Absolute Stereochemistry of Farfugin A[1]

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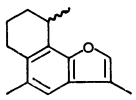
4,6-Dimethylcoumarin (**3**) was converted to an enantiomer (**1b**) of farfugin A, *via* a levorotatory carboxylic acid (**5b**). This led to the absolute configuration (**1a**) for farfugin A.

The structure of farfugin A, a dextrorotatory benzofuranosesquiterpene isolated from *Farfugium japonicum*, was shown to be **1**.[2] A skeletal rearrangement of furanoeremophilane-6β,10β-diol [(+)-**2**][3] gave farfugin A [(+)-**1**].[4] We wish to report the determination of an absolute configuration of farfugin A (**1a**), which is indispensable for elucidation of the mechanism of this rearrangement.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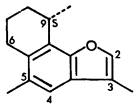
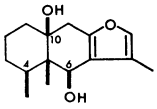

1a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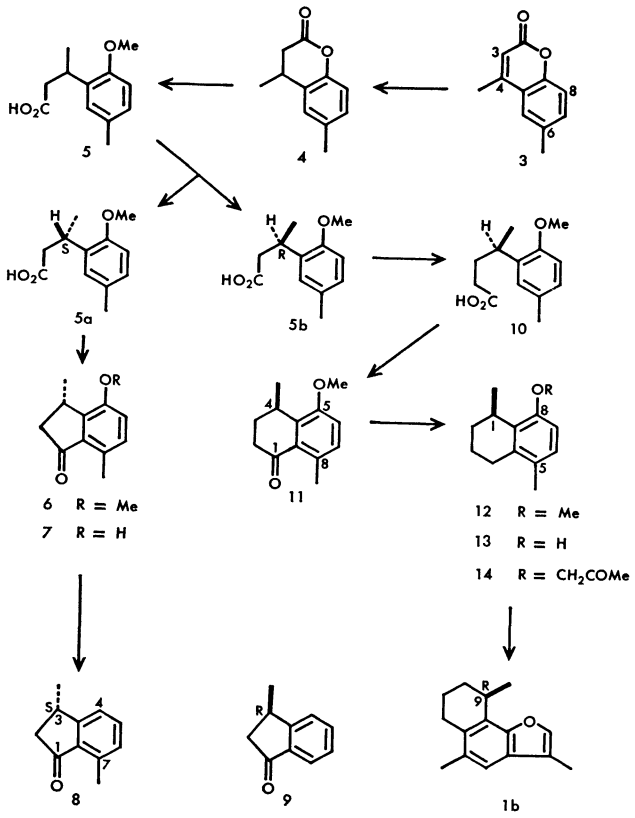
4,6-Dimethylcoumarin (**3**)[5] was hydrogenated over palladium-charcoal to yield a dihydro derivative (**4**;[6] mp 35—35.5 °C; yield: 90%). Alkaline hydrolysis of **4** followed by methylation with dimethyl sulfate gave 3-(2-methoxy-5-methylphenyl)butanoic acid (**5**; mp 60.5—61.5 °C; yield: 89%). A resolution of the (+)- and (−)-acid [(+)- and (−)-**5**] was carried out *via* their strychnine salts to give a dextrorotatory acid [**5a**; mp 60—60.5 °C, $[\alpha]_D$ +19° (C_6H_6)][7] and a levorotatory acid [**5b**; mp 60 °C, $[\alpha]_D$ −27° (C_6H_6)].[7]

The dextrorotatory acid (**5a**) was converted to (+)-3,7-dimethylindan-1-one (**8**) to determine an absolute configuration of **5a**. When **5a** was treated with polyphosphoric acid, **5a** was cyclized to give (+)-4-methoxy-3,7-dimethylindan-1-one (**6**; an oil; y: 94%), which was demethylated to yield a phenol (**7**;[8] mp 203 °C; yield: 68%). The phenol (**7**) was phosphorylated according to Kenner and Williams,[9] reduced with lithium in liquid ammonia, and then oxidized with Jones' reagent to give (+)-3,7-dimethylindan-1-one (**8**; an oil; y: 50%). These indanone derivatives (**6** and **8**)[10] showed the ORD curves which were almost mirror images to that of known (−)-(3R)-3-methylindan-1-one (**9**).[11] An asymmetric center of the dextrorotatory acid (**5a**) must therefore be in the configuration (S), and that of levorotatory acid (**5b**) in the configuration (R).

