tography afforded 182 mg (95%) of allylic alcohol **24**, identical in all respects with that prepared previously.

Synthesis of Compounds 29 and 30 by Raney Nickel Hydrogenation. The procedure for the synthesis of compound **30** is representative. Compound **17** (180 mg, 0.466 mmol) and Raney nickel W-7 prepared from 2.5 g of alloy[28] were shaken in 40 mL of absolute ethanol in a Parr shaker under 60 psi of hydrogen for 48 h. The mixture was then diluted with ether, filtered, washed twice with brine, and dried over $MgSO_4$. Flash chromatography afforded 141 mg (83%) of compound **30**: R_f 0.35 (4:1 hexanes/ethyl acetate); ^1H NMR ($CDCl_3$) δ 0.88 (3 H, t, J = 5 Hz, CH_3), 1.2–1.9 (31 H, m), 2.3 (2 H, t, J = 7 Hz, CH_2CO), 3.7 (4 H, s, overlapping peaks, OCH_3, C*H*OH); IR (neat) 3430 (OH), 1740 (C=O) cm^{-1}; ^{13}C NMR ($CDCl_3$) δ 174.14, 72.02, 71.06, 51.27, 46.34, 37.68, 36.81, 36.21, 33.99, 31.88, 30.69, 29.60, 29.33, 29.06, 26.73, 26.62, 25.27, 24.84, 22.56, 15.30, 13.95, 11.40; MS for $C_{23}H_{40}O_3$, m/z calcd 364.29775, found 364.29664.

Compound 29: 82% yield; R_f 0.37 (4:1 hexanes/ethyl acetate); ^1H NMR ($CDCl_3$) δ 0.9 (3 H, t, J = 6 Hz, CH_3), 1.1–1.9 (30 H, m), 1.9–2.1 (3 H, br s), 2.3 (2 H, t, J = 7 Hz, CH_2CO), 3.7 (4 H, s, overlapping peaks, OCH_3, C*H*OH); IR (neat) 3420 (OH), 1740 (C=O) cm^{-1}; ^{13}C NMR ($CDCl_3$) δ 174.22, 72.38, 72.05, 51.31, 46.82, 46.56, 40.77, 37.78, 37.52, 37.39, 34.01, 32.65, 31.86, 29.91, 29.52, 29.13, 25.75, 25.56, 25.30, 24.91, 22.57, 13.98; MS for $C_{23}H_{42}O_3$, m/z calcd 366.31340, found 366.31398.

Synthesis of Compounds 31 and 32. The synthesis of compound **31** is representative. Compound **29** (125 mg, 0.342 mmol) was refluxed for 30 min in 10 mL of a 4:1 mixture of methanol and 2 N KOH. Upon cooling, the reaction was diluted with ether, acidified with 10 drops of concentrated HCl, washed with brine, and dried over $MgSO_4$. Purification by chromatography afforded 104 mg (86%) of compound **31**: R_f 0.43 (1:1 hexanes/ethyl acetate); ^1H NMR ($CDCl_3$) δ 0.95 (3 H, t, J = 7 Hz, CH_3), 1.2–1.8 (30 H, m), 2.0 (2 H, br s), 2.37 (2 H, t, J = 7 Hz, CH_2CO), 3.7 (1 H, m, C*H*OH), 6.35 (2 H, br s, OH, CO_2H); IR (neat) 3410 (OH), 1720 (C=O) cm^{-1}; ^{13}C NMR ($CDCl_3$) δ 179.16, 72.77, 72.38, 46.95, 46.63, 40.90, 37.78, 37.46, 34.08, 32.78, 31.93, 30.04, 29.52, 29.00, 25.95, 25.56, 25.36, 24.71, 22.70, 14.05; MS for $C_{22}H_{38}O_2$ ($M^{\cdot+} - H_2O$), m/z calcd 334.28718, found 334.28753.

Compound 32: 95% yield; R_f 0.39 (1:1 hexanes/ethyl acetate); ^1H NMR ($CDCl_3$) δ 0.8–1.1 (3 H, t, J = 7 Hz, CH_3), 1.2–2.1 (30 H, m), 2.3 (2 H, t, J = 6 Hz, CH_2CO), 3.5–3.7 (1 H, m, C*H*OH), 6.5 (2 H, br s, OH, CO_2H); IR (neat) 3400 (OH), 1730 (C=O) cm^{-1}; ^{13}C NMR ($CDCl_3$) δ 178.90, 72.31, 46.50, 37.59, 37.33, 37.07, 36.35, 34.08, 32.00, 30.63, 29.59, 29.26, 28.81, 26.79, 25.36, 24.65, 22.70, 15.41, 15.22, 14.05, 11.51; MS for $C_{22}H_{36}O_2$ ($M^{\cdot+} - H_2O$), m/z calcd 332.27153, found 332.27232.

Acknowledgment. We gratefully acknowledge the National Institutes of Health and the American Heart Association, Iowa Affiliate, for financial support; Proctor and Gamble for fellowship support for D.R.L.; Johnson Matthey Inc. and Engelhard Industries for generous loans of palladium salts; and Bristol Laboratories of Syracuse, NY, for carrying out the biological testing.

Synthesis of Optically Pure Enantiomers of Grandisol

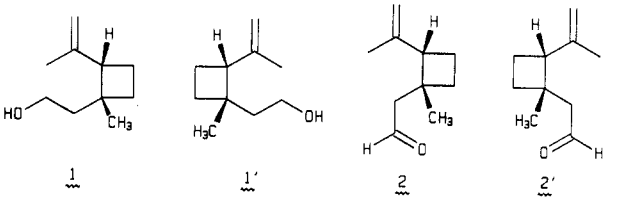
Francis X. Webster and Robert M. Silverstein*

State University of New York, College of Environmental Science and Forestry, Syracuse, New York 13210

Received July 30, 1986

The synthesis of both enantiomers of grandisol (**1** and **1'**) of greater than 99% optical purity is described. The key step is the separation of diastereomeric amides **11** and **12** and subsequent cleavage to give optically pure acids **8** and **8'**. Since **8** and **8'** contain a quaternary chiral center, the optical purity of derived grandisol **1** and **1'** is ensured.

Work in our laboratories has been directed at determining the composition of aggregating pheromones for several bark weevils of the genus *Pissodes* Germar. *P. strobi*, the white pine weevil, is notorious among forest insects for its deformation of pines and spruces throughout North America.[1] The northern pine weevil, *P. approximatus*, is not as economically important as *P. strobi*, although larvae may kill stressed trees and intense feeding by adults may be injurious to small trees.[2] The first evidence of an aggregation pheromone was reported by Booth and Lanier.[3] Subsequently, the suspected pheromone components for both species have been isolated and identified.[4] These components are the same for both species, namely, grandisol (*cis*-2-isopropenyl-1-methylcyclobutaneethanol) (**1** and **1'**) and grandisal (the corresponding aldehyde) (**2** and **2'**). Grandisol (**1** and **1'**) is well-known as one of the components of the aggregation pheromone of the cotton boll weevil (*Anthonomus grandis*).[5] In field tests, synthetic, racemic grandisol and



1 **1'** **2** **2'**

grandisal, along with suitable host material (red pine bolt), attracted beetles in numbers statistically identical with those of caged males (natural source of pheromone) for *P. approximatus*.[4] *P. strobi*, however, did not respond to the synthetic racemic compounds. Since the importance of optically pure semiochemicals has been well established,[6] we considered the possibility that *P. strobi* produces and responds to a single enantiomer or a specific blend of enantiomers.

