EtOH); IR (film) 3400, 1355, 1152, 1110, 1078, 1015, 948, 930, 840 cm^{-1}; NMR (CCl_4) δ 0.9–1.9 (m, 13 H), 2.50 (s, 1 H, OH), 3.45 (*t*, *J* = 6 Hz, 2 H), 3.80 (s, 4 H).

Anal. Calcd for $C_{11}H_{20}O_3$: C, 65.97; H, 10.07. Found: C, 65.73; H, 10.09.

3-(3,3-Ethylenedioxycyclohexyl)propyl *p*-Toluenesulfonate (17). Treatment of (−)-**16**, $[\alpha]_D$ −1.9° (5.00 g, 25.0 mmol), with *p*-toluenesulfonyl chloride (5.20 g, 27.5 mmol) according to Becker's procedure[5c] gave 7.1 g (80% yield) of **17** as an oil. IR (film): 1600, 1360, 1190, 1178, 1078, 945, 815 cm^{-1}.

(+)-3-(3-Bromopropyl)cyclohexanone (18) was obtained from **17** in a similar manner to that described by Becker:[5c] 3.35 g (76% yield); bp 103–104 °C (0.3 mm); $[\alpha]^{30}_D$ +3.0° (*c* 1.45, EtOH); IR (film) 1712, 1345, 1312, 1250, 1225 cm^{-1}.

Anal. Calcd for $C_9H_{15}OBr$: C, 49.33; H, 6.90; Br, 36.47. Found: C, 49.60; H, 7.00; Br, 36.25.

(+)-3-(3-Oxocyclohexyl)propyltriphenylphosphonium bromide (19) was prepared from (+)-**18** in the same manner as described by Becker:[5c] 5.35 g (76% yield); $[\alpha]^{28}_D$ +3.6° (*c* 0.827, CH_2Cl_2); IR (KBr) 1705, 1438, 1111, 992, 755, 740, 738, 695 cm^{-1}.

Anal. Calcd for $C_{27}H_{30}OBrP$: C, 67.36; H, 6.28. Found: C, 67.29; H, 6.25.

(−)-(*S*)-Bicyclo[3.3.1]-1(2)-nonene (7). Sodium hydride (1.05 g, 43.6 mmol), washed oil free with dry pentane, and (+)-**19**, $[\alpha]_D$ +3.6° (5.25 g, 10.9 mmol), were suspended in dry tetraglyme (40 mL) containing 2-methyl-2-butanol (0.96 g) under nitrogen. After the mixture was heated to 70 °C for 30 min, the temperature was raised gradually to 120 °C during 4 h, and the mixture was kept at this temperature for 20 min. Distillation in vacuo (120 °C, 10 mm) removed low-boiling fractions, and the residue was vacuum distilled (oil-bath temperature 120–125 °C) (5 mm) into a cold trap. The distillate was diluted with dry pentane, dried over anhydrous Na_2SO_4, and chromatographed on Florisil. Elution with dry pentane yielded 360 mg of **7** (27% yield) as a colorless oil, which was further purified by distillation: bp 80–85 °C (air-bath temperature) (12 mm); $[\alpha]^{30}_D$ −259° (*c* 0.574, $CHCl_3$); $[\alpha]^{30}_D$ −237° (*c* 0.500, EtOH); CD (*c* 9.11 × 10^{-4}, isooctane) [θ] −4.88 × 10^4 deg cm^2/dmol (213 nm); IR (film) 3022, 1620, 1455, 1230, 1212, 1098, 1022, 992, 956, 860, 810, 712 cm^{-1}; NMR (CCl_4) δ 0.8–2.6 (m, 13 H), 5.60 (t, *J* = 7 Hz, 1 H); mass spectrum *m/e* 122 (M^+).

Anal. Calcd for C_9H_{14}: C, 88.45; H, 11.55. Found: C, 88.41; H, 11.41.

