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Hetero-Diels–Alder reaction of [60]fullerene with nitrosoalkene

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ABSTRACT

A new type of stable C_{60}-fused dihydrooxazine derivatives was successfully prepared by the hetero-Diels–Alder reaction of C_{60} with nitrosoalkene generated in situ by extrusion of HBr from the corresponding α-bromooxime.

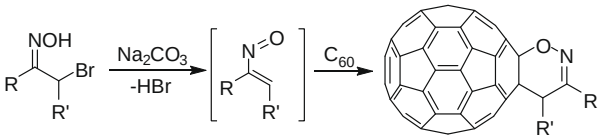
Since [60]fullerene, the most abundant representative of the fullerene family, was produced in macroscopic quantities for the first time in 1990,[1] a wide variety of reactions of fullerenes have been developed to synthesize a great diversity of fullerene compounds,[2] some of which have found widespread use in chemical, biological, and materials sciences.[3] Cycloaddition reaction is among the most outstanding and expeditious methods for the functionalization of C_{60} and has been applied to a variety of [*n*+2]cycloadditions (*n* = 1–4). Diels–Alder reaction has been particularly useful in the chemical modification of C_{60} to construct six-membered fullerocycles. However, many of the Diels–Alder cycloadducts of C_{60} were found to be thermally unstable and undergo cycloreversion to give the component molecules. Stable Diels-Alder adducts of C_{60} were first explored by Müllen and Rubin in their pioneering work using *o*-quinodimethane and its analogues as reactive dienes.[4]

Although the Diels–Alder reaction has been widely explored in the functionalization of C_{60}, the hetero-Diels–Alder reaction was seldom investigated. For example, the reaction of C_{60} with the oxo,[5] thia,[6] selenium,[7] and aza[8] heterologs of *o*-quinodimethanes, and with a 1,3-disubstituted-2-aza-1,3-diene,[9] has been reported to date. C_{60}-fused tetrahydropyridazine has been synthesized through heterocycloaddition of thermally generated 1,2-diaza-1,3-butadienes with [60]fullerene.[10] The reaction of C_{60} with 1,2,3-triazine[11] or 1,2,4,5-tetrazine[12] gave azacyclohexadiene-fused fullerene derivative through [4+2] cycloaddition/nitrogen-extrusion. There are also other methods to construct six-membered fulleroheterocycles such as the photochemical addition reaction of fullerene with 1,2-ethylenediamine and piperazine, which could give a derivative directly bonded to two nitrogen atoms.[13] Recently a novel protocol for the preparation of C_{60}-fused δ-lactones from benzenediazonium-2-carboxylates controlled by organic bases has been explored.[14]

We aimed at developing a new method to prepare fullerene derivatives with yet unknown novel structure. To the best of our knowledge, 5,6-dihydro-4*H*-oxazines are easily accessible from α-halolximes and olefinic substrates such as enol ethers, enamines, alkenes, and allenes.[15] These processes have been identified as inverse-electron demanded hetero-Diels–Alder reactions involving transient nitrosoalkenes,[16] that is, with electron-deficient heterodienes and electron-rich alkenes. However, C_{60} usually behaves as an electron-deficient dienophile and reacts with numerous electron-rich dienes in Diels–Alder reactions. The direct Diels–Alder reaction of fullerene C_{60} with nitrosoalkene should be a rather unfavorable one. We were wondering whether this kind of reaction could be applied to the functionalization of C_{60}.

To our satisfaction, when a mixture of C_{60} (54.0 mg), 2-bromo-1-phenylethanone oxime **1a** (80.0 mg, 5 equiv), and Na_2CO_3 (40.0 mg, 5 equiv) in 30 mL toluene was stirred at room temperature for 15 h the desired dihydrooxazine-fused C_{60} derivative **2a** was obtained in 26% (67% based on consumed C_{60}) yield (Scheme 1).

