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Unexpected synthesis and structure of a cage-like aza[3,3,3]propllane carbene

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Abstract

A stable, propeller-like *N*-heterocyclic cage carbene with a protective umbrella was unexpectedly synthesized in the hydrogen proton transfer catalytic hydrogenolysis. Its structural and spectral characteristics are obviously different from those of conventional imidazolin-2-ylidenes. Two nitrogen atoms of aza[3,3,3] propllenan-2-ylidene ring are in a plane environment.

Keywords

NHC-carbene; stable; synthesis; structure; aza[3,3,3]propllane

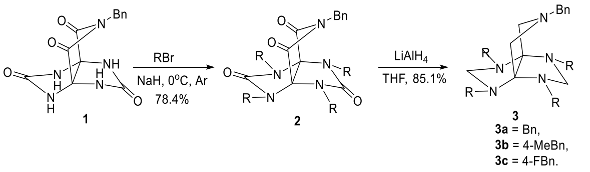
Introduction

Fused azacyclic cage structures have emerged as the key skeletons for Functional materials, especially high-energy-density compounds (HEDCs) such as 4,10-dinitro-2,6,8,12-tetraoxa-4,10-diazaisowur-tzitane, TEX) [1], 2,4,6,8,10,12-hexanitro-2,4,6,8,10,12-hexaazaiso-wurtzitane (HNIW, CL-20) [2], 2,4,9-trinitro-2,4,9-triaza-adamantane [3]. In 2014, Kim et al [4] successfully synthesized 2,4,6,8,10-pentabenzyl-2,4,6,8,10-pentaaza[3.3.3]propellane **3a**. Due to the suitable ring strain, high symmetry and a maximum nitrogen content of this skeleton, it can be a core building block to satisfy high energy density requirements of high energy compound after debenzylation followed by nitration of **3a**. So we studied systematically the debenzylation of compound **3a**. It is surprising that the high resolution mass spectrum of white debenzylation product **4a** of pentabenzylpentaaza[3.3.3]propellane was not the signal of expected debenzylation product, but the signal of losing a molecule of H2. What is this product? How to get it? Fortunately, we have successfully obtained a single crystal of **4a**, which shows that it is a new and very stable cage-like aza[3,3,3]propllenan-2-ylidene carbene. Here, we will report these results in detail.

Results and Discussion

In order to obtain a variety of multisubstituted azaspironanes, a modified synthetic strategy for suitable precursors [4] was developed (Scheme 1). Polysubstituted

3,7,9,11-tetraoxo-2,4,6,8,10-pentaaza-[3.3.3]propellanes **2** were obtained by the alkylation of 10-benzyl-3,7,9,11-tetraoxo-2,4,6,8,10-pentaaza [3.3.3]propellane **1** with RX in the catalyst of NaH at 0 ^{o}C in a mixed solvent of DMF/DMSO, and then the carbonyl groups of **2** were reduced by lithium aluminum hydride in tetrahydrofuran (THF) at low temperature to provide three pentaaza[3.3.3] propellane derivatives with different N-substituted benzyl groups **3** (Scheme 1).



Scheme 1: The modified syntheses of fully substituted 2,4,6,8,10-pentaaza[3.3.3] propellanes.

2,4,6,8,10-Pentabenzyl-2,4,6,8,10-pentaaza[3.3.3]propellane **3a** is a white solid with a melting point of 142-144 ^{o}C. Due to some flaws in the structure of **3a** reported by Kim [4] and the comparison of the structure of debenzylation of **3a** reported later, its structure was again confirmed by X-ray diffraction analysis. An X-ray diffraction analysis (Figure 1) shows that all C-N bond lengths of imidazolines are normal single bond. All N atoms are in a pyramidalized environment (the sum of the internal angles around N1, N3, N5 and N7 are 337.0^{o}, 342.0^{o}, 336.0^{o} and 339.0^{o}, respectively). The configurations of three five-membered rings of aza[3.3.3]propellane are envelopes in inversed clockwise direction like a propeller. The structures of the two imidazoline rings are almost same, and the angles of N-C-N are 103.6^{o}. All cyclic C-N bond lengths in **3a** lie within 1.436-1.474 Å, a typical value in aza[3.3.3]propellane derivatives, and the cyclic C-C bond lengths are between 1.525 to 1.565 Å. The longest C-C bond (1.565 Å) is the axis C-C bond, agreeing with the literature reported one [5].

