



Harnessing light energy with molecules

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Harnessing light energy with molecules

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Editorial

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Photoirradiation is one of the most effective ways of introducing energy into a molecule with high spatiotemporal resolution. From photoexcited states, molecules can relax via various pathways, which essentially converts photon energy to other forms of energy, including chemical and thermal energy. This thematic issue highlights various photochemical processes, for example by which some of the photon energy is stored within the molecule and can be potentially used at a later stage. A strong emphasis is on molecular photoswitches (photochromic molecules) that upon irradiation undergo *cis/trans* isomerization, intramolecular photocycloaddition, or an electrocyclic reaction. In addition, several articles describe absorption tuning by structural modifications of the chromophores, aiming for example at moving their absorption from the ultraviolet spectral region to the visible region. This is of importance for efficient exploitation of solar energy, i.e., matching molecular absorption with the solar emission spectrum, or for photodynamic therapies using molecular light harnessing.

So-called molecular solar thermal (MOST) energy storage systems are one type of photoresponsive systems [1-3].

These have attracted increasing interest in the past decade for the storage of solar energy by photoisomerization of a molecular photoswitch, recently coined as a “mostophore” [3]. Such energy storage systems have also been referred to as solar thermal fuels or solar thermal batteries. After light harnessing, photoisomerization generates a metastable compound of higher energy. Thermal back-reaction results in the release of the energy again as heat. This process is preferably induced by an external stimulus or by a catalyst, which enables a controlled energy release when needed. Overall, the process corresponds to a closed cycle of energy uptake and release.

This thematic issue has a strong focus on MOST systems and showcases various approaches of optimization with regard to their light harnessing efficiency, energy storage capacity, and storage time. Structural modifications and studies of the norbornadiene/quadracyclane (NBD/QC) photo-/thermoswitch couple are covered in several articles. In a publication by Kerzig, Ihmels, and co-workers [4], the π -system of monoaryl-substituted NBDs was synthetically extended by acetylenic bridges.

In addition, Hebborn, Ihmels, and co-workers [5] show that ^{19}F NMR spectroscopy enables unambiguous identification of mono- and bisQC intermediates in the sequential photoreactions of a fluorinated trisNBD-benzene, overcoming the signal overlap that limits conventional ^1H NMR analysis. Further, the consequences on the absorption properties, photoisomerization, and QC lifetime were studied. In another article by Krappmann and Hirsch [6], the implications of replacing the methylene bridge of the NBD structure by a heteroatom (oxygen or nitrogen) in donor–acceptor, push–pull NBD derivatives are reported. In a computational study, Pawar and co-workers [7] further expanded the NBD structure by elongating the unsaturated bridge with different heteroatoms or functional groups. Azobenzenes, interconverting between *trans* and *cis* isomers, represent another class of photoswitches, which were reviewed as mostophores in a Perspective by Wang, Wu, and co-workers [8].

Besides MOST systems, molecular photoswitches are interesting for a variety of potential applications when incorporated as photoresponsive units in larger systems or smart materials [9]. Photoswitches are, for example, relevant functional units for information storage or molecular electronic devices. They can serve to control ion transport, molecular assembly/disassembly, or the relative movement of units within molecular machines. In a Review, García-López and co-workers [10] describe how the integration of a variety of molecular photoswitches into mechanically interlocked systems, i.e., rotaxanes, can be explored for light-controlled movements, and hence for controlling advanced functions of smart materials and biofunctional systems. In another publication, Leung and co-workers [11] describe how amphiphilic donor–acceptor Stenhouse adducts can be employed in supramolecular nanostructures controlled by visible light, which is of particular interest for the development of biomedical materials. Jones, Evans, and co-workers [12] studied X-ray-induced isomerization within micelles generated from two different photosurfactants (containing either an azobenzene or arylazopyrazole photoswitch), thereby creating guidelines for using small-angle X-ray scattering to study photoresponsive materials of potential applications in solar energy storage, catalysis, or controlled drug delivery. In the article by Venkataramani, Gopakumar, and co-workers [13], it is shown how a fluorinated tripodal N-functionalized arylazo-3,5-dimethylpyrazole derivative, self-assembled on a graphite surface, can be switched between eight states in a tunneling junction at ambient conditions and hence be used as an 8-bit operation unit. Molecular photoswitches are also interesting for temperature sensing applications. Thus, in their publication, Priimagi and co-workers [14] show a strong temperature-dependence of azobenzene protonation in 1,2-dichloroethane.

Systematic tuning of photochromic properties is the focus of several articles in this thematic issue. Kitagawa, Kobatake, and co-workers [15] studied the effect of the substitution position of aryl groups on the thermal back-reaction of azadiarylethene photoswitches. Simeth and co-workers [16] present a study of substituent effects in a large selection of N-acetylated phenylazopyrazole photoswitches. Pittelkow, Antonov, and co-workers [17] present a study on tautomerism and switching in 7-hydroxy-8-(azophenyl)quinoline and similar π -expanded azobenzene compounds. The photoisomerization quantum yield is a key property for characterizing the light harnessing efficiency of a photoswitch. In the article by Volker, Steen, and Crespi [18], a convenient and reliable fiber optic spectroscopic setup for determining this quantum yield is reported and was benchmarked for azobenzene against other methods.

Photoinduced charge separation is a key process in the development of systems for artificial photosynthesis, photovoltaics, and photocatalysis. Kobayashi and co-workers [19] studied in detail the excited-state dynamics of donor–acceptor dyads based on perylene and phenothiazine, in which triphenylamine units and a phenyl spacer were introduced to modulate donor strength and spatial separation. The work underscores the crucial role of excited-state structural relaxation in tuning photoinduced charge separation. In another study, Kerzig and co-workers [20] show how polyaza[7]helicene can function as a singlet-state photoredox catalyst in the sulfonylation/arylation of styrenes and as a triplet sensitizer in energy transfer catalysis.

In addition to the photoredox contribution mentioned above, this thematic issue contains two publications on photochemical reactions beyond photoisomerizations. In the article by Wahl and co-workers [21], ring-opening of photogenerated azetidionols was used as a strategy for the convenient synthesis of aminodioxolanes. Photochemical denitrogenation reactions of bicyclic azoalkanes present a way to prepare strained bicyclic compounds. Further, Gomes and Lopez [22] report a computational study on the mechanism of photodenitrogenation of diazabicyclo[2.2.1]heptenes.

We are grateful to all authors who have contributed to this thematic issue. The contributions show how harnessing of light energy can be finely tuned by structural modifications and used for diverse applications.

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Data Availability Statement

Data sharing is not applicable as no new data was generated or analyzed in this study.

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Novel route to enhance the thermo-optical performance of bicyclic diene photoswitches for solar thermal batteries

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Full Research Paper

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Abstract

Harnessing solar energy by employing chemical photoswitches in molecular solar thermal (MOST) energy storage systems is a topic of appealing research interest. However, incorporating all the features desired for an ideal MOST system in a single photo-switching couple is challenging. Inspired by experimental synthesis, herein we report our attempt to enhance both the thermochemical and photophysical properties in a single-bridged bicyclic diene (BBD)-based photoswitch by elongating the unsaturated bridge with different heteroatomic units. To elucidate the best elongation unit, the energy storage capacity and the TBR barriers were accounted using the DLPNO-CCSD(T) and (8,8)-CASPT2 methods, respectively. The photophysical properties including the absorption onset, excitation wavelengths, and the absorption intensities were extensively investigated with the time-dependent calculations. The result provides information on the most versatile solvent to exhibit the best photoswitching behaviour which is beneficial for real-life energy storage applications. Additionally, the stability and reversibility of the photoswitching system with elongated unsaturated bridges have also been assessed. By means of the studied modification, the storage energy of 158.57 kJ/mol, energy storage density of 1.48 MJ/kg, TBR barrier of 136.36 kJ/mol, and the absorption onset of 305.00 nm is achieved in acetonitrile. These values are substantially higher when compared with the storage energy (96.06 kJ/mol), energy storage density (1.04 MJ/kg), and TBR barrier (121.76 kJ/mol) of prototype NBD/QC in the gas phase. The outcomes render useful insights into the stability and properties of bicyclic diene-based photoswitches having elongated unsaturated bridges and indeed paves the way for the rational design of practical MOST systems.

Introduction

Energy is an inevitable necessity of society and its rate of consumption is continuously increasing across the world due to increasing population and technological developments [1,2].

Fossil fuels like natural gas, oil, and coal are currently the chief energy resources whose excessive utilization causes serious environmental issues [2,3]. Further, their reserves are in a threat

of being exhausted [3,4]. The sun is the most fundamental and green energy resource that has potential to meet the increasing energy crises in a sustainable manner [2–4]. However, technological devices must be developed that enable a direct capture, conversion, and storage of the solar energy [2,5–7]. Molecular solar thermal (MOST) energy storage is one of the most promising approaches for this purpose [8–13].

The MOST system employs a photoswitchable molecular couple for harvesting, conversion, and storage of solar energy [8–13]. Upon exposure to sunlight, a parent molecule undergoes photoexcitation which induces its chemical transformation into a high energy photoisomer [8–13]. This photoisomer then can be stored for a certain period and thermal energy can be released when triggered with heat, light, catalyst, etc. The back isomerization of the metastable photoproduct regenerates the parent molecule for continuing the photoswitching cycle [8–13]. This enables the harvesting, conversion, and storage of solar energy into thermal energy via a reversible and closed photoswitching cycle.

The photoswitching couple must exhibit distinct features to be applicable for solar energy harvesting and storage [10]. These properties include the large storage energy, high gravimetric energy storage density, large barrier for thermal back isomerization reaction, photoabsorption in the visible range, high quantum yield of photoisomerization, and so forth [10]. Photoswitches like dihydroazulene/vinylheptafulvene, azobenzenes, tetracarbonyl(fulvalene)diruthenium complexes, norbornadiene/quadracyclane (NBD/QC), anthracenes, etc. exhibit a few promising properties for MOST applications [10,12,13]. However, these photoswitching couples still lack one or more important properties required in MOST systems and impose a serious limitation for their practical applications [8–13]. It is believed that the rational design of the molecular structure can assist to endow all the necessary properties in a single photoswitch [14]. Therefore, engineering of novel photochromic couples with an intention to incorporate all desired features within a single photoswitch is a focus of current research [15–30].

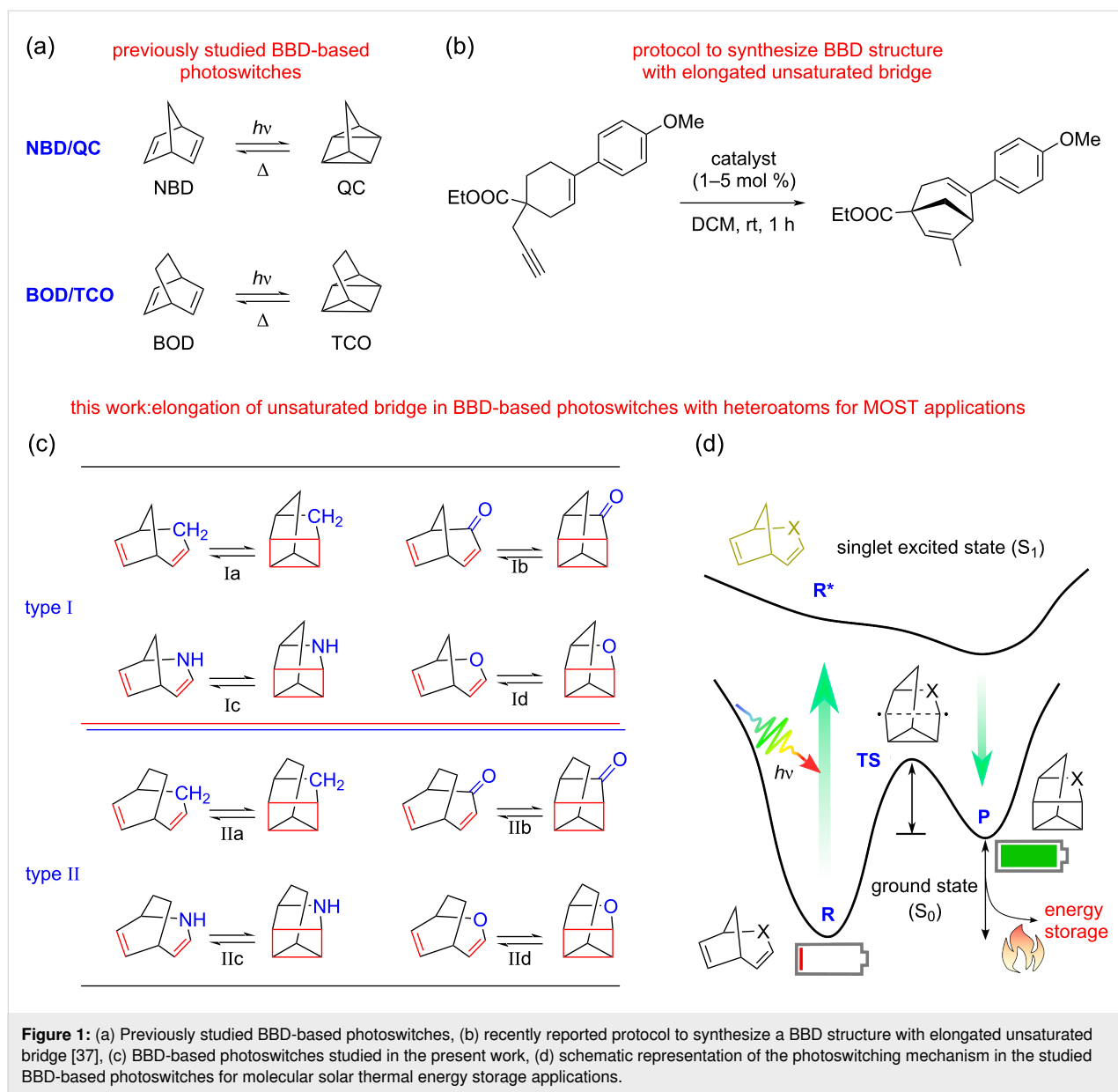
The bridged bicyclic diene (BBD)-based NBD/QC couple involves a reversible $[2 + 2]$ -cycloaddition and the chemical transformation during its photoswitching is depicted in Figure 1a. The NBD/QC couple is capable to chemically store huge amounts of solar energy due to the incorporation of large strain during the photoconversion and is thus recognized as a potential MOST candidate [8–10,13]. However, the optical absorption of unsubstituted NBD in the UV region hinders its practical applicability in MOST systems [8–10,13]. Several attempts have been made to red-shift the absorption wavelength in direction of the visible region by introducing different

substitutions which often compromised the thermochemical properties [8–10,13]. Thus, the improvement of both the thermochemical and photophysical properties of a photoswitching couple is a challenging task.

The bicyclooctadiene/tetracyclooctane (BOD/TCO) couple structurally resembles the NBD/QC pair but has an extended saturated bridge due to the additional methylene ($-\text{CH}_2-$) unit. An experimental report has evidenced that the BOD/TCO couple shows similar photoswitching behaviour (Figure 1a) and possesses a significantly better energy storage density, making it an interesting candidate for MOST applications [31]. The BOD molecule is likely to undergo a thermal degradation producing an aromatic ring via a kinetically controlled retro-Diels–Alder pathway [31]. However, the reversibility of the photoswitching cycle is a prerequisite for a closed MOST system. Recent studies have demonstrated that structural modifications in the basic BBD skeleton can alter the intrinsic properties of a photoswitch and may be crucial to impart novel photoswitching properties [31–36]. Further, the presence of heteroatoms in the bicyclic diene is also decisive to modulate the photoswitching behaviour [35,36]. This provides the impetus for rational designing of novel BBD photoswitches to endow all the essential functionalities in an individual system for a real-life MOST application.

Hitherto, studies have mainly focussed on the influence of saturated-bridge modifications on the photoswitching properties for applications in solar energy harvesting and storage [31–34]. A recent experimental study has reported a facile synthetic protocol (Figure 1b) to obtain BBD molecule which shows structural similarity with the NBD but has an elongated unsaturated bridge length [37]. Despite its potential, the photoswitching behaviour of this molecule has not been anticipated and the thermochemical and photophysical parameters relevant for MOST applications are still elusive.

Inspired by these earlier reports, herein we report our attempts to assess the impact of the unsaturated-bridge length elongation with different heteroatomic units on the thermochemical and photophysical properties of BBD-based photoswitches. The various BBD-based systems scrutinized in the present investigation are displayed in Figure 1c. These systems are rationally designed with elongated unsaturated bridge in both the NBD/QC and BOD/TCO pairs. Thus, these photoswitches can be basically classified into two types: (a) type-I is generated by increasing the unsaturated bridge length of the NBD/QC pair thus having a short saturated bridge, and (b) type-II designed by elongating the unsaturated bridge of the BOD/TCO pair thus have elongated saturated bridge, too. Further, the effect of the presence of different polarity solvents on the photoswitching



properties has also been investigated for a real-life MOST application. The stability and the reversibility of the photoswitches have also been verified to attain a closed cyclic photo-switching process for practical MOST system.

Results and Discussion

As can be seen from Figure 1a, the previously studied BBD-based photoswitches (NBD/QC and BOD/TCO) generate photoisomers with two strained 3-membered rings. In contrast, the photoinduced chemical transformation of all studied bicyclic dienes yield photoproducts containing one 4-membered and one 3-membered ring. Therefore, the metastable photoisomers of the studied photoswitches have a larger ring size and can be stabilized for longer time. Consequently, the

TBR barrier can be enhanced which ultimately enables the harvested solar energy to be stored for an extended period of time. Further, elongating the unsaturated bridge with heteroatoms can assist to improve the photophysical properties. Thus, the studied photoswitches are rationally designed to incorporate both thermochemical and photophysical properties in a single photoswitching couple as desired in an ideal MOST system for solar energy harvesting and storage.

A schematic representation of the photoswitching mechanism operating in the studied BBD-based switches for MOST application is illustrated in Figure 1d. The parent BBD molecules absorb incoming photons from solar radiation and undergo photoinduced electronic excitation. The excited diene thereafter

converts into a high-energy metastable photoproduct via a photoconversion process. The energy difference between the metastable photoproduct and the parent diene is the storage energy of the photoswitching pair and reflects the energy storage capacity of the MOST system. Thus, the larger energy difference between the two photoswitching isomers increases the amount of energy harnessed from solar radiation. Owing to its high energy, the metastable photoisomer shows a propensity to revert back to the parent diene and heat is released during this process. The regenerated parent diene further continues the photoswitching cycle. The activation energy required to trigger the transformation of the metastable photoisomer to the parent diene is called the thermal back isomerization barrier. The TBR barrier governs the duration of storage of harvested solar energy in the MOST devices. Photoswitching systems exhibiting a large TBR barrier store solar energy for long periods of time.

Thermochemical properties

En route to probe the energy storage capacity of the studied BBD-based photoswitches, initially the storage energy and energy storage density (ESD) have been calculated. Figure 2 displays the energy storage capacity of the studied photoswitches calculated employing M062X/6-311++G** and DLPNO-CCSD(T)/Def2TZVP level. The calculated storage energy and energy density values are provided in Table 1.

The storage energies calculated using the DLPNO-CCSD(T) level are in the range of 141.15 to 158.38 kJ/mol for the type-I

switches and 138.28 to 165.74 kJ/mol for the type-II photoswitches. It is worth to mention that the storage energy of the studied BBD-based switches is significantly higher than that of the prototype NBD/QC pair (96.06 kJ/mol) [36]. It is also apparent from Figure 2 that type-II photoswitches which are based on the BOD/TCO pair have a higher storage energy than the type-I systems which are based on the NBD/QC couple. These results are consistent with a previous report which demonstrated that the energy storage capacity of the BOD/TCO system (192.80 kJ/mol) is higher than that of the NBD/QC couple (96.30 kJ/mol) [33]. Moreover, the energy storage density ranges from 1.21 to 1.48 MJ/kg for type-I switches and 1.13 to 1.37 MJ/kg for type-II switches. The gravimetric energy densities of the studied photoswitches is higher than that of the NBD/QC pair (1.04 MJ/kg) [36]. Therefore, the elongation of the unsaturated bridge results in a higher energy storage capacity compared to the unsubstituted NBD/QC photo-switch.

It has also been observed that M062X/6-311++G** considerably underestimates the energy storage capacity of the studied BBD-based photoswitches when compared with the DLPNO-CCSD(T)/Def2TZVP level (Table 1). Also, the energy storage capacity of type-Ia, Ib, Ic and IIa, IIb, and IIc systems is the highest among all the studied photoswitches. This infers that $-\text{CH}_2-$, $-(\text{CO})-$, and $-\text{NH}-$ are better elongation units of the studied BBD-based photoswitches for improving energy storage capacities.

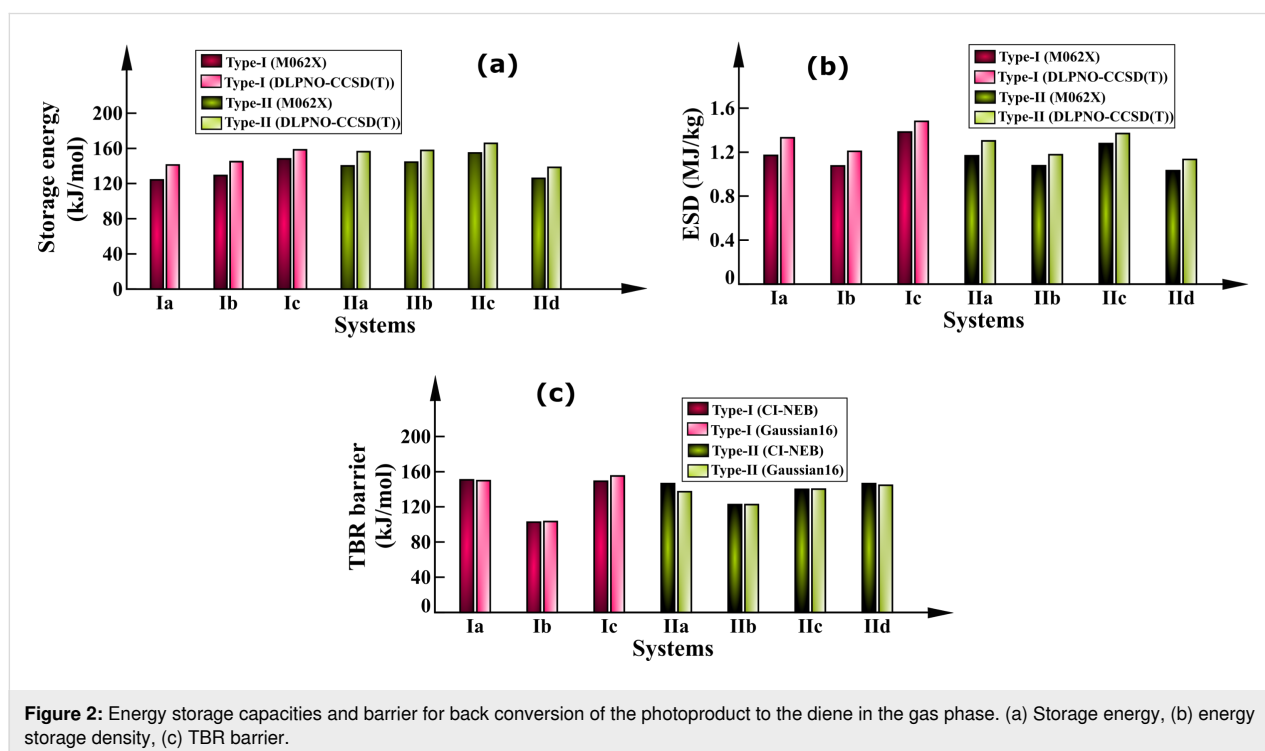


Figure 2: Energy storage capacities and barrier for back conversion of the photoproduct to the diene in the gas phase. (a) Storage energy, (b) energy storage density, (c) TBR barrier.

Table 1: Thermochemical properties of the studied BBD-based photoswitches and previously reported NBD/QC and BOD/TCO pairs in the gas phase.^a

Systems	Storage energy (kJ/mol)		ESD (MJ/kg)		TBR barrier (kJ/mol)	
	M062X	DLPNO-CCSD(T)	M062X	DLPNO-CCSD(T)	CI-NEB	Gaussian16
Ia	124.14	141.15	1.17	1.33	150.71	149.64
Ib	129.11	144.91	1.08	1.21	102.56	103.37
Ic	148.08	158.38	1.38	1.48	149.23	155.19
IIa	140.08	156.35	1.17	1.30	146.49	137.14
IIb	144.38	157.66	1.08	1.18	122.57	122.59
IIc	154.83	165.74	1.28	1.37	139.85	140.02
IId	125.93	138.28	1.03	1.13	146.43	144.58
NBD/QC	96.30		1.05		124.10	
BOD/TCO	192.80		1.82		118.10	

^aThe thermochemical properties of the NBD/QC and BOD/TCO pairs are taken from the previous study where energy storage capacities were calculated with CPS(D-4) for geometries optimized with M06-2X/6-311++G** and TBR barriers were accounted at the (8,8)-CASPT2/6-311++G** level for the TS obtained using the NEB [33].

The TBR barrier plays a decisive role in determining the energy storage time of the photoswitching system. The singlet biradicaloid TS involved during the thermal back isomerization of photoproduct to the parent bicyclic diene were initially predicted with the PBE functional employing CI-NEB method analogous to the previous studies [33,36]. The obtained TSs were re-optimized with PBE/6-311++G** level utilizing the Gaussian16 and vibrational analysis was performed at the same level of theory. The TS was confirmed as a first-order saddle point by the presence of a single imaginary frequency whose displacement vectors are in the direction of bond forming and breaking. The optimized geometry of the TSs along with the displacement vectors in the direction of bond forming and breaking is provided in Figure S1 (Supporting Information File 1).

The TBR barrier estimated using the (8,8)-CASPT2/6-311++G** method for the TS geometry obtained using CI-NEB and Gaussian16 is shown by histograms in Figure 2c. These TBR barriers calculated using both methods are also provided in Table 1. It is clear from Figure 2c that the TBR barrier solely depends on the type of heteroatom unit used to extend the unsaturated bridge length of the bicyclic diene. The TBR barrier is low only for type-Ib (103.37 kJ/mol) and IIb (122.59 kJ/mol) systems, while the other studied photoswitches have higher TBR barriers (137.14 to 155.19 kJ/mol). Noteworthy, these TBR barriers are significantly higher than those of the unsubstituted NBD/QC (124.10 kJ/mol) and BOD/TCO (118.10 kJ/mol) couples [33]. This is indeed expected due to the formation of comparatively stable and large rings in the metastable photoproducts. Among all the studied BBD switches, the barrier height for back isomerization of the photoproduct to the diene is

largest for systems whose unsaturated bridge was extended with $-\text{CH}_2-$, $-\text{NH}-$, and $-\text{O}-$ units. Interestingly, these TBR barriers for the studied BBD-based photoswitches with elongated unsaturated bridges are substantially higher and can store the energy for several months and even longer.

Overall, the studied BBD-based photoswitches with elongated unsaturated bridges have higher energy storage capacities than the NBD/QC pair. The storage energy is found to be higher for systems whose unsaturated bridge lengths are extended with $-\text{CH}_2-$, $-(\text{CO})-$ and $-\text{NH}-$ units. Additionally, extension of the unsaturated bridge of the BBD molecule relieves strain in the metastable photoisomer and thus, enhances the TBR barrier. The calculated energy barrier of TBR was found to be largest for the systems whose unsaturated bridge was extended with $-\text{CH}_2-$, $-\text{NH}-$, and $-\text{O}-$ units. Therefore, it is worth to mention that elongating the unsaturated bridge length of BBD molecule improves the thermochemical properties. As a result, the studied BBD-based photoswitches show the potential for efficiently harvesting solar radiation and long-term storage of energy in the chemical bonds of the photoproduct. More particularly, the BBD-systems whose unsaturated bridge was extended using $-\text{CH}_2-$ and $-\text{NH}-$ units exhibit the best storage energy capacities as well as the highest TBR barriers.

It can be noted that we were unable to find the TS for the thermal back conversion of the type-Id system by employing CI-NEB and Gaussian 16. Several attempts to search the TS structure instead resulted in a distinct TS geometry than that involved in thermal back conversion. The optimized geometry of the TS for the Id system along with the important geometrical parameters are shown in Figure 3. Analysis of the geomet-

rical parameters reveals that the TS is associated with dissociation of the photoproduct. To validate the interconnection of the TS with the metastable photoisomer and the expected degradation product, IRC calculations were performed. The IRC calculations confirm that the obtained TS interlinks the metastable photoproduct with an undesired byproduct (Figure 3).

Calculations reveal that the barrier for thermal dissociation of the photoproduct type-Id (209.43 kJ/mol) is significantly larger than the TBR barrier accounted for all the studied photoswitches. Nevertheless, the results reflect the propensity of the type-Id system to yield an undesired byproduct due to thermal dissociation. Consequently, the type-Id switch does not meet the criteria for reversible photoswitching desired for an ideal MOST system. This leads to the inference that the heteroatom used to extend the unsaturated bridge of the BBD molecules plays a crucial role in determining the stability of the metastable photoproduct against undesired thermal degradation.

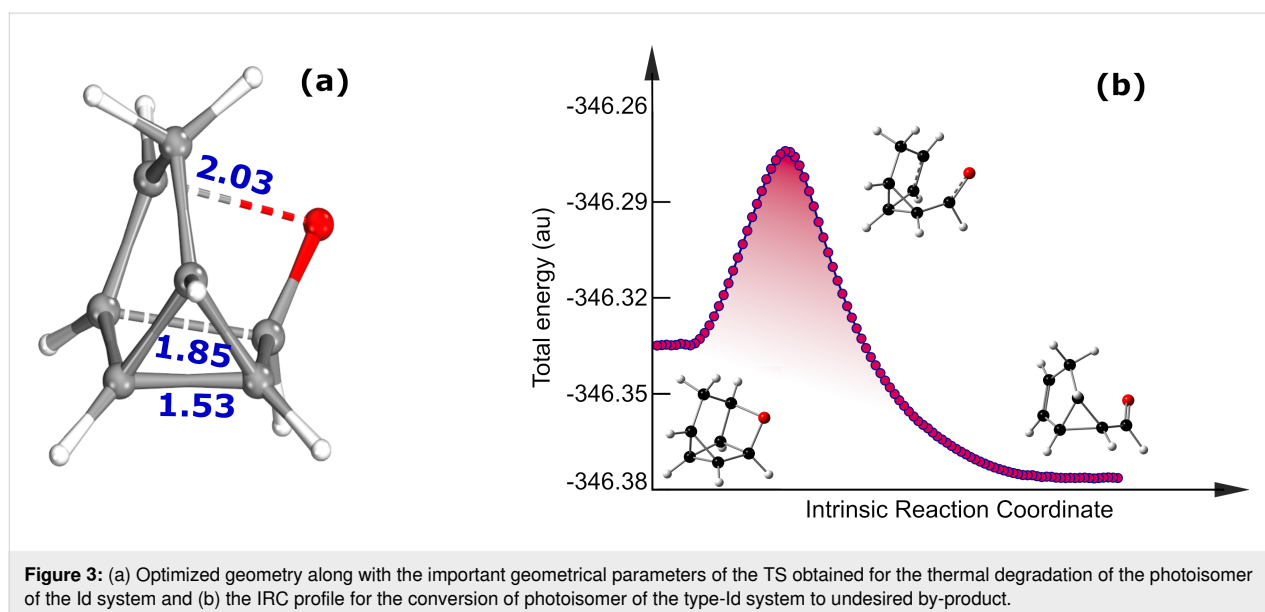
Photophysical properties

Photoabsorption of bicyclic dienes in the visible region of the solar spectrum is one of the prerequisites for their applicability as photoswitches in MOST systems. Therefore, forecasting the photophysical properties of BBD switches is one of the prominent objectives of the present investigation. The optical spectra of the dienes and photoproducts of both the types of BBD switches are depicted in Figure 4.

The optical spectra were obtained as the outcome of the first fifteen singlet vertical electronic excited state energy values computed with the TD-M062X/6-311++G** utilizing Gaussian

16. The data was extracted by considering the half width of 0.33 at the half height of the optical spectrum. The calculated spectral data including the absorption onset (λ_{onset}), the first important electronic excitation wavelength (λ) whose oscillatory strength (f) surpasses 0.01, and the molar absorption coefficient (ϵ) are systematically tabulated in Table 2. The results are compared with the optical properties previously reported for the NBD/QC and BOD/TCO pairs computed at the resolution-of-identity-CC2 model in conjunction with the 6-311++G** basis set [33].

From the figure, it can be clearly seen that the molar absorption coefficient of the parent dienes is significantly larger when compared with those of the metastable photoproducts. Close analysis of the optical spectra unraveled that the unit used to elongate the unsaturated bridge of the BBD-based photoswitch plays a critical role in altering the photophysical properties. The calculated first important electronic excitation wavelength and the absorption onset are longest for the diene whose unsaturated bridge length was extended using $-(\text{CO})-$ and $-\text{NH}-$ units. The calculated λ (λ_{onset}) for the dienes of type-Ib, Ic, IIb, and IIc photoswitches are 247.18 (275.00), 249.65 (295.60), 235.86 (261.50), and 251.62 (292.20) nm, respectively (Table 2). These absorption wavelengths are significantly longer than the previously reported λ for NBD (213.65 nm), BOD (196.44 nm), QC (190.74 nm), and TCO (204.92 nm) calculated at the resolution-of-identity-CC2 model in conjunction with the 6-311++G** basis set [33]. Also, the calculated λ for the photoproducts of type-Ib, Ic, IIb, and IIc photoswitches are 195.18, 177.38, 198.93, and 202.79 nm, respectively (Table 2). Therefore, the optical absorption spectra unveil that the extension of the unsaturated bridge length with $-(\text{CO})-$ and $-\text{NH}-$ units as in type Ib,



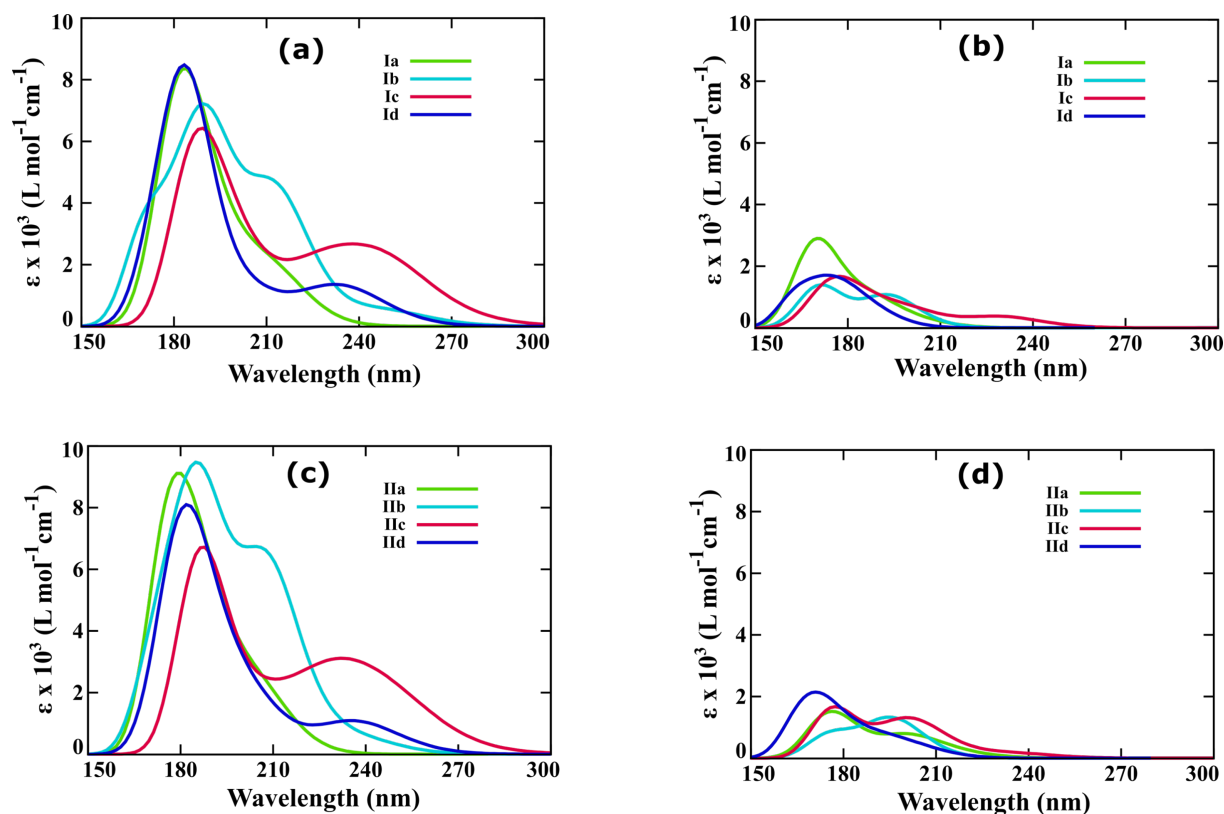


Figure 4: Photophysical properties of the studied BBD photoswitches with elongated unsaturated bridges. (a) Optical spectra of dienes of type-I switches and (b) optical spectra of photoproducts of type-I photoswitches, (c) optical spectra of dienes of type-II photoswitches, and (d) optical spectra of photoproducts of type-II switches.

Table 2: Spectral data for dienes and photoproducts of the studied BBD-based photoswitches calculated with M062X/6-311++G** level of theory and previously reported NBD/QC and BOD/TCO pairs.^a

Systems	λ_{onset}	f	λ (nm)	ϵ (L mol ⁻¹ cm ⁻¹)	λ_{onset}	f	λ (nm)	ϵ (L mol ⁻¹ cm ⁻¹)
diene				photoproduct				
Ia	241.12	0.029	212.80	2151.00	216.48	0.010	185.09	1377.58
Ib	275.00	0.013	247.18	602.84	215.60	0.014	195.18	1027.32
Ic	295.60	0.043	249.65	2375.97	251.20	0.011	177.38	1669.30
Id	268.50	0.021	238.21	1266.49	205.28	0.013	177.10	1638.78
IIa	233.92	0.022	206.58	2697.24	229.96	0.010	172.85	1376.49
IIb	261.50	0.013	235.86	877.54	220.40	0.013	198.93	1245.59
IIc	292.20	0.029	251.62	2162.12	247.40	0.013	202.79	1292.60
IId	269.50	0.015	240.38	1028.23	220.24	0.010	194.97	791.19
NBD/QC	—	0.017	213.65	—	—	0.019	190.74	—
BOD/TCO	—	0.041	196.44	—	—	0.027	204.92	—

^aThe spectral data of NBD/QC and BOD/TCO pairs was previously reported at the resolution-of-identity-CC2 model in conjunction with 6-311+ +G** basis set [33].

Ic, IIb, and IIc photoswitches red-shifts the excitation wavelength of the bicyclic diene and helps improving the photophysical properties.

More importantly, the differences between the first important excitation wavelength of the diene and photoproduct are 52 and 72 nm for the type-Ib and Ic photoswitches and are larger than

that of the NBD/QC pair (30 nm) [36]. This implies that the spectral overlap between the diene and the photoproduct is slightly reduced for the type-I photoswitches whose unsaturated bridge were extended using $-(CO)-$ and $-NH-$ units. This will assist to avoid achieving photostationary state (PSS) during the optical excitation of the diene. Therefore, elongation of an unsaturated bridge using a single unit has the potential to improve the photophysical properties, particularly the absorption cross-section, excitation wavelength, and spectral overlap. Despite this, the parent dienes of the studied BBD-based photoswitches show absorption in the UV region of the electromagnetic spectrum. Harvesting solar energy reaching the Earth's surface requires efforts to be devoted to red-shift the absorption wavelengths of the bicyclic diene in the visible range. As previous reports have demonstrated, this can be practically achieved by substitution with electron-releasing or accepting groups [8,9,33].

The energy storage capacity of the photoswitches should always be less than the actual solar energy harnessed by the bicyclic molecule. To perform this reality check, the photon energy (E_{photon}) for the first important electronic excitation (whose oscillatory strength is higher than 0.01) was compared with the sum of the storage energy and TBR barrier ($SE + \text{TBR barrier}$) for the studied photoswitches. The calculated values are provided in Table S1 of Supporting Information File 1. The sum of storage energy and TBR barrier is always less than the photon energy ($SE + \text{TBR barrier} < E_{\text{photon}}$) involved in the first important electronic excitation. This validates the reality of the photoswitches and reliability of the obtained outcomes. The solar energy conversion efficiencies ($\eta_{\text{efficiency}}$) of the studied photoswitches have also been estimated as demonstrated in a recent report [34]. The calculated results are also provided in Table S1 of Supporting Information File 1 and are within the range of 7.78 to 10.31% for the studied BBD-based photoswitches. These $\eta_{\text{efficiency}}$ values are in agreement with the solar energy conversion efficiencies of the BBD-based photoswitches with modified saturated bridges [34].

Effect of solvation

Knowledge of the best suitable environmental conditions for the photoswitching system is essential to achieve high performance in the real-life MOST devices. Therefore, attention has also been devoted to envisage the impact of different polarity solvents on the properties of the BBD-based photoswitching couples. Herein, the influence of solvation has been measured only for type-Ia, Ic, IIa, and IIc photoswitching couples. Initially, the geometries of the bicyclic dienes and photoproducts of the studied photoswitches were optimized in the presence of different polarity solvents at the M062X/6-311++G** level considering the SMD model. Thereafter, the storage ener-

gies were computed by performing the single point energy calculations at DLPNO-CCSD(T)/Def2TZVP and including the thermal correction at the M062X/6-311++G** level. Likewise, the geometries of the TS were optimized with PBE/6-311++G** in presence of different polarity solvents considering SMD model and TBR barrier were accounted at the (8,8)-CASPT2/6-311++G** level.

The effect of different polarity solvents on the thermochemical properties of the photoswitching couples considering the SMD solvation model is illustrated with histograms in Figure 5. The estimated data for storage energy, energy storage density, and TBR barriers in the presence of different solvents are given in Table S2 of Supporting Information File 1.

As can be seen from Figure 5 the storage energy and energy storage density appreciably increase due to solvation of the photoswitches in the different polarity solvents considering the SMD solvation model. The increase in energy storage capacity becomes more pronounced with increasing polarity of the solvent. The extent of increment in storage energy upon solvation is largest for the type-Ia (2.42–5.07 kJ/mol) and IIa (2.60–5.20 kJ/mol) photoswitching couples while the variation is least for the Ic (0.18–0.43 kJ/mol) switches. The trend observed for the effect of solvation on energy storage capacity is in agreement with a recent investigation on solvated BOD/TCO systems [38]. Juxtaposition to this, mostly the TBR barrier considerably decreases as the polarity of the solvent increases. The largest decrease in the TBR barrier is noticed for the type-Ia (1.37–4.38 kJ/mol) and Ic (–1.75–18.83 kJ/mol) photoswitches whereas the decrease in TBR for the type-IIc (0.19–0.32 kJ/mol) photoswitch is only marginal. Additionally, a little enhancement in the barrier for the thermal back isomerization is noticed for the type-IIa (0.30–0.36 kJ/mol) photoswitch with increasing polarity of the solvent. Due to the large convergence issue for the solvated systems of the type-IIc photoswitch, the electronic energies with (8,8)-CASPT2/6-311++G** were calculated with loose SCF criterion and may attribute to the large deviation between the TBR barriers in different polarity solvents (Figure 5). The result signifies that the energy storage capacity of the type-Ia and Ic photoswitches can be improved with increasing polarity of solvents but at the cost of the TBR barrier. Further, the high polarity solvents can improve the energy storage capacity of the photoswitches without compromising the TBR barrier for type-IIa and IIc photoswitches.

To probe the effect of solvation model, the calculations were performed by considering the polarizable continuum model (PCM) solvation model and systematically compared with the SMD model. The influence is assessed by evaluating the storage

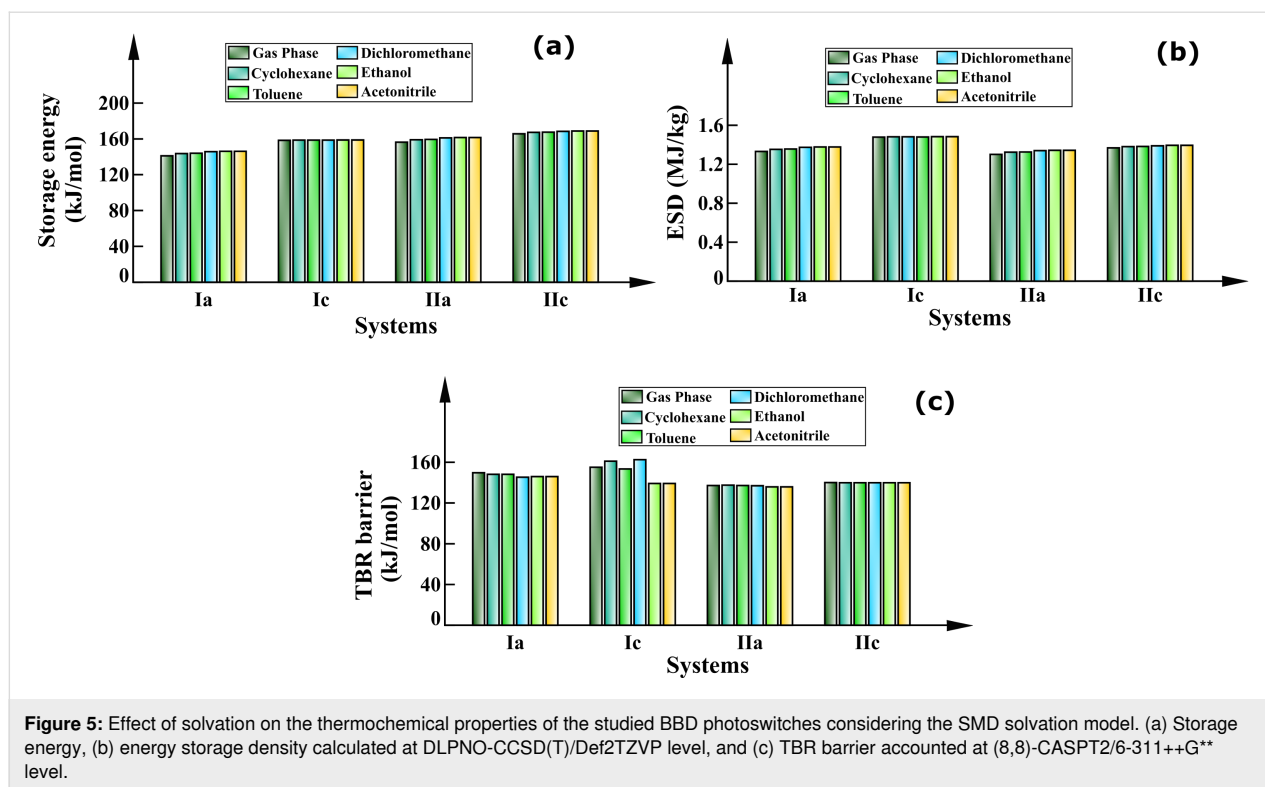


Figure 5: Effect of solvation on the thermochemical properties of the studied BBD photoswitches considering the SMD solvation model. (a) Storage energy, (b) energy storage density calculated at DLPNO-CCSD(T)/Def2TZVP level, and (c) TBR barrier accounted at (8,8)-CASPT2/6-311++G** level.

energies of the type-Ia and Ic photoswitches in different polarity solvents using both the solvation models at the M062X/6-311++G** level of theory. The calculated energy values are displayed by histograms in Figure S2 of Supporting Information File 1. The trend observed for the storage energies of the photoswitches in different polarity solvents calculated with M062X/6-311++G** (PCM solvation model) closely resembles with those obtained with DLPNO-CCSD(T) (SMD model). However, the storage energies of the photoswitches in different polarity solvents calculated at the M062X/6-311++G** level considering the SMD model are lower than the PCM model. Since the effect of solvation model is assessed at the M062X/6-311++G** level, the computed energy values are different than those obtained with the DLPNO-CCSD(T) level of theory. However, the influence of the solvation model on the overall storage energies in presence of different polarity solvents is only marginal.

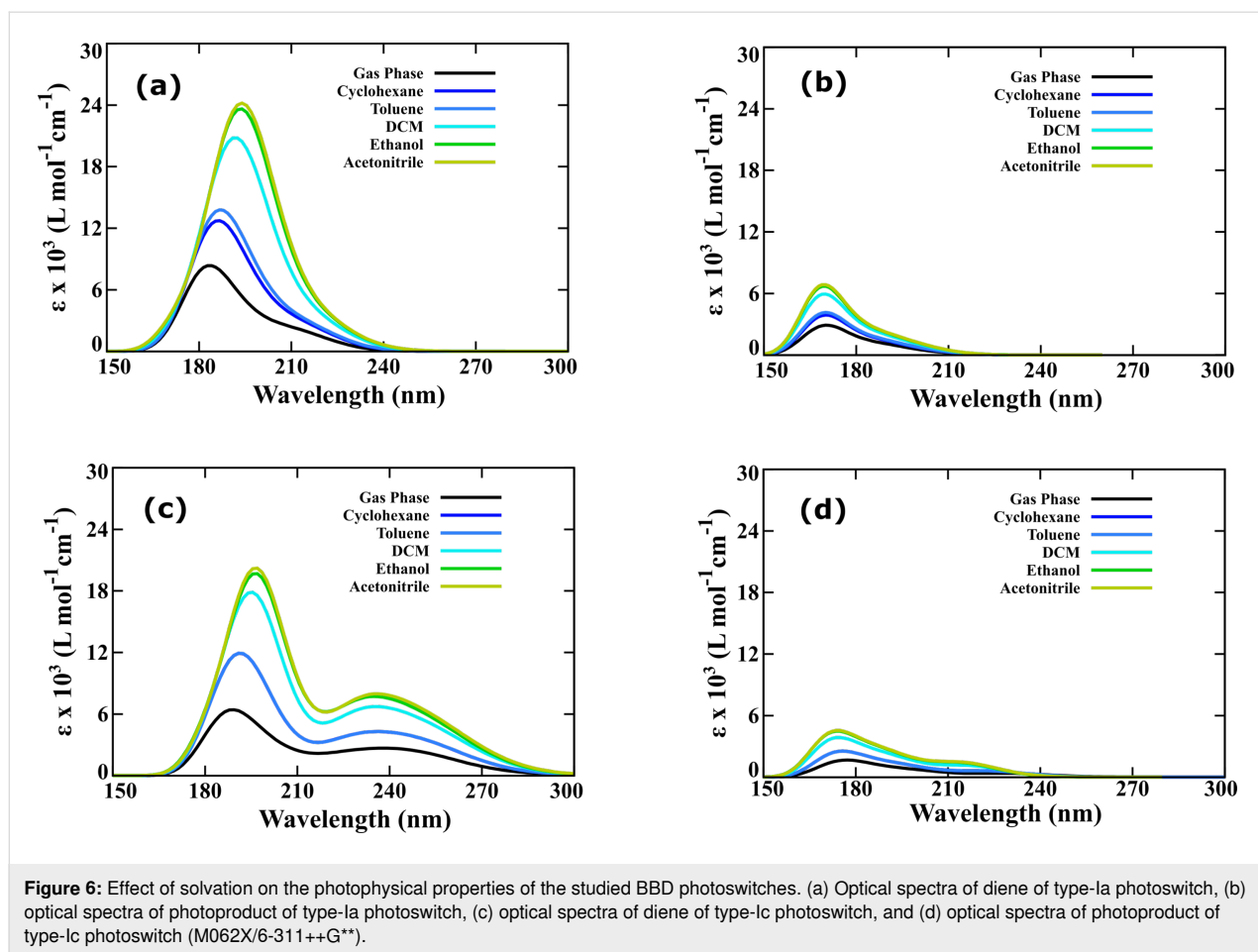
Furthermore, the influence of different polarity solvents on the photophysical properties of the parent dienes and the metastable photoproducts has also been forecasted. The optical absorption spectra for the solvated dienes and photoproducts of type-Ia, and Ic photoswitches are displayed in Figure 6. The calculated absorption spectra for the solvated diene and photoproducts of type-IIa and Ic photoswitches are provided in Figure S3 of Supporting Information File 1. The calculated spectral data in the presence of different solvents are systemati-

cally tabulated in Table S3 and Table S4 of Supporting Information File 1.

Figure 6 clearly elucidates that the absorption intensity of the diene and photoproduct remarkably enhances with solvation. The molar absorption coefficient is maximum for the highest polar solvent. Additionally, the absorption cross section is largest in the presence of the highly polar solvent, acetonitrile (dielectric constant = 35.688). The increase in absorption intensity is more pronounced for the diene when compared to the metastable photoproduct. Therefore, the difference in the absorption coefficients of the diene and corresponding photoproduct becomes larger with increasing polarity of the solvent. It is interesting to note that a considerable bathochromic shift in the excitation wavelength is also noticed with increasing polarity of the solvents. The red-shift of 7.56 to 12.30 nm is observed in the presence of highly polar acetonitrile. Noteworthy, the absorption onset of the bicyclic diene of type-Ic and IIc is red-shifted to 305 and 304 nm, respectively, in the presence of acetonitrile. This evidences that the solvation of the photoswitches with highly polar solvents improves their photophysical properties.

Thermal degradation of photoisomers

The reversibility of the photoswitching process is one of the key requisites for the applications in molecular solar thermal energy storage. Therefore, the feasibility of the thermally reversible



photoswitching in the studied BBD-based systems has also been assessed. Initially, the relative energy profiles for the conversion of the photoproducts to the dienes and undesired thermal degradation products were generated. The thermal stability and reversibility of the photoswitching cycle of the type-IIa photoswitch was analyzed using the *ab initio* molecular dynamics (AIMD) simulations.

The proposed mechanism for the thermal back conversion and undesired thermal degradation of the photoproduct is illustrated in Figure 7. As mentioned earlier, the dissociation of the two newly formed σ -bonds proceeds in a highly asynchronous mechanism. Therefore, initially, only one of the two σ -bonds denoted as α bond in the photoproducts (Figure 7) dissociates to form a TS structure having singlet biradicaloid. Subsequently, there exists a competition for the dissociation of the β or γ -bond that yields undesired thermal degradation products through pathway A or the parent diene via pathway B, respectively. This dissociation follows a highly asynchronous but concerted reaction mechanism and may involve bispericyclic post-transition state bifurcation (PTSB) of the PES [39,40]. Consequently, the reaction tends to produce two different products from a single

TS. Thus, the reaction resembles a peculiar ambimodal reaction that can produce multiple products from a single TS structure [41].

Owing to the formation of two singlet biradicaloids in the TS structure, the single reference DFT functionals are inappropriate to describe the TS. Despite this, the previous benchmark study has demonstrated that the PBE functional is still superior for predicting the geometry of the TS [42]. Therefore, the geometry of TS structures was herein determined using the PBE/6-311++G** method utilizing the Gaussian 16. Thereafter, the relative energy profiles were generated by computing the electronic energies of the point structures at the (8,8)-CASPT2/6-311++G** level of theory. Attempts to find the TS (both with CI-NEB and Gaussian 16) for the thermal back isomerization of the photoproduct of type-Id photoswitch to the corresponding diene have resulted in a TS that is associated with undesired thermal degradation (Figure 3). The obtained TS follows a conventional, synchronous and concerted dissociation mechanism to produce the undesired carbonyl compound (Id-P₂) shown in Figure 7. Cartesian coordinates of all the optimized geometries are provided in Supporting Information File 1.

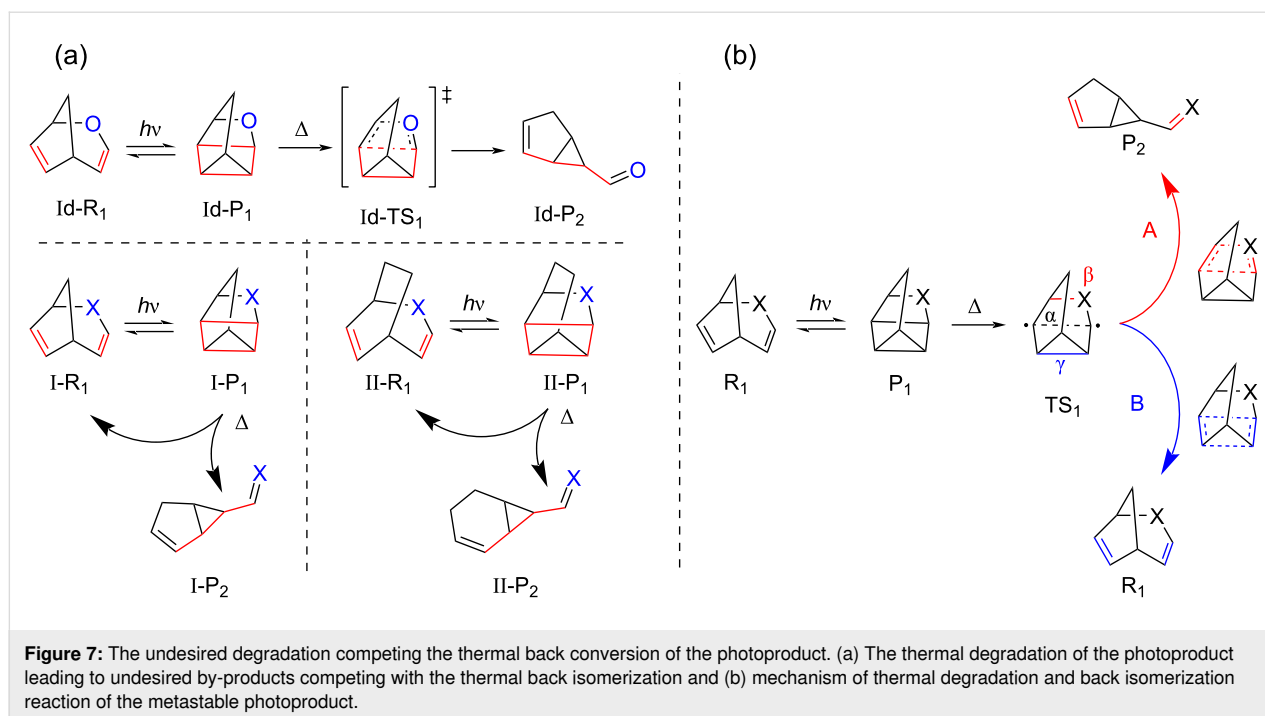


Figure 8 depicts the calculated relative energy profiles for the reversible thermal back conversion of the photoproduct to the bicyclic diene and the undesired thermal degradation of the photoproduct.

It is evident from the energy profiles that the parent dienes (R₁) obtained by thermal back isomerization of the photoproducts (P₁) are energetically more stable when compared with the thermally degraded products (P₂). Since a single TS is involved in regenerating the parent diene and producing the undesired product resembling the ambimodal reaction, the reversible photoswitching is more probable due to the energetic stability of the parent diene. Further, it has been noticed that the energetic stability of the undesired product depends on the unit used to extend the unsaturated bridge of the bicyclic diene. The energetic stability of the undesired byproduct is lowest for the photoswitching system whose bridge length is elongated with $-(CO)-$ and $-CH_2-$ units followed by $-NH-$ and $-O-$ units.

The calculated energy difference between the parent diene and the competing byproduct is largest for Ia (22.42 kcal/mol), IIa (22.57 kcal/mol), Ib (23.96 kcal/mol), IIb (23.80 kcal/mol) photoswitches. On the other hand, the energy difference between the parent diene and competing byproduct is least for the Id (5.76 kcal/mol) and IId (1.84 kcal/mol) photoswitches. This increases the propensity of the Id and IId couples towards the undesired thermal degradation product. This clearly indicates that the unit used for elongation of the unsaturated bridge is crucial to control the reversibility of the photoswitching cycle

or the stability of the photoproduct against undesired thermal degradation. Among the studied BBD-based system, the metastable photoproducts of the photoswitching couple whose unsaturated bridge was extended using the $-O-$ (Id and IId, respectively) are prone to undergo undesired thermal degradation. In contrast, the metastable photoproducts of the photoswitching couple whose unsaturated bridge was extended using the $-(CO)-$, $-CH_2-$, and $-NH-$ show thermodynamic feasibility for reversible photoswitching.

Furthermore, the thermal reversibility of the photoswitching process has been validated by AIMD simulations initiated using the biradicaloid TS structure of the IIa photoswitch. The variation in α , β , and γ -bond distances calculated during the AIMD dynamic trajectory is displayed in Figure 8. It is apparent from the figure that the α and γ -bond distances increase during the course of the simulations whereas the β distance almost remained constant. This signifies that subsequent formation of the TS, reversible photoswitching is more feasible over the thermal degradation of the metastable photoproduct. The outcomes of the AIMD simulations can be clearly visualized in a movie provided in Supporting Information File 2.

Conclusion

The outcomes of the simulations advocate that the heteroatomic unit used to elongate the unsaturated bridge is crucial in determining the stability, reversibility, and photoswitching properties of bicyclic dienes. DLPNO-CCSD(T) and (8,8)-CASPT2 results reveals that the photoswitches whose unsaturated bridge

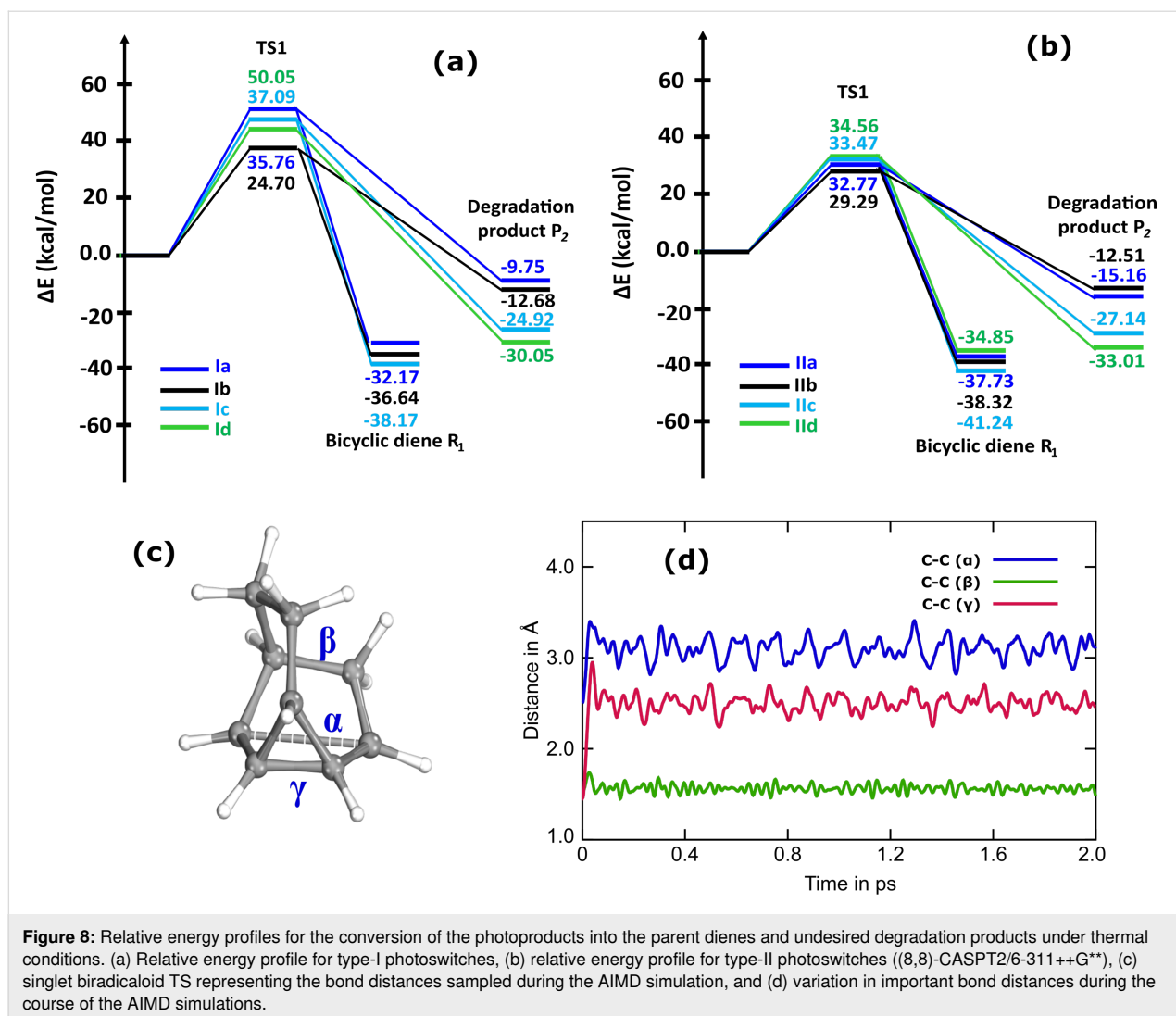


Figure 8: Relative energy profiles for the conversion of the photoproducts into the parent dienes and undesired degradation products under thermal conditions. (a) Relative energy profile for type-I photoswitches, (b) relative energy profile for type-II photoswitches ((8,8)-CASPT2/6-311++G**), (c) singlet biradicaloid TS representing the bond distances sampled during the AIMD simulation, and (d) variation in important bond distances during the course of the AIMD simulations.

was extended using $-\text{CH}_2-$ and $-\text{NH}-$ units exhibit the best storage energy capacities and high TBR barriers. The calculated energy storage capacities (138.28–165.74 kJ/mol) of the studied bridged bicyclic dienes are ≈ 1.5 times higher than the prototype NBD/QC (≈ 96 kJ/mol) pair in the gas phase. The estimated energy barriers for the thermal back isomerization in the studied photoswitching systems are large enough to store the harvested energy for several months or longer in the gas phase. The time-dependent calculations using the TD-M062X functional reveal that an elongation of the unsaturated bridge using $-(\text{CO})-$ and $-\text{NH}-$ red-shifts the absorption onset and excitation wavelength and thus are the best elongation units to improve the photophysical properties. The energy storage capacity of the type-Ia and Ic photoswitches increases as the polarity of solvent goes on increasing (0.18–5.07 kJ/mol) while the TBR barrier considerably decreases (1.36–18.83 kJ/mol). Surprisingly, the energy storage capacity of the type-IIa (5.20 kJ/mol) and IIc (3.14 kJ/mol) photoswitches appreciably

increases with the polarity of the solvent without compromising the TBR barrier. The solvation of studied photoswitching systems displays a bathochromic shift in the absorption onset and excitation wavelength and remarkably enhances the absorption intensities. The effect of solvation is more pronounced with the increasing polarity of the solvents. The photoswitching systems may show propensity for the undesired thermal degradation of the photoisomer via an ambimodal pathway, however the energetic stability of the parent diene favours the reversible photoswitching. Extending the unsaturated bridge of the bicyclic diene with an $-\text{O}-$ unit promotes the thermal degradation of the photoproduct to the carbonyl compounds. Among the studied systems, the bicyclic diene photoswitch whose unsaturated bridge length has been extended using a $-\text{NH}-$ unit exhibits the best storage energy (158.57 kJ/mol), energy storage density (1.48 MJ/kg), TBR barrier (136.36 kJ/mol), and absorption onset (305.00 nm) in the presence of acetonitrile. These values are substantially higher when compared with the storage

energy (96.06 kJ/mol), energy storage density (1.04 MJ/kg), and TBR barrier (121.76 kJ/mol) of the prototype NBD/QC pair in the gas phase. This work provides a new avenue to design bridged bicyclic dienes to achieve improved photoswitching properties in a single system and the results will certainly have a remarkable impact for applications in solar energy harvesting and storage.

Computational Details

The molecular structures of all studied dienes and photoproducts were fully relaxed without any geometrical or symmetrical constraints. The geometry optimization was performed using the M062X functional in combination with the 6-311++G** Pople-type basis set. This method was employed since the previous benchmarking studies have reported that the M062X/6-311++G** level performs well for prediction of the geometry and photoswitching properties of the BBD based systems. The analytical second order derivatives were also calculated to characterize the nature of the point structures. The critical point structure with no imaginary frequency was confirmed as a local minimum on the potential energy surface (PES). These optimized geometries were utilized for the further calculations including single point electronic energy, thermochemical and photophysical properties, etc.

The photophysical properties of the dienes and photoproducts were determined using the time-dependent TD-M062X/6-311++G** level of theory. The calculations were performed to determine the vertical excitation energy and oscillatory strength for the first fifteen singlet electronic excited states. To assess the influence of solvents, the geometries were optimized and photoswitching properties were determined in different polarity solvents (dielectric constant) including cyclohexane (2.0165), toluene (2.3741), dichloromethane or DCM (8.93), ethanol (24.852), and acetonitrile (35.688). Initially, the geometries of the bicyclic dienes and photoproducts of the studied photo-switches were optimized in the presence of different polarity solvents at the M062X/6-311++G** level considering the SMD model. Thereafter, the storage energies were computed by performing the single point energy calculations at DLPNO-CCSD(T)/Def2TZVP and including the thermal correction at the M062X/6-311++G** level. Likewise, the geometries of the TS were optimized with PBE/6-311++G** in presence of different polarity solvents considering SMD model and TBR barrier were accounted at the (8,8)-CASPT2/6-311++G** level. These calculations performed in the presence of solvents were modelled using the continuum solvation model density (SMD) solvation model. The pure implicit SMD solvation model has poor reliability to predict the pK_a values, and therefore, the storage energy was also calculated using the polarizable continuum model (PCM) [43]. The storage energy calculated using

both the methods are systematically compared. All the above-mentioned calculations were accomplished using the density functional theory (DFT) implemented in Gaussian 16 [44].

The storage energy (ΔG_{str}) is the amount of harvested solar energy that can be converted and stored as chemical energy in the metastable photoisomer. It measures the energy storage capability and the amount of thermal energy that can be obtained from a photoswitch in a MOST system. It can be calculated employing the following equation:

$$\Delta G_{\text{str}} = G_{\text{photoproduct}} - G_{\text{diene}}, \quad (1)$$

where G_{diene} and $G_{\text{photoproduct}}$ indicate the Gibbs free energy of the bridged bicyclic diene molecule and the corresponding photoproduct. The ΔG_{str} was herein calculated by computing the Gibbs free energy of the diene and photoproduct using the M062X/6-311++G** level for the geometries optimized using the same level of theory. Further, the single point energy of the diene and photoproduct were also accounted at the DLPNO-CCSD(T)/Def2TZVP level of theory to predict the more accurate storage energy values at a low computational cost. This storage energy is herein designated as $\Delta G_{\text{str}}^{\text{CCSD(T)}}$ and was estimated by including the thermal correction at M062X/6-311++G** level to the electronic energies computed at the DLPNO-CCSD(T)/Def2TZVP for the geometries optimized with M062X/6-311++G**.

$$\Delta G_{\text{str}}^{\text{CCSD(T)}} = \Delta E_{\text{str}}^{\text{CCSD(T)}} + \Delta T, \quad (2)$$

where $\Delta E_{\text{str}}^{\text{CCSD(T)}}$ is the difference in electronic energies (DLPNO-CCSD(T)/Def2TZVP) of the diene and photoproduct and ΔT is the difference in thermal contribution to the Gibbs free energy (M062X/6-311++G**) of the two photoisomers.

The thermal back reaction (TBR) barrier is the energy barrier that the photoproduct must overcome to revert back into the parent isomer for continuing the photoswitching cycle. The dissociation of two newly formed σ -bonds during the thermal back isomerization proceeds in a highly asynchronous mechanism. Initially, only one of the two newly formed σ -bonds is dissociated leading to the formation of singlet biradicals in the transition state (TS) structure. Therefore, the TS involved in the back reversion of the metastable photoisomer to the parent molecule exhibits multireference character. The single reference DFT functionals are unable to properly describe this multiconfigurational behaviour and often overestimate the TBR barrier. Therefore, the multireference complete active space (CAS)

methods like CASPT2 are required to accurately predict the behaviour of TS. However, the multiconfigurational CAS methods are computationally demanding and cannot be routinely employed for the calculations. A previous benchmarking study has demonstrated that the single reference DFT-based PBE method is still better to predict the geometry of TS using nudged elastic band (NEB) calculations and multireference methods determine the activation energy values close to the experiments [42].

In the present investigation, the geometry of all the TS structures was obtained with the climbing image NEB (CI-NEB) calculations implemented in the Quantum Espresso package analogous to the earlier reports [33,36,42,45]. Thereafter, the single point energy calculations were performed at the (8,8)-CASPT2/6-311++G** level for the singlet biradicaloid TS and the photoproduct. The TBR barrier was accounted by computing the electronic energy difference between for the TS and the corresponding photoproduct.

The TBR barrier can be calculated using the following equation:

$$TBR_{\text{CI-NEB}} = E_{\text{TS(CI-NEB)}}^{\text{CASPT2}} - E_{\text{photoproduct}}^{\text{CASPT2}}, \quad (3)$$

where $TBR_{\text{CI-NEB}}$ designates the TBR barrier calculated by using the TS geometry obtained with CI-NEB, $E_{\text{TS(CI-NEB)}}^{\text{CASPT2}}$ is the electronic energy computed with the (8,8)-CASPT2/6-311++G** level for the TS structure obtained with CI-NEB and $E_{\text{photoproduct}}^{\text{CASPT2}}$ is the electronic energy of photoproduct calculated with (8,8)-CASPT2/6-311++G**.

The geometries of TS obtained with CI-NEB method were re-optimized at the PBE/6-311++G** level employing Gaussian 16 [44]. The nature of the point structure was verified as a saddle point with the harmonic frequency calculations at the same level of theory. Afterwards, the TBR barrier was also predicted by performing a single point energy calculation at (8,8)-CASPT2/6-311++G** utilizing the TS geometries obtained with PBE/6-311++G**. The energy barrier for back isomerization reaction was calculated as:

$$TBR_{\text{Gaussian16}} = E_{\text{TS(Gaussian16)}}^{\text{CASPT2}} - E_{\text{photoproduct}}^{\text{CASPT2}}, \quad (4)$$

where $TBR_{\text{Gaussian16}}$ designates the TBR barrier calculated by using the TS geometry obtained with Gaussian16, and $E_{\text{Gaussian16}}^{\text{CASPT2}}$ is the electronic energy of TS computed with the

(8,8)-CASPT2/6-311++G** for TS structure obtained with Gaussian16. The TBR barriers accounted by using the TS geometries obtained with PBE functional using CI-NEB method are systematically compared with those obtained with PBE/6-311++G** level using Gaussian16.

The vibrational corrections obtained in the TS with the single-reference DFT functionals are inappropriate to include the electronic energies computed with (8,8)-CASPT2/6-311++G** due to cusp in energy landscape obtained with the single-reference methods [42]. Further, the vibrational analyses are computationally expensive with multireference methods and even inaccurate due to numerical differentiation [42]. A previous benchmarking study has also suggested that the electronic energy difference ($\Delta E^{\ddagger}$) accounts the TBR barrier closer to the experimental enthalpy difference ($\Delta H^{\ddagger}$) [42]. Therefore, the TBR barriers were predicted with the difference in electronic energy of the TS and photoisomer ($\Delta E^{\ddagger}$) akin to the earlier study. All the single point electronic energy calculations at the DLPNO-CCSD(T)/Def2TZVP and (8,8)-CASPT2/6-311++G** level were carried out using ORCA [46].

Intrinsic reaction coordinate (IRC) calculations have also been performed to validate the interconnection of the TS with the expected local minima on the PES. To confirm the reversible photoswitching in the studied BBD-based switches, ab initio molecular dynamics (AIMD) simulations were carried out. The simulations were initiated using the singlet biradicaloid TS of the IIa photoswitch. The simulations were performed for 2 ps with the time step of 1 fs by employing the CP2K package [47]. The Nosé–Hoover thermostat was employed to regulate the temperature of the systems at 300 K during the entire simulations. The AIMD simulations were executed employing the DZVP basis set, Goedecker–Teter–Hutter (GTH) pseudopotential and Perdew–Burke–Ernzerhof (PBE) functional along with the inclusion of the Grimme's D3 dispersion correction.

Supporting Information

Supporting Information File 1

Additional tables, figures and Cartesian coordinates.

[<https://www.beilstein-journals.org/bjoc/content/supplementary/1860-5397-20-93-S1.pdf>]

Supporting Information File 2

AIMD simulation movie.

[<https://www.beilstein-journals.org/bjoc/content/supplementary/1860-5397-20-93-S2.mpg>]

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Conflict of Interest

The authors declare there are no conflicts of interest.

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Data Availability Statement

All data that supports the findings of this study is available in the published article and/or the supporting information to this article.

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Mechanistic investigations of polyaza[7]helicene in photoredox and energy transfer catalysis

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Full Research Paper

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Abstract

Organic photocatalysts frequently possess dual singlet and triplet photoreactivity and a thorough photochemical characterization is essential for efficient light-driven applications. In this article, the mode of action of a polyazahelicene catalyst (Aza-H) was investigated using laser flash photolysis (LFP). The study revealed that the chromophore can function as a singlet-state photoredox catalyst in the sulfonylation/arylation of styrenes and as a triplet sensitizer in energy transfer catalysis. The singlet lifetime is sufficiently long to exploit the exceptional excited state reduction potential for the activation of 4-cyanopyridine. Photoinduced electron transfer generating the radical cation was directly observed confirming the previously proposed mechanism of a three-component reaction. Several steps of the photoredox cycle were investigated separately, providing deep insights into the complex mechanism. The triplet-excited Aza-H, which was studied with quantitative LFP, is formed with a quantum yield of 0.34. The pronounced triplet formation was exploited for the isomerization reaction of (*E*)-stilbene to the *Z*-isomer and the cyclization of cinnamyl chloride. Catalyst degradation mainly occurs through the long-lived Aza-H triplet (28 μ s), but the photostability is greatly increased when the triplet efficiently reacts in a catalytic cycle such that turnover numbers exceeding 4400 are achievable with this organocatalyst.

Introduction

The emergence of photoredox chemistry in recent years was pioneered by the introduction of photocatalysts (PC) based on metals such as Ru and Ir [1–6]. However, due to the high cost and limited availability of precious metals, organic photocata-

lysts have become a focal point of academic and industrial research [7–15]. Most of the established organic catalysts (acridinium salts [16–19], cyanoarenes [8,20–22], quinones [23,24], etc.) [10,25] are cationic or electron-deficient and tend to act as

excited state oxidants in a reductive quenching cycle. Only recently, more reducing catalyst classes have been investigated, including second-generation cyanoarenes [8], arylamines [26], phenothiazines, phenazines and phenoxazines [9,27,28], which can act as excited state reductants comparable to precious metal-based photoredox catalysts. Singlet-excited organic chromophores often have short lifetimes, limiting their use in collision-based electron/energy transfer reactions unless high substrate concentrations are used [29,30]. In contrast, triplet states populated via intersystem crossing (ISC) have much longer lifetimes and can efficiently react at lower substrate concentrations [30]. Prominent examples include: (i) carbonyl compounds such as benzophenone [31,32] and thioxanthone [33–35], (ii) TADF emitters with small singlet-triplet energy splitting [8,36], (iii) substitution with heavy atoms such as sulphur [37] and halides [38] for fast ISC, or a combination of the above-mentioned methods [39]. However, the longer lifetime of the triplet state usually comes at the expense of a lower energetic driving force. Helicenes in particular show an increased ISC rate compared to planar molecules, which is attributed to an enhanced spin-orbit coupling that is sensitive to their degree of non-planarity [40], where the helical structure allows for mixing between the singlet and triplet π, π^* -states [41,42]. In addition, the insertion of heteroatoms such as nitrogen further enhances ISC due to a spin-orbit coupling between n, π^* -states and π, π^* -states [40], as stated by El Sayed's rule [43]. However, helicenes have not been broadly considered as potential photocatalysts or sensitizers or their applications were unsuccessful [44]. Recently, one of our groups exploited the highly reducing polyaza[7]helicene (Aza-H, see Scheme 1 for its structure) for sulfonylation/arylation three-component reactions (3-CRs) and it has been shown that substituting the helicene core with functional groups is a viable approach to fine-tune the photochemical properties [45,46], as has been demonstrated for other organic and metal-based chromophores.

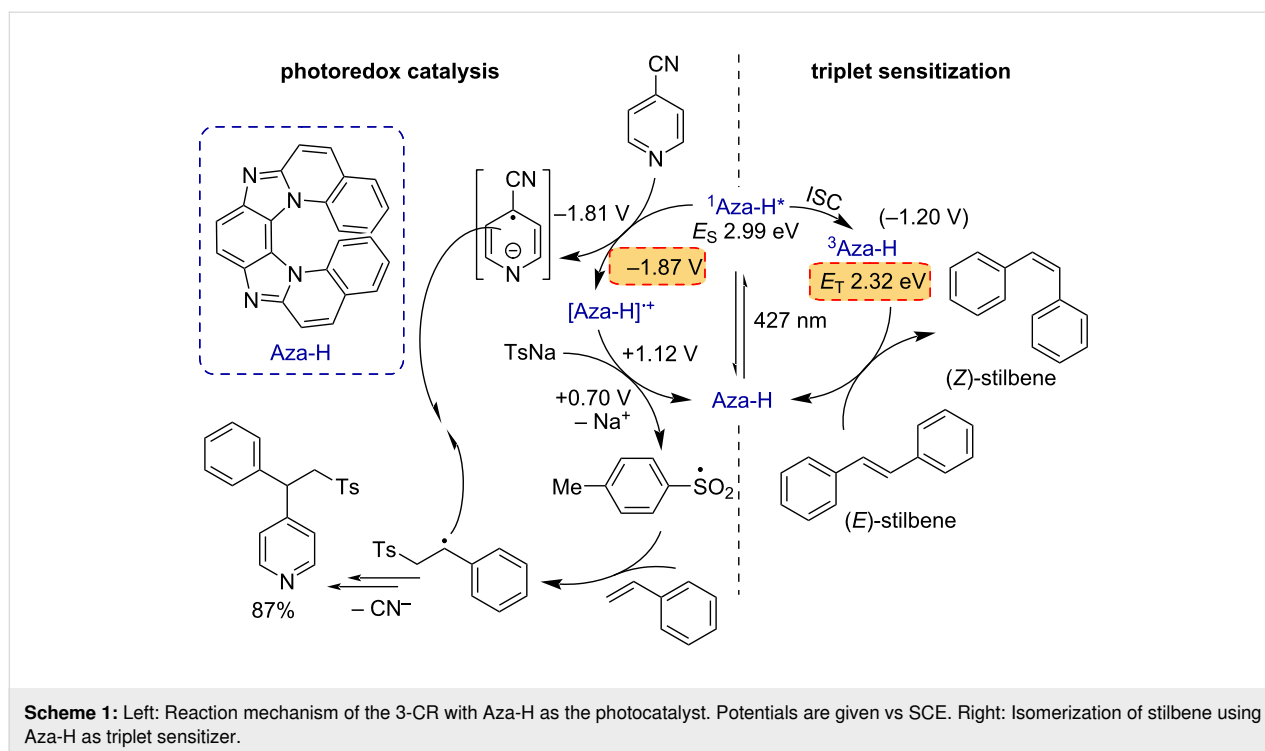
Our study focused on investigating the reaction mechanism of the recently reported sulfonylation/arylation [45,46] reaction using laser flash photolysis (LFP). LFP is a powerful spectroscopic tool in photocatalysis that allows us not only to distinguish between energy and electron transfer but also to detect transient triplet states and radicals, yielding clear-cut evidence for the proposed reaction mechanism [47–57]. We found that quenching of the singlet-excited Aza-H by 4-cyanopyridine is the main pathway for the 3-CR, while the triplet state of our catalyst, which is formed with a quantum yield as high as 0.34, is essentially non-reactive under our conditions. Cyanopyridine- and sulfinate-derived radicals are produced in equal concentrations in the catalytic cycle, suggesting that radical coupling is indeed the final reaction step to give the stable sulfonylation/arylation product. The triplet of Aza-H with its relatively high

formation quantum yield and an energy of 2.32 eV can be used for isomerizing photoswitches like stilbene and for the cyclization of cinnamyl chloride. Our goal was not only to clarify the reaction pathway but also to provide a clear method for distinguishing between singlet and triplet reactivity of the Aza-H photocatalyst through spectroscopic measurements. The careful characterization of the versatile Aza-H photochemistry might contribute to the development of a new class of photoactive catalysts that can compete with traditional metal complexes and well-known organic chromophores (as listed above).

Results and Discussion

A thorough understanding of the operation principles of a photocatalyst is essential for the development of improved catalysts and efficient photoreactions. To this end, the photochemical properties of photocatalysts such as metal complexes and organic chromophores and their roles in catalytic cycles have been extensively studied leading to numerous findings and novel reaction pathways [55,58–61]. Lately, polyazahelicenes have gained some attention by synthetic groups [62–66]. However, this chromophore class is underexplored concerning its photochemical reactivity. The main reaction class catalyzed by excited-state polyazahelicene Aza-H so far is the redox-neutral addition of sulfonates and cyanopyridines, under elimination of cyanide, to styrenes in a three-component reaction. The proposed mechanism was derived from the redox potentials of Aza-H and the substrates and initial steady-state fluorescence quenching experiments (Scheme 1, left), but detailed mechanistic insights and direct evidence of the transient radical ions could not be obtained yet [45].

Figure 1A illustrates the absorption and emission spectra of Aza-H in MeCN/H₂O (9:1). The low reduction potential of singlet-excited Aza-H ($PC^{*+}/PC^* = -1.87$ V vs SCE) led us to propose that the singlet-excited photocatalyst is oxidized by 4-cyanopyridine (4CP) ($4CP/4CP^{\bullet-} = -1.81$ V vs SCE) as the first step in this multicomponent reaction (Scheme 1, left). The oxidized photocatalyst ($PC^{*+}/PC = +1.12$ V vs SCE) is then regenerated by an electron transfer from sodium *p*-toluenesulfinate (TsNa) ($Ts^{\bullet}/Ts^- = +0.70$ V vs SCE) closing the photocatalytic cycle [45]. Unlike other prominent photocatalysts, little to nothing is known about the reactivity, the photophysical properties or the radical ions of polyazahelicenes. The moderate fluorescence quantum yield of 48% (in MeCN) [46] implies that a non-emissive triplet-excited state (at room temperature) could also be generated via intersystem crossing, potentially initiating electron transfer reaction sequences. 77 K emission measurements were thus carried out and they showed short-lived fluorescence and long-lived emission (phosphorescence) that was assigned to the triplet state of Aza-H with an energy of 2.32 eV (Figure 1A). Quantum mechanical computations of the Aza-H



Scheme 1: Left: Reaction mechanism of the 3-CR with Aza-H as the photocatalyst. Potentials are given vs SCE. Right: Isomerization of stilbene using Aza-H as triplet sensitizer.

triplet state yielded a triplet energy of 2.17 eV (adiabatic), which is in good agreement with the experimental value (see Supporting Information File 1 for further information). Consequently, triplet reactivity cannot be excluded, given that photo-induced electron transfer reactions with excited singlet states or singlet radical pairs frequently suffer from low cage escape quantum yields [67,68].

Aza-H exhibits a relatively long singlet lifetime of 9.6 ns (see Figure 4E), which is sufficient for diffusion-controlled energy or electron transfer at moderate substrate concentrations. Transient absorption (TA) spectra of an Ar-saturated Aza-H solution were recorded with an LFP setup using 355 nm pulses (20 mJ) of $\approx 5 \text{ ns}$ duration (see Supporting Information File 1 for experimental details). A delay of 250 ns was used between excitation and detection, which is sufficiently long to avoid the detection of the singlet-excited state (Figure 1B, black). Two broad TA bands peaking at 441 nm and 640 nm were observed that we assign to $^3\text{Aza-H}$. However, on longer time scales the shape of the spectrum changes significantly (Figure S4, Supporting Information File 1) indicating that more than one absorbing species is generated. Measurements on an air-saturated solution under otherwise identical conditions gave a completely different spectrum (Figure 1B, red) and we assume that the triplet state of Aza-H is almost fully quenched by oxygen at the selected delay, which is supported by additional kinetic measurements (see below). The second transient species is identified as the ionization product resulting from a consecutive

two-photon absorption at the selected high laser intensity [69,70], yielding the corresponding long-lived radical cation with second-order decay that is typical for oxidized/reduced species, and a solvated electron as by-product. The latter is in equilibrium with the dimeric solvent radical anion in MeCN, it weakly absorbs in our detection window and this species is rather short-lived compared to the triplet as well as the radical cation [71]. The oscillator strengths for the electronic transitions of $^3\text{Aza-H}$ (purple) and the radical cation $\text{Aza-H}^{\cdot+}$ (red) were computed using TD-DFT (see Supporting Information File 1 for details). These computational results, which are included in Figure 1B, align well with the experimentally observed absorption bands in the visible region, supporting our assignment.

The observed behavior of the Aza-H transient species in Ar-saturated/air-saturated solution is also reflected in the kinetic traces at 440 nm and 640 nm (Figure 1B, inset). Following the decay of the transient triplet species ($^3\text{Aza-H}$), essentially the same signal is reached irrespective of the presence of oxygen or argon in the solution. The contribution of the radical cation to the TA signal at 640 nm is only minor, which allows us to estimate a triplet lifetime of $\approx 28 \mu\text{s}$ at this detection wavelength. Based on our observations, an isolated triplet spectrum can be obtained from the spectral difference between the black and the red spectrum in Figure 1B, as shown in the purple spectrum displayed in Figure 1B (compare to Figure 3B, where the generated radical cation is fully quenched by TsNa).

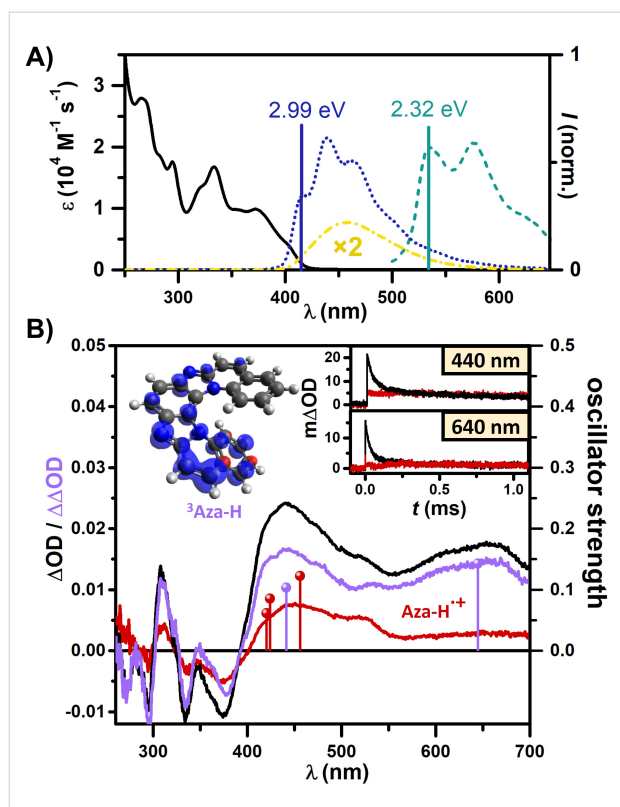


Figure 1: A) Room-temperature absorption (black) and emission (yellow) spectra of Aza-H recorded in MeCN/H₂O (9:1), and fluorescence (blue) and phosphorescence (green) spectra measured at 77 K in MeOH/EtOH (4:1). B) Transient absorption spectra of 25 μM (initial ground-state absorbance at the laser wavelength, 0.2) Aza-H in Ar-saturated (black) and air-saturated (red) MeCN/H₂O (9:1) recorded after 250 ns and the difference spectrum of both (purple) upon excitation with 355 nm laser pulses. Spin density of ³Aza-H and the predicted electronic transitions in the visible region (transitions with oscillator strengths *f* below 0.05 are not shown) of ³Aza-H (purple) and Aza-H^{•+} (red). Inset: Kinetic measurements at 440 nm and 640 nm.

Since all substrate compounds in the 3-CR mixture (4CP, TsNa and α -methylstyrene) cause fluorescence quenching, albeit to different degrees (see Supporting Information File 1), we recorded post-quenching TA spectra with Aza-H and the different substrates. Adding 200 mM 4CP to a deoxygenated solution of Aza-H quenches the fluorescence almost completely ($\eta > 93\%$). The post-quenching TA spectrum (250 ns delay) strongly correlates with what we identified as the radical cation, Aza-H^{•+}, which is in perfect agreement with our proposed photoinduced electron transfer step, while no triplet-excited Aza-H is observed (Figure 2A, blue spectrum). Since the direct ionization of Aza-H also contributes to this spectrum, we recorded a spectrum of only Aza-H in air-saturated solution (red spectrum) and used it to separate the signal that only stems from the oxidative quenching step (green spectrum). This correction likely overestimates the contribution of the two-photon process to the radical cation signal in the presence of 4CP, considering that quenching competes with ionization already during the laser

pulse. Kinetic measurements of the radical cation species show multiexponential decay, probably due to recombination of the radical cation and radical anion (Figure 2A, inset). Despite the reported absorption maximum for 4CP^{•−} at 398 nm [72], we were unable to detect this species, as emphasized by Figure S5 and the discussion in Supporting Information File 1. Similarly, our attempts to identify 4CP^{•−} in an analogous experiment that employed Ir(ppy)₃ as a well-characterized reference photoreductant were also unsuccessful [73,74], probably due to an overall small extinction coefficient of the radical anion (Figure S6 in Supporting Information File 1 and the corresponding discussion). To investigate the triplet reactivity of Aza-H, a lower concentration of 4CP (5 mM) was used, quenching the singlet excited photocatalyst only partially ($\eta \approx 25\%$) and allowing triplet-excited Aza-H to be generated (Figure 2B). Kinetic traces of the triplet state show minor quenching upon the addition of 4CP (Figure 2B, inset), while the initial triplet signal is reduced as expected. However, considering the rather long triplet lifetime (in comparison to the singlet-excited state lifetime), the quenching rate constant is roughly four orders of magnitude lower than singlet quenching ($k_q \approx 10^5 \text{ M}^{-1} \text{ s}^{-1}$). This is in good agreement with the reported high triplet energy of 4CP [75] at 3.08 eV compared to 2.32 eV of ³Aza-H and the lower reduction potential provided by the Aza-H triplet (−1.20 V vs SCE).

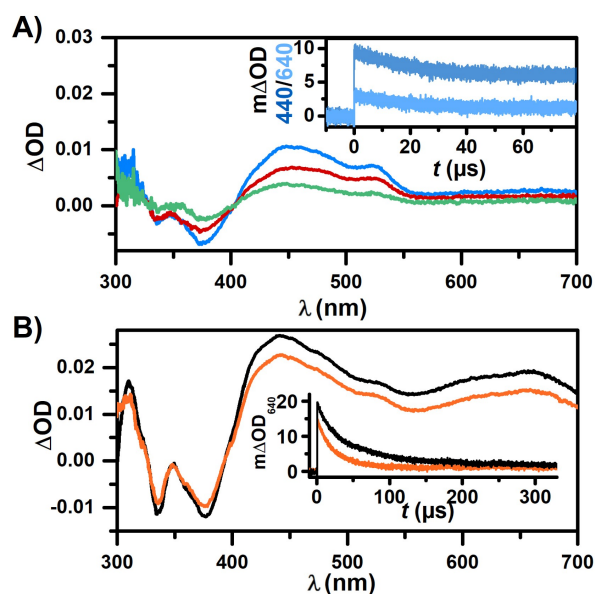


Figure 2: Mechanistic LFP experiments of 25 μM Aza-H with 4CP in MeCN/H₂O (9:1) after 355 nm laser pulses. A) TA spectra recorded after 250 ns of solely Aza-H in air-saturated solution (red), in Ar-saturated solution with 200 mM 4CP (blue) and the difference spectrum of both (green). Inset: Kinetic traces of Aza-H with 200 mM 4CP at 440 nm and 640 nm. B) TA spectra recorded after 250 ns of Aza-H in Ar-saturated solution in the absence (black) and presence (orange) of 5 mM 4CP. Inset: Kinetic traces at 640 nm.

Hence, we concluded that triplet quenching by 4CP plays a negligible role at typical substrate concentrations (>100 mM) used for lab-scale irradiation experiments. Following the proposed mechanism, the catalyst is then regenerated by an electron transfer from TsNa. However, we also observed minor fluorescence quenching of the photocatalysts by TsNa (see Figure S8, Supporting Information File 1), which prompted us to conduct additional LFP experiments to eliminate this as the primary reaction pathway (Figure 3A). Unlike quenching by 4CP, the addition of TsNa only shows signals that we assigned to the triplet spectrum of Aza-H in Figure 1B. Although the singlet-excited photocatalyst is quenched by TsNa, indicated by the reduced triplet formation of Aza-H, our conclusion is that this quenching is unproductive as no new photoproducts are observed. Interestingly, in contrast to all previous measurements, no signal of the Aza-H radical cation generated through two-photon absorption is detected. This can be easily rationalized as the radical cation is most likely rapidly quenched by TsNa (compare the proposed reaction mechanism regenerating the oxidized catalyst). That reasoning is consistent with kinetic traces at 440 nm that show the isolated decay of triplet Aza-H when TsNa is present, while the longer-lived signatures of Aza-H^{•+} are only visible in the absence of TsNa (Figure 3A, inset). In order to analyse the thermal electron transfer, we prepared an aerated solution of Aza-H with a lower concentration of TsNa (200 μM). We presumed this would enable us to exclusively monitor Aza-H^{•+} quenching by TsNa, since any triplet Aza-H would be deactivated by oxygen (see above). The ionization efficiency of Aza-H exhibits a quadratic dependence on the laser intensity. Consequently, focussing the laser on a narrow excitation spot on the sample ensured a significant generation of Aza-H^{•+} while minimizing the concentration of triplet-excited Aza-H. Initially, the same amount of radical cation is detected after the addition of TsNa, but the Aza-H^{•+} signal at 460 nm decays much faster and reaches the baseline after only 10 μs (Figure 3B). Kinetic measurements yielded a rate constant as high as $\approx 10^9 \text{ M}^{-1} \text{ s}^{-1}$ for the reaction between Aza-H^{•+} and TsNa (Figure 3B, inset), which implies that potential side reactions cannot compete. The TA spectra clearly reach baseline level after Aza-H^{•+} quenching by TsNa, indicating that the catalyst is regenerated (ground-state bleach recovery below 400 nm in Figure 3A and 3B) by that reaction, which is in line with the proposed thermal electron transfer. However, both the sulfonyl radical and 4CP^{•-} do not absorb in our detection window, hampering further kinetic and mechanistic investigations. Nevertheless, both radicals must be formed as quenching by-products based on our spectroscopic studies, either in the photoinduced or in the subsequent and rapid thermal electron transfer. For stoichiometry reasons, these radicals are formed in equal concentrations in the catalytic cycle and, therefore, the proposed radical recombination to yield the final product (with

intervening addition of the sulfonyl radical to excess styrene, see Scheme 1) can be regarded as most-likely reaction pathway. Furthermore, we carried out pK value determinations for the protonation of Aza-H, both in its ground state and in the excited singlet state (see Figure S10 in Supporting Information File 1 and the corresponding section for details). Based on our studies in aqueous ethanol, Aza-H is a weak photobase but protonation is seen to be unimportant in neutral and alkaline solutions. However, these studies might be important for explaining reactivity changes when Aza-H is employed in photoreactions requiring or releasing Brønsted acids. During the 3-CR experiment, we observed a decomposition of the catalyst that occurred faster than in the absence of any additives (see studies on inherent photostability presented below). Our observations also revealed that while the styrene does not significantly quench the singlet state of Aza-H, it quenches the triplet state, suggesting that the formation of triplet-excited styrene via energy transfer is feasible (see Figure S7, Supporting Information File 1) [76]. A reaction course plot in the absence of 4CP and TsNa revealed rapid decomposition of the photocatalyst, presumably in a [2 + 2]-photocycloaddition with the styrene component as observed in mass spectrometry (see Figure S17 and Figure S18 in Supporting Information File 1 for details).

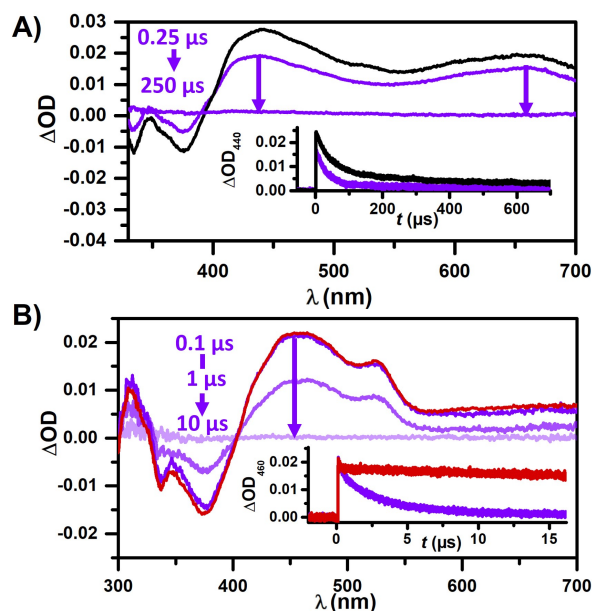


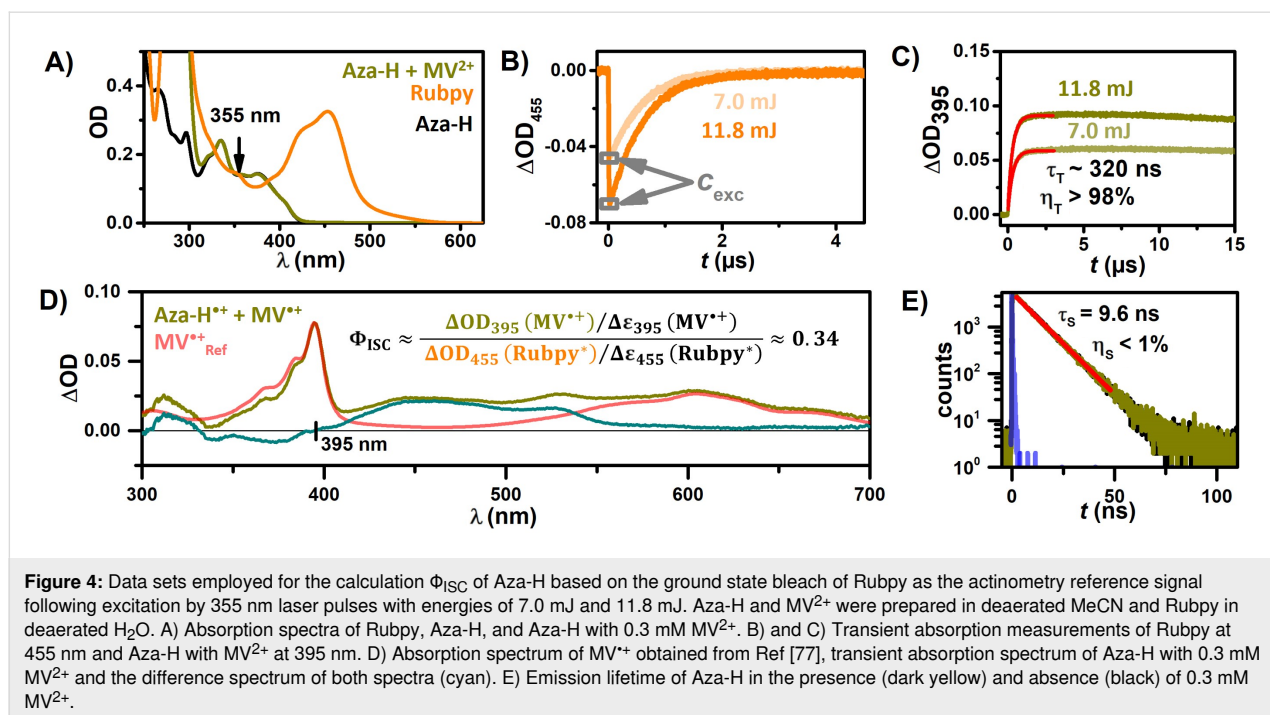
Figure 3: Mechanistic investigations of Aza-H with TsNa by LFP studies. A) Transient absorption measurements of 25 μM Aza-H in the absence of TsNa recorded after 0.25 μs (black) and presence of 50 mM TsNa recorded after 0.25 μs and 250 μs (purple) in deaerated MeCN/H₂O (9:1). Inset: Kinetic measurements at 440 nm. B) TA spectra of the radical cation of Aza-H (aerated MeCN/H₂O (9:1) solution) in the absence of TsNa recorded after 0.1 μs (red) and in the presence of TsNa after 0.1 μs, 1 μs and 10 μs (purple). Inset: Kinetic traces at 460 nm.