Since chromatographic and spectrometric methods of determining the enantiomeric composition of grandisol by

(1) (a) MacAloney, H. J. *N. Y. State Coll. For. Syracuse Univ., Tech. Publ.* **1930**, *3*, 1. (b) Taylor, R. L. *Entomol. Am.* **1930**, *9*, 167.
(2) Finnegan, R. J. *Can. Entomol.* **1958**, *90*, 348.
(3) Booth, D. C.; Lanier, G. N. *Ann. Entomol. Soc. Am.* **1974**, *67*, 992.
(4) Booth, D. C.; Phillips, T. W.; Claesson, A.; Silverstein, R. M.; Lanier, G. N.; West, J. R. *J. Chem. Ecol.* **1983**, *9*, 1.
(5) Tumlinson, J. H.; Hardee, D. D.; Gueldner, R. C.; Thompson, A. C.; Hedin, P. A.; Minyard, J. P. *Science (Washington, D.C.)* **1969**, *166*, 1010.
(6) Silverstein, R. M. In *Chemical Ecology: Odour Communication in Animals*; Ritter, F. F. Ed.; Elsevier/North Holland: Amsterdam, 1979; pp 133–158.

0022-3263/86/1951-5226$01.50/0

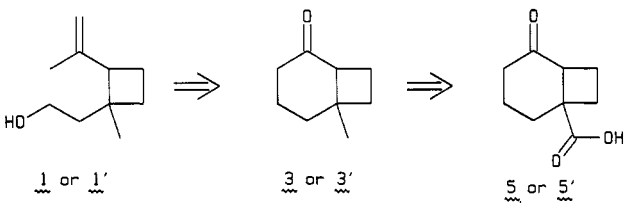


Figure 1. Retrosynthetic route from grandisol to the key resolvable carboxylic acid.

forming diastereomeric derivatives with a chiral derivatizing reagent have uniformly been unsuccessful and the minute amount available precludes determination of the optical activity of the natural material, we decided to synthesize both enantiomers of grandisol (which can readily be oxidized to grandisal) and test them in the field. The synthesis was designed to yield gram amounts of both enantiomers of very high optical purity (>99%).

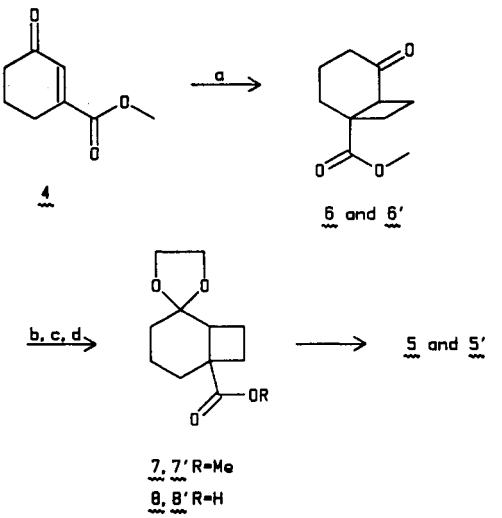
Because of the importance of the cotton boll weevil and because of the unique structure of grandisol, considerable synthetic work on grandisol has been reported,[7] but only two groups have been concerned with optically active grandisol. Hobbs and Magnus[8] reported the synthesis of (+)-grandisol of about 90% optical purity from (−)-β-pinene, but their work is not suitable for our purpose because it would be difficult to produce both enantiomers of high purity. Their work did, however, determine the absolute stereochemistry of (+)-grandisol (1*R*,2*S*), and it showed that optically pure grandisol should have an optical rotation of $[\alpha]_D$ +18.4° (*c* 1, *n*-hexane). Mori synthesized both enantiomers of 80% optical purity (determined with an NMR chiral shift reagent)[9] and the (−)-enantiomer of 90–98% optical purity (determined only by optical rotation).[10]

Results and Discussion

Since we were unable to find a suitable pair of enantiomers, both of very high optical purity, on which to base a synthesis, we devised a scheme that depended on resolution of a key intermediate with proof that the resolution was complete. Bicyclic keto acid **5** and **5′**[11] was chosen as the key intermediate to resolve because it contains both chiral centers found in grandisol and because this compound has been reported in the literature.[12] Figure 1 contains a retrosynthetic analysis relating grandisol to the key carboxylic acid **5** and **5′** through ketone **3** and **3′**, the basis of Zurflüh's stereospecific synthesis of racemic grandisol.[12]

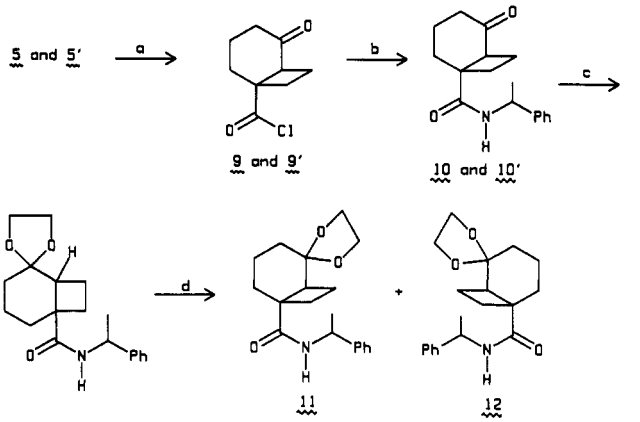
The synthesis of keto acid **5** and **5′**, outlined in Scheme I, parallels that of Agosta and Lowrance[13] but with some differences. We began with unsaturated keto ester **4**.[14] Agosta and Lowrance report that ethylene photocyclization gave the bicyclic keto ester **6** and **6′** in 98% yield. We have found that the product obtained in 98% yield on distillation of the solvent was not pure **6** and **6′** but contained about 16% of a much less volatile substance, probably the dimer of starting **4**. Simple distillation gave an 82% yield

Scheme I[a]



[a] Reagents: (a) $CH_2{=}CH_2$, C_6H_6, *hν*; (b) $HOCH_2CH_2OH$, PTSA, C_6H_6; (c) KOH, MeOH, H_2O; (d) 6 N HCl to pH 3; (e) 1 N HCl, Et_2O.

