Pergamon

Tetrahedron: Asymmetry, Vol. 8, No. 4, pp. 537–546, 1997

Printed in Great Britain
PII: S0957-4166(96)00539-3 0957-4166/97 $17.00 + 0.00

Axially chiral 1,1′-binaphthyls with non-identical groups in 2,2′-positions. Synthesis of the enantiomerically pure 2-hydroxy-2′-thiol and substituted 2-amino-2′-thiols

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Abstract: Enantiomerically pure hydroxy thiol (*S*)-(+)-**6**, amino thiol (*S*)-(+)-**12**, and *N*,*N*-dimethylamino thiol (*S*)-(−)-**16** have been synthesized from BINOL (*S*)-(−)-**1** and the amino alcohol (*S*)-(−)-**7**, respectively, via the Newman–Kwart rearrangement of the corresponding thiocarbamoyl derivatives (*S*)-(−)-**2**, (*S*)-(−)-**10**, and (*S*)-(−)-**14**. Configurational stability of the binaphthyl unit has been observed. © 1997 Elsevier Science Ltd. All rights reserved.

Introduction

2,2′-Disubstituted 1,1′-binaphthyls with identical groups in positions 2 and 2′, such as BINOL **1**, BINAP, and their congeners, are established ligands in asymmetric catalysis.[1] By contrast, their analogues with non-identical substituents in these positions are rare, Hayashi's MOP (with OMe and PPh_2 groups)[2] and our amino alcohol **7** (NOBIN)[3–5] being among the few examples reported to date.[6]

Whereas symmetrically disubstituted binaphthyls are readily available via the oxidative coupling of 2-naphthol as a strategic step,[1,3,4] their non-symmetrical counterparts are more difficult to synthesize since the procedure usually requires selective manipulation of one of the two identical groups (e.g. in **1**).[2,6] One possible solution to this problem is the selective cross-coupling of two different naphthalene derivatives.[3,4,7] We have demonstrated that this approach is particularly successful in the synthesis of NOBIN **7** and related binaphthyls.[3,4] However, its scope is limited by the stringent electronic demands of the reacting partners[4] and by the requirement that the reactants be capable of covalent bonding to the oxidizing agent (e.g., Cu^{2+}).[3,7e] Another limiting factor is the nature of the functional groups. Thus, for instance, the thio-analogue of BINOL, i.e., the dithiol **4**, cannot be prepared by the oxidative coupling of 2-thionaphthol since, in this instance, S-arylation dominates over the C-1 arylation.[8]

While this work was in progress, the dithiol **4** was prepared by De Lucchi[9] and Smith[10] from BINOL **1** via the Newman–Kwart[11] rearrangement of the thiocarbamate **2** followed by hydrolysis of the resulting carbamate **3**. In spite of the relatively severe conditions of the Newman–Kwart rearrangement (>250°C), no racemization has been detected when the enantiomerically pure **1** was utilized as the starting material,[9] which is in full agreement with our own, unpublished experience.[12] Racemic hydroxy thiol (±)-**6** has also been synthesized by the same group via a partial rearrangement of (±)-**2** followed by hydrolysis (**2** → **5** → **6**).[13] A recent report by Woodward[14] on the highly efficient synthesis of (±)-**6** via an elegant, selective functionalization of (±)-**1**, prompted us to disclose our results. Herein, we report on the syntheses of enantiomerically pure hydroxy thiol (*S*)-(+)-**6**, amino thiol (*S*)-(+)-**12**, and *N*,*N*-dimethylamino thiol (*S*)-(−)-**16**.

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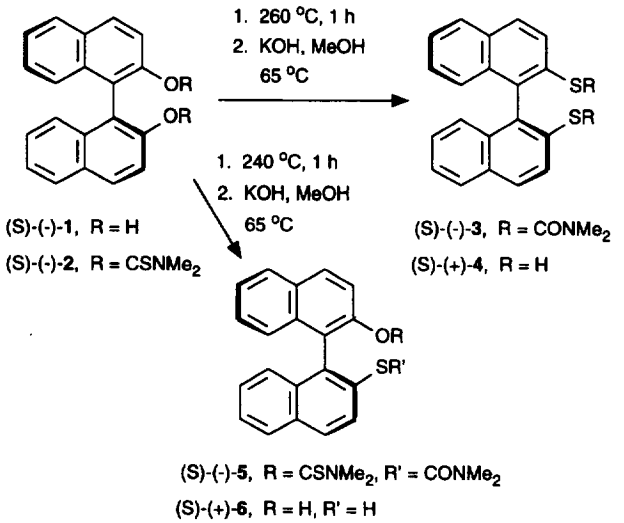


