Pergamon

Tetrahedron: *Asymmetry* 10 (1999) 3243–3248

TETRAHEDRON: *ASYMMETRY*

A highly efficient method for the resolution of 8,8′-dihydroxy-1,1′-binaphthyl

Kaoru Fuji,[a,*] Xiao-Shen Yang,[b] Hiroshi Ohnishi,[a] Xiao-Jiang Hao,[b] Yumiko Obata[c] and Kiyoshi Tanaka[c]

[a]*Institute for Chemical Research, Kyoto University, Uji, Kyoto 611-0011, Japan*
[b]*Kunming Institute of Botany, Chinese Academy of Sciences, Kunming 650204, China*
[c]*School of Pharmaceutical Sciences, University of Shizuoka, 52-1 Yada, Shizuoka 422-8526, Japan*

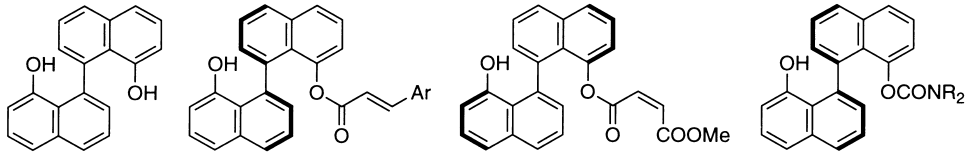
Received 9 July 1999; accepted 26 July 1999

Abstract

The diastereomeric mixture of monoesters of racemic 8,8′-dihydroxy-1,1′-binaphthyl and *N*-CBZ-L-proline was easily separated. Each diastereomer gave enantiomerically pure (*R*)- or (*S*)-8,8′-dihydroxy-1,1′-binaphthyl in good yields after hydrolysis.

1. Introduction

Derivatives of optically active 8,8′-dihydroxy-1,1′-binaphthyl **1** have been used in the fields of asymmetric synthesis as well as recognition of chiral molecules. The former includes the one-step synthesis of β-substituted ketones[1] by successive 1,4- and 1,2-addition of lithium dialkylcuprates to (*R*)-**2** and highly diastereoselective Diels–Alder cycloadditions of (*S*)-**3**.[2] Monocarbamates (*R*)-**4** have been used as chiral proton sources.[3] Chiral recognition of amino acid derivatives by optically active 8,8′-dihydroxy-1,1′-binaphthyl **1** has been reported.[4] (*R*)-8,8′-Dihydroxy-1,1′-binaphthyl **1** was used as a chiral derivatizing agent for the ^{1}H NMR determination of the absolute configuration of carboxylic acids.[5]



(*dl*)-**1** (*R*)-**2** (*S*)-**3** (*R*)-**4**

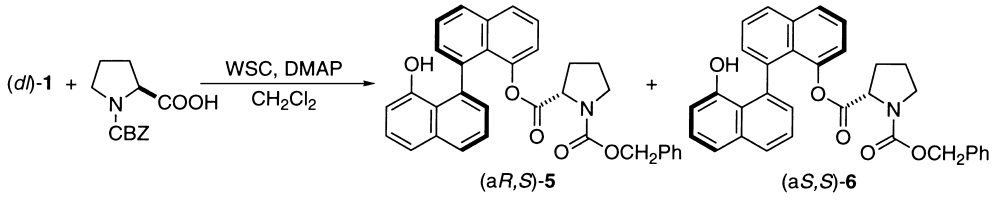
* Corresponding author. Fax: +81-774-38-3197; e-mail: fuji@scl.kyoto-u.ac.jp

0957-4166/99/$ - see front matter
PII: S0957-4166(99)00340-7

Although racemic 8,8′-dihydroxy-1,1′-binaphthyl **1** was synthesized by Cram et al.[6] in 1985, the resolution of **1** was not attempted. Resolution of **1** involving esterification with (*S*)-*O*-acetylmandelic acid,[3] or (−)-menthyl chloroformate[7] was reported in 1995. The former gives enantiomerically pure (*R*)-**1**, but not (*S*)-**1**. The latter gives enantiomerically pure (*S*)-**1**, but gives (*R*)-**1** in only 74% ee. Here we report a highly efficient method for resolution of racemic **1** giving both enantiomers with high ee in good yield. Attempted kinetic resolution of racemic **1** and the corresponding diacetate by several enzymes was not promising.

