Pergamon

Tetrahedron: *Asymmetry* 12 (2001) 1999–2004

TETRAHEDRON:
ASYMMETRY

Resolution of 8′-alkoxy- and hydroxy-1,1′-binaphthalen-8-ols

Duy H. Hua,[a,]* Trieu X. C. Nguyen,[a] James W. McGill,[a] Yi Chen[a] and Paul D. Robinson[b]

[a]*Department of Chemistry, Kansas State University, Manhattan, KS 66506, USA*
[b]*Department of Geology, Southern Illinois University at Carbondale, Carbondale, IL 62901, USA*

Received 18 June 2001; accepted 7 August 2001

Abstract—Enantiopure 8′-ethoxy-, 8′-hydroxy-, and 8′-methoxy-1,1′-binaphthalen-8-ol were readily resolved by separating the corresponding chiral camphanic esters [derived from the esterification of the alcohols with (−)-(1*S*)-camphanic chloride] based upon their differing solubility in diethyl ether and their differing chromatographic behavior. © 2001 Elsevier Science Ltd. All rights reserved.

1. Introduction

Chiral 8,8′-disubstituted 1,1′-binaphthyls have recently attracted great attention regarding their synthesis,[1] resolution,[2] and utilization[3] in asymmetric catalysis. In our studies of asymmetric catalysis involving transition metals, a series of enantiopure 8,8′-dialkoxy-1,1′-binaphthalenes, 8′-alkoxy-1,1′-binaphthalen-8-ols, and 1,1′-binaphthalen-8,8′-diol were required. Herein, we report an easy resolution of the naphtholic molecules via the camphanic ester derivatives.

2. Results and discussion

We first attempted to resolve 1,1′-binaphthalene-8,8′-diol **1** via the reported bis-l-menthyl carbonate method[2b] through recrystallization, but no crystals were obtained after several trials.[4] Resolution via a diastereomeric mixture of camphanic esters was then investigated. Hence, treatment of racemic diol **1** with (−)-(1*S*)-camphanic chloride **2**, triethylamine, and a catalytic amount of 4-(*N*,*N*-dimethylamino)pyridine (DMAP) in methylene chloride gave a 1:1 mixture of diastereomers **3R** and **4S** (Scheme 1). Fortunately, the more polar diastereomer, **3R** ($R_f = 0.23$ in hexane:CH_2Cl_2:toluene:ether = 3:2:2:1) is much less soluble in diethyl ether than **4S** ($R_f = 0.31$), so that the addition of diethyl ether to a mixture of **3R** and **4S** resulted in a solution which was highly enriched in **4S**. The remaining insoluble material was identified as pure (−)-**3R** {40% yield; $[\alpha]_D^{22} = -207$ (*c* 0.5; $CHCl_3$)}. The ether solution was concentrated and subjected to silica gel column chromatography to give a 47% yield of pure (+)-**4S** {$[\alpha]_D^{22} = +75$ (*c* 0.53; $CHCl_3$)} along with a 7% yield of (−)-**3R** (a total of 47% yield of **3R** was obtained). ^{1}H NMR spectra of **3R** and **4S** indicate pure diastereomers (the chemical shifts of **3R** and **4S** are different). The stereochemistry along the C1,1′ axis was easily determined by basic hydrolysis of **3R** and **4S** separately with KOH in methanol and 1,4-dioxane at 25°C to give diols (−)-(*R*)-**1R** {$[\alpha]_D^{22} = -21$ (*c* 0.69; $CHCl_3$)}[5] and (+)-(*S*)-**1S** {$[\alpha]_D^{22} = +20$ (*c* 0.69; $CHCl_3$)}, which are reported in the literature.[2b,2c,3i]

Similarly, enantiopure 8′-methoxy-8-hydroxy-1,1′-binaphthyl **5R** or **5S** and 8′-ethoxy-8-hydroxy-1,1′-binaphthyl **6R** or **6S** were obtained from (±)-**5** and (±)-**6**, respectively (Scheme 2). Esterification of racemic methyl ether (±)-**5** or ethyl ether (±)-**6** with 1 equiv. of (−)-(1*S*)-camphanic chloride **2**, triethylamine and DMAP in methylene chloride gave, respectively, a 1:1 mixture of **7R** and **8S** or **9R** and **10S**. When the mixture was treated with ether **7R** dissolved completely (less polar in TLC; hexane:CH_2Cl_2:ether = 1:1:0.5; $R_f = 0.16$), along with a trace amount of **8S** (more polar in TLC; hexane:CH_2Cl_2:ether = 1:1:0.5; $R_f = 0.10$).

