AXIALLY CHIRAL 3,3′-BI(1-BENZOTHIOPHENE)-2,2′-DICARBOXYLIC ACID AND ITS DERIVATIVES

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Dedicated to the memory of Professor Otakar Červinka.

Ullmann dimerization of substituted methyl 3-X-1-benzothiophene-2-carboxylates **1**–**7** (X = Cl, Br) gave rise to the corresponding dimeric 3,3′-bi(1-benzothiophene) esters **8**–**13**. Resolution of the title acid **20** by fractional crystallization of its mono- and bisquininium salt afforded pure (*R*)- and (*S*)-enantiomers, the optical purity and absolute configuration of which was confirmed by CD spectrometry and by X-ray crystallography. Ullmann dimerization of chiral oxazolines **23** and **24** derived from **2** proceeded without any diastereodifferentiation. Reduction of (*R*)- and (*S*)-**20** afforded the corresponding (*R*)- and (*S*)-diols **29**, which served as chiral ligands in a model enantioselective reduction of acetophenone. (*R*)- and (*S*)-1-phenylethan-1-ol were formed in 28 and 29% e.e., respectively.

Keywords: Ullmann reaction; Homocouplings; Benzothiophenes; Bi(1-benzothiophene); Resolution; Stereoselective reduction; Biaryls; Axial chirality; CD spectroscopy.

Calamitic liquid crystals[1] are characterized by the presence of a rigid core in their molecules, often represented by a biphenyl residue. To induce ferroelectricity[2] in smectic C phase, chiral element is necessary to be present in the liquid-crystalline molecule. This requirement is fulfilled in most studied compounds, which possess a carbon stereogenic center in one of the alkyl chains elongating the structure. On the other hand, this center can also be replaced by an axially chiral structural unit located in the long axis of the molecule, *e.g.* by 1,1′-binapthalene-2,2′-diol[3], substituted allene[4,5], alkylidenecycloalkane[6,7], and biphenyl derivatives[8–10]. In addition, a hetero-

cyclic unit in the core supports formation of the chiral smectic C phase (SmC*) in a broad temperature range. Recently we introduced[11–13] novel heterocyclic systems based on thieno[3,2-*b*][1]benzofuran, thieno[3,2-*b*][1]-benzothiophene and [1]benzothieno[3,2-*b*][1]benzothiophene to liquid crystal cores to create new liquid-crystalline materials exhibiting switchable mesophases.

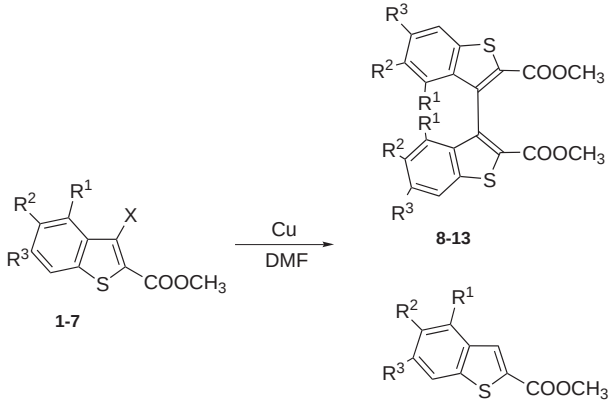
Axially chiral biaryls show[14] wide application as chiral templates for stoichiometric and asymmetric catalytic reactions. In particular the transition metal-catalyzed synthesis, *e.g.* asymmetric hydrogenation of prochiral organic substrates with bidentate phosphorus ligands such as BINAP or related systems has found wide use[15]. Recently axially chiral diphosphine ligands of 3,3′-bithiophene and 3,3′-bi(1-benzothiophene) (BITIANP) were described[16]. It has been found[16,17] that Ru(II) complexed with BITIANP shows excellent stereodifferentiation comparable with BINAP in reductions of α- and β-oxo esters to the corresponding hydroxy esters.

Earlier we applied substituted 3-chloro-1-benzothiophene-2-carboxylic acid derivatives[18,19] for synthesis of new lipoxygenase inhibitors. Easy accessibility of this structural motif inspired us to utilize such type of compounds for synthesis of novel atropoisomeric bi(1-benzothiophene) compounds, which can be used in designing of new types of liquid crystals and chiral auxiliaries for various stereoselective syntheses. In the present paper we report results of the synthesis of the title bi(1-benzothiophene) derivatives, resolution and characterization of enantiomers and preliminary results of their application in stereoselective reductions.

Formation of an aryl–aryl bond can be accomplished by various transition-metal-catalyzed coupling reactions of haloarenes[20–22]. Symmetrical biaryls are accessible by the copper-mediated homocoupling of aryl halides (Ullmann reaction[23]). Introducing a chiral oxazoline moiety to the haloarene molecule substantially influenced the Ullmann reaction diastereoselectivity[10,24–26]. To study the Ullmann dimerization of 3-halo-1-benzothiophene-2-carboxylic acid derivatives, model compounds **1**–**7** were chosen. Although reactivity of chloroarenes in the Ullmann reaction is generally low[23], we expected that due to the lower aromaticity of the thiophene ring (in comparison with benzene), it would be high enough for them to enter the coupling reaction. Nevertheless, dimerization of the related bromo ester **1** was also considered. A methyl group was also introduced in position 4 (ester **3**) with respect to requirement for eventual influencing the barrier to rotation about the 3,3′-bond of the axially chiral molecule. In addition, methoxy group, fluorine and chlorine atoms in **4**–**7** are typical lateral substituents affecting mesomorphic properties of liquid crystals. The

starting methyl esters were prepared by known procedures described elsewhere[18,27–29].

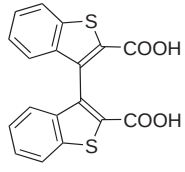
Homocoupling was achieved by heating esters **1**–**7** with activated copper bronze in *N*,*N*-dimethylformamide to 170 °C (Scheme 1). Under optimized conditions (4 h for **1**, 16 h for the other esters), corresponding diesters **8**–**13** were obtained in good yields (66–86%) along with a small portion of halogene reduction products – esters **14**–**19** (yield 6–13%). From mixtures of products, the dimeric esters were easily isolated by a single crystallization. The short reaction time for bromo ester **1** confirmed the known trend of haloarene reactivity in Ullmann reaction. An attempted dimerization of ester **2** under Ni(0) catalysis[30,31] afforded the desired diester **8** only in 9% yield.



In formulae **1** X = Br; **2-7** X = Cl; **1, 2, 8, 14** R^1-R^3 = H; **3, 9, 15** R^1 = CH_3, R^2, R^3 = H; **4, 10, 16** R^1, R^3 = H, R^2 = CH_3O; **5, 11, 17** R^1, R^2 = H, R^3 = F; **6, 12, 18** R^1, R^2 = H, R^3 = Cl; **7, 13, 19** R^1, R^2 = H, R^3= CH_3O

SCHEME 1

To obtain and characterize enantiomers of the formed racemic dimers **8**–**13**, the representative ester **8** was hydrolyzed to diacid **20**. Resolution of the diacid was attempted with various chiral bases, the best results being obtained with quinine. Triple crystallization of the monoquininium salt of



20

20 provided a pure diastereomeric salt, from which the (+)-**20** was liberated ($[\alpha]_D^{23}$ +75). Due to its very low solubility in common solvents, optical purity of (+)-**20** was determined by HPLC analysis of its dimethyl ester, which was obtained by esterification of (+)-**20** with diazomethane. It was found that purity of (+)-**20** is higher than 99% e.e. The overall preparative yield of (+)-**20** reached 15%.

Acid **20** enriched with the (–)-isomer showed only 79% optical purity. To obtain the enantiomerically pure (–)-isomer, it was subsequently fractionally crystallized with cinchonine. However, no separation of the diastereomeric cinchoninium salt proceeded. Surprisingly, we found that fractional crystallization of the bisquininium salt of **20** led to separation of a diastereomeric salt, which after liberation from the salt afforded the (–)-**20** ($[\alpha]_D^{23}$ –72), also in a high optical purity (97.5% e.e.) and in overall 18% yield. Optical purity of both the enantiomers was also confirmed by their CD spectra (Fig. 1). The spectra show nearly textbook perfect mirror image like characteristics. There are two couplets of CD bands centered on single absorption features, the most intense of which is the short wavelength couplet at 201 and 211 nm centered on the absorption feature at 206 nm. The much less intense couplet is found at the long wavelength end of the spectra. It involves CD bands 314 and 336 nm and it is centered on absorption band at 326 nm. A single CD band corresponds to the absorption feature at 286 nm and several low intensity CD bands are found in the region between 220 and 260 nm. The spectra might be interpretable using coupled oscillator theory, once the directions of transition moments within the substituted 1-benzothiophene chromophores are established.

