Preparation of Enantiomerically Pure 1,1′-Binaphthalene-2,2′-diol and 1,1′-Binaphthalene-2,2′-dithiol

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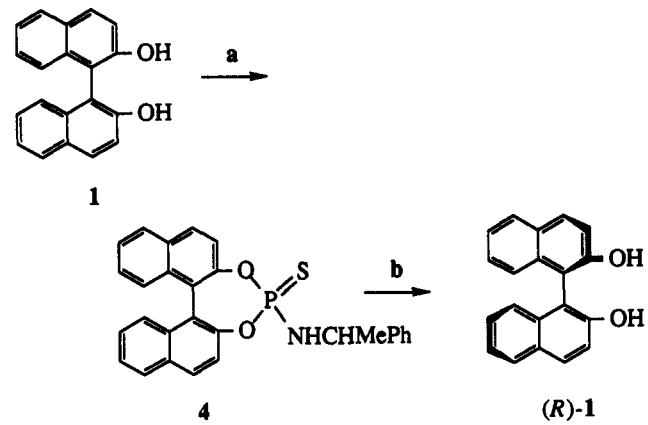
A practical preparation of enantiomerically pure 1,1′-binaphthalene-2,2′-diol (1) and 1,1′-binaphthalene-2,2′-dithiol (2) is reported. Enantiopure 2 is obtained from enantiopure 1 via Newman–Kwart rearrangement of the thiocarbamoyl derivative 5 under controlled reaction conditions. The enantiopure starting diol 1 was obtained by a simple and inexpensive method engaging condensation of thiophosphoryl chloride and (*S*)-(−)-α-methylbenzylamine in pyridine and reaction of the resulting phosphoramidate 3 with racemic binaphthol 1 to give quantitatively a 1:1 mixture of diastereoisomers 4 that were cleanly separated by a single recrystallization from a chloroform–ethanol mixture in very high yield. The procedures can be scaled up easily.

1,1′-Binaphthalene-2,2′-diol (1)[1] and 1,1′-binaphthalene-2,2′-dithiol (2)[2] have emerged as efficient chiral auxiliaries in a number of asymmetric reactions. These molecules may be considered prototypes of the larger class of atropisomeric chiral molecules with C_2-symmetry and are the starting materials for the preparation of several derivatives of comparable efficiency and potential.[3] Herein we report a practical method for the preparation of 2 in enantiomerically pure form starting from enantiomerically pure 1 for which we also provide a rapid and convenient method of resolution. Previously published procedures for the resolution of 1 involve, among other methods,[1] separation of the diastereomeric salts derived from 1,1′-binaphthyl-2,2′-diyl hydrogen phosphate and (+)-cinchonine[4] or (*R*)-(−)-aminobutanol.[5] The method described here, though rather similar to that recently reported by Gong et al.,[6] was independently developed in our laboratory and offers advantages which, in our opinion, render it among the most practical, reliable, and inexpensive methods available.

Equimolar quantities of thiophosphoryl chloride and (*S*)-(−)-α-methylbenzylamine were condensed in pyridine to afford the corresponding phosphoramidate 3 that was then reacted with racemic binaphthol 1. This procedure gave a quantitative yield of a 1:1 mixture of diastereoisomers 4 which were cleanly separated by recrystallization from a chloroform–ethanol mixture in very high yield (Scheme I). The large difference in solubilities between the two diastereoisomers of 4 allowed for their complete separation in a single recrystallization. The diastereoisomer that crystallized first was levorotatory and was shown to be the one derived from (*R*)-(−)-1,1′-binaphthol.

Scheme I[a]



[a] Key: (a) (*S*)-(−)-$Cl_2P(S)NHCHMePh$ (3), pyridine; (b) (i) selective recrystallization, (ii) $LiAlH_4$, THF.

