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Azidophosphonium salt directed chemoselective synthesis of (*E*)/(*Z*)-cinnamyl-1*H*-triazoles and regiospecific access to bromo-methyl coumarins from Baylis-Hillman adducts

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Abstract

Direct transformation of Baylis Hillman adducts into molecules of interest is a crucial process, thereby allylic hydroxy protected or halogenated BH adducts are commonly preferred. Herein, we report a azidophosphonium salt catalysed (QPS) straight forward protcol for synthesising structurally demanding (*E*) / (*Z*) cinnamyl-*1H*-1,2,3-triazoles and halomethyl coumarins from unaltered BH adducts. Novel methodology, efficient catalyst and direct utilization of BH adducts in presence mild reaction conditions identifies the reported procedures as a powerful synthetic tool.

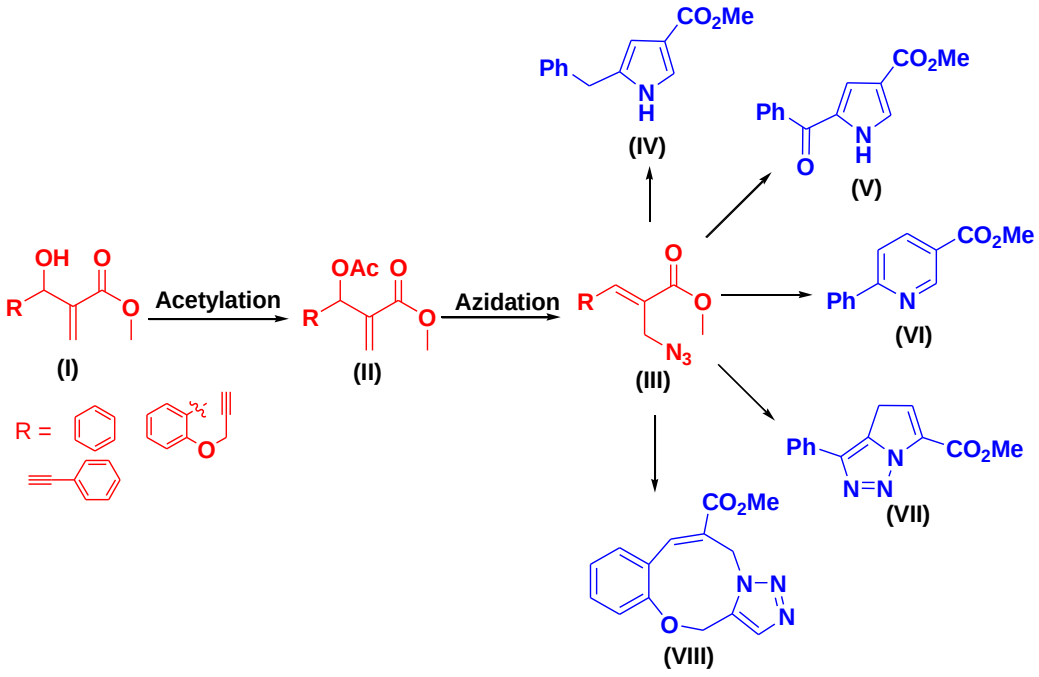
Introduction

The presence of rich functional groups in close proximity recognizes Baylis-Hillman adducts as key privileged scaffold among synthetic organic chemists. Accordingly, BH adduct has been explored as strategic intermediate for synthesis of interesting molecules such as carbamates of unsaturated β-amino acids,[1a] β-phenylsylfenyl-α-cyanohydrocinnamaldhydes,[1b] 2-carbonylalkyl-1-indals,[1c] dihydropyrazoles,[1d] tetrahydroacridines,[1e] γ-lactams,[1f] quinolin-5-ones,[1g] spiro-bisglutarimides,[1h] indolizines[1i] and spiro carbocyclic[1j] frameworks. However most of the reported synthetic transformations utilize either allylic hydroxyl protected or allyl halide substituted BH adducts.[2-4]

Among the known synthetic transformations using functionalized BH adducts, cycloaddition reactions are challenging and attractive among synthetic organic

chemists. In this context, acetate functionalized Baylis-Hillman adducts has been extensively utilized than other precursors. For example heterocycles such as, pyrroles (**IV**),[5a] keto pyrroles (**V**),[5b] pyridines (**VI**),[5c] pyrrolo triazoles (**VII**),[5d] and triazolo benzoxazonines (**VIII**)[5e] (**Scheme 1**) are the outcome of BH acetates. From these synthetic elaborations, three successive steps are universally utilized (i) acetylation, (ii) azidation and (iii) cycloaddition (**IV-VIII**). In spite of broad scope and synthetic utility, it is evident that the multi-step synthetic methodology is the only existing module for cycloaddition reactions.

Our research group has been focusing on developing one-pot synthetic transformations for complicated molecules.[6] Two individual research groups[7a,7b] have reported the multi-step pathway to access cinnamyl-1*H*- 1,2,3-triazole derivatives (IX) (Scheme 2) from acetates of BH adducts. The other preferable moiety for triazole transformation is the allyl halide of BH adducts however their (E) and (Z) isomers proximity limits their usage.[8] After a careful bibliographic investigation it was evident that one-pot protocols for direct transformation of BH adducts to cinnamyl triazoles had not been reported elsewhere.. The outcome of developing facile and economically useful one-pot synthetic strategy might also be worthwhile for pharmacologically important triazoles such as isavuconazole, tazobactum and ravuconazole.[9]

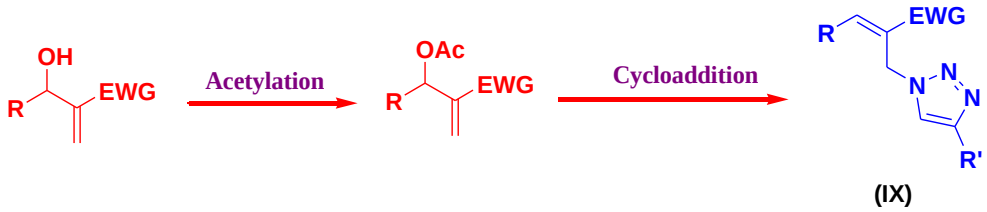


Scheme 1: Literature reported cycloaddition reactions of BH acetates involving azide and alkyne.[5a-e]