The levorotatory acid (**5b**) was subjected to the Arndt-Eistert homologation to give (−)-4-(2-methoxy-5-methylphenyl)-pentanoic acid (**10**; mp 87.5 °C; y: 75%),[12] which was converted *via* **11** and **12** to (+)-8-hydroxy-1,5-dimethyl-1,2,3,4-tetrahydronaphthalene (**13**; mp 91 °C; y: 72%) according to the procedures described in the literatures.[12] By the reaction sequence already reported,[2] **13** was converted to a (−)-8-acetonyloxy-1,5-dimethyl-1,2,3,4-tetrahydronaphthalene (**14**; mp 77 °C; y: 61%), which was then cyclized to give a levorotatory benzofuran [**1b**; mp



78 °C, $[\alpha]_D$−27° (EtOH); y: 55%). This compound (**1b**) was found to be an enantiomer of natural (+)-farfugin A[2] (*cf.* Experimental). Thus, the absolute stereochemistry of natural farfugin A was shown to be **1a** whose configuration at C-9 must be (S).

Experimental

IR spectra were measured using a Hitachi EPI-G2 spectrometer in Nujol mull, unless otherwise stated. UV spectra were determined on a Hitachi EPS-3 spectrophotometer. ORD measurements were carried out on a JASCO ORD/UV-5 spectrometer. Optical rotations were measured on a JASCO DIP-SL polarimeter. Mass spectra were taken on a Hitachi RMU-6-Tokugata mass spectrometer with a direct inlet system operating at 70 eV. PMR spectra were measured using a JEOL PS-100 (100 MHz) or a Hitachi R-20 (60 MHz) spectrometer. Chemical shifts were expressed in δ downfield from TMS as internal standard, and coupling constants in Hz. Thin layer chromatography (tlc) was carried out on Kieselgel PF_{254} (E. Merck, Darmstadt). For column chromatography Wakogel C-200 (Wako Pure Chemical Ind.) was used. All mps were determined on a hot block and reported uncorrected.

4,6-Dimethylcoumarin (3). According to the known procedures,[5] *p*-cresol (76 g) was condensed with ethyl aceto-

acetate (90 g) in polyphosphoric acid [prepared from phosphoric acid (85%; 300 ml) and phosphorus pentoxide (500 g)] at 80 °C for 1 hr to give 4,6-dimethylcoumarin (**3**; 55 g; y: 45%), mp 150—151.5 °C [crystallized from a mixture of light petroleum and benzene (1 : 1)] (lit,[5a] mp 148 °C; lit,[5b] mp 150 °C); IR: 1720, 1627, 1612, 1573, 1491, 1200, 938, 860, and 830 cm^{-1}; PMR ($CDCl_3$): δ 2.41 (6H, s; $C_{(4)}$-CH_3 and $C_{(6)}$-CH_3), 6.22 (1H, m; $C_{(3)}$-H), and 7.2—7.4 (3H, m; $C_{(5)}$-H, $C_{(7)}$-H, and $C_{(8)}$-H); mass spectrum: *m/e* 174 (M^+) and *m/e* 145 (base peak). Found: C, 75.87; H, 6.02%. Calcd for $C_{11}H_{10}O_2$: C, 75.84; H, 5.79%; mol wt 174.2.

