spectrum: m/e 258 (M^+). ^{19}F NMR ($CDCl_3$): φ 121.4 (d, J = 31.0 Hz). Anal. Calcd for $C_{11}H_{11}FO_4S$: C, 51.16; H, 4.26. Found: C, 51.02; H, 4.37.

(*Z*)-*cis*,*trans*-Methyl 2,2-Dimethyl-3-[2-fluoro-2-(methoxycarbonyl)vinyl]cyclopropanecarboxylate (15). To a solution of 589 mg (1.94 mmol) 3-fluoro-4,4,4-trimethoxy-2-butenyl phenyl sulfone and 486 mg (4.26 mmol) of methyl senecioate in dimethylformamide (4 mL) at 20 °C in a pear-shaped 50-mL flask was added 280 mg (5.19 mmol) of sodium methoxide. The flask was equipped with a magnetic stirrer and stirred for 48 h under an N_2 atmosphere. The reaction mixture was poured into 5% aqueous hydrochloric acid and the mixture was extracted with diethyl ether. Evaporation of solvent yielded a crude liquid which was diluted with 10 mL of methanol. *p*-Toluenesulfonic acid (10 mg) was added to the solution and the resulting solution was stirred for 1 h. The reaction mixture was diluted with excess 5% sodium bicarbonate solution and diethyl ether. The ether layer was washed with brine and then dried over anhydrous magnesium sulfate. Evaporation of the solvent in vacuo gave the crude diester which was purified by chromatography on silica gel to give 178 mg (40.0%) of (*Z*)-*cis*,*trans*-methyl 2,2-dimethyl-3-[2-fluoro-2-(methoxycarbonyl)vinyl]cyclopropanecarboxylate (trans:cis = 85:15). ^1H NMR (300 MHz, $CDCl_3$): δ 1.19, 1.26 (trans *gem*-dimethyl), 1.23 (cis *gem*-dimethyl), 1.73 (trans isomer, d, J = 5.0 Hz), 2.39 (trans isomer, dd, J = 5, 10 Hz), 1.94 (cis isomer, d, J = 9 Hz), 2.10 (cis isomer, dd, J = 9, 10 Hz), 5.84 (trans isomer, dd, J = 10, 32 Hz), 6.59 (cis isomer, dd, J = 10, 31 Hz). Mass spectrum: m/e 231 ($M^+ + 1$). ^{19}F NMR ($CDCl_3$): φ 131.6 (d, J = 32.0 Hz, trans), 132.7 (d, J = 31.1 Hz, cis). Anal. Calcd for $C_{11}H_{15}FO_4$: C, 57.36; H, 6.57. Found: C, 57.25; H, 6.61.

(*Z*)-3,4,4,4-Tetrafluoro-2-butenyl Phenyl Sulfone (16). Potassium fluoride (239 mg, 3.1 mmol; Aldrich Gold Label) was added to a solution of 237 mg (0.83 mmol) of 3-chloro-4-(phenylsulfonyl)-1,1,2-trifluoro-1-butene in 2 mL of dry dimethylformamide in a 20-mL round-bottom flask. The mixture was stirred for 15 h at room temperature. At this point the contents of the flask were poured into ice-water, and the mixture was extracted with diethyl ether. The ether layer was washed once with brine and then dried over anhydrous magnesium sulfate. Evaporation of solvent yielded crude solid, which was purified by recrystallization from 30% ethyl acetate in hexanes to give 184 mg (82.5%) of 3,4,4,4-tetrafluoro-2-butenyl phenyl sulfone as white crystals, mp 83.0–84.0 °C. ^1H NMR (300 MHz, $CDCl_3$): δ 3.94 (2 H, d, J = 9 Hz), 5.73 (1 H, dt, J = 8, 31 Hz), 7.6–7.9 (5 H, phenyl protons). Mass spectrum: m/e 268 (M^+). ^{19}F NMR ($CDCl_3$): φ 72.7 (d, $J(CF_3\text{–}F)$ = 10.3), 127.3 (dqt, J(F–H trans) = 31.0 Hz, $J(F\text{–}CF_3)$ = 10.3 Hz). Anal. Calcd for $C_{10}H_8F_4SO_2$: C, 44.76; H, 3.01. Found: C, 44.58; H, 3.02.