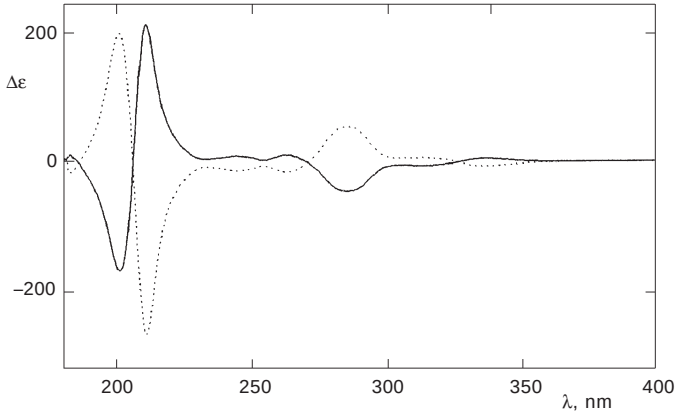


FIG. 1
CD spectra of (*R*)- (——) and (*S*)-**20** (·····) in acetonitrile

The couplet like characteristics of the CD spectra suggest presence of molecular excitons and an interpretation of the relation between CD bands signs and absolute configuration of **20** might be attempted, for the intense CD couplet centered at 206 nm. If we assume that the transition moment for this rather intense transition is oriented along the long axis of the benzothiophene chromophore then for the (–)-*R* configuration and the orientation of the two benzothiophene units according to X-ray result the exciton mechanism suggests that the longer wavelength lobe of the CD couplet (the band at 211 nm) should be of positive sign in accord with experimental data. Validity of such an interpretation of course assumes that the two benzothiophene units in the molecule of **20** are only weakly electronically coupled.

Single crystals of (–)-**20** suitable for X-ray diffraction were obtained from ethyl acetate. By X-ray diffraction analysis, absolute configuration of (–)-**20** was found to be (*R*) (Fig. 2). The value of Flack enantiopole parameter[32], F = 0.03(1), proved the expected absolute configuration. Conformation of the (*R*)-**20** molecule is characterized by two torsion angles: C2–C3–C3′–C2′ = –121.7(2)° and C3a–C3–C3′–C3a′ = –109.3(2)°. Two 1-benzothiophene planar units contain an angle of 113.2(3)°. A molecule of ethyl acetate is built into the crystal structure through two hydrogen bonds (intramolecular: O2–H1···O3 and intermolecular: O2′–H1′···O3 ($-x - 1, +y - 1/2, -z - 1$), which leads to the formation of interesting chains with the molecule of **20**

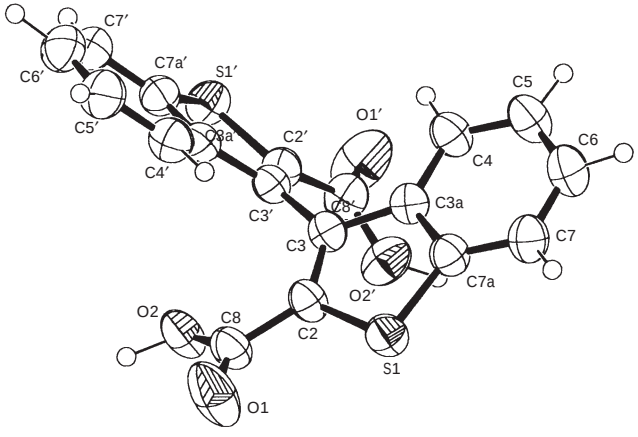


FIG. 2
ORTEP drawing of **20**, showing the numbering scheme. Thermal ellipsoids are drawn at 50% probability

in $y \rightarrow 0$ direction (Fig. 3). Small channels can be also found in the structure from the $y \rightarrow 0$ point of view (Fig. 4). The program ORTEP [33] vas used for visualisation and program PARST [34] for further calculations.

For the planned application of the enantiomers of acid **20**, a racemization study was further accomplished. We found that even at long term heating

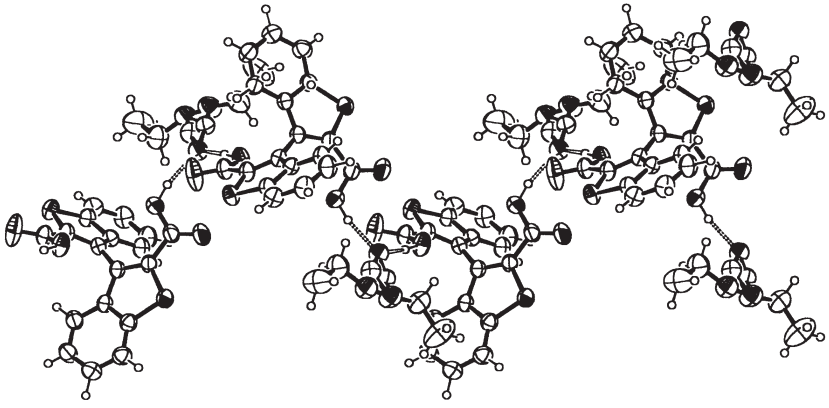


FIG. 3
ORTEP drawing, intermolecular chains in crystal structure of **20** in $0 \rightarrow y$ direction, viewing $0 \rightarrow x$ direction. Thermal ellipsoids are drawn at 50% probability

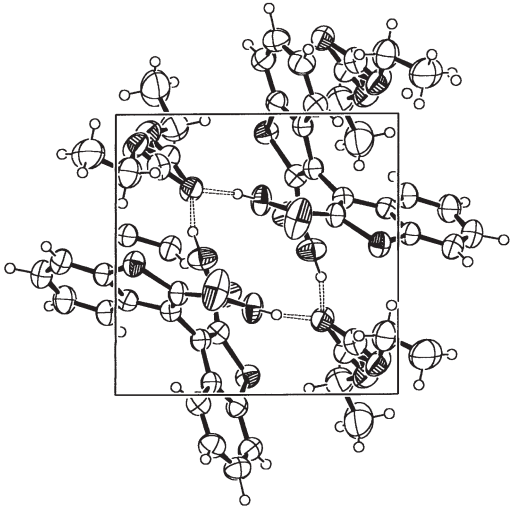
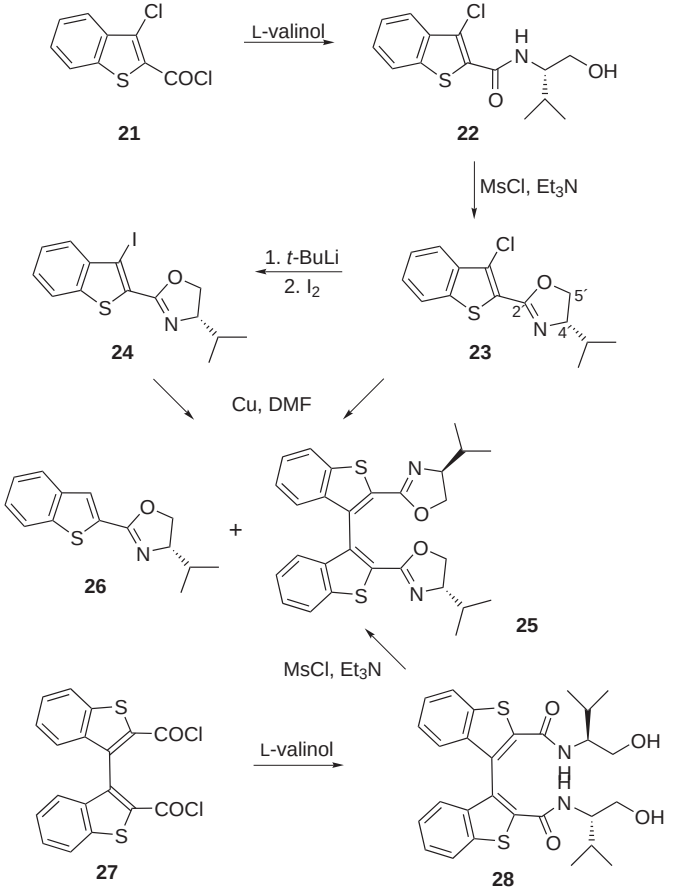


FIG. 4
ORTEP drawing, small channels formed by ethyl acetate and molecule of **20**, viewing $0 \rightarrow z$ direction. Thermal ellipsoids are drawn at 50% probability

to 100 °C in diglyme, optical rotation of (*R*)-**20** did not change at all**.** Only heating to higher temperatures led to a slow racemization. On the basis of the very high value of the determined rotation barrier ($\Delta G^{\ddagger} \approx 130$ kJ/mol at 128 °C), it can be emphasized that enantiomers of **20** do not practically racemize at room temperature. These results seem surprising when considering a substantial different bonding relation in 3,3′-bi(1-benzothiophene)s in comparison with those in 2,2′-disubstitued 1,1′-binaphthalenes.

