2.8 (s, 1 H), 2.6 (s, 1 H), 2.5 (d, J = 3 Hz, 1 H), 2.0 (s, 3 H), 1.5–1.0 (m, 8 H), 0.8 (t, J = 6 Hz, 3 H); ^{13}C NMR δ 209.79, 67.56, 49.94, 36.36, 31.76, 30.77, 25.11, 22.61, 14.03. ^{1}H NMR analysis ($CDCl_3$, 0.02 M, $C(O)CH_3$, $\Delta\Delta\delta$ 0.15 ppm) using Eu(hfc)$_3$, tris-[3-heptafluoropropylhydroxymethylene)-*d*-camphorato]europium(III) (1.1 equiv), as the chiral shift reagent[17] indicated a 95:5 mixture of isomers (90% ee).

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An Asymmetric Synthesis of Enantiomerically Pure (*S*)-(+)-Linalool (3,7-Dimethyl-1,6-octadien-3-ol) and a Formal Synthesis of (*R*)-(−)-Linalool

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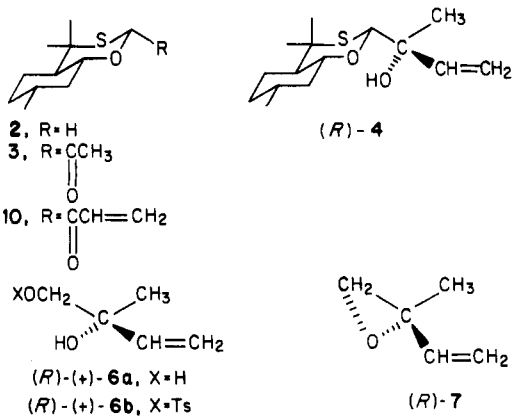
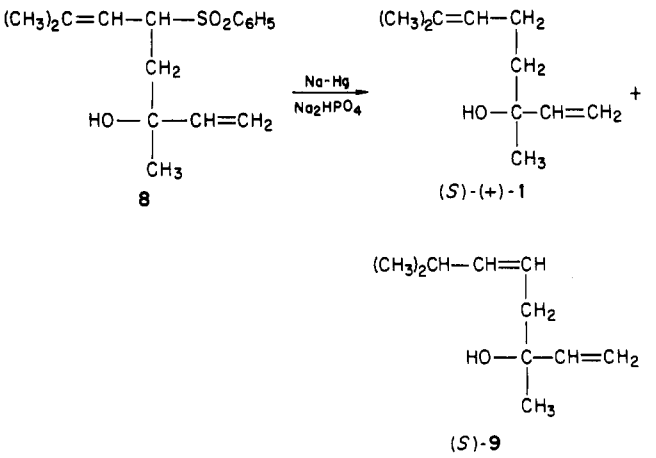
The terpene alcohol linalool (1) occurs in nature in both dextrorotatory (coriandrol) and levorotatory (licareol) forms as a constituent of essential oils,[1] and the correct configuration of the (−)-isomer as *R* was established in the 1960s by two groups of investigators.[2] Although the *dl* isomer has been synthesized by several routes, it has, so far, been only partially resolved.[3] However, a synthesis of enantiomerically pure (−)-**1** in nine steps from a resolved precursor [(*S*)-$C_6H_5CH_2OC(CH_3)(CO_2C_2H_5)CO_2H$[4]] has been reported.[5] We describe here a synthesis of enantiomerically pure (+)-**1** using our previously published[6] asymmetric synthesis employing the readily accessible oxathiane **2**[7] as the chiral template (Scheme I).

Treatment of **3**, obtained from **2** as described,[8] with vinylmagnesium bromide and magnesium chloride at −78 °C gave carbinol (*R*)-**4** in 84% de (92:8 ratio of diastereomers). The major diastereomer was obtained in pure form (as checked by NMR) by recrystallization (52% yield) and was cleaved by *N*-chlorosuccinimide–silver nitrate[9] to (*R*)-2-hydroxy-2-methyl-3-butenal [(*R*)-CH_2=CH(CH_3)C(OH)CHO, (*R*)-**5**], reduced in situ by sodium borohydride to (*R*)-(+)-**6a**, in 62% yield. The latter was converted to the primary mono-*p*-toluenesulfonate (*R*)-(+)-**6b** (83% yield) which, on treatment with ground potassium hydroxide in tetrahydrofuran yielded (*R*)-1,2-epoxy-2-methyl-3-butene (isoprene 1,2-monoepoxide, **7**).

