Pergamon

Tetrahedron: *Asymmetry* 11 (2000) 2801–2807

TETRAHEDRON: *ASYMMETRY*

First enantioselective syntheses of (2*R*,3*R*)- and (2*S*,3*S*)-3-(4-hydroxy-3-methoxyphenyl)-2-hydroxymethyl-1,4-benzodioxan-6-carbaldehyde

Wenxin Gu,[a] Xiaochuan Chen,[a] Xinfu Pan,[a,*] Albert S. C. Chan[b] and Teng-Kuei Yang[c]

[a]*Department of Chemistry, National Laboratory of Applied Organic Chemistry, Lanzhou University, Lanzhou 730000, PR China*

[b]*Union Laboratory of Asymmetry Synthesis and Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hong Kong, Hong Kong*

[c]*Department of Chemistry, National Chung-Hsing University, Taichang, Taiwan*

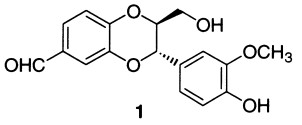
Received 24 May 2000; accepted 12 June 2000

Abstract

An enantioselective and regioselective total synthesis approach to chiral 1,4-benzodioxane lignans (2*R*,3*R*)- and (2*S*,3*S*)-3-(4-hydroxy-3-methoxyphenyl)-2-hydroxymethyl-1,4-benzodioxan-6-carbaldehyde is reported.

1. Introduction

The 1,4-benzodioxane framework has often been found in biologically active lignans. Silybin[1] and americanin A[2] are antihepatotoxic, and haedoxan A[3] has insecticidal activity. Silybin has been used as a folk medicine in Jammu aur Kashmir and Europe.[1] This type of natural product, which has shown a variety of bioactivities, is of synthetic interest. Recently, several efficient syntheses of natural 1,4-benzodioxane lignans have been reported.[4] Recently, we reported the total synthesis of (±)-sinaiticin, a natural flavonolignan.[5] An unsolved problem in this area has been the asymmetric synthesis of chiral 1,4-benzodioxane lignans.[6]



1

We now report the first enantioselective and regioselective synthetic approach to the 3-aryl-1,4-benzodioxane moiety, the important structure of natural 1,4-benzodioxane lignans.[1] In this

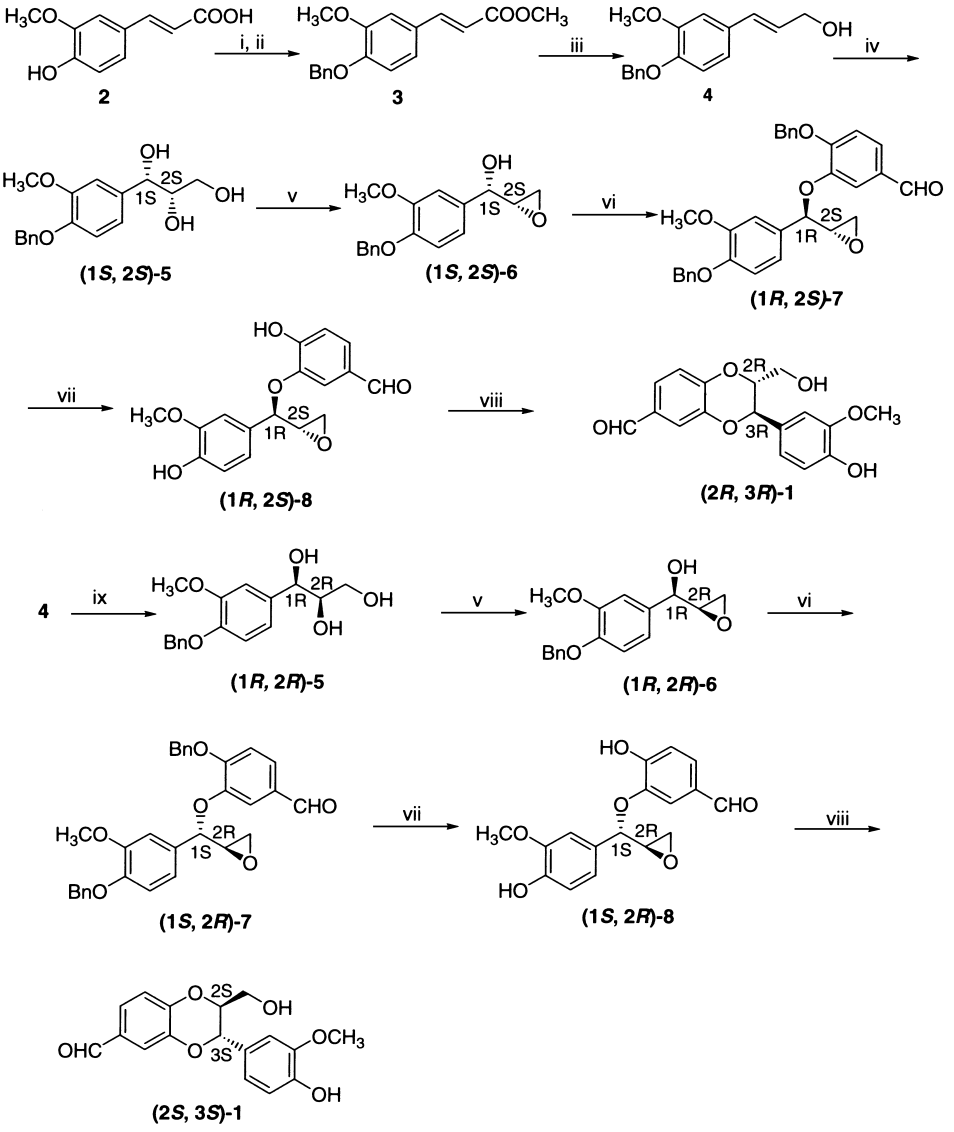
* Corresponding author. E-mail: panxf@lzu.edu.cn

