1,3,4,9a-Tetrahydro-12-methyl-2-oxo-1,4-ethano-3,4a-(iminoethano)-4a*H*-carbazole-9(2*H*)-carboxaldehyde (1d). A solution of 1.26 g (5 mmol) of **1a** and 1 mL of 37% of formaldehyde in 6 mL of 100% formic acid was refluxed for 3 h and subsequently evaporated to dryness. The residue was taken up with cold aqueous K_2CO_3 and extracted with 50 mL of ethyl acetate. The organic extract was washed, dried (Na_2SO_4), and evaporated. Crystallization of the residue from ethyl acetate–diisopropyl ether gave 0.4 g of **1d**: mp 148–149 °C; UV (CH_3OH) λ_{max} 251 nm (ϵ 15 100), 280 (3500); IR (KBr) 1724 (ketone C=O), 1668 (anilide C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.70 (CH_3-12), 2.97 (d, $J_{3,4}$ = 3.0 Hz, 1 H, H-3), 4.36 (d, $J_{9a,1}$ = 4.0 Hz, 1 H, H-9a), 7.00–7.28 (m, 4 H, Ar), 9.95 (s, 1 H, CHO); mass spectrum, *m/e* 296. Anal. Calcd for $C_{18}H_{20}N_2O_2$: C, 72.95; H, 6.80; N, 9.45. Found: C, 73.01; H, 6.49; N, 9.26.

1,3,4,9a-Tetrahydro-*N*,12-dimethyl-2-oxo-1,4-ethano-3,4a-(iminoethano)-4a*H*-carbazole-9(2*H*)-carboxamide (1f). A solution of 0.2 g of **1c**, 0.2 g of CH_3NCO, and 1 drop of *N,N*-diethylethanamine in 5 mL of CH_2Cl_2 was allowed to stand for 24 h at 23 °C. After the solution was evaporated, the solid residue was crystallized from ethyl acetate, giving 0.15 g of **1f** as white crystals, mp 211–212 °C; UV (CH_3OH) λ_{max} 250 nm (ϵ 15 150), 281 (3500); IR (KBr) 3450, 3330 (NH), 1723 (ketone C=O), 1658, 1533 (NHCO) cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 2.52 (s, CH_3-12), 2.63 (d, J = 5.4 Hz, $NHCH_3$), 2.93 (d, $J_{3,4}$ = 3.0 Hz, 1 H, H-3), 4.41 (d, $J_{9a,1}$ = 3.5 Hz, 1 H, H-9a), 6.70 (q, J = 5.4 Hz, 1 H, D_2O-exchangeable, $NHCH_3$), 6.85 (m, 1 H, H-6), 7.07–7.18 (m, 2 H, H-5, H-7), 7.83 (d, J = 8.0 Hz, 1 H, H-8); mass spectrum, *m/e* 325. Anal. Calcd for $C_{19}H_{23}N_3O_2$: C, 70.13; H, 7.12; N, 12.91. Found: C, 70.25; H, 7.19; N, 12.95.

3a,4,4a,5,10,10a-Hexahydro-3a-hydroxy-3-methyl-1,9b:4,10-diethanoimidazo[4,5-*b*]carbazol-2(3*H*)-one (2a). Methyl isocyanate (0.29 g, 5 mmol) and 1 drop of *N,N*-diethylethanamine were added to a solution of 1.47 g (5 mmol) of **1a** in 10 mL of CH_2Cl_2 and allowed to stand at 23 °C for 4 days. The resulting white crystals (1.2 g) of **2a** of analytical purity were collected, mp 292–293 °C dec. Evaporation of the filtrate and trituration with ethanol gave additional product **2a** (total yield, 88%): mp 291–292 °C; UV (CH_3OH) λ_{max} 250 nm (ϵ 15 000), 290 (2770); IR (KBr) 3400, 3250 (OH, NH), 1673 (C=O) cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 2.59 (s, 3 H, CH_3), 5.54 (d, J = 1.6, 1 H, D_2O-exchangeable, NH), 6.15 (s, 1 H, D_2O-exchangeable, OH), 6.49 (m, 2 H, Ar), 6.88 (m, 2 H, Ar); mass spectrum, *m/e* 311. Anal. Calcd for $C_{18}H_{21}N_3O_2$: C, 69.43; H, 6.80; N, 13.50. Found: C, 69.39; H, 6.94, N, 13.74.

3,3a,4,4a,10,10a-Hexahydro-3a-hydroxy-*N*,3-dimethyl-2-oxo-1,9b:4,10-diethanoimidazo[4,5-*b*]carbazole-5(2*H*)-carboxamide (2b). To a solution of 2 mmol of **2a** in 10 mL of dry tetrahydrofuran was added 2 mmol of MeNCO and 1 drop of Et_3N. After 2 days at 23 °C, the solution was evaporated in vacuo and the solid residue recrystallized from ethanol, giving 0.3 g of pure **2b**, mp 280–281 °C. The analytical and spectral data as well as a mixture of melting point are identical with product obtained directly when equivalent amounts of **1a** and MeNCO were employed.[1]

***N*-Cyclohexyl-1,2,3,4,9,9a-hexahydro-2-oxo-1,4-ethano-3,4a-(iminoethano)-4a*H*-carbazole-12-carboxamide (1h).** A solution of 2 mmol of **1a**, 1 mmol of cyclohexyl isocyanate, and 1 drop Et_3N in 15 mL of CH_2Cl_2 was allowed to stand overnight at 23 °C. After the solvent was removed under diminished pressure, the residue was crystallized from a mixture of 2-propanol–diisopropyl ether to give 0.4 g of **1h**: mp 155–156 °C; UV (CH_3OH) λ_{max} 249 nm (ϵ 16 800) 284 (3100); IR (KBr) 3440, 3330 (NH), 1726 (ketone C=O), 1655, 1528 (NHCO) cm^{-1}; mass spectrum, *m/e* 379. Anal. Calcd for $C_{23}H_{29}N_3O_2$: C, 72.79; H, 7.70; N, 11.07. Found: C, 72.53; H, 7.85; N, 10.86.

3-Cyclohexyl-3a,4,4a,5,10,10a-hexahydro-3a-hydroxy-1,9b:4,10-diethanoimidazo[4,5-*b*]carbazol-2(3*H*)-one (2c). A solution of 0.3 g of **1h** in 30 mL of xylene was refluxed for 2 h and subsequently evaporated under diminished pressure. The solid residue was crystallized from ethanol, giving 0.2 g of **2d**: mp 229–230 °C; UV (CH_3OH) λ_{max} 251 nm (ϵ 15 300), 291 (2780); IR (KBr) 3400, 3260 (OH, NH), 1671 (C=O) cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 5.70 (br, 1 H, D_2O-exchangeable, NH), 6.12 (s, 1 H, D_2O-exchangeable, OH); mass spectrum, *m/e* 379. Anal. Calcd for $C_{23}H_{29}N_3O_2$: C, 72.79; H, 7.70; N, 11.07. Found: C, 72.61; H, 7.73; N, 11.02.

