CYCLOADDITION REACTION OF C_{60} WITH 2-DIAZO-1,3-DITHIANE AND OXIDATION OF THE CYCLOADDUCT TO SULFOXIDE DERIVATIVES

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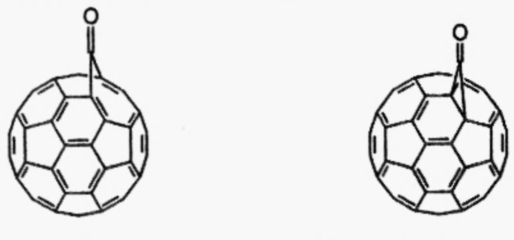
Abstract: Cycloaddition reaction of C_{60}, directed toward synthesis of homo[60]fullerenone, was carried out with 2-diazo-1,3-dithiane generated by Bamford-Stevens and diazo-tranfer reactions. As a result, dithiane ring connection occurred as a methanofullerene type rather than a fulleroid type. Such reactivity distinguished between [2+1] and [3+2] cycloaddition routes of this diazo compounds. Oxidation of the addend wiith mCPBA proceeded smoothly to give the corresponding sulfoxide derivatives.

Derivatization of fullerenes developed quite rapidly after discovery of a method for bulk production of fullerenes by Krätschmer and Huffman (1), and a variety of organic derivatives of C_{60} and to a minor extent of C_{70} have been synthesized (2); many of them exhibit promising potential as new materials and pharmaceuticals (3). Among them, fullerene derivatives functionalized with heterocycles are of particular interest because; i) even a simple combination of fullerenes with structurally diverse heterocycles provides a multitude of derivatives, ii) heterocycles are themselves intriguing and important functional groups, iii) functional conversions can be carried out with relative ease by heterocyclic modification and heterocyclic ring-opening, and iv) bond-formation between fullerene-carbons and various heteroatoms provide a new aspect of functionalization.

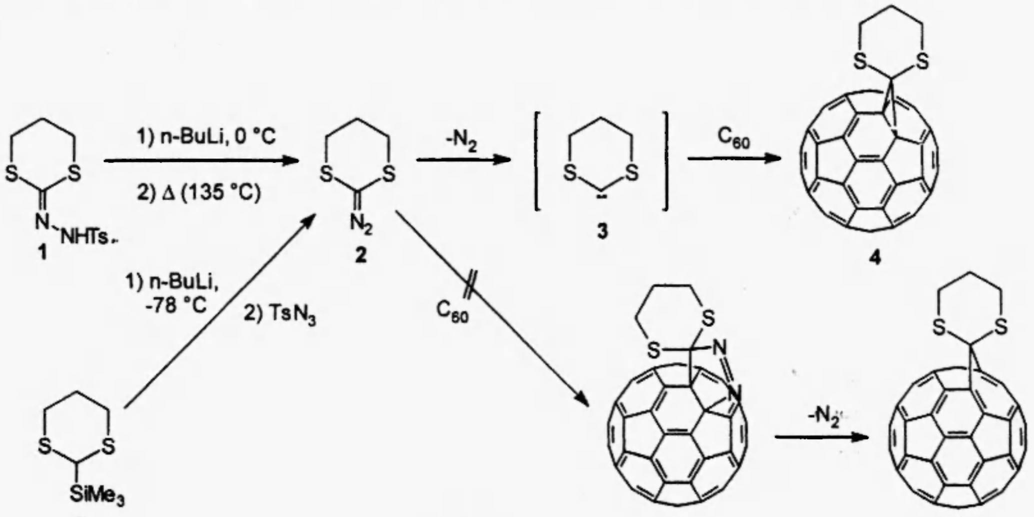
Fullerene-heterocycle combinations can range widely over a variety of heterocyclic systems, and synthesis of some heterocycle-containing fullerene derivatives have already been documented by us and other groups (4). We have now focused on a dithiane ring, which is an interesting class of heterocycle in synthesis but not yet exploited in fullerene chemistry; since a dithiane ring is able to serve as an efficient protecting group for a carbonyl function (5), this heterocycle may be useful as a precursor for synthesis of "homo[60]fullerenone". For this hypothetical and attractive fullerene derivative, two possible structures are considered; one is a [6,6]-closed methanofullerene type and the other is a [5,6]-opened fulleroid type (6). The former is supposed to be unstable because facile cheletropic elimination brings about spontaneous decomposition to pristine C_{60} and carbon monoxide, and in this sense the latter is expected to be a practical candidate. Such a [5,6]-opened fulleroid type of adduct is known to occur favorably from [3+2] cycloaddition reaction with diazo compounds under thermal conditions (6,7). These are enough to prompt us to examine the cycloaddition reaction of C_{60} with 2-diazo-1,3-dithiane as an approach to incorporate a carbonyl function on the C_{60} surface.