To examine the scope and limitation of the used substrates, various α-bromooximes **1a–g** were synthesized by the reactions of α-bromoketone with hydroxylamine hydrochloride and applied to the hetero-Diels–Alder reactions of C_{60}.[17] The reaction times and isolated yields along with recovered C_{60} for the reactions of C_{60}



1 **2**

1a, **2a**: R = Ph, R' = H
1b, **2b**: R = 4-$CH_3OC_6H_4$, R' = H
1c, **2c**: R = 4-$NO_2C_6H_4$, R' = H
1d, **2d**: R = CH_3, R' = H
1e, **2e**: R, R' = -$(CH_2)_4$-
1f, **2f**:

Scheme 1.

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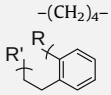
with α-bromooximes compounds **1a–f** and Na_2CO_3 in a molar ratio of 1:5:5 in toluene at proper temperature are listed in Table 1. The effect of other bases such as triethylamine, pyridine, and sodium ethoxide was also examined. The result showed that triethylamine and pyridine did not work because they could react with the bromooxime to form an organic salt which could not react with C_{60}. In addition, sodium ethoxide could not initiate the reaction either.

As far as we know the electron-rich alkene was widely used in the hetero-Diels–Alder reaction of nitrosoalkene; however, there are few reports that the electron-deficient alkenes were used as dienophiles in this kind of reversed-electron demanded reaction.[18] As can be seen from Table 1, **1a–f** reacted well with C_{60}. When R was an aromatic group and R′ was hydrogen (**1a–c**) the yields were higher and the electronic property of the substituent on the phenyl had little influence on the reaction. While R was an aliphatic group (**1d–e**) the reaction needed higher temperature and proceeded much slower and the yields decreased notably. The possible explanation was that the nitrosoalkene generated from **1a–c** might be formed easily and might have higher stability due to the conjugation of aromatic cycle with the C=C and N=O double bonds when R was an aromatic group, thus benefitting the reaction. It is to be noted that when R was CO_2Et group and R′ was hydrogen no product was obtained at 100 °C in spite of prolonging the reaction time to 48 h. Because fullerene is an electron-deficient alkene, the increase of electron-withdrawing ability of nitrosoalkene would decrease the reactivity. From this result we predicted that the nitrosoalkene with R being a phenyl group and the R′ being an alkyl or a phenyl group would be formed easily and had higher stability, and the reaction would proceed easier than **1a–c**. Firstly, we synthesized **1f** which reacted with C_{60} in shorter time (1.5 h) and gave higher yield (47%). That **1f** had higher reactivity than **1a–c** proved our prediction. But we failed in synthesizing the substrate with R and R′ being all phenyl group because the solvolysis reaction occurred. All new compounds **2a–f** were very stable. There was not any decomposition in solid state at room temperature even when placed for two months or in toluene solution at 110 °C for 24 h.

The identities of compounds **2a–e** were fully established by their MS, ^{1}H NMR, ^{13}C NMR, FT-IR, and UV–vis spectra. Taking **2a** as an example, the APCI mass spectrum of **2a** showed the molecular ion peak at *m/z* 853. The ^{1}H NMR spectrum of **2a** displays a singlet at 4.57 ppm for methylene and peaks of the five hydrogens for the phenyl ring. In the ^{13}C NMR spectrum of **2a**, there are 30 peaks due to the sp^2-C of the C_{60} skeleton in the range of 153.09–136.45 ppm and two sp^3-C of the C_{60} cage at 95.57 and 65.25 ppm along with 4 peaks for the phenyl rings in the range of 133.4–126.9 ppm, 1 peak at 175.15 ppm for the ON=*C* moiety, and 1 peak at 35.56 ppm for the *C*H_2 group, consistent with the C_s symmetry of its molecular structure. The resonance of the sp^3-C of C_{60} cage was close to that directly attached to an oxygen atom in the recent report of 1,2-adducts of C_{60}.[19,14] Other dihydrooxazine-fused C_{60} derivatives (**2b–e**) except **2f**, which could not be characterized by ^{13}C NMR because of its very low solubility, were characterized in the same way.