Scheme II[a]



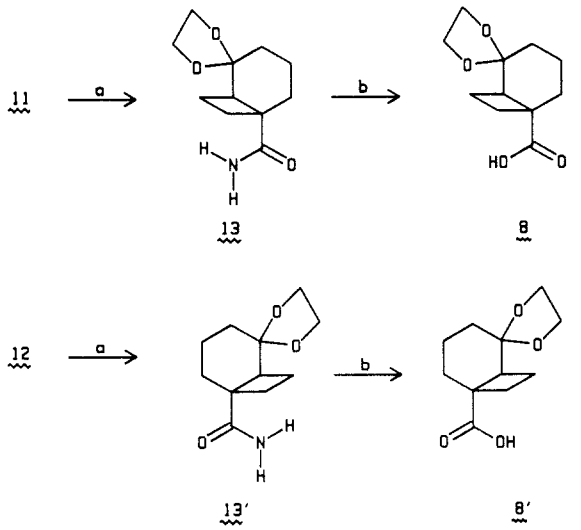
[a] Reagents: (a) oxalyl chloride, C_6H_6; (b) $NH_2CH(CH_3)Ph$, pyridine; (c) $HOCH_2CH_2OH$, C_6H_6, PTSA; (d) flash chromatography, recrystallization.

of pure **6** and **6′**. Basic hydrolysis of keto ester **6** and **6′** to keto acid **5** and **5′** was tried since Agosta and Lowrance reported a 98% yield for this reaction. However, in our hands, the reaction, even when run under milder conditions, gave an impure acid that proved difficult to purify. Since Mori[9] had the same problem with a similar system and since he used an acetal group successfully, we made acetal **7** and **7′**. Basic hydrolysis of acetal ester **7** and **7′** gave crystalline acetal acid **8** and **8′**. Mild hydrolysis of **8** was effected in a two-phase system of ether and 1 N HCl to give keto acid **5** and **5′**.

The resolution of acids by purifying diasteromeric salts is usually an attractive method because the acids can be regenerated easily. The resolution can often be monitored by ^{13}C NMR spectrometry directly on the diastereomeric salts.[15] However, preliminary work with various amine bases on **5** and **5′** gave only oils. The use of amides to resolve carboxylic acids has been very successful,[16] but the main problem has been to regenerate the acid without racemization. Since racemization of our quaternary acid

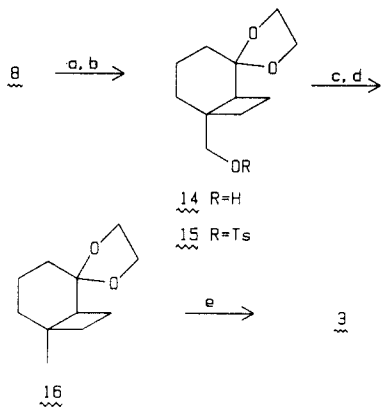
(7) Katzenellenbogen, J. A. *Science (Washington, D.C.)* **1976**, *194*, 139.
(8) (a) Hobbs, P. D.; Magnus, P. D. *J. Chem. Soc., Chem. Commun.* **1974**, 85. (b) Hobbs, P. D.; Magnus, P. D. *J. Am. Chem. Soc.* **1976**, *98*, 4594.
(9) Mori, K. *Tetrahedron* **1978**, *34*, 915.
(10) Mori, K.; Tamada, S.; Hedin, P. A. *Naturwissenschaften* **1978**.
(11) In the numbering of figures the primed numbers refer to antipodes of unprimed numbers. Racemic compounds have both primed and unprimed numbers.
(12) Zurflüh, R.; Durham, L. L.; Spain, V. L.; Siddall, J. B. *J. Am. Chem. Soc.* **1970**, *92*, 425.
(13) Agosta, W. C.; Lowrance, W. W., Jr. *J. Org. Chem.* **1970**, *35*, 3851.
(14) Webster, F. X.; Silverstein, R. M. *Synthesis*, in press.
(15) Webster, F. X.; Xeng, Z.-n.; Silverstein, R. M. *J. Org. Chem.* **1982**, *47*, 5225.
(16) (a) Jacques, J.; Colet, A.; Wilson, S. H. In *Enantiomers, Racemates, and Resolution*; Wiley: New York, 1981; pp 329–330. (b) Sonnet, P. E. *J. Org. Chem.* **1982**, *47*, 3739.

Scheme III[a]



[a] Reagents: (a) Li, NH_3, H_2O, THF; (b) KOH, $HOCH_2CH_2OH$, Δ.

Scheme IV[a]

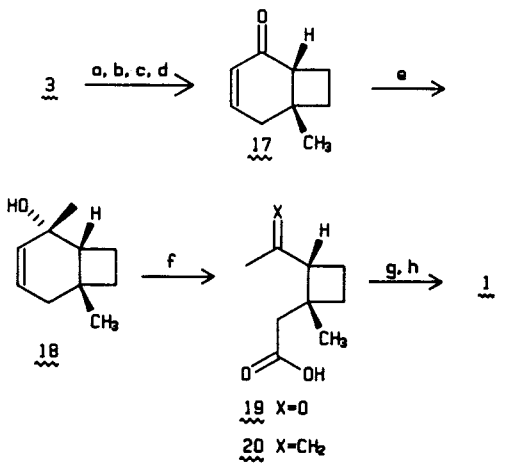


[a] Reagents: (a) $LiAlH_4$, Et_2O; (b) TsCl, pyridine; (c) $Li(Et)_3BH$, THF; (d) NaOH, H_2O, H_2O_2; (e) 1 N HCl, Et_2O.

5 and 5′ was not a concern, we used diastereomeric α-methylbenzylamides to resolve keto acid 5 and 5′ (Scheme II). The acid chloride 9 and 9′ of carboxylic acid 8 and 8′ was treated with (*S*)-(−)-α-methylbenzylamine to give the diastereomers of keto amide 10. Although these diastereomers could not be separated by either recrystallization or HPLC,[17] the acetal of 10 was readily separated into the diastereomers 11 and 12. Separation of 11 and 12 was carried out by large-scale flash chromatography (>95% pure) prior to recrystallization. By this method 11 and 12 can be purified to >99% purity[18] on a large scale and with high recovery.

Since published procedures for cleaving hindered amides[19] were not effective on the very highly hindered amides 11 or 12, we devised a satisfactory two-step procedure:[20] treatment of 11 or 12 with lithium in liquid ammonia followed by cleavage with KOH in hot ethylene glycol to give 8 or 8′ (Scheme III). If racemization in the latter step

Scheme V[a]



[a] Reagents: (a) PhSeCl, EtOAc; (b) $HOCH_2CH_2OH$, C_6H_6, PTSA; (c) H_2O_2, CH_2Cl_2, pyridine; (d) 1 N HCl, Et_2O; (e) MeLi, Et_2O; (f) RuO_4, $NaIO_4$, CCl_4, CH_3CN, H_2O; (g) CH_3Ph_3PBr, BuLi, THF; (h) $LiAlH_4$, Et_2O.

is of concern—as it was not for our amides—Olah's procedure may be used.[20,21]

Transformation of 8 or 8′ to the key bicyclic ketone 3 and 3′ was straightforward with excellent yields at each step (Scheme IV): reduction with $LiAlH_4$ and tosylation to give 15 and 15′, followed by immediate treatment with lithium triethylborohydride[22] and hydrolysis with dilute aqueous acid/ether to give 3 and 3′ with $[\alpha]^{23}_D$ −163° (*c* 2.0, $CHCl_3$) and $[\alpha]^{22}_D$ +165° (*c* 1.7, $CHCl_3$), respectively.