The preparation of the two diastereoisomers 4 could be carried out in one pot from thiophosphoryl chloride, (*S*)-(−)-α-methylbenzylamine, and binaphthol, substantially reducing the preparation time of the entire operation. Lithium aluminium hydride released the enantiomerically pure diol 1 in quantitative yield. (This step was not optimized in terms of identifying a cheaper reagent to perform the same operation.) Enantiomerically unchanged (*S*)-(−)-α-methylbenzylamine could also be easily recovered in very high yield from the mother liquors and could be reused in further resolutions. It should be noted, however, that both enantiomers of α-methylbenzylamine are rather inexpensive.

The preparation of enantiopure 2 from enantiopure 1 was carried out with optimization of the reaction conditions in the thermolysis of the Newman–Kwart rearrangement

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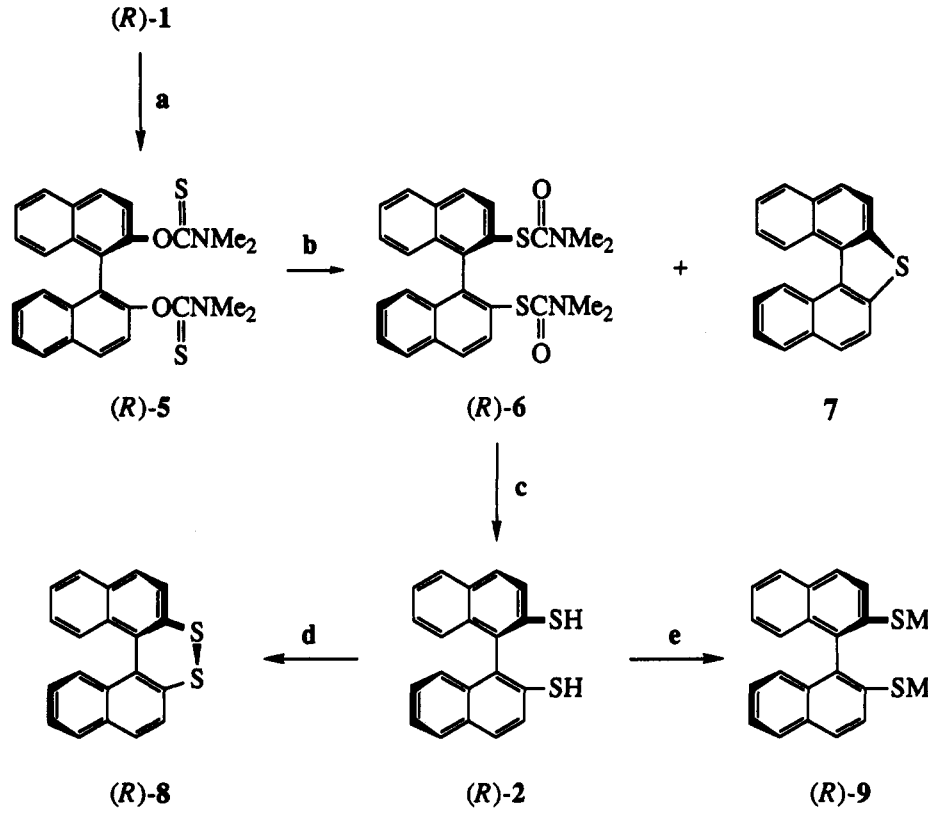
Scheme II[a]



[a] Key: (a) (i) NaH (oil dispersion), DMF, (ii) $Me_2NC(S)Cl$; (b) neat, 285 °C, 22 min; (c) $LiAlH_4$, THF; (d) I_2, $CHCl_3$; (e) Et_3N, MeI, MeOH.

of **5** into **6**[7,8] (Scheme II). Immersion of neat (*R*)-**5** into a glycerol bath at 285 °C for 22 min provided the rearranged product (*R*)-**6** and the thiophene **7**. Despite the rather high temperature, no loss of enantiomeric purity with respect to the starting material (*R*)-**5** was noted in the formation of (*R*)-**6** under the reaction conditions described. The thermolysis has been carried out several times with 5-g quantities with consistent success. Conversely, higher temperatures or longer reaction times provided (*R*)-**6** with variable losses of enantiomeric purity.