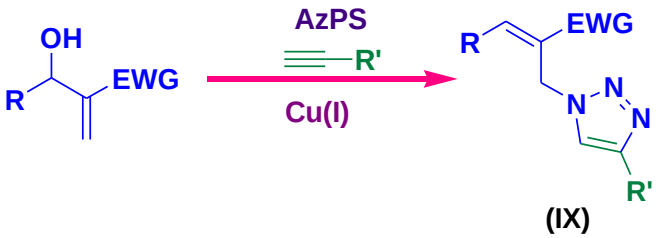
Results and discussion

Initially phosphonium salts were least utilised or exploited in a number of synthetic transformations. Later in 2014 phosphonium and quaternary phosphonium salts were widely employed as catalyst[10] for several organic transformations. Nevertheless their synthetic utility was not only confined as catalyst but also as intermediates for synthesis of 1*H*-indazoles,[11a] promoters for steroselective rearrangement[11b] and temporary protectors of O,P acetals[11c] which apparently branded them as promising motifs. Apart from these reports the convincingly Radosevich and co-workers[12] disclosed ethynylphosphonium salt as a facile reactant for synthesis of Z-enediynes. The above reports and the Lewis acid character of quarternary phosphonium salt (QPS)[13-16] recognizes them as reliable catalyst for the proposed methodology. The most studious process in the proposed methodology is the protection and elimination of allylic-OH. We believed this crucial strategy could be primarily resolved by quaternary phosphonium salt. After initial screening of various quaternary phosphonium salts we finally concluded the azido-phosphonium salt $[Ph_3P^+\text{-}CBr_3]N_3^-$ reported by Blanco and co-workers to accomplish our goal.[17-19] The azido-phosphonium salt (AzPS) surprisingly synchronised with functional and structural requirements of the proposed work. Therefore the azido-phosphonium salt was generated and purified accordingly to a modified literature procedure.[17]

a) Literature reported indirect triazolation of BH adducts.[7]



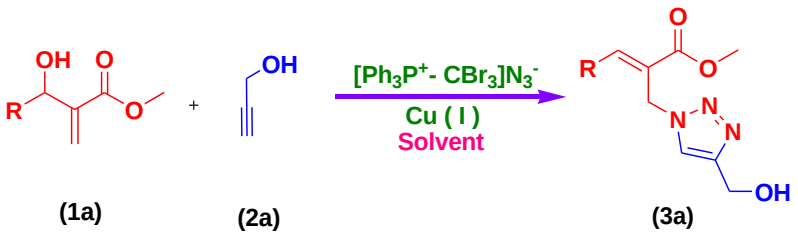
b) This work: Phosphonium salt catalysed triazolation of BH adducts.



Scheme 2: Synthetic methodologies for triazolation of BH adducts

The one-pot model reaction was investigated using BH adduct **1a** (1 equiv.), propargyl alcohol **2a** (1.2 equiv.) in presence of quaternary phosphonium salt (AzPS) $[Ph_3P^+$-$CBr_3]N_3^-$ and Cu(I). In this precedent reaction the adduct (1a) and propargyl alcohol (2a) in THF was treated with AzPS (1 equiv.), and CuI (3 mol %) at room temperature. To our expectations the reaction affords (*E*)-cinnamyl-1*H*-1,2,3-triazole at a very low yield of 24% (entry 1). Thereby we anticipated that an increase in the proportion of AzPS to substantially increase the yield of 3a (entry 2 & 3), unexpectedly the reaction demonstrated unsatisfactory yield. However on attempting the reaction with an improved ratio of CuI (5 mol %) and AzPS (2 equiv.) the expected product 3a was obtained at a moderate yield (71%, entry 4). However, a further increase in the ratio of AzPS ascertained a gradual decrease in the yield of 3a (entry 5 & 6). The outcome of this analysis might be due to the plethora of by-product, triphenylphosphine oxide which impediments the purification process and declines the yield of 3a. In due time alternative Cu(I) catalysts, CuCl and CuBr were also attempted at 5 mol%, however the combination shows no potential increase in the yield of 3a (entry 7 & 8). Comprehensive investigations reveal AzPS (2 equiv.) and CuI (5 mol %) as the optimized catalytic combination. Further the optimized reaction was screened in presence of various solvents, (entry 9-13) and the outcome divulges acetonitrile (3a, 83%) as the most preferable solvent. Interestingly, the efficiency of this reaction (entry 11) did not reduce even at high dilution of the solvent.

Table 1: Optimization of triazolation in BH adducts (1a)