Although the conversion of ketone 3 to grandisol 1 (or of 3′ to 1′) has been described, we found it necessary to modify several steps. Zurflüh et al.[13] converted 3 into its corresponding α,β-unsaturated ketone by the classical method of bromination/dehydrobromination, but we found the product difficult to purify. A much purer product was obtained by selenation/selenoxide elimination (Scheme V). Ketones 3 and 3′ were selenated with benzeneselenenyl chloride (PhSeCl) in ethyl acetate. It has been shown for cyclic α-phenylseleno ketones that direct oxidation and subsequent elimination of benzeneselenenic acid (PhSeOH) gives a poor yield of enone.[23] The same authors have shown, however, that if the ketone is protected as an acetal, the oxidation/elimination reaction proceeds in high yield. Therefore, the α-phenylseleno ketone was acetalized, the selenium was oxidized with a hydrogen peroxide/methylene chloride suspension, and the benzeneselenenic acid was eliminated in hot CCl_4. The resulting protected enone was deprotected with dilute HCl in ether. Enone 17 (or 17′) was alkylated with methyllithium in ether[13] to give tertiary allylic alcohol 18 (or 18′) as an unstable crystalline solid. Zurflüh et al.[12] oxidatively cleaved racemic 18 with osmium tetraoxide and sodium periodate to give keto acid 19 instead of the expected keto aldehyde. In our hands, the reaction gave erratic rresults, usually in low yield. Since ruthenium tetraoxide/sodium periodate cleavage[24] of 18 would be expected to give 19, we studied this reaction on various substrates and found that it was quite general and proceeded in high yield.[25] Treatment of 18 (or 18′) with these reagents gave a good

(17) Even though 10 is a mixture of diastereomers, ^{13}C NMR analysis gave a single set of peaks (15 peaks). We have found that, in general, diastereomers that do not give a separate set of peaks in ^{13}C NMR are very difficult to separate.

(18) HPLC analysis showed no trace of the undesired diastereomer in both cases. We estimate that our error is less than 1%.

(19) Sonnet, P. E.; Heath, R. R. *J. Chem. Ecol.* **1982**, *8*, 41.

(20) Webster, F. X.; Millar, J. G.; Silverstein, R. M. *Tetrahedron Lett.* **1986**, *27*, 4941.

(21) Olah, G. A.; Olah, J. A. *J. Org. Chem.* **1965**, *30*, 2386.

(22) (a) Krishnamurthy, S.; Brown, H. C. *J. Org. Chem.* **1976**, *41*, 3064.

(23) Reich, H. J.; Renga, J. M.; Reich, I. L. *J. Am. Chem. Soc.* **1975**, *97*, 5434.

(24) Carlsen, P. H. J.; Katsuki, J.; Martin, V. S.; Sharpless, K. B. *J. Org. Chem.* **1981**, *46*, 3938.

(25) Webster, F. X.; Silverstein, R. M. *J. Org. Chem.*, in press.

yield of **19** (or **19'**) uncontaminated by its trans isomer.

Wittig methyleneation of **19** (or **19'**) completes the construction of the isopropenyl group. This reaction has been reported many times with varying amounts of epimerization. Mori, for example, found that 20% isomerization occurred in his reaction.[9] Zurflüh et al. found that under their conditions about 3% isomerization occurred.[12] The key factor in these reactions seemed to be the proportion of dimethyl sulfoxide used. In fact, Stork and Cohen methyleneated a very similar compound in pure THF, and they found no trace of isomerization.[26] Therefore, we ran the Wittig reaction in THF with BuLi as the base and found no sign of epimerization.

To complete the synthesis, the Wittig product was reduced with $LiAlH_4$ in ether to give (1*R*,2*S*)-(+)-grandisol: $[\alpha]^{25}_D$ +18.4° (*c* 1.1, *n*-hexane). Since the quaternary center from **11** has remained intact and since **11** was shown to be >99% pure, the enantiomeric excess in **1** must also be >99%. In a similar manner, (1*S*,2*R*)-(−)-grandisol (**1'**), $[\alpha]^{25}_D$ −18.1° (*c* 1.2, *n*-hexane), was synthesized. These rotations agree with the value calculated from the work of Hobbs and Magnus[8] (see the introduction above).

Experimental Section

Melting points were obtained on a Mel-Temp apparatus and are uncorrected. Electron impact (70 eV) mass spectral data were obtained on a Finnigan 4000 mass spectrometer by either GC on a 30 m × 0.2 mm i.d. DB-1 capillary column in a Finnigan GLC 9500 (16 psi He) or by direct inlet to the ionizing source. Both ^1H NMR (100 MHz) and ^{13}C NMR (25.2 MHz) spectra were obtained on a Varian XL-100; all samples were run in $CDCl_3$ and were recorded as ppm from internal Me_4Si. IR spectra were obtained on a Perkin Elmer 1310 and were run, unless otherwise noted, as thin films between NaCl plates. A Perkin Elmer 141 polarimeter was used to obtain optical rotations. Silica gel (230–400 mesh) used for flash chromatography was obtained from Sigma.

Methyl (1*RS*,6*RS*)-5-Oxobicyclo[4.2.0]octane-1-carboxylate (6 and 6'). In an immersion-type photoreaction vessel, 20.0 g (0.13 mol) of methyl 3-oxo-1-cyclohexenecarboxylate (**4**) was dissolved in 2 L of benzene. The reaction vessel was equipped with a magnetic stirrer, a 450-W Hanovia UV lamp, and an outlet connected to a column of mercury acting as a pressure regulator and a blow-off valve. The stirred benzene solution was saturated with ethylene, pressurized to about 7–8 psi, and irradiated under pressure for 24 h. The apparatus was disassembled, and the benzene was evaporated. Distillation of the residue gave 19.4 g (82%) of **6** as a clear, colorless oil: bp 88 °C (0.1 mmHg); IR 2950, 2860, 1725, 1700, 1430, 1235, 1100, 900 cm^{-1}; ^1H NMR δ 1.72–2.74 (m, 10 H), 3.31 (crude t, *J* = 8 Hz, 1 H), 3.75 (s, 3 H); MS, *m/e* (relative intensity) 39 (78), 40 (28), 41 (76), 42 (11), 43 (10), 51 (9), 53 (17), 55 (100), 59 (22), 65 (19), 66 (23), 67 (58), 68 (19), 77 (9), 79 (28), 80 (11), 81 (21), 83 (11), 94 (19), 95 (39), 98 (14), 104 (20), 105 (27), 111 (8), 122 (23), 123 (22), 126 (28), 139 (4), 150 (17), 154 (9), 164 (10), 182 (8).

Methyl (1*RS*,6*RS*)-5,5-(Ethylenedioxy)bicyclo[4.2.0]octane-1-carboxylate (7 and 7'). In a 2-L round-bottom flash was placed a solution of 100.0 g (0.593 mol) of **6** and **6'**, 500 mg (2.6 mmol) of *p*-toluenesulfonic acid monohydrate (PTSA), and 40.44 g (0.652 mol) of ethylene glycol in 1 L of anhydrous benzene. The flask was equipped with a magnetic stirrer, a Dean–Stark trap, a reflux condenser, and a heating mantle. The reaction was heated and stirred under reflux until water no longer separated (about 4 h). When the reaction was complete, the mixture was cooled and extracted two times with 300 mL of saturated $NaHCO_3$. The organic solution was dried (Na_2SO_4), the solvent was evaporated, and the remaining oil was distilled to give 115.3 g (86%) of **7** and **7'** as a clear, viscous oil: bp 91 °C (0.1 mmHg); IR 2955, 2880, 1725, 1450, 1435, 1310, 1235, 1145, 1105, 1040, 945 cm^{-1}; ^1H NMR δ 1.40–2.45 (m, 10 H), 2.87 (crude t, *J* = 10 Hz, 1 H), 3.73 (s, 3 H), 3.92 (m, 4 H); ^{13}C NMR δ 18.9, 20.6, 28.8, 29.2, 31.5, 41.6, 46.1, 54.3, 63.9, 64.1, 107.7, 175.3; MS, *m/e* (relative intensity) 39 (7), 41 (10), 55 (20), 67 (5), 79 (4), 86 (8), 99 (100), 100 (6), 113 (14), 167 (3), 181 (1), 226 (4).