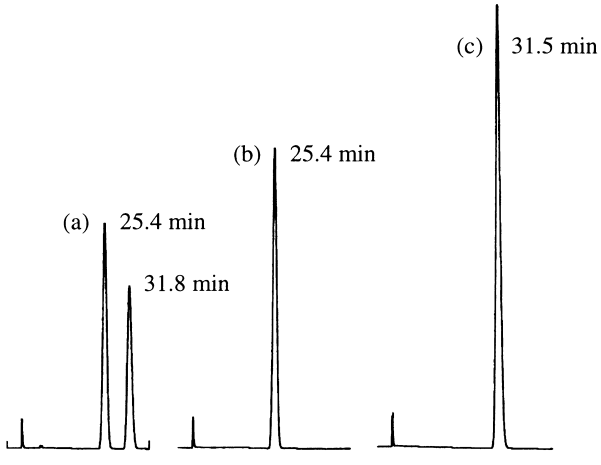
2. Results and discussion

For the resolution of **1**, carbobenzyloxy-L-proline (CBZ-L-proline) was shown to be the best among the chiral acids tested. Thus, esterification of racemic **1** with CBZ-L-proline afforded a diastereomeric mixture of (a*R*,*S*)-**5** and (a*S*,*S*)-**6** in good yield (Scheme 1). The former was easily crystallized from the crude reaction mixture in ether. Although **5** and **6** show a single peak on HPLC analysis (Fig. 1), they exist as a 3:2 mixture in $CDCl_3$ due to restricted rotation across the *N*–CBZ bond as determined by ^1H NMR spectroscopy. Fig. 2 shows the signal for the benzyl protons of **5** at various temperatures. Coalescence temperature was observed at 45°C. The free energy of activation for the C–N bond rotation was calculated to be 14.6 kcal/mol at 45°C.



Scheme 1.

Hydrolysis of (a*R*,*S*)-**5** with KOH in aqueous dioxane gave (*R*)-8,8′-dihydroxy-1,1′-binaphthyl **1** in 91% yield. Since the ee was >98% at this stage (Fig. 3), it could be used without further purification.



HPLC conditions: CHIRALCEL AD (Daicel),
15% isopropanol-hexane, 1 ml/min.

Figure 1. HPLC profile of (a) a mixture of **5** and **6**; (b) **5**; and (c) **6**

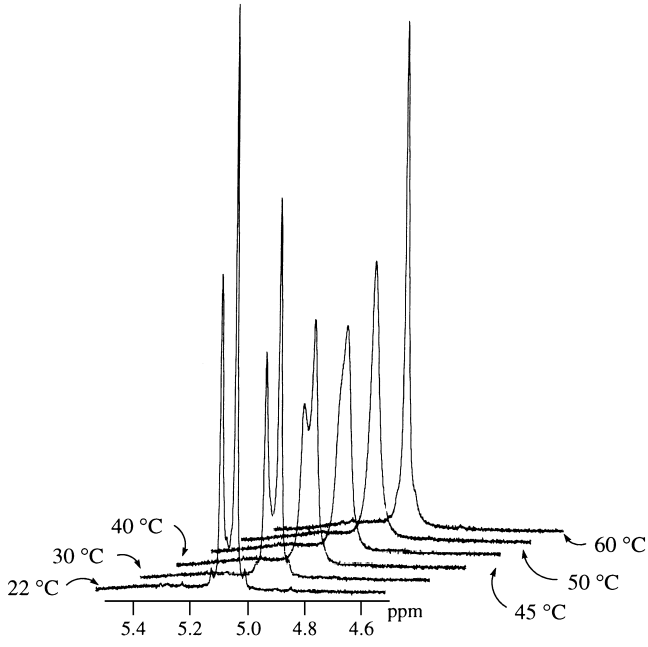
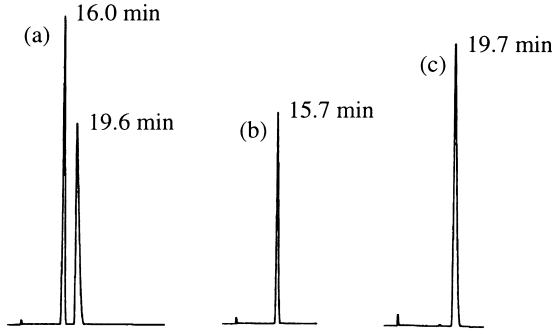