On addition of 1 equiv of cyclohexyl isocyanate to a solution of **2c** in tetrahydrofuran, *N*-3-dicyclohexyl-3,3a,4,4a,10,10a-hexahydro-3a-hydroxy-2-oxo-1,9b:4,10-diethanoimidazole-5-(2*H*)-carboxamide (**2d**) was obtained, mp 203–204 °C dec. The analytical and spectral data of **2d** are identical with the product obtained by thermal cyclization of the dicyclohexylurea derivative.[1]

General Chiral Route to Irregular Monoterpenes via a Common Intermediate: Syntheses of (*S*)-Lavandulol, *cis*-(1*S*,3*R*)-Chrysanthemol, (1*S*,2*R*)-Rothrockene, and (*R*)-Santolinatriene

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Treatment of (*S*)-*O*-benzylglycidol (**6**) with senecioic acid in the presence of LDA, followed by acid workup, yielded a mixture of lactones **9** and **10**, whose enolate **11** on exposure to hydrochloric acid (10%) gave the α/γ-syn lactone **12** as a single product via stereo- and regioselective protonation. With lactone **12** as a common intermediate, four of five irregular monoterpenoid skeletons so far known have been synthesized. Thus, **12** afforded (*S*)-lavandulol (**16**) as the lavandulyl, *cis*-(1*S*,3*R*)-chrysanthemol (**21**) as the chrysanthemyl, (1*S*,2*R*)-rothrockene (**26**) as the rothrockyl, and (*R*)-santolinatriene (**33**) as the santolinyl groups, respectively, without difficulties.

Irregular monoterpenes which do not obey the isoprene rule have so far been found in nature in five skeletal systems divided into lavandulyl (1), chrysanthemyl (2), artemisyl (3), rothrockyl (4), and santolinyl (5) groups (Chart I).[1,2] These compounds are of particular interest since their generation via common chrysanthemyl pyrophosphate has been proposed for the biosynthetic pathway.[3,4] Although a number of synthetic entries into each skeletal type of these compounds has been reported,[5,6] no

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(2) Epstein, W. W.; Gaudioso, L. A. *J. Org. Chem.* **1982**, *47*, 176.

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(4) King, C.-H. R.; Poulter, C. D. *J. Am. Chem. Soc.* **1982**, *104*, 1413 and related papers.

(5) (a) Thomas, A. F. In "The Total Synthesis of Natural Products"; ApSimon, J., Ed.; Wiley: New York, 1973; Vol. 2, p 1. (b) Thomas, A. F.; Bessiere, Y. In "The Total Synthesis of Natural Products"; ApSimon, J., Ed.; Wiley: New York, 1981; Vol. 4, p 451.

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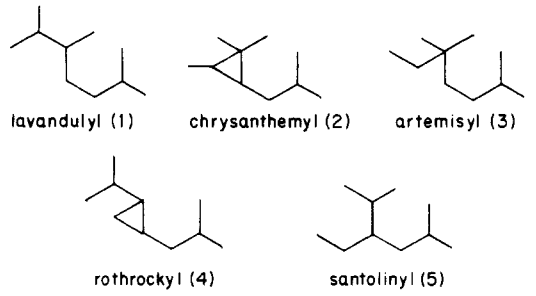
0022-3263/85/1950-0931$01.50/0

Chart I



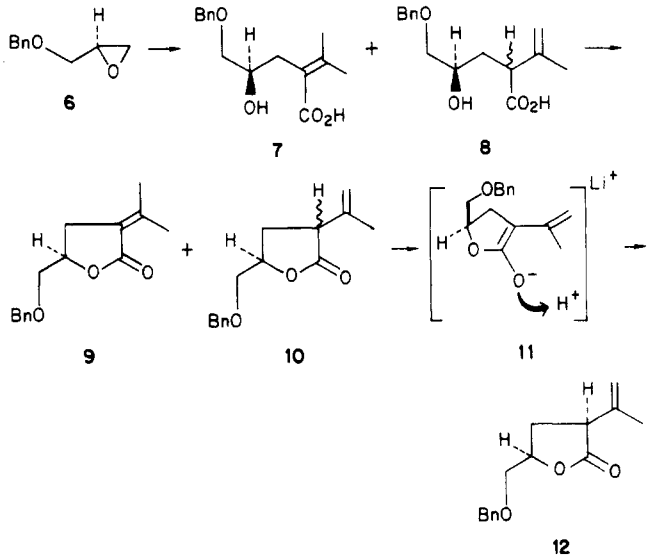
general chiral routes which lead to production of all these skeletons exist to date.

We report a general chiral route to four of the five skeletal compounds from (*S*)-*O*-benzylglycidol[23] (**6**) via the common γ-lactone intermediate **12**. Treatment of (*S*)-*O*-benzylglycidol (**6**), prepared from (*R*)-1-*O*-benzylglycerol,[7] with the dianion generated from senecioic acid and lithium diisopropylamide (LDA) (2 molar equiv) in tetrahydrofuran (THF) at −78 °C to room temperature yielded a mixture of the isomeric α,β- (**7**) and β,γ-unsaturated (**8**) acids. Formation of other isomeric hydroxy acids originated from attack at the C-4 position of the acid was negligeble. This mixture was refluxed in toluene with azeotropic removal of water to give a mixture of a conjugated and two unconjugated isomeric lactones (ca. 2:1:1). Without separation the mixture was treated with LDA (1 molar equiv) in THF at −78 °C to −20 °C to generate enolate **11**, which an exposure to excess hydrochloric acid (10%) added in one portion at −78 °C resulted in highly efficient regio- and stereoselective protonation at the α position from the less hindered face of the enolate and afforded deconjugated lactone **12** possessing the α/γ-syn configuration in 62% isolated yield (overall yield from **6**) (Scheme I). Although the stereochemistry of the newly generated chiral center could not be determined at this stage, it was eventually confirmed to have *S* configuration as expected. We have already reported an efficient chirality transfer method in terms of stereoselective protonation using a γ-lactone substrate,[8] however, the present single-step regio- and stereoselective reaction to form unsaturated lactone **12** from a mixture of unsaturated lactones **9** and **10** via unsaturated enolate **11** may be novel and noteworthy.

Having obtained the pivotal intermediate **12**, we first converted it into (*S*)-lavandulol (**16**),[9] one of two lavandulyl skeletal monoterpenes reported thus far.[5b] Reduction of **12** with lithium aluminum hydride in THF gave the diol **13** in 94% yield. Subsequent debenzylation of **13** with lithium in liquid ammonia yielded the water-soluble triol **14** which was treated without isolation with aqueous sodium periodate in the same flask, affording the lactol **15** by concomitant ring closure. Treatment of **15** with isopropylidenetriphenylphosphorane furnished (*S*)-lavandulol (**16**), in 53% overall yield from **12**. As a consequence, the configuration of the α position of the lactone precursor **12** has been now unambigously determined to be *S* at this stage.

Using the lactol **15** we next synthesized *cis*-(1*S*,3*R*)-

Scheme I



chrysanthemol (**21**). Although *cis*-chrysanthemol (**21**) has not been found in nature, its conversion into the naturally occurring trans isomer via *cis*- and *trans*-chrysanthemic acids is known.[10] Moreover, acquisition of compound **21** implies formal synthesis of artemisyl terpenoids which cannot be obtained directly from **12**, since an efficient chemical conversion of chrysanthemol into artemisyl compounds has been already established especially by Poulter and co-workers.[11] Upon oxidation with pyridinium chlorochromate (PCC) in methylene chloride, **15** produced the β-isopropenyl γ-lactone **17** in 79% overall yield from **12**. The lactone **17** was then treated with hydrogen chloride in acetic acid[12] at room temperature to give the tertiary chloride **18** in 67% yield. Treatment of **18** with potassium *tert*-butoxide (1.2 molar equiv) in THF afforded the cyclopropane lactone **19** in 79% yield, the racemate of which has been already synthesized.[13-15] Reduction of **19** with diisobutylaluminum hydride (Dibal-H) (1 molar equiv) gave the lactol **20** which on Wittig reaction with isopropylidenetriphenylphosphorane afforded *cis*-(1*S*,3*R*)-chrysanthemol (**21**)[16] in 67% overall yield.

