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Fullerenyl azide: synthesis and reactivity

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ABSTRACT

Trimethylsilyl azide adds to the carbonyl carbon in a cage-opened fullerene derivative to form the first fullerenyl azide compound. The fullerene-bound azido group exhibits some unusual reactivity compared with that exhibited by other organic azido compounds. Heating the azidofullerene at 100 °C only led to the cleavage of peroxo groups in the compound, whereas the azido group remained unchanged. Triphenylphosphine reacted with the azido group to form isolable iminophosphorane, which could not be hydrolyzed under normal acidic and basic conditions.

Organic azido compounds are among the most useful reagents in the organic synthesis. The azido group has a strong tendency to extrude diatomic nitrogen as shown in many rearrangement processes such as Curtis rearrangement, which leads to useful organic transformations that are difficult to be realized by other reactions.[1] The reduction of the azido group to $-NH_2$ allows them to serve as precursors for amines.[2] The 'click chemistry'[3] based on the Huisgen 1,3-dipolar cycloaddition of organic azides and alkynes[4] has become a hot topic in recent years.[5]

In fullerene chemistry, organic azido compounds have been extensively employed for fullerene functionalization and preparation of novel fullerene derivatives.[6] For example, the first open-cage fullerene[7] and the first heterofullerene (azafullerene)[8] were both synthesized starting from the [2+3] cycloaddition reaction of azido compounds and fullerene. Meanwhile, a number of azido-containing fullerene derivatives have also been prepared for special purposes. For example, azidophenyl group was attached to pyrrolidinofullerene to form photoaffinity labels for enzyme tagging.[9] Further functionalization of the azido group through the click chemistry[3] has been proven as an efficient method for introduction of new functionalities onto the fullerene system. Up to 15 sugar moieties[10] and up to 12 porphyrins[11] have been readily introduced to [60]fullerene core through such click strategy. A sixfold click reaction was also reported on a hexaazido macrocyclic methanofullerene recently.[12] However, the azido group in all the reported fullerene derivatives is attached to the addend, not directly on the C_{60} cage. So far there has been no fullerene-bound azido compound. Can the fullerenyl azide compound be prepared? Will this species show the same reactivity as the conventional azido compounds? Will the directly bonded azido group undergo rearrangement and insert into the fullerene skeleton? In this Letter, we show that the azido group can be directly connected to fullerene through the Lewis acid-promoted cage-close reactions. The reactivity and thermo stability of this kind of new azido compounds are also discussed.

The cage-opened compound **2** was prepared from a fullerendiol precursor $C_{60}(OH)_2(OO^tBu)^4$ **1** by oxidation with $PhI(OAc)_2$ as we have reported previously.[13] The structure of **2** was determined previously by spectroscopic data. During the course of the present work, we obtained single crystals of **2** by slow evaporation of its solution in a mixture of CH_2Cl_2 and ethanol. The X-ray diffraction data confirmed our earlier structural assignment (Fig. 1). The two pentagons containing the carbonyl groups adopt an envelop shape with the two carbonyl carbons lifted out of the cage surface by about 0.5 Å. The two carbonyls are in close contact as shown on the CPK model in Figure 1. The distances between the two carbonyl oxygen atoms and the two carbon atoms are 2.581 and 2.636 Å, respectively.

The proximity of the carbonyls results in their easy coupling reaction when treated with nucleophiles. In the presence of a Lewis

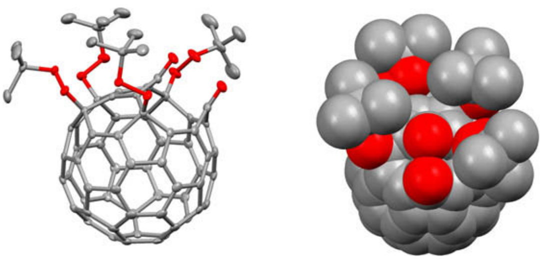

Figure 1. Ellipsoid and CPK models of the X-ray structure of **2**. The ellipsoids were drawn at 50%. For clarity hydrogen atoms are not shown. Color scheme: gray, C; red, O.

