Anal. Calcd for $C_{12}H_{16}$: C, 89.94; H, 10.06. Found: C, 89.96; H, 10.10.

From 23. A mixture of **23** (1.20 g, 5.94 mmol), KOH (2.86 g), 80% hydrazine hydrate (4.00 g), and triethylene glycol (13 mL) was treated in a manner similar to that above. A white solid was purified by sublimation at 60–70 °C (15 mm) to afford 500 mg of **5** (53% yield); mp 132–133 °C (in a sealed tube).

Anal. Calcd for $C_{12}H_{16}$: C, 89.94; H, 10.06. Found: C, 89.82; H, 9.95.

***C*$_2$-Methanotwistane (6). From 24.** A mixture of **24** (350 mg, 1.73 mmol), KOH (0.84 g), 80% hydrazine hydrate (1.20 g), and triethylene glycol (4 mL) was heated for 1.5 h at 110 °C and then for an additional 2 h at 190–200 °C. During this period a white solid was observed to condense on the inner wall of the condenser. After cooling, this was dissolved in *n*-pentane and the pentane solution was washed with water, dried ($MgSO_4$), and concentrated. Purification through sublimation at 80–90 °C (5 mm) gave 240 mg of **6** (79% yield): mp 95 °C (in a sealed tube); IR (KBr) 1460, 1445, 1325, 1292, 1280, 1170, 960, 920, 810 cm^{-1}; ^{13}C NMR ($CDCl_3$) δ 19.7, 23.2, 30.7, 37.0, 38.2, 39.4, 41.3; mass spectrum *m/e* 174 (M^+).

Anal. Calcd for $C_{13}H_{18}$: C, 89.59; H, 10.41. Found: C, 89.80; H, 10.25.

From 25. A mixture of **25** (150 mg, 0.743 mmol), KOH (0.36 g), 80% hydrazine hydrate (0.51 g), and triethylene glycol (2 mL) was treated by the same manner as above. Sublimation of the product afforded 84 mg of **6** (65% yield); mp 94–96 °C (in a sealed tube).

Anal. Calcd for $C_{13}H_{18}$: C, 89.59; H, 10.41. Found: C, 89.74; H, 10.30.

Registry No. (–)-**3**, 62928-75-0; (–)-**4**, 61473-77-6; (–)-**5**, 70209-47-1; (±)-**5**, 70267-03-7; (±)-**6**, 70224-69-0; **10**, 69685-89-8; **12**, 712-25-4; **13**, 62111-05-1; **15**, 60749-69-1; **16**, 70209-48-2; **17**, 70209-49-3; (±)-**18**, 70209-50-6; (–)-**19**, 61393-99-5; (–)-**20**, 61473-76-5; (–)-**21**, 70209-51-7; (±)-**22**, 70209-52-8; (±)-**23**, 70224-75-8; (±)-**24**, 70224-76-9; (±)-**25**, 70224-77-0; (±)-**26**, 70209-53-9; (–)-**30**, 64727-80-6; (–)-D_3-trishomocubyl hydrogen phthalate, 64727-85-1; diazomethane, 334-88-3.

Synthesis of the First Optically Active Anti-Bredt-Rule Compound with Known Absolute Configuration. (–)-(*S*)-Bicyclo[3.3.1]-1(2)-nonene

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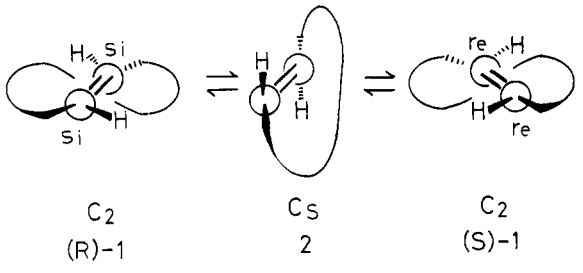
As the first member of optically active anti-Bredt-rule compounds, (–)-(*S*)-bicyclo[3.3.1]-1(2)-nonene (**7**) was prepared from (–)-(1*R*,3*S*)-*cis*-3-hydroxycyclohexanecarboxylic acid (**8**).

