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Heterocycloaddition of thermally generated 1,2-diaza-1,3-butadienes to [60]fullerene

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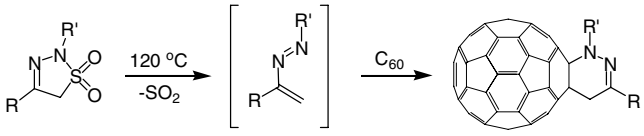
Abstract—Stable C_{60}-fused tetrahydropyridazine derivatives were synthesized through the hetero-Diels–Alder cycloaddition of C_{60} with 1,2-diaza-1,3-butadienes, which were generated in situ by the thermal extrusion of sulfur dioxide from 2,5-dihydro-1,2,3-thiadiazole-1,1-dioxides.

Chemical modification of [60]fullerene (C_{60}) to generate novel C_{60} derivatives with new structures and properties has attracted great attention over the last two decades for their potential material and medicinal applications.[1] Cycloaddition reaction is among the most outstanding and expeditious methods for the functionalization of C_{60}, which behaves as a good dienophile and reacts with a large variety of dienes. Diels–Alder reaction has been particularly useful in the chemical modification of C_{60}. However, many of the Diels–Alder cycloadducts of C_{60} were found to be thermally unstable and underwent cycloreversion to give the component molecules.[2] 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.[3] These highly reactive species, generated in situ from a variety of precursors, are efficiently trapped by C_{60}, which gains extra stabilization because of the restoration of the aromatic system.

Although the Diels–Alder reaction has been widely employed in the derivatizations of C_{60}, the hetero-Diels–Alder reaction was seldom investigated. Only few examples, that is, the hetero-Diels–Alder reaction of C_{60} with the oxo,[4] thia[5] and aza[6] heterologs of *o*-quinodimethanes, and with a 1,3-disubstituted 2-aza-1,3-diene,[7] have been reported to date. To the best of our knowledge, 1,2-diaza-1,3-butadienes, which contain two nitrogen atoms and are known to react with electron-rich alkenes, electron-deficient alkenes, and unconjugated alkenes,[8] have not been applied to the functionalization of C_{60} yet. In continuation of our interest in fullerene chemistry,[9] herein we report the new hetero-Diels–Alder reactions of 1,2-diaza-1,3-butadienes with C_{60} to give stable C_{60}-fused tetrahydropyridazine derivatives.

The 1,2-diaza-1,3-butadienes we investigated were generated in situ by the thermal extrusion of SO_2 from 2,5-dihydro-1,2,3-thiadiazole-1,1-dioxides **1a**–**e**, which were prepared according to the reported procedures.[10] In order to examine the generality of reagents **1**, R and R′ substituents as both aromatic and aliphatic groups have been explored. To our satisfaction, the reaction of C_{60} with **1a**–**e** in refluxing toluene gave the desired **2a**–**e** (Scheme 1).[11]

The yields and reaction times along with recovered C_{60} for the reaction of C_{60} with **1a**–**e** in toluene



1 **2**

1a, **2a**: R = Ph, R' = Ph
1b, **2b**: R = 4-ClPh, R' = Ph
1c, **2c**: R = 4-CH_3OPh, R' = Ph
1d, **2d**: R = CH_3, R' = Ph
1e, **2e**: R = Ph, R' = 4-$ClPhCH_2$

Scheme 1.

Keywords: [60]Fullerene; Hetero-Diels–Alder reaction; 1,2-Diaza-1,3-butadienes.
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Table 1. Yields, reaction times and recovered C_{60} for the reaction of C_{60} with **1a**–**e** at 120 °C

Product	R	R′	Time (min)	Yield[a] (%)	Recovered C_{60} (%)
2a	Ph	Ph	60	47	42
2b	4-ClPh	Ph	45	48	47
2c	4-MeOPh	Ph	40	48	45
2d	CH_3	Ph	180	36	48
2e	Ph	4-ClPhCH_2	480	27	61

[a] Isolated yield.

heated in an oil bath preset at 120 °C are listed in Table 1.

