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Iodo-Controlled Selective Formation of Pyrrolidino[60]fullerene and Aziridino[60]fullerene from the Reaction between C_{60} and Amino Acid Esters

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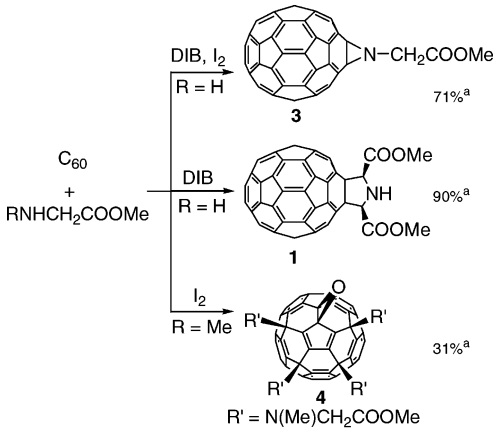
Abstract: The reaction between glycine methyl ester and C_{60} can be effectively controlled by different iodo-reagents. Addition of DIB ((diacetoxyiodo)benzene) yields the 2,5-bismethoxycarbonyl pyrrolidino[60]fullerene under ultrasonic irradiation; whereas addition of DIB-iodine results in the *N*-methoxycarbonylmethyl aziridino[60]fullerene under ultrasonic irradiation. The reaction of sarcosine methyl ester with C_{60} is similar to that of glycine methyl ester under these two conditions. Addition of just iodine to a mixture of sarcosine methyl ester and C_{60} affords the tetra(amino)[60]-fullerene epoxide $C_{60}(O)((Me)NCH_2COOMe)_4$. Possible mechanisms are discussed.

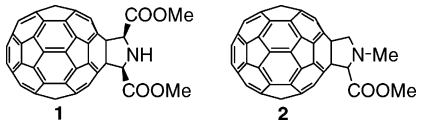
The reaction between amines and fullerene is one of the first reported fullerene reactions and has been widely studied.[1] Both primary and secondary amines can add directly onto fullerenes to form fullerene derivatives with the nitrogen attached to the fullerene cage,[2] whereas tertiary amines form pyrrolidinofullerene derivatives under photolysis through a [2+3] cycloaddition between the two carbons α to the nitrogen and a fullerene double bond.[3] Different mechanisms have been proposed for such a cycloaddition reaction in the literature.

Amino groups of amino acid esters exhibit a different reactivity toward fullerenes. No nitrogen bonded fullerene derivative was detected from the reaction between C_{60} and amino acid esters under various conditions. The reaction is very slow in darkness, and yielded pyrrolidinofullerene derivatives under photolysis for most amino acids and its derivatives.[4] Thus as reported in our previous study, glycine methyl ester gave the 2,5-bismethoxycarbonyl pyrrolidinofullerene **1**, and sarcosine methyl ester gave both **1** and **2**. Singlet oxygen was shown to be involved in the reaction mechanism.[5]

SCHEME 1. Selective Formation of Fullerene Derivatives



[a] Yields are based on converted C_{60}, conversions are 57%, 63% and 12% for **3**, **1** and **4** respectively.



In an effort to further clarify the mechanism of the amino acid reaction and also to make nitrogen-bonded amino acid fullerene derivatives, we treated a mixture of glycine methyl ester and C_{60} with the DIB-iodine system, which has been used as a unique oxidant in many reactions.[6] The mixture was stirred at room temperature or irradiated with ultrasonic sound, which accelerated the reaction. To avoid the effect of singlet oxygen the reaction flask was wrapped with aluminum foil. Aziridinofullerene **3**[7] was isolated together with some bis-adducts as a mixture of regioisomers. Unlike the photochemical reaction, there is no pyrrolidinofullerene detectable from this reaction (Scheme 1) when benzene or chlorobenzene was used as the solvent. When CS_2 was used as the solvent, both compounds **3** and **1** can be detected under lab light after the solution was stirred for 1 day. More **3** was produced than **1** under this condition as indicated by TLC.