0957-4166/00/$ - see front matter
PII: S0957-4166(00)00234-2

approach the important key intermediate for the synthesis of silybin[7] (2*R*,3*R*)- and (2*S*,3*S*)-3-(4-hydroxy-3-methoxyphenyl)-2-hydroxymethyl-1,4-benzodioxan-6-carbaldehyde is synthesized.

2. Results and discussion

As shown in Scheme 1, ferulic acid **2** was converted to a benzyl ether **3** in 94% yield by esterification with acidic methanol followed by treatment with benzyl chloride. Reduction of **3**



Scheme 1. Reagents and conditions: (i) MeOH, H_2SO_4, 90°C, 16 h; (ii) BnCl, DMF, K_2CO_3, 160°C, 3 h (i and ii 94%); (iii) LAH, THF, –10°C, 1 h (88%); (iv) AD-mix-α, $MeSO_2NH_2$, *t*-BuOH, H_2O, 0°C, 20 h (94%); (v) *N*-tosylimidazole, NaH, THF, rt, 2 h (71%); (vi) DE (83%); (vii) Pd/C (5%), H_2, EtOAc, rt, 6 h (90%); (viii) K_2CO_3, MeOH, rt, 1 h (98%); (ix) AD-mix-β, $MeSO_2NH_2$, *t*-BuOH, H_2O, 0°C, 20 h (90%)

gave the corresponding unsaturated alcohol **4** in 88% yield. Asymmetric dihydroxylation of **4** by AD-mix-α afforded (1*S*,2*S*)-**5** in 92% e.e. and 94% yield.[8] (1*S*,2*S*)-**5** was treated with *N*-tosylimidazole[9] in dry THF giving oxirane (1*S*,2*S*)-**6** in 71% yield. Mitsunobu reaction[10] between (1*S*,2*S*)-**6** and 4-benzyloxy-3-hydroxybenzaldehyde[11] gave a characterized ether (1*R*,2*S*)-**7** in 83% yield. In this reaction the absolute configuration of the C_1-position was converted completely by a S_N2-type nucleophilic displacement of 4-benzyloxy-3-hydroxybenzaldehyde. Two benzyl groups of (1*R*,2*S*)-**7** were removed by hydrogenolysis under an atmospheric pressure of hydrogen in the presence of 5% palladized charcoal in ethyl acetate to afford (1*R*,2*S*)-**8** in 90% yield as well as the epoxide moiety remaining intact.[12] (1*R*,2*S*)-**8** underwent cyclization with potassium carbonate to afford (2*R*,3*R*)-**1** in 98% yield. In this reaction an intramolecular nucleophilic attack at the C_2-position of oxirane by the phenol hydroxyl as its potassium salt led to a complete inversion of the absolute configuration of the C_2-position and the formation of 1,4-benzodioxane.[13] In the ^{1}H NMR spectrum of (2*R*,3*R*)-**1** H-3 resonated a doublet signal at δ 5.10 with a coupling constant ($J = 8$ Hz) indicating a typical of *trans*-isomer and *threo* configuration. ^{13}C NMR spectrum showed δ 61.5, 77.5, 79.5 indicating a six-membered 2-hydroxymethyl-3-aryl-1,4-benzodioxane skeleton.[14] Similarly, asymmetric dihydroxylation of **4** by AD-mix-β afforded (1*R*,2*R*)-**5** in 91% e.e. and 90% yield.[8] (1*R*,2*R*)-**5** was treated in the same four steps to afford (2*S*,3*S*)-**1** in good yield.