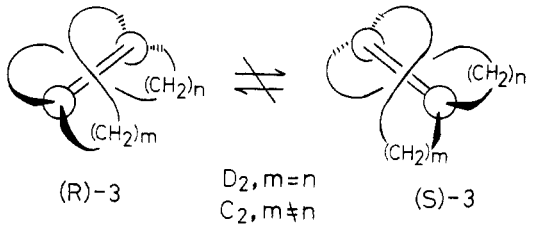
The gyrochiral[1] conformation (*R*)-**1** of a *trans*-cycloalkene with C_2 symmetry can be converted into its enantiomeric (*S*)-**1** conformation via schematically achiral planar C_s conformation **2**. Equilibration with the opposite process results in racemization whose rate is to be determined by the height of the energy barrier which the molecule should experience in passing through the planar transition conformation **2**.



Shortening the trans bridge should increase the nonbonding interaction in the transition state resulting in "frozen" enantiomeric conformers which can be isolated separately, and this has been unambigously demonstrated in Cope's classic optical resolution of *trans*-cyclooctene **6**.[2] Accompanying the (*R*)-**1** ⇌ (*S*)-**1** conformational transformation, simultaneous inversion of planar chirality of the double bond faces takes place as can be seen from the chirality specification change *si-si* ⇌ *re-re* for their respective outside faces.

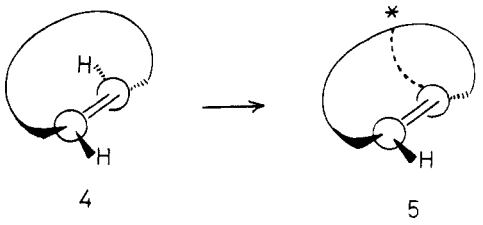
Replacing the pair of homotopic hydrogen atoms in C_2 *trans*-cycloalkene by an extra trans bridge leads to formation of the trans doubly bridged ethylene **3**, preparation of whose series of homologues ($m = n = 8$; $m = 8$, $n = 10$; $m = n = 10$) has been reported recently from our and Marshall's laboratories.[3]

In these trans doubly bridged ethylenes, the type of conformational chirality inversion observed in (*R*)-**1** ⇌ (*S*)-**1** cannot be realized; (*R*)-**3** ⇌ (*S*)-**3** inversion, being



essentially configurational rather than conformational, should only be achieved by a bond cleavage–recombination process between two trans bridges.

Another obvious and direct way to prevent (*R*)-**1** ⇌ (*S*)-**1** conformational inversion is provided by spanning a bridge (showed by the broken line in **5**) between the olefinic



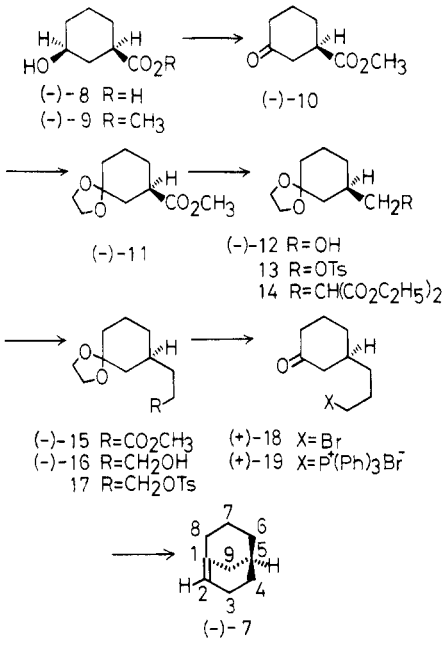
(1) Nakazaki, M.; Naemura, K.; Kadowaki, H. *J. Org. Chem.* **1976**, *41*, 3725. Nakazaki, M.; Yamamoto, K.; Tanaka, S. *Ibid.* **1976**, *41*, 4081.

(2) Cope, A. C.; Ganellin, C. R.; Johnson, Jr., H. W.; Van Auken, T. V.; Winkle, H. J. S. *J. Am. Chem. Soc.* **1963**, *85*, 3276. Cope, A. C.; Mehth, A. S. *Ibid.* **1964**, *86*, 5626.

(3) Nakazaki, M.; Yamamoto, K.; Yanagi, J. *J. Chem. Soc., Chem. Commun.* **1977**, 206. Nakazaki, M.; Yamamoto, K.; Yanagi, J. *J. Am. Chem. Soc.* **1979**, *101*, 147; Marshall, J. A.; Lewellyn, M. *J. Am. Chem. Soc.* **1977**, *99*, 3508.

