Chiral Bisazafulleroids†

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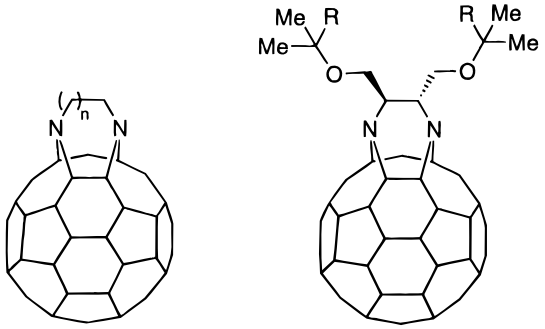
The reactions of C_{60} with C_2 chiral 1,4-*tert*-alkoxy-2,3-bisazidobutanes give the corresponding chiral bisazafulleroids **2**. The enantiomeric pairs of chiral bisazafulleroids **2** exhibit mirror image CD curves.

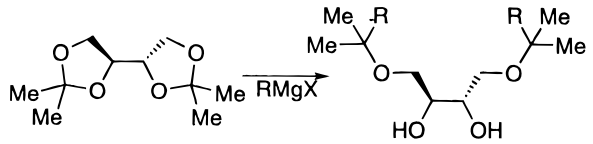
There has been an ever burgeoning interest in the synthesis of chiral fullerene derivatives.[1,2] The chirality is transferred from the chiral substituent to the polyconjugated fullerene moiety as witnessed by its circular dichroitic properties.[2] It is noteworthy that the presence of a C_2 symmetry in the chiral substituent may significantly enhance the chirospectroscopic response.[2d−f] The addition of organic azides to C_{60} so far appears to be one of the most versatile reactions in the derivatization of fullerene. Three kinds of monoadducts[3−5] and three kinds of bisadducts[6−11] have been uncovered. We recently reported the synthesis of bisazafulleroids **1** from the reaction of C_{60} with bisazides tethered by an ethylene or trimethylene bridge.[8] Bisazafulleroids **1** exhibit characteristic absorption profile in the UV−visible spectra. It was felt that the chirospectroscopic properties of the corresponding chiral bisazafulleroids would demonstrate certain unique properties. In this paper, we describe the first synthesis and circular dichroitic properties of chiral bisazafulleroids **2**.



1a n = 1
1b n = 2

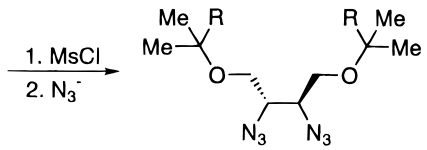
2a R = Me
2b R = Ph

The strategy was based on our recent synthesis of tunable C_2 chiral diols **4** from threitol bisketals **3**.[12,13] Treatment of **4** with MsCl in the presence of Et_3N



3

4a R = Me
4b R = Ph



6a R = Me
6b R = Ph

† Dedicated to Professor P. E. Eaton on the occasion of his 60th birthday.

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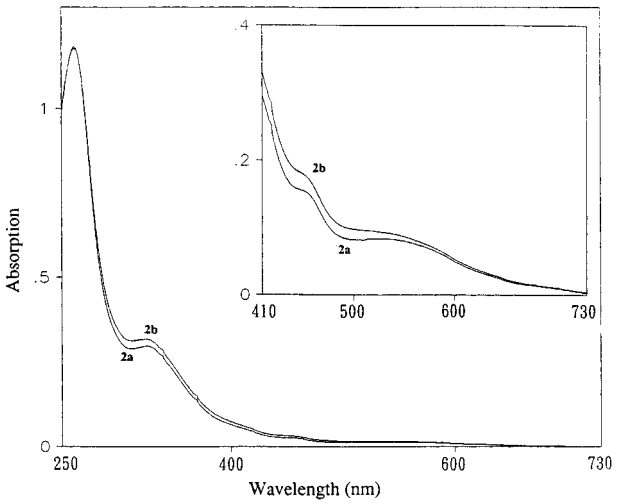

Figure 1. Uv−visible spectra for **22a** and **22b** in $CHCl_3$ ($c = 1.0 \times 10^{-5}$ mol dm^{-3}). Inset: $c = 5.0 \times 10^{-5}$ mol dm^{-3}).

yielded the corresponding bismesylates **5**, which were allowed to react with NaN_3 in the presence of 15-crown-5 in DMF/H_2O to give **6**. Without further purification, **6** was treated with C_{60} in refluxing chlorobenzene for 6−8 h and the reaction was monitored by TLC. As soon as the bis-adducts started to form, the reaction was stopped. After the usual workup, chiral bisazafulleroids (2*R*,3*R*)-**2a**, (2*S*,3*S*)-**2a**, (2*R*,3*R*)-**2b**, and (2*S*,3*S*)-**2b** were isolated in 54%, 49%, 56%, and 51% yields, respectively. The UV−visible spectra (Figure 1) for **2a** and **2b** are characteristic for the bisazafulleroid skeleton.[8] The ^{1}H and ^{13}C NMR data are consistent with the structures.

