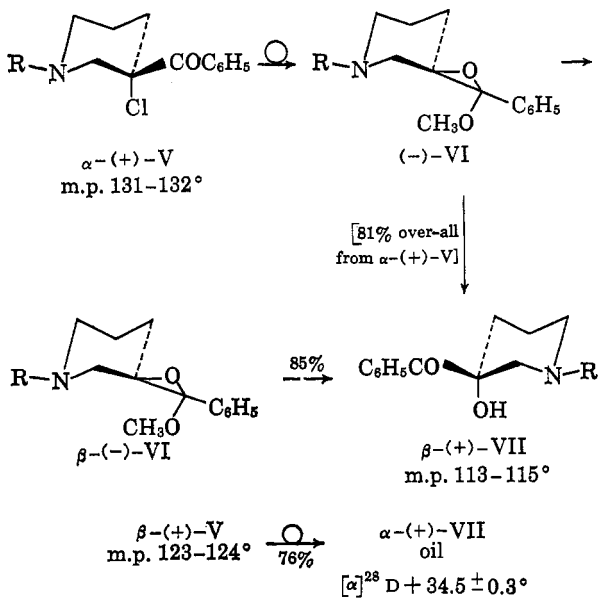
Treatment of α-(+)-V with methanolic sodium methoxide afforded a levorotatory diastereoisomeric mixture of epoxy ethers, 2-methoxy-2-phenyl-5-(10-camphorsulfonyl)-1-ox-5-azaspiro[2.5]octanes (VI), from which an optically pure diastereoisomer, β-(−)-VI, was isolated in 28% yield by fractional crystallization. Isolation of an optically pure, *solid* α-hydroxy ketone, β-(+)-1-(10-camphorsulfonyl)-3-benzoyl-3-hydroxypiperidine [β-(+)-VII], m.p. 113–115°, in 85% yield, upon treatment of β-(−)-VI with 0.2 *N* hydrochloric acid in 1:4 aqueous acetone, confirms retention of configuration through β-C–O cleavage of the epoxy ether.[2,3f,4] Moreover, the quantitative polarimetric analysis of this reaction reveals total retention of configuration within the limits of experimental error.

The mechanism of epoxy ether formation from α-halo ketones was clearly demonstrated by conversion of α-(+)-V directly to the same solid, β-(+)-VII, through the total epoxy ether mixture (VI) in 81% over-all yield. Thus, inversion of configuration normally occurs in epoxy ether formation, while anchimeric assistance[4] is responsible for the anomalous symmetrization (−)-I. Finally, from the fact that β-(+)-V afforded an *oil*, α-(+)-VII, $[\alpha]^{28}D$ +34.5 ± 0.3°, lit.[6a] $[\alpha]^{28}D$ +34.0 ± 0.4° (optically pure), which we have been unable to crystallize, it can be concluded that both "normal" epoxy ether formation and cleavage are virtually, if not in fact, 100% optically specific.



R = 10-camphorsulfonyl moiety derived from (+)-10-camphorsulfonic acid

Experimental Section[6b]

α-(+)- and β-(+)-1-(10-Camphorsulfonyl)-3-benzoyl-3-chloropiperidine [α-(+)-V and β-(+)-V].—These solids, m.p. 131–132° and 123–124°, respectively, were prepared as described earlier.[5]

Epoxy Ether Formation from α-(+)-V [VI and β-(−)-VI].—To 50 ml. of methanolic sodium methoxide (from 0.7 g. of freshly cut sodium and absolute methanol) was added 5.0 g. (11.4 mmoles) of optically pure α-(+)-V in 25 ml. of anhydrous benzene. After standing for 24 hr. at room temperature, the solution was filtered and the solvent was removed under reduced pressure. The residual gum was partitioned between benzene and water. The benzene extracts were dried over sodium sulfate, treated with carbon, filtered through sintered glass, and evaporated to dryness under reduced pressure. The residue (VI) was recrystallized from hexane and then petroleum ether (b.p. 20–60°) to constant melting point, 135–137°, and specific rotation, $[\alpha]^{28}D$ −32.2 ± 0.3° (*c* 1.18, methanol), to give 1.40 g. (3.1 mmoles, 28%) of β-(−)-VI.