0022-3263/79/1944-2438$01.00/0

Scheme I

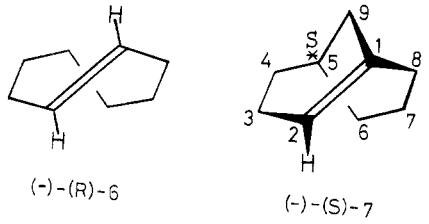


carbon atom and the trans bridge. This bridging degrades the original C_2 symmetry inherent to the *trans*-cyclooctene (**4**) to C_1 symmetry creating a new asymmetric center (*) at the ring juncture.

The resulting bicyclic compound has an unsaturated center at the bridgehead position and is an "anti-Bredt-rule" compound.[4] There appears to have been no explicit denunciation on this intrinsic chiral nature of an anti-Bredt-rule compound, and this together with our successful preparation of [8][8] and [8][10] trans doubly bridged ethylene **3** prompted us to prepare a first optically active anti-Bredt-rule compound. In this paper, we report the synthesis of (−)-(*S*)-bicyclo[3.3.1]-1(2)-nonene (**7**),[5] a methylene-bridged derivative of (−)-(*R*)-*trans*-cyclooctene (**6**), from (−)-(1*R*,3*S*)-*cis*-3-hydroxycyclohexanecarboxylic acid (**8**).

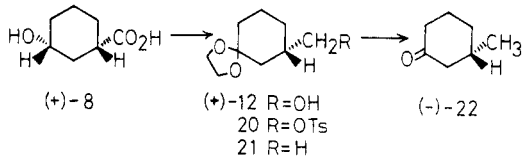
Results and Discussion

Synthesis of (−)-(*S*)-Bicyclo[3.3.1]-1(2)-nonene (7). Among several reported synthetic approaches to **7**, our



choice was Becker's,[5c] involving the intramolecular Wittig reaction of the triphenylphosphonium bromide (**19**) in the last and the most important strategic step. This made our immediate task to be securing a synthetic route from some easily accessible optically active starting material with known absolute configuration (hopefully with known optical purity) to the optically active modification of this Wittig compound (**19**).

Scheme II



Scheme I summarizes our projected sequence of steps from (−)-*cis*-3-hydroxycyclohexanecarboxylic acid (**8**) to the (−)-anti-Bredt-rule hydrocarbon **7**. The racemic hydroxy acid **8**, prepared following Noyce's procedure,[6] was optically resolved via the cinchonidine salts providing (−)-**8**, $[\alpha]_D$ −6.2° (EtOH), and (+)-**8**, $[\alpha]_D$ +5.6° (EtOH). The (−)-hydroxy acid **8** with the (1*R*,3*S*) configuration[7] was converted into the (−)-methyl ester **9** whose Jones' oxidation in acetone furnished an 88% yield of the (−)-keto carboxylate **10**, $[\alpha]_D$ −3.8° (EtOH).

After the carbonyl group had been protected by converting it into the (−)-ketal **11**, the side chain was modified by a routine chain-extension procedure involving $LiAlH_4$ reduction to the (−)-alcohol **12**, tosylation to **13**, and malonate ester synthesis to **14**. Saponification of **14**, decarboxylation of the resulting dicarboxylic acid followed by diazomethane esterification afforded a 38% overall yield of the homologous (−)-carboxylate **15** from **12**.

Lithium aluminum hydride reduction transformed the ester **15** into the (−)-alcohol **16**, $[\alpha]_D$ −1.9° (EtOH), whose identity was established by spectroscopic (IR and NMR) comparison with the reported racemic modification.[5c] The tosylate **17** obtained from **16** was refluxed with lithium bromide in acetone for 43 h to furnish a 60% yield of the (+)-bromide **18**, $[\alpha]_D$ +3.0° (EtOH), which was converted into the (+)-triphenylphosphonium bromide **19**, $[\alpha]_D$ +3.6° (CH_2Cl_2) (76% yield). The intramolecular Wittig reaction of (+)-**19** by heating with sodium hydride in tetraglyme completed our synthesis of (−)-bicyclo[3.3.1]-1(2)-nonene (**7**) whose purification through Florisil chromatography and distillation gave a 27% yield of a specimen with bp 80–85 °C (12 mm), $[\alpha]_D$ −259° ($CHCl_3$), and *m/e* 122 (M^+).