(*Z*)-4-Bromo-1,1,1,2-tetrafluoro-2-butene (17). A solution of 3.50 g (19.7 mmol) of *N*-bromosuccinimide and 20 mL of hydrogen fluoride–pyridine complex was prepared in a 100-mL polyethylene flask at −20 °C under a nitrogen atmosphere. The flask was fitted with a gas bubbling glass tube. Into this solution was bubbled 2.30 g (21.3 mmol) of 1,1,2-trifluoro-1,3-butadiene with a stream of nitrogen gas over half an hour. The solution was stirred further for 2 h at −20 °C and let stand at room temperature overnight. The contents of the flask were poured into a large excess of ice–water, and the liquid was extracted twice with diethyl ether. The combined ether layers were washed successively with 5% aqueous potassium hydroxide solution and brine and then dried over anhydrous magnesium sulfate. Evaporation of the solvent gave crude liquid, which was distilled to obtain 2.13 g (52.4%) of (*Z*)-4-bromo-1,1,1,2-tetrafluoro-2-butene as a clear liquid, bp 73.0–75.0 °C (760 mmHg). ^1H NMR (300 MHz, $CDCl_3$): δ 4.00 (2 H, d, J = 9 Hz), 5.88 (1 H, dt, J = 9, 30 Hz). ^{19}F NMR ($CDCl_3$): φ 73.2 (d, $J(CF_3\text{–}F)$ = 10.3 Hz), 131.2 (dqt, J(F–H trans) = 28.9 Hz, $J(F\text{–}CF_3)$ = 10.3 Hz).

(*E*)-1,2-Difluoro-1-phenyl-1,3-butadiene (18). To a solution 3.2 g (29.6 mmol) of 1,1,2-trifluoro-1,3-butadiene in tetrahydrofuran (40 mL) at −70 °C in a round-bottom 100-mL flask was added 15 mL (30 mmol) of phenyllithium (2 M). The reaction mixture was stirred for 2 h at −70 °C and for 10 h at 20 °C. The contents of the flask were poured into an excess of cold 5% hydrochloric acid, and the liquid was extracted twice with diethyl ether. The ether layers were combined, washed once with brine, and then dried over anhydrous magnesium sulfate. Evaporation of solvent gave a yellow oil which was chromatographed on silica gel (hexanes) to give 3.40 g (69.4%) of (*E*)-1,2-difluoro-1-phenyl-1,3-butadiene. (It contained 10% of *Z* isomer.) ^1H NMR (300 MHz, $CDCl_3$): δ 5.32 (1 H, d, J = 12 Hz, *E* isomer), 5.62 (1 H, d, J = 16 Hz, *E* isomer), 5.26 (1 H, d, J = 12 Hz, *Z* isomer), 5.69 (1 H, d, J = 16 Hz, *Z* isomer), 6.39 (1 H, m, *Z* isomer), 6.72 (1 H, m, *E* isomer), 7.5–7.8 (phenyl protons, 5 H). Mass spectrum: m/e 167 (M + 1). ^{19}F NMR ($CDCl_3$): φ trans isomer F^1 = 154.4, F^2 = 159.0, $J(F^1F^2)$ = 113.7 Hz, $J(F^1H^3)$ = 6.2 Hz, $J(F^2H^3)$ = 26.9 Hz; cis isomer F^1 = 127.5, F^2 = 146.5 Hz, $J(F^1F^2)$ = 12.4 Hz, $J(F^2H^3)$ = 26.6 Hz.

(*E*)-2,3-Difluorocinnamaldehyde (19). To a solution of 513 mg (3.09 mmol) of 1,2-difluoro-1-phenyl-1,3-butadiene (*E*:*Z* = 90:10) in 20 mL of dichloromethane at −70 °C in a 50-mL round-bottom flask was bubbled ozone gas. As soon as the starting diene disappeared on TLC, bubbling of ozone gas was stopped. Nitrogen gas was bubbled to remove excess ozone. At this point dimethyl sulfide (2 mL) was added to the solution, the mixture was left to stand overnight at room temperature and poured into water, and the mixture was extracted with diethyl ether. The ether layer was washed once with brine and then dried over anhydrous magnesium sulfate. Evaporation of solvent yielded crude oil which was purified by recrystallization from hexanes to give 333 mg (64.0%) of (*E*)-2,3-difluorocinnamaldehyde as yellow crystals, mp 32.0–33.0 °C. ^1H NMR (300 MHz, $CDCl_3$): δ 7.4–7.6 (3 H, m, phenyl protons), 7.84 (2 H, dd, J = 2, 8 Hz, phenyl protons), 9.98 (1 H, dd, J = 2, 18 Hz). Mass spectrum: m/e 168 (M^+), 169 (M + 1), 170 (M + 2). ^{19}F NMR ($CDCl_3$): φ F^1 = 148.3, F^2 = 166.9, $J(F^1F^2)$ = 119.9 Hz, $J(F^2H)$ = 16.5 Hz. Anal. Calcd for $C_9H_6F_2O$: C, 64.27; H, 3.61. Found: C, 65.17; H, 3.61.