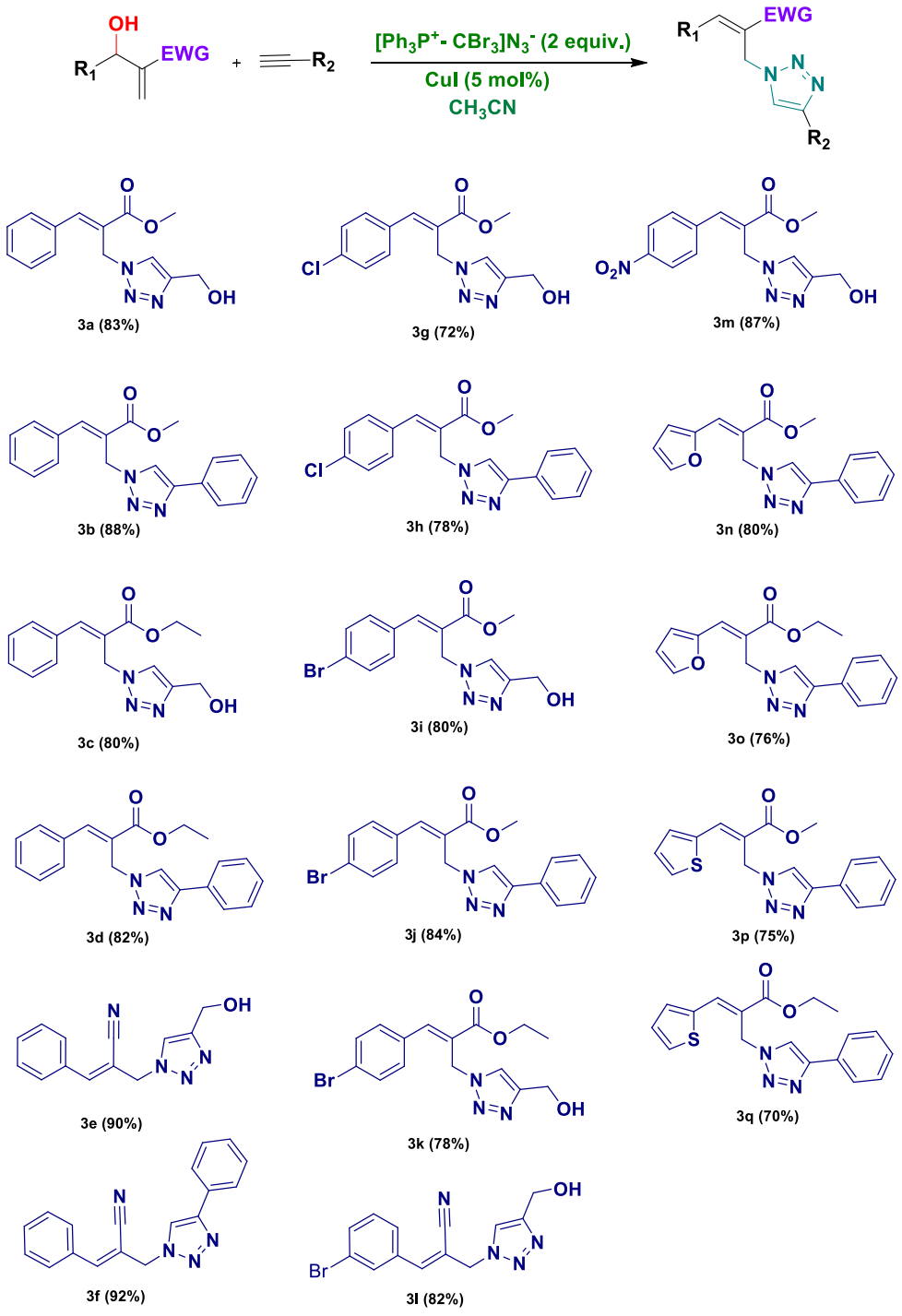


(1a) (2a) (3a)

Entry	Quat.phosph.salt (equiv.)	Cu(I) (mol%)	Solvent	Yield (%)
1.	AzPS (1)	CuI (3)	THF	24
2.	AzPS (1.5)	CuI (3)	THF	33
3.	AzPS (2)	CuI (3)	THF	42
4.	AzPS (2)	CuI (5)	THF	71
5.	AzPS (3)	CuI (5)	THF	45
6.	AzPS (4)	CuI (5)	THF	36
7	AzPS (2)	CuCl (5)	THF	47

8.	AzPS (2)	CuBr (5)	THF	54
9.	AzPS (2)	CuI (5)	EtOAc	66
10.	AzPS (2)	CuI (5)	Acetone	69
11.	**AzPS (2)**	**CuI (5)**	**CH_3CN**	**83**
12.	AzPS (2)	CuI (5)	DMF	64
13.	AzPS (2)	CuI (5)	DMSO	69

Table 2. Scope of the one-pot cascade reaction of unprotected Baylis-Hillman adducts (3a-q)



The substrate scope of the optimized reaction and its limitations was further extended to structurally distinct BH adducts (**Table 2**). BH-adducts derived from methoxy and ethoxy acrylates, stereochemically affords (*E*)-cinnamyl 1,4-disubstituted 1,2,3-triazole derivatives (**3a-d, 3g-k, & 3m-q**) at a yield of 70%-88%. Distinctly the cyano acrylate substituted BH adduct, stereoselectively affords (*Z*)-cinnamyl 1,4-disubstituted 1,2,3-triazole derivatives (**3e, 3f & 3l**) at a yield of 82-92%. In general irrespective of the acetylene moiety, BH adducts derived from acrylonitrile affords cinnamyl 1,4-disubstituted 1,2,3-triazole derivatives at an improved yield to that of methyl and ethyl counterparts. Notably BH adducts derived from *para*-bromo, *para*-chloro and *para*-nitro benzaldehydes favourably assisted the formation of the corresponding (*E*)-cinnamyl 1,4-disubstituted 1,2,3-triazole derivatives (**3g-m**) at a yield of 72-87%. Alternatively, *ortho*- and *meta*- substituted aryl BH-adducts were hostile towards the optimized reaction condition, and it presumably may be due to the apparent steric hindrance. Similarly BH adducts derived from salicylaldehydes and methyl or methoxy substituted benzaldehydes were also inert under the optimized reaction condition. Therefore it is evident that electronic variation of substituents on aromatic moiety of the BH adducts plays a crucial role in determining the outcome of the products. Similarly the aliphatic aldehydes were inert to the current reaction. We further extended the scope of this transformation to five membered heterocyclic BH adducts. To our delight except pyrroles the proposed methodology was amenable to BH adducts of furan and thiophene (**3n-q,** 70-80%).