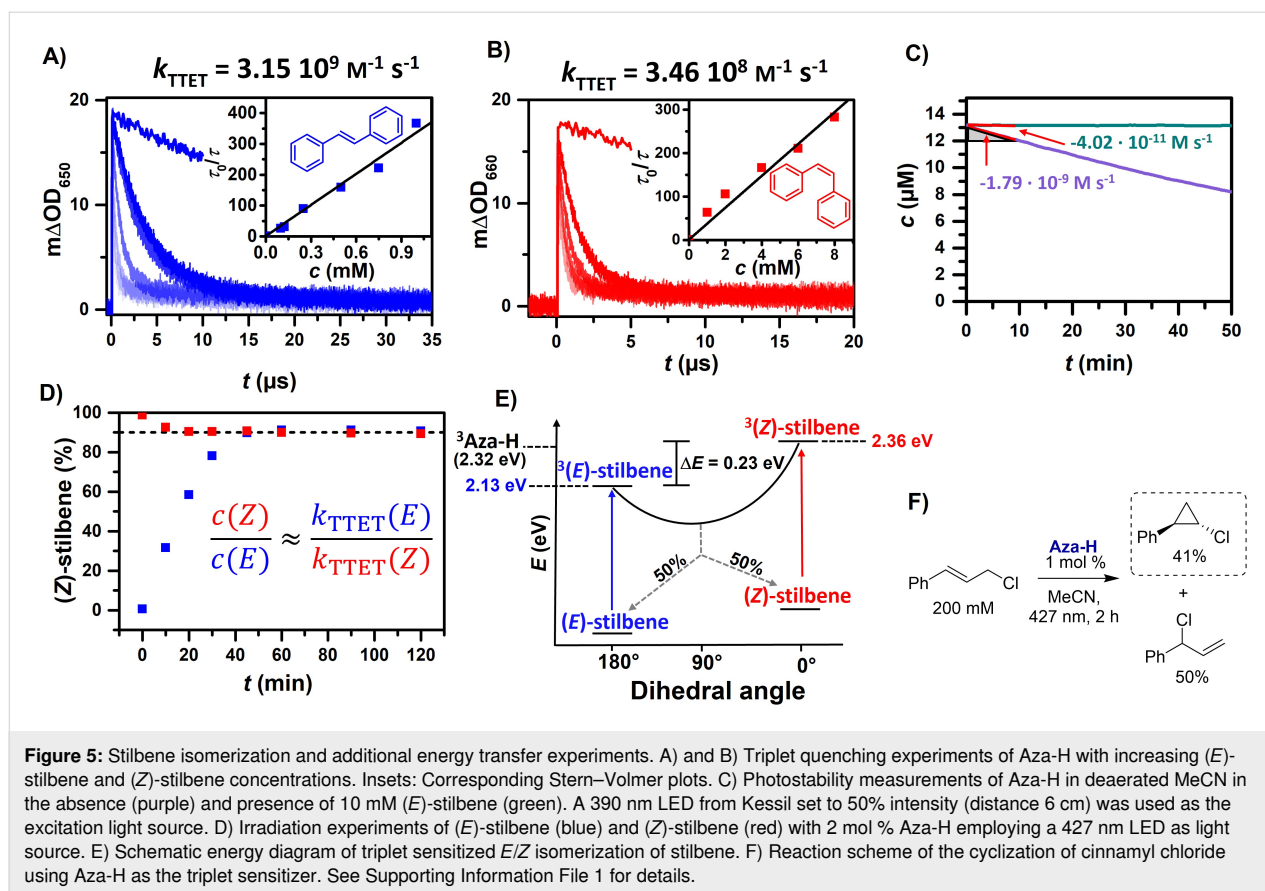
Consequently, the degradation of Aza-H is more efficient at the end of the reaction when incomplete deactivation of the excited singlet state leads to the (more efficient) formation of the triplet state. The occurrence of triplet reactivity of the catalyst as an undesirable side reaction highlights the importance of investigating the triplet state properties and this also initiated our search for a productive use of $^3\text{Aza-H}$. The moderate fluorescence quantum yield of 0.48 indicates that pronounced triplet state formation might take place. Quantitative LFP measurements were performed to determine the ISC quantum yield, Φ_{ISC} , using the well-studied photosensitizer $[\text{Ru}(\text{bpy})_3]\text{Cl}_2$ (Rubpy) as reference for actinometry [78–80]. This approach involved employing identical excitation conditions at 355 nm (Figure 4A) and monitoring the GSB of Rubpy with a literature-reported difference extinction coefficient, $\Delta\epsilon_{455}(\text{Rubpy}^*) = -10100 \text{ M}^{-1} \text{ cm}^{-1}$ [37,79], following excitation (Figure 4B). 0.3 mM methyl viologen (MV^{2+}) were added to Aza-H to quantitatively quench the triplet-excited photocatalyst in an electron transfer reaction yielding Aza-H^{*+} and MV^{*+} , which are clearly observed in the TA spectrum (Figure 4D). For the Φ_{ISC} determination described below, we assume a cage escape quantum yield of 100%, which is reasonable for the photoinduced electron transfer between a heavy atom-free sensitizer-quencher pair in the triplet manifold [67,68,81]. Quenching of the short-lived singlet excited Aza-H at our low quencher concentration was excluded by lifetime-based quenching experiments (Figure 4E). By observing the kinetic traces at the isosbestic point of Aza-H^{*+} (395 nm), we were able to exclusively track the formation of MV^{*+} (Figure 4C). To rule out the formation of

any other products apart from Aza-H^{*+} , we utilized a reference spectrum of MV^{*+} obtained through spectroelectrochemistry [77]. The difference spectrum depicted in Figure 4D closely resembles the Aza-H radical cation spectrum already obtained through photoionization and singlet state quenching (see above), substantiating the reliability of our procedure. Taking the literature-known extinction coefficient of the methyl viologen radical cation $\Delta\epsilon_{395}(\text{MV}^{*+}) \approx 39000 \text{ M}^{-1} \text{ cm}^{-1}$ [82] to calculate its concentration and the initial Aza-H excited-state concentration obtained through Rubpy* actinometry allows us to determine the ISC quantum yield. This procedure was conducted at two excitation intensities: 7.0 mJ and 11.8 mJ (see Supporting Information File 1 for details) yielding an ISC quantum yield of 0.34. The mild excitation energies also ensured that the formation of directly ionized Aza-H was negligible for the evaluation of the ISC quantum yield.

With a promising ISC quantum yield of 0.34 and a triplet energy of approximately 2.32 eV, the triplet-triplet energy transfer (TTET) to (*E*)-stilbene ($E_{\text{T}} = 2.13 \text{ eV}$) [76] should be feasible, while an energy transfer to (*Z*)-stilbene ($E_{\text{T}} = 2.36 \text{ eV}$) [76] is energetically uphill and therefore much slower. Triplet quenching experiments of Aza-H with increasing (*Z*)-stilbene and (*E*)-stilbene concentrations were performed (Figure 5A and B). We obtained quenching efficiencies and rate constants that are in line with our measured triplet energy of Aza-H.

Irradiating a 50 mM solution of either (*E*)-stilbene or (*Z*)-stilbene and Aza-H (2 mol %) in MeCN (Figure S19, Supporting





Information File 1) reaches an equilibrium at an Z/E-ratio of 91:9 (Figure 5D). Moreover, the Z/E-ratio is perfectly reflected by the ratio of the triplet energy transfer rates, which is in line with reported similar efficiencies for the formation of both isomers starting from the perpendicular triplet state (Figure 5E) [35,83].

In contrast to styrene substrates, mass spectrometry shows no addition products of catalyst and stilbene. Hence, the photocatalyst is not consumed by side reactions. Photostability measurements have also demonstrated that the inclusion of a triplet quencher like stilbene significantly enhances the longevity of the Aza-H chromophores, outperforming other well-known organic and metal-based photocatalysts such as 4CzIPN, riboflavin and [Ru(bpy)₃](PF₆)₂ (Figure 5C and Supporting Information File 1). A remarkable turnover number of 4440 was achieved when 1 M stilbene was used (see Supporting Information File 1 for more information). Furthermore, the photocatalyst was utilized in a photosensitized cyclization reaction of cinnamyl chloride [84]. This photoreaction was originally established by Xu et al., but its success was limited to costly Ir-based photocatalysts. Lifetime-based quenching experiments of ³Aza-H with increasing cinnamyl chloride concentration revealed an energy transfer rate of 10⁶ M^{−1} s^{−1} (Figure S9, Sup-

porting Information File 1). Although this rate is four orders of magnitude slower than the diffusion limit in MeCN, the long triplet lifetime ensures a quenching efficiency of 85% when a concentration of 200 mM cinnamyl chloride is used. Exposed to 427 nm irradiation with 1 mol % Aza-H 41% of the chlorocyclopropane and 50% of the branched allylic chloride was produced, which can be recycled to the cinnamyl chloride as demonstrated recently [84].

Conclusion

The experiments presented in this paper have demonstrated the wealth of information accessible by laser spectroscopic studies with a novel polyazahelicene photocatalyst. Its excited singlet state is the key species in a three-component sulfonylation/arylation reaction, whereas the unexplored triplet state is responsible for the decomposition of the photocatalyst. Photoinduced radical cation formation and thermal regeneration could be unambiguously observed, providing deep mechanistic insights into the underlying reaction mechanism. On the other hand, the relatively high triplet formation quantum yield of Aza-H along with its triplet energy on the order of 2.3 eV permit efficient and metal-free reactions via energy transfer catalysis, as shown for the photosensitized isomerization of stilbene and cinnamyl chloride. We believe that our findings pave the way for a

broader usage of the inherently chiral polyazahelicene photocatalyst class, both in photoredox and energy transfer catalysis.

Supporting Information

Supporting Information File 1

General information, detailed experimental procedures, additional spectroscopic data, quantum-mechanical calculations, photostability and photoisomerization experiments.

[<https://www.beilstein-journals.org/bjoc/content/supplementary/1860-5397-20-106-S1.pdf>]

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Data Availability Statement

All experimental data sets supporting the findings of this study are available in the main article and/or the supporting information. The data sets shown in the main paper and DFT output files are accessible via the JGU library and the homepage of the corresponding author.

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Supramolecular assemblies of amphiphilic donor–acceptor Stenhouse adducts as macroscopic soft scaffolds

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Abstract

In the design of photoharvesting and photoresponsive supramolecular systems in aqueous medium, the fabrication of amphiphilic photoswitches enables a noninvasive functional response through photoirradiation. Although most aqueous supramolecular assemblies are driven by high-energy and biodamaging UV light, we have previously reported a design of amphiphilic donor–acceptor Stenhouse adducts (DASAs) controlled by white light. Herein, we present a series of DASA amphiphiles (DAs) with minor structural modifications on the alkyl linker chain length connecting the DASA motif with the hydrophilic moiety. The excellent photo-switchability in organic medium and the photoresponsiveness in aqueous medium, driven by visible light, were investigated by UV–vis absorption spectroscopy. The assembled supramolecular nanostructures were confirmed by electron microscopy, while the supramolecular packing was revealed by X-ray diffraction analysis. Upon visible-light irradiation, significant transformations of the DA geometry enabled transformations of the supramolecular assemblies on a microscopic scale, subsequently disassembling macroscopic soft scaffolds of DAs. The current work shows promising use for the fabrication of visible-light-controlled macroscopic scaffolds, offering the next generation of biomedical materials with visible-light-controlled microenvironments and future soft-robotic systems.

Introduction

Solar energy is of paramount importance to life on the earth for various reasons, such as maintenance of a stable temperature and enabling photosynthesis as the basis of the food chain.

Inspired by the natural photosynthetic processes, synthetic molecules were designed and functionalized with photoresponsive and photoabsorbing functional motifs, serving as the counter-

part of natural photosystems. This allowed to construct smart materials that harvest light energy, e.g., solar cells, photosensitizers, and photochromic materials [1–4]. Supramolecular assemblies are commonly found in nature in order to enable different biological functions in a precise manner, e.g., actin in biological molecular motors, the cytoskeleton, and cell membrane [5–8]. Mimicking natural supramolecular assemblies in aqueous medium, the intrinsic supramolecular dynamicity, stimuli-responsiveness, and molecular functional tunability of synthetic supramolecular systems can be precisely controlled through the delicate design and synthesis of organic molecules [9–14]. Synthetic supramolecular systems can respond to various external stimuli, e.g., light, pH, organic solvents, ions, and heat [15–22]. Light enables noninvasive stimulation with high spatial and temporal precision to control structural transformations of supramolecular assemblies in organic and aqueous media [19,23–25]. Various photochromic and photoresponsive moieties, such as, stiff-stilbene [26], azobenzene [27,28], molecular motors [19,29,30], spiropyran [31–33], indigo [34,35], and donor–acceptor Stenhouse adducts (DASAs) [36,37], have been used in supramolecular systems for photoswitchable smart electronic, optoelectronic, and biomedical materials [30,38–40].

Photoresponsive supramolecular amphiphiles are responsive, complex, and adaptable in aqueous medium [41–43]. Supramolecular assemblies of photoresponsive molecular amphiphiles in aqueous medium can undergo transformation in solution or at the air–water interface and even sustained artificial muscle-like functions [17,43,44]. To tackle poor biocompatibility observed in UV-driven supramolecular assemblies of photoresponsive molecular amphiphiles, visible-light-active supramolecular systems enabling transformations across multiple length scales are urgently required. Some visible-light-driven supramolecular assemblies on a microscopic length scale, such as those containing spiropyran, azobenzenes, and indigos, have been used in transformations in aqueous medium [35,45,46]. However, very few examples of visible-light-driven supramolecular transformation on a macroscopic length scale are available. UV-light-driven supramolecular transformations on a macroscopic length scale were pioneered by Leung and Feringa [42,43]. Besides, we recently reported the first indigo amphiphiles in fabrication of macroscopic soft scaffolds with photoshrinking properties as a smart functional cell-material interfaces [34].

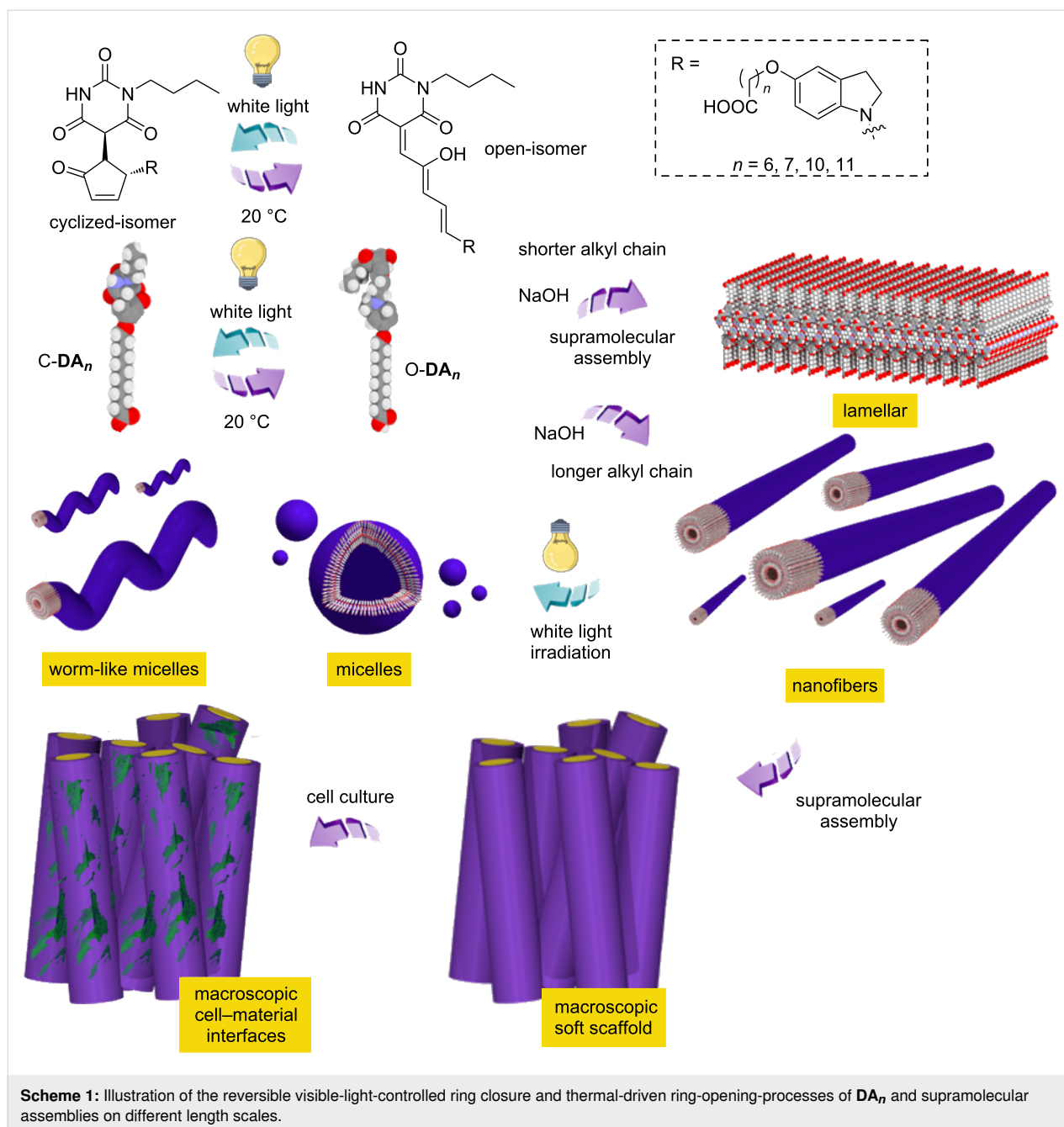
Alternatively, the visible-light-responsiveness of DASAs was firstly reported by Read de Alaniz [47,48]. The significant structural changes upon transformation of the open-isomer to the cyclized-isomer, and the simple modular synthesis of DASAs, enabled various applications in photochromic systems

and smart functional materials [47,49–59]. Inspired by the molecular designs of DASAs, we developed the first DASA amphiphiles (DAs) assembled into large-aspect-ratio nanostructures in aqueous medium while sustaining the visible-light-controlled supramolecular structural transformations [37]. The large-aspect-ratio DA nanostructures assembled into macroscopic soft scaffolds, for which the disassembly process on a macroscopic length scale was controlled by white light. Furthermore, the red-light-responsiveness of the DAs could be regained in aqueous medium upon coassembly with stiff-stilbene amphiphile due to reduced intermolecular stacking [36]. The excellent photoresponsiveness of DAs across multiple length scales significantly increases the urgency to investigate the biocompatibility and molecular structural derivatives. Based on the molecular design of the reported DAs, we designed and synthesized a series of DAs featuring a second-generation DASA switching motif and different chain lengths of the alkyl linker (i.e., **DA_n**) that connects the DASA indoline motif with the hydrophilic part (i.e., the carboxylic acid motif, Scheme 1). The alkyl linker length allowed fine adjustment of the hydrophobic volume of **DA_n**, enabling significant packing parameters changes upon supramolecular assembly in aqueous medium. On a microscopic length scale, the expected supramolecular assembly and the related assembly transformations can be controlled systematically by visible light irradiation. On a macroscopic length scale, the soft **DA_n** scaffolds were able to perform macroscopic structure disassembly upon visible-light irradiation. The biocompatibility of the macroscopic soft **DA_n** scaffolds was investigated, revealing limited cytotoxicity. The current work could open up new prospects in the development of biomedical materials with visible-light-controlled microenvironments and future soft robotic systems.

Results and Discussion

Synthesis and design of DAs

We designed and synthesized a series of **DA_n** with different chain lengths of the alkyl linker, i.e., number of methylene groups in the alkyl linker (n) = 11 (in **DA₁₁**), 7 (in **DA₇**), and 6 (in **DA₆**). The effect of the alkyl linker length in **DA₁₁**, **DA₇**, and **DA₆** is discussed and compared to our previously reported **DA₁₀** [37]. The donor part of **DA_n** was synthesized by alkylation in the presence of K_2CO_3 in a nitrogen atmosphere, followed by reduction of the indole motif in compound **1_n** to indoline in **2_n**. The ester group in compound **2_n** was deprotected under basic conditions to give compound **3_n** (Scheme 2). **DA_n** with different chain lengths of the alkyl linker were synthesized through an aza-Piancatelli rearrangement between a barbiturate–furan adduct **4** and compound **3_n** under ambient conditions in dichloromethane and hexafluoro-2-propanol (HFIP). The synthetic procedures and characterization of all newly synthesized compounds, including **DA₁₁**, **DA₇**, and **DA₆**,

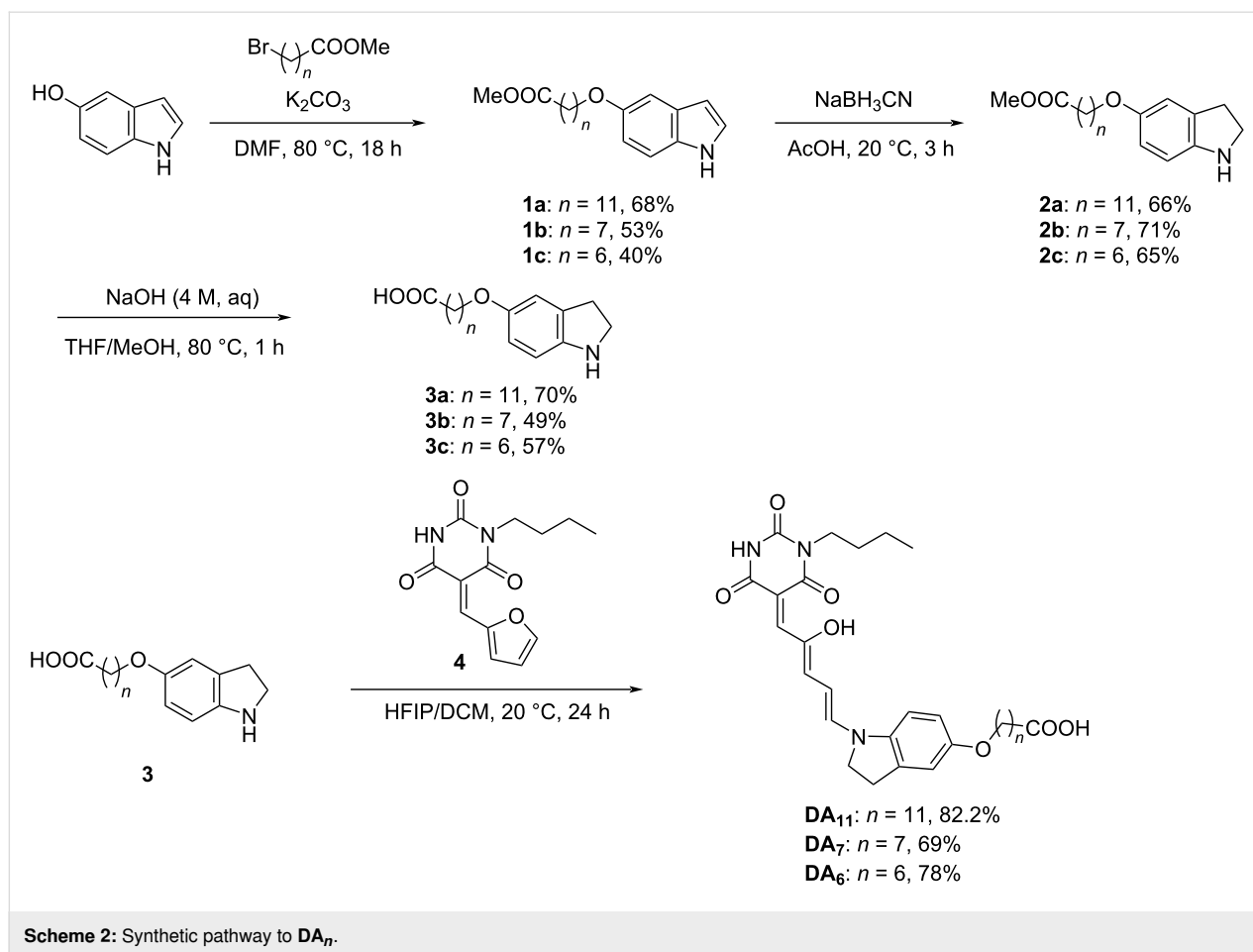


are summarized in Supporting Information File 1, Figures S13–S33.

Photochemical properties of **DA_n** in organic medium

The photochemical properties of **DA_n** were first studied in organic solvent by UV-vis absorption spectroscopy. The synthesized **DA₁₁** in THF solution (20 μM) showed a strong absorption band at 470–685 nm in the UV-vis absorption spectrum (Figure 1a). Upon 625 nm red-light irradiation for 60 s at 20 °C to reach the photostationary state (PSS), the strong

absorption band at 470–685 nm was diminished, with a clear isosbestic point at 259 nm (Figure 1a, red line), which indicates a selective photoisomerization process from the open-isomer **O-DA₁₁** (Figure 1a, black line and Figure 1b blue line) to the cyclized-isomer **C-DA₁₁** (Figure 1a, red line). The resulting solution continued to be irradiate with 625 nm red light for 60 s at 20 °C and subsequently stored in the dark at 20 °C for 60 min for the thermal back reaction to occur to test the reversibility and photostability in organic solvent (Figure S1a and S1b, Supporting Information File 1). The photoisomerization between **O-DA₁₁** and **C-DA₁₁**, upon irradiation with 625 nm red light



and thermal back reaction in the dark, could be repeated for over five cycles, with only 5% absorbance decreases per cycle (Figure S1a and S1b, Supporting Information File 1). In contrast, the previously studied reversibility of the photo-switching of **DA₁₀** had revealed 10% absorbance decreases per cycle [37], indicating a mild improvement to the fatigue resistance of **DA₁₁**.

To further investigate the photostability and reversibility of the other compounds, **DA_n** with shorter alkyl linkers were also examined in THF solvent by UV–vis absorption spectroscopy, where they showed photochemical properties similar to those of **DA₁₁** (Figure 1a and Figure 1b). THF solutions of **DA₇** and **DA₆** showed a strong absorption band at 470–685 nm (Figure 1c and Figure 1e). Upon red-light irradiation at 625 nm for 60 s at 20 °C to reach the PSS, the strong absorption band was diminished, similarly to **DA₁₁**, with a clear isosbestic point at 259 nm (Figure 1c and Figure 1e, red line). After thermal back reaction in the dark at 20 °C for 60 min (Figure 1d and Figure 1f, blue line), the strong absorption band had recovered and indicated a selective photoisomerization process from the open-isomers **O-DA₇** and **O-DA₆** (Figure 1c–f, black and blue

lines) to the cyclized-isomers **C-DA₇** and **C-DA₆** (Figure 1d and Figure 1f, red line). The results showed feasible photoreversibility of **DA₇** and **DA₆** for five additional photoswitching cycles. However, a more significant fatigue effect was observed in **DA₇** (Figure S1c and S1d, Supporting Information File 1) and **DA₆** (Figure S1e and S1f, Supporting Information File 1), with 15% absorbance decline per cycle. As a stronger fatigue effect was observed in the photoisomerization of **DA₇** and **DA₆**, this might be attributed to stabilization through hydrogen bonding and a favored cyclized-isomer in polar solvents. The increased alkyl linker length of **DA₁₀** and **DA₁₁** provided an improved photostability compared to **DA₇** and **DA₆**, possibly due to the reduced stabilization and improved fatigue resistance of the cyclized-isomer in a polar environment.

Photochemical properties of **DA_n** in aqueous medium

Delighted by the good photoswitchability performance of **DA_n** in organic solvent, the photochemical properties and supramolecular assembly were investigated in aqueous medium. An aqueous solution of 5.0 wt % **DA₁₁** in Milli-Q water was prepared, followed by deprotonation with 1.0 equivalent of NaOH,

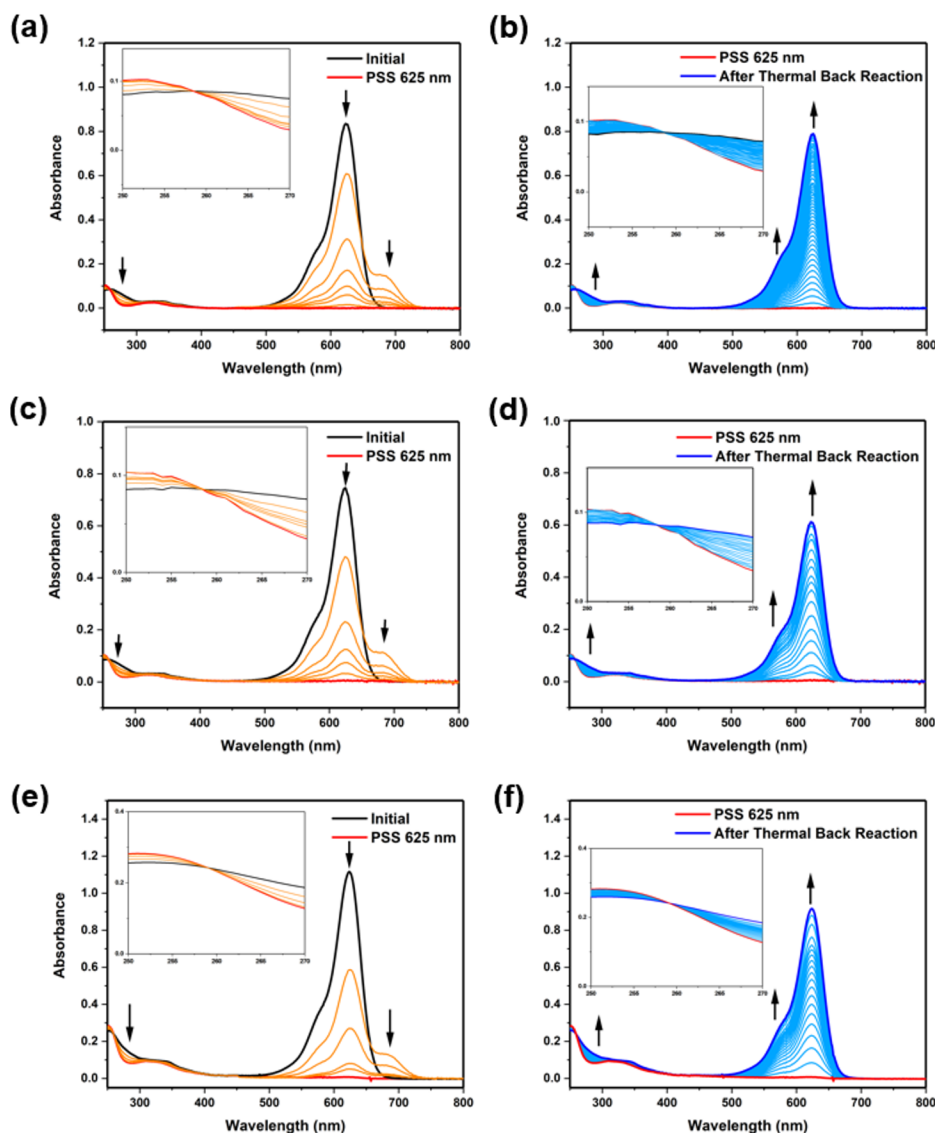


Figure 1: UV-vis-absorption-spectral changes of DA_n in THF solution (20 μ M). (a) DA_{11} , (c) DA_7 , (e) DA_6 solutions in the beginning (black line), upon 625-nm irradiation over the course of 1 min (orange lines), and after irradiation to reach the PSS (red line). (b) DA_{11} , (d) DA_7 , (f) DA_6 upon thermal back reaction over the course of 60 min at 20 °C (cyan lines) and after thermal back reaction (blue line). Insets: enlarged 250–270 nm range. Irradiation was carried out using a Thorlabs model M625F2 high-power LED (625 nm, 1.0 A) positioned at a distance of 1 cm from the sample.

showing excellent solubility up to 93 mM, giving a deep purple solution. An aqueous 43 μ M solution DA_{11} , diluted from the 5.0 wt % stock solution, was investigated by UV-vis absorption spectroscopy. Absorption bands at 250–325 nm and 430–800 nm were observed (Figure 2a), wherein the maximum at 667 nm was accompanied by a shoulder at 561 nm, similarly to the spectrum of DA_{10} [37]. A significant spectral shift and peak broadening of DA_{11} were observed compared to the THF solution (Figure 1a, black line), possibly due to supramolecular assembly in aqueous medium. Because of the broad absorption range of DA_{11} in aqueous medium, photoisomerization could not be effectively accomplished by a 625 nm LED light source

with a narrow emission wavelength range, similarly to our previously studies [37]. Thus, a white-light source with a broad emission wavelength range was employed for the photoisomerization of DA_n in aqueous medium. Photoisomerization of DA_{11} was induced by white-light irradiation for 60 min at 20 °C (Figure 2a, orange line), upon which the absorption band at 430–800 nm decreased and that at 250–325 nm increased. At the same time, isosbestic points were clearly observed at 286 nm, 357 nm, and 443 nm (Figure 2a, red line). The results indicated a slower selective photoisomerization process from O- DA_{11} to C- DA_{11} in aqueous medium compared to the THF (Figure 1a). The thermal back reaction in the resulting aqueous

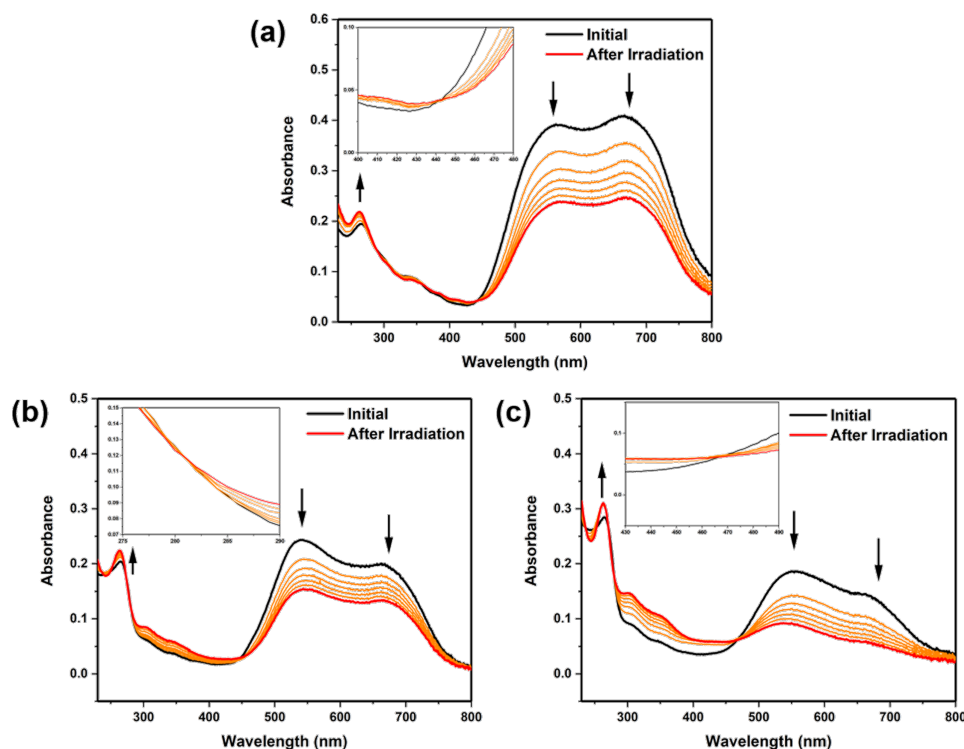


Figure 2: UV-vis absorption spectra of **DA_n** in aqueous solution (43 μ M). (a) **DA₁₁** (inset: enlarged 400–480 nm area), (b) **DA₇** (inset: enlarged 275–290 nm area), (c) **DA₆** (inset: enlarged 430–490 nm area) in the beginning (black line), upon white-light irradiation over the course of 60 min (orange lines), and after 60 min (red line). Irradiation was carried out at 20 $^{\circ}$ C using a light-guide-equipped BBZM-I xenon light source (380–800 nm, 300 W) positioned at a distance of 1 cm from the sample.

solution was further studied, showing no reverse switching to O-**DA₁₁** upon storage in the dark at 20 $^{\circ}$ C (Figure S2, Supporting Information File 1). It has previously been observed that the cyclized-isomers of common DASAs remained stable in aqueous medium, rendering the photoisomerization process irreversible [47,48,60]. The hindered thermal back reaction of **DA₁₁** should also be attributed to a phenomenon similar to that observed in our previously reported **DA₁₀** [37].

The **DA_n** with a shorter alkyl linker, i.e., **DA₇** and **DA₆**, in aqueous solution were also investigated in a protocol identical to that outlined above. An aqueous 43 μ M solution of **DA₇** had absorption bands at 250–325 nm and 430–800 nm, with a maximum at 543 nm, accompanied by a shoulder at 667 nm (Figure 2b). An aqueous 43 μ M solution of **DA₆** similarly had absorption bands at 250–325 nm and 430–800 nm, a broad absorption peak at 557 nm with a shoulder at 667 nm, and a maximum at 263 nm (Figure 2c). Upon white-light irradiation for 60 min at 20 $^{\circ}$ C, the absorption band at 430–800 nm was decreased, which could be observed in both **DA₇** (Figure 2b, orange line) and **DA₆** (Figure 2c, orange line), whereas the absorption band at 250–470 nm was increased. After irradiation for 60 min at 20 $^{\circ}$ C, distinct isosbestic points were located at 286 nm and 449 nm for **DA₇** (Figure 2b, red line,) and at

467 nm and 283 nm for **DA₆** (Figure 2c, red line.), indicating selective photoisomerization from O-**DA₇** to C-**DA₇** and from O-**DA₆** to C-**DA₆** in aqueous solutions. No thermal back reaction was observed for **DA₇** (Figure S3, Supporting Information File 1) and **DA₆** (Figure S4, Supporting Information File 1), similarly to **DA₁₁** and **DA₁₀**. The results indicated that even a subtle modification of the alkyl linker length could induce an obvious spectral shift, implying different supramolecular assemblies of **DA_n** in aqueous medium.

Photocontrolled supramolecular assemblies of **DA_n** in aqueous medium

A freshly prepared aqueous solution of **DA₁₁** (4.1 mM, 0.25 wt %), in the presence of 1.0 equivalent of NaOH, was further diluted to prepare various aliquots with a concentration ranging from 1.0×10^{-4} –0.1 mM in order to estimate the critical aggregation concentration (CAC) by using static light scattering (SLS). An aqueous solution of **DA₁₁** was estimated to have a CAC of <6.0 μ M (Figure S5, Supporting Information File 1). Negative-stain transmission electron microscopy (TEM) was employed to investigate the supramolecular transformations in aqueous medium. An aqueous solution of **DA₁₁** (82 mM, 5.0 wt %) was diluted to 4.1 mM (0.25 wt %), revealing large-aspect-ratio supramolecular nanofiber assem-

blies bundled ≈ 100 nm in width and hundreds of nm in length (Figure 3a and Figure S8a, Supporting Information File 1). Upon white-light irradiation for 60 min at 20 °C, the photoisomerization of **DA**₁₁ at 4.1 mM transformed the supramolecular assembly from bundled nanofibers into a mixture of worm-like micelles and micelle structures 3–4 nm in diameter (Figure 3b and Figure S8b, Supporting Information File 1). The supramolecular structure of **DA**₁₁ and the supramolecular transformation were similar to those observed in **DA**₁₀ [37]. This subtle increase in alkyl linker length in **DA**₁₁ gave an essentially identical performance compared to **DA**₁₀ on a microscopic length scale. Using the same protocol, aqueous solutions of **DA**₇ (0.25 wt %, 4.5 mM) and **DA**₆ (0.25 wt %, 4.6 mM) were prepared by dilution of a 5.0 wt % solution in the presence of 1.0 equivalent of NaOH. The CAC of aqueous solutions of **DA**₇ and **DA**₆ was estimated to be <0.05 mM (Figure S6, Supporting Information File 1) and <0.1 mM (Figure S7, Supporting Information File 1), respectively. This suggested that a longer **DA**_{*n*} alkyl chain led to a lower CAC due to the higher propensity for supramolecular assembly into nanostructures. In aqueous solution, **DA**₇ (0.25 wt %) formed lamellar structures ≈ 200 nm in length and ≈ 40 nm in width (Figure 3c and Figure S8c, Supporting Information File 1), as observed by TEM. A similar lamellar structure was found in an aqueous solution of **DA**₆ (Figure 3e and Figure S8e, Supporting Information File 1). More significant structural variations were revealed upon decreasing the alkyl linker length from $n = 11$ to $n = 7$ or 6. Similarly, the lamellar structure of **DA**₇ disassembled

into worm-like micellar structures upon white-light irradiation (Figure 3d and Figure S8d, Supporting Information File 1), while the lamellar structure of **DA**₆ remained unchanged (Figure 3f and Figure S8f, Supporting Information File 1), possibly due to the stability of the resulting supramolecular structures. The photoswitchability and structural transformations of the supramolecular assemblies on a microscopic length scale opened up possibilities for **DA**_{*n*} to be used for the fabrication of macroscopic soft scaffolds after charge screening with complementary ions.

Fabrication and characterization of macroscopic soft scaffolds of **DA**_{*n*} in aqueous medium

A freshly prepared aqueous solution of **DA**₁₁ (5.0 wt %, 82 mM) was deep blue and remained stable for months. By applying the shear-flow method, negatively charged nanofibers of **DA**₁₁ were assembled into a macroscopic soft scaffold when the solution was ejected into a shallow pool of calcium chloride solution (150 mM, Figure 4a). The high binding affinity between calcium ions and carboxylate groups enabled charge screening of **DA**₁₁ and stabilization as macroscopic soft scaffold. Under an optical microscope, a deep-blue string with a diameter of ≈ 560 μ m was observed in the macroscopic soft scaffold of **DA**₁₁ (Figure S9, Supporting Information File 1), without any birefringence under crossed polarizers. A macroscopic soft scaffold of **DA**₁₁ was imaged by scanning electron microscopy (SEM) to reveal bundled nanofibers partially aligned with

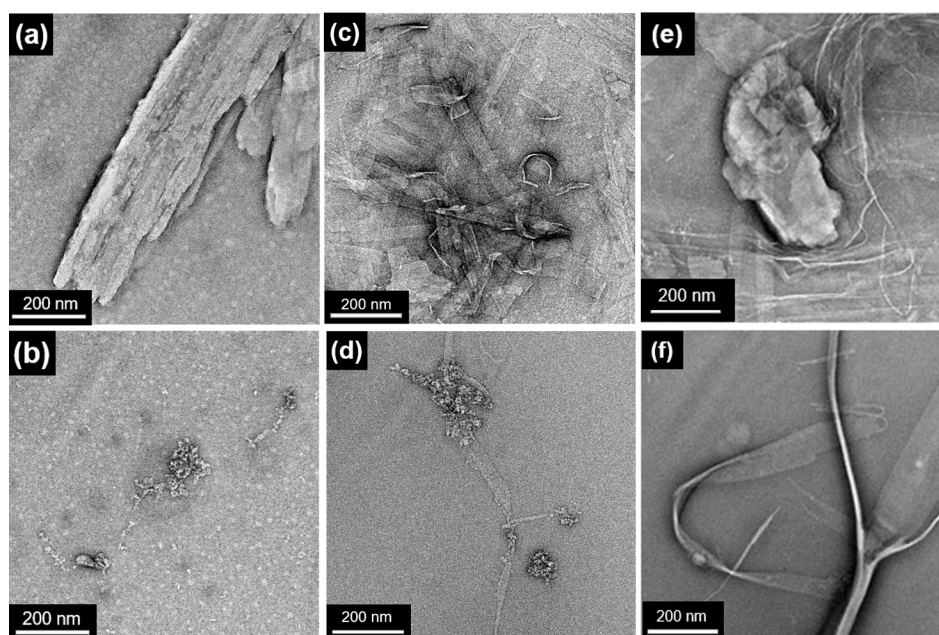


Figure 3: TEM images of freshly prepared aqueous solutions before irradiation of (a) **DA**₁₁ (0.25 wt %, 4.1 mM), (c) **DA**₇ (0.25 wt %, 4.5 mM), and (e) **DA**₆ (0.25 wt %, 4.6 mM). The solutions of (b) **DA**₁₁, (d) **DA**₇, and (f) **DA**₆ were irradiated with white light for 60 min at 20 °C.

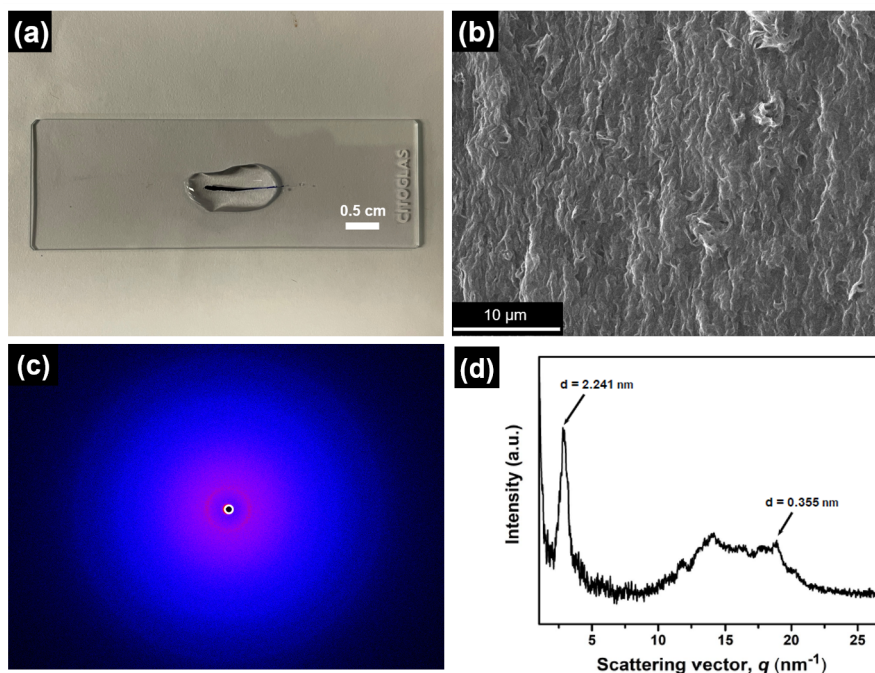


Figure 4: Photograph of a freshly prepared aqueous **DA**₁₁ solution (82.0 mM) ejected into a shallow pool of **CaCl**₂ solution (150 mM), (b) SEM image of a macroscopic **DA**₁₁ scaffold prepared from a solution of **CaCl**₂ (150 mM), (c) 2D WAXD image of **DA**₁₁ macroscopic soft scaffold with an X-ray exposure time of 20 min, and (d) 1D WAXD pattern of a 2D WAXD image of a **DA**₁₁ macroscopic soft scaffold in (c).

the long axis of the macroscopic soft scaffold (Figure 4b). The degree of alignment (structural parameters and orientational order) of macroscopic soft scaffolds of **DA**₁₁ were investigated with through-view wide-angle X-ray diffraction (WAXD). The 2D WAXD image of the macroscopic soft scaffold of **DA**₁₁ showed a diffraction ring in the region of $q = 0.5\text{--}5.0\text{ nm}^{-1}$ (Figure 4c), which was similar to that of **DA**₁₀ [37]. A low degree of angular dependency was observed in the macroscopic soft scaffold of **DA**₁₁, with a pair of weak peak maxima with full-width half-maxima at $\approx 110^\circ$ (Figure S10, Supporting Information File 1), while the **DA**₁₀ macroscopic soft scaffold showed no obvious peak maximum. The results indicated subtle unidirectional alignment of bundled **DA**₁₁ with respect to the long axis of the macroscopic soft scaffold, while no significant unidirectional alignment was observed in the **DA**₁₀ macroscopic soft scaffold. The 1D WAXD pattern of the 2D WAXD image of the **DA**₁₁ macroscopic soft scaffold showed diffraction peaks at $d = 2.24\text{ nm}$ and 0.36 nm (Figure 4d). The diffraction peak at $d = 2.24\text{ nm}$ could be attributed to the longer molecular axis of **DA**₁₁ in dimer form, while that at $d = 0.36\text{ nm}$ originated from π – π stacking of the DASA motif. Consistently, diffraction from the longer molecular axis of **DA**₁₀ in dimer form was shorter ($d = 2.19\text{ nm}$) than that of **DA**₁₁, revealing the subtle alkyl linker length variation of **DA**_{*n*} even on a macroscopic length scale. Further verifying this variation in the packing structure, the 2D WAXD images of **DA**₇ and **DA**₆

macroscopic soft scaffolds (Figures S11a and S12a, Supporting Information File 1, respectively) showed diffraction rings with d -spacings at 1.50 nm and 1.45 nm , respectively (Figure S11b and Figure S12b, Supporting Information File 1), revealing the shortened longer molecular axis of **DA**₇ and **DA**₆ in dimer form compared to **DA**₁₁ and **DA**₁₀. The observed major diffraction peaks of **DA**₇ and **DA**₆ macroscopic soft scaffolds also originated from π – π stacking of the DASA motifs. However, no significant unidirectional alignment was observed in WAXD and SEM images of **DA**₇ and **DA**₆ macroscopic soft scaffolds (Figure S11a and S11c as well as S12a and S12c, Supporting Information File 1, respectively). Electron microscopy and WAXD revealed that a longer alkyl linker length of **DA**_{*n*} could slightly improve the degree of unidirectional alignment of **DA**_{*n*} nanostructures in the corresponding macroscopic soft scaffolds, possibly due to the higher tendency to bundle.

Photocontrolled disassembly and biocompatibility of macroscopic soft scaffolds of **DA**_{*n*}

Macroscopic soft scaffolds of **DA**_{*n*} were shown to have an excellent structural stability and to undergo supramolecular transformations through visible light. A macroscopic **DA**₁₁ soft scaffold was monitored over the course of visible-light irradiation under an optical microscope. At the start, a deep-blue string with a diameter of $\approx 240\text{ }\mu\text{m}$ was observed (Figure 5a and Sup-

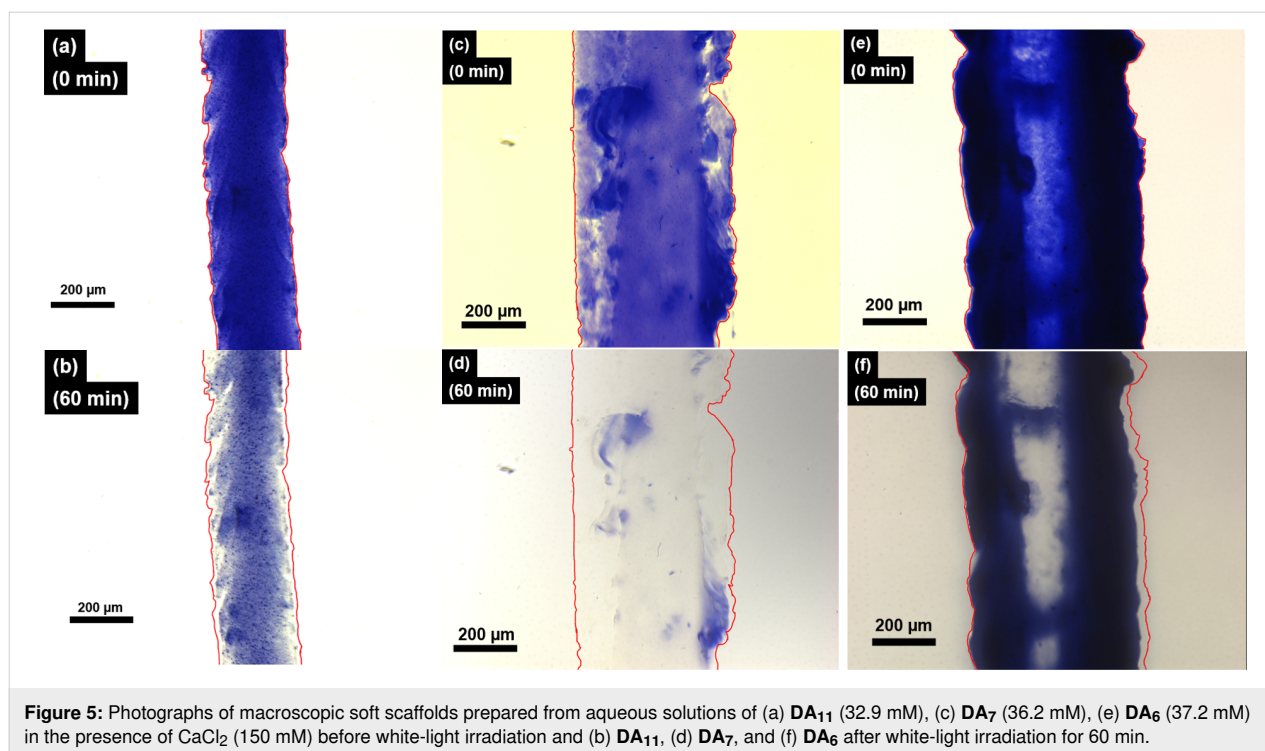


Figure 5: Photographs of macroscopic soft scaffolds prepared from aqueous solutions of (a) **DA**₁₁ (32.9 mM), (c) **DA**₇ (36.2 mM), (e) **DA**₆ (37.2 mM) in the presence of **CaCl**₂ (150 mM) before white-light irradiation and (b) **DA**₁₁, (d) **DA**₇, and (f) **DA**₆ after white-light irradiation for 60 min.

porting Information File 2). The macroscopic soft scaffold weakened and shrank in the process. It also partially disassembled upon irradiation for 60 min (Figure 5b), consistent with the behavior of the **DA**₁₀ macroscopic soft scaffold. With the same treatment, the macroscopic soft scaffolds of **DA**₇ and **DA**₆ showed deep-blue strings with diameters of ≈ 500 μm and ≈ 570 μm , respectively (Figure 5c and Figure 5e as well as Supporting Information File 3 and Supporting Information File 4). After 60 min of white-light irradiation, the **DA**₇ and **DA**₆ scaffolds had significantly disassembled, and the deep-blue color had significantly faded as well (Figure 5d and Figure 5f). The results indicated that **DA**_{*n*} macroscopic soft scaffolds enabled a photocontrolled disassembly process across multiple length scales.

Macroscopic soft **DA**_{*n*} scaffolds were freshly prepared by ejecting 5.0 wt % **DA**_{*n*} solutions onto a bioinert glass-bottomed Petri dish by the shear-flow method, rinsing with PBS, and incubating with human-bone-marrow-derived mesenchymal stem cells (hBM-MSCs) at 37 °C and 5% **CO**₂ for 3 days. hBM-MSCs have demonstrated importance in controlled differentiations and clinical translations. The **DA**₁₁ scaffold remained intact after incubation at 37 °C, while the hBM-MSCs cells grew and attached onto the scaffold surface (Figure 6a and Figure 6b). However, the structural properties of the macroscopic soft **DA**₁₁ scaffold could not be transferred to the attached cells. Besides, the **DA**₁₀, **DA**₇, and **DA**₆ scaffolds, prepared in the same way, also showed intact macroscopic

structures for 3 days of incubation at 37 °C, and hBM-MSCs cells attached onto the scaffold surfaces (Figure 6c–h). Though coverage of the **DA**_{*n*} scaffolds surface with hBM-MSCs cells was limited, the cellular compatibility was good. These **DA**_{*n*} biocompatibility results are the first example showing the intrinsic cytocompatibility of macroscopic soft **DA** scaffolds.

Conclusion

Amphiphilic DASAs with alkyl linkers of different length connecting to a carboxylic acid were prepared. Photochemical properties of the **DA**_{*n*} were investigated in both organic and aqueous media, revealing good photoswitchability in organic medium, while the thermal back reaction was hindered in aqueous medium. The large aspect ratio of the supramolecular **DA**_{*n*} nanofibers in aqueous medium enabled supramolecular transformations upon white-light irradiation. The good stability of the nanostructures further allowed fabrication of macroscopic soft scaffolds with limited unidirectional alignment. The obtained **DA**_{*n*} scaffolds showed photoresponsiveness in the form of partial weakening and disassembly after 60 min of irradiation. The scaffolds were further incubated with hBM-MSCs cells, promoting the attachment of cells onto the surface. The limited cytotoxicity and good stability of **DA**_{*n*} macroscopic soft scaffolds points at an application as cell–material interface and even offers opportunities for the fabrication of biomedical materials with visible-light-controlled microenvironments and future soft robotic systems.

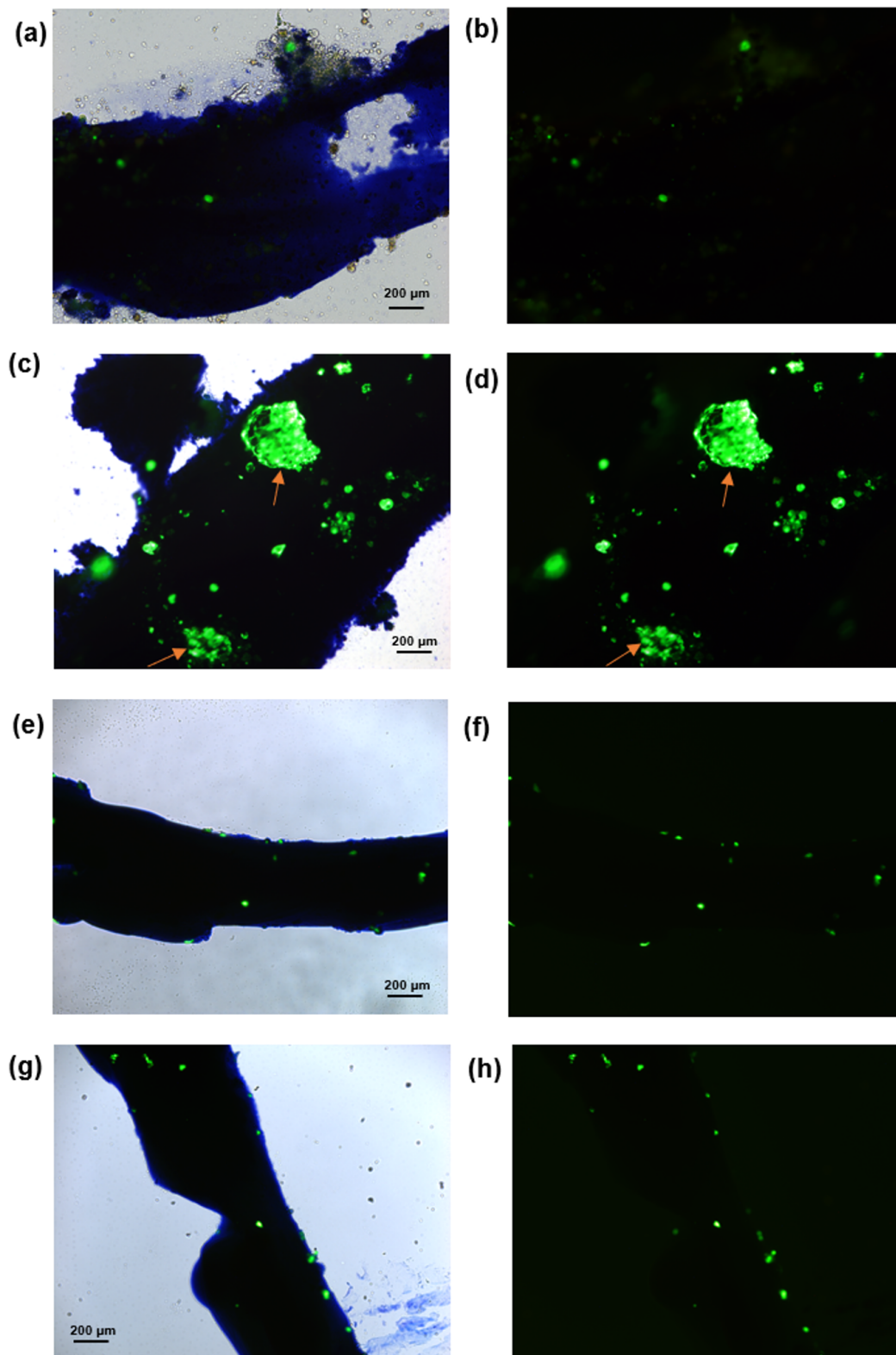


Figure 6: Macroscopic soft DA_n scaffolds fabricated by the shear-flow method. Images taken during fluorescence microscopy. Photographs of freshly prepared (a) DA_{11} , (c) DA_{10} , (e) DA_7 , and (g) DA_6 , merged image of bright field and fluorescence with hBM-MSCs after 3 days of incubation. Fluorescence images of live cells in (b) DA_{11} , (d) DA_{10} , (f) DA_7 , and (h) DA_6 after 3 days of incubation to observe the cell affinity on the hydrogel surface. Scale bar: 200 μm , applied for all panels. The large fluorescent particles pointed at by orange arrows in (c) and (d) are the clustered hBM-MSCs.

Experimental

Materials

All commercial reagents were purchased from Acros Organics, Aladdin, Alfa Aesar, Bidepharm, Dieckmann, Macklin, Sigma-Aldrich, and Tokyo Chemical Industry and used as received unless otherwise specified. All reactions were performed under nitrogen unless otherwise specified. Analytical thin-layer chromatography (TLC) was performed with Macherey-Nagel silica gel 60 UV254 aluminum plates, and visualization was accomplished by UV light (254 nm or 365 nm) or by staining with phosphomolybdic acid and heating. Flash column chromatography was performed using Macherey-Nagel silica gel 60 (230–400 mesh). Deuterated solvents were purchased from Cambridge Isotope Laboratories.

UV-vis spectroscopy

UV-vis measurements were performed on an Agilent Cary 60 UV-vis spectrophotometer with a quartz cuvette of 1 cm path length. A Luma 40/Cary 60 temperature-controlled cuvette holder with four optical ports was mounted in the sample compartment. UV-vis irradiation was carried out at 20 °C using a Thorlabs model M625F2 high-power LED (625 nm, 1.0 A) (625 nm, 1.0 A) and a light-guide-equipped BBZM-I xenon light source (380–800 nm, 300 W) positioned at a distance of 1 cm from the sample.

Preparation of aqueous samples

All aqueous solutions of **DA_n** were prepared according to the following general procedure: **DA_n** (5.0 wt %) was mixed with 1.0 equivalent NaOH in Milli-Q water. The obtained aqueous solution was sonicated for 10 min at room temperature to afford a deep-purple solution. The obtained solution was directly used or diluted for microscopic and spectroscopic measurements.

TEM

TEM was performed on a JEOL model JEM-2010 transmission electron microscope with tungsten hair pin type filament operating at 120 kV, equipped with a Gatan 794 CCD camera. TEM samples were prepared by depositing sample solutions (5.0 µL) onto a carbon grid (micro to nano, EMR carbon support film on copper, 400 square mesh) for 20 s. The sample solution was removed by blotting, and UranylLess EM stain solution (5.0 µL, Electron Microscopy Science) was directly deposited onto the grid for 20 s, and the stain was removed by blotting.

SEM and polarized optical microscopy analysis

Polarized optical microscopy was performed on a Leica DM2700-P optical polarizing microscope. SEM was performed on a Tescan VEGA3 scanning electron microscope. The prepa-

ration of soft scaffolds composed of **DA₆**, **DA₇**, and **DA₁₁**, respectively, on a glass substrate was done as follows: Aqueous solutions of **DA₆** (5.0 wt %, 92.9 mM), **DA₇** (5.0 wt %, 90.5 mM), and **DA₁₁** (5.0 wt %, 82.2 mM) were manually added to an aqueous solution of CaCl₂ (150 mM) by pipette, whereupon a noodle-like soft scaffold with an arbitrary length formed. After removal of the metal chloride solution, the soft scaffold was washed three times with Milli-Q water, and the resulting soft scaffold was used directly for POM experiments. A soft scaffold for SEM analysis was directly prepared on conductive carbon adhesive tape and air-dried for 48 h before measurement.

SLS

The scattering intensity of the samples was determined by SLS measurements using a Wyatt Technology DynaPro NanoStar. The scattering intensity was recorded as a parameter signifying the assembly size since the objects in solution were anisotropic, and the models used by Wyatt software are fitted to spherical objects. To determine the CAC of **DA₆**, **DA₇**, and **DA₁₁**, the scattering intensity of solutions of **DA₆** (1.0×10^{-4} –0.5 mM), **DA₇** (1.0×10^{-4} –0.5 mM), and **DA₁₁** (1.0×10^{-4} –0.1 mM) was recorded at 20 °C. This scattering rate was normalized by the concentration of the solution to yield the molar scattering intensity. Ten replications were performed, and the data was averaged to show the molar scattering intensity and the error standard deviation.

WAXD

WAXD of DA scaffolds was measured on a sapphire substrate ($\phi = 2.0$ cm) using a Rigaku NANOPIX equipped with a HyPix-6000 (Rigaku) detector. The scattering vector ($q = 4\pi\sin(\theta)/\lambda$), scattering angle θ , and the position of the incident X-ray beam on the detectors were calibrated using several orders of layer reflections from silver behenate ($d = 58.380$ Å), where λ refers to the wavelength of the X-ray beam (Cu K α irradiation, 1.54 Å). The sample-to-detector distance was ≈ 100 mm. The obtained diffraction patterns were integrated along the Debye–Scherrer ring to afford 1D intensity data using the Rigaku 2DP software.

Attachment of hBM-MSCs onto **DA_n** scaffold surface

The preparation of **DA_n** stock solutions [61] and the fabrication of macroscopic scaffolds followed the standard methods outlined above. An aqueous solution of **DA_n** (5.0 wt %) was manually added to a calcium chloride solution (150 mM) in a bioinert surface dish to fabricate the macroscopic scaffold. After removal of the calcium chloride solution, the obtained **DA_n** macroscopic scaffold was washed three times with fresh Milli-Q water, followed by the addition of 0.5 mL of a growth

medium consisting of minimum essential medium (MEM α , no phenol red, Gibco), 10% fetal bovine serum (FBS, Gibco), and 1% antibiotic–antimycotic (Gibco). Then, hBM-MSCs (Lonza) were added to the culture dish and cultured for 3 days at 37 °C and 5% CO₂ in an incubator. After incubation, the **DA_n** macroscopic scaffold with cells attached was used directly for fluorescent microscopy measurements.

Supporting Information

Supporting Information File 1

Experimental details, supporting figures, and copies of spectra.

[<https://www.beilstein-journals.org/bjoc/content/supplementary/1860-5397-20-142-S1.pdf>]

Supporting Information File 2

Monitoring of **DA₁₁** under visible-light irradiation.

[<https://www.beilstein-journals.org/bjoc/content/supplementary/1860-5397-20-142-S2.mp4>]

Supporting Information File 3

Monitoring of **DA₇** under visible-light irradiation.

[<https://www.beilstein-journals.org/bjoc/content/supplementary/1860-5397-20-142-S3.mp4>]

Supporting Information File 4

Monitoring of **DA₆** under visible-light irradiation.

[<https://www.beilstein-journals.org/bjoc/content/supplementary/1860-5397-20-142-S4.mp4>]

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Author Contributions

Ka-Lung Hung: investigation; writing – original draft. Leong-Hung Cheung: investigation; resources. Yikun Ren: investigation. Ming-Hin Chau: investigation. Yan-Yi Lam: investigation. Takashi Kajitani: investigation. Franco King-Chi Leung: conceptualization; funding acquisition; supervision; writing – original draft; writing – review & editing.

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Data Availability Statement

The data that supports the findings of this study is available from the corresponding author upon reasonable request.

Preprint

A non-peer-reviewed version of this article has been previously published as a preprint: <https://doi.org/10.3762/bxiv.2024.24.v1>

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61. The cell attachment experiment of hBM-MSCs on **DA_n** macroscopic scaffold was performed in a manner similar to [34].

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Ring opening of photogenerated azetidinols as a strategy for the synthesis of aminodioxolanes

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Letter

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Abstract

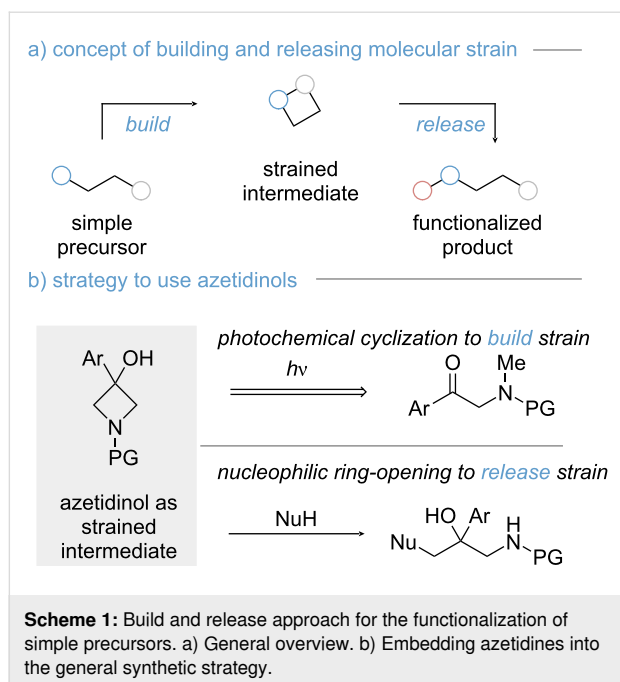
α -Aminoacetophenones are identified as promising building blocks for the synthesis of highly substituted dioxolanes. The presented strategy is founded on the build and release of molecular strain and achieves a formal transposition of a methyl group. During light irradiation, 3-phenylazetidinols are forged as reaction intermediates, which readily undergo ring opening upon the addition of electron-deficient ketones or boronic acids. Key to the successful development of this two-step process is the identification of a benzhydryl-protecting group, which orchestrates the photochemical Norrish–Yang cyclization and facilitates the subsequent ring opening.

Introduction

Identifying efficient methods for the preparation of densely functionalized molecules is one of the central goals of modern organic chemistry. In this context, application of strained molecules has garnered increasing attention due to their intrinsic reactivity [1,2]. However, accessing strained molecules continues to pose a synthetic challenge because many reported methods require harsh conditions for the preparation. An attractive alternative to traditional synthesis can be found in photochemical methods, bypassing energetic constraints by the utilization of photon energy. Thus, endergonic transformations can be real-

ized [3]. A promising strategy for the synthesis of complex products lies in the combination of photochemical cyclization and strain-release reaction (Scheme 1a) [4]. In this ‘build and release approach’, a simple precursor is cyclized upon irradiation. Subsequently, a functionalization step such as a ring-opening event is implemented, facilitated by the pre-installed strain energy of the four-membered ring [5–7].

The implementation of a build and release strategy, as depicted in Scheme 1a, necessitates the full compatibility of both indi-



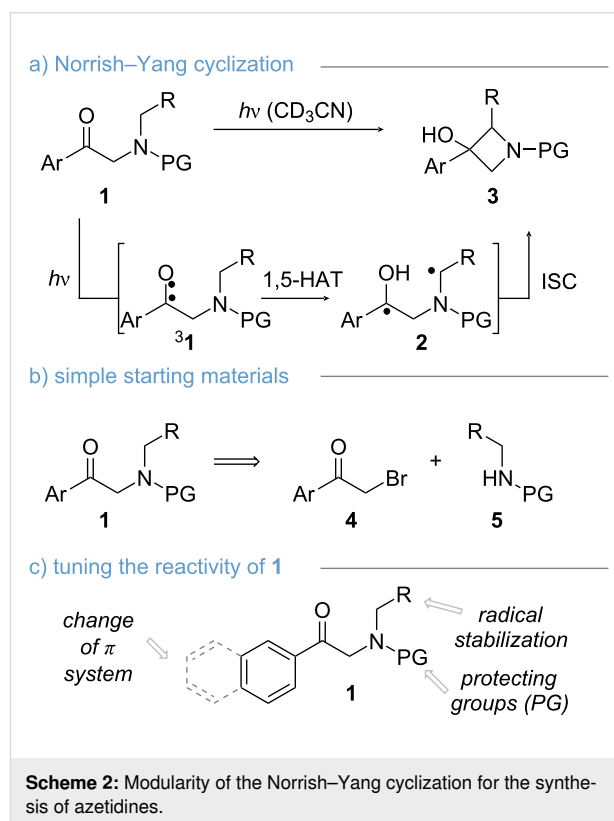
vidual reaction steps, thus placing stringent demands on the selection and assessment of substrates. In our quest to identify a suitable system, we were attracted by the use of azetidines as potential reaction intermediates (Scheme 1b) [8–10]. Azetidines were chosen because of existing literature precedent for their photochemical assembly by Norrish–Yang cyclization, which employs easily accessible α -aminoacetophenones as starting materials [11–15]. Furthermore, ring-opening reactions of azetidines have been recently achieved using sulfur and oxygen nucleophiles [16–25]. However, methods that target a combination of photochemical ring closure and subsequent functionalization are still underdeveloped [4–7]. Within this work, we describe our endeavours in identifying a suitable substrate to meet the photochemical requirements of the Norrish–Yang cyclization and allow for subsequent ring-opening reactions. In this regard, we uncovered a novel entry to dioxolanes by intramolecular ring opening of azetidines using ketones and boronic acids.

Results and Discussion

Photocyclization

We initiated our study by a systematic investigating of the Norrish–Yang cyclization for the synthesis of azetidins. Mechanistically, the Norrish–Yang cyclization involves a 1,5-hydrogen abstraction (HAT) step followed by ring closure to forge the azetidine scaffold (Scheme 2a, **1** $\rightarrow$ **3**, via 1,4-biradical **2**) [26]. The respective α -aminoacetophenones **1** were synthesized using a modular approach starting from α -bromoacetophenones **4** and disubstituted amines **5** (Scheme 2b). Three different criteria were chosen to evaluate the photochemical cycli-

zation (Scheme 2c). We hypothesized that changes in the π -system of the aromatic ring would have an impact on the efficiency of triplet generation (**1** $\rightarrow$ **3**). The corresponding protecting group (PG) was thought to control the conformation of the 1,4-biradical **2**, which is known to be important for efficient Norrish–Yang cyclizations [27,28]. Furthermore, the PG was deemed crucial for the development of further functionalizations of the azetidins (vide infra). Thirdly, we wanted to assess substitution α to the nitrogen (R), as this was thought to impact the stability of the intermediary 1,4-biradical **2** [29,30]. To obtain comparable results, all reactions were performed in a LuzChem photoreactor under identical conditions. Deuterated acetonitrile was chosen as a preferred solvent because it is known to facilitate Norrish–Yang-cyclizations and allows simple analysis by nuclear magnetic resonance (NMR) spectroscopy [10].



Our results are summarized in Table 1. When *p*-toluenesulfonyl (Ts) was used as a PG at nitrogen, azetidine **3a** was obtained in 81% yield along with 14% acetophenone (**6**) as the major side product (Table 1, entry 1). Acetophenone (**6**) is thought to be generated by a Norrish type II cleavage of biradical **2a**. Changes at the aromatic core, as demonstrated by acetophenone **1b**, resulted in low conversions (Table 1, entry 2). When extending the reaction time to reach full conversion, significant amounts of Norrish type II cleavage were obtained and product

Table 1: Comparison of the effect of structural variations on the photoreaction.

Entry	Substrates 1			Conversion (%)	Yield 3 (%)	Yield 6 (%)
1	Ar = Ph	PG = Ts	R = H (1a)	>99	81	14
2	Ar = Nph	PG = Ts	R = H (1b)	23	11	4
3	Ar = Ph	PG = Ts	R = CH ₃ (1c)	>99	54 (dr 54:46)	26
4	Ar = Ph	PG = Ts	R = Ph (1d)	>99	63 (dr 60:40)	20
5	Ar = Ph	PG = Ms	R = H (1e)	>99	67	14
6	Ar = Ph	PG = Ms	R = CH ₃ (1f)	>99	44 (dr 51:49)	42
7	Ar = Ph	PG = Ms	R = Ph (1g)	>99	37 (dr 52:48)	22
8	Ar = Ph	PG = Ph	R = H (1h)	90	12	3
9	Ar = Ph	PG = Ph	R = CH ₃ (1i)	27	2 (dr 52:48)	6
10	Ar = Ph	PG = Me	R = H (1j)	87	<1	53
11	Ar = Ph	PG = Bn	R = H (1k)	>99	<1	65
12	Ar = Ph	PG = Bzh	R = H (1l)	94	10	74

^aConversions and yields were determined by ¹H NMR spectroscopy using mesitylene as an internal standard. ^bDiastereomeric ratios were determined by ¹H NMR spectroscopy. Reactions were run on 25 μM scale. Ts = *p*-toluenesulfonyl. Nph = 2-naphthyl. Ms = methanesulfonyl. Bzh = benzhydryl = CH(Ph)₂.

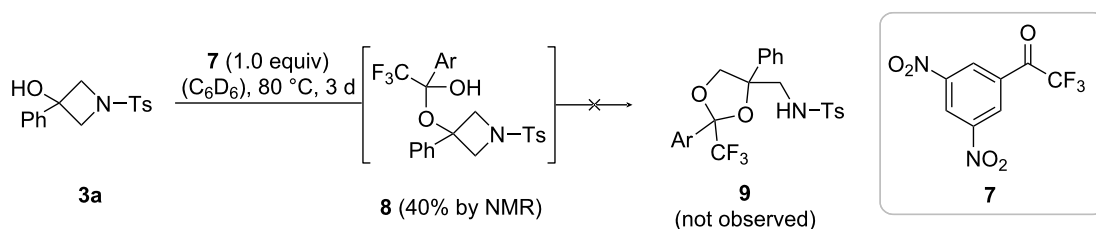
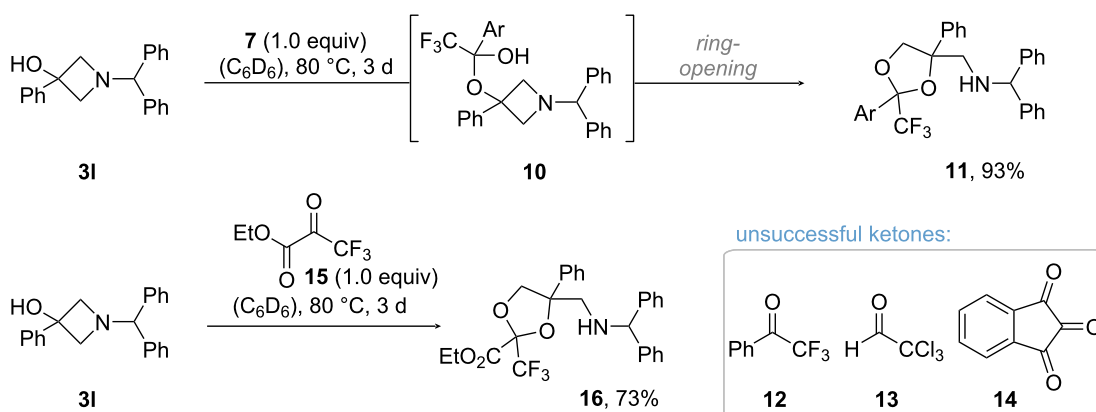
3b was isolated in only 16% yield. This substrate was therefore abandoned. Interestingly, ethyl (**1c**) and benzyl (**1d**) substitution was detrimental to the cyclization, indicated by the 54% and 63% yield, respectively (Table 1, entries 3 and 4). We observed an increase in Norrish II fragmentation in these cases. The observed diastereoselectivity was poor, supporting the radical character of the ring-closing event. A similar trend was observed when studying the methanesulfonyl (Ms) protecting group (entries 5–7 in Table 1). When changing to phenyl substitution at the nitrogen, azetidinol **3h** was formed in 12% yield with a substantial amount of unselective side reactions (Table 1, entry 8). By introducing an ethyl group (**1i**), only 27% conversion were achieved, with 2% product formation (Table 1, entry 9). The notable influence of steric and electronic parameters of the PG prompted us to investigate a range of sterically diverse alkyl substituents. Interestingly, while only fragmentation products were obtained for methyl and benzyl groups (Table 1, entries 10 and 11), the sterically demanding benzhydryl (Bzh) group showed progress towards azetidinol **3l** with a yield of 10% (Table 1, entry 12).

As it can be extracted from our study, sulfonyl-based protecting groups hold a unique role in the Norrish–Yang cyclization of α -aminoacetophenones, which was underpinned by the good

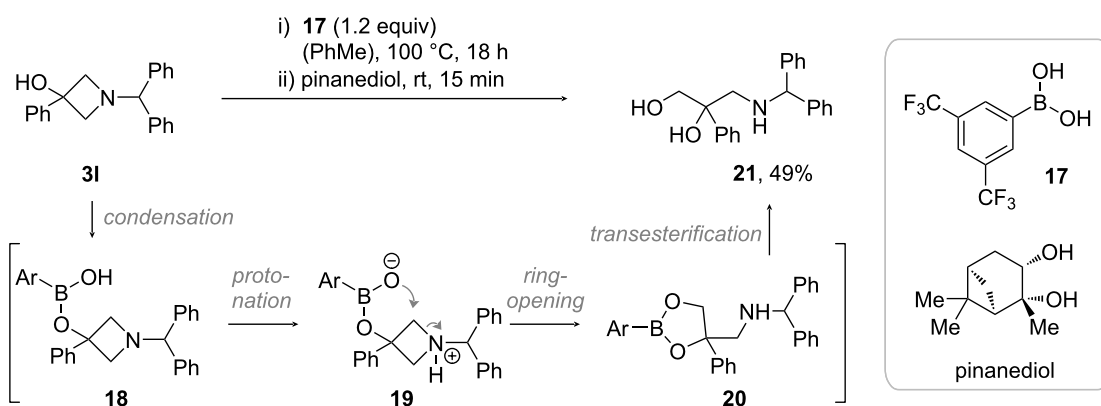
performances of substrates **1a** and **1e**. On the other hand, increasing steric demand at the α -aminocarbon has a detrimental effect on the cyclization, as indicated by the poor performances of ethyl and benzyl substitution (**1c** and **1d**). In contrast, sterically demanding groups at the nitrogen can have a positive effect on product formation, potentially by changing the substrate's conformation.

Ring opening

Based on its outstanding performance in the photoreaction, we selected Ts-protected azetidinol **3a** as our preferred substrate to test ring-opening reactions. However, initial attempts were met with limited success. Being conscious about the challenges associated with intermolecular ring openings at four-membered heterocycles, we considered an in situ tethering approach, which has proved an attractive alternative in our recent study on oxetane-ring openings [31]. Therefore, electron-deficient ketone **7** was added to **3a** (Scheme 3a). Formation of hemiketal **8** was expected to occur, which would facilitate ring opening by a 5-*exo-tet* cyclization. While we did observe the formation of hemiketal **8** by NMR spectroscopy, we were unable to detect any ring-opened products **9**, even when adding Lewis acids or Brønsted acids to the reaction mixture (see Supporting Information File 1 for further details). Finally, we decided to evaluate

a) attempted ring opening of azetidinol **3a**b) successful ring openings of azetidinol **3l**

c) synthesis of the free aminodiol



Scheme 3: Ring-opening reactions using electron-deficient ketones and boronic acids.

the electronic effects of the PG on the ring opening, which is why we opted to try the benzhydryl-protected substrate **3l** in our envisioned transformation. Several recent publications have indicated the unique role of the benzhydryl group for azetidinol reactivity [32–34]. To our delight, **3l** cleanly underwent ring opening via hemiketal **10** to deliver dioxolane **11** as a single diastereomer in 93% yield (Scheme 3b). With this result at hand, we tested several other carbonyls known to form stable hemiacetals [35–40]. While we were unable to isolate ring-opened products from trifluoroacetophenone (**12**), chloral (**13**), and indane-1,2,3-trione (**14**), ethyl trifluoropyruvate (**15**) furnished the desired dioxolane **16**, which was isolated as a

mixture of diastereomers in 73% yield. Mechanistically, we believe that the hemiketal protonates the azetidine before a nucleophilic attack can occur. Therefore, the ring opening is critical to the acidity of the transient hemiacetals and to the basicity of the respective azetidines, explaining the unsuccessful attempts with **3a**.

Dioxolanes **11** and **16** are inherently stable and we were unable to cleave the ketal after reaction. Thus, we investigated the feasibility to use boronic acids in the ring-opening reaction (Scheme 3c). Phenylboronic acid **17** is known to exhibit a similar acidity as the corresponding hemiacetals providing a promis-

ing starting point for pursuing this ring-opening attempt [41]. We hypothesized that this approach would allow the synthesis of 3-amino-1,2-diols, a motif commonly found in pharmaceuticals such as, e.g., β -blockers [42]. Our envisioned one-pot protocol features protonation of the azetidine from boronic monoester (**18** $\rightarrow$ **19**) followed by ring opening, in accordance to the hemiketal reactions. We decided to directly cleave dioxaborolane **20** after the reaction has stalled to facilitate separation. After a brief optimization of the reaction conditions (details are provided in Supporting Information File 1), we successfully conducted the desired sequence by raising the temperature to 100 °C to initiate ring opening, and employing a mild transesterification method for diol release [43–45]. Thus, we were able to isolate 3-amino-1,2-diol **21** in 49% yield.

Conclusion

Within this work, we demonstrated that the build and release of strain energy can be combined in a simple reaction sequence when appropriately tuning the reaction parameters. Our system relies on a photochemical Norrish–Yang cyclization of α -aminoacetophenones, which provides a sustainable entry to highly strained azetidins. It was shown that subsequent ring opening can be triggered by the addition of electron-deficient ketones or boronic acids, which resembles a novel strategy for azetidinol desymmetrization. The nature of the protecting group was found to be critical for the two-step process to be effective, which resulted in the synthesis of highly functionalized dioxolanes and 3-amino-1,2-diols. We believe that the concept of building and releasing strain energy, particularly when paired with photochemical means, is of general interest and its structural simplicity should allow for an expansion to other substrates.

Supporting Information

Supporting Information File 1

Experimental procedures, characterization data and copies of NMR spectra.

[<https://www.beilstein-journals.org/bjoc/content/supplementary/1860-5397-20-148-S1.pdf>]

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Data Availability Statement

All data that supports the findings of this study is available in the published article and/or the supporting information to this article.

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A fiber-optic spectroscopic setup for isomerization quantum yield determination

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Abstract

A spectroscopic setup for isomerization quantum yield determination is reported. The setup combines fiber-coupled LEDs, a commercially calibrated thermopile detector for measurement of the photon flux, and a fiber-coupled UV-vis spectrometer. By solving the rate equations numerically, isomerization quantum yields can be obtained from the UV-vis absorption spectra. We show that our results for the prototypical photoswitch azobenzene are in excellent agreement with the literature. The analysis of the errors showed that the quantum yields determined using this method are in the same order of magnitude as when using actinometry, thus demonstrating the reliability of our setup.

Introduction

Photoswitches are molecules that can undergo a light-driven structural rearrangement to populate a metastable state of the initial reactant. This isomerization can be reversed by light of a different wavelength or thermal stimuli. Depending on the nature of the reactant, different classes of photoreactions can be utilized: double bond isomerizations, electrocyclization, cyclo-additions, and electron-, hydrogen-, or group transfer [1].

Among the different switches known in the literature, azobenzene is a textbook example of a photoswitch operating via a double bond isomerization mechanism, with the first reports of

its *trans*-to-*cis* interconversion under direct sunlight dating back to the work of Hartley in 1937 [2]. Over the decades, azobenzene and its derivatives [3,4] have found numerous applications in the development of novel materials [5,6], photopharmacology [7-9] but also as actinometers [10,11], due to the large geometry changes upon isomerization [12] and easily accessible derivatives [1,7,13,14].

The absorption spectra of the two isomers each show distinct bands, as shown in Figure 1. For *trans*-azobenzene, there is a $\pi \rightarrow \pi^*$ band around 320 nm and a very weak (symmetry-

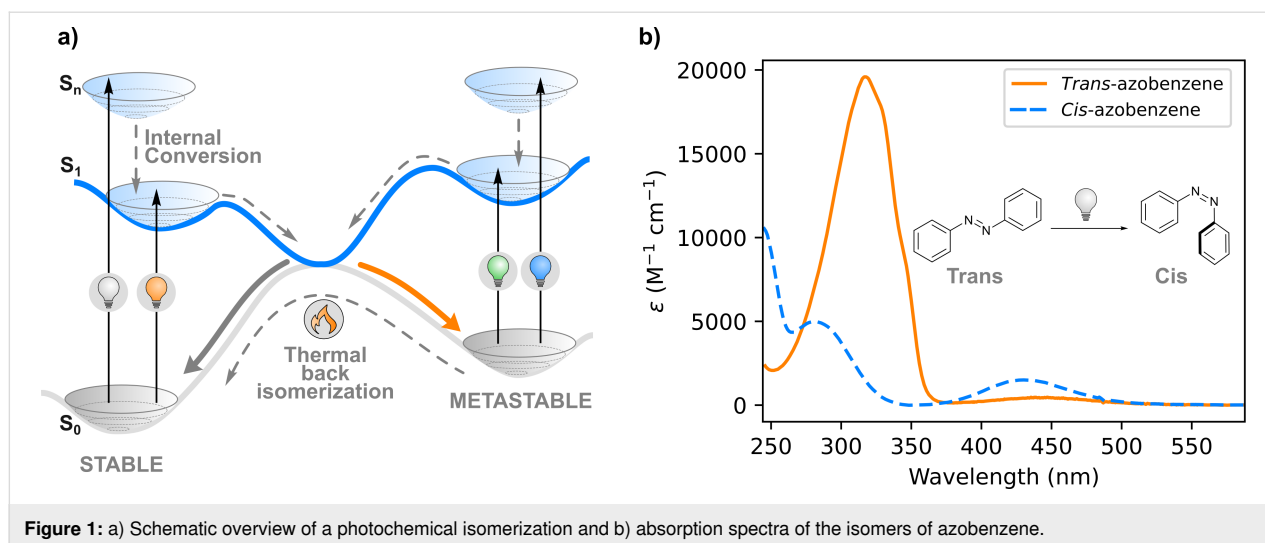


Figure 1: a) Schematic overview of a photochemical isomerization and b) absorption spectra of the isomers of azobenzene.

forbidden) $n \rightarrow \pi^*$ band around 440 nm. *cis*-Azobenzene shows two bands at 240 and 280 nm, and the $n \rightarrow \pi^*$ transition is slightly more allowed than for *trans*-azobenzene [15]. As the bands of *cis*- and *trans*-azobenzene overlap, irradiation results in a photostationary state (PSS) which is a mixture of the isomers. The distribution of the isomers at the PSS differs for irradiations at different wavelengths [16]. Irradiation at 340–350 nm, where the ratio $\epsilon_{trans}/\epsilon_{cis}$ is the highest, results in the formation of >95% *cis*-azobenzene [17].

The quantum yields (Φ) of isomerization of this process have been determined using different irradiation wavelengths, solvents, and methods [18–24]. One of the most interesting properties of azobenzene is the dependence of the Φ on the irradiation wavelength [25]. Clear differences are reported between irradiation of the different absorption bands, due to the so-called anti-Kasha behavior of this molecule, i.e., the wavelength dependency of the quantum yield of reaction [22,24].

Despite its textbook example status, the photoisomerization of azobenzene is still under active investigation. Over the past two decades, both experimental [23,26] and theoretical work [27–32] has been performed to explain the differences in quantum yield. Not only the exact details of the photoisomerization are still under debate, but also the absorption spectrum of *cis*-azobenzene has been redetermined as recently as 2017 [17]. With the re-evaluated values for the molar absorptivities, the Φ of azobenzene were recalculated by the same group immediately afterwards [24].

As shown by Vetráková et al. [17], the spectrum of *trans*-azobenzene can be easily obtained by careful preparation of the sample in the dark. The absorption spectrum of *cis*-azobenzene, however, is challenging to obtain via direct measurement, due

to its intrinsic thermal instability and sensitivity to ambient light. The authors showed that the *cis*-azobenzene previously isolated by extensive irradiation [2], liquid chromatography [22], or preparative TLC [21,33] contained some of the *trans*-isomer. Their work highlights the care that needs to be taken to obtain correct values for the molar absorptivities of *cis*-azobenzene. This conclusion holds for any photoswitch where only one isomer can be isolated successfully. During the measurement and at the PSS, the relative concentrations of the two isomers are unknown. The total absorbance (Abs_{obs}) at a given total concentration (c) of the sample is a linear combination of the absorbance of each isomer, as illustrated by Equation 1.

$$Abs_{obs} = c \cdot Abs_{trans} + (1 - c) \cdot Abs_{cis} \quad (1)$$

The value for c at the PSS can be found using other spectroscopic methods, such as NMR spectroscopy [17] or the TEM (for Thulstrup, Eggers, and Michl) method [34,35]. With a known value for c , the spectrum of the second component can be found by a simple scaled subtraction [14]. Another powerful method to obtain the spectrum of the second isomer is global and target analysis, where time-resolved spectra can be analyzed to find the number of spectral components and the evolution of their concentration over time [36,37]. Additional information, such as a kinetic model describing the components and the non-negativity constraint on the absorbance, can help to guide the decomposition of the data into chemically meaningful concentration traces and species-associated spectra (SAS) [38]. Global and target analysis is one of the methods employed in recent literature to find the spectrum of *cis*-azobenzene [17].

To calculate the quantum yields, both the molar absorptivities of the isomers and the number of photons absorbed by the sam-

ple needs to be known very accurately. Utilizing chemical actinometers remains the most used method for the determination of photon flux, i.e., the number of photons impinging a unit area of the sample in a unit of time [10]. Potassium ferrioxalate [39,40] is one of the most used actinometers while also some azobenzene derivatives have been reported as reaction quantum yield standards [11,22]. Although new chemical actinometers are being proposed [41,42], actinometry is dependent on quantum yields determined decades ago [10,43]. Using chemical actinometers is often labor-intensive, and measurements are restricted to irradiation wavelengths where the actinometer absorbs. With high-quality and reliable thermopile and solar cell detectors now being commercially available at a reasonable cost, instructions for building laboratory apparatus for quantum yield determination using direct measurement of photon flux using solar cell detectors have been reported by Riedle and co-workers [44,45]. With the design reported by Stadler et al. [46], on the other hand, it is possible to follow the isomerization in operando, while the photon flux can be obtained by disassembling the setup and reading the power of the excitation source using an integrating sphere.

In this paper, we introduce a relatively simple setup that combines the positive features of the aforementioned designs, which can be used to determine the forward and backward quantum yields of molecular switches without the need for actinometry, by combining fiber-coupled LEDs with a commercially calibrated thermopile detector and following the isomerization of a molecular switch by UV-vis absorption spectroscopy in operando. We provide all the information necessary to build the setup as well as the scripts and examples to retrieve the quantum yields of forward and backward isomerization of a molecular photoswitch following the evolution of the absorption in the low absorption regime [47] upon irradiation.

Results and Discussion

Azobenzene was chosen as the model compound for testing, as the recent work by Vetráková et al. [17] and Ladányi et al. [24] has provided us with very reliable molar absorptivities and quantum yields to use for validating our methods.

A molecular photoswitch generally has a stable state A and a metastable state B, which would be the *trans*- and *cis*-isomers, respectively, for azobenzene. The rate equations of the isomerization can be described in terms of the quantum yields and the molar absorption coefficients. It is possible to show that the change in the concentration of A is given by Equation 2 [47]:

$$\frac{d[A]}{dt} = -\frac{\Phi_{A \rightarrow B} \cdot q_A}{N_A \cdot V} + \frac{\Phi_{B \rightarrow A} \cdot q_B}{N_A \cdot V} + k_{B \rightarrow A}[B] \quad (2)$$

The first term gives the photochemical reaction from A to B, which is governed by the number of photons absorbed at a given wavelength, q_A , as well as the quantum yield $\Phi_{A \rightarrow B}$ for this reaction. N_A is Avogadro's number, V is the total volume of the sample. When the *cis*-isomer absorbs at the same wavelength, the reverse reaction will happen photochemically as well, as described by the second term. The last term describes the thermal reaction converting *cis*-azobenzene into the stable *trans*-azobenzene. For the selected example, the rate constant for the thermal back isomerization is $7.2 \cdot 10^{-7} \text{ s}^{-1}$ at 20 °C [24]. This value is generally disregarded for routine experiments where the isomerization happens in the minute timescale, however we explicitly included it in our quantum yield determination for better accuracy.

Using the Beer–Lambert law, the light absorbed by the sample, Abs_{tot} , in a setup with a given path length l can be expressed as the sum of the absorbances of the single species A and B and consequently in terms of the concentrations of A and B and their respective molar absorption coefficients (ϵ_A and ϵ_B):

$$Abs_{\text{tot}} = Abs_A + Abs_B = l\epsilon_A[A] + l\epsilon_B[B] \quad (3)$$

For absorbances below 2, not all photons are absorbed when passing through the sample. In this case, the number of photons absorbed by a species (q_A for species A in the following example) can be given by Equation 4 [47]:

$$q_A = \frac{[A] \cdot \epsilon_A}{[A]\epsilon_A + [B]\epsilon_B} q_0 \left(1 - 10^{-([A]\epsilon_A + [B]\epsilon_B) l} \right) \quad (4)$$

Where q_0 is the total number of photons absorbed by the sample. Combining Equations 2 and 4, the rate equations for the system are given by Equation 5 and Equation 6:

$$\frac{d[A]}{dt} = \frac{1}{V} \frac{q_0}{N_A} \frac{1 - 10^{-([A]\epsilon_A + [B]\epsilon_B) l}}{[A]\epsilon_A + [B]\epsilon_B} \left(\Phi_{B \rightarrow A}[B]\epsilon_B - \Phi_{A \rightarrow B}[A]\epsilon_A \right) + k_{B \rightarrow A}[B] \quad (5)$$

$$\frac{d[B]}{dt} = -\frac{d[A]}{dt} \quad (6)$$

So far, the spectral shape of the excitation light source (an LED in our case, vide infra) has not been explicitly considered and has been assumed to be monochromatic. Although this approximation is effective for many light sources with narrow bandwidths, the emission spectrum can be included in the rate equa-

tions. This correction is done by multiplying Equation 5 by the spectral distribution $f(\lambda)$ of the light source and integrating over all wavelengths [45]:

$$\frac{d[A]}{dt} = -\Phi_{A \rightarrow B} \int \frac{[A]\varepsilon_A}{[A]\varepsilon_A + [B]\varepsilon_B} \frac{q_0 \lambda f(\lambda)}{V N_A} P d\lambda + \Phi_{B \rightarrow A} \int \frac{[B]\varepsilon_B}{[A]\varepsilon_A + [B]\varepsilon_B} \frac{q_0 \lambda f(\lambda)}{V N_A} P d\lambda \quad (7)$$

where

$$P = 1 - 10^{-([A]\varepsilon_A(\lambda) + [B]\varepsilon_B(\lambda)) l} \quad (8)$$

Setup

The UV–vis irradiation experiments were performed using a setup assembled in-house, see Figure 2 and Supporting Information File 1. A Quantum Northwest Luma 40 Peltier-based temperature-controlled cuvette holder with an insulator jacket with four optical windows was used to allow irradiation perpendicular to the spectrometer light path. The light source is an Avantes AvaLight-DH-S-BAL light source coupled with a 400 μm fiber (Avantes FC-UVIR400-1-BX) to an SMA-to-SM1 fiber adapter (Thorlabs CVH100-COL) containing a plano-convex lens (20.1 mm focal length, Thorlabs LA4647) in a 1 inch diameter lens mount (Thorlabs LMR1S/M). The transmitted light is collected by a plano-convex lens (20.1 mm focal length, Thorlabs LA4647) in a 1 inch diameter lens mount (Thorlabs LMR1S/M) contained in an SMA-to-SM1 fiber adapter (Thorlabs CVH100-COL) connected to a 400 μm fiber (Avantes FC-UVIR400-1-BX). The spectrometer we used is an Avantes AvaSpec-ULS2048CL-EVO-RS. The light path for the irradiation consists of a fiber-coupled LED (Thorlabs M340F4,

M395FP1, M455F3) coupled to a 600 μm fiber (Thorlabs M114L01) to an adjustable fiber collimator (Thorlabs CFCS5-A) mounted on an adapter (Thorlabs AD15F2) in a 1 inch diameter lens mount (Thorlabs LMR1S/M). On the opposite side of the cuvette holder, a power meter (Thorlabs PM16-401) is mounted. The LED is powered by an LED driver with trigger mode (Thorlabs LEDD1B T-cube) controlled using an Arduino UNO R3 connected to a PC.

The AvaLight-DH-S-BAL light source is connected to the spectrometer via an interface cable (Avantes IC-DB26-RM), which allows the proprietary software AvaSoft from Avantes to control the internal shutter of the light source via a PC. With this configuration, starting a single measurement in AvaSoft sends a TTL signal to the light source that opens the shutter, which is followed by the acquisition of a spectrum, and finally a TTL signal is sent to close the shutter again. By utilizing scripts we developed (see Supporting Information File 1), it is possible to precisely control the timing of irradiation of the sample with the LED and the perpendicular illumination with the UV–vis probe. In this way, when a UV–vis spectrum is recorded, the shutter of the D₂-tungsten lamp is open and the excitation LED is switched off for the entirety of the measurement (average of 500 spectra acquired for 1.0 ms). When the measurement is finished, the script closes the shutter and the LED is switched on for a given amount of time. This sequence can be easily looped to obtain a desired illumination sequence (see Supporting Information File 1 for more detailed information on the loops and exact timings). The shutter prevents undesired illumination from the UV–vis probe that could influence the measurement altering the kinetics of isomerization, a known problem for similar setups [24].

