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Regioselective Oxygenative Tetraamination of [60]Fullerene. Fullerene-mediated Reduction of Molecular Oxygen by Amine via Ground State Single Electron Transfer in Dimethyl Sulfoxide

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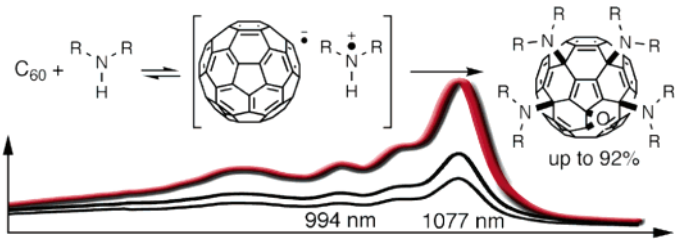

The reaction of [60]fullerene with a variety of a secondary aliphatic amines in 20% v/v dimethyl sulfoxide in chlorobenzene under an atmospheric pressure of molecular oxygen allows regioselective introduction of four amino groups and one epoxide group around one pentagon of the fullerene molecule in good to high yield. This new synthesis of tetraaminofullerene expoxide can be carried out with a simple procedure on a multigram scale at room temperature and affords a variety of functionalized fullerene derivatives. Near-infrared analysis of a mixture of [60]fullerene and piperidine in a deaerated dimethyl sulfoxide/chlorobenzene mixture indicated equilibrium formation of [60]fullerene radical anion ($C_{60}^{\bullet -}$) that persists at least for 2 weeks at room temperature but reacts immediately with molecular oxygen to give the tetraaminofullerene expoxide. The Benesi−Hildebrand analysis of the concentration dependency of the near-infrared absorption indicated that a [$C_{60}^{\bullet -}$ piperidine$^{\bullet +}$] radical ion pair is formed with an equivalent constant of $K = 0.62 \pm 0.02$ M^{-1} at 25 °C. This and other lines of evidence suggest that the oxygenative amination reaction involves C_{60}-mediated reduction of molecular oxygen by the amine.

Introduction

Amination of carbon clusters has been attracting the interest of chemists for a decade, for its own sake and for useful properties expected for the resulting amine-functionalized fullerene and carbon nanotube.[1,2] For instance, amino functionalization endows DNA-delivery ability to the parent carbon clusters[3,4] that are by themselves entirely insoluble in water and hence have few interactions with DNA.[5] The amination reaction of [60]fullerene (C_{60}) was reported as early as 1991.[1,6] The synthetic procedure called for mixing of fullerene and an amine at room temperature and afforded a mixture of aminated products of unknown structures.[1] Subsequently, Kampe and Hirsch reexamined the reaction for secondary amines and determined the structure of what appears to be a product reported in the original work to be a tetraaminofullerene epoxide **2**.[7,8] The product may

† PRESTO, Japan Science and Technology Agency.

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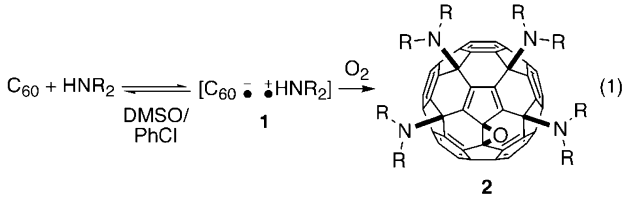
have formed through a series of 1,4-addition of amine molecules followed by epoxidation, but the reported yield was very modest. Sometime ago, we investigated this reaction synthetically and reported that the photoirradiation in an aerated solution accelerates the reaction to afford **2** in moderate to high yield.[9,10] The reaction, however, was synthetically still far from satisfaction for its narrow scope of the amine substrate, for the use of a large excess of the amine, and for poor scalability due to the use of light. In addition, light is productive at the beginning but destroys the desired product toward the end of the reaction. The lack of mechanistic information has hampered any further development of the chemistry. We report herein the results of the studies that have largely resolved these synthetic and mechanistic questions (eq 1). The key finding is that a mixture of C_{60} and

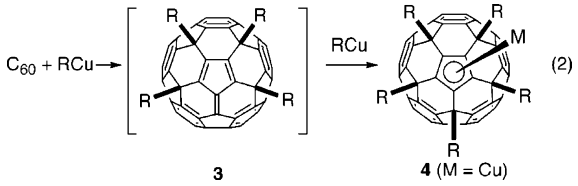


(1)

a secondary amine in a mixture of dimethyl sulfoxide (DMSO) and chlorobenzene generates a long-lived contact ion pair (**1**) of C_{60} radical anion and aminium radical as the result of amine-to-C_{60} single electron transfer (SET),[11] and this process makes it feasible to reduce molecular oxygen by the amine in the presence of C_{60}. Under the optimized conditions developed with this new information, a synthetically viable procedure has been developed: A near stoichiometric mixture of C_{60} and a secondary amine in DMSO/chlorobenzene at ambient temperature under oxygen atmosphere produces the desired tetraaminofullerene epoxide **2** essentially as an only amination product (eq 1). The reaction is applicable to cases where the previous photoreaction[9] entirely failed, and the isolated yield is generally 60−90%. The new reaction does not require any light, external heating, or hazardous or expensive reagents and adds to the repertoire of methods for large-scale preparation of functionalized fullerene derivative.