Because preparative yields of (*R*)- and (*S*)-**20** were relatively low, we attempted to extend the concept of the enantioselective Ullmann synthesis to 3,3′-bithiophene derivatives. Acylation of chloride **21** with L-valinol afforded the corresponding amido alcohol **22**, which was in the subsequent step cyclized by methanesulfonyl chloride to oxazoline derivative **23** in overall yield 83% (Scheme 2). We also attempted to modify the reactivity of

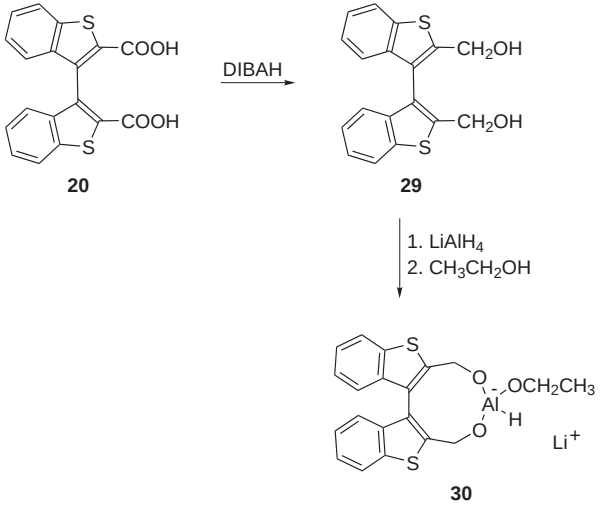


SCHEME 2

23 by substitution of the chlorine atom by iodine: lithiation of **23** with *t*-BuLi afforded the corresponding lithium salt, which was trapped with iodine to produce iodooxazoline **24** in 81% yield. Homocoupling of chlorooxazoline **23** was performed with copper bronze in DMF under the same conditions as for esters **2**–**7**. However, dimer **25** was isolated only in a very low yield (24%); the major product was the dechlorinated oxazoline **26** (yield 34%) (Scheme 2). Analogous reaction with the iodooxazoline afforded the bisoxazoline **26** in 62% yield. Analysis of ^{1}H NMR spectra of **26** showed that no diastereoselectivity of dimerization was achieved and both diastereomers of **26** were formed in the 1:1 ratio. In addition, we were not able to separate the corresponding diastereomers of **26** by chromatographic methods. We also used another approach to obtain bisoxazoline **26**. Racemic acid **20** was transformed with thionyl chloride to dichloride **27**. Acylation of L-valinol with dichloride **27** afforded bis(amidoalcohol) **28**, whose diastereomers could not be separated by chromatography. Finally, cyclization of **28** was achieved in a very slow reaction with methanesulfonyl chloride and bisoxazoline **26** was isolated in a good yield. To induce a diastereoselective course of dimerization, Ullmann reaction of oxazolines **23** and **24** was also performed under very mild conditions[35]. However, reaction of **23** and **24** catalyzed with copper(I) thiophene-2-carboxylate was unsuccessful.

Chirality transfer from various 1,1′-binaphthalene derivatives to prochiral molecules was shown to be essential, *e.g.* by reduction of multiple bonds with BINAP-complexed Rh(I) and Ru(II) [15,36,37] and by reduction of ketones with BINAL-H [38,39]. To achieve satisfactory enantiodifferentiation, other hydride agents were also modified with a broad scale of chiral ligands. Analogously, we attempted to utilize the acid **20** enatiomers for formulation of a chiral reducing agent for a model enantioselective reduction of acetophenone. Reduction of (*R*)-**20** and (*S*)-**20** with DIBAH afforded the corresponding (*R*)- and (*S*)-dimethanol **29** in high yield and optical purity (Scheme 3). From the values of rotational barrier to racemization of diol **29** enantiomers ($\Delta G^{\ddagger} \approx 112$ kJ/mol at 53 °C and 81 kJ/mol at 100 °C), it is evident, that steric requirements of the hydroxymethyl groups in **29** are substantially lower than that of the rigid carboxylic group in **20**. On the other hand, the determined values are high enough to prevent racemization of chiral dimethanol **29** at room temperature. Analogously to BINAL-H, lithium aluminium hydride was then derivatized with (*R*)- and (*S*)-dimethanol **29**, respectively, and an equivalent of ethanol to form the structure **30** of the reducing agent. Reduction of acetophenone with (*R*)- and (*S*)-**30** was

performed in ether at room temperature and (*R*)- and (*S*)-1-phenylethanol (**31**) were obtained with low optical purities of 28 and 29% e.e., respectively.



SCHEME 3

Structures of all new compounds were confirmed by IR and ^{1}H NMR spectra, and elemental analyses. The strong mutual shielding of both the aromatic systems in diesters **8**–**13** leads to substantial changes in chemical shifts of aromatic protons in comparison with chloro esters **2**–**7** and their reduced analogues **14**–**19** (Table I). While the H-4 and H-5 protons and protons of 4-methyl, 5-methoxy and the ester methoxy groups exhibit a strong up-field shift, the H-7 protons are shifted to lower fields. In Table II, comparison of ^{13}C NMR spectra of the pairs ester **2**/dimer **24** and oxazoline **23**/dimer **25** with the open chain amido alcohol **22** is shown. Dimerization of **2** leads to a strong down-field shift of the benzothiophene C-3,3′ atoms (127.4 *vs* 140.3 ppm) in dimer **24** and to slight shifts of the nearest carbon atoms (C-2,2′, C-3a,3′a). The same is for the pair **23** and **25**. In addition, formation of an equimolar mixture of diasteroisomers in **25** leads to duplication of most of the carbon atom signals in the spectrum.

In conclusion, the Ullmann reaction of 3-halo-1-benzothiophene-2-carboxylic esters provides a convenient synthetic route for preparation of the corresponding 3,3′-bi(1-benzothiophene) derivatives. Racemic diacid **20** was separated by fractional crystallization of the corresponding mono- and bisquininium salts yielding optically pure (*R*)- and (*S*)-diacid **20**, whose absolute configuration was determined by X-ray crystallography. No diastereodifferentiation was observed by the attempted oxazoline Ullmann

reaction. A new axially chiral reducing agent based on (*R*)- and (*S*)-dimethanol **29** was formulated for enantioselective reduction of acetophenone, which proceeded with 28 and 29% e.e. This preliminary results of prochiral acetophenone reduction support the potential applicability of 3,3′-bi(1-benzothiophene) derivatives in various enantioselective reactions, which will be the object of future research.

EXPERIMENTAL

Melting points were determined on a Leica VM TG block and are uncorrected. Elemental analyses were carried out on a Perkin–Elmer 2400. IR spectra (ν, cm^{-1}) were recorded on a Nicolet 740 FT-IR spectrometer in chloroform or KBr. NMR spectra (δ, ppm; *J*, Hz) were recorded on a Varian Gemini 300 HC (300 MHz for ^1H and 100 MHz for ^{13}C), deuteriochloroform or DMSO-d_6 was used as solvent and signals of the solvents served as inter-

TABLE I
Chemical shifts of aromatic protons in ^1H NMR spectra of **2**–**19**

Compound	Substituent	H-4	H-5	H-6	H-7	OCH_3
2	–	7.96	7.53	7.49	7.81	3.97
14	–	7.88	7.46	7.40	7.85	3.85
8	–	7.28	7.47	7.50	7.94	3.69
3	4-Me	2.93 (CH_3)	7.18	7.36	7.65	3.95
15	4-Me	2.63 (CH_3)	7.18	7.35	7.69	3.95
9	4-Me	1.89 (CH_3)	7.08	7.37	7.78	3.68
4	5-Me	7.32	–	7.17	7.67	3.91, 3.95
16	5-Me	7.28	–	7.11	7.72	3.88, 3.94
10	5-Me	6.65	–	7.15	7.80	3.65, 3.69
5	6-F	7.94	7.25	–	7.51	3.97
17	6-F	7.83	7.17	–	7.54	3.94
11	6-F	7.22	7.05	–	7.61	3.70
6	6-Cl	7.89	7.46	–	7.82	3.96
18	6-Cl	7.79	7.37	–	7.85	3.95
12	6-Cl	7.17	7.26	–	7.93	3.70
7	6-MeO	7.83	7.09	–	7.22	3.90, 3.95
19	6-MeO	7.74	7.02	–	7.28	3.89, 3.92
13	6-MeO	7.16	6.90	–	7.34	3.68, 3.90