Binaphthothiophene (**7**) did not exhibit any optical activity despite the conveivable helicene-type structure.[7] Studies on the conformational mobility of this and similar molecules are now in progress.

The procedure described herein is similar to the one reported for the preparation of racemic **6**[8] and is described in detail in the Experimental Section. The enantiomeric purity of the compounds was verified by NMR and HPLC. Since dithiol **2** does not lend itself to a clean determination of its enantiomeric purity as it oxidized to some extent to disulfide **8** and does not give sharp chromatographic peaks, it was oxidized by iodine to the disulfide **8**. The latter dithiin **8** showed optical activity almost identical to the reported values.[9] The dimethyl derivative **9** was also prepared because it showed clean enantiomeric separation in the HPLC using a Chiracel OD column. The enantiomeric purity of the compounds could thus be checked in this way with confidence in the precision.

Experimental Section

(*R,S*)-1,1'-Binaphthyl-2,2'-diyl *N*-((*S*)-α-Methylbenzyl)-thiophosphoroamidate (4). Two-Step Reaction. A solution of (*S*)-(−)-α-methylbenzylamine (12.11 g, 100 mmol) in pyridine (75 mL) was added dropwise with stirring to a cold (ice bath) solution of thiophosphoryl chloride (16.60 g, 98 mmol) in pyridine (100 mL) under N_2. The reaction mixture was stirred at 0 °C for 2 h and then at room temperature for 45 min. The resulting heterogeneous mixture was made slightly acidic with dilute sulfuric acid (10%, ca. 200 mL), and after adding water (200 mL), it was extracted with CH_2Cl_2 (3 × 100 mL) and dried over Na_2SO_4. Rotoevaporation of the solvent gave the *N*-((*S*)-(−)-α-methylbenzyl)thiophosphoroamidate **3**[10] (24.14 g, 97%) as a colorless oil: bp 305 °C/0.1 Torr; $[\alpha]^{25}_D$ −48.6 (*c* = 0.2, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.61 (dd, *J* = 6.6 and 0.9 Hz, $-CH_3$, 3 H), 4.41 (m, −NH−, 1 H), 4.78 (m, −CH−, 1 H), 7.22–7.40 (m, Ar, 5 H); ^{13}C NMR ($CDCl_3$) δ 23.78 (d, $^3J_{CP}$ = 28.2 Hz, $-CH_3$), 54.42 (d, $^2J_{CP}$ = 15.9 Hz, −CH−), 126.01, 127.85, 128.78, 128.80; IR (neat) 3329 (m), 3028 (w), 2970 (w), 1450 (m), 1402 (m), 1202 (m), 1114 (s), 1081 (s), 849 (m) cm^{-1}; MS *m/z* (M^+) 254, 220, 204, 184, 105.

N-((*S*)-α-Methylbenzyl)thiophosphoroamidate **3** (2 g, 7.87 mmol) was added dropwise with stirring to a solution of racemic 1,1'-binaphthalene-2,2'-diol (2.25 g, 7.87 mmol) in pyridine (70 mL) at rt under N_2. After 4 h at reflux, the reaction mixture was cooled and made slightly acidic with 10% sulfuric acid (ca. 200 mL). After water (200 mL) was added, the reaction mixture was extracted with CH_2Cl_2 (3 × 100 mL) and dried over Na_2SO_4. Removal of the solvent gave a ca. 1:1 diastereomeric mixture of **4** as a colorless crystalline material (3.53 g, 96%).

One-Step Reaction. A pyridine solution (70 mL) of (*S*)-(−)-α-methylbenzylamine (12.11 g, 100 mmol) was added dropwise with stirring to an ice-cooled solution of thiophosphoryl

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chloride (16.93 g, 100 mmol) in pyridine (100 mL) under N_2. The solution was stirred for 2 h at 0 °C and for 2 h at room temperature. Racemic 1,1′-binaphthol (27.20 g, 95 mmol) was added, and the reaction mixture was refluxed for 4 h. The solution was cooled and made slightly acidic with 10% sulfuric acid (ca. 200 mL). Water (200 mL) was added. Extraction with CH_2Cl_2 (3 × 100 mL), drying over Na_2SO_4, and removal of the solvent gave 4 as a colorless crystalline solid (42.19 g, 95%).