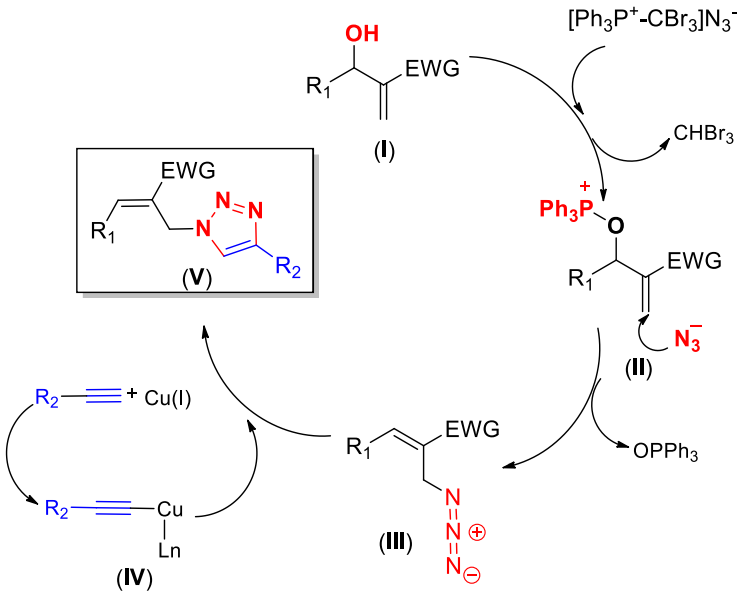
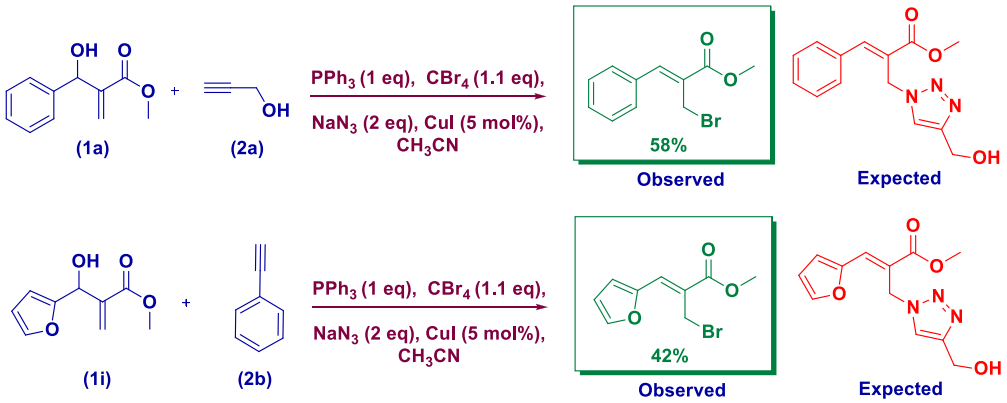


Figure 1: Proposed mechanism for the synthesis of 1,4-disubstituted triazoles.

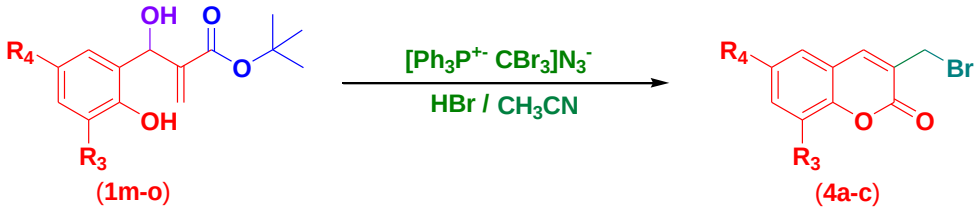
The mechanistic pathway for triazolation proceeds *via* nucleophillic attack of phosphonium ion (AzPS) by the allylic alcohol of BH adducts (**I**) to furnish facile oxy-phosphonium (**II**). Subsequently the azide ion (N_3^-) undergoes nucleophillic attack at the allylic carbon generating 2-azido alkene (**III**). Interestingly, the consecutive nucleophillic attack by azido ion (N_3^-) smoothly initiates the allylic rearrangement which thereby facilitates the facile removal of crucial phosphonium oxide. The outcome of this process is the structurally relevant azido moiety (**III**) which undergoes 1,3-dipolar cycloaddition with copper acetylide (**IV**) to furnish 1,4-disubstituted 1,2,3-triazoles (**V**) (Fig 1).



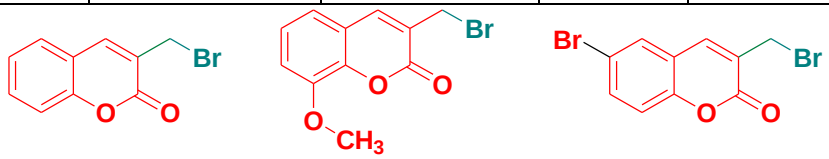
Scheme 3: Comparative analysis of sequential one-pot reaction

At this stage we sought to analyse the outcome of the proposed reaction for a sequential addition of the reagents utilised for synthesis of azido-phosphoium salt (AzPS). Therefore a preliminary investigation was attempted using BH adduct **1a** (1 equiv.), and propargyl alcohol **2a** (1.2 equiv.) in presence of CuI (5 mol%), triphenyl phosphine (1 equiv.), bromomethane (1.1 equiv.) and sodium azide (2 equiv.). Unexpectedly the reaction yields (Z)-methyl 2-(bromomethyl)-3-phenylacrylate (58%) over the expected triazoles. Similarly BH adducts derived from furan (**1i**) and phenyl acetylene (**2b**) also yields (Z)-methyl 2-(bromomethyl)-3-(furan-2-yl)acrylate (42%) rather than the triazoles (scheme 3). Thereby it is clearly evident that addition of individual reagents is void of delivering the complicated triazoles.

Table 3: Optimization of 3-bromomethyl coumarins from BH adducts



Entry	AzPS (equiv.)	HBr (equiv.)	Solvent	Yield (%)
1.	2	-	CH_3CN	-
2.	2	1	CH_3CN	33
3.	**2**	**2**	**CH_3CN**	**78**
4.	2	3	CH_3CN	62
5.	2	4	CH_3CN	31
6.	3	2	CH_3CN	65
7.	4	2	CH_3CN	57



Interestingly BH adducts derived from salicylaldehydes being inert to triazolation smoothly affords bromomethyl coumarin in presence of AzPS and HBr. The reaction was optimized using salicylaldehyde (1 equiv.) as a trial molecule in presence of AzPS (2 equiv.) and HBr (2.0 equiv.). The reaction affords 3-bromomethyl coumarin at a yield of 78 % (Table 3). The synthetic utility of the reaction was further extended to *ortho*-vanillin and *para*-bromomethyl coumarin to afford the corresponding halomethyl coumarins. However this regiospecific transformation is restricted only to BH adducts derived from salicyladehydes and *tert*-butyl acrylates rather than its methyl and ethyl counterparts.[20] Among the reported methodologies[21] on synthesis of halomethyl coumarins, the present methodology is attractive for its good yield under simplistic reaction conditions.

As shown in figure 2 the mechanistic pathway for 4a-c progress via temporary protection of allylic-OH (I) in presence of phosphine moiety of AzPS, where the counterion bromine facilitates the nucleophillic attack at the vinylic centre (II) and facilitates spontaneous deprotection of phosphine oxide and hydrazoic acid. A consecutive intramolecular nucleophilic attack of the hydroxyl moiety at the carbonyl

carbon (III) further drives the cyclisation & subsequent deprotection (IV) to afford bromomethyl coumarin (V).