(−)-3-Methylcyclohexanone (22). The same procedure as described for the preparation of (−)-**12** afforded (+)-**12**, $[\alpha]^{24}_D$ +3.5° (*c* 1.85, EtOH), from (+)-**8**, $[\alpha]_D$ +5.6°. Tosylation of (+)-**12**, $[\alpha]_D$ +3.5° (1.00 g, 5.81 mmol), was carried out with *p*-toluenesulfonyl chloride (1.30 g, 6.97 mmol) and 3 mL of dry pyridine by a similar manner to that described for tosylation of (−)-**12** to yield 1.80 g of the tosylate **20** as an oil. The tosylate **20** (1.80 g), without further purification, was dissolved in dry ether (20 mL), and the solution was added to a suspension of $LiAlH_4$ (0.44 g, 11.6 mmol) in dry ether (40 mL). The mixture was refluxed for 5 h, and the reaction complex was decomposed with 5% HCl. An inorganic solid was filtered off and the filtrate was washed with saturated $NaHCO_3$ solution and water, dried ($MgSO_4$), and concentrated. To the residue was added 10% sulfuric acid (10 mL), and the mixture was stirred for 28 h at room temperature and extracted with ether. The extract was washed with saturated $NaHCO_3$ solution and water, dried ($MgSO_4$), and concentrated. The residue was chromatographed on silica gel, and the eluent with pentane–ether (7:3 (v/v)) was distilled to give 160 mg of (−)-**22** (25% yield based on (+)-**12**): bp 172–175 °C (air-bath temperature) (760 mm); $[\alpha]^{27}_D$ −4.1° (*c* 1.62, EtOH); IR (film) 1710, 1275, 1225 cm^{-1}; NMR (CCl_4) δ 1.02 (d, *J* = 6 Hz, 3 H), 1.2–2.1 (m, 5 H), 2.1–2.4 (m, 4 H).

Anal. Calcd for $C_7H_{12}O$: C, 74.95; H, 10.78. Found: C, 75.06; H, 10.92.

Registry No. (−)-(*S*)-**7**, 70144-90-0; (±)-**8**, 49543-05-7; (−)-**8** cinchonidine salt, 70222-83-2; (−)-**8**, 21531-44-2; (+)-**8**, 21531-45-3; (−)-**9**, 70144-91-1; (−)-**10**, 21531-47-5; (−)-**11**, 70116-85-7; (−)-**12**, 70116-86-8; (+)-**12**, 70116-87-9; **13**, 70116-88-0; **14**, 70116-89-1; (−)-**15**, 70116-90-4; (−)-**16**, 70116-91-5; **17**, 70116-92-6; (+)-**18**, 70116-93-7; (+)-**19**, 70130-70-0; **20**, 70116-94-8; (−)-**22**, 24965-87-5; ethylene glycol, 107-21-1; ethyl malonate, 105-53-3.

Non-Head-to-Tail Monoterpenes. Synthesis of (*S*)-Lyratol and (*S*)-Lyratyl Acetate from (1*R*,3*R*)-Chrysanthemic Acid[1]

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Received November 14, 1978

(+)-(*S*)-Lyratol (1-OH) and (+)-(*S*)-lyratyl acetate (1-OAc) were synthesized from (1*R*,3*R*)-chrysanthemic acid ((1*R*,3*R*)-**2**-OH). The key steps in the sequence were the stereospecific oxidation of the (*E*)-methyl group in the isobutenyl moiety of chrysanthemyl acetate ((1*R*,3*R*)-**3**-OAc) with selenium dioxide and the regiospecific cleavage of the C(1)–C(2) cyclopropane bond in aldehyde methanesulfonate (1*R*,3*R*)-**4**-OMs to give the santolinyl skeleton found in lyratol. Since the synthesis began with (1*R*,3*R*)-chrysanthemic acid ((1*R*,3*R*)-**2**-OH) and did not alter the configuration at C(3), (+)-lyratol and (+)-lyratyl acetate are the (*S*) enantiomers. The absolute configurations of synthetic lyratol and lyratyl acetate are the same as those of their naturally occurring counterparts isolated from *Cyanthocline lyrata*.

Irregular monoterpenes, those which do not follow the common 1′–4 bonding pattern,[3] are most commonly found in a closely related group of plants in the Compositae family.[4] These compounds were considered to be biosynthetic curiosities until the discovery that the irregular terpenes presqualene[5] and prephytoene pyrophosphate[6]

(1) This investigation was supported by National Institutes of Health Grant GM 21328 and the University of Utah Research Committee.

(2) (a) Recipient of Research Career Development Award HL 00084 from the National Institutes of Health; (b) Alfred P. Sloan Fellow.