Results

The 1991 report[6] on the reaction of an amine and C_{60} was rather ambiguous, like many other earlier reports on the reactions of fullerene.[2] In 1995, Hirsch identified one of the amination products to be a tetraaminofullerene epoxide **2** that was formed in low yield.[8] We were intrigued by the similarity of this structure with the structure of C_5-symmetric pentaorganofullerene metal complexes **4** obtained by penta-addition of an organocopper reagent to C_{60} (eq 2) that we were then studying[12] and investigated the mechanism and the synthetic potential of the amination reaction. This reaction involves



(2)

a fulvene intermediate that accepts the fifth nucleophile at the end of a series of addition reactions.[13] Being aware of the photoreactivity of fullerenes,[11,14] we examined photosensitization in the presence of air in chlorobenzene and raised the yield to a synthetically acceptable level.[9] In an effort to understand the elements that control the reaction, to maximize the yield, and to expand the scope of the reaction, we reexamined a number of variables associated with the reaction.

Synthesis of Tetraaminofullerene Epoxides. After careful reexamination of the original photoreaction for the addition of piperidine, we discovered that addition of DMSO to the reaction mixture allows the reaction to take place without photoirradiation. The experimental procedure thus has become very simple: Stirring of a mixture of C_{60} and 4−6 equiv of piperidine in 20% v/v DMSO in chlorobenzene under an atmospheric pressure of molecular oxygen in the dark at 25 °C smoothly converts the fullerene to the desired tetraaminofullerene epoxide **2** (R,R = $(CH_2)_5$). The use of 4 equiv of the amine afforded **2** in 79% yield (the reaction slows down toward the end of reaction), and 6 equiv ensured complete consumption of fullerene after 12 h to afford the desired product in 92% yield after silica gel column chromatography. No reaction takes place in the absence of molecular oxygen (deaerated DMSO/PhCl under nitrogen, 100% recovery of C_{60}).[9] The reaction under air is slow (88% after 18 h), and excess oxygen supplied by continuous bubbling of oxygen gas also slows down the reaction (**2** in 84% yield after 48 h).[15] We can scale-up the reaction effortlessly to 5.0 g of C_{60} to isolate 6.6 g of **2** in 89% yield. The reaction temperature may be elevated from room temperature to 50 °C for some beneficial rate-accelerating effects.

The reaction also produced a few products of higher complexity in about 5% combined yield, which can be removed by chromatography or crystallization. Unlike in the photoreaction,[9] however, we did not detect the formation of a diaminated compound **10** that is an intermediate of the reaction (Scheme 1, vide infra). The

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(10) Other examples: Balch, A. L.; Cullison, B.; Fawcett, W. R.; Ginwalla, A. S.; Olmstead, M. M.; Winkler, K. *J. Chem. Soc., Chem. Commun.* **1995**, 2287−2288. Maggini, M.; Scorrano, G.; Bianco, A.; Toniolo, C.; Prato, M. *Tetrahedron Lett.* **1995**, *36*, 2845−2846. Butts, C. P.; Jazdzyk, M. *Chem. Commun.* **2003**, 1530−1531. Zhang, X.; Gan, L.; Huang, S.; Shi, Y. *J. Org. Chem.* **2004**, *69,* 5800−5802.

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(14) Arbogast, J. W.; Darmanyan, A. P.; Foote, C. S.; Diederich, F. N.; Whetten, R. L.; Rubin, Y.; Alvarez, M. M.; Anz, S. J. *J. Phys. Chem.* **1991**, *95*, 11−12. Tokuyama, H.; Nakamura, E. *J. Org. Chem.* **1994**, *59*, 1135−1138.

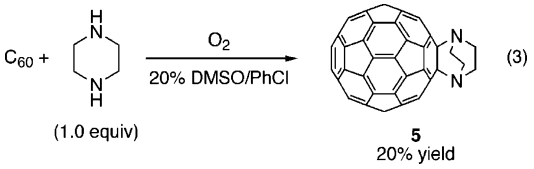
(15) Sawamura, M.; Kawaguchi, Y.; Nakamura, E. *Synlett* **1997**, 801−802.

reaction does not require light, but can be performed with the same efficiency in the presence of ambient light.

To define the synthetic scope of the new amination method, we examined the reaction of a variety of amines with C_{60} and summarize the results in the second column from the right in Table 1. In the far right column are the data obtained under the previous photoirradiated conditions. Comparison of the two data sets indicates that the new procedure is far superior to the photochemical method in terms of the range of applications and the product yield.

For simple substrates in the top half of the table, there is certain parallelism between the two conditions, which we ascribe largely to the steric problem in the final product. Piperidine is the highest yielding (entry 1), which is followed by pyrrolidine (entry 3) and secondary methylamines (entries 5 and 6). Bulkier acyclic secondary amines (such as dibutylamine; data not shown) gave a complex mixture where we could not identify the desired product. Small and reactive azetidine (entry 2) afforded a number of products, from which the desired product was isolated by chromatography in 20% yield. Azacycloheptane is less reactive but gave a reasonable yield when the reaction was performed at concentration four times higher than the one used for more reactive amines (entry 4). High concentration, however, tends to produce more side products. Aniline derivatives were found to be unreactive (data not shown). Primary amines are much more reactive than secondary amines, but gave a mixture of uncharacterizable products.