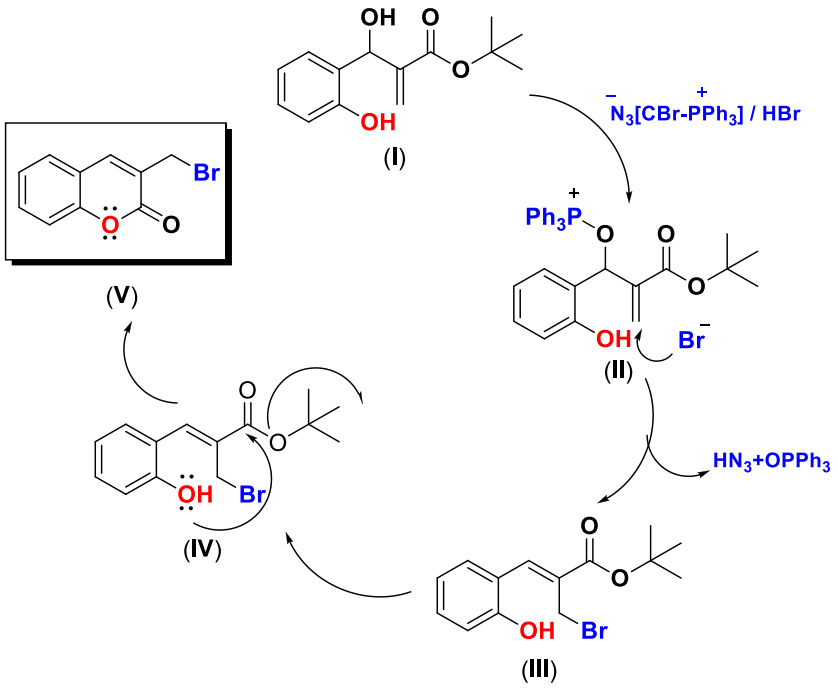


Figure 2: Proposed mechanism of the synthesis of 3-bromo methyl coumarins.

Conclusions

In summary we have reported the first protocol on quaternary phosphonium salt mediated direct synthesis of cinnamyl triazoles and 3-bromomethyl coumarins from Baylis Hillman adducts. On contrast to the contending reports on synthesis of 1,2,3-triazoles and halomethyl coumarins from BH adducts, our studies report moderate reaction conditions with improved yield. The above investigation provides a useful synthetic tool for synthetic organic chemists. Synthesis of biologically important triazoles using the reported methodology is underway in our laboratory.

Experimental Section

A. General Information: Chemicals were purchased from Sigma Aldrich, Spectrochem (P) Ltd., Central Drug House (P) Ltd., Rankem, India and were used without further purification. The solvents were purified by standard procedures. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance 300 MHz spectrometer using $CDCl_3$ and DMSO-d_6 as the solvent with tetramethylsilane (TMS) as an internal standard at room temperature. Chemical shifts are given in δ relative to TMS. High-

resolution mass spectra were recorded on an Agilent Technologies 6540 UHD Accurate-Mass Q-TOF LC/MS spectrometer. Melting point data are uncorrected. The compounds were purified using column chromatography on silica gel (100–200 mesh) using hexane:ethyl acetate and chloroform:methanol as eluent.

B. Typical Procedure for quaternary phosphonium salt:

Typically, triphenyl phosphine, bromomethane and sodium azide at an equivalence ratio of 1.1: 1.1: 5 was utilized for synthesising the quaternary phosphonium salt. Initially triphenylphosphine and sodium azide were stirred at 0°C in dimethylformamide (5mL) for 30 minutes. To the mixture bromomethane in DMF was added slowly to avoid sudden increase in temperature. The reaction was slowly warmed to room temperature and stirred for another 30 minutes. Finally the reaction was quenched with addition of diethyl ether. The filtration of insoluble inorganic salts results in transparent liquid which on concentration by evaporation results in a crude oily residue. The residue was dissolved in ethyl acetate, washed with brine and dried over sodium sulphate to yield a clear oily residue of quaternary phosphonium salt.

B. Typical Procedure (3a-3q)

A solution of AzPS (2 equiv.) in acetonitrile (5mL) was added to a solution of Baylis-Hillman adduct 1a (1 equiv.) in acetonitrile (3mL). The reaction mixture was then stirred for an hour, to which 1.2 equiv of propargyl alcohol and CuI (5 mol%) were added. The reaction mixture was stirred for another 4 hours and followed by TLC. After the completion of the reaction the solution was concentrated, diluted and extracted with EtOAc. The combined extracts were washed with brine, filtered through celite bed and dried over anhydrous Na_2SO_4. Thereafter the solvent was removed and the isolated crude oily product was purified over silica gel ($CHCl_3$:MeOH) to acquire 3a as a white solid.

(*E*)-Methyl-2-((4-hydroxymethyl)-1*H*-1,2,3-triazol-1-yl)methyl)-3-phenylacrylate (3a)

Yield: 295 mg (83%); white solid; mp 92-94 °C.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 3.83 (s, 3H, estr-CH_3), 4.78 (s, 2H, Trz-CH_2), 5.37 (s, 2H, Trz-CH_2OH), 7.43-7.45 (m, 3H, Aro-H), 7.61-7.64 (m, 2H, Aro-H), 7.74 (s, 1H, Trz-CH), 8.08 (s, 1H, Alkene-CH).

^{13}C NMR ($CDCl_3$, 300 MHz): δ = 47.23, 52.98, 56.75, 123.15, 125.30, 129.39, 130.07, 130.43, 133.91, 146.44, 147.84, 167.52.

HRMS: m/z Calcd for $C_{14}H_{15}N_3O_3$ $[M+H]^+$: 274.1113; found: 274.1136.

(*E*)-Methyl-3-phenyl-2-((4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl)acrylate (3b)

Yield: 365 mg (88%); yellowish white solid; mp 114-116 °C.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 3.84 (s, 3H, estr-CH_3), 5.42 (s, 2H, Trz-CH_2), 7.38-7.48 (m, 5H, Aro-H), 7.68-7.85 (m, 5H, Aro-H), 7.98 (s, 1H, Trz-CH), 8.10 (s, 1H, Alkene-CH).