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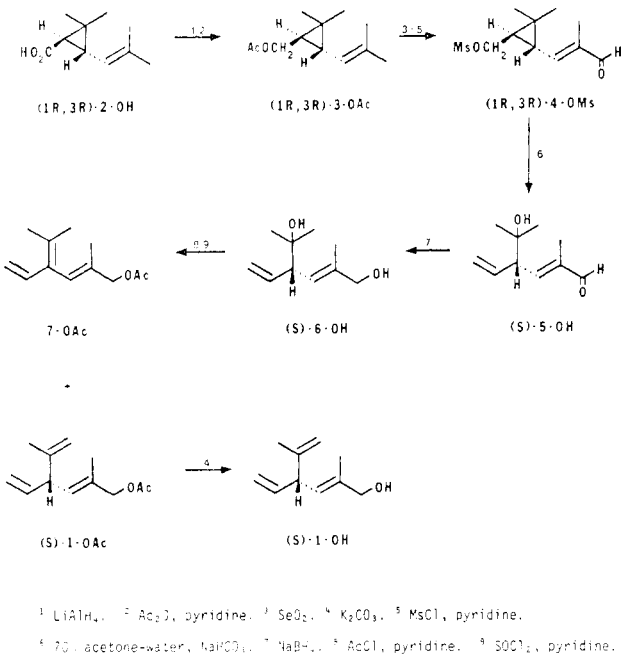
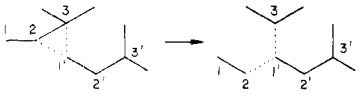
Scheme I. Synthesis of (*S*)-Lyratol ((*S*)-1-OH)



[1] $LiAlH_4$. [2] Ac_2O, pyridine. [3] SeO_2. [4] K_2CO_3. [5] MsCl, pyridine. [6] 70% acetone–water, $NaHCO_3$. [7] $NaBH_4$. [8] AcCl, pyridine. [9] $SOCl_2$, pyridine.

were normal intermediates in the sterol and carotenoid pathways. Although biological data for the C_{10} compounds are still not conclusive,[7] most current theories place the irregular structures after branch points which involve coupling of two regular allylic terpene pyrophosphates.[7,8] The lavandulyl (1′–2) and chrysanthemyl (1′–2–3) structures have been proposed as the initial products of the non-head-to-tail condensation reactions with artemisyl (1′–3), santolinyl (2–1′–3), and head-to-head (1′–1) structures arising from rearrangements of the 1′–2–3 system.[7]

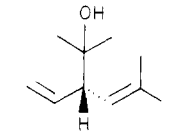
The proposed mechanism (1) for the chrysanthemyl to

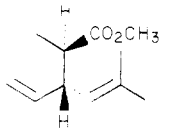


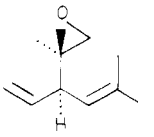
(1)

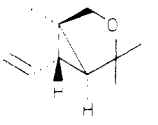
santolinyl rearrangement leaves the configuration at C(1′) intact, and as a corollary the absolute configuration of C(1′) in the 1′–2–3 precursor should be retained in the 2–1′–3 derivatives. Thus far, only the (1*R*,3*R*) enantiomer of the *trans*-chrysanthemic system has been isolated from natural sources.[4,7d] We recently demonstrated that the absolute configuration in santolina alcohol, a 2–1′–3 monoterpene isolated from *Oremenis multicaulis*, is the same as that

Chart I


(*S*)-santolina alcohol


(2*R*,3*S*)-methyl santolinate


(2*R*,3*R*)-oxidosantolina triene


(1*R*,5*S*,6*S*)-artemeseole

in naturally occurring 1′–2–3 terpenes[9] and now report the synthesis of (+)-(*S*)-lyratol (1-OH) and (+)-(*S*)-lyratyl acetate (1-OAc), 2–1′–3 monoterpenes found in *Cyanthocline lyrata*.[10]

Results and Discussion

The synthesis of (*S*)-lyratol (1-OH) and the corresponding acetate from readily available (+)-(1*R*,3*R*)-chrysanthemic acid ((1*R*,3*R*)-**2**-OH)[11] is outlined in Scheme I. The key step in the synthetic plan involves the regiospecific cleavage of the C(1)–C(2) cyclopropane bond to give the santolinyl skeleton while retaining the stereochemistry at C(3). In previous work, we demonstrated that low (ca. 0.5%) yields of santolina alcohol were obtained during solvolysis of suitable derivatives of chrysanthemol (**3**-OH).[3,12] However, the majority of the products was derived from an allylic cation produced by cleavage of the C(1)–C(3) cyclopropane bond. Thus, for this approach to succeed, it was necessary to suppress the cleavage of the C(1)–C(3) bond in order to allow C(1)–C(2) opening to compete. Since the C(1)–C(3) cleavage transfers substantial amounts of positive charge into the vinyl moiety attached to C(3), we reasoned that replacing the (*E*)-vinyl methyl by an electron-deficient group would suppress the undesired bond cleavage, and the group could be used later to introduce hydroxyl or acetate functionality at that position.