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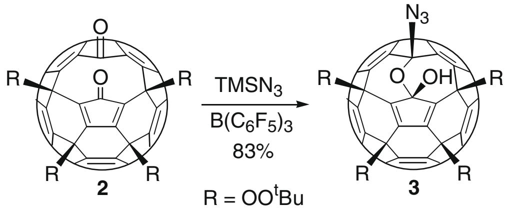
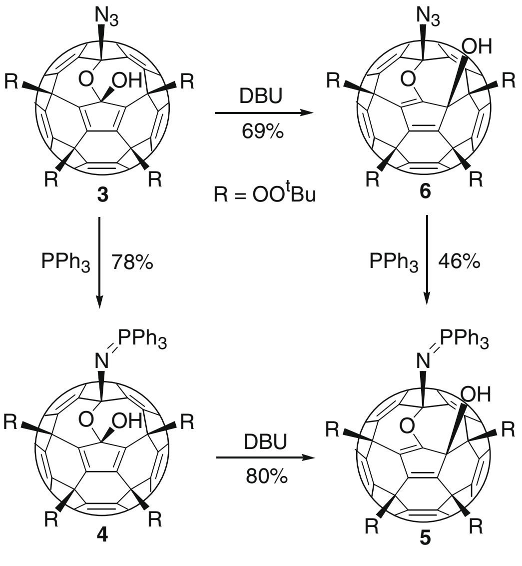
acid, trimethylsilyl azide $TMSN_3$ effectively closes the opening to form compound **3** through formation of hemiacetal and the azido moieties (Scheme 1).[14] Trace amount of water in the solvent may provide the proton source for the hydroxyl group in **3**. The present addition pattern is the same as the reaction between alcohols and compound **2**, but different from the addition pattern of hydroxylamine and primary amines which add to the alkene double bond on the central pentagon and lead to the formation of hemiacetal moiety.[15]

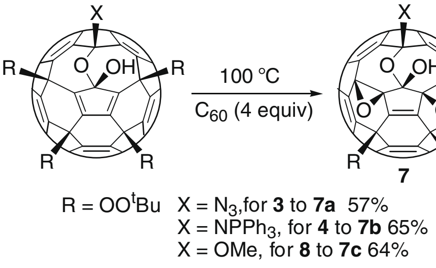
The azidofullerene derivative **3** shows different reactivity from classical organic azido compounds. Attempted 'click reaction'[3] with alkynes did not give the expected triazofullerene derivatives. In an attempt to reduce the azido group into an amino group, we treated **3** with triphenylphosphine and obtained the iminophosphorane derivative **4** (Scheme 2). Unlike many of the traditional substrates in Staudinger reactions, the iminophosphine group of **4** is quite stable. Treating **4** with common acids failed to hydrolyze it into the corresponding ammonia adduct. Under basic conditions, the hydroxyl group on the central pentagon rearranged to a position next to a *t*-butylperoxo group to form **5**, but the iminophosphine group remained unchanged. Similarly, treatment of compound **3** with a base induced the shift of OH group to form **6**. Addition of triphenylphosphine converted **6** to **5**. The base-induced shift of OH group on the central pentagon has been observed before for similar fullerene derivatives.[16]



Scheme 1. Formation of fullerenyl azide.



Scheme 2. Reactions of fullerenyl azide.



Scheme 3. Formation of epoxy azidofullerene by thermolysis.