^{13}C NMR ($CDCl_3$, 300 MHz): δ = 47.34, 53.02, 121.20, 125.39, 126.14, 126.50, 128.54, 129.22, 129.33, 129.41, 130.18, 130.46, 133.95, 146.55, 147.92, 167.69.

HRMS: m/z Calcd for $C_{19}H_{17}N_3O_2$ $[M+H]^+$: 320.1321; found: 320.1311.

(*E*)-Ethyl-2-((4-hydroxymethyl)-1*H*-1,2,3-triazol-1-yl)methyl)-3-phenylacrylate (3c)

Yield: 278 mg (80%); white solid; mp 81-83 °C.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.30-1.34 (t, *J* = 6 Hz, 3H, estr-CH_3), 3.50 (s, 1H, CH_2-OH), 4.24-4.31 (q, *J* = 6Hz, 2H, estr-CH_2), 4.78 (s, 2H, Trz-CH_2), 5.36 (s, 2H, Trz-CH_2OH), 7.41-7.61 (m, 5H, Aro-H), 7.74 (s, 1H, Trz-CH), 8.07 (s, 1H, Alkene-CH).

^{13}C NMR ($CDCl_3$, 300 MHz): δ = 14.59, 47.22, 56.73, 62.03, 123.14, 125.64, 129.35, 130.04, 130.32, 133.99, 146.09, 147.86, 167.02.

HRMS: m/z Calcd for $C_{15}H_{17}N_3O_3$ $[M+H]^+$: 288.1270; found: 288.1258.

(*E*)-Ethyl-3-phenyl-2-((4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl)acrylate (3d)

Yield: 331 mg (82%); white crystals; mp 100-102 °C.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.29-1.34 (t, *J* = 6 Hz, 3H, estr-CH_3), 4.24-4.31 (q, *J* = 6 Hz, 2H, estr-CH_2), 5.40 (s, 2H, Trz-CH_2), 7.30-7.85 (m, 10H, Aro-H), 7.98 (s, 1H, Trz-CH), 8.08 (s, 1H, Alkene-CH).

^{13}C NMR ($CDCl_3$, 300 MHz): δ = 14.60, 47.27, 61.95, 121.10, 125.92, 126.09, 128.40, 129.16, 129.33, 130.10, 130.27, 131.19, 134.12, 145.99, 147.82, 167.04.

HRMS: m/z Calcd for $C_{20}H_{19}N_3O_2$ $[M+H]^+$: 334.1477; found: 334.1453.

(*Z*)-2-((4-(hydroxymethyl)-1*H*-1,2,3-triazol-1-yl)methyl)-3-phenylacrylonitrile (3e)

Yield: 339 mg (90%); yellowish solid; mp 103-105 °C.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.86 (s, 1H, Trz-CH_2-OH), 4.53 (s, 2H, Trz-CH_2), 5.09 (s, 2H, Trz-CH_2-OH), 7.15 (s, 1H, Alkene-CH), 7.22-7.55 (m, 5H, Aro-H), 7.64 (s, 1H, Trz-CH).

^{13}C NMR ($CDCl_3$, 300 MHz): δ = 58.51, 61.15, 110.21, 122.11, 127.67, 134.16, 134.36, 136.57, 137.46, 153.20, 154.41.

HRMS: m/z Calcd for $C_{13}H_{12}N_4O$ $[M+H]^+$: 241.1011; found: 241.1023.

(*Z*)-3-phenyl-2-((4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl)acrylonitrile (3f)

Yield: 413 mg (92%); white crystals; mp 128-130 °C.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 5.30 (s, 2H, Trz-CH_2), 7.33-7.84 (m, 10H, Aro-H), 7.87 (s, 1H, Alkene-CH), 7.98 (s, 1H, Trz-CH).

^{13}C NMR ($CDCl_3$, 300 MHz): δ = 54.03, 104.94, 117.41, 120.28, 126.25, 128.88, 129.32, 129.49, 129.71, 130.52, 132.04, 132.48, 148.56, 149.01.

HRMS: m/z Calcd for $C_{18}H_{14}N_4$ $[M+H]^+$: 287.1218; found: 287.1209.

(*E*)-Methyl-3-(4-chlorophenyl)-2-((4-(hydroxymethyl)-1*H*-1,2,3-triazole-1-yl)methyl)acrylate (3g)

Yield: 244 mg (72%); white solid; mp 125-127 °C.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 3.38 (s, 1H, Trz-CH_2OH), 3.82 (s, 3H, estr-CH_3), 4.77 (s, 2H, Trz-CH_2), 5.31 (s, 2H, Trz-CH_2OH), 7.40-7.43 (d, *J* = 9 Hz, 2H, Aro-H), 7.61-7.63 (d, *J* = 6 Hz, 2H, Aro-H), 7.75 (s, 1H, Trz-CH), 7.99 (s, 1H, Alkene-CH).

^{13}C NMR ($CDCl_3$, 300 MHz): δ = 47.03, 52.99, 56.74, 123.32, 125.95, 129.65, 131.45, 132.33, 136.60, 144.88, 167.27.

HRMS: m/z Calcd for $C_{14}H_{14}ClN_3O_3$ $[M+H]^+$: 308.0724; found: 308.0719.

(*E*)-Methyl-3-(4-chlorophenyl)-2-(4-phenyl-1*H*-1,2,3-triazole-1-yl)methyl)acrylate (3h)

Yield: 304 mg (78%); white solid; mp 141-143 °C.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 3.76 (s, 3H, estr-CH_3), 5.29 (s, 2H, Trz-CH_2), 7.33-7.38 (m, 5H, Aro-H), 7.62-7.65 (d, *J*= 9Hz, 2H, Aro-H), 7.80-7.82 (d, *J*= 6Hz, 2H, Aro-H), 7.93 (s, 1H, Trz-CH), 8.01 (s, 1H, Alkene-CH).

^{13}C NMR ($CDCl_3$, 300 MHz): δ = 47.11, 53.00, 121.67, 125.95, 126.05, 128.53, 129.22, 129.56, 130.92, 131.60, 132.40, 136.41, 144.77, 147.76, 167.29.