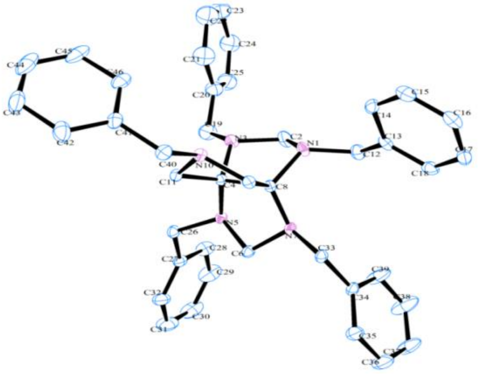
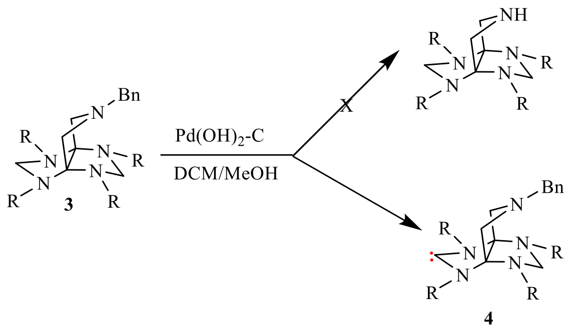


Figure 1: X-ray structures of **3a** with thermal ellipsoids drawn at 50% probability level. N1–C2 1.457(5), C2–N3 1.436(6), N3–C4 1.453(5), C4–N5 1.474(5), N5–C6 1.452(5), C6–N7 1.444(4); N7–C8 1.467(5), C8–N1 1.470(5), C8–C4 1.565(5). C8-N1-C2 104.4(3), C8-N1-C12 120.8(4), C12-N1-C2 112.5(4), N1-C2-N3 103.6(1), C2-N3-C4 104.3(3), C2-N3-C19 115.0(4), C19-N3-C4 123.1(4), N3-C4-C8 104.7(3), N3-C4-N5 112.6(3), N5-C4-C8 104.2(3). C4-N5-C6 106.1(3), C4-N5-C26 117.3(3), C26-N5-C6 112.8(3), N5-C6-N7 103.6(3), C6-N7-C8 107.3(3), C6-N7-C33 113.7(3), C33-N7-C8 118.5(3), N7-C8-N1 113.4(3), N7-C8-C4 103.8(3), C4-C8-N1 103.3(3)

Several practicing debenzylation experiments were performed to explore the debenzylation of **3a**, the debenzylation products could not be obtained under the conditions of H_2/Pd-C, O_2/t-BuOK, NBS and nitric acid/acetic anhydride. The debenzylation of of **3a** in the catalyst of $Pd(OH)_2/C$ with potassium tert-butoxide in DCM at different temperature also did not get any useful information. But luckily, when we repeated this test in a mixed solvent of DCM/MeOH, a new spot emerging up the raw material point was detected by TLC (ethyl acetate : methanol = 5 : 1). After workup, a pure white solid **4a** was obtained, and its melted point was at 192-193 ^oC (Scheme 2).



4a, R = Bn, 62.7%
4b, R = 4-MeBn, 63.7%
4c, R = 4-FBn, 54.8%

Scheme 2: Synthetic ways of stable NHC-carbenes.

The ^{1}H NMR spectrum of **4a** (See SI Fig. 34) in chloroform-d shows resonances at δ 7.67-6.83 ppm for the aromatic ring proton of the benzyl groups, but the methylene chemical shifts fall over a fairly wide range. The nuclear magnetic signal of one proton is located at δ 10.58 ppm, while the other is lower at δ 1.45-1.27 ppm. Its ^{13}C NMR chemical shifts of **4a** is shockly high-field-shift (δ 156.65 ppm). The high-resolution mass spectrum (EI/80 eV) give a base peak at m/z = 604.3398. The High resolution mass spectrometry (See SI Fig. 36) of **4a** revealed that its molecular weight is 2 less than that of reactant **3a**, which is obviously due to the loss of a molecule of hydrogen in **3a**. So what is the structure of **4a**, and how is it formed?

Fortunately, the crystal for X-ray determination was obtained by slowly evaporation solution of **4a** in ethyl acetate/THF. **4a** (Figure 2) is a triclinic, and two independent molecules were found in the unit cell. Obviously, the structure of **4a** is starkly different from that of raw material **3a**. Firstly, the imidazoline ring of **4a** is essentially planar. Secondly, the N-C-N angle (113.7°) at the carbene center is significantly enlarged relative to saturated imidazolin-2-ylidene (104.7°) [6] and unsaturated imidazol-2-ylidenes (101.4°) [7]. The larger N-C-N angle relative to **4a** may reflect strain introduced by the longer C4-C8 bonds that result from the special cage structure of aza[3,3,3]propllenan-2-ylidene bearing donor substituent and steric effect. Two nitrogen atoms of this imidazoline are in a plane environment, and the sums of the internal angles around N1 and N3 are 359.9° and 359.0°, respectively. Thirdly, the endocyclic C-N bonds lengths of imidazolidin-2-ylidene (1.316(4) Å and 1.318(3) Å, respectively) are significantly shorter than that of saturated l,3-dimesityl-imidazolin-2-ylidene (1.349 Å) [8], which suggests a significant interaction of the occupied 2p orbitals of nitrogen atoms and the unoccupied 2p orbital of the adjacent carbene carbon atom in **4a**, and the lengths of the N1-C8 and N3-C4 bonds clearly identify as single bonds. Additionally, the axis C4-C8 bond length (1.563 Å) of carbene ring is an axial C-C bond length of a typical [3.3.3]propellane and almost equal to the corresponding bond length of the raw material [9]. Thus, a new type of aza[3,3,3] propllenan-2-ylidene carbene **4a** rather than the expected debenzylation product was mainly produced in the hydrogen proton transfer catalytic hydrogenolysis **3a** (Scheme 2).