(S)-(-)-**1**, R = H
(S)-(-)-**2**, R = $CSNMe_2$

(S)-(-)-**3**, R = $CONMe_2$
(S)-(+)-**4**, R = H

(S)-(-)-**5**, R = $CSNMe_2$, R' = $CONMe_2$
(S)-(+)-**6**, R = H, R' = H

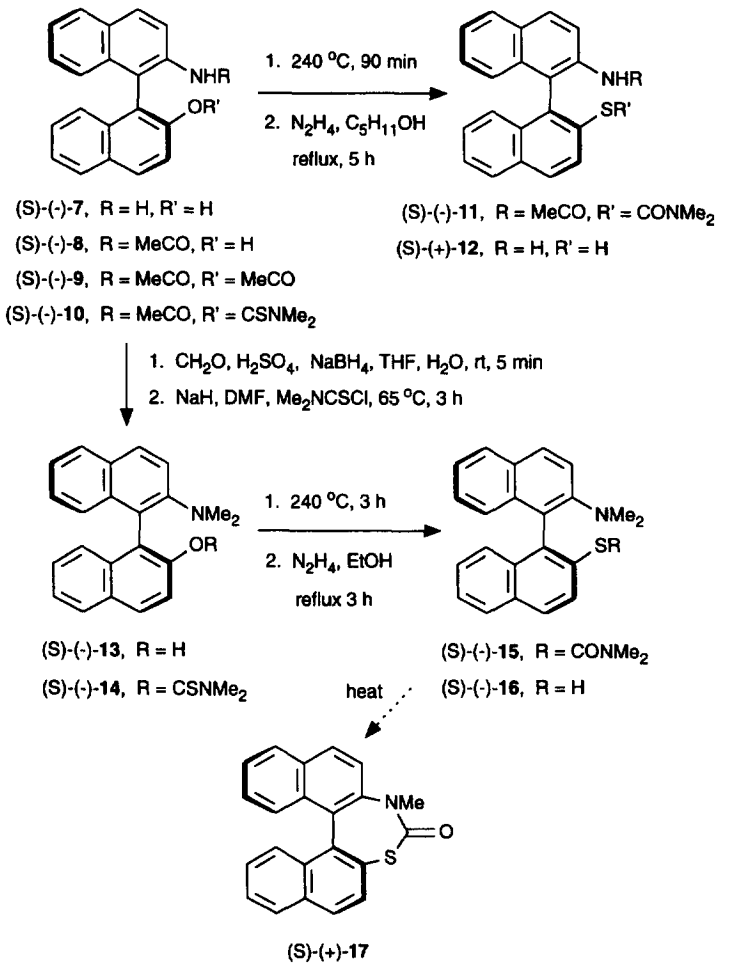
Results and discussion

The bis-thiocarbamate (*S*)-(−)-**2**, obtained from the enantiomerically pure BINOL (*S*)-(−)-**1** by treatment of its sodium salt with Me_2NCSCl in DMF, was subjected to the Newman–Kwart rearrangement. Whereas at ≥260°C the reaction mainly furnished the doubly rearranged product (*S*)-(−)-**3**, under controlled conditions (240°C for 60 min), the mono-rearranged *O,S*-derivative (*S*)-(−)-**5** was obtained as the major product (40%), accompanied by the bis-rearranged *S,S*-isomer (*S*)-(−)-**3** (25%) and unreacted starting material (10%), which were separated by flash chromatography. Although not being an ideal preparation, this experiment demonstrated that the *O,S*-derivative **5** can be prepared without loss of enantiomeric purity,[15] which is consistent with the experimental value of >35 kcal mol^{-1} for the barrier of racemization in 2,2′-disubstituted binaphthyls.[16] Moreover, at the higher temperature, dinaphtho[2,1-*b*;1′,2′-*d*]thiophene[9,10] was detected as the major contaminant; by contrast, its formation was almost entirely suppressed at 240°C.[17] Hydrolysis of pure **5** gave the enantiomerically pure hydroxy thiol (*S*)-(+)-**6**.

The amino thiol **12** could not be prepared in the same way since the attempted conversion of the amino alcohol **7** into the corresponding *N,O*-bis-thiocarbamoyl derivative led to a complex, intractable mixture of products. Therefore, (*S*)-(−)-**7** (>99% ee)[18] was first protected via *N*-acetylation and the resulting amide (*S*)-(−)-**8** (67%) was then converted into the thiocarbamate (*S*)-(−)-**10** (94%). The Newman–Kwart rearrangement of the latter compound, which was carried out at 240°C for 90 min, turned out to be much less successful than that in the *O,O*-series; from the resulting mixture of products the desired *N,S*-derivative (*S*)-(−)-**11** (99% ee) was isolated in only 20% yield.[19] Hydrazinolysis of the latter compound produced the pure amino thiol (*S*)-(+)-**12** (89%), which was also characterized as its hydrobromide (97.4% ee).

The *N,N*-dimethylamino alcohol (*S*)-(−)-**13**, required for the synthesis of *N,N*-dimethylamino thiol **16**, was prepared via a modified[20] Eschweiler–Clarke methylation[21] of the amino alcohol (*S*)-(−)-**7** in 84% yield (>99% ee).[22] The thiocarbamate (*S*)-(−)-**14** (98.2% ee), obtained in 95% yield from the sodium salt of (*S*)-(−)-**13** on reaction with Me_2NCSCl, was then heated at 240°C to afford (*S*)-(−)-**15**. In this case, the Newman–Kwart rearrangement proved much more successful than that in the instance of **11**, giving the desired product **15** in 78% yield, with very little racemization (*vide infra*). Cyclic thiocarbamate (*S*)-(+)-**17** has been identified as a byproduct (8%; 52.8% ee)[23] in this instance; a control experiment, carried out on a small scale, demonstrated that **17** arises from **15** by prolonged heating, presumably via an initial attack by the NMe_2 on the C=O group. Hydrazinolysis of (*S*)-(−)-

15 led to the *N,N*-dimethylamino thiol (*S*)-(−)-**16** (85%; 92.0% ee) which, on crystallization, afforded pure material of 96.2% ee.



Conclusion

We have demonstrated that the Newman–Kwart rearrangement can be employed as a crucial step for the synthesis of nonsymmetrically substituted 1,1′-binaphthyls with the thiol group as one of the substituents. Enantiomeric purity of the starting diol **1** and amino alcohol **7** is preserved in the resulting hydroxy thiol **6** and amino thiols **12** and **16**, respectively, in spite of the seemingly drastic condition of the rearrangement. We currently work on the application of some of the chiral ligands thus obtained in asymmetric catalysis.