(1*RS*,6*RS*)-5,5-(Ethylenedioxy)bicyclo[4.2.0]octane-1-carboxylic Acid (8 and 8'). In a 2-L round-bottom flask was placed a solution of 56.0 g (1.0 mol) of potassium hydroxide dissolved in a mixture of 400 mL of MeOH and 100 mL of H_2O. The flask was equipped with a heating mantle, a reflux condenser, and a magnetic stirrer. Under N_2, 115.0 g (0.51 mol) of **7** and **7'** was added all at once, and the solution was heated to reflux for 1 h. The solution was cooled, and all of the methanol was evaporated. The mixture was diluted with 400 mL of H_2O and placed in a large beaker. The solution was cooled in an ice bath and carefully acidified to pH 3 (pH meter) with 6 N HCl. The ice-cold solution (now containing a large amount of solid material) was extracted three times with 400 mL of CH_2Cl_2, the organics were dried (Na_2SO_4), and the solvent was evaporated. The residue was dissolved in a minimum of refluxing Et_2O and chilled to 0 °C. Filtration gave 84.3 g (78%) of **8** and **8'** as prisms: mp 100–101 °C; ^1H NMR δ 1.50–2.45 (m, 10 H), 2.78 (t, *J* = 9 Hz, 1 H), 3.97 (m, 4 H), 10.48 (s, 1 H); ^{13}C NMR δ 19.0, 20.9, 29.3, 29.9, 31.5, 41.9, 46.2, 64.1, 64.4, 108.0, 181.0; MS/*m/e* (relative intensity) 41 (23), 42 (9), 43 (7), 45 (9), 53 (7), 55 (37), 67 (8), 79 (6), 86 (13), 99 (100), 101 (7), 113 (9), 124 (3), 167 (2), 212 (4).

Anal. Calcd for $C_{11}H_{16}O_4$: C, 62.25; H, 7.60. Found: C, 62.31; H, 7.63.

(1*RS*,6*RS*)-5-Oxobicyclo[4.2.0]octane-1-carboxylic Acid (5 and 5'). In a 2-L Erlenmeyer flask containing 500 mL of 1 N HCl and 500 mL of Et_2O was dissolved 84.0 g (0.396 mol) of **8** and **8'** with magnetic stirring. The flask was stoppered and stirred at room temperature for 10 h. The layers were separated, and the ether layer was washed with saturated brine, dried (Na_2SO_4), and evaporated. The residue was dissolved in hot toluene and chilled to 0 °C. Filtration gave 61.9 g (93%) of **5** as clear prisms: mp 65–66 °C; ^1H NMR δ 1.70–2.70 (m, 10 H), 3.34 (m, 1 H), 10.72 (s, 1 H); ^{13}C NMR δ 20.9, 21.2, 28.6, 30.2, 38.0, 45.9, 47.8, 180.3, 214.5.

(1*RS*,6*RS*)-5-Oxobicyclo[4.2.0]octane-1-carbonyl Chloride (9 and 9'). In a 1-L round-bottom flask was dissolved 61.5 g (0.366 mol) of **5** and **5'** in 400 mL of anhydrous benzene with magnetic stirring. The flask was equipped with a reflux condenser and drying tube. To this vigorously stirred solution was added 69.7 g (0.549 mol) of oxalyl chloride; the solution was stirred for 9 h at room temperature. The benzene and excess oxalyl chloride were evaporated, and the residual oil was distilled to give 49.9 g (73%) of **9** and **9'** as a light yellow colored oil: bp 83 °C (0.1 mmHg); IR 2950, 1780, 1705, 1475, 1230, 960, 740, 675 cm^{-1}; ^1H NMR δ 1.80–2.80 (m, 10 H), 2.20–2.54 (m, 1 H).

(1*RS*,6*RS*)-5-Oxo-*N*-((*S*)-1-phenylethyl)bicyclo[4.2.0]octane-1-carboxamide (10). A 1-L, three-neck flask, equipped with N_2 inlet, dropping funnel, reflux condenser, and drying tube, was charged with 450 mL of dry CH_2Cl_2, 31.6 g (0.40 mol) of pyridine, and 32.3 g (0.267 mol) of (*S*)-(−)-1-phenylethylamine (Aldrich Chem. Co.). In the dropping funnel was placed 49.8 g (0.267 mol) of **9** and **9'**. The CH_2Cl_2 solution was cooled with an ice bath, and the acid chloride was added over a period of 15 min. After the addition was complete, the ice bath was removed and the solution was stirred for an additional hour. The reaction mixture was washed two times with 300 mL of 1 N HCl and once with 300 mL of saturated $NaHCO_3$ and dried (Na_2SO_4), and the solvent was stripped to give 65.8 g (91%) of **10** as a solid with a broad melting range: ^1H NMR δ 1.45 (d, *J* = 7 Hz, 3 H), 1.63–2.61 (m, 10 H), 3.29 (m, 1 H), 5.08 (m, 1 H), 6.21 (m, 1 H), 7.29. (br s, 5 H); ^{13}C NMR δ 20.8, 21.6, 28.7, 28.9, 31.3, 38.5, 45.6, 48.7, 49.0, 125.7, 126.5, 128.0, 143.3, 174.9, 212.0; MS, *m/e* 41 (22), 42 (5), 53 (6), 55 (22), 67 (13), 77 (17), 79 (24), 81 (7), 95 (15), 104 (16), 105 (70), 106 (18), 107 (100), 108 (5), 120 (78), 121 (5), 123 (12), 148 (2), 186 (1), 188 (4), 202 (1), 225 (<1), 243 (<1), 253 (<1), 256 (<1), 271 (<1).

(1*RS*,6*RS*)-5,5-(Ethylenedioxy)-*N*-((*S*)-1-phenylethyl)-bicyclo[4.2.0]octane-1-carboxamide (11 and 12). In a 1-L flask containing 400 mL anhydrous benzene, 350 mg (1.8 mmol) PTSA,

(26) Stork, G.; Cohen, J. F. *J. Am. Chem. Soc.* **1974**, *96*, 5270.

(27) **Note Added in Proof.** Recently, the enantiomeric composition (88% ee) of a synthetic (−)-grandisol was determined by ^1H NMR of Mosher's derivative (Meyers, A. I.; Fleming, S. A. *J. Am. Chem. Soc.* **1986**, *108*, 306).

and 16.5 g (0.266 mol) ethylene glycol was dissolved 65.4 g (0.242 mol) of **10** and **10'** with magnetic stirring. The ketal was formed as above. The oil obtained (64.0 g, 84% yield) was purified as follows.