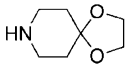
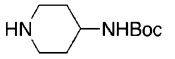
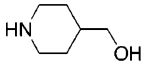
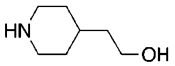
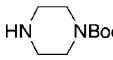
The new procedure offers a new synthetic possibility to introduce a variety of functional groups to the fullerene core. For instance, we introduced the free hydroxy group attached to a piperidine ring (entry 9 and 10). This transformation under the previous photoconditions gave black insoluble material and none of the desired product. Morpholine and a Boc-protected piperazine (entries 11 and 12) are moderate-yielding substrates and gave some unidentified side products. We consider that the complication is due to participation of the internal heteroatom. In support of this conjecture, we found that free piperazine reacted under the same conditions to give an intramolecular 1,2-addition product **5** in 20% yield instead of the expected tetraaminated product (eq 3).[8]



Experimental Observations Relevant to Reaction Mechanism. Mechanistic relationship between the previous photoreaction and the present thermal reactions is of much interest. We gathered several pieces of mechanistic information for the reaction of piperidine and C_{60}.

The epoxide oxygen atom in the product obviously originates from molecular oxygen. We found evidence for reduction of molecular oxygen under the reaction conditions: The final mixture was found to contain a small amount of hydrogen peroxide (38 mol % of the amount of **2** formed).

TABLE 1. Synthesis of Tetraaminofullerene Epoxides

entry	amine	method[a]	time (h)	yield (%)[b]	photo reaction (% yield)[c]
1		A	12	92	53
2		A	6	20	16
3		A	6	85	62
4		B	72	64	0
5		C	24	59	42
6		C	24	61	24
7		A	96	90	86
8		A	12	88	0
9		A	24	84	–
10		A	18	78	0
11		A	12	69	53
12		C	48	76	67

[a] Reaction conditions: All of the reactions were carried out at ambient temperature (25−30 °C). Method A: amine = 6.0 equiv, $[C_{60}]$ = 2.8 mm, 20% DMSO/PhCl, O_2 (1×10^5 Pa). Method B: amine = 6.0 equiv, $[C_{60}]$ = 11 mm, 20% DMSO/*o*-$Cl_2C_6H_4$, O_2 (1×10^5 Pa). Method C: amine = 6.0 equiv, $[C_{60}]$ = 22 mm, 20% DMSO/*o*-$Cl_2C_6H_4$, O_2 (1×10^5 Pa). See the Experimental Section for details. [b] Isolated yield. [c] Data reported in ref 9 (entries 1−7, 11, 12) or obtained under the reported conditions (other entries): amine = 32 equiv, $[C_{60}]$ = 2.8 mm, PhCl, air (1×10^5 Pa), *hν* (visible light).

The key difference between the present conditions and those employed previously by Kampe, Hirsch, and ourselves[7−9] is the use of DMSO as solvent. Other polar solvents also exerted the beneficial effect but to a lesser extent: The reaction in a solvent containing 80% v/v chlorobenzene and 20% v/v of dimethylformamide (DMF), acetonitrile, or benzonitrile in the place of DMSO afforded the adduct **2** in 68% (reaction time: 96 h), 19% (3 weeks), and 14% yield (3 weeks), respectively.[16] This decreasing order appears to be related to the decreasing donor number and permittivity of the solvent[17] as has also been reported for electrochemical reduction of C_{60}.[18] It is

(16) The concentrations of the radical ion pair in the solvents other than DMSO were too low to carry out reliable Benesi−Hildebrand analysis of the NIR spectra.

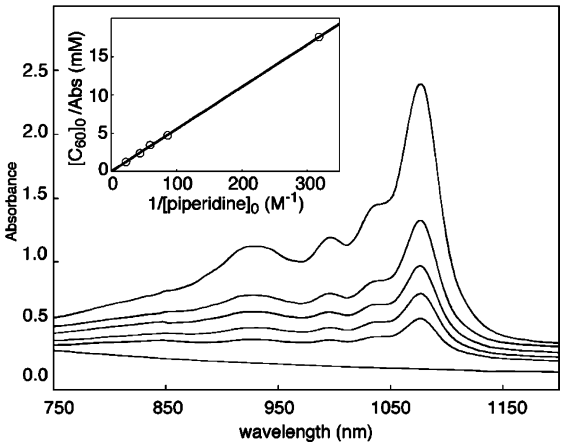


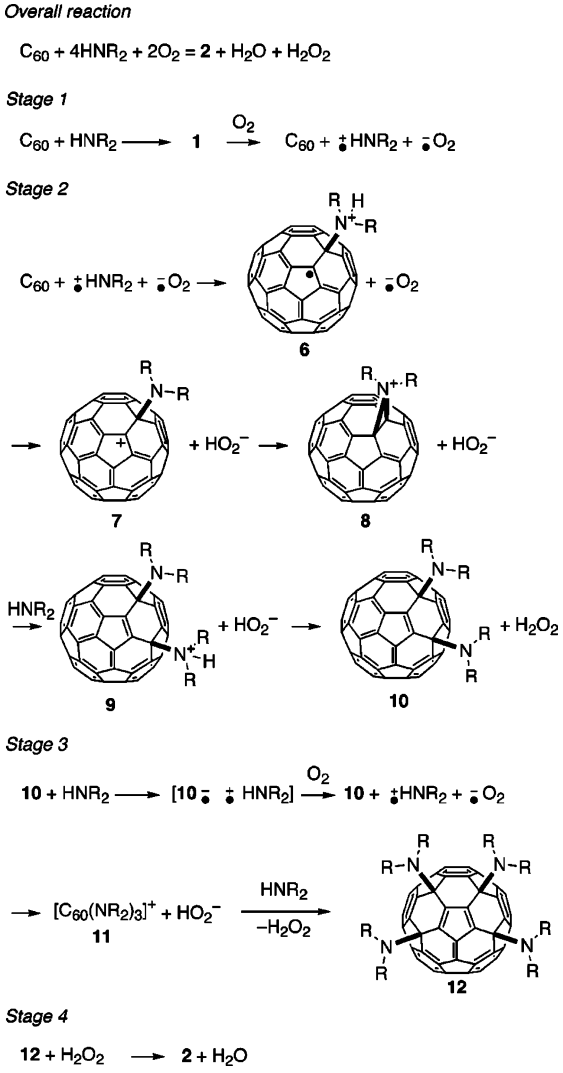
FIGURE 1. NIR spectra of a mixture of C_{60} (2.8 mm) and piperidine in deaerated 20% DMSO/PhCl at 25 ± 2 °C. The absorbance of radical anion $C_{60}^{\bullet-}$ appears at 850−1150 nm (major bands at 994 and 1077 nm), and the absorbance increases with increasing the concentration of piperidine (from bottom to top; 0, 3.1, 12, 17, 23, and 45 mm). Inset: the Benesi−Hildebrand analysis (correlation coefficient = 0.97) of the absorbance intensity at 1077 nm against the concentration of piperidine.