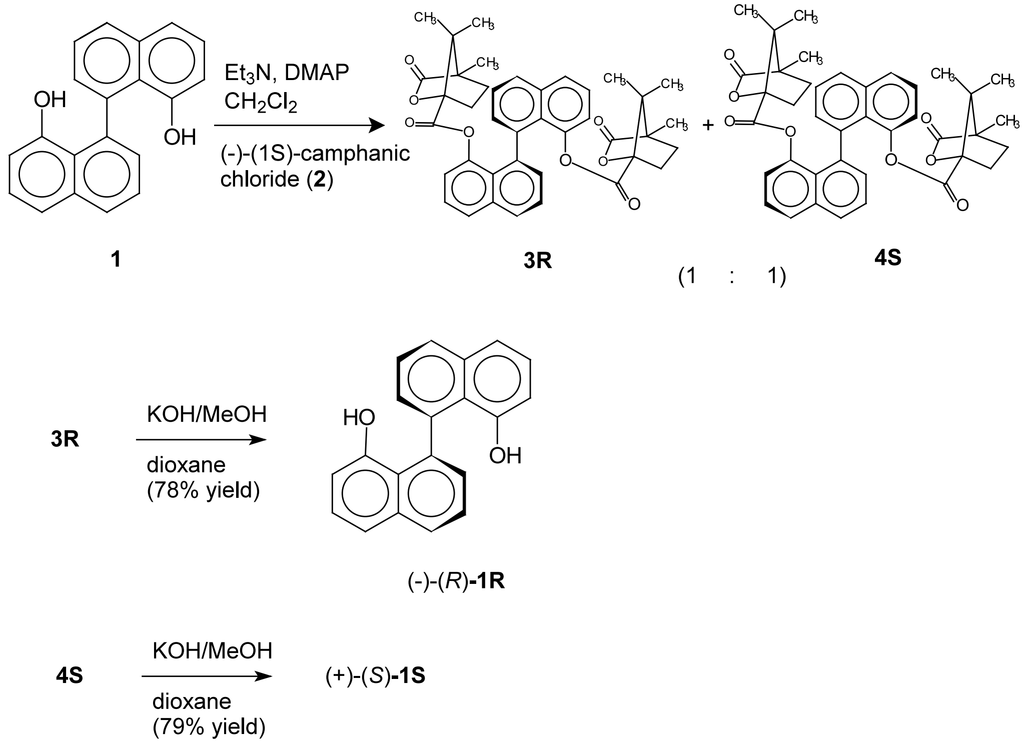
The ether soluble material was purified by column chromatography to give a 43% yield of pure (−)-**7R** and 4% yield of **8S**. The ether insoluble material was found to be pure (+)-**8S** based on ^{1}H NMR analysis (40% yield; total yield 44%).

The ethyl derivatives (−)-**9R** and (+)-**10S** were similarly separated. Again, the **10S** diastereomer has a smaller R_f

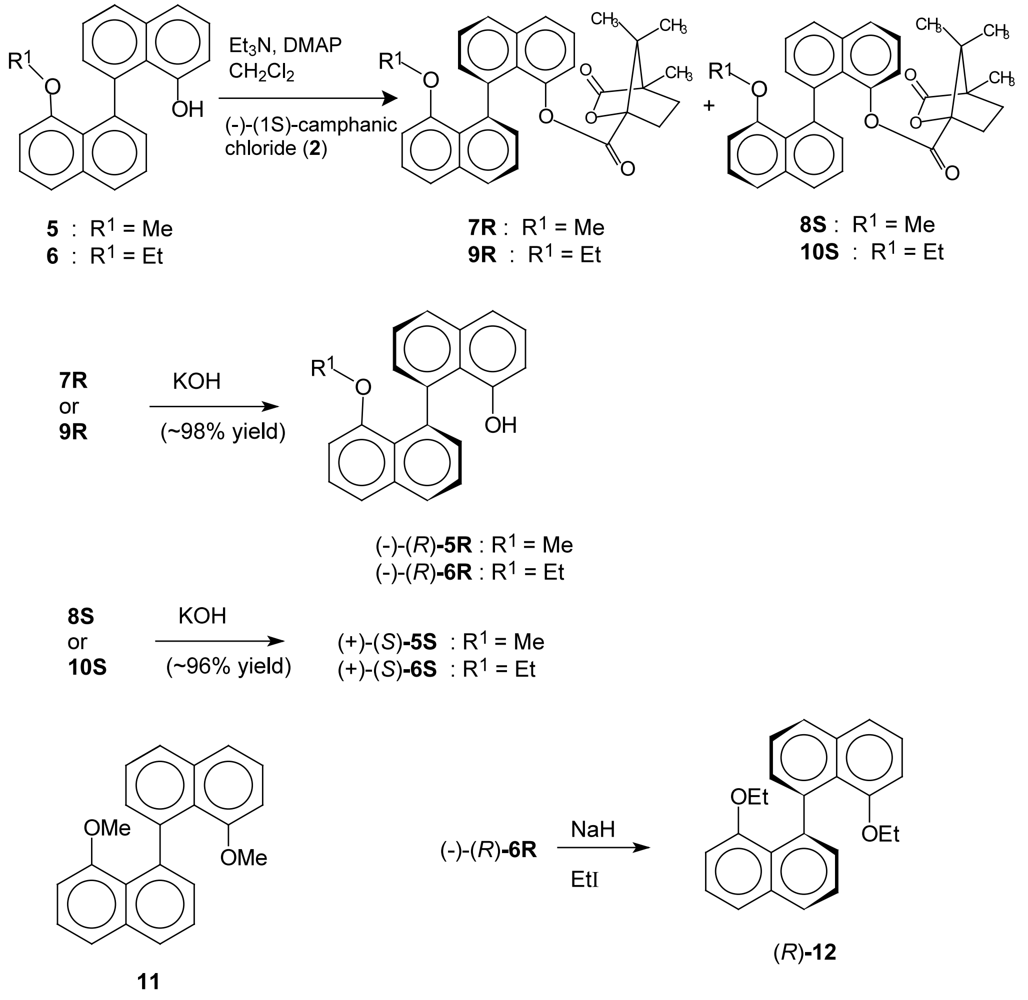
---

* Corresponding author. E-mail: duy@ksu.edu

0957-4166/01/$ - see front matter © 2001 Elsevier Science Ltd. All rights reserved.
PII: S0957-4166(01)00361-5



Scheme 1.



Scheme 2.

value, is less soluble in ether, and was obtained in 47% yield; the less polar isomer, **9R**, was obtained in 42% yield, via chromatographic separation. The relative stereochemistry of (+)-**10S** was confirmed by a single-crystal X-ray analysis (Fig. 1).[6] Based on the known absolute configuration of the (1*S*)-camphanic ester, the absolute configuration of the axially dissymmetric binaphthyl ring was determined to be (*S*). Based on the directions of their optical rotations, the absolute configurations of **7R** and **8S** were assigned.