Anal. Calcd. for $C_{28}H_{31}NO_5S$: C, 63.71; H, 7.21; N, 3.23; S, 7.39. Found: C, 63.59; H, 7.39; N, 3.44; S, 7.38.

The carbonyl band at 1670 cm.$^{-1}$ (1740 cm.$^{-1}$, camphor carbonyl) in the infrared spectrum of α-(+)-V was absent in the spectrum of β-(−)-VI.

Epoxy Ether Cleavage [β-(−)-VI → β-(+)-VII].—To 0.3128 g. (0.724 mmole) of β-(−)-VI in 7 ml. of acetone, was added 2 ml. of 1 *N* hydrochloric acid and enough acetone to bring the final volume to 10.00 ml. No change (±0.01°) in rotatory power could be observed, undoubtedly owing to the speed of the acidolysis.[4] Assuming 100% conversion to α-hydroxy ketone VII (after 24 hr.), from the weight of β-(+)-VII equivalent to that of β-(−)-VI introduced and the observed rotation, the calculated specific rotation, $[\alpha]^{28}D$ +12.9 ± 0.3° (0.2 *N* hydrochloric acid–1:4 water–acetone), of product(s) in the solution indicated total formation, within experimental error, of β-(+)-VII. This could be isolated in 85% yield (0.258 g., 0.62 mmole), m.p. 113–115°, $[\alpha]^{28}D$ +13.2 ± 0.3° (*c* 3.88, 0.2 *N* hydrochloric acid–1:4 water–acetone), by evaporation of the solvent under a stream of dry nitrogen and recrystallization of the residue from hexane.

Anal. Calcd. for $C_{22}H_{29}NO_5S$: C, 62.98; H, 6.97; N, 3.34. Found: C, 62.83; H, 7.03; N, 3.55.

The infrared spectrum of β-(+)-VI exhibited carbonyl absorptions at 1660 and 1740 cm.$^{-1}$ and hydroxyl absorption at 3450 cm.$^{-1}$.

Epoxy Ether Formation and Cleavage [α-(+)-V → (−)-VI → β-(+)-VII].—Treatment of 1.028 g. (2.34 mmoles) of α-(+)-V with methanolic sodium methoxide followed by subjection of the total epoxy ether mixture (VI) to acidolysis afforded 0.800 g. (1.91 mmoles, 81%) of β-(+)-VII, m.p. 113–115°, $[\alpha]^{28}D$ +13.4 ± 0.5° (*c* 3.28, 0.2 *N* hydrochloric acid–1:4 water–acetone).

Epoxy Ether Formation and Cleavage [β-(+)-V → (+)-VI → α-(+)-VII].—After treatment of 1.6 g. (3.65 mmoles) of β-(+)-V as described for the α isomer, the solution was filtered. The water-soluble precipitate contained no organic material. The solvent was removed under reduced pressure. The total residue was dissolved in about 25 ml. of 0.2 *N* hydrochloric acid in acetone–water (4:1). After 24 hr. the solvent was removed under a stream of dry nitrogen. The resulting oil was dissolved in purified hexane. The solution was treated with carbon and sodium sulfate, filtered through sintered glass, and subjected to a stream of dry nitrogen to give 1.2 g. (2.86 mmoles, 76%) of a colorless oil, α-(+)-VII, $[\alpha]^{28}D$ +34.5 ± 0.3° (*c* 5.54, 0.2 *N* hydrochloric acid–1:4 water–acetone), lit.[6a] $[\alpha]^{28}D$ +34.0 ± 0.4° (0.2 *N* hydrochloric acid–1:4 water–acetone) (optically pure).

Anal. Calcd. for $C_{22}H_{29}NO_5S$: C, 62.98; H, 6.97. Found: C, 63.09; H, 7.11.