(1*R*,3*R*)-Chrysanthemyl acetate ((1*R*,3*R*)-**3**-OAc), obtained by reduction and acetylation of (1*R*,3*R*)-chrysanthemic acid ((1*R*,3*R*)-**2**-OH), was oxidized stereospecifically with selenium dioxide to give aldehyde acetate (1*R*,3*R*)-**4**-OAc in an overall yield of 34%. The acetyl group was removed, and the resulting alcohol (1*R*,3*R*)-**4**-OH was converted to the corresponding methanesulfonate, (1*R*,-3*R*)-**4**-OMs. This highly reactive material was solvolyzed without purification to yield alcohol aldehyde (*S*)-**5**-OH, and the unstable product was immediately treated with sodium borohydride to prevent racemization of the asymmetric center. The resulting diol (*S*)-**6**-OH was obtained from (1*R*,3*R*)-**4**-OAc in an overall yield of 85%. Elimination of the tertiary hydroxyl group was carried out with thionyl chloride in pyridine at −20 °C, and gave a 10:1

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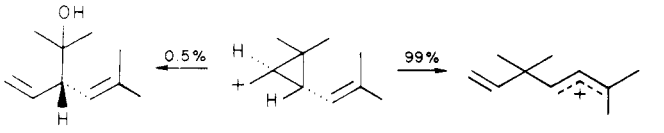
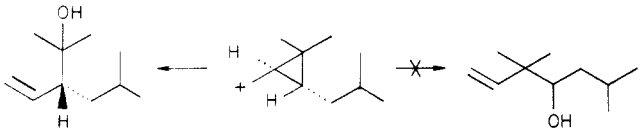
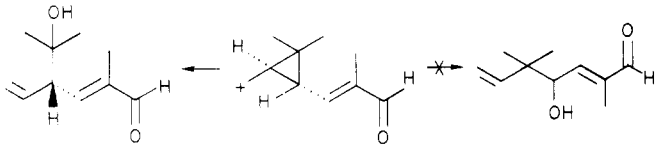
mixture of (+)-(*S*)-lyratyl acetate[10d] and cross-conjugated triene 7-OAc. Hydrolysis of (*S*)-1-OAc yielded (+)-(*S*)-lyratol in an overall yield of 19% from (1*R*,3*R*)-2-OH. Infrared and mass spectral data for the synthetic alcohol matched those reported by Devgan and co-workers[10c] for lyratol isolated from natural sources. In addition, the NMR spectrum we obtained was identical with that which was published.[10c]



(*S*)-santolina alcohol



(*R*)-dihydrosantolina alcohol



(*S*)-5-OH

As we surmised, the regiochemistry of the cyclopropylcarbinyl–homoallyl rearrangement in the chrysanthemyl system is extremely sensitive to the electronic properties of the substituents at C(3). At one extreme, the C(1)–C(3) cyclopropane bond opens regioselectively via isomerization of the initially formed primary cyclopropylcarbinyl cation to its more stable allylic isomer prior to reaction with solvent.[3] At the other extreme, saturation of the double bond in the side chain removes the driving force for the cyclopropylcarbinyl–allyl rearrangement and nucleophilic attack occurs exclusively at C(2) of the *intact* cyclopropane ring.[9] Introduction of the oxo moiety adjacent to the side-chain double bond also completely suppresses the cyclopropylcarbinyl to allyl rearrangement and nucleophilic attack at C(3). Thus, solvent adds regiospecifically at C(2), presumably by backside attack,[13] to yield the homoallylic product. Since the configuration of C(3) in chrysanthemic acid is preserved throughout the sequence of reactions, (+)-lyratol and (+)-lyratyl acetate are the (*S*) enantiomers, the same as isolated from *Cyanthocline lyrata*. After we corrected for the fact that the starting material for our synthesis was only 97% optically pure, the rotations of synthetic lyratol and lyratyl acetate matched those of the natural products.