Advantages of the synthetic approach include: (i) 2-aryl- and 3-aryl-1,4-benzodioxane lignans can be synthesized regioselectively when 3-benzyloxy-4-hydroxybenzaldehyde and 4-benzyloxy-3-hydroxybenzaldehyde was used, respectively; and (ii) S_N2-type nucleophilic displacement on the two stereogenic carbons led to the complete conversion of their absolute configurations, so that the absolute configuration of 1,4-benzodioxane can be assigned since the *trans*-isomers are the only products.

3. Experimental

3.1. General

The ^{1}H NMR and ^{13}C NMR data were recorded with Bruker AM-80 or AM-400 MHz spectrometers. The chemical shifts are reported in ppm relative to TMS. Optical rotations were determined on a JASCO J-20C polarimeter with 0.2 dm tube. Mass spectra were recorded on a ZAB-HS mass spectrometer. Microanalyses were performed on a MOD-1106 elemental analyser. Chiral analysis was performed on Varian Dynamax SD-300 using Chiralcel column CDMPC (150×4.6 mm D) with hexane/isopropyl alcohol as eluant. Flash column chromatography was generally performed on silica gel (200–300 mesh) eluting with petroleum ether:EtOAc and TLC inspections on silica gel GF_{254} plates with petroleum ether:EtOAc, if not noted especially below.

3.2. 4-Benzyloxy-3-methoxycinnamyl alcohol *4*

At –10°C, to a suspension of $LiAlH_4$ (1.7 g, 45 mmol) in dry diethyl ether (100 mL), compound **7** (8.9 g, 30 mmol) in dry THF (100 mL) was added dropwise. The mixture was stirred at this temperature for 1 h. Then the reaction was quenched with ice-water, extracted with ether and the combined organic layer was washed with brine, then dried with Na_2SO_4. The solvent was distilled

off under reduced pressure, the residue was flash chromatographed using petroleum ether and ethyl acetate (5:1, v/v) as eluent. A white solid **4** (7.1 g) was obtained in 88% yield. M.p. 89–90°C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.90 (s, 3H), 4.30 (d, 2H, J = 5.3 Hz), 5.16 (s, 2H), 6.26 (dt, 1H, J = 5.8, 15.8 Hz), 6.55 (d, 1H, J = 16.0 Hz), 6.81–7.44 (m, 8H). MS (EI): 270, 179, 151, 119, 91 (Found: C, 75.60; H, 6.73. $C_{17}H_{18}O_3$ requires: C, 75.53; H, 6.71%).