TABLE II
^{13}C NMR spectra of compounds **2**, **14**, **22**–**25**

Compound	C-2	C-3	C-3a	C-4	C-5	C-6	C-7	C-7a	C=O (C-2′)	OCH_3	C-4′	C-5′	CH	CH_3
2	125.4	127.4	138.5	122.7	125.4	128.1	123.7	136.9	161.6	52.5				
14	129.8	140.3	139.3	122.7	125.0	127.3	124.6	136.5	162.4	52.3				
23	123.8	127.1	137.9	122.4	125.2	127.1	123.1	137.1	158.1		72.5	70.5	32.7	17.95, 18.82
25	128.35	139.9	139.5	122.19	124.5	126.1	124.18	132.33	159.46		72.16	70.84	32.61	18.00, 18.08
	128.42	140.0		122.21			124.27	132.56	159.67		72.30		32.82	18.73, 18.80
22	118.6	123.0	138.0	122.8	125.4	127.4	123.1	136.9	161.6		58.1	64.1	29.2	18.7, 19.7

nal standards. HPLC analyses were performed on Chiralcel OD-H, elution with hexane/propan-2-ol 90:10 v/v. CD spectra of (*R*)- and (*S*)-**20** were measured on a Jobin Yvon Mark VI instrument in acetonitrile solution (≈1.3 × 10^{-3} mol l^{-1}). The spectra were measured in quartz cells with the path-length of 0.5 and 1.0 mm and represent computer averages of three consecutive scans each. Optical rotations are given in 10^{-1} deg cm^2 g^{-1}.

Methyl ester **1** (m.p. 69–70.5 °C, ref.[40] m.p. 71.5 °C) was prepared by a three-step route starting from 1-benzothiophene according to refs[40–42]. ^{1}H NMR: 3.97 s, 3 H (OCH_3); 7.51 m, 1 H (arom.); 7.53 m, 1 H (arom.); 7.84 dd, 1 H, J_1 = 8.0, J_2 = 2.2 (H-7); 7.99 dd, 1 H, J_1 = 8.0, J_2 = 2.2 (H-4).

Methyl 3-Chloro-4-methyl-1-benzothiophene-2-carboxylate (**3**)

A mixture of 3-chloro-4-methyl-1-benzothiophene-2-carbonyl chloride[43] (8.50 g, 34.7 mmol) and methanol (50 ml) was heated to boiling for 1 h. After cooling, the precipitated product was filtered off and washed with cold methanol. An amount of 7.29 g (87%) of **3** was obtained, m.p. 79–81 °C. For $C_{11}H_9ClO_2S$ (240.7) calculated: 54.89% C, 3.77% H, 14.73% Cl, 13.32% S; found: 54.76% C, 3.59% H, 14.54% Cl, 13.11% S. IR: 1725 (C=O). ^{1}H NMR: 2.93 s, 3 H (CH_3); 3.95 s, 3 H (OCH_3); 7.18 d, 1 H, J = 7.1 (H-5); 7.36 t, 1 H, J = 7.7 (H-6); 7.65 d, 1 H (H-7).

Analogously, methyl esters **2**, **4**–**7** were obtained from the corresponding substituted 3-chloro-1-benzothiophene-2-carbonyl chlorides. Ester **2**, m.p. 79–80 °C (methanol), ref.[29] m.p. 81.3 °C. ^{1}H NMR: 3.97 s, 3 H (OCH_3); 7.49 dt, 1 H, J_1 = 7.7, J_2 = 2.0 (H-6); 7.53 dt, 1 H (H-5); 7.81 dd, 1 H, J_1 = 8.0 (H-7); 7.96 dd, 1 H, J_1 = 8.0, J_2 = 2.2 (H-4). Ester **4**, m.p. 115–116 °C (methanol), ref.[44] m.p. 116 °C. ^{1}H NMR: 3.91 s, 3 H (OCH_3); 3.95 s, 3 H (OCH_3); 7.17 dd, 1 H, J_1 = 8.8, J_2 = 2.2 (H-6); 7.32 d, 1 H (H-4); 7.67 d, 1 H, J = 9.0 (H-7). Ester **5**, m.p. 119–120 °C (methanol), ref.[28] m.p. 119–121 °C. ^{1}H NMR: 3.97 s, 3 H (OCH_3); 7.25 ddd, 1 H, $^3J_{HH}$ = 8.9, $^3J_{HF}$ = 8.9, $^4J_{HH}$ = 2.5 (H-5); 7.51 dd, 1 H, $^3J_{HF}$ = 8.5, $^4J_{HH}$ = 2.2 (H-7); 7.94 dd, 1 H, $^3J_{HH}$ = 9.0, $^4J_{HF}$ = 4.5. Ester **6**, m.p. 133–134 °C (methanol), ref.[28] m.p. 131–133 °C. ^{1}H NMR: 3.96 s, 3 H (OCH_3); 7.46 dd, 1 H, J_1 = 8.8, J_2 = 2.0 (H-5); 7.82 d, 1 H (H-7); 7.89 d, 1 H (H-4). Ester **7**, m.p. 139–141 °C (methanol), ref.[27] m.p. 138–138.5 °C. ^{1}H NMR: 3.90 s, 3 H (OCH_3); 3.95 s, 3 H (OCH_3); 7.09 dd, 1 H, J_1 = 8.8, J_2 = 2.5 (H-5); 7.22 d, 1 H, J = 2.5 (H-7); 7.83 d, 1 H, J = 8.8 (H-4).

Dimethyl 3,3′-Bi(1-benzothiophene)-2,2′-dicarboxylates **8**–**13**

A mixture of ester **1**–**7** (15 mmol), activated copper bronze (3.81 g, 60 mmol) and dry DMF (12 ml) was heated under stirring in nitrogen atmosphere at 170 °C (bath temperature) for 4 h (compound **1**) or 16 h (compounds **2**–**7**). The mixture was diluted with chloroform (100 ml) and the inorganic material was filtered off. The organic solution was evaporated to dryness, dissolved in chloroform (150 ml), washed with brine and dried with anhydrous magnesium sulfate. After evaporation of the solvent, methanol (50 ml) was added to the residue; the heterogenous mixture was heated to boiling for 5 min, allowed to cool to room temperature and the precipitated crude product **8**–**13** was filtered off and washed with methanol. Pure compounds **8**–**13** were finally obtained by crystallization. From methanolic mother liquors, dehalogenated products **14**–**19** were isolated by column chromatography (silica gel, eluent toluene).

Dimethyl 3,3′-bi(1-benzothiophene)-2,2′-dicarboxylate (**8**). Yield 86% (from **1**), 63% (from **2**), m.p. 209–211 °C (ethanol). For $C_{20}H_{14}O_4S_2$ (382.5) calculated: 62.81% C, 3.70% H, 16.73% S; found: 62.48% C, 3.93% H, 16.53% S. IR: 1722 (C=O). ^{1}H NMR: 3.69 s, 6 H (OCH_3); 7.28dd, 2 H, J_1 = 7.7, J_2 = 2.3 (H-4, H-4′); 7.47 m, 2 H (H-5, H-5′); 7.50 m, 2 H (H-6, H-6′); 7.94 d, 2 H, J = 8.2 (H-7, H-7′).

Dimethyl 4,4′-dimethyl-3,3′-bi(1-benzo[b]thiophene)-2,2′-dicarboxylate (**9**). Yield 74%, m.p. 205–207 °C (ethanol). For $C_{22}H_{18}O_4S_2$ (410.5) calculated: 64.37% C, 4.42% H, 15.62% S; found: 64.52% C, 4.69% H, 15.55% S. IR: 1723 (C=O). ^{1}H NMR: 1.89 s, 6 H (CH_3); 3.68 s, 6 H (OCH_3); 7.08 d, 2 H, J = 7.1 (H-5, H-5′); 7.37 t, 2 H, J = 7.2 (H-6, H-6′); 7.78 d, 2 H, J = 8.2 (H-7, H-7′).