*3,4-Dihydro-4,6-dimethylcoumarin (**4**).* 4,6-Dimethylcoumarin (**3**; 45 g) dissolved in a mixture of ethyl acetate (200 ml) and acetic acid (1.8 l) was hydrogenated in the presence of 10% palladium-charcoal (10 g) for 4 hr at 100 °C. The catalyst was removed by filtration and the solvents were evaporated to give a residue, which was extracted with ether. A usual treatment gave an oil which solidified to afford 3,4-dihydro-4,6-dimethylcoumarin (**4**; 41 g; y: 90%), mp 35—35.5 °C (lit,[6] bp 100—105 °C/5 mmHg); IR: 1760, 1620, 1595, 1500, 1260, 1212, 1176, and 832 cm^{-1} (lit,[6] 1770 cm^{-1}); PMR ($CDCl_3$): δ 1.30 (3H, d, J=7 Hz; $C_{(4)}$-CH_3), 2.33 (3H, s; $C_{(6)}$-CH_3), and 6.95 (3H, m; $C_{(5)}$-H, $C_{(7)}$-H, and $C_{(8)}$-H); mass spectrum: *m/e* 176 (M^+) and *m/e* 134 (base peak). Found: C, 75.07; H, 6.75%. Calcd for $C_{11}H_{12}O_2$: C, 74.97; H, 6.86%; mol wt 176.2.

*3-(2-Methoxy-5-methylphenyl)butanoic Acid (**5**).* To a solution of 3,4-dihydro-4,6-dimethylcoumarin (**4**, 90 g) in ethanol (300 ml) was added 2 M sodium hydroxide (1 l), and the mixture was heated under reflux for 2 hr. To the cooled mixture dimethyl sulfate (65 g) was added dropwise with stirring at 0 °C, and the whole was heated under reflux for 8 hr. These procedures were repeated by further addition of dimethyl sulfate (20 g) and 2 M sodium hydroxide (90 ml). The cooled reaction mixture was acidified with 2 M sulfuric acid and heated under reflux for 2 hr. The mixture was cooled, alkalized with 2 M sodium hydroxide, and extracted with chloroform. The organic layer was separated and the solvents (chloroform and ethanol) were removed to give the starting material (**4**: 17 g). The alkaline layer was acidified with 2 M sulfuric acid, and then extracted with chloroform. The chloroform layer was separated, washed with brine, and dried over anhydrous sodium sulfate. The solvent was removed and the residue was distilled at 153 °C under 1 mmHg pressure. The distillate solidified to give 3-(2-methoxy-5-methylphenyl)-butanoic acid (**5**; 95 g; y: 89%), mp 60.5—61.5 °C; IR: *ca.* 3000 (br.), 1710, 1610, 1502, 1250, and 812 cm^{-1}; PMR ($CDCl_3$): δ 1.30 (3H, d, J=7 Hz; *s*-CH_3), 2.27 (3H, s; aromatic CH_3), 3.80 (3H, s; OCH_3), and 6.65—6.95 (3H, m; aromatic protons); mass spectrum: *m/e* 208 (M^+) and *m/e* 149 (base peak). Found: C, 69.36; H, 7.53%. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74%; mol wt 208.2.

*Resolution of (+)- and (−)-3-(2-Methoxy-5-methylphenyl)butanoic Acid [**5a** and **5b**].* To a solution of the racemic acid (**5**; 20 g) and strychnine (32 g) in chloroform (25 ml), ethanol (80%; 80 ml) was added. The resulting solution was concentrated to a volume of 20 ml. Water (10 ml) was added, and the solution was kept at room temperature overnight. There appeared the strychnine salt [18 g; $[\alpha]_D$ −68 ° (*c* 2.0, H_2O)], which was separated by filtration and crystallized thrice from ethanol (50%) to give the levorotatory strychnine salt. The rotation values of the salt at different stages of crystallization were: first crystallization, $[\alpha]_D$ −78.7 °; second, $[\alpha]_D$ −81.8 °; third, $[\alpha]_D$ −82.2 ° (*c* 2.0, H_2O).