The power readings from the thermal power sensor were recorded by using Thorlabs' Optical Power Monitor (OPM) software. The resulting data showed some fluctuations depending

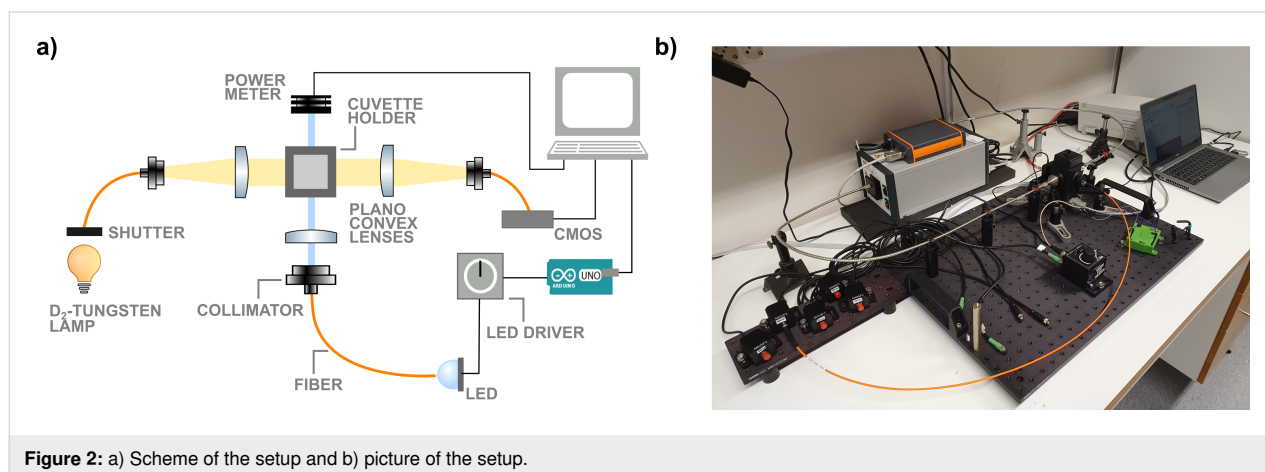


Figure 2: a) Scheme of the setup and b) picture of the setup.

on environment temperature and air movement. The background power was therefore monitored to get an accurate power reading before turning on the LED. The raw data was then fitted with a simple polynomial baseline using a Python script (see Supporting Information File 1). After baseline subtraction, the average power and standard deviation for the power were determined, as shown in Figure 3. Since transmission through quartz cuvettes and windows is not complete [48], we also corrected for the power loss.

The power of the LED was first determined without any quartz elements in the path between the collimator and the sensor. Then the LED power was determined with the insulated jacket for the cuvette holder and a cuvette containing solvent in place. The power loss at the sample was approximated to be half of the total power loss recorded for the system. Table S1 in Supporting Information File 1 gives an overview of the measured powers and averages. The loss was between 6–8%, with no marked dependence on the wavelength of the LED. The final power was taken to be the weighted mean of 3–4 measurements, using the reciprocal of the variance as the weights. The average error in the measured power is 10^{-6} W. These results grant a precision which is high enough to calculate the quantum yields, as our total error on the determined Φ is of the same order of magnitude as the ones earlier reported (vide infra) [22,24].

The current output of the LED driver is set by a manual dial, which adds another variable to the setup, inevitably causing some variation in the output power between different days. To avoid reproducibility errors, we measured the output current of the LED associated with a given power readout utilizing a multimeter connected to the LED driver. Nevertheless, we also

checked the reproducibility of the measurements with different currents to test the stability of the setup (see Supporting Information File 1).

Quantum yield determination

A concentrated solution of azobenzene (Sigma-Aldrich) in methanol (Supelco LiChrosolv) was prepared by dissolving an aliquot of crystalline azobenzene in 1.00 mL of solvent. Samples of 3.00 mL were prepared in a quartz cuvette (Hellma 117-100F QS) by diluting an aliquot of the concentrated solution in methanol, to obtain an absorbance of the $\pi \rightarrow \pi^*$ band between 0.8 and 1.0. The samples of azobenzene were kept at 20 °C and stirred throughout the measurement (1200 rpm). The samples were irradiated for 1 h, while a UV–vis absorption spectrum was recorded every 30 s. The results for one such determination are shown in Figure 4A.

We utilized the powers obtained following the procedure described in the previous section to retrieve the quantum yields of isomerization, assuming strictly monochromatic light at first [24,49]. We chose the peak of the emission spectrum of the LED as the approximated monochromatic wavelength, since this value can substantially differ from the nominal wavelength of the LED, e.g., the 455 nm LED from ThorLabs has a peak in the emission spectrum at 445 nm. We furthermore determined the quantum yields again, taking the emission spectrum of the LED into account. The emission spectra were measured using our spectrometer by connecting the LEDs to the detector (Figure S1 in Supporting Information File 1). The following input parameters were used in both methods: the photon flux was calculated from the weighted mean of the power measured; molar absorptivities, ϵ_A and ϵ_B , as well as the thermal rate constant, $k_{B \rightarrow A}$, were taken from the most recent study reporting

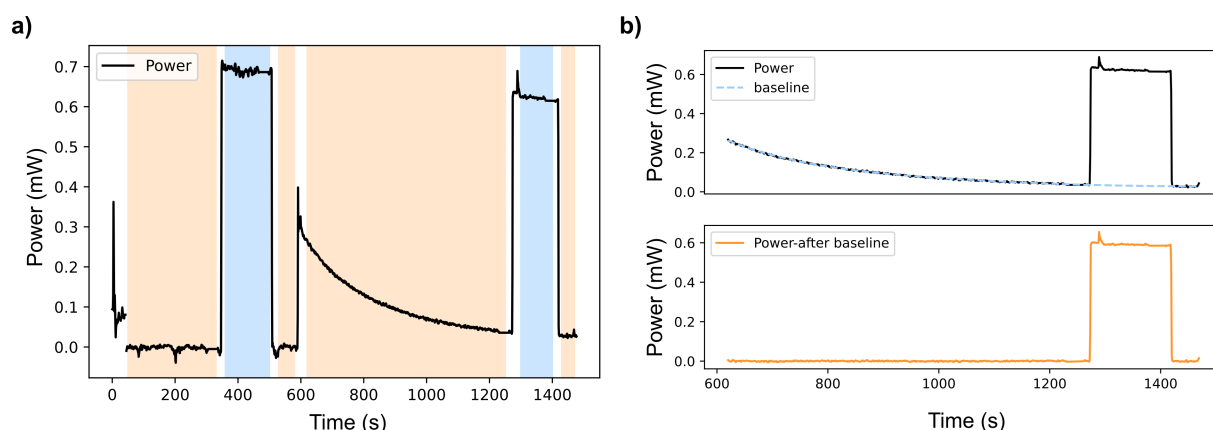
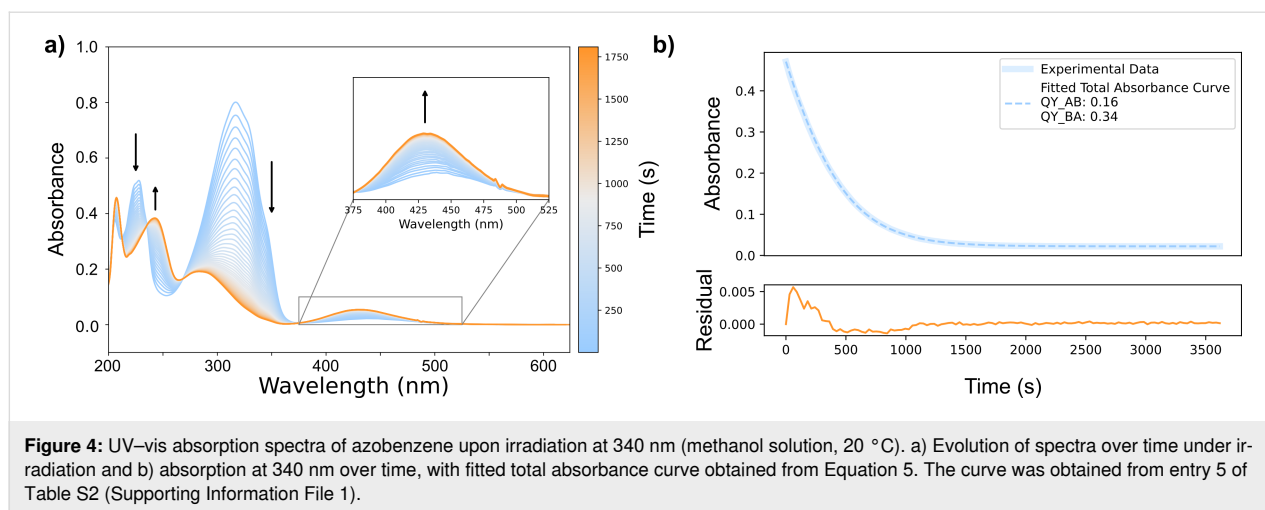


Figure 3: A visual example of the power determination. a) Power without any elements (left) and with insulated jacket and cuvette (right side, the change in baseline is noticeable), b) power with insulated jacket and cuvette after baseline subtraction.



these values [17]. The initial spectrum was confirmed to contain 100% *trans*-azobenzene by comparison with the known absorption spectrum of the pure switch [17].

To retrieve the quantum yield values for forward and backward isomerization, we solved rate equations Equations 5 and 6 (or Equation 6 and Equation 7, when the monochromatic excitation light approximation was not considered) numerically using two different python scripts (provided in Supporting Information File 1). The rate equations are ordinary differential equations (ODEs) and can thus be solved numerically using existing methods in the SciPy package [50]. An absorbance function was constructed, which takes the solution of the ODEs to model the absorbance over time. This absorbance function was then fitted to the measured absorbance at the wavelength of irradiation (or wavelengths, for a non-monochromatic excitation light). The parameters $\Phi_{A \rightarrow B}$ and $\Phi_{B \rightarrow A}$ were evaluated to minimize the residual sum of squares (RSS) between the measured and fitted absorbance values. This minimization is done by a Levenberg–Marquardt algorithm [51] as implemented in the lmfit package [52]. Using this package, the standard error of the fitted parameters is also obtained.

By evaluating the magnitude of the errors, we noticed that the largest source of uncertainty comes, not surprisingly, from the LED power measurement. This error is not included in the standard error of the fit, making the latter a poor reflection of the uncertainty in the retrieved quantum yields.

To overcome this limitation, we decided to evaluate the quantum yields using the powers corresponding to the lower and upper limits recorded with the thermopile. This procedure leads to two different values of quantum yields, $\Phi_{\text{min power}}$ and $\Phi_{\text{max power}}$, respectively, for both $\Phi_{A \rightarrow B}$ and $\Phi_{B \rightarrow A}$. In order to include the uncertainty of the fit ($\Delta\Phi_{\text{fit}}$), we corrected the thus

obtained quantum yields using Equation 9 and Equation 10 to derive Φ_{min} and Φ_{max} :

$$\Phi_{\text{min}} = \Phi_{\text{min power}} - \Delta\Phi_{\text{min power}} \quad (9)$$

$$\Phi_{\text{max}} = \Phi_{\text{max power}} + \Delta\Phi_{\text{max power}} \quad (10)$$

The total uncertainty on the quantum yield of a single measurement obtained by employing the weighted mean of the power ($\Phi_{A \rightarrow B}$ in the following example), is:

$$\Delta\Phi_{A \rightarrow B} = \max(|\Phi_{A \rightarrow B} - \Phi_{\text{min}}|, |\Phi_{A \rightarrow B} - \Phi_{\text{max}}|) \quad (11)$$

The values listed in Table 1 are the weighted means and sample standard deviations of multiple measurements, using the reciprocal of the variance of the quantum yields as the weights. For completeness, we report all the primary data that were utilized to compile Table 1 in Supporting Information File 1.

The measured quantum yields show good agreement with the values reported in the literature [22,24], especially for the 340 nm irradiation. It should be noted that an exact match of the quantum yields should not be expected, as the irradiation wavelengths are slightly different from the ones in the previous studies, because different excitation sources were used (non-monochromatic LED in our case, versus monochromatic light). In line with the findings of Ladányi et al., the precision of $\Phi_{\text{trans} \rightarrow \text{cis}}$ is generally better than the precision for the reverse photoreaction. This difference in precision could be attributed to the *trans* $\rightarrow$ *cis* reaction being more dominant, especially for irradiation in the $\pi \rightarrow \pi^*$ band, where the absorption of *trans*-azobenzene is considerably higher than the *cis* (see Figure S4 in Supporting Information File 1). The use of Equation 7 to take the emission spectrum of the LED into account increased the

Table 1: Calculated quantum yields and related quantum yields from the literature.

Wavelength of irradiation (nm)		This work; single wavelength	This work; integrated emission	Ladányi et al. (2017) [24]	Gauglitz and Hubig (1985) [22]
340 ^a /334 ^b	<i>trans</i> → <i>cis</i>	0.160 ± 0.003	0.166 ± 0.003	0.155 ± 0.006	0.15 ± 0.02
	<i>cis</i> → <i>trans</i>	0.376 ± 0.070	0.384 ± 0.069	0.388 ± 0.053	0.30 ± 0.03
395 ^a /405 ^b	<i>trans</i> → <i>cis</i>	0.314 ± 0.050	0.264 ± 0.030	0.288 ± 0.007	0.20 ± 0.02
	<i>cis</i> → <i>trans</i>	0.578 ± 0.076	0.513 ± 0.040	0.452 ± 0.018	0.57 ± 0.03
436	<i>trans</i> → <i>cis</i>	–	–	0.315 ± 0.002	0.22 ± 0.03
	<i>cis</i> → <i>trans</i>	–	–	0.469 ± 0.003	0.63 ± 0.05
455	<i>trans</i> → <i>cis</i>	0.352 ± 0.003	0.354 ± 0.025		
	<i>cis</i> → <i>trans</i>	0.542 ± 0.034	0.569 ± 0.009		

^aIrradiation used in this work; ^birradiation used in literature.

quantum yield values by a few percent. The difference when using the integration is larger for $\Phi_{cis \rightarrow trans}$. Since the emission of the LED has a larger bandwidth than the emission using a monochromator and filter, the integration over the bandwidth of the LED should be performed for the most accurate results. We would recommend measuring the emission spectra of the LEDs if possible. Although we did not find any significant changes between the quantum yields found using the measured emission spectra and the ones provided by the vendor, it is known that small variations in the LED spectral distribution can occur per lot [53].

Conclusion

In this work, we report a simple setup for the determination of quantum yields using LEDs for irradiation and a thermopile detector for the direct determination of the power. The setup is built from commercially available optical elements and (together with the scripts provided in Supporting Information File 1) can be replicated at moderate financial costs. The inclusion of a temperature-controlled cuvette holder and the possibility for simultaneous UV–vis absorption spectroscopy makes this setup ideally suitable for a wide range of photoswitches, including those with fast thermal back isomerization. Our setup was tested by determining the quantum yields of azobenzene for different wavelengths of irradiation. The measured quantum yields showed good agreement with the most recently reported values [24], making this method and setup a viable alternative to actinometry.

Supporting Information

Supporting Information File 1

Scripts description, configuration and supplementary data.
[<https://www.beilstein-journals.org/bjoc/content/supplementary/1860-5397-20-150-S1.pdf>]

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Data Availability Statement

The data generated and analyzed during this study is openly available in a figshare repository at <https://doi.org/10.6084/m9.figshare.25818016>.

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Understanding X-ray-induced isomerisation in photoswitchable surfactant assemblies

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Abstract

Dynamic, responsive materials can be built using photosurfactants (PS) that self-assemble into ordered nanostructures, such as micelles or liquid crystals. These PS contain photoswitchable groups, such as azobenzene (Azo) or, more recently, arylazopyrazoles (AAPs), which change shape and polarity on photoisomerisation between the *E* and *Z* states, thus changing the self-assembled structure. Small-angle X-ray scattering (SAXS) is a powerful technique to probe the morphology of PS and can be used to measure the mechanisms of structural changes using in-situ light irradiation with rapid, time-resolved data collection. However, X-ray irradiation has been shown previously to induce *Z*-to-*E* isomerisation of Azo-PS, which can lead to inaccuracies in the measured photostationary state. Here, we investigate the effect of light and X-ray irradiation on micelles formed from two different PS, containing either an Azo or AAP photoswitch using SAXS with in-situ light irradiation. The effect of X-ray irradiation on the *Z* isomer is shown to depend on the photoswitch, solvent, concentration and morphology. We use this to create guidelines for future X-ray experiments using photoswitchable molecules, which can aid more accurate understanding of these materials for application in solar energy storage, catalysis or controlled drug delivery.

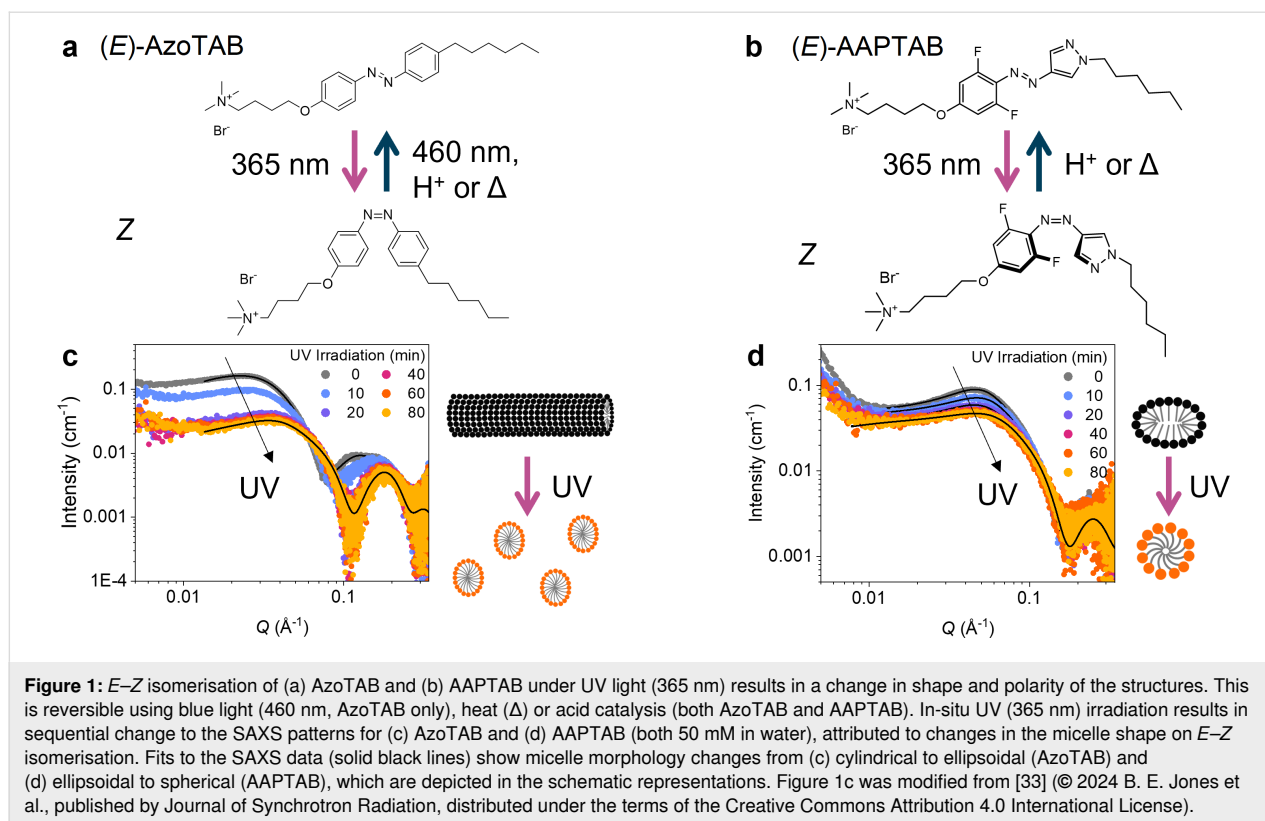
Introduction

The design of smart materials whose properties can be controlled using external stimuli is of significant interest for diverse applications spanning soft robotics [1], energy storage [2] and drug delivery [3]. Light is an ideal stimulus as it is non-invasive and can be administered selectively with high spatiotemporal control. To build responsive materials, surfactants are particularly attractive due to their ability to self-assemble into different morphologies depending on their molecular structure and chemical environment. To that end, photo-switchable chromophores can be incorporated into amphiphilic molecules to create photosurfactants (PS), whose molecular shape and polarity can be modified using light [4–6]. Of the PS studied, most use an azobenzene (Azo) photoswitch that undergoes *trans*-to-*cis* (*E*-to-*Z*) isomerization on irradiation with UV light, typically forming a photostationary state (PSS) that contains mostly *Z* isomers. This can be reversed using blue light or heat in a process that is stable over many cycles [7]. Isomerisation of azobenzene leads to a change in its conformation and polarity which, when combined into a surfactant molecule, modifies the resulting molecular geometry and hydrophilicity [6]. This, in turn, affects the interfacial and self-assembly properties of the PS [4–6]. The uniquely tuneable properties of these photoswitchable molecules have led to their successful application in areas such as DNA compaction [8], photorheological fluids [9,10] and micellar catalysis [11]. However, the potential scope for Azo in practice is limited by its incomplete photo-switching to the metastable isomer in the PSS and its rapid thermal reversion to the *E* isomer [12,13]. To tackle this, arylazopyrazoles (AAPs) have emerged as promising alternatives, where one of the phenyl rings of Azo is replaced by a pyrazole, which improves several aspects of their performance, including quantitative photoswitching between isomers and significantly enhanced thermal stability of the *Z* isomer [13–15]. This has led to recent reports on the integration of AAPs into surfactants to form systems with phototuneable interfacial [16–18] and self-assembly properties [19,20]. However, further understanding of factors which affect the isomerisation of these new surfactants, and the effect this has on their self-assembled structures, is still needed to tailor them towards application.

Small-angle scattering is a powerful technique that can be used to determine the structure and interactions of materials on length scales of 1–100s of nm. As a result, it has been used to study the changes in self-assembled morphologies of PS on irradiation with light [4,21–25]. In particular, the high brilliance of synchrotron X-ray sources enables the mechanisms of structural changes in PS to be studied, using in-situ light irradiation with time-resolved data collection. For example, Tribet and co-workers used this approach to explore the kinetics of micellisation and dissolution of cationic Azo-PS, both on their own

and in mixed micelles with lipids, on irradiation with either UV or blue light [21,22]. In addition, Ober et al. showed that in-situ UV irradiation stimulates a steady decrease in bilayer thickness for vesicles formed using Azo-modified phosphatidylcholine lipids, due to the shorter lipid tail length in the *Z* isomer [26]. Notably, these authors observed that the X-rays themselves also induced *Z*–*E* isomerisation in Azo-lipids, which they attributed to the X-ray radiolysis of water, which produces radicals and reactive species that can catalyse *Z*–*E* conversion [27]. This effect was greater using low-energy X-rays (8 keV) due to their greater photoabsorption in water, thus leading the authors to conclude that higher energy (≈ 36 keV) should be used for future small-angle X-ray scattering (SAXS) experiments on photo-switchable systems. However, this may not always be achievable, depending on the X-ray energy available from laboratory or synchrotron sources. Moreover, this effect may have significant consequences when measuring any light-responsive materials using X-rays, from self-assembled PS systems (using SAXS) to crystalline or powder samples (using X-ray diffraction) [28,29]. In addition to this, damage to amphiphilic samples due to X-ray irradiation has been widely reported, leading to effects such as ionisation and structural reordering [30,31]. It follows that improved understanding of the effect of X-rays on photoswitchable surfactants is needed to design protocols that ensure the *Z*-rich PSS can be measured appropriately.

To address this, here we investigate the effects of light- and X-ray irradiation on PS assemblies to further understand the parameters which influence X-ray-induced *Z*–*E* isomerisation. Two different cationic PS molecules are studied, based on the ubiquitous cetyltrimethylammonium bromide (CTAB), which contain either an Azo (i.e., AzoTAB, Figure 1a) or arylazopyrazole (i.e., AAPTAB, Figure 1b) photoswitch. AzoTAB and AAPTAB were chosen as they display distinct changes in micelle morphology on irradiation with UV light to form the *Z*-rich PSS [4,19]. In addition to this, AAPTAB has a high thermal half-life at room temperature (5.7 years [19]), meaning there is no significant contribution from thermal *Z*–*E* isomerisation over the course of these experiments. Using in-situ UV- and visible-light irradiation with SAXS, here we measure the intermediate structures formed during photoisomerisation of these PS for the first time. Once isomerised to the *Z*-rich PSS, the effect of X-ray irradiation is studied using time-resolved SAXS collection, where the photoswitch, solvent and concentration are all shown to impact the rate and extent of structural change. With comparison to the rate of *Z*–*E* isomerisation on addition of acid to the PS systems, we show that factors beyond the production of protons (H^+) upon X-ray radiolysis of water may have an effect to produce the large, rapid



structural changes observed using SAXS. To conclude, we create a set of guidelines for X-ray experiments using photo-switchable molecules, which is required to ensure these systems are understood accurately on designing them for applications such as solar energy storage [32], catalysis [11] or drug delivery [3].

Results and Discussion

Effect of light irradiation

First, in-situ UV irradiation with SAXS was used to determine the mechanisms for morphology changes in AzoTAB and AAPTAB systems on *Z*–*E* isomerisation. A concentration of 50 mM in water was chosen for these experiments, as this is well above the critical micelle concentration (CMC) for both surfactants (CMC in water for (*E*)-AzoTAB = 0.2 mM [4], (*E*)-AAPTAB = 5.4 mM [20]), and previous SAXS measurements have shown morphology changes between micelles formed for the *E* and *Z* isomers at or near this concentration [4,19]. For AzoTAB as the native, *E*-isomer, the SAXS pattern is characteristic of interacting micelles and can be fitted to an ellipsoidal cylindrical shell model (Figure 1c), consistent with previous results [4,33]. A Hayter–Penfold structure factor was incorporated into the fits to account for screened Coulombic repulsion between the charged micelles [34]. In-situ UV (365 nm) irradiation triggers a sequential change in the SAXS profile from the AzoTAB (Figure 1c), resulting in a steady de-

crease in the scattering intensity and a shift in the Guinier plateau to higher Q values. These changes are visible within 10 minutes of UV irradiation and stabilise with no further structural changes after around 20 minutes. It should be noted that a lag between the time taken to reach the PSS and the time for the new micelle morphology to form is expected. This is due to the additional time that is required for diffusion and reassembly of the AzoTAB in the *Z* conformation into the new equilibrium structure [22]. The scattering curve for the UV-induced PSS fits to an ellipsoidal core-shell micelle model (see Figure 1c and Table S1, Supporting Information File 1 for full fit details), which indicates that the initial cylindrical micelles break up into smaller fragments along their length on irradiation, resulting in micelles with a higher spontaneous curvature [33]. Previously, samples of lower concentration (20 mM, still > CMC) showed no change from the cylindrical morphology on isomerisation [4]. Here, we propose that the shorter cylinder length, due to the higher concentration, could result in the structure being closer to the cylindrical-ellipsoidal morphology boundary. Furthermore, a tendency to form higher-curvature morphologies on *E*–*Z* isomerisation has been seen for various Azo-PS, both with shorter and longer alkyl chain tails and spacer groups in comparison to the AzoTAB structure studied here. This can be explained by an increased tail-group volume of the *Z* isomer, which favours a higher spontaneous curvature in the amphiphile packing [4].

Similarly, the SAXS signal for AAPTAB shows a sequential change on UV irradiation (Figure 1d), reaching an equilibrium state after 40 minutes. Model fitting indicates that this is a result of an ellipsoid-to-sphere morphology change in the AAPTAB micelles, which matches reports from previous work using ex-situ irradiation [19]. The dimensions of the micelles change from a polar and equatorial radius of 24 and 13 Å to a single spherical radius of 18 Å (Table S2, Supporting Information File 1). This morphology change can be attributed to two changes in the AAPTAB on *E*–*Z* isomerisation [19]. Firstly, the shape change of the AAPTAB to the bent, “T-shape” conformation prevents the π – π stacking which was previously possible in the more planar, *E* isomers that were arranged in elongated, ellipsoidal micelles. Secondly, the change in geometry and polarity of the AAP photoswitch on isomerisation to the *Z* state [35] results in an effective incorporation of the AAP group into the hydrophilic headgroup of the PS. This means that the hydrophobic tail-group becomes just the pendant hexyl chain. This acts to increase the headgroup area of the surfactant and the spontaneous curvature of the resulting self-assembled micelles [4]. In-situ UV irradiation shows that *E*–*Z* isomerisation results in changes to the morphology of AzoTAB and AAPTAB micelles, where intermediate structures are formed, which could be due to the presence of a mixed state of *E* and *Z* isomers or gradual equilibration of the system into the new morphologies adopted by the *Z* isomer.

Effect of X-ray irradiation

Next, the effect of X-ray irradiation on the *Z*-rich PSS was investigated. AzoTAB (50 mM in water) was first irradiated with UV light in-situ to reach the PSS (80 min). The subsequent effect of X-ray irradiation (13 keV) was tracked over a total time of 50 s, taking individual exposures of 500 ms, separated by a delay-time of 100 ms. Irradiation with X-rays results in a partial return of the scattering pattern to that of the native, *E* isomer (Figure 2). Changes occur immediately, after 1 s of X-ray exposure, and saturate after ca. 5 s. The changes are comparable to those observed on *Z*–*E* isomerisation induced

using blue (460 nm) light or heating to 55 °C but occur at a much faster rate (Figure S2, Supporting Information File 1). Fits to the data show a return to the cylindrical micelle morphology present in the *E* isomer, but with smaller dimensions of 98 Å length (cf. 136 Å in the *E* isomer), and radii of 13 and 15 Å in the polar and equatorial directions (Table 1). A similar reduction in micelle size was seen on reverse isomerisation using blue light (Table S1, Supporting Information File 1), which may suggest that the larger micelle size in the *E* isomer is obtained by slow agglomeration over time.

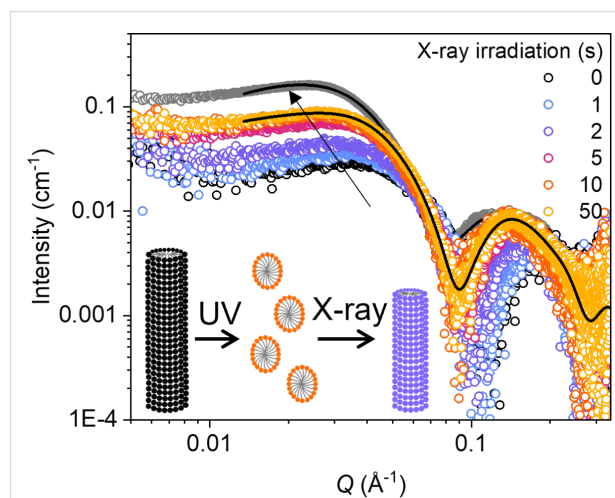


Figure 2: SAXS curves for AzoTAB (50 mM in water) showing the transition from the *Z*-rich PSS to the *E*-rich state with increasing X-ray exposure time. Fits to the data (black lines) indicate a morphology change from ellipsoidal to cylindrical micelles, as shown in the schematic insert (to scale). The grey circles indicate the original *E*-isomeric state before UV irradiation. The graphic is modified from [33] (© 2024 B. E. Jones et al., published by Journal of Synchrotron Radiation, distributed under the terms of the Creative Commons Attribution 4.0 International License).

The interaction of ionising radiation, such as X-rays, with water is known to result in a radiolysis process that generates a wide variety of primary species, including e^- , $HO^\bullet$, $H^\bullet$, $HO_2^\bullet$, H^+ , OH^- , H_2O_2 and H_2 [36]. For Azo photoswitches, the formation

Table 1: Micelle morphologies and dimensions for PS obtained from SAXS data fits after UV (365 nm) and X-ray irradiation.

PS	irradiation time		morphology	r_p^a (Å)	r_{eq}^b (Å)	l^c (Å)
	UV (min)	X-ray (s)				
AzoTAB	0	0	cylinder	31.4 ± 0.1	11.5 ± 0.1	136.0 ± 0.2
	80	0	ellipsoid	13.3 ± 0.1	19.3 ± 0.2	—
	80	50	cylinder	12.7 ± 0.1	14.7 ± 0.1	97.5 ± 0.6
AAPTAB	0	0	ellipsoid	23.8 ± 0.1	13.4 ± 0.1	—
	80	0	sphere	18.4 ± 0.1	—	—
	80	50	ellipsoid	23.8 ± 0.2	13.4 ± 0.1	—

^aPolar radius. ^bEquatorial radius. ^cLength of cylindrical micelle.

of H^+ species, i.e., the acidification effect, can catalyse the $Z-E$ isomerisation reaction. This is due to protonation of one of the nitrogen atoms in the azo bond ($N=N$), resulting in a decrease in the double bond character and a lowering of the energy barrier to isomerisation [37–39]. Additionally, $Z-E$ isomerisation can be catalysed electrochemically in the presence of free electrons [40] or holes [27]. The wide variety of radical and charged species produced on water radiolysis may therefore play a complicated role in inducing $Z-E$ isomerisation via a number of different mechanisms. No matter the mechanism, the morphology changes on X-ray irradiation appear consistent with the hypothesis that the E isomer is reformed, as shown by the return of the micelle shape of this isomer. The fast rate of the morphology change, in comparison to using blue light or heating to 55 °C, shows rapid rates of $Z-E$ isomerisation from X-ray-induced catalysis, which may be due to the presence of multiple different catalysing species and therefore isomerisation pathways. In contrast, there was negligible change in the SAXS pattern for AzoTAB in the native, E isomer over this irradiation time (Figure S4, Supporting Information File 1). This supports the hypothesis that the changes occur due to $Z-E$ isomerisation, rather than X-ray-induced ioni-

sation or beam damage to the AzoTAB, as seen in similar amphiphilic systems [30,31]. In the case of ionisation, both stereoisomers would be expected to be affected equally.

In comparison to Azo, the AAP moiety is much more stable as the Z isomer, with a thermal half-life of 5.7 years at room temperature [13]. This means that $Z-E$ isomerisation cannot be easily induced using gentle heating or visible light, as shown by the stability of the UV-vis absorbance spectra and SAXS patterns under these conditions (Figures S1 and S3, Supporting Information File 1). In contrast, irradiation with X-rays leads to significant changes in the SAXS patterns due to induced $Z-E$ isomerisation (Figure 3a). Model fitting to the SAXS data shows that X-ray irradiation induces a sequential increase in the radius of the spherical micelles from 0.5 to 2 s, and a return to the ellipsoidal morphology after 5 s (Figure 3c). After 50 s, the micelle dimensions match those obtained for the AAPTAB in the E -isomeric form (Table 1 and Table S2, Supporting Information File 1). As with the AzoTAB sample, there is little change to the SAXS profile for AAPTAB in the native, E isomer after the same X-ray irradiation time (Figure S4, Supporting Information File 1), suggesting that the X-ray irradiation

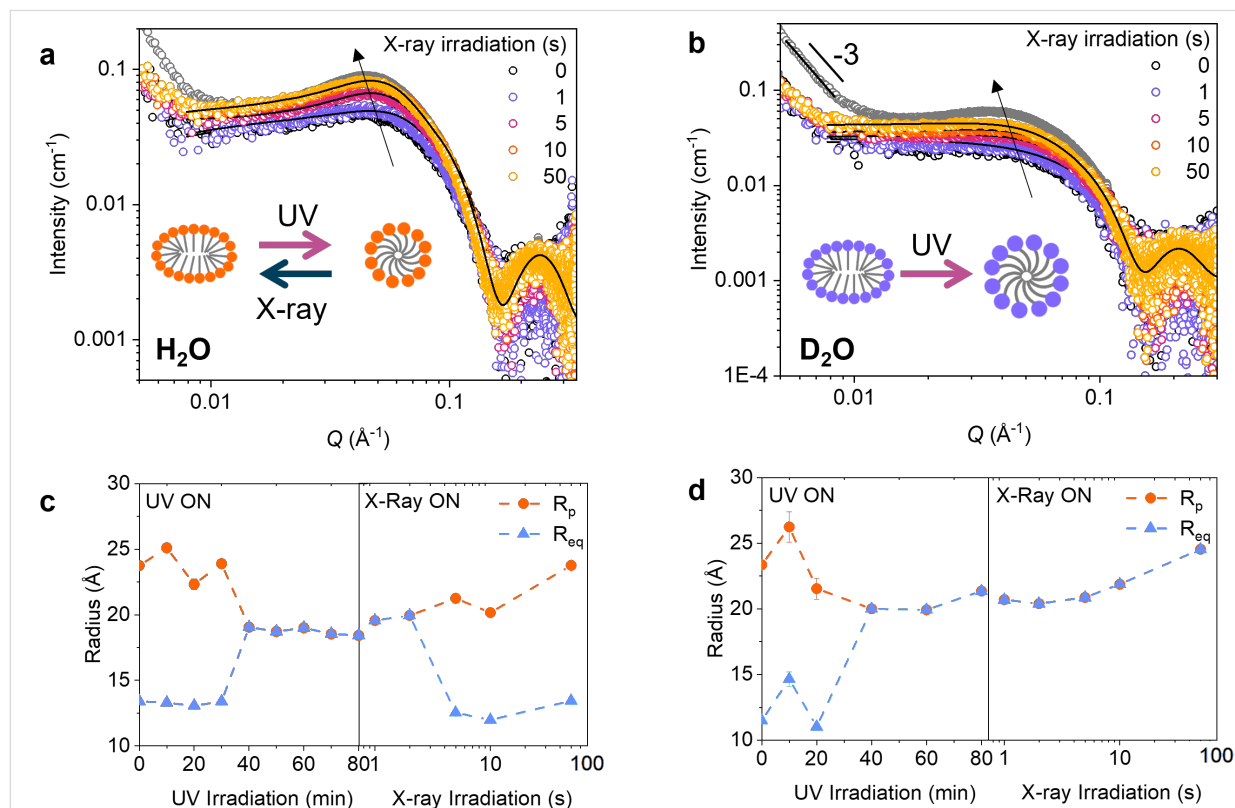


Figure 3: SAXS curves for the Z-rich PSS of AAPTAB (50 mM) in (a) water (H_2O) and (b) deuterium dioxide (D_2O) show changes to the micelle shape and size on X-ray exposure. Fits to the data (black lines) indicate that a spherical-to-ellipsoidal transition occurs in H_2O but not in D_2O . Note that the grey circles indicate the native, E -isomer state, and the slope of -3 at low Q values (b) indicates the presence of larger-scale aggregation. The dimensional changes to the ellipsoidal and spherical micelles are shown for (c) H_2O and (d) D_2O , where R_p is the polar radius and R_{eq} is the equatorial radius.

tion alone does not cause AAPTAB ionisation or affect the micelle morphology. As with Azo, *Z*–*E* isomerisation in AAP photoswitches can be catalysed efficiently using oxidising or reducing species [41]. This means that, despite the increased thermal stability of the *Z* isomer, AAP photoswitches are also susceptible to *Z*–*E* isomerisation on X-ray irradiation due to the presence of catalysing ionic and radical species from radiolysis of the surrounding water. This can be seen by a partial return of the UV–vis absorbance spectrum of AAPTAB from the *Z* to the *E* isomer after X-ray irradiation (Figure S7, Supporting Information File 1).

To further investigate the mechanism for *Z*–*E* isomerisation using X-rays and associated structural changes, we conducted an identical experiment using D₂O instead of H₂O. The change of solvent leads to an increase in the viscosity, from 0.89 in H₂O to 1.10 mPa·s in D₂O [42], which is attributed to slow diffusion of micelles within the medium. Furthermore, the rate of H⁺/D⁺ exchange between the solvent and the photoswitch will decrease due to the heavier deuterium atoms in D₂O, resulting in an effective weakening of the acidification effect from radiolytic D⁺ formation [43]. The change from H₂O to D₂O may also affect the surfactant self-assembly due to the change in hydrogen-bond strength [44]. Fitting to the SAXS data shows that AzoTAB and AAPTAB in the *E*-isomeric forms form elliptical cylindrical and ellipsoidal micelles, respectively, with comparable dimensions to those in H₂O (Tables S1 and S3, Supporting Information File 1). However, there is a large difference in the interactions between AAPTAB micelles on switching solvents, which can be seen as a decrease in the interaction hump in the SAXS pattern at $Q \approx 0.045 \text{ \AA}^{-1}$ (Figure 3a and Figure 3b). This may be due to a decrease in the CMC, as expected for TAB surfactants in D₂O in comparison to H₂O [45], which drives the formation of larger-scale aggregates within the solution. This is visible as a strong power-law decay in the low-*Q* region of the SAXS pattern, where $I(Q) \propto Q^{-3}$ (Figure 3b), and could result in fewer micelles in solution and fewer interactions between them. Despite this, both AzoTAB and AAPTAB undergo similar micelle morphology transitions on UV irradiation in D₂O as compared to those in H₂O (cylindrical-to-ellipsoidal and ellipsoidal-to-spherical, respectively, Tables S1 and S3, Supporting Information File 1).

On subsequent X-ray irradiation of the *Z*-rich PSS, AzoTAB in D₂O shows partial recovery of the elliptical cylindrical micelle shape present in the *E* isomer (Table S1, Supporting Information File 1); however, a longer exposure time is needed to induce changes compared to those occurring in H₂O (10 s cf. 5 s). The effect is much more pronounced for the AAPTAB system, where there is no evidence of the micelle morphology changing back to the *E* form on X-ray irradiation in D₂O. The fits instead

show a slow increase in the radius of the spherical micelles, from 20 to 25 Å after 50 s of irradiation (Figure 3d), but the morphology transition to the ellipsoidal shape is not complete. This could be due to both the slower rate of D⁺ exchange with the photoisomers, leading to a slower rate of *Z*–*E* isomerisation via this mechanism. Furthermore, the decreased rate of diffusion in the more viscous D₂O could lead to slower rearrangement after reverse isomerisation into the *E* isomer morphology. This demonstrates that the solvent plays a crucial role in X-ray-induced reverse isomerisation in these systems, not only due to catalysis from the radiolysis effect, but also as the medium for structural rearrangements.

Effect of acidification

The effect of acidification on isomerisation was further investigated using UV–vis absorbance spectroscopy, where excess hydrobromic acid (HBr) was added to AzoTAB and AAPTAB samples (25 μM) that had been preirradiated with UV light into the *Z*-rich PSS. HBr was selected as the acid to eliminate any effects from the Br[−] counterion on the self-assembly behaviour [36]. AzoTAB (in the *Z*-rich PSS) showed a rapid response to acidification with near-complete reversal to the *E* isomer within 60 minutes (Figure 4a). In contrast, for AAPTAB, the process was much slower, with minimal change over 1 hour, but near-complete transition to the *E* isomer after 20 hours (Figure 4b). The excess acid added in these experiments generates a pH value of 0.4 in the samples. In comparison, the calculated pH change expected due to the X-ray radiolysis of water (see section 6, Supporting Information File 1) was found to be from pH 7 to ≈ pH 5–6 for the X-ray irradiation doses used in these experiments. Interestingly, both AzoTAB and AAPTAB show little difference in their time-dependent absorbance spectra from the *Z*-rich PSS over the course of 200 minutes at pH 5, 6 and 7 (Figures S8 and S9, Supporting Information File 1). This suggests that the X-ray-induced formation of H⁺ ions alone may not be strong enough to induce *Z*–*E* isomerisation on the millisecond timescales on which structural changes were observed using SAXS. We note that the temperature change due to heating effects from the X-ray beam is <0.4 °C for a single 500 ms frame (see section 7, Supporting Information File 1), meaning that this will not affect the *Z*–*E* isomer ratio. The diverse range of reactive radical species formed in the radiolysis process must therefore play a key role in catalysing the *Z*–*E* isomerisation via multiple mechanisms.

Effect of solvent concentration

The solvent clearly plays a crucial role in enabling *Z*–*E* isomerisation of AzoTAB and AAPTAB on X-ray irradiation. To investigate this further, we decreased the concentration of solvent greatly to study two samples of AAPTAB at 10 and 90 wt % with respect to water. For such high surfactant loadings, addi-

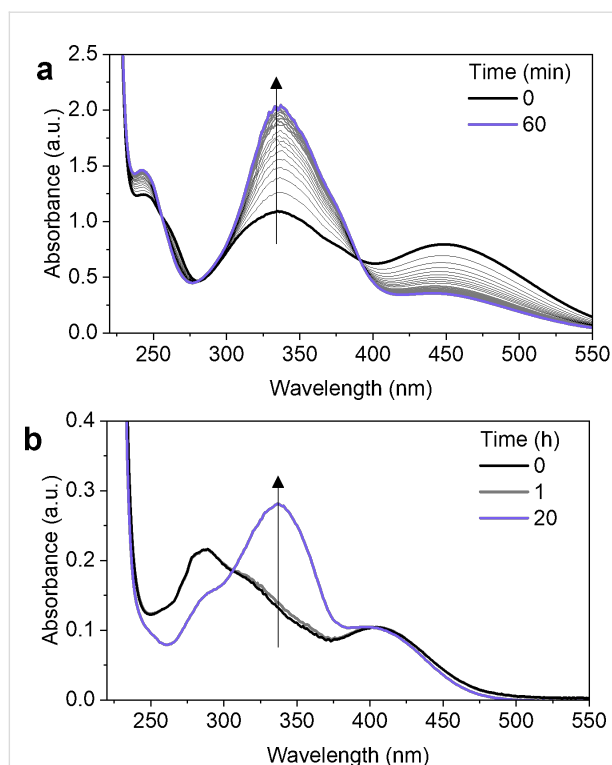


Figure 4: Addition of excess acid (pH = 0.4) induces *Z*–*E* isomerisation in AzoTAB and AAPTAB. UV–vis absorbance spectra for (a) AzoTAB (25 μ M in water) and (b) AAPTAB (100 μ M in water) after UV irradiation to form the *Z*-rich PSS and addition of excess hydrobromic acid as a function of time held in the dark. The grey lines indicate time intervals of (a) 3 minutes and (b) 1 hour.

tional factors must be considered such as increased absorbance and lower light penetration, as well as reduced diffusion due to higher viscosities. To counteract this, we chose to irradiate the

samples ex-situ for 3.5 hours to achieve a *Z*-rich PSS, where the percentage isomerised has been determined previously using ^1H NMR spectroscopy [20]. The 10 wt % sample was measured over 800 X-ray exposures of 250 ms each. The initial *Z*-rich PSS SAXS pattern shows a strong interaction peak at $Q \approx 0.08 \text{ \AA}^{-1}$, characteristic of an isotropic micellar mesophase with densely packed, strongly interacting micelles (Figure 5a). On X-ray irradiation, the interaction peak increases in intensity and shifts to lower Q values. This suggests that there is an increase in the micelle size on irradiation, which agrees with the previous results that the *E* isomer forms larger micelles than the *Z* isomer. The shift in the SAXS pattern was visible within 2.5 s of X-ray irradiation, with significant changes resulting after 200 s of irradiation. For AAPTAB at 90 wt % in water, a number of sharp, Bragg peaks are visible in the SAXS pattern (Figure 5b), which are characteristic of the long-range order present in a lyotropic liquid crystal (LLC) mesophase that can form from the self-assembly of surfactants at high concentrations in a solvent. An inverse bicontinuous gyroid cubic mesophase can be assigned using the Q positions of the Bragg peaks, which are in a characteristic ratio of $\sqrt{6}:\sqrt{8}:\sqrt{14}:\sqrt{16}:\sqrt{20}:\sqrt{22}$ [20]. The sample was measured over 20 exposures of 250 ms each, with little evidence of a change to the LLC order over this period. The lower rate of *Z*–*E* isomerisation on X-ray irradiation can be explained by several different factors. The lower free volume in the ordered, LLC structure could prevent rapid *Z*–*E* isomerisation on X-ray irradiation, despite the formation of ions and radical species which would catalyse the reaction. Alternatively, the lower volume of water within the sample (only 10 wt %) would mean that there is less X-ray radiolysis, fewer catalysing species produced and therefore a lower effect on the *Z*–*E* reaction. Interestingly, it has

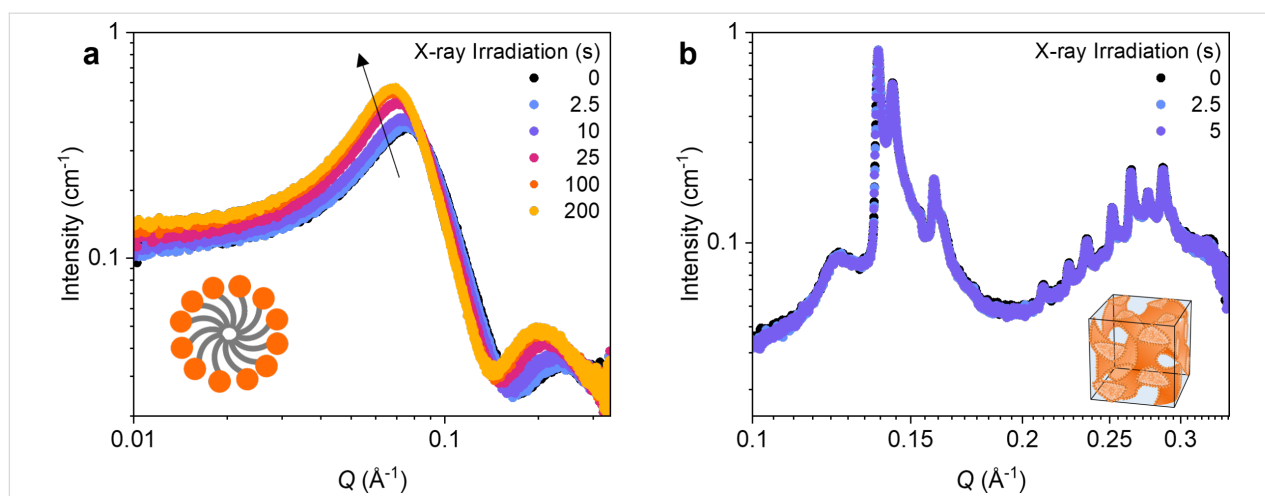


Figure 5: Effect of X-ray exposure time on high-concentration samples of AAPTAB in water, (a) 10 wt % and (b) 90 wt %, after ex-situ UV irradiation to form the *Z*-rich PSS. The schematic inserts illustrate the morphologies for the (a) isotropic micellar and (b) inverse bicontinuous gyroid cubic phases. The graphic depicted in Figure 5b was reproduced from [20] © 2024 B. E. Jones et al., published by American Chemical Society, distributed under the terms of the Creative Commons Attribution 4.0 International License).

been shown previously that the efficiency of electron or hole catalysis of *Z*–*E* isomerisation increases with increasing photo-switch concentration, due to the closer proximity leading to more efficient transfer of the catalysing species between molecules [40]. This suggests that there is a breakdown in the efficiency of the catalytic transfer at the concentrations studied here, or there is a critical water concentration needed to produce a sufficient number of species to catalyse isomerisation. X-ray-induced *Z*–*E* isomerisation therefore has a prevalent effect up to solvent concentrations of 90 wt % water; however, the effects are significantly slowed on formation of dense, LLC phases with low solvent concentrations (10 wt %).

Conclusion

In summary, with in-situ UV irradiation both AzoTAB and AAPTAB undergo morphological transitions due to *E*–*Z* isomerisation, producing micelles of higher spontaneous curvature. On subsequent X-ray irradiation both AzoTAB and AAPTAB in the *Z*-rich PSS revert to the micelle morphologies formed by the initial *E* isomers. It is thought that this is due to X-ray-induced radiolysis of water, which produces many primary species, including H^+ ions, that are known to catalyse the *Z*–*E* isomerisation reaction. By switching the H_2O solvent to D_2O , we observed that the increased viscosity and reduced acidification acted to slow the reversal process, especially for the AAPTAB, supporting this hypothesis. However, investigations into the degree of isomerisation at different pH values for AzoTAB and AAPTAB in water suggest that the pH change caused by X-ray radiolysis alone may not be sufficient to result in the structural changes on the timescales observed using SAXS. The presence of additional radical and ionic species, other than H^+ ions, must therefore play a crucial role in producing the observed rapid changes in SAXS profiles, through mechanisms such as electron or hole catalysis. Despite this, we saw that on increasing the concentration of PS to form higher-concentration LLC mesophases, the X-ray-induced reversal was less pronounced, likely due to the lower water content available for radiolysis.

The X-ray irradiation time required to obtain a good signal-to-noise ratio differs depending on the specific synchrotron beamline or laboratory instrument on which the SAXS experiments are conducted. We have found that the X-ray reversal process can be very fast (<1s), meaning that only a few frames will truly capture the *Z*-isomeric PSS. As the reversal effects are highly sample dependent, varying with photoswitch, concentration, solvent and morphology (e.g., micelles or LLCs), care must be therefore taken when conducting X-ray experiments with photo-switchable materials. As such, a broad-brush approach cannot be applied across all experiments. Instead, we suggest that the *Z*-rich PSS is first irradiated with X-rays for an extended period,

whilst taking many short X-ray exposure frames to determine at what point the changes in the scattering pattern become significant. A balance can then be struck between obtaining good-quality data and accurately probing the *Z*-rich PSS for the specific sample and instrument being used. It is only with this additional care that there can be confidence in the structural determination of photoswitchable materials using X-ray radiation. This understanding is vital as the field advances to harness the improved properties of new photoswitches with greater isomerisation control, such as aryliminopyrazoles [46], and to optimise these systems towards applications in solar energy storage, drug delivery or catalysis.

Experimental Materials

Photosurfactants AzoTAB and AAPTAB were synthesised according to previously reported procedures [4,19]. Water was obtained from a Millipore Simak 2 water purification system. Hydrobromic acid (48%) and deuterium oxide (99.9 atom %) were supplied by Merck.

Sample preparation

To produce micellar samples, light-responsive PS were shaken with the solvent (50 mM in either H_2O or D_2O) until homogeneous. For samples of higher concentration, AAPTAB was added to water (10 and 90 wt %), and the samples were heated to 60 °C, whilst stirring until homogenous. Samples were left to cool to room temperature whilst stirring.

For the photoisomerisation studies using UV–vis absorbance spectroscopy, samples were irradiated to the PSS in a custom-built LED light box with UV (365 nm, irradiance = $6.00 \text{ mW}\cdot\text{cm}^{-2}$), blue (455 nm, $5.16 \text{ mW}\cdot\text{cm}^{-2}$) or green (525 nm, $0.06 \text{ mW}\cdot\text{cm}^{-2}$) light. For the SAXS studies at high concentration, samples were irradiated in a custom-build LED light box with UV (365 nm) light at an irradiance of $1.24 \text{ mW}\cdot\text{cm}^{-2}$ for 3.5 h. This resulted in 98 ± 2 and $71 \pm 4\%$ *E*-to-*Z* isomerisation for 10 and 90 wt % AAPTAB, respectively, as determined previously using ^1H NMR [20].

SAXS

SAXS measurements were performed at the high-throughput SAXS beamline B21, Diamond Light Source (Oxfordshire, UK) [47]. The X-ray beam energy was 13.0 keV and the detector distance set to 3.7 m, giving a Q range of $0.0045\text{--}0.34 \text{ \AA}^{-1}$.

For the studies at low concentration (50 mM), samples were loaded into a 96 well PCR plate and stored at 25 °C before injection into a quartz capillary and held at 25 °C during measurement. 10 μL of sample was injected into the capillary and held in place during light and X-ray exposure. Frames of

500 ms were taken, and the 2D diffraction patterns were radially averaged and integrated to obtain 1D data. The solvent background was subtracted and frames were averaged using the ScÅtter software [48]. The number of frames averaged was varied to strike a balance between accessing greater time-resolution and achieving a better signal-to-noise ratio. For an X-ray irradiation time of ≤ 2 s, a single X-ray frame (500 ms) was used, whereas for > 2 s, an average of 3 frames was used.

For the measurements at high concentration, samples were loaded into a polyethyleneimine (PEI) capillary (90 wt % water) or using Kapton tape and a 3D-printed lolly stick (10 wt % water). Frames of 250 ms were taken, with a 50 ms wait time between each frame. A total of 900 and 20 frames were taken for the 10 and 90 wt % samples, respectively. The 2D diffraction patterns were radially averaged and integrated to obtain 1D data. The container background was subtracted and sets of three frames were averaged using the ScÅtter software [48].

In-situ light irradiation was achieved using the custom-made setup at beamline B21, using a fibre-coupled pE-4000 (coolLED) focussed onto the sample position and coincident with the X-ray beam [33]. An irradiance of 0.96, 4.00 and $0.42 \text{ W}\cdot\text{m}^{-2}$ was achieved for a wavelength of 365, 460 and 525 nm, as measured before the experiment using a photodiode calibrated to a photothermal power meter.

Model fitting for SAXS data

SAXS data were fitted using SASFit (version 0.94.11) [34]. The first 50 data points were removed due to aggregation effects in some samples. A linear, horizontal background was set to an appropriate value. The data were fitted to either: ellipsoidal cylindrical core-shell, ellipsoidal core-shell or spherical core-shell structures, with a Gaussian distribution around the (polar) radius to incorporate polydispersity into the model. Data were fitted to the radii (both polar and equatorial for ellipsoidal form factors), shell thickness, scattering length density and length (for cylindrical form factors). The structure factor was fitted using the Hayter–Penfold rescaled mean spherical approximation (RMSA) model to determine the charge and volume fraction of the micelles. Full details of the models used are included in section 3, Supporting Information File 1.

UV–vis absorbance spectroscopy

UV–vis absorbance spectra were recorded using a Perkin Elmer Lambda 750 spectrometer with a slit width of 2 nm and a scan speed of $266.75 \text{ nm}\cdot\text{min}^{-1}$. Measurements were taken at 1 nm intervals from 700–200 nm, using quartz cuvettes with a 10 mm path length. The temperature was regulated to 25°C using a Perkin Elmer Peltier temperature controller 201. For the isomerisation experiments using excess acid, HBr (8.9 M,

100 μL) was added to a quartz cuvette containing either AzoTAB (25 μM) or AAPTAB (100 μM) in water in the Z-rich PSS. UV–vis absorbance spectra were taken sequentially over 20 cycles every 3 minutes and after leaving the solution overnight in the dark. For experiments over the pH range 5–7, HBr (20 mM) was added to 2 mL of either AzoTAB (100 μM) or AAPTAB (100 μM) in water in the Z-rich PSS in a volume of 10 μL for pH 6 and 100 μL for pH 5. UV–vis absorbance spectra were taken sequentially over 66 cycles every 3 minutes.

To investigate the *Z*–*E* isomerisation on X-ray irradiation, UV–vis absorbance spectra were taken using a NanoDrop 1000 spectrometer. Samples (2 μL) were loaded onto the instrument and absorbance from 220 to 750 nm measured.

Supporting Information

Supporting Information File 1

UV–vis absorbance spectra for photoisomerisation, SAXS using in-situ irradiation, models used for SAXS fitting, micelle dimensions from SAXS fits, calculations for the pH change on X-ray irradiation and UV–vis absorbance spectra for acid-induced isomerisation.

[<https://www.beilstein-journals.org/bjoc/content/supplementary/1860-5397-20-176-S1.pdf>]

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Data Availability Statement

The data generated and analyzed during this study is openly available in the Apollo data repository at <https://doi.org/10.17863/CAM.109905>.

Preprint

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Extension of the π -system of monoaryl-substituted norbornadienes with acetylene bridges: influence on the photochemical conversion and storage of light energy

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Full Research Paper

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Abstract

The photochromic norbornadiene/quadricyclane pair is a promising system for molecular solar thermal (MOST) energy storage, with which solar energy may be converted, stored, and released as heat in one integral molecular system. Herein, we present the synthesis of mono-, bis-, and tris-norbornadiene derivatives with alkynylbenzene and alkynyl-naphthalene core units, along with studies of their photochemical properties. The target compounds were synthesized by Sonogashira–Hagihara coupling reactions of 2-bromonorbornadiene and the corresponding arylacetylenes. The norbornadienes showed absorption maxima in the range of 310–345 nm and long-wavelength zero onsets of up to 420 nm. The photoisomerization quantum yields were as high as 59% per photoisomerization event and the resulting quadricyclanes showed half-lives of up to 8 h at room temperature. Furthermore, the norbornadienes were transformed quantitatively into their quadricyclane photoproducts by irradiation with green light (520 nm) in the presence of a photosensitizer.

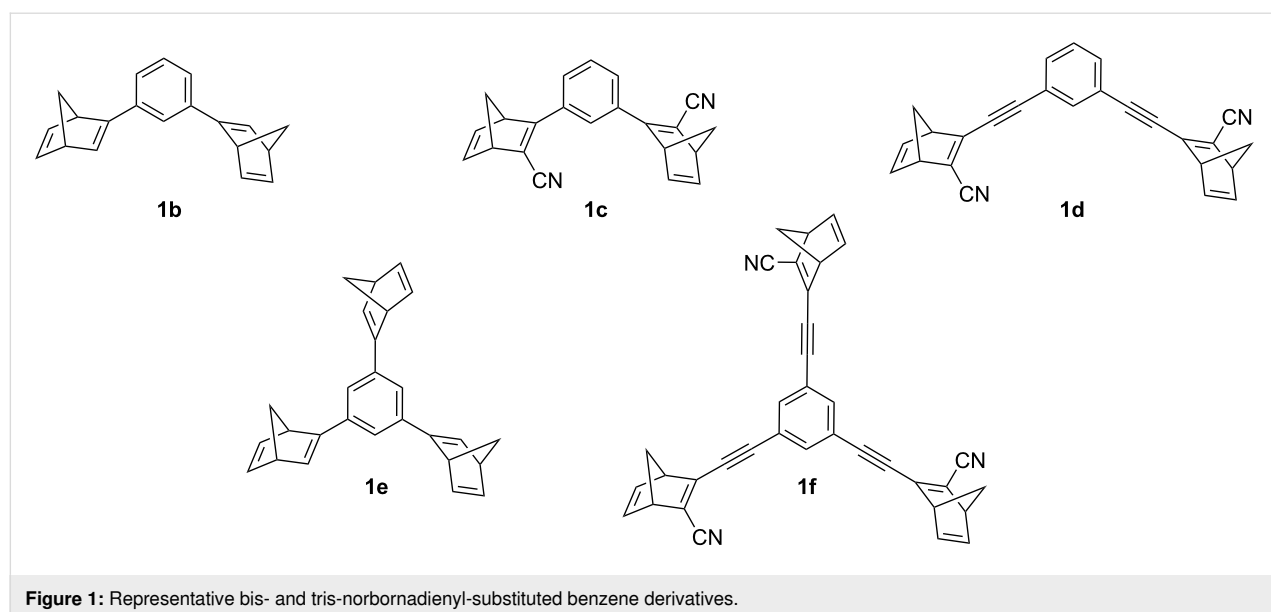
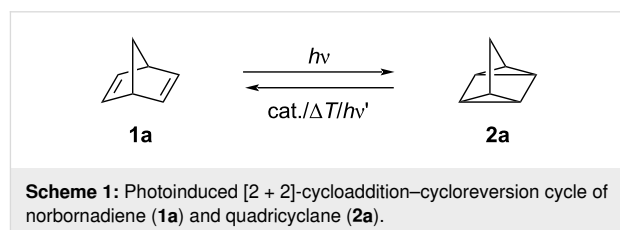
Introduction

The application of sustainable energy storage and supply has become a very important issue both from an economic and ecological point of view. In particular, the global energy demand is continuously expanding because of the increasing population,

the development of new, energy-intensive technologies and overconsumption of energy [1,2]. In this context, windpower plants and solar photovoltaic systems have become increasingly important contributions to the overall available energy, al-

though both technologies still pose some problems regarding the storage of the converted energy [3–8]. This drawback may be solved with the progress in battery technology, however, the use of high-performance batteries still requires some problematic materials, which are difficult to access, hardly recyclable, or which may harm the environment [9]. Thus, in the present situation, the efficient and flexible conversion and storage of energy requires the variable combination of different, complementary storage systems, and as a consequence, the development of alternative methods for energy storage is still an important task to contribute to the mix of storage systems. One promising approach towards storage of solar energy is represented by the molecular solar thermal (MOST) energy storage systems, which have the ability to convert and store (sun)light energy in reversible photochemical reactions. Specifically, this approach is based on photoactive compounds that are converted into photoisomers with higher energy upon absorption of light. In turn, this reaction is reversible, thus allowing to release the stored chemical energy as heat in a specifically triggered back reaction [7,8,10–13]. For a practicable MOST system, some key parameters have to be ensured, such as absorption in the range of the solar spectrum, a high quantum yield of the photoreaction, long half-lives of the photoproducts, and a high energy storage density [7,8,12–14]. In this context, several different MOST systems have been explored, including, for example, anthracenes [15], azobenzenes [16–19], dihydroazulenes [20,21], or azaborines [22,23]. However, the most prominent feasible MOST system is the [2 + 2] photocycloaddition–cycloreversion cycle between norbornadiene (**1a**) and quadricyclane (**2a**), which has several advantageous properties (Scheme 1) [8,14,24]. In particular, this system shows a high energy storage capacity of up to 1 MJ/kg, and the energy can be

conveniently released in form of heat by controlled photolysis, thermolysis, or catalysis [8,14]. However, the parent norbornadiene (**1a**) only absorbs ultraviolet light, which is of limited availability in sunlight. Furthermore, the photoisomerization quantum yield is very low and therefore not suitable for an application [7,8,14]. One promising way to overcome these disadvantages is the introduction of a donor–acceptor system at the norbornadiene double bonds, which has resulted in the development of new generations of modified norbornadiene derivatives with diverse variations of donor and acceptor substituents [25–32]. However, such a modification often leads to higher molar masses and thus to lower energy densities [7,25,33]. Consequently, further fine tuning of the substituents is necessary to accomplish a reasonable balance between the MOST parameters. Hence, to increase the energy density and to induce a decent red shift of the absorption, two, three or even more norbornadiene units may be combined in one integral molecule by attachment to a shared, linking arene unit, such as realized in bis- and tris-norbornadienes **1b–f** (Figure 1) [7,12,30,34,35]. In this particular case, derivatives with only one substituent at the norbornadiene double bond exhibited favorable storage properties because of a lower molecular weight, however, their absorption still lies in the UV range [30]. Therefore, we aimed at further modification of the core structure of bis- and tris-

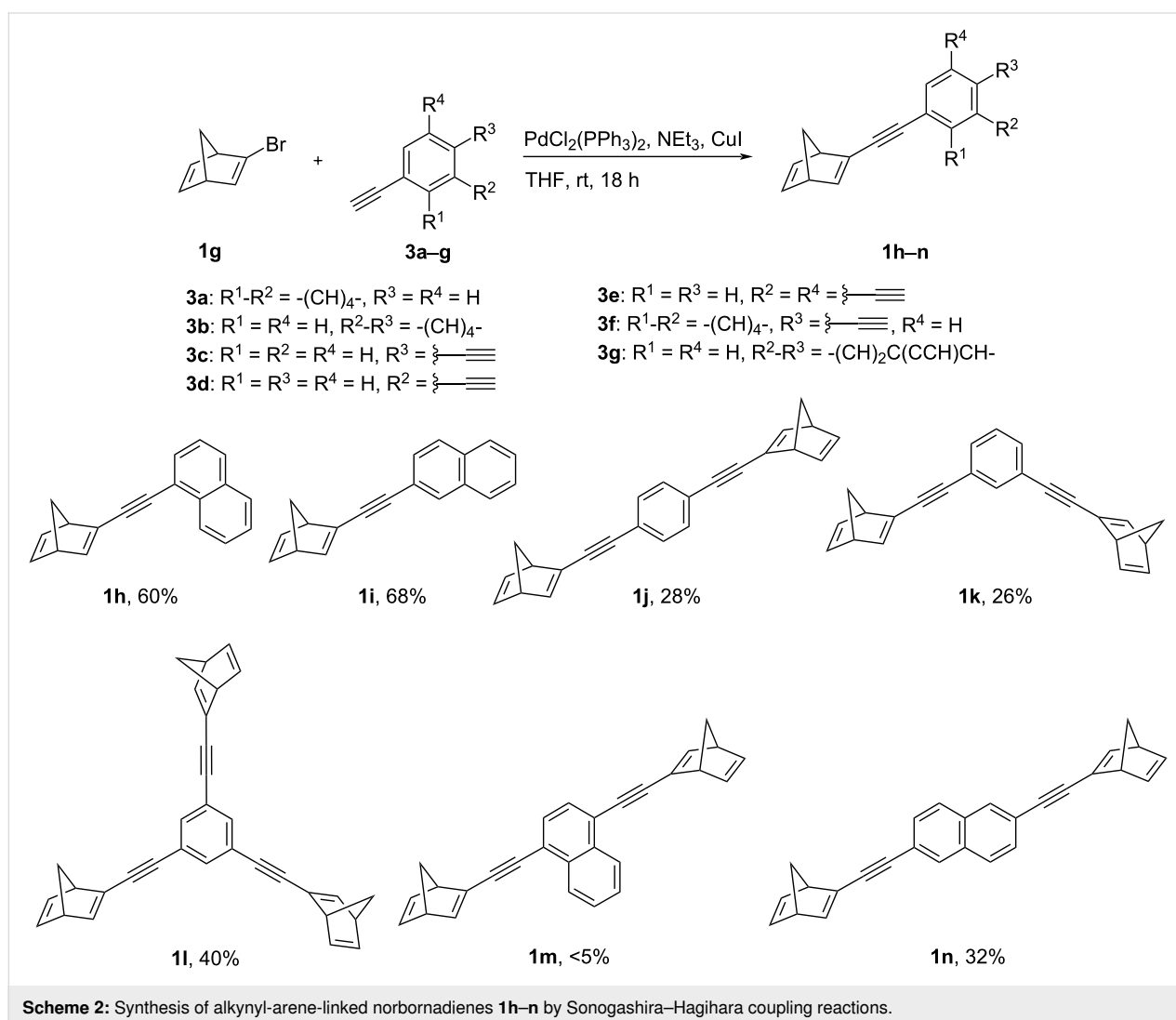


norbornadienes, which may lead to a more pronounced red shift of the absorption while maintaining the high energy density. As this has been shown in other cases already [34], we anticipated that the integration of an acetylene bridge between the arene core and the norbornadiene units in compounds **1h–n** may induce these effects. Herein, we present the synthesis of these target molecules and our studies of their photochemical and physicochemical properties with a focus on energy conversion and storage.

Results and Discussion

The norbornadiene derivatives **1h–l,n** were synthesized by Sonogashira–Hagihara coupling reaction of 2-bromonorbornadiene (**1g**) [36] with the corresponding arylacetylenes **3a–g** (Scheme 2). As an exception, 1,4-bis-norbornadienylnaphthalene (**1m**) could not be obtained by this route because the product could not be separated from the complex product mixture. The monosubstituted derivatives **1h** and **1i** were isolated in

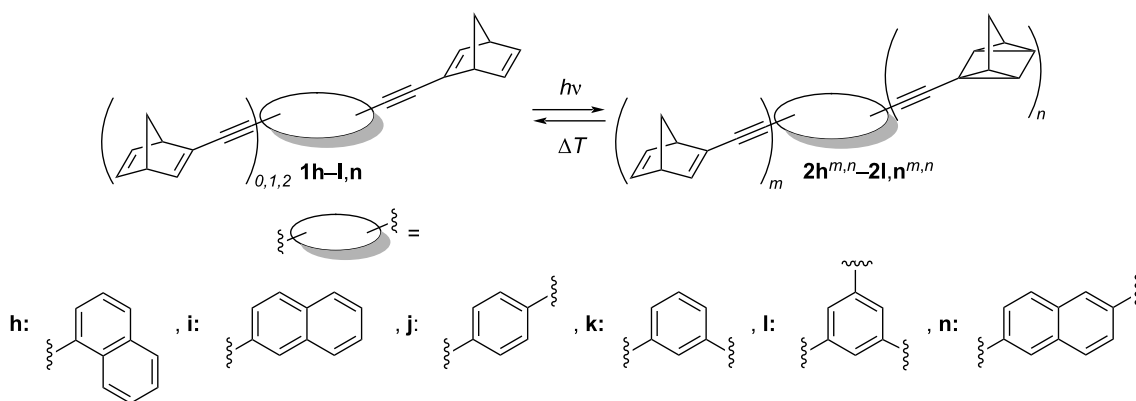
good yields (60–68%), whereas the bis- and tris-substituted derivatives **1j–l,n** were only obtained in low yields (26–40%). The latter were more difficult to isolate because by-products interfered with the chromatographic separation; however, these yields are similar to the ones reported for resembling norbornadienes [34,37]. The novel compounds **1h–l,n** were identified and fully characterized by NMR spectroscopy (^1H , ^{13}C , COSY, HSQC, HMBC), melting point, and elemental analysis. All products showed the characteristic ^1H NMR spectroscopic signals of norbornadienes, in particular two signals at ca. 2.10 ppm and 2.20 ppm (7-CH₂) and two broad singlets between 3 and 4 ppm (bridgehead 1- and 4-CH). In addition, typical ^{13}C NMR shifts of the aryl-substituted acetylenes at ca. 85 ppm and 95 ppm were observed. The norbornadienes **1h–l,n** exhibit very good solubility in organic solvents, like ethyl acetate, chloroform, or benzene, whereas they have poor solubility in cyclohexane, acetonitrile, or ethanol. In polar protic solvents, like methanol or water, they are insoluble.



The absorption spectra of compounds **1h–l,n** were recorded in different solvents (Table 1, cf., Supporting Information File 1, Figure S1). In general, the employed solvents had only a marginal influence on the absorption properties of each compound. With slight variations caused by the different substitution patterns, the compounds **1h–l,n** showed the characteristic long-wavelength bands with maxima between 310 nm (**1k**) and 345 nm (**1n**) and low-energy zero onsets from 345 nm (**1k**) to 420 nm (**1n**). Hence, the red shift of the absorption bands correlates with the size of the respective π -system of the derivatives, and is, thus, more pronounced for the naphthalene-bridged compounds. Likewise, the increased size of the conjugated π -system also led to a red shift of the absorption bands in comparison with the ones of the corresponding norbornadiene derivatives without acetylene bridges (**1b,e**) [29,30]. Accordingly, a

slightly more pronounced red shift (20 nm) has been reported for derivatives **1d** and **1f** which carry an additional electron-acceptor in the 3-position of the norbornadiene unit [33,34].

The photoisomerization of the norbornadiene derivatives **1h–l,n** (Scheme 3) was investigated photometrically in cyclohexane (20 μ M, Figure 2), because the norbornadienes and the corresponding quadricyclanes are sufficiently soluble in this solvent and because it allows direct comparison with literature data [30,34]. As a general trend, the long-wavelength absorption maximum of each substrate decreased for all derivatives during the photoreaction, whereas the blue-shifted maximum of the photoproduct was formed. In addition, isosbestic points were observed for the derivatives **1h** (A), **1i** (B), **1k** (D), and **1l** (E). The irradiations of the derivatives **1h**, **1i**, **1k**, and **1l** were



Scheme 3: Photoisomerization of norbornadiene derivatives **1h–l,n** (20 μ M) to quadricyclanes **2h–l,n** in cyclohexane, m = number of norbornadienylethynyl units, n = number of quadricyclylethynyl units.

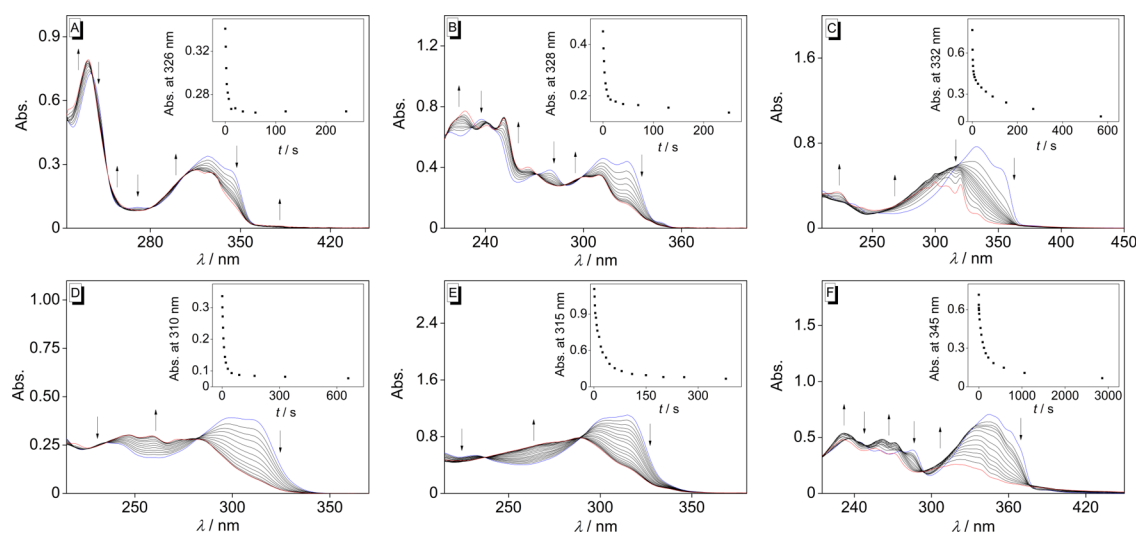


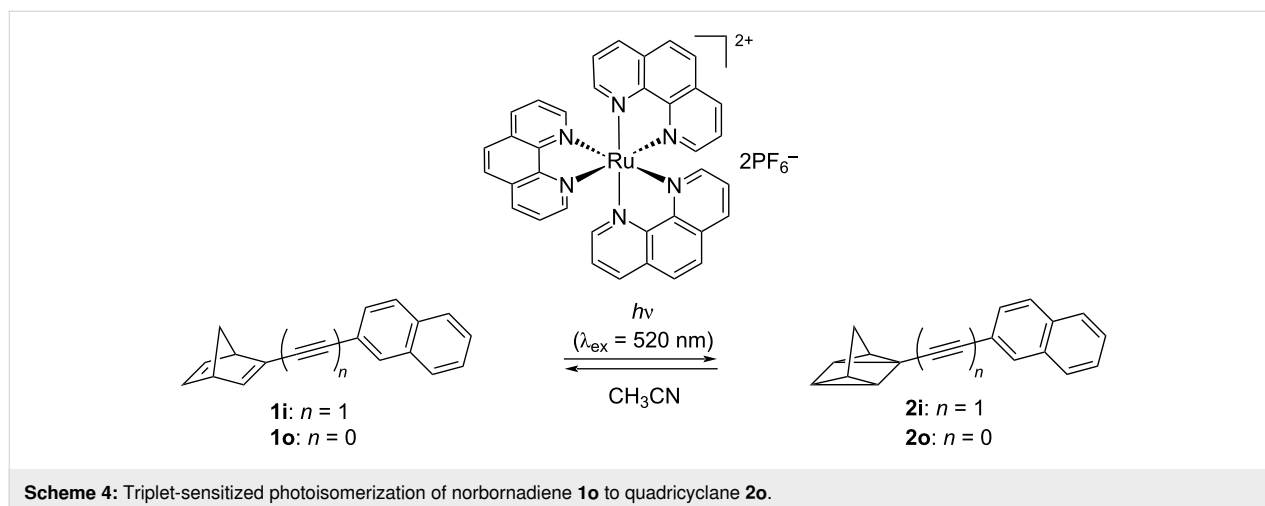
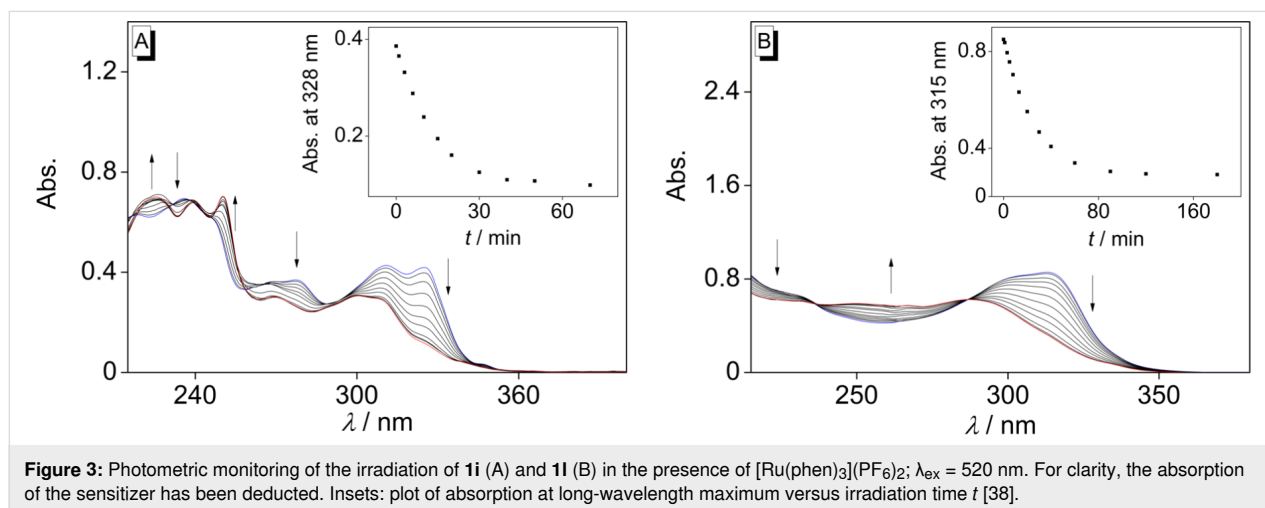
Figure 2: Photometric monitoring of the irradiation of **1h** (A), **1i** (B), **1j** (C), **1k** (D), **1l** (E), and **1n** (F); λ_{ex} = 315 nm (**1h**, **1i**, **1k**, and **1l**) or 340 nm (**1j**, **1n**). Insets: plot of absorption at long-wavelength maximum versus irradiation time t .

stopped once no more changes of the absorbance spectra were observed. In the case of compounds **1j** and **1n**, the endpoint of the photoreaction could not be identified, as a steady decrease of the whole absorption spectra during irradiation indicated secondary decomposition reactions.

We previously reported triplet energy transfer between $^3[\text{Ru}(\text{phen})_3](\text{PF}_6)_2$ and the corresponding arylnorbornadienes without an acetylene bridge, such as **1o**, leading to efficient and quantitative conversion to the quadricyclanes (Scheme 4) [38]. Hence, we assumed that triplet-sensitized isomerization of the mono-, bis-, and tris-norbornadiene derivatives with an alkynylbenzene and alkynyl-naphthalene core is also feasible. Quenching experiments of $[\text{Ru}(\text{phen})_3](\text{PF}_6)_2$ (triplet energy $E_T = 2.19$ eV [39]) with **1i** in acetonitrile yielded a triplet energy transfer rate of $k_{\text{ET}} = 5.8 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ indicating very efficient deactivation of the triplet sensitizer (Figure S4 in Supporting Information File 1). This rate is approximately an order of magnitude faster compared with the corresponding naphthyl-

norbornadiene **1o** without the acetylene bridge, which has a reported triplet energy of 2.41 eV (for details, see Supporting Information File 1, chapter S7). These results suggest that the triplet energy of **1i** is significantly lower than 2.4 eV and even triplet sensitizers with lower triplet energies than that of $[\text{Ru}(\text{phen})_3](\text{PF}_6)_2$ could be employed for this reaction, which might even allow red light-driven switching.

In addition to these kinetic studies, the photoisomerization reactions of **1i** and **1l** (20 μM) were investigated in the presence of $[\text{Ru}(\text{phen})_3](\text{PF}_6)_2$ (20 μM) at $\lambda_{\text{ex}} = 520$ nm in acetonitrile (Scheme 4). This solvent was required because of the solubility of the sensitizer. Under these conditions, both derivatives **1i** and **1l** showed the same development of absorption spectra during irradiation as upon direct irradiation, although the reaction times were significantly higher, most likely because of the much weaker molar absorption coefficient of $[\text{Ru}(\text{phen})_3](\text{PF}_6)_2$ at 520 nm ($\approx 900 \text{ M}^{-1} \text{ cm}^{-1}$), and the fact that the photosensitization process is bimolecular (Figure 3). Indeed, the quenching



efficiency of triplet-excited $[\text{Ru}(\text{phen})_3](\text{PF}_6)_2$ by **1i** was calculated to be as low as 5% under the highly diluted conditions required for the experiments in Figure 3.

In order to gain structural information about the photoproducts, the photoisomerization reactions were also examined by ^1H NMR spectroscopy. Initially, all derivatives showed the isomerization reactions to the corresponding quadricyclane derivatives, as identified by the characteristic ^1H NMR signal pattern of the quadricyclane fragment with five multiplets at around 1.6 ppm, 1.7 ppm, 1.8 ppm, 2.1 ppm, and 2.2 ppm. However, after relatively short irradiation times of only 30 min, additional signals were detected in the spectrum, which could not be assigned to distinct by-products or secondary products. Unfortunately, the NMR signals of the by-products overlapped with the ones of the norbornadiene and the quadricyclane signals, so that the quantitative analysis of the photostationary state was not possible with NMR spectroscopy. These observations are surprising, since the 3-acceptor-substituted derivatives and the ones without acetylene linkers have been reported to be converted quantitatively into their corresponding quadricyclanes [24,29,30,34].

As the photometric analysis of the photosensitized reaction of **1i** and **1l** pointed to a relatively clean and robust reaction, the irradiation of **1i** in the presence of $[\text{Ru}(\text{phen})_3](\text{PF}_6)_2$ at $\lambda_{\text{ex}} = 520$ nm was additionally monitored by in situ NMR spectroscopy [40] (Figure S41 in Supporting Information File 1). With this experiment, it was shown unambiguously that **1i** was quantitatively converted into the corresponding quadricyclane **2i** in the presence of the triplet sensitizer, as clearly indicated by the exclusive formation of the NMR signals of the photoproduct **2a** at 1.60–1.63 ppm, 1.69–1.71 ppm, 1.82–1.85 ppm, 2.07–2.11 ppm, and 2.21–2.25 ppm. Thus, it is possible to convert this monosubstituted norbornadiene efficiently into the corresponding quadricyclane with visible light, and thus also by

sunlight. Unfortunately, the derivatives **1h** and **1j–1,n** could not be investigated in the presence of the photosensitizer because these substrates have no sufficient solubility in acetonitrile.

To assess the efficiency of the photoreactions, photoisomerization quantum yields were determined in cyclohexane by actinometry ($\lambda_{\text{ex}} = 310$ nm or 340 nm) [41,42]. The quantum yields varied from only 1% per conversion event, i.e. per norbornadiene unit, for the naphthyl-substituted derivative **1n** to 59% for the *m*-phenyl-linked derivative **1k** (Table 1). In general, the derivatives **1h–1,n** showed significantly lower quantum yields than the 3-cyano-substituted derivatives **1d** and **1f** and the analogues **1c** and **1e** without an alkyne linker [29,30,34]. As the only exception, the *m*-substituted derivative **1k** has a higher quantum yield than its analog **1b**, which is, however, still lower than the one of the cyano-substituted norbornadiene **1c** [30,34]. In addition, substitution at the 2- and 2,6-position of the naphthalene unit resulted in low quantum yields, whereas the attachment of the norbornadiene at the 1- or 1,4-position led to significantly higher quantum yields, which is in accordance with previous observations with naphthyl-substituted derivatives [29,30]. Apparently, there is no obvious correlation between the quantum yields of the photoreactions and substitution pattern of the norbornadiene in this series, except for a rough trend that naphthyl-linked derivatives, in particular the ones substituted in the 2-position, have lower quantum yields than the phenyl-linked ones. This lack of correlation may indicate that several different factors and processes contribute to different extent to the course of the photoreaction, for example, steric hindrance and resulting torsion angles between the arene unit and norbornadiene, deactivation of the excited state by intersystem crossing (ISC), internal conversion (IC), or quenching by structural relaxation, etc.

Finally, the half-life, $t_{1/2}$, of the quadricyclane derivatives **2h–1,n** was determined by kinetic analysis of the thermally in-

Table 1: Photochemical and physicochemical parameters of the norbornadiene–quadricyclane interconversion of **1h–1,n** in cyclohexane.

	λ_{max} [nm] ^a	λ_{onset} [nm] ^b	λ_{onset} [nm] ^c	Φ [%] ^d	$\Delta G^\ddagger$ [kJ mol ^{−1}] ^e	$t_{1/2}$ [h] ^f
1h	326	386	366	31 (31)	97	3.6
1i	328	352	357	6 (6)	96	3.0
1j	332	400	392	10 (5)	97	3.1
1k	310	345	336	59 (30)	99	7.8
1l	315	345	355	16 (8)	99	7.6
1n	345	420	412	1 (0.5)	n.d. ^g	n.d. ^g

^aLong-wavelength absorption maximum of norbornadiene. ^bZero-onset of norbornadiene absorption (at $\epsilon = 10$ L mol^{−1} cm^{−1}). ^cLong-wavelength absorption of quadricyclane (at $\epsilon = 10$ L mol^{−1} cm^{−1}). ^dQuantum yield of photoisomerization per photoconversion event, absolute value in brackets, determined by actinometry. ^eActivation enthalpy of thermally induced cycloreversion of the quadricyclane; determined from Eyring equation. ^fHalf-life of the quadricyclane at 20 °C, determined from Eyring equation. ^gNot determined.

duced cycloreversion to the corresponding norbornadiene derivatives **1h–1,n** at 60 °C. From these data, the rate constants of the cycloreversion reactions were generated according to first-order kinetics and used to calculate the enthalpy and entropy of activation with the Eyring equation (Table 1, cf. Supporting Information File 1, equation S5). The analyses revealed half-lives of the quadricyclanes from 3.0 h to 7.8 h, which are essentially in the same range as the ones of analogues with an acceptor-substituent in the 3-position of the norbornadiene [34]. Notably, the quadricyclane derivatives with sterically more demanding substituents in the 2-position of the norbornadiene unit, such as **1e**, showed longer half-lives. Therefore, compounds **1h–1,n** have significantly lower half-lives than the corresponding analogues without an alkyne linker [29,30].

Conclusion

In summary, a small series of mono-, bis-, and tris-norbornadiene derivatives with alkynylbenzene and alkynyl-naphthalene core units was made available in reasonable yields by Sonogashira–Hagihara coupling reactions and the potential of these compounds for MOST applications was assessed. In particular, the compounds showed red-shifted absorption of up to 420 nm. Upon direct irradiation, the norbornadienes are converted into the corresponding quadricyclanes, which have short half-lives of only a few hours. The photoisomerization quantum yields were, with one exception, relatively low, as compared with the ones of other, structurally resembling norbornadiene derivatives [30,34]. Moreover, upon prolonged reaction time, significant amounts of unidentified by-products formed. Nevertheless, it was shown exemplarily that the photoisomerization can be performed under milder conditions and upon excitation with visible light in the presence of [Ru(phen)₃](PF₆)₂ as a photosensitizer. Under these conditions, the derivatives **1i** and **1l** were converted quantitatively into quadricyclanes by irradiation with green light. Thus, it was shown with the latter results that the photosensitization with suitable triplet sensitizers enables mild conversion of visible light in chemical energy in quantitative photoreactions of norbornadienes, even in cases that are rather problematic under direct irradiation.

The original target design, starting from the promising class of solely hydrocarbon-based, monoaryl-substituted norbornadienes, aimed primarily at the optimization of the absorption properties without adversely affecting the other advantageous MOST properties. However, although the integration of alkyne-linker units into otherwise unsubstituted arene-linked mono-, bis-, and tris-norbornadienes resulted in the anticipated red shift of the absorption, this slight advantage was established to the disadvantage of other relevant MOST properties, especially photostability. From these results, it may be concluded that the sole addition of alkyne units to optimize MOST materials

should be handled carefully because in some cases, like the one reported herein, it may result in an unfavorable tradeoff between the distinct MOST properties. After all, it still remains a challenge to design MOST materials with well-balanced advantageous properties. Based on the results presented herein, it may be proposed that the optimization of monoaryl-substituted norbornadienes along these lines should focus more on the factors that lead to improved stability, energy storage capacity and back reaction of the quadricyclane, and not primarily on the implementation of red-shifted absorption into the visible range. Specifically, the latter can easily be addressed in a more efficient way by the application of a suitable photosensitizer, as shown exemplarily in this work.

Supporting Information

Supporting Information File 1

Experimental section and complete set of NMR spectra.

[<https://www.beilstein-journals.org/bjoc/content/supplementary/1860-5397-20-254-S1.pdf>]

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Data Availability Statement

All data that supports the findings of this study is available in the published article and/or the supporting information of this article.

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Effect of substitution position of aryl groups on the thermal back reactivity of aza-diarylethene photoswitches and prediction by density functional theory

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Full Research Paper

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Abstract

Aza-diarylethene has been developed as a new family of photochromic compounds. This study explores the photochromic properties and thermal back reactivities of various aza-diarylethene regioisomers (**N1–N4** and **I1–I4**) in *n*-hexane. These molecules exhibit fast thermally reversible photochromic reactions driven by 6π aza-electrocyclization. Kinetic analysis of the thermal back reaction revealed activation parameters, highlighting how the substitution position of the aryl group affects the thermal stability. Additionally, density functional theory calculations identified M06 and MPW1PW91 as the most accurate functionals for predicting the thermal back reactivity, closely matching the experimental data. These findings offer valuable insights for the design of advanced photochromic materials with tailored thermal and photophysical characteristics.

Introduction

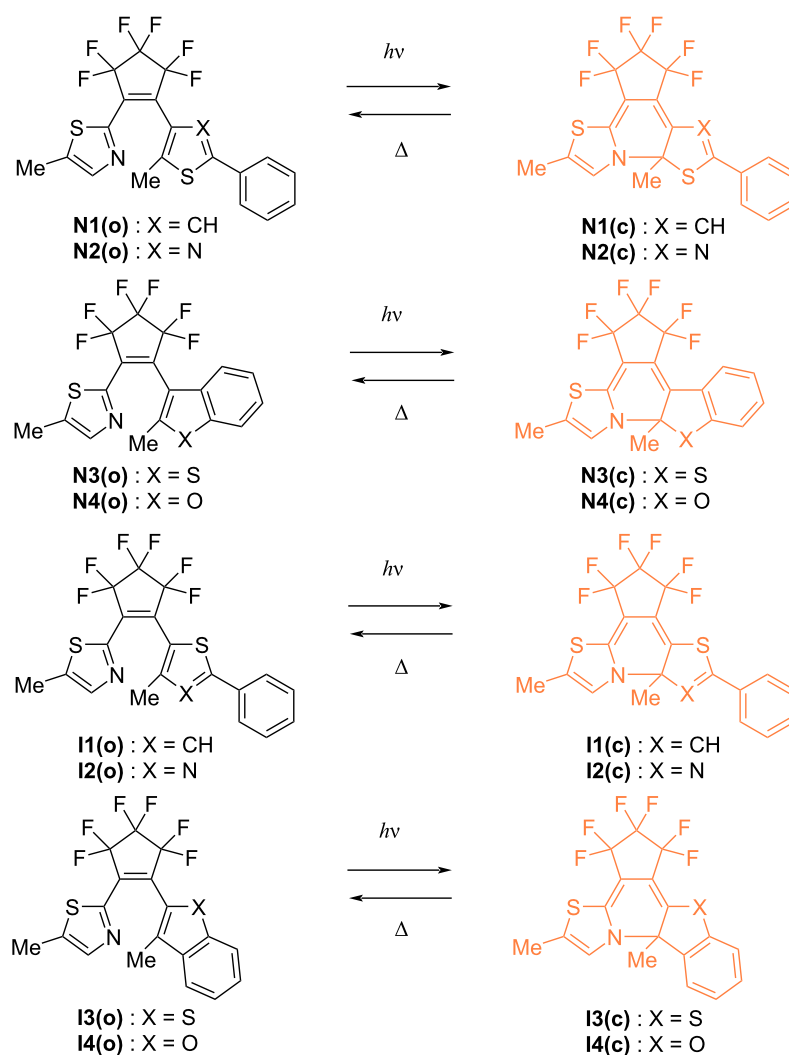
Molecular photoswitches have been studied for a long time because their physicochemical properties such as refractive index [1,2], dipole moment [3,4], conductivity [5,6], magnetism [7,8], and fluorescence [9–11] can be spatiotemporally modulated by light without physical contact. Therefore, various application examples of molecular photoswitches have been reported so far including volumetric 3D printing [12,13], photoreponsive semiconductors [14–17], photopharmacology [18,19], energy storage materials [20–23], data storage materials [24], super-resolution microscopy [25–27], photomechanical materi-

als [28–32], and so on. As seen in these representative application examples, the thermal stability of the colorless and colored isomers is one of the essential properties of molecular photoswitches. For example, the photochemically reversible-type (P-type) photoswitches [33,34], in which molecules isomerize upon photoirradiation and can maintain their state for a long time in the dark, are used for optical memories [35], displays [36,37], and photoresponsive actuators [38,39]. In contrast, the thermally reversible-type (T-type) photoswitches [40–42], in which the photogenerated isomers are thermally unstable at

room temperature and return to the initial isomers not only by photoreaction but also by the thermal back reaction, are utilized for eyeglass lenses [43], security inks [44], and real-time holograms [45]. Especially, it is important to control and predict the thermal reactivity of T-type molecules, and many researchers have made their efforts to control the thermal reactivity in various molecular systems by performing chemical modifications on the molecular structures [46–48]. For instance, Aprahamian and co-workers reported that replacing the rotor pyridyl group of a hydrazone switch with a phenyl group afforded long-lived negative photochromic compounds [49]. In addition, Hecht and co-workers reported that the thermal stability of indigos can be tuned by *N*-functionalization [50,51]. They revealed that the introduction of electron-withdrawing substituents on the *N*-aryl moieties enhanced the thermal stability of the *Z*-isomers while maintaining the advantageous photoswitching properties upon irradiation with red light [52]. The effect of

substituents on the thermal *cis*–*trans* isomerization of azobenzenes has also been widely studied, and push–pull derivatives bearing electron-donating and electron-withdrawing groups at the *para*-position of the benzene rings are known to exhibit very fast thermal isomerizations [53]. Velasco and co-workers also reported that a pyrimidine-based azophenol exhibits thermal back reaction on the nanosecond time scale [54]. Langton and co-workers demonstrated that the thermal isomerization rate of azobenzenes can be tuned over a time scale spanning 10^7 seconds by introducing appropriate chalcogens and halogens at the *ortho*-position of the benzene rings [55]. Thus, investigation of the strategies to modulate the thermal reactivity in each molecular system is very important.

Recently, we have developed aza-diarylethenes **N1** and **N2** shown in Scheme 1, in which one of the reactive carbons of the diarylethene is replaced by nitrogen, as a new class of T-type



Scheme 1: Photochromic reaction of aza-diarylethene derivatives **N1–N4** and **I1–I4** investigated in this work.

photochromic compounds [56,57]. Aza-diarylethenes undergo fast thermal back reaction from the closed-ring isomer to the open-ring isomer with the half-life time of millisecond order. For the further development of aza-diarylethenes, it is essential to establish molecular design guidelines for controlling the thermal back reactivity. As one of the effective methods for predicting the thermal back reactivity, density functional theory (DFT) calculations can be considered [51,58–62]. For example, in previous studies on the thermal back reactivity of diarylbenzene that is an analogue of diarylethene, we found that the M06-2X level of theory in combination with the 6-31G(d) basis set well reproduces the experimental value of the activation energy for the thermal back reaction of various diarylbenzenes, resulting in the accurate prediction of the half-life time [58,63]. Thus, the combination of experiments and theoretical calculations can be a powerful tool for molecular design.

In this work, we newly synthesize various aza-diarylethene derivatives **N3**, **N4**, and **I1–I4** with different substitution positions of the aryl group, and investigate their photochromic behaviors and thermal back reactivities as the data set for the prediction of thermal back reactivity. Moreover, we attempt to find the optimal functional for achieving a high correlation with experimental values by DFT calculation.

Results and Discussion

Photochromic properties in *n*-hexane

Compounds **N1–N3** were synthesized according to the procedures described in the previous work [56,57], whereas compounds **N4** and **I1–I4** were synthesized according to Scheme 2 in the Experimental section. The chemical structures of all compounds were confirmed by ^1H NMR and ^{13}C NMR spectroscopy and high-resolution mass spectrometry. ^1H NMR and ^{13}C NMR spectra are shown in Supporting Information File 1.

The photochromic properties of **N3**, **N4**, and **I1–I4** were investigated in *n*-hexane. Figure 1a,b and Figure S1 in Supporting Information File 1 show the absorption spectral changes of **N3**, **N4**, and **I1–I4** in *n*-hexane upon UV light irradiation. Compounds **N3(o)**, **N4(o)**, and **I1(o)–I4(o)** have absorption maxima (λ_{max}) at 299, 307, 291, 301, 307, and 369 nm, respectively. The molar absorption coefficients at λ_{max} of **N3(o)**, **N4(o)**, and **I1(o)–I4(o)** were determined to be 12200, 12700, 47800, 22700, 12900, and 12700 $\text{M}^{-1} \text{cm}^{-1}$, respectively. Upon irradiation with 365 nm, a new absorption band appeared in the visible region for all molecules, in which a visible absorption maximum was observed at 487, 467, 447, 454, and 440 nm for **N3(c)**, **N4(c)**, and **I1(c)–I3(c)**. Note that the λ_{max} of **I4(c)** could not be determined due to the overlapping absorption bands of

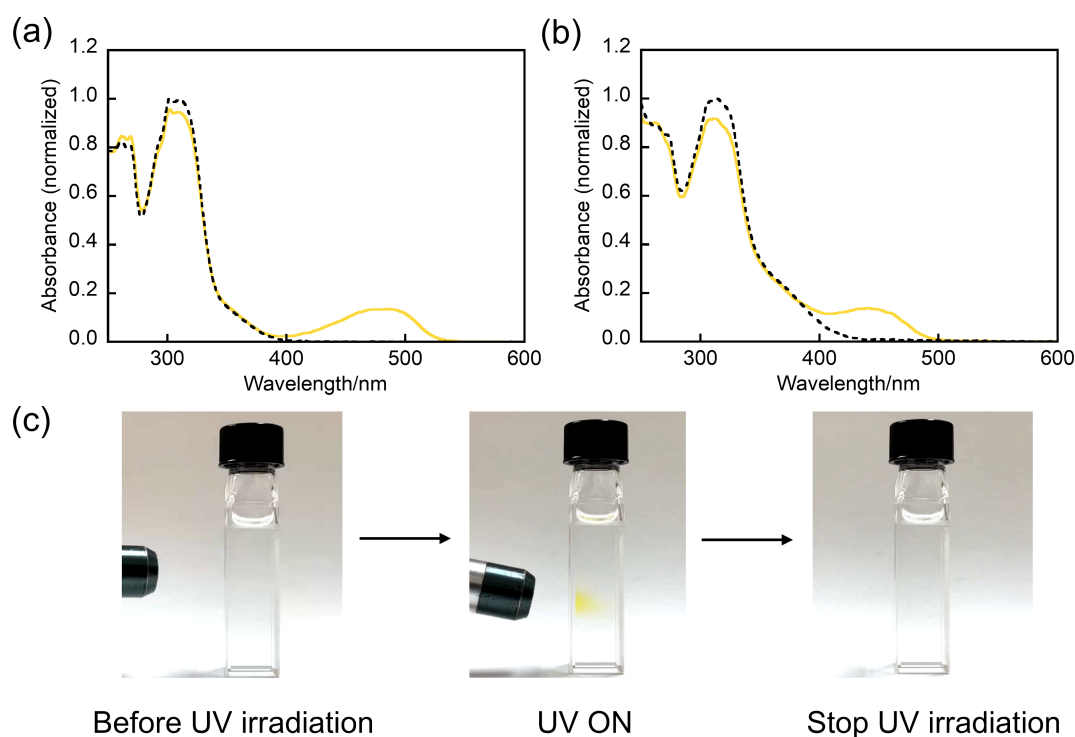


Figure 1: Absorption spectral changes of (a) **N3** and (b) **I3** in *n*-hexane at 253 K for **N3** and 203 K for **I3**: open-ring isomer (black line) and under irradiation at 365 nm (yellow line). (c) Photochromic reaction of **N4** in *n*-hexane at room temperature ($[\text{N4}] = 7.0 \times 10^{-4} \text{ M}$).

the open-ring and closed-ring isomers. The absorption band in the visible region disappeared and returned to the initial one by stopping UV light irradiation. These results indicate that all molecules exhibit T-type photochromic reactions based on 6 π aza-electrocyclic reaction. The absorption bands of compounds **I1(c)**–**I4(c)** are blue-shifted compared to **N1(c)**–**N4(c)**, which is due to the localization of the π conjugation in the central part of the molecular skeleton as reported in inverse-type diarylethenes [64]. Figure 1c and the video (Supporting Information File 2) show the photochromic behavior of **N4** at room temperature in *n*-hexane. It was confirmed that the colorless solution of **N4(o)** turned yellow upon irradiation with UV light and returned to the

initial color upon removal of the irradiation. The photophysical properties of **N3**, **N4**, and **I1–I4** are summarized in Table 1 together with the data of **N1** and **N2**.