3.3. (1S,2S)-1-(4-Benzyloxy-3-methoxyphenyl)-2,3-dihydroxypropanol (1S,2S)-5

To a stirred solution of *t*-BuOH (50 mL) and H_2O (50 mL) was added AD-mix-α (14 g), $MeSO_2NH_2$ (950 mg), and the mixture was stirred at room temperature until both phases were clear, and then cooled to 0°C. Compound **4** (2.7 g, 0.1 mol) was added at once, and the mixture was stirred vigorously at 0°C until TLC revealed the absence of **4**. The reaction was quenched at 0°C by addition of Na_2SO_3 (15 g), then warmed to room temperature and stirred for 0.5 h. The reaction mixture was extracted with CH_2Cl_2 (3×100 mL) and dried (Na_2SO_4), then the CH_2Cl_2 was distilled off. The residue was flash chromatographed using petroleum ether and ethyl acetate (1:1, v/v) as eluent. A white powder (1*S*,2*S*)-**5** (2.9 g) was obtained in 94% yield. Enantiomeric purity: 92% e.e. (Chiralcel column CDMPC, 150×4.6 mm D, *n*-hexane:isopropyl alcohol, 50:1, 1 mL/min, 25°C, retention times 26.6 min). M.p. 155–156°C. $[\alpha]_D^{25} = -76$ (*c* 1.50, MeOH). ^{1}H NMR (400 MHz, d_6-acetone): δ 3.39 and 3.47 (2dd, 2H, J = 3.0, 9.7 Hz), 3.80 (m, 1H), 3.86 (s, 3H), 4.64 (d, 1H, J = 6.5 Hz), 5.13 (s, 2H), 6.78–7.44 (m, 8H). MS (EI): 304, 286, 243, 153, 91. (Found: C, 66.98; H, 6.64. $C_{17}H_{20}O_5$ requires: C, 67.09; H, 6.62%).

3.4. (1R,2R)-1-(4-Benzyloxy-3-methoxyphenyl)-2,3-dihydroxypropanol (1R,2R)-5

By a procedure similar to the preparation for (1*S*,2*S*)-**5**, the reaction of **4** (2.7 g, 0.1 mmol), AD-mix-β (14 g), $MeSO_2NH_2$ (950 mg), *t*-BuOH (50 mL) and H_2O (50 mL) gave (1*R*,2*R*)-**5** (2.7 g) in 90% yield. (1*R*,2*R*)-**5**: A white powder. Enantiomeric purity: 91% e.e. (Chiralcel column CDMPC, 150×4.6 mm D, *n*-hexane:isopropyl alcohol, 50:1, 1 mL/min, 25°C, retention times 30.4 min). M.p. 139–140°C. $[\alpha]_D^{25} = +74$ (*c* 1.50, MeOH) (Found: C, 67.05; H, 6.63. $C_{17}H_{20}O_5$ requires: C, 67.09; H, 6.62%). Other spectra data were the same as those of (1*S*,2*S*)-**5**.

3.5. (1S,2S)-2,3-Expoxy-1-(4-benzyloxy-3-methoxyphenyl)propanol (1S,2S)-6

Sodium hydride (50% oil dispersion) (270 mg, 5.6 mmol) was placed in a dry flask equipped with a magnetic stirrer and drying tube, and washed free of oil with pentane. Dry THF (10 mL) was added followed by (1*S*,2*S*)-**5** (850 mg, 2.8 mmol), and the mixture was stirred for 1 h at room temperature. *N*-Tosylimidazole (650 mg, 2.9 mmol) was then added and the suspension stirred for a further 3 h. The reaction mixture was then poured with stirring into ice-water, extracted with diethyl ether and the combined organic layer was washed with brine, then dried with Na_2SO_4. The solvent was distilled off under reduced pressure, the residue was flash chromatographed using petroleum ether and ethyl acetate (4:1, v/v) as eluent to afford (1*S*,2*S*)-**6** (570 mg, 71%) as a colorless oil. Enantiomeric purity: 92% e.e. (Chiralcel column CDMPC, 150×4.6 mm D, *n*-hexane: isopropyl alcohol, 50:1, 1 mL/min, 25°C, retention times 15.7 min). $[\alpha]_D^{20} = -52$ (*c* 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.77 and 2.81 (2dd, 2H, J = 3.1, 8.8 Hz), 3.19 (m, 1H), 3.89 (s, 3H), 4.37 (d, 1H, J = 6.3 Hz), 5.14 (s, 2H), 6.82–7.43 (m, 8H). MS (EI): 286, 268, 256, 243, 177, 91 (Found: C, 71.28; H, 6.32. $C_{17}H_{18}O_4$ requires: C, 71.31; H, 6.34%).