Dimethyl 5,5′-dimethoxy-3,3′-bi(1-benzothiophene)-2,2′-dicarboxylate (**10**). Yield 66%, m.p. 203–204 °C (ethanol/toluene). For $C_{22}H_{18}O_6S_2$ (442.5) calculated: 59.71% C, 4.10% H, 21.69% S; found: 59.74% C, 4.12% H, 21.41% S. IR: 1723 (C=O). ^{1}H NMR: 3.65 s, 6 H (OCH_3); 3.69 s, 6 H (OCH_3); 6.65 d, 2 H, J = 2.5 (H-4, H-4′); 7.15 dd, 2 H, J_1 = 9.0, J_2= 2.5 (H-6, H-6′); 7.80 d, 1 H (H-7, H-7′).

Dimethyl 6,6′-difluoro-3,3′-bi(1-benzothiophene)-2,2′-dicarboxylate (**11**). Yield 67%, m.p. 189–191 °C (ethanol). For $C_{20}H_{12}F_2O_4S_2$ (418.4) calculated: 57.41% C, 2.89% H, 15.33% S; found: 57.23% C, 2.56% H, 15.18% S. IR: 1721 (C=O). ^{1}H NMR: 3.70 s, 6 H (OCH_3); 7.05 ddd, 2 H, $^3J_{HH}$ = 8.8, $^3J_{HF}$ = 8.8, $^4J_{HH}$ = 2.2 (H-5, H-5′); 7.22 dd, 2 H, $^3J_{HH}$ = 8.8, $^4J_{HF}$ = 5.5 (H-4, H-4′); 7.61 dd, 2 H, $^3J_{HF}$ = 8.5, $^4J_{HH}$ = 2.2 (H-7, H-7′).

Dimethyl 6,6′-dichloro-3,3′-bi(1-benzothiophene)-2,2′-dicarboxylate (**12**). Yield 66%, m.p. 238–240 °C (ethanol/toluene). For $C_{20}H_{12}Cl_2O_4S_2$ (451.4) calculated: 53.22% C, 2.68% H, 15.71% Cl, 14.21% S; found: 53.09% C, 2.63% H, 15.34% Cl, 14.12% S. IR: 1722 (C=O). ^{1}H NMR: 3.70 s, 6 H (OCH_3); 7.17 d, 2 H, J = 8.8 (H-4, H-4′); 7.26 dd, 2 H, J_1 = 8.8, J_2 = 1.9 (H-5, H-5′); 7.93 d, 2 H (H-7, H-7′).

Dimethyl 6,6′-dimethoxy-3,3′-bi(1-benzothiophene)-2,2′-dicarboxylate (**13**). Yield 67%, m.p. 180–182 °C (ethanol). For $C_{22}H_{18}O_6S_2$ (442.5) calculated: 59.71% C, 4.10% H, 21.69% S; found: 59.65% C, 3.98% H, 21.46% S. IR: 1723 (C=O). ^{1}H NMR: 3.68 s, 6 H (OCH_3); 3.90 s, 6 H (OCH_3); 6.90 dd, 2 H, J_1 = 8.8, J_2 = 1.9 (H-5, H-5′); 7.16 d, 2 H (H-4, H-4′); 7.34 d, 2 H, J = 2.2 (H-7, H-7′).

Methyl 1-benzothiophene-2-carboxylate (**14**). Yield 18% (from **1**) and 11% (from **2**), m.p. 71–72 °C (methanol), ref.[45] m.p. 71–72 °C. IR: 1714 (C=O). ^{1}H NMR: 3.85 s, 3 H (OCH_3); 7.40 m, 1 H (H-6); 7.46 m, 1 H (H-5); 7.85 dd, 1 H, J_1 = 8.8, J_2 = 2.2 (H-7); 7.88 dd, 1 H, J_1 = 8.8, J_2 = 2.2 (H-4); 8.06 s, 1 H (H-3).

Methyl 4-methyl-1-benzothiophene-2-carboxylate (**15**). Yield 13%, m.p. 51–53 °C (methanol). For $C_{11}H_{10}O_2S$ (206.3) calculated: 64.05% C, 4.89% H, 15.55% S; found: 63.90% C, 5.03% H, 15.59% S. IR: 1721 (C=O). ^{1}H NMR: 2.63 s, 3 H (CH_3); 3.95 s, 3 H (OCH_3); 7.18 d, 1 H, J = 7.1 (H-5); 7.35 t, 1 H, J = 7.7 (H-6); 7.69 d, 1 H, J = 8.2 (H-7); 8.15 s, 1 H (H-3).

Methyl 5-methoxy-1-benzothiophene-2-carboxylate (**16**). Yield 6%, m.p. 102–104 °C (methanol), ref.[44] m.p. 102.5–103.5 °C. For $C_{11}H_{10}O_3S$ (222.3) calculated: 59.44% C, 4.54% H, 14.43% S; found: 59.27% C, 4.51% H, 14.33% S. IR: 1720 (C=O). ^{1}H NMR: 3.88 s, 3 H (OCH_3); 3.94 s, 3 H (OCH_3); 7.11 dd, 1 H, J_1 = 8.8, J_2 = 2.2 (H-6); 7.28 d, 1 H (H-4); 7.72 d, 1 H, J = 8.8 (H-7); 7.98 s, 1 H (H-3).

Methyl 6-fluoro-1-benzothiophene-2-carboxylate (**17**). Yield 12%, m.p. 84.5–86 °C (methanol). For $C_{10}H_7FO_2S$ (210.2) calculated: 57.13% C, 3.36% H, 15.25% S; found: 57.02% C, 3.07% H, 15.33% S. IR: 1721 (C=O). ^{1}H NMR: 3.94 s, 3 H (OCH_3); 7.17 ddd, 1 H, $^3J_{HH}$ = 8.9, $^3J_{HF}$ = 8.9,

$^4J_{HH}$ = 2.2 (H-5); 7.54 dd, 1 H, $^3J_{HF}$ = 8.5, $^4J_{HH}$ = 2.2 (H-7); 7.83 dd, 1 H, $^3J_{HH}$ = 8.8, $^4J_{HF}$ = 5.2 (H-4); 8.02 s, 1 H (H-3).

Methyl 6-chloro-1-benzothiophene-2-carboxylate (**18**). Yield 14%, m.p. 104–106 °C (methanol). For $C_{10}H_7ClO_2S$ (226.7) calculated: 52.99% C, 3.11% H, 15.64% Cl, 14.14% S; found: 52.67% C, 2.98% H, 15.44% Cl, 15.11% S. IR: 1721 (C=O). ^{1}H NMR: 3.95 s, 3 H (OCH_3); 7.37 dd, 1 H, J_1 = 8.8, J_2 = 2.2 (H-5); 7.79 d, 1 H, J = 8.5 (H-4); 7.85 d, 1 H, J = 2.2 (H-7); 8.02 s, 1 H (H-3).

Methyl 6-methoxy-1-benzothiophene-2-carboxylate (**19**). Yield 8%, m.p. 119–120 °C (methanol). For $C_{11}H_{10}O_3S$ (222.3) calculated: 59.44% C, 4.54% H, 14.43% S; found: 59.18% C, 4.67% H, 14.26% S. IR: 1717 (C=O). ^{1}H NMR: 3.89 s, 3 H (OCH_3); 3.92 s, 3 H (OCH_3); 7.02 dd, 1 H, J_1 = 8.8, J_2 = 2.2 (H-5); 7.28 d, 1 H, J = 2.4 (H-7); 7.74 d, 1 H (H-4); 7.97 s, 1 H (H-3).

3,3′-Bi(1-benzothiophene)-2,2′-dicarboxylic Acid (**20**)

A mixture of diester **8** (10.4 g, 27.3 mmol), sodium hydroxide (6.7 g, 168 mmol) and 50% aqueous ethanol (180 ml) was heated under stirring to reflux for 2 h. After cooling to the room temperature, it was acidified with dilute hydrochloric acid (1:1) to pH 2. The precipitate was filtered a washed with water. Crystallization of the product from acetic acid afforded 8.79 g (91%) of diacid **20**, m.p. 273–275 °C. For $C_{18}H_{10}O_4S_2$ (354.4) calculated: 59.38% C, 3.48% H, 16.10% S; found: 59.44% C, 3.64% H, 16.10% S. IR (KBr): 3415 (OH), 1721 (C=O). ^{1}H NMR (DMSO): 7.14 d, 2 H, J = 8.2 (H-4, H-4′); 7.34 t, 2 H, J_1 = 7.2, J_2 = 7.7 (H-5, H-5′); 7.54 t, 2 H (H-6, H-6′); 8.13 d, 2 H, J = 8.2 (H-7, H-7′).

