



Synthesis and Crystal Structure of Chiral Bifunctional Helicenes with π -Deficient Pyridine and π -Excessive Thiophene Units

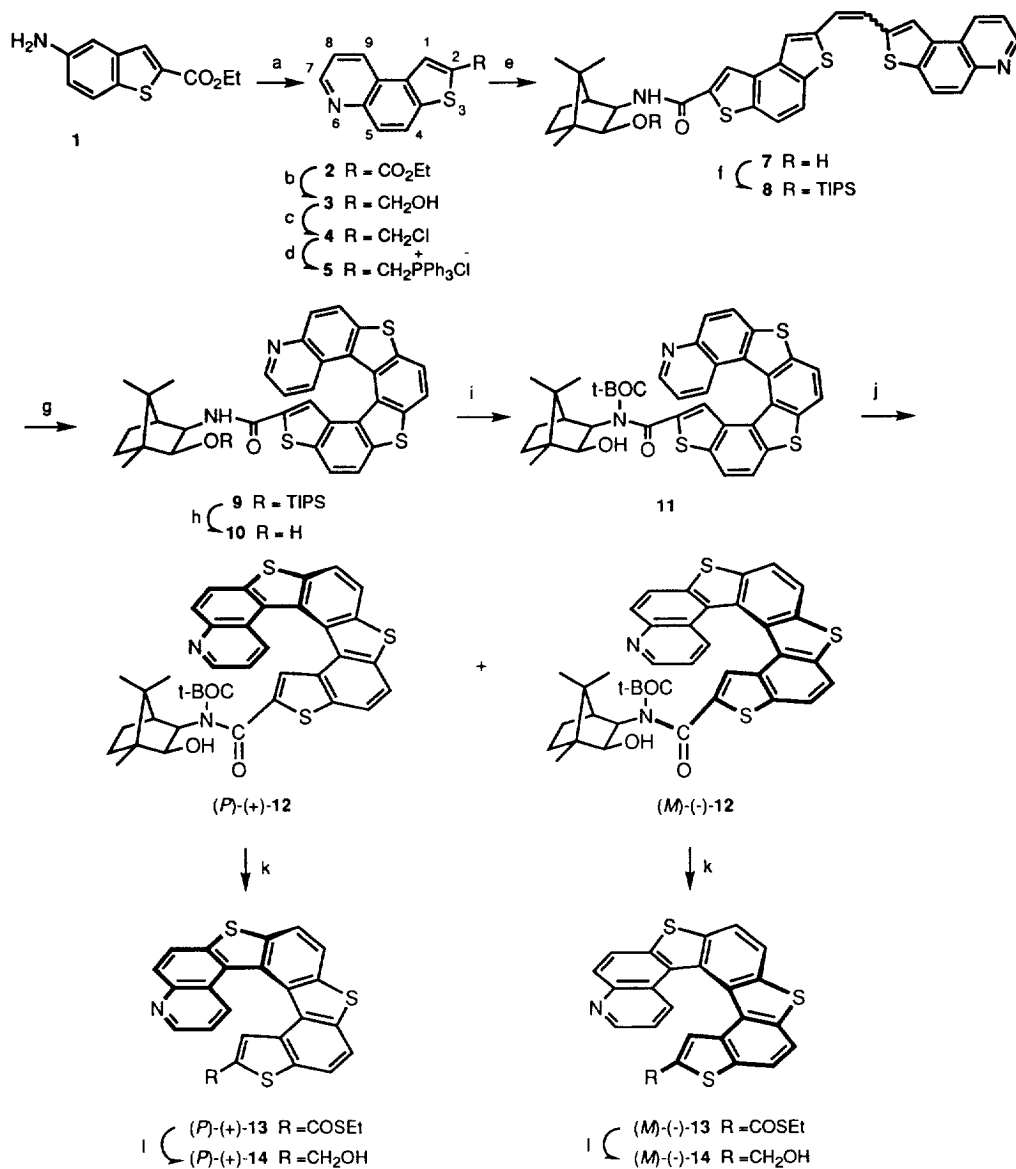
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Abstract: Both enantiomers of new bifunctional helicenes constructed from π -excessive 2-(hydroxymethyl)thiophene and π -deficient pyridine rings have been prepared using (1*R*,2*S*,3*R*,4*S*)-3-amino-2-hydroxybornane as a chiral auxiliary. The X-ray crystal structure reveals the intermolecular hydrogen bond between the hydroxy group of the helicene and the pyridine nitrogen atom of the adjacent molecule. The non-bonded distance between the nitrogen atom and the oxygen atom is 2.72 Å, and the interplanar angle between the terminal rings is 45.3°. Copyright © 1996 Elsevier Science Ltd