therefore likely that DMSO facilitates SET from the amine to C_{60}.

Direct evidence of the SET was obtained by near-infrared (NIR) spectroscopic analysis of a mixture of C_{60} and piperidine in DMSO/chlorobenzene in the absence of molecular oxygen (Figure 1). The mixture exhibited absorption (major bands at 994 and 1077 nm) characteristic of the C_{60} radical anion ($C_{60}^{\bullet-}$).[19] This absorption was not observed at all for a mixture that does not contain DMSO nor for a mixture in 20% benzonitrile/chlorobenzene containing excess amount of piperidine (179 mm, 64 equiv). Notably, this absorption persisted for 2 weeks without any appreciable decay but vanished immediately upon contact with air with concomitant appearance of the amination product **2**.

The fullerene radical anion $C_{60}^{\bullet-}$ can exist either as a contact ion pair of $C_{60}^{\bullet-}$ and an aminium radical cation (**1**) or as a solvent-separated ion pair.[14] These two possibilities can be differentiated by the Benesi−Hildebrand double-reciprocal analysis of the concentration-dependent NIR absorbance. It will also give us the formation constant and extinction coefficient of $C_{60}^{\bullet-}$. As shown in Figure 1, the NIR bands due to $C_{60}^{\bullet-}$ increased with increasing piperidine concentration, indicating that the neutral molecule and the radical ion are in equilibrium with each other. The double reciprocal plot fitted (correlation efficient of 0.97) into the Benesi-Hildebrand equation under the assumption of contact ion pair formation (Figure 1, inset; see details in the Experimental Section).[20] The molar absorbance coefficient of $C_{60}^{\bullet-}$ ($\epsilon = (2.9 \pm 0.1) \times 10^4$) obtained by the plot is close to the data previously determined by other methods ($\epsilon = (1.1-2.4) \times 10^4$).[14] The calculated equilibrium constant was found to be very large, $K = 0.62 \pm 0.02\ M^{-1}$ (25 ± 2 °C) that corresponds to the Gibbs energy difference of 1.2 kcal/mol.[21]

SCHEME 1. Suggested Stoichiometry and Pathway of Oxygenative Tetraamination of [60]Fullerene with a Secondary Amine and Molecular Oxygen



Discussion

We have described several pieces of experimental evidence that shed light to the reaction pathway of the reaction; that is, the formation of hydrogen peroxide in the reaction mixture, the formation of a substantial concentration of $C_{60}^{\bullet-}$ in the DMSO/chlorobenzene solution, its rapid reaction with molecular oxygen, and the

(17) Donor number is a quantitative measure of Lewis basicity. See: Reichardt, C. *Solvents and Solvents Effects in Organic Chemistry*, 3rd ed.; Wiley: Weinheim, 2003. Marcus, Y. *J. Solution Chem.* **1984**, *13*, 599−624.

(18) Dubois, D.; Moninot, G.; Kvtnew, W.; Jones, M. T.; Kadish, K. M. *J. Phys. Chem.* **1992**, *96*, 7137−7145. Wu, M.; Wei, X.; Qi, L.; Xu, Z. *Tetrahedron Lett.* **1996**, *37*, 7409−7412.

(19) We could not detect the aminium radical by UV−vis−NIR spectra because the absorption at 290 nm overlaps with the intense fullerene absorption. See: Wagner, B. D. Ruel, G.; Lusztyk, J. *J. Am. Chem. Soc.* **1996,** *118,* 13−19.

(20) Benesi, H. A.; Hildebrand, J. H. *J. Am. Chem. Soc.* **1949**, *71*, 1, 2703−2707.

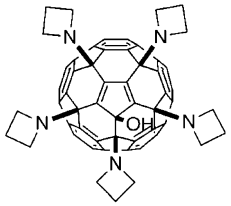
(21) On the basis of this equilibrium constant, we expect the concentration of the radical ion pair under the concentration of C_{60} used for the synthetic experiment (2.8 mM, 6.0 equiv of piperidine) is 31 μM. Because of the limited solubility of C_{60} in a DMSO/chlorobenzene mixture, NMR detection of the radical ion pair was unsuccesssful.

resulting formation of the desired amination product. In addition, the product structure bears similarity to those of the penta-addition of an organocopper reagent (eq 2).