Scheme I



Scheme II



Compounds **5**, **6a**, and **7** are chiral isoprenoid synthons. Since direct conversion of **7** to the monoterpene linalool **1** with prenyl organometallic reagents $(CH_3)_2C$=$CHCH_2M$ appears unfeasible,[10,11] **7** was allowed to react with the anion of prenyl phenyl sulfone, $(CH_3)_2C$=$CHCH_2SO_2C_6H_5$ as previously reported by Julia.[5,10] Reduction of sulfone **8** with sodium amalgam in anhydrous methanol led to linalool, as previously described,[5,10] along with the expected position isomer **9** (Scheme II). Use of the modified reducing conditions described by Trost,[12] i.e., use of disodium hydrogen phosphate (Na_2HPO_4) in the amalgam reduction, improved the ratio of **1**:**9** from the reported[10] 2:1 to 3:1, and **1** could be separated from the position isomer **9** by chromatography on silica gel (gradient elution) to give chemically and enantiomerically pure (+)-**1**. Chemical purity was checked by comparison of proton and ^{13}C NMR spectra with those of authentic samples of (+)-linalool; enantiomeric purity (≥99% ee) was determined by using a chiral shift reagent, Eu(hfc)$_3$.[13]

(*S*)-(−)-**6a** in 94% ee was similarly asymmetrically synthesized from the acryloyl derivative of **2**, **10**, obtained by treating the lithium derivative of **2** with acrolein followed by Swern oxidation.[14] Reaction of **10** with methylmagnesium bromide followed by oxathiane cleavage and sodium borohydride reduction (vide supra) gave (*S*)-(−)-**6a**. Unfortunately the diastereomer of (*S*)-**4** obtained in the

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Grignard reaction in a 97:3 ratio (94% de) was not crystalline in our hands nor could its diastereomeric purity be enhanced by chromatography. Attempts to purify the monotosylate (*S*)-(−)-**6b** derived from (*S*)-(−)-**6a** by crystallization and thus to enhance its enantiomeric purity also failed. In any case, since (*S*)-(−)-**6a** and its tosylate have been converted to (*R*)-(−)-**1**, previously,[5] their asymmetric synthesis in 94% ee [checked in the case of (*S*)-(−)-**6b** by NMR in the presence of Eu(hfc)$_3$] constitutes a formal asymmetric synthesis of (−)-**1** in 94% ee.

Our original intention had been to convert **3** to the chiral aldehyde $(CH_3)_2C{=}CHCH_2C(CH_3)(OH)CH{=}O$ by treatment with $(CH_3)_2C{=}CHCH_2CH_2MgBr$, followed by oxathiane cleavage.[9] The aldehyde could then have been converted to linalool by a Wittig reaction.[15] However, although the Grignard addition proceeded as planned and the diastereomeric purity of the adduct could be enhanced by chromatography, the NCS/$AgNO_3$ cleavage failed,[15] apparently because the reagent also (or preferentially) attacks the trisubstituted double bond, which was lost in the attempted cleavage reaction.

Experimental Section

General Methods. Melting points were taken on an Electrothermal melting point apparatus and are uncorrected. IR spectra were taken on a Beckman 4250 spectrometer calibrated with the 1601-cm^{-1} band of polystyrene. ^{1}H NMR spectra were recorded in $CDCl_3$ with Me_4Si as an internal reference on either a Bruker WM-250 or a Bruker AC-200 instrument. ^{13}C NMR spectra were similarly obtained at 62.8 MHz or 50.2 MHz; the 77.0 ppm resonance of $CDCl_3$ was used as an internal reference. Optical rotations were measured on a Perkin–Elmer Model 141 polarimeter equipped with sodium and mercury light sources in a 1-dm thermostated cell; reported temperatures are uncorrected.