HRMS: m/z Calcd for $C_{19}H_{16}ClN_3O_2$ $[M+H]^+$: 354.0931; found: 354.0928.

(*E*)-Methyl-3-(4-bromophenyl)-2-((4-(hydroxymethyl)-1*H*-1,2,3-triazol-1-yl)methyl)acrylate (3i)

Yield: 259 mg (80%); white solid; mp 116-118 °C.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 3.83 (s, 3H, estr-CH_3), 4.79 (s, 2H, Trz-CH_2), 5.32 (s, 2H, Trz-CH_2OH), 7.58 (s, 4H, Aro-H), 7.77 (s, 1H, Trz-CH), 7.98 (s, 1H, Alkene-CH).

^{13}C NMR ($CDCl_3$, 300 MHz): δ = 47.05, 53.07, 56.63, 123.46, 124.98, 125.98, 131.66, 132.64, 132.75, 144.99, 147.82, 167.28.

HRMS: m/z Calcd for $C_{14}H_{14}BrN_3O_3$ $[M+H]^+$: 352.0219; found: 352.0210.

(*E*)-Methyl-3-(4-bromophenyl)-2-((4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl)acrylate (3j)

Yield: 308 mg (84%); yellow solid; mp 132-134 °C.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 3.85 (s, 3H, estr-CH_3), 5.38 (s, 2H, Trz-CH_2), 7.34-7.86 (m, 9H, Aro-H), 8.01 (s, 1H, Trz-CH), 8.02 (s, 1H, Alkene-CH).

^{13}C NMR ($CDCl_3$, 300 MHz): δ = 47.13, 53.07, 121.40, 125.02, 126.10, 128.55, 129.22, 130.94, 131.77, 132.65, 132.80, 145.02, 147.91, 167.40.

HRMS: m/z Calcd for $C_{19}H_{16}BrN_3O_2$ $[M+H]^+$: 398.0426; found: 398.0435.

(*E*)-Ethyl-3-(4-bromophenyl)-2-((4-(hydroxymethyl)-1*H*-1,2,3-triazol-1-yl)methyl)acrylate (3k)

Yield: 250 mg (78%); white solid; mp 110-112 °C.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.30-1.34 (t, *J* = 6 Hz, 3H, estr-CH_3), 3.09 (s, 1H, CH_2-OH), 4.23-4.31 (q, *J* = 9 Hz, 2H, estr-CH_2), 4.78 (s, 2H, Trz-CH_2), 5.31 (s, 2H, Trz-CH_2-OH), 7.57-7.64 (m, 4H, Aro-H), 7.75 (s, 1H, Trz-CH), 7.97 (s, 1H, Alkene-CH).

^{13}C NMR ($CDCl_3$, 300 MHz): δ = 14.60, 47.06, 56.78, 62.17, 123.42, 124.90, 126.29, 131.65, 132.62, 132.83, 144.69, 147.82, 166.80.

HRMS: m/z Calcd for $C_{15}H_{16}BrN_3O_3$ $[M+H]^+$: 366.0375; found: 366.0383.

(*Z*)-3-(4-bromophenyl)-2-((4-(hydroxymethyl)-1*H*-1,2,3-triazol-1-yl)methyl)acrylonitrile(3l)

Yield: 274 mg (82%); white solid; mp 114-116 °C.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 4.65 (s, 2H, Trz-CH_2), 5.17 (s, 2H, Trz-CH_2-OH), 7.28-7.31 (d, *J* = 9 Hz, 2H, Aro-H), 7.39 (s, 1H, Alkene-CH), 7.48-7.51, (d, *J* = 9 Hz, 2H, Aro-H), 7.69 (s, 1H, Trz-CH).

^{13}C NMR ($CDCl_3$, 300 MHz): δ = 48.01, 56.34, 109.87, 118.21, 123.04, 125.43, 131.23, 132.69, 134.36, 147.93, 149.54.

HRMS: m/z Calcd for $C_{13}H_{11}BrN_4O$ $[M+H]^+$: 319.0116; found: 319.0125.

(*E*)-Methyl-2-((4-(hydroxymethyl)-1*H*-1,2,3-triazol-1-yl)methyl)-3-(4-nitrophenyl)acrylate (3m)

Yield: 291 mg (87%); yellow solid; mp 143-145 °C.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.77 (s, 1H, Trz-CH_2OH), 3.86 (s, 3H, estr-CH_3), 4.80 (s, 2H, Trz-CH_2), 5.29 (s, 2H, Trz-CH_2-OH), 7.78 (s, 1H, Trz-CH), 7.90-7.92 (d, *J* = 6 Hz, 2H, Aro-H), 8.06 (s, 1H, Alkene-CH), 8.30-8.33 (d,*J* = 9 Hz, 2H, Aro-H).

^{13}C NMR ($CDCl_3$, 300 MHz): δ = 46.67, 53.16, 56.56, 123.61, 124.34, 128.70, 130.86, 140.31, 143.04, 148.46, 148.60, 166.53.

HRMS: m/z Calcd for $C_{14}H_{14}N_4O_5$ $[M+H]^+$: 319.0964; found: 319.0954.

(*E*)-Methyl-3-(furan-2-yl)-2-((4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl)acrylate (3n)

Yield: 339 mg (80%); reddish oil.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 3.84 (s, 3H, estr-CH_3), 5.74 (s, 2H, Trz-CH_2), 6.56 (s, 1H, Het-H), 6.98 (s, 1H, Aro-H), 7.30-7.32 (d, *J* = 6Hz, 1H, Het-H), 7.37-7.42 (m, 2H, Aro-H), 7.64 (s, 1H, Trz-CH), 7.73 (s, 1H, Alkene-CH), 7.79-7.82 (m, 2H, Aro-H), 7.84 (s, broad, 1H, Het-H).

^{13}C NMR ($CDCl_3$, 300 MHz): δ = 47.19, 53.03, 113.20, 119.94, 120.31, 126.11, 128.44, 129.15, 130.99, 131.27, 146.86, 150.15, 167.78.

HRMS: m/z Calcd for $C_{17}H_{15}N_3O_3$ $[M+H]^+$: 310.1113; found: 310.1122.