We suggest an overall stoichiometry in the top line of Scheme 1 and, below that, a four-stage reaction pathway that largely accounts for the experimental observations but is obviously a mere book-keeping scheme rather than a true mechanism. Stage 1 involves ground-state SET from the amine to C_{60} in the DMSO/chlorobenzene mixture. The formation of a stable C_{60} radical anion through electron transfer from an amine in the dark to C_{60} has not been reported before.[11] Being capable of stabilizing polarized species in solution, DMSO must be responsible for the formation of the stable ion pair **1**.[17] In the second stage, addition of two amine molecules generates a diaminofullerene **10**, which undergoes the same reaction in the third stage to generate a tetraaminofullerene **12**. This intermediate has a highly electrophilic fulvene moiety, and therefore undergoes base-catalyzed epoxidation by hydrogen peroxide in the final stage. Details are discussed in the following paragraphs.

The formation of the contact ion pair **1** is the most important first event (stage 1, Scheme 1). Once generated, $C_{60}^{\bullet-}$ reduces molecular oxygen[22] to generate superoxide anion $O_2^{\bullet-}$, neutral C_{60}, and an aminium radical ($HNR_2^{\bullet+}$). This first stage represents a C_{60}-mediated reduction of molecular oxygen by a secondary amine. In stage 2, the latter two molecules react together to form a protonated aminofullerene radical **6** perhaps before they escape from the solvent cage. Superoxide anion then deprotonates **6**, and the resulting radical $HO_2^{\bullet}$ must be a powerful enough oxidant to convert to **6** into a cation **7** (and HO_2^-).[23,24] Having carbocation next to the amine group, **7** immediately cyclizes to a three-membered ring ammonium **8**. Such a process is known for primary amines.[10] Another equivalent of the amine undergoes "allylic" alkylation with this intermediate **8** to form a diaminofullerene **10** and hydrogen peroxide. Given the feasibility of 1,2-addition demonstrated by the formation of **5** in eq 3, the highly regioselective 1,4-additions taking place in the formation of **12** looks rather strange: The intermediacy of **7** and the second amination taking place in a 1,3-allylic substitution fashion provides a satisfying explanation of the net 1,4-addition of the two amine molecules to the hexagon system (though it could still be due to steric hindrance in the product). Stage 3 repeats the same diamination reaction on the diaminofullerene **10** to generate one equivalent of the tetraaminofullerene **12** and a second equivalent of hydrogen peroxide. The exclusive regioselectivity of this second diamination parallels the one observed for the copper pentaaddition (eq 2), which is considered to take place in such a manner that fullerene's ring strain is effectively released and intermediary anion achieves maximum planarity for better conjugation.[25]

In stage 4, **12**, which is a highly electrophilic fulvene, undergoes base-catalyzed epoxidation reaction with hydrogen peroxide to give the final product **2**. The epoxidation of the fulvene **12** must be occurring in competition with the addition of the fifth amine, but should be much faster than the latter because of the steric hindrance of the amine. In support of this conjecture, we isolated, in the reaction of azetidine, a small amount of pentaaddition product **13** whose structure is tentatively assigned to be indicated below.



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We consider that the mechanism of the photoreaction[9] is essentially the same except that the reaction in the absence of DMSO needs photon to promote SET from the amine to C_{60}. The DMSO effect is so significant that we do not see the effect of visible light irradiation when DMSO is present in the reaction mixture.

In summary, the discovery of the striking effect of DMSO in promoting SET from an amine to C_{60} led us to develop an efficient new method for the synthesis of tetraaminofullerene epoxides possessing functionalities useful for further elaboration. The experimental procedure is simple, scalable and often high-yielding, does not need hazardous chemicals nor expensive equipments, and therefore will be useful for applications in chemical, biological or materials science.[5] The NIR detection and the Benesi−Hildebrand analysis provided experimental evidence of the formation persistent $C_{60}^{\bullet-}$. Having been informed for a long time that fullerene is readily aminated by amines,[6] we are intrigued by the fact that a carefully deaerated mixture of piperidine and C_{60} in DMSO does not produce any amination products but generates stable radical ion pair. We consider that the present findings will advance mechanistic understanding of the chemical reactivities of fullerene and would also be useful for functionalization of carbon clusters.[2,26]

Experimental Section

6,12,15,18-Tetra(piperidin-1-yl)-6,12,15,18-(tetrahydro)-oxireno[2′,3′:1,9](C$_{60}$-*I*$_h$)[5,6]fullerene.[27] **Method A.** To a solution of C_{60} (250 mg, 0.347 mmol) in PhCl (100 mL) was added DMSO (25 mL), and the mixture was stirred under continuous bubbling of O_2 for 5 min. To the solution was then added piperidine (177 mg, 2.08 mmol; 6.0 equiv), and the mixture was stirred under an atmospheric pressure of O_2 at 25 °C. HPLC analysis (eluent: *i*-PrOH/toluene = 7/3) of the mixture showed that C_{60} was completely consumed after 12

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h. The mixture was washed with saturated aqueous NH_4Cl (100 mL). The amount of H_2O_2 in the aqueous layer (120 mL) was measured as 2.8 μM by titration with iodine.[28] The organic layer was washed further with saturated aqueous NH_4Cl (100 mL) and saturated aqueous $NaHCO_3$ (100 mL), dried over anhydrous $MgSO_4$, and concentrated in vacuo. The crude material (405 mg) was purified by silica gel column chromatography (15 g, eluent: 3% ethyl acetate/toluene) and recrystallization from CS_2/MeOH to give the title compound (345 mg, 92%) as an analytically pure brown powder. The product was identical with an authentic sample[9] by HPLC, IR, NMR, and MS analyses.