Basic hydrolyses of **7R** and **9R** with KOH in MeOH–dioxane gave ~98% yields of (–)-(*R*)-**5R** and (–)-(*R*)-**6R**, respectively. (–)-(1*S*)-Camphanic acid (96% yield) was also isolated from the hydrolysis and was converted into the (–)-(1*S*)-camphanic chloride by treatment with oxalyl chloride. Similarly, hydrolysis of (+)-**8S** and (+)-**10S** gave ~96% yields of (+)-(*S*)-**5S** and (+)-(*S*)-**6S**, respectively. 8′-Methoxy-1,1′-binaphthalen-8-ol **5** was obtained in a 71% yield from the selective demethylation of 8,8′-dimethoxy-1,1′-binaphthyl **11**[1a] with 3 equivalents of boron trichloride in methylene chloride at 25°C for 2 days along with a 15% yield recovery of binaphthyl **11**. Alkylation of enantiopure binaphthalenol **5R** or **6R** with various alkyl halides provided enantiopure 8,8′-disubstituted 1,1′-binaphthyls. For instance, alkylation of **6R** with NaH and ethyl iodide gave a quantitative yield of (–)-(*R*)-8,8′-diethoxyl-1,1′-binaphthyl **12**.

3. Conclusion

In conclusion, enantiopure 1,1′-binaphthalen-8,8′-diols **1R** and **1S**, 8′-methoxy-1,1′-binaphthalen-8-ol **5R** and **5S**, and 8′-ethoxy-1,1′-binaphthalen-8-ol **6R** and **6S** were readily resolved by separating the corresponding diastereomeric chiral camphanic esters based upon their differing solubilities in diethyl ether and their differing chromatographic behaviors. Studies of these compounds as ligands in asymmetric catalysis will be reported in due course.

4. Experimental

4.1. General

Nuclear magnetic resonance spectra were obtained at 400 MHz for ^{1}H and 100 MHz for ^{13}C in deuteriochloroform. Infrared spectra are reported in wavenumbers (cm^{-1}). Mass spectra were taken from a Hewlett–Packard 5890A Series II, GC–MS. FAB spectra were taken by using Xe beam (8 KV) and *m*-nitrobenzyl alcohol as matrix. 1-Methoxynaphthalene 3, *tert*-butyllithium, boron trichloride, and boron tribromide were purchased from Aldrich Chem. Co. Davisil silica gel, grade 643 (200–425 mesh), was used for the flash column chromatographic separation. Tetrahydrofuran and diethyl ether were distilled from sodium and benzophenone before use. Methylene chloride and cyclohexane were distilled from CaH$_2$ and toluene and benzene were distilled from LiAlH$_4$.

4.2. 8,8′-Bis{(1*S*,4*R*)-[3-oxo-4,7,7-trimethyl-2-oxabicyclo[2.2.1]heptan]-1-carbonyl}oxy-(a*R*)-1,1′-binaphthalene 3R and 8,8′-bis{(1*S*,4*R*)-[3-oxo-4,7,7-trimethyl-2-oxabicyclo[2.2.1]heptan]-1-carbonyl}oxy-(a*S*)-1,1′-binaphthalene 4S

To a solution of **1**[1a] (0.58 g, 2.02 mmol), 4-(*N*,*N*-dimethylamino)pyridine (DMAP, 0.10 g, 0.8 mmol) and (–)-(1*S*)-camphanic chloride (0.88 g, 4.04 mmol) in methylene chloride (10 mL) under argon, was added triethylamine (1.7 mL, 12 mmol) via syringe. The solution was stirred at 25°C for 18 h, diluted with aqueous ammonium chloride (80 mL), and extracted three times with diethyl ether. The combined extracts were washed with brine, dried (Na$_2$SO$_4$), and concentrated to give **3R** and **4S** as solids (1.30 g). ^{1}H NMR indicated two diastereomers (1:1). Diethyl ether (~15 mL) was added to the solids, stirred, and the ether was decanted. This process was repeated with smaller amounts of ether until the remaining solid (less soluble in ether) was shown by TLC to be a single isomer (hexane:CH$_2$Cl$_2$:ether = 2:2:0.5 as eluent; R_f = 0.1). The solid was dried under vacuum to give pure (–)-(a*R*)-**3R** (0.523 g, 40%). The diethyl ether layers were combined, concentrated, and purified by column chromatography on silica gel using a gradient mixture of hexane, methylene chloride, and ether as solvent to give pure (–)-(a*S*)-**4S** (0.614 g, 47%, less polar on TLC compared with **3**) and **3R** (0.091 g). Compound (+)-(a*S*)-**4S**: Mp 289–

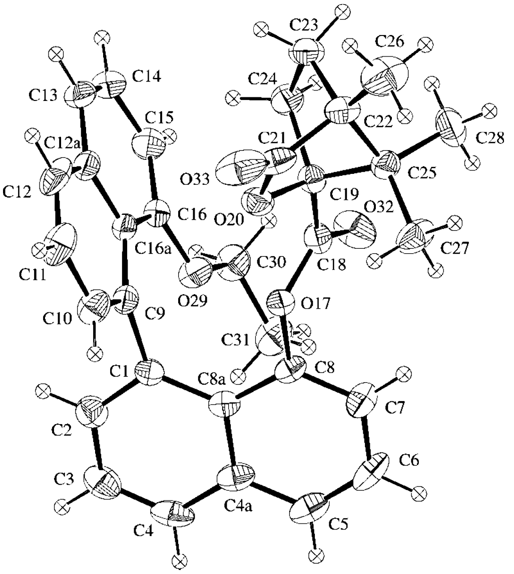


Figure 1. ORTEP drawing of the structure of (+)-**10S** as determined by X-ray crystallography.