Thermal back reactivity in *n*-hexane

To quantitatively evaluate the thermal back reaction of compounds **N3**, **N4**, and **I1–I4**, we measured the absorbance decay of the close-ring isomer at various temperatures as shown in Figure 2a,d, and Figure S2 in Supporting Information File 1. The absorbance decay curves obeyed the first-order kinetics and the rate constants (k) of the thermal back reactions at various temperatures were determined (Figure 2b,e and Supporting

Table 1: Photophysical properties and activation parameters for the thermal back reaction of compounds **N1–N4** and **I1–I4** in *n*-hexane.

	Open-ring isomer		Closed-ring isomer		$\Delta H^\ddagger$ [kJ mol ^{−1}]	$\Delta S^\ddagger$ [J mol ^{−1} K ^{−1}]	$\Delta G^\ddagger_{(\text{exp})}$ [kJ mol ^{−1}] ^a	k [s ^{−1}] ^a	$t_{1/2}$ [ms] ^a
	λ_{max} [nm]	ϵ [M ^{−1} cm ^{−1}]	λ_{max} [nm]						
N1 ^b	297	25200	522		61	−3.0	62	100	6.8
N2 ^b	300	25200	524		62	−5.2	63	56	12
N3	299	12200	487		57	−25	64	42	17
N4	307	12700	467		64	−4.9	66	20	35
I1	291	47800	447		49	−19	55	1600	0.44
I2	301	22700	454		58	−20	64	38	18
I3	307	12900	440		58	11	55	1700	0.41
I4	369	12700	—		66	9.5	63	59	12

^aAt 298 K. ^bReference [56].

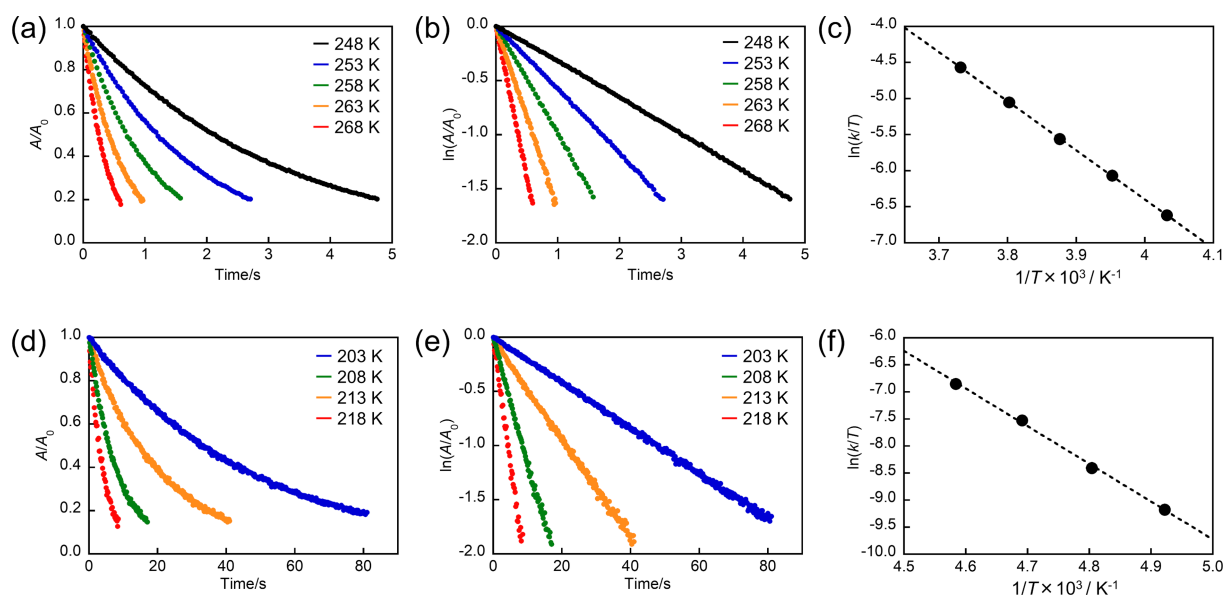


Figure 2: Absorbance decay curves and first-order kinetics profiles for (a,b) **N3** and (d,e) **I3** in *n*-hexane at various temperatures. Absorbance was monitored at λ_{max} . (c) and (f) show Eyring plots for the thermal back reaction of **N3** and **I3**, respectively.

Information File 1, Figure S3 and Tables S1–S6). Figure 2c and 2f, and Figure S4 in Supporting Information File 1 show the temperature dependence of k (Eyring plots) for compounds **N3**, **N4**, and **I1–I4**. The activation enthalpy ($\Delta H^\ddagger$) and activation entropy ($\Delta S^\ddagger$) in the thermal reaction were determined from the intercept and slope. Using these values, the experimental activation free energy ($\Delta G^\ddagger_{\text{(exp)}}$), the k value, and the half-life ($t_{1/2}$) at 298 K were calculated and the results are summarized in Table 1 with the data of **N1** and **N2**. The $\Delta G^\ddagger_{\text{(exp)}}$ values of **N3**, **N4**, and **I1–I4** were 64, 66, 55, 64, 55, and 63 kJ mol^{−1}, respectively. The $t_{1/2}$ values of **N3**, **N4**, and **I1–I4** were 17, 35, 0.44, 18, 0.41, and 12 ms, respectively, indicating that the compounds **N3**, **N4**, and **I1–I4** have fast thermal back reactivities on the order of sub-ms to ms as well as **N1** and **N2**. These thermal back reaction rates are comparable to those of diarylbenzene derivatives, hexaarylbiimidazole derivatives, and naphthopyran derivatives, which are known as fast T-type molecules [41,65,66].

Investigating the $\Delta H^\ddagger$ and $\Delta S^\ddagger$ values from the viewpoint of substitution position, when the aryl group is phenylthiophene (**N1** and **I1**) or phenylthiazole (**N2** and **I2**), both the $\Delta H^\ddagger$ and the $\Delta S^\ddagger$ values decreased by the change of the substitution position of the aryl group from **N** to **I**. In contrast, when the aryl group is benzothiophene (**N3** and **I3**) or benzofuran (**N4** and **I4**), the $\Delta H^\ddagger$ values were almost the same, but the $\Delta S^\ddagger$ values became larger and took positive values by the change of the substitution position of the aryl group from **N** to **I**. Furthermore, comparing the $\Delta G^\ddagger_{\text{(exp)}}$ and the $t_{1/2}$ values, when the aryl group is phenylthiophene (**N1** and **I1**) or benzothiophene (**N3** and **I3**), the $\Delta G^\ddagger_{\text{(exp)}}$ value decreased and the $t_{1/2}$ became shorter by the change of the substitution position of the aryl group from **N** to **I**. On the other hand, when the aryl group is phenylthiazole (**N2** and **I2**) or benzofuran (**N4** and **I4**), the $\Delta G^\ddagger_{\text{(exp)}}$ and the $t_{1/2}$ values were almost similar regardless of the substitution posi-

tion of the aryl group. At the present time, there is no clear answer that can explain how the substitution position affects these values, but our results indicate that the substitution position of the aryl group can affect the thermal back reactivity of aza-diarylethenes, which is a valuable information for the molecular design to modulate the thermal back reactivity of aza-diarylethenes.

Quantum chemical calculations

Based on the thermal back reactivity of aza-diarylethenes described above, we explored the most suitable functional that well reproduces the $\Delta G^\ddagger_{\text{(exp)}}$ values in DFT calculations. According to the previous studies on the prediction of the thermal back reactivity of diarylethene and diarylbenzene derivatives using DFT calculations, we performed geometry optimizations and harmonic frequency calculations of the closed-ring isomer and transition state for **N1–N4** and **I1–I4** using various functionals in combination with a 6-31G(d) basis set. The theoretical activation free energy ($\Delta G^\ddagger_{\text{(calc)}}$) at 298 K was determined as the difference in the sum of electronic energy and thermal free energy correction between the closed-ring isomer and the transition state (see Tables S7–S14 in Supporting Information File 1). Table 2 shows the differences in $\Delta G^\ddagger$ between the theoretical value obtained by DFT calculations and the experimental value, i.e., $\Delta G^\ddagger_{\text{(calc)}} - \Delta G^\ddagger_{\text{(exp)}}$. The B3LYP and M05 functionals underestimated the $\Delta G^\ddagger$ value, while the BMK, CAMB3LYP, M05-2X, M06-2X, and ω B97X-D functionals overestimated the $\Delta G^\ddagger$ value. Moreover, it was found that when M06 and MPW1PW91 were used as functionals, the theoretical values well reproduced the experimental values for all compounds. The errors between $\Delta G^\ddagger_{\text{(calc)}}$ and $\Delta G^\ddagger_{\text{(exp)}}$ values were within 6.6 kJ mol^{−1} and the mean absolute error is within 3.76 kJ mol^{−1}. This value is comparable to those described in previous studies [58–60,62,63]. The difference between $\Delta G^\ddagger_{\text{(calc)}}$ and $\Delta G^\ddagger_{\text{(exp)}}$ values is visualized in Figure 3. Thus, we

Table 2: The differences in $\Delta G^\ddagger$ between the theoretical value by DFT calculations and the experimental value (in kJ mol^{−1}).

	N1	N2	N3	N4	I1	I2	I3	I4	MAE ^a	RMSE ^b
B3LYP	−9.29	−7.15	−8.76	−12.7	−15.2	−15.4	−13.6	−14.4	12.0	77.0
BMK	12.7	14.6	14.4	5.51	7.34	7.99	6.95	10.1	9.94	55.0
CAMB3LYP	5.43	7.96	7.89	3.47	3.48	3.86	5.66	6.99	5.59	17.2
M05	−9.22	−7.07	−9.31	−13.3	−12.9	−13.5	−9.27	−9.95	10.6	58.3
M06	0.00644	3.15	−1.78	−5.59	−6.60	−5.91	−3.04	−4.02	3.76	9.27
M05-2x	6.39	9.66	7.09	4.62	5.15	3.09	7.14	7.79	6.37	22.1
M06-2x	5.85	8.94	7.32	2.70	4.30	3.42	7.39	8.11	6.00	20.3
MPW1PW91	−0.710	1.98	−0.744	−3.53	−6.16	−6.00	−2.79	−3.92	3.23	7.16
ω B97X-D	7.41	10.5	8.61	3.84	7.11	7.10	9.35	10.3	8.03	34.3

^aMAE : Mean absolute error. ^bRMSE : Root mean squared error.

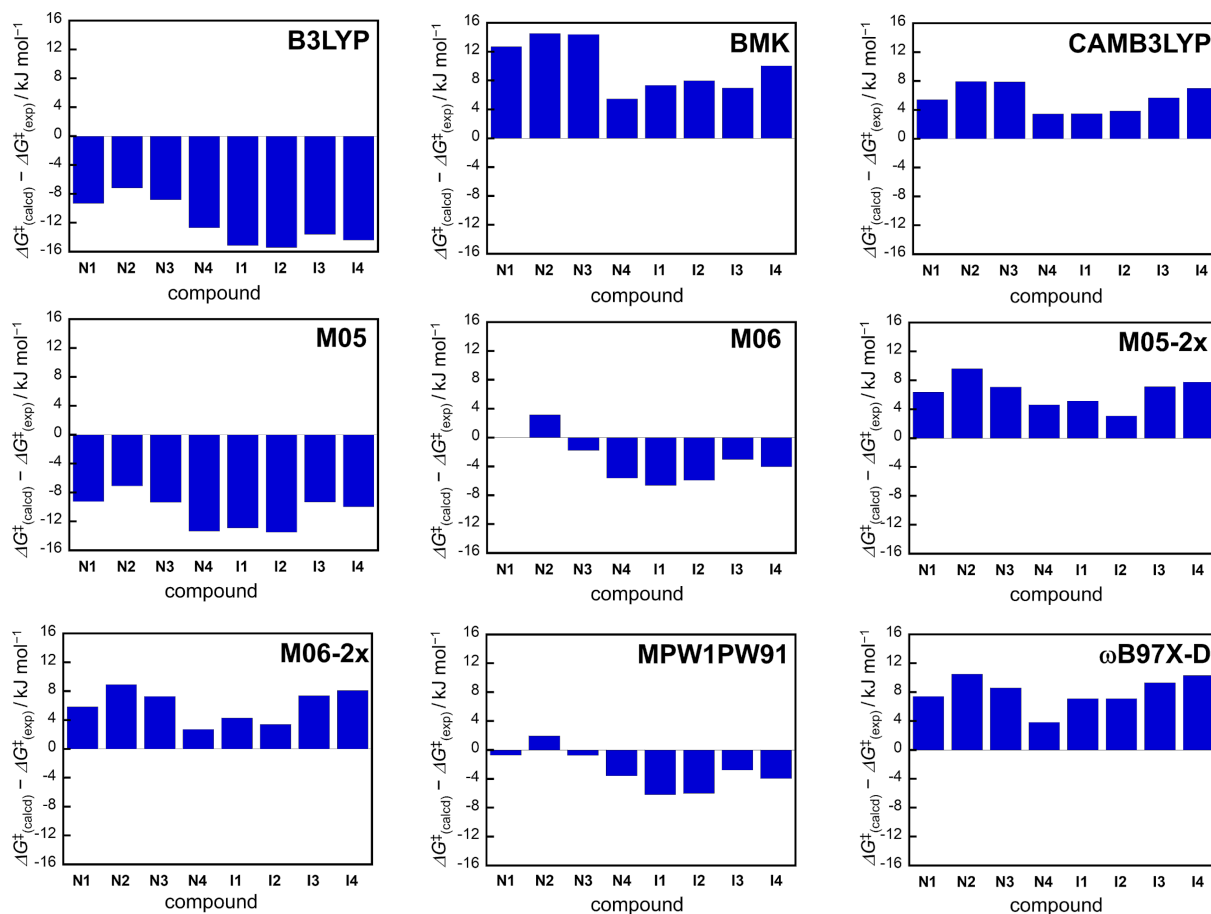


Figure 3: Visualization of the difference between $\Delta G^\ddagger_{(\text{calcd})}$ and $\Delta G^\ddagger_{(\text{exp})}$ for **N1–N4** and **I1–I4** by calculation using various functionals.

have found functionals that allow more accurate prediction of the thermal back reactivity of aza-diarylethenes.

Conclusion

In this study, we investigated the photochromic properties and thermal back reactivities of compounds **N1–N4** and **I1–I4** in *n*-hexane. All molecules exhibited T-type photochromic reactions through 6π aza-electrocyclic reactions, with significant changes in the absorption spectra upon UV irradiation. Notably, compound **N4** turns bright yellow under UV light, adding a new color to the photochromic reaction of azadiarylethenes. The analysis of the thermal back reaction revealed activation parameters and highlighted the influence of the substitution position of the aryl group on thermal reactivity, providing a foundation for future molecular modifications. Furthermore, DFT calculations identified M06 and MPW1PW91 as the most suitable functionals for accurately predicting the thermal back reactivity of aza-diarylethenes, achieving a high correlation with experimental values. These results contribute to the design of ad-

vanced photochromic materials with tailored thermal and photo-physical properties.

Experimental

General

Commercially available reagents were used as received for the syntheses. Solvents used for spectroscopy were of spectroscopic grade or purified by distillation before use. ^1H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded on a Bruker AV-300N spectrometer with tetramethylsilane (TMS) as the internal standard. High-resolution mass spectra (HRMS) were measured on a JEOL AccTOF LC mass spectrometer. UV–vis absorption spectra were recorded using a JASCO V-560 absorption spectrometer or an Ocean Optics FLAME-S multichannel analyzer. Photoirradiation (365 nm) to solution samples was carried out using a 200 W mercury–xenon lamp (MORITEX MSU-6) with a band-pass filter or a 365 nm UV-LED lamp (Keyence UV-400) as a light source. The solution samples were not degassed. The temperature control for

UV–vis absorption spectral measurements was carried out using a UNISOKU CoolSpek UV/CD or an Ocean Optics CUV-QPOD.

Material

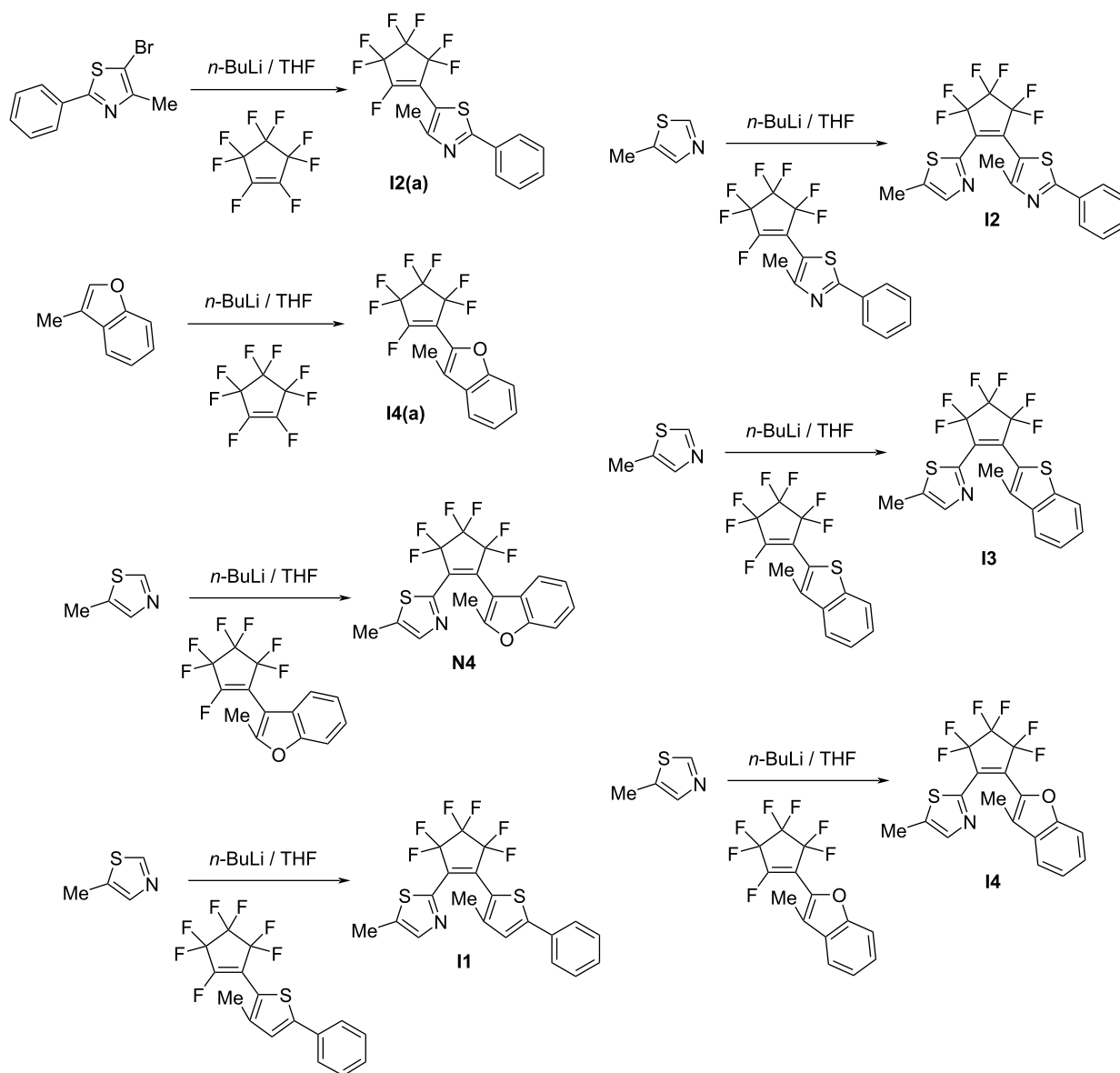
Synthesis of compounds **N4** and **I1–I4**

The synthesis of the compounds is shown in Scheme 2.

4-Methyl-5-(perfluorocyclopent-1-en-1-yl)-2-phenylthiazole (**I2(a)**)

Compound **I2(a)** was synthesized in a manner similar to a procedure from [67]. 5-Bromo-4-methyl-2-phenylthiazole (2.0 g, 7.9 mmol) was dissolved in anhydrous THF (200 mL) under argon atmosphere. A 1.6 M *n*-BuLi hexane solution

(5.4 mL, 8.7 mmol) was slowly added dropwise to the solution at -78°C , and the mixture was refluxed for 20 min. Perfluorocyclopentene (1.2 mL, 8.7 mmol) was added, and the mixture was stirred for 2 h. An adequate amount of distilled water was added to the mixture to quench the reaction. The reaction mixture was neutralized by an aqueous HCl solution, extracted with ether, washed with brine, dried over MgSO_4 , filtered, and concentrated in vacuo. The crude product was purified by column chromatography on silica gel using *n*-hexane and ethyl acetate 95:5 to give 1.4 g of **I2(a)** in 50% yield. ^1H NMR (300 MHz, CDCl_3 , TMS) δ = 2.55 (d, J_{HF} = 3.2 Hz, 3H, CH_3), 7.45–7.50 (m, 3H, aromatic H), 7.93–7.97 (m, 2H, aromatic H); ^{13}C NMR (75 MHz, CDCl_3) δ = 17.25, 17.31, 111.87, 126.93,



Scheme 2: Synthetic route to aza-diarylethenes **N4** and **I1–I4**.

129.29, 131.31, 132.62, 157.67, 171.07, 171.09; HRMS–DART+ (m/z): $[M + H]^+$ calcd for $C_{15}H_9F_7NS^+$, 368.0344; found, 368.0350.

3-Methyl-2-(perfluorocyclopent-1-en-1-yl)benzofuran (I4(a)). Compound **I4(a)** was synthesized in a manner similar to a procedure from [56]. 3-Methylbenzofuran (2.0 g, 15 mmol) was dissolved in anhydrous THF (200 mL) under argon atmosphere. A 1.6 M *n*-BuLi hexane solution (10 mL, 17 mmol) was slowly added dropwise to the solution at -78°C , and the mixture was refluxed for 40 min. Perfluorocyclopentene (2.2 mL, 17 mmol) was added, and the mixture was stirred for 5 h. An adequate amount of distilled water was added to the mixture to quench the reaction. The reaction mixture was neutralized by HCl aqueous solution, extracted with ether, washed with brine, dried over MgSO_4 , filtered, and concentrated in vacuo. The crude product was purified by column chromatography on silica gel using *n*-hexane to give 2.8 g of **I4(a)** in 56% yield. ^1H NMR (300 MHz, CDCl_3 , TMS) δ = 2.42 (s, 3H, CH_3), 7.29–7.34 (m, 1H, aromatic H), 7.40–7.46 (m, 1H, aromatic H), 7.49–7.53 (m, 1H, aromatic H), 7.59–7.62 (m, 1H, aromatic H); ^{13}C NMR (75 MHz, CDCl_3) δ = 8.78, 8.81, 8.86, 8.90, 111.83, 120.64, 122.65, 122.70, 123.54, 127.61, 129.11, 137.03, 137.12, 155.39, 155.41; HRMS–DART+ (m/z): $[M + H]^+$ calcd for $C_{14}H_8F_7OS^+$, 325.0463; found, 325.0467.

1-(5-Methylthiazol-2-yl)-2-(2-methylbenzo[*b*]furan-3-yl)perfluorocyclopentene (N4). Compound **N4** was synthesized in a manner similar to a procedure from [56]. 5-Methylthiazole (0.20 g, 2.1 mmol) was dissolved in anhydrous THF (30 mL) under argon atmosphere. A 1.6 M *n*-BuLi hexane solution (1.4 mL, 2.3 mmol) was slowly added dropwise to the solution at -78°C , and the mixture was refluxed for 40 min. 2-Methyl-3-(perfluorocyclopent-1-en-1-yl)benzofuran [68] (0.73 g, 2.3 mmol) dissolved in THF (5 mL) was added, and the mixture was stirred for 2 h. An adequate amount of distilled water was added to the mixture to quench the reaction. The reaction mixture was neutralized by HCl aqueous solution, extracted with ether, washed with brine, dried over MgSO_4 , filtered, and concentrated in vacuo. The crude product was purified by column chromatography on silica gel using *n*-hexane and ethyl acetate 8:2 and recycling HPLC using chloroform as the eluent to give 0.49 g of **N4** in 61% yield. ^1H NMR (300 MHz, CDCl_3 , TMS) δ = 2.38 (s, 3H, CH_3), 2.39 (s, 3H, CH_3), 7.21–7.36 (m, 3H, aromatic H), 7.51–7.54 (m, 1H, aromatic H), 7.21–7.36 (m, 3H, aromatic H), 7.66–7.67 (m, 1H, aromatic H); ^{13}C NMR (75 MHz, CDCl_3) δ = 11.9, 13.3, 104.0, 111.4, 119.7, 123.8, 125.0, 126.6, 139.9, 142.8, 152.3, 155.0, 155.9; HRMS–DART+ (m/z): $[M + H]^+$ calcd for $C_{18}H_{12}F_6\text{NOS}^+$ 404.0543; found, 404.0550.

1-(5-Methylthiazol-2-yl)-2-(3-methyl-5-phenylthiophen-2-yl)perfluorocyclopentene (I1). Compound **I1** was synthesized in a manner similar to a procedure from [56]. 5-Methylthiazole (0.27 g, 2.7 mmol) was dissolved in anhydrous THF (20 mL) under argon atmosphere. A 1.6 M *n*-BuLi hexane solution (1.9 mL, 3.1 mmol) was slowly added dropwise to the solution at -78°C , and the mixture was refluxed for 30 min. 3-Methyl-2-(perfluorocyclopent-1-en-1-yl)-5-phenylthiophene [69] (1.0 g, 2.7 mmol) dissolved in THF (8 mL) was added, and the mixture was stirred for 2 h. An adequate amount of distilled water was added to the mixture to quench the reaction. The reaction mixture was neutralized by an aqueous HCl solution, extracted with ether, washed with brine, dried over MgSO_4 , filtered, and concentrated in vacuo. The crude product was purified by column chromatography on silica gel using *n*-hexane and ethyl acetate 8:2 and recycling HPLC using chloroform as the eluent to give 0.68 g of **I1** in 56% yield. ^1H NMR (300 MHz, CDCl_3 , TMS) δ = 2.09 (s, 3H, CH_3), 2.46 (s, 3H, CH_3), 7.27 (s, 1H, aromatic H), 7.35–7.45 (m, 3H, aromatic H), 7.62–7.66 (m, 2H, aromatic H), 7.70–7.71 (m, 1H, aromatic H); ^{13}C NMR (75 MHz, CDCl_3) δ = 12.1, 15.0, 119.3, 126.0, 126.8, 128.7, 129.2, 133.2, 140.3, 141.8, 142.9, 148.6, 152.6. HRMS–DART+ (m/z): $[M + H]^+$ calcd for $C_{20}H_{14}F_6\text{NS}_2^+$, 446.0472; found, 446.0480.

1-(5-Methylthiazol-2-yl)-2-(4-methyl-2-phenyl-5-thiazol-yl)perfluorocyclopentene (I2). Compound **I2** was synthesized in a manner similar to a procedure from [56]. 5-Methylthiazole (0.24 g, 2.4 mmol) was dissolved in anhydrous THF (30 mL) under argon atmosphere. A 1.6 M *n*-BuLi hexane solution (1.5 mL, 2.4 mmol) was slowly added dropwise to the solution at -78°C , and the mixture was refluxed for 30 min. 4-Methyl-5-(perfluorocyclopent-1-en-1-yl)-2-phenylthiazole (0.80 g, 2.2 mmol) dissolved in THF (5 mL) was added, and the mixture was stirred for 4 h. An adequate amount of distilled water was added to the mixture to quench the reaction. The reaction mixture was neutralized by an aqueous HCl solution, extracted with ether, washed with brine, dried over MgSO_4 , filtered, and concentrated in vacuo. The crude product was purified by column chromatography on silica gel using *n*-hexane and ethyl acetate 8:2 and recycling HPLC using chloroform as the eluent to give 0.39 g of **I2** in 41% yield. ^1H NMR (300 MHz, CDCl_3 , TMS) δ = 2.31 (s, 3H, CH_3), 2.47 (s, 3H, CH_3), 7.47–7.51 (m, 3H, aromatic H), 7.72 (q, 1H, aromatic H), 7.98–8.01 (m, 2H, aromatic H); ^{13}C NMR (75 MHz, CDCl_3) δ = 12.1, 16.4, 114.8, 126.9, 129.3, 131.2, 132.8, 140.6, 143.2, 155.8, 171.2; HRMS–DART+ (m/z): $[M + H]^+$ calcd for $C_{19}H_{13}F_6\text{N}_2\text{S}_2^+$, 447.0424; found, 447.0430.

1-(5-Methylthiazol-2-yl)-2-(3-methylbenzo[*b*]thiophen-2-yl)perfluorocyclopentene (I3). Compound **I3** was synthesized

in a manner similar to a procedure from [56]. 5-Methylthiazole (0.36 g, 3.6 mmol) was dissolved in anhydrous THF (30 mL) under argon atmosphere. A 1.6 M *n*-BuLi hexane solution (2.3 mL, 3.6 mmol) was slowly added dropwise to the solution at -78°C , and the mixture was refluxed for 1 h. 3-Methyl-2-(perfluorocyclopent-1-en-1-yl)benzo[*b*]thiophene [69] (1.1 g, 3.6 mmol) dissolved in THF (5 mL) was added, and the mixture was stirred for 1 h. An adequate amount of distilled water was added to the mixture to quench the reaction. The reaction mixture was neutralized by an aqueous HCl solution, extracted with ether, washed with brine, dried over MgSO_4 , filtered, and concentrated in vacuo. The crude product was purified by column chromatography on silica gel using *n*-hexane and ethyl acetate 9:1 and recycling HPLC using chloroform as the eluent to give 0.83 g of **I3** in 60% yield. ^1H NMR (300 MHz, CDCl_3 , TMS) δ = 2.29 (s, 3H, CH_3), 2.39 (s, 3H, CH_3), 7.48–7.51 (m, 2H, aromatic H), 7.69–7.70 (m, 1H, aromatic H), 7.80–7.84 (m, 1H, aromatic H), 7.92–7.95 (m, 1H, aromatic H); ^{13}C NMR (75 MHz, CDCl_3) δ = 12.0, 12.8, 120.8, 122.9, 123.2, 124.8, 126.2, 135.9, 139.7, 140.7, 141.1, 142.9, 152.3; HRMS–DART+ (m/z): $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{18}\text{H}_{12}\text{F}_6\text{NS}_2^+$, 420.0315; found, 420.0314.

1-(5-Methylthiazol-2-yl)-2-(2-methylbenzofuran-2-yl)perfluorocyclopentene (I4). Compound **I4** was synthesized in a manner similar to a procedure from [56]. 5-Methylthiazole (0.38 g, 3.8 mmol) was dissolved in anhydrous THF (30 mL) under argon atmosphere. A 1.6 M *n*-BuLi hexane solution (2.6 mL, 4.2 mmol) was slowly added dropwise to the solution at -78°C , and the mixture was refluxed for 30 min. 3-Methyl-2-(perfluorocyclopent-1-en-1-yl)benzofuran (1.4 g, 4.2 mmol) dissolved in THF (5 mL) was added, and the mixture was stirred for 4 h. An adequate amount of distilled water was added to the mixture to quench the reaction. The reaction mixture was neutralized by an aqueous HCl solution, extracted with ether, washed with brine, dried over MgSO_4 , filtered, and concentrated in vacuo. The crude product was purified by column chromatography on silica gel using *n*-hexane and ethyl acetate 8:2 and recycling HPLC using chloroform as the eluent to give 0.49 g of **I4** in 31% yield. ^1H NMR (300 MHz, CDCl_3 , TMS) δ = 2.20 (s, 3H, CH_3), 2.49 (s, 3H, CH_3), 7.33–7.36 (m, 1H, aromatic H), 7.41–7.56 (m, 1H, aromatic H), 7.49–7.52 (m, 1H, aromatic H), 7.60–7.63 (m, 1H, aromatic H), 7.70 (q, J = 1.1 Hz, 1H, aromatic H); ^{13}C NMR (75 MHz, CDCl_3) δ = 9.3, 12.0, 111.9, 120.6, 122.5, 123.4, 127.1, 129.3, 139.0, 140.0, 143.0, 152.3, 155.6. HRMS–DART+ (m/z): $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{18}\text{H}_{12}\text{F}_6\text{NOS}^+$, 404.0544; found, 404.0550.

Theoretical calculations

DFT calculations were performed in a manner similar to procedures from [58]. Geometry optimizations and frequency calcu-

lations of closed-ring isomers (closed) and transition states (TS) were carried out using Gaussian 16 Rev. C.01 program package. The TS structure was optimized using Opt = TS keyword with Berny algorithm. To obey unrestricted Kohn–Sham solution, the broken-symmetry guess was generated and followed using the keyword Guess (mix, always). The frequency calculation for the TS was carried out to confirm that there is only one imaginary frequency corresponding to the stretching vibration between the nitrogen and the carbon atoms at the reactive site. The frequency calculation for closed-ring isomers was carried out to confirm that there is no imaginary frequencies. Various functionals (B3LYP, BMK, CAMB3LYP, M05, M06, M05-2X, M06-2X, MPW1PW91, and $\omega\text{B97X-D}$) in combination with a 6-31G(d) basis set were used for the calculations.

Supporting Information

Supporting Information File 1

Experimental details and analyses of thermal back reactions.

[<https://www.beilstein-journals.org/bjoc/content/supplementary/1860-5397-21-16-S1.pdf>]

Supporting Information File 2

Movie for photochromic behavior of **N4**.

[<https://www.beilstein-journals.org/bjoc/content/supplementary/1860-5397-21-16-S2.mp4>]

Supporting Information File 3

Cartesian coordinates in DFT calculations.

[<https://www.beilstein-journals.org/bjoc/content/supplementary/1860-5397-21-16-S3.xlsx>]

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Data Availability Statement

All data that supports the findings of this study is available in the published article and/or the supporting information of this article.

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Synthesis and photoinduced switching properties of C₇-heteroatom containing push–pull norbornadiene derivatives

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Full Research Paper

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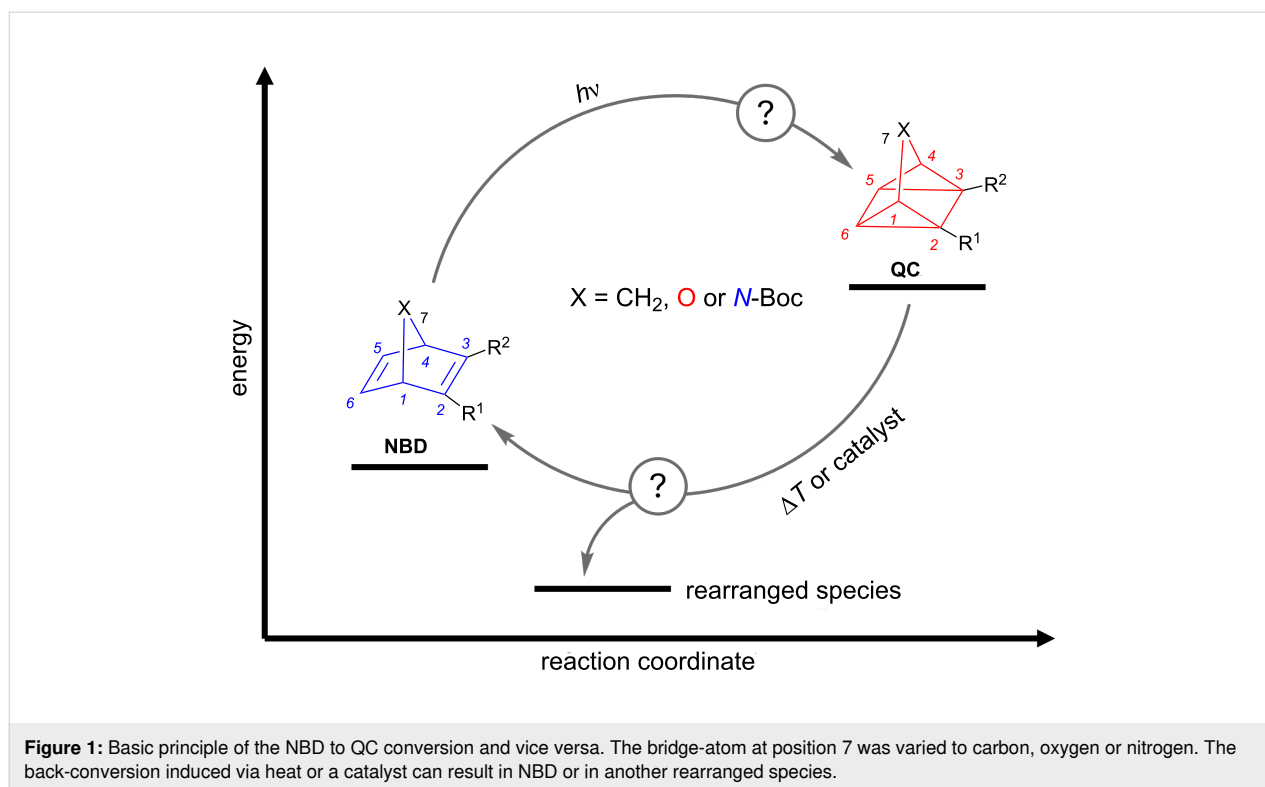
Abstract

We report the synthesis and characterization of heteroatom-incorporated norbornadiene (NBD) derivatives. Push–pull substitution on the 2 and 3 position as well as introduction of oxygen or nitrogen at position 7 of the NBD scaffold have led to the development of a new family of photoswitches. We studied the potential conversion of norbornadiene to quadricyclane (QC) isomers. As main investigation tools, UV–vis and NMR spectroscopy were utilized. We determined significant spectral features of the formed NBD species, including λ_{max} and λ_{onset} values, all of which exhibit redshifts compared to their isocyclic counterparts. Additionally, the selected QC isomers were subjected to thermal and catalytic back-conversion studies.

Introduction

In recent decades, the demand for renewable energy has increased tremendously [1]. A promising alternative to fossil fuels is the utilization of so-called molecular solar thermal (MOST) systems [2]. These systems operate on the principle of converting an energy-lean isomer into an energy-rich form by irradiating it with sunlight, effectively storing energy in the form of chemical strain energy [3]. On demand, by application of an external stimulus such as heat, catalysis, or an electrochemical input [4–6], the stored energy can be released

converting the molecule back in the parent form (Figure 1). Typical MOST systems are azobenzenes (*E/Z*-isomerization) [7–10], the isomerization of dihydroazulenes/vinylheptafulvenes [11–13], conversion of azaborines [14,15] to the corresponding Dewar isomer and the norbornadiene/quadricyclane (NBD/QC) couple [16–18]. Notably, the NBD/QC couple exhibits characteristics superior to those of the other mentioned photoswitches, including the highest energy storage density [19]. For MOST systems, it is essential not only to achieve a



high storage density and good quantum efficiency for the isomerization process but also to ensure large half-lives and durability in switching reliability [20]. By making structural adjustments to the parent carbon scaffold, it is possible to target specific variations in the switching properties. However, it is important to note that altering one property typically impacts other characteristics as well [21,22].

In this regard, both the substitution of the NBD periphery to produce push–pull derivatives and the variation of the central scaffold itself have been explored. For instance, incorporation of a C_2H_4 moiety into the bridge led to the formation of [2.2.2]-bicyclooctadiene derivatives with increased storage capacities but significantly reduced half-lives compared to analogues NBD derivatives [23,24]. Additionally, introduction of one or more heteroatoms at various positions of the NBD scaffold were envisioned, although such modifications have primarily been investigated theoretically thus far [25–28]. Recently, high-throughput calculations were conducted to screen a wide array of hetero-substituted NBD species. These studies predominantly considering the carbon-based scaffold as superior regarding their properties, while also highlighting some unique properties exhibited by heterocyclic derivatives [21].

C_7 -substituted NBD species have been scarcely investigated in terms of their switching behavior but have been employed as synthetic intermediates in total [29,30] and bio-synthesis proto-

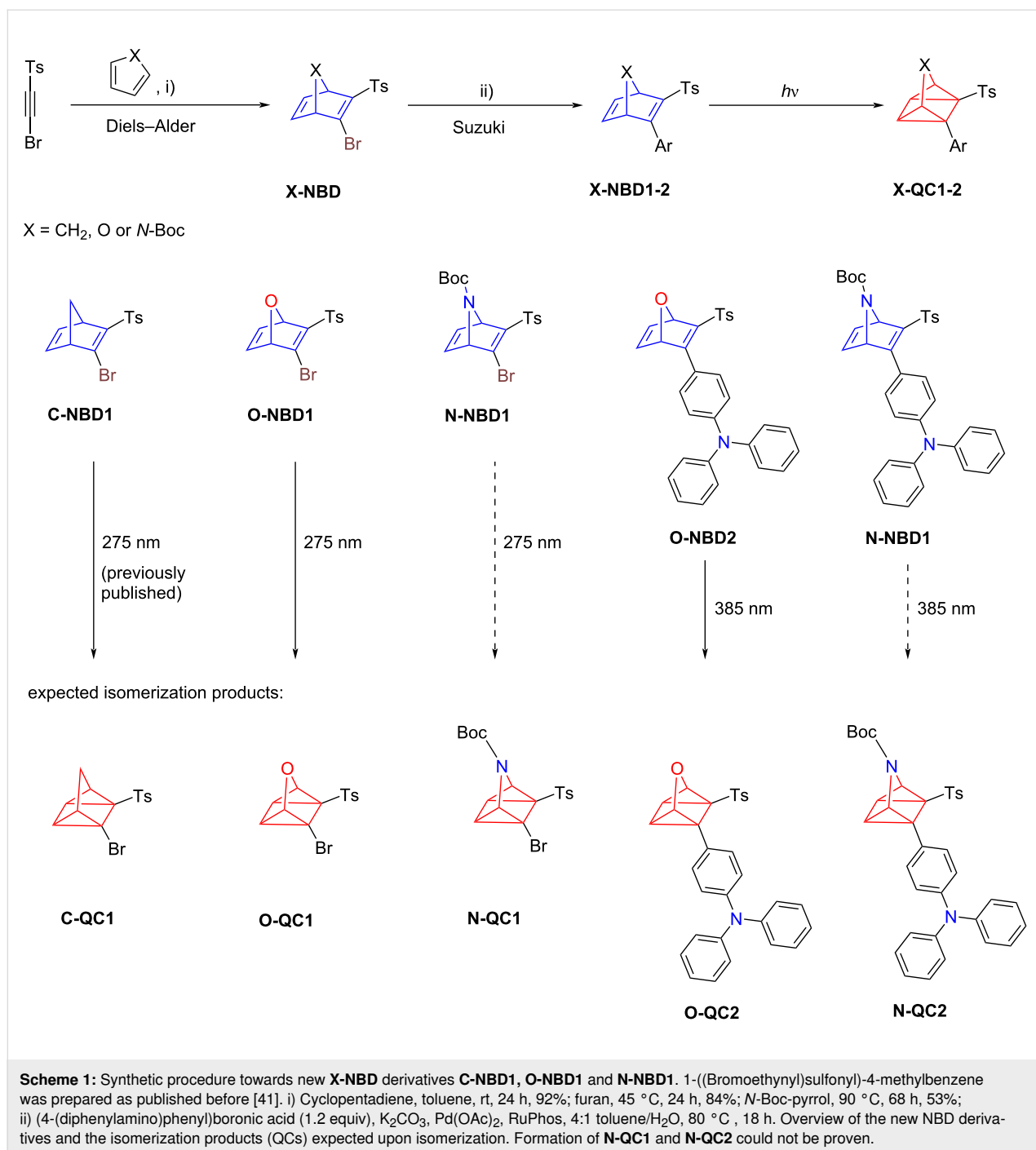
cols [31], e.g., in inositol chemistry [32] or towards aminocyclitols [33]. The potential of these compounds as functional photo-switches was primarily assessed in the 1960s and 1970s by Prinzbach and co-workers, who identified a variety of rearrangement products alongside the formation of the desired QCs [32,34–38]. Despite this, the focus has largely been on symmetrical 2,3-substituted derivatives, with reports primarily on the reversible isomerization of oxa-NBD to oxa-QC derivatives [39].

Asymmetrical push–pull derivatives have received little attention in the literature, with investigations largely limited to forward conversions [35]. Here, we present 2,3-heteroatom-incorporated NBD derivatives and compare their properties with those of previously published isocyclic derivatives. By utilizing push–pull functionalization and incorporating larger heteroatoms in the bridge moiety, we anticipate a bathochromic shift that would facilitate absorption match with the solar emission spectrum.

Results and Discussion

Synthesis

The library of new heterocyclic NBD molecules synthesized and investigated in this study is presented in Scheme 1. Starting with 1-((bromoethynyl)sulfonyl)-4-methylbenzene, which was previously prepared and characterized [40,41], Diels–Alder reaction with either cyclopentadiene, furan or Boc-protected



pyrrol, resulted in the NBD precursors **C-NBD1**, **O-NBD1** and **N-NBD1**, respectively [31,42]. With these precursors in hand a subsequent Suzuki cross-coupling reaction with (4-(diphenylamino)phenyl)boronic acid was performed. The reaction conditions were adapted from prior experiments with **C-NBD1** [40] and further refined for the heterocyclic analogues. Optimal results were achieved using K₂CO₃, Pd(OAc)₂ and RuPhos with the corresponding boronic acid in a degassed toluene/H₂O mixture (4:1, v/v) which was heated to 80 °C for 18 h (for detailed

information see Supporting Information File 1). Using the described procedure, the oxygen containing derivatives **O-NBD2** and nitrogen substituted **N-NBD2** were successfully synthesized (Scheme 1, bottom). In contrast to the previously synthesized large library carbon-based NBDs [40], only a few heterocyclic derivatives were successfully isolated. During the monitoring of additional reactions attempting to reproduce the literature scope, in most cases traces of new NBD species were observed. However, purification was not possible. Furthermore, an

alternative commonly used synthetic strategy involving the Diels–Alder reaction of a pre-functionalized push–pull acetylene with furan or pyrrol derivatives proved unsuccessful [4,43]. All synthesized NBD derivatives were characterized using UV–vis and NMR spectroscopy, as well as high-resolution mass spectrometry. An overview of the synthetic and spectroscopic data for all derivatives is provided in Table 1, while the specific spectroscopic properties of the individual QC analogues can be found in Supporting Information File 1.

Photoswitching

The photoswitching of the NBDs to corresponding QCs was monitored by UV–vis and ^1H NMR spectroscopy. With increasing electronegativity of the bridge-atom, a slight bathochromic shift in the absorption spectra of the parent NBD precursors **O-NBD1** and **N-NBD1** was found (Figure 2a and 2c). For the comparison with the data obtained for **C-NBD1** we refer to previous literature studies [40]. As with **C-NBD1**, clean conversion of **O-NBD1** into the corresponding **O-QC1** was observed upon irradiation at 275 nm. The absorption maximum at $\lambda_{\text{max}} = 278$ nm decreased, correlating with a simultaneous increase in the absorbance of the QC band at $\lambda_{\text{max}} = 229$ nm. The isomerization was completed after 360 s without any indication of photodecomposition. The appearance of isosbestic points demonstrate clean conversion. To further validate these findings, similar irradiation experiments were conducted and monitored by NMR spectroscopy. Upon irradiation at 275 nm, complete formation of **O-QC1** was confirmed after 18 h. A decrease over time of the **O-NBD1** multiplet centered signals at 7.06 ppm, 5.57 ppm and 5.35 ppm assignable to the NBD scaffold can be observed. New multiplet signals at 5.08 ppm, 4.65 ppm, 3.22 ppm and 2.64 ppm belonging to the scaffold of **O-QC1** arise. Further, the singlet signal corresponding to the CH_3 group of the tosyl moiety shifts from 2.45 ppm to 2.47 ppm. A spectrum containing approximately a 45:55 ratio of **O-NBD1**/**O-QC1** can be found after 140 minutes of irradiation (Figure 2b, green).

A different behavior was observed for **N-NBD1** (Figure 2c). In the UV–vis experiments, a decrease in the absorption maximum at $\lambda_{\text{max}} = 289$ nm was noted, accompanied by a significant emergence of a new band at $\lambda_{\text{max}} = 218$ nm. Additionally, either an increase in the baseline at wavelengths longer than 315 nm or the generation of a new absorption band with a maximum around $\lambda_{\text{max}} = 346$ nm was observed. However, the absence of isosbestic points, along with the atypical line shape of the final species after 360 seconds of irradiation, precluded the conclusion of a clean isomerization to **N-QC1**.

The corresponding ^1H NMR experiments reveal two significant signal changes (Figure 2d). First, the CH_3 singlet signal belonging to the tosyl group shifted from 2.44 ppm to 2.45 ppm and began to split into a pseudo-doublet. Second, the singlet signal corresponding to the nine protons of the Boc group at 1.30 ppm vanishes while two new singlet signals at 1.52 ppm and 1.50 ppm are formed, which combined integrate to nine. Due to the inversion of the nitrogen located in the bridge, not only the splitting of the signals, but also the line broadening of the signals corresponding to the NBD scaffold can be explained. Specifically, the multiplet signals at 7.06–6.88 ppm (H^1 and H^2) and 5.22–5.04 ppm as well as the singlet at 5.36 ppm (H^3 and H^4) correspond to the carbon framework of **N-NBD1**. During the experiment, these signals decreased in intensity, and a set of new signals appeared in the aromatic region, alongside a new multiplet signal in the range of 6.15–5.90 ppm. However, due to the lack of new formed aliphatic signals, and in comparison to literature [35], formation of **N-QC1** is very unlikely. Furthermore, additional signals in the region below 2.0 ppm indicate the formation of decomposition products. Studies conducted by Bansal and co-workers [44] revealed the potential formation of aza-QC derivatives at low temperatures. However, isolation of these derivatives proved difficult, as rapid rearrangement to azepine analogues occurred at temperatures exceeding 0 °C. On the basis of the quadricyclane or azepine structure, various light-, heat-, and acid-induced rearrangements have been re-

Table 1: Overview of spectroscopic data of the newly synthesized compounds. The data given for the carbon analogues **C-NBD1** (2-bromo-3-tosylbicyclo[2.2.1]hepta-2,5-diene) and **C-NBD2** (*N,N*-diphenyl-4-(3-tosylbicyclo[2.2.1]hepta-2,5-dien-2-yl)aniline) were previously published [40].

Compound	Yield [%]	λ_{max} (ϵ) ^a [nm]	$\lambda_{\pi-\pi^*}$ (ϵ) ^a [nm]	λ_{onset} ^b [nm]
C-NBD1 ^c	92	269 (6500)	243 (12500)	317
O-NBD1	84	278 (4500)	239 (11200)	343
N-NBD1	53	289 (3800)	240 (11800)	341
C-NBD2 ^c	62	370 (19200)	294 (14000)	452
O-NBD2	29	392 (15600)	295 (14600)	498
N-NBD2	26	393 (17300)	294 (14200)	479

^aExtinction coefficients are given in $\text{M}^{-1}\text{cm}^{-1}$; ^bonset values are defined as $\log(\epsilon) = 2$; ^cdata are provided for easier comparability based on literature [40].

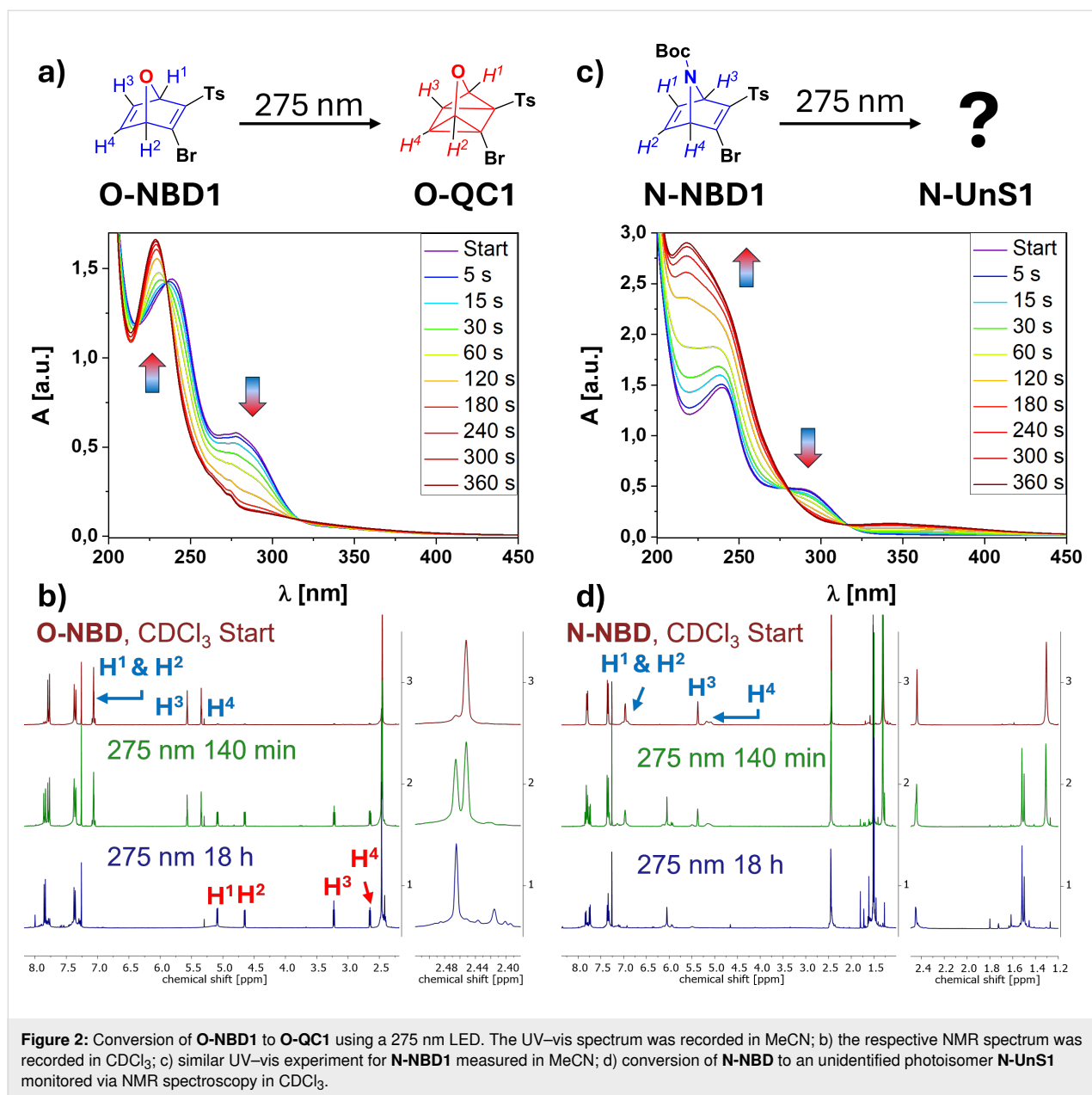


Figure 2: Conversion of **O-NBD1** to **O-QC1** using a 275 nm LED. The UV-vis spectrum was recorded in MeCN; b) the respective NMR spectrum was recorded in CDCl₃; c) similar UV-vis experiment for **N-NBD1** measured in MeCN; d) conversion of **N-NBD** to an unidentified photoisomer **N-UnS1** monitored via NMR spectroscopy in CDCl₃.

ported [35], complicating the distinct structural determination of these compounds. In comparison to published NMR and UV-vis data, formation of neither known species can be assumed with certainty.

Last, through addition of mono-carboxylic acid-Co^{II}-porphyrin (**POR**, see Supporting Information File 1), which was already available within our group [4], regeneration of the parent **N-NBD1** was unsuccessful (Supporting Information File 1). Consequently, the presence of **N-QC1** can be excluded, and the spectroscopic data likely corresponds to an unknown photoisomer (**N-UnS1**). Structural investigations using exhaustive 2D-correlation NMR spectroscopy were also inconclusive.

Next, the push-pull functionalized derivatives **O-NBD2** and **N-NBD2** were investigated. Notably, **N-NBD2** exhibited the most pronounced red shift (Table 1) and was the only nitrogen-containing push-pull derivative that could be synthesized in rather high quantity and purity. Monitoring first the switching process from **O-NBD2** to **O-QC2** by UV-vis spectroscopy showed complete formation of **O-QC2** was achieved after 5 seconds, indicated by the major decrease of the NBD signal at $\lambda_{\text{max}} = 392$ nm and the simultaneous increase of the QC's band at $\lambda_{\text{max}} = 301$ nm accompanied by the presence of isosbestic points (Figure 3). Extended irradiation times resulted in a decrease in the QC signal, accompanied by a slight blue shift and the emergence of a new absorption band at $\lambda_{\text{max}} = 382$ nm,

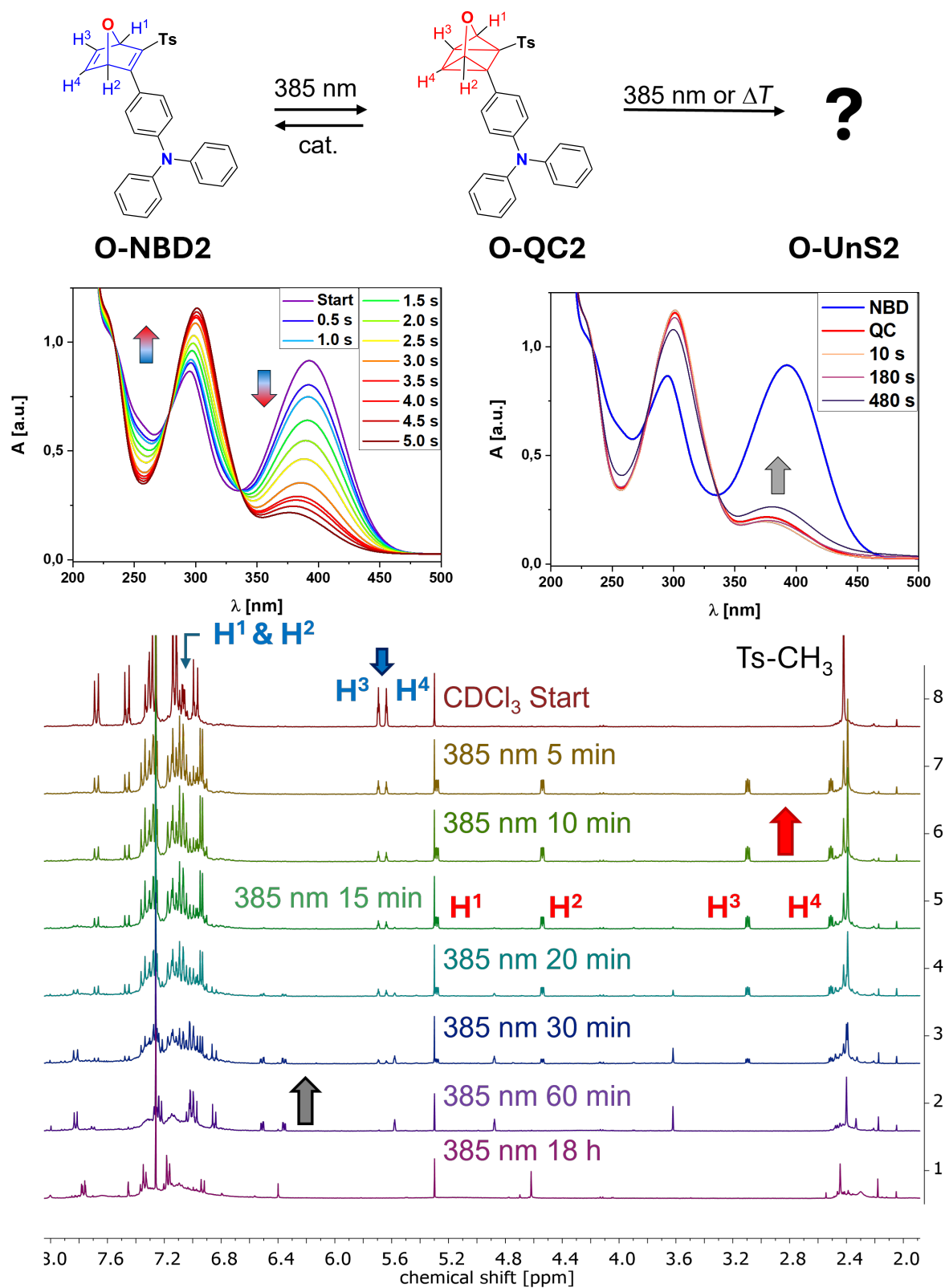


Figure 3: Rearrangement of **O-NBD2** to **O-QC2** using a 385 nm LED. The UV-vis measurement in the middle were conducted in MeCN, NMR spectra at the bottom with 6.9 mg substance in 650 μL CDCl_3 . Prolonged irradiation resulted first in the formation of an unidentified species **O-UnS2** (after 60 min) and further unknown rearrangement combined with photodecomposition after 18 h.

suggesting potential further rearrangements or photodecomposition.

To gain a better understanding of the ongoing conversion processes, we conducted NMR spectroscopy. The assignment of individual proton signals was supported by 2D correlation NMR spectroscopy (Supporting Information File 1). First, **O-NBD2** is characterized by the multiplet signal around 7.07 ppm for the olefinic (H^1 and H^2) and the two pseudo-triplet signals at 5.69 ppm (H^3) and 5.64 ppm (H^4) corresponding to the bridgehead protons. In addition, a sharp singlet signal assigned to the CH_3 protons of the tosyl group is found at 2.42 ppm like for the precursor **O-NBD1**. Upon irradiation at 385 nm, after 15 minutes, approximately 70% of **O-NBD2** are converted to **O-QC2**, indicated by the emerge of new signals at 5.28 ppm, 4.54 ppm, 3.09 ppm and 2.51 ppm, corresponding to H^1 , H^2 , H^3 and H^4 respectively. Furthermore, the CH_3 singlet is shifted to 2.39 ppm. However, after longer irradiation times (60 minutes), the remaining NBD signals, along with the newly formed QC signals, completely vanish, and a new set of signals corresponding to an unidentified species (**O-UnS2**) appears, as already noted during the UV-vis analysis.

Prinzbach, Stusche and Vogel have described a variety of potential rearrangements for oxa-NBD and oxa-QC derivatives [32,34,36,37]. Therefore, in-depth 2D NMR analysis combined with mass spectrometry was attempted to elucidate the structure of **O-UnS2**. Notably, an additional singlet proton signal (integrated as 1 proton) corresponding to the unidentified species was observed, which cannot be present in the structure of **O-QC2**. Further irradiation over 18 hours resulted in additional rearrangements or photodecomposition, which were not analyzed further.

At slightly lower concentrations (5.0 mg substance in 650 μ L $CDCl_3$) quantitative formation of **O-QC2** was achieved after 15 minutes (Supporting Information File 1). Next, thermally induced back-conversion to **Q-NBD2** was attempted by heating the sample to 50 °C overnight. This process resulted in the initial formation of **O-UnS2**, followed by further rearrangement, consistent with the observations made during prolonged irradiation experiments. Due to the thermal instability of **O-QC2** noted during the investigation, kinetic experiments for determining the half-life time $t_{1/2}$ were not conducted. However, the addition of Co^{II} -porphyrin **POR** allowed for the successful regeneration of the parent **O-NBD2** (Supporting Information File 1), demonstrating the intermediate availability of **O-QC2**.

In a similar manner, the aza analogue **N-NBD2** was investigated. The UV-vis experiments (Figure 4) yielded results compa-

rable to those obtained for **N-NBD1**. Initially, the conversion to **N-QC2** is anticipated at short time scales with irradiation at 385 nm, as indicated by a decrease in the NBD signal at $\lambda_{max} = 393$ nm. However, during this initial time segment, no isosbestic points developed, and no distinct new QC signal was detected. Instead, there was a slight redshift and an increase in the previously observed $\pi-\pi^*$ absorption from $\lambda_{\pi-\pi^*} = 294$ nm to 298 nm was found. Prolonged irradiation up to 660 s led to a complete change in the overall absorption properties with maxima at $\lambda = 348$ nm and 297 nm and an absorption shoulder at $\lambda = 228$ nm suggesting photodecomposition.

Next, NMR monitoring of the irradiation experiment was conducted. The signal sets for **N-NBD2** were generally similar to those of **O-NBD2**. As previously described, the possibility of inversion of the nitrogen's lone pair led to significant line broadening, particularly evident in the proton signals of the carbon scaffold near the heteroatom. As an additional significant signal, the singlet at 1.34 ppm corresponding to the nine protons of the Boc group can be found. After 5 minutes of irradiation, the majority of **N-NBD2** is consumed, finished after 15 minutes with the complete generation of a newly formed species. The spectral features were largely consistent with those described for **N-NBD1**, suggesting the formation of a similar unidentified species, designated as **N-UnS2**. Again, comprehensive 2D NMR spectroscopic investigations did not deliver satisfactory results unravelling the structure. Further irradiation first seems to induce no additional spectroscopic changes, while the initially yellow solution turned deep black in the time frame between 15 and 60 minutes (Supporting Information File 1). Prolonged irradiation overnight ultimately resulted in complete photodecomposition, indicated by the absence of significant signals corresponding to either **N-NBD2** and **N-UnS2**. Addition of the previously used Co^{II} -catalyst **POR** did not result in regeneration of the parent **N-NBD2** species strongly excluding the presence of **N-QC2**.

Given the challenges in generating heterocyclic QC derivatives – successfully achieved only for oxa derivatives – the investigation of photophysical key properties for molecular solar thermal (MOST) systems was not pursued at this stage. The limited availability of material, combined with the thermal instability of the formed QC species, precluded the determination of half-lives and storage densities. Additionally, as all NBD to QC conversions were either incomplete due to photodecomposition or led to the formation of additional species, it was not feasible to ascertain isomerization quantum yields.

Conclusion

In summary, we have presented the synthesis and photophysical properties of a library of heterocyclic push-pull NBD deriv-

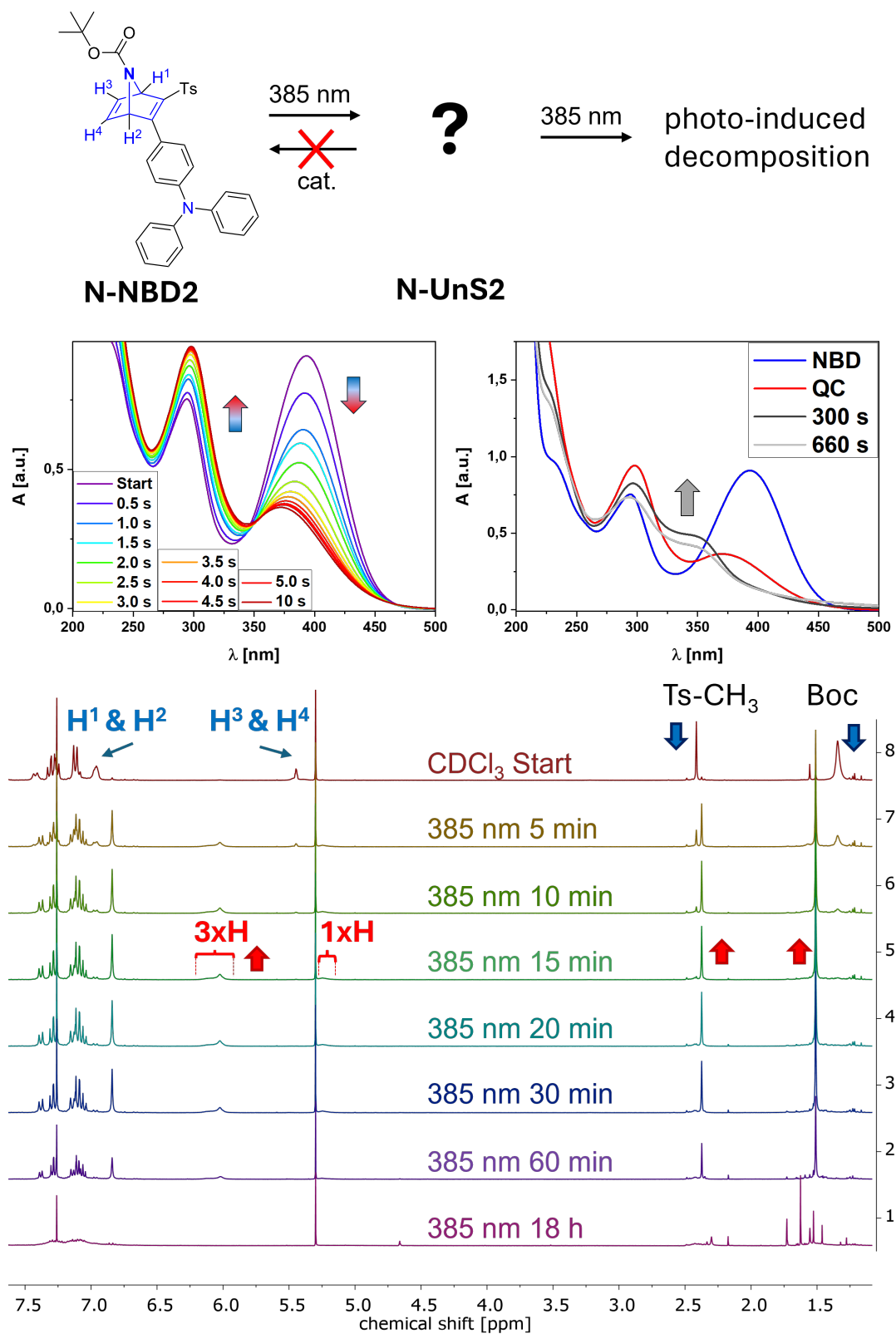


Figure 4: Rearrangement of **N-NBD2** using a 385 nm LED. The UV-vis measurement in the middle were conducted in MeCN, NMR spectra at the bottom with 6.9 mg substance in 650 μL CDCl_3 . Generation of the new photoisomer **N-UnS2** is completed after 20 minutes, while further irradiation induces photodecomposition.

atives. All interconversions were studied by UV–vis spectroscopy and confirmed with ^1H NMR measurements. Both oxa-NBD derivatives could be converted to the QC counterparts upon irradiation. A detailed description of the conversion of **O-NBD2** to **O-QC2** is provided, noting that **O-QC2** further isomerizes into another species with prolonged irradiation. The formation of the same species was also observed while attempting the back-isomerization of **O-QC2** to **O-NBD2** at elevated temperatures. However, prolonged heating resulted in rearrangement to a 4th unidentified species. Clean recovery of **O-NBD2** from the respective QC derivative was accomplished by addition of a Co^{II} -porphyrin catalyst. For the nitrogen containing NBDs **N-NBD1** and **N-NBD2** photoinduced generation of an unidentified species was observed, followed by complete photodecomposition upon extended irradiation. The formation of **N-QC2** was excluded, as evidenced by the unsuccessful attempts to catalytically back-convert it. The distinct determination of the unknown structures was attempted through exhaustive NMR spectroscopy, however, these efforts were ultimately unsuccessful. When compared to literature values, a notable redshift in the absorption maximum and onset was observed for the heterocyclic derivatives in relation to their isocyclic analogues.

Supporting Information

Supporting Information File 1

Experimental, characterization data, copies of NMR spectra and switching experiments.

[<https://www.beilstein-journals.org/bjoc/content/supplementary/1860-5397-21-64-S1.pdf>]

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Author Contributions

Daniel Krappmann: conceptualization; data curation; formal analysis; writing – original draft. Andreas Hirsch: conceptualization; funding acquisition; resources; supervision; writing – review & editing.

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Data Availability Statement

Data generated and analyzed during this study is available from the corresponding author upon reasonable request.

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Substituent effects in *N*-acetylated phenylazopyrazole photoswitches

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Abstract

Phenylazopyrazole photoswitches proved to be valuable structural motifs for various applications ranging from materials science to medicine. Despite their potential, their structural diversity is still limited and a larger pool of substitution patterns remains to be systematically investigated. This is paramount as electronic effects play a crucial role in the behavior of photoswitches and a deeper understanding enables their straightforward development for specific applications. In this work, we synthesized novel *N*-acylpyrazole-based photoswitches and conducted a comparative study with 33 phenylazopyrazoles, comparing their photoswitching properties and the impact of electronic effects. Using UV-vis and NMR spectroscopy, we discovered that simple acylation of the pyrazole moiety leads to increased quantum yields of isomerization, long *Z*-isomer life-times, good spectral separation, and high photo-stability.

Introduction

Organic photoswitches are molecules reversibly changing their optical and chemical properties upon irradiation. These features offer easy, precise, and reversible control over the system they are embedded in and make them attractive modulators for diverse applications. In the last decades, many classes of photoswitches have been described and extensively studied [1,2].

Among these, azobenzenes belong to the most common ones [3]. They were firstly explored almost 200 years ago [4] and initially used mainly as dyes or pigments [5]. Relatively recently, azobenzenes started to become an important part of state-of-the-art technologies ranging from energy-storage materials [6,7] to pharmacology [8–11], materials chemistry [12,13],

control of peptides structure [14,15] or proteins [16], as antibacterial agents [17,18], smart coating [19], or multivalent photoreponsive systems [20,21], to name only a few examples.

Azobenzene and its derivatives show two characteristic absorption bands, namely a $\pi \rightarrow \pi^*$ transition around 330 nm and an $n \rightarrow \pi^*$ one around 450 nm, respectively [22]. The molecule can populate the thermodynamically metastable *Z* isomer by addressing these transitions in the thermally stable *E* form. The relative position of the absorption bands in the azobenzene derivatives depends on the substitution pattern on the aromatic rings, which can act as a handle to affect the absorption properties of the compound class [3]. For instance, push–pull systems or the introduction of tetra-*ortho* substituents were reported to either bathochromically shift the UV–vis absorption spectrum or lead to a better separation of the $n \rightarrow \pi^*$ bands of the two photoisomers and allow for visible-light-responsive switches [23–26].

In recent years, heteroaryl azobenzene derivatives have revealed superior properties to classical azobenzenes. Heterocyclic rings offer, for example, enhanced polarity, electron pairs for metal coordination [27], better water-solubility, and variable pK_a [28,29]. Special attention has been given to 5-membered *N*-heterocyclic azobenzenes, which not only maintain the azobenzenes properties but often show higher quantum yields and increased thermal half-life of the metastable state. For the half-life, the choice of the heterocycle is crucial, as revealed through density functional theory (DFT) calculations, which showed that a 5-membered ring promotes the stability of the *Z* isomer [30]. Within these, azo-photoswitches based on a 1,3,5-trimethylpyrazole ring (phenylazopyrazole; **PAP**) became particularly popular, showing almost quantitative back and forward photoswitching and high thermal stability [31]. Moreover,

1*H*-pyrazole derivatives [32] and arylazopyrazolium [33] compounds were investigated in detail and allowed to correlate thermal relaxation rates and steric or electronic effects as well as mechanistic peculiarities, which has been in the spotlight recently for different classes of azobenzenes [34].

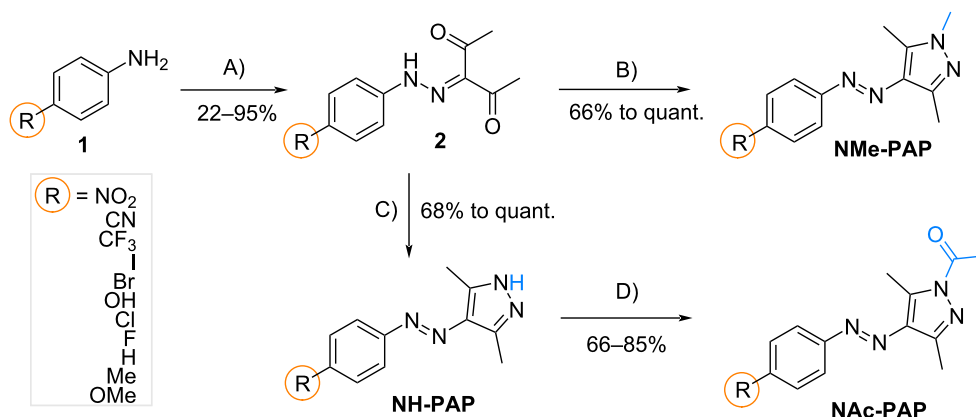
Despite these studies, the variety of substitution patterns in **PAPs** is limited compared to classical azobenzenes and remains to be better understood. Interestingly, Leistner et al. recently reported that introducing a formyl group in the *para* position of tetra-*ortho*-fluoro or -chloro-substituted azobenzenes leads to the decrease of the HOMO–LUMO gap resulting in a significant 50 nm bathochromic shift of the $n \rightarrow \pi^*$ absorption band further moving their UV–vis absorption spectrum towards the therapeutic window [35]. Moreover, a similar modification in stilbene-based photoswitches and molecular motors showed an increase in performance and photoisomerization quantum yield [36,37].

Consequently, we were interested to study the photoswitching properties of eleven novel *N*-acetylated analogous **NAc-PAPs** and the influence of substituent effects. Furthermore, we compared their photochromism with a set of 22 known *N*-methylated (**NMe-**) and unfunctionalized (**NH-**) **PAPs** in moderate to good yields (66–85%).

Results and Discussion

Synthesis

The **PAPs** in this study were obtained in a straightforward, three-step metal-free synthesis from commercially available aniline derivatives adapting known procedures [31,38]. An overview of the compounds used in this study and their synthesis is displayed in Scheme 1. First, a diazotization of a given aniline **1** and reaction with 2,4-pentanedione gave intermediate



Scheme 1: Reaction pathway for synthesizing MH-substituted, methylated-, and acetylated arylazopyrazoles. Conditions: A) NaNO_2 , $\text{AcOH} + \text{HCl}$ at 0°C , then, 2,4-pentanedione, NaOAc in $\text{EtOH} + \text{H}_2\text{O}$, reflux; B) MeNHNH_2 , EtOH , reflux; C) NH_2NH_2 , EtOH , reflux; D) AcCl , NaOAc in DCM , 0°C to rt.

2, with yields which strongly depended on the residue in the *para*-position. Specifically, the residues bearing an electron-donating group (EDG) such as -OMe or -OH showed low yields because of the poor reactivity of the diazonium salt. When strong electron-withdrawing groups (EWGs) were introduced, the yield was also reduced, likely due to the low nucleophilicity of the aniline derivative and the ineffective formation of a diazonium salt. An annulation reaction of compound **2** was performed with either hydrazine or methylhydrazine to yield **NH-PAPs** or **NMe-PAPs**, respectively, in high to quantitative yields. The **NAc-PAPs** were synthesized via an acetylation reaction of **NH-PAPs** with acyl chloride, forming the novel **NAc-PAPs**. While the molecules could be extracted and purified by column chromatography without further issue, we observed some instability at acidic pH during analysis. Thus, we tested the stability of **NAc-PAP-H** (1 mM, MeOH, ambient conditions, 2 h) at pH 2, 12, and in the presence of DBU (10^{-2} M) and found that the acetyl group was lost (cf. Supporting Information File 1, section 2.4).

UV-vis absorption spectroscopy

With a set of photoswitches at hand, we studied the obtained **PAPs** through UV-vis absorption spectroscopy. The photochemical properties are summarized in Table 1. All compounds show absorption maxima in the range of 324–368 nm in CH_3CN , which corresponds to the strongly allowed $\pi \rightarrow \pi^*$ transition, while the weaker $n \rightarrow \pi^*$ band shows absorption maxima in the range of 410–451 nm in CH_3CN .

The introduction of methyl and acyl groups on one nitrogen of the pyrazole ring led to a hyperchromic effect and a minor bathochromic shift. Also, the introduction of an EDG or EWG

on the R position led to minor hyperchromic effects and a bathochromic shift (exemplary the UV-vis absorption spectra of **NAc-PAPs** are displayed in Figure 1 and a full set is available in Supporting Information File 1, section 3.5). In the case of EWGs, we observed positive hyperchromic effects while for EDGs negative hyperchromic effects compared for **NH-** and **NMe-PAP-H**.

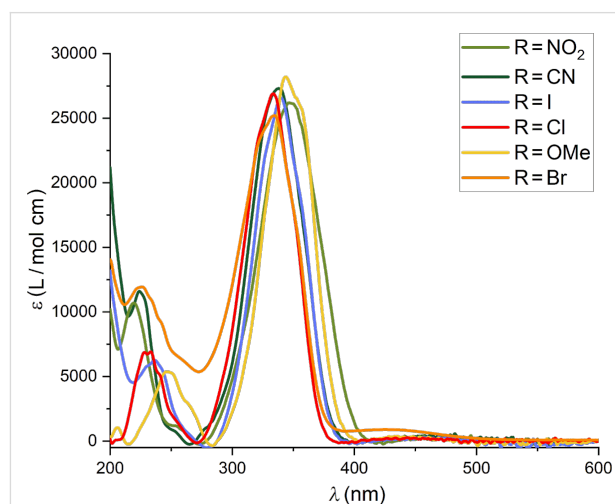


Figure 1: UV-vis absorption spectra of selected **NAc-PAP** derivatives in CH_3CN . The strong $\pi \rightarrow \pi^*$ can be observed in the region of 330–360 nm.

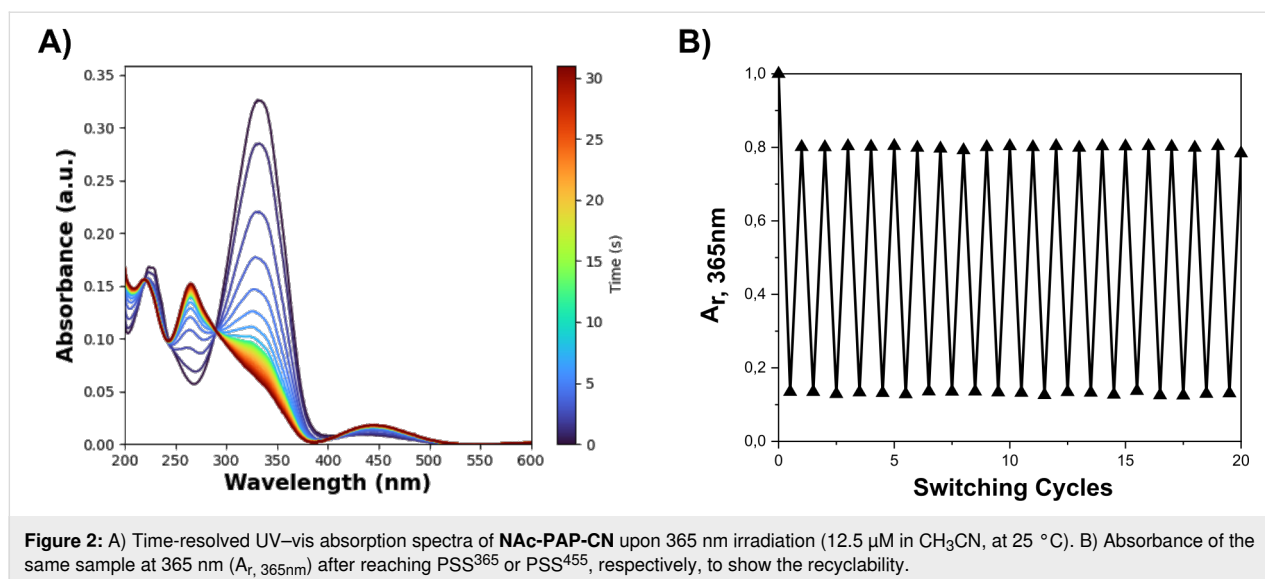
Photochemical isomerization

Upon irradiation with a 365 nm LED (exemplarily displayed for **NMe-PAP-CN** in Figure 2), we observed a decrease of the $\pi \rightarrow \pi^*$ band for the *E* isomers. Simultaneously the $\pi \rightarrow \pi^*$ bands around 253–369 nm and the $n \rightarrow \pi^*$ bands around 426–457, re-

Table 1: Photophysical properties of synthesized **PAP** derivatives in CH_3CN .

R:	NH-PAP			NMe-PAP			NAc-PAP		
	λ_{max} [nm]	$\pi \rightarrow \pi^*$	$\epsilon (\pi \rightarrow \pi^*) 10^3$ [L/(mol·cm)]	λ_{max} [nm]	$\pi \rightarrow \pi^*$	$\epsilon (\pi \rightarrow \pi^*) 10^3$ [L/(mol·cm)]	λ_{max} [nm]	$\pi \rightarrow \pi^*$	$\epsilon (\pi \rightarrow \pi^*) 10^3$ [L/(mol·cm)]
OH	342	415*	16.8 ± 0.5	345	^a	18.0 ± 0.3	344	443	13.0 ± 0.1
OMe	344	410	18.9 ± 0.8	345	^a	19.4 ± 1.1	344	447	28.3 ± 0.4
Me	336	413*	19.1 ± 0.9	338	434	21.8 ± 1.3	333	425	24.1 ± 0.4
H	330	440	18.9 ± 0.1	337	433	19.5 ± 1.1	327	427	24.5 ± 0.4
F	332	437	17.2 ± 0.7	335	435	17.3 ± 0.5	327	426	20.2 ± 0.1
Cl	336	441	20.9 ± 0.6	341	447	22.1 ± 1.1	333	414	26.9 ± 0.3
Br	341	450	17.8 ± 0.5	343	451	27.1 ± 0.1	334	429	25.2 ± 0.2
I	343	451	24.2 ± 0.1	347	445	22.1 ± 1.3	340	422	29.1 ± 0.6
CF ₃	335	442	16.3 ± 0.1	341	444	23.3 ± 0.1	324	435	23.5 ± 0.5
CN	345	448	24.1 ± 1.4	352	451	13.8 ± 0.2	333	444	27.3 ± 0.5
NO ₂	361	449	21.3 ± 1.0	368	^a	13.8 ± 0.1	345	448	26.4 ± 0.5

^aTransition band appears as shoulder.



spectively, of the *Z* isomers increased until reaching the photo-stationary state (PSS).

The UV-vis absorption spectra of the *Z* isomers show a more intense $n \rightarrow \pi^*$ transition and less intense $\pi \rightarrow \pi^*$ absorption band compared to the *E* isomers, because of the loss of the molecule's planarity [30,39]. This change in color can also be seen by naked eye with the solution changing from pale to dark yellow (cf. Supporting Information File 1, Figure S2). In Table 2, the absorption maxima of *Z*-PAP derivatives in CH_3CN are summarized. For EWGs, such as CF_3 , CN, or NO_2 , the absorption maxima are redshifted, while for EDGs, such as OH or OMe, they are shifted towards the blue. Especially for **NAc-PAPs**, we observe a higher spectral separation of the $\pi \rightarrow \pi^*$ and the $n \rightarrow \pi^*$ transitions of the *Z* isomers compared to **NMe-PAPs** and **NH-PAPs**. For instance, the separation for the $\pi \rightarrow \pi^*$ transition band and the $n \rightarrow \pi^*$ is 176 nm for **NAc-PAP-CN**, while for **NMe-PAP-CN** 146 nm and for **NH-PAP-CN** 102 nm are found.

Subsequent illumination with a 445 nm LED led to the formation of the *E* isomer, which is accompanied by an increase of its $\pi \rightarrow \pi^*$ band until reaching the PSS⁴⁴⁵. However, judging from the intensity of the *E* isomers' $\pi \rightarrow \pi^*$ band, the photostationary distribution (PSD) of the initial dark state could not be fully regenerated by photochemical means for all 33 PAPs (vide infra, ex-situ NMR measurements and thermal half-lives).

The recyclability of **NH-PAPs** was previously studied by Rustler et al. by altered irradiation with 365 and 420 or 455 nm light, showing a great photostability of these compounds [32]. We performed the same experiment on our **NAc-PAPs** (see Table 3 and section 3.2 in Supporting Information File 1) and

Table 2: UV-vis absorption maxima of *Z*-PAP derivatives in CH_3CN (obtained through 365 nm irradiation to the corresponding PSS³⁶⁵).

R	NH-PAP		NMe-PAP		NAc-PAP	
	λ_{max} [nm]	λ_{max} [nm]	λ_{max} [nm]	λ_{max} [nm]	λ_{max} [nm]	λ_{max} [nm]
	$\pi \rightarrow \pi^*$	$n \rightarrow \pi^*$	$\pi \rightarrow \pi^*$	$n \rightarrow \pi^*$	$\pi \rightarrow \pi^*$	$n \rightarrow \pi^*$
OH	304	436	307	435	309	445
OMe	307	426	307	411	307	445
Me	331	457	301	456	279	439
H	300	433	358	455	280	442
F	334	441	299	445	280	442
Cl	358	454	302	456	277	437
Br	366	452	302	457	275	435
I	366	455	366	456	279	445
CF_3	369	453	304	442	253	440
CN	361	463	311	457	265	441
NO_2	350	463	372	448	280	448

did not observe any fatigue after 10–20 cycles of photo-switching, showing high photostability also of **NAc-PAPs**.

To quantify the extent of photoisomerization, the isomer distributions of **NAc-PAPs** at the PSS³⁶⁵ and PSS⁴⁴⁵ were investigated using UV-vis and NMR spectroscopy. For the ex-situ ^1H NMR irradiation experiments, we irradiated our samples in a cuvette until the PSS was reached and measured immediately afterwards the ^1H NMR spectrum. We compared these results to simply estimating the isomer distribution at the PSS (cf. Supporting Information File 1, section 3.1) from the UV-vis spectra and observed good agreement, meaning the results from UV-vis spectroscopy can be used for rough PSD estimation, due to good spectral separation of the isomers. Since we en-

Table 3: PSS distribution of various **NAc-PAP** derivatives.^a

R:	365 nm <i>E</i> : <i>Z</i> UV-vis	365 nm <i>E</i> : <i>Z</i> NMR	445 nm <i>E</i> : <i>Z</i> UV-vis	445 nm <i>E</i> : <i>Z</i> NMR
OH	8:92	a	81:19	a
OMe	10:90	5:95	76:24	78:22
Me	4:96	4:96	77:23	77:23
H	22:78	22:78	81:19	81:19
F	8:92	8:92	79:21	79:21
Cl	16:84	4:96	73:27	75:25
Br	2:98	4:96	77:23	75:25
I	6:94	6:94	75:25	75:25
CF ₃	17:83	17:83	78:22	78:22
CN	15:85	5:95	78:22	78:22
NO ₂	14:86	27:73	84:16	88:12

^aNot determined; relaxation towards the *Z* isomer is too fast.

countered fast back isomerization only for **NAc-PAP-OH** (vide infra), the PSDs could only be determined from the UV-vis spectra.

NAc-PAPs showed high to quantitative formation of the *Z*-configured isomers. For example, **NAc-PAP-Br** showed an isomerization distribution of 98% *Z* by UV-vis and 96% *Z* by ¹H NMR. EWGs, such as **NAc-PAP-CF₃**, on the other hand, showed a lower PSD for the *Z* isomer of 83% by both UV-vis and ¹H NMR spectroscopy. For **NMe-** and **NAc-PAPs**, we observed increased *Z* content to almost quantitative photoisomerization after 365 nm illumination for most cases compared to **NH-PAPs**. For **NMe-PAPs**, West et al. attributed this to a pronounced spectral separation between the $\pi \rightarrow \pi^*$ bands of *E* and *Z*-isomers, which we also found for **NAc-PAPs** [31].

For the back isomerization with 445 nm light, favoring the *E* isomer, we observed that the amount of *E* isomer present in the dark state could not be reached for any of the **NAc-PAPs**. For example, for **NAc-PAP-Cl** 73% of the *E* isomer could be reformed and for **NAc-PAP-NO₂** 84%. Since we observed for **NAc-PAPs** a decrease of spectral separation of the $n \rightarrow \pi^*$ bands for the *E* and *Z* isomers, a non-quantitative PSD upon irradiation with 445 nm can be explained by the presence of a competing *E*→*Z* isomerization at the same wavelength. In general, **NAc-PAPs** show only a minor substitution effect on the PSD upon irradiation with 365 or 445 nm LED light.

Next, we studied the photoisomerization quantum yields (QYs) $\Phi_{E \rightarrow Z}$ and $\Phi_{Z \rightarrow E}$ and the impact of substitution effects on the *para* position, using two types of LEDs (365 nm and 445 nm, details see Supporting Information File 1, section 3.5). The values determined are provided in Table 4.

Table 4: Quantum yield values for the *E*→*Z* and *Z*→*E* photoisomerization of **PAP** derivatives with the corresponding 365 nm and 445 nm LED in CH₃CN.^a

R:	X = H $\pi \rightarrow \pi^*$ [%]	X = Me	X = Ac	X = Ac $n \rightarrow \pi^*$ [%]
OH	33	44	56	a
OMe	29	38	65	28
Me	18	45	44	31
H	11	22	14	30
F	29	56	72	61
Cl	26	36	59	42
Br	21	32	55	39
I	29	40	45	32
CF ₃	25	27	69	30
CN	25	26	26	10
NO ₂	21	18	16	20

^aNot determined.

For $\Phi_{E \rightarrow Z}$, we could observe for nearly all **NAc-PAP** derivatives, higher values compared to **NMe-PAPs**, followed by **NH-PAPs** in a descending order. For example, for **NH-PAP-CF₃** we found a QY of 25%, which went towards 27% for the **NMe-PAP-CF₃** and finally to 69% for the **NAc-PAP-CF₃**. Especially for EDGs and weak EWGs, the **NAc-PAPs** showed higher $\Phi_{E \rightarrow Z}$ compared to **NMe-PAPs** and **NH-PAPs**, while strong EWGs show a higher to equal $\Phi_{E \rightarrow Z}$. Interestingly, for R = Me and H, we recorded higher QYs in **NMe-PAPs** than in **NAc-PAPs** (22% and 45% for R = H and R = Me in **NMe-PAP** vs 14% and 44% for the acetylated ones).

In contrast to the excitation of the $\pi \rightarrow \pi^*$ state in **NAc-PAPs**, the isomerization process varies in efficiency when the $n \rightarrow \pi^*$ transition is selectively addressed, with similar or markedly reduced quantum yields. A deviation from Kasha's rule with the opposite outcome (viz. the quantum yield of isomerization proceeding from the excitation of the $\pi \rightarrow \pi^*$ state is lower than the one from the $n \rightarrow \pi^*$) is reported in various studies on azobenzene [32,40]. Another interesting aspect, that could point to a more complex picture in the excited state landscape of these switches, is that the QYs of **NAc-PAPs** with R = NO₂ and R = H are lower for the $\pi \rightarrow \pi^*$ than for the $n \rightarrow \pi^*$ transition, while for the other substituents the opposite was found. We thus suspect that the substituents play a crucial role in the population of the respective excited state and we can at this state not rule out a contribution also from the triplet state.

Moreover, we could not find a quantitative correlation between the R-substituents and $\Phi_{E \rightarrow Z}$, however, some trends can be observed; EWG and EDG lead to higher $\Phi_{E \rightarrow Z}$ for the $\pi \rightarrow \pi^*$ tran-

sition, while the opposite can be seen for the $n \rightarrow \pi^*$ transition. We also observed increased numbers for the $\Phi_{E \rightarrow Z}$ of $\pi \rightarrow \pi^*$ for **NMe-PAPs** compared to **NH-PAPs**. However, the highest values were observed for our newly synthesized **NAc-PAPs**. For example, for **NH-PAP-CF₃** we observed that the $\Phi_{E \rightarrow Z}$ has a value of 25%, for **NMe-PAP-CF₃** 27%, while for **NAc-PAP-CF₃** we observed an increase of $\Phi_{E \rightarrow Z}$ to 69%.

Thermal half-lives

The metastable *Z* isomers can be converted back to the thermodynamically favored *E* form by thermal means. Four mechanisms were predicted using quantum chemistry to describe the $Z \rightarrow E$ isomerization in azobenzenes, namely: rotation, inversion, inversion-assisted rotation, and concerted inversion depending on the structure of the azobenzene [40–44]. For **PAPs**, Calbo et al. showed by DFT calculations that the inversion mechanism is one of the fastest relaxation mechanism for heterocyclic azobenzenes (typically for most of the azo dyes [45]). However, the nature of the mechanism is still a matter of current debate, and additional factors, such as the presence of tautomerizable groups [46,47], and the involvement of the triplet state [48], appear to play a role.

Specifically, the rotation mechanism does not explain the low activation entropy observed in azobenzene systems [49] sparking new discussions on the possibility of alternative isomerization pathways [34]. Recently, Reimann et al. computationally showed that the involvement of a triplet state mechanism, which crosses the transition state for the $Z \rightarrow E$ relaxation, could explain the low values of the activation entropy. The same authors also showed experimental evidence for this proposal by an external heavy atom effect on $Z \rightarrow E$ isomerization.

To understand the thermal $Z \rightarrow E$ isomerization in our newly synthesized **NAc-PAPs**, we recorded the process by time-resolved UV–vis absorption spectroscopy and calculated the thermal half-lives of back isomerization (Table 5 and Supporting Information File 1, section 3.6). EDGs and weakly EWGs, such as halogen substituents, exhibited thermal half-lives for thermal back isomerization in the range of days. For instance, **NAc-PAP-Cl** or **-Br** converts back to the form with half-lives of roughly 1.5 days. In contrast, **NAc-PAP-H** or **-Me** demonstrated significantly longer thermal half-lives, ranging from 9 days to 21.5 days. Notably, **NAc-PAP-OMe**, with a thermal half-life of 4.38 days, extends the thermal half-life significantly compared to the 19.7 minutes observed for **NH-PAP-OMe**.

We subsequently analyzed the electronic effects on the thermal relaxation rates in our **NAc-PAPs** using Hammett parameters for the substituents in the *para*-position and found a trending behavior (cf. Figure 3). Specifically, the Hammett plot shows

Table 5: Overview over thermal half-lives for **NAc-PAPs** in CH₃CN at 30 °C.

R:	$\tau_{1/2}$ [d]
OMe	4.38
Me	8.97
H	21.5
F	13.3
Cl	1.51
Br	1.57
I	3.26

R	$\tau_{1/2}$ [s]
OH	19.0
CF ₃	1992
CN	696
NO ₂	608

linear trends for both EWGs and EDGs, with a minimum for electron-neutral $R = H$ and $R = OH$ as an outlier, likely due to a contribution of tautomerization [50]. Both linear fits show high slope values, indicating a great dependency on the nature of the substituent. The observed trend behavior indicates an apparent change of mechanism for thermal relaxation to the *E* isomer. This was previously observed for **NH-PAPs** [32] **N-PEG-PAPs** [20], and for azopyrazolium salts [33].

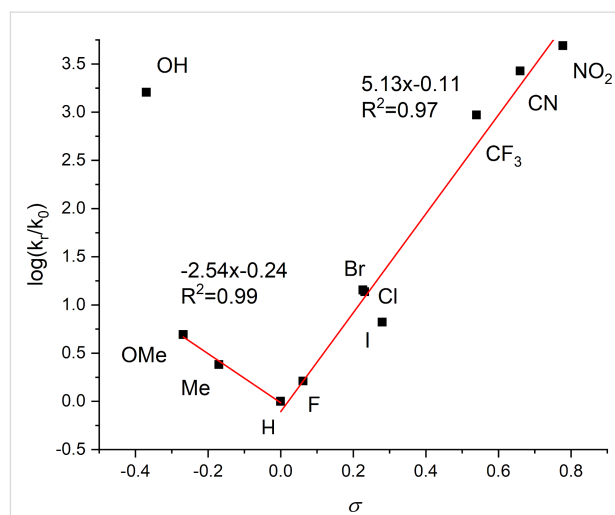


Figure 3: Hammett plot of **NAc-PAP** derivatives.

To obtain a deeper understanding of the transition states thermodynamic properties, we decided to perform an Eyring analysis of two representative **PAPs**. We chose **NAc-PAP-CN** and **NAc-PAP-OMe**, which lie on two different ends of the Hammett plot and hence should reveal the difference in relaxa-

tion mechanism. We measured the temperature-dependency of their relaxation rates in toluene to access higher temperatures (Table 6 and Supporting Information File 1, section 3.7). The Eyring plot for **NAc-PAP-CN** and **NAc-PAP-OMe** are depicted in Figure 4.

Table 6: Eyring analysis of **NAc-PAP-CN** and **NAc-PAP-OMe** determined in toluene (for details see Supporting Information File 1, section 3.7).

	NAc-PAP-CN	NAc-PAP-OMe
$\Delta G^\ddagger$ / kJ/mol	99.1 ± 0.07^a	104.3 ± 0.1^a
$\Delta H^\ddagger$ / kJ/mol	90.0 ± 0.7	93.0 ± 1.0
$\Delta S^\ddagger$ / J/(mol·K)	-30.0 ± 2.0	-39.0 ± 4.0

^aAt 298 K.

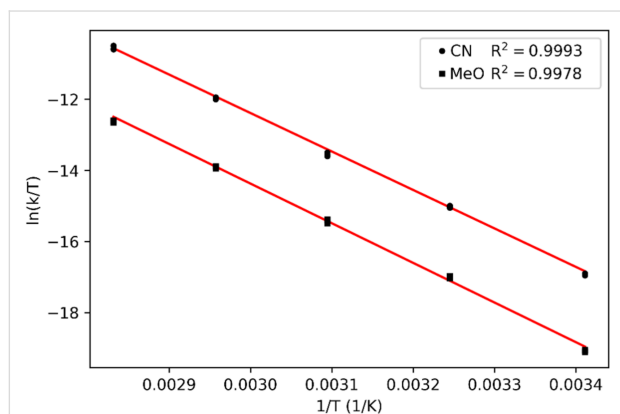


Figure 4: Eyring plots for **NAc-PAP-CN** and **NAc-PAP-OMe**.

