FUSION OF C_{60} WITH CYCLIC AMINO ACID AND THIOUREA BY HETERO DIELS-ALDER REACTIONS†

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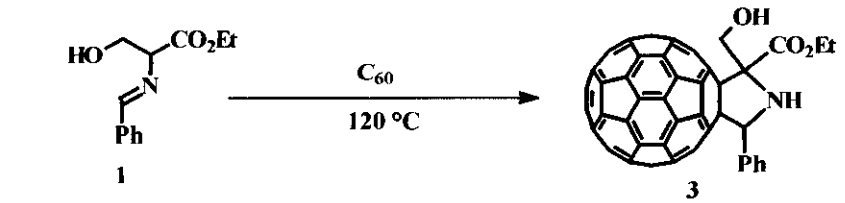
Abstract- C_{60} underwent hetero Diels-Alder reaction with a carbethoxy-substituted 2-aza-1,3-butadiene and trimethylsilylthio-substituted 1,3-diaza-1,3-butadiene (which possibly reacts as trimethylsilylamino-substituted 1-thia-3-aza-1,3-butadiene) to give C_{60} derivatives fused with cyclic amino acid and thiourea, respectively. The latter was explained to arise under equilibrated conditions.

We have been interested in synthesis of fullerene-heterocycles as a combination of sterically and electronically unique structure of C_{60} and specific functionalities of individual heterocycles.[1] For this aim, two modes of cycloaddition are envisaged for direct fusion of C_{60} with heterocycles. Since the double bond on C_{60} has considerable addition reactivity attributable to its low LUMO level,[2] 1,3-dipolar cycloaddition reactions have been frequently used for fusion with five-membered heterocycles.[3] The oxidative formal [3+2] cycloaddition and ring-expansion reactions were also developed for accessible routes to this class of compounds.[4] On the other hand, fusion with six-membered heterocycles has been attained chiefly by hetero Diels-Alder reactions. These were firstly demonstrated by us in the reactions with an *o*-quinone methide and the sulfur analog.[5] Following 1-thia- and 2-aza-1,3-butadiene cases have recently been reported to give dihydrothiopyrane and δ-lactam derivatives of C_{60}.[6] In this paper, we wish to describe that cyclic amino acid and thiourea can be introduced on the surface of C_{60} by this methodology.

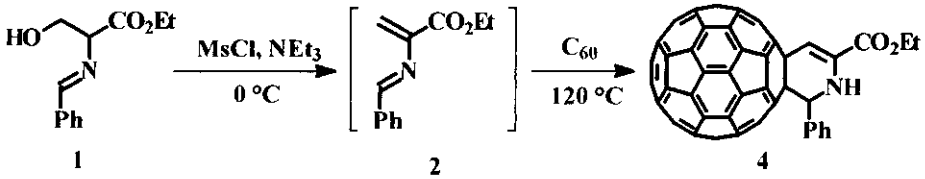
First examined was the fusion of C_{60} with a cyclic amino acid by the cycloaddition reaction using a carbethoxy-substituted 2-aza-1,3-butadiene (**2**) The required azadiene was *in situ* formed from dehydration of *N*-benzylideneserine ethyl ester (**1**) based on the reported procedure.[7] However, the precedented dehydration with carbonyldiimidazole/triethylamine was unsuccessful in this case, and instead methanesulfonyl chloride/triethylamine, which was effective in the formation of a carbethoxy-substituted 1,3-butadiene,[8] was applied. Further, the precursor (**1**) itself can react as a 1,3-dipole as was shown in the related system;[9] in fact, when **1** (1 equiv.) was allowed to react with C_{60} at 120 °C for 3 h in chlorobenzene, the pyrrolidine derivative (**3**) was obtained in 34% yield based on consumed C_{60} (64% recovery) (eq 1).[10] In order to avoid this competitive reaction, the reaction with **1** (10 equiv.) was

†Dedicated to the memory of the late Professor Shun-ichi Yamada.