Figure 2. Temperature-dependent ^{1}H NMR signals for the benzyl group of **5**



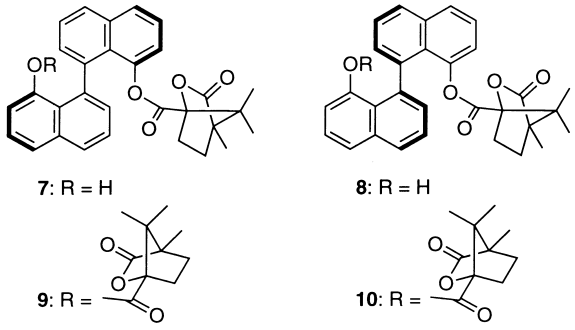
HPLC conditions: CHIRALCEL AD (Daicel),
15% isopropanol-hexane, 1 ml/min.

Figure 3. HPLC profile of (a) (*dl*)-**1**; (b) (*R*)-**1**; and (c) (*S*)-**1**

The crystals turned pale brown after standing overnight. However, the product, recrystallized from cyclohexane–hexane, can be kept unchanged for at least 3 months at room temperature.

(*S*)-Camphanic acid is another resolving agent for **1**. Thus, monoacylation of racemic **1** with 0.8 equiv. of (1*S*)-camphanic chloride gave **7** and **8** in 32 and 21% yield, respectively. Diesters **9** (18%) and **10** (32%) were obtained when 2.2 equiv. of (1*S*)-camphanic chloride were used. The esters **8**–**10** readily decompose during the purification and on standing at room temperature. Reduction of the esters with $LiAlH_4$ afforded (a*R*)- or (a*S*)-**1** in good yield.

It is worth noting that 8,8′-disubstituted-1,1′-binaphthyls have attracted attention in the field of asymmetric synthesis due to the highly dissymmetric microenvironment around the substituents at C-8 and C-8′.[8–10]



3. Experimental

3.1. General

Melting points are uncorrected. ^{1}H NMR spectra were taken at 400 or 270 MHz in $CDCl_3$ with chemical shifts being reported as δ ppm from tetramethylsilane as an internal standard. Dichloromethane was distilled from calcium hydride. TLC analyses were performed on commercial glass plates bearing a 0.25 mm layer of Merck Kieselgel 60 F_{254}. Silica gel column chromatography was carried out with Wakogel C-200.

3.2. (aR)- and (aS)-8,8′-Dihydroxy-1,1′-binaphthyl ester (5 and 6) of N-carbobenzyloxy-L-proline