290.5°C; $[\alpha]_D^{22}$ +75 (c=0.53; $CHCl_3$); ^1H NMR δ 7.94 (dd, J=8, 1.6 Hz, 2H), 7.86 (dd, J=8, 1.6 Hz, 2H), 7.54 (dd, J=8, 8 Hz, 2H), 7.48 (dd, J=8, 8 Hz, 2H), 7.21 (dd, J=8, 1.6 Hz, 2H), 6.99 (dd, J=8, 1.6 Hz, 2H), 1.52–1.43 (m, 2H), 1.26–1.16 (m, 4H), 0.96 (s, 6H, Me), 0.95 (s, 6H, Me), 0.82 (s, 6H, Me), 0.05–0.02 (m, 2H); ^{13}C NMR δ 177.6 (s, C=O, 2C), 166.1 (s, C=O, 2C), 146.7 (s, 2C), 136.7 (s, 2C), 136.3 (s, 2C), 130.8 (d, 2C), 128.0 (d, 2C), 127.4 (d, 2C), 126.0 (d, 2C), 125.4 (d, 2C), 124.8 (s, 2C), 120.1 (d, 2C), 90.3 (s, 2C, C-O), 54.7 (s, 2C), 54.5 (s, 2C), 28.6 (t, 2C), 28.0 (t, 2C), 16.9 (q, Me), 16.5 (q, Me), 9.6 (q, Me). Anal. calcd for $C_{40}H_{38}O_8$: C, 74.29; H, 5.92. Found: C, 74.01; H, 6.17%.

Compound (−)-(a*R*)-**3R**: Mp 280–281°C (dec.); $[\alpha]_D^{22}$ −207 (c=0.5; $CHCl_3$); ^1H NMR δ 7.88 (dd, J=8, 1.6 Hz, 2H), 7.84 (dd, J=8, 1.6 Hz, 2H), 7.53 (dd, J=8, 8 Hz, 2H), 7.42 (dd, J=8, 8 Hz, 2H), 7.12 (dd, J=8, 1.6 Hz, 2H), 7.04 (dd, J=8, 1.6 Hz, 2H), 1.61–1.55 (m, 4H), 1.34–1.27 (m, 2H), 0.93 (s, 6H, Me), 0.93–0.86 (m, 2H), 0.84 (s, 6H, Me), 0.81 (s, 6H, Me); ^{13}C NMR δ 177.6 (s, C=O, 2C), 166.8 (s, C=O, 2C), 147.4 (s, 2C), 137.8 (s, 2C), 136.1 (s, 2C), 129.8 (d, 2C), 128.1 (d, 2C), 127.3 (d, 2C), 126.2 (s, 2C), 126.0 (d, 2C), 125.2 (d, 2C), 120.6 (d, 2C), 89.0 (s, 2C, C-O), 54.8 (s, 2C), 54.5 (s, 2C), 29.6 (t, 2C), 28.6 (t, 2C), 16.9 (q, Me), 16.7 (q, Me), 9.7 (q, Me). Anal. calcd for $C_{40}H_{38}O_8$: C, 74.29; H, 5.92. Found: C, 73.98; H, 5.66%.

4.3. General procedure for the basic hydrolysis of camphanyl ester. (+)-(a*S*)-1,1′-Binaphthalene-8,8′-diol 1S

To a solution of (+)-(*S*)-**4S** (0.27 g, 0.42 mmol) in MeOH (10 mL) and 1,4-dioxane (10 mL), was added KOH (0.234 g, 4.2 mmol). The mixture was stirred at 25°C for 2 h then acidified with 1N HCl and extracted three times with ethyl acetate. The combined organic extract was washed twice with saturated aqueous sodium bicarbonate, once with brine, dried ($MgSO_4$), concentrated, and purified by column chromatography on silica gel using a gradient mixture of hexane and ether as eluent to give of (+)-(a*S*)-**1S** (95 mg, 79%); $[\alpha]_D^{22}$=+20.4 (c=0.69; $CHCl_3$); lit.[2b] +16.5 (c 1.0, $CHCl_3$); mp 118–119°C (lit.[1a] 117–119). ^1H NMR data are the same as those reported.[1a] The aqueous sodium bicarbonate layer was acidified with HCl and extracted twice with ethyl acetate. The ethyl acetate layers were dried ($MgSO_4$) and concentrated to give (−)-camphanic acid (0.160 g, 96%).

4.4. (−)-(a*R*)-1,1′-Binaphthalene-8,8′-diol 1R

Similar reaction conditions to those described above were used in the basic hydrolysis of (−)-(a*R*)-**3R**. Column chromatographic purification of the crude product gave a 78% yield of (−)-(a*R*)-**1R**. $[\alpha]_D^{22}$=−21 (c=0.69; $CHCl_3$).

4.5. (±)-8′-Methoxy-1,1′-binaphthalen-8-ol 5

To a solution of (±)-8,8′-dimethoxy-1,1′-binaphthyl **11**[1a] (2.00 g, 6.40 mmol) in methylene chloride (130 mL) under argon was added BCl_3 (1 M solution in heptane, 32 mL, 0.032 mol) and the resulting solution was stirred at 25°C for 2 days. The solution was carefully poured into water (125 mL) and extracted with CH_2Cl_2 three times. The combined extracts were washed with aqueous sodium bicarbonate and brine, dried ($MgSO_4$), concentrated, and purified by column chromatography on silica gel using a gradient mixture of hexane and methylene chloride as eluent to give (±)-**5** (1.363 g, 71%) and (±)-**11** (0.300 g, 15% recovery). Compound **5**: IR (neat) ν 3300, 3052, 2925, 2853, 1665, 1578, 1456, 1254 cm^{-1}; ^1H NMR δ 7.94 (d, J=8 Hz, 1H), 7.81 (d, J=8 Hz, 1H), 7.56–7.38 (m, 5H), 7.35 (dd, J=8, 8 Hz, 2H), 7.06 (dd, J=8, 1.6 Hz, 1H), 6.80 (dd, J=8, 1.6 Hz, 1H), 6.75 (d, J=8 Hz, 1H), 5.47 (s, 1H, OH), 3.14 (s, 3H, OMe); ^{13}C NMR δ 157.0 (s), 153.7 (s), 139.4 (s), 137.0 (s), 135.8 (s), 135.2 (s), 129.5 (d), 129.4 (d), 127.5 (d), 127.2 (d), 126.9 (d), 126.4 (d), 125.7 (d), 124.6 (d), 124.4 (s), 123.0 (s), 121.4 (d), 120.9 (d), 111.1 (d), 107.3 (d), 55.7 (q, Me). MS, CI, m/z 301 (M+1). Anal. calcd for $C_{21}H_{16}O_2$: C, 83.98; H, 5.37. Found: C, 83.69; H, 5.11%.