Resolution of Diacid **20**

Method A. Diacid **20** (3.11 g, 8.8 mmol) was dissolved in acetone (30 ml) by heating. To the solution, quinine (2.84 g, 8.8 mmol) was added and the mixture was heated to reflux for 45 min. After cooling, the precipitated crystals were filtered off and washed with cold acetone. An amount of 3.47 g (58%) of monoquininium salt of diacid **20** was obtained, which after two crystallizations from acetone, afforded 1.01 g (17%) of pure diastereomeric salt, m.p. 182–183 °C, $[\alpha]_D^{23}$ –91.0 (*c* 0.85, DMF). For $C_{38}H_{34}N_2O_6S_2$ (678.8) calculated: 67.24% C, 5.05% H, 4.13% N; found: 67.04% C, 5.10% H, 4.01% N.

The salt was dissolved in water (100 ml) and concentrated hydrochloric acid (4 ml) was added under stirring. The liberated acid was filtered off, washed thoroughly with water and dried *in vacuo*. An amount of 0.467 g (1.32 mmol) of (*R*)-(+)-acid **20** was obtained (overall yield 15%), m.p. 187–189 °C, $[\alpha]_D^{23}$ +75.0 (*c* 0.54, diglyme). Optical purity of (*R*)-(+)-acid **20** was determined by HPLC analysis (Chiralcel OD-H) of the corresponding (+)-methyl ester obtained by esterification of (*R*)-**20** with ethereal diazomethane.

X-Ray data for (–)-**20**: $C_{18}H_{10}O_2S_2{\cdot}C_4H_8O_2$, M = 441.493, monoclinic system, space group $P12_11$ (No. 4)[46], a = 8.626(2) Å, b = 14.079(3) Å, c = 8.634(1) Å, β = 90.32 (1)°, V = 1048.5(4) Å^3, Z = 2, D_c = 1.3983 g cm^{-3}, μ(CuKα) = 26.232 cm^{-1}, crystal dimensions 0.6 × 0.8 × 0.9 mm. Data were measured at 293 K on an Enraf–Nonius CAD4 diffractometer with graphite monochromatized CuKα radiation. The structure was solved by direct methods[47] and anisotropically refined by full matrix least-squares on F values[48] to final R = 0.0560, R_w = 0.0413 and S = 1.0135 with 329 parameters using 3769 independent reflections (θ_{range} = 3.14–67.90°). Hydrogen atoms linked to carbon atoms were located from the expected geometry and were not refined. The acid hydrogen atoms H1 and H11 were found from Fourier

difference electron density map and their positions were refined. Ψ-scan was used for absorption correction.

CCDC 196033 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge *via* www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge, CB2 1EZ, UK; fax: +44 1223 336033; or deposit@ccdc.cam.ac.uk).

Method B. From the original mother liquor, diacid **20** (1.21 g, 3.42 mmol) enriched with the (*S*)-enantiomer was obtained (78% e.e.). Its crystallization with quinine (2.25 g, 7.0 mmol) in acetone (40 mmol) by method *A* afforded 2.64 g (77%) of the crude bisquininium salt. After three crystallizations from acetone, 0.686 g (20%) of the pure bisquininium salt was obtained, m.p. 182–184.5 °C, $[\alpha]_D^{23}$ +219.9 (*c* 1.61, DMF). For $C_{58}H_{58}N_4O_8S_2$ (1003.3) calculated: 69.44% C, 5.83% H, 5.58% N; found: 69.03% C, 5.92% H, 5.32% N.

The (*S*)-(–)-acid **20** (0.224 g, 0.63 mmol) (overall yield 18%), m.p. 188–190 °C, $[\alpha]_D^{23}$ –72.0 (*c* 0.47, diglyme). Optical purity (97.5% e.e.) was determined analogously to the (*R*)-acid.

N-[(*S*)-1-(Hydroxymethyl)-2-(methylpropyl)]-3-chloro-1-benzothiophene-2-carboxamide (**22**)

A solution of chloride[18] **21** (7.4 g, 32 mmol) in dichloromethane (50 ml) was dropwise added to a solution of (*S*)-valinol[49] (3.7 g, 35.9 mmol) and triethylamine (20 ml) in dichloromethane (100 ml) at 0 °C in nitrogen atmosphere. After stirring at room temperature for 2 h, the mixture was successively washed with water (100 ml), 5% aqueous hydrochloric acid (50 ml) and water (100 ml), and dried with anhydrous magnesium sulfate. Evaporation of the solvent left a residue, which on crystallization from toluene afforded the 8.71 g (91%) of amide **22**, m.p. 154–155 °C, $[\alpha]_D^{23}$ –36.5 (*c* 1, $CHCl_3$). For $C_{14}H_{16}ClNO_2S$ (297.8) calculated: 56.46% C, 5.42% H, 11.90% Cl, 4.70% N; found: 56.70% C, 5.31% H, 11.89% Cl, 4.70% N. IR: 3422 (OH), 1640 (C=O). ^{1}H NMR: 1.071 d, 3 H, J = 6.6 (CH_3); 1.073 d, 3 H, J = 6.6 (CH_3); 2.09 m, 1 H (CH); 2.57 t, 1 H, J = 5.5 (OH); 3.84 dd, 2 H, J_1 = 7.7, J_2 = 4.4 (CH_2); 4.04 m, 1 H (CH); 7.38 d, 1 H (NH); 7.49 m, 2 H (H-5, H-6); 7.84 m, 2 H (H-4, H-7).

(*S*)-2-(3-Chloro-1-benzothiophen-2-yl)-4-isopropyl-4,5-dihydrooxazole (**23**)

A solution of amide **22** (1.20 g, 4 mmol) and triethylamine (2.25 ml) in dichloromethane (30 ml) was cooled to 0 °C in nitrogen atmosphere. Methanesulfonyl chloride (0.5 ml, 6.5 mmol) was added dropwise and the mixture was stirred at room temperature for 3 h, washed with water (50 ml) and brine, and dried with anhydrous magnesium sulfate. The residue after evaporation was purified by column chromatography (silica gel, chloroform) and 0.98 g (87%) of the title compound **23** was obtained, m.p. 84–86 °C, $[\alpha]_D^{23}$ –50.1 (*c* 0.51, $CHCl_3$). For $C_{14}H_{14}ClNOS$ (279.8) calculated: 60.10% C, 5.04% H, 12.67% Cl, 5.01% N; found: 60.31% C, 5.05% H, 12.50% Cl, 4.85% N. IR: 1638 (C=N). ^{1}H NMR: 0.96 d, 3 H, J = 6.6 (CH_3); 1.05 d, 3 H (CH_3); 1.91 m, 1 H (CH); 4.21 m, 2 H (CH + 1 H of CH_2); 4.48 dd, 1 H, J_1 = 6.6, J_2 = 6.2 (1 H of CH_2); 7.48 m, 2 H (H-5, H-6); 7.92 m, 2 H (H-4, H-7).

(*S*)-2-(3-Iodo-1-benzothiophen-2-yl)-4-isopropyl-4,5-dihydrooxazole (**24**)

tert-Butyllithium (5.3 ml of a 1.7 M solution in pentane) was added dropwise to a solution of oxazoline **23** (1.78 g, 6.36 mmol) in dry tetrahydrofuran (20 ml) under stirring at –78 °C in nitrogen atmosphere. The mixture was stirred for 2 h and the formed lithium salt was

trapped by addition of an iodine (2.42 g, 9.54 mmol) solution in tetrahydrofuran (5 ml). The cooling bath was removed and the mixture was stirred at room temperature for 1 h, added to a 5% aqueous solution of sodium thiosulfate (200 ml) and washed with chloroform (100 ml). The organic layer was washed with water (50 ml), dried with anhydrous magnesium sulfate and evaporated. Column chromatography (silica gel, toluene) of the residue afforded 1.92 g (81%) of iodo derivative **24**, m.p. 59–61 °C. For $C_{14}H_{14}INOS$ (371.2) calculated: 45.30% C, 3.80% H, 34.18% I, 3.77% N; found: 44.88% C, 3.93% H, 33.82% I, 3.57% N. IR: 1634 (C=N). ^{1}H NMR: 0.99 d, 3 H, J = 6.6 (CH_3); 1.08 d, 3 H (CH_3); 1.92 m, 1 H (CH); 4.22 m, 2 H (CH + 1 H of CH_2); 4.49 dd, 1 H, J_1 = 6.6, J_2 = 6.2 (1 H of CH_2); 7.45 m, 2 H (H-5, H-6); 7.79 m, 1 H; 7.89 m, 1 H.

