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Facile synthesis of enantiopure 1,1′-binaphthyl-2,2′-dicarboxylic acid via lipase-catalyzed kinetic resolution

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Abstract

Enantiopure 1,1′-binaphthyl-2,2′-dicarboxylic acids (*R*)-**1** and (*S*)-**1** have been synthesized through the lipase-catalyzed kinetic resolution of the racemic 2,2-bis(hydroxymethyl)-1,1′-binaphthyl (±)-**2** and subsequent oxidation of the hydroxymethyl groups. © 2000 Elsevier Science Ltd. All rights reserved.

1. Introduction

Enantiopure 1,1′-binaphthyl-2,2′-dicarboxylic acids **1** have received considerable attention as chiral building blocks for such valuable compounds as chiral catalysts for asymmetric epoxidation.[1] The conventional method to prepare **1**, however, requires toxic brucine or quinine for the resolution.[2] To remove these drawbacks resolutions of (±)-**1** via 1-phenylethylamide[3] and diastereoselective Ullmann reactions with 2,2′-dihydroxy-1,1′-binaphthyl[4a] or an oxazoline as the chiral auxiliary have been reported.[4b] Although excellent yields and strereoselectivities were accomplished, they are not completely satisfactory for a practical use because they require a stoichiometric amount of the covalently-bonded chiral auxiliary. Another synthesis of enantiopure **1** through palladium-catalyzed methoxycarbonylation of a ditriflate of 2,2′-dihydroxy-1,1′-binaphthyl was reported.[5] However, it requires an expensive starting material and reagents such as enantiopure 2,2′-dihydroxy-1,1′-binaphthyl and trifluromethanesulfonic anhydride. A conceptually attractive catalytic asymmetric synthesis of enantiopure 2,2′-dimethyl-1,1′-binaphthyl, a possible precursor of **1**, has been reported.[6] While it should provide the best approach to **1**, further investigation on an economical synthesis of the chiral ferrocenyl phosphine ligand or development of an inexpensive alternative is needed for a practical large-scale preparation. We report herein a novel and facile synthesis of **1** by means of the lipase-catalyzed kinetic resolution of the racemic 2,2′-bis(hydroxymethyl)-1,1′-binaphthyl (±)-**2**.

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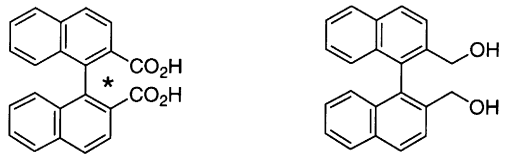
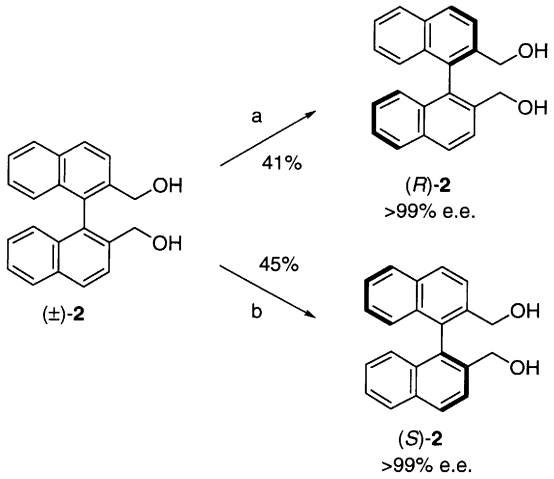


(*R*)-**1**, (*S*)-**1** (±)-**2**

2. Results and discussion

The enzymatic resolution of biaryls carrying axial chirality has so far been rarely described except for an enantioselective reduction of racemic 2-formyl-1,1′-binaphthyls by baker's yeast,[7] and lipase-catalyzed asymmetric acylation or hydrolysis of racemic 2,2′-dihydroxy-1,1′-binaphthyl derivatives.[8] We first attempted the enzymatic resolution of racemic 1,1′-binaphthyl-2,2′-dicarboxylic acid (±)-**1**. However, all attempts failed even in the non-selective enzymatic esterification of (±)-**1**. The results are in good accordance with the reported observation in that an aromatic carboxylic acid cannot be a substrate for the enzymatic acyl-transfer reactions.[9]

The kinetic resolution of 1,1′-bis(hydroxymethyl)-2,2′-binaphthyl (±)-**2**,[10] a possible precursor of **1**, was thus investigated (Scheme 1