Optically Pure (4a*S*)-(+)- or (4a*R*)-(−)-1,4a-Dimethyl-4,4a,7,8-tetrahydronaphthalene-2,5(3*H*,6*H*)-dione and Its Use in the Synthesis of an Inhibitor of Steroid Biosynthesis

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Synthesis of the optically pure enone 1 is described. Reestimation of the optical purity and reexamination of the absolute stereochemistry of 1 have been studied. Usefulness of the enone 1 is demonstrated by a five-step synthesis of (−)-3, an inhibitor of steroid biosynthesis.

Numerous syntheses and synthetic studies of sesquiterpenes and diterpenes from the racemic Wieland–Miescher ketone analogue 1 have been described.[1] In contrast to the availability of either enantiomer of the

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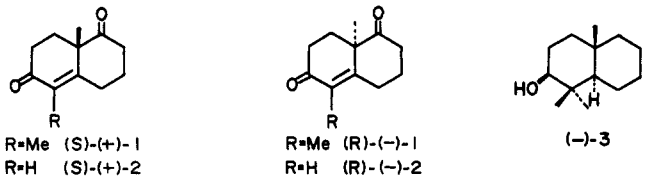
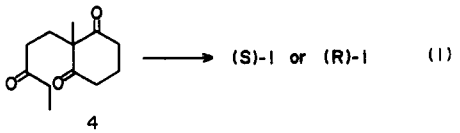


optically pure Wieland–Miescher ketone (2) by amino acid assisted asymmetric cyclization and subsequent recrystallization,[2] a convenient method for preparation of the enone 1 in high yield and high optical purity has not been reported. Our continuing interest in the synthesis of higher terpenoids using the Wieland–Miescher ketone analogue[3,4] required an efficient synthesis of optically active (*S*)- or (*R*)-1. We delineate herein an asymmetric synthesis of



optically pure (+)- or (−)-1, along with a reevaluation of its optical purity and absolute stereochemistry. Finally (−)-1 was employed in the synthesis of (−)-3, an inhibitor of steroid biosynthesis.

Results

Asymmetric Cyclization. The asymmetric cyclization of 4[5] was carried out on 10-mmol scale with an equivalent amount of L- or D-β-phenylalanine and 0.5 equiv of D-camphorsulfonic acid in acetonitrile (MeCN) or *N,N*-dimethylformamide (DMF) by the reported procedure,[4] in which control of the reaction temperature was important (see Experimental Section).

The asymmetric cyclization cited above using L-β-phenylalanine in acetonitrile gave optically active (+)-1 in 83% chemical yield which had a specific rotation of $[\alpha]_D$ +112° (*c* 1.31, MeOH). Furthermore, it was found that when DMF was employed as a solvent, the specific rotation $[\alpha]_D$ of the product 1 (79% chemical yield) increased to +128° (*c* 0.203, MeOH). In a similar fashion, the use of D-β-phenylalanine in DMF afforded (−)-enone 1 in 70% yield with a specific rotation of −125°.

Since the specific rotation of optically pure (+)-1 was previously estimated to be +79° (MeOH),[5] we carried out

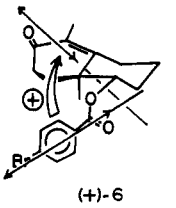
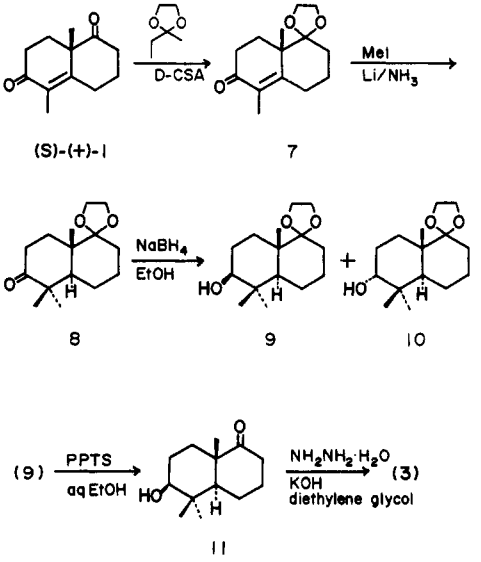
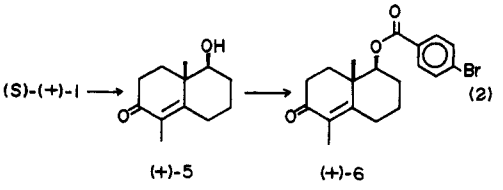


Figure 1.