Chiroptical Properties

The reported (1*R*,3*S*) absolute configuration of our starting material **8** automatically assigns the (5*S*) configuration to this first optically active anti-Bredt-rule hydrocarbon **7**, whose absolute rotation in turn was estimated through our correlating (+)-**8** (the enantiomer of our starting (−)-hydroxy acid **8**) with (−)-3-methylcyclohexanone (**22**)[8] (Scheme II).

The sequence of steps described for the (−)-enantiomer **8** (Scheme I) converted (+)-**8**, $[\alpha]_D$ +5.6° (EtOH), into the (+)-ketal alcohol **12**, $[\alpha]_D$ +3.5° (EtOH), which was then tosylated to give **20**. Refluxing the tosylate **20** with $LiAlH_4$ in ether for 5 h followed by acidic hydrolysis with 10% sulfuric acid afforded (−)-3-methylcyclohexanone (**22**), bp 172–175 °C, $[\alpha]_D$ −4.1° (EtOH).

Three reported absolute rotation values ($[\alpha]_D$ 12.5°,[8a] 11.7°,[8b] and 13.54°[8c]) for 3-methylcyclohexanone permitted us to estimate 33 ± 3% optical purity for our sample of (−)-3-methylcyclohexanone. This correlation assigns

(4) Köbrich, G. *Angew. Chem., Int. Ed. Engl.* **1973**, *12*, 464. Buchanan, G. L. *Chem. Soc. Rev.* **1974**, *3*, 41. Keese, R. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 528.

(5) For the synthesis of the racemic modification of this hydrocarbon, see: (a) Marshall, J. A.; Faubl, H. *J. Am. Chem. Soc.* **1967**, *89*, 5965. Marshall, J. A.; Faubl, H. *Ibid.* **1970**, *92*, 948. (b) Wiseman, J. R. *Ibid.* **1967**, *89*, 5966. Wiseman, J. R.; Pletcher, W. A. *Ibid.* **1970**, *92*, 956. (c) Becker, K. B. *Helv. Chim. Acta* **1977**, *60*, 81.

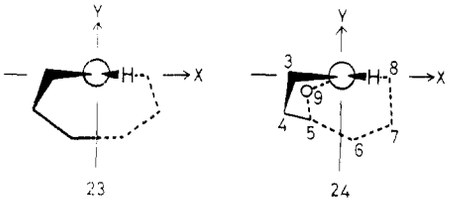
(6) Noyce, D. S.; Denny, D. B. *J. Am. Chem. Soc.* **1952**, *74*, 5912.

(7) Klyne, W.; Buckingham, J. "Atlas of Stereochemistry"; Chapman and Hall: London, 1974; p 42; and references cited therein.

(8) (a) Goering, H. L.; Silversmith, E. F. *J. Am. Chem. Soc.*, **1955**, *77*, 5172. (b) Macbeth, A. K.; Mills, J. A. *J. Chem. Soc.* **1947**, 205. (c) Rupe, H. *Justus Liebigs Ann. Chem.* **1927**, *459*, 206.

absolute rotation $[\alpha]_D$ +17.4 ± 1.3° to (−)-*cis*-3-hydroxycyclohexanecarboxylic acid (**8**) which eventually led us to calculate 36 ± 3% optical purity of our starting (−)-carboxylic acid **8** (Scheme I).

These roundabout correlations finally indicated absolute rotation $[\alpha]_D$ −725 ± 60° ($CHCl_3$) for the (−)-anti-Bredt-rule hydrocarbon **7**, which can be compared with absolute rotation $[\alpha]_D$ −458° (neat)[2] of closely related (−)-(*R*)-*trans*-cyclooctene (**6**). The close stereochemical relationship between **7** and **6** can also be seen in their respective Cotton curves with $[\Theta]$ −(13.6 ± 1.1) × 10^5 deg cm^2/dmol at 213 nm (isooctane)[9] and $[\Theta]$ −1.41 × 10^5 deg cm^2/dmol at 196 nm (cyclohexane).[10] These are found compatible with the prediction made from Scott's octant projection rule[10] which tells that (−)-anti-Bredt-rule hydrocarbon **24** has the extra methylene bridge in the



(+)-rear region which is expected to exert only a minor perturbation on the main chiral chromophore **23**.