In conclusion, the hetero-Diels–Alder reaction of C_{60} with nitrosoalkene generated in situ from the corresponding α-bromooximes by treatment with Na_2CO_3 was explored, and led to the formation of a new type of stable C_{60}-fused dihydrooxazine derivatives. These fullerene products may be further functionalized by the manipulation on the C=N double bond and weak N–O bond. Further work is underway to investigate functionalization of the C=N double bond and N–O bond on the dihydrooxazine ring.

Table 1
Yields and reaction time for the reaction of C_{60} with **1a–e** using Na_2CO_3 as a base

Substrate	R	R′	Temperature (°C)	Time (h)	Product	Yield[a] (%)
1a	Ph	H	25	15	**2a**	26 (67)
1b	4-$CH_3OC_6H_4$	H	25	15	**2b**	26 (59)
1c	4-$NO_2C_6H_4$	H	25	15	**2c**	31 (86)
1d	CH_3	H	100	25	**2d**	18 (60)
1e	$-(CH_2)_4-$		80	24	**2e**	16 (53)
1f			25	1.5	**2f**	47 (75)
1g	COOEt	H	100	48	—	—

[a] Isolated yield, that in the parentheses refers to the yield based on consumed C_{60}.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2009.10.060.

References and notes

1. Kratschmer, W.; Lamb, L. D.; Fostiropoulous, K.; Huffman, D. R. *Nature* **1990**, *347*, 354.
2. For reviews, see: Hirsch, A.; Brettreich, M. *Fullerenes: Chemistry and Reactions*; Wiley-VCH, 2005; (a) Hirsch, A. *Synthesis* **1995**, 895; (b) Diederich, F.; Thilgen, C. *Science* **1996**, *271*, 317; (c) Hirsch, A. *Top. Curr. Chem.* **1999**, *199*, 1; (d) Yurovskaya, M. A.; Trushkov, I. V. *Russ. Chem. Bull. Int. Ed* **2002**, *51*, 367; (e) Thilgen, C.; Diederich, F. *Chem. Rev.* **2006**, *106*, 5049.
3. (a) Martin, N.; Sánchez, L.; Llescas, B.; Pérez, I. *Chem. Rev.* **1998**, *98*, 2527; (b) Prato, M.; Maggini, M. *Acc. Chem. Res.* **1998**, *31*, 519; (c) Nakamura, E.; Isobe, H.; Tomita, N.; Sawamura, M.; Jinno, S.; Okayama, H. *Angew. Chem., Int. Ed.* **2000**, *39*, 4254; (d) Nakamura, E.; Isobe, H. *Acc. Chem. Res.* **2003**, *36*, 807; (e) Guldi, D. M.; Zerbetto, F.; Georgakilas, V.; Prato, M. *Acc. Chem. Res.* **2005**, *38*, 38; (f) Cremer, J.; Bauerle, P.; Wienk, M. M.; Janssen, R. A. J. *Chem. Mater.* **2006**, *18*, 5832.
4. (a) Belik, P.; Gügel, A.; Spickermann, J.; Müllen, K. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 78; (b) Rubin, Y.; Khan, S.; Freedberg, D. I.; Yeretzian, C. *J. Am. Chem. Soc.* **1993**, *115*, 344.
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. Nakahodo, T.; Takahashi, K.; Ishitsuka, M. O.; Tsuchiya, T.; Maeda, Y.; Fujihara, H.; Nagase, S.; Akasaka, T. *Tetrahedron Lett.* **2008**, *47*, 2302.
