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Synthesis, crystal structure and properties of thiaheterohelicenes containing phenolic hydroxy functions

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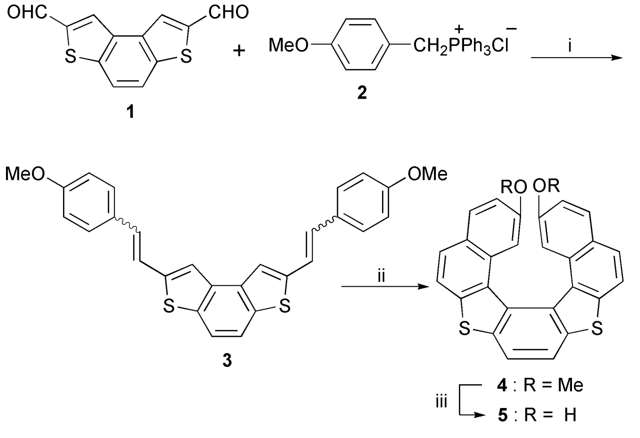
A convenient method for preparation of dimethoxythiahelicene 4 and dihydroxythiahelicene 5 is described; these helical molecules showed self-assembling properties such as enantiomorphic crystal growth and clathrate formation.

Optically active 1,1′-binaphthalene-2,2′-diol (BINOL) having an axial chirality has been widely used for asymmetric catalysis in organic synthesis,[1] where the phenolic hydroxy groups are essential for high stereo-differentiating reactions. However, the asymmetric synthesis based on helicity is known in few cases,[2,3] due to the difficulty in preparing a large amount of functionalized helicenes. Among helices such as helicenes,[4–6] helicates[7,8] and helixanes,[9] helicene skeletons have a rigid framework and possess high optical stability. Hence, the chiral bifunctionalized helicenes are very attractive chiral ligands from the viewpoint of asymmetric synthesis.

Olefin **3** was obtained by Wittig reaction of dialdehyde **1** and phosphonium salt **2** in 74% yield (Scheme 1).† Since the olefination reaction was very sluggish, 4 eq of phosphonium salt **2** were needed to complete the reaction. By irradiation of a mixture of the *cis-cis*, *cis-trans* and *trans-trans* stereoisomers of **3** with a high-pressure mercury lamp under Katz′s conditions,[10] dimethoxyhelicene **4** was obtained in 74% yield.‡ When the racemic helicene *PM*-**4** was recrystallized from a mixture of hexane and dichloromethane, pale yellow crystals suitable for X-ray analysis[11] were obtained. As shown in Fig. 1(A), the dimethoxyhelicene **4** exhibits intramolecular CH–π interaction[12] between the methoxy groups and benzene rings of the same molecule. Thus, the distances of C(32)···ring 2 and C(30)···ring 6 are 3.87 and 3.84 Å, respectively, and the shortest C···C lengths are 4.01 Å for C(32)···C(5) and 4.00 Å for C(30)···C(17), respectively.

Interestingly the crystals **4** exist as a conglomerate of crystals of different chilarity (space group $P2_12_12_1$) that can be separated by crystal picking. The circular dichroism (CD) spectra (Fig. 2) indicate that the two curves of enantiomorphic crystals are in a good mirror image relationship, indicating that the separation by crystal picking is satisfactory. Guest-free crystals suitable for X-ray analysis were obtained from the racemic mixture. In the chiral crystals of either (*P*)-**4** or (*M*)-**4** molecules of the same handedness are stacked by π–π interactions between two aromatic rings 1-2-3-4 and 7-6-5-4, where the shortest C···C distance of two aromatic rings is 3.5 Å, The interaction produces the helical stacking columns with 2_1 screw axis along the crystallographic *a* axis (Fig. 3). Treatment of *PM*-**4** with of BBr_3 in dichloromethane gave *PM*-**5** in 96% yield.§ Recrystallization of *PM*-**5** from acetone afforded a 1 : 1 inclusion complex (*PM*-**5**)·(acetone).

No clathrate complexes were obtained from dichloromethane, ethyl acetate and hexane. X-Ray analysis of (*PM*-



Scheme 1 *Reagents and conditions*: i, *t*-BuOK, dry DMF, 0 °C, then warm to 80 °C, 5 h, 74%; ii, I_2, propylene oxide, benzene, 3 h, 74%; iii, BBr_3, CH_2Cl_2, −78 °C, warm to rt, 96%.