initially conducted at 0 °C (2 h) to ensure mesylate formation and then heated to 120 °C for 3 h. Thus, the desired cyclic amino acid cycloadduct (**4**) was obtained in 11% yield [based on consumed C_{60} (30% recovery)] after chromatographic separation (eq 2). The low yield may be partly attributed to an electron-withdrawing substituent of the azadiene.[11] The structure was elucidated by spectral inspections The FABMS analysis indicated the expected molecular ion peak at m/z 923 with the base peak at m/z 720, and the IR spectrum had absorptions at 1713 (COOEt) and 527 (C_{60}) cm^{-1}. In the ^1H NMR (500 MHz, $CDCl_3$), observed were signals at δ 5.46 (s, 1 H) and 5.76 (s, 1 H) due to a tetrahydropyridine ring, 1.49 (t, *J*=7.0 Hz 3 H) and 4.50 (m, 2 H) due to an ethyl group, and 7 16-7.68 (m, 5+1 H) due to phenyl and imino groups. In the ^{13}C NMR (125 MHz, $CDCl_3$), signals at δ 64.23 and 73.19 were assignable to sp^3 fusion-carbons together with sp^2-carbon signals at δ 116.07 (HC=CNH), 128.55-157.49 (60 lines[12] due to all other ring carbons including C_{60}), and 163 93 (C=O).



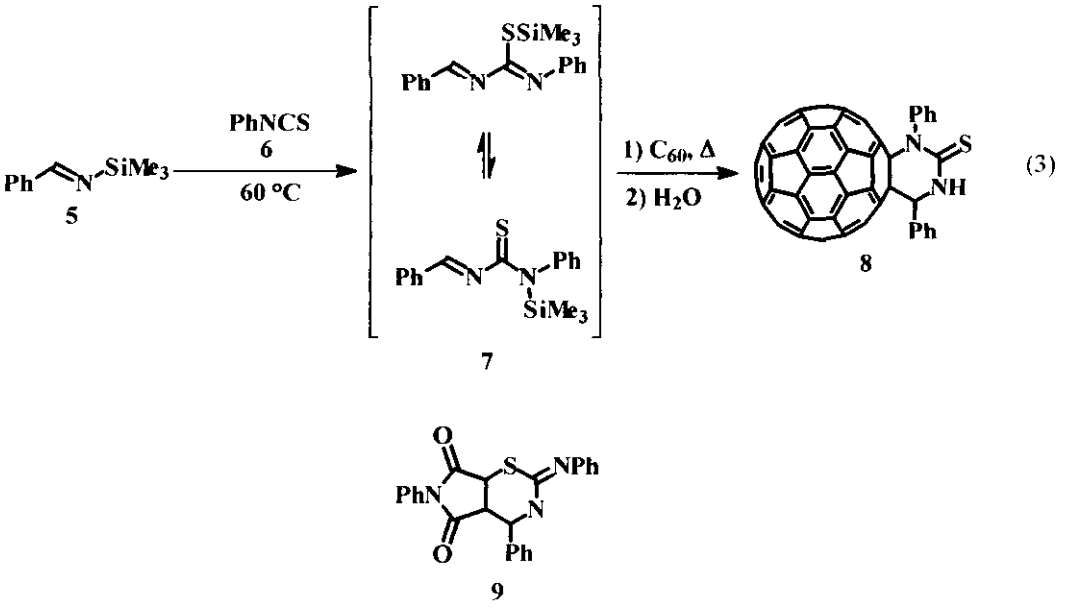
(1)



(2)

Next examined was the reaction with the heterodiene (**7**) prepared from *N*-trimethylsilylbenzylimine (**5**) and phenyl isothiocyanate (**6**) This diene was reported to act as 1-thia-3-aza-1,3-butadiene with electron deficient dienophiles such as *N*-phenylmaleimide and diethyl azodicarboxylate,[13] and as a 1,3-diaza-1,3-butadiene with aryl isocyanates and isothiocyanates.[14] While C_{60} was demonstrated to have nearly the same Diels-Alder reactivity as *N*-phenylmaleimide,[15] the cycloaddition of C_{60} with **7** occurred in a different way from *N*-phenylmaleimide Although the reported conditions for *N*-phenylmaleimide did not require the temperature higher than 60 °C to induce the cycloaddition with **7**, the reaction at this temperature gave no cycloadduct in the case of C_{60} Nevertheless, after the heterodiene (**7**) was formed from **5** and **6** (each 3 equiv.) at 60 °C overnight, this could be reacted with C_{60} at 110 °C for 24 h to give the desired 1:1 cycloadduct (**8**) in 33% yield based on consumed C_{60} (57% recovery) (eq 3). The yield was improved to 53% by heating at 150 °C (4 h). The structure was assigned as a cyclic thiourea rather than a cyclic isothiourea such as **9** obtained from *N*-phenylmaleimide and **5**/**6**, based on the following spectral data which was different from those reported for the cycloadducts related to **9**. The differences between them lie in chemical shifts in ^{13}C-NMR and fragmentation patterns in MS; the signals due to a C=N moiety in cyclic isothioureas were reported to appear at higher field than δ 150,[13] but the