On the other hand, the β-isopropenyl γ-lactone **17** was converted into rothrockene (**26**),[2] the only known rothrockyl monoterpene with unknown configuration. Thus, **17** was treated with thionyl chloride (10 molar equiv) in ethanol[17] to give the chloro ester **22** in 79% yield. Treatment of **22** with potassium *tert*-butoxide (1.2 molar equiv) in THF produced the cyclopropane ester **23** in 81% yield. The ester **23** was reduced with lithium aluminum hydride to give the alcohol **24** in 86% yield. Oxidation of **24** with pyridinium chlorochromate (PCC) yielded the aldehyde **25** which on Wittig reaction with isopropylidenetriphenylphosphorane furnished (+)-roth-

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(9) Chiral synthesis of lavandulol (**16**) has been carried out in both enantiomeric forms by using optically active methyl 3-hydroxybutanoate, see: Kramer, A.; Pfander, H. *Helv. Chim. Acta* **1982**, *65*, 293.

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(11) Poulter, C. D.; Marsh, L. L.; Hughes, J. M.; Argyle, J. C.; Satterwhite, D. M.; Goodfellow, R. J.; Moesinger, S. G. *J. Am. Chem. Soc.* **1977**, *99*, 3816 and related papers.

(12) Yanami, T.; Miyashita, M.; Yoshikoshi, A. *J. Org. Chem.* **1980**, *45*, 607.

(13) Franck-Neumann, M. *Angew. Chem., Int. Ed. Engl.* **1968**, *7*, 65.

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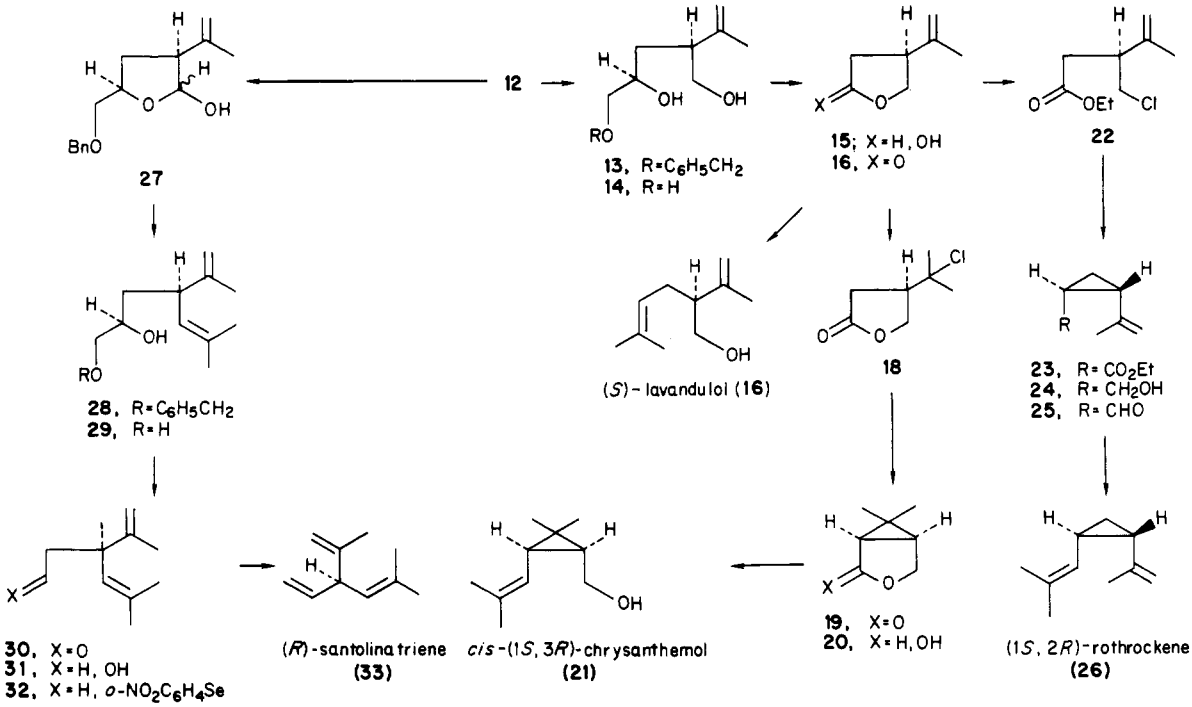
Scheme II



rockene (**26**)[18] in 25% overall yield. The observed optical rotation clearly indicated that the synthetic product, which should have the 1*S*,2*R* configuration, to be the antipode of the natural product,[2] and consequently the absolute configuration of the latter has been now unambigously deduced to be 1*R*,2*S*. This observation supported the earlier assumption made by Epstein and Gaudioso.[2]

Finally, we converted the lactone **12** into santolinatriene (**33**),[19-21] a representative of the santolynyl skeletal monoterpenes. Reduction of **12** with diisobutylaluminum hydride (Dibal-H) (1.5 molar equiv) yielded the lactol **27** which on Wittig reaction with isopropylidenetriphenylphosphorane produced the dienol **28** in 54% overall yield. On sequential treatment with lithium in liquid ammonia, aqueous sodium periodate, and sodium borohydride, **28** afforded, without isolation of the intermediates **29** and **30**, the primary alcohol **31** in 81% overall yield. The alcohol **31** could be transformed into (*R*)-santolinatriene (**33**) via the selenide **32** by employing the Sharpless–Grieco olefination reaction.[22] This reaction proceeded in ca. 10% yield due to instabilities of the target compound (Scheme II).

In summary, we have demonstrated a general chiral route to four of five existing irregular monoterpenoid skeletons via the common lactone intermediate **12** using (*S*)-*O*-benzylglycidol (**6**) as a chiral template. Since we have already developed an efficient conversion of (*R*)-1-*O*-benzylglycerol into the *S* enantiomer,[7] each monoterpene may also be obtained in antipodal forms.

Experimental Section

All reactions were carried out under argon.

(−)-(3*S*,5*R*)-5-[(Benzyloxy)methyl]-3-isopropenyltetrahydrofuran-2-one (12). To a solution of diisopropylamine (49.24 mL, 0.352 mol) in THF (300 mL) was added *n*-BuLi in *n*-hexane (10% (w/v), 215.24 mL, 0.336 mol) at −78 °C with stirring. After 20 min, senecioic acid (16.52 g, 0.16 mol) in THF (100 mL) was added dropwise into the mixture of the same temperature, and the reaction mixture was warmed gradually to room temperature and then again cooled to −78 °C. A solution of (*S*)-*O*-benzylglycidol (**6**) (26.24 g, 0.16 mol) in THF (150 mL) was added dropwise to the cooled mixture with stirring. The mixture was stirred at the same temperature for 30 min, warmed to room temperature, and stirred for 30 min. The mixture was poured into saturated $NaHCO_3$ and washed with ether. The aqueous layer was acidified with 6 N HCl and was extracted with CH_2Cl_2. The extract was washed with brine, dried ($MgSO_4$), and concentrated in vacuo to give a mixture of the acids **7** and **8** as a viscous oil (40.54 g). The mixture, without purification, was dissolved in toluene and was refluxed azeotropically for 10 h with a Dean–Stark apparatus. The mixture was washed with saturated $NaHCO_3$, dried ($MgSO_4$), and concentrated in vacuo to give a mixture of the lactones **9** and **10** (32.73 g). This was used immediately, without purification, in the next step. A small amount of sample was removed and separated by using a silica gel column for characterization to give (5*R*)-5-[(benzyloxy)methyl]-3-isopropylidenetetrahydrofuran-2-one (**9**) [IR (film) 1745, 1670 cm^{-1}; MS, *m/e* (relative intensity) 246 (M^+), 91 (100); ^1H NMR δ 1.83 (br t, 3 H, *J* = 1 Hz, $=C(CH_3)-$), 2.23 (br t, 3 H, *J* = 2 Hz, $=C(CH_3)-$), 2.55–2.95 (m, 2 H, $>CHCH_2(C=)-$), 3.57 (d, 2 H, *J* = 5 Hz, $-OCH_2CH<$), 4.33–4.78 (m, 1 H, $-(CH_2)CHO-$), 4.53 (s, 2 H, $ArCH_2O-$), 7.27 (s, 5 H, Ar H). Anal. Calcd for $C_{15}H_{18}O_3$: 246.1255 (M^+). Found: 246.1275 (M^+)], (3*R*,5*R*)-5-[(benzyloxy)methyl]-3-isopropenyltetrahydrofuran-2-one (**10**, α/γ-anti) [IR (film) 1765, 1645 cm^{-1}; MS, *m/e* (relative intensity) 246 (M^+), 91 (100); ^1H NMR δ 1.79 (br s, 3 H, $=C(CH_3)-$), 2.1–2,4 (m, 2 H, $>CHCH_2CH<$), 3.43 (br t, 1 H, *J* = 8.5 Hz, >CHCO–), 3.54 (dd, 1 H, *J* = 11, 4.3 Hz, $-OCH_2CH<$), 3.69 (dd, 1 H, *J* = 11, 3.6 Hz, $-OCH_2CH<$), 4.46–4.6 (m, 1 H, $-(CH_2)CHO-$), 4.54 (s, 2 H, $ArCH_2O-$), 4.9 (br s, 1 H, $=CH_2$), 4.94 (m, 1 H, $=CH_2$), 7.29 (s, 5 H, Ar H). Anal. Calcd for $C_{15}H_{18}O_3$: 246.1255 (M^+). Found:

(18) Racemic synthesis of this compound has been reported by Epstein and Gaudioso; see ref 2.

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(21) Racemic synthesis of this compound by fundamentally different approach has been reported; see: Sucrow, W. *Angew. Chem., Int. Ed. Engl.* **1968**, *7*, 629.

(22) Grieco, P. A.; Gilman, S.; Nishizawa, M. *J. Org. Chem.* **1976**, *41*, 1985.

(23) Compound **6** is (*S*)-*O*-benzylglycidol according to: Cahn, R. S.; Ingold, C.; Prelog, V. *Angew. Chem., Int. Ed. Engl.* **1966**, *5*, 385. When a revision of these rules (Prelog, V.; Helmchen, G. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 567–583) involving the way in which cyclic pathways are explored in order to rank attachments is used compound **6** is (*R*)-*O*-benzylglycidol. Chemical Abstracts Service started following the new rules in January 1984.

246.1254 (M^+)], and (3*S*,5*R*)-5-[(benzyloxy)methyl]-3-isopropenyltetrahydrofuran-2-one (**10**, α/γ-syn = **12**).

The lactone mixture (32.73 g, 0.133 mol) in THF (100 mL) was added to a solution containing LDA (prepared as above from diisopropylamine (18.6 mL, 0.133 mol) in THF (150 mL) and *n*-BuLi in *n*-hexane (10% (w/v), 85.2 mL, 0.133 mol) at −78 °C with stirring. The reaction mixture was stirred at the same temperature for 15 min, then warmed to room temperature, and, after 15 min, again cooled to −78 °C. To this mixture were added 10% HCl (120 mL) all at once and, after being warmed to room temperature, brine, and the mixture was extracted with ether and throughly with CH_2Cl_2. The combined extracts were dried ($MgSO_4$), concentrated in vacuo, and chromatographed on silica gel (800 g) using EtOAc:*n*-hexane (1:10) as an eluent to give the (−)-3*S*,5*R* lactone (**12**) (23.18 g, 62% from senecioic acid): $[\alpha]_D$ −10.52° (*c* 5.858, $CHCl_3$); IR (film) 1765, 1645 cm^{-1}; MS, *m/e* (relative intensity) 246 (M^+), 91 (100); ^1H NMR δ 1.79 (br s, 3 H, $=CCH_3$)–), 1.96–2.51 (m, 2 H, >CHCH_2CH<), 3.36 (dd, 1 H, *J* = 13, 9 Hz, –CH_2C*H*<), 3.57(dd, 1 H, *J* = 11, 4.7 Hz, –OCH_2CH<), 3.72 (dd, 1 H, *J* = 11, 4 Hz, –OCH_2CH<), 4.39–4.69 (m, 1 H, –(CH_2)C*H*O–), 4.57 (s, 2 H, ArCH_2O–), 4.96 (m, 2 H, $=CH_2$), 7.3 (s, 5 H, Ar H). Anal. Calcd for $C_{15}H_{18}O_3$: 246.1255 (M^+). Found: 246.1233 (M^+).

(+)-(3*S*,5*R*)-6-(Benzyloxy)-5-hydroxy-3-(hydroxymethyl)-2-methyl-1-hexene (13). To a stirred solution of $LiAlH_4$ (0.76 g, 20 mmol) in THF (50 mL) was added dropwise a solution of the lactone **12** (4.15 g, 17 mmol) in THF (50 mL) at 0 °C, and stirring was continued for 5 min at the same temperature. Concentrated NH_4OH was added dropwise to the reaction mixture at 0 °C to decompose any excess $LiAlH_4$ with stirring. The mixture was filtered by using Celite, and the filtrate was dried ($MgSO_4$) and concentrated in vacuo to give the diol **13** (4.09 g, 94.3 %) in practically pure state. A small amount of sample was removed and distilled in a Kugelrohr tube to yield pure **13**: bp ~150 °C (0.4 mmHg); $[\alpha]_D$ +5.78° (*c* 4.254, $CHCl_3$); IR (film) 3380, 1645 cm^{-1}; MS, *m/e* 251 ($M^+ + 1$), 91 (100); ^1H NMR δ 1.37–2.0 (m, 2 H, –CH_2CH<), 1.7 (br s, 3 H, $=C(CH_3)$–), 2.23–2.92 (m, 3 H, 2 H disappeared with D_2O, OH × 2, –CH_2C*H*<), 3.23–4.0 (m, 5 H, –OCH_2CH<, –(CH_2)C*H*OH, –CH_2OH), 4.52 (s, 2 H, ArCH_2O–), 4.73–4.95 (m, 2 H, $=CH_2$), 7.3 (s, 5 H, Ar H). Anal. Calcd for $C_{15}H_{22}O_3$: 250.1567 (M^+). Found: 250.1552 (M^+).

(2*RS*,4*S*)-2-Hydroxy-4-isopropenyltetrahydrofuran (15). The diol **13** (1.89 g, 7.56 mmol) in EtOH (2 mL) was added to liquid NH_3 (ca. 80 mL) in a flask equipped with a dry ice condenser. To this stirred mixture was added Li metal (0.48 g) portionwise, and the resulting solution was stirred at the same temperature for 1 h, followed by evaporation of NH_3 by removing the dry ice condenser. The residue was dissolved in water in the same flask, and the solution was made weak basic by introducing CO_2 gas. To this solution was added $NaIO_4$ (3.57 g, 16.7 mmol) in water (30 mL) at 0 °C with stirring. After neutralized by addition of 6 N HCl, the mixture was extracted with CH_2Cl_2. The extract was washed with brine, dried ($MgSO_4$), and concentrated in vacuo to give the lactol **15** (900 mg, 93%) in practically pure state: IR (film) 3400, 3080, 1645 cm^{-1}; MS, *m/e* (relative intensity) 128 (M^+), 69 (100); ^1H NMR δ 1.75 (d, 3 H, *J* = 1 Hz, $=C(CH_3)$–), 1.9–2.4 (m, 2 H, –CH_2CH<), 2.7–3.5 (m, 1 H, –CH_2C*H*<), 3.34 (br s, 1 H, disappeared with D_2O, –OH), 3.5–4.4 (m, 2 H, –CH_2O–), 4.78 (m, 2 H, $=CH_2$), 5.55 (m, 1 H, –(O)C*H*OH). Anal. Calcd for $C_7H_{12}O_2$: 128.0836 (M^+). Found: 128.0826 (M^+).