Separation of Diastereoisomers 4. The ca. 1:1 diastereomeric mixture of 4 (4 g) was dissolved in refluxing chloroform (120 mL). Absolute ethanol (60 mL) was added. After 24 h at 25 °C, the solution was filtered to obtain (−)-4 as colorless needles (1.74 g, 87%): mp 289–290 °C (EtOH); $[\alpha]^{25}_D$ −309 (c = 1.7, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.47 (d, J = 6.9 Hz, $-CH_3$), 3.47 (m, −NH−), 4.92 (m, −CH−), 6.60 (d, J = 8.7 Hz, Ar, 1 H), 7.20–7.45 (m, Ar, 11 H), 7.53 (d, J = 9.0 Hz, Ar, 1 H), 7.74 (d, J = 9.0 Hz, Ar, 1 H), 7.87 (t, J = 8.7 Hz, Ar, 2 H), 7.97 (d, J = 8.7 Hz, Ar, 1 H); ^{13}C NMR ($CDCl_3$) δ 24.0 (d, $J_{C,P}$ = 36 Hz, $-CH_3$), 52.5 (d, $J_{C,P}$ = 3 Hz, −CH−), 120.0 (d, $J_{C,P}$ = 12.0 Hz, $C_{3(3')}$), 121.4 (d, $J_{C,P}$ = 9.9 Hz, $C_{3'(3)}$), 125.4, 125.5, 125.5, 125.6, 126.2, 126.2, 126.4, 126.5, 126.8, 127.0, 127.5, 128.2, 128.4, 128.6, 128.6, 130.3, 130.4, 130.6, 130.7, 131.4, 131.7, 132.2; IR KBr disk) 3362 (m), 2975 (w), 1615 (m), 1459 (m), 1225 (s), 1065 (s), 955 (s), 835 (s), 750 (s), cm^{-1}. Anal. Calcd for $C_{28}H_{22}O_2NPS$: C, 71.93; H, 4.74; N, 2.99. Found: C, 71.68; H, 4.94; N, 3.07. The solution was rotoevaporated to dryness. CH_2Cl_2 (80 mL) and petroleum ether (50 mL) were added, and the solution was left at room temperature for 6 h. The solution was filtered, and more petroleum ether was added (20 mL). After 6 h the colorless crystals were filtered to obtain (+)-4 (1.60 g, 80%): mp 225–226 °C (CH_2Cl_2/petroleum ether); $[\alpha]^{25}_D$ +351 (c = 0.85, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.55 (d, J = 6.9 Hz, $-CH_3$), 3.59 (m, −NH−), 3.59 (m, −NH−), 4.66 (m, −CH−), 7.18–7.52 (m, Ar, 12 H), 7.59 (dd, J = 8.7, 1.0 Hz, Ar, 1 H), 7.86 (d, J = 9.0 Hz, Ar, 1 H), 7.92 (d, J = 8.1 Hz, Ar, 1 H), 7.94 (d, J = 8.1 Hz, Ar, 1 H), 8.05 (d, J = 9.0 Hz, Ar, 1 H); ^{13}C NMR ($CDCl_3$) δ 25.2 (d, $J_{C,P}$ = 15.19 Hz, $-CH_3$), 52.6 (d, $J_{C,P}$ − 2.5 Hz, −CH−), 120.9 (d, $J_{C,P}$ = 12.0 Hz, $C_{3(3')}$), 121.6 (d, $J_{C,P}$ = 9.9 Hz, $C_{3'(3)}$), 121.7, 123.1, 124.7, 125.5, 125.6, 125.8, 125.9, 126.4, 126.6, 126.9, 127.1, 127.3, 128.3, 128.4, 128.5, 128.5, 130.5, 130.8, 131.4, 131.8, 132.2, 132.3; IR (KBr disk) 3364 (w), 2966 (w), 1587 (m), 1225 (s), 1200 (s), 955 (s), 838 (s), 748 (s). Anal. Calcd for $C_{28}H_{22}O_2NPS$: C, 71.93; H, 4.74; N, 2.99. Found: C, 72.20; H, 4.87; N, 2.97.