Oxathianecarbinol (*R*)-4. A solution of 1.470 g (6.07 mmol) of methyl oxathianyl ketone **3**[8] in ca. 140 mL of dry THF containing 644 mg (6.76 mmol) of anhydrous magnesium dichloride was refluxed for 30 min and cooled to −78 °C with a dry ice–acetone bath. Freshly prepared vinylmagnesium bromide (23.0 mmol) in ca. 25 mL of THF was added dropwise to the above solution at −78 °C. The reaction mixture was stirred for 1.5 h at −78 °C, quenched with 25 mL of saturated NH_4Cl solution, and allowed to warm to 0 °C with stirring. The aqueous layer was extracted with 4 × 40 mL of ether and the combined organic layer washed with brine and dried over $MgSO_4$. Removal of the solvent at reduced pressure left 1.86 g of crude alcohol (*R*)-4 as a yellow oil, 84% de by ^{1}H NMR. Crystallization from pentane yielded 847 mg (52%) of pure alcohol (*R*)-4, 100% de by ^{1}H NMR: mp 51–53 °C; ^{1}H NMR ($CDCl_3$) δ 0.93 (d, 3 H, *J* = 7.5 Hz), 1.28 (s, 3 H), 1.36 (s, 3 H), 1.41 (s, 3 H), 2.66 (s, 1 H), 3.43 (dt, 1 H, *J* = 3.8, 11.3 Hz), 4.79 (s, 1 H), 5.14 (dd, 1 H, *J* = 1.4, 10.8 Hz), 5.37 (dd, 1 H, *J* = 1.4, 17.4 Hz), 5.95 (dd, 1 H, *J* = 10.8, 17.4 Hz); ^{13}C NMR (CDL_3) δ 21.87, 22.51, 23.05, 24.10, 29.45, 31.14, 34.40, 41.37, 42.83, 50.55, 74.19, 77.24, 85.09, 113.56, 140.73.

(*R*)-(+)-2-Methyl-3-butene-1,2-diol [(*R*)-(+)-6a]. To a solution of 4.31 g (25.4 mmol) of $AgNO_3$ and 3.14 g (23.5 mmol) of *N*-chlorosuccinimide in 90 mL of 80% CH_3CN/20% water were added successively 6.2 mL of 2,6-lutidine and 1.80 g (6.66 mmol) of oxathianecarbinol (*R*)-4 in 15 mL of CH_3CN at ambient temperature. After being vigorously stirred for 10 min, the above reaction mixture was filtered and the filtrate stirred for an additional 20 min before the successive addition of saturated aqueous solutions of Na_2SO_3 and Na_2CO_3 (7 mL each) at 1-min intervals. The resulting solution was filtered and treated with 793 mg (21.0 mmol) of $NaBH_4$ in 7 mL of water. After the mixture was stirred for 2.5 h, 25 mL of acetone was added to quench excess $NaBH_4$, the reaction mixture was filtered again, and the solvent was carefully removed by distillation under reduced pressure (water bath temperature below 35 °C) to leave an oil plus an aqueous layer. The mixture was extracted with 4 × 40 mL of hexanes and the extract washed with 2 × 35 mL of 0.12 N HCl and then with 35 mL of brine and dried over $MgSO_4$. Concentration of the solvent yielded 1.32 g (6.55 mmol, 98%) of the sultine[6] in crystalline form.

The water layer was extracted continuously for 2 days with 300 mL of chloroform. The extract was dried over $MgSO_4$ and the solvent concentrated below 35 °C at reduced pressure to afford a mixture of diol (*R*)-(+)-**6a** and crystalline succinimide. The mixture was dissolved in 20 mL of ether, and succinimide was crystallized out by adding 10 mL of hexanes at 0 °C. Careful removal of solvent gave 655 mg of crude diol (*R*)-(+)-**6a** (84% purity by ^{1}H NMR). Flash chromatography (50:50 EtOAc/hexanes) provided 423 mg (4.14 mmol, 62%) of purified diol (*R*)-(+)-**6a**: $[\alpha]_D$ +4.72° (*c* 3.05, CH_2Cl_2) [lit.[5] $[\alpha]^{20}_D$ −4.83° (*c* 1.37, $CHCl_3$) for *S* isomer]; ^{1}H NMR ($CDCl_3$) δ 1.27 (s, 3 H), 1.83 (br s, 1 H), 2.40 (br s, 1 H), 3.45, 3.51 (AB q, 2 H, *J* = 11 Hz), 5.18 (dd, 1 H, *J* = 2, 11 Hz), 5.32 (dd, 1 H, *J* = 2, 18 Hz), 5.87 (dd, 1 H, *J* = 11, 18 Hz) [lit.[5] δ 1.30, 3.20 (OH), 3.25 (OH), 3.45, 5.24, 5.93].