4.6. 8-Methoxy-8′-{(1*S*,4*R*)-[3-oxo-4,7,7-trimethyl-2-oxabicyclo[2.2.1]heptan]-1-carbonyl}oxy-(a*S*)-1,1′-binaphthalene 8S and 8-methoxy-8′-{(1*S*,4*R*)-[3-oxo-4,7,7-trimethyl-2-oxabicyclo[2.2.1]heptan]-1-carbonyl}oxy-(a*R*)-1,1′-binaphthalene 7R

To a solution of (±)-**5** (0.16 g, 0.53 mmol), 4-(*N*,*N*-dimethylaminopyridine (DMAP, 13 mg, 0.11 mmol) and (−)-(1*S*)-camphanic chloride (0.138 g, 0.64 mmol) in methylene chloride (10 mL) under argon, was added triethylamine (0.23 mL, 1.6 mmol) via syringe. The solution was stirred at 25°C for 10 h, diluted with aqueous ammonium chloride (80 mL) and extracted three times with diethyl ether. The combined extracts were washed with brine, dried (Na_2SO_4), and concentrated to give 0.26 g of solid. The ^1H NMR spectrum indicated two diastereomers (1:1) of **7R** and **8S**. Diethyl ether (∼10 mL) was added to the solids, stirred, and the ether was removed. This process was repeated with smaller amounts of ether until the remaining solid (less soluble in ether) was indicated by TLC to be a single isomer (hexane:CH_2Cl_2:ether=1:1:0.5 as eluent; R_f= 0.1). The solid was dried under vacuum to give pure (+)-**8S** (0.102 g, 40%). The diethyl ether layers were combined, concentrated, and purified by column chromatography on silica gel using a gradient mixture of hexane, methylene chloride, and ether as solvent to give pure (−)-**7R** (0.109 g, 43%) of (less polar on TLC compared with **8S**) and pure (+)-**8S** (0.01 g, 4%).

Compound (+)-**8S**: Mp 244.5–246.5°C; $[\alpha]_D^{22}$=+406 (c= 1; $CHCl_3$); IR (neat) ν 3051, 2965, 2930, 1790, 1768, 1575, 1256, 1097, 1042 cm^{-1}; ^1H NMR δ 7.86 (dd, J=8, 1.6 Hz, 2H), 7.80 (d, J=8 Hz, 1H), 7.52 (dd, J=8, 8 Hz, 1H), 7.48–7.41 (m, 3H), 7.34 (t, J=8 Hz, 1H), 7.28 (dd, J=8, 1.6 Hz, 1H), 7.06 (dd, J=8, 1.6 Hz, 1H), 6.94 (dd, J=8, 1.6 Hz, 1H), 6.63 (d, J=8 Hz, 1H), 3.07 (s, 3H, OMe), 1.47–1.40 (m, 1H), 1.29–1.19 (m, 1H), 0.95 (s, 3H, Me), 0.91 (s, 3H, Me), 0.9–0.79 (m, 1H), 0.75 (s, 3H, Me), 0.33–0.26 (m, 1H); ^{13}C NMR δ 177.9 (s, C=O), 166.5 (s, C=O), 157.0 (s), 147.6 (s), 140.3 (s), 139.3 (s), 135.8 (s), 135.3 (s), 129.3 (d), 128.4 (d), 127.5 (d), 127.4 (d), 127.1 (d), 126.4 (s), 126.3 (d), 126.1 (d), 125.3 (d), 124.9 (d), 124.7 (s), 121.0 (d), 119.3 (d), 105.8 (d), 90.6 (s, C-O), 55.2 (q, OMe), 54.9 (s), 54.7 (s), 28.8 (t), 28.2 (t), 17.1 (q, Me), 16.8 (q, Me), 9.8 (q, Me). MS, EI, *m*/*z* 481 (M+1), 300 (M−camphanyl+1), 268. Anal. calcd for $C_{31}H_{28}O_5$: C, 77.48; H, 5.87. Found: C, 77.53; H, 5.59%.