Previous to this work, absolute configurations have been reported for the four naturally occurring 2–1′–3 structures shown in Chart I. Three of the compounds, (*S*)-santolina alcohol (from *Ormenis multicaulis*[9]), (2*R*,3*S*)-methyl santolinate (from *Artemisia tridentata*[14]), and (1*R*,5*S*,-6*S*)-artemeseole (from *Artemisia tridentata*[15]), have the same configuration at the divinyl-methine carbon as (*S*)-lyratol and (*S*)-lyratyl acetate and could, in principle, be derived from the (1*R*,3*R*)-chrysanthemyl system. (1*R*,3*R*)-Chrysanthemol ((1*R*,3*R*)-3-OH) was recently found in the essential oil of *Artemisia ludoviciana*,[16] a variety of sage indigeneous to Utah and a close relative of the plants which produce 2–1′–3 monoterpenes. However, Epstein and Noble recently showed that oxidosantolina triene from *Artemisia tridentata* is the (2*R*,3*R*) enantiomer[17] and thus belongs to the opposite configurational series. In addition, samples of *Artemisia tridentata* which contain both enantiomers of santolina triene and oxidosantolina triene were found.[18] If the assumption that 2–1′–3 monoterpenes are derived from 1′–2–3 precursors is true, the divergence of stereochemistry must occur during biosynthesis of the cyclopropane ring. This could happen at an enantiomeric branch point where both enantiomers of the *trans*-chrysanthemyl intermediate are produced or at a diastereomeric branch point which produces (1*R*,3*R*)-trans and (1*R*,3*S*)- cis intermediates, as recently suggested by Epstein and Noble.[17] The final resolution of this question awaits appropriate incorporation experiments.

Experimental Section

General Procedures. All reactions were routinely monitored by thin-layer chromatography by using Baker Flex IB-F plates. The eluting solvent, unless reported otherwise, was a 16/84 (v/v) mixture of ethyl acetate and toluene. A Varian Aerograph 90-P3 gas chromatograph equipped with a 10% Carbowax on Chromosorb W-AW (63% 100/120, 37% 60/80 mesh) $^1/_8$ in. × 6 ft column was used for preparative separations. Medium-pressure chromatographic separations were achieved on silica gel with a "home-made" apparatus. Infrared spectra were obtained on a Beckman Acculab-3 infrared spectrophotometer. NMR spectra were measured on a Varian EM-390 spectrometer, and chemical shifts are reported in parts per million downfield (δ) from internal tetramethylsilane (Me_4Si). Ultraviolet spectra were obtained on a Beckman Model 24 spectrophotometer. Optical rotations were measured on a Perkin-Elmer Model 141 polarimeter. Carbon–hydrogen analyses were carried out by Chemalytics Inc. Routine mass spectra (chemical ionization and electron impact) were obtained with a Varian MAT 112-S mass spectrometer equipped with a computerized data system, and the high-resolution exact mass measurements were obtained with a Varian MAT 731 spectrometer.

(1*R*,3*R*)-2,2-Dimethyl-3-(2-methyl-1-propenyl)cyclopropanemethanol, (1*R*,3*R*)-Chrysanthemol ((1*R*,3*R*)-3-OH). The alcohol was prepared in 80% yield by reduction of the corresponding acid with lithium aluminum hydride.[3]

(1*R*,3*R*)-2,2-Dimethyl-3-(2-methyl-1-propenyl)cyclopropanemethyl Acetate, (1*R*,3*R*)-Chrysanthemyl Acetate ((1*R*,3*R*)-3-OAc). The acetate was prepared in 87% yield from (1*R*,3*R*)-chrysanthemol (97% optically pure) according to the procedure of Sasaki and co-workers;[19] $[\alpha]^{26}_{589}$ +20.40° (*c* 11.0 g/100 mL, cyclohexane).

(1*R*,3*R*)-(*E*)-2,2-Dimethyl-3-(2-methyl-3-oxo-1-propenyl)cyclopropanemethyl Acetate ((1*R*,3*R*)-4-OAc). To a refluxing solution of 5 g (0.026 mol) of (1*R*,3*R*)-3-OAc in 125 mL of toluene was added 6.15 g (0.055 mol) of selenium dioxide. After being heated at reflux for 1 h, the reaction mixture was allowed to cool slowly before filtering through a fine sintered glass funnel. The filtrate was washed with three 100-mL portions of 4% hydrogen peroxide, and solvent was removed under reduced pressure. The residue was bulb-to-bulb distilled to give 2.60 g (49%) of the desired aldehyde acetate: bp 110–113 °C (0.45 mm); R_f 0.62; IR (CCl_4) 2980, 2950, 2920, 1735, 1685, 1630, 1365, 1230, 1205, 1120, 1195, 1035 cm^{-1}; NMR (CCl_4) 1.1–1.9 (2, m, cyclopropyl), 1.20 (3, s, cyclopropyl methyl), 1.23 (3, s, cyclopropyl methyl), 1.79 (3, s, vinyl methyl), 2.05 (3, s, acetoxy methyl), 3.83–4.26 (2, m, acetoxy methylene), 6.16 (1, d, J = 10 Hz, olefinic H), 9.3 (1, s, aldehyde H) ppm; $[\alpha]^{25}_{589}$ +25.19° (*c* 0.84 g/100 mL, ethanol); λ_{max}^{EtOH} 246 nm (ε 17 150); a chemical ionization mass