A 100 ml, two-necked, round bottomed flask equipped with a magnetic stirring bar, a nitrogen inlet, and a rubber septum was charged with a solution of (*dl*)-8,8′-dihydroxy-1,1′-binaphthyl (**1**, 2.0 g, 7.0 mmol), *N*-CBZ-L-proline (1.9 g, 7.7 mmol, 1.1 equiv.), and 1-ethyl-3-(3-dimethylaminopropyl)-carbodimide hydrochloride (WSC, 2.0 g, 1.5 equiv.) in 60 ml of anhydrous CH_2Cl_2 at 0–5°C, and then 85 mg of 4-dimethylaminopyridine (DMAP) was added. After being stirred for 8 h at the same temperature (TLC control), the reaction mixture was quenched with 10 ml of water and the solution was evaporated in vacuo. The residue was partitioned between 300 ml of water and 300 ml of AcOEt and the aqueous layer was extracted with 200 ml of AcOEt again. The combined organic phase was washed successively with 0.1N HCl (200 ml), water (200 ml), and brine (150 ml×3), dried over $MgSO_4$, and evaporated in vacuo. The residue (4.0 g) was crystallized from ether (60 ml) to give 1.30 g (33%) of (a*R*,*S*)-**5** as white needles. Mp 204–206°C (from $CHCl_3$–hexane); $[\alpha]_D^{20}$ −296.5 (*c* 1.1, dioxane); IR ($CHCl_3$) cm^{-1}: 3480, 2320, 2280, 1760, 1700; ^{1}H NMR δ: 0.54 (m, 0.4H), 0.73 (m, 0.6H), 1.08–1.26 (1H), 1.46–1.71 (2H), 1.63 (br. s, 1H), 3.00 (dd, 0.6H, *J*=8.2, 3.6 Hz), 3.23–3.41 (1.4H), 4.89 (d, 0.6H, *J*=12.4 Hz), 5.04–5.17 (1.4H), 6.63 (d, 0.6H, *J*=7.3 Hz), 6.86 (d, 0.4H, *J*=7.3 Hz), 6.94 (d, 0.6H, *J*=7.3 Hz), 7.08 (d, 1H, *J*=6.8 Hz), 7.20–7.54 (12.4H), 7.77–7.83 (2H), 7.95 (d, 1H, *J*=8.2 Hz). Anal. calcd for $C_{33}H_{27}NO_5$: C, 76.58, H, 5.26, N, 2.71. Found: C, 76.52, H, 5.08, N, 2.63.

The residue (2.70 g) obtained from the mother liquor was chromatographed over silica gel (400 g). Elution with hexane:AcOEt (5:1) gave racemic **1** (100 mg, 5%). Further elution with hexane:AcOEt (2:1) successively gave (a*R*,*S*)-**5** (510 mg), a mixture (500 mg) of **5** and **6**, and (a*S*,*S*)-**6** (1.40 g, 35%) as white needles. Mp 170.5–172°C (from hexane–AcOEt); $[\alpha]_D^{20}$ 211.2 (*c* 1.1, dioxane); IR ($CHCl_3$) cm^{-1}: 3480, 2320, 2280, 1765, 1700; ^{1}H NMR ($CDCl_3$) δ: 0.54 (m, 0.4H), 0.73 (m, 0.6H), 1.08–1.26 (1H), 1.46–1.71 (2H), 1.63 (br. s, 1H), 3.00 (dd, 0.6H, *J*=8.2, 3.6 Hz), 3.23–3.41 (1.4H), 4.89 (d, 0.6H,

J=12.4 Hz), 5.04–5.17 (1.4H), 6.63 (d, 0.6H, *J*=7.3 Hz), 6.86 (d, 0.4H, *J*=7.3 Hz), 6.94 (d, 0.6H, *J*=7.3 Hz), 7.08 (d, 1H, *J*=6.8 Hz), 7.20–7.54 (12.4H), 7.77–7.83 (2H), 7.95 (d, 1H, *J*=8.2 Hz). A small amount of diester (40 mg) was obtained with further elution with AcOEt. The second chromatography of a mixture (500 mg) of **5** and **6** gave **5** (42 mg), a mixture (40 mg) of **5** and **6**, and **6** (290 mg). Total yields of (a*R*,*S*)-**5** and (a*S*,*S*)-**6** were 1.85 g (46%) and 1.69 g (42%), respectively.