As shown in Table 1, when both R and R′ were aromatic groups (**2a**–**c**) the yields were higher, and the electronic property of the substituent on the phenyl ring of the R group had little effect on the product yields. However, when the R or R′ group was replaced by an aliphatic group (**2d**,**e**), the yields decreased notably and the reactions proceeded much slower. The 1,2-diaza-1,3-butadienes generated from **1a**–**e** might be formed easily and have higher stability due to the conjugation with C=C and N=N double bonds when both R and R′ were aromatic groups, thus explaining the observed phenomenon. All new compounds **2a**–**e** were very stable at room temperature.

The identities of compounds **2a**–**e** were established by their MS, ^{1}H NMR, ^{13}C NMR, FT-IR, and UV–vis spectra.[12] Taking **2a** as an example, the APCI mass spectrum of **2a** showed the molecular ion peak at *m*/*z* 928. The ^{1}H NMR spectrum of **2a** displayed a singlet at 4.74 ppm for the methylene group and peaks of the 10 hydrogens for the two phenyl rings. In the ^{13}C NMR spectrum of **2a**, there were 30 peaks due to the sp^2-C of the C_{60} skeleton in the range of 153.8–135.3 ppm and two sp^3-C of the C_{60} cage at 84.99 and 67.78 ppm along with eight peaks for the two aromatic rings, one peak at 161.37 ppm for the NN=*C* moiety, and one peak at 37.46 ppm for the CH_2 group, consistent with the C_s symmetry of its molecular structure. The UV–vis spectrum of **2a** showed a peak at 431 nm, which was a characteristic absorption peak for the monoadduct of C_{60} at the [6,6] junction. All other tetrahydropyridazine-fused C_{60} derivatives (**2b**–**e**) were characterized in the same way.

In conclusion, the hetero-Diels–Alder reaction of C_{60} with 1,2-diaza-1,3-butadienes generated in situ by the thermal extrusion of SO_2 from 2,5-dihydro-1,2,3-thiadiazole-1,1-dioxides was realized, and led to the formation of new types of stable C_{60}-fused tetrahydropyridazine derivatives. These fullerene products could be converted into water-soluble ammonium salts, which may have applications in biology and nanoscience,[1e,f] and they could be further functionalized by the manipulation on the C=N double bond.

Acknowledgments

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11. Typical procedure for the synthesis of **2a**–**e**: A mixture of C_{60} (36.0 mg, 0.05 mmol) and **1a** (**1b**–**e**, 0.06 mmol) was dissolved in 30 mL of toluene and stirred in an oil bath preset at 120 °C for a desired time. After removing the solvent in vacuo, the residue was separated on a silica gel column with CS_2 or CS_2–toluene as the eluent to afford unreacted C_{60} and adduct **2a** (**2b**–**e**).
12. Compound **2a**: ^{1}H NMR (300 MHz, CS_2–DMSO-d_6) δ 8.10 (d, $J = 7.9$ Hz, 2H), 7.79 (d, $J = 7.4$ Hz, 2H), 7.51–7.42 (m, 3H), 7.31 (t, $J = 7.7$ Hz, 2H), 7.15 (t, $J = 7.3$ Hz, 1H), 4.74 (s, 2H); ^{13}C NMR (75 MHz, CS_2–DMSO-d_6, with Cr(acac)$_3$ as relaxation reagent) (all 2C unless indicated) δ 161.37 (1C, N*C*=), 153.78, 147.78, 147.09 (1C), 146.63 (1C), 146.32 (1C, aryl *C*), 145.68, 145.60, 145.30, 145.17, 144.97, 144.87, 144.75, 144.59, 144.40, 144.35, 143.87, 143.74, 143.59, 141.95, 141.78, 141.69, 141.55, 141.28, 141.24, 141.02, 140.79, 140.71, 139.38, 137.35, 135.94, 135.27, 135.04 (1C, aryl *C*), 129.35 (1C, aryl *C*), 128.11 (aryl *C*), 128.09 (aryl *C*), 127.42 (aryl *C*), 125.66 (1C, aryl *C*), 125.44 (aryl *C*), 84.99 (1C, sp^3-*C* of C_{60}), 67.78 (1C, sp^3-*C* of C_{60}), 37.46 (1C, *C*H$_2$); UV–vis