Experimental section

Materials and equipment

Optical rotations were measured on Pye Unicam 143A polarimeter with an error of $<\pm 0.5$. ^1H NMR spectra were recorded on Varian XL-400 (FT mode), Varian Gemini 300 (300 MHz), or Bruker ARX-250 (250 MHz) instruments for $CDCl_3$ solutions at 25°C with TMS as internal reference. The IR spectra were measured in chloroform on a Perkin–Elmer 490 instrument. The high resolution mass spectra were measured on a Jeol JMS D-100 double focusing spectrometer (70 eV, 3 kV) using direct inlet and the lowest temperature enabling evaporation; the accuracy was ≤5 ppm. Chromatography on

Chiralpak AD, Chiralcel OD-H, Chiralcel OF, Chiralcel OJ, and Chiralcel OS was used to determine ee (with UV detection at 254 nm). In each case the separability of enantiomers was tested with the corresponding racemate and the optimal conditions were chosen for the analysis of the actual samples. In all cases the (*S*)-enantiomer was the first to be eluted from the column except for **14** and **15**. All the solvents used for the reactions or for crystallization experiments were degassed by purging with argon (20 min; 60 mL Ar/min). Light petroleum refers to the fraction boiling in the range 40–60°C. Yields are given in mg of isolated product showing one spot on a chromatographic plate and no impurities detectable in the NMR spectra.

(S)-(−)-2,2′-Di[(N,N-dimethylthiocarbamoyl)oxy]-1,1′-binaphthyl (S)-(−)-2

Prepared from (*S*)-(−)-**1** (99% ee) in the same way as reported[9,13] in 84% yield: mp 158–160°C (EtOH), literature[13] gives 206–208°C (petroleum ether–CH_2Cl_2);[24,25] $[\alpha]_D$ −154 (*c* 0.1; $CHCl_3$) or −111° (*c* 1.0; THF), literature[13] gives $[\alpha]_D$ +103.5 (*c* 1; THF) for the (*R*)-enantiomer; chromatography on a Chiralpak AD column with a hexane–ethanol mixture (9:1) at rt showed 97.0% ee.

(S)-(−)-2-[(N,N-Dimethylthiocarbamoyl)oxy]-2′-[(N,N-dimethylcarbamoyl)mercapto]-1,1′-binaphthyl (S)-(−)-5

Bis-thiocarbamate (*S*)-(−)-**2** (12.00 g; 26 mmol; 97% ee) was heated under argon in a sealed tube at 240±1°C for 60 min. The tube was then cooled and the content was chromatographed on silica gel (600 g) with a petroleum ether–ethyl acetate mixture (4:1) to give dinaphthothiophene[9] (371 mg; 5%), unreacted **2** (1.20 g; 10%), the *O,S*-product **5** (4.80 g; 40%) and the *S,S′*-product[9] **3** (3.01 g; 25%; 97% ee according to chromatography on a Chiralcel OD-H column). Crystallization of the corresponding fraction from methanol gave the pure (*S*)-(−)-**5**: mp 183–184°C; $[\alpha]_D$ −144 (*c* 0.5; $CHCl_3$); chromatography on a Chiralcel OD-H column with a hexane–ethanol mixture (9:1) at rt showed >99% ee; ^{1}H NMR δ 1.57 (s, 3 H, $OCSNMe_2$) and 1.81 (s, 3 H, $OCSNMe_2$), 2.89 (s, 3 H, $SCONMe_2$), 2.96 (s, 3 H, $SCONMe_2$), 6.89 (d, *J*=8.5 Hz, 1 H, arom), 7.10 (d, *J*=8.8 Hz, 1 H, arom), 7.16–7.30 (m, 1 H, arom), 7.36–7.42 (m, 1 H, arom), 7.49–7.56 (m, 1 H, arom), 7.74 (d, *J*=8.5 Hz, 1 H, arom), 7.88–8.08 (m, 5 H, arom), 8.40 (d, *J*=8.8 Hz, 1 H, arom); ^{13}C NMR δ 23.99 (q), 36.85 (q), 37.18 (q), 122.01 (d), 124.81 (d), 124.84 (s), 125.31 (d), 126.43 (d), 126.66 (d), 127.25 (d), 127.52 (d), 127.95 (2×d), 128.07 (s), 128.64 (d), 129.52 (d), 130.63 (s), 133.13 (s), 133.16 (s), 133.35 (d), 134.07 (s), 134.99 (s), 140.73 (s), 168.59 (s), 169.21 (s); IR ν 1221 and 1535 (Ar–O–CS), 1658 (C=O) cm^{-1}; HRMS *m/z* (%) 460 ($M^{+\bullet}$, $C_{26}H_{24}N_2O_2S_2$, 4), 388 (1), 356 (1), 299 (2), 284 (48), 268 (2), 239 (3), 88 (79), 72 (100). Anal. Calcd for $C_{26}H_{24}N_2O_2S_2$: C, 67.78; H, 5.25; N, 6.08; S, 13.92. Found: C, 67.83; H, 5.18; N, 6.05; S, 13.83.

(S)-(+)-2-Hydroxy-2′-mercapto-1,1′-binaphthyl (S)-(+)-6

To the refluxing solution of the *O,S*-derivative (*S*)-(−)-**5** (920 mg; 2 mmol; >99% ee) in anhydrous methanol (80 mL), purged with argon, was slowly added a 10% solution of KOH in methanol (1 mL), and the mixture was refluxed under argon for 5 h. The mixture was then cooled to rt and poured to a degassed, 5% aqueous HCl. The resulting precipitate was filtered off and dried in vacuo to afford amorphous (*S*)-(+)-**6** (380 mg; 63%):[26] $[\alpha]_D$ +5.7 (*c* 0.9; EtOH);[27,28] IR ν 2568 (ArSH), 3536 (ArOH) cm^{-1}; ^{1}H NMR (400 MHz) δ 3.40 (br s, 1 H, SH), 4.91 (br s, 1 H, OH), 7.02–8.00 (m, 12 H, arom); ^{13}C NMR δ 116.55 (s), 117.75 (d), 123.31 (d), 124.20 (d), 125.01 (d), 125.63 (d), 126.62 (s), 126.94 (d), 127.16 (d), 127.63 (d), 128.28 (d), 128.29 (d), 129.32 (s), 129.65 (d), 130.76 (d), 131.84 (s), 132.69 (s), 133.65 (s), 133.66 (s), 151.04 (s); HRMS *m/z* (%) 302 ($M^{+\bullet}$, $C_{20}H_{14}OS$, 100), 282 (7), 273 (14), 269 ($C_{20}H_{13}O$, 52), 268 (22), 251 (12), 241 (12), 239 (23), 141 (13), 134.5 (14), 134 (17), 128 (17), 125.5 (16), 125 (15), 119.5 (19).