DIB is also used alone without iodine in many organic reactions. When just DIB was added instead of DIB-iodine, the above reaction gave the pyrrolidinofullerene

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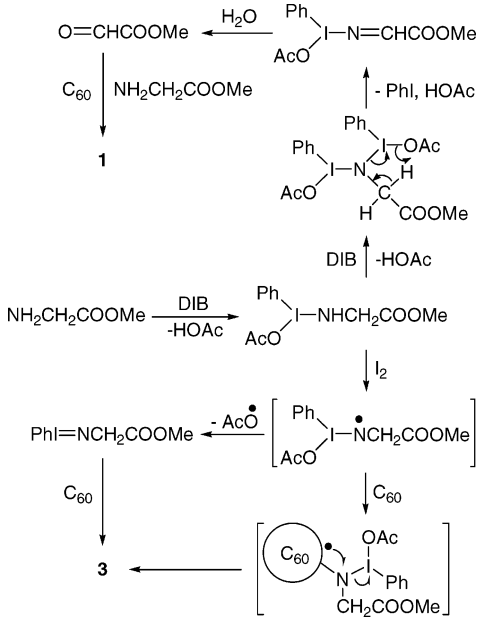
SCHEME 2. Possible Pathways for Formation of Compounds 1 and 3



1 as the only isolable product (Scheme 1). This result is essentially the same as the photolysis reaction including the stereochemistry of **1**.[4c] The yield of **1** is improved here. Sarcosine methyl ester gave the same product **3** or **1** when DIB-iodine or DIB was added, respectively. But yields are lower compared to those from glycine methyl ester.

Addition of iodine alone gave hardly any product for the reaction between C_{60} and glycine methyl ester. Sarcosine methyl ester afforded the multiadduct **4**. When the reaction was carried out without iodine, a small amount of compound **4** (less than 0.1%) formed after the solution was stirred for one month. Separation of the products was straightforward by column chromatography in all these reactions.

Spectroscopic data of **4** are in agreement with the structure as depicted. On the ^{13}C NMR spectrum there are 28 well-resolved signals for the sp^2 fullerene skeleton carbons as expected. The two signals at 147.91 and 145.28 ppm are half intensity compared to the rest, corresponding to the two sp^2 carbons on the mirror plane. The two sp^3 fullerene epoxide carbons at 76.48 and 71.64 ppm are also half intensity compared to signals of the other two sp^3 fullerene carbon signals at 74.78 and 71.12 ppm (both bonded to nitrogen), once again reflecting the existence of the mirror plane in the molecule. The MALDITOF-MS showed the molecular ion peak as the base peak. Structures of compounds **1**[4a,c] and **3**[7] were easily established by comparison to literature spectroscopic data.

Scheme 2 shows a possible pathway for the formation of **1** and **3** from the glycine ester reactions. The first step leads to an amidoiodane species, which reacts further with either iodine or another molecule of DIB. In the absence of iodine the amidoiodane reacts with DIB and gives methyl glyoxalate in three steps. The water molecule in this process may come from the neutralization of glycine methyl ester hydrochloride with sodium carbonate or impurity in the solvent. The so-formed glyoxalate then forms a 1,3-dipole with glycine methyl ester, which adds to C_{60} to form **1** following the well-known Prato reaction.[8] Iodobenzene was detected with a mole ratio of 1:9.5 between **1** and iodobenzene. Unidentified products including nonfullerene compounds may account for the extra iodobenzene.

In the presence of iodine, formation of the nitrogen-centered radical is apparently the major reaction. The nitrogen-centered radical may add to C_{60} directly to form **3** through the loss of an acetoxyiodobenzene radical. The nitrogen-centered radical may also form the iminoiodane PhI=NR, which then adds to C_{60} through the nitrene pathway. Iminoiodanes have been used in the aziridination of alkenes as nitrene precursors.[6] Aziridinofullerene derivatives have been prepared through reactions of azides and nitrene precursors.[7,9] Iodobenzene was also detected in the formation of **3**. The ratio between **3** and iodobenzene is 1:2.3. Unidentified products should account for the extra iodobenzene.