Scheme I



a reevaluation of the optical purity of the enone 1. (+)-Enone 1 ($[\alpha]_D$ +112°) was reduced by sodium borohydride to give the known equatorial alcohol 5,[6] which was then benzoylated with *p*-bromobenzoyl chloride (eq 2). HPLC



analysis of the resulting benzoate 6 using a chiral stationary phase column [Chiralpak OT(+)^R][7] revealed that the enantiomeric excess of the benzoate 6 was 80%. The antipodal benzoate (−)-6 derived from the (−)-enone 1 ($[\alpha]_D$ −125°), was 89% ee by HPLC analysis. From these data, the specific rotation of the optically pure (+)- or (−)-1 was calculated to be 140°. Moreover, both (+)- and (−)-enantiomers of 1 crystallized gradually on standing in a freezer, and repeated recrystallization from *n*-hexane to constant rotational values afforded crystals of mp 47–48 °C and specific rotation +(or−)140°.

The CD spectrum of the benzoate (+)-6 obtained from the (+)-enone 1 showed a strong positive first Cotton effect ($\Delta\epsilon$ +32.72 at 253.5 nm) and a negative second Cotton effect ($\Delta\epsilon$ −13.94 at 235 nm). This clearly indicates that the chirality between the two long axes of transition moments of enone and benzoate chromophores is positive as depicted in Figure 1.[4,8] Thus, the absolute stereochemistry

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of the (+)-enone 1 is unambiguously established as 4a*S* in agreement with the original assignment.[5]

A Synthesis of an Inhibitor of Steroid Biosynthesis. In 1978, Spencer and his co-workers[9] discovered that both (2*S*,4a*S*,8a*R*)-(−)-2β-hydroxy-1,1,4aβ-trimethyl-1,2,3,4,4a,5,6,7,8,8aα-decahydronaphthalene (**3**) and its enantiomer are specific inhibitors of cholesterol biosynthesis in either rat liver enzyme preparations or cultured mammalian cells. The syntheses of **3**, both in racemic and optically active forms, had been reported in 1958 before the discovery of the bioactivity of **3**.[10,11] Racemic **3** was resolved by Spencer et al., who found both enantiomers were effective as inhibitors.[9] Recently, Mori et al.[12] reported the eight-step synthesis of (−)-**3**, in which bakers' yeast reduction of an achiral cyclohexane-1,3-dione derivative was crucial in the realization of a high optical purity of (−)-**3**. We disclose a short alternative enantiomeric synthesis of (−)-**3**, starting from (*S*)-(+)-**1** (Scheme I).

Selective transacetalization of the (*S*)-(+)-enone **1** (91% ee) led to acetal **7** in 77% yield employing the ethylene acetal of 2-butanone and D-camphorsulfonic acid in ethylene glycol. Reductive alkylation of acetal **7** with methyl iodide in lithium–liquid ammonia afforded ketone **8** in 67% yield along with 10% of recovered acetal. Ketone **8** was reduced with sodium borohydride to give crystalline alcohol **9** in 85% yield accompanied by the oily isomeric alcohol **10** in 8% yield. The half-height width (16 Hz) of the proton signal at C-2 in the ^{1}H NMR spectrum of the major isomer (**9**) proves an equatorial orientation of the hydroxyl group. Treatment of the alcohol **9** with pyridinium *p*-toluenesulfonate in refluxing aqueous ethanol gave deprotected crystalline ketol **11** in 96% yield. Finally, the Wolff–Kishner reduction of the ketol **11** afforded the desired alcohol (−)-**3** in 73% yield. The spectral data (^{1}H and ^{13}C NMR and IR) are identical with those of an authentic sample. The optical rotation and mp show good agreement with the reported values [$[\alpha]_D$ −9.4° (*c* 0.35, MeOH) (lit.[12] $[\alpha]_D$ −11.3° (*c* 0.32, MeOH)); mp 87–88 °C (lit.[12] mp 86.5–87.4 °C)].

