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Practical Synthesis of Optically Pure Bifunctionalized Heterohelicenes

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Optically active 2-(hydroxymethyl)- and 2-(ethylthiocarbonyl)[1]benzothieno[5′,4′ : 2,3][1]benzothieno [4′,5 : 4,5]-thieno[3,2-*f*]quinolines containing π-excessive thiophene and π-deficient pyridine units were prepared by the use of *exo*-3-amino-2-hydroxybornane as a chiral auxiliary. This procedure consists of separation of the helical diastereomers prepared by photocyclization of 1,2-diarylethylenes and removal of the chiral auxiliary by a thiolate ion. Large scale preparation of the helicenes can be accomplished by a modified procedure of the photocyclization reaction. Optical purities of both enantiomers of 2-(hydroxymethyl)- and 2-(ethylthiocarbonyl)[1]benzothieno[5′,4′ : 2,3][1]benzothieno[4′,5′ : 4,5]-thieno[3,2-*f*]quinolines were >99.5%. Their absolute configurations were determined by comparison of CD spectra.

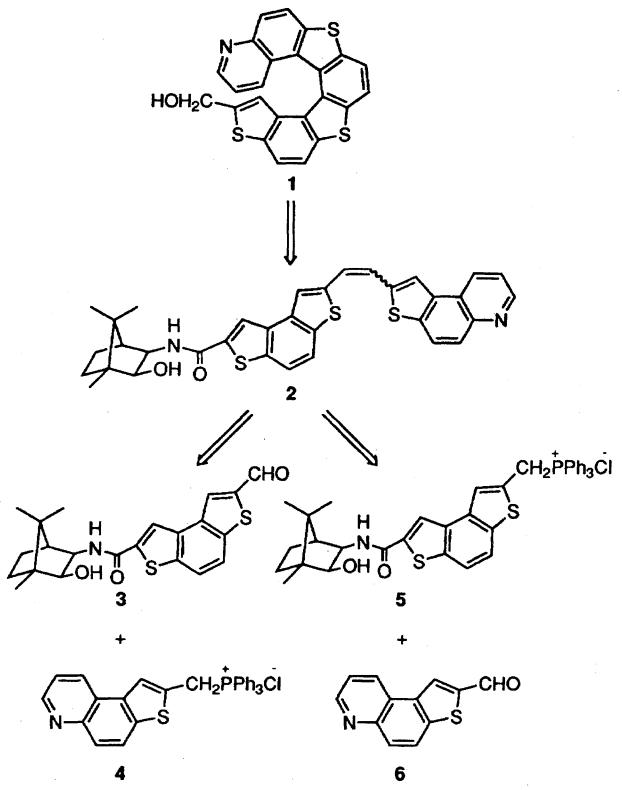
Since the first synthesis of hexahelicene ([6]helicene) which was made up of *ortho*-condensed six benzene rings by Newman in 1955,[1] the helical aromatic molecules have received considerable attention because of unique helical non-planar π-electron system and of their very high rotational values.[2,3] The helicenes containing more than six benzene rings (carbohelicenes) or seven heterocyclic rings (heterohelicenes) possess a rigid helical framework[2a,4] and are very stable toward acids, bases, and relatively high temperatures.[5] For this reason, chiral functionalized analogues are promising candidates for chiral ligands and auxiliaries in asymmetric syntheses. The syntheses of chiral helicenes, however, requires laborious methods such as (1) repeated recrystallization of diastereomeric charge transfer complexes from 2-(2,4,5,7-tetranitro-9-fluorenylideneaminooxy)propionic acid (TAPA),[1,6] (2) crystal picking of racemic mixtures,[7] or (3) separation by chiral column using High-Performance Liquid Chromatography (HPLC).[8]

Recently we have developed an efficient method for the synthesis of optically active monofunctionalized heterohelicenes[9] by the use of *exo*- and *endo*-3-amino-2-hydroxybornane as chiral auxiliaries,[10] which provides various types of optically pure functionalized heterohelicenes.[11] We now report a full account of the synthesis of potentially more valuable bifunctionalized heterohelicene such as 2-(hydroxymethyl)- and 2-(ethylthiocarbonyl)[1]benzothieno-[5′,4′ : 2,3][1]benzothieno[4′,5′ : 4,5]thieno[3,2-*f*]quinoline (**1**) and (**17**) consisting of π-excessive thiophene and π-deficient pyridine rings, as well as a practical method for the preparation of a large amount of heterohelicene by modifying the photocyclization of diaryl-olefins. The optical properties of the resulting heterohelicenes are also described in this paper.