Compound (−)-**7R**: Mp 141.5–143.5°C; $[\alpha]_D^{22}=-170$ ($c=1$; $CHCl_3$); IR (neat) ν 3051, 2967, 2932, 2835, 1790, 1770, 1616, 1575, 1256, 1099 cm^{-1}; ^{1}H NMR δ 7.87 (d, $J=8$ Hz, 2H), 7.79 (d, $J=8$ Hz, 1H), 7.48–7.38 (m, 5H), 7.19 (dd, $J=8$, 1.6 Hz, 1H), 7.08 (dd, $J=8$, 1.6 Hz, 1H), 6.96 (dd, $J=8$, 1.6 Hz, 1H), 6.70 (d, $J=8$ Hz, 1H), 3.11 (s, 3H, OMe), 1.55–1.54 (m, 1H), 1.30–1.24 (m, 1H), 1.12–1.07 (m, 1H), 0.96 (s, 3H, Me), 0.88 (s, 3H, Me), 0.83 (s, 3H, Me), 0.51–0.48 (m, 1H); ^{13}C NMR δ 177.6 (s, C=O), 166.4 (s, C=O), 156.6 (s), 147.4 (s), 140.3 (s), 139.7 (s), 135.5 (s), 135.0 (s), 129.1 (d), 127.4 (d), 127.3 (d), 127.0 (d), 126.9 (d), 126.6 (d), 126.2 (s), 125.1 (d), 125.0 (d), 124.7 (d), 124.6 (s), 120.5 (d), 119.0 (d), 106.1 (d), 90.2 (s, C-O), 54.9 (q, OMe), 54.4 (s), 54.3 (s), 28.5 (t), 28.4 (t), 16.7 (q, Me), 16.6 (q, Me), 9.5 (q, Me). MS, EI, *m*/*z* 481 (M+1), 300 (M−camphanyl+1), 268. Anal. calcd for $C_{31}H_{28}O_5$: C, 77.48; H, 5.87. Found: C, 77.20; H, 5.62%.

4.7. (+)-(a*S*)-8′-Methoxy-1,1′-binaphthalen-8-ol 5S

Following the above general procedure described for the basic hydrolysis. Hydrolysis of (+)-(a*S*)-**8S** (0.10 g, 0.21 mmol) afforded pure (+)-(a*S*)-**5S** (61 mg, 96%). Mp 117.5–120°C. ^{1}H NMR and TLC are identical with those of the racemic sample, **5**. $[\alpha]_D^{22}=+195$ ($c=0.52$; $CHCl_3$). The aqueous layer was acidified with 2N HCl and extracted twice with methylene chloride. The combined methylene chloride extracts were dried ($MgSO_4$) and concentrated to give pure (−)-(1*S*)-camphanic acid (40 mg; 98%): ^{1}H NMR δ 4.8 (broad s, 1H, OH), 2.47 (ddd, $J=14$, 11, 4 Hz, 1H), 2.1 (ddd, $J=14$, 9, 5 Hz, 1H), 1.96 (ddd, $J=14$, 11, 5 Hz, 1H), 1.73 (ddd, $J=14$, 9, 4 Hz, 1H), 1.14 (s, 3H, Me), 1.10 (s, 3H, Me), 1.02 (s, 3H, Me).

4.8. (−)-(a*R*)-8′-Methoxy-1,1′-binaphthalen-8-ol 5R

Reaction conditions similar to those described above were used in the basic hydrolysis of (−)-(a*R*)-**7R** to give a 98% yield of (−)-(*R*)-**5R**. $[\alpha]_D^{22}=-195$ ($c=0.5$; $CHCl_3$).

4.9. 8-Ethoxy-8′-{(1*S*,4*R*)-[3-oxo-4,7,7-trimethyl-2-oxabicyclo[2.2.1]heptan]-1-carbonyl}oxy-(a*S*)-1,1′-binaphthalene 10S and 8-ethoxy-8′-{(1*S*,4*R*)-[3-oxo-4,7,7-trimethyl-2-oxabicyclo[2.2.1]heptan]-1-carbonyl}oxy-(a*R*)-1,1′-binaphthalene 9R

To a solution of **6** (0.645 g, 2.00 mmol), DMAP (49 mg, 0.4 mmol) and (−)-(1*S*)-camphanic chloride (0.534 g, 2.47 mmol) in methylene chloride (30 mL) under argon, was added triethylamine (0.89 mL, 6.16 mmol) via syringe. The solution was stirred at 25°C for 10 h, diluted with aqueous ammonium chloride (70 mL) and extracted three times with diethyl ether. The combined extracts were washed with brine, dried (Na_2SO_4), and concentrated to give 1.00 g of solids. ^{1}H NMR indicated two diastereomers in a ratio of 1:1. Diethyl ether (~10 mL) was added to the solids, stirred, and the ether was removed. This process was repeated with smaller amounts of ether until the remaining solid (less soluble in ether) was shown by TLC to be a single isomer (hexane:CH_2Cl_2:ether = 1:1:0.5 as eluent; $R_f=0.1$). The solid was dried under vacuum to give pure (+)-(a*S*)-**10S** (0.459 g, 47%). The diethyl ether layers were combined, concentrated, and purified by column chromatography on silica gel using a gradient mixture of hexane, methylene chloride, and ether as solvent to give pure (−)-(a*R*)-**9R** (less polar on TLC compares with **10S** 0.410 g, 42%). Compound (+)-(a*S*)-**10S**: Single crystals were obtained from recrystallization of the solid with methylene chloride and ether and the structure was solved by single-crystal X-ray analysis (Fig. 1). Mp 223–224.5°C; $[\alpha]_D^{22}=+293$ ($c=0.5$; $CHCl_3$); IR (neat) ν 3052, 2977, 2926, 2880, 1782, 1748, 1615, 1574, 1263, 1101 cm^{-1}; ^{1}H NMR δ 7.86 (t, $J=8$ Hz, 2H), 7.81 (dd, $J=8$, 1.6 Hz, 1H), 7.53 (t, $J=8$ Hz, 2H), 7.46–7.41 (m, 3H), 7.32 (t, $J=8$ Hz, 1H), 7.26 (dd, $J=8$, 1.6 Hz, 1H), 7.05 (dd, $J=8$, 1.6 Hz, 1H), 6.94 (dd, $J=8$, 1.6 Hz, 1H), 6.59 (d, $J=8$ Hz, 1H), 3.56–3.42 (m, 2H, OCH_2), 1.48–1.4 (m, 1H), 1.29–1.21 (m, 1H), 0.96 (s, 3H, Me), 0.94–0.89 (m, 1H), 0.92 (s, 3H, Me), 0.77 (s, 3H, Me), 0.3–0.22 (m, 1H), 0.07 (t, $J=7$ Hz, 3H, Me); ^{13}C NMR δ 177.7 (s, C=O), 166.4 (s, C=O), 156.0 (s), 147.5 (s), 140.3 (s), 139.2 (s), 135.7 (s), 135.3 (s), 128.9 (d), 128.1 (d), 127.3 (d), 127.1 (d), 126.7 (d), 126.5 (s), 125.9 (d), 125.8 (d), 125.2 (d), 124.6 (d), 124.1 (s), 120.3 (d), 119.1 (d), 105.2 (d), 90.3 (s, C-O), 62.8 (t, OCH_2), 54.7 (s), 56.4 (s), 28.6 (t), 27.9 (t), 16.9 (q, Me), 16.5 (q, Me), 12.8 (q, Me), 9.6 (q, Me). MS, EI, *m*/*z* 495 (M+1), 314 (M−camphanyl+1), 286.