(S)-(−)-2-(Acetamido)-2′-hydroxy-1,1′-binaphthyl (S)-(−)-8

To the solution of (*S*)-(−)-**7** (2.85 g; 10 mmol; >99% ee) in dry pyridine (40 mL) was slowly added acetyl chloride (0.8 mL; 10.5 mmol) at 0°C and the mixture was then kept at rt for 8 h. The mixture was

poured onto ice and water and extracted with chloroform. The extract was successively washed with water, 5% aqueous HCl, water, sat. aqueous $NaHCO_3$, and water and dried with Na_2SO_4. The solvent was evaporated and the residue was chromatographed on silica gel (250 g) with a toluene–acetone mixture (8:1) to give the diacetate **9** (610 mg; 16%) followed by (*S*)-(−)-**8** (2.20 g; 67%): mp 208–208.5°C (EtOH); $[\alpha]_D$ −79 (*c* 0.5; $CHCl_3$); chromatography on a Chiralpak AD column with a hexane–ethanol mixture (1:1) at 40°C showed >99.0% ee; ^{1}H NMR δ 1.75 (s, 3 H, CH_3CO), 5.66 (bs, 1 H, OH), 6.95 (bs, 1 H, NH), 6.99 (d, *J*=8.5 Hz, 1 H, arom), 7.14–7.45 (m, 6 H, arom), 7.85–8.00 (m, 4 H, arom), 8.46 (d, *J*=8.8 Hz, 1 H, arom); ^{13}C NMR δ 24.33 (q), 112.99 (s), 118.04 (d), 118.74 (s), 121.27 (d), 123.87 (d), 124.10 (d), 125.30 (d), 125.43 (d), 127.10 (d), 127.32 (d), 128.17 (d), 128.32 (d), 129.32 (d), 129.16 (s), 129.91 (d), 130.99 (d), 131.28 (s), 132.72 (s), 133.07 (s), 135.48 (s), 152.03 (s), 169.02 (s); IR ν 1690 (C=O), 3407 (NH), 3530 (OH) cm^{-1}; HRMS *m/z* (%) 327 ($M^{+\bullet}$, $C_{22}H_{17}NO_2$, 48), 285 ($C_{20}H_{15}NO$, 100), 284 (11), 268 (32), 267 (21), 256 (12), 254 (10), 239 (15), 43 (14). Anal. Calcd for $C_{22}H_{17}NO_2$: C, 80.73; H, 5.23; N, 4.28. Found: C, 80.72; H, 5.15; N, 4.26.

*(S)-(−)-2-(Acetamido)-2′-acetoxy-1,1′-binaphthyl (S)-(−)-**9***

Obtained along with **8** as a less polar byproduct and isolated via chromatography (610 mg; 16%): mp 162–163°C (MeOH); $[\alpha]_D$ −88 (*c* 1; $CHCl_3$); ^{1}H NMR (80 MHz) δ 1.78 (s, 3 H), 1.83 (s, 3 H), 7.00–8.45 (m, 12 H, arom); IR ν 1686 and 1750 (C=O), 3398 (NH) cm^{-1}; HRMS *m/z* (%) 369 ($M^{+\bullet}$, $C_{24}H_{19}NO_3$, 27), 327 (47), 286 (21), 285 (100), 268 (21), 267 (18), 256 (9), 239 (10), 43 (15). Anal. Calcd for $C_{24}H_{19}NO_3$: C, 78.03; H, 5.18; N, 3.79. Found: C, 77.63; H, 5.12; N, 3.82.

*(S)-(−)-2-(Acetamido)-2′-[(N,N-dimethylthiocarbamoyl)oxy]-1,1′-binaphthyl (S)-(−)-**10***

