dl-**Elwesine (Dihydrocrinine) 2a.**—Amine **21c** (234 mg) was freed from its hydrochloride salt by dissolution in water, addition of 3 *M* NaOH, and extraction of the precipitated free base with ether. The ether was removed and the free base was dissolved in 5 ml of MeOH to which 2.4 ml of 37% formalin was added. After 10 min of stirring at room temperature the mixture was poured into 80 ml of 6 *N* HCl and stirred overnight. The slightly yellow solution was treated with charcoal, neutralized with concentrated NH_4OH, and extracted three times with $CHCl_3$. The organic extracts were combined, washed with H_2O, and dried over Na_2SO_4. Removal of the solvent provided 130 mg (61%) of a white crystalline solid which was essentially pure elwesine. Recrystallization from MeOH and drying *in vacuo* provided crystals, mp 216–220°. The solution ir spectra ($CHCl_3$) of this substance and that of an authentic sample[20] of elwesine were identical, as was their behavior on tlc.

Registry No.—*dl*-**2a**, 33531-72-5; *dl*-**2b**, 32209-87-3; **16a**, 33522-14-4; **16b**, 33522-15-5; **16b** (2,4-D), 33522-16-6; **17a**, 33522-17-7; **17b**, 32042-34-5; **18a**, 33608-35-4; **18b**, 33522-19-9; **19b**, 32209-88-4; **21a**, 33531-75-8; **21b**, 33531-76-9; **21b** (picrate), 33531-77-0; **21c**, 33531-78-1; **21c** (HCl), 33531-79-2; **21d**, 32209-89-5; **21d** (HCl), 33531-81-6.

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The Synthesis of (±)-Guaiol and (±)-7-Epiguaiol

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The synthesis of guaiol was carried out in two stages. In the first stage methyl *cis*-4-methyl-1(9)-octalin-2-one 10-carboxylate (**1**) was converted *via* enol acetylation and reduction ($NaBH_4$ followed by mesylate formation and Li–NH_3 reduction) to *cis*-5-methyl-10-hydroxymethyl-1(9)-octalin (**5**). Ring contraction *via* ozonolysis of the corresponding benzyl ether and aldol cyclization of the resulting ketoaldehyde afforded *cis*-7-methyl-7a-benzyloxymethyl-2,4,5,6,7,7a-hexahydroindene 3-carboxaldehyde (**8**). This intermediate was subjected to deconjugation–reduction through treatment of the enolate with ethanolic sodium borohydride followed by hydrogenolysis of the derived mesylate with Li–NH_3–*tert*-BuOH to give *cis*-3,7-dimethyl-7a-hydroxymethyl-5,6,7,7a-tetrahydroindan (**11**). The corresponding mesylate derivative upon acetolysis afforded *cis*-6,10-dimethylbicyclo[5.3.0]dec-1(7)-en-3-yl acetate (**13**) stereoselectively. The second stage of the synthesis was concerned with the introduction of a 1-methyl-1-hydroxyethyl grouping at the 3 position of this acetate. This transformation was finally achieved through carbonation of the Grignard reagent derived from the corresponding bromide. The sequence afforded a 2:1 mixture of acids in which the 7-epi isomer **16b** predominated. Equilibration of the derived methyl esters gave a 1:1 mixture of cis and trans esters **17a** and **17b** which yielded (±)-guaiol (**18**) and (±)-7-epiguaiol in the same ratio upon treatment with methyllithium. These epimeric alcohols were separated by preparative gas chromatography and identified through comparison with authentic material.

A major problem of synthesis relating to hydroazulene natural products[2] is the rational control of stereochemistry. An examination of molecular models clearly indicates the inherent stereochemical ambiguities of synthetic approaches which allow equilibration of chiral centers on the hydroazulene ring system. Thus particular effort must be made to avoid reactions and intermediates where such equilibration might occur. An especially fruitful approach to substituted hydroazulenes utilizes as a key step the skeletal rearrangement of relatively rigid bicyclic systems under conditions such that epimerization does not take place.[3] Such schemes have employed cyclohexane rings to good advantage for the control of stereochemistry in the various bicyclic precursors. This report describes a partially successful approach of this type to the total synthesis of guaiol, the structural prototype and first recognized member of the guaiane family of sesquiterpenes.[4–6]

Our synthetic plan was based on the expected rearrangement of a bicyclo[4.3.0]nonyl derivative through a formal ring expansion of the six-membered ring facilitated by homoallylic participation. This type of reaction has been examined in some detail by Tadanier using C-19 functionalized Δ^5 steroids as substrates.[7] Applications to bicyclo[4.3.0]nonyl systems have recently been reported by us[8] and by Scanio.[9] Our previous studies indicated that the methanesulfonate **12** (Chart I) would be the intermediate of choice for a projected synthesis of guaiol along these lines.[8] Accordingly, the known *cis*-methyloctalonecarboxylic ester **1**[10] was subjected to deconjugation–reduction *via* treatment of the enol acetate **2**[11] with ethanolic sodium borohydride.[12] The resulting hydroxy ester **3** readily lactonized upon work-up unless care was taken to avoid heating. Further reduction was effected through treatment of the methanesulfonate derivative **4** with lithium–ammonia–*tert*-butyl alcohol to give the unsaturated alcohol **5**, which was protected as the benzyl ether **6**.

The requisite ring contraction of octalin **6** was achieved through ozonolysis and subsequent aldol cyclization of the intermediate ketoaldehyde **7**. Double-

(1) National Institutes of Health Predoctoral Fellow, Institute of General Medical Sciences (Fellowship 4 FO1 GM38262), 1967–1970.