The third crop (14 g) was added to 1 M sodium hydroxide (80 ml). The resulting mixture was extracted with chloroform, and the organic layer was discarded. The aqueous layer was then acidified with 2 M sulfuric acid and extracted with chloroform. The chloroform layer was washed with brine, dried over anhydrous sodium sulfate, and evaporated to yield an oil which was distilled at 150 °C under 1 mmHg pressure. The distillate solidified to give (−)-3-(2-methoxy-5-methylphenyl)butanoic acid (**5b**; 5 g), mp 60 °C, $[\alpha]_D$ −27 ° (*c* 2.0, C_6H_6).[7]

The mother liquor after separating the levorotatory strychnine salt was concentrated to a volume of *ca.* 20 ml to give the salt of **5b** (1 g); no salt was precipitated on further concentration of the mother liquor. The mother liquor was then alkalized with 1 M sodium hydroxide. The subsequent treatments were followed as before to give an oil which was distilled at 150 °C under 1 mmHg pressure. The distillate solidified to give (+)-3-(2-methoxy-5-methylphenyl)butanoic acid (**5a**; 9 g), mp 60—60.5 °C, $[\alpha]_D$ +19 ° (*c* 2.0, C_6H_6).[7]

*(+)-4-Methoxy-3,7-dimethylindan-1-one (**6**).* The dextrorotatory acid (**5a**; 7 g) was dissolved in polyphosphoric acid [prepared from phosphoric acid (85%; 80 ml) and phosphorus pentoxide (130 g)] at 30 °C, and the resulting solution was then heated at 100 °C for 1 hr. The cooled reaction mixture was poured into a mixture of ice and water and extracted with chloroform. The organic layer was washed with brine, dried, and evaporated to give an oil (6 g; y: 94%). A part of this material was purified by preparative tlc to give (+)-4-methoxy-3,7-dimethylindan-1-one (**6**), an oil; IR (liquid): 1715, 1590, 1500, 1270, 820, and 760 cm^{-1}; UV (cyclohexane): λ_{max} 317 nm (ε 3300), 308 (3500), 252.5 (8600), 246 (8300), and 238 (8000); PMR ($CDCl_3$): δ 1.34 (3H, d, J=7 Hz; $C_{(3)}$-CH_3), 2.20 (1H, dd, J=19 and J=3 Hz; $C_{(2)}$-H), 2.53 (3H, s; $C_{(7)}$-CH_3), 2.85 (1H, dd, J=19 and J=7 Hz; $C_{(2)}$-H), 3.45 (1H, m; $C_{(3)}$-H), 3.82 (3H, s; OCH_3), 6.88 and 7.00 (each 1H, d, J=8 Hz; $C_{(5)}$-H and $C_{(6)}$-H); ORD (*c* 0.18, cyclohexane): $[\Phi]_{589}$ +40 °, $[\Phi]^{peak}_{365}$ +1100 °, $[\Phi]^{trough}_{358}$ +720 °, $[\Phi]^{peak}_{350}$ +1000 °, $[\Phi]^{trough}_{340}$ +220 °, $[\Phi]^{peak}_{335}$ +330 °, $[\Phi]_{325}$ −1200 ° (shoulder), $[\Phi]^{trough}_{313}$ −2200 °, and $[\Phi]_{297}$ 0°; mass spectrum: *m/e* 190 [$M^+(C_{12}H_{14}O_2)$] and *m/e* 175 (base peak).