Reduction of (−)-4. Diasteromerically pure (−)-1,1′-binaphthyl-2,2′-diyl *N*-((*S*)-α-methylbenzyl)thiophosphoroamidate (4) (1.0 g, 2.13 mmol) in dry THF (30 mL) was cooled at 0 °C under argon. Lithium aluminium hydride (0.40 g, 10.60 mmol) was added in portions under vigorous magnetic stirring. After 2 h, water (50 mL) and dilute hydrochloric acid were cautiously added until the solution tested slightly acidic. The solution was then extracted with CH_2Cl_2 (2 × 80 mL), dried over Na_2SO_4, and rotoevaporated to give 95% yield of enantiopure (*R*)-(+)-1,1′-binaphthol as a colorless crystalline solid: mp 209–210 °C; $[\alpha]^{25}_D$ +34.0 (c = 1, THF). The acidic aqueous solution was neutralized with dilute NaOH and extracted with CH_2Cl_2 (2 × 50 mL), dried over sodium sulfate, evaporated, and bulb to bulb distilled (ca. 80 °C, 10 Torr) to obtain (*S*)-α-methylbenzylamine in 93% yield: $[\alpha]^{20}_D$ −31.3 (c = 1, EtOH).

Reduction of (+)-4. Diastereomeric pure (+)-1,1′-binaphthyl-2,2′-diyl *N*-((*S*)-α-methylbenzyl)thiophosphoroamidate (4) was reduced similarly to the (−)-diastereoisomer giving enantiopure (*S*)-(−)-1,1′-binaphthol as colorless crystals: mp 209–210 °C; $[\alpha]^{25}_D$ −34.0 (c = 1, THF), The acidic aqueous solution was neutralized with dilute NaOH and extracted with CH_2Cl_2 (2 × 50 mL), dried over Na_2SO_4, evaporated, and bulb to bulb distilled (10 Torr) to obtain (*S*)-(−)-α-methylbenzylamine in 90% yield: $[\alpha]^{20}_D$ −31.3 (c = 1, EtOH).

(*R*)-(+)-1,1′-Binaphthalene-2,2′-diyl *O,O*-Bis(*N,N*-dimethylthiocarbamate) (5). An ice-cooled solution of (*R*)-(+)-1,1′-binaphthol (28.63 g, 100 mmol) in 200 mL of dry DMF under N_2 was treated under mechanical stirring with NaH (50% oil dispersion) (10.56 g, 220 mmol). To the resulting yellow mixture was added *N,N*-dimethylthiocarbamoyl chloride (27.19 g, 220 mmol), and the solution was warmed to 85 °C. After 1 h the reaction mixture was cooled to room temperature and poured into aqueous KOH (800 mL). The colorless precipitate was filtered, washed thoroughly with water, and dissolved in CH_2Cl_2. The CH_2Cl_2 solution was dried over Na_2SO_4 and rotoevaporated to obtain a colorless solid that was recrystallized from CH_2Cl_2/petroleum ether (41.45 g, 90%): mp 206–208 °C (lit.[2a] mp, 208–209.5 °C); $[\alpha]^{25}_D$ +103.5 (c = 1, THF).