To the solution of (*S*)-(−)-**8** (1.10 g; 3.40 mmol; >99% ee) in dry DMF (50 mL) was added sodium hydride (170 mg; 3.9 mmol; obtained from a 55%-oil suspension by washing with petroleum ether). When the evolution of hydrogen ceased, a solution of *N,N*-dimethylthiocarbamoyl chloride (450 mg; 3.6 mmol) in DMF (20 mL) was added. The mixture was then heated at 40°C for 2 h. The mixture was then cooled and poured into a 2% aqueous KOH (400 mL) and the resulting precipitate was filtered off and dried on air. The crude product was dissolved in chloroform and purified by filtration through a short column of silica gel (20 g) to furnish (*S*)-(−)-**10** (1.31 g; 94%), chromatography of which on a Chiralpak AD column with a hexane–ethanol mixture (1:1) at 40°C showed 94.8% ee: mp 66–68°C (*n*-heptane); $[\alpha]_D$ −20 (*c* 0.5; $CHCl_3$); chromatography of this sample on a Chiralpak AD column showed ≥99% ee; ^{1}H NMR δ 1.76 (s, 3 H, CH_3CO), 2.53 and 3.18 (2×s, 6 H, Me_2N), 7.87 (bs, 1 H, NH), 7.26, 7.32, 7.34, and 7.49 (4×ddd, *J*=8.3, 6.8, and 1.4 Hz, 4 H, 6-H, 6′-H, 7-H, 7′-H), 7.43, 7.96, 8.06, and 8.28 (4×d, *J*=8.7 Hz, 4 H, 3-H, 3′-H, 4-H, 4′-H), 7.17, 7.23, 7.88, 7.96 (4×brd, $J \cong$ 8.3 Hz, 4 H, 5-H, 5′-H, 8-H, 8′-H); ^{13}C NMR δ 24.17 (q), 37.92 (q), 42.98 (q), 121.41 (s), 122.69 (d), 122.87 (d), 125.00 (d), 125.43 (d), 125.55 (d), 124.97 (s), 126.25 (d), 126.34 (d), 127.40 (d), 127.92 (d), 128.14 (d), 128.90 (d), 129.86 (d), 130.90 (s), 131.97 (s), 132.91 (s), 132.97 (s), 135.08 (s), 150.40 (s), 165.99 (s), 168.77 (s); IR ν 1222 and 1502 ($OCSNMe_2$), 1681 (C=O), 3305 (NH) cm^{-1}; HRMS *m/z* (%) 414 ($M^{+\bullet}$, $C_{25}H_{22}N_2O_2S$, 23), 325 (9), 284 (36), 268 (6), 267 (7), 88 (100), 72 (32), 43 (7). Anal. Calcd for $C_{25}H_{22}N_2O_2S$: C, 72.44; H, 5.35; N, 6.76; S, 7.74. Found: C, 72.11; H, 5.01; N, 6.59; S, 7.48.

*(S)-(−)-2-(Acetamido)-2′-[(N,N-dimethylcarbamoyl)mercapto]-1,1′-binaphthyl (S)-(−)-**11***

The thiocarbamate (*S*)-(−)-**10** (1.31 g; 3.20 mmol; ≥99% ee) was heated under argon in a sealed tube at 240±1°C for 90 min. The tube was then cooled and the content was chromatographed on silica gel (60 g) with a toluene–acetone mixture (8:1) to give amorphous (*S*)-(−)-**11** (250 mg; 20%): $[\alpha]_D$ −190 (*c* 0.5; $CHCl_3$); chromatography on a Chiralcel OD-H column with a hexane–ethanol mixture (95:5) at 25°C showed ≥99% ee; ^{1}H NMR δ 1.81 (s, 3 H, CH_3CO), 2.89 (s, 3 H, Me_2N), 2.96 (s, 3 H, Me_2N), 6.89 (d, *J*=8.2 Hz, 1 H, arom), 7.10 (d, *J*=8.2 Hz, 1 H, arom), 7.15–7.29 (m, 1 H, arom), 7.36–7.42 (m, 1 H, arom), 7.49–7.55 (m, 1 H, arom), 7.74 (d, *J*=8.5 Hz, 1 H, arom), 7.88–8.08 (m, 5 H, arom), 8.40 (d, *J*=9.1 Hz, 1 H, arom); ^{13}C NMR δ 23.98 (q), 36.85 (q), 37.18 (q), 122.01

(d), 124.82 (d), 124.86 (s), 125.31 (d), 126.43 (d), 126.66 (d), 127.25 (d), 127.51 (d), 127.96 (2×d), 128.07 (s), 128.64 (d), 129.51 (d), 130.63 (s), 133.10 (s), 133.16 (s), 133.34 (d), 134.07 (s), 134.97 (s), 140.73 (s), 168.60 (s), 169.24 (s); IR ν 1590 and 1605 (arom), 1655 (SNC=O), 1692 (NC=O), 3319 (NH) cm^{-1}; HRMS *m/z* (%) 414 ($M^{+\bullet}$, $C_{25}H_{22}N_2O_2S$, 14), 325 (7), 300 (4), 284 (27), 283 (4), 267 (5), 72 (100), 43 (9). Anal. Calcd for $C_{25}H_{22}N_2O_2S$: C,72.44; H, 5.35; N, 6.76; S, 7.74. Found: C, 72.64; H, 5.33; N, 6.62; S, 7.43.

*(S)-(+)-2-Amino-2′-mercapto-1,1′-binaphthyl (S)-(+)-**12***

To a solution of (*S*)-(−)-**11** (200 mg; 0.48 mmol; ≥99% ee) in degassed 1-pentanol (6 mL) was added, strictly under an argon atmosphere, 80% hydrazine hydrate (4 mL) and the mixture was refluxed under argon for 5 h. The mixture was then cooled and evaporated to dryness. The residue was chromatographed on silica gel (20 g) with toluene as eluent to afford (*S*)-(+)-**12** (130 mg; 89%): mp 127–131°C (dec; EtOH); $[\alpha]_D$ +19 (*c* 0.1 $CHCl_3$); IR ν 1618 (C=C arom), 2558 (SH), 3367 and 3471 (NH_2) cm^{-1}; ^1H NMR (250 MHz) δ 3.42 (s, 1 H, SH), 3.59 (bs, 2 H, NH_2), 6.91 (d, 1 H, *J*=7.9 Hz, arom), 7.08–7.28 (m, 5 H, arom), 7.35–7.41 (m, 1 H, arom), 7.55 (d, 1 H, *J*=8.8 Hz, arom), 7.76–7.87 (m, 4 H, arom); ^{13}C NMR δ 114.72 (s), 118.23 (d), 122.58 (d), 123.59 (d), 125.20 (d), 125.31 (d), 126.88 (d), 127.02 (d), 127.23 (d), 128.16 (d), 128.20 (d), 128.26 (s), 128.70 (d), 129.85 (s), 129.91 (d), 131.95 (s), 132.29 (d), 133.15 (s), 133.22 (s), 141.95 (s); HRMS *m/z* (%) 301 ($M^{+\bullet}$; $C_{20}H_{15}NS$, 80), 284 (89), 283 (100), 282 (41), 268 (48), 267 (40), 266 (15), 265 (13), 252 (8), 239 (11), 148.5 (12), 141 (19), 134 (22), 133.5 (36), 132.5 (16). Anal. Calcd for $C_{20}H_{15}NS$: C, 79.70; H, 5.02; N, 4.65; S, 10.64. Found: C, 79.84; H, 4.96; N, 4.62; S, 10.34. Chromatography of its hydrobromide (prepared by precipitation with gaseous HBr in chloroform) on a Chiralpak AD column with a hexane–ethanol mixture (1:1) showed 97.4% ee.

