Pergamon

Tetrahedron Letters, Vol. 37, No. 51, pp. 9211-9214, 1996

0040-4039/96 $15.00 + 0.00

PII: S0040-4039(96)02185-5

δ-Valerolactam Derivative of C_{60} from Hetero Diels-Alder Reaction with 1,3-Bis(*tert*-butyldimethylsilyloxy)-2-aza-1,3-butadiene

Masatomi Ohno, Satoshi Kojima, Yuri Shirakawa, and Shoji Eguchi*

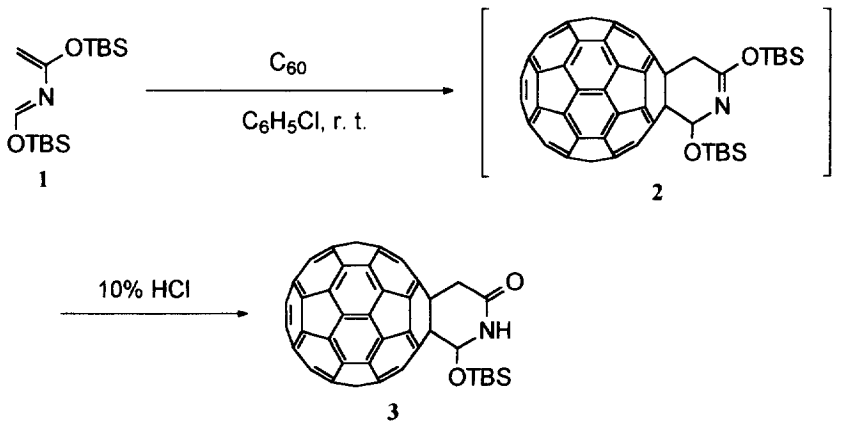
Department of Molecular Design and Engineering, Graduate School of Engineering,
Nagoya University, Chikusa, Nagoya 464-01, Japan

Abstract. The title 2-aza-1,3-diene reacted smoothly with C_{60} at room temperature to give 2-piperidone-fused C_{60} after hydrolysis. A silyoxy group on the piperidone ring was replaced by alkoxy groups by acid-catalyzed substitution reaction with alcohols *via* an iminium cation intermediate. This type of reaction was applied to reduction by use of triethylsilane to give the parent δ-valerolactam derivative of C_{60}. Copyright © 1996 Elsevier Science Ltd

Organic functionalization of C_{60} has been drawing keen and continuous attention after discovery of a method for bulk production,[1] and a variety of designed C_{60} derivatives have been constructed for material and pharmaceutical applications.[2] We have been interested in heterocycle-fused C_{60} (trivial [60]fullero-heterocycles), since heterocycles are themselves intriguing and important functional groups and are possibly converted into bifunctional derivatives by ring-opening.[3] In this context, the hetero Diels-Alder reaction[4] affords a reasonable strategy for the fusion of heterocycles with dienophilic C_{60} by exploiting various heterodienes. We have previously demonstrated that oxa- and thiadienes give chroman-, thiochroman- and dihydrothiopyran-fused C_{60} derivatives.[5-7] We wish to report here the first example of the azadiene case leading to δ-valerolactam derivatives of C_{60}. The Diels-Alder reaction of C_{60} sometimes encountered cycloreversion because of its intrinsic aromatic character.[8] However, in the present reaction using 1,3-bis(silyloxy)-2-aza-1,3-diene, the cycloadduct can avoid this undesired process by transforming the formed double bond (N=COSi) to a single bond (NH-C=O) by facile hydrolysis.[9]

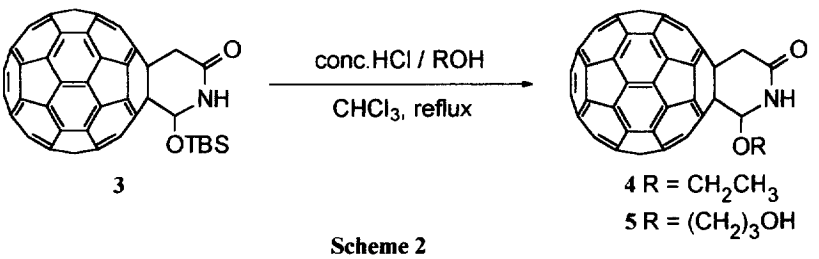
1,3-Bis(*tert*-butyldimethylsilyloxy)-2-aza-1,3-butadiene (**1**) is known as an electron-rich heterodiene[10] and, therefore, the cycloaddition with low LUMO-lying C_{60} proceeded smoothly at room temperature. A solution of C_{60} in chlorobenzene mixed with **1** (3 equiv.) under argon changed color from purple to brown within 4 h, and newly-formed products were observed by TLC. Without isolation of the primary cycloadduct **2**, the resulting reaction mixture was further treated with hydrochloric acid, and the hydrolyzed cycloadduct was separated by silica gel chromatography to give 2-piperidone-fused C_{60} **3** in 77 % yield based on consumed C_{60} (Scheme 1).[11] The structure was elucidated by spectral data.[12] FAB MS peaks appeared at m/z 921 (M^+) and 720 (base) showing one *tert*-butyldimethylsilyl (TBS) group retained in the 1:1 cycloadduct. IR absorptions were observed at 1699 cm^{-1} showing the presence of an amide group, together with 1256, 849 and