(6) (a) H. Patel and G. Hite, *J. Org. Chem.*, **30**, 4336 (1965); (b) *ibid.*, footnote 6.

Resin Acids. VII. Partial Synthesis of (−)-13-*epi*-Rimuane[1]

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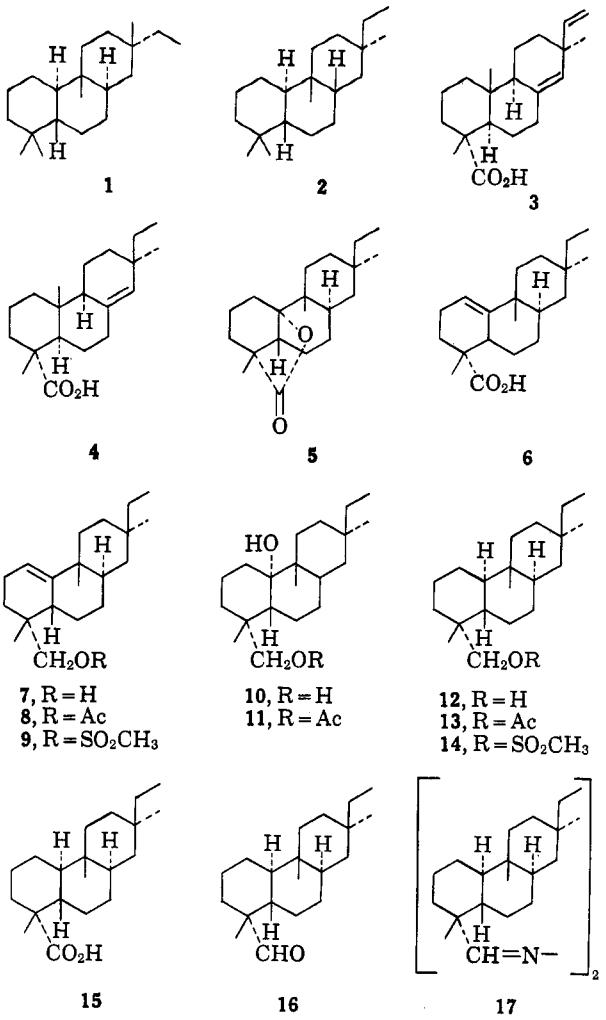
Although our recently described[2] partial synthesis of (−)-rimuane (1) from isopimaric acid defined the absolute configuration of rimuene, we had determined at the outset, because of uncertainty about the stereochemistry at C-13,[3] to synthesize concurrently the

(1) Previous paper: W. Herz and R. N. Mirrington, *J. Org. Chem.*, **30**, 3198 (1965). Work was supported in part by grants from the Petroleum Research Fund administered by the American Chemical Society and the National Science Foundation (G.P.-1962).

(2) W. Herz and R. N. Mirrington, *ibid.*, **30**, 3195 (1965).

(3) The total synthesis[4] of *dl*-rimuene did not establish the configuration at this center unambiguously.

(4) R. E. Ireland and L. N. Mander, *Tetrahedron Letters*, **No. 46**, 3453 (1964).



epimeric hydrocarbon **2** from pimaric acid **3** by a similar series of reactions. The synthesis of **1** was completed first and its identity with authentic tetrahydrorimuene established,[2] but, as a sequel, we now describe the partial synthesis of **2** which we name 13-*epi*-rimuane for convenience.

Partial hydrogenation of pimaric acid[5] followed by acid treatment of the dihydro derivative **4**[10] yielded the known γ-lactone **5**.[10,11] Hydrolysis of **5** with potassium hydroxide in refluxing diethylene glycol gave the known unsaturated acid **6**[12] whose hydrogenation was not attempted because of difficulties encountered with the analogous acid in the isopimaric series.[2] **6** was directly reduced to the unsaturated alcohol **7** with lithium aluminum hydride, and the latter was acetylated to **8**. The acetate **8** was also conveniently prepared by lithium aluminum hydride reduction of the lactone **5** to the diol **10** whose monoacetate **11** was smoothly dehydrated with thionyl chloride in pyridine. The nuclear magnetic resonance (n.m.r.) spectra of compounds **6**, **7**, **8**, and **9** all contained a multiplet near 5.4 p.p.m. due to one olefinic proton, confirming the presence of a trisubstituted double bond rather than the alternative tetrasubstituted $\Delta^{5(10)}$ isomer.

