

FUSION OF C₆₀ WITH CYCLIC AMINO ACID AND THIOUREA BY HETERO DIELS-ALDER REACTIONS†

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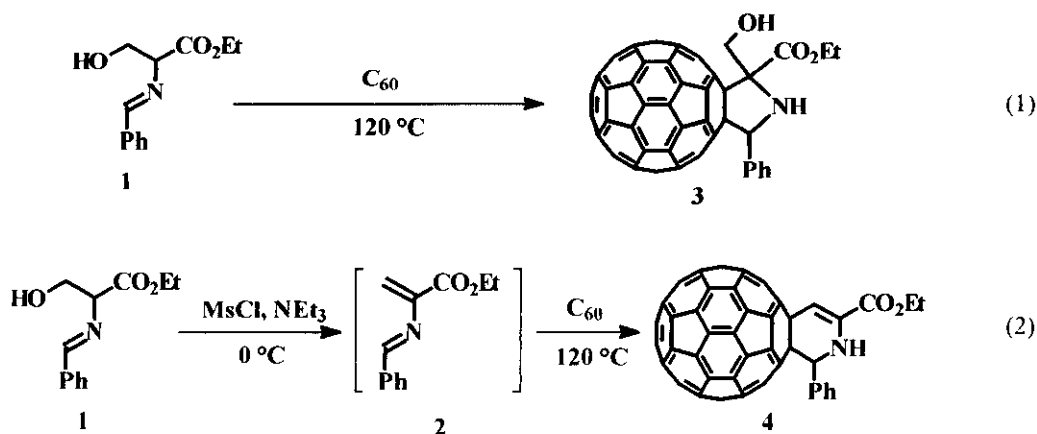
Abstract- C₆₀ underwent hetero Diels-Alder reaction with a carboxy-substituted 2-aza-1,3-butadiene and trimethylsilylthio-substituted 1,3-diaza-1,3-butadiene (which possibly reacts as trimethylsilylamino-substituted 1-thia-3-aza-1,3-butadiene) to give C₆₀ derivatives fused with cyclic amino acid and 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 C₆₀ and specific functionalities of individual heterocycles.¹ For this aim, two modes of cycloaddition are envisaged for direct fusion of C₆₀ with heterocycles. Since the double bond on C₆₀ 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 C₆₀.⁶ In this paper, we wish to describe that cyclic amino acid and thiourea can be introduced on the surface of C₆₀ by this methodology.

First examined was the fusion of C₆₀ with a cyclic amino acid by the cycloaddition reaction using a carboxy-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 carboxy-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 C₆₀ at 120 °C for 3 h in chlorobenzene, the pyrrolidine derivative (**3**) was obtained in 34% yield based on consumed C₆₀ (64% recovery) (eq 1).¹⁰ In order to avoid this competitive reaction, the reaction with **1** (10 equiv.) was

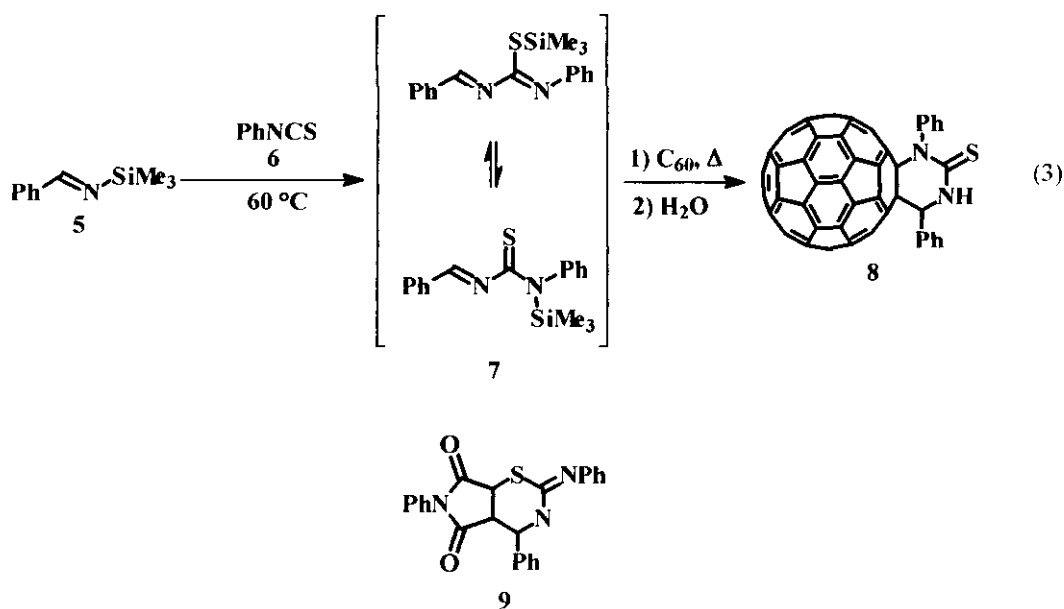
†Dedicated to the memory of the late Professor Shun-ichi Yamada.

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 lines¹² due to all other ring carbons including C_{60}), and 163.93 (C=O).



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 isothiurea 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 isothiureas 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 isothioureia 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 thioureia system rather than a cyclic isothioureia 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 reversible¹⁹ and thus it is reasonable to consider that the cycloadduct (**8**) is formed under equilibrated conditions.

ACKNOWLEDGMENT

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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, 146.77, 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
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