3.6. (1R,2R)-2,3-Expoxy-1-(4-benzyloxy-3-methoxyphenyl)propanol (1R,2R)-6

By a procedure similar to the preparation of (1*S*,2*S*)-**6**, the reaction of (1*R*,2*R*)-**5** (850 mg, 2.8 mmol) with *N*-tosylimidazole (650 mg, 2.9 mmol) gave (1*R*,2*R*)-**6** (550 mg) as a colorless oil in 68% yield. (1*R*,2*R*)-**6**: Enantiomeric purity: 91% e.e. (Chiralcel column CDMPC, 150×4.6 mm D, *n*-hexane:isopropyl alcohol, 50:1, 1 mL/min, 25°C, retention times 21.3 min). $[\alpha]_D^{20}=+52$ (*c* 1.00, $CHCl_3$) (Found: C, 71.25; H, 6.30. $C_{17}H_{18}O_4$ requires: C, 71.31; H, 6.34%). Other spectral data are the same as those of (1*S*,2*S*)-**6**.

3.7. (1R,2S)-4-Benzyloxy-3-[2,3-epoxy-1-(4-benzyloxy-3-methoxyphenyl)propoxy]benzaldehyde (1R,2S)-7

A solution of PPh_3 (520 mg, 2.0 mmol) and (1*S*,2*S*)-**6** (500 mg, 1.8 mmol) in dry THF (10 mL) was added dropwise to a solution of 4-benzyloxy-3-hydroxybenzaldehyde[11] (450 mg, 2.0 mmol) and DEAD (350 mg, 2.0 mmol) at room temperature under nitrogen. After stirring of the mixture overnight at room temperature, it was evaporated in vacuum. The residue was flash chromatographed using petroleum ether and ethyl acetate (2:1, v/v) as eluent. A white solid (1*R*,2*S*)-**7** (720 mg) was obtained in 83% yield. Enantiomeric purity: 92% e.e. (Chiralcel column CDMPC, 150×4.6 mm D, *n*-hexane:isopropyl alcohol, 50:1, 1 mL/min, 25°C, retention times 20.6 min). M.p. 76–78°C. $[\alpha]_D^{20}=+10$ (*c* 1.00, $CHCl_3$). ^1H NMR (400 MHz, d_6-acetone): δ 2.76 and 2.79 (2dd, 2H, $J=2.7$, 5.5 Hz), 3.38 (m, 1H), 3.76 (s, 3H), 5.08 (s, 2H), 5.31 (s, 2H), 5.42 (d, 1H, $J=4.0$ Hz), 7.00–7.72 (m, 16H), 9.77 (s, 1H). MS (EI): 496, 466, 375, 347, 269, 227, 91 (Found: C, 74.91; H, 5.66. $C_{31}H_{28}O_6$ requires: C, 74.98; H, 5.68%).

3.8. (1S,2R)-4-Benzyloxy-3-[2,3-epoxy-1-(4-benzyloxy-3-methoxyphenyl)propoxy]benzaldehyde (1S,2R)-7

By a procedure similar to the preparation of (1*R*,2*S*)-**7**, Mitsunobu reaction of (1*R*,2*R*)-**6** gave (1*S*,2*R*)-**7** (700 mg) in 81% yield. (1S, 2R)-**7**: A white powder. Enantiomeric purity: 91% e.e. (Chiralcel column CDMPC, 150×4.6 mm D, *n*-hexane:isopropyl alcohol, 50:1, 1 mL/min, 25°C, retention times 26.0 min). M.p. 90–92°C. $[\alpha]_D^{20}=-12$ (*c* 1.00, $CHCl_3$) (Found: C, 74.94; H, 5.66. $C_{31}H_{28}O_6$ requires: C, 74.98; H, 5.68%). Other spectral data were the same as those of (1*R*,2*S*)-**7**.