Catalytic reduction of acetate **8** with platinum oxide in acetic acid containing a trace of perchloric acid gave the expected[2] saturated acetate **13** which was saponified to furnish alcohol **12**. The hydrogenation was carried out on the acetate **8** rather than on the alcohol **7** to prevent formation of an unwanted cyclic ether as observed in the isopimaric series.[2]

Oxidation of **12** with excess Jones reagent at room temperature gave 13-*epi*-tetrahydrorimuic acid **15**, m.p. 192–193°, $[\alpha]D$ −13°, presumably identical with the acid, m.p. 190°, $[\alpha]D$ −15°, obtained by Le Van Thoi and Ourgaud[12] by catalytic hydrogenation of **6** (without perchloric acid) and also by Clemmensen reduction of lactone **5**. The latter procedure was unsuccessful in our hands, starting material being recovered quantitatively.

Oxidation of **12** with Jones reagent at 0° gave aldehyde **16** which, when subjected to Huang-Minlon reduction, afforded a 36% yield of the desired hydrocarbon **2**, m.p. 52–53°, $[\alpha]D$ −21°, obviously different from the previously obtained hydrocarbon **1** in the isopimaric series.[2]

Experimental Section[13]

Lactone 5.—Dihydropimaric acid **4**,[14] 14 g., was lactonized by the method of Edwards and Howe[10] to give a gum which was chromatographed on 300 g. of silica gel. Elution with benzene furnished 9.87 g. (70%) of lactone **5** which crystallized from methanol: m.p. 98–100° (lit.[10] m.p. 100°), infrared band at 1770 cm.$^{-1}$.

Unsaturated Acetate 8. A. *Via* **Unsaturated Acid 6.**—A mixture of 12.5 g. of lactone **5**, 80 ml. of anhydrous diethylene glycol, and 8 g. of potassium hydroxide was heated under reflux in a nitrogen atmosphere for 1.75 hr. and then worked up as described previously[2] to give 0.78 g. of unchanged **5** and 8.35 g. (71%) of acid **6** which crystallized from aqueous methanol as colorless needles: m.p. 156–157° (lit.[12] m.p. 160°); infrared band at 1700 cm.$^{-1}$; n.m.r. signals at 7.0 (broad, 1 proton, COO*H*), 5.35 (multiplet, 1 proton 1H), 1.22, 0.90, and 0.83 p.p.m. (methyl singlets). A solution of 3.0 g. of **6** in 250 ml. of anhydrous ether was added slowly to a swirled suspension of 2 g. of lithium aluminum hydride in 200 ml. of anhydrous ether and the mixture was refluxed for 2 hr. The excess reagent was destroyed carefully with water, and the washed and dried ether layer was evaporated to furnish a yellow oil which was chromatographed on 80 g. of alumina. Elution with benzene gave 2.35 g. (82%) of alcohol **7** as a colorless oil: infrared bands ($CHCl_3$) at 3700 (sharp), 3500 (broad) (free and bonded OH, respectively), 1020 (hydroxyl C—O stretch), and 1650 cm.$^{-1}$ (C=C); n.m.r. signals at 5.40 (multiplet, 1 proton, 1 H), 3.52, 3.32 (AB quartet, 2 protons, CH_2OH, J_{AB} = 10.5 c.p.s.), 0.93, 0.88, and 0.84 p.p.m. (methyl singlets).

Acetylation of **7** with acetic anhydride–pyridine at 25° for 16 hr. gave acetate **8** as an oil: infrared bands (CCl_4) at 1745, 1250 (acetate), and 1650 cm.$^{-1}$ (C=C); n.m.r. signals at 5.41 diffuse triplet (1 proton, 1H, $J \sim 3$ c.p.s.), 3.90 s (2 protons, CH_2OAc), 2.07 s (3 protons, acetate), 0.94, 0.88, and 0.84 p.p.m. (methyl singlets).