(+)-(*S*)-Lavandulol (16). *n*-BuLi in *n*-hexane (10% (w/v), 10.4 mL, 16.3 mmol) was added to a stirred suspension of isopropyltriphenylphosphonium iodide (7.35 g, 17.0 mmol) in THF (20 mL) at 0 °C, and the resulting dark red solution was stirred at 0 °C for 10 min. To this solution was added the lactol **15** (870 mg, 6.8 mmol) in THF (5 mL) dropwise at 0 °C, and the solution was stirred for 15 min at 0 °C. The reaction was worked up with saturated NH_4Cl and extraction with ether. The extract was washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was chromatographed on silica gel (70 g) using *n*-hexane:ether (3:1) as an eluent to give (+)-(*S*)-lavandulol (**16**) (550 mg, 53%): bp (Kugelrohr) ~110–115 °C (15 mmHg); $[\alpha]_D$ +10.05° (*c* 1.294, MeOH) (lit.[9] $[\alpha]_D$ +10.8° (*c* 0.94, MeOH); IR (film) 3360, 3080, 1645 cm^{-1}; MS, *m/e* (relative intensity) 154 (M^+), 69 (100); ^1H NMR δ 1.52 (br, 1 H, disappeared with D_2O, O*H*), 1.6 (s, 3 H, $=CCH_3$)–), 1.68 (s, 6 H, $=C(CH_3)_2$), 1.9–2.57 (m, 3 H, –CH_2C*H*<), 3.53 (d, 2 H, *J* = 6 Hz, –CH_2OH), 4.75–5.0 (m, 2 H, $=CH_2$), 5.08 (br t, 1 H, *J* = 6 Hz, –(=CH).

(+)-(4*S*)-4-Isopropenyltetrahydrofuran-2-one (17). The lactol **15** (2.56 g, 20 mmol) in CH_2Cl_2 (30 mL) was added dropwise to a stirred solution of pyridinium chlorochromate (PCC) (8.62 g, 40 mL) in CH_2Cl_2 (50 mL) at room temperature, and the resulting solution was stirred for 12 h at room temperature. The reaction mixture was diluted with ether and filtered through Florisil (50 g). The filtrate was concentrated in vacuo, and the residue was chromatographed on silica gel (50 g) using EtOAc: *n*-hexane (1:4) as an eluent to give the lactone **17** (2.06 g, 79%): bp (Kugelrohr) ~70 °C (0.4 mmHg); $[\alpha]_D$ +15.09° (*c* 4.958, $CHCl_3$); IR (film) 3090, 1780, 1645 cm^{-1}; MS, *m/e* (relative intensity) 126 (M^+), 68 (100); ^1H NMR δ 1.74 (br s, 3 H, $=C(CH_3)$–), 2.41 (dd, 1 H, *J* = 17, 9 Hz, –CH_2CO–), 2.66 (dd, 1 H, *J* = 17, 8 Hz, –CH_2CO–), 3.18 (m, 1 H, >CH–), 4.09 (dd, 1 H, *J* = 9, 7 Hz, –OCH_2CH<), 4.43 (dd, 1 H, *J* = 9, 7 Hz, –OCH_2CH<), 4.8 (br s, 1 H, $=CH_2$), 4.86 (br s, 1 H, $=CH_2$); ^{13}C NMR δ 176.601 (s), 142.370 (s), 112.076 (t), 71.626 (t), 42.212 (d), 32.995 (t), 20.255 (q). Anal. Calcd for $C_7H_{10}O_2$: 126.0679 (M_+). Found: 126.0636 (M^+).

(4*S*)-4-(1-Chloro-1-methylethyl)tetrahydrofuran-2-one (18). A solution of the lactone **17** (1.12 g, 8.9 mmol) in AcOH (110 mL) saturated with HCl was stirred at room temperature for 96 h. The mixture was poured into ice–water and extracted with CH_2Cl_2. The extract was washed succesively with water, saturated $NaHCO_3$, and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was chromatographed on silica gel (50 g) using EtOAc:*n*-hexane (1:5) as an eluent to give the chloride **18** (0.97 g, 67%): bp (Kugelrohr) ~78–83 °C (0.06 mmHg); $[\alpha]_D$ +15.72° (*c* 5.192, $CHCl_3$); IR (film) 1780 cm^{-1}; MS, *m/e* (relative intensity) 162 (M^+), 69 (100); ^1H NMR δ 1.53 (s, 6 H, –$C(CH_3)_2$), 2.47–2.9 (m, 3 H, –CH_2C*H*<), 4.23–4.53 (m, 2 H, –CH_2O–). Anal. Calcd for $C_7H_{11}O_2Cl$: 162.0447 (M^+). Found: 162.0442 (M^+).

(−)-(1*R*,5*S*)-2-Oxo-6,6-dimethyl-3-oxabicyclo[3.1.0]hexane (19). A solution of the chloride **18** (2.31 g, 14.2 mmol) in THF (50 mL) was added dropwise to a stirred solution of KOBu-*t* (2.07 g, 18.5 mmol) in THF (100 mL) at 0 °C, and the resulting mixture was stirred at the same temperature for 5 min. The reaction was worked up by adding saturated NH_4Cl and extracting with CH_2Cl_2. The extract was washed with brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was chromatographed on silica gel (70 g) using EtOAc: *n*-hexane (1:2) as an eluent to give the bicyclic lactone **19** (1.42 g, 79%): bp (Kugelrohr) ~70 °C (10.5 mmHg); $[\alpha]_D$ − 60.07° (*c* 2.374, $CHCl_3$); IR (film) 1765 cm^{-1}; MS, *m/e* (relative intensity) 126 (M^+), 67 (100); ^1H NMR δ 1.17 (s, 6 H, >$C(CH_3)_2$), 1.88–2.2 (m, 2 H, >C*H*CH<), 4.0–4.55 (m, 2 H, –CH_2O–). Anal. Calcd for $C_7H_{10}O_2$: 126.0679 (M^+). Found: 126.0661 (M^+).

(1*R*,2*RS*,5*S*)-2-Hydroxy-6,6-dimethyl-3-oxabicyclo-[3.1.0]hexane (20). A solution of diisobutylaluminum hydride (Dibal-H) in toluene (1.58 M, 5.78 mL, 9.1 mmol) was added dropwise to a stirred solution of the bicyclic lactone **19** (1.15 g, 9.1 mmol) in THF (30 mL) at −78 °C, and the resulting mixture was stirred at the same temperature for 5 min. The reaction was worked up by adding MeOH (5 mL), followed by saturated NH_4Cl (5 mL). The mixture was filtered through Celite, and the filtrate was extracted throughly with CH_2Cl_2. The extract was washed with brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was chromatographed on silica gel (50 g) using *n*-hexane:ether (2:1) as eluent to give the bicyclic lactol **20** (0.87 g, 74%): IR (film) 3420 cm^{-1}, MS, *m/e* (relative intensity) 128 (M^+), 67 (100); ^1H NMR δ 1.03 (s, 6 H, >$C(CH_3)_2$), 1.17–1.9 (m, 2 H, >C*H*CH<), 2.83 (br d, 1 H, *J* = 5 Hz, disappeared with D_2O, OH), 3.7–4.33 (m, 2 H, –CH_2O–), 5.23 (br d, 1 H, *J* = 5 Hz, –(–O)C*H*OH). Anal. Calcd for $C_7H_{12}O_2$: 128.0836 (M^+). Found: 128.0830 (M^+).

