Synthesis of Oxy Aminated [60] and [70]Fullerenes with Cumene Hydroperoxide as Oxidant

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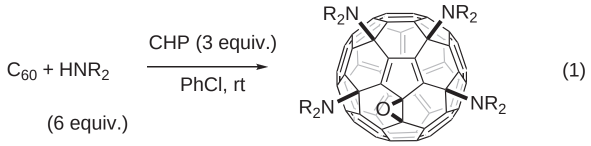
Treatment of [60] or [70]fullerene with excess secondary amine and 3 equiv. of cumene hydroperoxide regioselectively afforded a mono-oxygenated tetraamino or diamino fullerene in good to high yield. The reaction is operationally simple and applicable to a large-scale synthesis.

As a ton-scale commercial plant for production of [60]fullerene has been in operation for some years,[1] development of practical and scalable synthetic methods for functionalization of fullerenes have become a realistic target of research.[2,3] Among numerous derivatives of [60]fullerene (C_{60}), tetraaminofullerene epoxides[4] (**1**) are particularly interesting for their ability to generate a wide variety of compounds that are to be useful in biological[5] and materials science,[6] and for the simplicity and the mildness of the reaction conditions of their preparation (vide infra). The compounds have previously been synthesized in high yield by stirring a solution of C_{60} and a secondary amine in a mixture of dimethyl sulfoxide (DMSO) and chlorobenzene under oxygen atmosphere (cf. Table 1, Entry 1).[7–9] The use of molecular oxygen, however, poses a safety problem in an industrial synthesis[10] and hence is to be avoided. We herein report a new synthesis of **1**, wherein much safer cumene hydroperoxide (CHP) is used in place of O_2[11] and higher product yields may be obtained (eq 1). The method also allowed us for the first time to synthesize an oxygenated diamino[70]fullerene (C_{70}) (**7**) possessing a novel oxidoannulene structure. To our knowledge, no structural determination of amino[70]fullerene has previously been made.[12,13]



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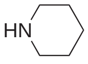
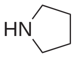
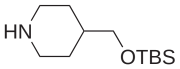
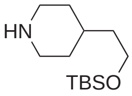
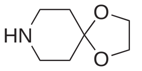
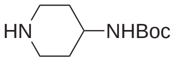
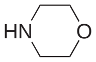
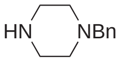
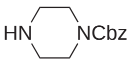
In our first attempt to avoid the use of O_2 gas, we utilized hydrogen peroxide because it is a likely reactive intermediate in the O_2 procedure.[7] Replacement of O_2 gas with 36% aqueous H_2O_2 (3 equiv.) and nitrogen gas otherwise under the same conditions converted a mixture of C_{60} and piperidine (6 equiv.) in chlorobenzene containing 20% v/v DMSO into the desired compound **1** in 55% yield (Table 1, Entry 2). The use of CHP,[14] 3 equiv. in particular, was found to give the best results of 70% (Entry 3). The peroxide reactions took place faster than the O_2 reaction, but produced more polar, higher molecular weight by-products of unknown structures. The adduct **1** was stable to CHP, but reacted further with a mixture of CHP and an amine in a DMSO/chlorobenzene mixture to give the same by-products. The formation of the by-products was suppressed by using chlorobenzene as a sole solvent, and the yield was improved to 84% (Entry 4).

Table 1. Synthesis of tetraamino[60]fullerene epoxide **1**

Entry[a]	Amine	Oxidant[b]	Solvent	Yield[c] /%
1[d]		O_2	DMSO/PhCl[e]	92
2		H_2O_2	DMSO/PhCl[f]	55
3		CHP	DMSO/PhCl[e]	70
4		CHP	PhCl	84
5		CHP	PhCl	81
6		CHP	PhCl	64
7		CHP	PhCl	98
8		CHP	PhCl	99
9		CHP	PhCl	85
10		CHP	PhCl	83
11		CHP	PhCl	96
12		CHP	PhCl	96
13		CHP	PhCl	76
14		CHP	PhCl	75 (71)