3.9. (1R,2S)-4-Hydroxy-3-[2,3-epoxy-1-(4-hydroxy-3-methoxyphenyl)propoxy]benzaldehyde (1R,2S)-8

A solution of (1*R*,2*S*)-**7** (500 mg, 1.0 mmol) in ethyl acetate (10 mL) was hydrogenated over 5% Pd–C (50 mg) under an H_2 atmosphere. The reaction mixture was filtered and the filtrate was concentrated. The residue was flash chromatographed using petroleum ether and ethyl acetate (1:2, v/v) as eluent. A white solid (1*R*,2*S*)-**8** (280 mg, 90%) was obtained. Enantiomeric purity: 92% e.e. (Chiralcel column CDMPC, 150×4.6 mm D, *n*-hexane:isopropyl alcohol, 50:1, 1 mL/min, 25°C, retention times 28.4 min). M.p. 135–136°C. $[\alpha]_D^{25}=+8.3$ (*c* 1.00, MeOH). ^1H NMR (d_6-acetone, 400 Hz): δ 2.83 and 2.86 (2dd, 2H, $J=2.5$, 12.2 Hz), 3.41 (m, 1H), 3.82 (s, 3H), 5.34 (d, 1H, $J=4.0$ Hz), 6.80–7.43 (m, 6H), 9.70 (s, 1H). MS (EI): 316, 179, 151, 137, 123, 93. IR (KBr/cm^{-1}): 3506, 3286, 3010, 2844, 1707, 1596, 1514, 1271, 1237 (Found: C, 64.61; H, 5.11. $C_{17}H_{16}O_6$ requires: C, 64.55; H, 5.10%).

3.10. (1S,2R)-4-Hydroxy-3-[2,3-epoxy-1-(4-hydroxy-3-methoxyphenyl)propoxy]benzaldehyde (1S,2R)-8

By a procedure similar to the preparation of (1*R*,2*S*)-**8**, debenzylation of (1*S*,2*R*)-**7** (500 g, 1.0 mmol) gave (1*S*,2*R*)-**8** (270 mg) in 85% yield. (1*S*,2*R*)-**8**: A white powder. Enantiomeric purity: 91% e.e. (Chiralcel column CDMPC, 150×4.6 mm D, *n*-hexane:isopropyl alcohol, 50:1, 1 mL/min, 25°C, retention times 32.0 min). M.p. 157–159°C. $[\alpha]_D^{25} = -7.6$ (*c* 1.00, MeOH) (Found: C, 64.58; H, 5.09. $C_{17}H_{16}O_6$ requires: C, 64.55; H, 5.10%). Other spectral data were the same as those of (1*R*,2*S*)-**8**.

3.11. (2R,3R)-3-(4-Hydroxy-3-methoxyphenyl)-2-hydroxymethyl-1,4-benzodioxan-6-carbaldehyde (2R,3R)-1

A mixture of (1*R*,2*S*)-**8** (100 mg, 0.3 mmol) and anhydrous K_2CO_3 (140 mg, 1.0 mmol) in MeOH (5 mL) was stirred at room temperature for 30 min. The solvent was evaporated and 2N HCl (2 mL) was added, then the mixture was extracted with EtOAc. The combined organic was washed with brine and dried with Na_2SO_4. The solvent was removed under reduced pressure. The residue was flash chromatographed using petroleum ether and ethyl acetate (1:2, v/v) as eluent to afford (2*R*,3*R*)-**1** (98 mg, 98%) as a white solid. Enantiomeric purity: 92% e.e. (Chiralcel column CDMPC, 150×4.6 mm D, *n*-hexane:isopropyl alcohol, 50:1, 1 mL/min, 25°C, retention times 34.3 min). M.p. 112–113°C. $[\alpha]_D^{25} = +13$ (*c* 0.9, $CHCl_3$). ^{1}H NMR (d_6-acetone, 400 Hz): δ 3.51 and 3.78 (2dd, 2H, $J = 12.5$, 4.0 Hz), 3.76 (s, 3H), 4.15 (m, 1H), 5.10 (d, 1H, $J = 8.0$ Hz), 6.71–7.47 (m, 6H), 9.86 (s, 1H). ^{13}C NMR (d_6-acetone, 100 Hz): 55.8, 61.5, 77.5, 79.5, 112.9–133.0, 191.2. MS (FAB): 317 (M+1). IR (KBr/cm^{-1}): 3444, 3351, 2937, 2856, 1739, 1606, 1598, 1270, 1246 (Found: C, 64.52; H, 5.08. $C_{17}H_{16}O_6$ requires: C, 64.55; H, 5.10%).