In the case of the sarcosine methyl ester reaction, demethylation of the nitrogen-bonded methyl group may be the first step giving off glycine methyl ester, which then follows the above reaction pathway. *N*-Alkylsulfonamides could be dealkylated by DIB-iodine to give free sulfonamides and aldehydes. Nitrogen-centered radicals and unstable imino intermediates were generated in such a dealkylation process.[10]

When iodine is added alone to the sarcosine system, it simply acts as the oxidant to give compound **4** according to the cyclopentadiene mode of fullerene reactions. Compounds with analogous structure to **4** have been reported through the photochemical addition of certain secondary amines to C_{60} in the presence of oxygen.[11] Singlet oxygen is the oxidant in such reactions.[5]

Fullerene amino acid derivatives exhibit many potential applications in medicinal chemistry and material science.[12] Various methods have been reported for their synthesis mostly through the further functionalization of fullerene derivatives.[13] The present work shows that direct interaction between amino acid esters and C_{60} can be well controlled by iodo-reagents to afford pyrrolidinofullerene or aziridinofullerene derivatives in moderate to good yields.

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Experimental Section

All reagents were used as received. Solvents for reaction were distilled by standard methods. Reactions were carried out in air unless specified.

Synthesis of *N*-Methoxycarbonylmethyl Aziridino[60]-fullerene 3. To a C_{60} chlorobenzene (100 mg, 0.14 mmol in 20 mL) solution were added DIB (224 mg, 0.69 mmol) and I_2 (88 mg, 0.35 mmol), being dissolved under ultrasonic irradiation (Branson 5210 Ultrasonic Cleaner). Glycine methyl ester hydrochloride (87 mg, 0.69 mmol) and sodium carbonate (74 mg, 0.69 mmol) were then added. The flask was wrapped with aluminum foil and irradiated with an ultrasonic processor (Gmbh 200s, amplitude set at 60%, cycle set at 0.5). Progress of the reaction was monitored by TLC. The reaction was stopped after 7 min. Excess $Na_2S_2O_3$ solution was added to the reaction mixture to reduce unreacted oxidants. The organic layer was separated and evaporated. The residue was dissolved in a minimum of toluene and chromatographed on silica gel (160−200 mesh). Toluene eluted unreacted C_{60} (43 mg, 57% conversion) as the first band, followed by a small amount of an unknown compound as the second band, then compound **3** as the third band (45.7 mg, 0.057 mmol, yield 71% based on converted C_{60}). The ^{1}H and ^{13}C NMR MALDI-TOF mass spectra are the same as those in the literature.[7]

Synthesis of *cis*-2,5-Bismethoxycarbonyl Pyrrolidino-[60]fullerene 1. To a C_{60} chlorobenzene (100 mg, 0.14 mmol in 50 mL) solution was added DIB (224 mg, 0.69 mmol), being dissolved under ultrasonic irradiation (Branson 5210 Ultrasonic Cleaner). Glycine methyl ester hydrochloride (117 mg, 0.93 mmol) and sodium carbonate (116 mg, 1.1 mmol) were then added. The flask was wrapped with aluminum foil and irradiated with an ultrasonic processor (Gmbh 200s, amplitude set at 60%, cycle set at 0.5). Progress of the reaction was monitored by TLC. The reaction was stopped after 1 h. The solution was directly poured onto a silica gel column. Toluene eluted C_{60} as the first band (37 mg, 63% conversion), and compound **1** as the second band (70 mg, 0.08 mmol, yield 90% based on converted C_{60}). The ^{1}H NMR MALDI-TOF mass spectra are the same as those in the literature.[4a,4c]

Both the solvent and concentration are important factors for the above two reactions. When more concentrated chlorobenzene solutions than those described above were used, the reaction was too fast to allow TLC to follow the progress. Toluene gave lower yields and required longer reaction time. Stirring the solution without ultrasonic irradiation could give the same product but in a much longer time.