(*R*)-(+)-2-Methyl-2-hydroxy-3-buten-1-yl *p*-Toluenesulfonate [(*R*)-(+)-6b]. To a solution of 254 mg (2.49 mmol) of diol (*R*)-(+)-**6a** in ca. 3 mL of dry pyridine was added a solution of 517 mg (2.71 mmol) of *p*-toluenesulfonyl chloride in 2 mL of dry pyridine at 0 °C. The mixture was stored in the refrigerator overnight, poured into ca. 30 mL of cold water, and extracted with 5 × 15 mL of ether. The combined ether extract was washed with 4 × 10 mL of 10% H_2SO_4 solution, 15 mL of brine, and 15 mL of saturated $NaHCO_3$ solution and dried over $MgSO_4$. Concentration gave a pale yellow oil, which was purified by flash chromatography (25:75 EtOAc/hexanes) to yield 526 mg (2.05 mmol, 83%) of tosylate (*R*)-(+)-**6b** as crystals: mp 43–44 °C; $[\alpha]^{20}_D$ +14.85° (*c* 3.23, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.30 (s, 3 H), 2,23 (br s, 1 H), 2.47 (s, 3 H), 3.93 (s, 2 H), 5.16 (dd, 1 H, *J* = 1.2, 10.0 Hz), 5.31 (dd, 1 H, *J* = 1.2, 17.0 Hz), 5.83 (dd, 1 H, *J* = 10.0, 17.0 Hz), 7.35 (d, 2 H, *J* = 8.0 Hz), 7.80 (d, 2 H, *J* = 8.0 Hz).

Sulfone 8. (a) Epoxide (*R*)-7. To a solution of 526 mg (2.05 mmol) of tosylate (*R*)-(+)-**6b** in ca. 4 mL of dry THF was added 834 mg of ground KOH in one portion at 10 °C. After being stirred for 1 h at 10 °C, the resulting reaction mixture was filtered through Celite, and the white precipitate formed was washed with ca. 6 mL of THF. The filtrate was distilled at atmospheric pressure to obtain a THF solution of epoxide (*R*)-**7**.