In summary, we showed that amino acid assisted asymmetric cyclization of **4** under selected conditions provided either enantiomer of chiral **1** in high optical and chemical yields. To demonstrate the usefulness of the optically active enone **1**,[13] we have completed a six-step (from the achiral triketone **4**) enantioselective synthesis of the alcohol (−)-**3**, an inhibitor of steroid biosynthesis.

Experimental Section

All melting points are uncorrected. Anhydrous solvents were distilled from calcium hydride (DMF, MeCN, pyridine) or lithium aluminum hydride (tetrahydrofuran). All infrared spectra were obtained with a Jasco A-3 spectrophotometer for solutions in carbon tetrachloride unless otherwise indicated. Ultraviolet spectra were run on a Jasco UVIDEC-505 spectrophotometer. The circular dichroism was obtained with a Jasco-400X spectropolarimeter. ^{1}H NMR spectra were recorded with Jeol PMX-60 (60 MHz) or FX-90Q (90 MHz) instruments, and the ^{13}C NMR spectra were also obtained with an FX-90Q (22.5 MHz) instrument. Chemical shifts were reported δ values relative to tetramethylsilane. Optical rotations were determined for solutions in methanol on a Jasco DIP-4S polarimeter at ambient temperature. Analytical high-pressure liquid chromatographies (HPLC) and preparative medium-pressure liquid chromatographies (MPLC) were carried out on Waters 510 and Jasco PRC-50 systems, respectively. High-resolution mass spectra were obtained with a Jeol JMS DX-300 mass spectrometer. Merck 60 GF-254 silica-gel was used for preparative thin-layer chromatographies (PLC). Combustion microanalyses were carried out in the microanalytical laboratory of this Institute.

(4a*S*)-(+)-1,4a-Dimethyl-4,4a,7,8-tetrahydronaphthalene-2,5(3*H*,6*H*)-dione (1). A solution of the triketone **4** (2.13 g, 10 mmol), L-β-phenylalanine (1.66 g, 10 mmol), and D-camphorsulfonic acid (1.16 g, 5 mmol) in DMF (150 mL) was stirred at room temperature under a nitrogen atmosphere overnight. Then the mixture was heated at 30 °C for 24 h, and the temperature was raised in 10 °C intervals in every 24 h during 4 days. After the mixture was stirred at 70 °C for 24 h, the oil bath was removed. The resulting solution was poured into cold aqueous $NaHCO_3$ and extracted with ether (50 mL × 2). Evaporation of ether followed by column chromatography of the residue afforded 1.54 g (79%) of the enone **1** as a viscous oil ($[\alpha]_D$ +128° (*c* 0.203), 91% optical purity), which crystallized on standing in a freezer. Recrystallization from *n*-hexane in an ice bath gave colorless long needles: mp 46–47 °C; $[\alpha]_D$ +140° (*c* 0.200); IR ν 1720, 1678, 1618 cm^{-1}; ^{1}H NMR (60 MHz) δ 1.40 (s, 3 H), 1.80 (s, 3 H), 1.7–3.2 (m, 10 H). Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.94; H, 8.46.

(4a*R*)-(−)-1,4a-Dimethyl-4,4a,7,8-tetrahydronaphthalene-2,5(3*H*,6*H*)-dione (1). The triketone **4** (429 mg, 2 mmol), D-β-phenylalanine (332 mg, 2 mmol), and D-camphorsulfonic acid (232 mg, 1 mmol) in DMF (35 mL), under the same reaction condition cited above, afforded 274 mg (70%) of the *R*-(−)-enone **1** as an oil ($[\alpha]_D$ −125° (*c* 0.54), 89% optical purity), which was recrystallized from *n*-hexane to give needles: mp 47–48 °C ($[\alpha]_D$ −140° (*c* 0.200)). Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.71; H, 8.49.

(4a*S*,5*S*)-(+)-1,4aβ-Dimethyl-5β-hydroxy-4,4a,5,6,7,8-hexahydronaphthalen-2(3*H*)-one (5). A solution of 2.2 mg (0.06 mmol) of sodium borohydride in 1 mL of ethanol was added to a stirring solution of 32.2 mg (0.17 mmol) of the (+)-enone **1** ($[\alpha]_D$ +112° (*c* 1.31)) at an ice bath temperature. After an additional 20 min the excess hydride was decomposed by addition of two drops of acetic acid. The solvent was evaporated under reduced pressure and the residue was taken up in ether. After washing the organic layer with water and brine and drying over Na_2SO_4, the solvent was evaporated. The residue was purified on a PLC to give 30.4 mg (94%) of **5**: $[\alpha]_D$ +142° (*c* 0.202) (lit.[6] $[\alpha]_D$ +162.6° (*c* 2.17, $CHCl_3$)); IR ν 3650, 3450, 1670, 1615 cm^{-1}; ^{1}H NMR (60 MHz) δ 1.17 (s, 3 H), 1.77 (s, 3 H), 1.2–2.9 (m, 12 H), 3.42 (dd, *J* = 10, 5 Hz, 1 H).