***cis*-(−)-(1*S*,3*R*)-Chrysanthemol (21).** *n*-BuLi in *n*-hexane (10% (w/v), 10.0 mL, 15.6 mmol) was added to a stirred suspension of isopropyltriphenylphosphonium iodide (6.75 g, 15.6 mmol) in THF (20 ml) at 0 °C, and the resulting dark red solution was stirred at 0 °C for 10 min. To this solution was added dropwise the bicyclic lactol **20** (800 mg, 6.25 mmol) in THF (5 mL) dropwise, and the solution was stirred for 15 min at 0 °C. The reaction was worked up by adding saturated NH_4Cl and extracting with ether. The extract was washed with brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was chroma-

tographed on silica gel (30 g) using EtOAc:*n*-hexane (1:5) as an eluent to give *cis*-(1*S*,3*R*)-chrysanthemol (**21**) (0.88 g, 91%): bp (Kugelrohr) ~120 °C (15 mmHg); $[\alpha]_D$ -30.40° (*c* 4.908, $CHCl_3$); IR (film) 3350 cm^{-1}; MS, *m/e* (relative intensity) 154 (M^+), 122 (100); ^1H NMR δ 0.8–1.6 (m, 2 H, >C*H*C*H*<), 1.02 (s, 3 H, =CCH_3), 1.1 (s, 3 H, =C(CH_3), 1.68 (s, 6 H, =C(CH_3)$_2$), 1.8 (br, 1 H, disappeared with D_2O, -O*H*), 3.63 (d, 2 H, *J* = 7 Hz, -CH_2OH), 4.96 (br d, 1 H, *J* = 8 Hz, -(=CH). Anal. Calcd for $C_{10}H_{18}O$: 154.1358 (M^+). Found: 154.1375 (M^+).

Ethyl (-)-(3*S*)-3-(Chloromethyl)-4-methyl-4-pentenoate (22). To a stirred solution of the lactone **17** (2.80 g, 22.2 mmol) in EtOH (200 mL) was added thionyl chloride (16.2 mL, 222 mmol) at room temperature, and the resulting mixture was stirred at room temperature for 1 h and at 60 °C for 4 h. The mixture was concentrated in vacuo and the residue was chromatographed on silica gel (150 g) using EtOAc:*n*-hexane (1:10) as an eluent to give the chloro ester **22** (3.35 g, 79.2%): bp (Kugelrohr) ~ 50–53 °C (0.12 mmHg); $[\alpha]_D$ -3.25° (*c* 4.304, $CHCl_3$); IR (film) 3080, 1725, 1640 cm^{-1}; MS, *m/e* (relative intensity) 154 (M^+ - HCl), 81 (100); FDMS, *m/e* 192, 190 (M^+); ^1H NMR δ 1.25 (t, 3 H, *J* = 7 Hz, -OCH_2CH_3), 1.78 (s, 3 H, =CCH_3)-), 2.4–2.73 (m, 2 H, -CH_2CO-), 2.78–3.2 (m, 1 H, >CH-), 3.62 (d, 2 H, *J* = 6 Hz, -CH_2Cl), 4.13 (q, 2 H, *J* = 7 Hz, -OCH_2CH_3), 4.9 (m, 2 H, =CH_2). Anal. Calcd for $C_9H_{15}ClO_2$: C; 56.69, H; 7.93, Cl; 18.59. Found: C; 56.23; H, 7.76, Cl; 18.78.

***trans*-(+)-(1*S*,2*S*)-1-(Hydroxymethyl)-2-isopropenylcyclopropane (24).** A solution of the chloro ester **22** (1.03 g, 5.4 mmol) in THF (10 mL) was added dropwise to a stirred solution of KOBu-*t* (730 mg, 6.5 mmol) in THF (15 mL) at 0 °C, and the resulting mixture was stirred at the same temperature for 10 min. The reaction was worked up by adding saturated NH_4Cl and extracting with ether. The extract was washed with brine, dried (K_2CO_3), and concentrated in vacuo to give the crude cyclopropane ester **23** (760 mg) which was accompanied by ca. 9% of inseparable *tert*-butyl ester **23** (Et replaced by *t*-Bu).

The crude ester **23** (760 mg) in THF (10 mL) was added dropwise to a stirred solution of $LiAlH_4$ (190 mg, 5 mmol) in THF (20 mL) at 0 °C, and the resulting mixture was stirred at the same temperature for 30 min. The reaction was treated with concentrated NH_4OH to decompose any excess $LiAlH_4$, and the mixture was filtered by using Celite. The filtrate was dried ($MgSO_4$) and concentrated in vacuo, and the residue was chromatographed on silica gel (30 g). Elution using EtOAc:*n*-hexane (1:10) yielded the unreacted *tert*-butyl ester **23** (Et replaced by *t*-Bu) (90 mg) contaminated, and elution using ether yielded and cyclopropane alcohol **24** (420 mg, 69.4% overall yield from **22**). The recovered ester could be converted into the desired alcohol **24** under more forcing conditions. Thus, the *tert*-butyl ester **23** (Et replaced by *t*-Bu) (320 mg, 1.76 mmol) in THF (15 mL) was added dropwise to a stirred solution of $LiAlH_4$ (67 mg, 1.76 mmol) in THF (30 mL) at 0 °C, and the mixture was stirred at 0 °C for 30 min, at room temperature for 30 min, and at reflux temperature for 30 min to give the same cyclopropane alcohol **24** (160 mg, 81.2%): bp (Kugelrohr) ~85–95 °C (15 mmHg); $[\alpha]_D$ +42.83° (*c* 3.876, $CHCl_3$); IR (film) 3350, 3090, 1640 cm^{-1}; MS, *m/e* (relative intensity) 112 (M^+), 68 (100); ^1H NMR δ 0.38–1.05 (m, 2 H, -CH_2-), 1.1–1.5 (m, 2 H, >C*H*C*H*<), 1.65 (s, 3 H, =C(CH_3)—), 2.03 (br, 1 H, disappeared with D_2O, -OH), 3.5 (br d, 2 H, *J* = 6 Hz, -CH_2OH), 4.68 (s, 2 H, =CH_2). Anal. Calcd for $C_7H_{12}O$: 112.0887 (M^+). Found: 112.0871 (M^+).

***trans*-(1*S*,2*S*)-1-Formyl-2-isopropenylcyclopropane (25).** The cyclopropane alcohol **24** (410 mg, 3.66 mmol) in CH_2Cl_2 (10 mL) was added dropwise to a stirred solution of pyridinium chlorochromate (PCC) (1.58 g, 7.33 mmol) in CH_2Cl_2 (20 mL) at 0 °C, and the resulting solution was stirred at 0 °C for 30 min and at room temperature for 14 h. The mixture was filtered by using Celite, and the residue was mixed with Florisil (2 g) and extracted for 6 h with ether (50 mL). The combined organic layers were evaporated and the residue was chromatographed on silica gel (15 g) using *n*-hexane:ether (2:1) as an eluent to give the aldehyde **24** (320 mg, 79.5%) as a very volatile oil: IR (film) 3080, 1700, 1635 cm^{-1}; MS, *m/e* (relative intensity) 110 (M^+), 95, 41 (100); ^1H NMR δ 1.15–1.53 (m, 2 H, -CH_2-), 1.68 (d, 3 H, *J* = 1 Hz, =C(CH_3)—), 1.8–2.33 (m, 2 H, >C*H*C*H*<), 4.82 (s, 2 H, =CH_2), 9.15 (d, 1 H, *J* = 4.5 Hz, -CH=O). Anal. Calcd for C_7H_9O: 109.0636 (M^+ - 1). Found: 109.0656 (M^+ - 1).