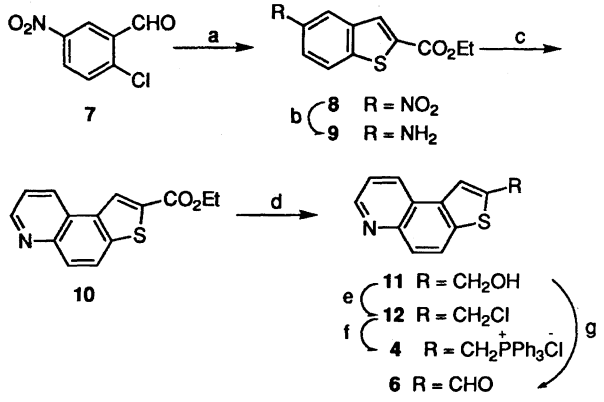
Results and Discussion

Our strategy for the synthesis of **1** is based upon the regioselective synthesis of olefin **2**, in which the thiophene appendages not only lead to the regioselective α-functionalization[12] of the ring systems, but can also participate in the regioselective photocyclization at their β-positions.[4,13] The pyridine nitrogen in the chiral helicene can serve as a hydrogen acceptor as well as a metal chelating agent for chirality recognition. Two routes are possible in the preparation of olefin **2** (Scheme 1), a precursor of the desired heterohelicene which was readily obtained by Wittig reactions of **3** and **4**, or **5** and **6**. Although benzo [1,2-*b* : 4,3-*b*′]dithiophene derivatives **3** and **5** possessing a chiral auxiliary derived from D-camphor have already been reported,[9b] thieno[3,2-*f*]quinoline derivatives like **10** could not be obtained from the corresponding diaryl-olefin by photocyclization.[14] We devised an improved method using Skraup type reaction[15] as shown in Scheme 2. Thus, reaction of 2-chloro-5-nitrobenzaldehyde **7** and ethyl mercaptoacetate in the presence of potassium carbonate in DMF smoothly proceeded at rt to give 5-nitrobenzo[*b*]thiophene-2-carboxylate **8** in 88% yield. Selective reduction of the nitro group of **8** was accomplished by iron powder and hydrochloric acid in absolute ethanol to afford ethyl 5-aminobenzo[*b*]thiophene-2-caboxylate **9** in 96% yield. The resulting amine **9** was then treated with a mixture of glycerol and concentrated sulfuric acid in the presence of sodium *m*-nitrobenzenesulfonate and boric acid, and the reaction mixture was esterified by acidic ethanol to give the desired ethyl thieno[3,2-*f*]quinoline-2-caboxylate **10** in 73% yield. Reduction of **10** with $LiAlH_4$ provided alcohol **11**, which was converted into chloride **12** with $SOCl_2$ in the presence of triethylamine. Reaction of **12** and triphenylphosphine in refluxing benzene gave phosphonium salt **4** in 94% yield and aldehyde **6** was obtained by oxidation of **11** with pyridinium dichromate (PDC) in CH_2Cl_2 in 65% yield.

Wittig reactions of **3** with **4** and of **5** with **6** gave **2** in 84 and 76% yields, respectively (Scheme 3). The olefin **2**, however, has low solubility in common organic solvents, which hampered subsequent manipulations. In order to improve the

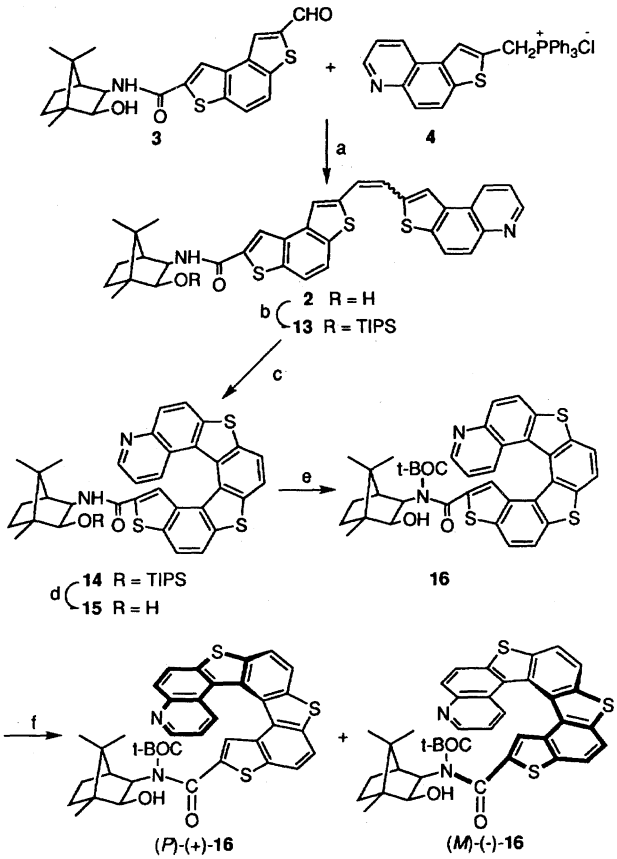


Scheme 1.



Scheme 2. Reagents and conditions: (a) $HSCH_2CO_2Et$, K_2CO_3, DMF, 88%; (b) iron powder, HCl, ethanol, 84%; (c) (i) H_2SO_4, glycerol, sodium *m*-benzenesulfonate, H_3BO_3; (ii) cat. H_2SO_4, ethanol, 73%; (d) $LiAlH_4$, THF, 91%; (e) $SOCl_2$, Et_3N, 74%; (f) PPh_3, benzene, 94%; (g) PDC, CH_2Cl_2, 65%.

solubility of the olefin, **2** was converted into the corresponding triisopropylsilyl ether[16] **13** in 94% yield. The silyl ether **13** was dissolved in benzene (0.30 g in 1.6 L of benzene, 0.25 mM) and irradiated with a high-pressure mercury lamp in the presence of a stoichiometric amount of iodine and an excess amount of propylene oxide under inert atmosphere[17] to give helicene **14** in 59% yield as a mixture of diastereoisomers in ratio of 38 : 62 determined by HPLC analysis.[18] Since the yield of the helicene by intramolecular photocyclization reaction is highly dependent on the concentration of starting material, the dilute solution should be used in this



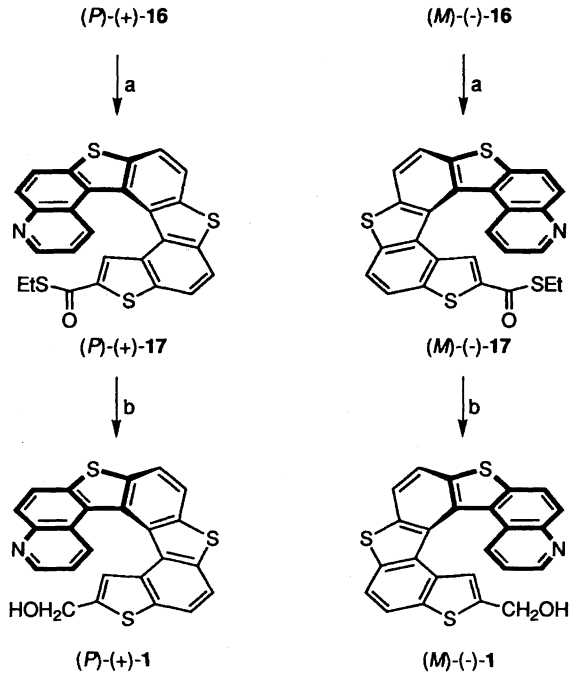
Scheme 3. Reagents and conditions: (a) *t*-BuOK, THF, methanol, 89%; (b) triisopropylsilyl trifluoromethanesulfonate, 2,6-lutidine, CH_2Cl_2, 94%; (c) iodine, propylene oxide, argon, benzene, 73%; (d) TBAF, THF, 96%; (e) di-*t*-butyl dicarbonate, DMAP, CH_2Cl_2, 83%; (f) column chromatography on silica gel.