3.3. (R)-8,8′-Dihydroxy-1,1′-binaphthyl **1**

To a solution of (a*R*,*S*)-**5** (1.0 g) in dioxane (10 ml) and water (30 ml) was added KOH (1.0 g) at room temperature, then the mixture was stirred for 5 h (TLC control). After addition of 30 ml of water, the mixture was extracted with ether (200 ml×2).[11] The organic phase was washed successively with water (200 ml) and brine (200 ml×3), dried ($MgSO_4$), and evaporated in vacuo to give a residue. Silica gel column chromatography of the residue with hexane:AcOEt (5:1) as an eluent gave (*R*)-1,1′-binaphthalene-8,8′-diol (**1**, 0.5 g, 91%). Mp 103–105°C; $[\alpha]_D^{20}$ −336.5 (*c* 1.1, THF); lit.[3] $[\alpha]_D^{20}$ −361.0 (*c* 0.6, THF); ^{1}H NMR δ: 5.42 (br. s, 1H), 6.83 (dd, 1H, *J*=1.3, 7.5 Hz), 7.30–7.60 (m, 4H), 7.95 (dd, 1H, *J*=1.3, 8.2 Hz); ^{13}C NMR (99.45 MHz, $CDCl_3$) δ: 112.2, 120.9, 121.6, 124.5, 127.3, 128.4, 129.6, 134.3, 135.3, 152.7; IR ($CHCl_3$) cm^{-1}: 3500, 1620, 1580, 1510, 1458, 1340, 1280, 1230, 820. Anal. calcd for $C_{20}H_{14}O_2$: C, 83.90, H, 4.93. Found: C, 84.18, H, 4.98. Recrystallization from 10 ml of cyclohexane:hexane (1:1) gave (*R*)-**1** (400 mg, 73%).

3.4. (S)-8,8′-Dihydroxy-1,1′-binaphthyl **1**

Through the same procedure as that for (a*R*,*S*)-ester **5**, (a*S*,*S*)-ester **6** gave (*S*)-1,1′-binaphthalene-8,8′-diol (**1**, mp 104.5–106°C; $[\alpha]_D^{20}$ +329.0 (*c* 1.1, THF); lit.[7] $[\alpha]_D^{25}$ +16.5 (*c* 1.0, $CHCl_3$) in 71% yield after recrystallization from cyclohexane–hexane.

3.5. Camphanates **7** and **8**

(−)-Camphanic chloride (86 mg, 0.4 mmol, 0.8 equiv.) was added to a stirred solution of racemic **1** (143 mg, 0.5 mmol) in pyridine (2.0 ml) at 0°C and the mixture was stirred for 25 h at room temperature. The reaction mixture was concentrated to half volume in vacuo and then poured into ice-water, and extracted with AcOEt. The organic extract was successively washed with dil. HCl and brine, and then dried over $MgSO_4$. Evaporation of the solvent in vacuo gave an oil (220 mg), which was subjected to column chromatography on silica gel with toluene:CH_2Cl_2 (1:1). The starting material **1** (38 mg) was recovered from the least polar fractions. From the successive fractions, **7** (75 mg, 32%) was obtained as an off-white solid, which was recrystallized from ether–hexane. Following fractions contained the mixture of **7** and **8** (1:1 ratio, 7 mg), and from the most polar fractions **8** (48 mg, 21%) was afforded as an amorphous solid. The compound **8** turned out to be rather unstable on standing, so most of the sample was used for the next reduction without further purification.

Compound **7**: mp 210°C (prisms, from ether–hexane); $[\alpha]_D^{25}$ 54.3 (*c* 1.1, $CHCl_3$); ^{1}H NMR δ: 0.18 (m, 1H), 0.75 (s, 3H), 0.94 (s, 3H), 0.96 (s, 3H), 5.21 (s, 1H, exchangeable with D_2O), 6.90–8.04 (12H); IR (KBr) cm^{-1} 3414, 1767. Anal. calcd for $C_{30}H_{26}O_5$: C, 77.23; H, 5.62. Found: C, 77.48; H, 5.62.

Compound **8**: amorphous solid; $[\alpha]_D^{22}$ −111.9 (*c* 1.0, $CHCl_3$); ^{1}H NMR δ: 0.80 (s, 3H), 0.88 (s, 3H), 0.95 (s, 3H), 5.14 (s, 1H, exchangeable with D_2O), 6.85–8.00 (12H); IR ($CHCl_3$) cm^{-1} 3524, 1788. HRMS calcd for $C_{30}H_{26}O_5$: 466.1780. Found: 466.1775. Purity was assayed by ^{1}H NMR.