Counterintuitively, the calculated thermodynamic data of the transition states show, within the error margin, similar values of activation enthalpy $\Delta H^\ddagger$ and $\Delta S^\ddagger$. In particular, **NAc-PAP-CN** showed a negative $\Delta S^\ddagger = -30.0 \pm 2.0$ J/(mol·K), while **NAc-PAP-OMe** showed a relatively similar value (-39.0 ± 4.0 J/(mol·K)), hinting towards the same mechanism of relaxation operating for both compounds. Comparing these values to the calculations for azobenzene, we hypothesize that both compounds undergo isomerization via triplet intermediacy [34].

Contrary to what was observed by Reimann et al. [34], however, we did not observe any heavy atom effect. This could be explained by the different ways in which the heavy atom is introduced: in our case as a substituent, in the case of the literature example by adding tetrabutylammonium iodide to the solution.

Conclusion

In this study, we synthesized and systematically investigated various **PAP** derivatives, including **NAc-PAPs**, **NMe-PAPs**,

and **NH-PAPs**. As similar functional groups were reported as highly beneficial for the photochemical properties in other classes of photoswitches, our focus was on the novel **NAc-PAPs**, which exhibit an acetyl group on one of the pyrazole nitrogens. The functional group could be installed easily via acetylation from the corresponding **NH-PAPs** in high yields to result in a set of eleven novel compounds that we could compare to a set of 22 **NMe-PAPs** and **NH-PAPs**.

We then analyzed the molecules' photophysical and photochemical properties and studied the metastable isomers' thermal relaxation mechanism. In particular, photophysical studies highlighted the impact of structural modifications on the $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions, showing that substitution of nitrogen with methyl or acetyl groups resulted in a small bathochromic shift and hyperchromic effects.

Anti-Kasha behavior was observed with distinct trends in the $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions when studying the quantum yields ($\Phi_{E \rightarrow Z}$ and $\Phi_{Z \rightarrow E}$). Strong EWGs or EDGs enhanced the quantum yields for the $\pi \rightarrow \pi^*$ transitions, whereas the $n \rightarrow \pi^*$ transitions exhibited no clear correlation with substitution patterns. Notably, the acetylation of nitrogen significantly increased the $\Phi_{E \rightarrow Z}$ for $\pi \rightarrow \pi^*$ transitions in almost all compounds studied (excluding **NAc-PAP-H** and **-Me**), even surpassing the effects of methylation.

Hammett analysis showed that the thermal population of the triplet state seem to be preferred as the thermal relaxation mechanisms of the back isomerization. EWGs and EDGs accelerated the relaxation dynamics compared to **NAc-PAP-H**. Acylation of the pyrazole moiety led to an enhanced metastable half-life compared to the **NH-PAPs**. For **NAc-PAP-H**, we observed increased half-lives (21.5 days, 30 °C), compared to the reported **NH-PAP-H** (0.066 days; 25 °C [51]) or **NMe-PAP-H** (10 days; 25 °C [31], all in CH_3CN). In the presence of OH as substituent, tautomerism can become feasible and result in particularly fast relaxation rates. These results highlight the complex interplay between electronic effects and thermal isomerization pathways in this class of compounds.

To summarize, this work provides a comprehensive understanding of how structural modifications affect the synthesis, photochemical, and thermal behavior of **PAP** derivatives introducing **NAc-PAPs** as novel compound set with enhanced photochemical performance. Our findings provide valuable guidance for designing functional **PAPs** with tailor-made photochemistry and photophysical properties, which may broaden their application in areas such as molecular switches, photodynamic materials, and optoelectronics.

Supporting Information

Supporting Information File 1

Materials and methods, analytical equipment, experimental procedures, compound characterization, UV–vis spectra at different concentrations, photochemical experiments, thermal isomerization analysis, and NMR spectra.
[<https://www.beilstein-journals.org/bjoc/content/supplementary/1860-5397-21-66-S1.pdf>]

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Author Contributions

Radek Tovtik: conceptualization; data curation; formal analysis; investigation; methodology; visualization; writing – original draft; writing – review & editing. Dennis Marzin: conceptualization; formal analysis; investigation; methodology; visualization; writing – original draft; writing – review & editing. Pia Weigel: data curation; formal analysis; writing – original draft. Stefano Crespi: data curation; formal analysis; methodology; writing – review & editing. Nadja A. Simeth: conceptualization; funding acquisition; investigation; supervision; validation; writing – review & editing.

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Data Availability Statement

All data that supports the findings of this study is available in the published article and/or the supporting information of this article.

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Tautomerism and switching in 7-hydroxy-8-(azophenyl)-quinoline and similar compounds

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Abstract

Tautomerism in two new azo dyes, based on 7-hydroxyquinoline, has been considered from the viewpoint of the proton crane concept. Although 8-(phenyldiazenyl)quinolin-7-ol exists in solution as a mixture of azo and two hydrazone tautomers, as shown by the experimental and theoretical results, upon irradiation switching, based on long-range proton transfer, occurs in a limited extent. 8-(4-Hydroxy-1,2,3,5-tetrafluorophenyldiazenyl)quinolin-7-ol exists as a single enol (azo) tautomer and the reduced basicity of the azo group nitrogen atoms does not allow shift of the tautomeric state neither upon changing the solvent, nor upon irradiation. Possibilities for molecular design, allowing to improve the capacity of 7-hydroxy-8-(azophenyl)quinolines, are considered in terms of stabilization of the azo tautomer and making possible long range proton transfer to the quinolyl nitrogen atom.

Introduction

Azo compounds have long been utilized as dyes in industries such as textiles, printing, and coloring agents for various materials, due to their excellent color fastness, high stability, and ease of synthesis. The azo functionality allows for a wide range of colors to be achieved by altering the substituents on the azo

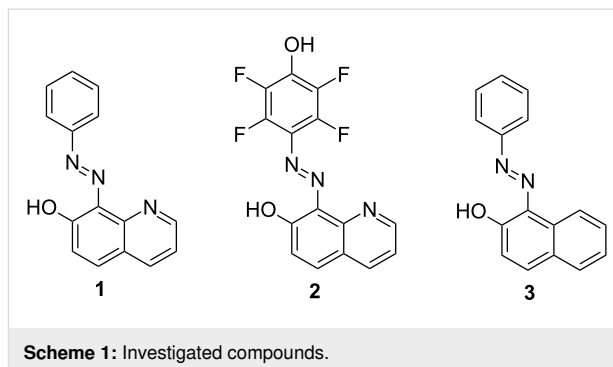
group, improving the color intensity, lightfastness, and wash resistance [1–4]. In addition to their conventional use, azodyes have unique optical properties, defined by the *E/Z* isomerization [5,6] and by the tautomeric proton exchange [3,7–11], when a OH or NH group is present on a suitable position in the mole-

cule. Both processes are strongly influenced by the structural variations and the environment (temperature, solvent properties, acidity and presence of other molecules).

The *E/Z* isomerization of the azodyes, caused by light irradiation [12–14] or electrochemically [15,16], has paved the way for the development of innovative materials and systems, including gels [17], metal-organic frameworks [18–21], photocatalysts [22,23], container molecules [24–26], drug delivery systems [27–29], photoresponsive polymers [30–37], photoswitches [12,13,38–41], optical storage devices [42–45] and systems for energy storage [46,47]. The phototautomerism of azodyes refers to the reversible isomerization process that occurs upon exposure to light, leading to exchange of a proton [48,49]. The obtained tautomeric forms have different optical and chemical properties, which make these molecules good candidates for molecular switches [50].

Recently, we have developed a series of 7-hydroxyquinoline Schiff bases, where the tautomeric proton transfer causes intramolecular twisting upon irradiation [51]. The process happens in the excited state and the competition between proton transfer and *E/Z* isomerization around the C=N bond leads to reduced efficiency of the tautomeric based switching [52].

In this respect, based on the excellent stability of the azo compounds, it is interesting to understand the effect of the competitive proton transfer and *E/Z* switching by replacement of the azomethine group with an azo group. Therefore, two new compounds, based on 7-hydroxyquinoline (**7OHQ**), namely (*E*)-8-(phenyldiazenyl)quinolin-7-ol (**1**, Scheme 1) and 8-(4-Hydroxy-1,2,3,5-tetrafluorophenyldiazenyl)quinolin-7-ol (**2**) were synthesized and studied in variety of solvents. The implemented

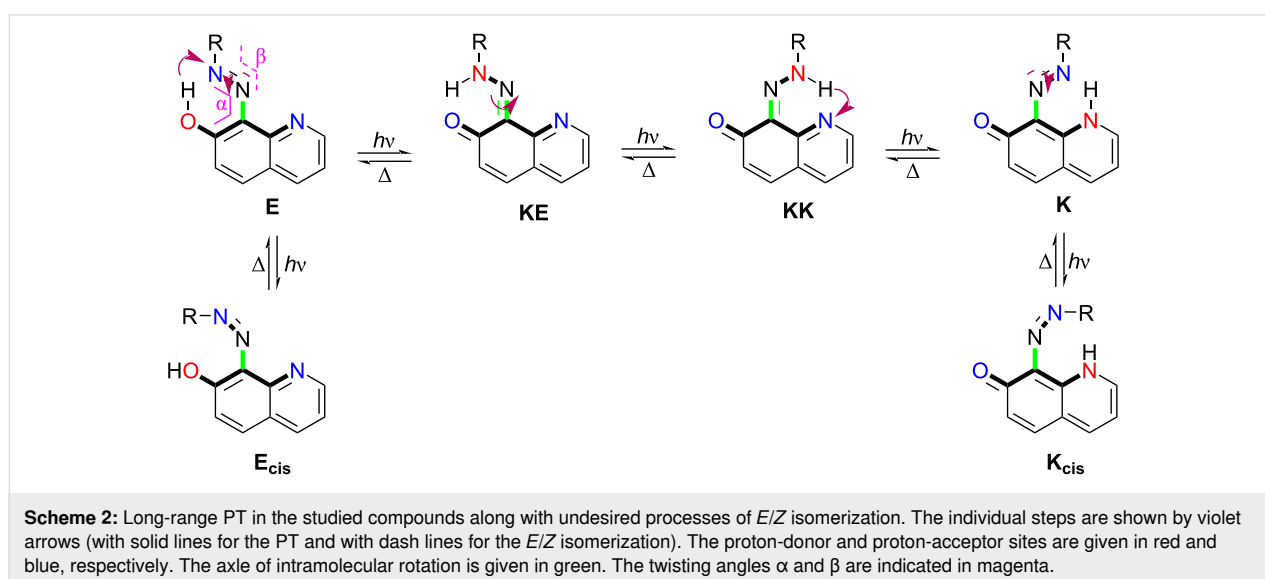


additional OH functionality in compound **2** gives possibility to influence the tautomerism in this compound dynamically by protonation/deprotonation. The tautomeric and switching properties of compounds **1** and **2** have been revealed by using quantum-chemical calculations, UV–vis and NMR spectroscopy and UV irradiation. Compound **3**, whose tautomeric properties are well known and studied [11,53–55] is used as a model compound in which only short range proton transfer is possible.

Results and Discussion

Tautomerism in the ground state

As shown in Scheme 2, the studied compounds possess multiple tautomeric forms, allowing long-range proton transfer starting from the enol, azo, (**E**) and finishing to the end keto form **K**. As described in similar compounds, ideally for switching, the process begins with excitation of **E**, which, in the excited state, exhibits excited-state proton transfer (PT) to **KE***. This changes the nature of the axle from single to double bond and leads to twisting, where conical intersection region is reached with the protonated crane (HN–N bond) and the deprotonated tautomeric frame (**7OHQ**) being almost perpendicular to each other. Then,



the system relaxes to the ground state, populating both **KE** and **KK**, which undergo ground-state PT to **E** and **K**, respectively. Therefore, it is crucial to have the intermediate keto tautomers **KE** and **KK** higher in energy in the ground state, comparing to the paired terminal **E** and **K**, respectively, in order to provide efficient switching. The additional factors that are important include relatively low PT barriers (**TS(E-KE)** and **TS(K-KK)**) and relatively large twisting barrier (**TS(KE-KK)**). The former provides fast PT to the corresponding terminal states, while the latter allows accumulation of the **KK** and **K** as a result of the irradiation. When the crane part is flexible, the excitation of **E** can lead to *E/Z* isomerization, which competes with the initial excited-state PT process, reducing its efficiency [52].

The theoretical data, collected in Table 1, can shed light on the potential energy landscape in the ground state for the studied compounds. According to them neither **1** nor **2** is suitable for switching from **E** to **K** for couple of reasons. The most important one is the higher relative energy of **K** in respect of **KK**. This means that if **KK** is populated, according to the above described mechanism, the tautomeric proton cannot be released to **K**, i.e. the terminal form of the switching process is **KK**. This is also a kind of switching, which could be detected, because the

TS(KE-KK) is large enough to allow accumulation of the switched form **KK**. As will be discussed in the next paragraph, in the case of compound **1**, the enol form is not the only existing tautomer, which means that the switching would not be clean.

According to relative energies and relative Gibbs free energies, collected in Table 1, compound **1** should co-exist as a three component (**E**, **KE** and **KK**) tautomeric mixture in both toluene and acetonitrile. If the relative energies are taken into account in toluene **E** and **KE** are approximately equal as amount with a small presence ($\approx 10\%$) of **KK**. The change of the solvent to acetonitrile does not change much the situation for the relatively equally polar **E** and **KE**, but leads to substantial stabilization of the more polar **KK**. The use of the relative free energies changes the ratios between these three tautomers, but does not change the overall situation in respect of the tautomerism. These theoretical results, obtained at the M06-2X DFT level, can be validated in several ways. The usual theoretical approach is to compare them to higher level of theory (either MPn or CCSD(T)) single point energies as shown in Table S1 (Supporting Information File 1). As seems from a comparison between the data from Table 1 and these in Table S1, the tautomeric fractions from **E** to **K**, obtained by MP4 correspond

Table 1: Relative stability (M06-2X/TZVP) and spectral characteristics of the ground-state tautomers of the studied compounds as well as relative energies of the transition states between them in toluene and in acetonitrile (in parentheses).

Structure /dipole moment [D]	ΔE [kcal/mol]	ΔG^0 [kcal/mol]	UV-vis ^a (B3LYP/TZVP// M06-2X/TZVP)		¹ H NMR [ppm]	
			$\lambda_{\max}$ [nm]	<i>f</i>		
1E_{cis} 4.8	17 (16)	18 (17)	464 (467)	0.03 (0.04)	OH	3.97 (4.15)
1TS(E-E_{cis}) 4.4	49 (49)	48 (47)				
1E 1.7	0.0 (0.28)	0.0 (0.0, 0.0 ^b)	398 397	0.67 (0.65)	OH	15.11 (15.21)
1TS(E-KE) 1.5	3.9 (3.9)	2.5 (2.1, 1.9 ^b)				
1KE 2.1	0.11 (0.0)	1.6 (1.2, 1.0 ^b)	432 (429)	0.64 (0.60)	NH	16.17 (16.05)
1TS(KE-KK) 9.3	41 (35)	42 (37, 37 ^b)				
1KK 7.8	1.3 (0.16)	2.4 (0.52, 0.53 ^b)	439 (436)	0.59 (0.57)	NH	15.53 (15.90)
1TS(K-KK) 9.1	9.8 (7.1)	7.7 (4.5, 4.5 ^b)				
1K 9.9	7.5 (3.8)	8.4 (4.4, 4.3 ^b)	456 (453)	0.02 (0.01)	NH	17.40 (16.98)
1TS(K-K_{cis}) 11.1	54 (–)	54 (–)				
1K_{cis} 11.2	27 (22)	28 (23)	515 (517)	(0.03) (0.04)	NH	7.58 (8.22)

Table 1: Relative stability (M06-2X/TZVP) and spectral characteristics of the ground-state tautomers of the studied compounds as well as relative energies of the transition states between them in toluene and in acetonitrile (in parentheses). (continued)

2E_{cis} 4.4	14 (14)	17 (16)	468 (470)	0.06 (0.06)	OH	4.07 (4.17)
2TS(E-E_{cis}) 5.8	49 (49)	48 (48)				
2E 3.4	0.0 (0.0)	0.0 (0.0)	408 (406)	0.78 (0.74)	OH	14.06 (14.24)
2TS(E-KE) 3.7	5.0 (4.7)	3.5 (2.6)				
2KE 4.3	2.3 (1.8)	2.5 (2.4)	434 (434)	0.67 (0.65)	NH	16.12 (15.58)
2TS(KE-KK) 7.3	75 (42)	78 (42)				
2KK 6.2	2.7 (1.5)	4.0 (2.0)	438 (437)	0.62 (0.61)	NH	15.81 (16.20)
2TS(K-KK) 8.0	8.6 (6.3)	7.5 (4.3)				
2K 9.0	5.8 (2.2)	6.6 (2.9)	450 (453)	0.32 (0.01)	NH	16.74 (16.30)
2TS(K-K_{cis})	N/A (N/A)	N/A (N/A)				
2K_{cis} 10.5	23 (N/A)	26 (N/A)	513 (N/A)	0.07 (N/A)	NH	7.93 (N/A)
c						
3E_{cis} 3.2	18 (17)	20 (18)	498 (492)	0.06 (0.06)	OH	3.77 (3.96)
3TS(E-E_{cis}) 2.2	48 (48)	47 (47)				
3E 1.3	0.0 (0.23)	0.0 (0.03)	432 (428)	0.55 (0.52)	OH	14.56 (14.64)
3TS(E-KE) 1.5	4.3 (4.3)	2.4 (1.3)				
3KE 1.8	0.25 (0.0)	1.1 (0.0)	450 (448)	0.59 (0.57)	NH	15.92 (15.73)
3TS(KE-KK) 11.1	47 (40)	48 (41)				
3KK 6.5	12 (9.8)	14 (11)	451 (448)	0.39 (0.42)	NH	9.71 (10.03)

^aS₀–S₁ transitions, the simulated absorption spectra are shown as follows: **1** – in Figure 1 in toluene and in Supporting Information File 1, Figure S1 in acetonitrile; **2** – in Supporting Information File 1, Figure S2 in toluene; **3** – in Figure S3 in toluene; ^bthe values at 243 K are underlined; ^cexperimental ΔG values for the tautomeric equilibrium in **3** at room temperature [53]: 0.42 (cyclohexane), 0.34 (CCl₄), –0.15 and 0.25 [56] (acetonitrile) kcal/mol.

very well to the M06-2X relative energies from Table 1, while the relative Gibbs' free energies are very near to the CCSD(T). Since this comparison does not answer the question about the reliability of the DFT data for **1**, it can be relied to a compound that is well-studied before. Compound **3** is a well-known tautomeric compound, a backbone of a large number of industrially used azo dyes [1,3] and therefore its tautomerism is studied in details. The existing experimental data for low polar solvents (cyclohexane and tetrachloromethane) indicate a ΔG value of around 0.4 kcal/mol [53] at room temperature, which gives a prevalence of the **E**-tautomer (a molar fraction roughly between 60 and 70%). The relative energy between **3E** and

3KE, given in Table 1, is 0.25 kcal/mol (60% **E** and 40% **KE**) in toluene, which very well corresponds to the experiment bearing in mind that toluene is slightly more polar and could stabilize the more polar **KE** tautomer. The relative Gibbs' free energies suggest a distribution of 88% **E** and 12% **KE**. The theoretical results for acetonitrile show that the tautomer fractions are almost equal, which reflects to the existing experimental ΔG values in acetonitrile, obtained by two different approaches (–0.15 [53] and 0.25 [56] kcal/mol).

Of course, the best way to validate the theoretical data for compound **1** is to study its tautomerism experimentally. The simu-

lated absorption spectra of **1** are shown in Figure 1, while the experimental spectra in various solvents are given in Figure 2. It is obvious from the latter that solvent-influenced tautomerism takes place, but its interpretation is not a trivial work. The curves, shown in Figure 1, indicate why. It seems that the spectra of **KE** and **KK** are almost identical as position and intensity,

which is reasonable, because they share the same chromophore system and, due to the stabilizing intramolecular hydrogen bonding, keep planarity. However, this situation means that changes in their molar fractions cannot be detected by use of UV–vis spectroscopy, i.e. the tautomerism could be considered only in the frame of change between **E** and (**KE**+**KK**). In the

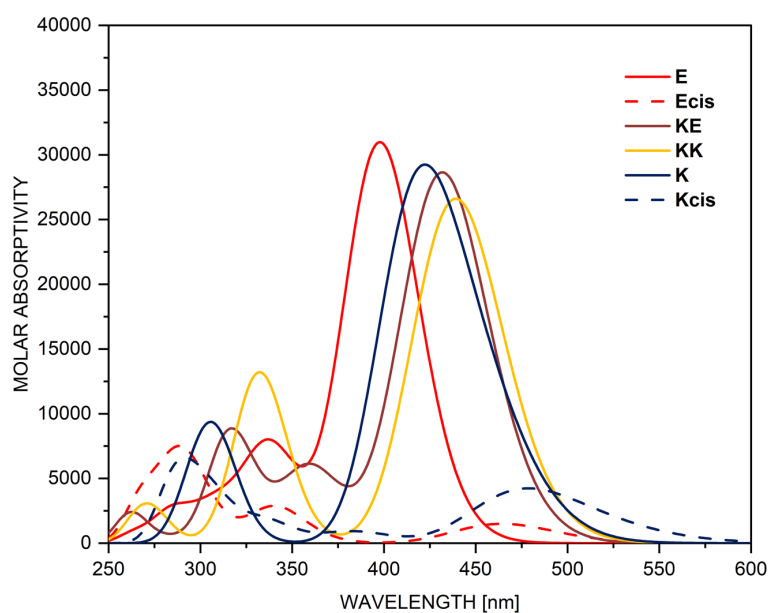


Figure 1: Simulated absorption spectra of the tautomers of **1** in toluene. The spectra in acetonitrile are shown in Figure S1 in Supporting Information File 1.

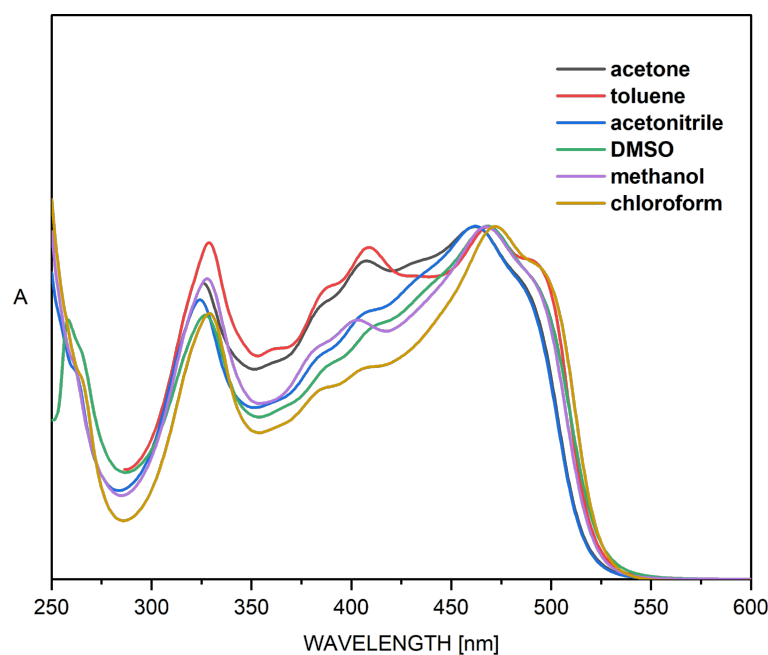


Figure 2: Normalized absorption spectra of **1**.

spectra, shown in Figure 2, two distinct spectral regions could be defined – around 400 nm, where the **E**-form absorbs (in analogy with the prediction from Figure 1 and the known individual spectra of the tautomers of **3** [55]) and around 450 nm, where the mixture of **KE** and **KK** absorbs. Bearing in mind that the predicted molar absorptivities of the tautomers are almost equal, it could be concluded that in toluene the ratio **E**/(**KE**+**KK**) is around 1, which corresponds very well to the relative energies from Table 1, predicting **E**/**KE**/**KK** as 52%/43%/5%. As seen from Figure 1 in all other solvents the content of (**KE**+**KK**) increases without disappearance of **E**. The reasons are different. While in acetonitrile this is the effect of the increased polarity of the solvent, leading to stabilization of the more polar keto tautomers, in the non-polar chloroform it is caused by its proton-donative nature (formation of a stabilizing intermolecular hydrogen bonding with the C=O group of the keto tautomers [51,56]). The effects of acetone, methanol and DMSO, as seen, are based only on the increased (comparing to toluene) dielectric constant of the solvent, stabilizing in different extent the more polar **KE** and **KK**. The further increase of the polarity of the environment by addition of water to acetonitrile (Figure 3) lead to increase of the content of the keto tautomers, but the enol form is still present.

As suggested by the theoretically predicted chemical shifts of the tautomeric proton (Table 1), the use of NMR could shed more light on the tautomeric composition in solution, again with some assumptions. The proton-transfer barrier between **E** and

KE (**TS**(**E-KE**), Table 1) is almost negligible, which makes the process very fast for the NMR timescale. Consequently, the OH (in **E**) and NH (in **KE**) signals cannot be distinguished from each other, giving one average peak. This makes possible to analyze the tautomerism in **1** as a function of (**E**+**KE**) and **KK**. The NMR spectra of **1** in acetonitrile-*d*₃ are in agreement with the above analysis of tautomeric equilibration based on theoretical calculations and UV spectra. At room temperature the proton signals are very broad and therefore the sample was cooled to 243 K (Figure 4). At this temperature the exchange process is slowing down and it is possible to register two exchanging protons (Figure S4 and Figure S5 in Supporting Information File 1). From COSY and NOESY spectra (Figure S6 and Figure S7 in Supporting Information File 1) most of the proton signals for the major and minor components can be assigned (see the note below Figure S4).

The calculated energy barrier of the process from **1E** to **1KE** in acetonitrile (2.11 kcal/mol, Table 1) is very low and this process should be fast in the NMR time scale. The cooling to 243 K does not change it much (Table 1, the italicized values). The calculated energy barrier of process from **1KE** to **1KK** in acetonitrile (37 kcal/mol in Table 1) is relatively high and this process should be slow in the NMR time scale. The conclusion from these calculations is that the major conformer is a result of fast exchange between **1E** and **1KE** and the minor conformer can be attributed to **1KK**. The measured carbon spectrum of **1** in CD₃CN at 243 K (Figure S8 in Supporting Information

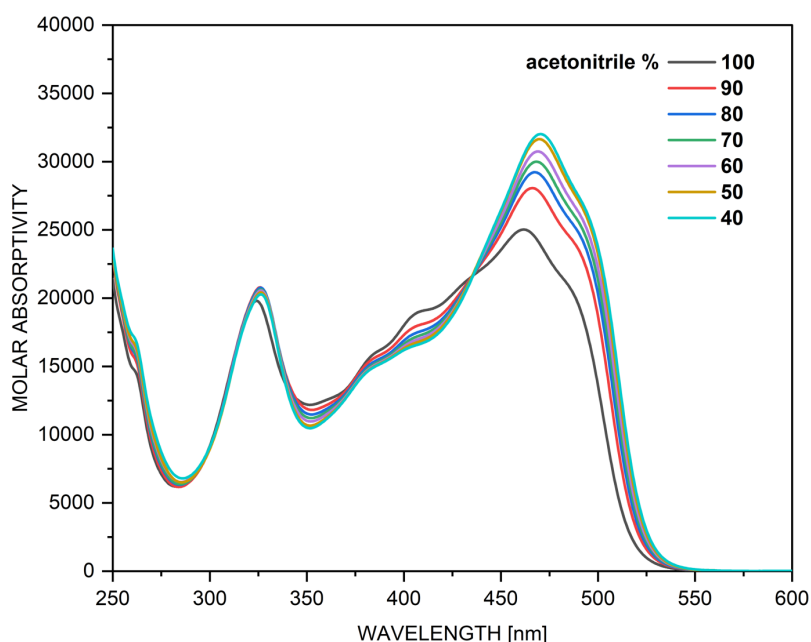


Figure 3: Absorption spectra of **1** in acetonitrile with stepwise addition of water.

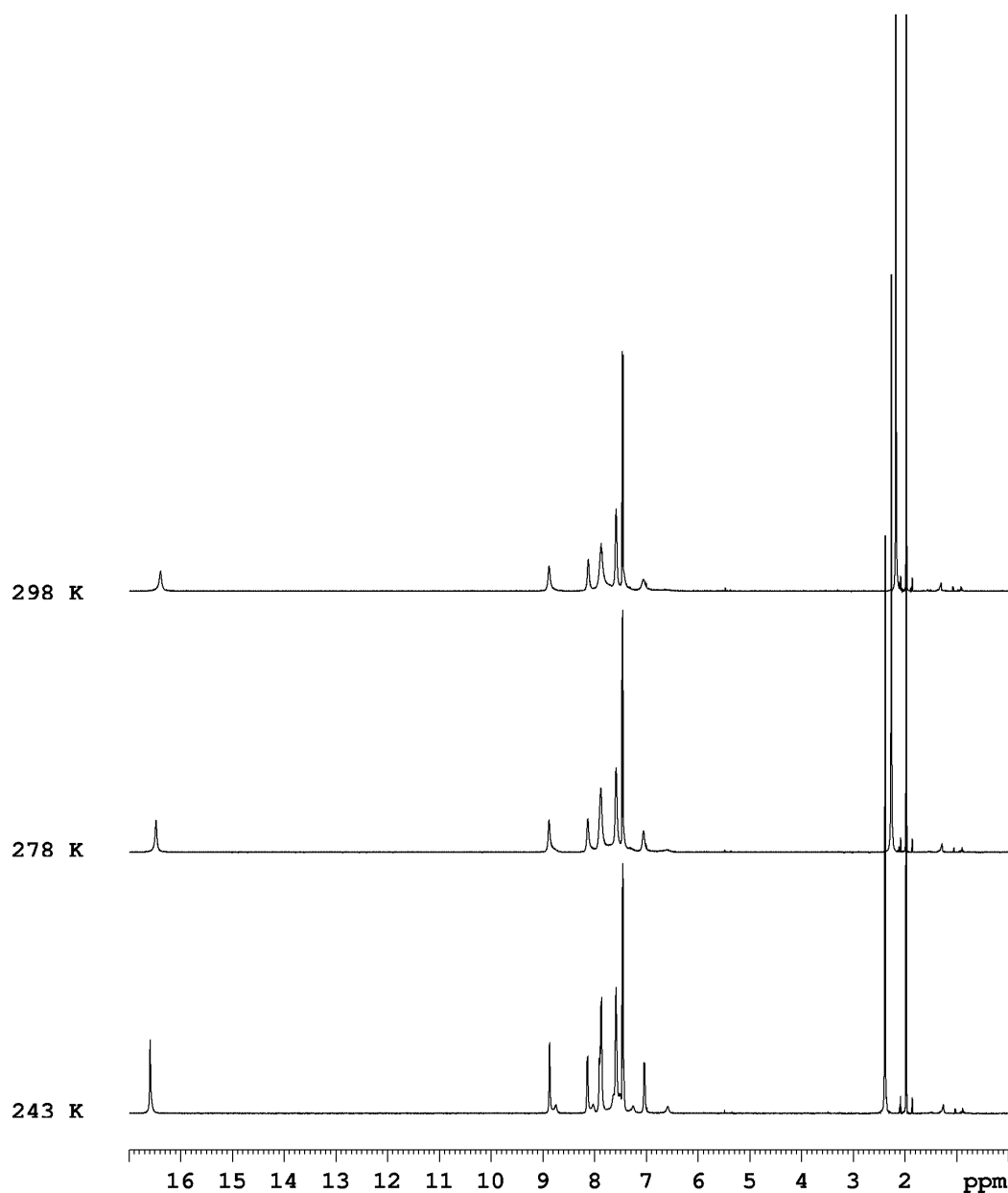


Figure 4: VT ^1H NMR spectra of compound **1** in acetonitrile- d_3 .

File 1) supports this assignment as well. The HSQC spectrum (Figure S9 in Supporting Information File 1) helps in the assignment of the carbon spectrum.

The proton signal at 16.59 ppm seems to be a sum of two signals and a deconvolution with Lotenzian bandshape function was performed (Figure S5 in Supporting Information File 1). The obtained two signals have an integral intensity of 78 to 22, which is in agreement with other integrals in the proton spectrum. This means that at 243 K the mixture **1E**+**1KE** is still dominating, but the content of **1KK** slightly increases

comparing to room temperature. This is not surprising bearing in mind that in the case of compound **3** the cooling in non-protic solvents (i.e. without the ability to form hydrogen bonding with the solute) shifts the equilibrium in direction of the keto tautomer [57].

According to the theoretical data, collected in Table 1, the enol form of **2** is substantially more stable and should predominantly exist in toluene. In acetonitrile some traces of **KE** and **KK** (both below 5%) could be observed in amounts around the detection limit of optical spectroscopy, which finally should not

lead to substantial spectral changes comparing to toluene. The absorption spectra, shown in Figure S10 (Supporting Information File 1), suggest a different story. The spectra in toluene and CHCl_3 are almost identical, with two intensive bands around 390 nm (assumed to **E** according to the simulated spectra, Figure S2) and 470 nm (assumed to **KE/KK**), which is rather surprising bearing in mind that chloroform, as a strong proton-donor solvent, always shifts the tautomeric equilibrium towards C=O-group-containing structures. In addition, the spectra in the remaining solvents show a single band around 500 nm independent on the nature of the solvent. Obviously, these data cannot be interpreted in the frame of the concept for a tautomeric equilibrium. The rotor in **2** contains a OH group surrounded by fluorine atoms, which could spontaneously deprotonate in polar solvents, while the tautomeric OH/NH group is always a part of strong intramolecular hydrogen bonding and the possibility for deprotonation is low. The deprotonation of the phenyl OH group is also supposed by the computational quantum chemistry calculations. As seen from Table S2 in Supporting Information File 1, the deprotonation of the tautomeric proton requests substantially more energy, while the deprotonation of the phenyl OH group leads to a single E^- tautomer. This fact is confirmed by a simple experiment. As seen from Figure 5, in the spectrum of **2** in acetonitrile a single band is observed at 500 nm. Upon addition of a very small amount of trifluoroacetic acid this band disappears and a new band at 400 nm

appears, suggesting that the red-shifted band can be attributed to E^- . The spontaneous deprotonation in acetonitrile is not completed, because the addition of triethylamine leads to rise of the band at 500 nm. The hypothesis for deprotonation in acetonitrile is nicely confirmed by the simulated spectra of **E** and E^- , shown in Figure S11 and Figure S12 in Supporting Information File 1. As seen the intensity of the E^- is substantially larger, exactly as observed in Figure 5.

Excited-state proton transfer and switching

The lack of emission in the azo dyes is attributed to the availability of non-bonding electron pairs at the nitrogen atoms from the azo group and the possibility for *cis/trans* isomerization upon excitation, which leads to conical intersection deactivation from the excited to the ground state. And while there is substantial number of experimental and theoretical (some of them at very high level of theory [58-60]) investigations concerning the *cis/trans* isomerization in azobenzenes [61-74], the number of studies, dealing with the excited-state behavior of compounds where an OH group is situated on the ortho position in respect of the azo group, is very limited. It is not surprising because in these cases a possibility for ESIPT exists along with the *cis/trans* isomerization, creating a rather complicated interplay between two competitive processes. Experimental [49,75-80] and theoretical [81-84] studies of compound **3** and derivatives clearly indicate the excited-state competition be-

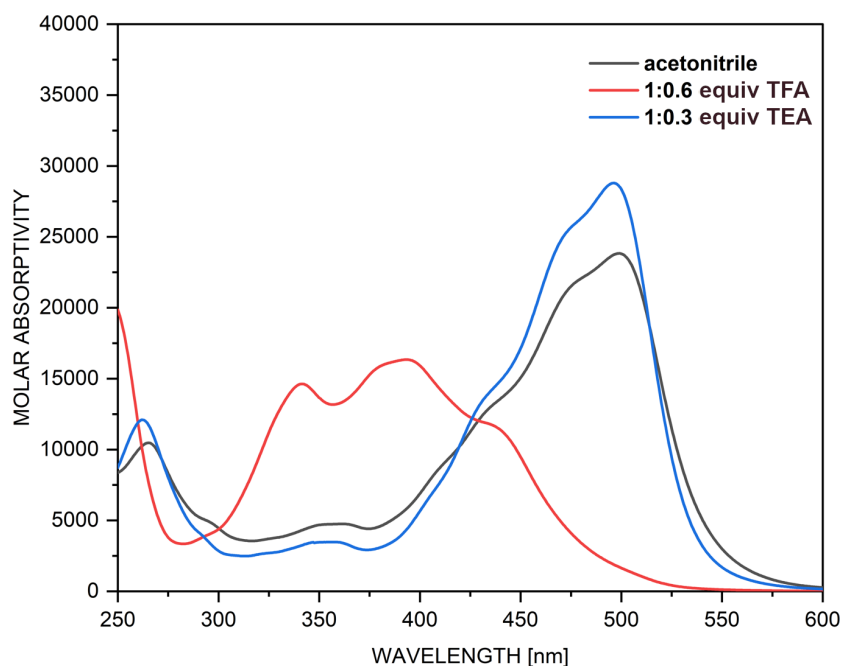


Figure 5: Changes in the absorption spectrum of **2** in acetonitrile upon addition of trifluoroacetic acid (TFA) and triethylamine (TEA). The addition of more TFA or TE does not cause further spectral changes.

tween the ESIPT from enol to keto form, which leads to very weak emission, and the *trans* to *cis* isomerization, leading to emissionless deactivation to the ground state.

The potential energy surfaces (PESs) of **1** in the ground and excited state, sketched in Figure 6, show a very complicated picture. The ground-state tautomerism, discussed above, leads to a tautomeric mixture of **E**, **KE**, and **KK**, each of them being excited upon irradiation. As already shown [82], the first singlet excited state of **E** is dark. According to the results from Figure 6, **E*** can spontaneously go to the *trans* to *cis* conical intersection (CI) via twisting ground the N=N bond (angle β) returning back to the ground state. Although from the spectral point of view (Figure 1) the obtainment of a mixture of **E** and **E_{cis}** should result in a decrease of intensity of the band around 400 nm, the same process in **3** is very fast to be recorded by conventional UV–vis spectroscopy, suggesting preferable population of intramolecular hydrogen bonding stabilized **E**. Comparing the angles α of the **E*** form (13°) and the transition state between **E** and **E_{cis}** (60°) the former is nearer to the geometry of **E**, suggesting preferable population. The excitation of **KE** gives three possible pathways: returning back to ground state by emitting, ESIPT to **E*** (and relaxation to the ground state by CI in the N=N bond isomerization region) and twisting around the double bond axle C=N (change of α) to the CI in the twisting region populating **KE** and **KK** in the ground state. No measurable emission of **1** was detected in any of the studied solvents, excluding the first pathway. The ESIPT process is practically barrierless leading to the CI in the N=N bond isomerization region with preferential population of **E** as discussed above. The third pathway could lead to population of **KK**, rise

of its existing amount and, consequently, to rise of the absorption band at around 470 nm and restoration with the time of the equilibrium tautomeric state. No appearance of **K** is expected as a result of higher energy as discussed previously.

Actually, the third process is shown in Figure 7. Upon irradiation at 365 nm a slight rise of the absorbance around 470 nm is observed. The process is fast ($0.738 \pm 0.029 \text{ s}^{-1}$ for the forward transition from the equilibrium mixture **E**+**KE** to **KK** and $0.177 \pm 0.031 \text{ s}^{-1}$ for the transition back) and fully reversible, indicating that a switching between **E**+**KE** and **KK** occurs from the PT region I to the PT region II as indicated in Figure 6. The switching is observed in toluene, but not in acetonitrile, which is probably due to the substantial decrease of **TS(KE-KK)** relative energy (see Table 1) moving it to the shorter time window. The dipole moments of **KE*** and the surrounding transition states are approximately the same, which excludes changes in the stabilization going from toluene to acetonitrile. The results indicate that the excitation of **KE** leads preferably to return to the ground state via CI in the N=N bond isomerization region and, in a very limited extent, to switching to **KK**. According to the PESs in Figure 6, the excited **KK** behaves in a way similar to **KE** and the spectral changes cannot be distinguished from these of **KE** due to the similarities in the absorption spectra.

Compound **2** does not emit in the studied solvents and its absorption spectra in toluene do not show detectable changes upon irradiation. The twisting barrier (**2TS(KE-KK)** in Table 1) here is substantially larger comparing to **1**, which means that if switching to **KK** occurs the relaxation process back should be slower. The theoretical calculations give the

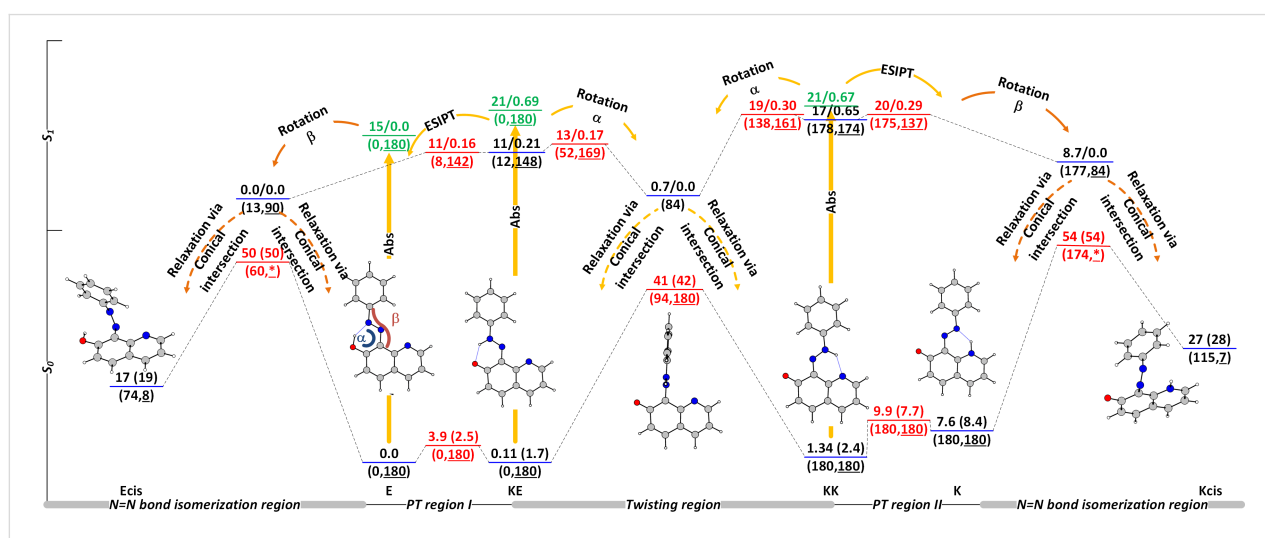


Figure 6: Ground (M06-2X/TZVP) and excited (CAM-B3LYP/TZVP) state potential energy surface of compound **1** in toluene presented as relative energies in kcal/mol. The values of the angles α and β (see also Scheme 2) are given in brackets (β is underlined). The asterisk indicates *trans* to *cis* isomerization via inversion mechanism [67]. In the excited state the relative energy is followed by the oscillator strength of the corresponding state. The Franck–Condon states of the tautomers, existing in solution, are given in green.

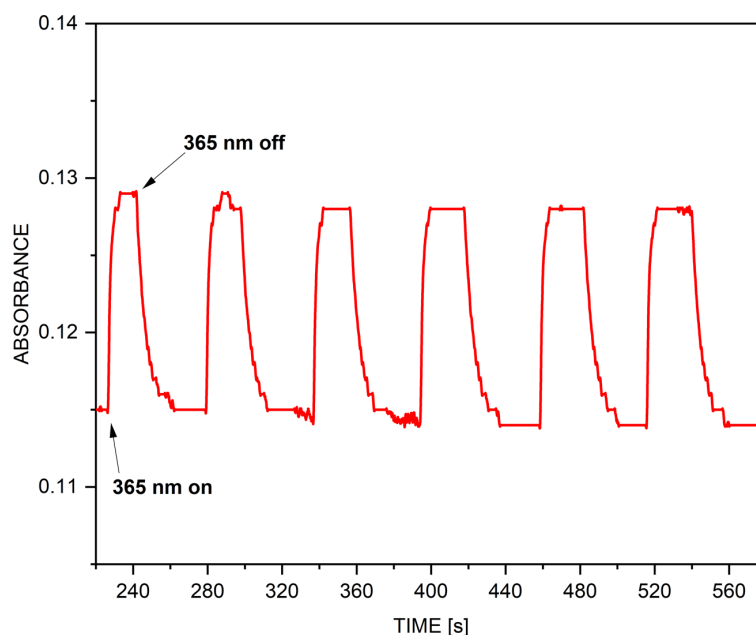


Figure 7: Changes of the absorbance of compound **1** at 465 nm in toluene upon turning on and off the irradiation source (365 nm).

possible reason for lack of switching – due to the low basicity of the proton-accepting nitrogen atom, the **KE*** form spontaneously goes to **E***, which closes the channel to the twisting region. On the other side there is substantial number of papers describing the very long-lived *cis* isomers in *ortho*-halogen-substituted azobenzenes [38,85–88]. Obviously, in the case of compound **2** the relaxation back to the ground state through the CI in the N=N bond isomerization region, which is the only option in this compound to return back to the ground state, populates exclusively the ground state **E** instead of **Ecis**.

Is there a potential for clean switching in **1**?

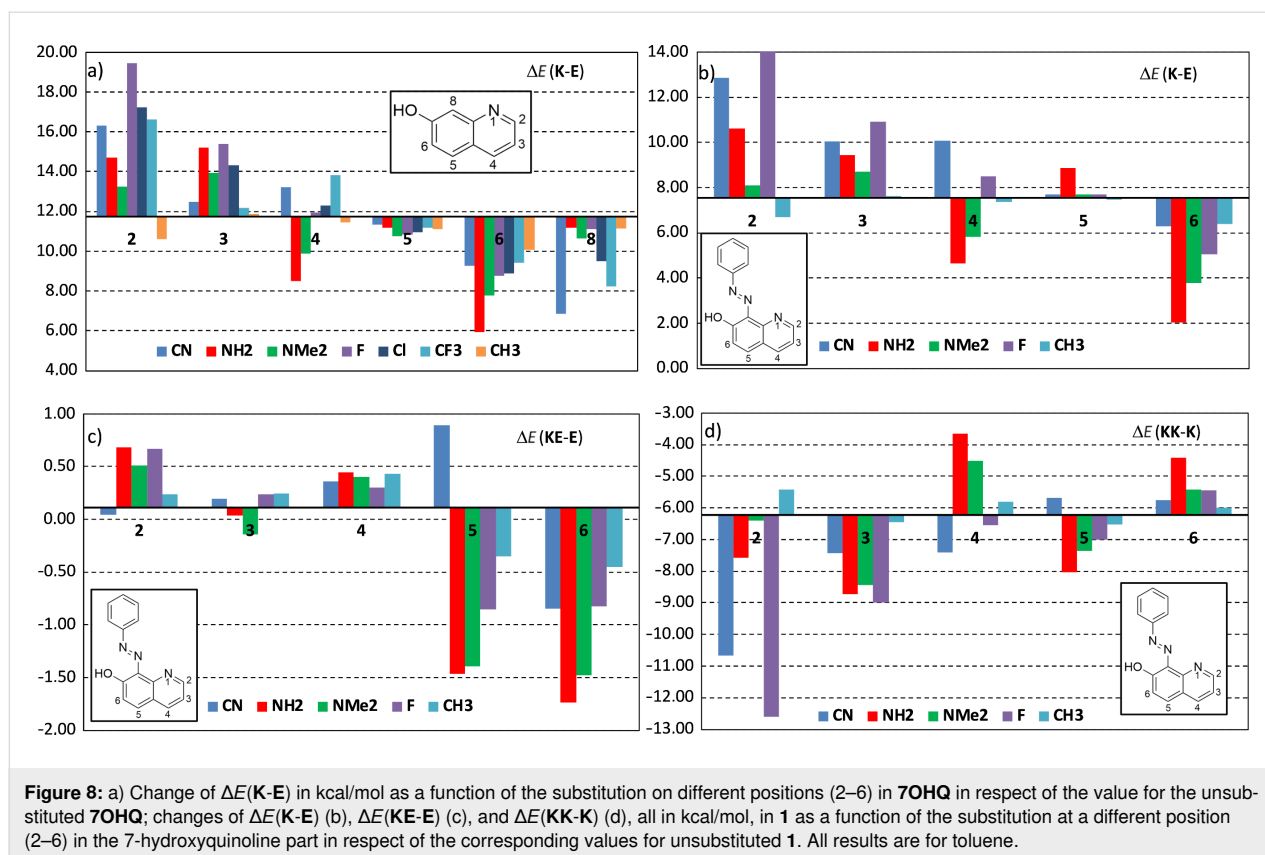
Although it was shown above that there is a switching from the mixture **E+KE** to **KK** in **1** in toluene, the compound does not fulfil the requirements for clean switching. Returning back to Scheme 2, the clean switching can be defined, in general terms, as transition from the pure **E** (or **KE**) to the pure **K** (or **KK**). In order to classify compound **1** as a real proton crane, the switching has to be from **E** to **K**.

As shown above, in the case of **1**, there is a mixture between **E**, **KE** and **KK** (problem with a clean off-state of switching) and the end tautomer **K** is higher in energy comparing to **KK** (problem with possibility to achieve a clean on-state of switching). All this means that structural changes are needed in order to find an azo compound, based on 7-hydroxyquinoline, where the individual tautomers have energies ranked in the following way: $E_E < E_{KE}$, E_{KK} and $E_K < E_{KE}$, E_{KK} , $E_E < E_K$. In order to assure

that in the initial solution (prior irradiation) only **E** is present, the relative energy of **K** should be at least 2 kcal/mol higher to be considered negligible from the viewpoint of optical spectroscopy. In other words, three conditions can be defined for clean switching:

- The relative energy between **K** and **E**, $\Delta E(\mathbf{K-E}) > 2$ kcal/mol, in order to have only pure **E** in solution;
- $\Delta E(\mathbf{KE-E}) > 2$ kcal/mol, again to assure presence only of **E**;
- $\Delta E(\mathbf{KK-K}) > 2$ kcal/mol in order to provide conditions for complete transfer from **KK** to **K** upon irradiation.

The relative stabilization of **K** in respect of **E** depends mainly on the substitution in the **7OHQ** moiety. The relative energies of **K** in respect of **E** under various substitution in **7OHQ** are collected in Tables S3 (Supporting Information File 1) and the directions of change are illustrated in Figure 8a. It seems that substitution on positions 2 (with exception of a CH_3 group) and 3 leads to destabilization of **K**, while placing a substituent in positions 5 (weakly) and 6 stabilizes it. The effect on position 4 is mixed – electron donors stabilize the **K** form, while acceptors rise its energy. All substituents in position 8 stabilize **K**, but the effect of the acceptors is more pronounced. The effect of the amino group is stronger comparing to NMe_2 due to the steric hindrance in the latter. Since in **1** the azo group, an acceptor, is placed on position 8, it is also expended to bring additional inherent stabilization of the **1K** tautomer.



The effect of the substitution in the **7OHQ** part of **1** is illustrated in Figure 8b–d and the corresponding values are collected in Table S4, Supporting Information File 1. In **1** all three criteria for clean switching are not fulfilled and it is interesting to see how the substitution can change the situation. In respect of $\Delta E(\text{K-E})$ (Figure 8b) the needed reduction is observed in position 2 for CH_3 group (weakly), substantially for NR_2 in position 4 and strongly for all substituents in position 6. The value of $\Delta E(\text{KE-E})$ (Figure 8c) has to be larger than 2, but it cannot be achieved. Almost all functional groups on position 2 and all on position 4 lead to changes in the desired direction. The substitution on positions 5 and 6 leads to strong stabilization of **KE**, which is not needed. The cyano group on position 5 destabilizes **KE** strongly. The value of $\Delta E(\text{KK-K})$ has also to be larger than 2 and, as seen from Figure 8d, it cannot be achieved with the used substituents. Most of the substituents destabilize **K** with exception of the electron donor ones on position 4 and all in position 6. Again, the cyano group on position 5 is acting in the desired direction, but the effect is weak. Considering the fact that some substituents act positively in some cases and negatively in others, it can be concluded substitution on position 4 by NR_2 or CH_3 and on position 5 by CN leads to desired changes in all three parameters. The effect on substitution in position 6 is contradictory in respect of $\Delta E(\text{KE-E})$ and $\Delta E(\text{KK-K})$.

Based on the previous knowledge about the relative stabilities of **E** and **KE** in **3**, it can be stated that electron-acceptor substituents in the phenyl ring shift the equilibrium towards **KE**, while electron donors do the same in direction of **E**. In this charge transfer model, the N=N group plays a role of acceptor, stabilized by donors in the phenyl ring, while N-NH is a donor, favored by acceptors in Ph [3,7,89]. Following this model, a suitable substitution in the Ph ring of **1** can stabilize or destabilize **KE** and **KK** in respect to **E** and **K**. This opens an additional channel for fulfilling the requirements for a clean switching. It should be noted, however, that the relative stabilization of **KE** and **KK** depends, in addition, on the strength of the intramolecular hydrogen bonding. The interaction $\text{C=O}\cdots\text{H-N}$ is much stronger, which leads to better stabilization of **KE**.

Some border cases of substitution in the phenyl ring of **1** are considered in Table 2. As expected, the substitution with electron-donor substituents destabilizes the **KE** and **KK** tautomers leading to changes of $\Delta E(\text{KE-E})$ and $\Delta E(\text{KK-K})$ in the desired direction. At the same time, they destabilize **K**, which is not desired. Para-substituted NO_2 and CN compounds feature undesired stability of **KE** and **KK** (and hence, low values of $\Delta E(\text{KE-E})$ and $\Delta E(\text{KK-K})$), but the increased number of CN substituents leads to a rise of $\Delta E(\text{KE-E})$ and $\Delta E(\text{KK-K})$ and,

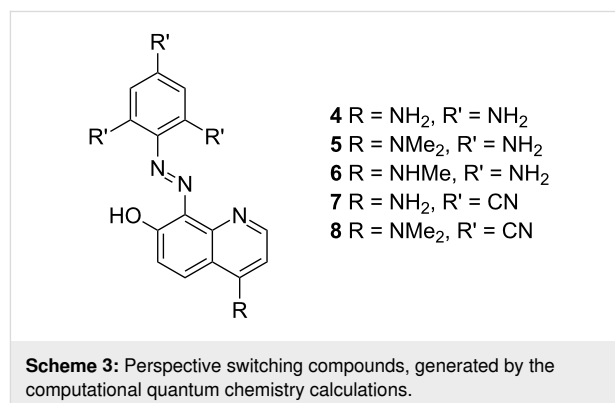
Table 2: Relative stability of the tautomers of compound **1** in toluene as a function of the substituents in Ph ring.

Position	Subst.	ΔE [kcal/mol]				ΔG^0 [kcal/mol]			
		E	KE	KK	K	E	KE	KK	K
	H	0.00	0.11	1.3	7.5	0.00	1.7	2.4	8.4
<i>p</i>	NO ₂	0.81	0.00	0.65	6.9	0.00	0.08	0.69	5.0
<i>p</i>	CN	0.52	0.00	0.77	6.9	0.00	0.67	1.4	6.1
<i>o,o'</i>	CN	0.00	1.6	0.54	2.7	0.00	0.82	0.13	2.1
<i>o,o',p</i>	CN	1.1	1.4	0.00	1.9	0.17	0.91	0.00	1.5
<i>m,m'</i>	CN	0.00	0.15	0.81	5.7	0.00	1.4	1.9	5.4
<i>p</i>	NH ₂	0.00	1.6	3.2	8.5	0.00	2.0	3.8	8.8
<i>o,o',p</i>	NH ₂	0.00	5.5	7.5	9.6	0.00	5.1	8.1	10
<i>p</i>	NMe ₂	0.00	1.8	3.5	8.7	0.00	2.4	4.7	9.8
<i>o,o',p</i>	NMe ₂	0.00	2.7	4.5	9.1	0.00	2.5	4.8	9.5
<i>p</i>	N(<i>t</i> -Bu) ₂	0.00	0.35	1.6	7.7	0.00	0.86	2.2	8.0
	julolidine	0.00	2.0	3.9	9.1	0.00	1.7	3.9	9.5
<i>o,o',m,m',p</i>	F	0.00	1.6	2.0	5.3	0.00	1.7	2.4	8.4

also, to the requested stabilization of **K**. Considering the data in Table 2, there is no compound that nears to the ground-state PES, requested for clean switching. Obviously, a cooperative effect between substitution in the Ph ring and the 7-OH quinoline part is needed.

In Scheme 3 and Table 3 the most suitable examples for cooperative substitution are shown. It seems that the substitution with strong donor substituents in the phenyl ring and on position 4 in 7-OH quinoline leads to results that are near to the desired (compounds **4–6**). Very interesting is the result with strong electron-acceptor-substituted phenyl ring and donor substitution in **7OHQ** part (compounds **7** and **8**). Actually **7** and **8** fulfill most of the requirements for clean switching if the **K** tautomer is considered as off-state and the **E** one as on-state. The predicted spectra of the terminal **E** and **K** tautomers of compounds **4** and **7** are compared with those of compound **1** in Figure S13 in Supporting Information File 1. The increased

charge-transfer character of compound **4** compared to **1** leads to a red shift in the absorption spectra of both tautomers. At the same time the long-wavelength maximum of **7K** is blue shifted in respect to **7E**, which in practical means would lead again to a red shift when switching from the more stable former to latter.

**Table 3:** Relative stability of the tautomers of compounds **4–7** in toluene.

compound	ΔE [kcal/mol]				ΔG^0 [kcal/mol]			
	E	KE	KK	K	E	KE	KK	K
4	0.00	5.8	7.2	7.0	0.00	5.4	7.7	6.9
5	0.00	5.8	7.5	8.4	0.00	5.4	7.7	8.3
6	0.00	6.0	7.5	7.2	0.00	5.6	7.3	7.6
7	2.5	3.4	1.0	0.00	3.3	4.4	1.6	0.00
8	1.6	2.3	0.48	0.00	0.84	1.7	0.00	0.39

Of course, the results in this part should be considered with care. They originate from computational quantum chemistry calculations in toluene and their aim is not to suggest definite compounds, but to show directions of structural modifications that can solve one of the problems with the switching of compounds originating from **1** – the unsuitable relative stability of the ground-state tautomers. Changing the solvent can also change the results, because **KK** and, especially, **K** could be much more stabilized in polar solvents. The problem with avoiding the *cis/trans* isomerization, which reduces sharply the PT switching is also a problem pending solution.

Conclusion

Two novel azo dyes originating from 7-hydroxyquinoline have been synthesized and studied by a variety of experimental and theoretical methods. It has been shown that 8-(phenyldiazenyl)quinolin-7-ol exists in solution as an equilibrium mixture of three different tautomers, whose proportion depends on the solvent environment. Upon irradiation reversible switching is detected in toluene, based on proton transfer and intramolecular switching. The reduced basicity in the azo nitrogen atoms in the case of 8-(4-hydroxy-1,2,3,5-tetrafluorophenyldiazenyl)quinolin-7-ol does not allow a ground-state tautomeric process to occur.

Bearing in mind the requirements for clean switching, where the tautomeric proton is transferred from the oxygen atom to the nitrogen atom of the quinolyl moiety (i.e. from **E** to **K**), a theoretical design was performed in order to see the most suitable substituents and their position. It seems that the substitution with strong donor substituents in the phenyl ring and on position 4 in 7-hydroxyquinoline leads to results that are near to the desired. Very interesting is the result with strong electron-acceptor-substituted phenyl ring and donor substitution in 7-OH quinoline, where the most of the requirements for clean switching are achieved if the **K** tautomer is considered as off-state and the **E** one as on-state.

Experimental

Synthesis and structure elucidation

Materials

The starting reagents and solvents were purchased from Sigma-Aldrich and Fluorochem and used as received. The solvents used for the experimental synthesis (HPLC grade) were purchased from Sigma-Aldrich. All other materials were commercial products of analytical grade and used as supplied. Analytical TLC (thin-layer chromatography) was performed on Merck silica gel 60 F254 precoated TLC plates (0.2 mm thick). The identity of all compounds was confirmed employing various spectroscopic techniques including NMR and HRMS–ESI high-resolution mass spectrometry. The ^1H and ^{13}C NMR spectra

were recorded in CDCl_3 or $\text{DMSO}-d_6$ at 25 °C on a Bruker Ultrashield Plus 500 spectrometer using 5 mm tubes. The corresponding operating frequencies were 500.13 MHz and 125.77 MHz, respectively. The chemical shifts are quoted in parts per million (ppm) with an accuracy of 0.01 ppm. The coupling constants (J) are described in Hz and determined with an accuracy of 0.1 Hz. To describe the spin multiplicity in the ^1H NMR spectra, the following abbreviations were used: s = singlet, br s = broad singlet, d = doublet, t = triplet, dt = double triplet, dd = doublet of doublets, m = multiplet. The HRMS spectra were recorded on a Dionex Acclaim RSLC 120 C18 2.2 mm 120 Å 2.1×50 mm column maintained at 40 °C. The measurements were done on a Bruker MicrOTOF-QII-system coupled with an ESI source with a nebulizer: 1.2 bar, dry gas 8.0 L min^{-1} , dry temperature 200 °C, capillary 4500 V and plate offset 500 V.

Synthesis of 8-(phenyldiazenyl)quinolin-7-ol (**1**)

A 50 mL round-bottomed flask equipped with a mini magnet was charged with aniline (0.33 g, 3.5 mmol) and 1 N aqueous HCl (12 mL), and stirred at 0 °C for 30 min. A cold solution of sodium nitrite (0.38 g, 5.5 mmol, dissolved in 4.0 mL H_2O) was added dropwise during 10 min and the resulting mixture was stirred at 0 °C for 2 h. The mixture was diluted by adding pre-cooled methanol (4.0 mL). In a separate round-bottomed flask, 7-hydroxyquinoline (0.29 g, 2.0 mmol) and potassium hydroxide (0.163 g, 3.0 mmol) were dissolved in methanol (6.0 mL) and cooled to 0 °C. This solution was treated under constant stirring by dropwise addition of the cold diazonium solution during 20 min. The resulting red-orange mixture was stirred at 0 °C for 2 h, and at rt for 15 h. The mixture was neutralized with 1 N aqueous sodium hydroxide, filtered, washed with cold water (5 mL) and dried under vacuum. The dark orange crude material was purified by flash column chromatography on silica gel, using dichloromethane/ethyl acetate 6:1 as eluent to obtain the pure product as bright orange solid (0.31 g, 62% yield). ^1H NMR (500 MHz, CDCl_3) δ 8.93 (dd, $J = 1.2 \text{ Hz}$, 4.6 Hz, 1H), 7.95 (d, $J = 8.0 \text{ Hz}$, 1H), 7.87 (d, $J = 8.0 \text{ Hz}$, 2H), 7.70 (d, $J = 9.5 \text{ Hz}$, 1H), 7.49 (t, $J = 8.0 \text{ Hz}$, 2H), 7.73–7.33 (m, 2H), 7.02 (d, $J = 9.5 \text{ Hz}$, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 171.3, 151.3, 148.5, 145.0, 137.7, 136.5, 131.0, 129.7, 128.8, 125.8, 123.2, 120.7, 120.0; HRMS–ESI (m/z): $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{15}\text{H}_{12}\text{N}_3\text{O}^+$, 250.09749; found, 250.09739.

Synthesis of 8-(4-hydroxy-1,2,3,5-tetrafluorophenyldiazenyl)quinolin-7-ol (**2**)

Diazotization of pentafluoroaniline has been recommended to be carried out in nonaqueous media or concentrated mineral acid, otherwise the coupling product always contains a hydroxy group on the perfluorophenyl ring at the position para to the azo group. It appears that when solutions of the diazonium salts are

made alkaline the para-fluorine atom is so readily replaced by a hydroxy group, and that the 4-hydroxy-2,3,5,6-tetrafluorobenzene cation is the entity formed first [90,91]. A 50 mL round-bottomed flask equipped with a mini magnet was charged with pentafluoroaniline (0.64 g, 3.5 mmol) and 1 N aqueous HCl solution (12.0 mL) and methanol (7.0 mL). The mixture was stirred at rt for 2 h, then cooled in an ice bath to 0 °C, and treated slowly with a cold solution of sodium nitrite (0.38 g, 5.5 mmol) in distilled water (3.0 mL). The mixture was left stirring at 0 °C for 2 h. In a separate 50 mL flask, 7-hydroxyquinoline (0.29 g, 2.0 mmol) dissolved in methanol (4.0 mL) was treated with potassium hydroxide (0.16 g, 3.0 mmol). The solution was stirred at 0 °C for 20 min, then the cooled diazonium salt solution was added slowly to the cold solution of 7-hydroxyquinoline during 30 min. Upon addition, a red-orange color formed. The mixture was left stirring at 0 °C for 2 h, then at rt overnight. The mixture was filtered, the filtrate was neutralized with 1 N aqueous potassium hydroxide solution, diluted with dichloromethane (75 mL) and stirred overnight. The orange solid formed, was washed with water several times and dried. The crude material was purified by column chromatography on silica gel, eluting with dichloromethane. Evaporation of the solvent afforded the pure target compound as orange solid (0.26 g, 38% yield). ^1H NMR (500 MHz, DMSO- d_6) δ 14.7 (br s, 1H), 8.90 (dd, $J = 1.7$, $J = 4.3$, 1H), 8.28 (dd, $J = 1.7$, $J = 8.2$, 1H), 7.86 (d, $J = 9.2$ Hz, 1H), 7.44 (dd, $J = 4.2$ Hz, $J = 4.2$ Hz, 1H), 7.25 (d, $J = 9.2$ Hz, 1H); ^{13}C NMR (125 MHz, DMSO- d_6) δ 156.5, 153.0, 151.0, 145.2, 144.0 (d, $J = 240$ Hz), 141.2 (d, $J = 240$ Hz), 136.5, 131.2, 131.1, 123.0, 120.9, 120.0, 110.5; ^{19}F NMR (470 MHz, DMSO- d_6) δ 154.5 (d, $J = 17.7$ Hz), -169.2 (d, $J = 17.7$ Hz); HRMS–MALDI–TOF [m/z]: [$M + H$] $^+$ calcd for $\text{C}_{15}\text{H}_8\text{F}_4\text{N}_3\text{O}_2^+$, 338.05471; found, 338.05477.

Spectral investigations: The NMR spectra were recorded on a Bruker Avance II+ spectrometer operating with frequency 500 MHz for ^1H NMR and 125 MHz for ^{13}C NMR in CD_2Cl_2 and 600 MHz for ^1H NMR and 151 MHz for ^{13}C NMR in CDCl_3 and CD_3CN . ATR-FTIR spectra of the compounds were recorded on a Bruker Tensor 27 FTIR spectrophotometer in the range of 4400–600 cm^{-1} with a resolution of 2 cm^{-1} at room temperature. The external reflection diamond crystal was used and the samples were scanned 128 times. The UV–vis spectra were measured on a Jasco V-570 UV–vis–NIR spectrophotometer using spectral grade solvents in the concentration range $\approx 10^{-5}$ mol/L. The steady-state fluorescence spectra were recorded with a FluoroLog 3-22 (HORIBA) spectrofluorometer in the range 200–800 nm with a resolution of 0.5 nm and double-grating monochromators using as excitation wavelength a value near the absorption maxima of the compounds with concentrations of $\approx 10^{-6}$ mol L^{-1} .

The irradiation experiments were performed with an experimental setup designed and constructed by us [92]. The configuration allows to use two light sources whose beams path orthogonally through a cuvette. The absorbance spectra were measured using a fiber-optic micro-spectrometer QE 65000 (Ocean Optics, Inc., Dunedin, FL, USA) with approximately 0.7 nm spectral resolution in the range 250–1000 nm. The spectra were recorded with the specialized software SpectraSuite (Ocean Optics, Inc., Dunedin, USA).

Computational quantum chemistry calculations: Quantum-chemical calculations in the ground state were performed using the Gaussian 16 C.01 program suite [93]. All structures (in both ground and excited state) were optimized without restrictions, using tight optimization criteria and an ultrafine grid in the computation of two-electron integrals and their derivatives. The true minima were verified by performing frequency calculations in the corresponding environment. The implicit solvation was described using the polarizable continuum model [94] (the integral equation formalism variant, IEFPCM, as implemented in Gaussian 16). The transition states were estimated using the STQN method [95] and again verified by performing frequency calculations in the corresponding environment.

The M06-2X [96,97] functional with the TZVP [98] basis set was used for the structure optimizations in the ground state. The use of M06-2X provides very good predictability in the ground state [51,53,99–103] of the tautomeric composition in tautomeric compounds and proton cranes as well as the *E/Z* isomerization ratio in rotary switches. In compound **1** the obtained values for the relative energies are validated by using Møller-Plesset MP2-4 [104–107] and CCSD(T) [108,109] single point energies (M06-2X/TZVP geometry) in the corresponding solvent environment.

The TD-DFT method [110,111] was used for singlet excited-state optimizations. CAM-B3LYP [112] with the TZVP basis set was used for the optimizations. The selection of CAM-B3LYP is based on its better performance (in comparison with a variety of density functionals, including M06-2X) in describing electronic excitation energies, excited-state geometries, dipole moments and oscillator strengths in a variety of systems [113–116], including ESIPT ones [117], as well as on our own previous experience in describing the overall shape of the excited-state PES [51,52,92].

Bearing in mind that M06-2X systematically underestimates the absorption band positions [118], the UV–vis spectral data were predicted by the B3LYP [119] functional (TZVP basis set) using the M06-2X optimized ground-state geometries.

The NMR chemical shieldings of selected tautomeric forms of the studied compounds were calculated using the GIAO approximation [120]. The calculated absolute shieldings were transformed to chemical shifts using the reference compound tetramethylsilane ($\text{Si}(\text{CH}_3)_4$), for hydrogen and carbon atoms: $\delta = \delta_{\text{calc}}(\text{ref}) - \delta_{\text{calc}}$. Both $\delta_{\text{calc}}(\text{ref})$ and δ_{calc} were evaluated at the same computational level (M06-2X/TZVP).

Supporting Information

Supporting Information File 1

Additional figures and tables.

[<https://www.beilstein-journals.org/bjoc/content/supplementary/1860-5397-21-105-S1.pdf>]

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Author Contributions

Lidia Zaharieva: data curation; formal analysis; investigation; writing – review & editing. Vera Deneva: data curation; formal analysis; investigation; writing – review & editing. Fadhil S. Kamounah: data curation; writing – review & editing. Nikolay Vassilev: formal analysis; investigation; writing – review & editing. Ivan Angelov: data curation; investigation; writing – review & editing. Michael Pittelkow: conceptualization; data curation; writing – review & editing. Liudmil Antonov: conceptualization; data curation; formal analysis; funding acquisition; project administration; writing – original draft; writing – review & editing.

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Data Availability Statement

Data generated and analyzed during this study is available from the corresponding author upon reasonable request.

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Highly distinguishable isomeric states of a tripodal arylazopyrazole derivative on graphite through electron/hole-induced switching at ambient conditions

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Full Research Paper

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Abstract

Manipulating the energy barrier and extending the half-life of nonequilibrium states in photochromic switches presents viable solutions for applying them in molecular electronics. Typically, the half-life of the *Z* isomer of azobenzene (AB) is a few days. Arylazo-pyrazole-based molecular switches are one of the profoundly explored systems in recent times due to their superior bidirectional photoswitching and long half-life (over a thousand days at room temperature) of *Z* isomers. Herein, we utilize an efficient solid-state photoswitchable fluorinated tripodal *N*-functionalized arylazo-3,5-dimethylpyrazole derivative (FNAAP) to envisage and access multiple metastable states on the surface. The tripodal molecule forms well-ordered, large crystalline domains on graphite through non-bonding interactions between the molecules. By injecting electron/hole pairs into the self-assembled molecules on a surface using a scanning tunneling microscope (STM) tip, they are switched between 8 states (*EEE*, *EEZ*, *EZE*, *ZEE*, *EZZ*, *ZEZ*, *ZZE* and *ZZZ*) in a tunneling junction at ambient conditions. Contrary to the degeneracy-controlled four states in solution phase, all the eight states are remarkably stable on the surface and are well distinguishable by the tunneling current passing through the molecule at the tunneling junction. The change in current upon switching between these states is approximately an order of magnitude. This is particularly notable at positive sample voltage compared to negative sample voltage. The exceptional stability of the states at ambient conditions provides an opportunity to use a single FNAAP molecule as an 8-bit operation unit, with a potential storage capacity of ≈ 200 Tbits per 1 cm^2 area using an atomically precise write and read tool like an STM tip.

Introduction

Molecular electronic devices have been predicted to outperform silicon-based devices [1,2]. Reprogrammable arrays of molecular switches with multiple states [3], logic-in-memory operations using single-metallofullerenes [4], multistate molecular switches [5], molecular memory and logic processing based on guest capture/release [6], etc., have demonstrated the possibility of using single molecules in logic operations. Manipulating molecular spin states [7–9] and electronic states [10,11] using tunneling electrons/holes have shown the potential to revolutionize quantum information processing. For a single molecular switch possessing multiple spins [7–9] or electronic states [10,11], the functional unit can be suitably triggered through external stimuli to induce the switching and to modulate the function. Photo-triggerable molecular switches like azobenzene (AB) [10–13], spiropyran [14], diarylethene [15] and multifunctional AB [16] have attracted a lot of interest due to the distinct differences in the electronic and optical properties of switchable states.

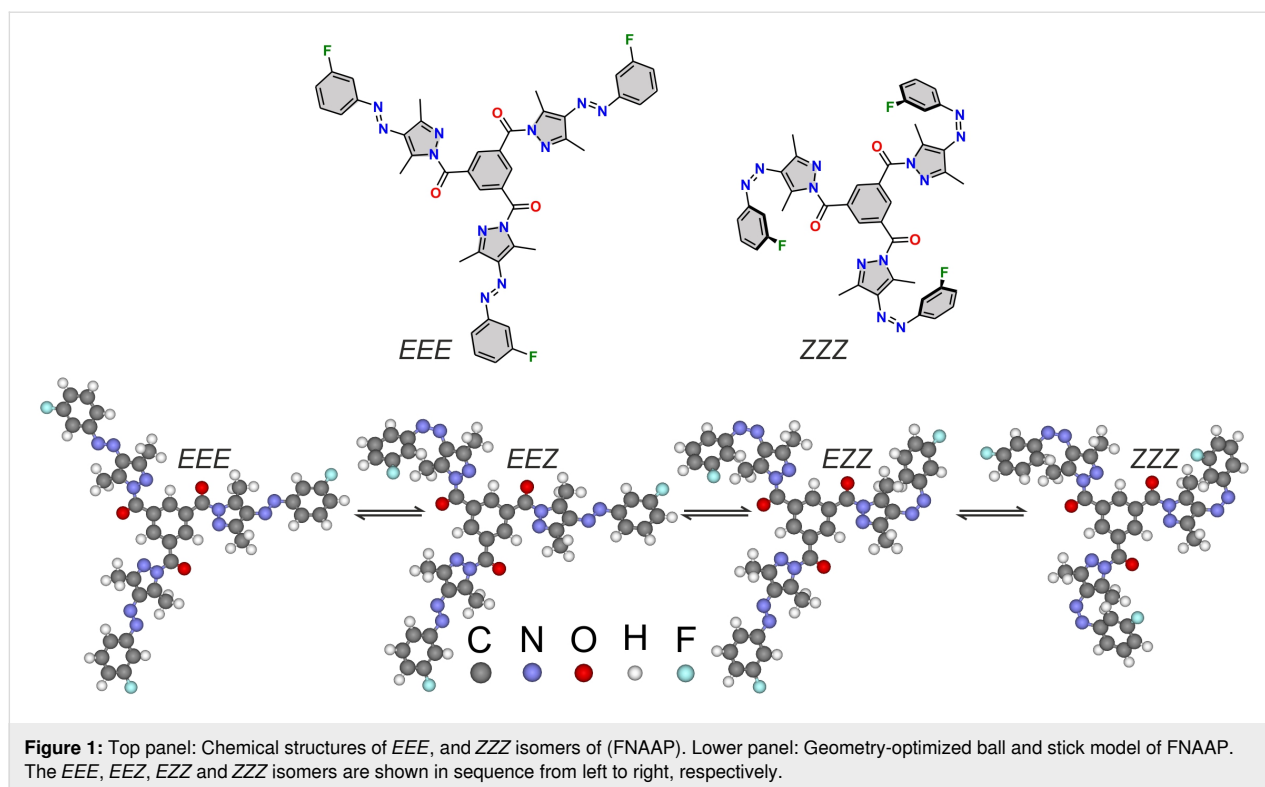
The applicability of molecular switches relies on the efficiency, reversibility, and the half-life associated with different non-equilibrium states. Typically, the half-life of the *Z* isomer of AB is a few days [17]. Chemical modifications of AB derivatives play a crucial role in realizing efficient bidirectional photo-switches with longer half-lives [18,19]. In particular, replacing one of the phenyl units in AB with a five-membered heterocycle and the resulting *Z* isomer of phenylazoheteroarenes has extended half-life ranging up to 1000 days and imparted quantitative and reversible photoswitching [20,21]. The long-term photoswitching stability and tunable half-lives of *Z* isomers of azopyrazole-based switches [20–22] have made their way to several applications in thermal energy storage [23], photo-switchable inhibitor [24], photoswitchable hydrogelator [25], photoregulation of DNA nanosystems [26], in controlling surface wettability [27], and in solar energy conversion [28]. Considering these advantages, we synthesized C_3 symmetric tripodal azopyrazole-based derivatives having a trimesoyl core and aroylazole connections as a solid-state switchable probe for light-driven reversible printing and erasing applications [29]. Besides exhibiting excellent photoswitching in solution phase, the tripodal photoswitches exhibit extended half-life of the *ZZZ* isomer in the solid-state as well [22,29]. The overall efficiency of the molecular switch could be attributed to the electronically decoupled individual photoswitchable units by 1,3,5-functionalization and attainment of non-planar geometry [30]. Molecular switches with multiple switching units having extended lifetime for their non-equilibrium states will be a unique tool for fabricating multi-functional molecular switches on the surface. Molecular switches with multiple switching units are scarce on the surface [10,31] and mostly studied under low temperatures.

If such multi-functional molecular switches, with stable non-equilibrium states, can be reversibly switched under ambient conditions, quantum information processing based on single molecules can be revolutionized.

In this article, we show the single molecule electron/hole-induced switching of a fluorinated tripodal *N*-functionalized arylazo-3,5-dimethylpyrazole derivative (FNAAP), a multi-functional molecular switch, on a graphite surface at ambient conditions. The fluorine substitution is chosen in FNAAP for its better photoisomerization efficiency (in solution as well as in solid state) and higher molecular stability [29]. Possible photoisomers of FNAAP, *EEE*, *EEZ*, *EZZ* and *ZZZ* are shown in Figure 1. FNAAP molecules assemble into well-ordered large domains on graphite and are revealed by atomic force microscopy (AFM) and scanning tunneling microscopy (STM) studies. The molecular level arrangement in the assembly reveals a hexagonal packing through weak non-bonding interactions between the carbonyl and aromatic hydrogen, and is further understood by reactive force-field (ReaxFF) simulation [32]. Using electron/hole under a tunneling junction, molecules are switched between 8 stable states (*EEE*, *EEZ*, *EZE*, *ZEE*, *EZZ*, *ZEZ*, *ZZE* and *ZZZ*) at ambient conditions. These states are remarkably stable and are well distinguishable by the tunneling current passing through the molecule at the tunneling junction. The electron/hole-induced switching reveals that the electron injection yields a higher switching probability than that through hole injection. It is also observed that the overall switching probability of FNAAP on the surface is several-fold higher than that of molecular switches with a single switching unit known. The comparison is made for an AB derivative (4-(phenylazo)benzoic acid) (PABA) and a pyrazole-AB derivative (*E*-4-((1,3,5-trimethyl-1*H*-pyrazol-4-yl)diazanyl)benzoic acid) (PyABA) on a graphite surface under similar experimental conditions. The choice of molecules that can be studied under ultra-high vacuum (UHV) is limited due to the requirement of their thermal stability and UHV compatible sublimation temperature. Therefore, the solution-based preparation method and solid-state measurements at ambient conditions hold their importance in exploring novel and thermally less stable molecular switches.

Results and Discussion

Typical AFM phase images of an ultra-thin film of FNAAP deposited from ethanolic solution on highly oriented pyrolytic graphite (HOPG) are shown in Figure 2. The corresponding topographs are shown in Supporting Information File 1. The AFM images of the ultra-thin film reveal domains of assembled molecules shown as bright contrast, marked by green and yellow dashed lines in Figure 2a,b. The pristine graphite sur-



face has a median contrast. The molecular domains are growing as long islands with well-defined growth facets. We tag the domains as one-dimensional (1D) phase, as noted by their 1D growth. The typical apparent height of the FNAAP islands is ≈ 0.7 nm, indicating that the islands are monolayers (see Supporting Information File 1, section 2 for height profile of islands). The apparent height measured is consistent with monolayer islands of planar molecules [33]. It is also noted that the molecular islands are typically oriented by $\approx 0^\circ$, 120° , and 240° , with respect to the long edges of the islands. The angles of orientation are determined using a 2D fast Fourier transform (2D FFT) of high-resolution images, and an example is shown in Figure 2d. The resonances in the 2D-FFT are originated from the moiré pattern of the super-lattice. Two distinct orientations are visible in the 2D-FFT. The 3-fold orientation of islands suggests that the molecular lattices are oriented with respect to the graphite lattice, which has 3-fold symmetry [33–35]. Each of the orientations has a mirror domain as well, making a total of six orientations for the islands on the surface. The orientations of the islands are marked by yellow and green 3-fold arrowheads in Figure 2a,b. The mirror orientations are originating due to the incommensurate alignment of the molecular lattices along the graphite compact lattices at an angle. The angle between the mirror domains is $\approx 7^\circ$, that is, the molecular lattice is oriented by $\approx 3.5^\circ$ with respect to the graphite compact lattice. This clearly suggests that the molecular lattice is not a commensurate lattice with respect to graphite [33–35].

A high-resolution AFM phase image of a few islands in 1D phase is shown in Figure 2c. Molecular domains reveal line-like features within the domains and extend through the length of the islands. Adjacent line-like features are indicated by green double-headed arrows and are separated by 6.3 ± 0.1 nm. The magnitude of the spacing suggests that the line-like features are originating due to a super-periodic pattern of molecular assembly, namely a moiré pattern [33–35]. This further suggests that the molecular adlayer is forming an incommensurate lattice with respect to the graphite lattice and leading to a super-lattice.

In addition to the 1D phase, we also observed a two-dimensional (2D) phase, named due to the 2D nature of the growth. We noted that the surface is covered by $\approx 88\%$ of the 1D phase, and the remaining is covered by the 2D phase. Interestingly, high-resolution images revealed no line-like features due to the moiré pattern within the islands in the 2D phase. As suggested earlier, the moiré pattern is typical for incommensurate structures. Thus, we propose that in the 2D phase, the molecules organize commensurate with respect to the graphite lattice. An AFM image corresponding to a 2D phase of FNAAP is provided in Supporting Information File 1, section 3. It is to be noted that the majority of the islands in the 2D phase appear with nearly hexagonal-like facets, indicating that they are most likely originating from a hexagonal type of lattice.

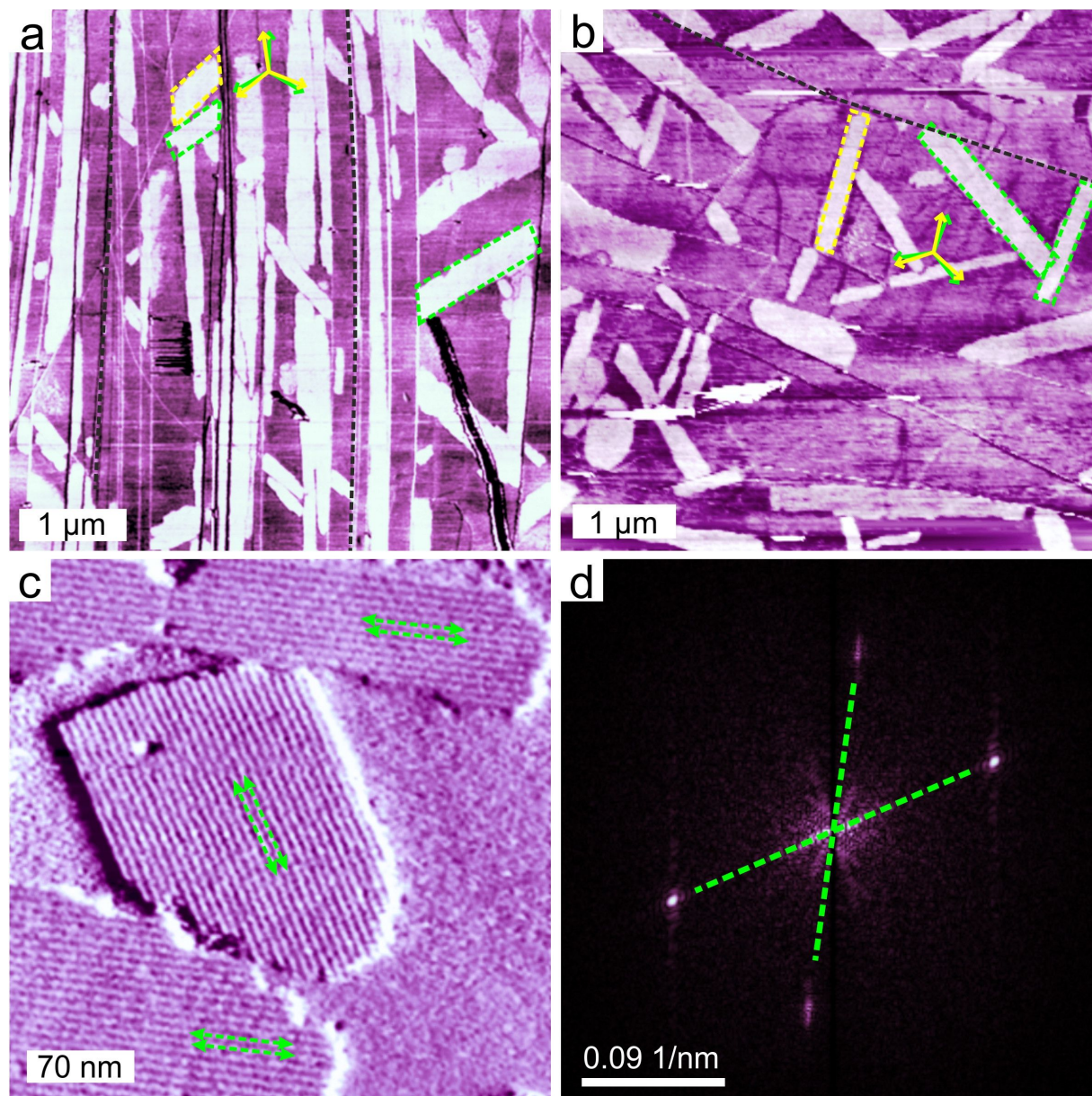


Figure 2: AFM phase images (a, b and c) of ultra-thin films of FNAAP deposited from ethanolic solution on HOPG (0001) and are obtained from independent areas. Domains in the 1D phase of FNAAP are marked by green and yellow dashed lines. The green and yellow three-fold arrows depict the orientation of the long edges of the islands with respect to each other. A few graphite step edges are marked by black dashed lines. Double-headed arrows in (c) indicate line-like features within the domains of the 1D phase, which is due to the moiré pattern originating from the super-lattice. (d) 2D-FFT taken on (c). The resonances corresponding to the super-lattice are indicated by green dashed lines. Two resonances are rotated by $\approx 120^\circ$ and correspond to the major orientations of the domains in the 1D phase.

To further understand the microscopic structure of the assembly, we have performed STM experiments on ultra-thin films of FNAAP. Figure 3a,b shows constant current STM topographs of ultra-thin films of an FNAAP adlayer on HOPG (0001) at different resolutions. Single molecules appear as bright spots, and the arrangement of the molecules reveals a hexagonal packing. The green dashed arrow indicates two adjacent molecular lattices, and the green oblique indicates the

unit cell of the assembly. The unit lattice vectors are a (1.9 ± 0.1 nm), b (1.9 ± 0.1 nm) and γ ($\approx 120^\circ$), the angle between the vectors. The intermolecular distance obtained from STM corresponds to the lateral length of the *EEE* isomer (F to F distance is $22.06 \text{ \AA}$). Thus, we conclude that the adlayer is formed by the energetically most favorable *EEE* isomer. This is also consistent with the NMR data, which reveals that the majority (>98%) of molecules in the solution are in the thermo-

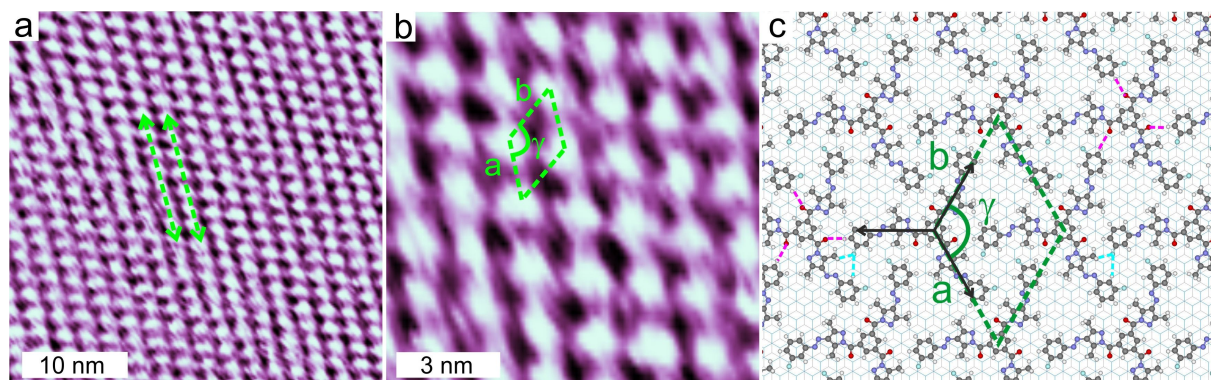


Figure 3: Constant current STM topographs (300 pA, 0.3 V) of the FNAAP adlayer on HOPG (a, b) deposited from the corresponding ethanolic solution. Imaging is performed at the HOPG–air interface. Green dashed lines depict two adjacent molecular lattices, and the green dashed oblique depicts the unit cell of the assembly. (c) Force field optimized geometry of the adlayer of FNAAP (*EEE* isomer) on bilayer graphite. The unit lattice vectors of the adlayer are a , b and γ is the angle between the vectors. Black arrows indicate the compact lattice directions of graphite. Magenta dashed lines depict possible non-bonding interactions between carbonyl groups and aromatic hydrogen atoms. Blue dashed lines depict the same between fluorine and aromatic/methyl hydrogen atoms.

dynamically stable *EEE* form (see Supporting Information File 1, section 4 for a UV–vis spectrum of FNAAP in ethanol–chloroform mixture, which resembles the reported spectrum in chloroform [29]). Long 1D islands are visible in large-area STM images as well. A super-periodic pattern is visible at low resolution, and the periodicity (≈ 6.1 nm) matches with the AFM measurements. Additional STM images of the ultra-thin film of FNAAP at different resolutions are provided in Supporting Information File 1, section 5.

Next, we propose a molecular-level model for the adlayer of the *EEE* isomer of FNAAP. Based on the experimental lattice parameters, an initial geometry was modelled and subjected to geometry optimization using ReaxFF. The optimized assembly of FNAAP on bilayer graphite is shown in Figure 3c. The calculations assume a commensurate hexagonal lattice. The graphite lattice directions are marked by the 3-black arrows. The unit cell parameters of optimized geometry ($a = 1.968$ nm, $b = 1.968$ nm and $\gamma = 120^\circ$) match well with the experiments. The microscopic arrangement of the molecules is clearly visible. It is to be noted that the fluorine atoms are oriented toward the aromatic and aliphatic hydrogen and the carbonyl group to aromatic hydrogen. This suggests possible directional non-bonding interactions between the molecules. For molecules with 3-fold symmetry, the 3-fold orientation within the assembly is not a surprise [10,36]. Therefore, it is summarized that the typical intermolecular interactions are of van der Waals type and interactions dominantly driven by steric packing. We note that the STM experiments reveal only a hexagonal type of arrangement of molecules, as shown in Figure 3 (additional STM images are provided in Supporting Information File 1, section 5). Based on the microscopic details obtained from STM

and AFM images, we propose possible geometric models for incommensurate lattice and commensurate lattice and are included in Supporting Information File 1, section 6. Both incommensurate ($a = 1.96$ nm, $b = 1.86$ nm and $\gamma = 117.6^\circ$) and commensurate lattices ($a = 1.97$ nm, $b = 1.97$ nm and $\gamma = 120^\circ$) are hexagonal-type with slightly different lattice parameters. Thus, we summarize that both 2D and 1D phases have comparable arrangements of molecules with slightly different lattice parameters. This is also possibly the reason why we observe only a hexagonal-type of lattice in the STM experiments. Since the incommensurate lattice leads to the formation of super-periodicity, we observe a moiré pattern (line-like pattern) for the 1D phase (see Supporting Information File 1, section 6 for details).

Next, we show the electron/hole-induced *E–Z* isomerization of a single FNAAP within the assembly. By placing the STM tip on selected molecules, the sample voltage is ramped, and the corresponding change in current is measured. These measurements are tagged as current–voltage (*I–V*) characteristics. Electrons and holes are injected into molecules at negative and positive sample voltages, respectively. It is known that upon injection of electrons or holes, molecules get transiently charged on the graphite surface and undergo isomerization (switch) [11,37,38]. Figure 4a shows two independent *I–V* measurements obtained on two single FNAAP molecules. Additional *I–V* measurements are provided in Supporting Information File 1, section 7 for reference. Unlike the expected continuous variation of current as a function of voltage, we observed abrupt increases and decreases in the tunneling current, as indicated using up/down arrow heads. The abrupt change in current is an indication of geometrical changes at the tip–molecule tunneling junction. We presume that the change in current is due to the

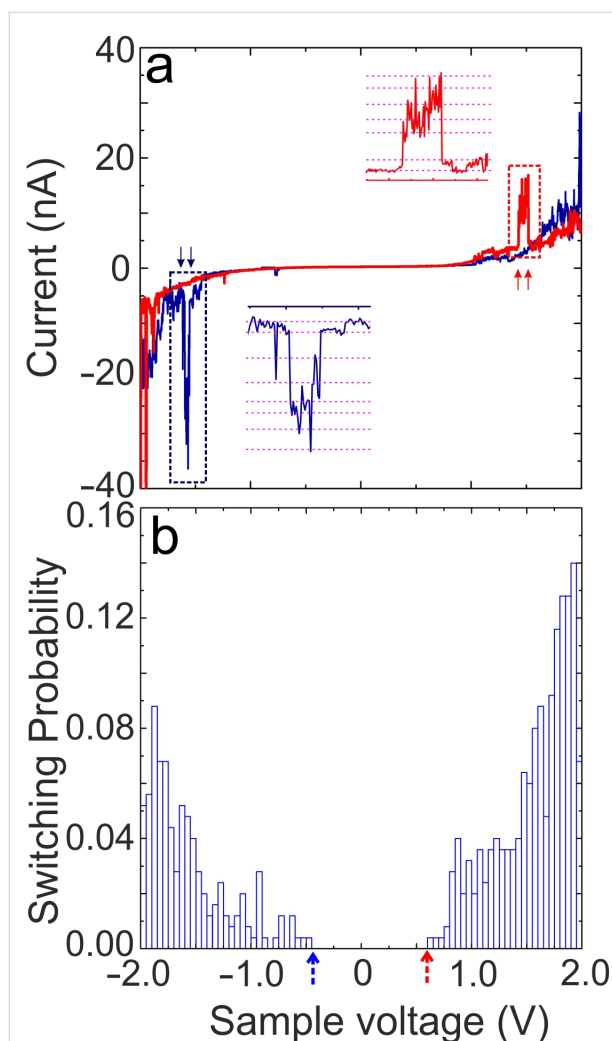


Figure 4: (a) Current versus sample voltage (I - V) recorded on a single FNAAP within the assembly. The I - V measurements are recorded by stabilizing the current at ≈ 0.5 nA and at -2 V. Arrows indicate the switching of FNAAP molecules between E and Z forms. Insets show the zoomed section of the I - V curves indicated using dashed rectangles. Distinct levels of current can be discerned and are indicated by dashed magenta lines. (b) Statistical analysis of all the switching events (voltage value corresponding to the up and down arrows). The switching probability is obtained by taking the ratio of the number of times switching is observed in a given voltage window to the total number of I - V measurements performed. The binning of I - V measurements is 10 mV. Each data point depicts the average probability for switching in intervals of 50 mV. Blue and red arrowheads depict the threshold voltage for switching at negative and positive sample voltages, respectively.

switching of molecules and is in accordance with previous reports [7,10-12,15,33,38]. Insets of Figure 4a show a zoomed section of the I - V curves indicated using dashed rectangles. Distinct levels of current can be discerned and are indicated by dashed magenta lines. We attribute these fluctuations in the current to the interconversion between different possible geometrical isomeric states of the molecule, that is, reversible E - Z isomerization. It will be shown later that the isomerization is

electron/hole-induced, which is initiated by injecting electrons into molecular orbitals [7,10-12,15,33,38]. It is to be noted that within a given interval of voltage/time, the current repeatedly goes through similar values. The fluctuations in current have a step-like nature, and they can be clearly established by following the dashed magenta lines. Thus, it is concluded that the origin of the fluctuations in current is due to distinct reversible isomeric changes of the molecule; i.e., molecules go through different geometrical isomerization multiple times. These distinct levels and fluctuations in the current further confirm that they are not random noise or instabilities but switching between geometrical isomeric states of FNAAP. If the fluctuation in current was simply due to environmental instabilities, we would not have obtained I - V curves with such reproducible fluctuation (step-like nature) in the current. Additionally, the well-defined step-like nature of the fluctuation in current is visible in the time traces given in the upper panel of Figure 5. It is interesting to note that the abrupt changes are reversible (each increase in current is associated with a step involving a decrease in current), which indicates the molecular switching between two associated states.

The geometrical isomerization between the EEE and ZZZ forms of the molecule leads to structural changes, and the average distance between the tip and molecules is expected to change. The current changes drastically as it is exponentially dependent on the distance. Once a molecule is injected with an electron/hole, it changes its geometry, which in turn, causes a decrease or increase in the tunneling gap and thus the current changes abruptly. In other words, the abrupt change in current is caused by isomerization or geometrical changes in the molecule. The change in tunneling current has been earlier used to identify geometrical changes/isomerization of spin-cross-over molecule [7] and azobenzene derivatives [10-12,15,33,38] on the surface. Other degrees of freedom, like molecular vibrations, are also associated with configurational switching. However, such small changes may not lead to a distinguishable signal (change in current) in the I - V at ambient conditions. Therefore, we mainly rely on the sharp and abrupt change in current that is highly distinguishable from the background noise.

To understand the switching further, we have performed a statistical analysis of the voltages associated with every switching event (indicated by up or down arrows). Figure 4b shows the statistical analysis of all the switching events observed. We have included I - V curves recorded on 160 independent locations (each presumably from a few molecules) from different molecular domains. Some of the I - V curves used for the analysis are shown in Supporting Information File 1, section 7. The number of switching events is normalized by the number of I - V measurements used for the analysis. Thus, the ratio

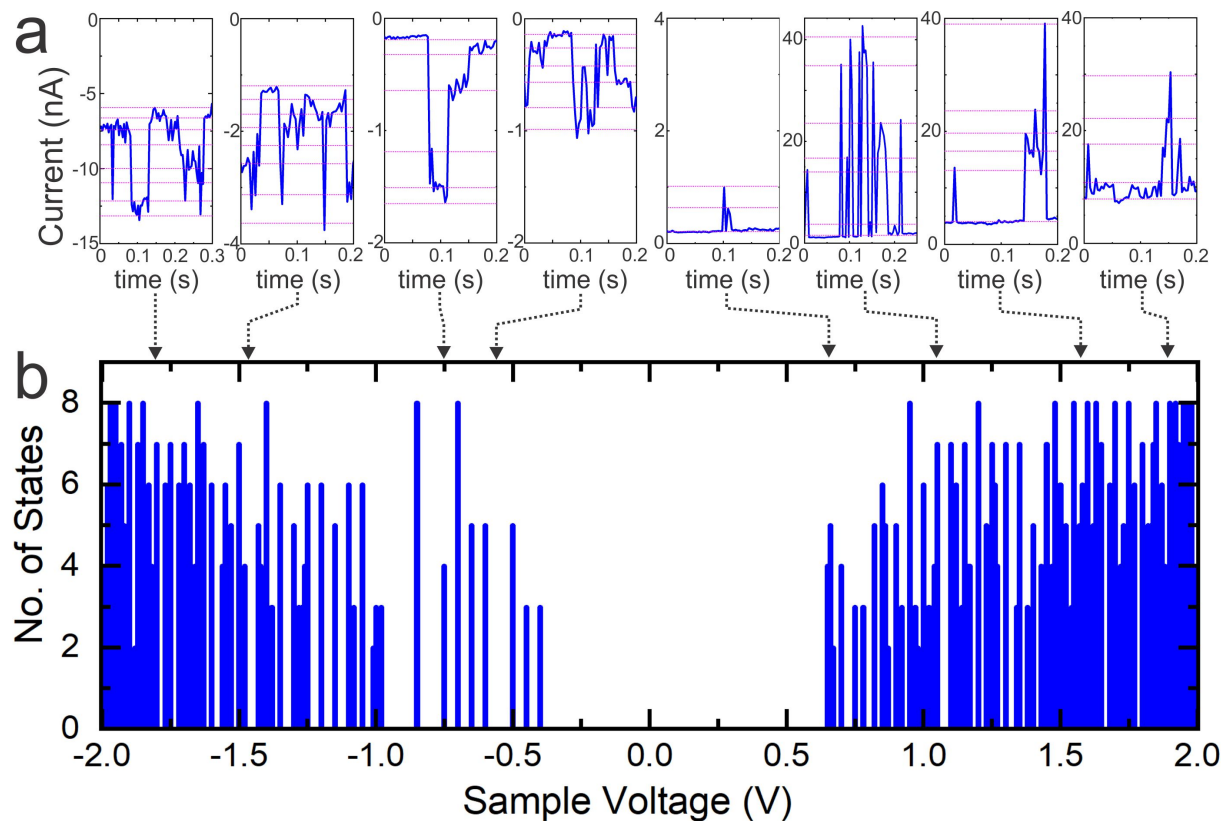


Figure 5: (a) Current versus time (time trace) at selected voltage intervals acquired on the adlayer of FNAAP on HOPG at ambient conditions. The time traces are part of I - V curves measured by stabilizing the feedback at ≈ 0.5 nA and at -300 mV. The mean value of the sample voltage at which the time traces are recorded is marked by dashed arrows. Magenta dashed lines represent stable recurring levels of current, which correspond to different isomeric states. (b) Statistical analysis of the number of states as obtained from multiple time traces in intervals of ≈ 100 mV voltage versus sample voltage.

of the number of switching events to the number of I - V used directly corresponds to the switching probability. The following observations are noted from the statistical analysis. 1) a threshold voltage is observed for the isomerization of the molecules at both positive and negative sample voltages (marked by red/blue arrow heads); 2) the switching probability increases exponentially with increasing voltage; 3) the switching probability at positive voltage is almost double than that at negative sample voltage; 4) a strong asymmetry in the switching probability induced by electrons and holes.