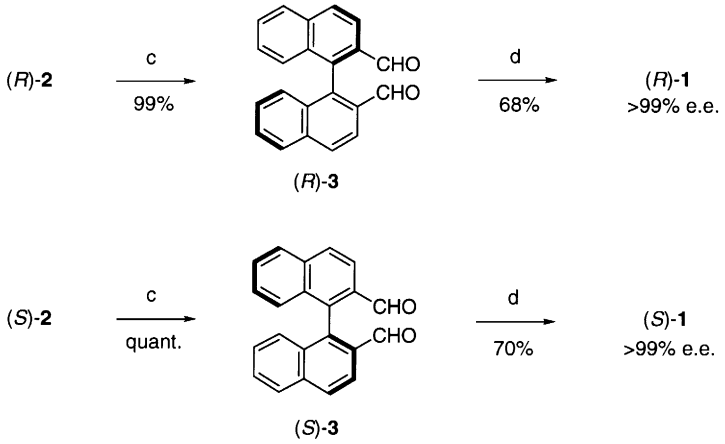


Scheme 1. a: Lipase SM, vinyl hexanoate, *tert*-BME, 30°C, 45 h; b: Lipase CE, vinyl hexanoate, *tert*-BME, 30°C, 24 h

) as an alternative. The compound (±)-**2** was prepared in four steps from 1-bromo-2-methylnaphthalene according to the reported procedure.[10b] Several enzymes were tested for the asymmetric acylation of (±)-**2** with vinyl acetate used as an acyl donor in *tert*-butyl methyl ether (*tert*-BME). Among them, lipase SM[11] (*Serratia marcescens*, lyophilized powder, Tanabe Seiyaku Co., Ltd) was found to catalyze selectively the acylation of (*S*)-**2** to leave virtually enantiopure diol (*R*)-**2** (>99% e.e.) in 29% yield. In contrast to the lipase-catalyzed monoacylation of 2,2′-dihydroxy-1,1′-binaphthyl,[8b] mono- and diacylation took place in the reaction to give the monoacylated (*S*)-**2** in 60% yield with poor selectivity (43% e.e.) along with diacylated compound in 10% yield (29% e.e.). The yield of (*R*)-**2** was improved when vinyl hexanoate was employed as the acyl donor to give (*R*)-**2** (>99% e.e.) in 41% yield.

The oxidation of the hydroxymethyl groups of (*R*)-**2** to the dicarboxylic acid (*R*)-**1** was then investigated. The reported method to prepare an aldehyde **3** requires three steps involving the treatment with toxic

silver nitrate; direct oxidation of **2** to **3** using dinitrogen tetroxide failed.[12] We found that treatment of the enantiomerically pure diol (*R*)-**2** with manganese(IV) oxide in toluene at ambient temperature provided an aldehyde (*R*)-**3** in 99% yield. The aldehyde (*R*)-**3** was treated with sodium chlorite in the presence of hydrogen peroxide to give the desired dicarboxylic acid (*R*)-**1** (>99% e.e.) in 68% yield (Scheme 2).



Scheme 2. c: MnO_2, toluene; d: $NaClO_2$, H_2O_2, NaH_2PO_4, H_2O, CH_3CN

Further screening of the enzyme was required in order to obtain the antipode (*S*)-**1** because the acylated (*S*)-**2** of high enantiomeric purity was not obtained in the lipase SM-catalyzed asymmetric acylation of (±)-**2**. As a result of the screening, lipase CE (*Humicola* sp., Amano Pharmaceutical Co., Ltd) was found to selectively acylate (*R*)-**2**, leaving (*S*)-**2** in >99% e.e. and 45% yield. The enantiomerically pure diol (*S*)-**2** was subjected to the two-step oxidation to provide the corresponding dicarboxylic acid (*S*)-**1** (>99% e.e.) in 70% yield.

In conclusion, a facile synthesis of enantiopure 1,1′-binaphthyl-2,2′-dicarboxylic acids (*R*)-**1** and (*S*)-**1** was accomplished. Either enantiomer of **1** can be prepared by proper choice of the enzyme, i.e. lipase SM for the *R*-isomer and lipase CE for the *S*-isomer. The present synthesis is advantageous in terms of simple operations and high yields of the enzymatic resolutions without the use of any toxic resolving agents.

3. Experimental

Melting points were measured using a Yamato melting point apparatus and are uncorrected. Infrared spectra were taken by the use of a Perkin–Elmer 1600 infrared spectrometer and are reported as $\lambda_{max}(cm^{-1})$. ^1H NMR were recorded on a Bruker AC-200 (200 MHz) spectrometer and are reported in δ values. Mass spectra were taken by using a HITACHI M-2000A mass spectrometer at an ionizing potential of 70 eV. Microanalyses were performed by a Perkin–Elmer 2400 Series II CHNS/O analyser. Optical rotations were measured on a Perkin–Elmer 243 polarimeter, and $[\alpha]_D$-values are given in 10^{-1} deg cm^2 g^{-1}.

