ORGANIC LETTERS

2000
Vol. 2, No. 23
3663−3665

One-Step Multiple Addition of Amine to [60]Fullerene. Synthesis of Tetra(amino)fullerene Epoxide under Photochemical Aerobic Conditions

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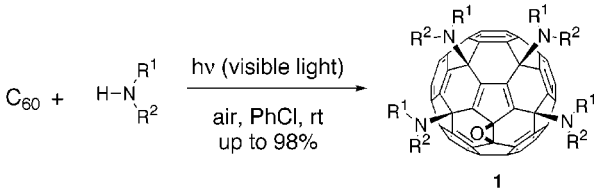
Received September 11, 2000

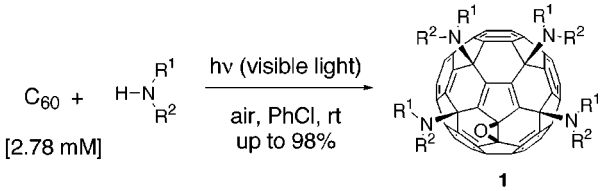
ABSTRACT



A secondary amine undergoes a one-step multiple addition to [60]fullerene under photochemical aerobic conditions to produce tetra(amino)-fullerene epoxide 1 in moderate to excellent yield.

Multiple addition of a nucleophile to [60]fullerene sometimes looks much easier than a monoaddition reaction. For instance, an alkylcopper reagent undergoes a remarkable one-step 5-fold addition to the [5]radialene structure of [60]fullerene to generate a pentaalkylated [60]fullerene in quantitative yield.[1,2] We now report that a secondary amine likewise undergoes a one-step multiple addition to [60]fullerene under photochemical aerobic conditions to produce tetra(amino)-fullerene epoxide **1** (Scheme 1). The reaction performed with functionalized piperazine was found to be especially efficient and simple to carry out, producing the multiple addition product in quantitative yield.

Scheme 1



The experimental procedure for the addition reaction is very simple: A mixture of [60]fullerene (100 mg, 0.139 mmol) and 1-methylpiperazine (488 μL, 4.44 mmol) in chlorobenzene (50 mL) was stirred under open air for 20 h under irradiation with a 60-W incandescent light at room temperature. Volatile material was removed in vacuo. The residual brown solid was made pure simply by repeated washing with hexane (155 mg, 98%).[3] The product may be purified on silica gel if necessary. The present

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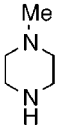
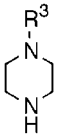
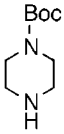
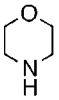
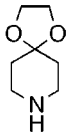
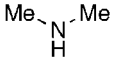
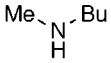
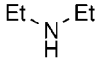
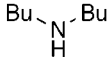
(2) (a) Krusic, P. J.; Wasserman, E.; Keizer, P. N.; Morton, J. R.; Preston, K. F. *Science* **1991**, *254*, 1183. (b) Birkett, P. R.; Avent, A. G.; Darwish, A. D.; Kroto, H. W.; Taylor, R.; Walton, D. R. M. *J. Chem. Soc., Chem. Commun.* **1993**, 1230. (c) Schick, G.; Kampe, K.-D.; Hirsch, A. *J. Chem. Soc., Chem. Commun.* **1995**, 2023. (d) Murata, Y.; Shiro, M.; Komatsu, K. *J. Am. Chem. Soc.* **1997**, *119*, 8117.

(3) Spectral data: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.38 (s, 6 H), 2.42 (s, 6 H), 2.1−2.5 (br m, 16 H), 2.5−3.5 (br m, 16 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 46.07, 46.09, 50.42, 50.78, 55.65, 55.76, 71.53, 71.83, 75.44, 76.31, 140.07, 141.48, 142.71, 142.90, 143.30, 143.41, 143.68, 143.87, 144.09, 144.45, 144.93, 145.10, 145.96, 146.12, 146.65, 146.71, 146.76, 146.79, 146.81, 146.91, 147.22, 147.50, 147.58, 148.88, 149.11, 149.14, 149.17, 151.21.