*(+)-4-Hydroxy-3,7-dimethylindan-1-one (**7**).* To a solution of crude (+)-4-methoxy-3,7-dimethylindan-1-one (**6**; 6 g) in acetic acid (30 ml) was added 5.9 M hydrobromic acid (12 ml), and the mixture was heated under reflux for 8 hr. The solvent was removed under reduced pressure to give a residue. The residue was extracted with ether, washed with 1 M sodium carbonate and then brine, dried over anhydrous sodium sulfate, and evaporated to give a residue, which was crystallized from a mixture of benzene and ether (1 : 1) to yield (+)-4-hydroxy-3,7-dimethylindan-1-one (**7**; 3.8 g; y: 68%), mp 203 °C (lit,[8] racemic **7**, mp 175 °C), $[\alpha]_D$ +25 ° (*c* 0.28, EtOH); IR: *ca.* 3200, 1670, 1590, 1505, 1380, 1305, 1285, and 1250 cm^{-1}; PMR (acetone-d_6): δ 1.36 (3H, d, J=7 Hz; $C_{(3)}$-CH_3), 2.14 (1H, dd, J=19 and J=3 Hz; $C_{(2)}$-H), 2.45 (3H, s; $C_{(7)}$-CH_3), 2.82 (1H, dd, J=19 and J=7 Hz; $C_{(2)}$-H), *ca.* 3.4 (1H, m; $C_{(3)}$-H), and 6.88 (2H, s; $C_{(5)}$-H and $C_{(6)}$-H); mass spectrum: *m/e* 176 (M^+) and *m/e* 161 (base peak). Found: C, 75.29; H, 6.67%. Calcd for $C_{11}H_{12}O_2$: C, 74.97; H, 6.86%; mol wt 176.2.

*(+)-3,7-Dimethylindan-1-one (**8**).* To a solution of (+)-4-hydroxy-3,7-dimethylindan-1-one (**7**; 3.5 g) in a mixture of carbon tetrachloride (30 ml) and ether (10 ml), was added diethyl phosphite (5 ml) and triethylamine (4 ml). The mixture was kept overnight at room temperature, and

then extracted with chloroform. The organic layer was washed successively with 2 M hydrochloric acid, 1 M sodium hydroxide, and brine, dried over anhydrous sodium sulfate, and evaporated to give an oil (6 g). Lithium (4 g) was added to a solution of this oil (6 g) in liquid ammonia (120 ml), and the whole was stirred for 1 hr. Ethanol (20 ml) and then water (40 ml) were added, and the ammonia was allowed to evaporate. The resulting mixture was extracted with ether, washed successively with 1 M sodium hydroxide and brine, dried over anhydrous sodium sulfate, and evaporated to give an oil, which was oxidized with Jones' reagent at 0 °C. The product was taken up in ether and treated as usual to give a residue, which was chromatographed on a column of silica gel (320 g). Elution with a mixture of light petroleum and ether (40 : 3) gave an oil (1.6 g; y: 50%). A part of this material was purified by preparative tlc to afford (+)-3,7-dimethylindan-1-one (**8**) an oil, IR (liquid): 1715, 1600, 1480, and 795 cm^{-1}; UV (cyclohexane): λ_{max} 297.5 nm (ε 2600), 294 (shoulder), 287.5 (2500), 260 (shoulder), and 234 (12000); PMR (CCl_4): δ 1.38 (3H, d, J=7 Hz; $C_{(3)}$-CH_3), 2.26 (1H, dd, J=19 and J=4 Hz; $C_{(2)}$-H), 2.65 (3H, s; $C_{(7)}$-CH_3), 2.90 (1H, dd, J=19 and J=7 Hz; $C_{(2)}$-H), 3.40 (1H, m; $C_{(3)}$-H), and 7.0—7.6 (3H, m; $C_{(4)}$-H, $C_{(5)}$-H, and $C_{(6)}$-H); ORD (c 0.44, cyclohexane): $[\Phi]_{589}$ +8° $[\Phi]_{368}^{peak}$ +600°, $[\Phi]_{359}^{trough}$ +410°, $[\Phi]_{352}^{peak}$ +640°, $[\Phi]_{339}$+60° (shoulder), $[\Phi]_{324}$ −1200° (shoulder), $[\Phi]_{311}$ −2000° (shoulder), $[\Phi]_{300}^{trough}$ −2700°, and $[\Phi]_{290}$−2300°; mass spectrum: *m/e* 160 [M^+ ($C_{11}H_{12}O$)] and *m/e* 145 (base peak).