The CD curves for these compounds are shown in Figure 2. It is noteworthy that the enantiomeric pairs of **2a** and of **2b** exhibited mirror image CD curves. Like many other chiral fullerene derivatives, the CD spectra for **2** are complicate and no direct correlation with the UV−visible spectra can be concluded. However, the fine patterns of the CD spectra of bisazafulleroids **22** are somewhat different from those of other chiral fullerene derivatives.[2]

In summary, we have described the first chiral bisazafulleroids **2** having C_2 chiral auxiliary. Our results established that our tunable chiral substituent significantly enhances the chirospectroscopic response in these polyconjugated fullerene derivatives. Since the tertiary alkyl group in **2** can easily be removed, further derivatization of **2** is underway for the synthesis of water-soluble chiral fullerene derivatives.

Experimental Section

(2*S*,3*S*)-1,4-Bis(*tert*-butoxy)butane-2,3-diyl Dimesylate (5a). To a solution of (2*S*,3*S*)-1,4-(*tert*-butoxy)-2,3-butanediol [(2*S*,3*S*)-**4a**, 1.0 g, 4.3 mmol] and Et_3N (4.05 g, 40 mmol) in CH_2Cl_2 (25 mL) was added at 0 °C MsCl (2.5 g, 21.5 mmol) in CH_2Cl_2 (10 mL); the mixture was stirred for 10 h, quenched with aqueous HCl (10%), and washed with NaOH (10%), and water. The organic layer was dried ($MgSO_4$) and evaporated in vacuo to give the crude (2*S*,3*S*)-**5a** (0.32 g, 60%): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.17 (s, 18H), 3.12 (s, 6H), 3.64 (m, 4H), 3.83 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 27.33, 38.75, 61.02, 80.32. This crude (2*S*,3*S*)-**5a** was used directly for the next reaction without further purification.

In a similar manner, (2*R*,3*R*)-**5a** was prepared in 67% yield.

(2*R*,3*R*)-1,4-(*tert*-Butoxy)-2,3-diazidobutane (6a). A mixture of (2*R*,3*R*)-**5a** (0.32 g, 0.9 mmol), 15-crown-5 (1 drop) in DMF (30 mL), and water (1 mL) was treated with NaN_3 (0.30 g, 5.4 mmol), and the mixture was refluxed for 24 h. After cooling to room temperature, water (50 mL) was added and the mixture was extracted with ether. The organic layer was washed with aqueous HCl (10%) and then with water, dried ($MgSO_4$), and evaporated in vacuo to give crude diazide (2*R*,3*R*)-**6a** (0.14 g, 55%), which was used for the next reaction without further purification: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.20 (s, 18H), 3.60 (m, 6H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 27.33, 61.15, 62.05, 73.81; IR (neat) ν 2099 cm^{-1}.