*(S)-(+)-2-(N,N-Dimethylamino)-2′-hydroxy-1,1′-binaphthyl (S)-(−)-**13***

To a stirred solution of 20% aqueous H_2SO_4 (1 mL) and 40% aqueous formaldehyde (1 mL; 12 mmol) in THF (3 mL) were simultaneously added, over a period of 5 min, a solution of (*S*)-(−)-**7** (285 mg; 1.0 mmol; >99% ee) in THF (20 mL) and solid $NaBH_4$ (279 mg; 7 mmol) and the mixture was stirred at rt for 5 min and then poured into 2% aqueous KOH (200 mL). The product was extracted with ethyl acetate (3×20 mL), the combined extracts were dried with $MgSO_4$ and the solvent was evaporated. The residue was chromatographed on silica gel (50 g) using toluene as eluent, to give pure (*S*)-(−)-**13** (263 mg; 84%): mp 194–195.5°C (toluene); $[\alpha]_D^{30}$ −32.6 (*c* 1; THF);[29] chromatography on a Chiralpak AD column with a hexane–ethanol mixture (60:40) at rt showed >99% ee; ^1H NMR (300 MHz) δ 2.66 (s, 6 H, Me_2N), 7.05–7.54 (m, 8 H, arom), 7.84–7.99 (m, 4 H, arom); ^{13}C NMR δ 43.53 (q), 118.27 (d), 118.39 (s), 119.39 (d), 122.09 (s), 123.15 (d), 124.13 (d), 125.68 (d), 125.85 (d), 126.25 (d), 126.44 (d), 127.87 (d), 128.09 (d), 129.19 (s), 129.62 (d), 129.84 (d), 130.00 (s), 133.88 (s), 134.06 (s), 149.38 (s), 151.55 (s); IR ν 1595 and 1619 (C=C arom), 3523 (OH) cm^{-1}; HRMS *m/z* (%) 313 ($M^{+\bullet}$, $C_{22}H_{19}NO$, 98), 312 (10), 282 (16), 281 (31), 269 (29), 268 ($C_{20}H_{12}O$, 100), 267 (15), 239 (21), 100 (12), 157 (11), 127 (12), 119.5 (12). Anal. Calcd for $C_{22}H_{19}NO$: C, 84.31; H, 6.11; N, 4.47. Found: C, 84.27; H, 6.04; N, 4.41.

*(S)-(−)-2-(N,N-Dimethylamino)-2′-[(N,N-dimethylthiocarbamoyl)oxy]-1,1′-binaphthyl (S)-(−)-**14***

To a solution of (*S*)-(−)-**13** (313 mg; 1 mmol; >99% ee) in dry DMF (5 mL) was added a 55% suspension of NaH in mineral oil (50 mg; 1.15 mmol) under argon and the mixture was stirred at rt until the evolution of hydrogen ceased (5 min). A solution of *N,N*-dimethylthiocarbamoyl chloride (136 mg; 1.1 mmol) in DMF (5 mL) was then added and the mixture was stirred at 65°C for 3 h under argon. The cooled mixture was then poured into 2% aqueous KOH (100 mL) and the product was extracted with ethyl acetate (3×20 mL). The combined extracts were dried with $MgSO_4$ and the solvent was evaporated. The residue was chromatographed on silica gel (50 g) using toluene as eluent, to give (*S*)-(−)-**14** (380 mg; 95%): mp 120–122°C (CH_2Cl_2–heptane); $[\alpha]_D^{30}$ −8.8 (*c* 1; THF); chromatography on a Chiralcel OF column with a hexane–ethanol mixture (9:1) at 40°C showed 98.2% ee; ^1H NMR

(300 MHz) δ 2.53 (s, 6 H, *Me*$_2$N–Ar), 2.57 and 3.18 (two s, 2×3 H, Me$_2$N–CSO), 7.13–7.49 (m, 7 H, arom), 7.71–7.99 (m, 5 H, arom); ^{13}C NMR δ 37.79 (q), 42.66 (q), 43.38 (2×q), 118.96 (d), 120.95 (s), 123.29 (d), 124.14 (d), 125.33 (d), 125.86 (d), 125.92 (d), 126.18 (d), 126.56 (d), 127.38 (d), 127.42 (d), 127.66 (s), 128.08 (d), 128.96 (s), 129.03 (d), 131.63 (s), 133.78 (s), 133.87 (s), 148.88 (s), 149.95 (s), 186.20 (s); IR ν 1220 and 1530 (OCSNMe$_2$), 1595 and 1619 (C=C arom); HRMS *m/z* (%) 400 ($M^{+\bullet}$, $C_{25}H_{24}N_2OS$, 21), 328 (3), 312 (5), 296 (52), 295 (13), 294 (14), 281 (22), 268 (13), 239 (7), 88 (100), 72 (12). Anal. Calcd for $C_{25}H_{24}N_2OS$: C, 74.97; H, 6.04; N, 6.99; S, 8.01. Found: C, 74.76; H, 5.81; N, 6.96; S, 7.85.