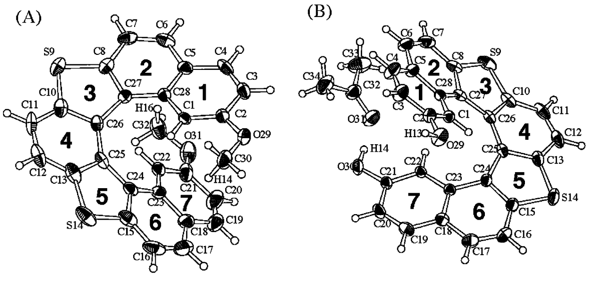


Fig. 1 Numbering scheme of ORTEP drawings of **4** (A) and **5**·acetone (B). Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as spheres of arbitrary radii.

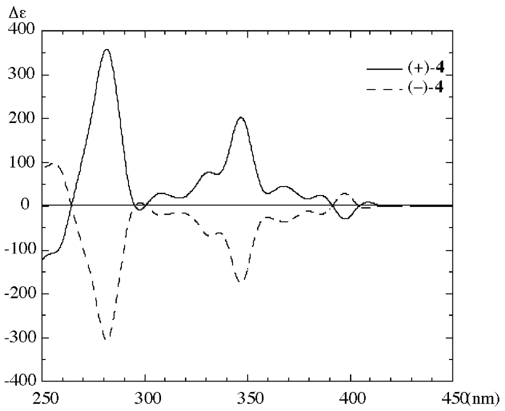


Fig. 2 CD spectra of helicene **4** (in chloroform).

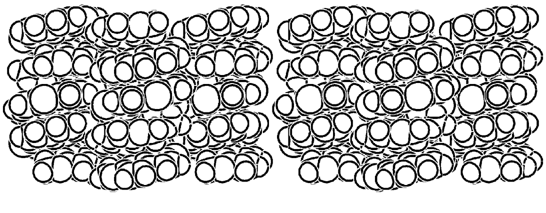


Fig. 3 Stereoview of helical stacking columns of left-handed helicenes **4** along *a* axis.

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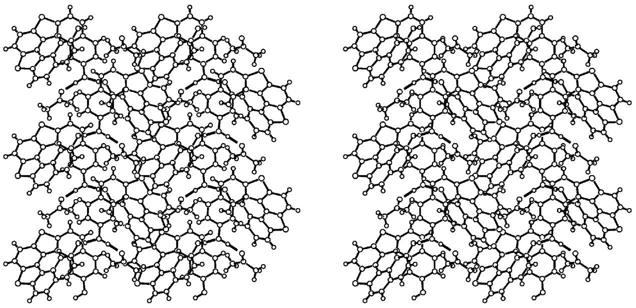

Fig. 4 Stereoview of homochiral hydrogen-bonding networks (*P*-**5**)·(acetone) in crystal (*PM*-**5**)·(acetone).

5)·(acetone) indicates that helicenediols with the same helicity are aligned along the crystallographic *b* direction by intermolecular hydrogen bonds with the O···O distance of 2.77 Å and the O–H···O angle of 169°. The oxygen atom of a guest molecule interacts with one of the hydroxy functions of a helicenediol to form the hydrogen bond with the O···O distance of 2.65 Å and the O–H···O angle of 173° (Fig. 4). These hydrogen bondings are important in stabilizing the helical networks in the crystal lattice, forming two chiral supramolecular structures consisting of (*P*-**5**)·(acetone) and (*M*-**5**)·(acetone). Although the bond lengths of aromatic frameworks of **4** and **5** are essentially the same, the dihedral angle between two terminal thiophene rings 1 and 7 increases from 41.3° for **4** to 47.0° for **5** (Table 1). This is due to the flexible helicene framework, so that introduction of suitable substitutes can change the helical pitches, and eventually change the properties of the helicene molecules such as guest-binding and self-assembling properties.

Table 1 Non-bonding contacts (Å) and dihedral angles between terminal benzene rings (°)

Crystal	(*P*)- or (*M*)-**4**[11]	(*PM*-**5**)·(acetone)
C1–C22	3.20	3.10
C1–C23	3.06	3.10
C1–C24	3.15	3.24
C22–C27	3.17	3.15
C22–C28	3.08	3.29
O29–O30	5.91	5.62
Dihedral angle	41.3	47.0

The reaction chemistry of these helical compounds as well as their potential applications as resolving agents and chiral auxiliaries in organic synthesis are in progress and will be reported in due course.