To test the thermal stability of the azido and peroxo groups, we heated **3** in dichlorobenzene. A complex mixture was observed at 100 °C, probably as a result of decomposition of the peroxo groups. To improve the selectivity excess pristine C_{60} was added into the solution because pristine C_{60} should react with those reactive species resulting from decomposition of the *t*-butylperoxo group (Scheme 3). Indeed, compound **7a** with the azido group intact was then obtained in 57% yield. In the process two *t*-butylperoxo groups were converted into two epoxy groups located symmetrically alongside the hemiacetal moiety. Prolonged heating at 100 °C or higher temperature could not afford any characterizable skeleton rearranged fullerenes through the expected in situ formation of highly reactive nitrene species from the decomposition of azido group, just led to decomposition mixtures. Compounds **7b** and **7c** were obtained under similar conditions starting from the corresponding precursors **4** and **8**,[13] respectively. It is worth noticing that the azido and iminophosphorane groups remained unchanged in the thermal conversion of **4** to **7**.

Spectroscopic data are in agreement with the structures depicted in the Schemes. Compounds **3**, **4**, and **7** are all C_s symmetric. Their NMR spectra showed the expected pattern. For example, the azido derivative **3** showed two *t*-butyl signals at 1.46 and 1.47 ppm, and one OH signal at 5.1 ppm on the ^{1}H NMR spectrum. There are 28 sp^2 and 4 sp^3 fullerene skeleton carbon signals on the ^{13}C NMR spectrum. The two acetal carbons appear at 97.5 and 106.9 ppm. The IR spectrum showed a band at 2109 cm^{-1}, characteristic of the azido stretching band. But these data cannot differentiate different C_s symmetric structures such as location of the two epoxy groups in compounds **7**. Single crystal structure data are needed to verify the assignment.

Various conditions were tested to grow single crystals. Slow evaporation of the methoxyl derivative **7c** in a mixture of toluene and *n*-hexane yielded suitable single crystals. The X-ray structure of compound **7c** is shown in Figure 2. The epoxy groups are located around the acetal moiety. The hydroxyl group is on the central pentagon, and methoxy group is on the less hindered acetal carbon. Thus, methanol attacks the carbonyl group on the outside in the coupling reaction of the diketone compound **2**. The distance between the two acetal carbons is 2.492 Å, much shorter than that in the diketone compound **2** (2.636 Å).

In summary, the first fullerenyl azide was prepared through Lewis acid-promoted addition of trimethylsilyl azide to a cage-opened fullerene derivative. This species shows chemical reactivity

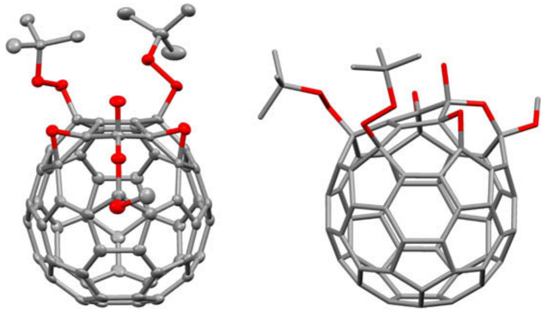


Figure 2. Ellipsoid and stick models of the X-ray structure of **7c**. Ellipsoids were drawn at 50%. For clarity hydrogen atoms are not shown. Color scheme: gray, C; red, O.

different from that of conventional azido compounds, such as no activity in click reaction and its Staudinger reduction stops at the aza-ylide stage. Work is in progress to study the detailed electronic and steric effect of the fullerene moiety on the reactivity of the azido group.

Acknowledgments

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Supplementary data

Supplementary data (experimental procedure and spectroscopic data for all new compounds) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2009.11.032.