(b) Sulfone 8. A solution of 870 mg (4.14 mmol) of prenyl phenyl sulfone[10] in ca. 6 mL of dry THF was treated with 3.73 mL of *n*-BuLi solution (1.1 M in hexanes) at −78 °C. The resulting wine-red solution was stirred for 15 min at −78 °C and for an additional 15 min without cooling, it was then cooled to −78 °C again, and the above prepared solution of (*R*)-**7** was added rapidly to it. After being stirred for 5 h at ambient temperature, the reaction mixture was poured into a cold saturated NH_4Cl solution, the aqueous layer was extracted with 4 × 20 mL of ether, and the combined organic layer was washed with 30 mL of brine, dried over $MgSO_4$, and evaporated to obtain 1.07 g of sulfone 8 plus excess starting sulfone as a yellow oil. The material was purified by flash chromatography on silica gel (30:70 EtOAc/hexanes) to give 483 mg (1.64 mmol, 80% from (*R*)-(+)-**6b**) of sulfone 8 as a mixture of two diastereomers: $[\alpha]^{20}_D$ +16.96° (*c* 3.06, $CHCl_3$); ^{1}H NMr ($CDCl_3$) δ [major isomer] 1.08 (d, 3 H, *J* = 1.9 Hz), 1.25 (s, 3 H), 1.60 (d, 3 H, *J* = 3.0 Hz), 1.84 (dd, 1 H, *J* = 7.5, 15.0 Hz), 2.13 (br s, 1 H), 2.57 (dd, 1 H, *J* = 3.7, 15.0 Hz), 3.94 (m, 1 H),* 4.99 (dd, 1 H, *J* = 1.9, 11.2 Hz), 4.94–5.03 (m, 1 H), 5.23 (dd, 1 H, *J* = 1.9, 16.9 Hz), 5.74 (dd, 1 H, *J* = 11.2, 16.9 Hz), 7.46–7.55 (m, 2 H),* 7.56–7.67 (m, 1 H),* 7.77–7.86 (m, 2 H)* [lit.[5] δ 1.10 (d), 1.27 (s), 1.6 (d), 1.9 (m), 2.6 (m), 3.9 (m), 5.1 (m), 5.8, 5.9 (d), 7.7 (m)], [minor isomer] 1.00 (d, 3 H, *J* = 1.9 Hz), 1.32 (s, 3 H) [lit.[5] δ 1.31], 1.64 (d, 3 H, *J* = 3.0), 1.92 (dd, 1 H, *J* = 9.4, 15.0 Hz), 2.50 (dd, 1 H, *J* = 3.0, 15.0 Hz), 2.66 (br s, 1 H), 3.94 (m, 1 H),* 5.03–5.11 (m, 1 H), 5.11 (dd, 1 H, *J* = 1.9, 11.2 Hz), 5.21 (dd, 1 H, *J* = 1.9, 16.9 Hz), 5.90 (dd, 1 H, *J* = 11.2, 16.9 Hz), 7.46–7.55 (m, 2 H),* 7.56–7.67 (m, 1 H),* 7.77–7.86 (m, 2 H)* [*peaks overlapped]; IR (neat) 3500 (br s), 3180 (w), 3160 (w), 2970 (s), 2930 (s), 1740 (s), 1600 (m), 1445 (vs), 1300 (vs), 1285 (vs), 1240 (s), 1140 (vs), 1080 (vs), 995 (s), 920 (s), 750 (s), 730 (vs) cm^{-1} [lit.[5] 3350, 1300, 1145, 1000, 925 cm^{-1}].

(*S*)-(+)-Linalool [(+)-1]. To a suspension of 418 mg (1.63 mmol) of sulfone 8 and 933 mg (6.57 mmol) of anhydrous Na_2-

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HPO_4 in ca. 16 mL of MeOH (dried over molecular sieves) was added 2.52 g of 6% sodium amalgam at −4 °C, and then the reaction mixture was allowed to warm to ambient temperature. The progress of the reduction was followed by TLC (15:75 hexanes/CH_2Cl_2). After the mixture was stirred for 6.5 h, 698 mg (4.92 mmol) of anhydrous Na_2HPO_4 and 1.90 g of 6% of sodium amalgam was added to the mixture at 25 °C to complete the reaction. After stirring for an additional 2.5 h, the reaction mixture was poured into 20 mL of cold saturated NH_4Cl solution and extracted with 4 × 20 mL of pentane and dried over $MgSO_4$. The solvent was removed carefully by distillation at atmospheric pressure to leave 272 mg (80% purity) of crude oil containing some solvent. The oil was chromatographed by using gradient elution (pentane and then 50:50 pentane/CH_2Cl_2) to give 164 mg (65%) of (+)-**1**. Enantiomeric excess of (+)-**1** was determined by means of a chiral shift experiment[13] [(+)-**1**/Eu(hfc)$_3$ = 0.15] to be greater than 99% ee: ^{1}H NMR ($CDCl_3$) δ 1.28 (s, 3 H), 1.51–1.65 (m, 3 H), 1.60 (s, 3 H), 1.68 (s, 3 H), 1.96–2.11 (m, 2 H), 5.07 (dd, 1 H, J = 1.9, 11.2 Hz), 5.08–5.17 (m, 1 H), 5.21 (dd, 1 H, J = 1.9, 16.9 Hz), 5.91 (dd, 1 H, J = 11.2, 16.9 Hz).

2-Acryloyl-1,3-oxathiane 10. (a) 2-(1-Hydroxyallyl)-1,3-oxathiane 11. To a solution of 4.07 g (20.3 mmol) of 1,3-oxathiane in ca. 50 mL of dry THF was added 15.2 mL (24.4 mmol, 1.2 equiv) of *n*-BuLi solution (1.6 M in hexanes) at −78 °C. After being stirred for 30 min at −78 °C the reaction mixture was allowed to warm for 30 min and then recooled to −78 °C. A solution of 1.37 g (24.4 mmol) of freshly distilled acrolein in ca. 40 mL of dry THF was added dropwise to the solution of lithio-1,3-oxathiane **2** at −78 °C. After being stirred for 4 h at −78 °C, the reaction mixture was poured into 40 mL of cold saturated NH_4Cl solution. The aqueous layer was extracted with 4 × 30 mL ether; the combined organic layer was washed with brine and dried over $MgSO_4$. Concentration of the solvent gave 5.75 g of alcohol **11** as a yellow oil. This material was used for the next oxidation reaction without further purifications.