The alcohol **7** was characterized for analysis as its mesylate **9**, which crystallized from aqueous methanol as colorless needles: m.p. 86–87°; infrared bands at 1650 (C=C), 1360, 1340, 1180,

(5) Correlation[6,7] of pimaric acid with sandaracopimaric acid, whose absolute stereochemistry has been defined by correlation with testosterone[8] and 3β-acetoxy-androst-5-en-17-one,[9] established that the absolute stereochemistry of pimaric acid is represented as **3**.

(6) O. E. Edwards, A. Nicolson, and M. N. Rodger, *Can. J. Chem.*, **38**, 663 (1960).

(7) O. E. Edwards and R. Howe, *Chem. Ind.* (London), 537 (1959).

(8) A. K. Bose and S. Harrison, *ibid.*, 254 (1963).

(9) M. Fétizon and M. Golfier, *Bull. soc. chim. France*, 167 (1963).

(10) O. E. Edwards and R. Howe, *Can. J. Chem.*, **37**, 760 (1959).

(11) Le Van Thoi and J. Ourgaud, *Bull. soc. chim. France*, 202 (1956).

(12) Le Van Thoi and J. Ourgaud, *ibid.*, 205 (1956).

(13) Melting points are uncorrected. Analyses were performed by Dr. F. Pascher, Bonn, Germany. Infrared spectra were run as Nujol mulls unless otherwise specified, rotations in chloroform. N.m.r. spectra were run on an A-60 spectrometer in deuteriochloroform with tetramethylsilane as internal standard, chemical shifts being recorded as δ values.

(14) Isolated from "Staybelite" resin kindly supplied by Dr. T. F. Sanderson, Hercules Powder Co., and also prepared by hydrogenation of pimaric acid over palladium–charcoal catalyst.[10] A generous sample of pimaric acid was furnished by Mr. B. L. Hampton.

and 1170 cm.$^{-1}$ (sulfonate),[15] no hydroxyl; n.m.r. signals at 5.30 diffuse triplet (1 proton, 1 H, $J \sim 3$ c.p.s.), 3.90 s (2 protons, $CH_2OSO_2CH_2$), 2.92 s (3 protons, mesylate), 0.98, 0.84, and 0.82 p.p.m. (methyl singlets).

Anal. Calcd. for $C_{21}H_{36}O_3S$: C, 68.42; H, 9.84; S, 8.70. Found: C, 69.06; H, 9.59; S, 8.63.

B. *Via* **Diol 10.**—A solution of 8.37 g. of lactone **5** in 300 ml. of anhydrous ether was added to a swirled suspension of 6.0 g. of lithium aluminum hydride in 400 ml. of anhydrous ether and the mixture was refluxed for 3 hr. The excess reagent was decomposed in the usual way, the aqueous layer was extracted with ether, and the extracts were combined with the original ether layer, washed with water, dried, and evaporated to furnish 8.3 g. of diol **10**, which crystallized from acetone as colorless needles: m.p. 176–179° (the analytical sample had m.p. 182–183°); infrared bands at 3300–3400 and 1080 cm.$^{-1}$ (hydroxyl); n.m.r. signals at 3.80 s (2 protons, OH, removed on exchange with D_2O), 3.68, 3.16 (AB quartet, 2 protons, CH_2OH, $J_{AB} = 11$ c.p.s.), 0.87, 0.87, and 0.78 p.p.m. (methyl singlets).

Anal. Calcd. for $C_{20}H_{36}O_2$: C, 77.86; H, 11.76. Found: C, 77.86; H, 11.61.