527 cm^{-1} characteristic of a TBS group and C_{60}. The ^1H NMR spectrum indicated a methylene signal at δ 4.05 and 5.08 (each 1 H, d, J = 14 Hz), a methine signal at δ 6.49 (1 H, d, J = 5.5 Hz), and an NH signal at δ 8.96 (1 H, d, J = 5.5 Hz) due to a 2-piperidone ring together with methyl signals at 0.34 (3 H, s), 0.48 (3 H, s) and 1.12 (9 H, s) due to a TBS group. The ^{13}C NMR spectrum indicated signals due to two sp^3 junction carbons at δ 61.76 and 70.53 together with 53 lines[13] of sp^2 carbons at δ 135.50 - 155.87 being observable because of lack of C_s symmetry. The other signals at δ -4.71, -3.96, 18.59, 25.96, 45.65, 84.26 and 173.00 were compatible with the piperidone ring and its substituent.



Scheme 1

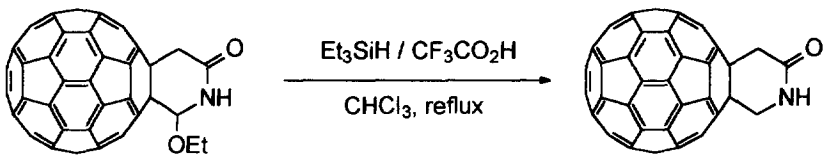
The TBSO group of the obtained product **3** could be replaced by alkoxy groups. Action of an acid on **3** having an $NHCH_2OR$ moiety possibly generates a cyclic iminium cation intermediate which is allowed to react with alcohols. Thus, treatment of **3** (55 mg) with conc. HCl (1 mL) in $CHCl_3$ (10 mL) including EtOH (0.3 mL) under reflux for 12 h afforded 6-ethoxy derivative **4** in a quantitative yield (48 mg) (Scheme 2). This was evidenced by the expected molecular ion (m/z 835) in FAB MS and an ethoxy signal [δ 1.57 (3 H, t, J = 7 Hz), 3.99 and 4.29 (each 1 H, dq, J = 14.5 and 7 Hz)] in ^1H NMR.[14] Similarly, the reaction with 1,3-propanediol for a longer period (3 days) gave 6-(3-hydroxypropoxy) derivative **5** (62 % yield based on consumed **3**).[15]



Scheme 2

When this type of substitution is performed by hydride attack, reduction is expected to occur to give the

parent δ-valerolactam derivative **6**. Thus, **4** was refluxed in $CHCl_3$ with excess CF_3COOH and Et_3SiH for 12 h and the expected product **6** was obtained in 88 % yield after chromatographic separation (Scheme 3). FAB MS peaks at m/z 792 (M^+) and 720 (base) and IR absorptions at 1687 and 527 cm^{-1} were the spectral data as anticipated. The ^1H NMR spectrum showed two pairs of broad singlet signals at δ 4.14 and 4.52 and at δ 4.90 and 5.32, respectively, which coalesced at 35 °C, indicating that piperidone ring-flipping occurs at near room temperature. Because of C_s symmetry and fortuitous superimposability, the ^{13}C NMR spectrum exhibited a simple pattern of 18 lines[16] due to sp^2 carbons at δ 140.51 - 155.01. The other 5 lines were observed at δ 46.80 and 53.58 (piperidone), 63.89 and 66.33 (junction sp^3 carbons) and 172.99 (carbonyl).



4 **6**

Scheme 3

The above conversions by substitution at the position adjacent to a junction carbon are indicative of the synthetic potentiality of **3** and **4**; some designed nucleophiles can be introduced near the C_{60} surface *via* the iminium cation intermediate.