8. (a) Martín, N.; Martínez-Grau, A.; Sánchez, L.; Seoane, C.; Torres, M. *J. Org. Chem.* **1998**, *63*, 8074; (b) Ohno, M.; Sato, H.; Eguchi, S. *Synlett* **1999**, 207.
9. Ohno, M.; Kojima, S.; Shirakawa, Y.; Eguchi, S. *Tetrahedron Lett.* **1996**, *37*, 9211.
10. Yang, H.-T.; Wang, G.-W.; Xu, Y.; Huang, J.-C. *Tetrahedron Lett.* **2006**, *47*, 4129.
11. Murata, Y.; Murata, M.; Komatsu, K. *J. Org. Chem.* **2001**, *66*, 8187.
12. (a) Miller, G. P.; Tetreau, M. C. *Org. Lett.* **2000**, *2*, 3091; (b) Murata, Y.; Suzuki, M.; Rubin, Y.; Komatsu, K. *Bull. Chem. Soc. Jpn.* **2003**, *76*, 1669.
13. (a) Wang, N.-X. *Tetrahedron* **2002**, *58*, 2377; (b) Butts, C. P.; Jazdzyk, M. *Chem. Commun.* **2003**, 1530.
14. Wang, G.-W.; Zhu, B. *Chem. Commun.* **2009**, 1769.
15. (a) Wabnitz, T. C.; Saaby, S.; Jørgensen, K. A. *Org. Biomol. Chem.* **2004**, *2*, 828; (b) Gallos, J. K.; Sarli, V. C.; Varogli, A. C.; Papadoyanni, C. Z.; Papaspyrou, S. D.; Argyropoulos, N. G. *Tetrahedron Lett.* **2003**, *44*, 3905; (c) Zimmer, R.; Collas, M.; Czerwonka, R.; Hain, U.; Reissig, H.-U. *Synthesis* **2008**, 237.
16. (a) Gilchrist, T. L. *Chem. Soc. Rev.* **1983**, 53; (b) Arnold, T.; Orschel, B.; Reissig, H.-U. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1033; (c) Yoon, S. C.; Kim, K.; Park, Y. J. *J. Org. Chem.* **2001**, *66*, 7334.
17. *Typical procedure for the synthesis of* **2a–f**: A mixture of C_{60} (54.0 mg, 0.075 mmol), **1** (0.375 mmol), and Na_2CO_3 (0.375 mmol) was dissolved in 30 mL of toluene and stirred at proper temperature for a desired time. The product was separated on a silica gel column with CS_2 or CS_2-toluene as the eluent to afford unreacted C_{60} and adduct **2**.
Compound **2a**: ^{1}H NMR (500 MHz, CS_2–$CDCl_3$) δ 8.11 (dd, J = 6.5, 2.1 Hz, 2H), 7.61–7.55 (m, 2H), 4.57 (s, 2H); ^{13}C NMR (125 MHz, CS_2–$CDCl_3$, all 2C unless indicated) δ 175.15 (1C, *C*=N), 153.09, 148.30 (1C), 148.07, 147.76 (1C), 146.64, 146.55, 146.42, 146.27, 146.18, 145.71, 145.63, 145.44, 145.42, 145.34, 144.71, 144.58, 144.50, 142.81, 142.70, 142.69, 142.46, 142.37, 142.07, 142.06, 141.58, 141.52, 140.22, 139.95, 137.94, 136.45, 133.37 (1C, aryl *C*), 131.58 (1C, aryl *C*), 129.20 (aryl *C*), 126.87 (aryl *C*), 95.57 (1C, sp^3-*C* of C_{60}), 65.25 (1C, sp^3-*C* of C_{60}), 35.56 (1C, CH_2);) UV–vis ($CHCl_3$) λ_{max} nm 256, 316, 690; FT-IR ν/cm^{-1} (KBr) 2920, 2850, 1462, 1425, 1347, 1181, 1114, 1104, 967, 918, 767, 759, 687, 575, 563, 554, 526; MS (+APCI) *m/z* 853.