(*E*)-Ethyl-3-(furan-2-yl)-2-((4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl)acrylate (3o)

Yield: 313 mg (76%); yellowish solid; mp 95-97 °C.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.28-1.32 (t, *J* = 6Hz, 3H, estr-CH_3), 4.23-4.29 (q, *J* = 6Hz, 2H, estr-CH_2), 5.72 (s, 2H, Trz-CH_2), 6.54 (s, 1H, Het-H), 6.97 (s, 1H, Aro-H), 7.30-7.39 (m, 3H, Aro-H& Het-H), 7.61 (s, 1H, Trz-CH), 7.71 (s, 1H, Alkene-CH), 7.78-7.81 (m, 2H, Aro-H), 7.85 (s, broad, 1H, Het-H).

^{13}C NMR ($CDCl_3$, 300 MHz): δ = 14.65, 47.11, 61.98, 113.16, 119.71, 120.21, 120.73, 126.02, 128.32, 129.12, 130.90, 131.19, 146.71, 147.75, 150.20, 167.22.

HRMS: m/z Calcd for $C_{18}H_{17}N_3O_3$ $[M+H]^+$: 324.1270; found: 324.1256.

(*E*)-Methyl-2-((4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl)-3-(thiophen-2-yl)acrylate (3p)

Yield: 307 mg (75%); yellowish solid; mp 107-109 °C.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 3.87 (s, 3H, estr-CH_3), 5.63 (s, 2H, Trz-CH_2), 7.19 (m, 1H, Aro-H), 7.34 (m, 1H, Het-H), 7.41-7.42 (m, 2H, Aro-H), 7.61 (s, 1H, Trz-CH), 7.70 (s, 1H,Alkene-CH), 7.82-7.84 (m, 2H, Aro-H), 7.90 (m, 1H, Het-H), 8.17 (s, 1H, Het-H).

^{13}C NMR ($CDCl_3$, 300 MHz): δ = 30.10, 53.09, 120.23, 128.47, 128.90, 129.16, 129.33, 130.98, 132.11, 134.69, 136.72, 138.28, 148.00, 167.80.

HRMS: m/z Calcd for $C_{17}H_{15}N_3O_2S$ $[M+H]^+$: 326.0885; found: 326.0879.

(*E*)-Ethyl-2-((4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl)-3-(thiophen-2-yl)acrylate (3q)

Yield: 279 mg (70%); yellow oil.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.37-1.41 (t, *J* = 6Hz, 3H, estr-CH_3), 4.35-4.41 (q,*J* = 6Hz, 2H, estr-CH_2), 4.47 (s, 2H, Trz-CH_2), 7.40 (s, 1H, Aro-H), 7.42 (s, 1H, Het-H), 7.46 (s, 1H, Aro-H), 7.48 (s, 1H, Aro-H), 7.50 (s, 1H, Het-H), 7.84 (s, 1H, Trz-CH), 7.86 (s, 1H, Alkene-CH), 7.91-7.93 (m, 1H, Aro-H), 8.01 (s, 2H, Aro-H& Het-H),

^{13}C NMR ($CDCl_3$, 300 MHz): δ = 14.28, 46.98, 61.06, 125.75, 126.14, 126.60, 128.75, 129.00, 131.06, 131.64, 133.13, 134.26, 134.97, 137.70, 147.08, 166.98.

HRMS: m/z Calcd for $C_{18}H_{17}N_3O_2S$ $[M+H]^+$: 340.1041; found: 340.1029.

Typical Procedure (4a-c)

To a mixture of Baylis-Hillman adduct (1 equiv.) and AzPS (2 equiv.) in the acetonitrile (3mL), HBr (2 equiv.) was added carefully at room temperature. After 2hours the reaction mixture was quenched with water (20 mL) and then extracted with ethyl acetate. The organic layer was washed with brine and dried over anhydrous $MgSO_4$. Removal of solvent under vacuo affords the crude product which was purified over silica gel (using Hexane:EtOAc) to acquire 4a as white crystal.

3-(bromomethyl)-2*H*-chromen-2-one (4a)

Yield: 186 mg (78%); White crystal; mp 112-114 °C.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 4.55-4.57 (d, *J* = 6Hz, 2H, CH_2-Br), 7.31-7.57 (m,4H, Aro-H), 7.89-7.91 (d,*J* = 6Hz, 1H, Alkene-CH).

^{13}C NMR ($CDCl_3$, 300 MHz): δ = 41.49, 117.02, 119.16, 125.14, 125.33, 128.50, 132.45, 141.62, 153.90, 160.47.

HRMS: m/z Calcd for $C_{10}H_7BrO_2$ $[M+H]^+$: 238.9629; found: 238.9618.

3-(bromomethyl)-8-methoxy-2*H*-chromen-2-one (4b)

Yield: 208 mg (87%); White crystals; mp 151-153 °C.

^{1}H NMR (DMSO-D_6, 300 MHz): δ = 3.92 (s, 3H, Aro-O-CH_3), 4.63 (s, 2H, CH_2-Br), 7.31-7.32 (m, 3H, Aro-H), 8.22 (s, 1H, Alkene-CH).

^{13}C NMR (DMSO-D_6, 300 MHz): δ = 42.02, 56.61, 115.10, 119.63, 120.28, 125.22, 125.26, 143.01, 143.23, 146.88, 159.50.

HRMS: m/z Calcd for $C_{11}H_9BrO_3$ $[M+H]^+$: 267.9735; found: 267.9724.

6-bromo-3-(bromomethyl)-2*H*-chromen-2-one (4c)

Yield: 181 mg (75%); White crystals; mp 125-127 °C.

^{1}H NMR (CDCl3, 300 MHz,): δ = 4.42 (s, 2H, CH_2-Br), 7.23-7.25 (d, *J* = 6 Hz, 1H, Aro-H), 7.61-7.62 (d, *J* = 3Hz, 1H, Aro-H), 7.65 (s, 1H, Aro-H), 7.79 (s, 1H, Alkene-CH).

^{13}C NMR (CDCl3, 300 MHz,): δ = 27.14, 117.31, 118.47, 120.40, 126.79, 130.29, 134.87, 140.49, 152.53, 159.22.

HRMS: m/z Calcd for $C_{10}H_6Br_2O_2$ $[M+H]^+$: 317.8714; found: 317.8703.

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Conflicts of interest

There are no conflicts to declare

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