Experimental Section

Infrared spectra were taken with a Hitachi EPI-S2 spectrophotometer. NMR spectra were recorded on a JNM-C-60 HL. Optical rotations were measured with a JASCO-DIP-SL automatic polarimeter. Circular dichroism data were collected with a JASCO J-40 spectropolarimeter. Mass spectra were taken with a Hitachi RMS-4 spectrometer. Elemental analysis were determined on a Yanagimoto CHN-Corder Type II. All melting and boiling points are uncorrected.

Optical Resolution of *cis*-3-Hydroxycyclohexanecarboxylic Acid (8). *cis*-3-Hydroxycyclohexanecarboxylic acid (**8**) [mp 131.5–132 °C (lit.[6] mp 130.5–131.5 °C)] was prepared according to Noyce's method.[6]

The carboxylic acid **8** (55.5 g, 0.386 mol) and cinchonidine (113 g, 0.385 mol) were heated under reflux for 1 h in ethanol (400 mL). Standing overnight at room temperature deposited a solid, which was recrystallized three times from ethanol to give 81.5 g of a salt; $[\alpha]^{25}_D$ −89.0° (*c* 1.61, EtOH). A mixture of the salt (81.5 g) and NaOH aqueous solution (NaOH 15.0 g, water 200 mL) was stirred for 12 h at room temperature and cinchonidine was filtered off. The filtrate was made acidic with 18 N sulfuric acid and extracted with ether. Evaporation of the ether gave 25.5 g of **8**: mp 124–127 °C; $[\alpha]^{24}_D$ −6.2° (*c* 1.61, EtOH).

Anal. Calcd for $C_7H_{12}O_3$: C, 58.31; H, 8.39. Found: C, 58.28; H, 8.35.

Concentration of the mother liquor of the cinchonidine salt gave 19.0 g of a semisolid, which was treated with aqueous NaOH (NaOH 2.0 g, water 70 mL). The same procedure described above afforded 3.85 g of **8**: mp 123–127.5 °C; $[\alpha]^{28}_D$ +5.6° (*c* 0.930, EtOH).

Anal. Calcd for $C_7H_{12}O_3$: C, 58.31; H, 8.39. Found: C, 58.61; H, 8.41.

(−)-Methyl *cis*-3-Hydroxycyclohexanecarboxylate (9). To a chilled solution of (−)-**8**, $[\alpha]_D$ −6.2° (25.5 g, 0.177 mol), in ether (200 mL) was added an excess of CH_2N_2 ether solution, and the mixture was stirred for 2 h with ice cooling. After a usual workup, distillation of the product gave 26.5 g of (−)-**9** (95% yield): bp 125–130 °C (20 mm); $[\alpha]^{22}_D$ −5.1° (*c* 0.685, EtOH).

Anal. Calcd for $C_8H_{14}O_3$: C, 60.74; H, 8.92. Found: C, 60.82; H, 8.94.

(−)-3-Carbomethoxycyclohexanone (10). To a chilled solution of (−)-**9**, $[\alpha]_D$ −5.1° (26.0 g, 0.164 mol), in acetone (100 mL) was added an excess of Jones' reagent.[11] After the mixture was stirred for 3 h at room temperature, the organic phase separated by decantation was concentrated. The residue and an inorganic substance were diluted with water and extracted with ether. The extract was washed with saturated $NaHCO_3$ solution and water, dried ($MgSO_4$), and concentrated. The residue was distilled to afford 22.6 g of (−)-**10** (88% yield): bp 115–120 °C (20 mm); $[\alpha]^{26}_D$ −3.8° (*c* 2.46, EtOH); IR (film) 1730, 1715, 1280, 1225, 1198, 1178 cm^{-1}.

Anal. Calcd for $C_8H_{12}O_3$: C, 61.52; H, 7.75. Found: C, 61.39; H, 7.89.

(−)-3-Carbomethoxycyclohexanone Ethylene Ketal (11). To a mixture of (−)-**10** ($[\alpha]_D$ −3.8° (35.9 g, 0.230 mol)), *p*-toluenesulfonic acid (500 mg), and benzene (1.5 L), ethylene glycol (51.4 g, 0.828 mol) was added dropwise with refluxing. The mixture was refluxed for 1.5 h during which water was removed as an azeotropic distillate. After workup, the solvent was evaporated and the residue was distilled to give 41.1 g of (−)-**11** (89% yield): bp 124–126 °C (10 mm); $[\alpha]^{22}_D$ −15.2° (*c* 0.823, EtOH); IR (film) 1735, 1450, 1435, 1355, 1295, 1255, 1172, 1160, 1090, 1040 cm^{-1}.