reaction. Thus, photocyclization performed in more dilute solution (0.20 g in 1.6 L of benzene, 0.17 mM) increased the yield of **14** to 73% (diastereoisomer ratio 37 : 63). If the heterohelicene **14** is stable under conditions using intense irradiation of UV light, the olefin **13** can be added in the same vessel containing **14** after the photocyclization. Thus, **13** (0.20 g) dissolved in 1.6 L of benzene (0.17 mM) was irradiated with a high-pressure mercury lamp under the conditions described above. After the olefin **13** was consumed, as judged by TLC, additional portions of **13** (0.20 g, 0.27 mmol) and iodine (0.40 mmol) were added into the reaction mixture and the irradiation was repeated. After this procedure was repeated six times, 0.70 g of heterohelicene **14** was obtained in 59% yield from olefin **12** : Total amount was 1.20 g (1.62 mmol) and the diastereomer ratio of **14** was 37 : 63. This procedure can be successfully applied to other photocyclization reactions using a catalytic amount of iodine. Thus, the photocyclization of 1,2-di(2-thienyl)ethene (2.88 g, 15 mmol) in 1.7 L of benzene (9.5 mM) containing 0.45 mmol of I_2 was repeated four times to give 9.50 g (50 mmol) of benzo[1,2-*b* : 4,3-*b*']dithiophone in 83% yield.[19]

The diastereomers of the helicene could be separated by silica gel column chromatography after desilylation with

TBAF and subsequent *N*-*t*-butoxycarbonylation by di-*t*-butyl dicarbonate. Optical purities of both diastereomers, (+)-**16** and (−)-**16**, were determined as >99.5% by HPLC analysis.[20] Removal of chiral auxiliary was successfully carried out by transformation of **16** to the corresponding thioester **17** by LiSEt in THF (Scheme 4).[11,21]

Optical rotation of (−)-**17** obtained from the major diastereomer, (−)-**16**, was −2620 (*c* 0.0499, $CHCl_3$), whose absolute value shows good agreement with that of the enantiomer (+)-**17** obtained from (+)-**16**, +2670 (*c* 0.0500, $CHCl_3$). Both enantiomers of the thioester were converted into the corresponding alcohols by reduction with $LiAlH_4$ in 85% yield. Optical rotations of (−)-**1** and (+)-**1** were −2140 (*c* 0.0503, $CHCl_3$) and +2150 (*c* 0.0503, $CHCl_3$), respectively, and their optical purities were determined to be >99.5% by HPLC analysis (Fig. 1).[22] The CD spectra of thioester **17** and alcohol **1** (Figs. 2 and 3) clearly indicate that (+)-**17** and (+)-**1** have same helicity as that of the (*P*)-(+)-methyl [1]benzothieno[5,4-*b*]naphtho[1′,2′ : 4,5]thieno-[3,2-*e*][1]benzothiphene-2-carboxylate, whose absolute configuration was determined by X-ray structural analysis of the precursor.[9b,23] Thus, it is clearly shown that (+)-**1** has the helicity of *P*, and (−)-**1** has that of *M*. This result agrees with the fact that all of the levorotatory helicenes have same helicity *M*, and vise versa.[2c,24]



Scheme 4. Reagents and conditions: (a) EtSLi, THF, 89%; (b) $LiAlH_4$, THF, 85%.

The deviation from planarity of the helicene **1** could be confirmed by NMR analysis (Fig. 4). The chemical shifts for 1-H, 14-H, and 16-H in the spectrum of **1** show large upfield shifts compared to the corresponding chemical shifts of the alcohol **11** : $\Delta\delta$ (ppm) = +1.59 (1-H), +0.83 (14-H), +0.83 (16-H). This suggests that the helical structure exerted these protons in the anisotropic region of the aromatic rings of the same molecule. The chemical shift for 14-H (δ = 6.66) in **1** is almost the same as that of 2-H in benzo[*c*]phenanthro[1,2-*f*]quinoline (δ = 6.57),[25] however it is at higher field than that of 2-H in naphtho[1′,2′ : 4,5]thieno[3,2-*a*]-4,7-phenanthroline (δ = 7.05).[26] These results indicate that the heterohelicene **1** has a full turn of helix such as benzo-[*c*]phenanthro[1,2-*f*]quinoline, since the chemical shifts for the protons in terminal aromatic rings are dependent on the degree of overlapping of the two terminal rings.

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

Experimental

General: THF and ether were distilled under argon atmosphere from sodium benzophenone ketyl immediately before use. Dichloromethane and benzene were distilled from calcium hydride and stored over 4 Å molecular sieves. The hexane solution of butyllithium (Kanto chemicals) was titrated using diphenylacetic acid.[27]