Acetylation of 4.0 g. of diol **10** with acetic anhydride–pyridine for 2 hr. at 80° gave, after the usual working up, 4.5 g. (quantitative) of monoacetate **11** which crystallized from aqueous methanol as colorless flat needles: m.p. 101–102°; infrared bands at 3600, 1040 (OH), 1735, 1715, and 1280–1250 cm.$^{-1}$ (acetate). The infrared spectrum in carbon tetrachloride showed only one carbonyl band at 1740 cm.$^{-1}$. N.m.r. signals occurred at 4.67, 3.98 (AB quartet, 2 protons, CH_2OAc, $J_{AB} = 11$ c.p.s.), 2.01 s (3 protons, acetate), 0.93, 0.85, and 0.83 p.p.m. (methyl singlets).

Anal. Calcd. for $C_{22}H_{38}O_3$: C, 75.38; H, 10.93. Found: C, 75.61; H, 10.89.

A solution of 3.0 g. of **11** in 100 ml. of pyridine was cooled to 0° and treated slowly with 11 ml. of thionyl chloride. After addition was complete the ice bath was removed and the mixture was kept at 25° for 4 hr., then poured onto ice, and extracted three times with ether. The combined extracts were washed well with water, twice with 1 *N* hydrochloric acid, and again with water, dried, and evaporated to give 2.6 g. (92%) of acetate **8**, identical (infrared and n.m.r.) with the compound described in A.

Alcohol 12.—A solution of 1.4 g. of acetate **8** in 60 ml. of acetic acid and 3 drops of 61% perchloric acid was shaken under hydrogen at 20 p.s.i.g. pressure in the presence of platinum catalyst (from 0.2 g. of platinum oxide) for 22 hr. at room temperature. The catalyst was removed by filtration through Celite and the filtrate was diluted with water, saturated with salt, and extracted twice with ether. The combined ether extracts were washed successively with water, 2 *N* aqueous sodium hydroxide, and water, dried, and evaporated to give 1.3 g. of crude acetate **13**: infrared bands ($CHCl_3$) at 1735 cm.$^{-1}$ (acetate); n.m.r. signals at 4.31, 3.94 (AB quartet, 2 protons, CH_2OAc, $J_{AB} = 11$ c.p.s.), 2.06 s (3 protons, acetate), 0.96, 0.86, and 0.68 p.p.m. (methyl singlets), no olefinic resonances.

A mixture of the above oil in 60 ml. of methanol and 10 ml. of 2 *N* aqueous sodium hydroxide was heated on a steam bath for 1 hr., then diluted with water, and extracted thrice with ether. The combined extracts were washed successively with water, 1 *N* hydrochloric acid, and water, dried, and evaporated to yield 0.9 g. (73% from **8**) of alcohol **12** which crystallized from aqueous methanol as colorless needles: m.p. 114–115°; infrared bands at 3400 and 1040 cm.$^{-1}$ (OH); n.m.r. signals at 3.83, 3.51 (AB quartet, 2 protons, CH_2OH, $J_{AB} = 11$ c.p.s.), 0.96, 0.86, and 0.68 p.p.m. (methyl singlets).

Anal. Calcd. for $C_{20}H_{36}O$: C, 82.12; H, 12.40. Found: C, 82.50; H, 12.57.

The alcohol **12** was further characterized as its mesylate **14** which crystallized from methanol as colorless plates: m.p. 149.5–150°; infrared bands at 1350 and 1180 cm.$^{-1}$ (sulfonate), no hydroxyl or carbonyl absorption; n.m.r. signals at 4.60, 4.06 (AB quartet, 2 protons $CH_2OSO_2CH_3$, $J_{AB} = 9$ c.p.s.), 2.99 s (3 protons, mesylate), 1.01, 0.84, and 0.68 p.p.m. (methyl singlets).

Anal. Calcd. for $C_{21}H_{38}O_3S$: C, 68.05; H, 10.34; S, 8.65. Found: C, 68.26; H, 9.93; S, 8.34.