Detection of Iodobenzene. To avoid possible loss of iodobenzene in the evaporation process, the low-boiling benzene was used as the reaction solvent instead of chlorobenzene. Other conditions were the same as above. Longer reaction time and lower yields were observed (conditions were not optimized for the present purpose). The reaction was stopped after half of the starting C_{60} was consumed as monitored by TLC. The solution was directly poured onto a silica gel column. Benzene eluted C_{60} and iodobenzene as the first band, which was evaporated on a rotovap. Iodobenzene was extracted from the residue with ether. The ether solution was evaporated to give iodobenzene as oil, the identity of which was confirmed by comparing its ^{1}H and ^{13}C NMR spectra to those of a commercial sample. The mole ratio between product **1** and iodobenzene was 1:9.5.

A similar experiment was carried out for the reaction leading to compound **3**. To avoid the reduction of DIB by $Na_2S_2O_3$, the reduction step by $Na_2S_2O_3$ was omitted. The mole ratio between product **3** and iodobenzene was 1:2.3.

Synthesis of 1,2-Oxo-4,11,15,30-tetra(methylmethoxycarbonylmethylamino)-1,2,4,11,15,30-hexahydro[60]-fullerene 4. To a C_{60} toluene (500 mg, 0.69 mmol in 500 mL) solution under nitrogen were added sarcosine methyl ester hydrochloride (1.2 g, 8.6 mmol) and iodine (250 mg, 0.98 mmol). The mixture was stirred for 20 min followed by addition of 0.5 mL of DBU (3.3 mmol). The resulting solution was stirred for 10 days at room temperature. Throughout the reaction the flask containing the solution was wrapped with aluminum foil and kept under nitrogen. The reaction was quenched by adding 4 mL of 2 M H_2SO_4. The organic solution was evaporated on a rotovap. The residue was chromotographed on silica gel. Toluene first eluted 440 mg of unreacted C_{60} (12% conversion). Chloroform then eluted some iodine and compound **4** as a very narrow band (30 mg, 31% based on converted C_{60}).

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.33 (d, 16.4 Hz, 1H), 4.11 (d, 16.4 Hz, 2H), 3.97 (d, 16.4 Hz, 1H), 3.81 (s, 3H), 3.78 (s, 3H), 3.00 (s, 3H), 2.94 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.72, 171.38, 151.22, 149.97, 149.43, 149.18, 148.91, 147.91 (half intensity), 147.72, 147.42, 147.16, 147.05, 147.02 146.96, 146.94, 146.88, 146.32, 146.16, 145.28 (half intensity), 144.91, 144.41, 144.20, 143.94, 143.92, 143.59, 143.36, 143.22, 143.00, 141.46, 139.82, 76.48 (half intensity), 74.78, 71.64 (half intensity), 71.12, 56.50 (CH_2), 56.01 (CH_2), 51.92 ($COOCH_3$, broad and intense compared to the rest, due to two overlapped signals), 40.91 (CH_3), 40.28 (CH_3). DEPT (100 MHz, $CDCl_3$): δ 56.49 (CH_2), 56.01 (CH_2), 51.94 ($COOCH_3$, broad and intense compared to the rest, due to two overlapped signals), 40.91 (CH_3), 40.28 (CH_3). IR spectrum: 534, 849, 1040, 1124, 1201, 1378, 1446, 1638, 1743, 2861, 2932 cm^{-1}. UV−vis spectrum: 256, 275 (sh), 363 (sh), 401 (sh). MALDI-TOF-MS (rel intensity): 1144 (M^+, 15%), 1167 (M^+ + Na, 100%), 1183 (M^+ + K, 29%). Found (calcd) elemental analysis for $C_{76}H_{32}N_4O_9$: C 79.74 (79.72), H 2.97 (2.82), N 4.86 (4.89), O 12.01 (12.57).

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Supporting Information Available: Selected NMR and MS spectra for compounds **3** and **4**. This material is available free of charge via the Internet at http://pubs.acs.org.

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