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spectrum (methane) gave the base peak at m/e 211; exact mass measurements were made by scanning and by peak matching at m/e 209. Ionizing energy was 70 eV with the ion source temperature at 230 °C. The sample was introduced by a direct probe which was water cooled and heated gently. Expected peaks were seen at M − 1, m/e 209.1175, M − 15, m/e 195.1022, and M − 43, m/e 167.1070.

(1*R*,3*R*)-(*E*)-2,2-Dimethyl-3-(2-methyl-3-oxo-1-propenyl)cyclopropanemethanol ((1*R*,3*R*)-4-OH). A mixture of (1*R*,3*R*)-4-OAc (0.93 g, 4.4 mmol) and potassium carbonate (0.5 g, 5.9 mmol) in 20 mL of 90% methanol–water was stirred at room temperature until hydrolysis was complete (3 h). Most of the solvent was removed at reduced pressure and the residue was saturated with sodium chloride before extraction with three 20-mL portions of ether. The combined ether layers were dried over magnesium sulfate, and solvent was removed at reduced pressure. The residue was purified by medium-pressure chromatography (33/67 (v/v) ethyl acetate and toluene) giving 0.70 g (95%) of the desired aldehyde alcohol: R_f 0.075; IR (CCl_4) 3620, 3440 (broad), 2970, 2950, 2920, 2870, 2810, 2705, 1680, 1629, 1450, 1420, 1403, 1375, 1246, 1110, 1078, 1015, 860, 830, 693 cm^{-1}; NMR (CCl_4) 0.9–1.55 (2, m, cyclopropyl), 1.23 (6, d, cyclopropyl methyls), 1.75 (3, s, vinyl methyl), 3.2 (1, s, hydroxy H), 3.6 (2, d, J = 7.5 Hz, hydroxy methylene), 6.05 (1, d, J = 10 Hz, olefinic H), 9.2 (1, s, aldehyde H) ppm; $[\alpha]^{25}_{589}$ +51.26° (c 0.27 g/100 mL, ethanol); λ_{max}^{EtOH} 257 nm (ϵ 17 817); chemical ionization mass spectra (methane) gave a peak at m/e 171 (M + 1).

(*S*)-(*E*)-2,5-Dimethyl-4-ethenyl-2-hexene-1,5-diol ((*S*)-6-OH). A solution of 0.14 g (0.83 mmol) of (1*R*,3*R*)-4-OH in 25 mL of dry acetone was cooled to −20 °C before 80 μL (0.12 g, 1.0 mmol) of freshly distilled methanesulfonyl chloride and 170 μL (0.12 g, 1.2 mmol) of triethylamine were added in rapid succession.

After 20 min the mixture was poured through a sintered glass suction funnel into a solution of 0.13 g (1.5 mmol) of sodium bicarbonate in 25 mL of 70% acetone–water. The resulting solution was maintained at room temperature for 1 h before most of the solvent was removed at reduced pressure. The aqueous portion that remained was saturated with sodium chloride and extracted with three 20-mL portions of ether. Ether was removed under reduced pressure leaving 0.14 g of a yellow oil.

The oil was dissolved in 25 mL of absolute ethanol, and 0.10 g (2.6 mmol) of sodium borohydride was added. After 1 h, the reaction was quenched with 25 mL of saturated sodium chloride solution and extracted with three 25-mL portions of ether. The combined organic layers were washed with saturated sodium bicarbonate and dried over magnesium sulfate before solvent was removed under reduced pressure. Analysis of the mixture by gas chromatography indicated a single major component. Purification by medium-pressure chromatography (33/67 (v/v) ethyl acetate and toluene) gave (*S*)-(*E*)-2,5-dimethyl-4-ethenyl-2-hexene-1,5-diol: 0.13 g (90%); R_f 0.1 (33/67, ethyl acetate/toluene); IR (CCl_4) 3360, 3340 (broad), 3079, 2975, 2920, 2875, 1643, 1460, 1425, 1390, 1348, 1275, 1215, 1183, 1110, 1070, 1025, 933, 889, 675 cm^{-1}; NMR (CCl_4) 1.12 (6, s, methyls at C(5)), 1.6 (3, s, vinyl methyl), 2.87 (1, t, J = 9 Hz, H at C(4)), 3.56 (2, s, hydroxyl H's), 3.87 (2, s, H at C(1)), 4.75–5.1 (2, m, vinyl methylene), 5.4 (1, d, J = 10 Hz, vinyl H), 5.5–6.0 (1, m, H at C(3)) ppm; $[\alpha]^{24}_{589}$ +15.78° (c 0.59 g/100 mL, chloroform); chemical ionization mass spectra (methane) gave a peak at m/e 171 (M + 1); an electron impact mass spectrum gave a base peak at m/e 79 (M − 91) with characteristic peaks at m/e 139 (M − 31), 112 (M − 58), 94 (M − 76), 59 (M − 111).