Purification of (1*R*,6*R*)-5,5-(Ethylenedioxy)-*N*-((*S*)-1-phenylethyl)bicyclo[4.2.0]octane-1-carboxamide (11) and (1*S*,6*S*)-5,5-(Ethylenedioxy)-*N*-((*S*)-1-phenylethyl)bicyclo[4.2.0]octane-1-carboxamide (12). A 50-mm-diameter, flash chromatography column containing about 10 in. of silica gel was prepared with a solvent mixture of hexane, ethyl acetate, and isopropyl alcohol in a ratio of 7:3:1. This column was used to purify ten separate 6.5-g samples of the oil from the above reaction. The pooled fractions were analyzed by HPLC (Whatman Partisil 10 silica M9, 25 cm long, flow 8 mL/4 min, same solvent system, refractive index detector) and were >99% pure. The more polar diastereomer (shown to be **11**) was recrystallized twice from hexane/ethyl acetate (2:1) and gave 26.2 g (82% yield) of **11**: mp 113–114 °C; ^{1}H NMR δ 1.44 (d, J = 6 Hz, 3 H), 1.55–2.55 (m, 11 H), 3.60–4.07 (m, 4 H), 5.05 (m, 1 H), 7.31 (m, 6 H); ^{13}C NMR δ 17.9, 21.0, 22.3, 22.7, 30.0, 32.1, 42.8, 47.8, 48.6, 64.2, 64.9, 108.8, 126.11, 127.2, 128.6, 144.3, 176.7; MS, (relative intensity) m/e 41 (26), 42 (14), 43 (7), 45 (5), 53 (10), 55 (61), 67 (15), 73 (13), 77 (20), 79 (28), 81 (5), 86 (10), 95 (10), 99 (75), 103 (5), 104 (11), 105 (58), 106 (18), 107 (100), 108 (7), 113 (31), 120 (32), 123 (5), 167 (11), 188 (17), 203 (15), 243 (<1), 254 (1), 316 (1).

Anal. Calcd for $C_{19}H_{25}NO_3$: C, 72.35; H, 7.99; N, 4.44. Found: C, 72.36; H, 8.08; N, 4.56.

The less polar diastereomer (shown to be **12**) was recrystallized twice from cyclohexane (chilled to 10 °C) to give 23.7 g (74%) of **12**: mp 67–69 °C; ^{1}H NMR δ 1.44 (d, J = 6 Hz, 3 H), 1.55–2.55 (m, 11 H), 3.90 (m, 4 H), 5.05 (m, 1 H), 6.28 (m, 1 H), 7.31 (m, 5 H); ^{13}C NMR δ 17.9, 21.0, 22.3, 22.7, 29.8, 31.9, 42.5, 47.8, 48.5, 64.2, 64.9, 108.8, 125.9, 127.0, 128.6, 144.0, 176.7; MS, m/e 41 (31), 42 (16), 43 (10), 45 (7), 51 (5), 53 (11), 55 (54), 65 (5), 67 (14), 73 (12), 77 (20), 78 (6), 79 (23), 81 (5), 86 (11), 91 (5), 95 (10), 99 (65), 103 (7), 104 (12), 105 (52), 106 (17), 107 (100), 108 (9), 113 (31), 120 (31), 123 (5), 160 (5), 167 (12), 188 (18), 203 (19), 243 (1), 254 (2), 272 (1), 300 (1), 315 (6).

Anal. Calcd for $C_{19}H_{25}NO_3$: C, 72.35; H, 7.99; N, 4.44. Found: C, 72.51; H, 7.97; N, 4.54.

(1*R*,6*R*)-5,5-(Ethylenedioxy)bicyclo[4.2.0]octane-1-carboxamide (13). In a 2-L, three-neck flask was dissolved 26.0 g (82.5 mmol) of amide **11** in 220 mL of THF containing 17 mL of H_2O. The flask was equipped with an efficient mechanical stirrer, an ammonia inlet, and a cold-finger condenser containing solid CO_2 and acetone. Ammonia was admitted above the solution through a sintered-glass filter; about 900 mL of ammonia was collected, giving a homogeneous solution. As quickly as possible, 2.23 g (0.319 mol) of lithium wire cut into small pieces was added with vigorous stirring, which was continued until the blue color had completely disappeared. The solution was allowed to stand until the ammonia had evaporated. The residue was diluted with 200 mL of THF and filtered. The solids were washed well with 200 mL total of fresh THF, and the combined THF solution was evaporated to dryness. The residue was dissolved in CH_2Cl_2, washed well with water, dried (Na_2SO_4), and evaporated to give 16.5 g (95%) of **13**, which was used without further purification.

(1*S*,6*S*)-5,5-(Ethylenedioxy)bicyclo[4.2.0]octane-1-carboxamide (13'). In a similar manner 23.5 g (74.6 mmol) of amide **12** was treated to give 14.8 g (94%) of **13'**.

(1*R*,6*R*)-5,5-(Ethylenedioxy)bicyclo[4.2.0]octane-1-carboxylic Acid (8). Ethylene glycol (225 mL) containing 11.3 g (0.20 mol) of KOH was thoroughly purged with N_2 in a 500-mL three-neck flask equipped with a thermometer, magnetic stirrer, and reflux condenser. To this solution was added 16.5 g (0.0784 mol of **13**, and the solution was heated to 125–130 °C in an oil bath. The reaction was monitored by checking the N_2 at the mouth of the condenser with moist pH paper. After 10 h, the gases were neutral. The cooled reaction mixture was diluted with 1100 mL of H_2O and extracted two times with ether (350 mL each time). The aqueous solution was chilled with an ice bath and acidified to pH 3 with 6 N HCl (pH meter). The solution was extracted three times with CH_2Cl_2 (350 mL each time), the organic phase was dried (Na_2SO_4), and the solvent was evaporated to give 14.29 g (86%) of **8**, identical with the racemate in ^{1}H and ^{13}C NMR spectra and MS; however, the pure enantiomer was an oil in contrast with the racemate **8** and **8'**.

(1*S*,6*S*)-5,5-(Ethylenedioxy)bicyclo[4.2.0]octane-1-carboxylic Acid (8'). Similarly, 14.8 g (70.1 mmol) of **1'** gave 13.23 g (89%) of **8'** as an oil; it too was spectrally identical with the racemate.

(1*R*,6*R*)-5,5-(Ethylenedioxy)-1-(hydroxymethyl)bicyclo[4.2.0]octane (14). Lithium aluminum hydride (0.96 g, 25.3 mmol) was suspended in 200 mL of dry Et_2O in a 500-mL, three-neck flask with magnetic stirrer, dropping funnel, reflux condenser, and drying tube. In the dropping funnel was placed 14.92 g (67.4 mmol) of **8** dissolved in 10 mL of dry Et_2O, and this solution was added at a rate that maintained a gentle reflux. Stirring was continued for 1 h at room temperature, and the reaction was killed by the cautious sequential addition of 1 mL of H_2O, 1 mL of 15% NaOH, and 3 mL H_2O. The mixture was filtered and dried (Na_2SO_4), and the solvent was removed to give 10.94 g (82%) of **14** as an oil: IR 3390, 2890, 2805, 1430, 1345, 1070, 920 cm^{-1}; ^{1}H NMR δ 1.20–2.53 (m, 12 H), 3.48 (m, 2 H), 3.97 (m, 4 H); MS, m/e (relative intensity) 41 (18), 42 (6), 43 (7), 54 (5), 55 (32), 67 (6), 79 (5), 86 (9), 87 (10), 99 (100), 100 (87), 111 (2), 142 (2), 169 (1), 198 (1).