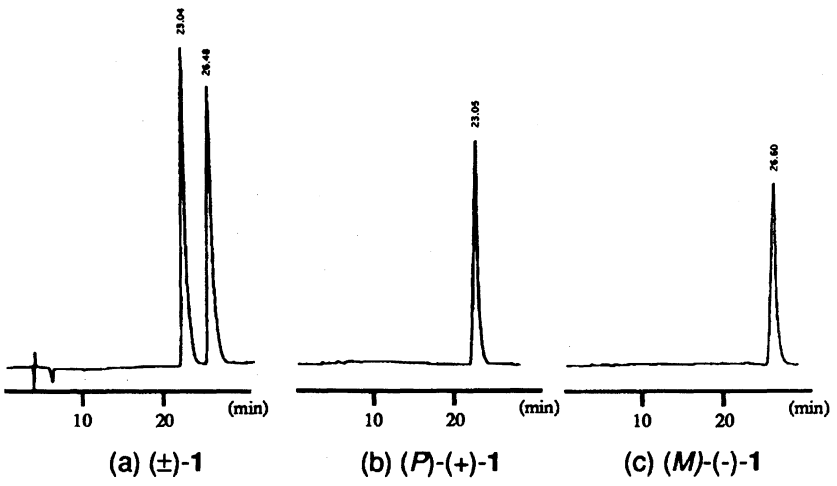


Fig. 1. HPLC chromatograms of heterohelicenes **1**. Column : SUMICHIRAL OA-2000l (4.6 mm i.d.×25 cm), Eluent : hexane/1,2-dichloroethane/methanol (100 : 100 : 3), Flow rate : 1 mL min^{-1}, Detector : 254 nm.

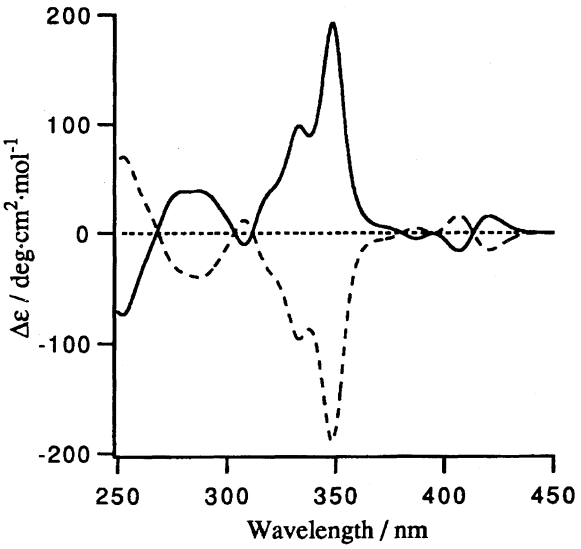


Fig. 2. CD spectra of (*P*)-(+)-**17** and (*M*)-(−)-**17** in chloroform.

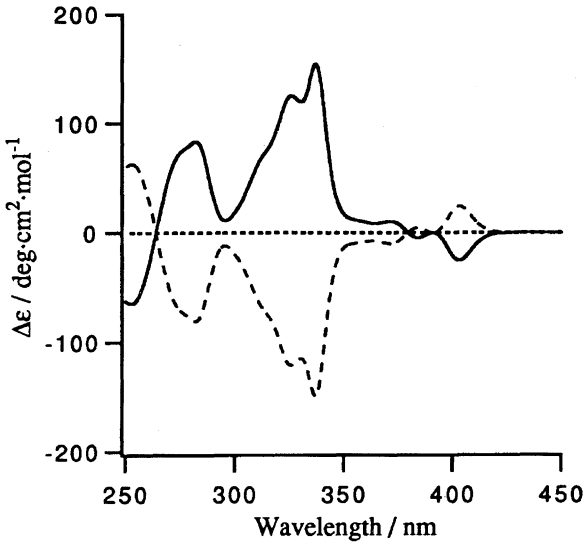


Fig. 3. CD spectra of (*P*)-(+)-**1** and (*M*)-(−)-**1** in chloroform.

Melting points were determined on a Yanagimoto hotstage apparatus and are not corrected. IR spectra were recorded on a Shimadzu FT IR DR 8000/8100 infrared spectrometer. NMR spectra were obtained with a Varian Gemini-200 (200MHz) spectrometer in $CDCl_3$ with tetramethylsilane as an internal standard, and J values are given in Hz. The CD spectra are recorded on a JASCO Model J-720W recording spectropolarimeter in $CHCl_3$. Optical rotation was measured in 1 dm lengths cells of 10 cm^3 on a JASCO Model DIP-181 polarimeter; $[\alpha]_D$ values are given in 10^{-1} deg cm^2 g^{-1}. Photocyclization reactions were performed in a water-cooled pyrex photoreactor using an Eikosha 500-W high-pressure mercury lamp. Thin layer chromatography was performed by using Merck precoated silica gel sheets 60F-254. Silica gel (Wakogel) of the size 100—200 mesh was used for column chromatography. Elemental analyses were performed by the Microanalytical Laboratory, operated by the Institute for Chemical Research, Kyoto University.

Ethyl 5-Nitrobenzo[*b*]thiophene-2-carboxylate (8): To a stirred solution of 5-nitro-2-chlorobenzaldehyde (18.56 g, 100 mmol) in 200 mL of dry DMF was added anhydrous K_2CO_3 (16.59 g, 120 mmol) and ethyl mercaptoacetate (11.0 mL, 100 mmol) at 0 °C, and the mixture was stirred at r.t. overnight. The reaction mixture was then poured into ice water and the solid was collected, washed with water, and dried in vacuo. The solid was recrystallized from ethyl acetate to give **8** as white needles (22.01 g, 88%). Mp 162—165 °C; ^{1}H NMR ($CDCl_3$) δ = 1.44 (t, J = 7.2 Hz, 3H), 4.45 (q, J = 7.2 Hz, 2H), 7.99 (d, J = 8.9 Hz, 1H), 8.17 (s, 1H), 8.30 (dd, J = 8.9 Hz, 2.2, 1H), 8.78 (d, J = 2.2 Hz, 1H); IR (KBr) 1694, 1534, 1341, 1302, 1273, 1073, 1053, 831, 760, 741 cm^{-1}. Found: C, 52.67; H, 3.55; N, 5.55%. Calcd for $C_{11}H_9NO_4S$: C, 52.58; H, 3.61; N, 5.57%.