(*S*)-(*E*)-2,5-Dimethyl-4-ethenyl-5-hydroxy-2-hexen-1-yl Acetate ((*S*)-6-OAc). A solution of 114 mg (0.67 mmol) of (*S*)-6-OH and 0.1 mL (1.34 mmol) of pyridine in 25 mL of carbon tetrachloride was cooled to 0 °C before slow addition of 48 μL (0.67 mmol) of acetyl chloride in 50 mL of carbon tetrachloride. After 30 min, the reaction was worked up as described for (1*R*,3*R*)-3-OAc, yielding 100 mg (78%) of the desired acetate. Analytical samples were obtained by preparative gas chromatography: R_f 0.75 (33/67 (v/v), ethyl acetate and toluene); IR (CCl_4) 3600, 3560, 3480 (broad), 3065, 2970, 2925, 2875, 1740, 1639, 1465, 1445, 1380, 1343, 1240, 1175, 1060, 1033, 1010, 929, 875, 670 cm^{-1}; NMR (CCl_4) 1.1 (6, s, methyls at C(5)), 1.64 (3, s, methyl at C(2)), 2.0 (3, s, acetoxy methyl), 2.28 (1, s, hydroxyl H), 2.9 (1, d of d, J = 7.8 and 10.2 Hz, H at C(4)), 4.42 (2, s, H at C(1)), 4.75–5.15 (2, m, J = 11.4 and J = 16.8 Hz, vinyl methylene), 5.45 (1, d, J = 10.2 Hz, H at C(3)), 5.5–6.0 (1, d of d of d, J = 7.8, 11.4, and 1.68 Hz, vinyl H); $[\alpha]^{24}_{589}$ +20.86° (c 0.38 g/100 mL, chloroform); chemical ionization mass spectra (methane) gave no M + 1 peak but showed major fragments at m/e 195 (M − 17), 135 (M − 77), 119 (M − 93), and 95 (M − 117); electron impact mass spectra gave the base peak at m/e 79 (M − 133) with other characteristic peaks at m/e 154 (M − 58), 94 (M − 118), 59 (M − 153), 43 (M − 169).

Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.88; H, 9.50. Found: C, 68.03; H, 9.70.

(*S*)-(*E*)-2,5-Dimethyl-4-ethenyl-2,5-hexadien-1-yl Acetate, (*S*)-Lyratyl Acetate ((*S*)-1-OAc). A solution of 100 mg (0.47 mmol) of (*S*)-6-OAc in 20 mL of pyridine was cooled to −20 °C before addition of 0.10 mL (1.4 mmol) of freshly distilled thionyl chloride. After the addition was complete, the resulting suspension was allowed to warm to room temperature. After 3 h, thin-layer chromatography indicated the reaction was complete and 5 g of cracked ice was added to the flask. The resulting solution was extracted with three 20-mL portions of ether, and the organic layer was washed in succession with three 10-mL portions of 2.4 N hydrochloric acid and water. The organic layer was dried over magnesium sulfate, and solvent was removed at reduced pressure to give 90 mg of a pale yellow oil which was judged to be a 91:9 mixture of two components by gas chromatography. The major product (89%), isolated by preparative gas chromatography, was (*S*)-lyratyl acetate:[10c,d] R_f 0.77; IR (CCl_4) 3090, 2980, 2950, 2880, 1745, 1650, 1635, 1540, 1380, 1255, 1235, 1025, 930, 910, 875 cm^{-1}; NMR (CCl_4) 1.65 (6, s, methyls at C(2) and C(5)), 1.98 (3, s, acetoxy methyl), 3.47 (d of d, J = 6 and 10 Hz, H at C(4)), 4.37 (2, s, H at C(1)), 4.69 (2, s, H at C(6)), 4.95 (1, d, J = 18 Hz, trans H at C(2′) of ethenyl moiety), 4.97 (1, d, J = 9 Hz, cis H at C(2′) of ethenyl moiety), 5.34 (1, d, J = 10 Hz, H at C(3)), 5.5–6.0 (1, d of d of d, J = 6, 9, and 19 Hz, vinyl H) ppm; $[\alpha]^{28}_{289}$ +22.9° (c 0.1 g/100 mL, chloroform); chemical ionization mass spectra (isobutane) gave a peak at m/e 195 (M + 1).