*(S)-(−)-2-(N,N-Dimethylamino)-2′-[(N,N-dimethylcarbamoyl)mercapto]-1,1′-binaphthyl (S)-(−)-**15***

The thiocarbamate (*S*)-(−)-**14** (400 mg; 1 mmol; 98.2% ee) was heated under argon in a sealed tube at 240±1°C for 3 h. The tube was then cooled and the solid content was dissolved in toluene and chromatographed on silica gel (50 g) with a toluene–ethyl acetate mixture (9:1) to give an inseparable mixture of the starting material **14** and the cyclic thiocarbamate **17** (82 mg) as the lipophilic fraction. The polar fraction contained the pure, oily (*S*)-(−)-**15** (312 mg; 78%): $[\alpha]_D$ −25 (*c* 0.4; $CHCl_3$); ^{1}H NMR (300 MHz) δ 2.48 (s, 6 H, Me$_2$N–Ar), 2.84 (bs, 6 H, Me$_2$N–COS), 6.97–7.48 (m, 7 H, arom), 7.80–7.96 (m, 5 H, arom); IR ν 1596 and 1919 (C=C arom), 1659 (C=O) cm^{-1}; HRMS *m/z* (%) 400 ($M^{+\bullet}$, $C_{25}H_{24}N_2OS$, 32), 328 (8), 296 ($C_{22}H_{18}N$, 100), 295 (41), 294 (58), 284 (14), 283 (15), 282 (30), 281 ($C_{21}H_{15}N$, 61), 280 (12), 278 (10), 252 (8), 72 (96).

*(S)-(−)-2-(N,N-Dimethylamino)-2′-mercapto-1,1′-binaphthyl (S)-(−)-**16***

A solution of (*S*)-(−)-**15** (400 mg; 1 mmol) and 100% hydrazine hydrate (14 mL) in ethanol (50 mL) was refluxed for 3 h. The mixture was then evaporated, the residue was suspended in water, and the product was extracted with ethyl acetate (3×20 mL). The combined extracts were dried with Na_2SO_4 and the solvent was evaporated. The residue was chromatographed on silica gel (50 g) using toluene as eluent to afford pure product (279 mg; 85%): mp 124–126°C (toluene–petroleum ether 1:1); $[\alpha]_D$ −27 (*c* 0.4; THF); chromatography on a Chiralcel OS column with a hexane–ethanol mixture (80:20) at 40°C showed 96.2% ee; before recrystallization the purity was 92.0% ee; ^{1}H NMR (300 MHz) δ 2.59 (s, 6 H, Me$_2$N), 3.40 (bs, 1 H, SH), 6.98 (ddd, 1 H, ^3J=8.5, ^4J=1.2, and ^4J=0.6 Hz, 5-H), 7.15 (ddd, 1 H, ^3J=8.2, ^4J=1.3, and ^4J=0.7 Hz, 5′-H), 7.20 (ddd, 1 H, ^3J=8.5, ^3J=6.8, and ^4J=1.2 Hz, 6-H), 7.24 (ddd, 1 H, ^3J=8.2, ^3J=6.8, ^4J=1.3 Hz, 6′-H), 7.31 (ddd, 1 H, ^3J=8.1 Hz, ^3J=6.8, and ^4J=1.4 Hz, 7-H), 7.39 (ddd, 1 H, ^3J=8.1 Hz, ^3J=6.8, and ^4J=1.3 Hz, 7′-H), 7.50 (d, 1 H, ^3J=9.0 Hz, 3-H), 7.55 (d, 1 H, ^3J=8.6 Hz, 3′-H), 7.81 (dd, ^3J=8.6 and ^4J=0.7 Hz, 4′-H), 7.83–7.87 (m, 2 H, 8-H and 8′-H), 7.95 (dd, 1 H, ^3J=9.0 and ^4J=0.6 Hz, 4-H); ^{13}C NMR δ 43.35 (2×q), 119.74 (d), 123.76 (d), 124.24 (s), 124.71 (d), 124.89 (d), 126.10 (d), 126.60 (d), 126.63 (d), 127.22 (d), 127.93 (2×d), 128.05 (d), 129.63 (d), 129.68 (s), 131.34 (s), 131.68 (s), 133.07 (s), 133.58 (s), 133.85 (s), 149.87 (s); IR ν 1595 and 1618 (C=C arom), 2567 (SH) cm^{-1}; HRMS *m/z* (%) 329 ($M^{+\bullet}$, $C_{22}H_{19}NS$, 9), 294 ($C_{22}H_{16}N$, 19), 284 ($C_{20}H_{12}S$, 100), 283 (77), 282 (30), 281 (18), 280 (7), 278 (6), 265 (6), 252 (8), 147.5 (7), 141 (9), 140.5 (7), 140 (8), 139.5 (7), 139 (7), 126 (6), 125 (6). Anal. Calcd for $C_{22}H_{19}NS$: C, 80.20; H, 5.81; N, 4.25; S, 9.73. Found: C, 80.47; H, 5.43; N, 4.25; S, 9.62.