Thin-layer chromatography was performed on E. Merck 0.25 mm precoated glass backed plates (60 F_{254}). Development was accomplished using either 20% phosphomolybdic acid in ethanol–heat or visualized by UV light where feasible. Flash chromatography was accomplished using Kieselgel 60 (230–400 mesh, E. Merck). Lipase CE was a generous gift from Amano Pharmaceutical Co., Ltd. Manganese(IV) oxide was purchased from Tosoh Corporation and used without further purification.

3.1. (R)-2,2′-Bis(hydroxymethyl)-1,1′-binaphthyl (R)-2 (acyl donor: vinyl acetate)

Into a mixture of (±)-**2** (1.0 g, 3.2 mmol) in *tert*-BME (100 mL) were added lipase SM[11] (lyophilized powder, 1.0 g), vinyl hexanoate (9.3 g, 0.11 mol) and water (50 μl), and the mixture was stirred at 30°C for 24 h. The mixture was filtered and the filtrate was evaporated in vacuo. The residue was purified by silica gel column chromatography (*n*-hexane:AcOEt, 4:1) to give (*R*)-**2** (290 mg, 29%) (>99% e.e.), monoacetyl (*S*)-**2** (679 mg, 60%) and diacetyl (*S*)-**2** (127 mg, 10%). (*R*)-**2**: colorless crystals; mp 170°C (lit.[10a] 168–170°C); IR (KBr) ν_{max} 3247, 3040, 2930, 2875 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.87 (brs, 2H), 4.09 (d, *J*=12 Hz, 2H), 4.36 (d, *J*=12 Hz, 2H), 7.00–7.04 (m, 2H), 7.18–7.26 (m, 2H), 7.40–7.49 (m, 2H), 7.74–7.78 (m, 2H), 7.90–8.01 (m, 4H). MS *m/z*: 314 (M^+); $[\alpha]_D^{25}$ +68.5 (*c* 1.0, $CHCl_3$) (lit.[10a] $[\alpha]_D^{23}$ +67.9 (*c* 1.06, acetone)). Anal. calcd for $C_{22}H_{18}O_2$: C, 84.05; H, 5.77. Found: C, 83.80; H, 5.66; >99% e.e. (HPLC: Chiralcel OD (Daicel), *n*-hexane:ethanol, 60:1, 1 mL/min, 30°C, 224 nm); monoacetyl (*S*)-**2** ((*S*)-2-acetoxymethyl-2′-hydroxymethyl-1,1′-binaphthyl): colorless oil; IR (Nujol) ν_{max} 3420, 3058, 1738 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.91 (s, 3H), 4.30 (s, 2H), 4.70–4.96 (m, 2H), 7.00–7.10 (m, 2H), 7.20–7.30 (m, 2H), 7.40–7.51 (m, 2H), 7.64–7.69 (m, 1H), 7.81–8.01 (m, 5H); MS *m/z*: 356 (M^+); 43% e.e. (HPLC: Chiralcel OD (Daicel), *n*-hexane:ethanol, 60:1, 1 mL/min, 30°C, 224 nm); diacetyl (*S*)-**2** ((*S*)-2,2′-bis(acetoxymethyl)-1,1′-binaphthyl): colorless oil; IR (Nujol) ν_{max} 1737 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.85 (s, 6H), 4.74–4.89 (m, 4H), 7.04–7.08 (m, 2H), 7.21–7.29 (m, 2H), 7.43–7.51 (m, 2H), 7.65–7.70 (m, 2H), 7.91–8.03 (m, 4H); MS *m/z*: 398 (M^+); 29% e.e. (The e.e. was determined by conversion to 2,2′-bis(hydroxymethyl)-1,1′-binaphthyl by the treatment with NaOMe in methanol followed by HPLC analysis (HPLC: Chiralcel OD (Daicel), *n*-hexane:ethanol, 60:1, 1 mL/min, 30°C, 224 nm).)

3.2. (R)-2,2′-Bis(hydroxymethyl)-1,1′-binaphthyl (R)-2 (acyl donor: vinyl hexanoate)

Into a mixture of (±)-**2** (200 mg, 0.64 mmol) in *tert*-BME (17 mL) were added lipase SM[7] (lyophilized powder, 40 mg), vinyl hexanoate (2.8 g, 16.4 mmol) and water (20 μl), and the mixture was stirred at 30°C for 45 h. The mixture was filtered and the filtrate was evaporated in vacuo. The residue was purified by silica gel column chromatography (*n*-hexane:AcOEt, 4:1) to give (*R*)-**2** (82 mg, 41%) (>99% e.e.) in colorless crystals. Mp, IR, ^1H NMR and MS spectra were identical with those of (*R*)-**2** obtained above; optical purity: >99% e.e. (HPLC: Chiralcel OD (Daicel), *n*-hexane:ethanol, 60:1, 1 mL/min, 30°C, 224 nm).