When the reaction was performed on a 5.0-g scale (6.9 mmol, 24-h reaction time), the product was obtained in 89% yield (6.6 g) after silica gel purification.

6,12,15,18-Tetra(azetidin-1-yl)-6,12,15,18-(tetrahydro)-oxireno[2′,3′:1,9](C_{60}-I_h)[5,6]fullerene. The compound was synthesized from azetidine (119 mg, 2.08 mmol) and C_{60} (250 mg, 0.347 mmol) by method A and obtained as an analytically pure brown powder (68 mg, 20% yield). The compound was purified by gel permeation chromatography (eluent: toluene), as it partially decomposes on silica gel. We also obtained a mixture of adducts bearing more than four amine moieties (structures unknown). The product was identical with an authentic sample[9] by HPLC, IR, NMR, and MS analyses.

6,12,15,18-Tetra(pyrrolidin-1-yl)-6,12,15,18-(tetrahydro)-oxireno[2′,3′:1,9](C_{60}-I_h)[5,6]fullerene. The compound was synthesized from pyrrolidine (148 mg, 2.08 mmol) and C_{60} (250 mg, 0.347 mmol) by method A and obtained as an analytically pure brown powder (301 mg, 85% yield). The product was identical with an authentic sample[9] by HPLC, IR, NMR, and MS analyses.

6,12,15,18-Tetra(1-azacycloheptan-1-yl)-6,12,15,18-(tetrahydro)oxireno[2′,3′:1,9](C_{60}-I_h)[5,6]fullerene. Method B. This procedure is essentially the same as method A except that substrate concentration was increased by four times by reducing the amount of the solvent mixture. The high concentration accelerates the reaction in the expense of side products, and to be used only for unreactive amines. To a solution of C_{60} (100 mg, 0.139 mmol) in *o*-dichlorobenzene (10 mL) was added DMSO (2.5 mL), and the mixture was stirred under continuous bubbling of O_2 oxygen for 5 min. To the solution was then added 1-azacycloheptane (82.6 mg, 389 mmol; 6.0 equiv), and the mixture was stirred under atmospheric pressure of O_2 at 25 °C. HPLC analysis (eluent: *i*-PrOH/toluene = 7/3) of the mixture showed that C_{60} was completely consumed after 18 h. The mixture was washed with saturated aqueous NH_4Cl (20 mL). The organic layer was washed with saturated aqueous $NaHCO_3$ (20 mL), dried over anhydrous $MgSO_4$, and concentrated in vacuo. The crude material (131 mg) was purified by a silica gel column chromatography (7 g, eluent: 1% ethyl acetate/toluene) to give the title compound (101 mg, 64%) as an analytically pure brown powder: IR (powder) 2923 (m), 2852 (w), 1739 (w), 1723 (w), 1713 (w), 1692 (w), 1659 (w), 1644 (w), 1632 (w), 1613 (w), 1451 (m), 1409 (w), 1391 (w), 1358 (m), 1335 (w), 1306 (w), 1285 (w), 1239 (w), 1223 (w), 1181 (m), 1113 (s), 1075 (s), 986 (m), 967 (m); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.06−1.1.60 (m, 24H), 2.32−2.54 (m, 8H), 3.00−3.15 (m, 8H), 3.52−3.92 (m, 8H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.09 (CH_2), 27.12 (CH_2), 29.47 (CH_2), 29.70 (CH_2), 52.07 (CH_2), 52.54 (CH_2), 71.12, 72.49, 76.04, 77.21, 139.68, 141.33, 142.62, 142.83, 143.55, 143.63, 143.72, 143.94, 144.99, 145.06, 145.43, 145.44, 146.33, 146.38, 146.83, 146.95, 146.96, 147.16, 147.18, 147.40, 147.65, 147.73, 148.56, 148.94, 149.24, 150.87, 150.96, 152.30; HRMS (ESI) calcd for $C_{84}H_{48}N_4O^+$ $[M]^+$1128.3828, found 1128.3841.

6,12,15,18-Tetra(dimethylamino)-6,12,15,18-(tetrahydro)oxireno[2′,3′:1,9](C_{60}-I_h)[5,6]fullerene. Method C. This procedure is essentially the same as method A except that substrate concentration was increased by eight times by reducing the amount of the solvent mixture. To a solution of C_{60} (250 mg, 0.347 mmol) in *o*-dichlorobenzene (12.5 mL) was added DMSO (3.13 mL), and the mixture was stirred under continuous bubbling of O_2 for 5 min. To the solution was added dimethylamine (50% w/w aqueous solution, 188 mg, 2.08 mmol; 6.0 equiv), and the mixture was stirred under atmospheric pressure of O_2. HPLC analysis (eluent: *i*-PrOH/toluene = 7/3) of the mixture showed that C_{60} was completely consumed after 6 h. The mixture was washed with saturated aqueous NH_4Cl (200 mL) and saturated aqueous $NaHCO_3$ (100 mL) and dried over anhydrous $MgSO_4$. The crude material was purified by a silica gel column chromatography (20 g, eluent: 10% ethyl acetate/toluene) to give the title compound (187 mg, 59%) as an analytically pure brown powder. The product was identical with an authentic sample[9] by HPLC, IR, NMR, and MS analyses.