(b) 2-Acryloyl-1,3-oxathiane 10. To a solution of 2.16 mL of dimethyl sulfoxide in ca. 40 mL of dry CH_2Cl_2 was added dropwise 4.30 mL of trifluoroacetic anhydride in 20 mL of dry CH_2Cl_2 at −78 °C over 1 h. The resulting white suspension was stirred for 30 min at −78 °C, and then 5.75 g of alcohol **11** in ca. 50 mL of dry CH_2Cl_2 was added slowly over 50 min. After being stirred for 1.5 h at −78 °C, the reaction mixture was quenched with 8.0 mL of dry triethylamine, allowed to warm, and then poured into 150 mL of cold 10% HCl solution. The aqueous layer was extracted with 3 × 50 mL of CH_2Cl_2, and the combined organic layer was washed with 50 mL of water and dried over $MgSO_4$. Removal of the solvent gave 7.70 g of crude ketone **10** as a yellow oil, which was purified by flash chromatography to yield 3.34 (13.1 mmol, 65% based on 1,3-oxathiane **2**) of pure ketone **10** as crystalline material. Recrystallization from hexanes provided an analytical sample: mp 56–57 °C; ^{1}H NMR ($CDCl_3$) δ 0.93 (d, 3 H, J = 8.3 Hz), 1.30 (s, 3 H), 1.49 (s, 3 H), 3.48 (dt, 1 H, J = 4.4, 10.4 Hz), 5.64 (s, 1 H), 5.82 (dd, 1 H, J = 1.8, 10.4 Hz), 6.46 (dd, 1 H, J = 1.9, 17.5 Hz), 6.78 (dd, 1 H, J = 10.4, 17.5 Hz); ^{13}C NMR ($CDCl_3$) δ 21.67, 22.16, 23.64, 28.95, 30.67, 34.17, 41.10, 43.71, 49.91, 76.56, 81.51, 129.88, 130.63, 192.51; IR ($CHCl_3$) 3020, 2960, 2920, 2865, 1705, 1615, 1455, 1400, 1385, 1366, 1300, 1188, 1145, 1115, 1082, 1060, 1000, 975, 962, 906 cm^{-1}. Anal. Calcd for $C_{14}H_{22}O_2S$: C, 66.10; H, 8.72. Found: C, 65.81; H, 8.86.

Oxathianecarbinol (*S*)-4. A mixture of 1.185 g (4.66 mmol) of acryloyl-1,3-oxathiane **10** and 1.40 (5.37 mmol) of magnesium bromide etherate in ca. 60 mL of dry THF was refluxed to obtain a clear solution and then was cooled to −78 °C. To the above solution was rapidly added 8.1 mL of methylmagnesium bromide solution (2.9 M in THF) at −78 °C. After the mixture was stirred for 2 h at −78 °C, 20 mL of saturated NH_4Cl solution was added to the reaction mixture. The aqueous layer was extracted with 3 × 30 mL of ether, and the combined organic layer was washed with 40 mL of brine and dried over $MgSO_4$. Concentration of the solvent at reduced pressure gave 1.39 g of crude oil (*S*)-**4**, 94% de (by ^{1}H NMR). This material was purified by flash chromatography (10:90 EtOAc/hexanes) to provide 1.09 g (4.04 mmol), 87%) of (*S*)-**4** as a colorless oil, 94% de by ^{1}H NMR: ^{1}H NMR ($CDCl_3$) δ 0.92 (d, 3 H, J = 6.5 Hz), 1.27 (s, 3 H), 1.33 (s, 3 H), 1.41 (s, 3 H), 2.73 (br s, 1 H), 3.38 (dt, 1 H, J = 4.3, 10.4 Hz), 4.83 (s, 1 H), 5.17 (dd, 1 H, J = 1.4, 10.7 Hz), 5.38 (dd, 1 H, J = 1.4, 17.2 Hz), 6.00 (dd, 1 H, J = 10.7, 17.2 Hz); ^{13}C NMR (acetone-d_6) δ 22.41, 23.19, 24.49, 29.94, 30.44, 32.02, 35.46, 42.53, 43.20, 51.72, 74.65, 78.00, 86.69, 112.79, 143.35.