corresponding signal was observed at δ 171.63 in **8**, which is better ascribable to a C=S moiety.[16] Further, the signal due to a sp^3 fusion-carbon was observed at δ 84.85 and it was more reasonably assigned to a carbon adjacent to a nitrogen atom than a sulfur atom.[17] In contrast to appearance of the molecular ion peak in isothiourea type of cycloadducts,[13] **8** gave no molecular ion but a fragmented peak at m/z 914 which originated from extrusion of H_2CS, and this behavior is likely to emerge in a cyclic thiourea system rather than a cyclic isothiourea system.[18] These facts were consistent with the assigned structure as above, which was also supported by other spectral data: IR (KBr); ν 1275 (C=S), 527 (C_{60}) cm^{-1}; UV/vis (hexane); λ 428 nm; ^1H NMR (500 MHz, $CDCl_3/CS_2$ 8/1) δ 7.25 (s, 1 H), 7.42-8.29 (m, 10 H).



The above difference in reactivity of the heterodiene (**7**) may be attributed to the intrinsic aromatic character of double bond on C_{60}. The [4+2] cycloaddition of C_{60} is known to be reversible[19] and thus it is reasonable to consider that the cycloadduct (**8**) is formed under equilibrated conditions.

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10 All the spectral data were compatible with the 1,3-dipolar cycloadduct (1:2 stereoisomeric mixture).

11 The corresponding 1,3-disiloxy-2-aza-1,3-butadiene was found to be much reactive· ref. 6b.

12 δ 128.55, 129.24, 130.52, 131.11, 133.54, 134 89, 135 64, 137 93, 138.17, 138.50, 138.95, 140.60, 140.76, 140.97, 141.20, 141.67, 141.82, 142.00, 142.18, 142.32, 142.37, 142 41, 142.53, 142.65, 142.72, 142.82, 142.85, 142.91, 143 31, 143 33, 143 36, 144.70, 144.77, 144.86, 145.06, 145.23, 145.27, 145 53, 145 55, 145.66, 145.73, 145.75, 145.89, 145 99, 146.01, 146.06, 146.20, 146 28, 146.30, 146.57, 146.69, 146.71, 46.77, 146 96, 147 82, 147.91, 147.95, 152 32, 155.67, 157.49.

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16 The other ^{13}C-NMR signals: δ 77.87, 88.42, 128.43, 128 62, 128.93, 129.21, 129 42, 130.84, 134.09, 134.69, 135.04, 136.45, 136 49, 140 01, 140.12, 140.37, 140 68, 141.82, 141.91, 141.96, 142.05, 142.11, 142.22, 142.33, 142.36, 142.45, 142.47, 142 65, 142 81, 142.88, 142.93, 143.35, 144.22, 144.24, 144 50, 144.62, 145.12, 145 16, 145 22, 145.26, 145.42, 145.54, 145.57, 145.70, 145.74, 145.77, 145.90, 145.99, 146.09, 146.12, 146 17, 146 50, 146.57, 146.75, 147.18, 147.35, 147.85, 148.86, 152.84, 155.29

17 The reported ^{13}C-NMR of 1,2-(3-phenyl-2-phenyliminotetrahydrothiazolino)-[60]fullerene was indicative of relative chemical shifts, δ 67.47 for fullerene sp^3-C-S and δ 84 86 for fullerene sp^3-C-N: W. Duczek, F. Tittelbach, B. Costisella, and H -J. Niclas, *Tetrahedron*, **1996**, *52*, 8733.

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