6,12,15,18-Tetra(2-azahexan-2-yl)-6,12,15,18-(tetrahydro)oxireno[2′,3′:1,9](C_{60}-I_h)[5,6]fullerene. The compound was synthesized from butylmethylamine (182 mg, 2.08 mmol) and C_{60} (250 mg, 0.347 mmol) by method C and obtained as an analytically pure brown powder (228 mg, 61% yield). The product was identical with an authentic sample[9] by HPLC, IR, NMR, and MS analyses.

6,12,15,18-Tetra(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)-6,12,15,18-(tetrahydro)oxireno[2′,3′:1,9](C_{60}-I_h)[5,6]-fullerene. The compound was synthesized from dioxa-8-azaspiro[4,5]decane (298 mg, 2.08 mmol) and C_{60} (250 mg, 0.347 mmol) by Method A, and obtained as an analytically pure brown powder (410 mg, 90% yield). The product was identical with an authentic sample[9] by HPLC, IR, NMR, and MS analyses.

6,12,15,18-Tetra[4-(*tert*-butoxycarbonylamino)piperidin-1-yl]-6,12,15,18-(tetrahydro)oxireno[2′,3′:1,9](C_{60}-I_h)-[5,6]fullerene. The compound was synthesized from 4-(*tert*-butoxycarbonylamino)piperidine (167 mg, 2.08 mmol) and C_{60} (250 mg, 0.347 mmol) by method A and obtained as an analytically pure brown powder (186 mg, 88% yield): IR (powder) ν 3437 (w), 2972 (w), 2928 (w), 2812 (w), 1714 (m), 1498 (m), 1449 (w), 1389 (w), 1364 (m), 1326 (w), 1310 (w), 1285 (m), 1256 (m), 1237 (m), 1171 (s), 1094 (m), 1044 (s), 1028 (s), 1011 (s), 978 (m), 944 (w), 886 (w), 860 (m), 843 (w), 802 (w), 787 (w), 750 (s), 706 (w), 675 (m); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.47 (s, 18H), 1.49 (s, 18H), 1.50 (m, 8H), 2.10 (m, 8H), 2.90 (m, 8H), 3.59 (m, 8H), 3.70 (m, 4H), 4.60 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.43, 28.45, 33.35, 33.61, 47.19, 47.63, 49.36, 49.74, 71.52, 71.82, 75.61, 76.51, 79.26, 140.15, 141.55, 142.85, 143.03, 143.09, 143.56, 143.86, 144.01, 144.37, 144.58, 145.07, 145.29, 146.16, 146.33, 146.85, 146.89, 146.98, 147.06, 147.12, 147.43, 147.70, 147.77, 149.08, 149.35, 149.59, 151.68, 155.11, 155.17; HRMS (APCI) calcd for $C_{100}H_{76}N_8O_9^+$ $[M]^+$ 1532.5735, found 1532.5747.

6,12,15,18-Tetra[4-(hydroxymethyl)piperidin-1-yl]-6,-12,15,18-(tetrahydro)oxireno[2′,3′:1,9](C_{60}-I_h)[5,6]-fullerene. The compound was synthesized from 4-(hydroxymethyl)piperidine (96.0 mg, 0.833 mmol) and C_{60} (100 mg, 0.139 mmol) by method A and obtained as an analytically pure brown powder (139 mg, 84% yield): IR (powder) ν 3280 (m), 2916 (m), 2850 (m), 2811 (m), 2752 (w), 1663 (w), 1636 (w), 1459 (m), 1418 (w), 1401 (w), 1391 (w), 1345 (w), 1333 (w), 1301 (m), 1264 (m), 1216 (w), 1196 (w), 1183 (w), 1136 (m), 1098 (s), 1038 (s), 1013 (s), 990 (s), 967 (s), 949 (m), 857 (s), 831 (w), 810 (w), 785 (w), 771 (w), 758 (w), 747 (w), 729 (w), 702 (m), 673 (m); ^{1}H NMR (400 MHz, DMSO-d_6/toluene-d_8 1/1) δ 1.36−1.42 (br m, 8H), 1.60−1.61 (br m, 8H), 1.87−2.02 (m, 8H), 2.65 (t, J = 12 Hz, 2H), 2.81 (m, 6H), 3.47 (m, 8H), 3.72 (d, J = 8 Hz, 4H), 3.91 (dd, J = 13, 12 Hz, 4H), 4.66 (t, J = 5 Hz, 2H), 4.70 (t, J = 5 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6/toluene-d_8 1/1) δ 30.35 (CH_2), 30.48 (CH_2), 30.53 (CH_2), 38.94 (CH), 39.25 (CH), 50.99 (CH_2), 51.44 (CH_2), 51.47 (CH_2), 51.88 (CH_2), 66.85 (CH_2), 66.97 (CH_2), 71.54, 72.73, 76.42, 77.02, 140.75, 141.66, 142.96, 143.12, 143.60, 143.78, 144.10, 145.25,

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145.53, 145.58, 145.68, 146.50, 146.51, 146.98, 147.03, 147.13, 147.27, 147.52, 147.54, 147.79, 147.85, 148.35, 149.10, 149.37, 150.38, 150.83, 152.60; HRMS (APCI) calcd for $C_{84}H_{48}N_4O_5^+$ $[M]^+$ 1192.3625, found 1192.3587.