Compound **2b**: ^{1}H NMR (500 MHz, CS_2–$CDCl_3$) δ 8.03 (d, J = 8.9 Hz, 2H), 7.03 (d, J = 8.9 Hz, 2H), 4.51 (s, 2H), 3.89 (s, 3H); ^{13}C NMR (125 MHz, CS_2–$CDCl_3$, all 2C unless indicated) δ 173.97 (1C, *C*═N), 162.27 (1C, aryl *C*), 153.13, 148.17 (1C), 147.65 (1C), 146.52, 146.45, 146.30, 146.16, 146.07, 145.68, 145.52, 145.36, 145.30, 145.23, 144.63, 144.48, 144.45, 142.71, 142.59, 142.58, 142.35, 142.28, 141.97, 141.95, 141.48, 141.44, 140.10, 139.85, 137.83, 136.42, 128.32 (aryl *C*), 125.55 (1C, aryl *C*), 114.49 (aryl *C*), 95.29 (1C, sp^3-*C* of C_{60}), 65.13 (1C, sp^3-*C* of C_{60}), 55.05 (1C, *C*H_3O), 35.18 (1C, *C*H_2); UV–vis ($CHCl_3$) λ_{max} nm 257, 315, 690; FT-IR ν/cm^{-1} (KBr) 2925, 2831, 1604, 1511, 1461, 1426, 1349, 1305, 1253, 1176, 1019, 968, 920, 868, 830, 768, 623, 575, 563, 554, 526; MS (+APCI) *m*/*z* 883.

Compound **2c**: ^{1}H NMR (500 MHz, CS_2–DMSO-d_6) δ 8.44 (d, J = 8.9 Hz, 2H), 8.38 (d, J = 8.9 Hz, 2H), 4.69 (s, 2H); ^{13}C NMR (125 MHz, CS_2–DMSO-d_6, all 2C unless indicated) δ 173.36 (1C, *C*═N), 152.27, 148.74 (1C, aryl *C*), 147.46 (1C), 147.22, 146.91 (1C), 145.84, 145.74, 145.60, 145.44, 145.37, 144.82, 144.76, 144.61, 144.59, 144.50, 144.06, 143.84, 143.79, 142.00, 141.91, 141.88, 141.61, 141.52, 141.28, 141.25, 140.74, 140.66, 139.24, 139.12, 138.07, 137.04, 135.44, 127.41 (aryl *C*), 123.37 (aryl *C*), 94.81 (1C, sp^3-*C* of C_{60}), 64.52 (1C, sp^3-*C* of C_{60}), 34.01 (1C, *C*H_2); UV–vis ($CHCl_3$) λ_{max} nm 256, 316, 690; FT-IR ν/cm^{-1} (KBr) 2920, 2849, 1509, 1463, 1425, 1340, 1181, 1102, 965, 914, 875, 849, 767, 751, 687, 574, 563, 554, 526; MS (+APCI) *m*/*z* 898.

Compound **2d**: ^{1}H NMR (500 MHz, CS_2–$CDCl_3$) δ 4.14 (s, 2H), 2.70 (s, 3H); ^{13}C NMR (125 MHz, CS_2–$CDCl_3$, all 2C unless indicated) δ 175.62 (1C, *C*═N), 153.18, 148.32 (1C), 148.05, 147.80 (1C), 146.65, 146.60, 146.42, 146.31, 146.22, 145.75, 145.63, 145.48, 145.44, 145.37, 144.74, 144.61, 144.50, 143.07, 142.86, 142.73, 142.71, 142.47, 142.39, 142.07, 141.60, 141.52, 140.20, 139.96, 137.84, 136.33, 94.98 (1C, sp^3-*C* of C_{60}), 64.63 (1C, sp^3-*C* of C_{60}), 37.81 (1C, *C*H_2), 21.80 (1C, *C*H_3); UV–vis ($CHCl_3$) λ_{max} nm 256, 316, 689; FT-IR ν/cm^{-1} (KBr) 2917, 2848, 1511, 1462, 1424, 1374, 1181, 984, 948, 921, 902, 878, 857, 767, 729, 644, 575, 561, 553, 526; MS (+APCI) *m*/*z* 791.