*(−)-4-(2-Methoxy-5-methylphenyl)pentanoic Acid (**10**).* Thionyl chloride (3 ml) was added with stirring to a cooled solution (at 0 °C) of the levorotatory acid (**5b**; 5 g) in a mixture of dry benzene (10 ml) and pyridine (0.5 ml). The mixture was kept at room temperature for 30 min and then warmed at 40 °C for 10 min. The precipitated solid was removed by filtration. To the filtrate was added dropwise at 0 °C with stirring a *ca.* 3% solution of diazomethane in ether (100 ml). After 40 min, the solvents were removed under reduced pressure at room temperature to give a residue. Anhydrous methanol (50 ml) and then silver oxide (0.8 g) were added to this residue. The mixture was warmed at 50 °C for 20 min (an evolution of nitrogen was observed) and then heated under reflux for 20 min. The cooled mixture was filtered, and the filtrate was evaporated to give a residue which was taken up in ether. The ethereal solution was treated with cold 1 M sodium hydroxide to give, after a work-up as usual, (i) a neutral and (ii) an acidic fraction. Ethanol (30 ml), water (20 ml), and potassium hydroxide (2 g) were added to the neutral product (i), and the whole was heated under reflux for 3 hr. The cooled reaction mixture was acidified with 2 M sulfuric acid and extracted with ether to give, after a treatment as usual, (−)-4-(2-methoxy-5-methylphenyl)pentanoic acid (**10**; 4 g; y: 75%), mp 87.5 °C (crystallized from benzene) (racemic **10** prepared by other routes: lit,[12a] mp 94 °C; lit,[12b] mp 93.5—94 °C), $[\alpha]_D$ −14° (c 2.0, EtOH), IR: 1710, 1610, 1500, 1250, 815, 805, and 750 cm^{-1}; PMR ($CDCl_3$): δ 1.20 (3H, d, J=7 Hz; s-CH_3), 2.28 (3H, s; aromatic CH_3), 3.76 (3H, s; OCH_3), and 6.5—7.0 (3H, m; aromatic protons); mass spectrum: *m/e* 222 (M^+) and *m/e* 149 (base peak). Found: C, 70.31; H, 8.31%. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16%; mol wt 222.3. The acidic fraction (ii; *ca.* 300 mg) was suggested to be a mixture (*ca.* 1 : 1) of the starting acid (**5b**) and the homoacid (**10**) by examination on tlc.

*(+)-5-Methoxy-4,8-dimethyl-1-oxo-1,2,3,4-tetrahydronaphthalene (**11**).* A cyclization of (−)-4-(2-methoxy-5-methylphenyl)pentanoic acid (**10**) to give **11** was accomplished according to the procedures described for the preparation of racemic **11**.[12b] The homoacid (**10**; 3.8 g) in polyphosphoric acid [prepared from phosphoric acid (85%; 100 ml) and phosphorus pentoxide (160 g)] was heated at 100 °C for 1 hr. After a treatment as usual, the product was purified by chromatography on a column of silica gel (60 g; elution with benzene) to give (+)-5-methoxy-4,8-dimethyl-1-oxo-1,2,3,4-tetrahydronaphthalene (**11**; 3.5 g; y: quantitative), mp 76.5—77 °C (crystallized from light petroleum) (lit, [12b] racemic **11**, mp 50—51 °C; lit, [12a] racemic **11** prepared by other route, bp 150—153 °C/7 mmHg), $[\alpha]_D$ +28° (c 2.0, EtOH); IR: 1675, 1575, 1270, 1045, and 815 cm^{-1}; PMR (CCl_4): δ 1.24 (3H, d, J=7 Hz; $C_{(4)}$-CH_3), 2.48 (3H, s; $C_{(8)}$-CH_3), 3.83 (3H, s; OCH_3), 6.75 and 6.90 (each 1 H, d, J=8 Hz; $C_{(6)}$-H and $C_{(7)}$-H); mass spectrum: *m/e* 204 (M^+) and *m/e* 189 (base peak). Found: C, 76.50; H, 7.60%. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90%, mol wt 204.3.