3.6. Camphanates **9** and **10**

The esterification of racemic **1** (143 mg, 0.5 mmol) with (−)-camphanic chloride (238 mg, 1.1 mmol, 2.2 equiv.) in pyridine (3.0 ml) was undertaken in the same manner as above to give a residue (352 mg). The precipitates of **10** (85 mg, 26%) were obtained when the residue was treated with AcOEt. After filtration, the mother liquor was concentrated and subjected to preparative TLC to give **9** (57 mg, 18%) as an amorphous solid together with 21 mg (6%) of **10** and 72 mg of the mixture of **9** and **10** (1:1). An analytical sample of **10** was obtained by recrystallization from AcOEt as prisms.

Compound **9**: mp 285–286°C (prisms, from AcOEt); $[\alpha]_D^{23}$ 41.0 (*c* 1.2, $CHCl_3$); ^{1}H NMR δ −0.06 (1H, m), 0.82 (3H, s), 0.95 (3H, s), 0.96 (3H, s), 6.98–7.95 (12H); IR ($CHCl_3$) cm^{-1} 1786. HRMS calcd for $C_{40}H_{38}O_8$: 646.2567. Found: 646.2576. Purity was assayed by ^{1}H NMR.

Compound **10**: mp 286°C (prisms, from AcOEt); $[\alpha]_D^{23}$ −166.5 (*c* 0.55, $CHCl_3$); ^{1}H NMR δ 0.81 (3H, s), 0.84 (3H, s), 0.93 (3H, s), 7.03–7.90 (12H); IR (KBr) cm^{-1} 1769. Anal. calcd for $C_{40}H_{38}O_8$: C, 74.28; H, 5.92. Found: C, 74.27; H, 5.88.

3.7. Reduction of **7**. General procedure for reductive removal of the camphanic group

A mixture of **7** (23 mg, 0.062 mmol), $LiAlH_4$ (8.0 mg, 0.22 mmol) in THF (5.0 ml) was stirred for 1 h at room temperature. After cooling to 0°C, excess reagent was decomposed by careful addition of cold aqueous $NaHCO_3$ solution, and the mixture was extracted with AcOEt. The organic extracts were washed with water, dried over $MgSO_4$, and then concentrated in vacuo to leave a residue (23 mg), which was subjected to preparative TLC on silica gel with hexane:AcOEt (3:1), to give (*S*)-**1** (15 mg, 85%).

In the same way as above, starting from **8** (20 mg), **9** (22 mg) and **10** (20 mg), the optically active (*R*)-**1** (9.0 mg, 72%, 98% ee), (*S*)-**1** (8.0 mg, 82%, 95% ee), and (*R*)-**1** (7.0 mg, 77%, 99% ee) were obtained, respectively.

References

1. Fuji, K.; Yang, S.; Tanaka, K.; Asakawa, Y.; Hao, X. *Tetrahedron Lett*. **1996**, *37*, 7373–7376.
2. Tanaka, K.; Asakawa, Y.; Nuruzzaman, M.; Fuji, K. *Tetrahedron: Asymmetry* **1997**, *8*, 3637–3645.
3. Fuji, K.; Kawabata, T.; Kuroda, A. *J. Org. Chem*. **1995**, *60*, 1914–1915.
4. Kawabata, T.; Kuroda, A.; Nakata, E.; Takasu, K.; Fuji, K. *Tetrahedron Lett*. **1996**, *37*, 4153–4156.
5. Fukushi, Y.; Shigematu, K.; Mizutani, J.; Tahara, S. *Tetrahedron Lett*. **1996**, *37*, 4737–4740.
6. Artz, S. P.; de Grandpre, M. P.; Cram, D. J. *J. Org. Chem*. **1985**, *50*, 1486–1496.
7. Fabbri, D.; Delogu, G.; De Lucchi, O. *J. Org. Chem*. **1995**, *60*, 6599–6601.
8. Meyers, A. I.; McKennon, M. J. *Tetrahedron Lett*. **1995**, *36*, 5869–5872.
9. Fuji, K.; Sakurai, M.; Kinoshita, T.; Tada, T.; Kuroda, A.; Kawabata, T. *Chem. Pharm. Bull*. **1997**, *45*, 1524–1525.
10. Meyers, A. I.; Price, A. *J. Org. Chem*. **1998**, *63*, 412–413.
11. Neither neutralization nor acidification was necessary before extraction.