Ethyl 5-Aminobenzo[*b*]thiophene-2-carboxylate (9): To a stirred suspension of **8** (11.30 g, 45 mmol) in 450 mL of ethanol was added 27 g of iron powder, and the mixture was heated under reflux. To the stirred suspension was added 27 mL of concentrated hydrochloric acid dropwise and this mixture was stirred for an additional 1 h under reflux. The reaction mixture was filtrated and the filtrate was evaporated. The residue was dissolved in CH_2Cl_2, successively washed with water, $NaHCO_3$ solution, and brine, and dried over Na_2So_4. The solvent was evaporated and the residue was recrystallized from hexane–ethyl acetate to give **9** as a yellow

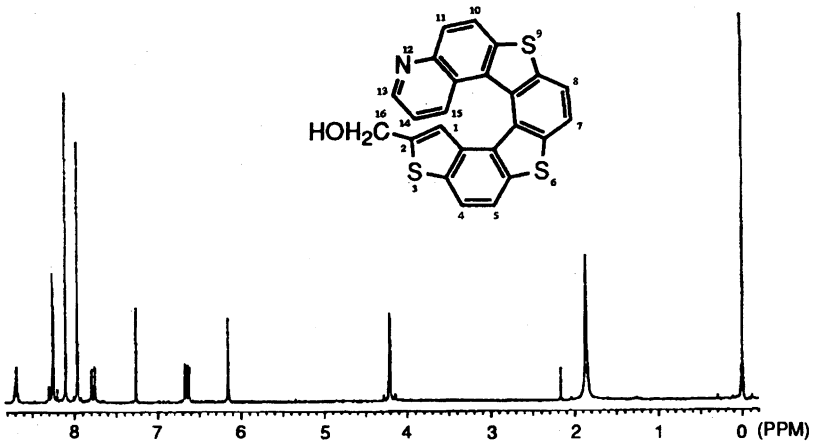


Fig. 4. NMR spectrum of heterohelicene **1**.

solid (9.60 g, 96%). Mp 80—81 °C; ^{1}H NMR ($CDCl_3$) δ = 1.40 (t, J = 7.2 Hz, 3H), 3.76 (br s, 2H), 4.38 (q, J = 7.2 Hz, 2H), 6.89 (dd, J = 8.7 Hz, 2.3, 1H), 7.11 (d, J = 2.3 Hz, 1H), 7.61 (d, J = 8.7 Hz, 1H), 7.86 (s, 1H); IR(KBr) 3382, 1674, 1636, 1522, 1302, 1293, 1240, 1156, 1076, 762 cm^{-1}. Found: C, 59.84; H, 5.02; N, 6.32%. Calcd for $C_{11}H_{11}NO_2S$: C, 59.71; H, 5.01; N, 6.33%.

Ethyl Thieno[3,2-*f*]quinoline-2-carboxylate (10): This compound was prepared according to the literature procedure.[15] Amine **9** (8.93 g, 40.4 mmol) was treated with glycerol (11.52 g, 125.1 mmol), sodium *m*-nitrobenzenesulfonate (4.54 g, 20.2 mmol), boric acid (1.90 g, 30.67 mmol), and concentrated sulfuric acid (12.27g, 125.1 mmol), and the mixture was heated at 170 °C for 1 h and then was cooled. Dry benzene (100 mL) was added and water was removed by azeotropic distillation. The excess of benzene was evaporated and dried in vacuo. To this reaction mixture, 100 mL of ethanol and concentrated sulfuric acid (1.7 mL) were added and the mixture was heated under reflux overnight. The solvent was evaporated and water was added to the mixture. The mixture was made alkaline by NaOH, extracted with ethyl acetate, washed with brine, and dried with Na_2So_4. The solvent was evaporated, and the residue was recrystallized from hexane–ethyl acetate to give the product **10** as white needles (73%, 29.3 mmol). Mp 140—142 °C; ^{1}H NMR ($CDCl_3$) δ = 1.45 (t, J = 7.1 Hz, 2H), 4.46 (q, J = 7.1 Hz, 2H), 7.57 (dd, J = 8.3, 4.4 Hz, 1H), 8.06 (d, J = 9.3 Hz, 1H), 8.12 (d, J = 9.3 Hz, 1H), 8.65 (dd, J = 8.3, 1.6 Hz, 1H), 8.66 (s, 1H), 8.98 (dd, J = 4.4, 1.6 Hz, 1H); IR (KBr) 1717, 1563, 1509, 1289, 1254, 1080, 1017, 804, 758, 741 cm^{-1}. Found: C, 65.39; H, 4.29; N, 5.43%. Calcd for $C_{14}H_{11}NO_2S$: C, 65.35; H, 4.31; N, 5.44%.

2-(Hydroxymethyl)thieno[3,2-*f*]quinoline (11): To a stirred solution of ester **10** (1.29 g, 5.0 mmol) in 30 mL of dry THF was added $LiAlH_4$ (0.19 g, 5.0 mmol) at 0 °C, and the mixture was stirred for 2 h at r.t. The reaction was quenched by careful addition of water, and the reaction mixture was filtrated through a celite pad, and then washed with $CHCl_3$. The organic phase was separated and washed with brine, and dried over Na_2SO_4. The solvent was evaporated, and the residue was recrystallized from ethyl acetate to give alcohol **11** as white needles (0.98 g, 91%). Mp 164—165 °C; ^{1}H NMR ($CDCl_3$) δ = 2.63 (br s, 1H), 5.05 (s, 2H), 7.49 (dd, J = 4.3, 8.3 Hz, 1H), 7.78 (s, 1H), 7.94 (d, J = 8.9 Hz, 1H), 8.03 (d, J = 8.9 Hz, 1H), 8.52 (dd, J = 8.3, 1.7 Hz, 1H), 8.91 (dd, J = 4.3, 1.7 Hz, 1H); IR (KBr) 3399, 3252, 2953, 1610, 1528, 1483, 1275, 1179, 1032, 600 cm^{-1}. Found: C, 66.86; H, 4.20; N, 6.46%. Calcd for $C_{12}H_9NOS$: C, 66.95; H, 4.21; N, 6.51%.