3.12. (2S,3S)-3-(4-Hydroxy-3-methoxyphenyl)-2-hydroxymethyl-1,4-benzodioxan-6-carbaldehyde (2S,3S)-1

By a procedure similar to the preparation of (2*R*,3*R*)-**1**, cyclization of (1*S*,2*R*)-**8** (100 mg, 0.3 mmol) gave (2*S*,3*S*)-**1** (90 mg) in 90% yield. (2*S*,3*S*)-**1**: A white powder. Enantiomeric purity: 91% e.e. (Chiralcel column CDMPC, 150×4.6 mm D, *n*-hexane:isopropyl alcohol, 50:1, 1 mL/min, 25°C, retention times 42.9 min). M.p. 137–139°C. $[\alpha]_D^{20} = -12$ (*c* 1.0, $CHCl_3$) (Found: C, 64.59; H, 5.09. $C_{17}H_{16}O_6$ requires: C, 64.55; H, 5.10%). Other spectral data were the same as those of (2*R*,3*R*)-**1**.

Acknowledgements

Support from the National Natural Science Foundation of China (No. 29972015) is gratefully acknowledged.

References

1. (a) Hansel, R.; Shulz, J.; Pelter, A. *J. Chem. Soc., Chem. Commun.* **1972**, 195–196; (b) *Chem. Commun.* **1975**, *108*, 1482–1501; (c) Wagner, H.; Horhammer, L.; Munster, R. *Arzneimittel-Forsch.* **1968**, *18*, 688; (d) Wanger, H.;

Diesel, P.; Seitz, M. *Arzneimittel-Forsch*. **1974**, *24*, 466–471; (e) Bandopadhyay, M.; Pardeshi, N. P.; Seshadri, T. R. *Indian J. Chem*. **1972**, *10*, 808; (f) Abraham, D. J.; Takagi, S.; Rosenstein, R. D.; Shiono, R. *Tetrahedron Lett*. **970**, 2675.
2. Woo, W. S.; Kang, S. S.; Wanger, H.; Chari, V. M. *Tetrahedron Lett*. **1978**, 3239–3242.
3. Taniguchi, E.; Imamura, K.; Ishibashi, F.; Matsui, T.; Nishio, A. *Agric. Biol. Chem*. **1989**, *53*, 631–649.
4. Merlini, L.; Zanarotti, A.; Pelter, A.; Rochefort, M. P.; Hansel, R. *J. Chem. Soc., Perkin Trans. 1* **1980**, 775.
5. She, X. G.; Jing, X. B.; Pan, X. F.; Chan, A. C.; Yang T. K. *Tetrahedron Lett*. **1999**, *40*, 4567–4570.
6. (a) Ward, R. S. *Nat. Prod. Rep*. **1997**, *14*, 43; (b) Ward, R. S. *Nat. Prod. Rep*. **1999**, *16*, 75–96.
7. Tanaka, H.; Shibata, M.; Ohira, K.; Ito, K. *Chem. Pharm. Bull*. **1985**, *33*, 1419–1423.
8. Sharpless, K. B.; Amberg, W.; Bennani, Y. L.; Crispino, G. A.; Hartung, J.; Jeong, K. S.; Kwong, H. L.; Morikawa, K.; Wang, Z. M.; Xu, D.; Zhang, X. L. *J. Org. Chem*. **1992**, *57*, 2768–2771.
9. Hicks, D. R.; Fraser-Reid, B. *Synthesis* **1974**, 203.
10. Mitsunobu, O. *Synthesis* **1981**, 1–26.
11. Kessar, S. V.; Guputa, Y. P.; Mohammad, T.; Goyal, M.; Sawal, K. K. *J. Chem. Soc., Chem. Commun*. **1983**, 400–401.
12. Taniguchi, E.; Yamauchi, S.; Nagata, S.; Ohnishi, T. *Biosci. Biotech. Biochem*. **1992**, *56*, 630–635.
13. Ganesh, T.; Krupadanam, G. L. D. *Synth. Commun*. **1998**, *28*, 3121–3131.
14. Fukiyama, Y.; Hasegawa, T.; Toda, M.; Kodama, M. *Chem. Pharm. Bull*. **1992**, *40*, 252.