The minor component (9%), also isolated by preparative gas chromatography, was identified as (*E*)-2,5-dimethyl-4-ethenyl-2,4-hexadien-1-yl acetate (7-OAc): R_f 0.77; NMR (CCl_4) 1.46, 1.66, 1.85 (9, three s, methyls at C(2) and C(5)), 2.00 (3, s, acetoxy methyl), 4.50 (2, s, H at C(1)), 4.70–5.03 (2, m, vinyl methylene), 5.81 (1, s, H at C(3)), 6.4–6.8 (1, d, vinyl H) ppm. Hydrolysis of the acetate using the procedure previously described for (1*R*,3*R*)-4-OH gave 6 mg (95%) of (*E*)-2,5-dimethyl-4-ethenyl-2,4-hexadien-1-ol (7-OH): R_f 0.43; IR (CCl_4) 3610, 3340, 3080, 2950, 2910, 2850, 1620, 1435, 1370, 1283, 1245, 1175, 1063, 1005, 983, 900, 860, 693 cm^{-1}; NMR (CCl_4) 1.44, 1.67, 1.83 (9, three s, methyls at C(2) and C(5)), 2.50 (1, s, hydroxyl H), 4.03 (2, s, H at C(1)), 4.8–5.1 (2, m, vinyl methylene), 5.78 (1, s, H at C(3)), 6.4–6.8 (1, m, vinyl H) ppm; λ_{max}^{EtOH} 239.5 nm (ϵ 13 802); a chemical ionization mass spectrum (methane) gave a peak at m/e 153 (M + 1); an electron impact mass spectrum gave a molecular ion at m/e 152 with characteristic peaks at m/e 121 (M − 31), 119 (M − 33), 91 (M − 61), 79 (M − 73).

(*S*)-(*E*)-2,5-Dimethyl-4-ethenyl-2,5-hexadien-1-ol, (*S*)-Lyratol, ((*S*)-1-OH). A solution of 37 mg (0.19 mmol) of (*S*)-lyratyl acetate and 50 mg (0.36 mmol) of potassium carbonate in 10 mL of 90% methanol water was stirred for 1 h. Workup as previously described for preparation of (1*R*,3*R*)-4-OH gave 28 mg (95%) of (*S*)-lyratol:[10c,d] R_f 0.43; IR (CCl_4) 3603, 3350, 3075, 2950, 2905, 1640, 1629, 1445, 1420, 1369, 1283, 1245, 1175, 1059, 1001, 913, 890, 860, 691 cm^{-1}; NMR (CCl_4) 1.45 (1, s, hydroxyl H), 1.5–1.7 (6, m, methyls at C(2) and C(5)), 3.35–3.65 (1, d of d, J = 6.75 and 9.0 Hz, H at C(4)), 3.9 (2, s, H at C(1)), 4.69 (2, s, H at C(6)), 4.75–5.1 (2, m, vinyl methylene), 5.3 (1, d, J = 9 Hz, H at C(3)), and 5.45–5.95 (1, d, J = 6.75 Hz, vinyl H) ppm; $[\alpha]^{24}_{589}$ +61.5° (c 0.17 g/100 mL, chloroform), reported $[\alpha]^{27}_{589}$ +62.3° (c 4.6 g/100 mL, chloroform); chemical ionization mass spectra (isobutane) gave a peak at m/e 153 (M + 1).

Registry No. (*S*)-1-OH, 19889-92-0; (*S*)-1-OAc, 20384-05-8; (1*R*,3*R*)-2-OH, 4638-92-0; (1*R*,3*R*)-3-OH, 32989-74-5; (1*R*,3*R*)-3-OAc, 70144-38-6; (1*R*,3*R*)-4-OH, 70101-73-4; (1*R*,3*R*)-4-OAc, 70101-74-5; (*S*)-5-OH, 70101-75-6; (*S*)-6-OH, 70101-76-7; (*S*)-6-OAc, 70101-77-8; 7-OH, 70101-78-9; 7-OAc, 70101-79-0.