In summary, the hetero Diels-Alder reaction of C_{60} with a 1,3-bis(silyloxy)-2-aza-1,3-diene and the following acid-catalyzed substitution reaction afforded [60]fulleropiperidones. The parent δ-valerolactam derivative of C_{60} seems to be an interesting precursor for C_{60}-based amino acid and polyamide compounds by means of ring-opening reaction.[17]

Acknowledgments: This research was supported by the Japan Securities Scholarship Foundation and a Grant-in-Aid for Developmental Scientific Research (No. 07555285) from the Ministry of Education, Science and Culture of Japan.

References and Notes

1. Krätschmer, W.; Lamb, L. D.; Fostiropoulos, K.; Hufmann, D. R. *Nature*, 1990, 347, No. 6271, p. 354.
2. For example, (a) Kroto, H.; Fischer, J. E.; Cox, D. E. *The Fullerenes*, Pergamon Press, Oxford, 1993. (b) Hirsch, A. *The Chemistry of Fullerenes*, Georg Thime Verlag, Stuttgart, 1994. (c) Williams, R. M.; Zwier, J. M.; Verhoeven, J. W. *J. Am. Chem. Soc.* **1995**, *117*, 4093 and references cited therein.
3. Synthesis of fullerene-heterocycles by the Diels-Alder reaction: (a) Prato, M.; Suzuki, T.; Foroudian, H.; Q. Li.; Khemani, K.; Wudl, F.; Leonetti, J.; Little, R. D.; White, T.; Rickborn, B.; Yamago, S.; Nakamura, E. *J. Am. Chem. Soc.* **1993**, *115*, 1594. (b) Diederich, F.; Jonas, U.; Gramlich, V.; Herrmann. A.; Ringsdorf, H.; Thilgen, C. *Helv. Chim. Acta.* **1993**, *76*, 2445. (c) Gügel, A.; Kraus, A.; Spikermann, J.; Belik, P.; Müllen, K. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 559. (d) Wilson, S. R.; Lu, Q. *Tetrahedron Lett.* **1993**, *34*, 8043. (e) Imahori, H.; Hagiwara, K.; Akiyama, T.; Taniguchi, S.; Okada, T.; Sakata, Y. *Chem. Lett.* **1995**, 265. (f) Linssen, T. G.; Durr, K.; Hanack, M.; Hirsch, A. *J. Chem. Soc., Chem. Commun.* **1995**, 103. (g) Ohkita, M. Ishigami, K.; Tsuji, T. *J. Chem. Soc., Chem. Commun.* **1995**, 1769. (h) Warrener, R. N.; Elsey G. M.; Houghton, M. A. *J. Chem. Soc., Chem. Commun.* **1995**, 1417.

Bifunctional Derivatization of fulleroheterocycles: Banks, M. R.; Cadogan, J. I. G.; Gosney, I.; Hodgson, P. K. G.; Langridge-Smith, P. R. R.; Miller, J. R. A.; Taylor, A. T. *Tetrahedron Lett.* **1994**, *35*, 9067.