(+)-(1*S*,2*R*)-Rothrockene (26). *n*-BuLi in *n*-hexane (10% (w/v), 5.54 mL, 8.63 mmol) was added to a stirred suspension of isopropyltriphenylphosphonium iodide (7.46 g, 17.26 mmol) in THF (20 mL) at 0 °C, and the resulting dark red solution was stirred at 0 °C for 20 min. To this solution was added dropwise the aldehyde **25** (730 mg) in THF (10 mL), and the mixture was stirred at the same temperature for 30 min. The reaction was worked up by adding saturated NH_4Cl and extracting with ether. The extract was concentrated in vacuo and the residue was chromatographed on silica gel (60 g) by using *n*-hexane as an eluent to give (1*S*,2*R*)-rothrockene (**26**) (320 mg, 35.4%) as a very volatile oil: bp (Kugelrohr) ~50–60 °C (18 mmHg); $[\alpha]_D$ +49.42° (*c* 0.518, $CHCl_3$) (lit.[2] $[\alpha]_D$ -64.8° (*c*, 1.33, $CHCl_3$)); IR (film) 3080, 1645, 1635 cm^{-1}; MS, *m/e* (relative intensity) 136 (M^+), 93 (100); ^1H NMR δ 0.5–0.7 (m, 1 H, -CH_2-), 0.85–1.05 (m, 1 H, -CH_2-), 1.2–1.6 (m, 2 H, >C*H*C*H*<), 1.67 (d, 3 H, *J* = 1 Hz, =C(CH_3)—), 1.68 (d, 3 H, *J* = 1 Hz, =C(CH_3)—), 1.71 (d, 3 H, *J* = 1 Hz, =CHCH_3), 4.66 (br s, 3 H, =CH_2, =CH-). Anal. Calcd for $C_{10}H_{16}$: 136.1252 (M^+). Found: 136.1258 (M^+).

(2*RS*,3*S*,5*R*)-5-[(Benzyloxy)methyl]-2-hydroxy-3-isopropenyltetrahydrofuran (27). A solution of diisobutylaluminum hydride (Dibal-H) in toluene (1.58 M, 15.2 mL, 24 mmol) was added dropwise to a stirred solution of the lactone **12** (3.94 g, 16 mmol) in THF (30 mL) at -78 °C, and the resulting mixture was stirred at the same temperature for 15 min. The reaction was worked up by adding MeOH (10 mL), followed by saturated NH_4Cl (10 mL). The mixture was filtered through Celite, and the filtrate was extracted throughly with CH_2Cl_2. The extract was washed with brine, dried ($MgSO_4$), and concentrated in vacuo to give the lactol **27** (3.92 g, 98.8%) in practically pure state: IR (film) 3425, 3050, 1645 cm^{-1}; MS, *m/e* (relative intensity) 248 (M^+), 247 (M^+ - 1), 91 (100); ^1H NMR δ 1.5–2.23 (m, 5 H, =C(CH_3)—, -CH_2CH<), 2.5–3.0 (m, 1 H, -CH_2C*H*<), 3.17 (br d, 1 H, *J* = 7 Hz, disappeared with D_2O, -OH), 3.4–3.7 (m, 2 H, >CHCH_2O—), 4.13–4.6 (m, 1 H, —(CH_2)C*H*O—), 4.6 (br s, 2 H, ArCH_2O-), 4.73–5.0 (m, 2 H, =CH_2), 5.2–5.5 (m, 1 H, -(O)C*H*OH), 7.3 (s, 5 H, Ar H). Anal. Calcd for $C_{15}H_{19}O_3$: 247.1333 (M^+ - 1). Found: 247.1286 (M^+ - 1).

(-)-(4*R*,6*R*)-7-(Benzyloxy)-6-hydroxy-4-isopropenyl-2-methyl-2-heptene (28). *n*-BuLi in *n*-hexane (10% (w/v), 24.6 mL, 38.4 mmol) was added to a stirred suspension of isopropyltriphenylphosphonium iodide (17.28 g, 40 mmol) in THF (50 mL) at 0 °C, and the resulting dark red solution was stirred at 0 °C for 10 min. To this solution was added dropwise the lactol **27** (3.92 g, 15.8 mmol) in THF (25 mL), and the solution was stirred for 15 min at 0 °C. The reaction was worked up by adding saturated NH_4Cl and extracting with ether. The extract was washed with brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was chromatographed on silica gel (150 g) using EtOAc:*n*-hexane (1:10) as an eluent to give the diene **28** (2.37 g, 54.7%): bp (Kugelrohr) ~120–125 °C (0.06 mmHg); $[\alpha]_D$ -37.44° (*c*, 5.232, $CHCl_3$); IR (film) 3450, 1640 cm^{-1}; MS, *m/e* (relative intensity) 275 (M^+ + 1), 109 (100); ^1H NMR δ 1.4–1.9 (m, 2 H, -CH_2CH<), 1.6 (s, 3 H, =CCH_3)-), 1.67 (br s, 6 H, =C(CH_3)$_2$), 2.33 (br, 1 H, disappeared with D_2O, -OH), 2.83–3.5 (m, 3 H, -CH_2C*H*<, -OCH_2CH<), 3.5–3.93 (m, 1 H, -(CH_2)C*H*OH), 4.52 (s, 2 H, ArCH_2O-), 4.72 (br s, 2 H, =CH_2), 5.07 (br d, 1 H, *J* = 9 Hz, >CHC*H*=), 7.27 (s, 5 H, Ar H). Anal. Calcd for $C_{18}H_{26}O_2$: 274.1932 (M^+). Found: 274.1917 (M^+).

(4*R*,6*R*)-6,7-Dihydroxy-4-isopropenyl-2-methyl-2-heptene (29). The diene **28** (1.75 g, 6.39 mmol) in EtOH (2 mL) was added to liquid NH_3 (ca. 80 mL) in a flask equipped with a dry ice condenser. To this stirred mixture was added Li metal (0.52 g) portionwise, and the resulting solution was stirred at the same temperature for 1 h. The reaction was quenched by adding NH_4Cl, and NH_3 was evaporated. The residue was extracted with CH_2Cl_2, and the extract was washed with brine, dried (Na_2SO_4), and concentrated in vacuo to give the diol **29** (1.20 g, 100%) which could be used for the next reaction: IR (film) 3370, 3080, 1640 cm^{-1}; MS, *m/e* (relative intensity) 184 (M^+), 109 (100); ^1H NMR δ 1.4–1.85 (m, 2 H, -CH_2CH<), 1.7 (br s, 9 H, =C(CH_3)-, =C(CH_3)$_2$), 1.9–2.35 (br, 2 H, disappeared with D_2O, -OH × 2), 2.83–3.42 (m, 1 H, -(CH_2)C*H*-), 3.42–3.93 (m, 3 H, -CH_2OH, >C*H*OH), 4.73 (s, 2 H, =CH_2), 5.1 (br d, 1 H, *J* = 9 Hz, -CH=). Anal. Calcd for $C_{11}H_{20}O_2$: 184.1462 (M^+). Found: 184.1497 (M^+).