6,12,15,18-Tetra[4-(2-hydroxyethyl)piperidin-1-yl]-6,-12,15,18-(tetrahydro)oxireno[2′,3′:1,9](C$_{60}$-*I*$_h$)[5,6]-fullerene. The compound was synthesized from 4-(hydroxyethyl)piperidine (108 mg, 0.833 mmol) and C_{60} (100 mg, 0.139 mmol) by method A and obtained as an analytically pure brown powder (136 mg, 78% yield): IR (powder) ν 3267 (m), 2916 (m), 2842 (m), 2811 (m), 1559 (w), 1517 (w), 1507 (w), 1459 (m), 1443 (m), 1418 (w), 1395 (w), 1374 (w), 1362 (w), 1302 (w), 1289 (w), 1262 (m), 1235 (w), 1194 (w), 1179 (w), 1133 (m), 1102 (m), 1081 (s), 1054 (s), 1015 (m), 980 (s), 859 (s), 785 (w), 771 (w), 758 (w), 747 (w), 729 (w), 702 (w), 673 (w); ^{1}H NMR (400 MHz, DMSO-d_6/toluene-d_8 1/1) δ 1.27−1.41 (br m, 8H), 1.49−1.56 (m, 12H), 1.76−1.91 (m, 8H), 2.57−2.62 (br m, 2H), 2.73−2.82 (m, 6H), 3.60−3.38 (m, 12H), 3.80 (dd, J = 17, 11 Hz, 4H), 4.48 (t, J = 5 Hz, 2H), 4.49 (t, J = 5 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6/toluene-d_8 1/1) δ 32.71 (CH_2), 32.97 (CH_2), 33.79 (CH_2), 33.84 (CH_2), 33.93 (CH), 33.96 (CH), 41.24 (CH_2), 51.31 (CH_2), 51.72 (CH_2), 51.85 (CH_2), 52.26 (CH_2), 59.43 (CH_2), 71.72, 72.88, 76.58, 77.17, 140.92, 141.80, 143.13, 143.31, 143.78, 143.97, 144.27, 145.41, 145.72, 145.84, 146.69, 147.17, 147.21, 147.31, 147.45, 147.70, 147.72, 147.98, 148.03, 148.53, 149.53, 149.29, 149.55, 150.51, 151.00, 152.74; HRMS (APCI) calcd for $C_{88}H_{56}N_4O_5^+$ $[M]^+$ 1248.4251, found 1248.4272.

6,12,15,18-Tetra(morpholin-4-yl)-6,12,15,18-(tetrahydro)-oxireno[2′,3′:1,9](C$_{60}$-*I*$_h$)[5,6]fullerene. The compound was synthesized from morpholine (181 mg, 2.08 mmol) and C_{60} (250 mg, 0.347 mmol) by method A and obtained as an analytically pure brown powder (255 mg, 69% yield). The product was identical with an authentic sample[9] by HPLC, IR, NMR, and MS analyses.

6,12,15,18-Tetra(4-*tert*-butoxycarbonylpiperazin-1-yl)-6,12,15,18-(tetrahydro)oxireno[2′,3′:1,9](C$_{60}$-*I*$_h$)[5,6]-fullerene. The compound was synthesized from 4-(*tert*-butoxycarbonyl)piperazine (248 mg, 2.08 mmol) and C_{60} (250 mg, 0.347 mmol) by method D and obtained as an analytically pure brown powder (392 mg, 76% yield). The compound was purified by silica gel column chromatography followed by a preparative HPLC using ODS column. The product was identical with an authentic sample[9] by HPLC, IR, NMR, and MS analyses.

1′,4′-Diazabicyclo[2.2.2]octano[2′,3′:1,9](C$_{60}$-*I*$_h$)[5,6]-fullerene. The compound was synthesized from piperazine (12.0 mg, 139 mmol) and C_{60} (100 mg, 0.139 mmol) by method A and obtained as an analytically pure brown powder (22.2 mg, 20% yield). The compound is spectroscopically identical with the one reported previously.[7]

NIR Spectroscopic Analysis of C$_{60}$ and Piperidine in DMSO/PhCl. A solution of C_{60} (50.0 mg, 69.4 μmol) in 20% v/v DMSO in PhCl (25 mL) was deaerated by three freeze−thaw cycles. A portion of the solution (4.0 mL) was transferred to a quartz cuvett (1 × 1 cm) through a rubber septum, and the NIR spectrum was recorded at 25 ± 2 °C. Incremental amounts of piperidine were added to make 3.1, 12, 17, and 45 mM solutions and spectra (Figure 1) were taken each time.

Benesi−Hildebrand Analysis of NIR Spectra.[11,20] Assuming equilibrium formation of a contact ion pair through single electron transfer from the amine to C_{60} (Scheme 1), we obtain the Benesi−Hildebrand equation (eq 4)

$$\frac{[C_{60}]_0}{\mathrm{Abs}} = \frac{1}{K\epsilon[\mathrm{piperidine}]_0} + \frac{1}{\epsilon} \qquad (4)$$

where Abs is the absorbance of $C_{60}^{\bullet-}$ in the contact ion pair, K is the equilibrium constant, and ϵ is the molar absorbance coefficient of the ion pair. We plotted $[C_{60}]_0$/Abs against $1/[\mathrm{piperidine}]_0$, taking the absorbance at 1077 nm as the absorbance due to the ion pair (Figure 1, inset).[11] From the intercept and the slope of the plot (correlation coefficient = 0.97), we obtained the molar absorbance coefficient and the equilibrium constant as $\epsilon = 2.9 \pm 0.1 \times 10^4$ and $K = 0.62 \pm 0.02$ M^{-1}, respectively. When we assumed the formation of solvent-separated ion pair, the experimental data did not fit in the corresponding Benesi−Hildebrand equation.

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Supporting Information Available: NMR and MS spectra of new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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