($CHCl_3$) λ_{max} nm ($\log\varepsilon$) 257 (5.16), 316 (4.73), 431 (3.52), 696 (2.60); FT-IR ν/cm^{-1} (KBr) 2922, 2853, 1594, 1512, 1489, 1463, 1425, 1357, 1234, 1183, 1071, 755, 692, 577, 527; MS (+APCI) m/z 928.

Compound **2b**: ^1H NMR (300 MHz, CS_2–DMSO-d_6) δ 8.03 (d, $J = 8.6$ Hz, 2H), 7.70 (d, $J = 7.3$ Hz, 2H), 7.36 (d, $J = 8.6$ Hz, 2H), 7.23 (t, $J = 7.7$ Hz, 2H), 7.08 (t, $J = 7.4$ Hz, 1H), 4.66 (s, 2H); ^{13}C NMR (75 MHz, CS_2–DMSO-d_6, with $Cr(acac)_3$ as relaxation reagent) (all 2C unless indicated) δ 160.29 (1C, N*C*═), 153.64, 147.69, 147.17 (1C), 146.72 (1C), 146.24 (1C, aryl *C*), 145.77, 145.69, 145.39, 145.26, 145.07, 144.87, 144.79, 144.69, 144.48, 144.44, 143.88, 143.80, 143.66, 142.04, 141.88, 141.79, 141.61, 141.36, 141.31, 141.05, 140.86, 140.79, 139.45, 137.46, 135.95, 135.55 (1C, aryl *C*), 135.33, 133.61 (1C, aryl *C*), 128.29 (aryl *C*), 128.15 (aryl *C*), 127.47 (aryl *C*), 126.79 (aryl *C*), 125.77 (1C, aryl *C*), 85.06 (1C, sp^3-*C* of C_{60}), 67.78 (1C, sp^3-*C* of C_{60}), 37.40 (1C, *C*H_2); UV–vis ($CHCl_3$) λ_{max} nm ($\log\varepsilon$) 256 (5.13), 316 (4.70), 431 (3.49), 695 (2.55); FT-IR ν/cm^{-1} (KBr) 2922, 2851, 1593, 1511, 1489, 1421, 1355, 1180, 1091, 1010, 826, 765, 696, 574, 526; MS (+APCI) m/z 962.

Compound **2c**: ^1H NMR (300 MHz, CS_2–DMSO-d_6) δ 8.03 (d, $J = 8.9$ Hz, 2H), 7.78 (d, $J = 7.3$ Hz, 2H), 7.29 (t, $J = 7.8$ Hz, 2H), 7.13 (t, $J = 7.3$ Hz, 1H), 6.95 (d, $J = 8.9$ Hz, 2H), 4.70 (s, 2H), 3.84 (s, 3H); ^{13}C NMR (75 MHz, CS_2–DMSO-d_6, with $Cr(acac)_3$ as relaxation reagent) (all 2C unless indicated) δ 160.93 (1C, N*C*═), 160.34 (1C, aryl *C*), 153.70, 147.79, 146.95 (1C), 146.51 (1C), 146.34 (1C, aryl *C*), 145.54, 145.47, 145.18, 145.04, 144.84, 144.80, 144.62, 144.46, 144.27, 144.23, 143.72, 143.61, 143.49, 141.83, 141.65, 141.57, 141.43, 141.16, 141.11, 140.90, 140.66, 140.59, 139.25, 137.25, 135.83, 135.20, 127.96 (aryl *C*), 127.54 (1C, aryl *C*), 127.24 (aryl *C*), 126.78 (aryl *C*), 125.40 (1C, aryl *C*), 113.41 (aryl *C*), 84.91 (1C, sp^3-*C* of C_{60}), 67.58 (1C, sp^3-*C* of C_{60}), 54.27 (1C, O*C*H_3), 37.28 (1C, *C*H_2); UV–vis ($CHCl_3$) λ_{max} nm ($\log\varepsilon$) 257 (5.17), 317 (4.76), 431 (3.53), 696 (2.62); FT-IR ν/cm^{-1} (KBr) 2924, 2851, 1607, 1514, 1487, 1425, 1358, 1252, 1176, 1031, 975, 829, 765, 698, 573, 527; MS (+APCI) m/z 958.