(1*S*,6*S*)-5,5-(Ethylenedioxy)-1-(hydroxymethyl)bicyclo[4.2.0]octane (14'). In a similar manner 13.23 g (62.4 mmol) of **8'** gave 10.62 g (86%) of **14'**. Its spectral properties were identical with those of **14**.

(1*R*,6*R*)-5,5-(Ethylenedioxy)-1-(hydroxymethyl)bicyclo[4.2.0]octane *p*-Toluenesulfonate (15). Alcohol **14** (10.94 g, 55.3 mmol) was dissolved in 125 mL of dry pyridine in a 500-mL round-bottom flash with magnetic stirrer and a drying tube. The flask was chilled to 0 °C, and 14.36 g (75.3 mmol) of *p*-toluenesulfonyl chloride was added. Stirring was continued at 0 °C until all of the acid chloride was dissolved. The flask was placed in a freezer at 0 °C for 24 h. The reaction was diluted with 700 mL of H_2O and extracted five times with ether (350 mL each time). The ether extracts were combined, washed with water (350 mL), washed two times with 1 N HCl (350 mL each), washed with brine, and dried (Na_2SO_4). Evaporation of the solvent gave 18.71 g (96%) of the neopentyl-type tosylate **15** as a lightly colored orange oil: IR 2930, 2865, 1592, 1455, 1355, 1182, 1170, 1105, 1091, 1030, 1010, 952, 918, 890, 860, 830, 810, 660 cm^{-1}; ^{1}H NMR δ 1.25–2.30 (m, 11 H), 2.46 (s, 3 H), 3.84 (m, 6 H), 7.33 (m, 2 H), 7.79 (m, 2 H).

(1*S*,6*S*)-5,5-(Ethlenedioxy)-1-(hydroxymethyl)bicyclo[4.2.0]octane *p*-Toluenesulfonate (15'). Tosylation of 10.62 g (53.7 mmol) of alcohol **14'** in similar fashion gave 17.98 g (95%) of **15'**, spectrally identical with **15**.

(1*S*,6*R*)-5,5-(Ethylenedioxy)-1-methylbicyclo[4.2.0]octane (16). In as 1-L, three-neck flask equipped with dropping funnel, condenser, N_2 inlet, drying tube, and magnetic stirrer was dissolved 18.71 g (53.1 mmol) of tosylate **15** in 200 mL of dry THF. The stirred solution was cooled to 0 °C, and the dropping funnel was charged with 160 mL (160 mmol) of 1 M lithium triethylborohydride in THF (Aldrich). The hydride solution was added over a period of 1 h. After the addition, the ice bath was removed, and the solution was stirred for 14 h at room temperature. The excess hydride was destroyed by gradual addition of 10 mL of water. The reaction mixture was then cooled with an ice bath, and 60 mL of 3 N NaOH was added followed gradually by 60 mL of 30% H_2O_2 (caution: the addition can cause a very violent reaction). The mixture was refluxed for 1 h, then cooled, and extracted three times with pentane (200 mL each). The pentane extracts were washed with water, dried (Na_2SO_4), and evaporated to give 7.83 g (81%) of **16** as a clear, colorless oil. This acetal was not characterized except for ^{1}H NMR spectrum to ensure completeness of reaction: ^{1}H NMR δ 1.08 (s, 3 H), 1.38–2.16 (m, 11 H), 3.90 (m, 4 H).

(1*R*,6*S*)-5,5-(Ethylenedioxy)-1-methylbicyclo[4.2.0]octane (16'). Reduction of 17.78 g (51.0 mmol) of tosylate **15'** gave 7.52 g (81%) of **16'**. Its ^{1}H NMR was identical with that of **16**.

(1*R*,6*S*)-6-Methylbicyclo[4.2.0]octan-2-one (3). In a 1-L Erlenmeyer flask with magnetic stirring was dissolved 7.83 g (43.0 mmol) of **16** in 250 mL of Et_2O. To the vigorously stirred solution was added 250 mL of 1 N HCl; stirring was continued for 12 h. The layers were then separated, and the ether layer was washed with brine and dried (Na_2SO_4), and the solvent was evaporated. Distillation gave 5.16 g (87%) of **3** as a clear oil: bp 75 °C (8 mmHg); IR 2940, 2860, 1698, 1454, 1369, 1223, 1038 cm^{-1}; ^{1}H NMR

δ 1.24 (s, 3 H), 1.38–2.67 (m, 11 H); ^{13}C NMR δ 20.1, 20.8, 28.6, 30.8, 34.8, 39.1, 40.4, 51.0, 214.0; MS, *m/e* (relative intensity) 41 (30), 42 (7), 53 (9), 54 (11), 55 (47), 67 (26), 68 (10), 69 (6), 70 (22), 79 (5), 81 (9), 82 (100), 83 (12), 95 (8), 110 (28), 123 (8), 178 (6); $[\alpha]^{23}_D$ −163° (*c* 2.0, $CHCl_3$).

(1*S*,6*R*)-6-Methylbicyclo[4.2.0]octan-2-one (3′). Acetal **16′** (7.52 g, 41.3 mmol) was similarly cleaved to give 5.13 g (90%) of **3′**: $[\alpha]^{23}_D$ +165° (*c*, 1.7, $CHCl_3$).

(1*R*,6*R*)-6-Methylbicyclo[4.2.0]oct-3-en-2-one (17). To a solution of 5.16 g (37.4 mmol) of **3** in 325 mL of ethyl acetate was added 8.70 g (45.3 mmol) of benzeneselenenyl chloride (PhSeCl) with stirring. The solution was stirred for 20 min (red-orange solution to pale yellow) and washed with 100 mL of H_2O. The solution was dried and evaporated. An acetal was formed with 2.55 g (41.1 mmol) of ethylene glycol and 220 mg (1.2 mmol) of PTSA as before. The product was dissolved in 300 mL of CH_2Cl_2 and 6.2 mL of pyridine. Hydrogen peroxide (30%, 84 mL) was added slowly with stirring (caution: reaction becomes more vigorous at the end), and stirring was continued for 1.5 h at room temperature. After removal of the aqueous phase, the CH_2Cl_2 was replaced with 100 mL of CCl_4 containing 6 mL of pyridine. The solution was refluxed for 1 min. The solution was extracted with saturated $NaHCO_3$ (100 mL) and two times with 1 N HCl (75 mL each) and dried (Na_2SO_4), and the solvent was removed. The residue was dissolved in 100 mL of Et_2O and 100 mL of 1 N HCl. The solution was stirred at room temperature for 12 h, extracted with brine, dried (Na_2SO_4), and evaporated. Distillation gave 2.29 g (45%) of **17** as an oil: bp 57–59 °C (1.0 mmHg); ^1H NMR δ 1.34 (s, 3 H), 1.55–2.72 (m, 7 H), 6.17 (dt, J = 10 Hz, J = 1 Hz, 1 H), 6.91 (dt, J = 10 Hz, J = 4 Hz, 1 H); MS, *m/e* (relative intensity) 41 (51), 42 (7), 51 (10), 52 (7), 53 (19), 54 (5), 55 (26), 65 (11), 66 (5), 67 (16), 68 (50), 77 (21), 78 (6), 79 (66), 80 (100), 81 (18), 91 (13), 93 (14), 94 (17), 95 (5), 107 (5), 108 (62), 109 (5), 121 (14), 136 (18).