(4a*S*,5*S*)-(+)-1,4aβ-Dimethyl-5β-[(*p*-bromobenzoyl)oxy]-4,4a,5,6,7,8-hexahydronaphthalen-2(3*H*)-one (6). A mixture of the hydroxy ketone **5** (43 mg, 0.22 mmol), *p*-bromobenzoyl chloride (640 mg, 2.9 mmol), and (*N*,*N*-dimethylamino)pyridine (19 mg, 0.15 mmol) in anhydrous pyridine (2 mL) was stirred at room temperature for 84 h under nitrogen. After addition of water (10 mL), stirring was continued for 1 h. The product was extracted with ether, and the organic layer was washed with water and brine. Evaporation of the solvent followed by repeated PLC of the residue afforded the benzoate **6** (88.4 mg, quant). The HPLC analysis was performed on a Chiralpak OT(+) column (4.6 mm × 250 mm) at 2000 psi (0.44 mL/min) by using 95% aqueous MeOH as the mobile phase with peak detection at 254 nm. The racemic benzoate **6** prepared analogously was analyzed to give two equal peaks, which eluted at 7 and 8.3 min, respectively. Injection of the optically active benzoate **6** gave major (90%) and minor (10%) peaks in the order of elution. Thus the optical purity of the starting (+)-enone **1** ($[\alpha]_D$ +112°) was 80% ee and specific rotation of the optically pure (+)-enone **1** was calculated to be +140°. The benzoate **6** exhibited $[\alpha]_D$ +180° (*c* 0.087): UV (EtOH) λ_{max} 244 nm (ε 32 480), 203.5 (19 530); CD (EtOH) λ_{ext} 253.5 nm (Δε +32.7), 235 (−13.9); IR ν 1720, 1672, 1267, 1100 cm^{-1}; ^{1}H NMR (90 MHz) δ 1.39 (s, 3 H), 1.82 (s, 3 H), 1.4–2.9 (m, 10 H), 4.91 (dd, *J* = 9.4, 4.4 Hz, 1 H), 7.56 (B part of AB-type q, *J* = 8.8 Hz, 2 H), 7.86 (A part of AB-type q, *J* = 8.8 Hz, 2 H); mass spectrum (70 eV), *m*/*e* (relative intensity) 378 (M^+, 6), 376 (M^+, 6), 185 (99), 183 (100), 176 (22), 118 (11); calcd for $C_{19}H_{21}O_3$

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(13) During the course of our work, Yamashita et al. reported the enantiomeric synthesis of trisporic acid starting from the (+)-enone **1**, which was prepared according to the same procedure as described herein: Takahashi, S.; Oritani, T.; Yamashita, K. *Agric. Biol. Chem.* **1987**, *51*, 2291.

^{81}Br *m/e* 378.06545 and $C_{19}H_{21}O_3$ ^{79}Br *m/e* 376.06742, found 378.06455 and 376.06702, respectively.

(4a*R*,5*R*)-(−)-1,4aβ-Dimethyl-5β-[(*p*-bromobenzoyl)oxy]-4,4a,5,6,7,8-hexahydronaphthalen-2(3*H*)-one (6). In an analogous manner, the (−)-enone 1 (26.5 mg, 0.14 mmol, $[\alpha]_D$ −125° (*c* 0.504)) in ethanol (0.5 mL) was reduced by sodium borohydride (2 mg, 0.05 mmol) in ethanol (1 mL), giving the hydroxy ketone **5** (21 mg, 79%), which was treated with *p*-bromobenzoyl chloride (320 mg, 1.5 mmol) and (*N*,*N*-dimethylamino)pyridine (11.8 mg, 0.1 mmol) in anhydrous pyridine (1 mL) to produce the benzoate **6** (30.4 mg, 75%). The HPLC analysis of **6** provided minor (5.5%) and major (94.5%) peaks in the order of elution. Thus the optical purity of the (−)-enone 1 and the specific rotation value of the optically pure (−)-1 were calculated to be 89% ee and −140°, respectively.