[5,6]-opened fulleroid type [6,6]-closed methanofullerene type

Required 2-diazo-1,3-dithiane 2 is accessible from the Bamford-Stevens (8) and diazo-transfer reactions (9). First, the cycloaddition reaction *via* the Bamford-Stevens reaction was attempted. *p*-Tosylhydrozone 1 was prepared from *p*-tosylhydrazine based on the reported procedure (8), and 2 was generated *in situ* by base treatment (nBuLi/THF, 0 °C, 30min) of 1 (2 equiv.) followed by thermolysis at 135 °C for 35 min in o-dichlorobenzene (ODCB) under an argon atmosphere, during which C_{60} was allowed to react with 2 (or otherwise with the derived carbene 3)(Scheme 1). The reaction proceeded smoothly as judged by the solution color changing from purple to dark brown and TLC analysis showing a new product (R_f = 0.4, hexane/toluene 3/1). After evaporation of the solvent under reduced pressure, the residue was subjected to chromatography. Unfortunately, the product could not be separated completely from unreacted C_{60} by silica gel chromatography (10) and even by preparative HPLC, but the structure could be analyzed as a crude form without interference of pristine C_{60}. The FAB-MS supported a 1:1 cycloadduct by a parent peak at m/z 838 together with a base peak at m/z 720. The UV/Vis spectrum had λ_{max} 430 nm, which is characteristic of [6,6]-closed cycloadduct of C_{60} (11), suggesting that the cycloadduct was methanofullerene 4. In accordance with this, NMR spectra were compatible with C_{2v} symmetricity of 4. While requisite signals at δ 2.40 (m, 2 H) and 3.30 (m, 4 H) due to a 1,3-dithiane ring were observed in ^{1}H-NMR (500 MHz), ^{13}C-NMR (125 MHz) showed 16 lines at δ 140.15 – 146.47 due to sp^2 spherical carbons (12) and 1 line at δ 66.18 due to sp^3 fusion carbons together with 3 lines at δ 26.46, 32.92 and 47.91 due to 1,3-dithiane ring carbons. These spectral inspections indicated that the method using the Bamford-Stevens reaction did not give the targeted fulleroid type of product (*i.e.*, 6 → 7).

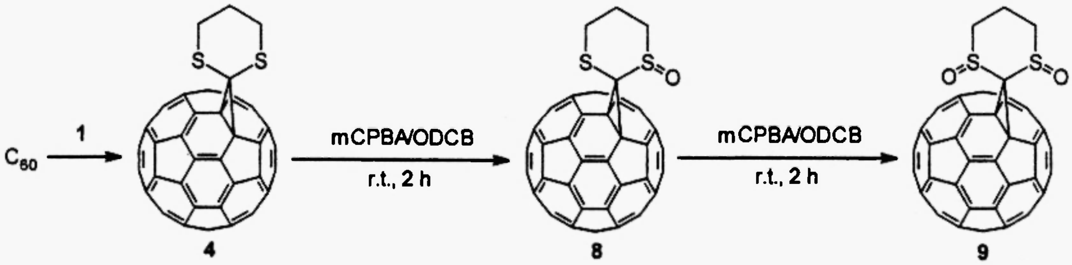
Then, an alternative reaction *via* the diazo-transfer route was attempted to avoid drastic thermal conditions. Recently, Benati et al. demonstrated that 2 *in situ* generated by diazo-transfer to 2-trimethylsilyldithiane 5 reacted with dimethyl fumarate to give the corresponding cyclopropane derivative either *via* [3+2]cycloaddition reaction of 2 followed by decomposition of the resulting pyrazoline intermediate or *via* direct [2+1]cycloaddition of the carbene intermediate derived from decomposition of 2; it remains unclear whether is actually operative (9). Since characteristic reactivity of [60]fullerene possibly distinguish between these two (*vide infra*) and milder conditions is fit for our purpose, this method was applied to C_{60}. Thus, a solution of **2** in THF-HMPA prepared from 5 (2.5 equiv.) and tosyl azide according to the reported procedure (9) was treated with C_{60} in *o*-dichlorobenzene at 0 °C for 2 h and then at room temperature for 2 h. The reaction also proceeded smoothly even at lower temperature than employed in the reaction of 1. The same workup and chromatography as above gave a nitrogen-extruded cycloadduct (Scheme 1), but yet spectral data of the cycloadduct obtained here was consistent with those of the above product *via* the Bamford-Stevens reaction.