2-(Chloromethyl)thieno[3,2-*f*]quinoline (12): To a stirred suspension of alcohol **11** (0.65 g, 3 mmol) in 50 mL of dry benzene was added thionyl chloride (0.45 mL, 6 mmol) and triethylamine (2 mL, 15 mmol), and the reaction mixture was heated under reflux for 2 h. Then the dark brown suspension was filtrated through a celite pad and washed with benzene. The filtrate was successively washed with water and brine, and dried over Na_2SO_4. The solvent was evaporated, and the residue was chromatographed on silica gel using hexane–ethyl acetate (3 : 1) as the eluent to give chloride **12** as a white solid (0.52 g, 74%). Mp 104—106 °C; ^{1}H NMR ($CDCl_3$) δ = 4.98 (s, 2H), 7.52 (dd, J = 8.4, 4.3 Hz, 1H), 7.94 (s, 1H), 8.00 (d, J = 9.2 Hz, 1H), 8.06 (d, J = 9.2 Hz, 1H), 8.56 (dd, J = 8.4, 1.8 Hz, 1H), 8.95 (dd, J = 4.3, 1.8 Hz, 1H); IR (KBr) 3023, 1568, 1495, 1252, 1186, 1153, 803, 704, 658, 642 cm^{-1}. Found: C, 61.55; H, 3.44; N, 5.95%. Calcd for $C_{12}H_8ClNS$: C, 61.67; H, 3.45; N, 5.99%.

(2-Thieno[3,2-*f*]quinolylmethyl)triphenylphosphonium Chloride (4): To a stirred solution of chloride **12** (0.52 g, 2.23 mmol) in 10 mL of dry benzene was added triphenylphosphine (1.75 g, 6.69 mmol), and the mixture was heated under reflux overnight. The resulting precipitation was filtrated and washed with dry ether, and the filtrate was concentrated in vacuo. The residue was dissolved in 5 mL of dry benzene, and the mixture was heated under reflux for an additional 2 d. The resulting precipitation was filtrated again, and washed with dry ether. The combined phosphonium salt was dried in vacuo (1.04 g, 94%), and was used without further purification. Mp 238—240 °C (decomp); ^{1}H NMR ($CDCl_3$) δ = 6.29 (s, 1H), 6.36 (s, 1H), 7.46 (dd, J = 8.4, 4.4 Hz, 1H), 7.56—7.93 (m, 17H), 8.33 (d, J = 3.8 Hz, 1H), 8.56 (dd, J = 8.4, 1.5, 1H), 8.88 (dd, J = 4.4, 1.5 Hz, 1H); IR (KBr) 3400, 1491, 1439, 1111, 839, 818, 720, 689, 581, 509 cm^{-1}. Found: C, 68.30; H, 5.09; N, 2.61%. Calcd for $C_{30}H_{23}ClNPS\cdot 2H_2O$: C, 67.73; H, 5.12; N, 2.63%.

Thieno[3,2-*f*]quinoline-2-carboxaldehyde (6): To a stirred suspension of alcohol **11** (1.38 g, 5.90 mmol) in dry CH_2Cl_2 was added PDC (4.44 g, 11.8 mmol), and the mixture was stirred overnight at r.t. The reaction mixture was filtrated through a celite pad, and the filtrate was washed with water and brine, and dried over Na_2SO_4. The solvent was evaporated, and the residue was recrystallized from ethyl acetate to give aldehyde **6** as white needles (0.89 g, 65%). Mp 212—213 °C; ^{1}H NMR ($CDCl_3$) δ = 7.61 (dd, J = 8.2, 4.4 Hz, 1H), 8.11 (d, J = 9.3 Hz, 1H), 8.17 (d, J = 9.3 Hz, 1H), 8.63 (s, 1H) 8.66 (dd, J = 8.2, 1.7 Hz, 1H), 9.01 (dd, J = 4.4, 1.7 Hz, 1H), 10.20 (s, 1H); IR (KBr) 1671, 1505, 1489, 1370, 1242, 1192, 1163, 810, 666, 486 cm^{-1}. Found: C, 67.48; H, 3.23; N 6.53%. Calcd for $C_{12}H_7NOS$: C, 67.59; H, 3.31; N, 6.57%.

***N*-[(1*R*,2*S*,3*R*,4*S*-2-(Triisopropylsilyloxy)-1,7,7-trimethylbicyclo[2.2.1]heptan-3-yl]-5-[2-(2-thieno[3,2-*f*]quinolyl)ethenyl)-benzo[1,2-*b*:4,3-*b*′]dithiophene-2-carboxamide (13): Method A (from 3 and 4):** To a stirred solution of aldehyde **3** (0.83 g, 2 mmol) in 20 mL of THF and 20 mL of methanol were successively added phosphonium salt **4** (0.99 g, 2 mmol) and potassium *t*-butoxide (0.45 g, 4 mmol) in 5 mL of methanol at 0 °C, and the mixture was stirred overnight at r.t. The resulting precipitate was filtrated, and sufficiently washed with methanol and benzene. The crude olefin **2** was dried in vacuo, and used without further purification.

To a stirred suspension of olefin **2** in 30 mL of dry CH_2Cl_2 were added 2,6-lutidine (0.48 mL, 4 mmol) and triisopropylsilyl trifluoromethanesulfonate (0.90 mL, 3.3 mmol) at −20 °C, and the mixture was stirred overnight at r.t. The resulting orange solution was washed with water and brine, and dried over Na_2So_4. The solvent was evaporated, and the residue was chromatographed on silica gel to give the silylated product **13** as a yellow solid (1.26 g, 84%).