4. Boger, D. L.; Weinreb, S. M. *Hetero Diels-Alder Methodology in Organic Chemistry*, Academic Press, New York, 1987.
5. Ohno, M.; Azuma, T.; Eguchi, S. *Chem. Lett.* **1993**, 1833.
6. Ohno, M.; Kojima, S.; Shirakawa, Y.; Eguchi, S. *Tetrahedron Lett.* **1995**, *36*, 6899.
7. Ohno, M.; Kojima, S.; Eguchi, S. *J. Chem. Soc., Chem. Commun.* **1995**, 565.
8. (a) Nie, B.; Rotello, V. M. *J. Org. Chem.* **1996**, *61*, 1870. (b) Tsuda, M.; Ishida, T.; Nogami, T.; Kurono, S., Ohashi, M. *J. Chem. Soc., Chem. Commun.* **1993**, 1296.
9. For a 2-silyloxy-1,3-diene case, (a) An, Y.-Z.; Anderson, J. L.; Rubin, Y. *J. Org. Chem.* **1993**, *58*, 4799. (b) Ohno, M.; Azuma, T.; Kojima, S.; Shirakawa, Y.; Eguchi, S. *Tetrahedron* **1996**, *52*, 4983. In our work, it was found that the primary Diels-Alder cycloadduct of C_{60} with 4-methyl-2-(trimethylsilyloxy)-1,3-pentadiene undergwent cycloreversion in a month if it was not hydrolyzed to a keto form.
10. Sainte, F.; Serckx-Poncin, B.; Hesbain-Frisque, A.-M.; Ghosez, L. *J. Am. Chem. Soc.* **1982**, *104*, 1428.
11. Experimental detail; a solution of C_{60} (137 mg, 0.19 mM) and **1** (180 mg, 0.57 mM) in dry *o*-dichlorobenzene (27 mL) was stirred at room temperature under argon for 4 h. To this solution was added 10% HCl (6 mL), and after being shaken well, the organic layer was washed with water, separated, dried over Na_2SO_4, and evaporated to dryness. The residue was chromatographed on silica gel column (Fuji-Davison BW-300) with toluene to give **3** (113 mg) after elution of the recovered C_{60} (26 mg).
12. The spectral data were obtained by measurements with methods shown in parentheses: FAB MS (matrix: *m*-nitrobenzylalcohol); IR (KBr); ^{1}H NMR (500 MHz) and ^{13}C NMR (125 MHz) in $CDCl_3/CS_2$ (1/1) for **3** and **4** and in *o*-dichlorobenzene-d_4 for **5** and **6**.
13. δ 135.50, 135.54, 136.85, 137.12, 140.17, 140.24, 140.34, 140.61, 141.60, 141.74, 141.79, 141.85, 141.94, 142.08, 142.14, 142.18, 142.23, 142.27, 142.62, 142.72, 142.75, 142.80, 143.16, 143.28, 144.59, 144.66, 144.70, 144.80, 144.84, 145.07, 145.21, 145.44, 145.48, 145.57, 145.59, 145.62, 145.67, 145.76, 145.78, 145.90, 146.31, 146.33, 146.45, 146.58, 146.60, 146.64, 146.68, 147.76, 147.80, 152.79, 152.86, 155.85, 155.87.
14. The other spectral data: IR 1692, 1084, 527 cm^{-1}; ^{13}C NMR δ 15.63, 45.88, 61.72, 64.84, 69.20, 89.50, 135.38, 135.90, 136.92, 137.05, 140.12, 140.23, 140.28, 140.66, 141.68, 141.70, 141.77, 141.80, 141.96, 142.08, 142.15, 142.18, 142.27, 142.29, 142.62, 142.72, 142.76, 142.82, 143.20, 143.34, 144.65, 144.72, 144.78, 144.88, 145.16, 145.34, 145.46, 145.50, 145.61, 145.66, 145.73, 145.79, 145.82, 145.93, 146.32, 146.45, 146.59, 146.64, 146.65, 146.72, 147.77, 147.83, 152.36, 152.91, 155.23, 155.71, 172.56.
15. **5**: FAB MS m/z 865 (M$^+$), 720 (base); IR 3422, 1688, 1071, 527 cm^{-1}; ^{1}H NMR δ 1.01 (1 H, br s), 1.86 (2 H, m), 3.72 (2 H, m), 3.78 and 4.14 (each 1 H, dt, J = 15 Hz and 6 Hz), 3.87 and 4.82 (each 1 H, d, J = 14.5 Hz), 5.83 (1 H, d, J = 5 Hz), 7.95 (1 H, br s); ^{13}C NMR δ 33.03, 46.54, 60.45, 62.20, 66.86, 69.65, 90.36, 135.20, 137.05, 140.29, 140.46, 140.76, 141.79, 141.84, 141.88, 142.16, 142.25, 142.33, 142.38, 142.40, 142.74, 142.81, 142.87, 142.90, 143.33, 143.39, 144.75, 144.81, 144.84, 144.87, 144.98, 145.58, 145.61, 145.78, 145.83, 145.86, 145.94, 146.05, 146.47, 146.56, 146.73, 146.75, 146.77, 146.84, 147.92, 147.96, 152.74, 156.11, 172.02.
16. δ 140.51 (4 C), 140.57 (4 C), 141.91 (1 C), 141.97 (1 C), 142.31 (6 C), 142.83 (4 C), 142.86 (2 C), 143.31 (2 C), 144.86 (4 C), 145.68 (4 C), 145.73 (2 C), 145.81 (2 C), 145.91 (2 C), 146.50 (6 C), 146.74 (4 C), 146.77 (4 C), 147.89 (2 C), 155.01 (4 C).
17. In a preliminary experiment, **6** was refluxed in conc. H_2SO_4, but formed was an uncharacterizable brown solid which was insoluble in most solvents such as water, ethanol, chloroform, toluene and *o*-dichlorobenzene.

(*Received in Japan* 19 *September* 1996; *revised* 30 *October* 1996; *accepted* 5 *November* 1996)