(-)-(3*R*)-3-Isopropenyl-5-methyl-4-hexenol (31). A solution

of $NaIO_4$ (1.39 g, 6.5 mmol) in water (30 mL) was added portionwise to a stirrd solution of the diol **29** (1.20 g, 6.5 mmol) in dilute MeOH (H_2O:MeOH, 3:5, 80 mL) at 0 °C, and the mixture was stirred for 5 min at 0 °C. To this mixture was added $NaBH_4$ (0.24 g, 6.5 mmol) portionwise at the same temperature, and the reaction was quenched with 6 N HCl. The mixture was extracted with CH_2Cl_2 and the extract was washed with brine, dried ($MgSO_4$), and concentrated. The residue was chromatographed on silica gel (40 g) by using EtOAc:*n*-hexane (1:8) as eluent to give the primary alcohol **31** (0.81 g, 80.9%): bp (Kugelrohr) ~120 °C (350 mmHg); $[\alpha]_D$ -67.81° (*c* 2.908, $CHCl_3$); IR (film) 3350, 3080, 1645 cm^{-1}; MS, *m/e* (relative intensity) 154 (M^+), 109 (100); ^1H NMR δ 1.43 (br, 1 H, disappeared with D_2O, -OH), 1.67 (d, 3 H, J = 1 Hz, =C(CH_3)—), 1.7 (br s, 6 H, =C(CH_3)$_2$), 1.53-2.1 (m, 2 H, -CH_2CH_2CH<), 2.7-3.42 (m, 1 H, -CH_2CH<), 3.65 (br t, 2 H, J = 7 Hz, -CH_2OH), 4.72 (s, 2 H, =CH_2), 5.05 (br d, 1 H, J = 9 Hz, >CHCH=). Anal. Calcd for $C_{10}H_{18}O$: 154.1356 (M^+). Found: 154.1330 (M^+).

(3*R*)-3-Isopropenyl-5-methyl-4-hexenyl 2-Nitrophenyl Selenide (32). To a stirred solution of the primary alcohol **31** (740 mg, 4.8 mmol) and 2-nitrophenyl selenocyanate (1.92 g, 7.2 mmol) in THF (10 mL) was added tri-*n*-butylphosphine (1.79 mL, 7.2 mL) dropwise at room temperature, and the mixture was stirred at the same temperature for 30 min. The mixture was concentrated under reduced pressure, and the residue was chromatographed on silica gel (70 g) by using *n*-hexane as eluent to give the selenide **32** (1.51 g, 93%): IR (film) 3080, 1640 cm^{-1}; MS, *m/e* (relative intensity) 339 (M^+), 109 (100); ^1H NMR δ 1.52-2.1 (m, 2 H, >CHCH_2CH_2-), 1.67 (br s, 6 H, =C(CH_3)$_2$), 1.73 (d, 3 H, J = 1 Hz, =C(CH_3)—), 2.73-3.3 (m, 1 H, >$CH$$CH_2$-), 2.87 (t, 2 H, J = 7.5 Hz, -CH_2CH_2Se-), 4.75 (s, 2 H, >C=CH_2), 5.05 (br d, 1 H, J = 9 Hz, >CHCH=), 7.08-7.62 (m, 3 H, Ar H), 8.25 (br d, 1 H, J = 8 Hz, Ar H). Anal. Calcd for $C_{16}H_{21}NO_2Se$: 339.0736 (M^+). Found: 339.0718 (M^+).

(-)-(*R*)-Santolinatriene (33). To a stirred solution of the selenide **32** (2.03 g, 6.0 mmol) in THF (5 mL) was added 30% H_2O_2 (5.21 mL, 60 mmol) dropwise at 0 °C, and the mixture was stirred for 5 h at the same temperature. Water (10 mL) was added to the reaction mixture, and the mixture was extracted with *n*-hexane. The extract was washed with saturated sodium carbonate and then with brine, dried ($MgSO_4$), and evaporated to leave crude santolinatriene (**33**) (750 mg, 92%). This was distilled immediately by using a Kugelrohr tube to minimize decomposition to give pure (*R*)-santolina triene (**33**) (120 mg, 15%): bp (Kugelrohr) 45° (14 mmHg) (lit.[20] bp_{20} 54.5 °C); $[\alpha]_D$ -55.58° (*c* 0.806, $CHCl_3$) (lit.[20] $[\alpha]_D$ +64°); IR (film) 3080, 1665, 1640, 1630 cm^{-1}; MS, *m/e* (relative intensity) 136 (M^+), 93, 79 (100); ^1H NMR δ 1.62 (s, 3 H, =C(CH_3)—), 1.72 (br s, 6 H, =C(CH_3)$_2$), 3.55 (m, 1 H, >CH-), 4.72 (br s, 2 H, =CH_2), 4.78-4.95 (m, 1 H, -CH=CH_2), 5.0-5.33 (m, 2 H, >C=CH—, -CH=CH_2), 5.5-6.1 (m, 1 H, -CH=CH_2). Anal. Calcd for $C_{10}H_{16}$: 136.1252 (M^+). Found: 136.1252 (M^+).

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Synthesis and Rearrangements of Alkyl Phosphorothioates

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Reaction of $PSCl_3$ with benzyl alcohol in triethyl phosphate followed by aqueous workup produces *S*-benzyl phosphorothioate, **2**, while similar reaction of cyclohexanol produces *O*-cyclohexyl phosphorothioate. The *S*-benzyl ester is postulated to arise from rearrangement of either *O*-benzyl phosphorodichloridate, **5**, or a hydrolysis product. Reaction of P^1-*O*-cyclohexyl P^2-*n*-propyl 1-thiodiphosphate, **3**, with BrCN in aqueous solutions buffered at pH 7.2 with lutidine or at pH 10.3 with triethylamine produces P^1-cyclohexyl P^2-*n*-propyl diphosphate, **4**, in essentially quantitative yield within 10 min. Similar reaction in $H_2{}^{18}O$ produces exclusively [P^1-^{18}O]**4** with no indication of the presence of ^{18}O at P^2. The reaction is postulated to involve the intermediate formation of P^1-*O*-cyclohexyl P^2-*n*-propyl 1-thiocyanatodiphosphate, **9**, by reaction of **3** with BrCN. **9** undergoes hydrolysis with displacement of SCN^- by H_2O, producing **4**. Similar reaction of P^1-*O*-cyclohexyl 1-thiodiphosphate in $H_2{}^{18}O$ produces cyclohexyl [1-^{18}O,2-^{18}O]diphosphate in high yield, with approximately 50% ^{18}O-enrichment at each position. This labeling pattern is postulated to arise from neighboring group participation by the terminal phosphoryl group. Initial reaction of P^1-*O*-cyclohexyl 1-thiodiphosphate produces the intermediate P^1-*O*-cyclohexyl 1-thiocyanatodiphosphate, **10**. The latter is partitioned between two pathways, direct displacement of SCN^- by water to form cyclohexyl diphosphate and internal displacement of SCN^- by the neighboring phosphoryl group to form cyclohexyl cyclodiphosphate, **11**, a highly reactive species which undergoes immediate hydrolysis to cyclohexyl diphosphate.

Reactions of adenosine 5′-*O*-[1-thiodiphosphate], ADPαS, and adenosine 5′-*O*-[2-thiotriphosphate], ATPβS, with BrCN in aqueous solutions produce ADP and ATP, respectively.[1a,b] These reactions carried out in $H_2{}^{18}O$ lead to the incorporation of ^{18}O into two positions within the di- or triphosphate moieties of ADP and ATP, demonstrating the operation of a complex mechanism. The mechanism involves a novel, spontaneous rearrangement of the polyphosphate moiety subsequent to the reaction of sulfur in ADPαS or ATPβS with BrCN to form the corresponding thiocyanato derivatives. The rearrangements lead to randomization of oxygens in the di- and triphosphate systems, as well as incorporation of oxygen from solvent at two positions[1a,b], and are thought to involve neighboring group participation by the terminal phosphoryl group leading to the formation of cyclodiphosphates as intermediates (see eq 1).

Factors governing the propensities of polyphosphates to form cyclodiphosphates are poorly understood. To

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