(*R*)-(+)-1,1′-Binaphthalene-2,2′-diyl *S,S*-Bis(*N,N*-dimethylthiocarbamate) (6) and Dinaphtho[2.1-*b*:1′.2-*d*]thiophene (7). A Pyrex vial fitted with a $CaCl_2$ drying tube, containing 1,1′-binaphthalene-2,2′-diyl *O,O*-bis(*N,N*-dimethylthiocarbamate) (5) (5 g, 10.85 mmol) was immersed for 22 min into a hot bath containing glycerol at 285 °C. After being cooled to room temperature, the yellow solid was dissolved in CH_2Cl_2 and purified by flash chromatography (silica gel, CH_2Cl_2). Dinaphtho[2.1-*b*:1′.2′-*d*]thiophene (7)[2a] (R_f = ca. 0.9, 0.60 g, 20%) and 1,1′-binaphthalene-2,2′-diyl *S,S*-bis(*N,N*-dimethylcarbamate) (6) (R_f = ca. 0.1, 3.5 g, 70%) were eluted in the order.

6: mp 247–249 °C (CH_2Cl_2/petroleum ether) (lit.[2a] mp 245–247 °C); $[\alpha]^{25}_D$ +40.6 (c = 1, THF).

(*R*)-(+)-1,1′-Binaphthalene-2,2′-dithiol (2). A solution of compound 6 (4.60 g, 10 mmol) in 40 mL of dry THF under N_2 was cooled at 0 °C, and lithium aluminium hydride (2.27 g, 60 mmol) was added in portions. The reaction mixture was refluxed for 4 h and then cooled to 0 °C. Water and 10% HCl were added until the solution was neutralized. The mixture was extracted with ether (3 × 80 mL), dried over Na_2SO_4, and rotoevaporated to give 2 as a colorless solid (2.86 g, 90%): mp 150–151 °C (benzene); $[\alpha]^{22}_D$ −85.9; $[\alpha]^{22}_{546}$ −103.8 (c = 1, $CHCl_3$) [lit.[9b] mp ca. 100 °C; $[\alpha]^{22}_{546}$ −33.0 (c = 0.49, $CHCl_3$)].

(*R*)-(−)-Dinaphtho[2,1-*c*:1′,2′-*e*][1,2]dithiin (8). To a solution of (*R*)-(−)-1,1′-binaphthalene-2,2′-dithiol (2) (3.18 g, 10 mmol) in $CHCl_3$ (30 mL), a few crystals of iodine were added. After the solution was stirred at room temperature for 12 h, the excess iodine was reduced with a saturated aqueous solution of sodium metabisulfite, extracted with CH_2Cl_2 (2 × 80 mL), dried over Na_2SO_4, and rotoevaporated. The resulting solid was purified by flash chromatography (silica gel, petroleum ether) to give yellow crystals (2.84 g, 90%): mp 259–260 °C; $[\alpha]^{25}_{546}$ −776.0 (c = 1, $CHCl_3$) [lit.[9d] mp 260–261 °C; $[\alpha]^{25}_{546}$ −777.1 (c = 0.5, $CHCl_3$)].

(*R*)-(+)-Bis(methylthio)-1,1′-binaphthalene (9). To an ice-cooled solution of 1,1′-binaphthalene-2,2′-dithiol (2) (3.18 g, 10 mmol) in triethylamine (20 mL), under N_2, was added a solution of methyl iodide (100 mmol) in methanol (20 mL). The reaction mixture was stirred at room temperature for 5 h, 10% aqueous HCl was added, and the solution was extracted with CH_2Cl_2 (2 × 80 mL), dried over Na_2SO_4, and rotoevaporated to obtain a colorless solid that was recrystallized from CH_2Cl_2/petroleum ether (3.29 g, 95%): mp 184–185 °C; $[\alpha]^{25}_{436}$ +39.2 (c = 1, $CHCl_3$) [lit.[9d] mp 185–186 °C (racemate); $[\alpha]^{25}_{436}$ +39.1 (c = 1.1, $CHCl_3$)]. HPLC on Chiracel (cellulose 3,5-dimethylphenyl carbamate) OD column [eluant *n*-hexane/*i*-PrOH (94:6), 0.6 mL/min, 254-nm UV detection] provided a clean separation of the enantiomers (α = 1.12) and confirmed the enantiomeric purity of 9 and of its precursors.

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