3.3. (S)-2,2′-Bis(hydroxymethyl)-1,1′-binaphthyl (S)-2

Using the same procedure as for the synthesis of (*R*)-**2** (experiment 3.2.) except using lipase CE and the reaction period of 24 h, the compound (*S*)-**2** was obtained in 45% yield. Mp 169°C; IR, ^1H NMR and MS spectra of (*S*)-**2** were identical with those of (*R*)-**2**; $[\alpha]_D^{25}$ −70.7 (*c* 1.05, $CHCl_3$). Anal. calcd for $C_{22}H_{18}O_2$: C, 84.05; H, 5.77. Found: C, 83.69; H, 5.69; >99% e.e. (HPLC: Chiralcel OD (Daicel), *n*-hexane:ethanol, 60:1, 1 mL/min, 30°C, 224 nm).

3.4. (R)-2,2′-Diformyl-1,1′-binaphthyl (R)-3

A mixture of (*R*)-**2** (500 mg, 1.6 mmol) in toluene (10 mL) was added MnO_2 (5 g) and the mixture was stirred at 25°C for 17 h. The mixture was filtered through Celite and the filtrate was evaporated in vacuo to give (*R*)-**3** (486 mg, 99%) in colorless oil. IR (Nujol) ν_{max} 1692, 1608, 1594 cm^{-1}; ^1H NMR

($CDCl_3$) δ 7.24 (dd, *J*=0.5, 8.4 Hz, 2H), 7.37 (ddd, *J*=1.3, 7.0, 8.3 Hz, 2H), 7.64 (ddd, *J*=1.3, 6.8, 7.8 Hz, 2H), 8.00 (d, *J*=8.2 Hz, 2H), 8.13 (d, *J*=8.7 Hz, 2H), 8.22 (d, *J*=8.2 Hz, 2H), 9.62 (d, *J*=0.8 Hz, 2H). MS *m/z*: 310 (M^+); $[\alpha]_D^{25}$ +3.2 (*c* 1.04, $CHCl_3$).

3.5. (S)-2,2′-Diformyl-1,1′-binaphthyl (S)-3

Using the same procedure for the synthesis of (*R*)-**3**, the compound (*S*)-**3** was obtained in quantitative yield as a colorless oil which showed the same IR, ^{1}H NMR and MS spectra as the compound (*R*)-**3** except specific rotation: $[\alpha]_D^{25}$ −3.1 (*c* 1.01, $CHCl_3$).

3.6. (R)-1,1′-Binaphthyl-2,2′-dicarboxylic acid (R)-1

Into a mixture of (*R*)-**3** (1 g, 3.2 mmol), $NaH_2PO_4 \cdot H_2O$ (260 mg, 1.9 mmol) and H_2O_2 (0.8 mL) in CH_3CN (10 mL) was added dropwise $NaClO_2$ (1 g, 11 mmol) in H_2O (10 mL) at 25°C for 15 min and the mixture was stirred at 40°C for 20 min. After adding Na_2SO_3 (60 mg, 0.5 mmol), the mixture was evaporated in vacuo. The mixture was acidified by adding 2N HCl and extracted with AcOEt. The extracts were washed with water, dried over anhydrous $MgSO_4$ and evaporated in vacuo. The crystals formed were collected by adding *n*-hexane to afford (*R*)-**1** (755 mg, 68%) in colorless crystals. Mp 200°C (dec.) (lit.[2b] 197–199°C (dec.)); IR (KBr) ν_{max} 1696 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 7.04–7.26 (m, 4H), 7.44–7.53 (m, 4H), 7.89–8.00 (m, 4H), 8.11–8.15 (m, 2H); MS *m/z*: 342 (M^+); $[\alpha]_{546}^{25}$ +127.0 (*c* 1.0, 1N NaOH) (lit.[2b] $[\alpha]_{546}^{25}$ +127.0 (*c* 1.0, 1N NaOH)). Anal. calcd for $C_{22}H_{14}O_4$: C, 77.18; H, 4.12. Found: C, 77.15; H, 3.99; >99% e.e. (HPLC: Chiralcel OD (Daicel), *n*-hexane:ethanol:trifluoroacetic acid, 90:10:0.1, 1 mL/min, 35°C, 254 nm).

3.7. (S)-1,1′-Binaphthyl-2,2′-dicarboxylic acid (S)-1

Using the same procedure for the synthesis of (*R*)-**1**, the compound (*S*)-**1** was obtained in 70% yield from (*S*)-**3** as colorless crystals which showed the same mp, IR, ^{1}H NMR and MS spectra as the compound (*R*)-**1** except specific rotation: $[\alpha]_{546}^{25}$ −127.0 (*c* 1.0, 1N NaOH) (lit.[2b] $[\alpha]_{546}^{25}$ −127.0 (*c* 1.0, 1N NaOH)).

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