*(−)-8-Methoxy-1,5-dimethyl-1,2,3,4-tetrahydronaphthalene (**12**).* (+)-5-Methoxy-4,8-dimethyl-1-oxo-1,2,3,4-tetrahydronaphthalene (**11**) was converted to **12** according to the procedures described for the preparation of racemic **12**.[12a] A mixture of the tetralone (**11**; 1 g), ethanol (15 ml), and 6.5 M hydrochloric acid (30 ml) was heated under reflux, and then amalgamated zinc (*ca.* 70 g) and 10 M hydrochloric acid (25 ml) were added in portions during 12 hr (under reflux). After a work-up as usual, the product was purified by chromatography on a column of silica gel (20 g; elution with light petroleum) to give (−)-8-methoxy-1,5-dimethyl-1,2,3,4-tetrahydronephthalene (**12**: 930 mg; y: quantitative), an oil (lit,[12a] racemic **12**, bp 120—122 °C/3 mmHg), $[\alpha]_D$ −65.5° (c 0.12, EtOH), IR (liquid): 1590, 1480, 1260, 1245, 1100, and 805 cm^{-1}; PMR ($CDCl_3$): δ 1.17 (3H, d, J=7 Hz; $C_{(1)}$-CH_3), 2.13 (3H, s; $C_{(5)}$-CH_3), 3.78 (3H, s; OCH_3), 6.62 and 6.96 (each 1H, d, J=8 Hz; $C_{(6)}$-H and $C_{(7)}$-H); mass spectrum: *m/e* 190 [M^+ ($C_{13}H_{18}O$)] and *m/e* 175 (base peak).

*(+)-8-Hydroxy-1,5-dimethyl-1,2,3,4-tetrahydronaphthalene (**13**).* (−)-8-Methoxy-1,5-dimethyl-1,2,3,4-tetrahydronaphthalene (**12**) was demethylated according to the procedures described for the preparation of racemic **13**.[12b] The methyl ether (**12**; 900 mg) in acetic acid (10 ml) was demethylated under reflux (for 7 hr) by addition of 5.9 M hydrobromic acid (3.5 ml). After a treatment as usual, the product was chromatographed on a column of silica gel (20 g; elution with benzene) to give the crude tetrahydronaphthol (**13**; 600 mg; y: 72%). A part of this material was purified by preparative tlc to afford (+)-8-hydroxy-1,5-dimethyl-1,2,3,4-tetrahydronaphthalene (**13**), mp 91 °C (crystallized from ethanol) (lit, [12b] racemic **13**, mp 93—94 °C), $[\alpha]_D$ +5° (c 2.1, EtOH); IR (liquid): 3400 (br.), 1590, 1485, 1460, 1270, 1015, and 810 cm^{-1}; PMR ($CDCl_3$): δ 1.23 (3H, d, J=7 Hz; $C_{(1)}$-CH_3), 2.13 (3H, s; $C_{(5)}$-CH_3), 6.53 and 6.85 (each 1H, d, J=8 Hz; $C_{(6)}$-H and $C_{(7)}$-H); mass spectrum: *m/e* 176 [M^+ ($C_{12}H_{16}O$)] and *m/e* 161 (base peak).