(4a*S*)-(+)-1,4aβ-Dimethyl-4,4a,7,8-tetrahydronaphthalene-2,5(3*H*,6*H*)-dione 5-Ethylene Acetal (7). A solution of the enone (+)-1 (898 mg, 4.7 mmol, $[\alpha]_D$ +128°, 91% ee) and D-camphorsulfonic acid (84 mg, 0.36 mmol) in ethylene acetal of 2-butanone (5 mL) and ethylene glycol (3 mL) was heated at 40 °C for 36 h under an atmosphere of nitrogen. After cooling in an ice bath, the resulting solution was poured into aqueous $NaHCO_3$, and the product was extracted with ether (30 mL × 2). The combined extracts were washed with water, brine, and dried over anhydrous Na_2SO_4. Evaporation of the solvent followed by MPLC purification of the residue provided the acetal **7** (850 mg, 77%) along with the starting enone 1 (41 mg, 6%). The acetal **7** exhibited $[\alpha]_D$ +100° (*c* 0.500): IR ν 1670, 1620, 1340, 1315, 1190, 1170, 1100 cm^{-1}; ^1H NMR (60 MHz) δ 1.30 (s, 3 H), 1.75 (s, 3 H), 1.3–1.9 (m, 10 H), 3.92 (s, 4 H). Anal. Calcd for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53. Found: C, 70.92; H, 8.58.

(4a*S*,8a*S*)-(−)-1,1,4aβ-Trimethyl-1,4,4a,7,8,8aα-hexahydronaphthalene-2,5(3*H*,6*H*)-dione 5-Ethylene Acetal (8). To a refluxing solution of lithium (61 mg, 8.7 mmol) in liquid ammonia (50 mL) was added dropwise a solution of the acetal **7** (502 mg, 2.1 mmol) in anhydrous tetrahydrofuran (15 mL). After a 2-h reflux, methyl iodide (1.4 mL, 22 mmol) was added as rapidly as possible, and the reaction mixture was refluxed over 1 h. Solid ammonium chloride (1 g) was added, and the mixture was allowed to stand at room temperature until almost all of ammonia was evaporated. The residue was poured into water, and the product was extracted with ether (30 mL × 2). The combined extracts were washed with water and brine and dried. Evaporation of the solvent followed by MPLC separation of the residue (silica gel, 1:1 *n*-hexane/ethyl acetate) afforded the ketone **8** (358 mg, 67%) along with the recovered starting material **7** (49 mg, 10%). The ketone **8** exhibited mp 69–70 °C (from *n*-hexane, lit.[14] 69.5–70 °C): $[\alpha]_D$ −42.4° (*c* 0.50) (lit.[14] $[\alpha]_D$ −34.8° (*c* 1.8, $CHCl_3$)); IR ν 1710, 1185, 1140 cm^{-1}; ^1H NMR (60 MHz) δ 1.03 (s, 3 H), 1.07 (s, 3 H), 1.23 (s, 3 H), 1.3–2.1 (m, 9 H), 2.1–2.8 (m, 2 H), 3.8–4.1 (m, 4 H). Anal. Calcd for $C_{15}H_{24}O_3$: C, 71.39; H, 9.59. Found: C, 71.30; H, 9.56.

(2*S*,4a*S*,8a*S*)-(−)-2β-Hydroxy-1,1,4aβ-trimethyl-1,2,3,4,4a,7,8,8aα-octahydronaphthalen-5(6*H*)-one Ethylene Acetal (9). To a stirred solution of the ketone **8** (377 mg, 1.5 mmol) in ethanol (5 mL) was added sodium borohydride (56 mg, 1.5 mmol) at −40 °C under a nitrogen. After stirring for 1.5 h at −10 °C, the resulting solution was poured into water. The product was extracted with ether (20 mL × 2), and the combined organic layers were washed with water and brine and dried. After evaporation of the solvent, the residue was separated by MPLC (silica gel, 1:1 *n*-hexane/ethyl acetate), giving the alcohol **9** (321 mg, 85%) accompanied with the minor alcohol **10** (31 mg, 8%). The major alcohol **9** crystallized spontaneously: mp 81–82 °C (from *n*-hexane); $[\alpha]_D$ −24.1° (*c* 0.883); IR ν 3640, 3500, 1110, 1070, 1045 cm^{-1}; ^1H NMR (90 MHz) δ 0.80 (s, 3 H), 0.99 (s, 3 H), 1.05 (s, 3 H), 1.2–1.9 (m, 12 H), 3.28 (m, $W_{1/2}$ = 16 Hz, 1 H), 3.8–4.1 (m, 4 H). Anal. Calcd for $C_{15}H_{26}O_3$: C, 70.83; H, 10.30. Found: C, 70.89; H, 10.28. The minor alcohol **10**: IR ν 3625, 3450, 1120, 1080, 1035, 915 cm^{-1}; ^1H NMR (90 MHz) δ 0.86 (s, 3 H), 0.96 (s, 3 H), 1.07 (s, 3 H), 1.1–2.5 (m, 12 H), 3.40 (d-like, *J* = 2.6, $W_{1/2}$ = 5.4 Hz), 3.8–4.1 (m, 4 H).