Compound **2e**: ^{1}H NMR (500 MHz, CS_2 CS_2–DMSO-d_6) δ 4.35 (dd, J = 10.5, 6.3 Hz, 1H), 3.09–3.05 (m, 1H), 2.92–2.85 (m, 1H), 2.52–2.41 (m, 2H), 2.17–2.05 (m, 3H), 1.93–1.90 (m, 1H); ^{13}C NMR (125 MHz, CS_2–DMSO-d_6, all 1C unless indicated) δ 177.76 (*C*═N), 151.46, 150.62, 150.50, 147.36, 146.87, 146.41, 145.77, 145.76, 145.73, 145.68, 145.61, 145.42, 145.38 (2C), 145.36, 145.30, 145.27 (2C), 144.76 (2C), 144.71, 144.68, 144.61, 144.56, 144.52, 144.47 (2C), 144.43, 144.07, 143.82, 143.75, 143.70, 142.00 (2C), 141.91, 141.88 (2C), 141.85, 141.67, 141.57, 141.52, 141.36 (2C), 141.30, 141.26, 141.09, 140.82, 140.64, 140.54, 140.53, 139.12, 139.11, 138.78, 138.41, 136.97, 136.64, 136.01, 135.22, 94.93 (1C, sp^3-*C* of C_{60}), 68.44 (1C, sp^3-*C* of C_{60}), 40.10 (1C, *C*H_2); UV–vis ($CHCl_3$) λ_{max} nm 256, 316, 689; FT-IR ν/cm^{-1} (KBr) 2932, 2861, 1511, 1462, 1426, 1181, 979, 943, 912, 879, 840, 728, 574, 563, 553, 526; MS (+APCI) *m*/*z* 831. Compound **2f**: ^{1}H NMR (500 MHz, CS_2–$CDCl_3$) δ 8.38 (d, J = 7.7 Hz, 1H), 7.50 (t, J = 7.5 Hz, 1H), 7.44 (d, J = 7.4 Hz, 1H), 7.34 (d, J = 7.4 Hz, 1H), 4.77 (dd, J = 10.7, 6.5 Hz, 1H), 3.20–3.09 (m, 2H), 2.93–2.86 (m, 1H), 2.71–2.63 (m, 1H); UV–vis ($CHCl_3$) λ_{max} nm 259, 317, 689; FT-IR ν/cm^{-1} (KBr) 2921, 2853, 1513, 1462, 1429, 1338, 1181, 1008, 973, 923, 875, 861, 760, 728, 625, 575, 563, 554, 526; MS (+APCI) *m*/*z* 879.

18. (a) Venkata, P.P.; Sarala, B.; Sarika, R.; Abhijit, R.; Sunanda, G.D. PCT Int. Appl. **2007**, WO 2007046022 A2.; (b) Tret'yakova, E. V.; Flekhter, O. B.; Galin, F. Z.; Tolstikov, G. A. *Chem. Nat. Compd.* **2004**, *40*, 391.
19. (a) Wang, G.-W.; Li, F.-B.; Zhang, T.-H. *Org. Lett.* **2006**, *8*, 1355; (b) Wang, G.-W.; Li, F.-B.; Xu, Y. *J. Org. Chem.* **2007**, *72*, 4774; (c) Wang, G.-W.; Li, F.-B.; Chen, Z.-X.; Wu, P.; Cheng, B.; Xu, Y. *J. Org. Chem.* **2007**, *72*, 4779; (d) Li, F.-B.; Liu, T.-X.; Wang, G.-W. *J. Org. Chem.* **2008**, *73*, 6417; (e) Wang, G.-W.; Lu, Y.-M.; Chen, Z.-X.; Wu, S.-H. *J. Org. Chem.* **2009**, *74*, 4841.