13-*epi*-Tetrahydrorimuic Acid 15.—A solution of 0.1 g. of alcohol **12** in 30 ml. of acetone was stirred at 25° with 1.0 ml. of Jones reagent for 1 hr. and then diluted with water. The precipitate was collected, washed well with water, and crystallized from aqueous acetone to give acid **15**: m.p. 192–193°; $[\alpha]D$ −13° (*c* 1.27) (lit.[12] m.p. 190°, $[\alpha]D$ −15°); infrared bands at 2650–2800 and 1700 cm.$^{-1}$ (carboxylic acid); n.m.r. signals at 1.23, 0.88, and 0.67 p.p.m. (methyl singlets); the carboxylic acid proton was superimposed on the methylene envelope.

13-*epi*-Rimuane 2.—Deaerated Jones reagent was added dropwise to a stirred solution of 0.8 g. of alcohol **12** in 60 ml. of acetone at 0° under nitrogen. When a brown color persisted, the mixture was diluted with water and extracted twice with ether. The combined extracts were washed, dried, and evaporated to yield crude aldehyde **16** as an oil: infrared bands ($CHCl_3$) at 2750 and 1725 cm.$^{-1}$ (aldehyde).

A mixture of this crude aldehyde, 70 ml. of diethylene glycol, 9 ml. of hydrazine hydrate, and 9 g. of potassium hydroxide was heated under reflux for 6.5 hr., then cooled, diluted with water, and extracted thrice with hexane. The combined extracts were washed twice with 1 *N* hydrochloric acid and twice with water, dried, and evaporated to furnish 0.58 g. of an oil which was taken up in hexane and chromatographed on 40 g. of alumina prepared in hexane. Elution with that solvent gave a colorless mobile oil which solidified on cooling and crystallized from methanol at −10° as colorless needles of 13-*epi*-rimuane **2** (yield 0.275 g., 36%): m.p. 52–53°; $[\alpha]D$ −21°; infrared bands (CCl_4) at 1385 and 1365 cm.$^{-1}$ (*gem*-dimethyl); n.m.r. signals at 0.83, 0.83, 0.79, and 0.66 p.p.m. (methyl singlets).

Anal. Calcd. for $C_{20}H_{36}$: C, 86.88; H, 13.12. Found: C, 86.62; H, 13.03.

Continued elution with hexane and ether afforded 0.2 g. of the azine **17** which crystallized from acetone as colorless needles: m.p. 220–221°; infrared bands at 1640 cm.$^{-1}$ (C=N); n.m.r. signals at 8.14 s (1 proton, C*H*=N—), 1.17, 0.87, and 0.70 p.p.m. (methyl singlets).

Anal. Calcd. for $C_{40}H_{68}N_2$: N, 4.85. Found: N, 4.76.

(15) L. J. Bellamy, "The Infra-red Spectra of Complex Molecules," Methuen and Co. Ltd., London, 1956, p. 300.

Arbiglovin. A New Guaianolide From *Artemisia bigelovii* Gray[1]

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In continuation of our study of American *Artemisia* species,[2] we have carried out a systematic search for sesquiterpene lactones in *Artemisia bigelovii* Gray. This resulted in the isolation of a new guaianolide, $C_{15}H_{18}O_3$, m.p. 201–203°, $[\alpha]D$ +199°, which we have called arbiglovin.

The ultraviolet spectrum of arbiglovin (**1**), λ_{max} 227 mμ (ϵ_{max} 19,500), indicated the presence of conjugation, the chromophore of a disubstituted α,β-unsaturated ketone being superimposed on that of a conjugated lactone. This was supported by the infrared spectrum which exhibited strong bands at 1705 and 1625 cm.$^{-1}$ reminiscent of β-alkyl-substituted cyclopentenones.[2] The remaining two oxygens were presumably present as a γ-lactone (infrared band at 1770 cm.$^{-1}$) conjugated with a methylene group (shoulder near 1660 cm.$^{-1}$).

The presence of an exocyclic methylene group conjugated with a lactone was shown chemically by ozonolysis (formation of formaldehyde) and preparation of a pyrazoline. The presence of two double bonds

(1) Supported in part by a grant from the Mallinckrodt Chemical Works.

(2) Previous paper: W. Herz and K. Ueda, *J. Am. Chem. Soc.*, **83**, 139 (1961).