Compound (−)-(a*R*)-**9**: Mp 164–165°C; $[\alpha]_D^{22}=-251.6$ ($c=0.5$; $CHCl_3$); IR (neat) ν 3051, 2973, 2932, 2878, 1791, 1748, 1615, 1575, 1257, 1098 cm^{-1}; ^{1}H NMR δ 7.86 (t, $J=8$ Hz, 2H), 7.78 (dd, $J=8$, 1.6 Hz, 1H), 7.47–7.35 (m, 5H), 7.17 (dd, $J=8$, 1.6 Hz, 1H), 7.06 (dd, $J=8$, 1.6 Hz, 1H), 6.95 (dd, $J=8$, 1.6 Hz, 1H), 6.65 (dd, $J=8$, 1.6 Hz, 1H), 3.52 (m, 2H, OCH_2), 1.56–1.5 (m, 1H), 1.33–1.25 (m, 1H), 1.06–0.98 (m, 1H), 0.96 (s, 3H, Me), 0.89 (s, 3H, Me), 0.84 (s, 3H, Me), 0.5–0.43 (m, 1H), 0.06 (t, $J=7$ Hz, 3H, Me); ^{13}C NMR δ 177.6 (s, C=O), 166.4 (s, C=O), 155.8 (s), 147.7 (s), 140.4 (s), 139.8 (s), 135.6 (s), 135.3 (s), 129.0 (d), 127.3 (d), 127.2 (d), 127.0 (d), 126.8 (d), 126.7 (d), 126.5 (s), 125.2 (d), 124.9 (d), 124.7 (d), 124.3 (s), 120.0 (d), 119.1 (d), 105.8 (d), 90.4 (s, C-O), 62.7 (t, OCH_2), 54.4 (s), 54.3 (s), 28.5 (t), 28.2 (t), 16.7 (q, Me), 16.7 (q, Me), 12.6 (q, Me), 9.5 (q, Me); MS, EI, *m*/*z* 495 (M+1), 314 (M−camphanyl+1), 286. Anal. calcd for $C_{32}H_{30}O_5$: C, 77.71; H, 6.11. Found: C, 77.60; H, 6.35%.

4.10. (+)-(a*S*)-8-Ethoxy-8′-hydroxy-1,1′-binaphthalene 6S

Similar reaction conditions as those described above were used in the basic hydrolysis of (+)-(*S*)-**8** to give a 96% yield of (+)-(*S*)-**6S**. Mp 139–140°C; $[\alpha]_D^{22}=+251$ ($c=0.5$; $CHCl_3$). Compound **6S**: IR (neat) ν 3360, 3050, 2923, 2852, 1652, 1575, 1270 cm^{-1}; ^{1}H NMR δ 7.94 (d, $J=8$ Hz, 1H), 7.82 (d, $J=8$ Hz, 1H), 7.55–7.33 (a series of m, 7H), 7.04 (d, $J=8$ Hz, 1H), 6.80 (d, $J=8$ Hz, 1H), 6.72 (d, $J=8$ Hz, 1H), 5.54 (s, 1H, OH), 3.55 (q, $J=7$ Hz, 2H, OCH_2), 0.127 (t, $J=7$ Hz, 3H, CH_3); ^{13}C NMR δ 157.4 (s), 153.7 (s), 136.8 (s), 135.6 (s), 129.2 (d), 129.2 (d), 127.2 (d), 127.0 (d), 126.6 (d), 126.1 (d), 125.3 (d), 124.4 (d), 123.2 (s), 120.7 (d), 120.6 (d), 110.7 (d), 106.5 (d), 63.1 (t, OCH_2), 12.8 (q, Me); MS, CI, *m*/*z* 315 (M+1). Anal. calcd for $C_{22}H_{18}O_2$: C, 84.05; H, 5.77. Found: C, 83.76; H, 6.03%.

4.11. (−)-(a*R*)-8-Ethoxy-8′-hydroxy-1,1′-binaphthalene 6R

Similar reaction conditions as those described above were used in the basic hydrolysis of (−)-(a*R*)-**9** to give a 98% yield of (−)-(a*R*)-**6R**. Mp 139–140°C; $[\alpha]_D^{22}=-264$ ($c=0.5$; $CHCl_3$).