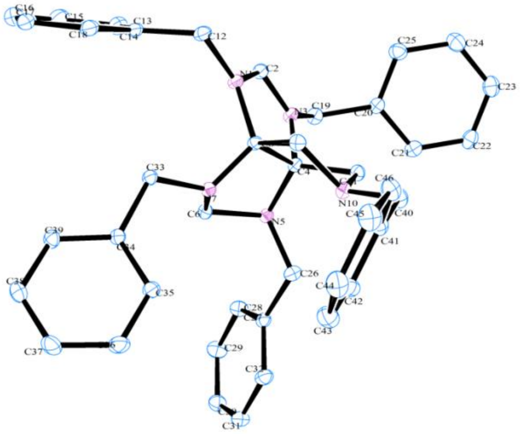


Figure 2: X-ray structures of **4a** with thermal ellipsoids drawn at 50% probability level. N1–C2 1.316(4), C2–N3 1.318(3), N3–C4 1.505(3), C4–N5 1.437(3), N5–C6 1.453(3), C6–N7 1.465(3); N7–C8 1.469(3), C8–N1 1.477(3), C8–C4 1.563(4). C8-N1-C2 111.4(2), C8-N1-C12 124.2(2), C12-N1-C2 124.3(2), N1-C2-N3 113.7(3), C2-N3-C4 109.9(2), C2-N3-C19 122.6(2), C19-N3-C4 126.5(2), N3-C4-C8 102.5(2), N3-C4-N5

116.4(3), N5-C4-C8 102.5(2). C4-N5-C6 106.2(2), C4-N5-C26 119.4(2), C26-N5-C6 117.1(2), N5-C6-N7 104.9(2), C6-N7-C8 102.7(2), C6-N7-C33 113.2(2), C33-N7-C8 117.1(2), N7-C8-N1 110.2(2), N7-C8-C4 107.2(2), C4-C8-N1 107.2(2).

The condition optimization indicated that the dehydrogenation of **3a** was achieved in the catalyst of $Pd(OH)_2$-C in DCM/MeOH, and protonated solvent was necessary, higher temperature was beneficial to the dehydrogenation. It is worth nothing that alkali was not essential, even argon protection was redundant (Table 1). To the best of our knowledge, this is a new and convenient synthetic method for N-heterocyclic imidazol-2-linene. We also used this method to synthesize the derivatives of **3a**, such as **4b** and **4c**, and their structures were characterized by IR, NMR and mass spectrometry.

Table 1: The debenzylation reaction of 3 in different conditions.

Entry	Catalyst	Solvent	Protective gas/Base	Temperature	Time	Yield
1	Pd/C	AcOEt	H_2/no	Ice salt bath	3d	-
2	Pd(OH)/C	AcOEt	H_2/no	Ice salt bath	4d	-
3	$Pd(OH)_2$-C	DCM	H_2/no	Ice salt bath	3d	-
4	O_2/t-BuOK	DCM	/	Ice salt bath	2d	-
6	NBS	DCM	/	Ice salt bath	3d	-
7	HNO_3/Ac_2O	DCM	/	R.T.	2d	-
8	$Pd(OH)_2$-C	DCM	Ar/ t-BuOK		2d	-
9	$Pd(OH)_2$-C	DCM/MeOH	Ar/ t-BuOK	refluxing	2d	8.29%
10	$Pd(OH)_2$-C	DCM/MeOH	Ar/no	refluxing	2d	54.73%
11	$Pd(OH)_2$-C	DCM/MeOH	/	refluxing	2d	62.71%
12	$Pd(OH)_2$-C	DCM/MeOH	Ar/$HCOONH_4$	R.T.	2d	8.31%
13	$Pd(OH)_2$-C	DCM/MeOH	Ar/$HCOONH_4$	refluxing	2d	12.15%
14	$Pd(OH)_2$-C	DCM	Ar/$HCOONH_4$	refluxing	2d	-
15	$Pd(OH)_2$-C	DCM/MeOH	Ar/NaH	refluxing	2d	34.83%

The possible mechanism is shown in Figure 3. Firstly, the palladium catalyst is inserted into the C-H bond of the substrate **3a** to form intermediate **I**, and then the proton solvent methanol is added to release hydrogen and to form intermediate **II**. The active transition state **II** eliminates the proton solvent and catalyst, and gives the product carbene.