The threshold voltage of switching suggests that the switching is electron/hole-induced [7,10–12,15,33,38]. The threshold voltage observed for the electron injection (marked by red arrowhead) and hole injection (marked by blue arrowhead) should match with the position of lowest unoccupied molecular orbital (LUMO) and highest occupied molecular orbital (HOMO), respectively for electron/hole-induced switching [7,10–12,15,33,38]. To understand the same, we have calculated the molecular orbitals at the B3LYP/6-311g level of

theory using Gaussian 03. The computed HOMO–LUMO gap of *EEE*, *EEZ*, *EZZ* and *ZZZ* isomers is 3.59 eV, 3.27 eV, 3.26 eV, and 3.35 eV, respectively (see details in Supporting Information File 1, section 8). The HOMO–LUMO gap obtained from the calculation is much higher than the gap obtained from the threshold voltage, which is ≈ 1.1 V. This suggests that while switching, the molecules may not be in their neutral state. Since the graphite–molecule interaction is weak and van der Waals-type, we use the gas-phase calculations and no major change in the electronic structure is expected for molecules upon adsorption on the surface.

To understand the low threshold voltage for switching and the possible scenario of charging of molecules, we have analyzed the density of states (DOS) of positively charged and negatively charged FNAAP. The HOMO–LUMO gap of all isomers in single negative/positive charge is substantially reduced (see Supporting Information File 1, section 9 and section 10 for details of calculated DOS). The calculated HOMO–LUMO gap of charged FNAAP is smaller than that of the neutral FNAAP,

which means the frontier molecular orbitals are closer to the Fermi level. The significantly smaller HOMO–LUMO gap observed for the charged species compared to their neutral counterparts suggests enhanced reactivity and a low charge injection barrier. In the case of negatively charged FNAAP, the LUMO shifts toward the Fermi level, facilitating low electron injection. In the case of positively charged molecules, the HOMO shifts toward the Fermi level and allows hole injection. These observations strongly point to the fact that molecules are in a charged state at the tunneling junction when bias is applied and require a lower threshold voltage for electron/hole injection. It is reported that if the molecules are negatively or positively charged, then the electron injection and hole injection can occur at much lower threshold voltage than that required for a neutral molecule [38,39]. As the switching is induced through the attachment of an electron or hole into the molecule, the process is referred to as electron or hole-induced switching. Depending on the polarity of the bias, either an electron is injected (at positive sample bias) or a hole (at negative sample bias). This may be directly compared to the electron or hole-catalyzed isomerization of molecules in solution [40–42].

Generally, the $E \rightarrow Z$ isomerization is fully limited without external stimulus due to the high energy barrier and endothermicity associated with the isomerization. It was shown earlier that when a positive or negative charge is attached to the molecule, the resultant energy landscape is rather shallow compared to a neutral molecule. This has been established both in solution [40–42] and on the surface [33]. That is, the isomerization is energetically less demanding once the molecule is charged. The change in the barrier is due to the drastic change in the geometry of the charged molecule. The optimized geometry of the charged FNAAP shows a drastic difference in the geometry, especially around the azo group, compared to the neutral case. The optimized geometry of the *EEE* and *ZZZ* isomers of FNAAP⁺ and FNAAP[−], along with the neutral one, is provided in Supporting Information File 1, section 11. That is, upon charging, the potential energy landscape of isomerization changes, which supports the isomerization. As graphite–molecule interaction is weak and makes a capacitive interface between them, the molecules are likely stabilized in their ionic forms when a bias is applied at the tunneling junction. Charging of molecules on graphite [38,39,43] and ultra-thin insulating surfaces [44] is known due to the weak electronic coupling between the molecule and the graphite/insulator surface. We propose that when a sample voltage is applied to the FNAAP adlayer on graphite, they are instantaneously negatively/positively charged (depending on the voltage) due to the capacitive interface between the molecule and graphite [38,39]. The charged state of the molecule requires a lower threshold voltage for electron/hole-induced switching [38]. This scenario does not

occur at molecules adsorbed on metal surfaces due to strong electronic coupling between molecules and the metal. We are unable to predict the exact number of charges in the molecule while switching, but what we could demonstrate is that charging can lead to a reduction in the HOMO–LUMO gap, as observed in the experiment. Thus, we propose that the reduction in the energy barrier and the low charge injection barrier for the charged FNAAP drives the isomerization.

For both positive and negative voltages, the switching probability increases exponentially as the voltage increases. The switching probability is directly proportional to the current flowing at the tunneling junction. As the current increases exponentially with applied voltage, it is expected that the switching probability also increases exponentially [38]. We also note that the switching probability at positive voltage is several folds larger than that at the negative voltage. This suggests that the electron injection yields a higher switching probability than that through hole injection. This could be due to high electron transport within the molecular layer compared to hole transport. We also note that the overall switching probability of FNAAP molecules in its *EEE* adlayer is several-fold higher than that for the adlayer of molecules with a single switching unit. We compared the switching probability of FNAAP with that of PABA and PyABA in the adlayer of their *E* isomer [33]. The comparison shows that the switching probability of FNAAP is an order of magnitude higher than that of PABA and PyABA. The switching experiments of PABA and PyABA were performed under similar experimental conditions. That is, by increasing the number of switching units, the overall probability of switching can be increased for molecular switches in their adlayers on surfaces. The number of switching states for FNAAP is higher (8; *EEE*, *EEZ*, *EZE*, *ZEE*, *EZZ*, *ZEZ*, *ZZE*, and *ZZZ*) compared to molecules with single switching units (2; *E* and *Z*) and thus the observed higher probability is expected. Though the switching is induced by placing the STM tip in a random position on the molecular island, each switching event observed in the time-traces corresponds to the switching/isomerization of a single molecule. That is, the calculated switching probability is per molecule. If harnessed, the increased probability of switching could be used in storing high-density of energy in the molecular system using an atomically precise write and read tool like an STM tip.

An obvious question at this stage is whether one can observe all possible 8 states and the type of interconversion between different switching states. If the tip is placed at the center, only 4 states are distinguishable: *EEE*, *EEZ*, *EZZ*, and *ZZZ*. However, all 8 states (*EEE*, *EEZ*, *EZE*, *ZEE*, *EZZ*, *ZEZ*, *ZZE* and *ZZZ*) become distinguishable if the tip is placed off-center. This is a more likely scenario due to the following reasons: we select a

random position on the molecular islands for I – V measurements; due to thermal drift, the tip may move to a random location during the I – V measurements. To understand the possible switching events and the number of states distinguishable during the switching experiments, we have analyzed current versus time (time traces) at different voltage intervals. Figure 5a depicts typical time traces obtained at selected sample voltages. The time traces are obtained from I – V curves, segments of ≈ 100 mV and analyzed the possible number of distinguishable states. The black dashed arrowhead indicates the mean voltage corresponding to the time trace shown in the figure. Interestingly, distinguishable states (marked by magenta dashed lines) are observed at both sample voltage polarities. The statistics of the number of states as a function of sample voltage are given in Figure 5b. The number of states increases as the voltage increases and reaches a maximum value of 8. We attribute the 8 distinguishable levels of current to the 8 states of the molecule. Except for a short voltage range (-0.5 to -0.75 V and 0.6 to 0.9 V), the maximum number of switching states is accessible at all voltages. That is, the onset voltages for switching are ≈ -0.5 and ≈ 0.6 V, which correspond to the onsets shown in Figure 4b. At this stage, we are unable to predict which current corresponds to which state; however, the clear distinguishability of states is remarkable for the experiments conducted in ambient conditions.

The average half-life of distinguishable states ranges up to a few tens of milliseconds as per the time traces (cf. Figure 5a). While metastable isomers often exhibit long lifetimes in solution [20,21] or solid-state environments [29,30], the ultra-short lifetimes of different states on the surface are surprising. During the STM experiments, electrons or holes under applied bias are continuously injected into the molecules, which vigorously drives the molecule between different possible states. That is, the half-life referred to the time-trace measurements corresponds to a constant external trigger, at a given bias and a given current. If the bias (and thus the current) is removed, it is plausible that the molecule could reside in a specific state for a longer duration, closer to its intrinsic thermal stability. We have observed that photo- and thermal-triggered AB and azopyrazole derivatives remain in the *Z*-isomeric state for several hours on the surface [45]. These exceptional lifetimes of non-equilibrium states of FNAAP are also particular for the condensed state on the surface, due to the confinement of several degrees of freedom when condensed on the surface. It is also noted that the change in current for switching between states is higher ($\approx$ one order of magnitude larger) for the positive sample voltage compared to negative sample voltage. This is also obvious in the cumulative number of states at positive sample bias compared to negative sample bias. This suggests that different states are better distinguished at positive sample voltage.

The following is understandable about the switching pattern from the time traces. (a) A stepwise change in current is observed generally, indicating that the molecule can switch between any given state, or any order does not exist for the switching. (b) The molecule can be switched from the lowest current state to the highest current state (cf. time trace taken at 1.1 V) without any intermediates. (c) All 8 states are accessible reversibly even at lower sample voltages, indicating that switching can be performed between any given state at a low threshold voltage. That is, all states are accessible and are remarkably stable at all sample voltages. It is concluded that the high energy barrier and the long lifetime of the non-equilibrium states are at the origin of their remarkable stability at room temperature. The remarkable stability of the states at ambient conditions provides an opportunity to use a single FNAAP molecule as an 8-bit operation. We propose to switch the molecule using an STM tip, which is a tool that can manipulate molecules at an atomic level. Thus, the selection of a single molecule and the selection of a part of molecules is not impractical. Once the selection is off-centered all isomers are distinguishable and non-degenerate. The molecule may be switched using an STM tip between multiple states and the state could be read using the magnitude of the current. Given the dimension of the molecule (≈ 2 nm² as obtained from the unit cell) one could accommodate ≈ 200 Tbits in a 1 cm² area. Such a remarkable density of bits is possible since each molecule acts as an 8-bit operation unit. If the states of the molecule are addressed as $|1\rangle, |2\rangle, \dots, |8\rangle$, one can use combinations of different states of molecules in an array to record information. For example, if FNAAP is in states $|2\rangle$, the operation is addressed as 0 1 0 0 0 0 0, which could be assigned to a number, letter, etc. Depending on the state of the adjacent molecules in an array, one can assign a combination of states to address number, letters etc. Thus, in an array of 8 molecules, 8^8 permutations are possible.

Conclusion

We have investigated the microscopic structure and electron/hole-induced conformational switching of a tripodal azopyrazole derivative (FNAAP) in its ultra-thin films on a HOPG surface at ambient conditions. Most of the molecules ($>98\%$) in the film are in the *EEE* configuration and form a hexagonal close-packed assembly. Molecules within the condensed phase of *EEE* isomeric states were switched between different isomers reversibly using electrons/holes injected from an STM tip. The electron/hole-induced switching is characterized by the observation of a threshold voltage for switching. The observed threshold voltages are lower than expected and indicate that the switching is mediated through a charged state of FNAAP. The observed switching probability is several-fold higher than that of other AB derivatives with one switching unit. The analysis of the number of switchable states as a function of sample voltage

reveals 8 maximum states. These states have distinguishable current values and are assigned to *EEE*, *EEZ*, *EZE*, *ZEE*, *EZZ*, *ZEZ*, *ZZE*, and *ZZZ*. The clear distinguishability of these states is remarkable for the experiments conducted in ambient conditions. The change in current for switching between states is higher ($\approx$ one order of magnitude larger) for positive sample voltage compared to negative sample voltage. The cumulative switching per unit voltage is higher at positive sample bias compared to negative sample bias. The remarkable stability of the states at ambient conditions provides an opportunity to use a single FNAAP molecule as an 8-bit operation and one could accommodate ≈ 200 Tbits in a 1 cm^2 area.

Experimental

Preparation of adlayer

The FNAAP molecule is synthesized as per our previous report [29]. Ultra-thin films were prepared by drop casting from ethanolic solutions of molecules (concentration between 10^{-5} to 10^{-6} M) on freshly cleaved highly oriented pyrolytic graphite (HOPG, ZYB grade from μ Masch). Approximately 4 μL of solutions of FNAAP were drop-casted on the HOPG surface, dried (a few minutes) in ambient conditions, and AFM/STM studies were performed. Relative humidity ($\approx 50\%$) and temperature ($22\text{--}25\text{ }^\circ\text{C}$) of the room were controlled by an air conditioner and a dehumidifier. While drop casting, the sample was kept at $\approx 20\text{--}30\text{ }^\circ\text{C}$ to ensure a smooth flow of the solvent over the substrate. After drop casting, all films were subjected to vacuum pumping (typically 0.01 mbar) for about 1 h. Before depositing molecules, freshly cleaved graphite surfaces were subjected to control AFM experiments to check for any contamination or impurities on the surface. We also note that no traces of ethanol remained on the surface after pumping, as confirmed by AFM images.

Instrumentation

All AFM and STM measurements were performed using an Agilent 5500 in soft tapping mode and an ATM300 from RHK Technology, respectively. Aluminum-coated silicon cantilevers from Nanosensors (PPP-NCHR) were used as AFM probes. The force constant and resonance frequency of the cantilevers during the imaging were $30\text{--}34\text{ N/m}$ and $\approx 300\text{ kHz}$, respectively. A Pt/Ir (80:20) tip was mechanically prepared and used as a probe for STM imaging. The XY and Z scales of STM images are calibrated using the graphite lattice. All the AFM and STM images are post-processed using WSxM from Nanotec [46]. Mesh averaging implemented in WSxM [46] is used for enhancing the contrast of STM images. Current–voltage (*I*–*V*) measurements and statistics of switching are performed in ambient conditions. The voltage is referred to with respect to the sample. Similar set point voltage and current were chosen for the *I*–*V* measurements included in the statistics in order to

ensure that the relative distance between the tip and the molecules is similar while performing the *I*–*V* measurements. Due to thermal drift during the *I*–*V* measurement, it is assumed that each *I*–*V* measurement includes the switching of a few molecules under the tip. However, every switching event corresponds to isomerization in a single molecule. To overcome the effect of drift, *I*–*V* measurements are recorded within an average time of $\approx 4\text{ s}$. This ensures that the location of the *I*–*V* measurement does not drastically drift from the originally selected point.

Details of force field simulation and computations

The Reax Force Field method implemented in Quantumwise ATK-classical is devised for geometry optimization. The graphite (previously optimized) was kept fixed during the simulations, and the molecular geometry was fully optimized. Parameter set: ReaxFF-CHO-2008 [32]. A force tolerance of $0.001\text{ eV/\AA}$, stress tolerance of $0.001\text{ eV/\AA}$, and a maximum step size $0.01\text{ \AA}$ were used for the optimization. The limited memory BFGS (L-BFGS) optimizer method was employed for optimization. L-BFGS is an optimization algorithm in the family of quasi-Newton that approximates the Broyden–Fletcher–Goldfrab–Shanno (BFGS) algorithm using a limited amount of computer memory. A pre-optimized two-layer graphite was used from the library data as provided in the Quantumwise DFT package. The lattice parameters for graphite are, $a = 2.4612\text{ \AA}$, $b = 2.4612\text{ \AA}$, $c = 6.709\text{ \AA}$, and $\alpha = 60^\circ$. Molecular orbitals were obtained from the calculations performed using the Gaussian 03 program suite [47].

Supporting Information

AFM topographs of ultra-thin film of FNAAP, height profile of FNAAP, AFM phase images of ultra-thin films of FNAAP, UV–vis spectrum of FNAAP, STM image of ultra-thin films of FNAAP, model for the incommensurate hexagonal adlayer of FNAAP on graphite, *I*–*V* measurements performed on adlayer of FNAAP, HOMO–LUMO gap of different isomers of FNAAP, DOS of *EEE* and *EEZ* isomers of FNAAP, DOS of *EZZ* and *ZZZ* isomers of FNAAP. Optimized charged geometries of *EEE*- and *ZZZ*-isomers of FNAAP. Chemical structures of *EEE*- and *ZZZ*-isomers of FNAAP and the azo derivatives used for comparison.

Supporting Information File 1

Additional information and spectra.

[<https://www.beilstein-journals.org/bjoc/content/supplementary/1860-5397-21-112-S1.pdf>]

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Data Availability Statement

All data that supports the findings of this study is available in the published article and/or the supporting information of this article.

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Azobenzene protonation as a tool for temperature sensing

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Full Research Paper

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Abstract

Azobenzenes can be protonated at one of the azo nitrogen atoms, leading to significant changes in their absorption and photochemical properties. While azobenzene protonation has been recently used as a tool in photoswitching studies, the factors influencing protonation itself have received little attention. Here, we report a strong temperature dependence of azobenzene protonation in 1,2-dichloroethane and highlight its potential for temperature sensing applications. Density functional theory calculations were performed to support our findings and to investigate the mechanisms of azobenzene–acid interactions, aiming to guide the design of azobenzene-based temperature sensors in future research.

Introduction

Molecular switches are molecules that can reversibly shift between distinct (meta)stable states in response to external stimuli such as light, pH changes, or electric fields [1]. Over the past decades, they have emerged as staple building blocks in smart materials, from light-responsive norbornadienes in molecular solar thermal energy storage [2] to pH-sensitive spiropyrans in cell imaging [3], and redox-active viologens in memory junctions [4]. Among the different molecular switches azobenzenes stand out due to their widespread use in biomedicine [5,6], energy storage [7,8], soft robotics [9,10], and sensing [11]. The key factors for their success are the efficient photochemical isomerization, causing large spatial, spectral, and electronic changes, as well as the relative ease of modification of the azobenzene core by introducing different functional groups to

the phenyl rings. For these reasons, azobenzenes can be sensitized to various stimuli and easily integrated into different types of materials.

While *cis*–*trans* isomerization is the most prominent property of interest for azobenzenes, there are also other transformations that can offer useful functionalities. These include ionization via protonation of one of the nitrogens forming the azo bond [12,13], azo–hydrazone tautomerization [14,15], and binding of analytes to side groups [16]. Such transformations depend on the azobenzene structure but they all typically result in significant changes in the absorption spectrum and/or alter the stability of the metastable isomer. In sensing, azobenzenes have been utilized, e.g., through changes in isomerization kinetics

[17,18] or colorimetric properties. The colorimetric sensors are effective for heavy metal detection [16,19] and humidity sensing [20]. The color changes can be either reversible or irreversible, depending on the mechanism of operation. Spectral tuning also enables switching with low-energy light, eliminating the need for potentially harmful UV irradiation [21].

Utilizing spectral changes caused by azobenzene protonation is a well-established concept, with methyl orange-based pH indicators dating back to the late 1800s [22]. Early studies primarily focused on characterizing these spectral changes, determining pK_a values, and elucidating the protonation mechanism of different azo compounds [23–25]. More recent work has harnessed protonation to enable red-light switching [12,13,26] and to control the stability of the *cis*-isomer [27–29]. These studies have focused on how protonation affects isomerization, with less attention given on how external stimuli affect the protonation itself.

In this study, we investigate the temperature dependence of azobenzene protonation with the aim of utilizing it in temperature sensing. We focus on steady-state behavior of azobenzene, 4-methoxyazobenzene, and 4,4'-dimethoxyazobenzene in solution. By tuning acid strength and solvent polarity, we demonstrate that the degree of protonation, and thus solution color, is highly temperature-dependent, changing from pale yellow to deep red as temperature decreases. We also present mechanistic insights and compare our experimental findings with computational results.

Results

Due to the lone pairs on their nitrogen atoms, azobenzenes are weak bases. Their basicity can be increased by electron-donating substituents on the benzene rings. *para*-Alkoxy substitution effectively increases the electron density at the azo-nitrogens without introducing additional protonation sites. We opted for methoxy substitution on one or both benzene rings as the simplest alkoxy substituent. The protonation of azobenzene (**1**), 4-methoxyazobenzene (**2**), and 4,4'-dimethoxyazobenzene (**3**) is schematized in Figure 1A. In the presence of a strong acid, these compounds form an equilibrium of neutral and protonated species. Protonation leads to a notable red-shift in the absorption spectrum from 320–360 nm to 420–510 nm, as shown in Figure 1B using methanesulfonic acid (MSA) in 1,2-dichloroethane (DCE). We assume that in DCE alone, no protonation occurs. In MSA, on the other hand, full protonation is assumed. Stronger electron donation gives rise to larger red-shift, and hence more pronounced color changes, upon protonation, as illustrated in Figure 1C. Figure 1D illustrates the shift in protonation equilibrium with increasing acidity when MSA is added to DCE solution of **3** at 25 °C. Due to the strong acidity

of MSA, moderate polarity of DCE, and the electron-donating substituents of **3**, only 76 equivalents of acid (3.08 mM) is needed for nearly full protonation as indicated by the almost complete disappearance of the absorption peak at 360 nm. Similar data for compounds **1** and **2** in MSA/DCE mixtures, as well as for **3** in MSA/acetonitrile mixture and for a weaker acid (trifluoroacetic acid), are shown in Supporting Information File 1, Figures S3–S6.

Given the large reversible absorption shift upon protonation, azobenzenes can act as pH indicators with tunable sensitivity through substituent modification. By combining a medium with temperature-dependent proton activity and an indicator molecule with systematic spectral changes, the system can be utilised for temperature sensing. Figure 2A shows the drastic change in the relative proportion of the neutral and protonated absorption peaks of **3** in DCE with 1.44 mM MSA over a 10–80 °C temperature range. Comparing the maximum absorbances at the neutral and protonated peaks provides a measure of sensitivity and optimal working range. Figure 2B presents this comparison for **1–3** in MSA/DCE solutions, calculated as the ratio between neutral and protonated peak maxima at each temperature (see Supporting Information File 1 for more details). Sensitivity is defined by the rate of change of ratio of absorption maxima ($A_{\text{neutral}}/A_{\text{protonated}}$) over a given temperature range, represented by the slope of the curves in Figure 2B. Within the optimal operation range, the rate of change should be both high and systematic. For example, in Figure 2B, the optimal range for **3** appears to be between 30 and 80 °C, where the rate of change is fastest and follows a clean, exponential trend. All three compounds show similar sensitivity in DCE, while the sensitivity of **3** is drastically reduced in MeCN (Figure S7 in Supporting Information File 1). This can be attributed to the less favorable protonation in MeCN as shown in Table 1.

The interaction between compounds **1–3** and MSA was studied computationally by geometry-optimizing their ion pairs, denoted as $1H^+MSA^-$, $2H^+MSA^-$, and $3H^+MSA^-$. Because the azo group contains two nitrogens with lone pairs and an excess of MSA was used in the experiments, geometry optimizations were also performed for complexes with two MSA molecules ($1H^+MSA^-MSA$, $2H^+MSA^-MSA$ and $3H^+MSA^-MSA$). In addition to protonation, we also considered hydrogen-bonded complexes between **1–3** and MSA ($X-MSA$ and $X-(MSA)_2$, $X = 1, 2$ or **3**). The geometry-optimized structure of $3H^+MSA^-MSA$ is shown in Figure 3. In this structure, the second MSA molecule does not bind directly to the azo group but forms a hydrogen bond with the mesylate anion, and one of its oxygen atoms interacts with the $3H^+$ ion. All geometry-optimized structures for compounds **1–3** are shown in Supporting Information File 1, Figures S19–S28).

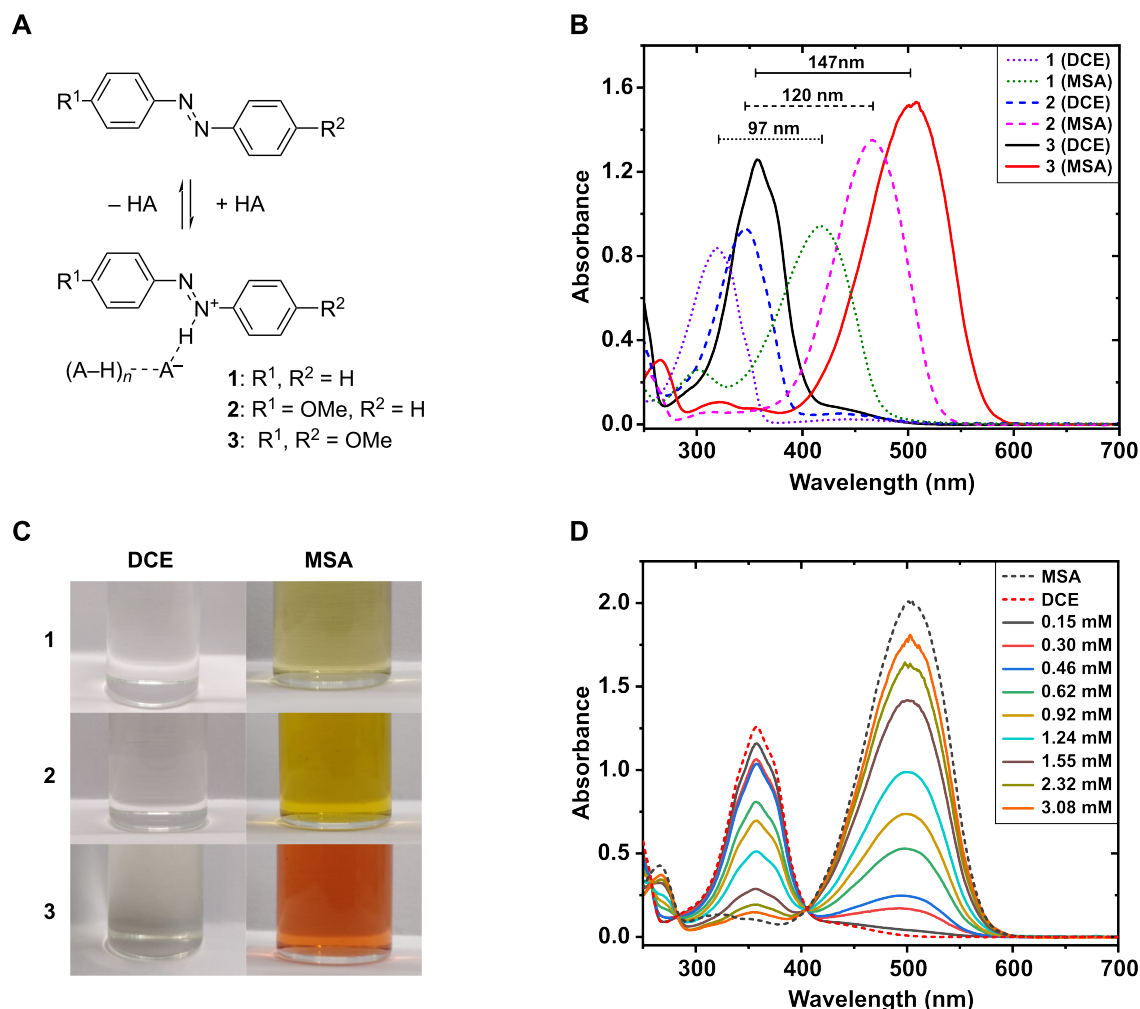


Figure 1: A) Protonation reaction scheme of azobenzene (**1**), 4-methoxyazobenzene (**2**), and 4,4'-dimethoxyazobenzene (**3**) with acid (HA). The parentheses indicate additional acid molecule(s) stabilizing the anion. B) Absorption spectra of **1**, **2**, and **3** in 1,2-dichloroethane (DCE) and methanesulfonic acid (MSA). C) Photographs showing the color change upon protonation, taken from 40 μ M solutions of each azobenzene in DCE and MSA. D) The effect of MSA concentration on the degree of protonation of **3** in DCE at 25 °C. Dashed lines represent the spectra of 40 μ M of **3** in pure DCE and MSA, calculated from the molar absorption coefficients. To account for slight azobenzene concentration variations the spectra have been dilution-corrected to 40 μ M at 405 nm, which acts as a pseudo-isosbestic point between the neutral and protonated forms.

Table 1 presents the calculated Gibbs free energy changes (ΔG°) for the complexes. Among the XH^+MSA^-MSA ($X = \mathbf{1}, \mathbf{2}$ or **3**) complexes, **3** shows the highest protonation propensity ($\Delta G^\circ = -5.81, -5.25$, and -2.55 kcal/mol for **3**, **2**, and **1**, respectively). The protonation is more favorable in DCE (ΔG° between -2.55 and -5.81 kcal/mol) than in MeCN (ΔG° between -1.74 and -4.74 kcal/mol), highlighting solvent effects on reactivity. For **3** in DCE, the addition of a second MSA molecule substantially enhances protonation, lowering ΔG° from -1.59 to -5.81 kcal/mol.

Spectral changes upon protonation were also studied computationally using time-dependent density functional theory (TDDFT). Analysis of the molecular orbitals involved in the

electronic transitions confirms that the absorption maxima for both neutral and protonated forms of compounds **1–3** correspond to $\pi \rightarrow \pi^*$ transition (see Supporting Information File 1, Figures S9–S14). In accordance with the experimentally observed red-shift upon protonation ($\Delta\lambda_{\max} = 97\text{--}147$ nm), the calculated spectra show comparable shifts ($\Delta\lambda_{\max} = 98\text{--}144$ nm) between compounds **1–3** and their protonated counterparts ($1H^+ \text{--} 3H^+$; Figures S16–S18 in Supporting Information File 1).

The experimental results are enticing from the applications point of view but offer little insight into details of the azobenzene–acid interactions. DFT calculations were performed to study these interactions at the molecular level. Better under-

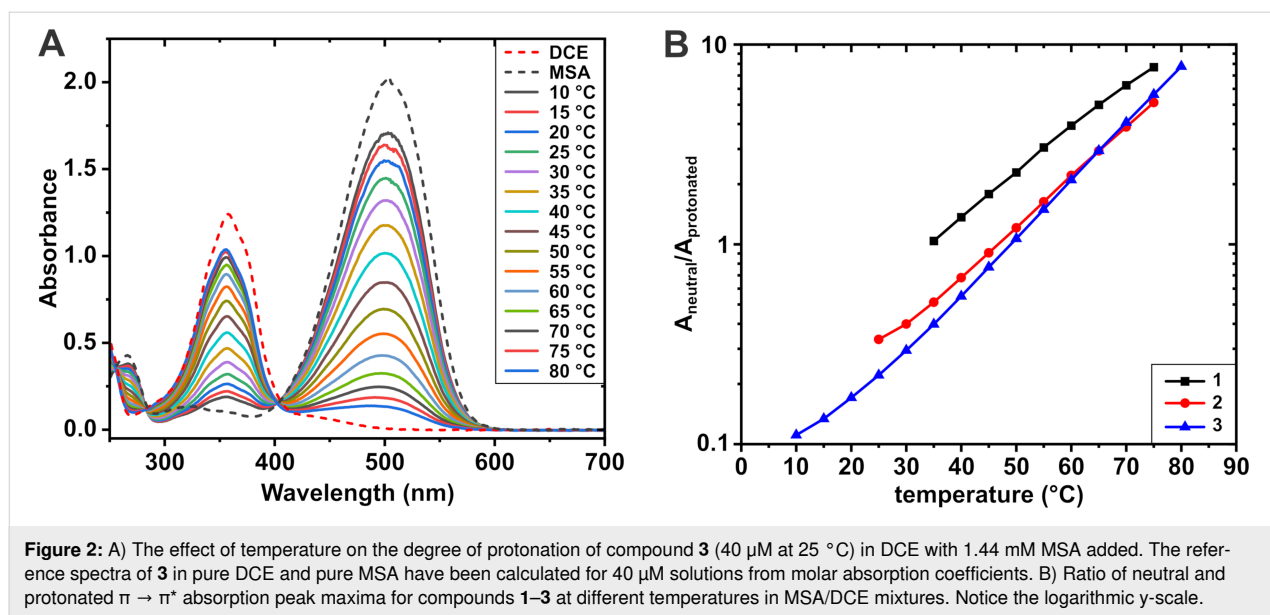


Figure 2: A) The effect of temperature on the degree of protonation of compound **3** (40 μ M at 25 $^{\circ}$ C) in DCE with 1.44 mM MSA added. The reference spectra of **3** in pure DCE and pure MSA have been calculated for 40 μ M solutions from molar absorption coefficients. B) Ratio of neutral and protonated $\pi \rightarrow \pi^*$ absorption peak maxima for compounds **1**–**3** at different temperatures in MSA/DCE mixtures. Notice the logarithmic y-scale.

Table 1: Computation ΔG° values for the complex and ion-pair formation of compounds **1**, **2**, and **3** with one or two molecules of methanesulfonic acid (MSA) in 1,2-dichloroethane (DCE) and acetonitrile (MeCN).

Complex or ion pair	ΔG° in DCE (kcal/mol)	ΔG° in MeCN (kcal/mol)
1 -MSA	−0.16	0.31
1H ⁺ MSA [−]	1.17	1.04
2 -MSA	−0.67	−0.30
2H ⁺ MSA [−]	−0.66	−1.03
3 -MSA	−0.45	0.17
3H ⁺ MSA [−]	−1.59	−1.37
1 -(MSA) ₂	1.62	2.45
1H ⁺ MSA [−] MSA	−2.55	−1.74
2H ⁺ MSA [−] MSA	−5.25	−4.53
3H ⁺ MSA [−] MSA	−5.81	−4.74

standing on the protonation process emerges from combining computational findings with experimental data, as discussed in the following section.

Discussion

Upon protonation, azobenzene and the conjugate base of the acid form either an ion pair or dissociated ions. The ion pair can be a contact ion pair (CIP), where the ions remain in close proximity through hydrogen bonding or electrostatic interactions, or a solvent-separated ion pair (SIP), where solvent molecules intervene and weaken these interactions [30]. In a moderately polar aprotic solvent such as DCE, we assume the formation of CIP, as supported by computational results. This discussion focuses on compound **3**, which showed most promising charac-

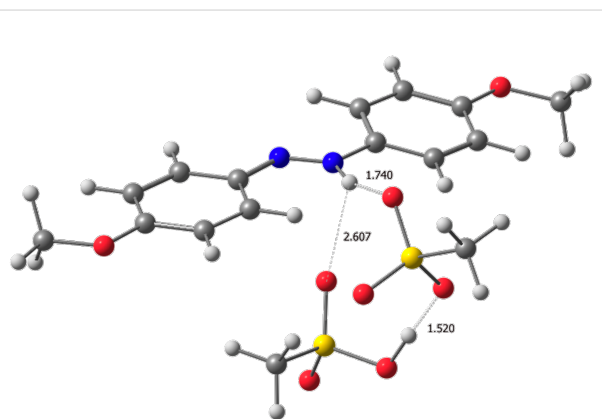


Figure 3: The geometry-optimized structure of **3H**⁺MSA[−]MSA.

teristics for temperature sensing, including a larger red-shift upon protonation and a broader sensing range.

DFT calculations revealed that a second acid molecule significantly enhances protonation, prompting further investigation into the reaction stoichiometry. Upon protonation of **3**, the $n \rightarrow \pi^*$ transition disappears and the $\pi \rightarrow \pi^*$ transition red-shifts from 358 nm to 502 nm (Figure 1B), resulting in a visible color change from pale yellow to bright red. Since the protonated **3** shows minimal absorption between 300–400 nm (Figure 1B), the degree of protonation can be estimated by comparing the absorbance at 358 nm (neutral) and 502 nm (protonated). As the degree of protonation and initial concentration are known, the equilibrium constant (K) can be determined using Equation 1, provided that the reaction stoichiometry (n) is known.

$$K = \frac{[3\text{H}^+\text{MSA}^-(\text{MSA})_{n-1}]}{[3][\text{MSA}]^n}, \quad n = 0, 1, 2, \dots \quad (1)$$

To determine the stoichiometry, the degree of protonation was measured for different acid concentrations and the corresponding K values were calculated. Using these K values, ΔG° can be determined using Equation 2. If the stoichiometry is correct, the calculated ΔG° values should not depend on the initial acid concentration.

$$\Delta G^\circ = -RT \ln K \quad (2)$$

We considered options where **3** forms ion pairs with one, two or three MSA molecules in DCE. The ΔG° values were calculated at three temperatures (15, 25, and 50 °C) for nine acid concentrations ($[\text{MSA}]_0 = 154\text{--}3080 \mu\text{M}$, or 10–200 ppm; see Tables S1–S9 in Supporting Information File 1). For one or three acid molecules ($n = 1$ or 3), the ΔG° values varied with the initial acid concentration, indicating incorrect stoichiometry. However, for $n = 2$, constant ΔG° values were obtained, irrespective of initial acid concentration (Supporting Information File 1, Table S10). This suggests that upon protonation, **3** forms an ion pair with two MSA molecules ($3\text{H}^+\text{MSA}^-\text{MSA}$), as supported also by DFT calculations.

Assuming the 1:2 stoichiometry between **3** and MSA, the reaction thermodynamics was studied using van't Hoff equation, i.e., by plotting $\ln K$ versus $1/T$. In an idealized case of temperature-independent enthalpy and entropy, this yields a straight line, allowing ΔH° and ΔS° to be extracted from the slope and intercept. However, a non-linear relationship was observed (see Supporting Information File 1, Figure S8), indicating temperature-dependent thermodynamics. To account for this, the polynomial form of the van't Hoff equation (Equation 3) was used, showing that both ΔH° and ΔS° vary significantly with temperature (see Supporting Information File 1, Table S11).

$$\begin{aligned} \ln K &= a + \frac{b}{T} + \frac{c}{T^2}, \\ \Delta H^\circ &= -R \cdot \left(b + \frac{2c}{T} \right), \text{ and} \\ \Delta S^\circ &= R \cdot \left(a - \frac{c}{T^2} \right) \end{aligned} \quad (3)$$

The calculated ΔH° values ranged from -11.1 kcal/mol at 10 °C to -16.5 kcal/mol at 80 °C, while ΔS° decreased from $-0.009 \text{ kcal/mol/K}$ to $-0.026 \text{ kcal/mol/K}$ over the same range. These trends suggest that the ion pair is more strongly bound at

higher temperatures. However, the increase in exothermicity is more than cancelled by the loss in entropy, resulting in a slight increase in ΔG° from -8.6 kcal/mol at 10 °C to -7.3 kcal/mol at 80 °C, in line with the observed temperature dependence of the protonation reaction.

The experimental and computational data indicate that the ions form a hydrogen-bonded ion pair ($3\text{H}^+\text{MSA}^-\text{MSA}$), which acts as a single thermodynamic unit. However, interactions with solvent molecules, underrepresented in implicit solvation models, may weaken this interaction in practice [31,32]. Since a solvent's dielectric constant increases when temperature decreases, the higher ΔH° values at lower temperatures could reflect enhanced solvation, leading to weaker ion pairing. Thus, the hydrogen-bonded geometry predicted computationally may better represent conditions at higher temperatures, when the dielectric constant is lower. Future work could explore how additional substituents on the azobenzene core influence ion-pairing strength, offering a strategy to further control the protonation behavior and enhance the temperature-sensing performance.

With improved understanding of azobenzene–acid interactions and good agreement between computations and experiments, a design-driven approach to temperature sensing becomes increasingly feasible. The aim is to create systems with tailored absorption wavelengths and spectral shifts, sensitivity, and well-defined operational ranges. While the experimental results are promising, the use of a hazardous, chlorinated solvent is a major limitation, highlighting the need for safer, non-toxic alternatives. Computational design can play a key role in minimizing trial and error during system development and optimization. Looking even further, utilizing azobenzene protonation in solid matrices can open new opportunities for practical sensing applications.

Experimental

1,2-Dichloroethane was purchased from Acros Organics (99.8% purity), acetonitrile from Honeywell ($\geq 99.9\%$ purity), methanesulfonic acid (MSA) from Sigma-Aldrich ($\geq 99.5\%$ purity), and trifluoroacetic acid (TFA) from TCI ($\geq 99.0\%$ purity). Azobenzene (98% purity) was bought from TCI and 4-methoxyazobenzene ($\geq 98\%$ purity) from Sigma-Aldrich. All of these were used as received. 4,4'-Dimethoxyazobenzene was synthesized according to the reaction depicted in Scheme S1 in Supporting Information File 1. The purity was confirmed by NMR spectroscopy (JNM-ECZR 500, JEOL).

UV–vis measurements were done with a Cary 60 UV–vis spectrometer (Agilent Technologies) in quartz cuvettes. Samples were prepared by first dissolving the azobenzene compounds in

1,2-dichloroethane to create stock solutions. MSA and TFA were added by creating acid–solvent mixtures of the desired acid concentration (e.g., 1000 ppm v/v in the target solvent). Samples of desired azobenzene concentration were then prepared by dilution from stock solutions into the desired acid–solvent mixture.

DFT calculations were performed with ORCA 6.0.1 [33] using the ω B97X-D4/def2-SVPD method. The conductor-like polarizable continuum model (CPCM) was used to account for the implicit solvation. Frequency calculations were performed for geometry-optimized structures to ensure that the structure was a true minimum energy structure (i.e., no imaginary frequencies). The molecular structures were visualized with ChemCraft version 1.8 (<http://www.chemcraft.org>) and Avogadro version 1.2.0 (<http://www.avogadro.cc>).

Supporting Information

Supporting Information File 1

Reaction schemes and characterization, UV–vis absorption spectra, determination of the stoichiometry, determination of thermodynamic parameters for $3\text{H}^+\text{MSA}^-\text{MSA}$, molecular orbitals, calculated absorption spectra and geometry-optimized structures.

[<https://www.beilstein-journals.org/bjoc/content/supplementary/1860-5397-21-115-S1.pdf>]

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Author Contributions

Antti Siiskonen: formal analysis; investigation; methodology; visualization; writing – original draft. Sami Vesamäki: formal analysis; investigation; visualization; writing – original draft.

Arri Priimagi: conceptualization; funding acquisition; project administration; resources; supervision; writing – review & editing.

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Data Availability Statement

All data that supports the findings of this study is available in the published article and/or the supporting information of this article.

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Thermodynamic equilibrium between locally excited and charge transfer states in perylene–phenothiazine dyads

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Full Research Paper

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Abstract

We report the excited-state dynamics of π -orthogonal donor–acceptor dyads based on perylene (Pe) and phenothiazine (PTZ), in which triphenylamine (TPA) units and a phenyl spacer were introduced to modulate donor strength and spatial separation. Among the series, Pe–PTZ(TPA)₂ exhibits a distinct thermal equilibrium between the locally excited (LE) state of the PTZ moiety and the photoinduced charge-transfer (CT) state. Femtosecond to microsecond transient absorption spectroscopy reveals that this equilibrium is facilitated not simply by enhanced donor ability, but presumably by excited-state planarization of the PTZ moiety, which lowers the energy of the LE state of the PTZ moiety. In contrast, Pe–Ph–PTZ(TPA)₂, in which the donor–acceptor distance is increased by a phenyl spacer, does not show clear equilibrium behavior. These results underscore the crucial role of excited-state structural relaxation in tuning photoinduced charge separation, and demonstrate that precise electronic and geometric design can enable controllable excited-state behavior in orthogonal molecular systems.

Introduction

Photoinduced electron transfer and charge separation are fundamental processes underlying a wide range of applications, including artificial photosynthesis, solar energy conversion, and photocatalysis [1–3]. In particular, the formation of long-lived charge-separated states is crucial for efficient energy conversion and advanced photofunctions driven by light. Among various donor–acceptor (D–A) architectures, π -orthogonal molecules, where the donor and acceptor moieties are spatially

decoupled, have attracted considerable attention [4–7]. This orthogonal arrangement can minimize ground-state electronic interactions while facilitating efficient photoinduced charge separation and spin–orbit charge-transfer intersystem crossing (SOCT-ISC), leading to unique excited-state behavior.

An important aspect of D–A systems is the interplay between the locally excited (LE) and the charge-transfer (CT) states

(denoted as diabatic states). A thermal equilibrium between local excited (LE) and charge-transfer (CT) states can be experimentally observed as dual fluorescence: a structured, higher-energy emission from the LE state and a broad, red-shifted emission from the CT state [8,9]. Classical systems such as 4-(*N,N*-dimethylamino)benzonitrile (DMABN) and pyrene-*o*-carborane exhibit such behavior, where LE and CT states dynamically interconvert depending on solvent polarity and temperature [10–12]. When the interconversion is faster than radiative decay, the two states can reach thermodynamic equilibrium, and their relative populations are determined by the energy gap between them.

Phenothiazine (PTZ) and perylene (Pe) are well-known molecular components for designing π -orthogonal D–A systems [13–15]. PTZ is an excellent electron donor due to its strong electron-donating ability and redox tunability, while Pe is often used as a robust acceptor featuring high photostability and strong visible absorption. Perylene–phenothiazine (Pe–PTZ) derivatives have been previously investigated for their excited-state dynamics [15].

Incorporating additional electron-donating groups such as triphenylamine (TPA) onto the PTZ core is expected not only to

enhance the donor property but also to lower the energy of the LE state of the PTZ moiety. Notably, while PTZ adopts a non-planar conformation in the ground state, it undergoes planarization in the excited state [16,17]. This conformational change is expected to further enhance the stabilization effect imparted by TPA. Such stabilization could bring the energy levels of the LE state of the PTZ moiety and the CT state into closer proximity, which may create conditions favorable for establishing a transient thermal equilibrium between the LE and CT states.

In this study, we designed and synthesized a series of novel Pe–PTZ derivatives by incorporating electron-donating triphenylamine (TPA) units and phenyl spacers to systematically modulate the donor strength and the spatial distance between the donor and acceptor. Four compounds – Pe–PTZ, Pe–PTZ(TPA), Pe–PTZ(TPA)₂, and Pe–Ph–PTZ(TPA)₂ – were synthesized and characterized (Figure 1). Their photophysical properties were comprehensively examined by steady-state and time-resolved emission and absorption spectroscopy. Furthermore, time-dependent density functional theory (TD-DFT) calculations were performed to support the experimental findings. Through these investigations, we aim to deepen the understanding of how molecular design parameters such as donor strength, spacer introduction, and π -orthogonality influence

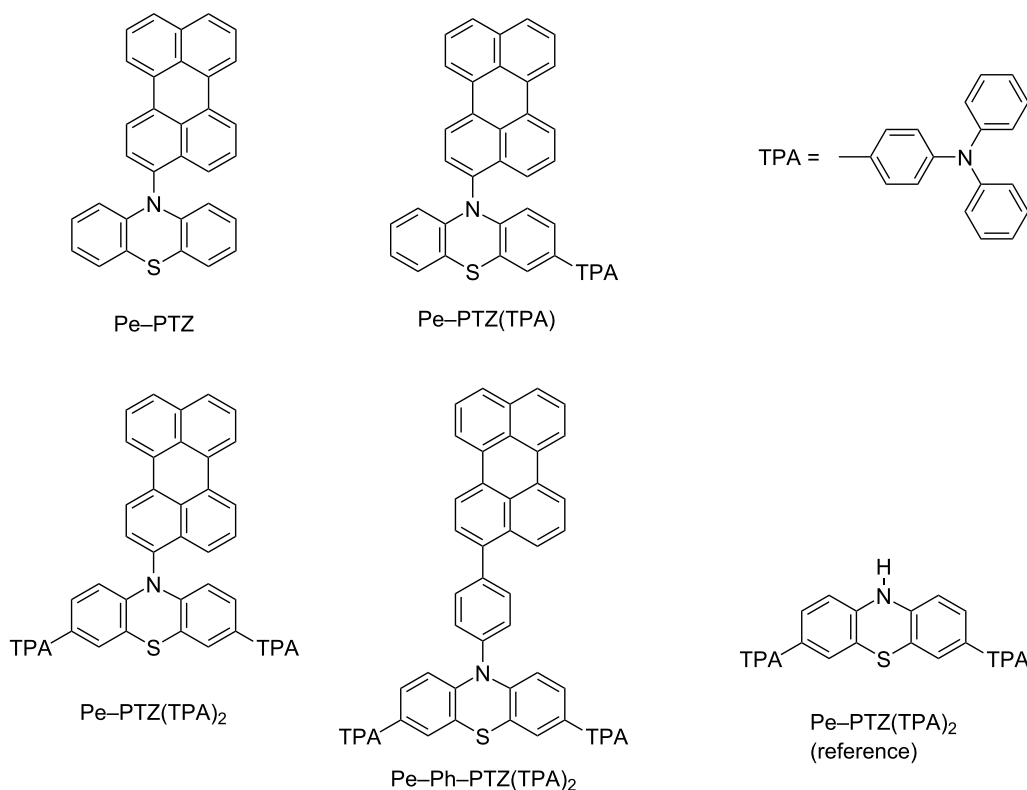


Figure 1: Molecular structures of Pe–PTZ, Pe–PTZ(TPA), Pe–PTZ(TPA)₂, and Pe–Ph–PTZ(TPA)₂.

excited-state equilibria and charge-transfer processes in π -orthogonal donor–acceptor systems.

Results and Discussion

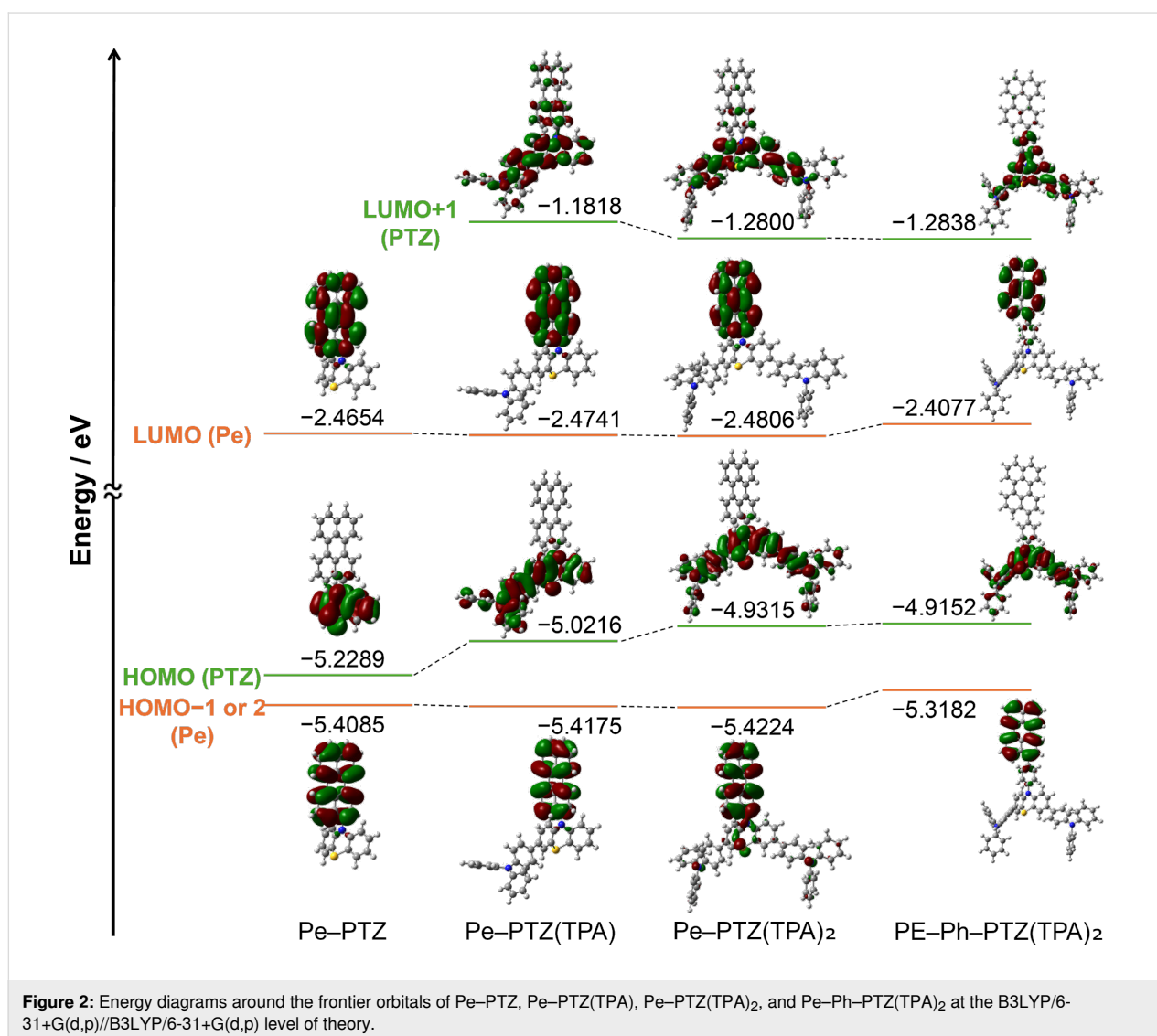
Synthesis and structural characterization

A series of π -orthogonal D–A molecules based on the Pe–PTZ framework were synthesized to systematically modulate the electronic properties and spatial arrangement between the donor and acceptor units. Structural features were designed to ensure orthogonality between the Pe and PTZ moieties, minimizing ground-state electronic interactions. In particular, the introduction of TPA groups aimed to enhance the electron-donating ability of the donor unit, while a phenyl spacer was introduced to modulate the distance between the donor and acceptor. The synthetic routes involved palladium-catalyzed cross-coupling reactions between bromo-substituted perylene or phenothiazine precursors and appropriate donor or linker units, followed by

purification via column chromatography and gel permeation chromatography (Figures S18–S21 in Supporting Information File 1). The details of the syntheses are shown in Supporting Information File 1.

Energy levels and steady-state optical properties

Time-dependent density functional theory (TD-DFT) calculations were performed to gain insights into the electronic structures of Pe–PTZ derivatives at B3LYP/6-31+G(d,p) level of theory (Figure 2) [18]. The calculations revealed that the highest occupied molecular orbitals (HOMOs) are localized at the PTZ or PTZ–TPA moieties in all compounds. In contrast, the lowest unoccupied molecular orbitals (LUMOs) are localized at the Pe moiety. This spatial separation of frontier orbitals suggests a weak electronic coupling in the ground state, consistent with the π -orthogonal molecular design. The introduction



of electron-donating TPA groups raises the HOMO energy levels, while the LUMO levels remain relatively unaffected, thereby reducing the HOMO–LUMO gaps. The presence of phenyl spacers in Pe-Ph-PTZ(TPA)_2 lowers the degree of electronic interaction between the donor PTZ and acceptor Pe moieties, as indicated by the decreased overlap between HOMO and LUMO.

UV–vis absorption spectra of the Pe–PTZ derivatives were recorded in benzene at room temperature (Figure 3a). All compounds exhibited characteristic absorption bands derived from the Pe moiety between 390 and 450 nm. A broad absorption feature around 320 nm, whose intensity increased with the number of TPA groups, was also observed. The increase in the absorption with the increase in the number of TPA groups is reproduced by TD-DFT calculations (Figure 3c, indicated by arrows), although the observed wavelength was slightly shifted to a longer wavelength. The calculations suggest that the absorption around this wavelength is explained by the optical transitions between the molecular orbitals, which are mainly distributed around the PTZ and TPA moieties (Figure 3d,

details are described in Figures S35–S38 in Supporting Information File 1). Absorption peaks associated with the Pe moiety are almost identical irrespective of the number of TPA groups, whereas they were slightly shifted to a longer wavelength in Pe-Ph-PTZ(TPA)_2 . This indicates that the absorption originated from the Pe moiety does not depend on the PTZ moieties, most probably due to the nearly orthogonal alignment. On the other hand, the absorption tail at 460–500 nm extended further into the lower energy region following the order $\text{Pe-PTZ} < \text{Pe-PTZ(TPA)} < \text{Pe-PTZ(TPA)}_2$. These absorption tails were ascribed to the CT transitions between the PTZ to Pe moieties. Pe-Ph-PTZ(TPA)_2 exhibited a less pronounced tailing, likely due to the increased spatial separation between the donor and the acceptor by a phenyl spacer, reducing electronic coupling. TD-DFT calculations indicated that, in TPA-substituted compounds, several weak absorption bands corresponding to CT transitions (primarily HOMO→LUMO) appear in the longer-wavelength region (Figure 3c), in good agreement with the experimental observations. Steady-state emission spectra of the Pe–PTZ derivatives displayed dual emission bands: a structured band in the 450–500 nm region associated with the LE

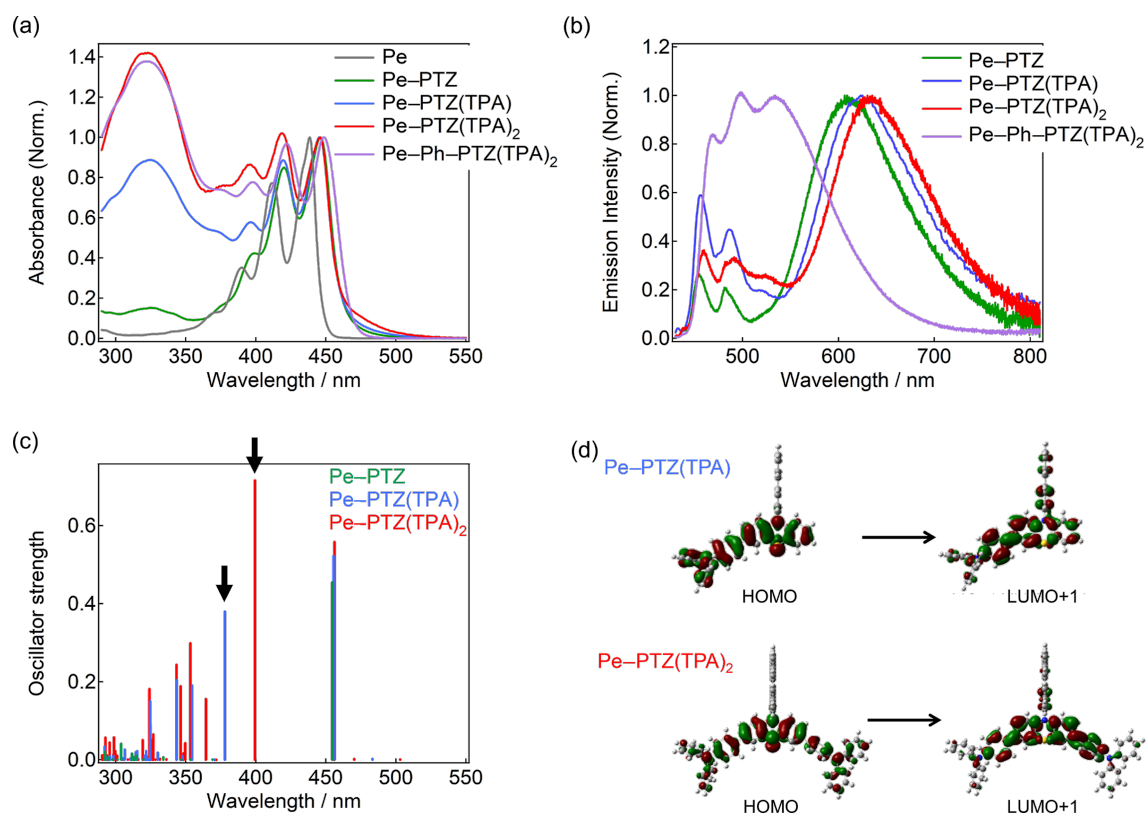


Figure 3: Steady-state (a) absorption and (b) emission spectra of Pe–PTZ, Pe–PTZ(TPA), Pe–PTZ(TPA)₂, and Pe–Ph–PTZ(TPA)₂ in benzene at room temperature. The excitation wavelength was 420 nm for Pe–PTZ, Pe–PTZ(TPA)₂, and Pe–Ph–PTZ(TPA)₂, and 415 nm for Pe–PTZ(TPA). (c) Simulated absorption spectra of these compounds (B3LYP/6-31+G(d,p)//B3LYP/6-31+G(d,p) level of theory), and (d) molecular orbitals mainly contributing to the optical transitions indicated by arrows.

state of the Pe moiety, and a broad, red-shifted band in the 550–750 nm region attributed to the CT emission (Figure 3b). The CT emission showed strong solvent dependence, i.e., shifting to longer wavelengths and decreasing in intensity as the solvent polarity increased, which are typical features of CT states (Figure S22 in Supporting Information File 1). The emission intensity of the CT band was almost comparable to that of the LE band of the Pe moiety in Pe–Ph–PTZ(TPA)₂, whereas the emission intensity of the CT band is larger than that of the LE band of the Pe moiety in other compounds. This suggests that the phenyl spacer effectively suppressed the CT interaction. It is noted that the substitution of the TPA group increases the relative amplitude of the CT emission band. On the other hand, it was found that the intensity does not necessarily depend on the number of TPA groups. The relative emission quantum yields (Φ_f) in benzene solution were 2.4, 3.1, 2.4, and 20% for Pe–PTZ, Pe–PTZ(TPA), Pe–PTZ(TPA)₂, and Pe–Ph–PTZ(TPA)₂, respectively. This order corresponds to the relative intensities of the CT band compared to the LE band of the Pe moiety. This result suggests that a stronger CT character leads to a lower overall fluorescence quantum yield. The Φ_f in other solvents are shown in Table S1 (Supporting Information File 1). In addition, a gradual increase in the emission intensity around 500–520 nm is observed with an increasing number of TPA substituents. This observation suggests the presence of an additional emission band originating from the PTA-substituted PTZ unit, in addition to the emissions from the LE state of the Pe moiety and the CT state. The assignment of this band will be discussed in detail based on fluorescence lifetime measurements in the following section.

Since the CT states of these molecules exhibit emissive properties, their excited-state lifetimes were determined from emission decay measurements. Time-resolved fluorescence measurements revealed that the decays of the CT emission band follow a single-exponential decay function in all compounds (Supporting Information File 1, Figure S23 and Figure S24). As a representative example, Figure 4 presents the emission decay profiles of Pe–PTZ(TPA)₂, with overlaid decay curves monitored at 600 nm and 460 nm. The lifetimes of the CT states were 10.7, 10.3, 9.7, and 10.8 ns for Pe–PTZ, Pe–PTZ(PTA), Pe–PTZ(PTA)₂, and Pe–Ph–PTZ(PTA)₂, respectively. At the probe wavelength corresponding to the LE band of the Pe moiety (460 nm), a subnanosecond decay attributable to the LE state of the Pe moiety (within the instrumental response function, IRF) was observed, along with a relatively slower decay component on tens of nanosecond timescales. Notably the lifetime of the slower component (15 ns) was clearly different from that of the CT emission (10 ns). This implies that the slower decay component at 460 nm is different from the CT state observed at the decay at 632 nm. Taking into account the broad

emission feature observed at 500–520 nm only in the TPA-substituted PTZ derivatives, the emission component may be assigned to another state derived from TPA moieties.

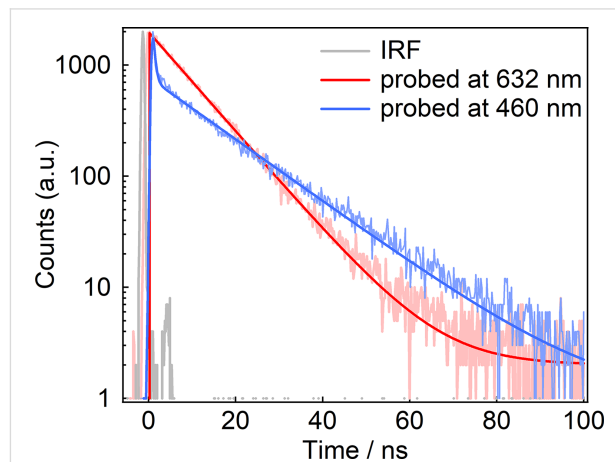


Figure 4: Emission decay curves of Pe–PTZ(TPA)₂ in benzene excited at 403 nm and probed at 460 and 632 nm.

Microsecond transient absorption spectroscopy

To elucidate the excited-state dynamics of these molecules, transient absorption spectroscopy measurements spanning the femtosecond to microsecond timescales were conducted. When electron transfer occurs between the donor and acceptor, the spin–spin interaction becomes weaker, facilitating the formation of triplet excited states upon recombination. This process is known as spin–orbit charge transfer intersystem crossing (SOCT-ISC), as described in the Introduction. Therefore, the dynamics of the triplet excited state were initially investigated using microsecond transient absorption spectroscopy. Upon excitation at 355 nm, all compounds exhibited transient absorption bands centered between 420 and 550 nm, attributed to the triplet LE (³LE) state of the Pe moiety (Figure 5a for Pe–PTZ(TPA)₂ and the spectra of the other compounds are shown in Figures S25–S27 in Supporting Information File 1). Under nitrogen atmosphere, the triplet signals displayed lifetimes in the order of several microseconds. In contrast, under an oxygen atmosphere, the transient absorption decayed significantly faster, confirming the triplet nature of these states (Figure 5b and Figures S25–S27 in Supporting Information File 1). Under a nitrogen atmosphere, the decay time constants were found to be 77, 46, 135, and 63 μ s for Pe–PTZ, Pe–PTZ(TPA), Pe–PTZ(TPA)₂, and Pe–Ph–PTZ(TPA)₂, respectively. The transient absorption spectral features closely matched those of the triplet state of perylene, indicating that the ³LE state of the Pe moiety is generated in all of these molecules. Pe is a rigid aromatic hydrocarbon, and exhibits significant overlap between the HOMO and LUMO, resulting in a

large singlet–triplet energy gap and a low-lying ^3LE state. These characteristics likely cause the excited states of all compounds to relax preferentially to the ^3LE state of the Pe moiety.

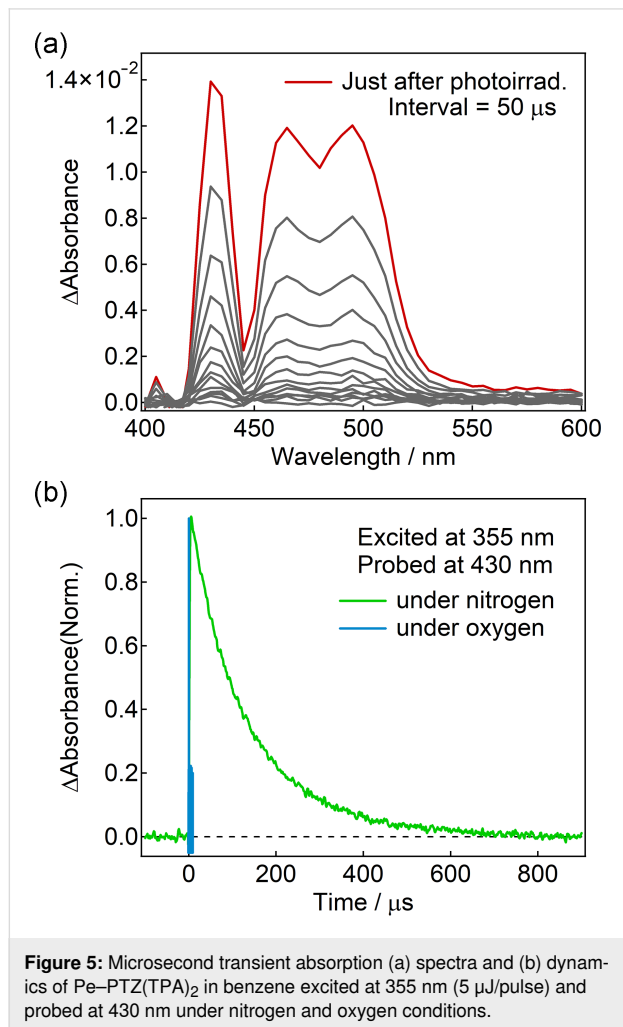


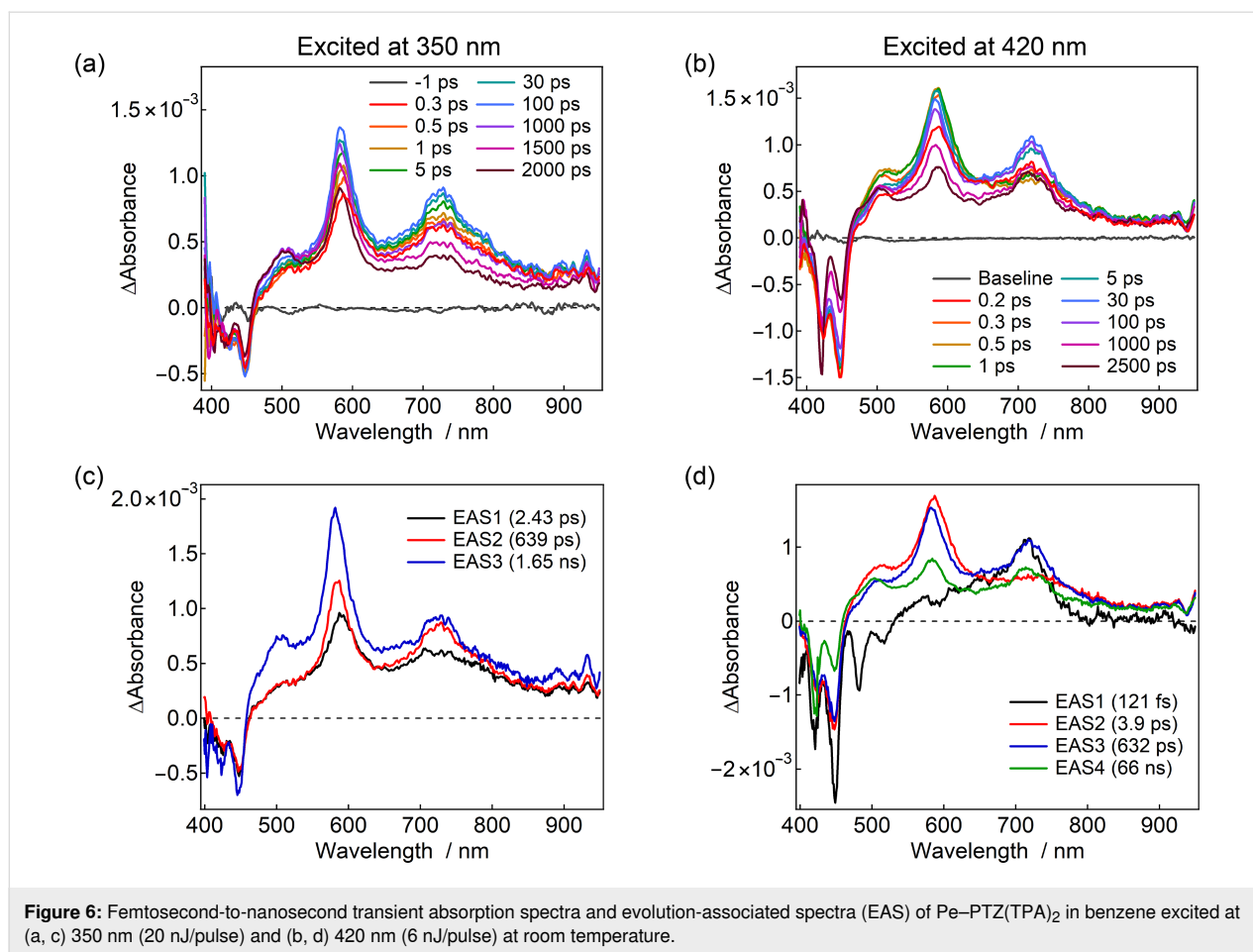
Figure 5: Microsecond transient absorption (a) spectra and (b) dynamics of Pe-PTZ(TPA)₂ in benzene excited at 355 nm (5 μJ/pulse) and probed at 430 nm under nitrogen and oxygen conditions.

Femtosecond-to-nanosecond transient absorption spectroscopy

To gain deeper insights into the effects of the electron-donating TPA substituents on the excited-state dynamics, femtosecond-to-nanosecond transient absorption spectroscopy measurements were carried out. While the excited-state dynamics of Pe-PTZ have been studied in a previous study [15], this study focused first on a detailed analysis of Pe-PTZ(TPA)₂, followed by a comparison with other derivatives. The transient absorption spectra were analyzed using global analysis based on singular value decomposition with the Glotaran program to resolve into the evolution-associated spectra (EAS) [19]. The spectral evolution over time was tentatively analyzed using a three- or four-component sequential decay model (for example, the four-state kinetic model is described as $\text{EAS1} \rightarrow \text{EAS2} \rightarrow \text{EAS3} \rightarrow \text{EAS4} \rightarrow \text{ground state}$).

Figure 6a and 6c show the transient absorption spectra and EAS of Pe-PTZ(TPA)₂ in benzene excited at 350 nm. The excitation at 350 nm predominantly corresponds to an absorption band enhanced by the introduction of TPA groups, suggesting preferential excitation of the PTZ(TPA)₂ moiety. Immediately after excitation, ground-state bleach signals at 425 and 445 nm and positive transient absorption bands at 505, 582, and 725 nm were observed (0.3 ps). The overall spectral features were highly similar to those previously reported for Pe-PTZ [15], particularly the characteristic band at 582 nm, which was assigned to the radical anion of the Pe moiety. Additionally, a shoulder signal observed near 500 nm was attributed to the radical cation of the PTZ(TPA) unit. However, although previous studies selectively excited the Pe moiety and attributed the 725 nm band to the LE state of Pe moiety, such an assignment may not be directly applicable to the present case because the PTZ(TPA)₂ moiety was predominantly excited in the present case.

To clarify the origin of the 725 nm band, a reference compound lacking the Pe moiety (PTZ(TPA)₂, Figure 1) was synthesized, and its transient absorption spectra were measured. Remarkably, a transient absorption band around 710 nm, similar to the ESA of the LE state of the Pe moiety, was observed (Supporting Information File 1, Figure S29a). This result indicates that the ^1LE states at both the PTZ(TPA)₂ and Pe moieties exhibit transient absorption near 710–720 nm, necessitating careful interpretation. Notably, as will be discussed later in Figure 6d, the ^1LE state of the Pe moiety can be identified by its characteristic stimulated emission in the 490–510 nm region. Based on these observations, it is concluded that selective excitation of the PTZ(TPA)₂ moiety at 350 nm generates both the ^1LE state of the PTZ(TPA)₂ moiety and the Pe radical anion almost instantaneously. The electron transfer occurs extremely rapidly (within the instrumental response function, <100 fs), likely via a direct CT transition. Subsequently, both signals showed growth components with time constants of 2.4 and 639 ps. Although the PTZ unit adopts a bent structure in the ground state, it is known to undergo a structural transformation to a planar conformation upon excitation, as the planar geometry becomes more stable in the excited state. For instance, the planarization time constant of a phenyl-substituted phenothiazine derivative, 12-phenyl-12*H*-benzo[*a*]phenothiazine, in toluene at room temperature has been estimated to be 28 ps (with an additional minor 0.7 ps component attributed to small-scale structural changes) [17]. It is also noted that the relaxation dynamics depend on the molecular structure and the surrounding environment. Considering that Pe-PTZ(TPA)₂ is significantly larger than that in the aforementioned study, and that benzene has a slightly higher viscosity than toluene (0.60 and 0.56 cP at 297 K, respectively), the time constant of 2.43 ps of the first EAS (EAS1) can be attributed to reorganization of solvent molecules associated with excited-



state charge redistribution and minor conformational changes. Meanwhile, the time constant of 639 ps of the second EAS (EAS2) may be ascribed to the planarization of the PTZ(TPA)₂ moiety.

Several hundred picoseconds after excitation, a new transient absorption band at ≈ 505 nm emerged, which was assigned to the ³LE state of the Pe moiety, as confirmed by microsecond transient absorption measurements. Interestingly, even after the formation of the Pe radical anion via electron transfer, the component corresponding to the ¹LE state of the PTZ(TPA)₂ moiety remained observable for nanoseconds or longer. This behavior, not seen in the parent Pe-PTZ, is attributed to the introduction of TPA groups.

Furthermore, when the same measurements were performed in acetonitrile, the signals derived from the LE state disappeared, leaving only the CT-state component (Supporting Information File 1, Figure S29b). Given that the CT states are relatively unstable (i.e., energetically higher-lying) in benzene, and that the LE emission from the PTZ(TPA)₂ moiety was concurrently observed with the CT emission in the emission decay measure-

ments, it is inferred that a transient equilibrium exists between the ¹LE state of the PTZ(TPA)₂ moiety and CT states (see Figure 8 for summarized energy diagrams). The introduction of TPA groups not only stabilizes the CT state but also stabilizes the LE state, bringing their energy levels into proximity and thus creating the observed equilibrium in nonpolar environments.

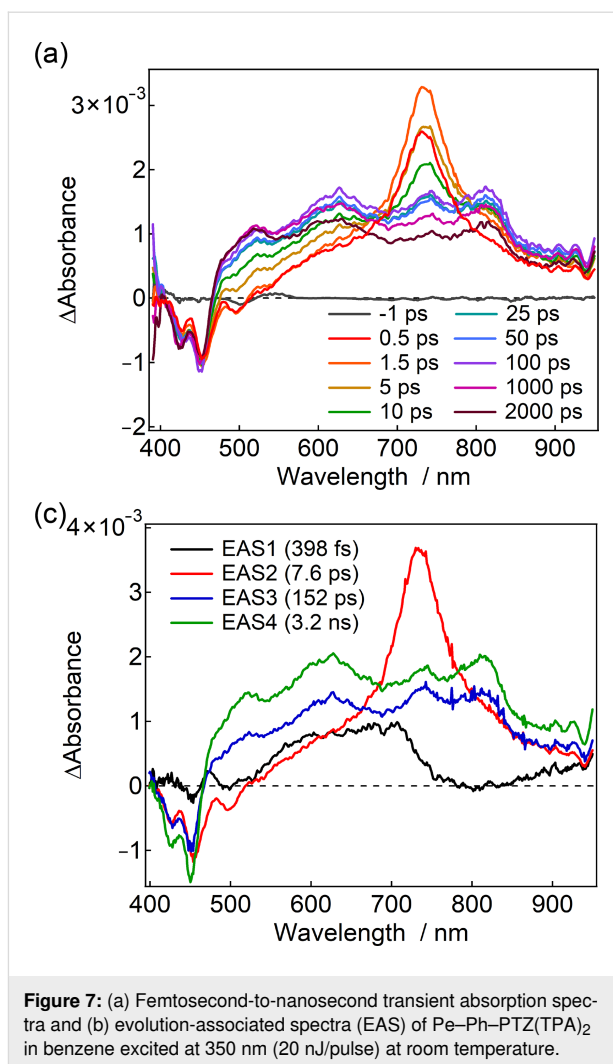
Subsequently, transient absorption measurements of Pe-PTZ(TPA)₂ in benzene were performed using a 420 nm excitation pulse, where the Pe moiety is predominantly excited (Figure 6b and 6d). Immediately after excitation, ground-state bleach, stimulated emission, and excited-state absorption signals corresponding to the ¹LE state of the Pe moiety were observed for a very short duration. Based on the characteristic stimulated emission signals of the Pe moiety at 480–510 nm as shown in Figure 6d, EAS1 can be safely assigned to the ¹LE state of the Pe moiety. With a time constant of ≈ 120 fs, a band at 582 nm, attributed to the Pe radical anion, was generated, clearly demonstrating that the time constant of the reductive electron transfer from the PTZ(TPA)₂ to the Pe moieties is ≈ 120 fs. Afterward, at 3.9 ps, a broader transient absorption

band near 710 nm reappeared, assigned to the thermal equilibrium between the CT state and the LE S_1 state of the PTZ(TPA)₂ moiety. These observations indicate that after initial electron transfer, the LE S_1 state of PTZ(TPA)₂ moiety and the CT state coexist transiently in a thermal equilibrium. Subsequently, the 500 nm band gradually increased, reflecting the formation of the 3 LE state of the Pe moiety.

The recombination process after electron transfer was measured using the randomly-interleaved pulse train (RIPT) method (Supporting Information File 1, Figure S28) [20]. The Pe radical anion signal decayed with a time constant of 10 ns, while the 500 nm band attributed to the 3 LE state of the Pe moiety persisted. The CT-state formation thus facilitated subsequent triplet generation via SOCT-ISC, enabled by the orthogonal arrangement of the donor and acceptor moieties.

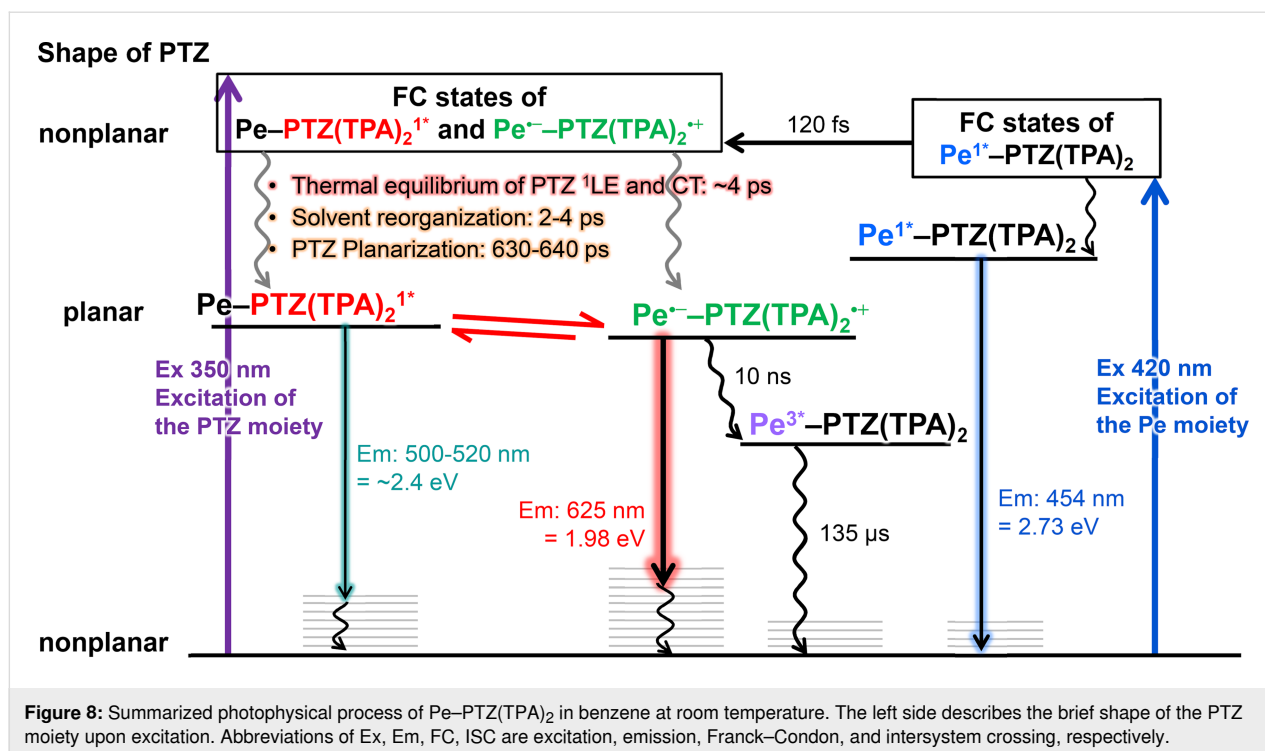
When Pe–PTZ(TPA) was excited at 350 nm in benzene, the transient absorption spectra and dynamics observed were generally similar to those of Pe–PTZ(TPA)₂ (Supporting Information File 1, Figure S29c). However, the broad band between 700–800 nm is split into two peaks at 720 and 790 nm, likely due to asymmetric substitution of a single TPA group. The time constants of photoinduced structural planarization of the PTZ(TPA) moiety were determined to be 6.2 and 470 ps. The acceleration of the planarization of the PTZ(TPA) moiety (470 ps vs 639 ps for PTZ(TPA)₂) can be attributed to the presence of only one TPA group, which facilitates structural reorganization of the PTZ moiety. Conversely, the deceleration of the early component (6.2 ps vs 2.4 ps for PTZ(TPA)₂), likely associated with solvent reorientation, may be explained by the larger dipole rearrangement induced by excitation in this asymmetric molecular framework, which in turn requires more time for the reorganization of the surrounding solvent molecules.

For Pe–Ph–PTZ(TPA)₂, the transient equilibrium behavior, like Pe–PTZ(TPA)₂, was obscured. Upon excitation at 390 nm, where both PE and PTZ(TPA)₂ moieties are expected to be excited, the transient absorption band at 720 nm and negative signals at 420–500 nm were instantaneously observed. These negative signals are ascribed to the bleach and stimulated emission of the PE moiety, suggesting that the transient absorption band at 720 nm is ascribed to the excited-state absorption of 1 LE state of the Pe moiety. These signals gradually decayed, and broad transient absorption features attributable to the Pe radical anion and the PTZ(TPA) radical cation appeared at $\approx$ 600 and $\approx$ 500 nm, respectively (Figure 7). The electron transfer time constant was determined to be 7.6 ps, significantly slower than that of Pe–PTZ(TPA)₂ (120 fs or faster), reflecting the effect of the phenyl spacer that increases the D–A distance and thus reduces the electronic coupling.



The photophysical processes of Pe–PTZ(TPA)₂ are summarized in Figure 8. Upon excitation of the PTZ moiety with a 350 nm pulse, transient absorption signals originating from both the excited PTZ moiety and the perylene radical anion were observed almost instantaneously. As the PTZ moiety relaxes from a nonplanar to a planar structure in the excited state, the transient absorption spectra evolve with time constants of several picoseconds and approximately 630–640 ps. During this process, the signal of the Pe radical anion gradually increases, while the signal attributed to the 1 LE state of the PTZ moiety remains. This result suggests that the 1 LE state of the PTZ moiety and the CT state coexist in a transient equilibrium. This equilibrium eventually leads to charge recombination, forming the 3 LE state of the Pe moiety with a time constant of 10 ns, which subsequently returns to the ground state with a lifetime of 135 μ s.

In contrast, when the Pe moiety is predominantly excited using a 420 nm pulse, the ground-state bleach and stimulated emis-



sion associated with the ¹LE state of the Pe moiety are initially observed. However, this state rapidly decays with a time constant of 120 fs, followed by the immediate formation of the CT state. Subsequently, a transient signal attributed to the ¹LE state of the PTZ moiety appears at 3.9 ps, indicating that the thermal equilibrium between the ¹LE state of the PTZ moiety and the CT state is established within approximately 4 ps. The later-stage dynamics follow a similar pathway as those observed upon 350 nm excitation, involving planarization of the PTZ moiety and triplet formation via charge recombination.

Conclusion

This study reveals the unique excited-state dynamics of π -orthogonal donor-acceptor systems, TPA-substituted Pe-PTZ derivatives. Femtosecond-to-microsecond transient absorption spectroscopy demonstrated that Pe-PTZ(TPA) and Pe-PTZ(TPA)₂ exhibit a transient equilibrium between the ¹LE state of the PTZ moiety and the photoinduced CT state. Notably, this equilibrium is not primarily driven by the enhanced electron-donating ability of the TPA units, but rather by the stabilization of the PTZ ¹LE state, which is facilitated by planarization of the PTZ moiety in the excited state and the resulting increase in π -conjugation. This behavior led to the persistent presence of ¹LE-state signals coexisting with those of the CT state, and ultimately to the formation of the Pe ³LE state via charge recombination. Such a dynamic interplay between the LE and CT states was obscured in Pe-Ph-PTZ(TPA)₂, where the spatial separation between the donor and acceptor

units is large, highlighting the critical role of the electronic D-A interaction and the stabilization of the ¹LE state of the PTZ moiety by excited-state induced planarization. These results highlight the importance of structural relaxation in the excited state for controlling photophysical properties, and demonstrate that even within a simple molecular framework, subtle intramolecular interactions – such as increased conjugation induced by planarization – can have a significant impact on the nature of photoinduced charge separation. Such molecules with finely tunable excited-state dynamics are expected to play an important role in the development of next-generation photoresponsive materials exhibiting complex and multifunctional responses [21].

Supporting Information

Supporting Information File 1

Experimental and computational details, synthesis and characterization of compounds, additional spectroscopic results, and theoretical calculations.

[<https://www.beilstein-journals.org/bjoc/content/supplementary/1860-5397-21-121-S1.pdf>]

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Author Contributions

Issei Fukunaga: formal analysis; investigation; visualization; writing – review & editing. Shunsuke Kobashi: formal analysis; investigation; visualization; writing – review & editing. Yuki Nagai: investigation; writing – review & editing. Hiroki Horita: investigation; writing – review & editing. Hiromitsu Maeda: investigation; resources; writing – review & editing. Yoichi Kobayashi: conceptualization; formal analysis; funding acquisition; investigation; methodology; software; supervision; visualization; writing – original draft; writing – review & editing.

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Data Availability Statement

Data generated and analyzed during this study is available from the corresponding author upon reasonable request.

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Understanding the origin of stereoselectivity in the photochemical denitrogenation of 2,3-diazabicyclo[2.2.1]heptene and its derivatives with non-adiabatic molecular dynamics

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Abstract

Photochemical denitrogenation reactions of bicyclic azoalkanes produce strained bicyclic compounds of interest to synthetic organic chemists. We report a computational study on the mechanism of diazabicyclo[2.2.1]heptenes to address long standing mechanistic questions. Indeed, the mechanism of these reactions has been disputed for over six decades. We employed non-adiabatic molecular dynamics (NAMD) simulations combined with state-of-the-art multireference quantum mechanical calculations to understand the photophysical properties and mechanisms of these diazabicyclo[2.2.1]heptenes. The energetically accessible lowest excitations are $n_{\text{NN}}(\sigma_{\text{CN}}) \rightarrow \pi^*$ and range from 3.94–3.97 eV. From the >292 trajectories, the reaction proceeds through a dynamically concerted but asynchronous denitrogenation reaction. One σ_{CN} bond breaks along the S_1 surface; the other σ_{CN} breaks after hopping to the S_0 . We identified two clusters of S_1/S_0 surface hopping points from these trajectories. In the first cluster, the methylene bridge is fully inverted relative to the reactant geometry. In the second cluster, the inversion is only partial, with one of the carbon atoms in the methylene bridge inverted relative to the reactant. We identified each cluster's corresponding minimum energy conical intersection (MECI), indicating at least two possible S_1/S_0 -MECIs. Our dynamics simulations illustrate that inversion begins in the excited state immediately after the first σ_{CN} bond breaks. This inversion is driven by the atomic momenta acquired after the bond breaks. These dynamical effects promote the formation of the inverted housane, thereby explaining the observed selectivities. A minority of trajectories undergo thermal conversion in the ground state, producing the minor retained housane product from inverted housane/diradical.

Introduction

Photochemical reactions utilize light as a sustainable energy source and are considered to be 'green' reactions [1,2]. Organic chromophores absorb light, accessing higher-lying excited

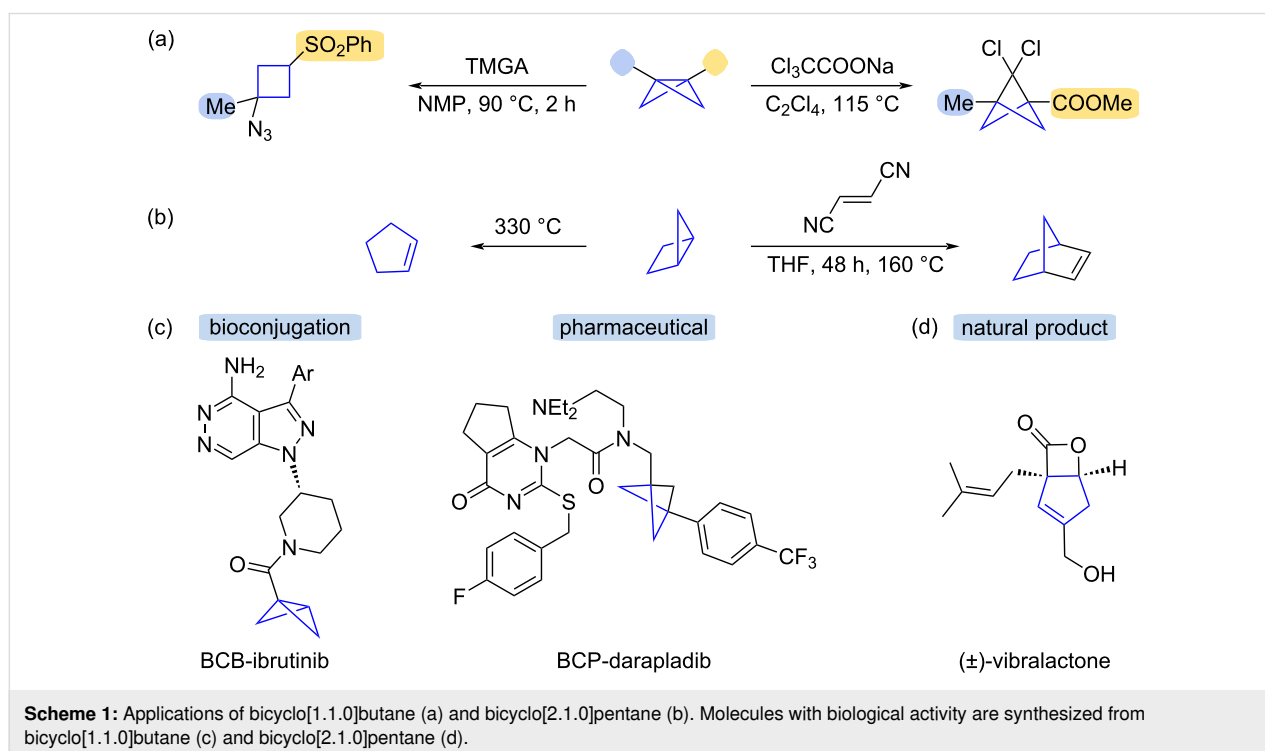
state(s) that exhibit distinct reactivities, leading to bond breaking and formation, irreversibly producing energy-dense compounds [2,3]. One promising strategy to access strained

compounds involves gas-evolution (e.g., CO or N₂) because of the associated entropic driving force; this approach has had wide utility in photomedicine and organic synthesis. For example, photochemical decarboxylation has been employed to release carbon monoxide at relatively safer doses in biological systems using photoresponsive CO-releasing molecules (photo-CORMs) [4] because these have shown anti-inflammatory activity [5,6]. Photochemical denitrogenation of azoalkanes has been utilized in the stereoselective synthesis of strained compounds such as bicyclo[1.1.0]butane (BCB) and bicyclo[2.1.0]pentane (housane).

The energy stored in strained σ_{CC} bonds of BCB and housane makes them important building blocks in the synthesis of complex molecular structures. BCBs have been employed in ring-opening reactions with nucleophiles [7–11], radicals [12–15] and electrophiles [16–18] to give cyclobutanes and cyclobutenes [19,20], which are building blocks in regio- and stereoselective synthesis [21–27] (Scheme 1a). Additionally, BCB has been used in bioconjugation due to its high chemoselectivity for cysteine alkylation under mild conditions, for example, BCB-ibrutinib [28] (Scheme 1c). BCB is also used as a precursor to bicyclo[1.1.1]pentanes, which are valuable motifs in drug design [19,20,29–33], such as BCP-darapladib (Scheme 1c) [30,31,34,35]. Housanes are versatile starting materials for different types of reactions including thermal isomerization to cyclopentenenes [36–38] and 1,4-pentadienes [37,38], chemical electron-transfer oxidations to cyclopentene [39] and cycloaddi-

tion reactions with electron-deficient alkenes and alkynes [38,40,41] (Scheme 1b). Housane derivatives were also used in an atom-economical synthesis of the antibiotic [42–44] and potentially anti-obesity drug [45–49], ($\pm$)-vibrallactone [42] (Scheme 1d).

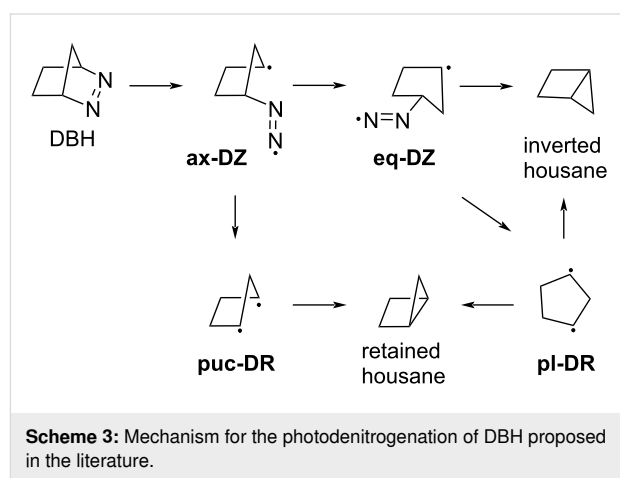
The thermolysis [50–60] and photolysis [57,58,60–78] mechanisms of cyclic azoalkenes have been studied with experimental and computational techniques for more than six decades, in solution [51,55,59–61,64,67,69,70,73–76,78,79], gas phase [50,55,62,64,65], and solid state [60,63]. The experimental studies on the thermal denitrogenation of diazabicyclo[2.1.1]hept-2-ene (DBH, **1**) indicate that both the parent compound and its derivatives undergo a concerted elimination of N₂ and the inverted product (*exo*-**2**) is preferentially formed [55,56]. Deuterium labeling of DBH was employed to experimentally measure the stereoselectivity of the reaction. In 1965, Crawford and co-workers experimentally found kinetic evidence for a 1,3-diradical from the thermal decomposition of **1** [56]. In 1963, Steel investigated the photolysis of diazabicyclo[2.1.1]hept-2-ene in solution, and the products were the same those obtained by thermolysis, nitrogen and bicyclo[2.1.0]pentane with quantum yield approaching unity [64]. Engel and co-workers explored further the reaction using transient spectroscopic methods and discovered that the rate of N₂ formation is significantly slower than that the S₁ fluorescence decay, suggesting that the N₂ is not released at S₁ state [80]. Roth and co-workers discovered a preference to form the



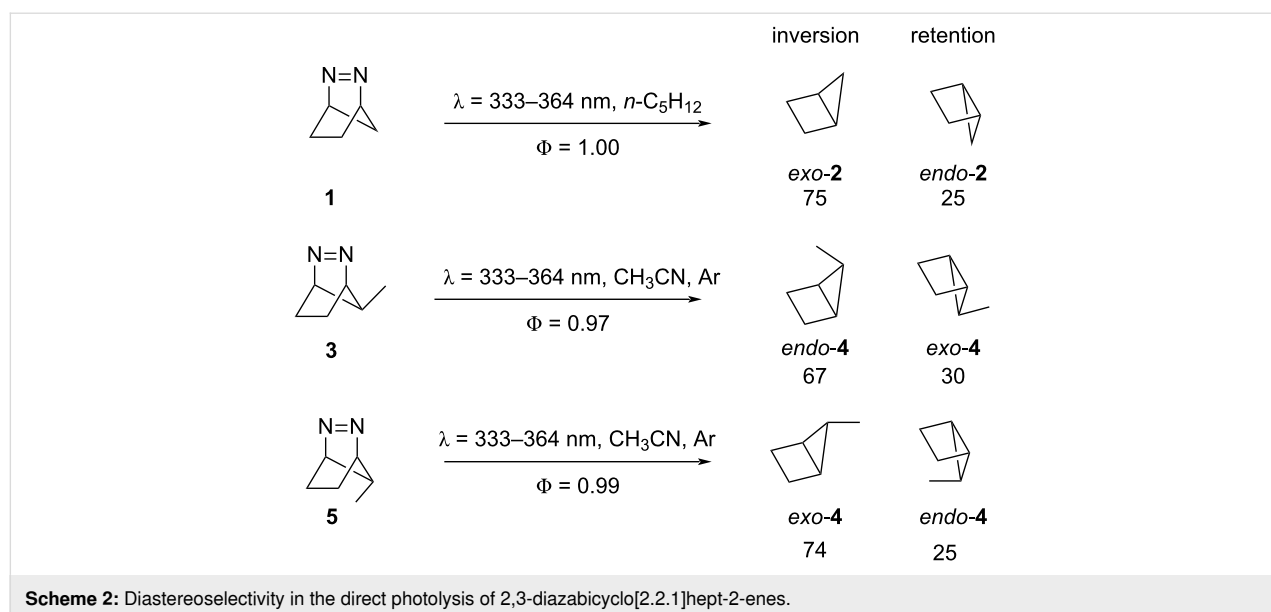
inverted product *exo*-2 from deuterated diazabicyclo[2.1.1]hex-2-ene (**1**) (Scheme 2) [71]. Adam and co-workers performed photochemical reactions with derivatives of **1**, including **3** and **5** (Scheme 2) through direct photolysis and with benzophenone as photosensitizer. No diastereomeric excess was observed [72] for reactions with photosensitizer. Trofimov and co-workers reported the temperature and solvent effect on the stereoselectivities [73–76] and observed a general preference for inversion across several derivatives of **1** [77,78]. These studies suggest that the thermal denitrogenation of diazabicyclo[2.1.1]hept-2-ene undergoes a concerted mechanism of elimination of nitrogen, while the photochemical reaction proceeds via a stepwise mechanism.

Quantum mechanical calculations have provided valuable insights into the photochemical stereoselectivities of cyclic azoalkenes. In 1998, Yamamoto and co-workers investigated the reaction paths for α -C–N and β -C–C bond cleavage during the direct and sensitized photolysis of DBH [81]. The minimum energy geometries in S_0 , S_1 , T_1 , and T_2 , conical intersections, transition structures, and singlet–triplet crossing were computed using CASSCF(10,8)/6-31G(d)//MP2/6-31G(d) [81]. The results suggested a stepwise C–N bond breaking with the formation of the diazenyl diradical intermediate [81]. In 2003, Olivucci and his co-workers investigated the inversion stereoselectivity of housane formation using CASPT2(12,10)/6-31G(d)//CASSCF(12,10)/6-31G(d). They also used a single classical trajectory with UB3LYP/6-31G(d) to probe the ground-state relaxation dynamics immediately after the conical intersection. They found that the axial diazenyl diradical (**ax-DZ** in Scheme 3) is selectively generated through a linear–axial conical intersection, providing access to five different reaction

pathways. The computed energetics show a production of a cyclopentane-1,3-diyl diradical with a 1:1 production of retained and inverted housane, which disagrees with experimental observations. They argued that the DZ intermediate reacts before thermal equilibration. The formation of inverted housane occurs via the pseudo-axial-to-equatorial inversion of DZ. From the axial DZ, the puckered-DR (**puc-DR** in Scheme 3) radical could be formed resulting in retained housane. From the equatorial DZ (**eq-DZ** in Scheme 3), the inverted housane can be formed through a homolytic substitution (S_H2) process or can be formed via a planar DR (**pl-DR** in Scheme 3) radical which affords retained and inverted housane [82].