*(−)-8-Acetonyloxy-1,5-dimethyl-1,2,3,4-tetrahydronaphthalene (**14**).* (+)-8-Hydroxy-1,5-dimethyl-1,2,3,4-tetrahydronaphthalene (**13**) was acetonylated to give **14** according to the procedures reported for the preparation of racemic **14**.[2] A solution of the crude tetrahydronaphthol (**13**; 400 mg) in dry acetone (20 ml) was refluxed with chloroacetone (0.4 ml), potassium iodide (150 mg), and potassium carbonate (1.5 g). After a work-up as usual, the product was purified by chromatography on a column of silica gel [25 g; elution with a mixture of light petroleum and ether (10 : 1)] to afford (−)-8-acetonyloxy-1,5-dimethyl-1,2,3,4-tetrahydronaphtha-

lene (**14**; 320 mg; y: 61%), mp 77 °C (crystallized from light petroleum) (lit,[2] racemic **14**, mp 50—51 °C), $[\alpha]_D$ −5° (*c* 1.7, EtOH), IR (liquid): 1725, 1590, 1475, and 1105 cm^{-1}; PMR ($CDCl_3$): δ 1.26 (3H, d, J=7 Hz; $C_{(1)}$-CH_3), 2.13 (3H, s; $C_{(5)}$-CH_3), 2.30 (3H, s; -$COCH_3$), 4.48 (2H, s; -OCH_2CO-), 6.46 and 6.92 (each 1H, d, J= 8 Hz; $C_{(6)}$-H and $C_{(7)}$-H); mass spectrum: *m/e* 232 [M^+ ($C_{15}H_{20}O_2$)] and *m/e* 174 (base peak).

(−)-*Farfugin A (**1b**; an Enantiomer of Natural Farfugin A).* (−)-8-Acetonyloxy-1,5-dimethyl-1,2,3,4-tetrahydronaphthalene (**14**) was converted to **1b** according to the procedures described for the preparation of racemic farfugin A [(±)-**1**].[2] The ether (**14**; 296 mg) was heated with polyphosphoric acid [prepared from phosphoric acid (85%; 10 g) and phosphorus pentoxide (16 g)] at 100 °C for 20 min. The cooled mixture was poured into a mixture of ice and water and extracted with ether. The organic layer was washed successively with 1% sodium hydroxide and brine, dried over anhydrous magnesium sulfate, and evaporated to give a residue, which was chromatographed on a column of silica gel. Elution with light petroleum gave (−)-farfugin A (**1b**; 150 mg; y: 55%), mp 78 °C (crystallized from ethanol) [lit.,[2] racemic farfugin A [(±)-**1**], mp 73—73.5 °C; lit,[2] natural (+)-farfugin A (**1a**), mp 80.5—82.5 °C], $[\alpha]_D$ −27° (*c* 0.7, EtOH)[7] [lit,[2] natural (+)-farfugin A, $[\alpha]_D$ +39° (*c* 0.34, EtOH)]; IR: 1590, 1540, 1525, 1430, 1325, 1100, 1018, 855, 780, and 765 cm^{-1}; UV (EtOH): λ_{max} 291 nm (ε 2500), 281 (2300), and 252 (10500); PMR ($CDCl_3$): δ 1.38 (3H, d, J=7.5 Hz; $C_{(9)}$-CH_3), 2.18 (3H, d, J=1.2 Hz; $C_{(3)}$-CH_3), 2.28 (3H, s; $C_{(5)}$-CH_3), 7.08 (1H, s; $C_{(4)}$-H), and 7.23 (1H, m; $C_{(2)}$-H); mass spectrum: *m/e* 214 (M^+) and *m/e* 199 (base peak). Found: C, 84.25; H, 8.64%. Calcd for $C_{15}H_{18}O$: C, 84.07; H, 8.47%; mol wt 214.2. The spectral data (IR, UV, PMR, and mass spectrum) of **1b** were identical with those[2] of natural (+)-farfugin A. The compound (**1b**) was thus shown to be an enantiomer of natural (+)-farfugin A.

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