(2*S*,4a*S*,8a*S*)-(−)-2β-Hydroxy-1,1,4aβ-trimethyl-1,2,3,4,4a,7,8,8aα-octahydronaphthalen-5(6*H*)-one (11). A solution of the hydroxy acetal **9** (393 mg, 1.5 mmol) and pyridinium *p*-toluenesulfonate (50 mg, 0.2 mmol) in 90% aqueous ethanol (11 mL) was heated under reflux for 1.5 h. The solvent was evaporated under reduced pressure, and the residue was taken up in ether. The organic layer was washed with water and brine and dried. Evaporation of the solvent afforded crystals of hydroxy ketone **11** (313 mg, 96%): mp 70–71 °C (from *n*-hexane); $[\alpha]_D$ −44° (*c* 0.200); IR ν 3650, 3500, 1715, 1045 cm^{-1}; ^1H NMR (60 MHz) δ 0.88 (s, 3 H), 1.02 (s, 3 H), 1.15 (s, 3 H), 1.4–2.7 (m, 12 H), 3.22 (m, 1 H). Anal. Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54. Found: C, 73.90; H, 10.79.

(2*S*,4a*S*,8a*R*)-(−)-2β-Hydroxy-1,1,4aβ-trimethyl-1,2,3,4,4a,5,6,7,8,8aα-decahydronaphthalene (3). A solution of the hydroxy ketone **11** (184 mg, 0.88 mmol) and hydrazine hydrate (100%, 0.7 mL) in diethylene glycol (8 mL) was heated at 150 °C for 1 h. Aqueous potassium hydroxide (50%, 2 mL) was added, and the resulting solution was heated at 150 °C for 30 min and then at 210 °C for 1.5 h. After cooling to room temperature, the product was extracted with ether (20 mL × 4). The combined extracts were washed with cold aqueous HCl, water, and brine and dried. After removal of the solvent, MPLC (silica gel, 1:3 ethyl acetate/*n*-hexane) purification of the residue gave the alcohol **3** (125 mg, 73%), which crystallized on evacuation: mp 87–88 °C (from *n*-hexane)(lit.[12] mp 86.5–87.4 °C); $[\alpha]_D$ −9.4° (*c* 0.35) (lit.[12] $[\alpha]_D$ −11.3° (*c* 0.32)); IR ν (KBr) 3275, 1462, 1448, 1390, 1370, 1035 cm^{-1}; ^1H NMR (90 MHz) 0.75 (s, 3 H), 0.91 (s, 3 H), 0.96 (s, 3 H), 1.0–2.0 (m, 14 H), 3.23 (dd, *J* = 8.8, 6.6 Hz, 1 H); ^{13}C NMR (22.5 MHz) 15.06, 19.19, 21.63, 21.76, 27.55, 27.68, 27.81, 34.19, 38.81, 40.30, 45.28, 52.79, 79.74 ppm. Anal. Calcd for $C_{13}H_{24}O$: C, 79.53; H, 12.32. Found: C, 79.36; H, 12.29.

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Registry No. (+)-**1**, 41722-49-0; (−)-**1**, 113666-06-1; (−)-**3**, 58193-61-6; **4**, 57440-68-3; (+)-**5**, 38405-15-1; (−)-**5**, 52842-07-6; (+)-**6**, 113584-70-6; (−)-**6**, 113584-71-7; (±)-**6**, 113666-07-2; (+)-**7**, 26742-33-6; (−)-**8**, 91547-50-1; (−)-**9**, 113666-03-8; **10**, 113666-04-9; (−)-**11**, 113666-05-0; L-β-phenylalanine, 63-91-2; D-β-phenylalanine, 673-06-3; *p*-bromobenzoyl chloride, 586-75-4; 2-butanone ethylene acetal, 126-39-6.

(14) Smith, A. B., III; Mewshaw, R. *J. Org. Chem.* **1984**, *49*, 3685.