(1*S*,6*S*)-6-Methylbicyclo[4.2.0]oct-3-en-2-one (17′). The same series of reactions on 5.13 g (37.2 mmol) of **16′** gave 2.44 g (48%) of **17′**.

(1*R*,6*R*)-2,6-Dimethylbicyclo[4.2.0]oct-3-en-2-ol (18). In a 500-mL, three-neck flask with a dropping funnel, N_2 inlet, condenser, drying tube, and magnetic stirrer was placed 100 mL of anhydrous ether containing 2.29 g (16.8 mmol) of enone **17**. The dropping funnel was charged with 18 mL (25.2 mmol) of a 1-M solution of MeLi in Et_2O (Aldrich). The stirred solution was cooled to 0 °C and the MeLi was added over a period of 15 min. The reaction was killed by the cautious addition of 1 mL of water. The reaction mixture was washed with brine, dried (Na_2SO_4), and evaporated to give 2.15 g (84%) of **18** as a white crystalline solid. This material was very labile and purification was not attempted: ^1H NMR δ 1.15 (s, 3 H), 1.19 (s, 3 H), 1.30–2.37 (m, 7 H), 5.82 (m, 2 H); ^{13}C NMR δ 17.3, 27.1, 30.9, 32.6, 35.4, 36.2, 51.0, 71.0, 126.3, 135.6.

(1*S*,6*S*)-2,6-Dimethylbicyclo[4.2.0]oct-3-en-2-ol (18′). In a like manner, alkylation of 2.44 g (17.9 mmol) of **17′** gave 2.23 g (82%) of **18′**.

(1*R*,2*S*)-2-Acetyl-1-methylcyclobutaneacetic Acid (19). Allylic alcohol **18** (2.15 g, 14.1 mmol) was dissolved in 28 mL of CCl_4 and 28 mL of acetonitrile in a 250-mL, three-neck flask equipped with a condenser and magnetic stirrer. Sodium periodate (16.59 g, 77.5 mmol) was suspended in the solution with vigorous magnetic stirring. Ruthenium(III) chloride (81.2 mg, 0.39 mmol), dissolved in 42 mL of H_2O, was added on one portion, and vigorous stirring was continued for 5 h. Sufficient water was then added to dissolve the separated sodium iodate. The solution was extracted three times with 150 mL of CH_2Cl_2, and the organic extracts were combined, dried (Na_2SO_4), and evaporated. The residue, which contained highly colored ruthenium species, was dissolved in 150 mL of ether and filtered through Celite. Evaporation of the ether gave 1.46 g (61%) of **19** as a viscous oil: ^1H NMR δ 1.42 (s, 3 H), 1.65–2.34 (m, 4 H), 2.12 (s, 3 H), 2.51 (m, 2 H), 3.09 (m, 1 H), 10.21 (s, 1 H); ^{13}C NMR δ 17.1, 27.3, 30.0, 30.3, 39.3, 41.0, 54.6, 176.6, 209.3; MS, *m/e* (relative intensity) 41 (25), 43 (100), 44 (8), 53 (8), 54 (6), 55 (26), 57 (5), 58 (7), 67 (7), 68 (5), 71 (57), 72 (9), 81 (10), 82 (16), 83 (5), 85 (6), 95 (7), 96 (7), 100 (7), 109 (10), 110 (13), 111 (14), 124 (5), 152 (4), 170 (1).

(1*S*,2*R*)-2-Acetyl-1-methylcyclobutaneacetic Acid (19′). Oxidative cleavage of 2.23 g (14.7 mmol) of **18′** gave 1.50 g (60%) of **19′** as a viscous oil, spectrally identical with **19**.

(1*R*,2*S*)-2-Isopropenyl-1-methylcyclobutaneacetic Acid (20). Methyltriphenylphosphonium bromide (7.68 g, 21.5 mmol) was suspended in 120 mL of dry THF in a 500-mL, three-neck, round-bottom flask with N_2 inlet, condenser, drying tube, dropping funnel, and magnetic stirrer. The dropping funnel was charged with 8.6 mL (21.5 mmol) of a 2.5 M solution of BuLi in hexane. The suspension was cooled in an ice bath, and the BuLi was added over a period of 10 min. The ylide solution was stirred for 1 h. In a new dropping funnel was placed 1.46 g (8.6 mmol) of keto acid **19** in 10 mL of THF. This was added over a 10-min period at 0 °C. After being stirred for 2.5 h at room temperature, the reaction mixture was poured into 150 mL of H_2O and extracted three times with 100 mL of Et_2O (discarded). The aqueous solution was acidified with 1 N HCl and extracted three times with 100 mL of CH_2Cl_2. These extracts were combined, dried (Na_2SO_4), and evaporated to give 980 mg (68%) of **20** as viscous oil: ^1H NMR δ 1.36 (s, 3 H), 1.71 (d, J = 1 Hz, 3 H), 1.61–2.20 (m, 5 H), 2.49–2.78 (m, 2 H), 4.72 (m, 1 H), 4.91 (m, 1 H), 10.37 (s, 1 H).

(1*S*,2*R*)-2-Isopropenyl-1-methylcyclobutaneacetic Acid (20′). Wittig methyleneation of 1.50 g (8.8 mmol) of **19′** gave 1.15 g (78%) of **20′**; its ^1H NMR was identical with that of **20**.

(1*R*,2*S*)-2-Isopropenyl-1-methylcyclobutaneethanol ((+)-Grandisol, 1). Lithium aluminum hydride reduction of 980 mg (5.8 mmol) of **20** as above gave an oil that was flash chromatographed on silica gel (20 mm × 15.25 cm, 85:15 hexane–ethyl acetate) to give 620 mg (70%) of (+)-grandisol: IR 3320, 2950, 2870, 1645, 1450, 1375, 1050, 880 cm^{-1}; ^1H NMR δ 1.18 (s, 3 H), 1.24–2.14 (m, 10 H), 2.56 (m, 1 H), 3.68 (m, 2 H), 4.66 (m, 1 H), 4.85 (m, 1 H); ^{13}C NMR δ 19.1, 23.2, 28.3, 29.2, 36.7, 41.2, 52.4, 59.5, 109.5, 144.9; MS, *m/e* (relative intensity) 41 (27), 42 (4), 43 (9), 53 (13), 55 (11), 56 (11), 67 (39), 68 (100), 69 (30), 70 (6), 71 (7), 79 (7), 81 (20), 85 (5), 93 (8), 95 (5), 107 (9), 108 (8), 109 (27), 111 (19), 121 (7), 123 (4), 139 (16), 154 (1); $[\alpha]^{25}_D$ +18.4° (*c* 1.1, *n*-hexane).

(1*S*,2*R*)-2-Isopropenyl-1-methylcyclobutaneethanol ((−)-Grandisol, 1′). Reduction of 1.15 g (6.9 mmol) of **20** gave, after purification, 770 mg (73%) of (−)-grandisol (**1′**): $[\alpha]^{25}_D$ −18.1° (*c* 1.2, *n*-hexane).

Acknowledgment. This study was supported by a grant from the National Science Foundation. We thank Dr. M. Mitchell and his group from the College for combustion analysis.