Method B (from 5 and 6): The reaction procedure is almost the same as that described above. From aldehyde **6** (0.13 g, 0.6 mmol) and phosphonium salt **5** (0.42 g, 0.6 mmol), olefin **13** was obtained as a yellow solid (0.34 g, 76%). Mp 135—137 °C (decomp); ^{1}H NMR ($CDCl_3$) δ = 0.83 (s, 3H), 0.85—2.36 (m, 8H) 1.03 (s, 3H), 1.14 (d, J = 5.2 Hz, 18H), 1.21 (s, 3H), 4.03—4.22 (m, 2H), 6.97 (d, J = 6.0 Hz, 1H), 7.34 (s, 2H), 7.52 (dd, J = 8.4, 4.4 Hz, 1H), 7.61 (s, 1H), 7.76—8.06 (m, 6H), 8.58 (dd, J = 8.4, 1.5 Hz, 1H), 8.94 (dd, J = 4.4, 1.5 Hz, 1H); IR (KBr) 2944, 2865, 1653, 1516, 1460, 1364, 1053, 884, 830, 681 cm^{-1}. Found: C, 68.50; H, 7.12; N, 3.37%. Calcd for $C_{43}H_{50}N_2O_2S_3Si$: C, 68.76; H, 6.71; N, 3.73%.

***N*-[(1*R*, 2*S*, 3*R*, 4*S*)-2-(Triisopropylsilyloxy)-1, 7, 7-trimethylbicyclo[2.2.1]heptan-3-yl][1]benzothieno[5′,4′ : 2,3][1]benzothieno[4′, 5′ : 4, 5]thieno[3.2-*f*]quinoline-2-carboxamide (14): Method A:** Olefin **13** (0.20 g, 0.27 mmol) and iodine (0.11 g, 0.40 mmol) were dissolved in 1.6 L of benzene, and argon was bubbled through the stirred solution for 2 h before photo-irradiation.

Propylene oxide (9.3 mL, 133 mmol) was added to the mixture and the resulting solution was irradiated for 15 h at r.t. with argon flow. The reaction mixture was washed with aqueous $Na_2S_2O_3$, aqueous $NaHCO_3$ and brine, and dried over Na_2SO_4. The solvent was evaporated, and the residue was chromatographed on silica gel using hexane–ethyl acetate to give the diastereomeric mixture (37 : 63) of heterohelicene **14** as a yellow solid (0.14 g, 73%).

Method B : Olefin **13** (0.20 g, 0.27 mmol) and iodine (0.11 g, 0.40 mmol) were dissolved in 1.6 L of benzene, and argon was bubbled through the stirred solution for 2 h before photo-irradiation. Propylene oxide (9.3 mL, 133 mmol) was added to the mixture and the resulting solution was irradiated at r.t. with argon flow. When most of the substrate was consumed (judged by TLC), the irradiation was stopped and the additional substrates, olefin **13** and iodine were dissolved in the above reaction mixture. The procedures were repeated six times, and olefin 1.20 g (1.62 mmol) of **13** was used in total. The reaction time depends on the step. Thus, the substrate was consumed by irradiation for 10 h in the first step, but the reaction took 24 h in the final one. The diastereomeric mixture (37 : 63) of heterohelicene **14** was obtained as a yellow solid (0.70 g, 59%).

***N*- [(1*R*, 2*S*, 3*R*, 4*S*)- 2- Hydroxy- 1, 7, 7- trimethylbicyclo-[2.2.1]heptan- 3- yl][1]benzothieno[5′, 4′ : 2, 3][1]benzothieno-[4′,5′ : 4,5]thieno[3,2-*f*]quinoline-2-carboxamide (15):** To a stirred solution of diastereomeric mixture of helicene **14** (0.67 g, 0.89 mmol) in 10 mL of THF was added TBAF (1.8 mL of a 1 M solution in THF, 1 M = 1 mol dm^{-3}) at r.t., and the mixture was stirred overnight. The reaction mixture was concentrated in vacuo, and the residue was dissolved in $CHCl_3$, washed with water and brine, and dried over Na_2SO_4. The solvent was evaporated, and the residue was chromatographed on silica gel to give the desilylated helicene **15** as a yellow solid (0.50 g, 96%).

***N*-*t*-Butoxycarbonyl-*N*-[(1*R*,2*S*,3*R*,4*S*)-2-hydroxy-1,7,7-trimethylbicyclo[2.2.1]heptan-3-yl][1]benzothieno[5′,4′ : 2,3][1]-benzothieno[4′,5′ : 4,5]thieno[3,2-*f*]quinoline-2-carboxamide (16):** To a stirred solution of diastereomeric mixture of helicene **15** (0.50 g, 0.85 mmol) in 20 mL of dry CH_2Cl_2 were added 4-dimethylaminopyridine (DMAP) (0.21 g, 1.7 mmol) and di-*t*-butyl dicarbonate (0.74 g, 3.4 mmol) at r.t. and the mixture was stirred overnight. The reaction mixture was washed with water and brine, and dried over Na_2SO_4. The solvent was evaporated, and the residue was passed through the short column on silica gel using hexane–ethyl acetate (2 : 1) as an eluent to give the diastereomeric mixture of the *t*-Boc-helicene **16** as a yellow solid (0.49 g, 83%). The column chromatography on silica gel using hexane–ethyl acetate (10 : 1—5 : 1) as an eluent gave both of the pure diastereomer (*P*)-(+)-**16** (0.12 g, 0.17 mmol) and (*M*)-(−)-**16** (0.20 g, 0.29 mmol) as optically pure form.

(*P*)-(+)-16: Mp 156—158 °C; ^{1}H NMR ($CDCl_3$) δ = 0.88 (s, 3H), 0.89 (s, 3H), 1.05—1.83 (m, 5H), 1.07 (s, 3H), 1.35 (s, 9H), 3.99 (t, J = 8.4 Hz, 1H), 4.70 (d, J = 8.4 Hz, 1H), 5.73 (d, J = 7.7 Hz, 1H), 6.62 (dd, J = 8.8, 4.2 Hz, 1H), 6.89 (s, 1H), 7.77 (dd, J = 8.8, 1.6 Hz, 1H), 7.97 (d, J = 8.4 Hz, 1H), 8.08 (d, J = 8.4 Hz, 1H), 8.10 (d, J = 8.4 Hz, 1H), 8.15 (d, J = 8.4 Hz, 1H), 8.28 (s, 2H), 8.71 (dd, J = 4.2, 1.6 Hz, 1H); IR(KBr) 2950, 2360, 1748, 1645, 1541, 1277, 1254, 1150, 1102, 805 cm^{-1}. Found: C, 67.86; H, 5.15; N, 3.91%. Calcd for $C_{39}H_{36}N_2O_4S_3$: C, 67.60; H, 5.24; N, 4.04%.