*Cyclic thiocarbamate (S)-(+)-**17***

Formed along with **15** (see above); the lipophilic fraction (82 mg) contained a mixture of **14** and **17**, which were separated via a semi-preparative HPLC on a Magnum 9 column (Whatman), using a petroleum ether–ether mixture (4:1) and RI detection. First eluted was the unreacted **14** (52 mg; 13%), whereas the slower moving component was identified as the cyclic thiocarbamate (*S*)-(−)-**17** (30 mg; 8% - based on the preparation of **15**): amorphous solid, $[\alpha]_D$ +114 (*c* 0.4, $CHCl_3$); chromatography on a Chiralpak AD column with a hexane–ethanol mixture (90:10) at 40°C showed 52.8% ee; ^{1}H NMR (400 MHz) δ 3.37 (s, 3 H, MeN), 7.16–8.03 (m, 12 H, arom); ^{13}C NMR 37.54 (q), 121.34 (d), 126.20 (d), 126.49 (d), 126.70 (d), 126.83 (d), 127.72 (d), 128.02 (d), 128.10 (d), 128.31 (d), 129.13 (d), 129.99 (d), 130.33 (2×d), 130.51 (s), 131.34 (s), 131.57 (s), 132.53 (s), 133.11 (s), 133.48 (s),

134.86 (s), 142.23 (s), 170.63 (s); IR ν 1596 and 1620 (C=C arom), 1655 (C=O) cm^{-1}; HRMS *m/z* (%) 341 ($M^{+\bullet}$, $C_{22}H_{15}NOS$, 32), 296 ($C_{20}H_{10}NS$, 21), 284 (100), 283 (92), 282 (56), 281 (50), 265 (13), 264 (10), 239 (9), 148.5 (13), 148 (13), 142 (17), 141.5 (17), 141 (35).

Acknowledgements

We thank the Grant Agency of the Czech Republic for grant No. 203/96/0694, the Grant agency of Charles University for Grant No. 86/95 GAUK, and the University of Leicester and Pfizer Central Research for financial support.

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15. Chromatography of **5** on a Chiralcel OD-H column indicated >97.4% ee for the crude product which, upon crystallization, gave pure material (>99% ee).
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17. Smith has reported dependence of the formation of the thiophene derivative on the solid-state modification of the starting, racemic thiocarbamate **2**, for which he could identify different conformations by X-ray diffraction.[10] However, there is no direct correlation of his results with those obtained by us for our experiments were carried out with the pure enantiomer.
18. Prepared from (±)-**7** by resolution with (1*S*)-(+)-10-camphorsulfonic acid. This method represents an alternative to our asymmetric coupling described earlier.[3b,c] For details of the resolution procedure, see: Smrčina, M.; Vyskočil, Š.; Polívková, J.; Poláková, J.; Kočovský, P. *Collect. Czech. Chem. Commun.* **1996**, *61*, 1520.
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22. Other methods gave unsatisfactory results. Thus, for instance, the *N*-monomethyl amino alcohol, prepared by reduction of the corresponding carbamate with $LiAlH_4$, resisted all attempts at further *N*-carbamoylation. The classical Eschweiler–Clarke reaction[21] with $(CH_2O)_n$ and HCO_2H at 150°C in autoclave was capricious (giving 30–65% yield and, in some batches, up to 40% of an unidentified byproduct), and led to a substantial racemization.
23. The relatively high degree of racemization observed in this case can be tentatively attributed to the change of the geometry of the binaphthyl system due to cyclization.
24. Crystallization of our sample of the enantiomerically pure (*S*)-(−)-**2** from a petroleum ether–CH_2Cl_2 mixture furnished the product of the same mp as that obtained from EtOH, i.e., 158–160°C. On the other hand, the corresponding racemate, prepared by us, had the mp identical to that reported by De Lucchi[9] for the pure enantiomer, i.e. 206–208°C (this value agrees with that previously reported by De Lucchi for the racemate[25]). A similar discrepancy can be demonstrated for (*S*)-(−)-**3**: we have found mp 108–110°C (MeOH or CH_2Cl_2–petroleum ether) as opposed to 247–249°C reported by De Lucchi;[9] $[\alpha]_D$ −81 (*c* 1; $CHCl_3$) and −43.5 (*c* 1; THF); De Lucchi reported $[\alpha]_D$ +40.6 (*c* 1; THF) for the (*R*)-enantiomer. These findings lead us to the belief that the mp reported by De Lucchi[9] for **2** and **3** correspond, in fact, to racemates rather than to pure enantiomers.
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26. The hydroxy thiol **6** (and the aminothiol **12** as well, but not **16**) tends to oxidatively dimerize to the corresponding disulfide on standing. From these samples, **6** (and **12**) can be regenerated via reduction (e.g., with $LiAlH_4$ in THF).
27. De Lucchi has reported $[\alpha]_D$ −27.9 (*c* 1.0, EtOH) for the compound that can now be assigned the opposite configuration (see comments in Note 28): Fabbri, D.; Delogu, G.; De Lucchi, O. *J. Org. Chem.* **1995**, *60*, 6599.
28. Determining the ee of this product proved difficult with the chiral columns available. De Lucchi reported[27] resolution of the racemic (±)-**6** via its derivatization with (1*R*)-(−)-menthyl

chloroformate. The two diastereoisomeric *O,S*-carbonates thus obtained exhibit distinctly different pattern in the methyl region of the ^{1}H NMR spectra. Significant for determining the ee are the highest field methyl doublets, which were reported to appear at 0.30 (d, J=8.1 Hz) and 0.61 (d, J= 6.9 Hz) ppm, respectively, for individual diastereoisomers.[27] With our sample, the latter signal could be easily identified [at 0.59 (d, J=6.9 Hz) ppm], whereas the former doublet was essentially missing. Other methyl doublets of our sample corresponded to those reported by De Lucchi for one of the diastereoisomers (within ~0.02 ppm), while those for the other could not be detected. These results indicate ≥98% ee for our sample. Moreover, the absolute configuration of **6** and the relative configuration of the De Lucchi's menthol-derived carbonates is thus unequivocally established.

29. Mutarotation has been observed with this sample of (*S*)-**13** in $CHCl_3$: starting at $[\alpha]_D$ +305 (*c* 2; $CHCl_3$), the solution reached an equilibrium in 2 days, and displayed $[\alpha]_D$ +50. By contrast, little changes were detected in THF over 24 h.

(Received in UK 2 December 1996)