Compound **2d**: ^1H NMR (300 MHz, CS_2–DMSO-d_6) δ 7.67 (d, $J = 7.4$ Hz, 2H), 7.25 (t, $J = 7.6$ Hz, 2H), 7.10 (t, $J = 7.2$ Hz, 1H), 4.28 (s, 2H), 2.64 (s, 3H); ^{13}C NMR (75 MHz, CS_2–DMSO-d_6, with $Cr(acac)_3$ as relaxation reagent) (all 2C unless indicated) δ 162.96 (1C, N*C*═), 153.69, 147.66, 146.85 (1C), 146.43 (1C), 145.97 (1C, aryl *C*), 145.44, 145.40, 145.09, 144.97, 144.74 (4C), 144.53, 144.36, 144.18, 144.15, 143.56, 143.52, 143.40, 141.77, 141.58, 141.48, 141.37, 141.06, 141.01, 140.80, 140.58, 140.48, 139.16, 137.14, 135.68, 134.99, 127.79 (aryl *C*), 127.10 (aryl *C*), 125.21 (1C, aryl *C*), 84.31 (1C, sp^3-*C* of C_{60}), 67.20 (1C, sp^3-*C* of C_{60}), 29.07 (1C, *C*H_2), 22.79 (1C, *C*H_3); UV–vis ($CHCl_3$) λ_{max} nm ($\log\varepsilon$) 256 (5.08), 314 (4.61), 431 (3.47), 695 (2.53); FT-IR ν/cm^{-1} (KBr) 2923, 2852, 1593, 1512, 1486, 1426, 1378, 1184, 1104, 1071, 1023, 765, 696, 573, 527; MS (+APCI) m/z 866.

Compound **2e**: ^1H NMR (300 MHz, CS_2–DMSO-d_6) δ 7.98–7.90 (m, 2H), 7.57 (d, $J = 8.2$ Hz, 2H), 7.44–7.37 (m, 3H), 7.32 (d, $J = 8.2$ Hz, 2H), 5.44 (s, 2H), 4.60 (s, 2H); ^{13}C NMR (75 MHz, CS_2–DMSO-d_6, with $Cr(acac)_3$ as relaxation reagent) (all 2C unless indicated) δ 161.74 (1C, N*C*═), 153.78, 147.51, 147.04 (1C), 146.57 (1C), 145.67, 145.54, 145.25, 145.16, 145.11, 144.66 (4C), 144.50, 144.41, 144.32,143.77 (4C), 143.54, 142.01, 141.79, 141.72, 141.38, 141.29, 141.19, 141.01, 140.75, 140.70, 139.43, 137.87, 137.22 (1C, aryl *C*), 136.72, 135.07, 134.69 (1C, aryl *C*), 132.20 (1C, aryl *C*), 129.89 (aryl *C*), 129.20 (1C, aryl *C*), 127.88 (aryl *C*), 127.59 (aryl *C*), 125.21 (aryl *C*), 83.09 (1C, sp^3-*C* of C_{60}), 68.54 (1C, sp^3-*C* of C_{60}), 57.27 (1C, N*C*H_2), 37.07 (1C, *C*H_2); UV–vis ($CHCl_3$) λ_{max} nm ($\log\varepsilon$) 256 (5.11), 315 (4.67), 430 (3.49), 694 (2.60); FT-IR ν/cm^{-1} (KBr) 2921, 2851, 1489, 1430, 1355, 1182, 1089, 1016, 847, 804, 762, 689, 573, 527; MS (+APCI) m/z 976.