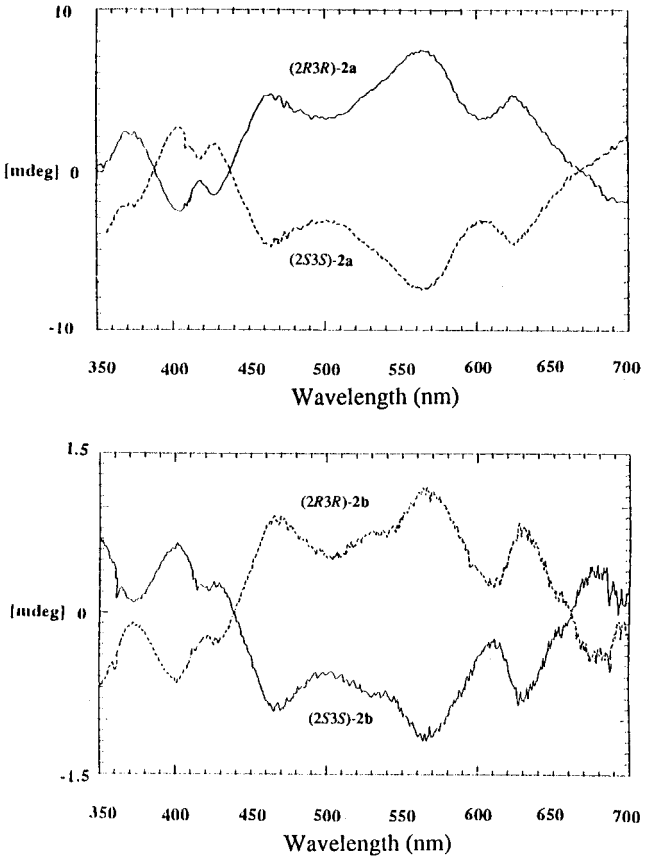

Figure 2. (top) CD curves for (2*R*,3*R*)-**2a** and (2*S*,3*S*)-**2a** in $CHCl_3$ ($c = 1.0 \times 10^{-5}$ mol dm^{-3}). (bottom) CD curves for (2*R*,3*R*)-**2b** and (2*S*,3*S*)-**2b** in $CHCl_3$ ($c = 1.0 \times 10^{-5}$ mol dm^{-3}).

In a similar manner, (2*S*,3*S*)-**6a** was obtained in 50% yield.

(2*S*,3*S*)-1,4-(1,1-Dimethyl-2-phenylethoxy)butan-2,3-diyl Dimesylate (5b). In a manner similar to that described above, (2*S*,3*S*)-**4b** (0.7 g, 1.8 mmol) was transformed into (2*S*,3*S*)-**5b** (0.6 g, 1.3 mmol, 72%): $[\alpha]_D^{26} = +29.1°$ (*c* 0.22, $CHCl_3$); mp 102−103 °C (MeOH); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.11 (s, 6H), 1.14 (s, 6H), 2.74 (s, 4H), 2.93 (s, 6H), 3.56−3.69 (m, 4H), 4.85−4.87 (m, 2H), 7.14−7.28 (m, 10H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.7, 25.1, 38.5, 47.2, 60.7, 76.2, 79.8, 126.3, 127.9, 130.6, 137.6; IR (neat) ν 3036, 2977, 2945, 2928, 1494, 1472, 1468, 1359, 1340, 1309, 1256, 1176, 1146, 1111, 1089, 1076, 1018, 986, 976, 936, 912, 889, 838, 815, 783, 770, 738, 704, 664 cm^{-1}.

In a similar manner, (2*R*,3*R*)-**5b** was obtained in 66% yield; $[\alpha]_D^{26} = -27.5°$ (*c* 0.30, $CHCl_3$); mp 100−103 °C (MeOH).

(2*R*,3*R*)-1,4-(1,1-Dimethyl-2-phenylethoxy)-2,3-diazidobutane (6b). In a manner similar to that described above, (2*R*,3*R*)-**5b** (0.3 g, 0.6 mmol) was converted into the diazide-(2*R*,3*R*)-**6b** (0.16 g, 61%), which was used for the next reaction without further purification: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.15 (s, 12H), 2.75 (s, 4H), 3.56 (s, 6H), 7.14−7.29 (m, 10H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.57, 24.62, 47.57, 61.19, 61.59, 76.03, 126.11, 127.74, 130.47, 137.89; IR (neat) ν 2102 cm^{-1}.

In a similar manner, (2*S*,3*S*)-**6b** was obtained in 66% yield.

General Procedure for the Reaction of Bisazide with C_{60}. Under a nitrogen atmosphere, to a refluxing chlorobenzene (360 mL) solution of C_{60} (360 mg, 0.5 mmol) was added dropwise bisazide (0.75 mmol) in chlorobenzene (100 mL). The

mixture was refluxed for 6−8 h and monitored by TLC. The solvent was removed in vacuo, and the residue was chromatographed on silica gel (hexane/toluene 3:1−1:1 as gradient eluent) to afford the desired product.