2,2′-Bis[(*S*)-4-isopropyl-4,5-dihydrooxazol-2-yl]-3,3′-bi(1-benzothiophene) (**25**)

Method A. Compound **23** (1.30 g, 4.64 mmol), activated copper bronze (2.3 g, 36.2 mmol) and dry DMF (20 ml) were heated to 170 °C (bath temperature) in nitrogen atmosphere for 20 h. The mixture was diluted with chloroform (50 ml) and the inorganic material was filtered off. The organic solution was evaporated to dryness, dissolved in chloroform (100 ml), washed with water (50 ml) and dried with anhydrous magnesium sulfate. The residue after evaporation was separated by column chromatography (silica gel, chloroform/methanol 99.5:0.5 v/v). An amount of 0.27 g (24%) of **25** as an equimolar diastereomeric mixture and 0.39 g (34%) of dechlorinated compound **26** were isolated.

Method B. By the same procedure as in method *A*, compound **24** (360 mg, 0.96 mmol), activated copper bronze (0.5 g, 7.8 mmol) and DMF (8 ml) afforded 145 mg (62%) of a diastereomeric mixture of **25** and 38 mg (16%) of deiodo product **26**.

Method C. A solution of compound **23** (300 mg, 1.07 mmol) in dry THF (5 ml) was treated with *tert*-butyllithium (0.67 ml of a 1.7 M solution in pentane, 1.14 mmol) at –78 °C in nitrogen atmosphere for 1 h. Anhydrous copper chloride (0.3 g, 2.23 mmol) was added and the mixture was stirred at room temperature for 4 h and heated to reflux for 1 h. The reaction mixture was worked up as in method *A* and 110 mg (0.45 mmol) of dechloro product **26** was isolated.

Method D. By the same procedure as for **23**, diamide **28** (4.09 g, 7.79 mmol), methanesulfonyl chloride (1.32 ml, 17.1 mmol) in the presence of triethylamine (6.5 ml, 46.7 mmol) in chloroform (70 ml) afforded after stirring at room temperature for 14 days and subsequent aqueous workup 2.16 g (57%) of a 1:1 diastereomeric mixture of compound **23**.

2,2′-Bis[(S)-4-isopropyl-4,5-dihydrooxazol-2-yl]-3,3′-bi(1-benzothiophene) (**25**). For $C_{28}H_{28}N_2O_2S_2$ (488.7) calculated: 68.82% C, 5.78% H, 5.73% N; found 69.13% C, 6.05% H, 5.80% N. IR: 1637 (C=N). ^{1}H NMR: 0.64 d, 3 H, J = 6.5 (CH_3); 0.68 d, 3 H, J = 6.5 (CH_3); 0.74 d, 3 H, J = 6.5 (CH_3); 0.80 d, 3 H, J = 6.5 (CH_3); 1.45 m, 2 H (CH); 1.56 m, 2 H (CH); 3.65 dd, 2 H, J_1 = 16.1, J_2 = 8.1 (1 H of CH_2); 3.77–3.94 m, 8 H (CH_2); 4.03 dd, 2 H, J_1 = 17.9, J_2 = 9.0 (1 H of CH_2); 7.15–7.22 m, 8 H (arom.); 7.33 m, 4 H (arom.); 7.82 d, 4 H, J = 8.1 (arom.).

(S)-2-(1-Benzothiophen-2-yl)-4-isopropyl-4,5-dihydrooxazole (**26**). M.p. 83–85 °C. For $C_{14}H_{15}NOS$ (245.4) calculated: 68.54% C, 6.16% H, 5.71% N; found: 68.35% C, 5.89% H, 5.42% N. IR: 1648 (C=N). ^{1}H NMR: 0.94 d, 3 H, J = 7.1 (CH_3); 1.04 d, 3 H, J = 6.6 (CH_3); 1.92 m, 1 H (CH); 4.18 m, 2 H (CH + 1 H of CH_2); 4.45 m, 1 H (1 H of CH_2); 7.38 m, 2 H (arom.); 7.82 s, 1 H (H-3); 7.79–7.86 m, 2 H (arom.).

3,3′-Bi(1-benzothiophene)-2,2′-bis(carbonyl chloride) (**27**)

To a slurry of diacid **20** (5.0, 14.1 mmol) in toluene (50 ml), thionyl chloride (5.1 ml, 71 mmol) was added dropwise and the mixture was heated to reflux 3 h and evaporated to dryness. Crystallization of the formed solid from heptane afforded 3.97 g (73%) of chloride **27**, m.p. 206–208 °C. For $C_{18}H_8Cl_2O_2S_2$ (391.3) calculated: 55.25% C, 2.06% H, 18.12% Cl, 16.39% S; found: 55.52% C, 1.99% H, 17.91% Cl, 16.55% S. IR: 1749 (C=O). ^{1}H NMR: 7.28 d, 2 H, J = 8.8 (H-4, H-4′); 7.36 dt, 2 H, J_1 = 8.2, J_2 = 1.3 (H-5, H-5′); 7.59 dt, 2 H (H-6, H-6′); 7.97 dd, 2 H, J_1 = 8.2, J_2 = 1.3 (H-7, H-7′).

N,*N*′-Bis[(*S*)-1-(hydroxymethyl)-2-methylpropyl]-3,3′-bi(1-benzobenzothiophene)-2,2′-dicarboxamide (**28**)

By the same method as for **22**, acylation of dichloride **27** (3.49 g, 9.0 mmol) with (*S*)-valinol (2.23 g, 21.6 mmol) in the presence of triethylamine (15 ml) and dichloromethane (25 ml) afforded, after aqueous workup, 4.51 g (96%) of oily dicarboxamide **28**. For $C_{28}H_{32}N_2O_4S_2$ (524.7) calculated: 64.10% C, 6.15% H, 5.34% N, 12.22% S; found: 64.01% C, 6.31% H, 5.08% N, 12.06% S. IR: 3409 (NH), 1642 (C=O). ^{1}H NMR of a mixture of diastereoisomers: 0.56 d, 6 H, J = 7.1 (CH_3); 0.68 d, 6 H, J = 7.2 (CH_3); 0.84 d, 6 H, J = 7.2 (CH_3); 0.98 d, 3 H, J = 7.1 (CH_3); 1.33 m, 2 H (CH); 1.55 m, 2 H (CH); 3.17 dd, 4 H, J_1 = 5.5, J_2 = 3.9 (CH_2); 3.33 dd, 2 H, J_1 = 11.5, J_2 = 5.5 (1 H of CH_2); 3.58 dd, 2 H, J_1 = 8.2, J_2 = 2.8 (1 H of CH_2); 3.72 m, 4 H (CH); 5.93 d, 4 H, J = 8.2 (NH); 7.16–7.38 m, 8 H (arom.); 7.52 m, 4 H (arom.); 8.00 d, 4 H, J = 8.3 (arom.).

(*R*)-3,3′-Bi(1-benzothiophene)-2,2′-dimethanol (**29**)

A slurry of (*R*)-**20** (300 mg, 0.85 mmol) in dry THF (50 ml) was cooled to –78 °C and diisobutylalumnium hydride (10.2 ml of a 1 M solution in hexanes, 10.2 mmol) was added dropwise under nitrogen atmosphere in 10 min. The stirring was continued for 30 min, the cooling bath was removed and the mixture was stirred at room temperature for 6 h. The reaction was quenched with methanol (2 ml) at –70 °C and subsequently decomposed with water (5.5 ml) at 0 °C. The mixture was filtered and the solid was washed with chloroform (50 ml). The filtrate was washed subsequently with water (3 × 30 ml), brine and dried with anhydrous magnesium sulfate. After removing the solvent, 170 mg (62%) of pure (*R*)-**29** was obtained, m.p. 177–179 °C, $[\alpha]_D^{23}$ +38.0 (*c* 0.76, $CHCl_3$), purity >99% e.e. (Chiralcel OD-H). For $C_{18}H_{14}O_2S_2$ (326.4) calculated: 66.23% C, 4.32% H, 19.64% S; found: 65.97% C, 4.25% H, 19.47% S. IR: 3392 (OH). ^{1}H NMR: 2.96 dd, 2 H, J_1 = 12.4, J_2 = 6.3 (OH); 4.62 dd, 2 H (CH_2); 7.24 m, 4 H (arom.); 7.38 t, 2 H, J = 7.4 (arom.); 7.92 d, 2 H, J = 8.0 (H-7, H-7′).