In 2020, Rollins and co-workers also investigated the diradical pathways resulting from thermal decomposition using UM06-2X/6-31G(d,p) with quasiclassical trajectories and machine-learning analysis [83]. The results suggested a correlation be-



tween the out-of-plane bending of the methylene bridge and the stereoselectivity of the formation of retained and inverted housane [83]. Chen and Li explored the potential energy surfaces and surface crossing points of 2,3-diazabicyclo[2.1.1]hex-2-ene with CASPT2(12,10)/6-31G(d)//CASSCF(12,10)/6-31G(d,p) in 2006 and concluded that on the S_1 surface one C–N bond is broken [84]. In 2011, Abe and co-workers investigated the denitrogenation mechanism of 7,7-diethoxy-2,3-diazabicyclo[2.2.1]hept-2-ene, showing that a stepwise C–N-bond cleavage is energetically favored using broken-symmetry (BS)-(U)CCSD/6-31G(d) and suggested that an equatorial conformation of the diazanyl diradical leads to the formation of the inverted product. An alternative route via an axial conformation of diazanyl diradical for the inverted product was suggested using Born–Oppenheimer molecular dynamics [85]. Most recently, our group performed multireference calculations with CASPT2(8,8)/ANO-S-VDZP//CASSCF(8,8)/ANO-S-VDZP and non-adiabatic molecular dynamics (NAMD) simulations of a series of diazabicyclo[2.1.1]hexenes. The minimum energy path showed stepwise σ_{CN} bond breaking and led directly to a minimum energy crossing point, corresponding to the inversion product. We also performed NAMD simulations on halogenated derivatives to test the role of hyperconjugative interactions; the NAMD simulations revealed that this stereo-electronic effect substantially perturbs the potential energy surface toward the retention products [86].

However, for 2,3-diazabicyclo[2.2.1]hept-2-enes, current theoretical reports only offer qualitative mechanistic understanding.

The previous studies omit dynamical effects in the photochemical denitrogenation; the overall mechanism and origin of stereoselectivity are still unknown. We used state-of-the-art computations and NAMD simulations to understand the origin of the reactivities and stereoselectivities for a series of 2,3-diazabicyclo[2.2.1]hept-2-enes (Scheme 2). This report shows the first multiconfigurational NAMD simulation studies to understand the photochemical denitrogenation mechanism of 2,3-diazabicyclo[2.2.1]hept-2-enes.

Results and Discussion

We started our studies on characterizing the photophysical properties of **1**, **3**, and **5**. We considered the molecular orbitals and electrons most critical for describing the electronic structure of the molecules in the reaction. The CASSCF [87]/ANO-S-VDZP [88] active space for **1** is shown in Figure 1; we considered 8 electrons and 9 orbitals, along with their average occupancies. For derivatives **3** and **5** with a methyl substituent, the active space also consisted of 8 electrons and 9 orbitals, with their active space and occupancies available in Supporting Information File 1.

We benchmarked the vertical excitation energy with a (8,9)-active space against those obtained with time-dependent density functional theory by computing the vertical excitation energy, oscillator strength, and nature of the electronic transition of **1**, **3**, and **5** with ω B97X-D [89]/aug-cc-pVTZ [90], SA(4)-CASSCF(8,9)/ANO-VDZP, and SA(4)-XMS-CASPT2 [91] (8,9)/ANO-S-VDZP levels of theory, as shown in Table 1.

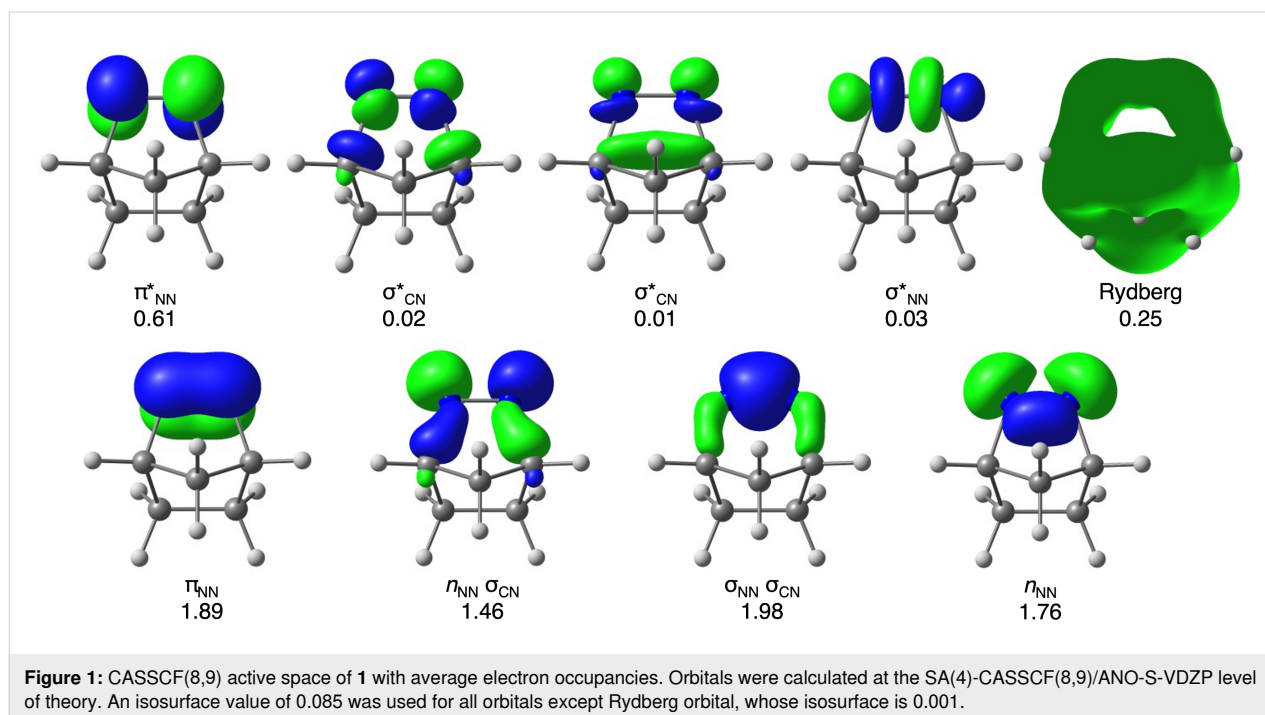


Figure 1: CASSCF(8,9) active space of **1** with average electron occupancies. Orbitals were calculated at the SA(4)-CASSCF(8,9)/ANO-S-VDZP level of theory. An isosurface value of 0.085 was used for all orbitals except Rydberg orbital, whose isosurface is 0.001.

Table 1: Vertical excitation energies, oscillator strengths, and electronic transitions for the first three excited states of **1**, **3**, and **5** at TD-DFT, CASSCF, and XMS-CASPT2 levels of theory.

Molecule	Method	State	Energy (eV)	Wavelength (nm)	Oscillator strength	Nature
1	ω B97X-D/ aug-cc-pVTZ	S ₁	3.58	346	0.001	$n_{\text{NN}}(\sigma_{\text{CN}}) \rightarrow \pi^*$
		S ₂	6.23	199	0.001	$n_{\text{NN}} \rightarrow \pi^*$
		S ₃	6.34	195	0.013	$n_{\text{NN}}(\sigma_{\text{CN}}) \rightarrow \text{Ryd}$
	XMS-CASPT2(8,9)/ ANO-S-VDZP	S ₁	3.97	312		$n_{\text{NN}}(\sigma_{\text{CN}}) \rightarrow \pi^*$
		S ₂	6.13	202		$n_{\text{NN}} \rightarrow \pi^*$
		S ₃	7.02	177		$n_{\text{NN}}(\sigma_{\text{CN}}) \rightarrow \text{Ryd}$
	SA4-CASSCF(8,9)/ ANO-S-VDZP	S ₁	4.64	267	0.013	$n_{\text{NN}}(\sigma_{\text{CN}}) \rightarrow \pi^*$
		S ₂	6.95	179	0.000	$n_{\text{NN}} \rightarrow \pi^*$
		S ₃	7.96	156	0.039	$n_{\text{NN}}(\sigma_{\text{CN}}) \rightarrow \text{Ryd}$
3	ω B97X-D/ aug-cc-pVTZ	S ₁	3.56	348	0.000	$n_{\text{NN}}(\sigma_{\text{CN}}) \rightarrow \pi^*$
		S ₂	6.13	202	0.000	$n_{\text{NN}} \rightarrow \pi^*$
		S ₃	6.38	194	0.008	$n_{\text{NN}}(\sigma_{\text{CN}}) \rightarrow \text{Ryd}$
	XMS-CASPT2(8,9)/ ANO-S-VDZP	S ₁	3.94	315		$n_{\text{NN}}(\sigma_{\text{CN}}) \rightarrow \pi^*$
		S ₂	6.27	198		$n_{\text{NN}} \rightarrow \pi^*$
		S ₃	7.01	177		$n_{\text{NN}}(\sigma_{\text{CN}}) \rightarrow \text{Ryd}$
	SA4-CASSCF(8,9)/ ANO-S-VDZP	S ₁	4.63	268	0.013	$n_{\text{NN}}(\sigma_{\text{CN}}) \rightarrow \pi^*$
		S ₂	6.92	179	0.000	$n_{\text{NN}} \rightarrow \pi^*$
		S ₃	8.02	155	0.033	$n_{\text{NN}}(\sigma_{\text{CN}}) \rightarrow \text{Ryd}$
5	ω B97X-D/aug-cc-pVTZ	S ₁	3.55	349	0.001	$n_{\text{NN}}(\sigma_{\text{CN}}) \rightarrow \pi^*$
		S ₂	6.19	200	0.001	$n_{\text{NN}} \rightarrow \pi^*$
		S ₃	6.31	196	0.008	$n_{\text{NN}}(\sigma_{\text{CN}}) \rightarrow \text{Ryd}$
	XMS-CASPT2(8,9)/ ANO-S-VDZP	S ₁	3.95	314		$n_{\text{NN}}(\sigma_{\text{CN}}) \rightarrow \pi^*$
		S ₂	6.42	193		$n_{\text{NN}} \rightarrow \pi^*$
		S ₃	7.04	176		$n_{\text{NN}}(\sigma_{\text{CN}}) \rightarrow \text{Ryd}$
	SA4-CASSCF(8,9)/ ANO-S-VDZP	S ₁	4.63	268	0.013	$n_{\text{NN}}(\sigma_{\text{CN}}) \rightarrow \pi^*$
		S ₂	6.96	178	0.000	$n_{\text{NN}} \rightarrow \pi^*$
		S ₃	8.06	154	0.045	$n_{\text{NN}}(\sigma_{\text{CN}}) \rightarrow \text{Ryd}$

The $S_0 \rightarrow S_1$ vertical excitation energy, calculated using XMS-CASPT2(8,9)/ANO-S-VDZP, ranges from 3.94 to 3.97 eV and has the electronic transition from $n_{\text{NN}}(\sigma_{\text{CN}})$ to π^* , with an oscillator strength of 0.013 for all molecules. The $S_0 \rightarrow S_2$ excitation involves an $n_{\text{NN}} \rightarrow \pi^*$ transition with all methods, and energy with XMS-CASPT2(8,9)/ANO-S-VDZP ranging from 6.13 to 6.42 eV with 0.000 oscillator strength. In contrast, $S_0 \rightarrow S_3$ excitation has an $n_{\text{NN}}(\sigma_{\text{CN}}) \rightarrow \text{Ryd}$ electronic transition, with energy ranging from 7.01 to 7.04 eV with XMS-CASPT2(8,9)/ANO-S-VDZP and an oscillator strength ranging from 0.033 to 0.045. These results show agreement between the electronic nature of the transition of TD-DFT, CASSCF, and

CASPT2, showing that the chosen active space can capture the photophysics of the molecules.

Table 1 provides the photophysical properties for the optimized ground-state geometry. However, experimentally, there is an ensemble of non-equilibrium geometries. To get a more realistic understanding of the absorption, we generated 500 geometries using the Wigner-sampling method to generate an ensemble of energetically accessible non-equilibrium geometries. We computed the gas-phase vertical excitation energies ($S_0 \rightarrow S_n$, $n = 1, 2, 3$) and corresponding oscillator strengths of the Wigner-sampled structures of **1**, **3** and **5** to explore the nature of

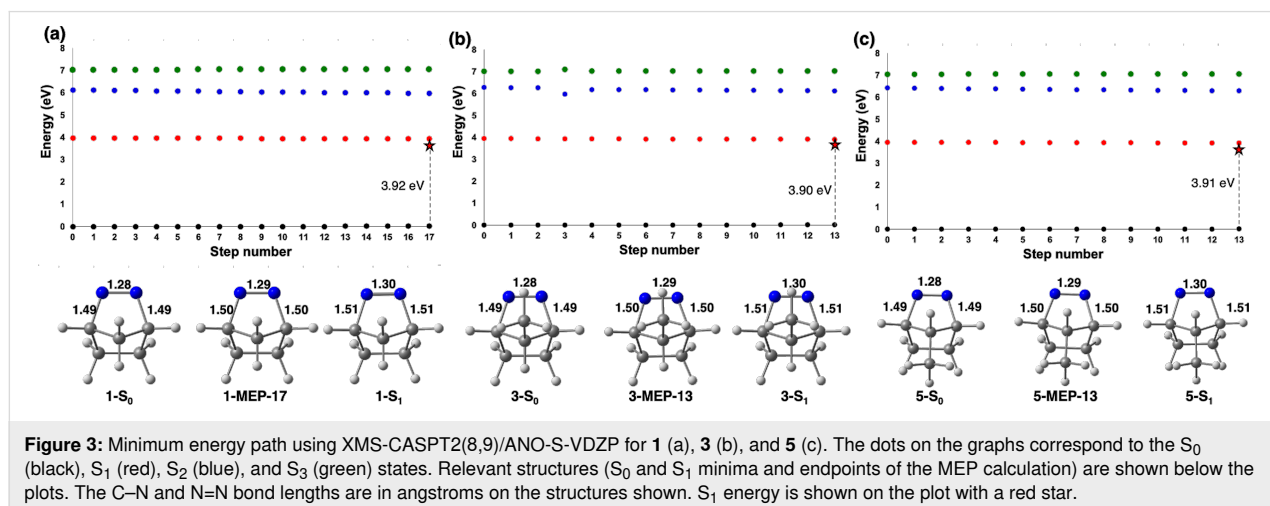
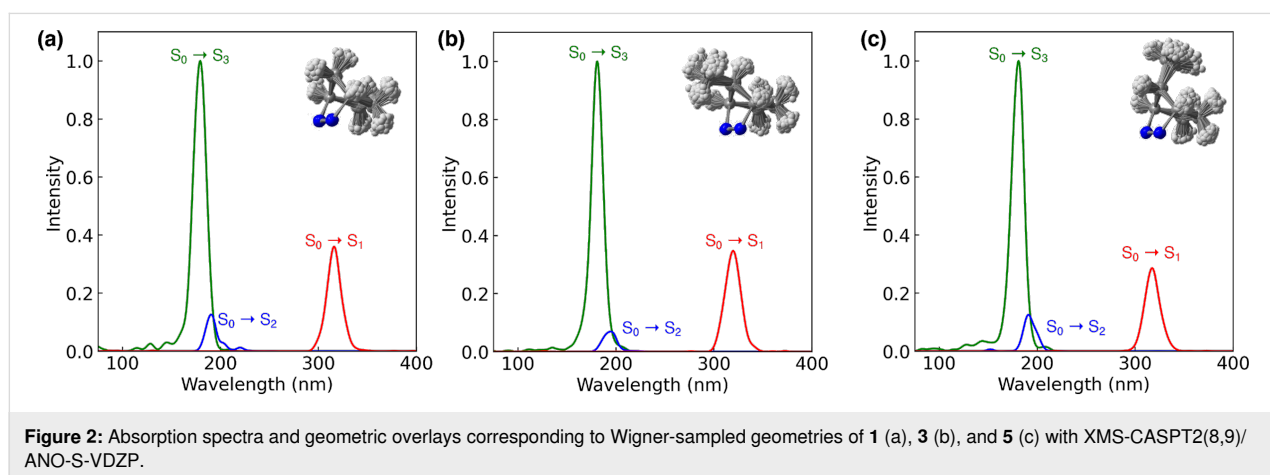
electronic excitations to the FC regions. This allowed us to predict an absorption spectrum with normalized oscillator strengths ($S_0 \rightarrow S_3$). Figure 2 shows the computed absorption spectra of **1**, **3**, and **5**.

Figure 2 shows the **1**, **3**, and **5** computed absorption spectra with three λ_{max} peaks. The S_0 to S_3 has a peak centered from 179 to 181 nm and corresponds to a majority $n_{\text{NN}}(\sigma_{\text{CN}}) \rightarrow \text{Ryd}$, the peak centered from 190 to 194 nm corresponds to a majority $n_{\text{NN}} \rightarrow \pi^*$ from S_0 to S_2 , and the peak centered from 316 to 319 nm corresponds to an $n_{\text{NN}}(\sigma_{\text{CN}}) \rightarrow \pi^*$ from S_0 to S_1 . The S_0 to S_3 has the highest intensity due to the allowed nature of the electronic transition $n_{\text{NN}}(\sigma_{\text{CN}}) \rightarrow \text{Ryd}$. On the other hand, the S_0 to S_1 peak is expected to have a lower intensity because of the forbidden nature of the $n_{\text{NN}}(\sigma_{\text{CN}}) \rightarrow \pi^*$ electronic transition. This aligns with the trends observed in oscillator strength within the optimized geometry, where the S_0 to S_3 transition shows a higher oscillator strength than the S_0 to S_1 transition. In the case of the S_0 to S_2 transition, the spectrum reveals that a non-equilibrium assembled geometry produced a non-zero

oscillator strength, unlike the optimized geometry, which exhibited zero. This difference is attributed to some mixing in the transition nature from S_0 to S_2 , involving $n_{\text{NN}}(\sigma_{\text{CN}}) \rightarrow \text{Ryd}$ and $n_{\text{NN}} \rightarrow \pi^*$ transitions. The $S_0 \rightarrow S_1$ peaks from 316 to 319 nm are closer to the range of irradiation wavelengths of the experimentally used light source (333–364 nm). For **1**, this peak is closer to experimental absorbance, $\lambda_{\text{max}} = 338$ nm [80]. The remaining peaks, shown in blue and green for S_2 and S_3 , respectively, absorb at higher energy than the experimental light source. Electronic transitions to these excited states are impossible in the experiment and thus will not be considered for this photochemical mechanistic study.

DBH photodenitrogenation mechanism

We then turned our attention to the photochemical reaction mechanisms leading to the formation of housane derivatives from 2,3-diazabicyclo[2.2.1]hept-2-enes. To determine the dominant mechanistic pathway, we started with a static exploration with the minimum steepest-descent energy path (MEP) from the FC-point along the S_1 reaction coordinate. Figure 3



shows the MEP and the structure of S_0 , the last point of MEP, and S_1 for **1**, **3**, and **5**. These structures are important for understanding the geometrical changes after light absorption and determining the dominant mechanism pathway, along the S_1 -reaction coordinate.

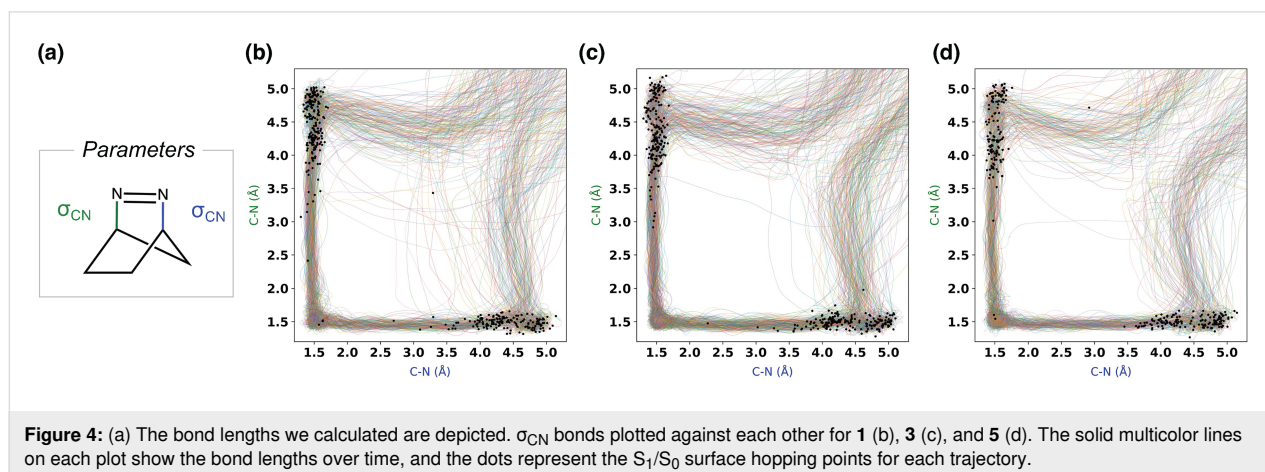
The MEP for **1** contains 17 geometries leading to the final structure **1-MEP-17**, and the MEP for **3** and **5** contain 13 geometries leading to final structures **3-MEP-13** and **5-MEP-13**, respectively. The dominant electronic transition is from $n_{\text{NN}}(\sigma_{\text{CN}}) \rightarrow \pi^*$ for all molecules, and the geometrical changes along the S_1 -MEP correspond to an increased population of the π_{NN}^* orbital. In all molecules, the π_{NN} bond length increased from 1.28 Å at the S_0 -optimized geometry to 1.29 Å at the last MEP structure, which is consistent with the electronic transition because the π_{NN}^* is being populated, resulting in a less stable π_{NN} . The σ_{CN} increased by 0.01 Å along the S_1 -MEP for all molecules. The final MEP structure has a large S_1 – S_0 energy gap ranging from 3.90 to 3.92 eV with XMS-CASPT2(8,9)/ANO-S-VDZP for all molecules. The large S_1 – S_0 energy gap suggests that the dominant mechanistic pathway is toward an S_1 minimum, as it does not indicate a possible crossing between the S_1 and S_0 potential energy surface. We used the last MEP structure as an input to optimize an S_1 minimum. The S_1 optimized geometries are shown in Figure 3 as **1-S₁**, **3-S₁**, and **5-S₁**. Their energies are 3.83 to 3.87 eV above the S_0 and have nearly identical structure and energy as the last point of the MEP. Based on this static MEP calculation, the experimental quantum yield ($\Phi = 0.97$ – 1.00) is inconsistent with this static analysis, since it suggests a non-productive and fluorescence pathway. We hypothesize that these S_1 minima are shallow excited-state minima that can be escaped towards a productive region of the conical intersection seam, or dynamical effects enable this reaction towards near-unity quantum yields. We performed non-adiabatic molecular dynamics (NAMD) simulations starting from the S_1 -FC region of **1**, **3**, and **5** to verify our hypotheses,

identify the dynamical effects that enable this reaction, and enumerate all possible mechanistic pathways.

Non-adiabatic molecular dynamics simulations

We performed an NAMD simulation using the Fewest Switches Surface Hopping (FSSH) algorithm [92–94], with OpenMolcas [95,96] and with Python Rapid Artificial Intelligence Ab Initio Molecular Dynamics (Pyrai²MD) [97–100] for **1**, **3**, and **5**. The NAMD simulation was performed with the CASSCF(8,9)/ANO-S-VDZP method to elucidate the origin of stereoselectivities and the overall singlet-mediated mechanism involved in denitrogenation. We generated initial conditions with an ensemble of 700 non-equilibrium geometries through Wigner sampling with 300 K velocities. The trajectories were then propagated from the S_1 Franck–Condon region for 1 ps. We defined a complete trajectory as one that reached 1 ps with a maximum energy drift of 0.06 a.u., resulting in 352, 396, and 292 completed trajectories for molecules **1**, **3**, and **5**, respectively; 98–99% of these trajectories end in the S_0 .

We wanted first to understand the synchronicity of the σ_{CN} -bond breaking and whether bond-breaking occurs on the S_1 and/or S_0 state(s). To address these questions, we plotted the two σ_{CN} bond lengths throughout the trajectories (Figure 4). We observed that one σ_{CN} bond breaks first, as indicated by an increase in the σ_{CN} bond length. For the majority of the trajectories, when the broken σ_{CN} bond length reaches 4.5 to 5.0 Å, we observed the breaking of the second bond, suggesting a sequential bond-breaking process. This observation aligns with previous computational studies on the photodenitrogenation of DBH. The black dots represent the hopping points, the geometries where the trajectory crosses from S_1 to S_0 . Figure 4 shows that the first σ_{CN} bond breaks on the S_1 surface, while the second σ_{CN} bond breaks after relaxation to S_0 . We determine that the denitrogenation is stepwise but on an ultrafast



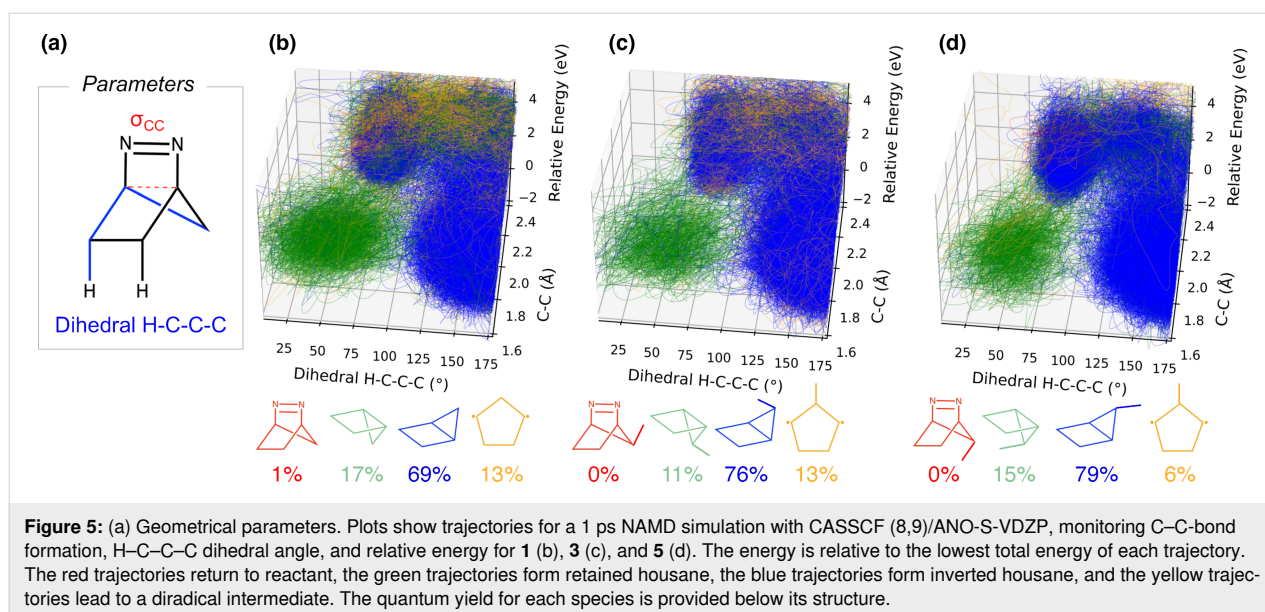
timescale, making it dynamically concerted. By analyzing the state population of the trajectories over time, the obtained time constants were 174 fs for **1**, 163 fs for **3**, and 201 fs for **5**. The plots are available in Supporting Information File 1.

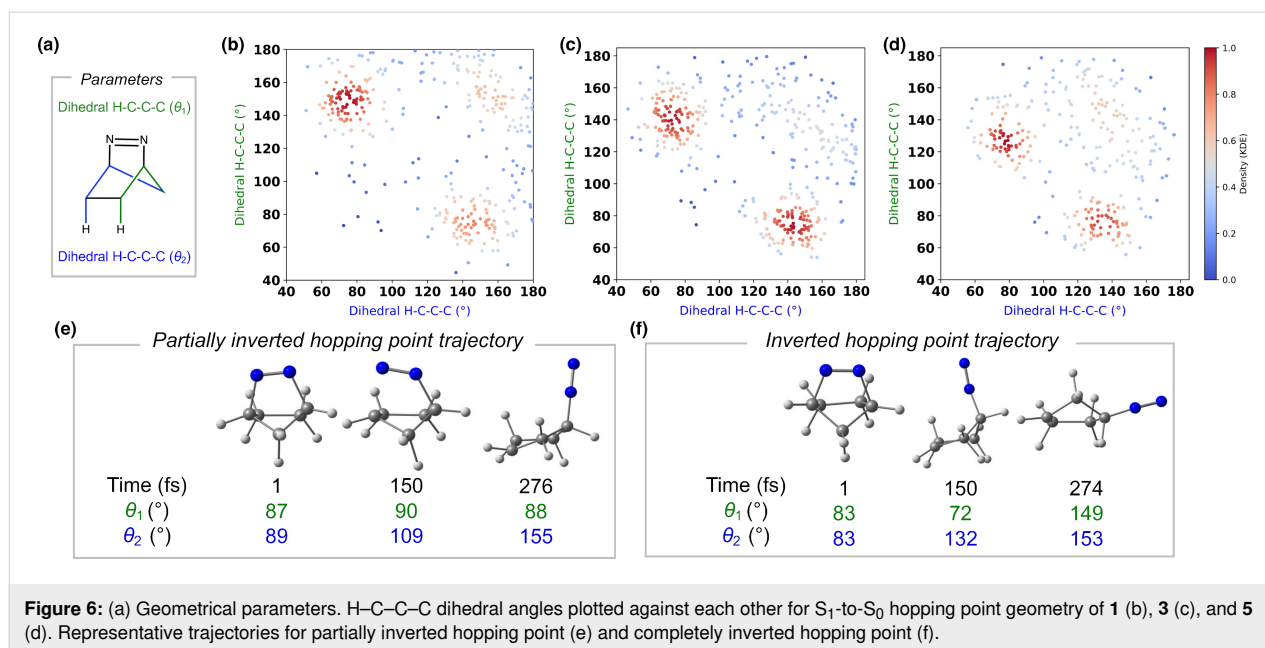
Next, we aimed to elucidate the reaction pathways originating from the S_1 Franck–Condon region for **1**, **3**, and **5**. We classified the final geometries of each trajectory to identify the resulting products and computed their respective quantum yields (QYs). We identified four pathways following the S_1 to S_0 crossing: the reversal to reactant, the inversion product, the retention product, and a diradical intermediate, as shown in Figure 5. Each pathway is shown in a different color, with the products shown at the bottom in their corresponding colors along with the quantum yields. Our computations indicate high photodenitrogenation quantum yields, ranging from 0.98 to 0.99, which align closely with the experimental QYs observed between 0.97 and 1.00. Some trajectories terminated prematurely at a diradical intermediate. We attempted to extend these trajectories by an additional 0.5 ps; however, most encountered convergence failures or exhibited energy drift exceeding 0.06 a.u. In the one case where the trajectory successfully reached 1.5 ps with conserved energy, we observed the formation of both inverted and retained housane, consistent with the existence of an intermediate. Nevertheless, due to the challenges in consistently achieving 1.5 ps extensions while maintaining energy conservation, these trajectories were excluded from the statistical analysis of the housane quantum yield.

The inverted housane exhibited the highest quantum yields, ranging from 0.69 to 0.79, consistent with the experimentally

observed preferred product. Notably, all trajectories leading to retained housane passed through a region characterized by dihedral angles exceeding 110° , corresponding to the inverted housane if the C–C bond is formed and to the inverted diradical if it is not. This observation offers new insights into the reaction mechanism, showing that inverted housane/diradical forms initially in the ground state and can thermally convert into retained housane. This finding represents a significant shift in mechanistic understanding, highlighting the importance of incorporating dynamical effects. Previous studies, summarized in Scheme 3, predicted that a diazenyl diradical (**az-DZ**) with one broken C–N bond would retain the stereochemistry of the reactant, leading directly to the formation of retained housane. However, this pathway was not observed when dynamical effects were included in our simulations. Our predicted inverted-to-retained housane ratios – 4, 7, and 5 for **1**, **3**, and **5**, respectively – are higher than the experimental ratios of 3, 2, and 3. We attribute this overestimation to the limited simulation time of 1 ps. Since retained housane forms via thermal conversion from inverted housane/diradical, longer timescales are likely required to capture its formation accurately. Nevertheless, we maintained the 1 ps simulation length to ensure energy conservation, as energy drift increases with longer trajectory times, and to obtain a statistically representative number of trajectories.

We analyzed the S_1/S_0 crossing by examining the geometries of the hopping points to understand the stereoselectivities of the inverted housanes. We plotted the two H–C–C–C dihedral angles, shown in Figure 6a, and estimated the local density for each hopping point using kernel density estimation, as shown in Figure 6b–d. By plotting the dihedral angles, we identified two





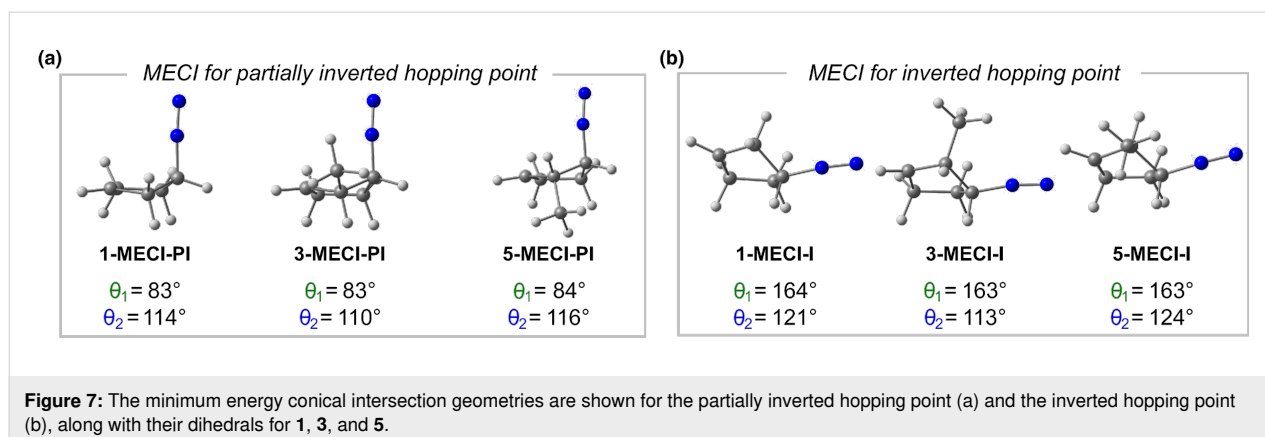
types of hopping points: one that is partially inverted and another that is fully inverted. The H-C-C-C dihedral angles of the reactant-optimized geometry range from 81° to 83° for compounds **1**, **3**, and **5**. By plotting the dihedral, two types of hopping points were identified. The first type, termed partially inverted hopping point, features one dihedral angle similar to that of the reactant, ranging from 60° to 90° across all molecules. In contrast, the other dihedral angle is significantly larger, with the highest density localized between 140° and 160° , 130° and 150° , and 120° and 140° for compounds **1**, **3**, and **5**, respectively. The lower dihedral angle ranges observed for the largest dihedral angle for derivatives **3** and **5** suggest that the methyl substituent on the methylene group restricts dihedral inversion. This restriction may arise from increased steric hindrance imposed by the methyl group on the methylene bridge of the derivatives. Two clusters represent the partially inverted hopping point, depending on which σ_{CN} breaks first. The second type, referred to as the inverted hopping point, occurs when both dihedral angles are significantly larger than those of the reactant, with both dihedral angles ranging from 140° and 160° , 130° and 150° , and 120° and 140° for compounds **1**, **3**, and **5**.

We selected representative trajectories from **1** to illustrate different types of hopping points. Figure 6e shows snapshots from a trajectory that leads to a partially inverted hopping point. At 1 fs, both dihedral angles are similar, with θ_1 at 87° and θ_2 at 89° . By 150 fs, the first σ_{CN} bond breaks. The dihedral angle θ_2 , corresponding to the carbon still bonded to N_2 , increases to 109° , while θ_1 rises slightly to 90° . At the hopping point (276 fs), θ_1 remains nearly unchanged at 88° , but θ_2 increases

significantly to 155° , indicating that the carbon bonded to N_2 is already inverted and positioned above the molecular plane. In contrast, the other carbons are in the plane or below it; we consider this hopping point geometry partially inverted. A trajectory snapshot leading to a fully inverted hopping point is shown in Figure 6f. At 1 fs, both dihedral angles are identical at 83° . At 150 fs, the σ_{CN} bond is broken, θ_1 decreases slightly to 72° ; θ_2 increases substantially to 132° , placing the carbon bonded to N_2 above the molecule plane. At the hopping point (274 fs), both θ_1 and θ_2 are significantly increased (149° and 153° , respectively). Here, all carbons of the methylene bridge are located above the molecular plane, indicating complete inversion of stereochemistry.

Using kernel density estimation [101], we found that partially inverted hopping points can be found in high-density regions, plotted in red within their respective clusters across all molecules. The observed geometric differences and distinct clustering patterns suggest the existence of two separate $S_1 \rightarrow S_0$ crossing channels. To test this hypothesis and investigate the preference for partially inverted hopping geometries, we performed optimizations of the minimum energy conical intersection (MECI). The MECI for the partially inverted hopping point (MECI-PI) and the inverted hopping point (MECI-I) for **1**, **3**, and **5** are shown in Figure 7.

The MECI-PI exhibits θ_1 between 83° and 84° , and θ_2 , a more elongated dihedral angle, ranging from 110° to 116° . In contrast, MECI-I displays two elongated dihedral angles: θ_1 ranges from 163° to 164° , and θ_2 from 113° to 124° . The significant geometrical difference supports the hypothesis of two



crossing regions between the S_1 and S_0 . The **MECI-PI** has lower energy for all molecules studied than the **MECI-I**, by being lower in energy by 0.15 eV, 0.19 eV, and 0.09 eV for **1**, **3**, and **5**, respectively. These results suggest that the gradient towards the **MECI-PI** is steeper than for **MECI-I**, making the pathway to the **MECI-PI** more favorable. All MECI structures show partial stereochemical inversion. Following the initial σ_{CN} -bond cleavage, the carbon atom still bonded to N_2 begins to move towards inversion, indicating that dynamic effects help promote the stereoselective inversion.

Conclusion

We used multiconfigurational quantum mechanical calculations and NAMD simulations to investigate the mechanism of photo-denitrogenation of 2,3-diazabicyclo[2.2.1]heptene and its derivatives, which produce the strained compound housane, important building blocks in the synthesis of complex molecular structures. We identified that the key electronic transitions are $S_0 \rightarrow S_1$ ($n_{\text{NN}}(\sigma_{\text{CN}}) \rightarrow \pi^*$) transitions, with excitation energies ranging from 3.94 to 3.97 eV. MEP calculations indicate that the dominant mechanistic pathway leads to an S_1 minimum, which is inconsistent with the nearly unity quantum yield observed experimentally. We employed NAMD to explore all possible mechanistic pathways and identify the dynamic effects that enable this reaction. The predicted quantum yields ranged from 0.98 to 0.99, aligning closely with the experimentally observed quantum yields of 0.97 to 1.00. Our simulations reveal that all productive trajectories involve a dynamically concerted but asynchronous denitrogenation reaction, characterized by breaking one σ_{CN} bond in the S_1 state and the second σ_{CN} bond in the S_0 state. After the first σ_{CN} bond breaks, the stereochemistry of the carbon bonded to N_2 begins to invert, suggesting that dynamic effects promote this inversion. The diazenyl diradical, which shares the same stereochemistry as the reactant – and was proposed in prior studies – was not observed when dynamic effects were included in our simulations. Following the S_1/S_0 surface hopping points, we identified four distinct

pathways: reversion to the reactant, formation of the inverted housane, formation of the retained housane, and formation of the diradical, which presumably undergoes ring-closing if given sufficient simulation time. These were unfortunately prohibitively expensive due to the CASSCF computation of the energy, gradients, and non-adiabatic couplings at each 0.5 fs timestep. Our results indicate that the retained stereochemistry of housane is generated in the ground state via thermal conversion from inverted housane/diradical.

Computational Details

Single reference methods

We used density functional theory (DFT) to optimize the ground-state global minima of **1**, **3**, and **5**. The molecular geometries were optimized using B3LYP/6-31(G) [102,103]. Time-dependent density functional theory (TD-DFT) was used to calculate the vertical excitation energies, wavelengths, and oscillator strength for the first 10 excited singlet states of **1**, **3**, and **5**. The TD-DFT calculations were performed using the range-separated hybrid density functional ω B97X-D [89] with the aug-cc-pVTZ [90,104] basis set. All single reference methods were run using the Gaussian 16 software [105].

Multiconfigurational methods

The multiconfigurational calculations were performed with a state-average complete active space self-consistent field (SA-CASSCF) [106,107] using OpenMolcas 19.11 [95,96]. The methods are described with the format SA(N)-CASSCF(m,n), where N is the number of the singlet states the calculation is averaged over. The variables m and n denote the number of electrons and orbitals used in the active space, respectively. For all included molecules, we used an (8,9) active space consisting of one π and π^* orbitals, one n_{NN} σ_{CN} , one σ_{NN} σ_{CN} , two σ^*_{CN} , one σ^*_{NN} , one n_{NN} , and a Rydberg orbital. The active space is shown in Figure 1, and Figures S1 and S2 in Supporting Information File 1 for **1**, **3**, and **5**, respectively. We employed SA(4)-

CASSCF(8,9)/ANO-S-VDZP [88] multiconfigurational calculations to optimize the geometries of both the ground and excited states, determine vertical excitation energies, oscillator strengths, and nature of the electronic transitions. Additionally, we conducted minimum energy path (MEP) calculations to track the reaction pathway along the excited state starting from the Franck–Condon (FC) point. All optimized structures were verified as stationary points by calculating their vibrational frequencies, ensuring no imaginary frequencies were present. To include partial dynamic correlation, we performed single-point energy calculations using extended multistate complete active space perturbation theory (XM2-CASPT2) [91] on the CASSCF-optimized geometries.

Non-adiabatic molecular dynamics (NAMD)

We performed NAMD using the fewest switches surface hopping (FSSH) [92,93] to investigate the photochemical pathways of compounds **1**, **3**, and **5** along the potential energy surfaces (PESs) of both ground and three excited states. The initial nuclear positions and velocities were sampled based on the Wigner distribution [108] at 300 K. All quantum mechanical calculations are performed in OpenMolcas using SA(4)-CASSCF(8,9)/ANO-S-VDZP. With the Python Rapid Artificial Intelligence Ab Initio Molecular Dynamics (PyRAI²MD) [97–99], we used FSSH to run the NAMD simulations. Trajectories were initiated from the S₁ Franck–Condon (FC) region, with a total simulation duration of 1 picosecond and a time step of 0.5 femtoseconds.

Supporting Information

Supporting Information File 1

Details for the active space for derivatives, time constants, the outcome of extended trajectories ending at the diradical intermediate, and the energy of minimum energy conical intersections (MECIs).

[<https://www.beilstein-journals.org/bjoc/content/supplementary/1860-5397-21-156-S1.pdf>]

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Data Availability Statement

All data that supports the findings of this study is available in the published article and/or the supporting information of this article. All optimized structures, output files for vertical excitation energy, MEP and dynamics (including energies, xyz, velocities for each trajectory) are available at <https://doi.org/10.6084/m9.figshare.25326076>

Preprint

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Solar thermal fuels: azobenzene as a cyclic photon–heat transduction platform

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Perspective

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Abstract

Azobenzene-based solar thermal fuels have undergone significant advancements over the past four decades, emerging as a promising technology for light-to-thermal energy conversion. While these materials exhibit considerable development potential, critical challenges remain that hinder their practical implementation. In this perspective, we systematically analyze four representative azobenzene-based solar thermal fuel systems including nanocarbon-hybrid, conjugated polymer, linear polymer, and small-molecule derivative formulations to trace their developmental trajectories and identify key limitations. Through this comparative analysis, we aim to clarify the current state of azobenzene-based solar thermal fuels, while mapping strategic pathways for future technological advancements in this rapidly evolving research field.

Introduction

Solar energy occupies a pivotal position among renewable energy sources. To date, solar energy conversion and storage technologies have experienced considerable progress, including artificial photosynthesis [1], solar thermal collectors [2], photovoltaic cells [3], and solar thermal fuels [4,5]. Among these innovations, solar thermal fuels based on photoswitchable mole-

cules are highly promising candidates for capturing and storing solar energy as heat [6,7].

In such systems, low-energy ground-state molecules absorb solar radiation and undergo isomerization to form high-energy photoexcited states (metastable configurations) through struc-

tural or bond rearrangements, thereby enabling solar energy storage. This reversible process is termed "energy charging", while the subsequent transformation of high-energy photoisomers back to their ground state – triggered by external stimuli such as light, heat, or catalysts – releases stored thermal energy in a controlled manner, a phase designated "energy discharging" (Figure 1). The core advantages of such closed-loop systems are primarily manifested in their reversible cycling capability, carbon neutrality characteristics, transportation convenience, and on-demand heat generation [8].

Significant progress has been made in developing molecular photochromic systems for solar thermal energy storage, with representative examples including anthracene derivatives [9–11], diphenylethylene [12,13], fulvalene-based tetracarbonyldiruthenium ($\text{FvRu}_2(\text{CO})_4$) [14–16], norbornadiene–quadricyclane (NBD–QC) complexes [17–23], dihydroazulene–vinylheptadiene (DHA–VHF) systems [24–30], and azobenzene derivatives [31–34] (Figure 2). In addition, other reversible photoisomers exhibit potential for development as solar thermal fuels [35–41]. Notably, the utilization of azobenzene-based materials in solar thermal storage applications is gaining

considerable attention due to their advantages in low synthesis cost, facile molecular design, exceptional cycling stability, and superior fatigue resistance [6,8].

Since Olmsted's pioneering exploration of azobenzene compounds as solar thermal fuels in 1983 [42], significant breakthroughs have been achieved through interdisciplinary integration of organic synthesis, functional materials engineering, photophysical mechanism analysis, and computational chemistry. So far, azobenzene-based solar thermal fuels mainly include: nanocarbon-based azobenzene polymers, conjugated azobenzene polymers, linear azobenzene polymers, and azobenzene small molecule derivatives. From this perspective, we review various azobenzene-based solar thermal fuels and their potential applications, highlighting key contributions in the field.

Discussion

Nanocarbon-based azobenzene polymer solar thermal fuels

Nanocarbon-based azobenzene polymer solar thermal fuels are constructed by grafting azobenzene moieties onto carbon nano-

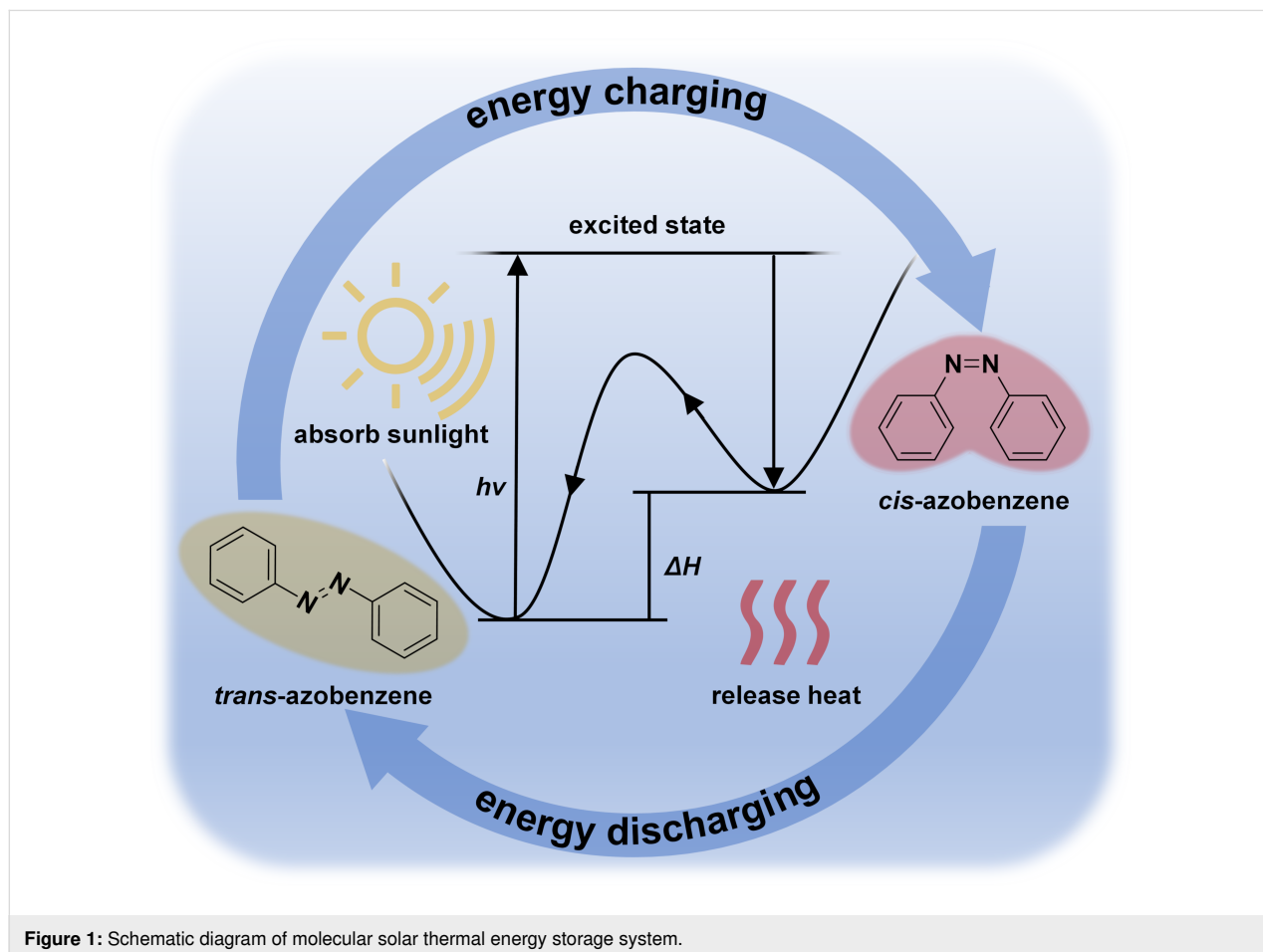


Figure 1: Schematic diagram of molecular solar thermal energy storage system.

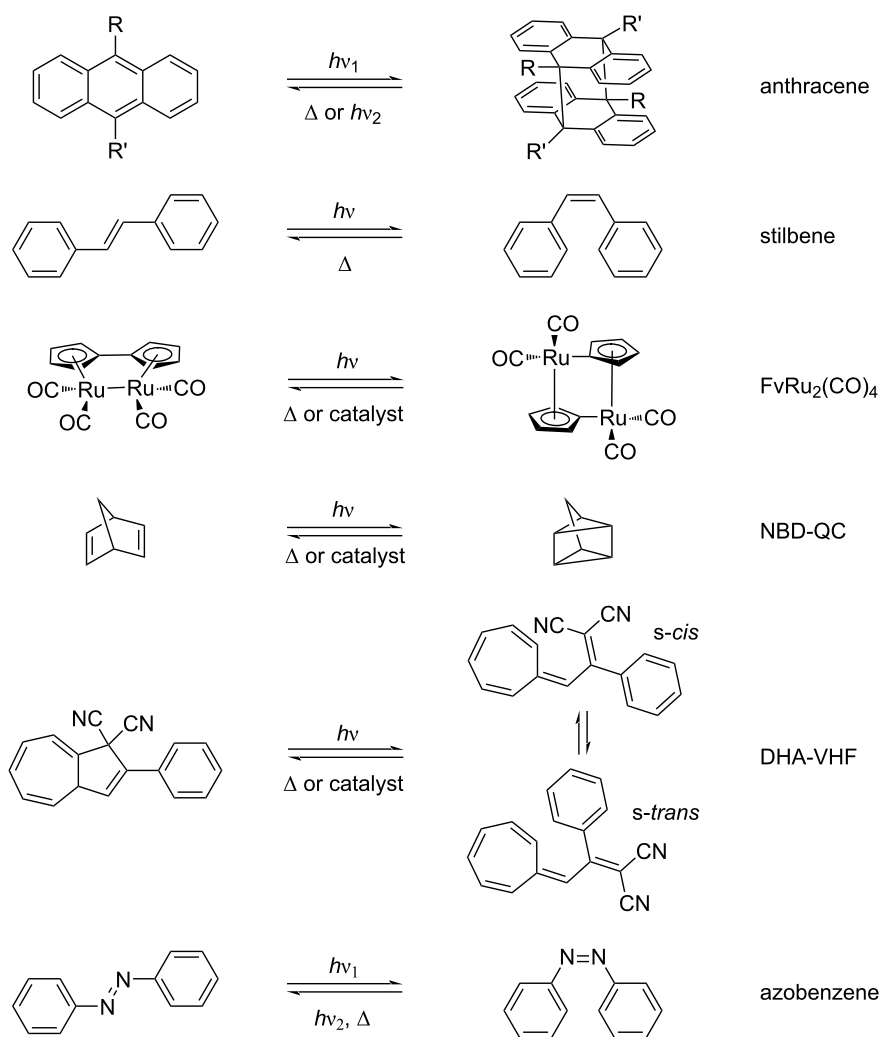
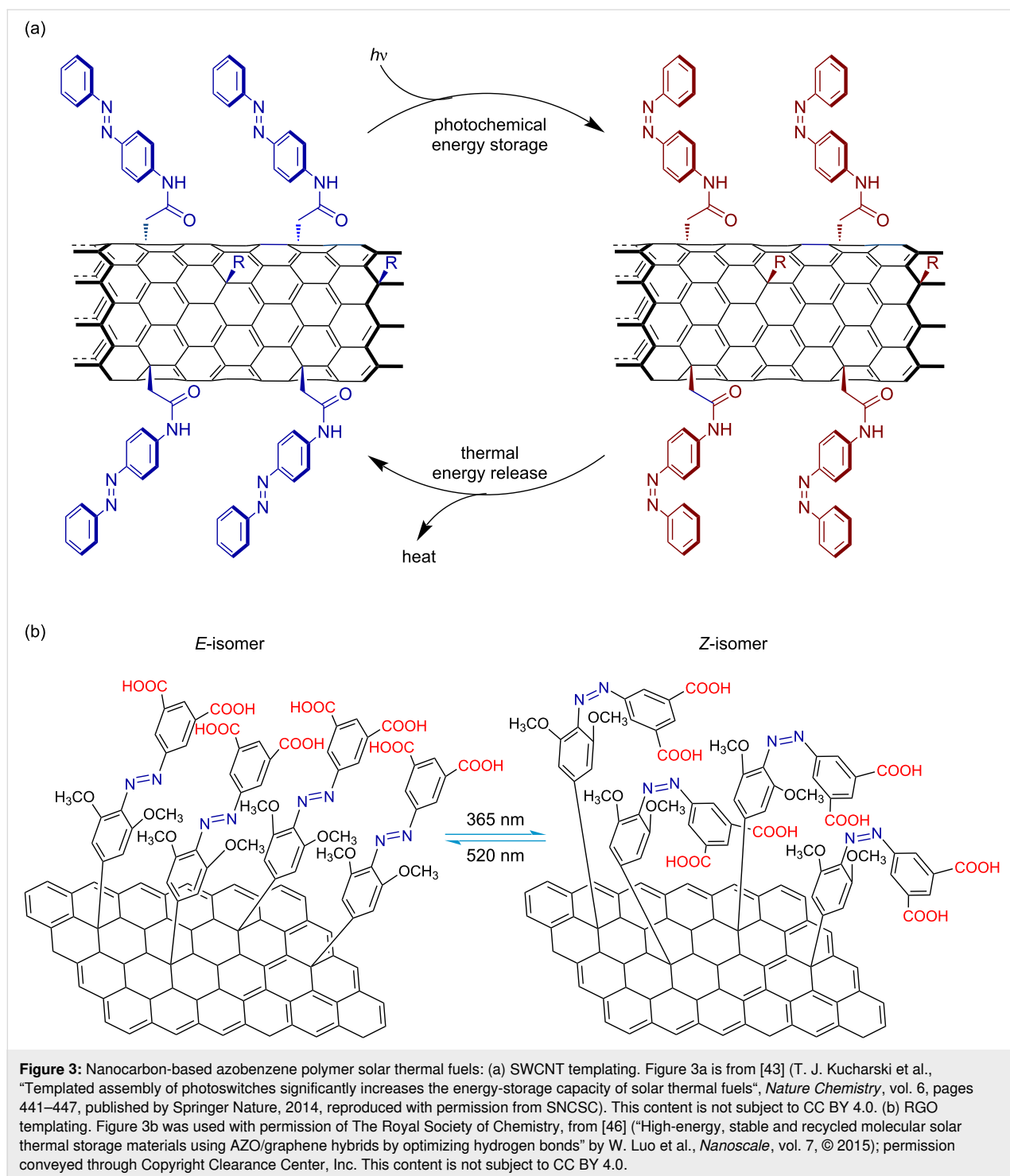


Figure 2: Photoisomerization of different types of molecular optical switches. Figure 2 was redrawn from [8].

tube [43–45] or reduced graphene oxide (RGO) templates. Grossman et al. synthesized azobenzene-functionalized single-walled carbon nanotubes (SWCNTs) (Figure 3a) and demonstrated their application as solar thermal fuels [43]. The conformational restriction imposed by the chromophore-template structure combined with photochemically generated spatial strain enables each azobenzene unit to store >200% more energy than isolated molecules, while achieving multi-order-of-magnitude improved storage lifetime and resistance to material degradation during repeated cycling. Feng and co-workers covalently grafted azobenzene groups onto RGO templates (Figure 3b) and investigated their solar thermal energy storage performance [46]. Key parameters governing the performance of azobenzene–RGO hybrid solar thermal fuels include hydrogen-bonding interactions, intermolecular distances between adjacent azobenzene groups, and electronic coupling effects.

Conjugated azobenzene polymer solar thermal fuels

Conjugated azobenzene polymer solar thermal fuels [47,48] utilize π -conjugated systems as templates for azobenzene chromophore photoisomerization, as schematically illustrated in Figure 4. Han et al. developed azobenzene-functionalized polydiacetylene-based solar thermal fuels [47], where the azobenzene moieties undergo reversible photoisomerization and thermally induced reverse isomerization, enabling "energy charging–discharging" cycles (Figure 4a). Under ultraviolet (UV) irradiation (254 nm), the closely packed diacetylene polymers undergo polymerization to form π -conjugated polydiacetylene structures, with an energy storage density reaching 243 J/g (Figure 4b). These azobenzene-functionalized polydiacetylenes exhibit structural analogy to azobenzene-modified carbon nanotubes and graphene in terms of photoresponsive behavior. Sert



et al. combined electroactive and light-harvesting carbazole units with photoresponsive azobenzene units in a unique macromolecular architecture (Figure 4c) [48]. The resulting cross-linked polycarbazole structure led to a high solar thermal storage capacity of 179.9 J/g and an extended half-life at 60 °C, increasing from 7 min for the monomer to 103 min for the polymer.

Linear azobenzene polymer solar thermal fuels

Linear azobenzene polymers possess excellent processability and serve as ideal solid-state matrices for photoisomerization [49–57], making them suitable candidates for solar thermal fuels. Zhitomirsky et al. studied a linear azobenzene polymer-based solid solar thermal fuel [58], which enables the fabrica-

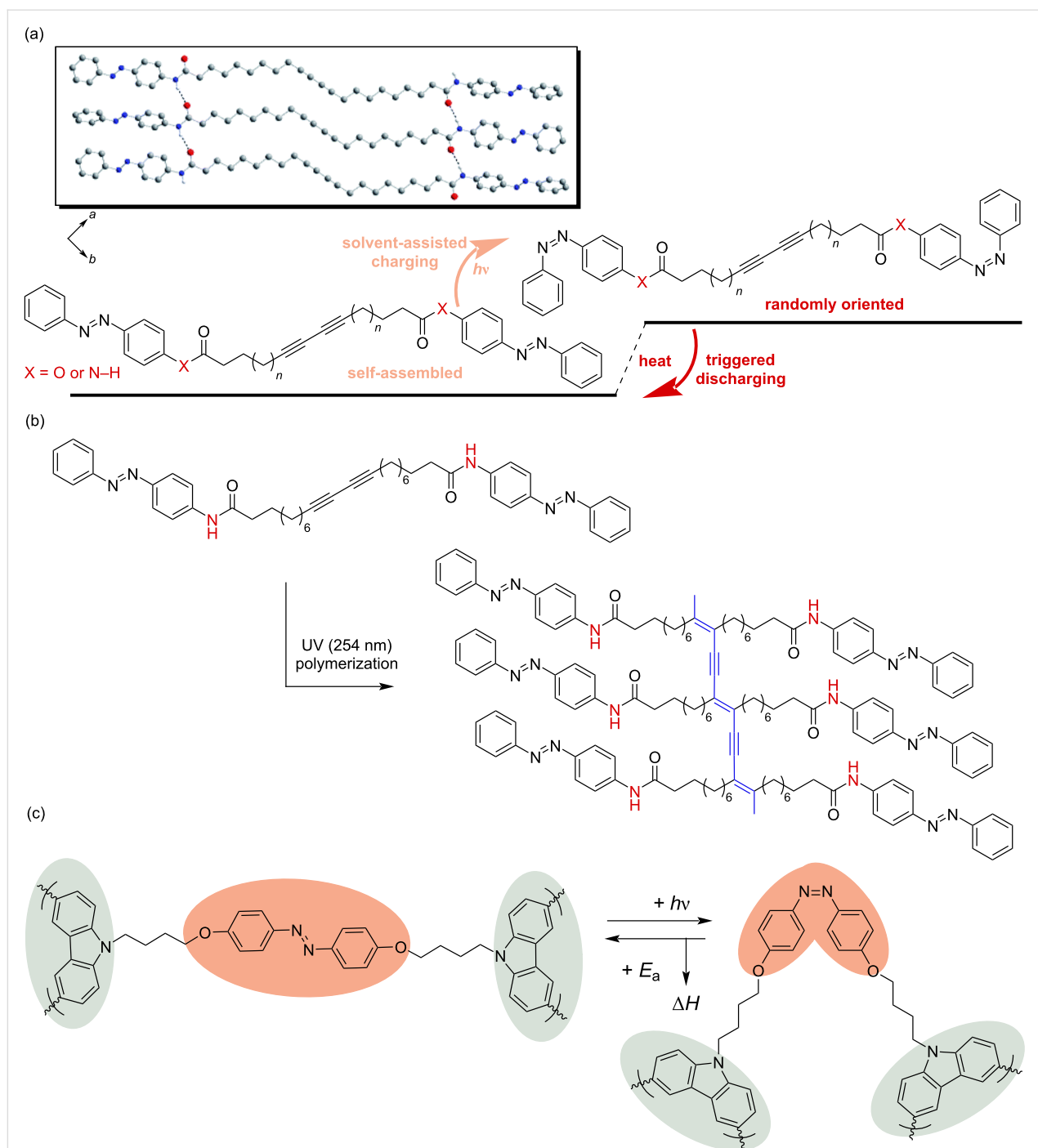


Figure 4: Conjugated azobenzene polymer solar thermal fuels: (a) Photoisomerization and thermally induced reverse isomerization of diacetylene monomers. The inset depicts the crystal structure of diacetylene monomer ($n = 6$, $X = \text{N-H}$) with dashed lines indicating intermolecular hydrogen bonds. Figure 4a was used with permission of The Royal Society of Chemistry, from [47] ("Photon energy storage materials with high energy densities based on diacetylene–azobenzene derivatives" by G. D. Han et al., *Journal of Materials Chemistry A*, vol. 4, © 2016); permission conveyed through Copyright Clearance Center, Inc. This content is not subject to CC BY 4.0. (b) Schematic illustration of diacetylene monomer photopolymerization and the conjugated polydiacetylene structure. Figure 4b was redrawn from [47]. (c) Photoisomerization of a conjugated azobenzene polymer with a carbazole backbone. Figure 4c was redrawn from [48].

tion of uniform thin films capable of storing up to 108 J/g of thermal energy (Figure 5a). Wu et al. designed an azobenzene polymer-based device capable of efficiently storing both UV

and visible light under sunlight irradiation [59], achieving a solar efficiency of 0.4% and a solid-state isomerization efficiency of 72.7% (Figure 5b). Feng and co-workers reported the

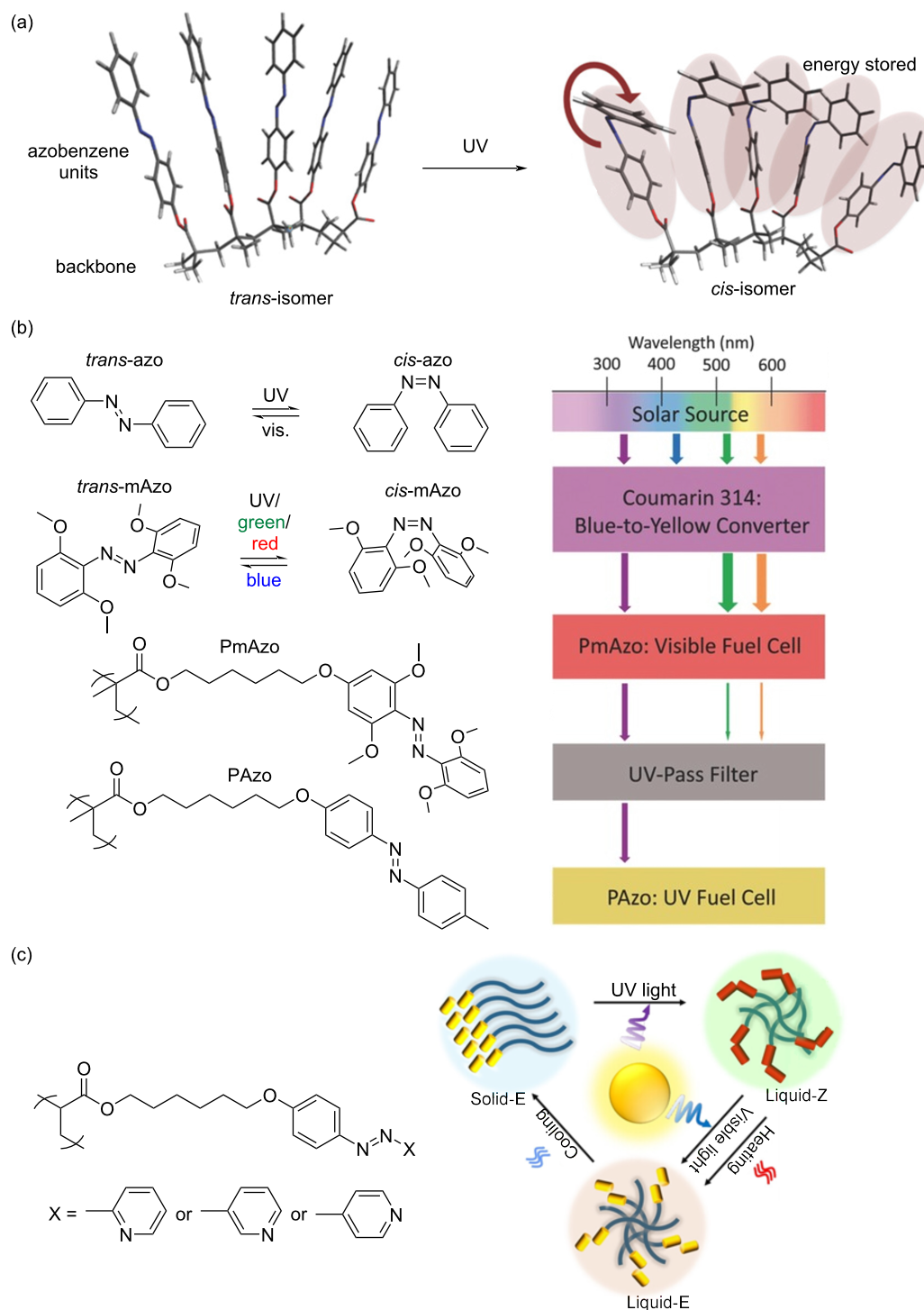


Figure 5: Linear azobenzene polymer solar thermal fuels: (a) Schematic illustration of the *trans*-to-*cis* isomerization of an azobenzene polymer upon UV illumination. Figure 5a was reproduced from [58], D. Zhitomirsky et al., "Solid-State Solar Thermal Fuels for Heat Release Applications", *Adv. Energy Mater.*, with permission from John Wiley and Sons. Copyright © 2015 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim. This content is not subject to CC BY 4.0. (b) Structure of the UV-vis solar-thermal cell. Figure 5b was adapted from [59], A. K. Saydjari et al., "Spanning the Solar Spectrum: Azopolymer Solar Thermal Fuels for Simultaneous UV and Visible Light Storage", *Adv. Energy Mater.*, with permission from John Wiley and Sons. Copyright © 2016 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim. This content is not subject to CC BY 4.0. (c) Schematic of the mechanism for photothermal energy and phase change energy storage of azopyridine polymers. Figure 5c was adapted from [60], R. Liang et al., "Azopyridine Polymers in Organic Phase Change Materials for High Energy Density Photothermal Storage and Controlled Release", *Angew. Chem., Int. Ed.*, with permission from John Wiley and Sons. Copyright © 2024 Wiley-VCH GmbH. This content is not subject to CC BY 4.0.

synthesis of three azopyridine polymers (*ortho*-, *meta*-, and *para*-) [60], with the *m*-azopyridine polymer exhibiting a significant photothermal energy storage capacity of 430 J/g (Figure 5c). This study presents potential implications for energy distribution and utilization in domestic consumer applications, and for photothermal-assisted insulation strategies.

Azobenzene small molecule derivative solar thermal fuels

Azobenzene small-molecule derivatives can be systematically categorized based on molecular structure into monoazobenzene derivatives [61–69], multiazobenzene derivatives [70–73], heteroaromatic azobenzene derivatives [74–81], and macrocyclic azobenzene derivatives [82–88]. From an energy charging perspective, some solvent-free systems store energy in the solid state [89] or via photoinduced solid–liquid phase transitions [61,69,74], which occur because the melting temperature (T_m) of *trans*-azobenzene is above room temperature and the T_m of the isomerized *cis*-azobenzene is below room temperature, while others require solvent-assisted charging mechanisms [70,71]. This structural and functional diversity makes them particularly valuable for solar thermal storage applications.

Feng et al. incorporated fluorinated azobenzene small molecules into polymer fibers [65], enabling solvent-free charging and discharging under visible light (Figure 6a). This material exhibited good capacity for releasing high-temperature heat (80–95 °C) at room temperature and in cold environments, along with an energy storage lifetime approaching two years, significantly exceeding the reported storage lifetime of other azobenzene-based solar thermal fuels. Han et al. synthesized a series of bisazobenzene small molecules with various substituents [90], all exhibiting photoinduced solid–liquid phase transitions. In contrast, comparable monoazobenzene small molecules showed substituent-dependent photoinduced solid–liquid phase transition behavior. This provides a feasible strategy for enhancing the energy density of azobenzene-based solar thermal fuels by controlling phase transitions (Figure 6b). Wu et al. conducted a comparative study on monoazobenzene versus multiazobenzene derivatives [91], demonstrating that in solution-assisted conditions, bisazobenzene derivatives achieve a peak energy density of 272 J/g. However, in the solid state, energy storage is limited to monoazobenzene derivatives due to photoinduced solid–liquid transition (Figure 6c), providing new insights into the structure–property relationships in azobenzene systems. Li et al. reported a series of rationally designed aryl-azopyrazole-based azobenzene derivatives [74] that enable simultaneous photon and environmental heat capture through their photoinduced solid–liquid transition behavior, achieving high gravimetric energy densities (300–400 J/g) with long-term storage stability (Figure 6d). Grossman and Durgun proposed

methods for incorporating azobenzenes into macrocyclic structures [82]. Their computational models indicated that the molecular rings connecting the molecules can improve energy density by imposing strain within the molecule. However, there are no experimental reports of these compounds and their synthesis is expected to remain a challenge in the future.

Applications of azobenzene-based solar thermal fuels

After more than four decades of research, our understanding of azobenzene-based solar thermal fuels has significantly advanced, driving continuous innovation in this field. The application scope of these materials has expanded beyond initial temperature monitoring [58,92,93] to practical energy utilization scenarios. For instance, Li et al. utilized charged solar thermal fuels for deicing tests [74], showing effective ice removal capability under green light irradiation (Figure 7a). Wang et al. developed a photostimulated self-heating wristband [94] that elevates surface temperature from 29 °C to 44 °C upon blue light irradiation, protecting users from frostbite (Figure 7b); and Li and Wang et al. fabricated fabrics containing azobenzene-based solar thermal fuels that exhibit high energy storage density and long half-lives [95], enabling photothermal stimulation for moxibustion at acupoints upon light irradiation (Figure 7c). These examples collectively highlight the transition from fundamental studies to real-world applications, where azobenzene-based systems now serve as enabling technologies for device deicing, wearable thermal management, and wearable smart textiles for acupuncture.

Conclusion and Future Directions

We summarized the development of azobenzene-based solar thermal fuels and demonstrated their potential applications. Nanocarbon-integrated azobenzene polymers: Their energy storage efficiency (up to >200%) and cycle life are primarily modulated by template confinement effects and electronic coupling. However, high costs and challenges in large-scale fabrication are inherent limitations. Conjugated azobenzene polymers undergo photoisomerization and thermally triggered back-isomerization, enabling cyclic "charging–discharging" of energy. However, their solid-state phase transition behavior is inherently governed by molecular packing, making solvent-independent energy cycling difficult to achieve. Linear azobenzene polymers exhibit excellent processability and solid-state photoisomerization performance. However, their moderate energy density is inherently limited by the mass fraction of non-active polymer segments. Small-molecule azobenzene derivatives achieve gravimetric energy densities of 300–400 J/g with long-term storage stability. However, solvent dependence or steric hindrance in multiazobenzene units remains an inherent challenge dictated by material type. These materials show

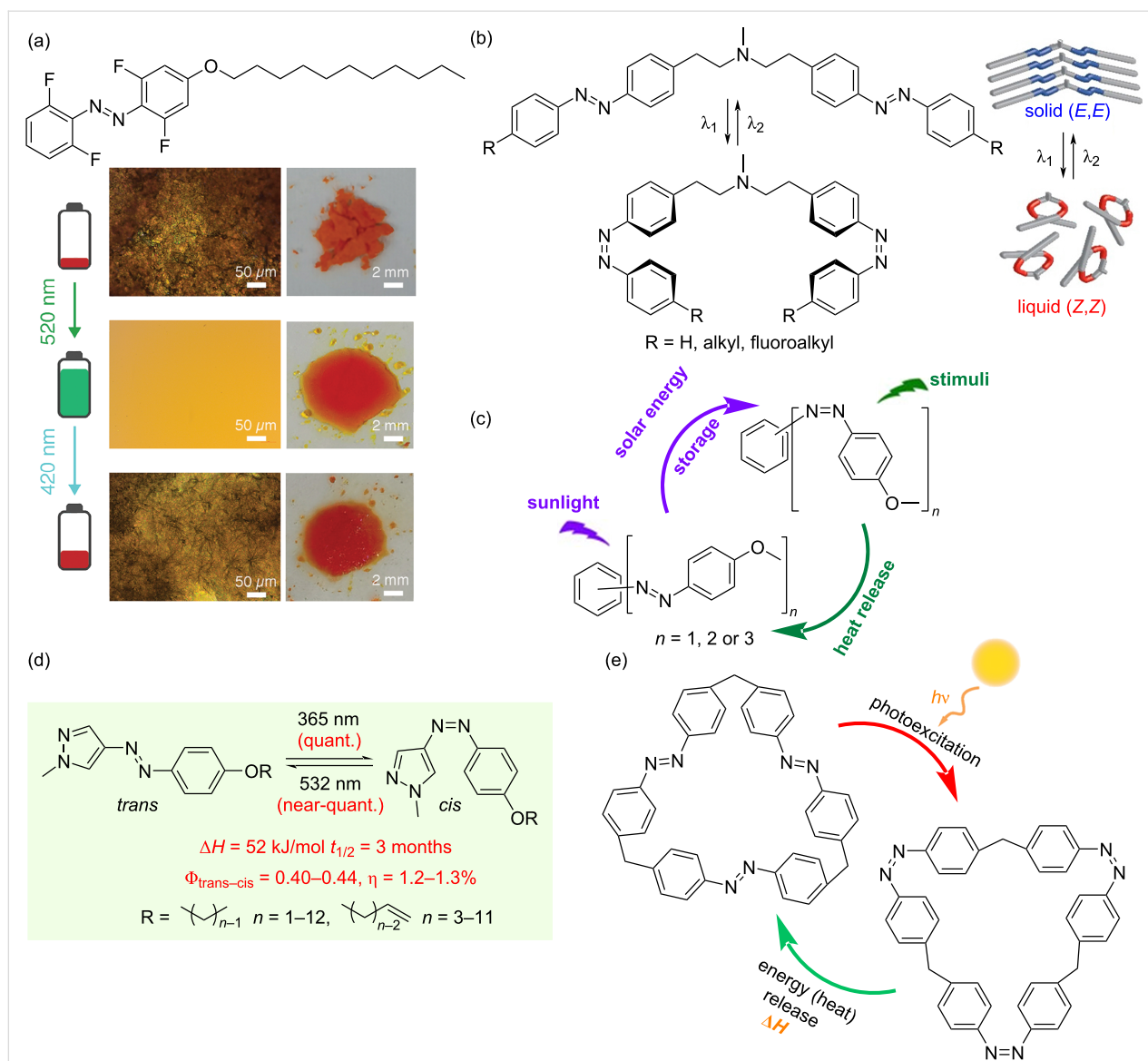


Figure 6: Representative examples of azobenzene small-molecule derivative solar thermal fuels. (a) Polarized light microscopy images and photographs of the solid-liquid transition of fluorinated azobenzene under visible light. Figure 6a was adapted from [65], Y. Wu et al., “An Innovative Azobenzene-Based Photothermal Fabric with Excellent Heat Release Performance for Wearable Thermal Management Device”, *Small*, with permission from John Wiley and Sons. Copyright © 2024 Wiley-VCH GmbH. This content is not subject to CC BY 4.0. (b) Schematic illustration of the isomerization of the bisazobenzene small molecule. Figure 6b was reproduced from [90] (© 2023 A. Gonzalez et al., published by American Chemical Society, distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International license, <https://creativecommons.org/licenses/by-nc-nd/4.0/>). This content is not subject to CC BY 4.0. (c) Photoisomerization and thermal reverse isomerization of small molecules incorporating diverse azo units. Figure 6c was used with permission of The Royal Society of Chemistry, from [91] (“Photoswitches with different numbers of azo chromophores for molecular solar thermal storage” by S. Sun et al., *Soft Matter*, vol. 18, © 2022); permission conveyed through Copyright Clearance Center, Inc. This content is not subject to CC BY 4.0. (d) Arylazopyrazole-based azobenzene derivatives. Figure 6d was adapted with permission from [74] Copyright © 2020 American Chemical Society. This content is not subject to CC BY 4.0. (e) Molecular structure of the trisazobenzenophane. Figure 6e was adapted with permission from [82] Copyright © 2013 American Chemical Society. This content is not subject to CC BY 4.0.

promising applications in device deicing, wearable thermal management, and wearable smart textiles for acupuncture.

While azobenzene-based solar thermal fuels excel in molecular designability and cycling stability, they exhibit significant gaps in spectral response range and energy density compared to non-

azobenzene systems. These comparisons highlight future directions for cross-material integration. The reversible *trans*–*cis* isomerization of azobenzene makes it an ideal model system for studying solar thermal fuels, as it enables both solar energy storage and heat release. While significant advances have been made, critical challenges persist. First, a major limitation is that

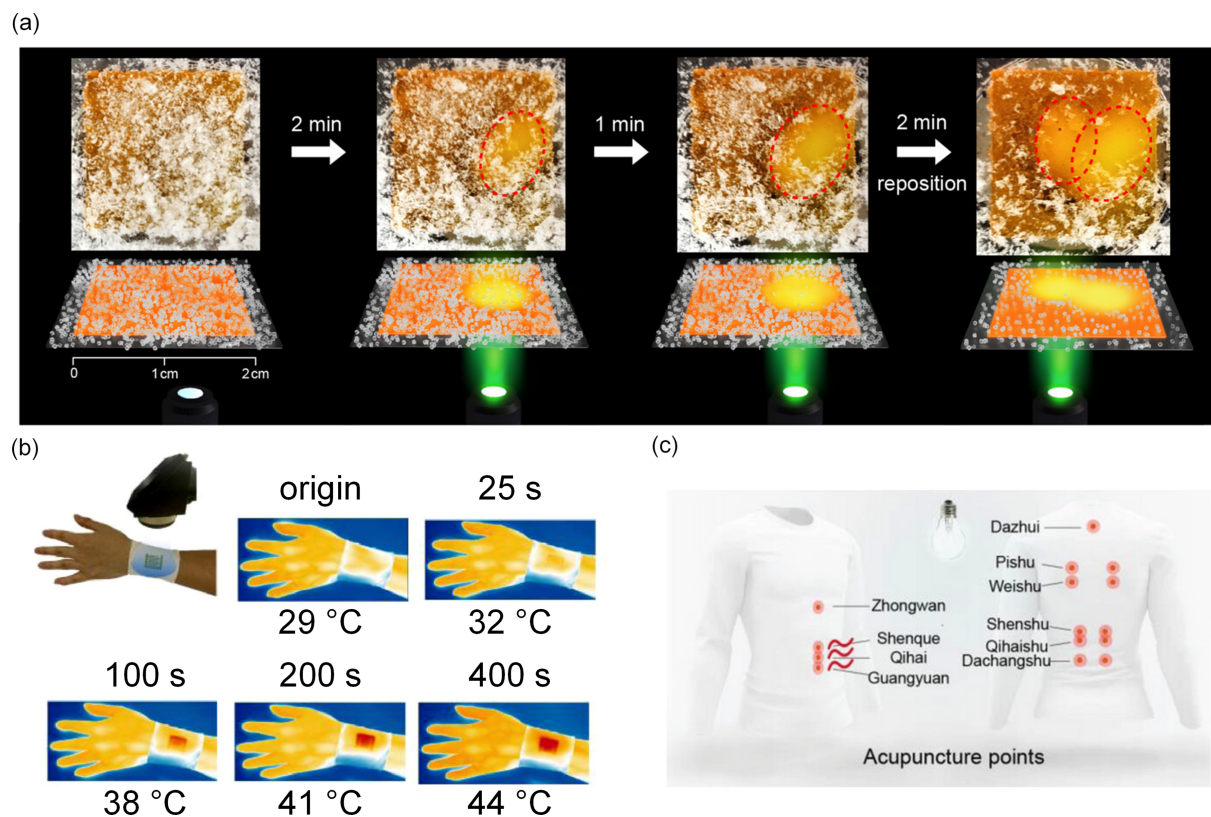


Figure 7: (a) Deicing test of charged solar thermal fuels under green light irradiation (550 nm). Figure 7a was reprinted with permission from [74] Copyright © 2020 American Chemical Society. This content is not subject to CC BY 4.0. (b) Real-time infrared thermal imaging images of a charged self-heating wristband under blue light irradiation (450 nm). Figure 7b was reprinted from [94], *Energy Storage Materials*, vol. 42, by L. Fei, Y. Yin, M. Yang, S. Zhang, C. Wang, "Wearable solar energy management based on visible solar thermal energy storage for full solar spectrum utilization", p. 636–644, Copyright (2021), with permission from Elsevier. This content is not subject to CC BY 4.0. (c) Schematic of the fabric with the printed acupuncture point pattern. Figure 7c was reproduced from [95], L. Fei et al., "Efficient and Robust Molecular Solar Thermal Fabric for Personal Thermal Management", *Advanced Materials*, with permission from John Wiley and Sons. Copyright © 2023 Wiley-VCH GmbH. This content is not subject to CC BY 4.0.

most azobenzene-based solar thermal fuels can only store UV or visible light, which represent a minor portion of the solar spectrum. In contrast, approximately 50% of the solar irradiance is in the form of near-infrared (NIR) radiation, highlighting the urgent need for NIR-responsive systems. Second, although azobenzene-based fuels have evolved from conceptual designs to functional materials, many still require solvent assistance during energy charging. The use of organic solvents exacerbates environmental concerns, increases costs, complicates operation, and hinders practical deployment. Third, azobenzene groups release energy through a process involving thermal relaxation or thermally induced *cis*–*trans* isomerization. Temperature critically governs the efficiency and kinetics of this process: elevated temperatures accelerate uncontrolled instantaneous heat release, while low temperatures induce phase transition-induced failures that compromise structural stability. Despite tunable photothermal parameters, achieving controlled heat release and structural robustness under extreme temperatures remains a pivotal challenge for azobenzene systems.

Looking forward, improving the energy storage density of azobenzene-based solar thermal fuels remains an important research direction. However, significant opportunities exist for developing azobenzene derivatives that absorb visible light to NIR. In terms of charging and discharging methods, solvent-free systems capable of efficient charging and discharging in the solid state or via photoinduced solid–liquid transitions will be advantageous. Simultaneously, enhancing the long-term stability of azobenzene energy storage is a key area for future research.

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Author Contributions

Jie Yan: conceptualization; data curation; writing – original draft; writing – review & editing. Shaodong Sun: conceptualization; writing – original draft; writing – review & editing. Minghao Wang: conceptualization; data curation; writing – review & editing. Si Wu: conceptualization; funding acquisition; supervision; writing – review & editing.

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Data Availability Statement

Data sharing is not applicable as no new data was generated or analyzed in this study.

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Rotaxanes with integrated photoswitches: design principles, functional behavior, and emerging applications

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Review

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Abstract

Integrating molecular photoswitches into rotaxanes offers unique opportunities for precise control over their structural, dynamic, and functional properties. By harnessing light as a non-invasive stimulus with high spatial and temporal resolution, these photoswitches allow for the modulation of the rotaxanes' intra- and intermolecular interactions, optoelectronic properties, and shuttling dynamics. In this review, we discuss key examples of photoswitchable rotaxanes, organized according to the position of the photoswitch, either embedded in the axle or incorporated into the macrocycle. We examine the major classes of photoswitches used, including their switching mechanisms and the resulting influence on rotaxane operation. Due to their architectural versatility and precise light control, photoswitchable rotaxanes hold promise for a broad range of applications, including light-responsive molecular machines, smart materials, and biofunctional systems. However, emerging applications increasingly require rethinking and developing new structural designs that incorporate more efficient and advanced photoswitches to fully realize their potential.

Introduction

Harnessing light energy to control intra- and intermolecular interactions is a powerful strategy for designing sophisticated molecular systems that operate across multiple length scales, from nanoscale dynamics to macroscopic functions [1-3]. Light is particularly attractive compared to other stimuli due to its non-invasive nature, high spatial and temporal precision in activating systems, and the ability to fine-tune responses by

adjusting wavelength, intensity, and exposure time. Additionally, photoswitchable molecules can often operate reversibly without generating chemical waste or requiring the addition of chemical fuels [4,5].

In the last three decades, photoswitches have been successfully integrated into a variety of supramolecular architectures, includ-

ing mechanically interlocked molecules (MIMs) such as rotaxanes, enabling new dynamic functions [6,7]. Rotaxanes are molecules composed of a macrocycle threaded onto a linear axle, with bulky stoppers at both ends to prevent dethreading (Figure 1) [1,8]. Functionalization of the axle with recognition sites allows the macrocycle to shuttle between positions in response to external stimuli, including light, redox, temperature, pH, and reactions with chemicals such as carbodiimides [9–12].

Depending on their structure, rotaxanes can be classified by the number of components involved. In [1]rotaxanes, the macrocycle is covalently attached to one end of the axle while remaining mechanically interlocked with another part of the axle (Figure 1) [13–15]. In contrast, [2]rotaxanes consist of a macrocycle and an axle held together purely by mechanical bonding without covalent linkage. More complex architectures, such as [3]rotaxanes, may feature two macrocycles threaded onto a single axle or one macrocycle threaded onto two axles (Figure 1) [16–19].

Integrating photoswitches into rotaxane frameworks has resulted in a rapidly expanding class of systems capable of light-driven molecular motion, controlled conformational changes, and tunable functional outputs. Consequently, photo-switchable rotaxanes provide unique design opportunities for a broad range of applications, including responsive materials, sensing, cargo delivery, information storage, and biotechnology [7,16,17,20–23].

In this review, we broadly discuss the design principles, functional behaviors, and emerging applications of rotaxanes that have integrated photoswitches. We classify key examples based on the location of the photoswitch within the rotaxane structure – either integrated into the axle or situated in the macrocycle.

Within these categories, we highlight widely used photo-switches, including acridane, anthracene, azobenzene, cycloheptatriene, dithienylethene, fumaramide, hydrazone, spirobenzopyran, stilbene and stiff-stilbene (Figure 2). Systems whose photoinduced behavior primarily depends on photoredox or energy-transfer mechanisms fall outside the scope of this review.

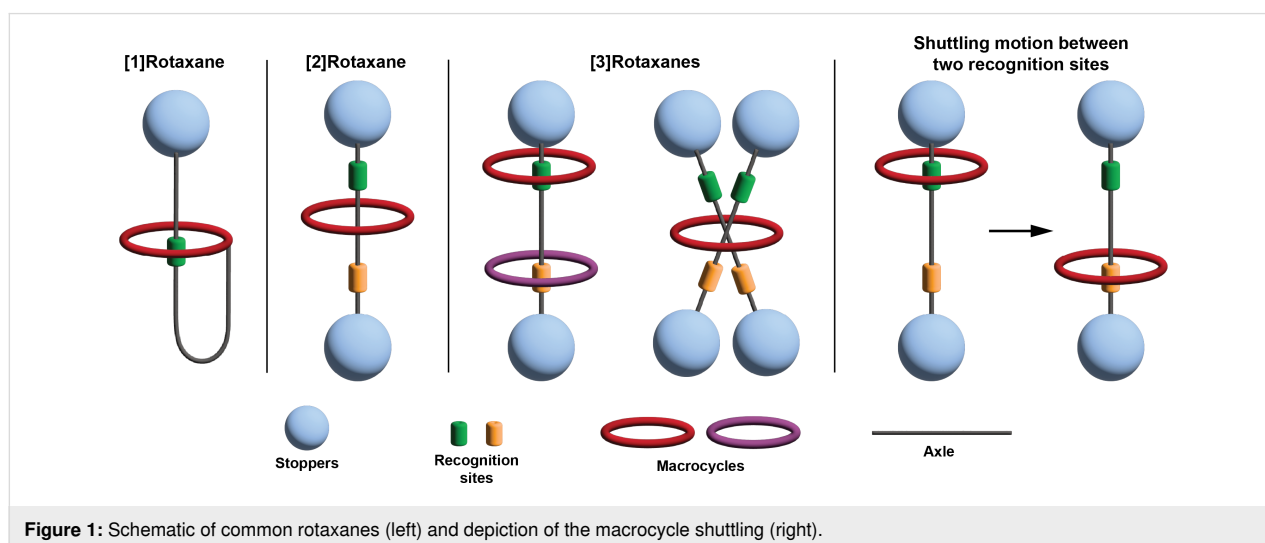
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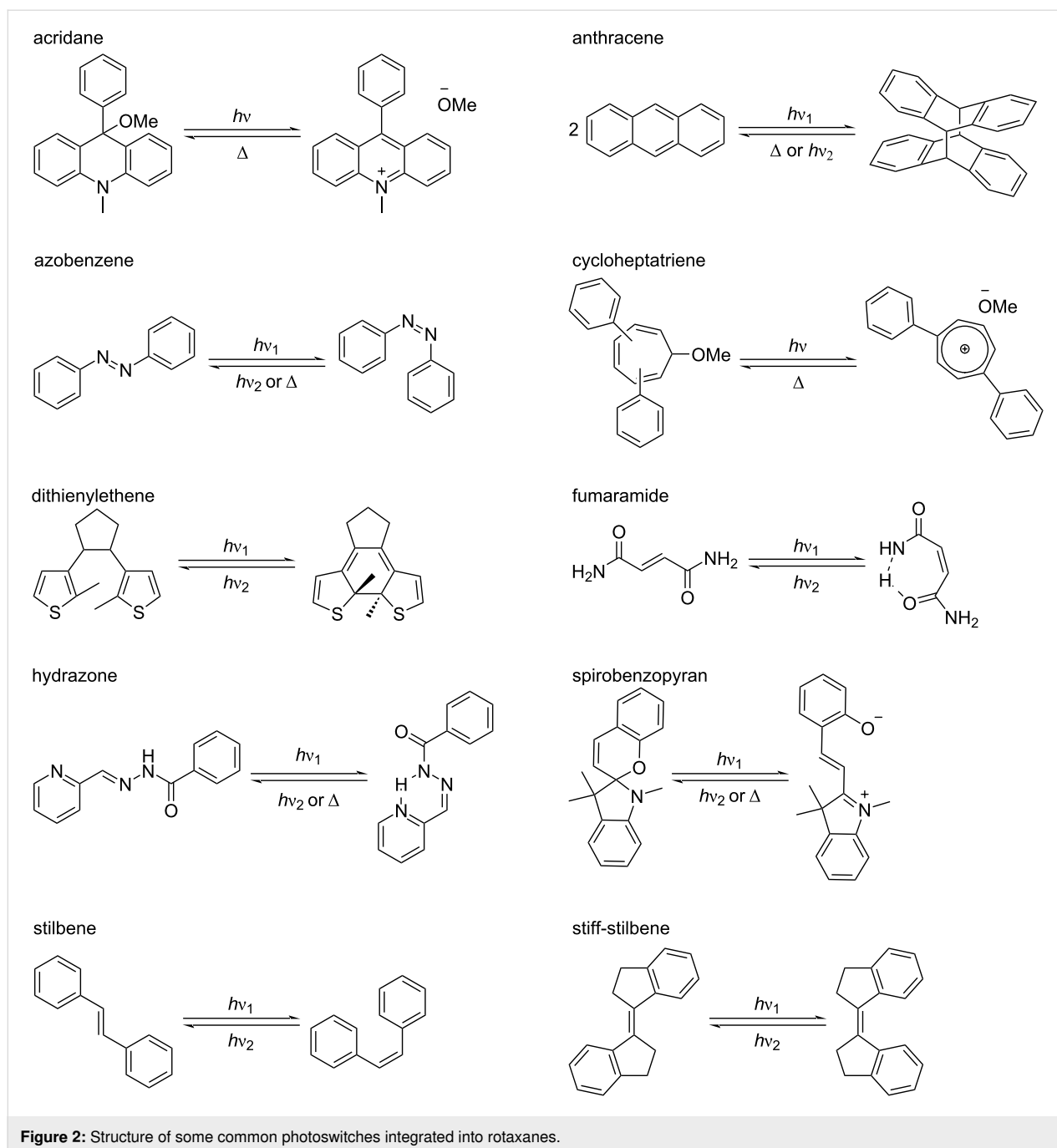
Rotaxanes featuring photoswitches on the axle

Rotaxanes that incorporate photoswitchable units into the axle are the most extensively developed and studied class of photo-switchable rotaxanes, in contrast to those in which the photo-switch is integrated into the macrocycle. Incorporating a photo-switch into the axle is used to modulate the non-covalent interactions between the macrocycle and the axle, thereby regulating the macrocycle's position and, when appropriate, its shuttling rate. This section highlights representative examples featuring the most widely used photoswitches.

Acridane

Acridane photoswitching involves its photoheterolysis, generating a positively charged acridinium and an alkoxide, typically a methoxide anion (Figure 2). The neutral acridane is restored through the thermal nucleophilic attack of the alkoxide on the acridinium ion. Abraham and co-workers exploited this dramatic change in the electronic nature and geometric shape of acridane to modulate the translation of cyclobis(paraquat-4,4-bisphenylene) (CBPQT⁴⁺) along the axle of rotaxanes [24]. Specifically, they used acridane as a recognition unit and stopper in a [2]rotaxane. Thus, the electron-rich acridane interacts with the electron-poor CBPQT⁴⁺, and upon light irradiation

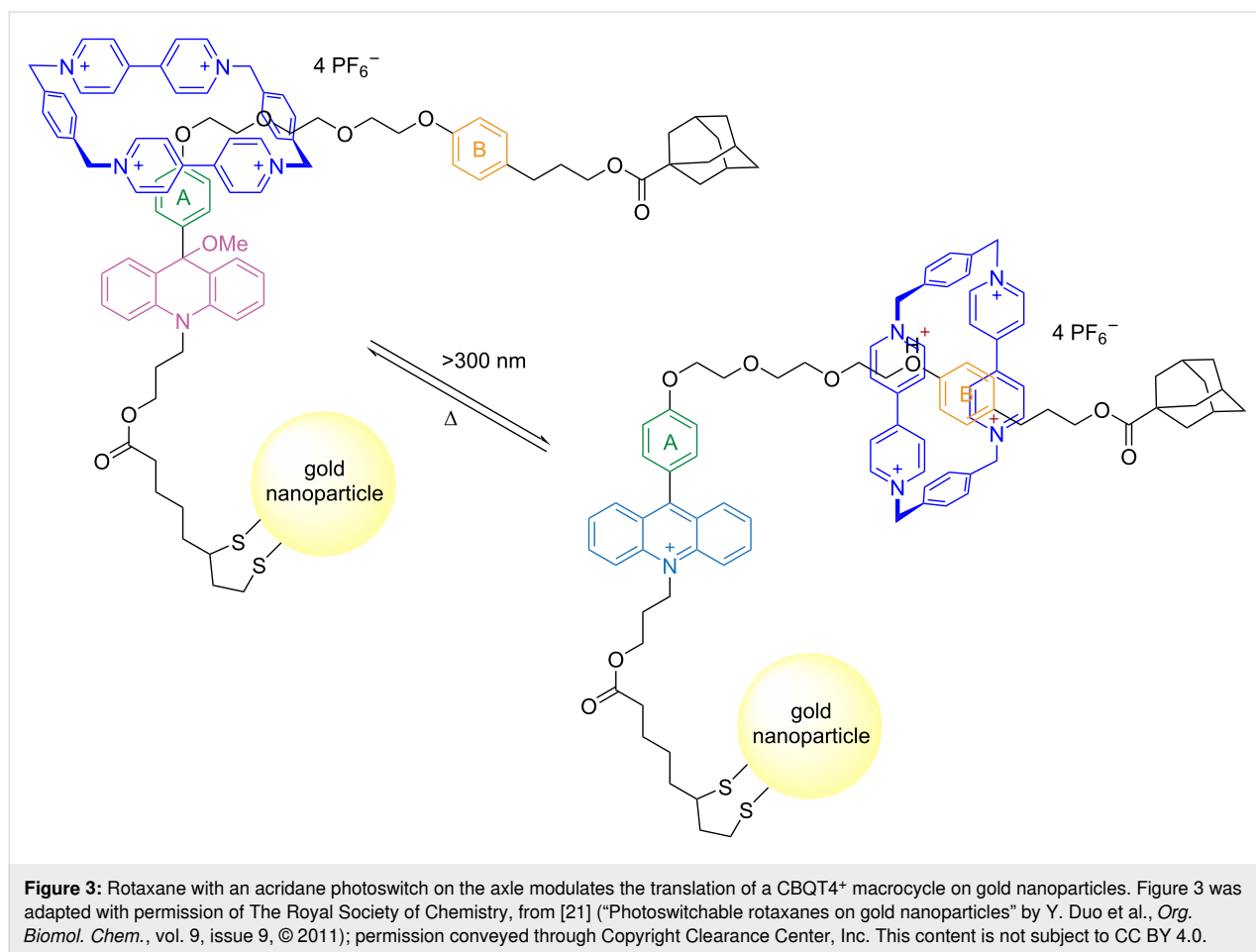




tion, the formation of the cationic acridinium repels the CBPQT⁴⁺ macrocycle and promotes its translation away from the acridane toward the secondary site. However, if the rotaxane contains only one recognition site, the macrocycle remains at the unfavorable acridinium station, interacting with the 9-aryl group. Therefore, substitution at this position was employed to tune the macrocycle interaction with the axle.

In a different approach, the authors demonstrated that the macrocycle can shuttle along an axle by incorporating

two acridane photoswitches at both ends. However, upon light activation, the macrocycle stops shuttling and remains in the middle of the axle, thereby avoiding the terminal cationic sites [25]. The shuttling is restored by the thermal reaction that regenerates the neutral acridane [24–26]. The same group also demonstrated that similar rotaxanes can be incorporated onto gold nanoparticles and retain their photoreactivity and switching behavior, enabling the translation of the macrocycle along the axle upon irradiation with light (Figure 3) [21].



Anthracene

Anthracene undergoes $[4\pi + 4\pi]$ dimerization upon irradiation with light, whereas cycloreversion is achieved thermally (Figure 2) [27]. Tron and co-workers synthesized a [2]rotaxane composed of a dibenzo-24-crown-8 (DB24C8) and an axle with anthracenes as stoppers on both ends [28]. Light irradiation at 365 nm triggered the dimerization of the anthracenes allowing the conversion of the [2]rotaxane into a [2]catenane. Cycloreversion and formation of the rotaxane was achieved thermally or upon irradiation with light at 280 nm.

Azobenzene

Azobenzene is one of the most widely utilized photoresponsive units in the design and synthesis of photo-switchable rotaxanes. These photo-switches undergo *trans*–*cis* isomerization and are classified as T-type, due to the thermal reversibility of the isomerization (Figure 2) [29]. In 1997, Nakashima and co-workers reported the first rotaxane where the azobenzene was located on the axle, acting as a recognition site for a β -cyclodextrin macrocycle. Photoisomerization of the azobenzene controlled the shuttling of the macrocycle [30]. Later, Stoddart and co-workers developed a rotaxane where the azobenzene was located be-

tween two phenyl rings that work as recognition sites for a CBPQT⁴⁺ macrocycle. Likewise, isomerization of the azobenzene modulates the shuttling of the macrocycle among the recognition sites [31]. In the same year, Anderson and co-workers reported the first [3]rotaxane with three azobenzene units in the axle and two α -cyclodextrins as the macrocycle. The rotaxane was obtained as a single stereoisomer, where the two narrow rings of the cyclodextrin point to each other. Although no photo-switching studies were conducted, ¹H NMR results showed that for the [2]rotaxane, the macrocycle shuttles along the axle very rapidly [32].

Two decades after the first reports of azobenzene-based rotaxanes, numerous studies have been published in which azobenzene units are incorporated into the axle to control the shuttling of various macrocycles. In some systems, the azobenzene functions also as a recognition site for macrocycles such as cyclodextrins [18,33–39], or CBPQT⁴⁺ [40–42], while in others, it serves merely as part of the axle structure without directly participating in macrocycle recognition. Examples of the latter include systems employing CBPQT⁴⁺ [43], cucurbit[7]uril [44], tetralactam [45], and pillar[5]arene [46].