Scheme 1

It is concluded from above results that the [6,6]-closed product (methanofullerene) is the sole product from the cycloaddition reaction of C_{60} with 2. In fullerene chemistry, cycloaddition with diazoalkanes produces a pyrazoline derivative in only the case of the parent diazomethane (7a), and those with all others produce [5,6]-opened cycloadducts (fulleroids) directly (7b-e) as a result of concomitant extrusion of nitrogen through the concerted manner (13). Methanofullerenes are formed after the rearrangement under various (thermal, photochemical, electrochemical, and acid-catalyzed) conditions (14). It is apparent that the carbene route results in the straightforward formation of methanofullerenes. In comparison with these facts, it is likely in the case of S,S-disubstituted diazoalkane 2 that the reactive carbene intermediate 3 participates preferentially and is responsible for exclusive formation of methanofullerene 4. Thus, it is of some value for [60]fullerene to play a role of guideline to distinguish the course of the reaction in the cycloaddition of 2(15).

Although cycloaddition of 2 was disappointed of our purpose, fullerene-dithiane combination was performed and the cycloadduct seems to be useful for further conversion. For example, oxidation reaction with *m*-chloroperbenzoic acid (mCPBA, 1 equiv.) at room temperature for 2 h using crude 4 as obtained from the above cycloaddition afforded mono-sulfoxide 8 in 38% overall yield (73% based on consumed C_{60}), which allowed the complete separation of the product 8 from C_{60} (silica gel column eluted with $C_6H_5CH_3/Et_2O$ 3/1) and unambiguous assignment by spectroscopic methods (16). Moreover, 8 was oxidized repeatedly with the same reagent to bis-sulfoxide 9 (17) in 74% yield (Scheme 2).



Scheme 2

In summary, 2-diazo-1,3-dithiane 2 generated by Bamford-Stevens and diazo-transfer reactions cycloadded to C_{60} to give a methanofullerene type of product exclusively. This product has thioether functionality but is not susceptible to self-sensitized photooxygenation with the same tendency as found in tetrahydrothiophene and thiochroman-fused C_{60} derivatives (4b, 18), and such stability is convenient for handling without care. On the other hand, intentional oxidation with mCPBA gave sulfoxide derivatives 8 and 9 efficiently. Mechanistically, the characteristic reactivity of fullerene gave testimony for **2** to undergo cycloaddition *via* the carbene route.

Acknowledgement

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(16) Spectral data: FAB MS m/z 854 (M^+), 720 (base peak); IR (KBr) ν (cm^{-1}) 1061, 527; UV ($CHCl_3$) λ (nm) 431; ^1H-NMR (1,1,2,2-tetrachloroethane-d_2) δ 2.94-3.00 (m, 2 H), 3.22-3.48 (m, 4 H); ^{13}C-NMR (1,1,2,2-tetrachloroethane-d_2) δ 22.26, 31.30, 47.76, 58.49, 77.14, 78.13, 138.66, 139.78, 139.98, 140.15, 140.74, 141.73, 141.87, 141.88, 141.90,142.09, 142.39, 142.63, 142.67, 142.74, 142.79, 142.92, 143.55, 143.63, 143.70, 143.73, 143.75, 143.77, 143.87, 143.97, 144.37, 144.48, 144.58, 144.63, 144.98, 145.06, 145.08, 145.28, 145.39, 145.45, 145.51, 145.53, 145.57, 145.62, 145.66, 145.72, 145.91, 145.93, 145.95, 145.97, 146.00, 146.02, 146.14.

(17) Elution: $CHCl_3$/EtOH 20/1. Spectral data: FAB MS m/z 870 (M^+), 720 (base peak); IR (KBr) ν (cm^{-1}) 1061,1057, 527; UV ($CHCl_3$) λ (nm) 431; Unfortunately, an NMR spectrum could not be obtained because of its quite low solubility in organic solvents. This compound has a pharmacological interest since the bis-sulfoxide of tetrahydrothiophene-fused fullerene is potentially attractive in association with *E. Coli* growth-inhibiting activity of bis-pyrrolidinum-fused fullerene (see ref. 4d).

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