References and notes

1. For review, see: (a) Labbe, G. *Chem. Rev.* **1969**, *69*, 345; (b) Scriven, E. F. V.; Turnbull, K. *Chem. Rev.* **1988**, *88*, 297.
2. For example, the synthesis of Reneza and Tamiflu. See review: Magano, J. *Chem. Rev.* **2009**, *109*, 4398.
3. Kolb, H. C.; Finn, M. G.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2001**, *40*, 2004.
4. Huisgen, R. *Angew. Chem., Int. Ed.* **1968**, *7*, 321.
5. For recent review, see: Amblard, F.; Cho, J. H.; Schinazi, R. F. *Chem. Rev.* **2009**, *109*, 4207.
6. Hirsch, A.; Brettreich, M. *Fullerenes: Chemistry and Reactions*; Wiley-VCH Verlag GmbH & Co. KGaA: Germany, 2005.
7. Hummelen, J. C.; Prato, M.; Wudl, F. *J. Am. Chem. Soc.* **1995**, *117*, 7003.
8. Hummelen, J. C.; Knight, B.; Pavlovich, J.; Gonzalez, R.; Wudl, F. *Science* **1995**, *269*, 1554.
9. Okada, E.; Komazawa, Y.; Kurihara, M.; Inoue, H.; Miyata, N.; Okuda, H.; Tsuchiyaa, T.; Yamakoshi, Y. *Tetrahedron Lett.* **2004**, *45*, 527.
10. Isobe, H.; Cho, K.; Solin, N.; Werz, D. B.; Seeberger, P. H.; Nakamura, E. *Org. Lett.* **2007**, *9*, 4611.
11. (a) Iehl, J.; Pereira de Freitas, R.; Delavaux-Nicot, B.; Nierengarten, J.-F. *Chem. Commun.* **2008**, 2450; (b) Pereira de Freitas, R.; Iehl, J.; Delavaux-Nicot, B.; Nierengarten, J.-F. *Tetrahedron* **2008**, *64*, 11409.
12. Pierrat, P.; Vanderheiden, S.; Muller, T.; Brase, S. *Chem. Commun.* **2009**, 1748.
13. Huang, S. H.; Wang, F. D.; Gan, L. B.; Yuan, G.; Zhou, J.; Zhang, S. W. *Org. Lett.* **2006**, *8*, 277.
14. Azidotrimethylsilane (12 mg, 0.10 mmol) and $B(C_6F_5)_3$ (4 mg, 0.0078 mmol) were added to a solution of **2** (72 mg, 0.065 mmol) in 10 mL CH_2Cl_2. The mixture was stirred in the dark at rt for 5 min. The mixture was chromatographed on silica gel eluting with toluene/petroleum ether/ethyl acetate = 2:2:1. Unreacted **2** (trace) was collected as the first band. Product **3** was then collected (62 mg, 83%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.10 (s, 1H), 1.47 (s, 18H), 1.46 (s, 18H). ^{13}C NMR (100 MHz, $CDCl_3$): All signals represent 2C except noted. δ 162.40, 149.67, 148.88, 148.86, 148.70 (1C), 148.51, 148.46, 148.25, 148.16 (1C), 148.07, 147.12, 146.97, 146.63, 146.61, 145.73, 145.63, 145.44, 145.16, 144.74, 144.72, 144.04, 143.44, 143.11, 142.88, 141.63, 141.57, 139.85, 132.68, 106.87 (1C, sp^3), 97.48 (1C, sp^3), 87.91 (2C, sp^3), 82.41 (2C-$(CH_3)_3$), 81.88 (2C-$(CH_3)_3$), 79.05 (2C, sp^3), 26.74 ($6CH_3$), 26.73 ($6CH_3$). FT-IR (microscope): 3536, 2979, 2929, 2109, 1388, 1364, 1230, 1193, 1104, 1067, 1020, 871, 756 cm^{-1}. HRMS (ESI) for $C_{76}H_{41}N_4O_{10}$ $[M+NH_4^+]$: calcd 1169.28172; found: 1169.28374.
15. Zhang, G. H.; Huang, S. H.; Xiao, Z.; Chen, Q.; Gan, L. B.; Wang, Z. M. *J. Am. Chem. Soc.* **2008**, *130*, 12614.
16. Jiang, Z. P.; Zhang, Y.; Gan, L. B.; Wang, Z. M. *Tetrahedron* **2008**, *64*, 11394.