Recently, remarkable success has been achieved in a number of asymmetric syntheses with optically active bidentate ligands based on central, axial, and planar chirality (*R* or *S*) such as amino alcohols,¹ binaphthols² and ferrocene derivatives.³ In contrast, only limited research has been carried out on the symmetric reactions using chiral ligands based on helicity (*P* or *M*) owing to the lack of efficient synthetic processes for optically pure helical ligands. Among helices such as helicenes, helicates, and helixanes,⁴ chiral functional helicenes are promising candidates for ligands in asymmetric syntheses because they have a rigid helical framework and possess high optical stability.

Our recent success in the synthesis of chiral monofunctional helicenes using *exo*-2-hydroxy-3-aminobornane⁵ as a chiral auxiliary led us to examine the potentially more valuable bifunctional analogues **13** and **14** comprising of π -excessive thiophene and π -deficient pyridine rings. For the synthesis of [7]helicenes, the thiophene appendages not only lead to the regioselective α -functionalization of the ring systems, they can also participate in the regioselective photocyclization at their β -positions. The pyridine nitrogen in the chiral helicenes can serve as a hydrogen acceptor as well as a metal chelating agent for chirality recognition.

Since thieno[3,2-*f*]quinoline derivatives like **2** could not be obtained by photocyclization⁶ from the corresponding olefin, *E*-1-(4-pyridyl)-2-(2-thienyl)ethene, we prepared **2** by an improved method of the Skraup reaction.⁷ Thus, ethyl 5-nitrobenzo[*b*]thiophene-2-carboxylate was subjected to reduction to give ethyl 5-aminobenzo[*b*]thiophene-2-carboxylate **1** in 84% yield. The resulting amine **1** was then treated with sodium *m*-nitrobenzene-sulfonate in a mixture of glycerol and concentrated sulfuric acid, and esterification gave the desired quinoline **2** in 73% yield. Reduction of **2** and chlorination of **3** followed by treatment with triphenylphosphine gave the corresponding phosphonium salt **5** in 63% overall yield. Coupling of *N*-[(1*R*,2*S*,3*R*,4*S*)-2-hydroxy-1,7,7-trimethylbicyclo[2.2.1]heptan-3-yl]-5-formylbenzo[1,2-*b*:4,3-*b'*]dithiophene-2-carboxamide^{8b} with **5** gave olefin **7** in 84% yield. The olefin has low solubility in common organic solvents, which hampered subsequent manipulation. To improve the solubility of the olefin, **7** was



Scheme 1. Reagents and conditions: (a) (i) H_2SO_4 , glycerol, sodium *m*-benzene-sulfonate, H_3BO_3 ; (ii) H_2SO_4 , ethanol, 73%; (b) LiAlH_4 , THF, 91%; (c) SOCl_2 , Et_3N , benzene, 74%; (d) PPh_3 , benzene, 94%; (e) *N*-[(1*R*,2*S*,3*R*,4*S*)-2-hydroxy-1,7,7-trimethylbicyclo-[2.2.1]heptan-3-yl]-5-formylbenzo[1,2-*b*:4,3-*b'*]dithiophene-2-carboxamide, *t*-BuOK, THF, methanol, 89%; (f) triisopropylsilyl trifluoromethanesulfonate, 2,6-lutidine, CH_2Cl_2 , 94%; (g) iodine, propylene oxide, argon, benzene, 73%; (h) TBAF, THF, 96%; (i) di-*tert*-butyl dicarbonate, DMAP, CH_2Cl_2 , 83%; (j) column chromatography on silica-gel; (k) EtSLi, THF, 89%; (l) LiAlH_4 , THF, 85%.