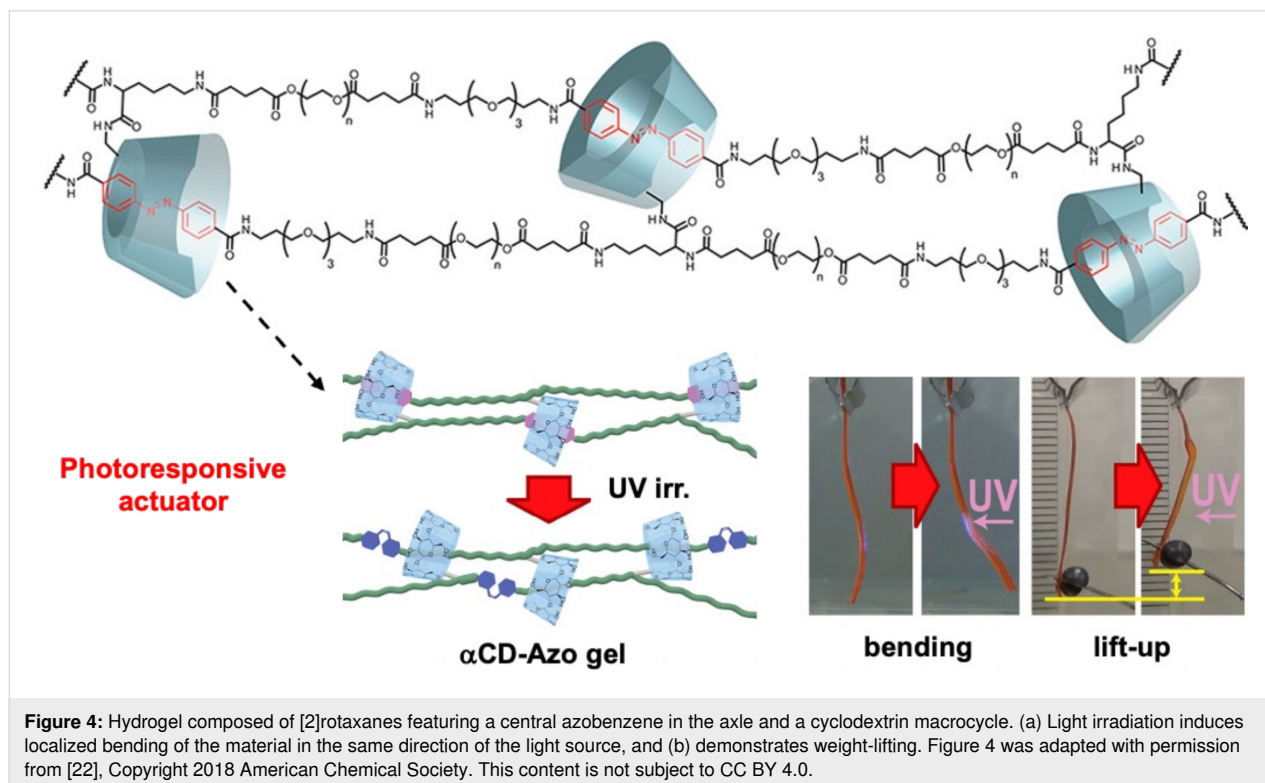
Moreover, Qu and co-workers synthesized [2]rotaxanes with a biphenyl and an azobenzene acting as recognition units for an α -cyclodextrin macrocycle, which has two distinct fluorescent bulky groups as stoppers. Upon both photoisomerization and thermal isomerization, the macrocycle motion along the axle is controlled, enhancing the fluorescence of the closer stopper while dimming the fluorescence of the farther stopper [47,48]. The authors later reported a [2]rotaxane containing both an azobenzene and a stilbene photoswitchable unit on the axle and an α -cyclodextrin macrocycle, where different wavelengths were required to induce isomerization of each photoswitch. Furthermore, after converting both units from *trans* to *cis*, the cyclodextrin was trapped in the middle of the axle. This reversible, light-driven shuttling of the cyclodextrin macrocycle was accompanied by alternations in fluorescence between two fluorescent stoppers [49].

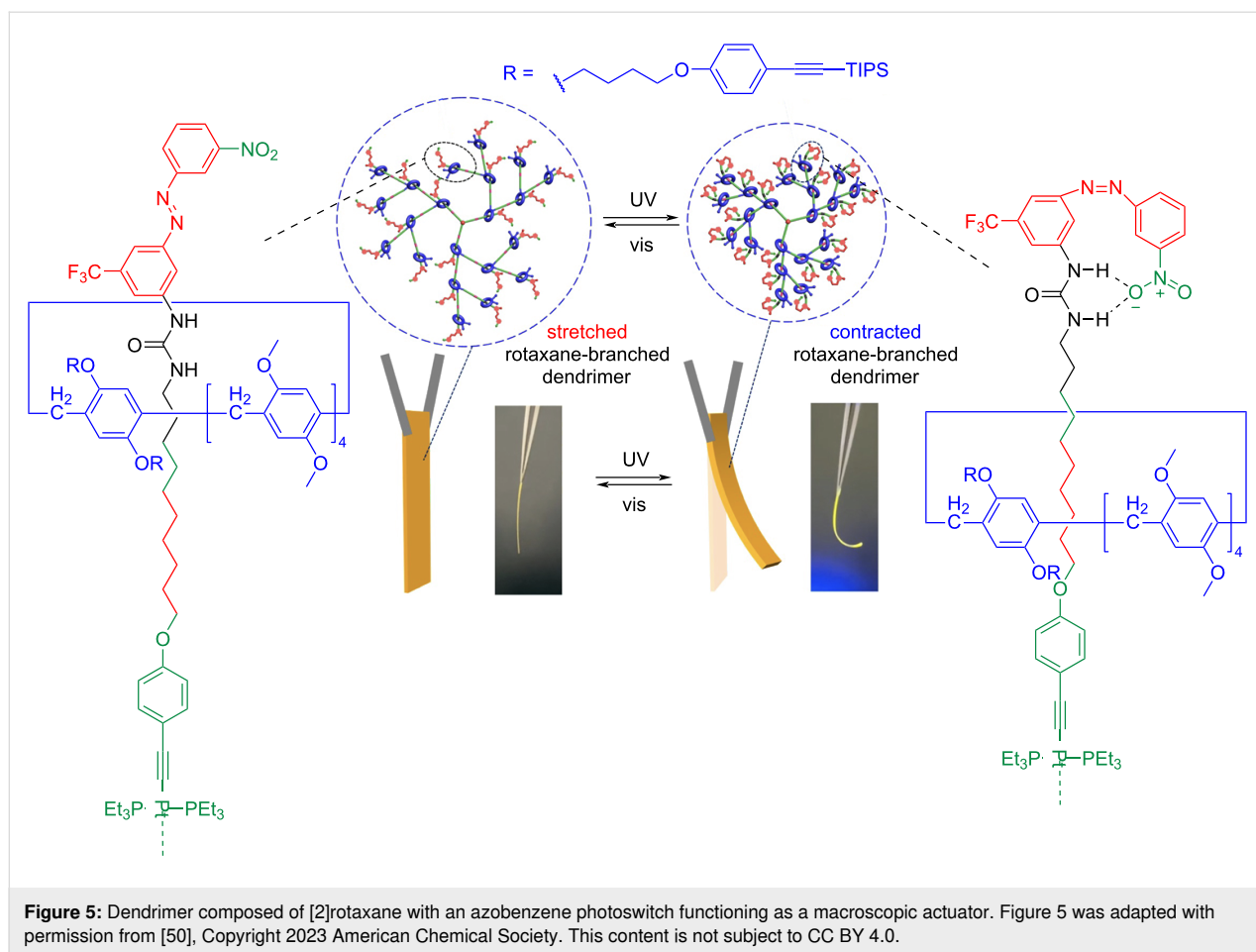
Takashima and co-workers developed a photoresponsive polymeric actuator utilizing [2]rotaxane units as topological cross-links in a polymer network, in which the azobenzene serves as a recognition site for an α -cyclodextrin macrocycle [22]. This material demonstrated remarkable mechanical properties, including a rupture strain of 2800%, which was attributed to the stress-dispersive sliding motion of the rotaxane cross-links. Moreover, the polymeric network exhibits reversible deformation upon irradiation with UV or visible light, which triggers the isomerization of the azobenzene moiety, leading to structural

changes in the rotaxane linkers. Notably, the dry state of the material, when uniaxially stretched, shows an enhanced response compared to its hydrogel form, achieving rapid mechanical actuation (Figure 4). This example illustrates the potential of topological cross-linking in advancing the field of stimuli-responsive materials, particularly in applications requiring efficient and durable artificial actuators.

Yang and co-workers reported a photoresponsive dendrimer that incorporates about 21 individual azobenzene-based rotaxanes serving as branches distributed within the dendrimer skeleton [50]. The [2]rotaxane consists of a pillar[5]arene macrocycle and an axle featuring a urea and alkyl chain as recognition sites. The azobenzene functioned as one of the stoppers. The molecular motion of the macrocycle during azobenzene photoswitching was utilized to demonstrate controllable and reversible shape transformation behaviors and to perform weightlifting and cargo transporting tasks (Figure 5). Therefore, these rotaxanes highlight their potential in applications as actuators in soft robotic devices.

Wang and collaborators developed a photoswitchable [2]rotaxane featuring a central azobenzene in the axle and two benzylalkylammonium (BAA) recognition sites. As a threaded macrocycle, they used dibenzo-24-crown-8 (DB24C8), which has a smaller benzo[18]crown-6 ring appended to it, capable of capturing K^+ ions (Figure 6) [51]. The authors demonstrated





that this rotaxane can be incorporated into model lipid bilayers and mediate K^+ ion transport across membranes through the shuttling motion of the macrocycle. In its *trans* configuration, the azobenzene allows unhindered macrocycle movement, enabling effective K^+ ion transport. Upon photoisomerization, the *cis* isomer restricts the macrocycle's motion and slows ion transport (Figure 6). Importantly, this switching is reversible, permitting precise light-triggered control of ion transport. Such photoswitchable and biomembrane-compatible rotaxanes are promising for designing artificial ion transporters to address channelopathies.

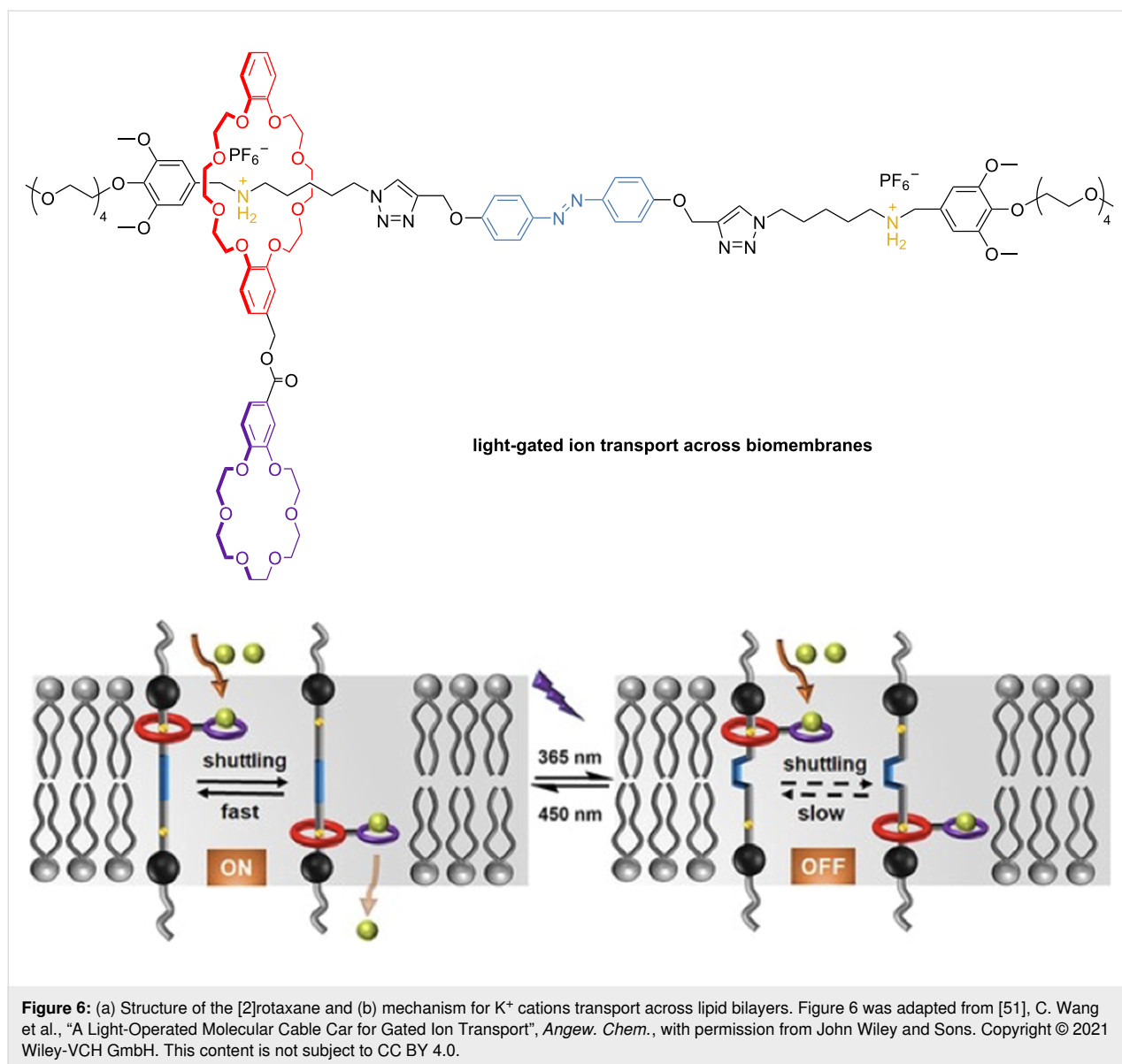
Song and co-workers developed a system in which the azobenzene in the axle is encapsulated within a chiral β -cyclodextrin, affording a self-locked [1]rotaxane [15]. The intramolecular host–guest interaction induces a chiral signal, while the azobenzene chromophore imparts photoswitching properties to the molecule. Furthermore, solvent-mediated hydrogen-bonding interactions tailored within the inner cyclodextrin cavity, combined with photocontrolled isomerization of the azo moiety, enable dual orthogonal manipulation of the rotaxane's conformational regulation and chiroptical switching properties. Thus,

this system functions as a phototriggered chiral on–off switch in polar aprotic solvents. These types of rotaxanes hold promise for developing simple information storage materials and anti-counterfeiting materials.

Credi and co-workers recently introduced photoswitchable axles containing azobenzene units to control the threading and dethreading of macrocycles such as crown ethers and cyclodextrins. Although these systems are pseudorotaxanes, they are noteworthy for their potential in the development of molecular pumps and ratchets [52,53].

Cycloheptatriene (CHT)

Cycloheptatriene is a 7-membered non-aromatic ring that can be interconverted into the corresponding tropylium ion via a photoheterolysis reaction, whereas back isomerization is achieved thermally (Figure 2). In 2004, Abraham and co-workers reported the first rotaxane containing a cycloheptatriene photoswitchable unit in a folded molecular axle and a CBQT⁴⁺ macrocycle [54]. The authors demonstrated that upon light exposure, the positively charged tropylium ion was generated, which repelled the CBPQT⁴⁺ macrocycle and modulated the



co-conformation of the rotaxane. However, the folded geometry of the axle restricts long-range movement of the macrocycle. Therefore, the authors later reported a photoswitchable rotaxane with an unfolded molecular thread, achieved by modifying the stopper groups and adjusting the linker chain length. These modifications enabled large-amplitude shuttling motions and created sufficient spatial separation, ensuring the macrocycle resides exclusively at one recognition site at a time [55].

Dithienylethene

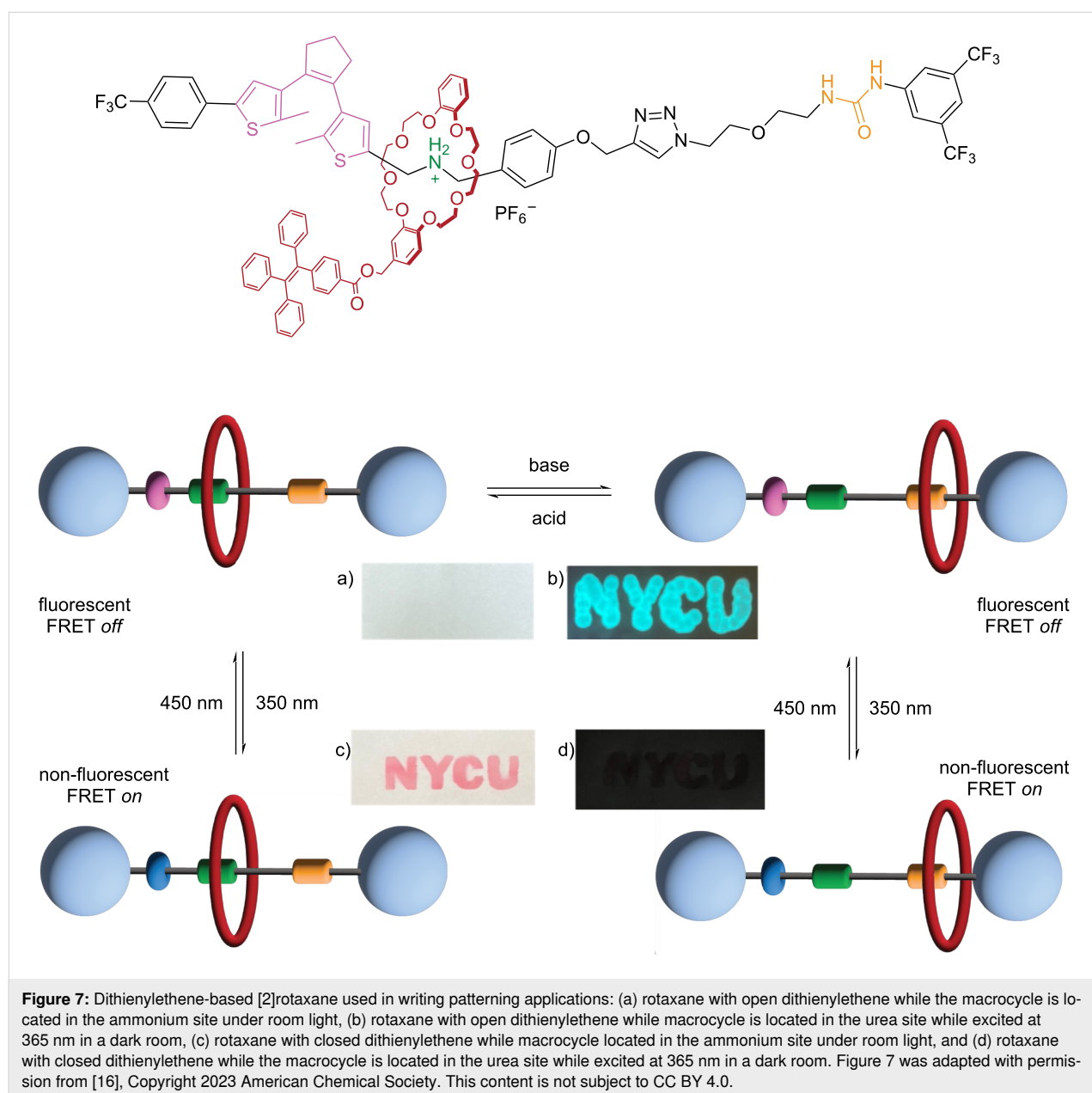
Dithienylethene photoswitches undergo an electrocyclic reaction, forming a closed-ring isomer upon irradiation with light. Notably, they are thermally irreversible, so the back isomerization occurs only upon irradiation with light at longer wavelengths. Although photocyclization leads to subtle structural

changes (Figure 2), the two isomers present very different photochemical and photophysical properties [56]. Contrary to azobenzenes, where the isomerization modulates the position of the macrocycle, in dithienylethene-based rotaxanes, it is the shuttling of the macrocycle that modulates the fluorescence and photoswitching behavior of the dithienylethene. For example, Yin and co-workers reported in 2014 the first examples of rotaxanes with a dithienylethene switch on the axle [57]. They synthesized [3]- and [5]rotaxanes with a symmetric axle containing a dithienylethene in the center and alkylammonium binding sites on each side, which interact with *N*-hetero crown ether macrocycles. Although no shuttling or energy transfer process was observed, both rotaxanes presented good photoisomerization behavior. Remarkably, the use of cucurbit[6]uril macrocycles enhanced the photoisomerization.

Later, Liu and co-workers designed a symmetric [3]rotaxane where the pH-responsive shuttling motion of the DB24C8 macrocycles can control the photocyclization of the dithienylethene. For instance, when the DB24C8 is positioned at the *N*-methyltriazolium (MTA) site, the photocyclization rate is enhanced because the macrocycle locks the antiparallel conformer of the dithienylethene. In contrast, the opposite occurs when DB24C8 is situated further away from the dithienylethene, at the dibenzylammonium site [58]. Moreover, the authors showed that the fluorescence of the dithienylethene can also be controlled by attaching a pyrene unit to the DB24C8 macrocycle. When the dithienylethene is closed, electron transfer from the pyrene to the dithienylethene acceptor occurs,

quenching its fluorescence. Moreover, faster quenching was observed when the macrocycles were closer to the dithienylethene unit [59].

Considering the discoveries on tunable fluorescence, Alene and co-workers combined the fluorescence quenching phenomena with aggregate-induced emission (AIE) in aqueous media. They synthesized a [2]rotaxane with one dithienylethene unit as a stopper, and one BAA and one urea binding site, as well as one DB24C8 macrocycle with a tetraphenylethene (TPE) fluorophore [16] (Figure 7). Addition of base results in the deprotonation of the ammonium site and shuttling of the macrocycle to the urea site. Whereas, upon addition of acid, the macrocycle



returns to the protonated BAA site. Notably, the rotaxane exhibited high fluorescence intensity due to aggregation in acetonitrile with high water content, compared to pure acetonitrile. Photocyclization of the dithienylethene with UV light quenches the fluorescence of the TPE due to Förster resonance energy transfer (FRET) between the TPE (donor) and the closed dithienylethene (acceptor). Irradiation with visible light triggers the cycloreversion, regenerating the fluorescence. Notably, the application of this rotaxane in photoswitchable patterning allowed for a sequence of letters to be “erased” with UV light (Figure 7).

Following similar principles, Khang and co-workers synthesized a [1]rotaxane featuring a dithienylethene photoswitch in

the axle, which had a DB24C8 macrocycle on one end and a TPE unit as the stopper on the other end (Figure 8) [60]. The shuttling between the BAA (*off*) and MTA (*on*) recognition sites, induced by changes in pH, enabled the photochromism of the rotaxane to be switched on and off. Specifically, the dithienylethene cannot undergo the photocyclization reaction when the macrocycle is in the BAA site due to conformational restraint. This system was used to form water-soluble nanoparticles to investigate their biological applications. The obtained nanoparticles exhibited bright red photoluminescence and the ability to generate singlet oxygen ($^1\text{O}_2$), which can be controlled through dithienylethene photoisomerization. Therefore, the authors investigated these nanoparticles for bioimaging and apoptosis of HeLa cells. When the dithienylethene is in the

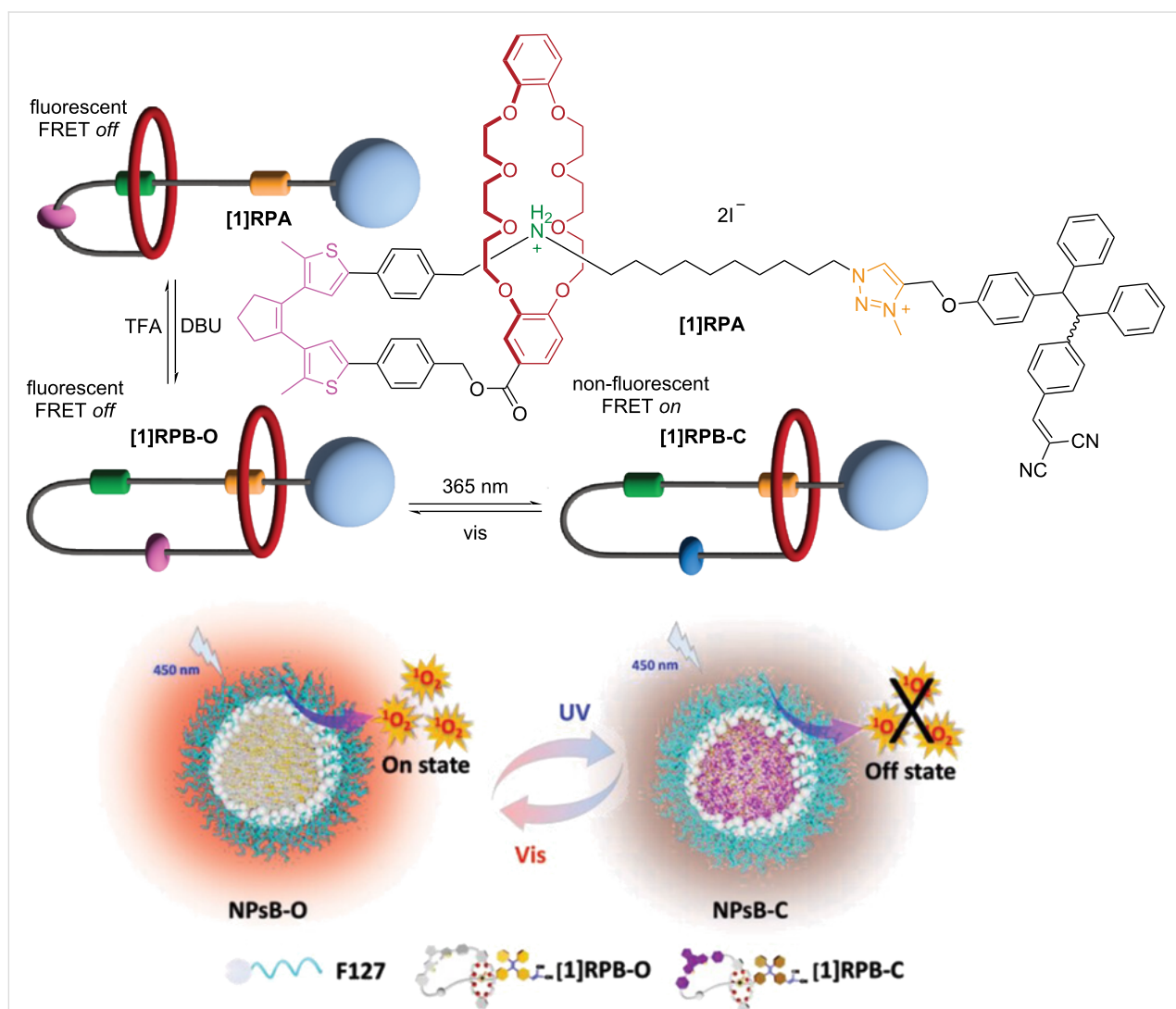


Figure 8: Dithienylethene-based [1]rotaxane shuttling motion triggered by pH changes (top). Dithienylethene photoswitch modulates singlet oxygen generation to kill HeLa cells (bottom). Figure 8 was adapted from [60], T. M. Khang et al., “Dual and Sequential Locked/Unlocked Photochromic Effects on FRET Controlled Singlet Oxygen Processes by Contracted/Extended Forms of Dithienylethene-Based [1]Rotaxane Nanoparticles”, *Small*, with permission from John Wiley and Sons. Copyright © 2022 Wiley-VCH GmbH. This content is not subject to CC BY 4.0.

open form, the nanoparticles have relatively high cytotoxicity due to the in-situ generation of toxic $^1\text{O}_2$.

Fumaramide

Fumaramide is a bisamide photoswitch with a thermally stable *trans*-olefin, which, upon UV light irradiation, undergoes *trans*-to-*cis* isomerization, affording the corresponding maleamide (Figure 2). These photoswitches are distinct due to their ability to form selective hydrogen bonds between the carbonyl oxygen of the fumaramide unit and the N–H groups of benzylic amide rings. Upon isomerization to the *cis* isomer, the hydrogen-bonding interactions are weakened, enabling the macrocycle to migrate to a second recognition station [61]. Despite their structural differences, fumaramide switches operate similarly to azobenzenes in rotaxanes, utilizing light-induced *trans*–*cis* isomerization to control the macrocycle shuttling [62].

Leigh and co-workers developed the first fumaramide-based rotaxanes, in which the photoswitchable unit was incorporated into the axle and allowed geometrical changes to occur, thereby modifying the nature and strength of the interaction between the macrocycle and the recognition sites [63,64]. Later, a new rotaxane was reported, which generates a strong induced circular dichroism response when the macrocycle is hydrogen-bonded to a chiral peptide station. This rotaxane works as a chiroptical switch by light-induced macrocycle movement along the axle [65]. The need to understand the photochemistry of fumaramides to aid their usage in various applications led to the design of rotaxanes containing different axles. Both experimental and theoretical studies involving these rotaxanes showed that no side reactions occur upon excitation, meaning these compounds can be operated continuously under illumination with very little efficiency loss, making them very effective photoactive units in nanodevices.

In 2005, Leigh and co-workers utilized a photoresponsive fumaramide [2]rotaxane as a macroscopic transporter for droplets of diiodomethane on the surfaces of glass and mica (Figure 9) [66]. This presents a promising method for liquid transport, with potential applications in lab-on-a-chip systems, including targeted analyte delivery and microscale chemical reactions, by allowing the controlled merging of droplets containing different reactants without the need for traditional reaction vessels.

Furthermore, Zhu and co-workers developed a rotaxane-based fluorescence switch in which photoinduced shuttling of the benzylic amide macrocycle occurs along a thread containing fumaramide and succinic amide ester units as recognition sites, with highly fluorescent perylene bisimide and pyrene serving as stoppers [67]. The macrocycle features two pyridine units that,

upon protonation, effectively quench the fluorescence of both chromophores via photoinduced electron and energy transfer within the pyrene–perylene dyad. This interlocked system functions as a fluorescence switch, presenting strong potential for optical applications.

Martínez-Cuezva and co-workers synthesized photoswitchable [2]rotaxanes for catalytic applications. They incorporated a photoswitchable fumaramide and a thiodiglycolamide unit as recognition sites along the axle of the interlocked system [68]. The catalytic performance of the [2]rotaxane was assessed in a TiCl_4 -promoted Baylis–Hillman reaction between *p*-nitrobenzaldehyde and 3-butyne-2-one, where the *trans*-fumaramide showed stereoselectivity. Upon photoswitching to the *cis* isomer, the macrocycle moved to the thiodiglycolamide site, which disrupted its ability to catalyze the reaction, leading to the loss of stereoselectivity. This work represents the first evidence of a light-responsive interlocked catalyst capable of modulating reaction stereoselectivity.

Hydrazone

Hydrazones undergo *trans*–*cis* isomerization at the C=N bond when exposed to light, and in some instances, they can also undergo thermal isomerization (Figure 2) [69]. Although there are early reports of hydrazone derivatives in rotaxanes [70], the incorporation of functional hydrazone photoswitches into rotaxanes began more recently with Leigh. Thus, these photoswitches are underexplored in MIMs.

Specifically, Leigh and co-workers synthesized [2]rotaxanes in which a pyridyl-acyl hydrazone moiety functioned as both photo- and thermal-switchable binding site, enabling precise control over molecular motion [71]. The incorporation of pyridyl-acyl hydrazone units is demonstrated to enable high binding (>95%) and reversible macrocycle shuttling between two binding sites (98%). Moreover, structural analysis revealed distinct intercomponent hydrogen-bonding patterns that dictate the position of the macrocycle.

Later, Leigh and co-workers introduced a new strategy for dynamically controlling asymmetric catalysis using a hydrazone-based rotaxane [72]. The axle features a hydrazone photoswitch and a pseudo-*meso* 2,5-disubstituted pyrrolidine organocatalytic unit. The photoisomerization of the hydrazone modulates the position of the tetraamide macrocycle around the pyrrolidine, breaking its symmetry and switching its handedness. This dynamic control was used to adjust the enantioselectivity of an enamine-mediated conjugate addition.

In 2024, the same group reported a [2]rotaxane with controlled shuttling motion of the macrocycle, which results in a revers-

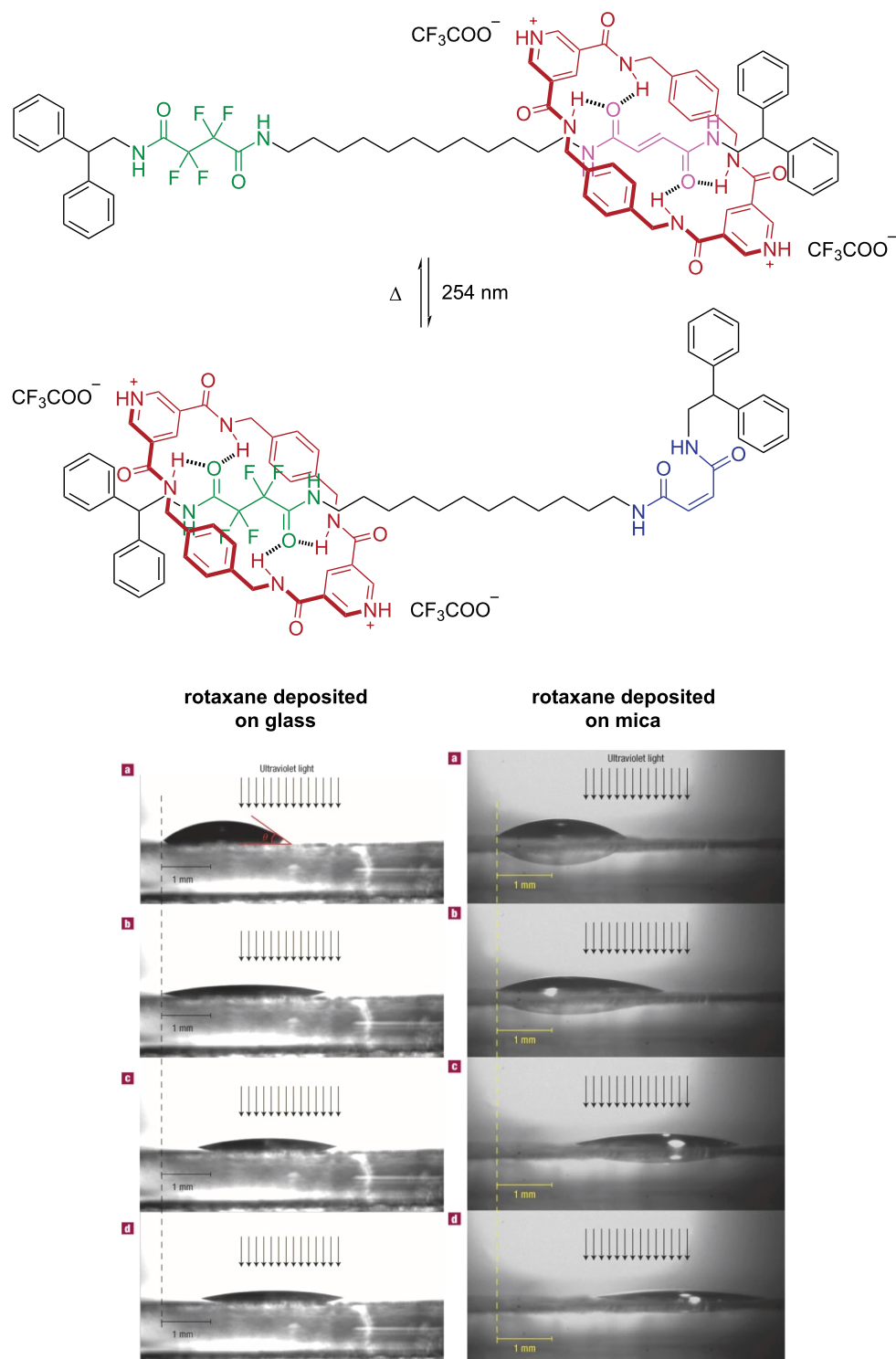


Figure 9: Depiction of a fumaramide-based [2]rotaxane photoswitching cycle and deposition on glass and mica surfaces for diiodomethane droplets transportation. Figure 9 was adapted from [66] (J. Berná et al., *Nat. Mater.*, 2005, 4, 704, © Springer Nature 2005). This content is not subject to CC BY 4.0.

ible control over liquid crystal helical pitch [73]. The system features a benzylic amide macrocycle that shuttles between a pyridyl-acyl hydrazone site and a glycyl- β -leucine site via

trans–*cis* photoisomerization of the hydrazone. When the macrocycle is closer to the chiral center (*cis* isomer), the rotaxane exhibits significantly enhanced chiral expression, as

confirmed by a stronger circular dichroism and an increase in the helical twisting power of the liquid crystal (Figure 10). This example demonstrates that mechanical motion within a rotaxane can propagate molecular-level stereochemical information to the macroscopic organization of soft matter, providing a new strategy for dynamic chirality control in functional materials.

Spiropyran

When spiropyrans are irradiated with UV light, the breaking of the C–O bond “opens” the molecule, generating the corresponding merocyanine (Figure 2). The reverse photocyclization can occur upon exposure to visible light. Remarkably, the two isomers differ in their chemical and physical properties such as polarity, molecular volume, dipole moment, fluorescence emission, net charge, and color, which distinguish them from other photoswitches. Thus, incorporating these photoswitches into rotaxanes enables the modulation of the macrocycle–axle interactions, leading to materials and biological applications. The first spiropyran-based rotaxane was reported in 2007 by Zhou and co-workers [74]. The spiropyran was positioned on the axle and served a dual purpose: as a recognition site and stopper. Photoisomerization led to the reversible shuttling of the macrocycle, which produced a visible absorption output signal that can be seen with the naked eye.

Later, Lin and co-workers reported [2]rotaxanes that contain naphthalimide fluorophores on the macrocycle and a spiropyran

as one of the axle stoppers [17]. The photoswitching of the spiropyran was used to modulate the photoluminescence of the rotaxane through Förster resonance energy transfer (FRET) with the naphthalimide. Specifically, red fluorescence was observed when the merocyanine formed, and green fluorescence when the spiropyran was generated. Notably, this rotaxane was employed for the detection of sulfite, where the addition of sulfite led to the deactivation of FRET. This occurs due to a Michael addition taking place at the active site ($C=C-C=N^+$) in the merocyanine unit in the presence of sulfite ions, resulting in color changes from red to green. This work represents a substantial advancement in the development of rotaxane-based fluorescent probes, providing highly sensitive and selective detection of sulfite for potential biological applications.

Furthermore, the same group reported a photoswitchable [2]rotaxane containing a spiropyran stopper and a macrocycle armed with tetraphenylethylene for photopatterning applications (Figure 11) [20]. The macrocycle has been shown to shuttle along the axle in response to pH changes, moving farther from the spiropyran upon the addition of acid. In the spiropyran form, no FRET occurs between the tetraphenylethylene fluorophore on the macrocycle (donor) and the spiropyran unit, regardless of their relative positions. However, upon photoisomerization to the merocyanine (open) form, FRET is activated – even when the macrocycle is relatively distant from the merocyanine – and becomes more pronounced as the donor ap-

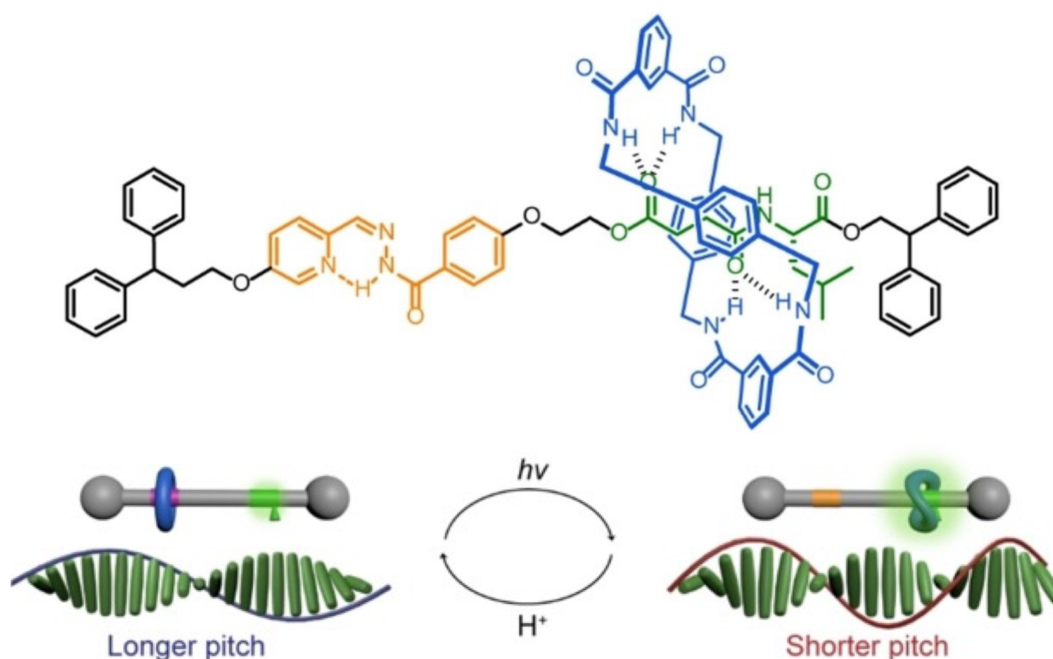
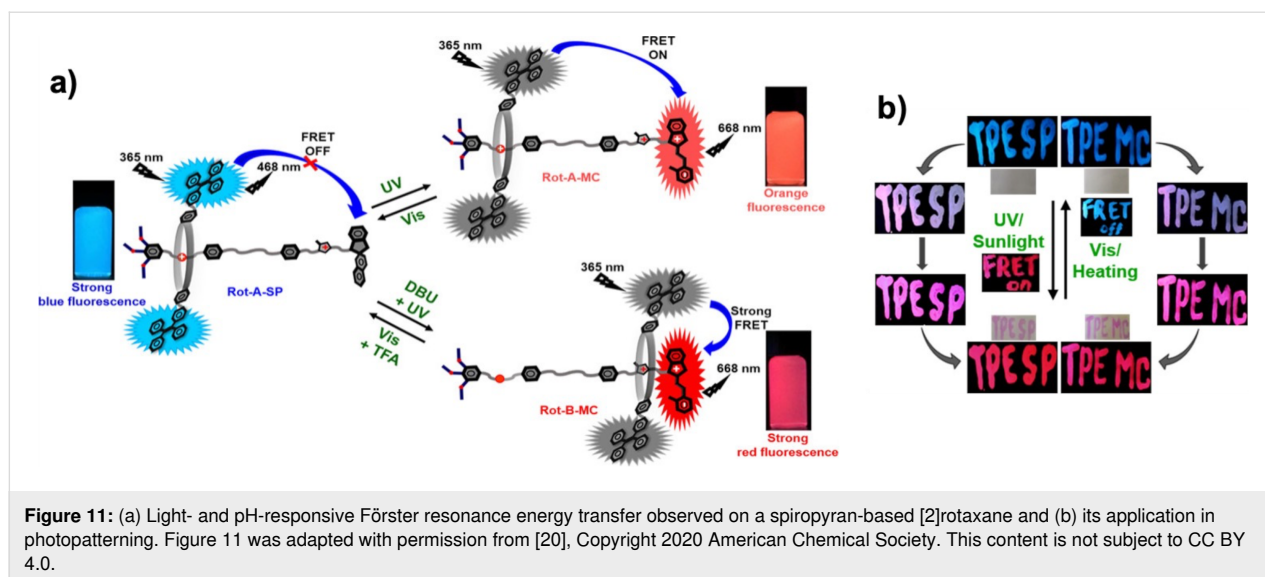


Figure 10: Hydrazone-based rotaxane controls helical pitch in a liquid crystal. Figure 10 was adapted from [73] (© 2024 S. Chen et al., *Angewandte Chemie* published by Wiley-VCH GmbH, distributed under the terms of the Creative Commons Attribution 4.0 International License, <https://creativecommons.org/licenses/by/4.0/>).



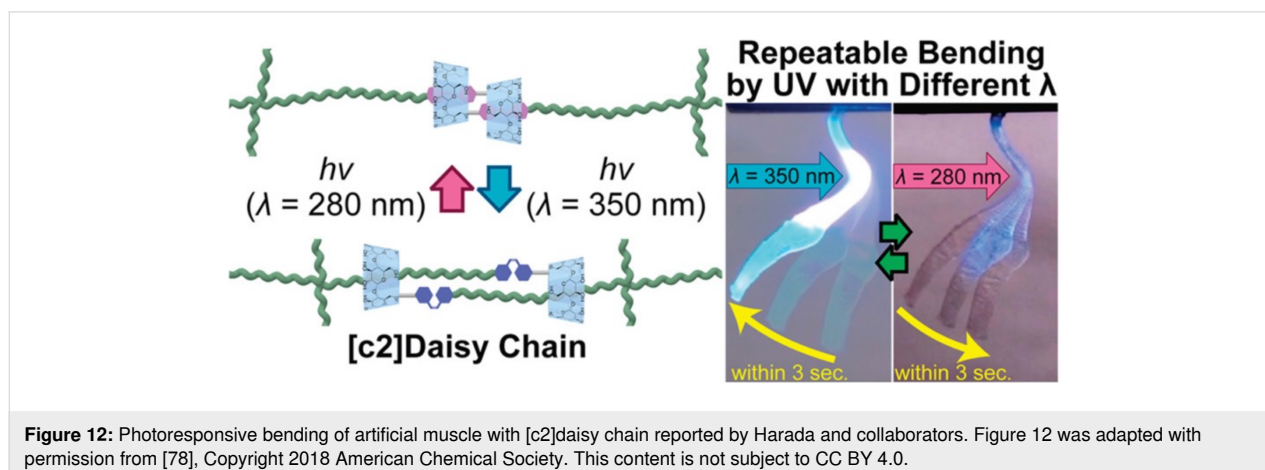
proaches the acceptor. Moreover, this rotaxane exhibited tunable photoluminescence properties in response to solvent polarity, pH, temperature, and acid–base stimuli. Additionally, this spiropyran-based rotaxane showed pronounced photochromic and fluorescent behavior in both powder and solid film under alternating UV/sunlight and visible light/heating conditions, highlighting its suitability for dynamic optical systems and anti-counterfeiting applications.

Stilbene and stiff-stilbene

Stilbene photoswitches consist of a central olefin with a phenyl group at each end. Upon light irradiation, they undergo *trans*-to-*cis* isomerization, with the reverse isomerization triggered photochemically at a different wavelength or thermally (Figure 2). However, the *cis* isomer may undergo a 6π -electrocyclization, forming dihydrophenanthrene intermediates that further oxidize into phenanthrene derivatives, thereby irreversibly deactivating the photoswitch [75].

The first stilbene-based rotaxane was reported by Anderson and co-workers in 2001, featuring a stilbene unit incorporated into the axle, which served as a recognition site for a cyclodextrin macrocycle [76]. However, in this initial study, the authors only investigated how the fluorescence properties of the stilbene were affected by its confinement in the cyclodextrin. Soon thereafter, the same group reported related [2]rotaxanes in which stilbene *trans*-to-*cis* photoisomerization induced the translocation of the cyclodextrin along the axle [77]. Remarkably, the movement of the macrocycle was unidirectional, driven by the asymmetric size difference between the two rims of the cyclodextrin.

Harada and co-workers demonstrated the potential of stilbene-based rotaxanes by developing artificial muscles [78]. They created gels based on [c2]daisy chains, which are double-threaded [2]rotaxane dimers with stilbene as the recognition unit for a cyclodextrin macrocycle (Figure 12). The photoisom-



erization of the stilbenes caused the cyclodextrin to displace along the axle, resulting in rapid and significant contraction or expansion of the gels. Moreover, stilbene photoisomerization was used to perform bending motions and lift a weight 15 times heavier than the dry gel.

Contrary to stilbenes, stiff-stilbenes have 5-membered rings fused to the carbon–carbon double bond, are more photostable, and undergo reversible photoisomerization with higher efficiency (Figure 2) [75]. Notably, their *cis* isomer exhibits higher thermal stability than that of other commonly used photo-switches, such as azobenzene. This property, in addition to facilitating their study and isolation, is advantageous for various applications.

The first stiff-stilbene-based rotaxane was reported in 2018 [79]. This [1]rotaxane used stiff-stilbene as one of the stoppers, and its photoisomerization produced the translation of a pillar[5]arene macrocycle along a hydrophobic axle with a central urea unit. More recently, a rotaxane incorporating a stiff-stilbene unit at the center of the axle was synthesized, featuring two DB24C8 macrocycles primarily positioned at quaternary ammonium recognition sites [80]. In this system, the *trans* isomer of the stiff-stilbene facilitated the formation of aggregates, resulting in organic room-temperature phosphorescence. The phosphorescent properties can be modulated by inducing macrocycle translation through acid–base stimuli or by disrupting the aggregates via stiff-stilbene photoisomer-

ization. The authors demonstrated that this system can be utilized in information encryption, anti-counterfeiting, and photorecording.

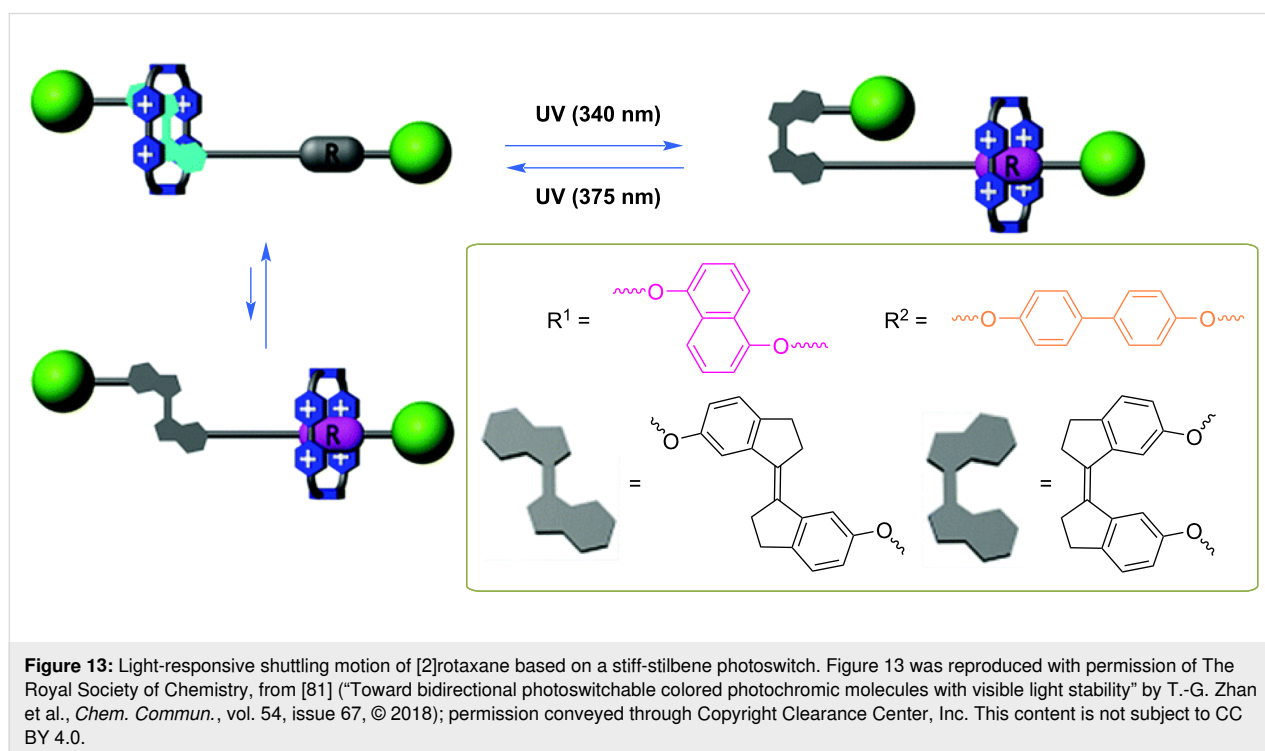
Zhan and co-workers synthesized a photochromic bistable [2]rotaxane in which the *trans*-stiff-stilbene served as the primary recognition unit for a CBPQT⁴⁺ macrocycle (Figure 13) [81]. The photoisomerization to the *cis* isomer caused the macrocycle to shift to a secondary recognition unit, either a 1,5-dioxynaphthalene or a biphenyl, resulting in a significant color change, a desired property for information storage.

Rotaxanes with different switchable units on the macrocycle

Rotaxanes incorporating photoswitchable units directly into the macrocycle remain relatively underexplored compared to their axle-based counterparts. This likely stems from the long-standing focus on the shuttling motion of the macrocycle as the hallmark of rotaxane function, which naturally led to early designs positioning photoswitches on the axle to control macrocycle movement. However, recent advances have revealed that embedding photoswitchable units within the macrocycle unlocks new and exciting functional possibilities as discussed below.

Acridane

Abraham and co-workers attempted to synthesize a [2]rotaxane incorporating an acridane photoswitch directly into a crown



ether macrocycle [82]. However, the synthesis proceeded with very low yield, and the small amount of rotaxane obtained was immediately converted to the acridinium form during purification. Attempts to regenerate the acridane were unsuccessful. Nevertheless, the authors successfully prepared the corresponding pseudorotaxane (lacking stopper groups), which underwent dethreading upon light activation, demonstrating the potential of acridane-based macrocycles for light-controlled mechanical motion in rotaxanes.

Anthracene

Hirose and co-workers developed [2]rotaxanes composed of a large crown ether macrocycle containing two anthracene moieties and an axle consisting of dibenzylammonium hexafluorophosphate [83]. Light-induced anthracene dimerization reduces the macrocycle's cavity, strengthening its interaction with the axle. As a result, the initially rapid dethreading is suppressed, and the macrocycle becomes effectively immobilized. The process is reversible upon heating. Later, Tron and co-workers synthesized a [2]rotaxane containing a barbiturate moiety in the axle, which serves as a template for a reversible clipping approach [84]. The macrocycle precursor is an acyclic Hamilton-like receptor with terminal anthracene moieties on both ends. Therefore, upon irradiation with light, the anthracene undergoes photodimerization, forming a macrocycle and capturing the axle to afford the [2]rotaxane. Notably, the photo-clipping approach is thermally reversible.

Azobenzene

Recently, the García-López group reported the first rotaxane featuring two azobenzene photoswitches integrated into a DB24C8 macrocycle (Figure 14) [23]. The azobenzene units retained their excellent photoswitching performance and photostability. In the *trans* isomer, the macrocycle exhibited shuttling motion along a 3.2 nm axle between two BAA recognition sites in acetonitrile solution. The behavior of this rotaxane was investigated in lipid bilayers of large and giant vesicles. Remarkably, the photoisomerization of the azobenzene units enabled modulation of the rotaxane's interaction with the lipid membrane, leading to reversible changes in giant lipid vesicles. In the *trans* isomer, the membrane tension decreased, resulting in deformation and pronounced membrane undulations. Isomerization to the *cis* form increased membrane tension, causing vesicle contraction. Molecular dynamics simulations revealed that while azobenzene photoisomerization can directly induce some degree of lipid packing reorganization, the dominant effect arises from changes in the position of the rotaxane within the membrane. Specifically, in the *trans* isomer, the macrocycle resides closer to the membrane–water interface, promoting local water accumulation and membrane permeabilization. In contrast, in the *cis* isomer, the macrocycle pene-

trates deeper into the hydrophobic core of the bilayer, reducing perturbation and water accumulation, thereby increasing membrane tension.

Light-driven membrane modulation holds great promise for drug delivery, therapeutics, and various biotechnological applications [85–88]. As a proof of principle, this rotaxane was used to trigger the light-induced release of hydrophilic cargo from large vesicles, highlighting its potential as a platform for controlled drug delivery.

Recently, Yang and co-workers reported a [2]rotaxane featuring a macrocycle constructed from two azobenzene photoswitches threaded onto an asymmetric axle [89]. Photoisomerization of the azobenzenes alters the geometry and size of the macrocycle, thereby modulating its affinity toward two distinct recognition sites on the axle – an ammonium and a pyridinium group. In the all-*trans* state, the macrocycle preferentially associates with the pyridinium site, whereas in the *cis* state it shuttles to the ammonium residue. Back isomerization, triggered either thermally or with light, returns the macrocycle to the pyridinium site. This light-driven shuttling was shown to be fatigue-resistant over multiple cycles, highlighting the robustness of the system. Notably, the authors also reported a general quantification of kinetic asymmetry in a multicycle chemical reaction network, establishing a framework applicable to other molecular systems.

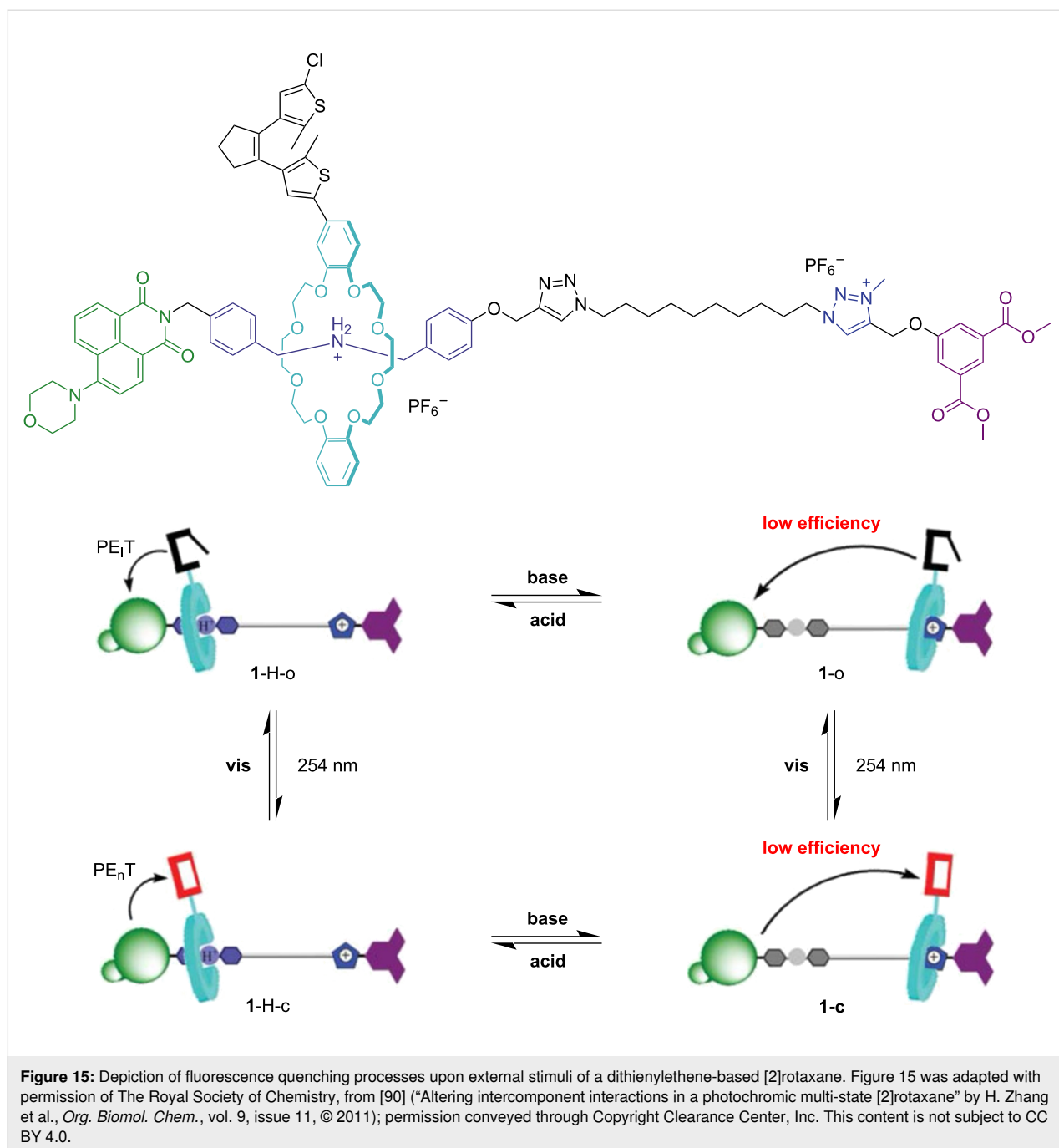
Dithienylethene

Incorporation of dithienylethene switches on the macrocycle of rotaxanes has been done primarily to modulate the fluorescence properties of the system. Tian and co-workers reported the first example of this type of rotaxane, followed by Li and co-workers [90–92]. The systems consist of [2]- and [3]rotaxanes where the dithienylethene units are directly attached to either *N*-hetero crown ether or DB24C8 macrocycles. BAA and MTA units served as recognition sites for the macrocycles. Notably, Tian's rotaxane showed fluorescence quenching when the dithienylethene is in the closed form, caused by photoinduced electron transfer (PET) from the fluorescent pyrene stopper to the acceptor dithienylethene (Figure 15). Moreover, the efficiency of the PET is modulated by the macrocycle shuttling motion between the two recognition sites due to differences in proximity to the fluorescent stopper. The reported findings involving dithienylethene-based rotaxanes prove their promising future in materials applications, mainly due to their high photofatigue resistance.

Spiropyran

While most spiropyran-based rotaxanes have the photoswitchable unit located on the axle, an exception has been reported by Zhou and co-workers, where the authors designed and synthe-

isomerization of the spiropyran led to the merocyanine. Thus, four different configurational states of the interlocked system were generated, which produce distinct fluorescence outputs (Figure 16). Therefore, this work presents a multistate



[2]rotaxane with light and pH-responsive fluorescence, highlighting its promising ability to design responsive optical materials and molecular logic gates.

Stiff-stilbene

Wezenberg and co-workers designed a photoswitchable macrocycle that incorporates a stiff-stilbene unit on one side and an isophthalamide moiety on the other [94]. The photoisomerization of the stiff-stilbene allows the macrocycle to adopt a narrow-elongated conformation in the *cis* state and a wider ge-

ometry in the *trans* state. This light-induced conformational change was utilized to control the anion-templated formation of a pseudorotaxane. Specifically, the axle contains a pyridinium bisamide that forms a complex with the isophthalamide unit of the macrocycle and a chloride anion when the stiff-stilbene is in the *cis* configuration (Figure 17). Upon switching to the *trans* isomer, the expanded geometry of the macrocycle disrupts the complex, resulting in the dethreading of the macrocycle. By introducing stopper groups to prevent dethreading, the authors demonstrated that the photoisomerization of stiff-stilbene can

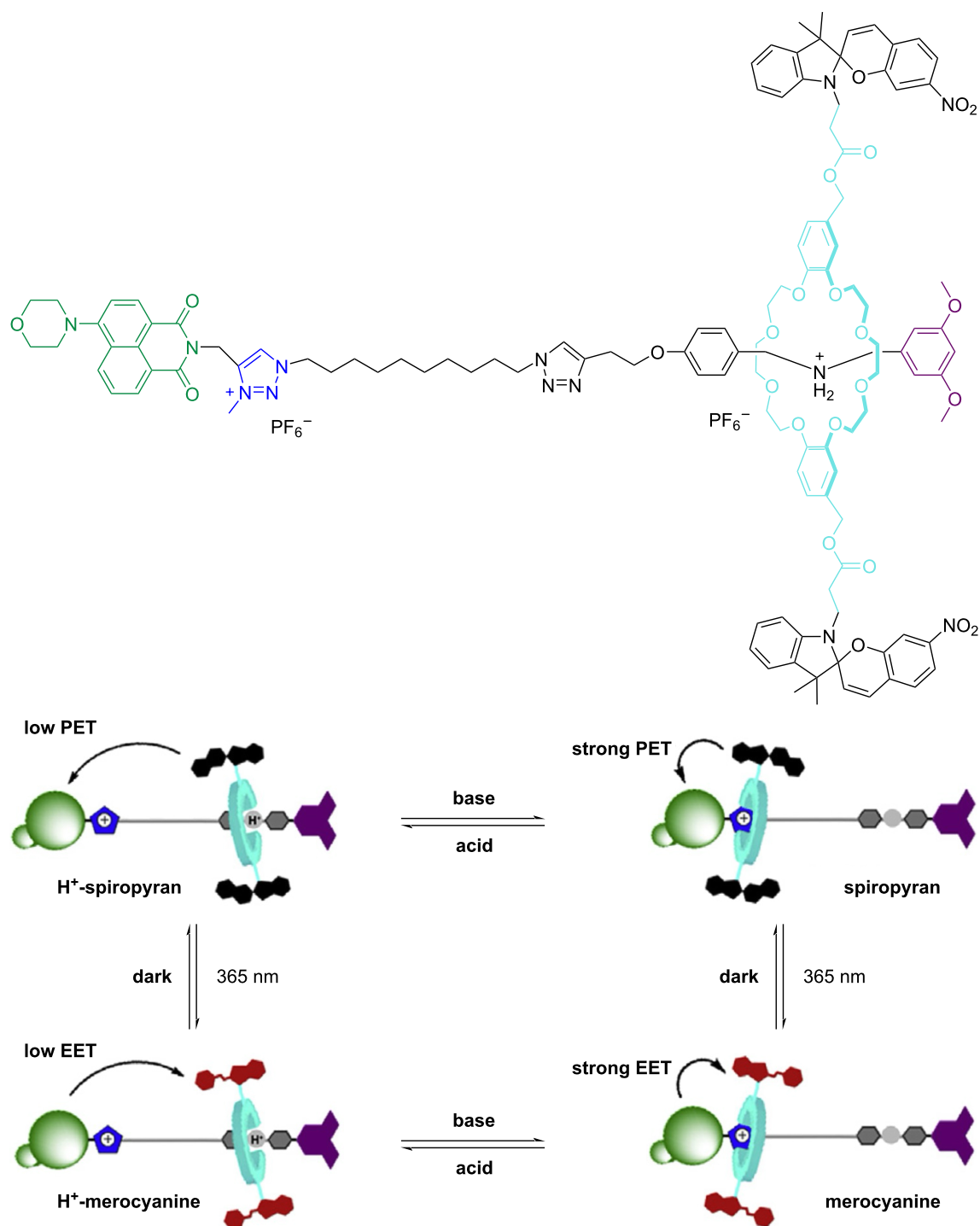


Figure 16: Diagrammatic illustration of rotaxane 1-H-SP depicting interconversions between the four isomeric states in response to both pH and light stimuli. Figure 16 was adapted from [93], *Tetrahedron*, vol. 69, by W. Zhou, H. Zhang; H. Li; Y. Zhang; Q.-C. Wang; D.-H. Qu, "A bis-spiropyran-containing multi-state [2]rotaxane with fluorescence output", pages 5319–5325, Copyright (2013), with permission from Elsevier. This content is not subject to CC BY 4.0.

reversibly modulate the chloride anion binding affinity of the system [95]. Due to its selectivity and light-controlled binding behavior, this system holds potential for applications in anion transport, extraction, and separation technologies.

Conclusion and Perspectives

The development of photoswitchable rotaxanes has mainly focused on controlling the position and movement of the macrocycle along the axle. Consequently, the vast majority of systems

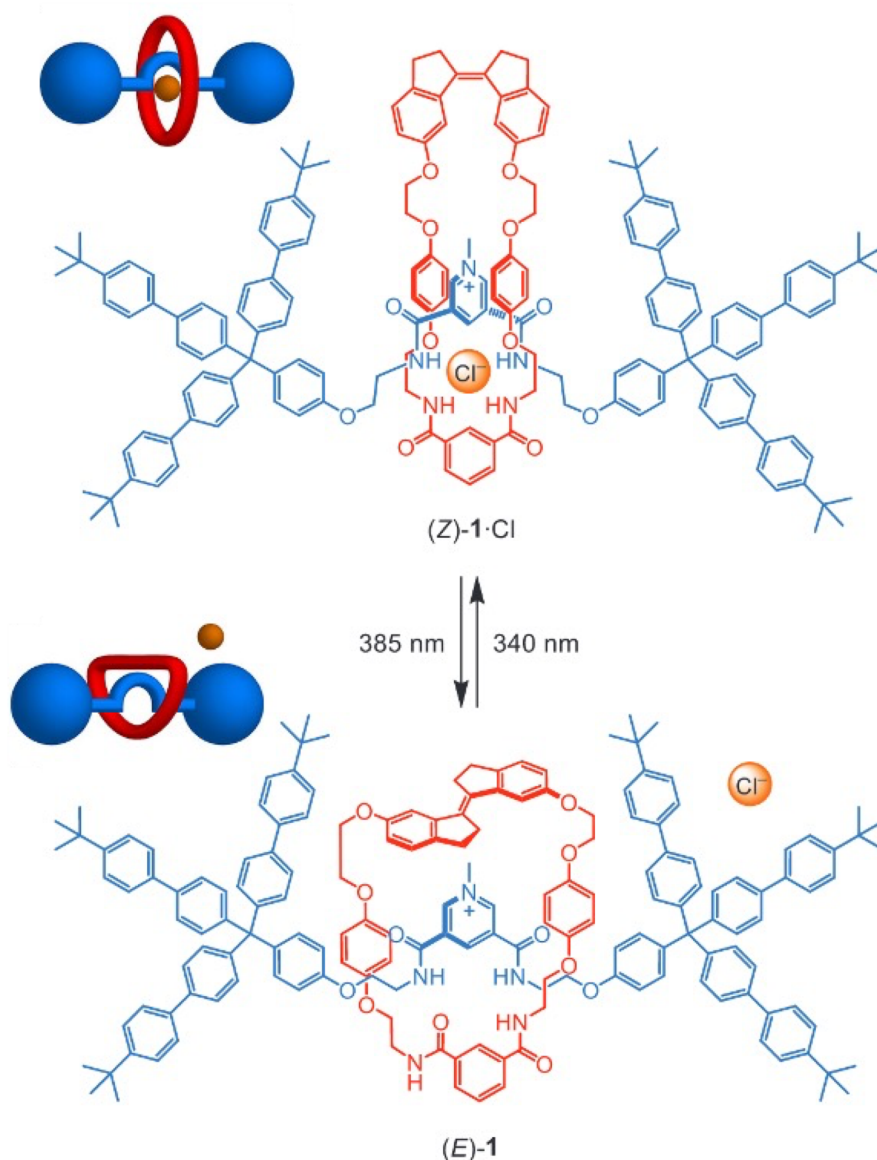


Figure 17: Representation of [2]rotaxane chloride binding modulated by photoisomerization of a stiff-stilbene. Figure 17 was reproduced from [95] (© 2025 J. de Jong et al., *Chemistry – A European Journal* published by Wiley-VCH GmbH, distributed under the terms of the Creative Commons Attribution 4.0 International License, <https://creativecommons.org/licenses/by/4.0/>).

reported to date incorporate photoswitches into the axle to regulate shuttling dynamics. However, emerging strategies that integrate photoswitches directly into the macrocycle are creating alternative avenues for modulating not only macrocycle–axle interactions but also the interactions of rotaxanes with their surrounding environment.

Controlling macrocycle shuttling via light activation has proven valuable for enabling secondary functions. For example, when integrated into polymers or gels, the mechanical motion of rotaxanes can be harnessed to control the macroscopic properties of materials or even generate mechanical work, such as

lifting objects. In other systems, photoswitchable rotaxanes have been used to modulate optoelectronic properties, creating opportunities for applications in information storage, sensing, optical devices, and anti-counterfeiting technologies.

Recently, the incorporation of photoswitchable rotaxanes into lipid membranes has revealed exciting opportunities for future biooriented applications. These applications include light-controlled systems for drug release, ion transport, rotaxane-based therapeutics, and molecular tools capable of modulating biological processes in living cells. However, most photoswitchable rotaxanes developed to date have been designed for use in

organic solvents or non-biological environments. To fully harness their potential in biomedical and biotechnological settings, it is essential to establish new design principles that ensure biocompatibility, stability, and functionality under physiological conditions.

Looking forward, incorporating newer and more efficient photoswitches, along with advancements in rotaxane architecture, will expand the functional landscape of these systems. Opportunities arise not only for more sophisticated molecular machines for fundamental studies but also for practical applications in smart materials, responsive systems, and biomedical technologies. The synergy between molecular design, light-driven control, and functional integration positions photo-switchable rotaxanes as a highly versatile and dynamic platform for future innovations across multiple disciplines.

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Author Contributions

Jullyane Emi Matsushima: writing – original draft; writing – review & editing. Khushbu: writing – original draft. Zuliah Abdulsalam: writing – original draft. Udyogi Navodya Kulathilaka Conthagamage: writing – original draft. Víctor García-López: conceptualization; funding acquisition; project administration; supervision; writing – original draft; writing – review & editing.

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Data Availability Statement

Data sharing is not applicable as no new data was generated or analyzed in this study.

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Get a better glimpse on sequential photoreactions of trisnorbornadienes with ^{19}F NMR spectroscopy

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Full Research Paper

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Abstract

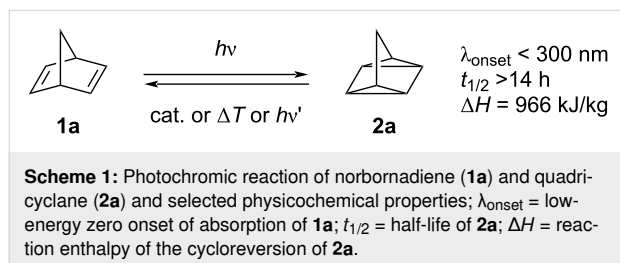
It is shown exemplarily with a trifluorinated trisnorbornadienylbenzene that ^{19}F NMR spectroscopy may be applied as a useful complementary method for the investigation of sequential photoreactions. The trisnorbornadiene core structure was used as it figures as promising scaffold for molecular solar thermal (MOST) energy storage. The target compound was readily synthesized by a Suzuki–Miyaura coupling reaction and examined with respect to the key properties for MOST applications. Upon direct or photo-sensitized irradiation, the trisnorbornadiene was transformed stepwise and almost quantitatively into the corresponding trisquadricyclane. Even though the reaction can be monitored by photometry or by in situ ^1H NMR spectroscopy, unambiguous assignment of the distinct intermediate mono- and bisquadricyclanes was not possible because of signal overlap. In contrast, this shortcoming is circumvented with in situ ^{19}F NMR-spectroscopic analysis. Contrary to the ^1H NMR spectra, the ^{19}F NMR spectra show significantly fewer characteristic and sufficiently separated signals that allow the unambiguous identification of all photoproducts and, thus, their detection in the course of the photoreaction.

Introduction

Photochromic compounds, which change their physical and chemical properties reversibly upon irradiation, figure as a versatile basis for the development of functional materials, whose performance can be switched or controlled by light [1–4]. To add to that, the photochromic reaction allows to convert the energy of the applied light into chemical energy, which can thus be stored and eventually released on demand as heat in the back

reaction. Therefore, photochromic reactions constitute the centerpiece of the emerging approach towards molecular solar thermal (MOST) energy storage [5–8]. In this context, norbornadienes are employed as well established photoswitches because they provide several favorable photochemical and physico-chemical properties [9,10]. In a photochromic intramolecular [2 + 2] cycloaddition reaction, these compounds are trans-

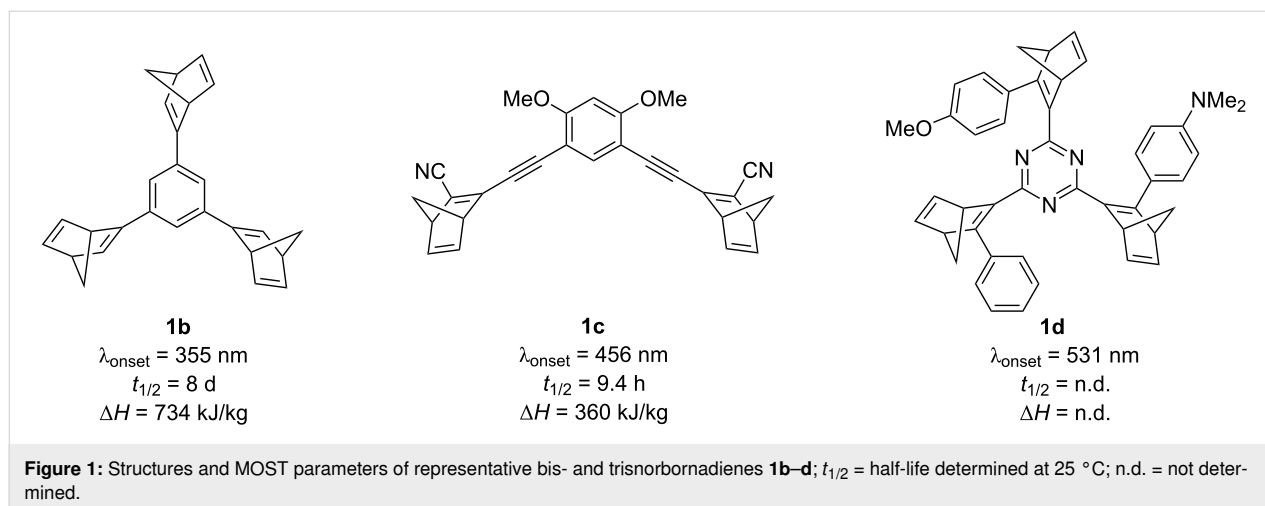
formed into an energy-rich metastable photoproduct that, upon application of an external stimulus, isomerizes back in a cycloreversion reaction to the starting compound with the release of heat (Scheme 1) [5,7]. In comparison with other photochromic compounds (e.g., azobenzenes [11,12], anthracenes [13–15], stilbenes [16,17], and bicyclooctadienes [18,19]), the photoisomers of norbornadienes, namely quadricyclanes, stand out with their high energy density, with the parent compound **2a** providing a ΔH value of 966 kJ/kg [20–23] and a half-life of the more than 14 h [24]. At the same time, however, norbornadiene (**1a**) has also some major drawbacks with regard to a real MOST application, namely minimal overlap of the absorption spectrum ($\lambda_{\text{onset}} < 300$ nm) [25–28] with the solar emission spectrum as well as a low quantum yield ($\Phi = 5\%$) [26,27].



In order to optimize the photophysical and physicochemical properties of norbornadiene (**1a**) with minimal impact on the energy density, scaffolds with multiple norbornadiene units have been investigated with the goal to accomplish higher energy storage density per molecule [20–22,29–33]. Furthermore, to shift the absorption towards lower-energy light in such compounds – and for that matter to the solar spectrum – push–pull systems [29,31], enlarged π systems [30,33], and heteroaromatic chromophores [32,34,35] have been introduced (Figure 1). Although this structural variation often leads to a red-shifted absorption, the half-lives of the corresponding

quadricyclanes are often decreased at the same time. In particular, the addition of an acetylene unit between the linking aromatic part and the norbornadiene often leads to short half-lives [29–31].

As arene-linked bis- and trisnorbornadienes are promising lead structures for further development of more efficient MOST materials, a detailed investigation of the photochemical reactions is necessary. However, such studies of multichromophore photo-reactions are often difficult, because the distinct reaction steps are not necessarily consecutive and may not be readily dissected. Furthermore, as the reaction intermediates are isomers with mainly similar structural fragments, it is difficult to distinguish them by the usually employed spectroscopic methods because of overlapping signals [22,30,33]. Along these lines, ^1H NMR spectroscopy is a very useful method to follow the photoreaction, ideally upon direct irradiation in the NMR probehead (in situ NMR), because it potentially enables accurate structure elucidation. But even though this method may enable the accurate monitoring of a stepwise photochromic reaction of multichromophores in some cases [36,37], significant overlap of NMR signals often interferes with the detailed identification of separate components. Therefore, we proposed that the analysis of the photoreaction of a fluorinated starting material with in situ ^{19}F NMR spectroscopy may add a useful complementary tool [38–41]. Firstly, the ^{19}F nucleus is only slightly less sensitive for NMR spectroscopy than the ^1H nucleus [42]. Additionally, fluoro substituents may be attached such that they will give well-separated signals in less complex spectra, thus allowing conclusive and quantitative product identification [38–40]. Herein, we will show in a proof-of-principle study with a fluorinated trisnorbornadiene derived from promising lead compound **1b** that in situ ^{19}F NMR spectroscopy may indeed be used to monitor sequential photoreactions of multichromophoric systems.



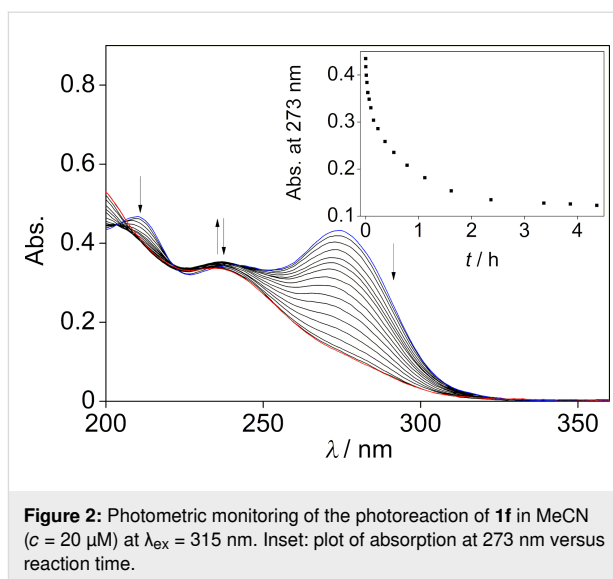
Results

The trisnorbornadiene **1f** was synthesized in 36% yield through a Suzuki–Miyaura coupling reaction of tribromotrifluorobenzene **3** with the 2-borononorbornadiene **1e** (Scheme 2) [43]. The product **1f** was identified and fully characterized by NMR spectroscopy (^1H , ^{13}C , ^{19}F , COSY, HSQC, HMBC), mass spectrometry, melting point, and elemental analysis. Norbornadiene **1f** is well soluble in alkanes, chlorinated and aromatic solvents, whereas it is hardly soluble in polar protic solvents and MeCN and insoluble in water.

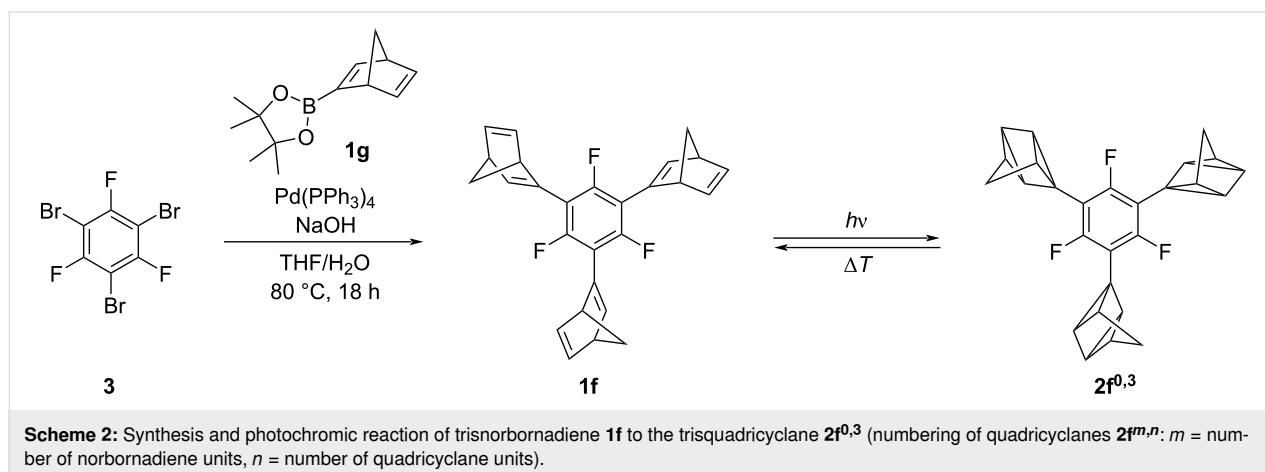
The absorption spectra of **1f** were recorded in MeCN, cyclohexane, MeOH, ethyl acetate, THF, CH_2Cl_2 , CHCl_3 , and benzene (see Supporting Information File 1, Figure S1). The absorption spectra have essentially the same key features, specifically absorption maxima at around 209 nm, 240 nm, and 273 nm, with a long-wavelength absorption onset at 350 nm. Both maxima and onset absorptions are hypsochromically shifted compared with the ones of the parent compound **1b** [22].

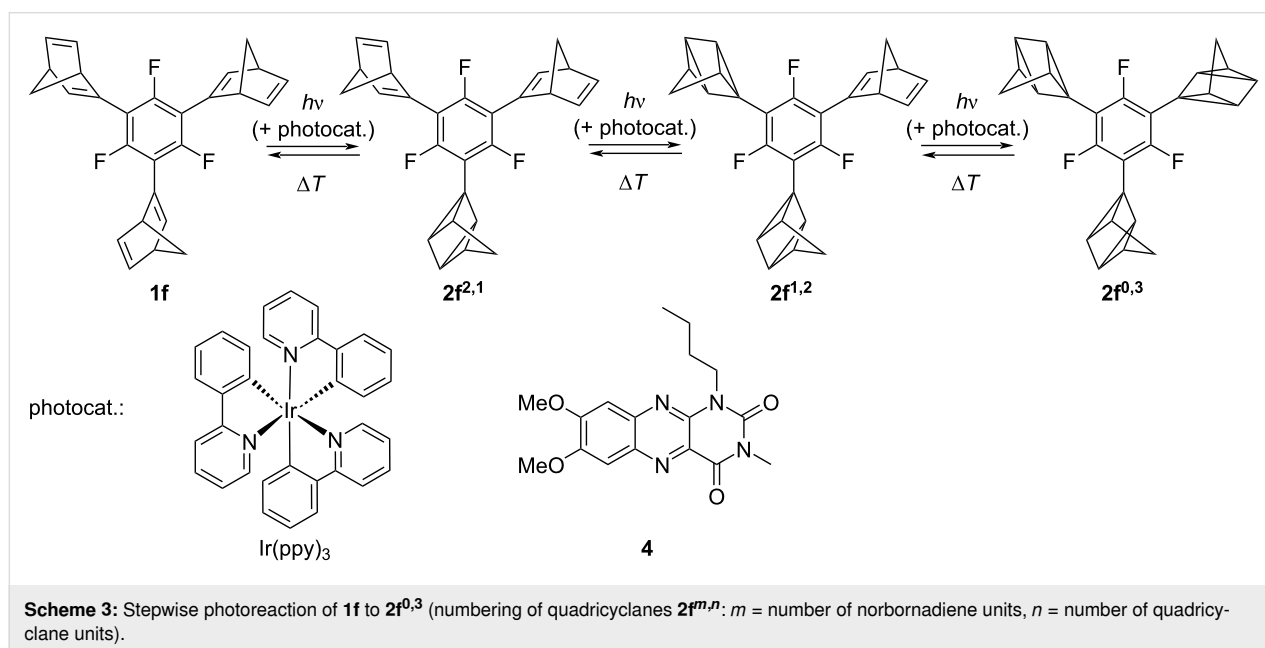
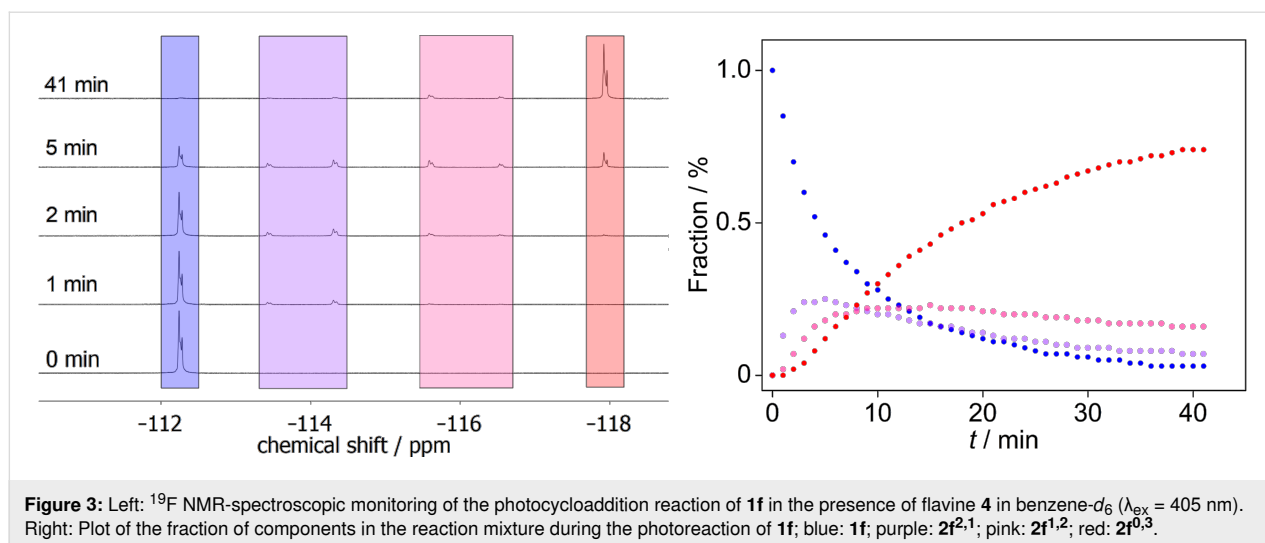
The [2 + 2] photocycloaddition reaction of **1f** was initiated by direct irradiation with 315 nm. The photoreaction was significantly slower (4 h to achieve photostationary state) compared with the one of the parent compound **1b** (0.5 h) [22]. Monitoring the photoreaction by absorption spectroscopy revealed the formation of a new maximum at 235 nm with no discernible isosbestic points, clearly indicating the presence of more than two differently absorbing compounds (Figure 2). In addition, the examination of the photoreaction with ^1H NMR spectroscopy showed that the quadricyclane **2f^{0,3}** was formed almost quantitatively as the photoproduct (>95%) (see Supporting Information File 1, Figure S11).

The photosensitized reaction in the presence of $\text{Ir}(\text{ppy})_3$ also afforded quadricyclane **2f^{0,3}** in almost quantitative yield (>95%), as shown by ^1H NMR spectroscopy (see Supporting



Information File 1, Figure S10). The photosensitized reaction in the presence of $\text{Ir}(\text{ppy})_3$ or 1-butyl-7,8-dimethoxy-3-methylalloxazin (**4**) as an alternative catalyst [44,45] with $\lambda_{\text{ex}} = 405$ nm (LED) was investigated by in situ ^1H NMR spectroscopy. In both cases, the photoreaction was almost quantitative (see Supporting Information File 1, Figures S13 and S14). To gain more information about the course of the photoreaction and sequential formation of intermediates, the photoreaction of **1f**, catalyzed by flavin **4**, was investigated with in situ ^{19}F NMR-spectroscopic analysis. During the irradiation, the NMR signals of two intermediates (approx. -114 ppm and -116 ppm) were observed (Figure 3 and Supporting Information File 1, Figure S15), which were assigned to monoquadricyclane **2f^{2,1}** and bisquadricyclane **2f^{1,2}** (Scheme 3, Figure 3). As expected, the quadricyclanes were formed consecutively, that is, from monoquadricyclane **2f^{2,1}** to bisquadricyclane **2f^{1,2}** and eventually the trisquadricyclane **2f^{0,3}**. The latter was only formed after a sufficient concentration of the intermediates was present (5 min).





From this point onwards, the fraction of the starting material **1f** and the intermediates $2f^{2,1}$ and $2f^{1,2}$ decreased steadily, while the content of the trisquadricyclane $2f^{0,3}$ increased (Figure 3). This proposed consecutive, stepwise photoreaction was supported by theoretical analysis which showed a consistent fitting of the experimental data to the proposed kinetic model (see Supporting Information File 1, Figure S16). Contrary to the ^1H NMR spectra, the ^{19}F NMR spectra showed significantly fewer signals (one or two per molecule) during the photoreaction because of the symmetry of norbornadiene **1f** and its photo-products and the less complex coupling pattern. Thus, the ^{19}F NMR spectra of the norbornadiene **1f** and the quadricyclane $2f^{0,3}$ showed a multiplet, respectively, whereas the ones of the intermediates resulted in two multiplets with a ratio of

1:2. Additionally, pronounced downfield shifts of the ^{19}F NMR signals were observed with increasing number of quadricyclane units (Figure 3).

To assess the physicochemical parameters of the light energy storage and release, the thermally induced cycloreversion of $2f^{0,3}$ was investigated. Analysis of the cycloreversion at different temperatures revealed a half-life, $t_{1/2}$, of 55 d at 25 °C, an activation enthalpy $\Delta H = 99.4$ kJ/kg, and an activation entropy of $\Delta S = -42$ J/K mol (see Supporting Information File 1, Figure S2).

The energy density of trisquadricyclane $2f^{0,3}$ was determined with simultaneous thermal analysis (STA) with a heat release of

458 kJ/kg. Additionally, a second exothermic peak ($>150\text{ }^{\circ}\text{C}$) correlated with a significant decrease in mass, indicating decomposition above this temperature (see Supporting Information File 1, Figure S3).

The cycloreversion of trisquadricyclane **2f^{0,3}** was also initiated in a ground-state reaction with magic blue (**5**), which has already been shown to be an effective catalyst for this reaction [46–48]. Upon addition of magic blue (**5**, 7.5 mol %) to a solution of quadricyclane **2f^{0,3}** in CDCl_3 , the norbornadiene **1f** was formed almost quantitatively in addition to very small traces of tri(4-bromophenyl)amine, i.e., the reduced catalyst (see Supporting Information File 1, Figure S12).

Discussion

A comparison of the synthesis and photophysical properties of the fluoro-substituted norbornadiene **1f** with the ones of the parent compound **1b** revealed that the yield of the Suzuki–Miyaura coupling reaction is significantly lower for the former [22], presumably because of the steric hindrance induced by the *ortho*-fluoro substituents. These substituents also induce a strong electron-withdrawing effect on the chromophore and thus lower the HOMO energy, likely leading to a larger HOMO–LUMO gap and to a small hypsochromic shift of the absorption (**1f**: $\lambda_{\text{max}} = 273\text{ nm}$; parent norbornadiene **1b**: $\lambda_{\text{max}} = 283\text{ nm}$) [49].

According to the results of the photosensitized reaction, the triplet state energy of the norbornadiene **1f** is higher than that of norbornadiene **1b** (2.08 eV) [50], as the sensitized photocycloaddition only took place with the photocatalyst $\text{Ir}(\text{ppy})_3$ (2.52 eV) [51] and with flavine (2.28 eV) [52]. In contrast, $[\text{Ru}(\text{phen})_3]^{2+}$ (2.19 eV) [53] does not catalyze the reaction of **1f**, but is still able to catalyze the one of **1b** [50].

Notably, the half-life of trisquadricyclane **2f^{0,3}** (55 d) is almost eight times longer than the one of the parent compound **2b** (8 d) [22], presumably because of additional steric hindrance induced by the fluoro substituents in the *ortho* positions [54]. It should be noted that there is only very limited data available to compare the effect of the substitution pattern on the half-life of aryl-substituted norbornadienes to support this interpretation [55]. However, the effect of *ortho* substituents has been examined in more detail for 2-cyano-3-arylnorbornadienes. And these studies have shown that the substituents in *ortho* position lead to an increased thermal stability in comparison with the *meta* and *para*-substituted isomers [54]. Although the longer half-life of the trisquadricyclane may be considered an improved property, the energy density of this compound is lower than that of the parent compound **2b** because of the higher molecular mass.

The experimental results showed a decomposition of trisquadricyclane **2f^{0,3}** at higher temperature, which is accompanied by significant loss of mass. This observation likely indicates the thermally induced retro-Diels–Alder reaction of the initially formed norbornadiene units and presumably subsequent reactions of the primary intermediates under these conditions. This unfavorable property may also be caused by the *ortho*-fluoro substituents as it was not observed with the parent compound **1b**. In fact, increased rates of retro-Diels–Alder reactions have been observed with acceptor-substituted substrates [56,57].

Although the course of the photoreaction of norbornadiene **1f** can be visualized by in situ ^1H NMR spectroscopy, significantly overlapping signals prevent the conclusive differentiation of the individual species that are formed throughout the reaction (see Supporting Information File 1, Figures S13 and S14), interfering with the complete assessment of this stepwise photoreaction. In contrast, it is demonstrated herein that this problem is circumvented by the application of in situ ^{19}F NMR-spectroscopic measurements. Contrary to the ^1H NMR spectra, the ^{19}F NMR spectra are less complex and show characteristic and sufficiently separated signals that allow the unambiguous identification of photoproducts **2f^{0,3}**, **2f^{2,1}**, and **2f^{1,2}** and, thus, their detection in the course of the photoreaction.

Conclusion

One ongoing problem during assessment of MOST systems is the examination of multichromophore photoreactions, because the intermediates share high structural similarities and are thus often difficult to be distinguished by ^1H NMR spectroscopy, i.e., the currently most applied method. We demonstrated in this proof-of-principle study that fluorinated norbornadiene **1f** is a well-designed substrate for in situ ^{19}F NMR-spectroscopic investigation. The advantages of ^{19}F NMR spectroscopy are obvious, as the ^{19}F NMR spectra comprise fewer and sufficiently separated signals as compared with the ^1H NMR spectra. To add to that, in principle only one well-placed fluoro substituent is necessary to take advantage of ^{19}F NMR spectroscopy as a useful complementary method for the investigation of sequential photoreactions.

At the same time, the norbornadiene/quadricyclane system **1f/2f^{0,3}** has some favorable MOST properties, namely a high energy density and a long half-life of the trisquadricyclane. In addition, the cycloaddition reaction can be initiated under mild conditions with visible light ($\lambda_{\text{ex}} = 405$ or 420 nm) in the presence of $\text{Ir}(\text{ppy})_3$ or flavine **4** as photocatalysts. However, these key parameters do not match the better ones of the parent norbornadiene **1b**. Furthermore, the fluoro-substituted derivative **2f^{0,3}** appears to be prone towards thermal decomposition. Thus, even though this compound serves as an ideal probe for

the investigation of the photoreaction by ^{19}F NMR spectroscopy, further structural optimization is necessary for application purposes.

Experimental

Synthesis

1,3,5-Tris(bicyclo[2.2.1]hepta-2,5-dien-2-yl)-2,4,6-trifluorobenzene (**1f**)

A mixture of 1,3,5-tribromo-2,4,6-trifluorobenzene (212 mg, 575 μmol), 4,4,5,5-tetramethyl-2-(bicyclo[2.2.1]heptadien-2-yl)-1,3,2-dioxaborolane (**1e**, 501 mg, 2.30 mmol), $\text{Pd}(\text{PPh}_3)_4$ (66.5 mg, 57.5 μmol , 5 mol %), THF (5.0 mL), and aq. NaOH (5.7 mmol, 2.7 M, 2.1 mL) was stirred at 80 °C for 16 h under anaerobic conditions [22]. After cooling the emulsion to room temperature, EtOAc (15 mL) was added and the organic layer was separated and dried with Na_2SO_4 . The drying agent was filtered off, the solvent was removed under reduced pressure, and the crude product was purified by column chromatography (SiO_2 , *n*-hexane, R_f = 0.44) and recrystallization from *n*-pentane. The product was obtained as colorless cubes (84.0 mg, 209 μmol , 36%); mp 107–109 °C; ^1H NMR (500 MHz, CDCl_3) δ 2.08 (dt, 2J = 6.0 Hz, 3J = 1.8 Hz, 3H, 7'-H, 7''-H, 7'''-H), 2.19 (dt, 2J = 6.0 Hz, 3J = 1.8 Hz, 3H, 7'-H, 7''-H, 7'''-H), 3.71 (br. s, 3H, 4'-H, 4''-H, 4'''-H), 3.89 (br. s, 3H, 1'-H, 1''-H, 1'''-H), 6.82 (dd, 3J = 5.0 Hz, 3J = 3.1 Hz, 3H, 5'-H, 5''-H, 5'''-H), 6.94 (dd, 3J = 5.0 Hz, 3J = 2.4 Hz, 3H, 6'-H, 6''-H, 6'''-H), 7.00 (d, 3J = 2.4 Hz, 3H, 3'-H, 3''-H, 3'''-H); ^{13}C NMR (125 MHz, CDCl_3) δ 50.7 (C4', C4'', C4'''), 54.6 (C1', C1'', C1'''), 73.1 (C7', C7'', C7'''), 111.2 (C1, C3, C5), 143.1 (C5', C5'', C5'''), 143.4 (C6', C6'', C6'''), 144.5 (C3', C3'', C3'''), 144.7 (C2', C2'', C2'''), 154.8 (dt, 1J = 251.0 Hz, 3J = 10.9 Hz, C2, C4, C6); ^{19}F NMR (470 MHz, CDCl_3) δ -112.1–112.2 (m, 3F, 2-F, 3-F, 6-F); APCIMS (*m/z*): $[\text{M} + \text{H}]^+$ 403; Anal. calcd for $\text{C}_{27}\text{H}_{21}\text{F}_3$: C, 80.58; H, 5.26; found: C, 80.51; H, 5.09.

General procedure (GP A) for the sensitized photocycloaddition reaction [48]

A solution of the norbornadiene (4.02–25.0 mg, 10.0–62.1 mmol) and the sensitizer $\text{Ir}(\text{ppy})_3$ or $[\text{Ru}(\text{phen})_3](\text{PF}_6)_2$ (5–10 mol %) in deaerated benzene or MeCN was irradiated with light (λ_{ex} = 420 or 520 nm) for 0.5–3 h. The solvent was removed under reduced pressure at 20 °C and the residue was suspended in *n*-pentane (10 mL) and filtered. The solvent was removed under reduced pressure at 20 °C.

1,3,5-Tris(tetracyclo[3.2.0.0^{2,7}.0^{4,6}]heptyl)-2,4,6-trifluorobenzene (**2f^{0,3}**)

Attempt 1: According to GP A, a solution of **1f** (4.02 mg, 10.0 μmol), $[\text{Ru}(\text{phen})_3](\text{PF}_6)_2$ (0.47 mg, 0.50 μmol , 5 mol %) in deaerated MeCN (10 mL) was irradiated with λ_{ex} = 520 nm

at rt for 30 min. The ^1H NMR-spectroscopic analysis showed no conversion of the starting material.

Attempt 2: According to GP A, a solution of **1f** (25.0 mg, 62.1 μmol), $\text{Ir}(\text{ppy})_3$ (4.08 mg, 6.21 μmol , 10 mol %) in deaerated benzene (4 mL) was irradiated with λ_{ex} = 420 nm at rt for 3 h. The product was obtained as an opaque viscous liquid (24.6 mg, 61.1 μmol , >95%). ^1H NMR (500 MHz, CDCl_3) δ 1.54–1.57 (m, 1H), 1.67 (ddd, 3J = 6.0 Hz, 3J = 4.5 Hz, 3J = 2.2 Hz, 1H), 1.73–1.78 (m, 1H), 1.84–1.89 (m, 1H), 2.10 (dt, 2J = 11.1 Hz, 3J = 1.4 Hz, 1H), 2.21 (dt, 3J = 4.5 Hz, 3J = 2.2 Hz, 1H), 2.24 (dt, 2J = 11.1 Hz, 3J = 1.4 Hz, 1H).

Supporting Information

Supporting Information File 1

Experimental section and copies of spectra.

[<https://www.beilstein-journals.org/bjoc/content/supplementary/1860-5397-22-38-S1.pdf>]

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Data Availability Statement

All data that supports the findings of this study is available in the published article and/or the supporting information of this article.

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