(*S*)-(−)-2-Methyl-3-butene-1,2-diol [(*S*)-(−)-6a]. The oxathianecarbinol (*S*)-**4** was treated with NCS, $AgNO_3$, and 2,6-lutidine as described for (*R*)-(+)-**6a**. Workup and continuous extraction as before followed by flash chromatography gave diol (*S*)-(−)-**6a** (61% yield), and the sultine[6] (99% yield): ^{1}H NMR ($CDCl_3$) δ 1.17 (s, 3 H), 3.40, 3.50 (AB q, 2 H, J = 10.3 Hz), 3.50 (br s, 2 H), 5.12 (dd, 1 H, J = 2.0, 12.0 Hz), 5.30 (dd, 1 H, J = 2.0, 17.4 Hz), 5.91 (dd, 1 H, J = 12.0, 17.4 Hz).

(*S*)-(−)-2-Methyl-2-hydroxybuten-1-yl *p*-Toluenesulfonate [(*S*)-(−)-6b]. The tosylate (*S*)-(−)-**6b** was prepared from diol (*S*)-(−)-**6a** as described above for the enantiomer in 61% yield (purified by flash chromatography): mp 37–41 °C; $[\alpha]^{20}_D$ −12.22° (*c* 2.97, $CHCl_3$). This material was further purified by recrystallization from ether–hexanes to give (*S*)-(−)-**6b** in 49% yield: mp 43–44 °C; $[\alpha]^{20}_D$ −14.01° (*c* 3.26, $CHCl_3$). The enantiomeric purity of (*S*)-(−)-**6b** was determined by means of a chiral shift experiment [(*S*)-(−)-**6b**/Eu(hfc)$_3$ = 0.29] to be 94% ee: ^{1}H NMR ($CDCl_3$) δ 1.28 (s, 3 H), 2.46 (s, 3 H), 3.89 (s, 2 H), 5.17 (dd, 1 H, J = 0.96, 10.7 Hz), 5.32 (dd, 1 H, J = 0.96, 17.3 Hz), 5.81 (dd, 1 H, J = 10.7, 17.3 Hz), 7.38 (d, 2 H, J = 8.48 Hz), 7.79 (d, 2 H, J = 8.48 Hz).

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Aromatic Norditerpenes from the Nudibranch *Chromodoris macfarlandi*

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Dorid nudibranchs are shell-less marine molluscs that are believed to have acquired a chemical defense against predation that compensates for the loss of the shell.[1] Members of the genus *Chromodoris* feed on sponges, from which they obtain their defensive chemicals.[2] In this paper, we report the isolation of two aromatic norditerpenes, macfarlandin A (**1**) and macfarlandin B (**2**) from *Chromodoris macfarlandi* (see Chart I). The macfarlandins **1** and **2** are closely related to the diterpene aplysulphurin (**3**), a metabolite of the sponge *Aplysilla sulphurea*.[3]

Twenty-two specimens of *Chromodoris macfarlandi* were collected by hand at a depth of approximately −30 m in Scripps Canyon, La Jolla. The dichloromethane-soluble material from an acetone extract of the animals contained a mixture of terpenoid compounds from which two aromatic norditerpenes, macfarlandin A (**1**), mp 183–184 °C, and macfarlandin B (**2**), a glass, were obtained.

It was immediately apparent that the macfarlandins were closely related isomers. Both compounds gave almost identical mass spectral data: the highest peak in the electron impact mass spectra at m/z 343.1545 for **1** and m/z 343.1523 for **2** corresponded to an $[M - CH_3]^+$ ion but the chemical ionization mass spectra both contained $[M + H]^+$ peaks at m/z 359, indicating the molecular formula $C_{21}H_{26}O_5$. The ^{13}C NMR spectrum of macfarlandin A (**1**)

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