Reaction of (2*R*,3*R*)-6a with C_{60}. According to the general procedure, a mixture of C_{60} (100 mg, 0.14 mmol) and (2*R*,3*R*)-**6a** (0.060 g, 0.21 mmol) was converted into (2*R*,3*R*)-**2a** (71.6 mg, 54%): $[\alpha]_D^{24} = +420°$ (*c* 1.2 × 10^{-3}, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.21 (s, 9H), 1.32 (s, 9H), 4.08−4.10 (m, 2H), 4.15−4.24 (m, 2H), 4.81−4.85 (m, 1H), 4.96−5.00 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 27.41, 27.64, 63.32, 63.76, 64.69, 65.52, 134.00, 134.95, 136.95, 137.03, 137.31, 137.54, 138.44, 138.50, 138.54, 139.06, 139.26,139.31, 139.50, 139.53, 139.78, 140.32, 140.55, 140.56, 140.91, 141.00, 141.04, 141.05, 141.19, 141.21, 141.67, 141.84, 143.05, 143.18, 143.57, 143.85, 143.86, 143.87, 144.11, 144.19, 144.25, 144.69, 144.76, 144.83, 144.86, 144.91, 145.00, 145.59, 145.61, 145.65, 145.77, 146.02, 146.11, 146.20, 146.23, 146.30, 146.45, 146.54, 147.34, 147.41, 148.39, 148.90, 151.03, 153.11; UV−visible ($CHCl_3$) λ_{max} nm (ϵ × 10^{-3} L mol^{-1} cm^{-1}) 529 (1.7), 449 (3.1), 326 (29.7), 262 (118.3); IR (KBr) ν 1536, 1510, 1465, 1442, 1406, 1385, 1360, 1303, 1289, 1256, 1231, 1220, 1188, 1087, 1053, 1037, 1014, 971, 941,.932, 909, 879, 841, 808, 795, 775, 756, 741, 711, 689 cm^{-1}. FABMS *m*/*z* 949.6.

In a similar manner, (2*S*,3*S*)-**2a** was obtained (65.0 mg, 0.069 mmol, 49%): $[\alpha]_D^{24} = -397°$ (*c* 1.2 × 10^{-3}, CH_2Cl_2).

Reaction of (2*R*,3*R*)-6b with C_{60}. According to the general procedure, a mixture of C_{60} (100 mg, 0.14 mmol) and (2*R*,3*R*)-**6b** (0.060 g, 0.21 mmol) was converted into (2*R*,3*R*)-**2b** (85.8 mg, 0.078 mmol, 56%): $[\alpha]_D^{24} = +477°$ (*c* 1.2 × 10^{-3}, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.15 (s, 6H), 1.25 (s, 3H), 1.28 (s, 3H), 2.76 (s, 2H), 2.86 (s, 2H), 4.07−4.19 (m, 3H), 4.26−4.29 (m, 1H), 4.85−4.89 (m, 1H), 4.97−5.02 (m, 1H), 7.14−7.25 (m, 10H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.80, 24.89, 25.23, 25.4, 47.37, 47.74, 63.28, 63.92, 64.20, 65.29, 76.15, 76.22, 126.14, 126.18, 127.90, 127.92, 130.58, 130.65, 133.99, 134.93, 136.94, 136.98, 137.30, 137.56, 138.12, 138.26, 138.47, 138.52, 138.58, 138.81, 139.03, 139.35, 139.51, 139.55, 139.74, 140.36, 140.50, 140.55, 140.89, 141.00, 141.05, 141.06, 141.07, 141.18, 141.68, 141.85, 143.06, 143.20, 143.57, 143.84, 143.86, 144.11, 144.13, 144.25, 144.64, 144.76, 144.83, 144.86, 144.91, 144.95, 145.59, 145.61, 145.63, 145.74, 145.89, 146.13, 146.21, 146.23, 146.44, 146.50, 147.32, 147.39, 148.37, 148.86, 150.61, 152.93; UV−visible ($CHCl_3$) λ_{max} nm (ϵ × 10^{-3} L mol^{-1} cm^{-1}) 530 (1.9), 450 (3.6), 325 (31.8), 262 (117.8); IR (KBr) ν 1801, 1774, 1754, 1737, 1493, 1465, 1443, 1379, 1362, 1290, 1220, 1204, 1190, 1172, 1142, 1121, 1079, 1070, 1029, 1017, 970, 907, 891, 871, 774, 761, 728, 697, 650, 610 cm^{-1}; FABMS *m*/*z* 1100.4.

In a similar manner, (2*S*,3*S*)-**2b** was obtained (78.1 mg, 51%): $[\alpha]_D^{24} = -423°$ (*c* 9.9 × 10^{-2}, CH_2Cl_2).

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra of (2*R*,3*R*)-**2a** and (2*R*,3*R*)-**2b** (4 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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