Anal. Calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05. Found: C, 59.70; H, 8.01.

(−)-3-Hydroxymethylcyclohexanone Ethylene Ketal (12). A solution of (−)-**11**, $[\alpha]_D$ −15.2° (20.0 g, 99.8 mmol), in dry ether (350 mL) was added dropwise to a suspension of $LiAlH_4$ (3.80 g, 99.8 mmol) in dry ether (240 mL), and the mixture was refluxed for 7 h. Saturated NH_4Cl solution was added to the chilled reaction mixture and an inorganic solid was filtered off. The filtrate was washed with water, dried ($MgSO_4$), and concentrated. Distillation of the residue gave 15.5 g of (−)-**12** (90% yield): bp 127 °C (5 mm); $[\alpha]^{24}_D$ −3.8° (*c* 1.95, EtOH); IR (film) 3400, 1450, 1355, 1280, 1235, 1162, 1105, 1078, 1032, 952, 932, 850 cm^{-1}.

Anal. Calcd for $C_9H_{16}O_3$: C, 62.76; H, 9.36. Found: C, 62.85; H, 9.26.

(−)-Methyl 3-(3,3-Ethylenedioxycyclohexyl)propionate (15). To a solution of (−)-**12**, $[\alpha]_D$ −3.8° (16.8 g, 97.5 mmol), in dry pyridine (50 mL) was added *p*-toluenesulfonyl chloride (22.3 g, 0.117 mol), and the mixture was stirred for 6 h with ice cooling. After standing overnight at room temperature, the reaction mixture was poured into ice–water, made acidic with HCl, and extracted with ether. After the usual workup, removal of the solvent gave 34.7 g of the tosylate **13** as an oil. Ethyl malonate (62.5 g, 0.390 mol) was added to a solution of sodium ethoxide prepared from sodium (6.6 g, 0.166 mol) and absolute ethanol (170 mL), and the mixture was refluxed for 3 h. To the mixture was added a solution of the crude tosylate (34.7 g) in absolute ethanol (230 mL), and the mixture was refluxed for 10 h. After evaporation of most of the ethanol under reduced pressure, the residue was poured into water and extracted with ether. The ethereal extract was washed with water, and the solvent with low boiling materials was removed by distillation in vacuo to afford 38.9 g of an oily product, which was dissolved in 50% aqueous methanol containing KOH (20.8 g). After refluxing for 5 h, the mixture was cooled with ice, made acidic with HCl, and extracted with ether. The extract was washed with water, and the solvent was evaporated. The residue (21.9 g) was placed in a distilling flask and heated (140–150 °C) under reduced pressure. The monocarboxylic acid obtained was distilled at 175 °C (0.4 mm) and then esterified with etheral CH_2N_2 by the same manner described for (−)-**9**. Distillation of the product gave 8.40 g of (−)-**15** (38% yield based on (−)-**12**): bp 116–118 °C (1.0 mm); $[\alpha]^{28}_D$ −0.64° (*c* 5.33, EtOH); IR (film) 1732, 1355, 1172, 1152, 1105, 1078, 952, 935 cm^{-1}.

Anal. Calcd for $C_{12}H_{20}O_4$: C, 63.13; H, 8.83. Found: C, 63.37; H, 8.67.

(−)-3-(3,3-Ethylenedioxycyclohexyl)propanol (16). Reduction of (−)-**15**, $[\alpha]_D$ −0.64° (17.3 g, 75.9 mmol) was carried out with $LiAlH_4$ (2.90 g, 76.3 mmol) by a similar manner to that described for (−)-**12**. Distillation of the product gave 10.8 g of (−)-**16** (71% yield): bp 130–132 °C (1.5 mm); $[\alpha]^{30}_D$ −1.9° (*c* 2.40,

(9) The $[\Theta]$ value is corrected to 100% optical purity according to its known optical purity.

(10) Scott, A. I.; Wrixon, A. D. *Tetrahedron* **1970**, *26*, 3695.

(11) Meinwald, J.; Crandall, J.; Hymans, W. E. "Organic Syntheses", Collect. Vol. V; Wiley: New York, N.Y., 1973; p 866.

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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(+)-(*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]

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