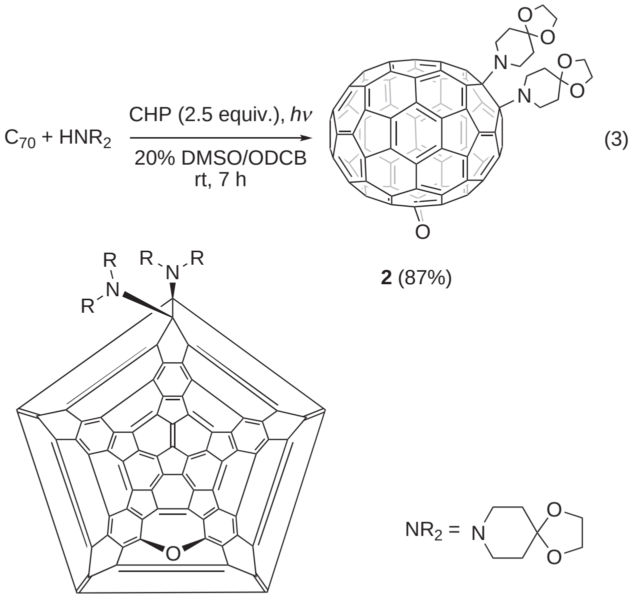
[a]The reaction was carried out at room temperature for several hours to several days till complete consumption of fullerene. We used 40–200 mg of C_{60} except in the reaction shown in the parenthesis of Entry 14 which was performed with 5 g of C_{60}. [b]In Entry 1, excess gaseous oxygen was used, and in others 3.0 equiv. of H_2O_2 or CHP was used. [c]Isolated yield of **1**. [d]Data taken from Ref. 5. [e]20% v/v of DMSO in PhCl. [f]0.04% v/v water in 20% v/v DMSO in PhCl.

The synthetic scope of the reaction as well as the product yield were generally comparable to those of the O_2 procedure[7] with some favorable exceptions. For instance, azetidine gave the desired product in much better yield (Entry 6, 64%) than by the O_2 procedure (20%). The reaction tolerates various functional groups such as silyl ether, acetal, ether, and amide groups (Entry 7–11). Protected piperazines smoothly take part in the reaction (Entries 12–14), while carbamate groups (e.g., benzyl (Cbz) and *tert*-butyl carbamate (Boc)) appear to suffer slightly. The conditions optimized on a 100-mg scale were applied equally well to a large scale preparation. Thus, the reaction of 5.0 g of C_{60} with Boc-protected piperazine gave 7.3 g of the desired product in 71% yield by precipitation from a chlorobenzene solution with methanol. The product was of 97% purity as judged by HPLC analysis. α-Cumyl alcohol was obtained in a nearly quantitative yield.[15]

On the basis of the experimental evidence obtained by the O_2-mediated reaction, we consider that CHP oxidizes the transient electron-transfer complex formed from the amine and fullerene. The formation of α-cumyl alcohol suggests that the oxidation took place via a two-electron transfer process[16] rather than a single-electron transfer (acetophenone formation expected).[17] We suggest the following stoichiometry for the C_{60} reaction.

$$C_{60} + 4HNR_2 + 3CHP = \mathbf{1} + 3\text{cumyl alcohol} + 2H_2O \quad (2)$$

The use of CHP under carefully optimized conditions allowed us to selectively aminate C_{70} in high yield. Through combination of photoirradiation,[8] DMSO-acceleration[7] and the use of CHP, we could convert C_{70} into a monooxy diaminofullerene (**2**) in 87% yield. The oxa-homo[70]fullerene structure of the product was deduced on the basis of the combination of mass spectrum (two amino groups and one oxygen atom), experimental (C_s symmetry and oxidoannulene) and computed NMR spectra (GIAO)[18] and quantum mechanically optimized structural analysis. The experimental data limited the structural possibilities into only three, among which the structure **2** was found to be the most stable and afforded a simulated ^{13}C NMR that showed by far the best matching with the experimental one.



(3)

2 (87%)

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This paper is dedicated to Professor Teruaki Mukaiyama on the occasion of his 80th birthday and in recognition of his outstanding contribution to synthetic organic chemistry.

References and Notes

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15 As a safety precaution, the crude reaction mixture was treated with dimethyl sulfide to reduce any remaining CHP.

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