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Notes and references

† *Synthesis of* **3**: To a stirred solution of dialdehyde **1** (1.00 g, 4.06 mmol)[13] and phosphonium salt **2** (6.80 g, 16.2 mmol)[14] in dry DMF (40 mL), was added 1.82 g (16.2 mmol) of *t*-BuOK in one portion at 0 °C. After stirring for 30 min, the reaction mixture was heated at 80 °C for 5 h. The resulting yellow suspension was collected by filtration, washed with methanol and dried *in vacuo*. The crude product **3** (1.37 g, 74%) was obtained as a yellow solid: mp 332–334 °C; IR (KBr) 2967, 1602, 1516, 1255, 1178, 1030 cm^{-1}; FAB(M$^+$) = 454.1 (calc. = 454.2).

‡ *Synthesis of* **4**: Olefin **3** (0.250 g, 0.55 mmol) and iodine (0.28 g, 1.1 mmol) were dissolved in benzene (1.8 L). Following addition of propylene oxide (10 mL) to the above solution, the mixture was irradiated for 3 h under bubbling argon. The reaction mixture was washed with aq. $Na_2S_2O_3$ and brine, dried (Na_2SO_4) and concentrated. The crude product was purified by silica gel column chromatography (hexane–EtOAc, 5 : 1). The pure helicene **4** (0.184 g, 74%) was obtained as a pale yellow solid: mp 271–273 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.08 (s, 2H) 7.8–7.9 (m, 4H), 7.74 (d, 2H, J = 9.0 Hz), 6.82 (dd, 4H, J = 8.1, 2.7 Hz), 6.76 (d, 2H, J = 2.4 Hz), 2.62 (s, 6H); IR (KBr) 3062, 2993, 2945, 2927, 2822, 1619, 1507, 1216 cm^{-1}; Anal. Calcd for $C_{28}H_{18}O_2S_2$: C, 74.64; H, 4.03; Found: C, 74.39; H, 4.04%.

Crystal data for **4**: $C_{28}H_{18}O_2S_2$, M = 450.57, orthorhombic, space group $P2_12_12_1$, a = 11.719(6), b = 17.730(4), c = 9.974(4) Å, V = 2072(1) Å^3, T = 298 K, Z = 4, μ = 2.82 cm^{-1}, $2\theta_{max}$ = 55.1°, R = 0.053 for 1759 data and 290 parameters, Rw = 0.077 [$I > 2.0\sigma(I)$] and GOF = 1.23. CCDC 175385. See http://www.rsc.org/suppdata/cc/b1/b110514k/ for crystallographic data in .cif or other format.

§ *Synthesis of* **5**: To a solution of **4** (86.9 mg, 0.193 mmol) in dry CH_2Cl_2 (5 mL), was added slowly a solution of BBr_3 (0.77 mmol) in CH_2Cl_2 (1.46 mL) at −78 °C. Stirring was continued overnight during which time the mixture was slowly warmed up to rt. The reaction mixture was poured into water (30 mL) and extracted twice with CH_2Cl_2. The combined organic extracts were dried and concentrated *in vacuo*. Purification by silica gel chromatography (hexane–EtOAc, 3 : 1) gave **5** (77.9 mg, 96%) as pale yellow solid (guest free): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.10 (s, 2H), 7.92 (s, 4H), 7.80 (d, 2H, J = 9.0 Hz), 6.85 (dd, 2H, J = 8.7, 2.4 Hz), 6.62 (d, 2H, J = 2.4 Hz), 4.30 (s, 2H); IR (KBr) 3314, 2922, 2849, 1685, 1619, 1509, 1220 cm^{-1}. Crystal (*PM*-**5**)·(acetone); mp 153–155 °C; Anal. Calcd for $C_{29}H_{20}O_3S_2$: C, 72.47; H, 4.19; Found: C, 72.04; H, 4.30%.

Crystal data for **5**: $C_{29}H_{20}O_3S_2$, M = 480.60, monoclinic, space group $P2_1/c$, a = 11.612(3), b = 10.361(1), c = 19.180(2) Å, β = 91.31(2)°, V = 2306.9(8) Å^3, T = 298 K, Z = 4, μ = 2.61 cm^{-1}, $2\theta_{max}$ = 55.0°, R = 0.042 for 3562 data and 307 parameters, Rw = 0.063 [$I > 2.0\sigma(I)$] and GOF = 1.27. CCDC 175386.

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