converted into the corresponding triisopropylsilyl ether **8** in 94% yield.⁵ The ether was dissolved in benzene and irradiated with a high-pressure mercury lamp⁹ to give the helicene **9** in 73% yield as a mixture of diastereoisomers in a ratio of 37:63 determined by HPLC analysis using Shim-Pack CLC-SIL(M).¹⁰ Separation of the diastereomers was readily accomplished by silica-gel column chromatography after desilylation with TBAF followed by *N-tert*-butoxycarbonylation.¹¹ Optical purities of both diastereomers, (*P*)-(+)-**11** and (*M*)-(-)-**11**, were determined as >99.5% by HPLC.¹⁰ Removal of the chiral auxiliary was carried out by transesterification to the corresponding thioester **13** by a modification^{5c} of the Damon procedure.¹² Optical rotation of (*M*)-(-)-**13** obtained from (*M*)-(-)-**11** was -2620 (c 0.0499, CHCl₃), whose absolute value is in good agreement with that of the enantiomer (*P*)-(+)-**13**, +2670 (c 0.0500, CHCl₃), and optical rotations of (*M*)-(-)-**14** and (*P*)-(+)-**14** were -2140 (c 0.0503, CHCl₃) and +2150 (c 0.0503, CHCl₃), respectively. Their optical purities were determined to be >99.5% by HPLC.¹³

Table 1. Dihedral angles between planes (degree)

plane	1(T)	2(B)	3(T)	4(B)	5(T)	6(B)
2(B)	6.2					
3(T)	10.3	7.4				
4(B)	21.1	20.2	12.9			
5(T)	30.0	29.2	21.9	9.1		
6(B)	37.8	38.1	31.0	18.3	10.0	
7(P)	45.3	46.9	40.4	28.4	21.2	11.7

T: thiophene, B: benzene, P: pyridine.

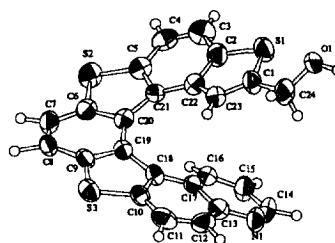
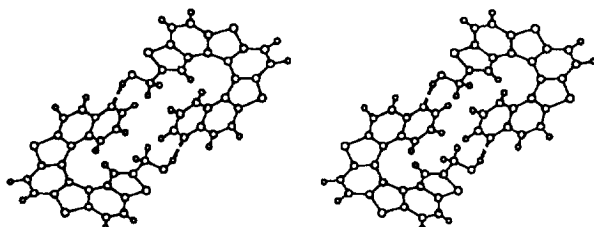


Figure 1. Numbering scheme of the crystal structure of **14**

Figure 2. Stereoview of hydrogen bonded binary aggregate

X-ray structural analysis shows that the angles between two adjacent planes vary from 6.2 to 12.9° (Table 1), which indicates that the strain seems to be localized in the inner aromatic rings.¹⁴ Hence, the outer bonds C(3)-C(4), C(7)-C(8), and C(11)-C(12) are shortened to 1.34-1.38 Å to the bond length in benzene (1.39 Å), whereas the inner bond distances C(17)-C(18), C(19)-C(23), and C(21)-C(22) are lengthened to 1.40-1.43 Å (see Fig. 1). The dihedral angles between the terminal rings is 45.3°, which is larger than that of bis-(hydroxymethyl)[7]thiaheterohelicene (38°).¹⁵ The deviation from planarity is also confirmed by ¹H NMR spectroscopy. Thus, the protons on C(23) (δ 6.15) and on C(15) (δ 6.65) of **14** resonate at higher field than the protons on C(8) (δ 7.50) and on C(1) (δ 7.78) of **3**. This suggests that the former protons are in the region of a shielding zone exerted by the helical aromatic structure.

The present "3+3" approach shows promise for the synthesis of a wide range of bidentate [7]helicenes with high enantiomeric purity, which might be useful in asymmetric reactions. Studies along this line are currently in progress.

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- The ratio of the diastereoisomers was determined by HPLC using Sumichiral OA-2000I (eluent : hexane/1,2-dichloroethane/methanol = 100/100/3).
- Recrystallization of **14** from CHCl₃ afforded a host-guest inclusion complex: monoclinic, P2₁/a, a = 7.568(3) Å, b = 20.912(2) Å, c = 15.031(3) Å, β = 100.93(3)°, V = 2335.9(9)Å³, Z = 2, R 0.113, R_w 0.156. The crystal contains a disordered guest species in its cavity. The X-ray structure of the clathrate will be reported in due course.
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