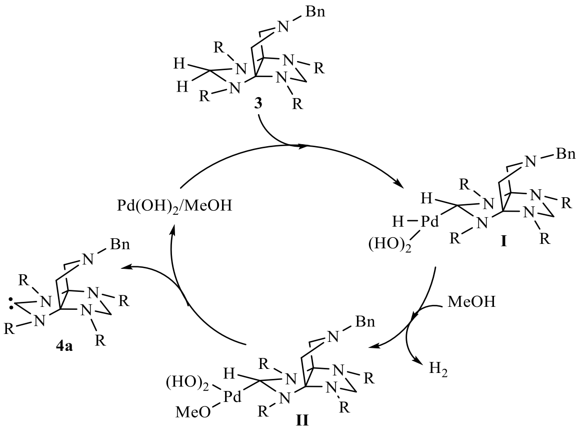


Figure 3: The Possible catalytic mechanism.

It is worth noting that **4a** is extremely stable, and its preparation and storage do not need dehydration, oxygen displacement and inert gas protection. In the cell, the carbene carbon of the crystal is clamped by two benzyl groups on the imidazolin-2-ylidene, and shielded by two other five-membered heterocycles attached benzyl substitutents like a hemispherical vault or a umbrella in the tail, and maybe covered up by other three benzene rings of benzyl groups in the other molecules in the cell. They together form a lipophilic and hydrophobic cavity which cleverly encapsulated carbene carbon of aza[3,3,3]propllenan-2-ylidene.

To get more insights into the stability of propeller-like NHC-carbene, the structure of 3a was optimized by using density functional theory (DFT) method with the long-range corrected hybrid exchange-correlation functional CAM-B3LYP and the polarized basis set 6-31g* [10]. Vibrational frequency analysis was performed at the same theoretical level to ensure that the optimized geometry was local minimum on the potential energy surface. All calculations were performed with the Gaussian 09 program package [11].

As shown in Figure 4, the five-membered ring containing the carbene C atom is almost planar, which is consistent with the X-ray result. The Mulliken charge on the carbene C atom is 0.195 e, while the two neighboring N atoms are negatively charged with Mulliken charge around -0.5 e. Interestingly, the highest occupied molecular orbital (HOMO) orbital of **3a** is almost localized on the carbene C atom, while the lowest unoccupied molecular orbital (LUMO) orbital is mainly delocalized on the phenyl ring far away from the carbene C atom. Their HOMO-LUMO energy gap of **3a** is up to 7.77 eV at CAM–B3LYP/6-31g*level, implying that the electron transfer from HOMO to LUMO is very difficult and the carbene is quite stable upon light. To the best of our knowledge, the HOMO-LUMO erengy gap of 7.77 eV is the highest value among those of NHC carbenes [12].

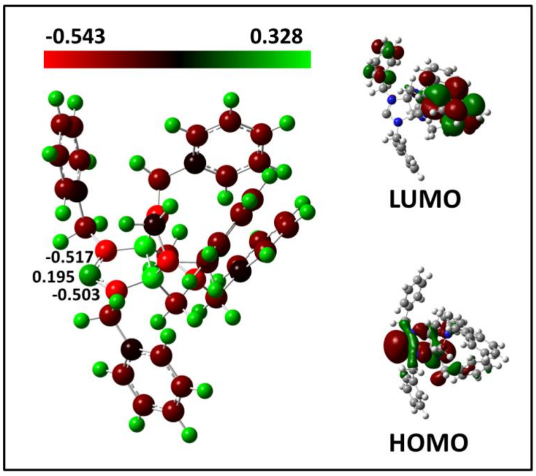


Figure 4: Mulliken charges (in electron) and the frontier orbitals (HOMO and LUMO) at the optimized structure of **4a**.

Conclusion

A new aza[3,3,3]propellan-2-ylidene was accidentally obtained by a the synthetic method in the hydrogen proton transfer catalytic hydrogenolysis of fivebenzylfiveaza[3,3,3]propellane. This three-dimensional, fan-like NHC-carbene is a fair stable, and not deteriorate even if exposed to air. Its carbene imidazoline system is entirely in a flat environment, the bond angle of carbene carbon is larger than that of any five-membered NHC-carbene reported, the lengths of two C-N bonds in the carbene ring are obviously shorter than that of the saturated imidazolin-2-ylidene, and the chemical shift of the carbene center in **4a** at δ 156.65 ppm is shockly high-field-shift. Further studies on formation mechanism, catalytic application of **4a** are ongoing.

Supporting Information

Supporting Information : Experimental procedures and characterization data

Acknowledgements

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