(*M*)-(−)-16: Mp 160—162 °C; ^{1}H NMR ($CDCl_3$) δ = 0.67 (s, 3H), 0.72—1.02 (m, 1H) 0.79 (s, 3H), 0.92(s, 3H), 1.09 (s, 9H), 1.05—1.89 (m, 4H), 4.07 (t, J = 7.7 Hz, 1H), 4.61 (d, J = 7.7 Hz, 1H), 5.16 (d, J = 8.1 Hz, 1H), 6.65 (dd, J = 8.2, 4.2 Hz, 1H), 6.68 (s, 1H), 7.42 (dd, J = 8.2, 1.6 Hz, 1H), 8.02 (d, J = 8.6 Hz, 1H), 8.08 (d, J = 8.6 Hz, 1H), 8.27 (d, J = 9.0 Hz, 1H), 8.35 (d, J = 9.0 Hz, 1H), 8.74 (dd, J = 4.2, 1.6 Hz, 1H), 9.15 (s, 2H); IR (KBr) 2957, 2360, 1748, 1665, 1655, 1522, 1275, 1254, 1155, 806 cm^{-1}. Found: C, 67.38; H, 5.24; N, 3.93%. Calcd for $C_{39}H_{36}N_2O_4S_3$: C, 67.60; H, 5.24; N, 4.04%.

***S*-Ethyl [1]Benzothieno[5′,4′ : 2,3][1]benzothieno[4′,5′ : 4,5]-thieno [3,2-*f*]quinoline-2-carboxylate (17):** To a stirred solution of ehtanethiol (0.13 mL, 2 mmol) in 5 mL of dry THF was added butyllithium (0.67 mL of a 1.50 M solution in hexane, 1 mmol) at −78 °C, and the mixture was allowed to warm to room temperature and stirred for 1 h at r.t. To the resulting white suspension was added *t*-Boc-helicene **17** (47.6 mg, 0.069 mmol) in 5 mL of dry THF at r.t., and the mixture was stirred overnight. The reaction mixture was washed with water and brine, and dried over Na_2SO_4. The solvent was evaporated, and the residue was chromatographed on silica gel using hexane–ethyl acetate (5 : 1) to give thioester **17** as a yellow solid (29.9 mg, 89%).

Mp 194—195 °C; ^{1}H NMR ($CDCl_3$) δ = 1.21 (t, J = 7.4 Hz, 3H), 2.85 (q, J = 7.4 Hz, 2H), 6.64 (dd, J = 8.6, 4.2 Hz, 1H), 7.13 (d, J = 0.9 Hz, 1H), 7.75 (dd, J = 8.6, 1.3 Hz, 1H), 8.01 (dd, J = 8.6, 0.9 Hz, 1H), 8.11 (d, J = 8.6 Hz, 1H), 8.12 (d, J = 8.4 Hz, 1H), 8.17 (d, J = 8.4 Hz, 1H), 8.28 (d, J = 8.9 Hz, 1H), 8.31 (d, J = 8.9 Hz, 1H), 8.70 (dd, J = 4.2, 1.3 Hz, 1H); IR (KBr) 1657, 1626, 1495, 1298, 1190, 1138, 866, 823, 804, 790 cm^{-1}. Found: C, 64.25; H, 3.16; N, 2.92%. Calcd for $C_{26}H_{15}NOS_4$: C, 64.30; H, 3.11; N, 2.88%. (*P*)-(+)-**17** $[\alpha]_D$ = +2670 (*c* 0.0500, $CHCl_3$); (*M*)-(−)-**17** $[\alpha]_D$ = −2620 (*c* 0.0499, $CHCl_3$).

2-(Hydroxymethyl)[1]benzothieno[5′,4′ : 2,3][1]benzothieno-[4′,5′ : 4,5]thieno[3,2-*f*]quinoline (1): To a stirred solution of the thioester **17** (28.0 mg, 0.065 mmol) in 5 mL of dry THF was added $LiAlH_4$ (10 mg, 0.26 mmol) at r.t., and the mixture was stirred for 1 h at r.t. The reaction was quenched by careful addition of water, and the reaction mixture was filtrated through a celite pad. The organic phase was separated form the filtrate, and washed with water and brine, and dried over Na_2SO_4. The solvent was evaporated, and the residue was chromatographed on silica gel using hexane–ethyl acetate (1 : 2) to give alcohol **1** as a yellow solid (23.8 mg, 85%). Mp 246—247 °C; ^{1}H NMR ($CDCl_3$) δ = 1.79 (br s, 1H), 4.18 (d, J = 14.4 Hz, 1H), 4.26 (d, J = 14.4 Hz, 1H), 6.19 (s, 1H), 6.66 (dd, J = 8.5, 4.3 Hz, 1H), 7.79 (dd, J = 8.5, 1.6 Hz, 1H), 7.95 (d, J = 8.0 Hz, 1H), 7.99 (d, J = 8.0 Hz, 1H), 8.11 (s, 2H), 8.21 (d, J = 8.9 Hz, 1H), 8.27 (d, J = 8.9 Hz, 1H), 8.69 (dd, J = 4.3, 1.6 Hz, 1H); UV ($CHCl_3$) λ_{max} 360, 400nm; IR (KBr) 3220, 2800, 1495, 1298, 1154, 1127, 1105, 1044, 812, 779 cm^{-1}. Found: C, 67.35; H, 3.00; N, 3.16%. Calcd for $C_{24}H_{13}NOS_3$: C, 67.42; H, 3.06; N, 3.28%. (*P*)-(+)-**1** $[\alpha]_D$ = +2150 (*c* 0.0503, $CHCl_3$); (*M*)-(−)-**1** $[\alpha]_D$ = −2140 (*c* 0.0503, $CHCl_3$).

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