4.12. (a*R*)-8,8′-Diethoxy-1,1′-binaphthyl 12

To a solution of **6R** (54 mg, 0.17 mmol) in DMF (5 mL, distilled from CaH_2) under argon at 0°C was added NaH (50% dispersion in oil, 0.17 mmol; 8.2 mg) and ethyl iodide (29 mg, 0.19 mmol). The solution was stirred at 0°C for 30 min and 25°C for 2 h, diluted with aqueous NH_4Cl, and extracted twice with ether. The combined extracts were washed with brine, dried ($MgSO_4$), concentrated, and purified by column chromatography on silica gel using a gradient mixture of hexane and ether as eluent to give **12** (59 mg, 100%). Mp 222–223°C; $[\alpha]_D^{22}=-464$ ($c=0.5$; $CHCl_3$); IR (neat) ν 3050, 2973, 2922, 1580, 1455, 1376, 1266, 1066 cm^{-1}; ^{1}H NMR δ 7.68 (dd, $J=8$, 1.6 Hz, 2H), 7.44 (t, $J=8$ Hz, 2H), 7.40 (t, $J=8$ Hz, 2H), 7.31 (t, $J=8$ Hz, 2H), 7.16 (dd, $J=8$, 1.6 Hz, 2H), 6.60 (d, $J=8$ Hz, 2H), 3.55–3.38 (m, 4H, CH_2), 0.07 (t, $J=7$ Hz, 6H, Me); ^{13}C NMR δ 156.0 (s, 2C), 135.0 (s, 2C), 132.0 (s, 2C), 126.6 (d, 2C), 126.2 (d, 2C), 125.3 (d, 2C), 124.9 (d, 2C), 123.5 (s, 2C), 120.4 (d, 2C), 105.2 (d, 2C), 62.9 (t, 2C), 12.8 (q, 2C); MS, CI, *m*/*z* 343 (M+1). Anal. calcd for $C_{24}H_{22}O_2$: C, 84.18; H, 6.48. Found: C, 84.42; H, 6.30%.

Acknowledgements

We gratefully acknowledge financial support from the National Science Foundation (CHE-0078921), National Institutes of Health, National Cancer Institute (CA86842), American Heart Association, Heartland Affiliate (0051658Z, 9951177Z), NASA-BioServe Space Technologies (NAGW-1197), and Great Plains Diabetes Research, Inc., and are grateful to Professors Kaoru Fuji and Kiyoshi Tanaka at Kyoto University for helpful communication. Support from the National Science Foundation, Research Experience for Undergraduates (CHE-9732103) to T.X.C.N. is also acknowledged.

References

1. Syntheses of (±)-8,8′-dimethoxy-1,1′-binaphthalene and 1,1′-binaphthalen-8,8′-diol: (a) Artz, S. P.; deGrandpre, M. P.; Cram, D. J. *J. Org. Chem.* **1985**, *50*, 1486–1496; (b) Ossor, H.; Pfeffer, M. *J. Chem. Soc., Chem. Commun.* **1985**, 1540–1541. Synthesis of chiral 2,2′-dimethyl-1,1′-binaphthalen-8,8′-diol: (c) Kolotuchin, S. V.; Meyers, A. I. *J. Org. Chem.* **1999**, *64*, 7921–7928.
2. Resolution of the 1,1′-binaphthalen-8,8′-diol: Use of the diester of (*S*)-*O*-acetyl mandelic acid: (a) Fuji, K.; Kawabata, T.; Kuroda, A. *J. Org. Chem.* **1995**, *60*, 1914–1915. Use of the dicarbonate derived from the diol and (−)-L-menthyl chloroformate: (b) Fabbri, D.; Delogu, G. *J. Org. Chem.* **1995**, *60*, 6599–6601. Use of the ester of *N*-CBZ-L-proline: (c) Fuji, K.; Yang, X.; Ohnishi, H.; Hao, X.; Obata, Y.; Tanaka, Y. *Tetrahedron: Asymmetry* **1999**, *10*, 3243–3248.
3. Enantioselective protonation of enolates: **2a**. (a) Fuji, K.; Kawabata, T.; Kuroda, A. *J. Org. Chem.* **1995**, *60*, 1914–1915. 1,4-Addition with cuprate reagents: (b) Fuji, K.; Yang, X.; Tanaka, K.; Asakawa, N. *Tetrahedron Lett.* **1996**, *37*, 7373–7376; (c) Tanaka, K.; Nuruzzaman, M.; Yoshida, M.; Asakawa, N.; Yang, X.; Tsubaki, K.; Fuji, K. *Chem. Pharm. Bull.* **1999**, *47*, 1053–1055. Chiral recognition with amines: (d) Kawabata, T.; Kuroda, A.; Nakata, E.; Takasu, K.; Fuji, K. *Tetrahedron Lett.* **1996**, *37*, 4153–4156. NMR chiral derivatizing reagent of carboxylic acids: (e) Fukushi, Y.; Shigematsu, K.; Mizutani, J.; Tahara, S. *Tetrahedron Lett.* **1996**, *37*, 4737–4740. Palladium-catalyzed reduction of allylic carbonates: (f) Fuji, K.; Sakurai, M.; Kinoshita, T.; Tada, T.; Kuroda, A.; Kawabata, T. *Chem. Pharm. Bull.* **1997**, *45*, 1524–1526; (g) Fuji, K.; Sakurai, M.; Kinoshita, T.; Kawabata, T. *Tetrahedron Lett.* **1998**, *39*, 6323–6326. In asymmetric Diels–Alder reactions: (h) Tanaka, K.; Asakawa, N.; Nuruzzaman, M.; Fuji, K. *Tetrahedron: Asymmetry* **1997**, *8*, 3637–3645. Cyclopropanation: **1c**. Asymmetric reduction and addition reactions with organometallic reagents: (i) Muller, P.; Nury, P.; Bernardinelli, G. *Helv. Chim. Acta* **2000**, *83*, 843–854.
4. Attempts at resolving the dimenthyl carbonate derivatives of 1,1′-binaphthalene-8,8′-diol in hexane failed. No crystals were obtained after sitting at either 0°C or room temperature for over 1 week.
5. The rotations of **1R** and **1S** are concentration and solvent dependent, see Refs. 2b, 2c, and 3i.
6. The author has deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 168001. The coordinates can be obtained on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.