10.1021/ol006573y CCC: $19.00
Published on Web 10/13/2000

conditions are far superior to the thermal conditions described by Hirsch,[2c] in which a morpholine adduct was obtained in 9% yield (53% under our conditions, entry 4, Table 1).

Table 1. Synthesis of Tetra(amino)fullerene Epoxide **1**

entry	amine	time/h[a]	yield/%[b]
1		20	98
2	 $R^3 = (CH_2CH_2O)_3CH_2CH_3$	22	90
3		36	67
4		36	53
5		22	86
6		8	53
7		6	62
8		2	16
9		12	0
10		5	42
11		6	24
12		14	0
13		6	0
14		4	0

[a] The reaction was terminated upon TLC confirmation of complete conversion of [60]fullerene and the 1,4-diadduct. [b] Isolated yield of **1**.

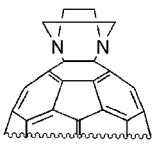
Careful studies on the reaction course revealed initial formation of a small amount of a 1,4-diaminated intermediate (structure not shown), which, however, was totally consumed toward the end of the reaction.[4] Note that a similar 1,4-diadduct has been demonstrated to be the first neutral intermediate in the penta-addition of organocopper reagent to [60]fullerene.[5] In addition, the present reaction obviously shares the same mechanism with a dimer-forming reaction between 1,3-propanediamine and [60]fullerene.[6] It is intriguing to note that none of the monoaminated product, which must have been formed at the outset of the reaction, could be detected.

As can be readily noticed in the data shown in Table 1, the reaction is subject to subtle structural effects. For instance, primary amines give no isolable adducts (entry 14), and among acyclic secondary amines, only *N*-methylamines give the product in decent yields (cf. entries 10, 11, 12, and 13). Note, however, that the 24% yield in entry 11 must be regarded as quite good since six carbon−heteroatom bonds are created in the reaction. It is notable that, in addition to the above-mentioned 1,4-diaminated intermediate,[5] other intermediary compounds could not be detected in the reaction mixture. Five- and six-membered cyclic amines (entries 1−7) appear to be the best starting materials for the present reaction, while four- and seven-membered ones are poor reactants (entries 8 and 9). Among the six-membered amines, piperazines (entries 1−3) are better than morpholine (entry 4) and piperidine (entry 6), and among piperazines, 1-alkylpiperazine is better than 1-Boc piperazine. Therefore, the electronic property of the nitrogen reaction center is critical to the success of the reaction.

Steric effects may also play an important role. For instance, careful examination of the crystallographic structure of a related compound obtained from 1,3-propanediamine[6] suggested that the amine substituents exert considerable interference with each other and that such a steric effect is a reason for the structural sensitivity of the present multiple addition reaction. The physical properties of the adduct are very dependent on the substituents, and the piperazine adducts are freely soluble in acidic aqueous media, whereas many other are not.

In summary, we have reported an extremely simple and efficient method for multiple functionalization of [60]-

(4) When a small excess of 1-methylpiperazine was used, a demethylative monoadduct (see below) formed as a major side product (ca. 10%; Kampe, K.-D.; Egger, N. *Liebigs Ann.* **1995**, 115), which does not form, however, when >16 equiv of the amine was used for the reaction. Note that this monoadduct does not react further with 1-methylpiperazine, failing to give the multiple adduct **1**.



(5) Sawamura, M.; Toganoh, M.; Suzuki, K.; Hirai, A.; Iikura, H.; Nakamura, E. *Org. Lett.* **2000**, *2*, 1919.
(6) Isobe, H.; Ohbayashi, A.; Sawamura, M.; Nakamura, E. *J. Am. Chem. Soc.* **2000**, *122*, 2669.
(7) Nakamura, E.; Isobe, H.; Tomita, N.; Sawamura, M.; Jinno, S.; Okayama, H. *Angew. Chem.* In press.

fullerene. The product aminofullerene will serve not only as a nanoscale scaffold for the preparation of giant molecules but also by itself as a possible candidate of an artificial vector for delivery of genes into the cell.[7]

Acknowledgment. Generous support from Intelligent Modeling Laboratory and Information Technology Center, the University of Tokyo, is gratefully acknowledged.
OL006573Y