In the same way, reduction of (*S*)-**20** afforded (*S*)-**29** in 75% yield, m.p. 176–178 °C, $[\alpha]_D^{23}$ –37.0 (*c* 0.65, $CHCl_3$), purity 97.4% e.e.

Reduction of Acetophenone with $LiAlH_4$/(*R*)-**29** and $LiAlH_4$/(*S*)-**29**

A solution of (*R*)-**29** (254 mg, 0.78 mmol) in dry ether (5 ml) was cooled to 0 °C, and solution of lithium aluminium hydride (3.90 ml of a 0.2 M solution in ether, 0.78 mmol) was added within 15 min. After 15 min stirring, ethanol (45 µl, 0.78 mmol) was added and the mixture stirred for another 1 h. Acetophenone was added (0.91 ml, 0.78 mmol) and stirring was continued at 0 °C for 3 h and at room temperature for 16 h. The reaction was stopped

with 4% aqueous sodium hydroxide (0.2 ml) and the precipitated salts removed by filtration. The ethereal solution was dried with anhydrous magnesium sulfate, evaporated to dryness and the residue separated by column chromatography (silica gel, toluene) afforded 76 mg (81%) of (*R*)-1-phenylethan-1-ol (**30**) with 28% e.e. and 228 mg (90%) of (*R*)-**29** was recovered with 98.2% e.e.

By the same procedure, reduction of acetophenone with $LiAlH_4$/(*S*)-diol **29** afforded (*S*)-1-phenylethan-1-ol (85%) with 29% e.e and (*S*)-**29** (88%) with 96.2% e.e.

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REFERENCES

1. Demus D., Goodby J., Gray G. W., Spiess H.-W., Vill V. (Eds): *Handbook of Liquid Crystals*. Wiley-VCH, Weinheim 1998.
2. Lagerwall S. T.: *Ferroelectric and Antiferroelectric Liquid Crystals*. Wiley-VCH Verlag, Weinheim 1999.
3. Dorfler H.-D., Gopfert A.: *Colloid Polym. Sci.* **2000**, *278*, 1085.
4. Lunkwitz R., Zab K., Tschierke C.: *J. Prakt. Chem.* **1998**, *340*, 662.
5. Lunkwitz R., Tschierke C., Langhoff A., Giesselmann F., Zugenmaier P.: *J. Mater. Chem.* **1997**, *7*, 1713.
6. Zhang Y., Schuster G. B.: *J. Org. Chem.* **1994**, *59*, 1855.
7. Lemieux R. P., Schuster G. B.: *J. Org. Chem.* **1993**, *58*, 100.
8. Solladie G., Zimmermann R.: *J. Org. Chem.* **1985**, *50*, 4062.
9. Solladie G., Hugelé P., Bartsch R., Skoulios A.: *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1533.
10. Solladie G., Hugele P., Bartsch R.: *J. Org. Chem.* **1998**, *63*, 3895.
11. Váchal P., Svoboda J., Glogarová M., Stibor I.: *Mol. Cryst. Liq. Cryst. Sci. Technol., Sect. A* **1999**, *328*, 367.
12. Černovská K., Svoboda J., Stibor I., Glogarová M., Vaněk P., Novotná V.: *Ferroelectrics* **2000**, *241*, 248.
13. Košata B., Kozmík V., Svoboda J., Novotná V., Vaněk P., Glogarová M.: *Liq. Cryst.* **2003**, *30*, in press.
14. Helmchen G., Hoffmann R. W., Mulzer J., Schaumann E. (Eds): *Houben–Weyl: Methods of Organic Chemistry*, Bd. E21a, *Stereoselective Synthesis*. G. Thieme Verlag, Stuttgart 1995.
15. Noyori R., Takaya H.: *Acc. Chem. Res.* **1990**, *23*, 345.
16. Bennincori T., Brenna E., Sannicolo F., Trimarco L., Antognazza P., Cesarotti E., Demartin F., Pilati T.: *J. Org. Chem.* **1996**, *61*, 6244.
17. Bennincori T., Piccolo O., Rizzo S., Sannicolo F.: *J. Org. Chem.* **2000**, *65*, 8340.
18. Nič M., Havelková M., Terinek M., Paleček J., Svoboda J., Jandera A., Panajotová V., Kuchař M.: *Cesk. Farm.* **1999**, *48*, 281.
19. Svoboda J., Štádler M., Jandera A., Panajotová V., Kuchař M.: *Collect. Czech. Chem. Commun.* **2000**, *65*, 1082.
20. Miyaura N., Suzuki A.: *Chem. Rev. (Washington, D. C.)* **1995**, *95*, 2457.
21. Negishi E.: *Acc. Chem. Res.* **1982**, *15*, 340.

22. Farina V.: *Pure Appl. Chem.* **1996**, *68*, 73.
23. Fanta P. E.: *Synthesis* **1974**, 9.
24. Nelson T. D., Meyers A. I.: *J. Org. Chem.* **1994**, *59*, 2655.
25. Meyers A. I., McKennon M. J.: *Tetrahedron Lett.* **1995**, *36*, 5869.
26. Meyers A. I., Price A.: *J. Org. Chem.* **1998**, *63*, 412.
27. Higa T., Krubsack A. J.: *J. Org. Chem.* **1976**, *41*, 3399.
28. Wright W. B., Brabander H. J.: *J. Heterocycl. Chem.* **1971**, *8*, 711.
29. Ried W., Oremek G., Ocakcioglu B.: *Justus Liebigs Ann. Chem.* **1980**, 1424.
30. Colon I., Kelsey D. R.: *J. Org. Chem.* **1986**, *51*, 2627.
31. Lin G., Hong R.: *J. Org. Chem.* **2001**, *66*, 2877.
32. Flack H. D.: *Acta Crystallogr., Sect. A: Fundam. Crystallogr.* **1983**, *39*, 876.
33. Farrugia L. J.: *J. Appl. Crystallogr.* **1997**, *30*, 565.
34. Nardelli M.: *PARST, System of Computer Routines for Calculating Molecular Parameters from Results of Crystal Structure Analysis*. University of Parma, Parma 1998.
35. Zhang S., Zhang D., Liebeskind L. S.: *J. Org. Chem.* **1997**, *62*, 2312.
36. Takaya H., Ohta T., Mashima K., Noyori R.: *Pure Appl. Chem.* **1990**, *62*, 1135.
37. Brown J. M.: *Chem. Soc. Rev.* **1993**, *22*, 25.
38. Noyori R.: *Pure Appl. Chem.* **1981**, *53*, 2315.
39. Noyori R., Tomino I., Tamimoto Y., Nishizawa M.: *J. Am. Chem. Soc.* **1984**, *106*, 6709.
40. Smirnov-Zamkov I., Zborovskii Y. L.: *Zh. Org. Khim.* **1975**, *11*, 1776.
41. Ried W., Bender H.: *Chem. Ber.* **1955**, *88*, 34.
42. Reinecke M. G., Newsom J. G., Almqvist K. A.: *Synthesis* **1980**, 327.
43. Tominaga Y., Pratap R., Castle R. N., Lee M. L.: *J. Heterocycl. Chem.* **1982**, *19*, 871.
44. Higa T., Krubsack A. J.: *J. Org.Chem.* **1975**, *40*, 3037.
45. Cooper J., Scrowston R. M.: *J. Chem. Soc., Perkin Trans. 1* **1972**, 414.
46. *International Tables for Crystallography*. D. Riedel Publishing Company, Boston 1983.
47. Altomare A., Cascarano G., Giacovazzo G., Guagliardi A., Burla M. C., Polidori G., Camalli M.: *J. Appl. Crystallogr.* **1994**, *27*, 435.
48. Watkin D. J., Prout C. K., Carruthers J. R., Betteridge P. W., Cooper R. I.: *Crystals*, p. 11. Chemical Crystallography Laboratory, Oxford (U.K.) 2001.
49. Meyers A. I., Dickman D. A., Bailey T. R.: *J. Am. Chem. Soc.* **1985**, *107*, 7974.