(2) *Cf.* P. de Mayo, "Mono and Sesquiterpenoids," Interscience, New York, N. Y., 1959, pp 244–262.

(3) *Cf.* J. A. Marshall and J. J. Partridge, *Tetrahedron*, **25**, 2159 (1969); C. H. Heathcock and R. Ratcliffe, *Chem. Commun.*, 994 (1968); M. Kato, H. Kosugi and A. Yoshikoshi, *ibid.*, 185 (1970).

(4) H. Minato, *Tetrahedron Lett.*, 280 (1961).

(5) For a recent nonstereoselective synthesis of guaiol, see G. L. Buchanan and G. A. R. Young, *Chem. Commun.*, 643 (1971).

(6) For a preliminary account of this work, see J. A. Marshall and A. E. Greene, *Tetrahedron Lett.*, 859 (1971); J. A. Marshall, A. E. Greene, and R. A. Ruden, *ibid.*, 855 (1971).

(7) J. Tadanier, *J. Org. Chem.*, **31**, 3204 (1966).

(8) J. A. Marshall and A. E. Greene, *ibid.*, **36**, 2035 (1971).

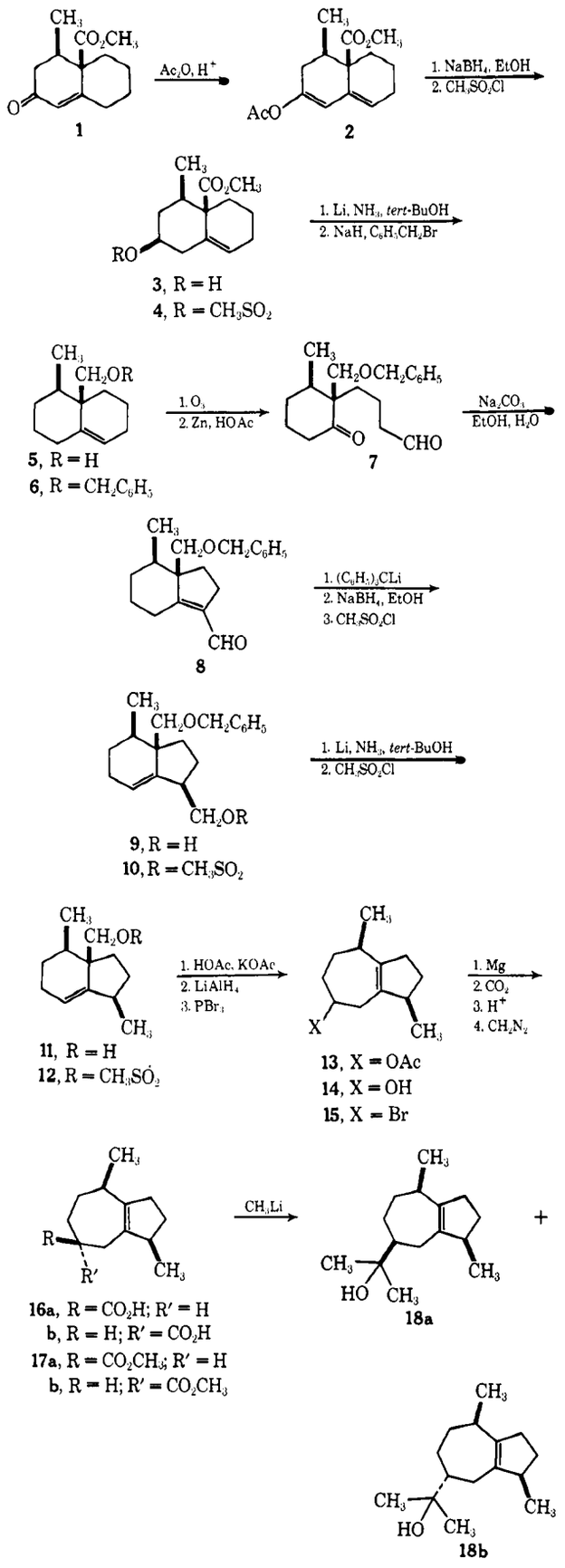
(9) C. J. V. Scanio and L. P. Hill, *Chem. Commun.*, 242 (1971).

(10) J. A. Marshall and T. M. Warne, Jr., *J. Org. Chem.*, **36**, 178 (1971).

(11) B. E. Edwards and P. N. Rao, *ibid.*, **31**, 324 (1966).

(12) W. G. Dauben and J. F. Eastham, *J. Amer. Chem. Soc.*, **73**, 4463 (1951).

CHART I



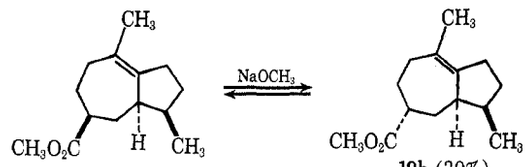
bond isomerization was achieved as before (*cf.* **1** → **3**) *via* deconjugation–reduction. In this case, however, enol acetylation of aldehyde **8** afforded appreciable amounts of by-products consisting largely of acylals. Accordingly, an alternative procedure was developed whereby aldehyde **8** was converted to its enolate using triphenylmethyllithium, and this enolate was allowed to protonate in aqueous ethanol containing a large excess of sodium borohydride to rapidly reduce the resulting β,γ-unsaturated aldehyde before conjugation or epimerization could take place.[8] In this manner a 2:1 mixture of alcohol **9** and its presumed double bond isomer was obtained. Separation of these isomers was unnecessary at this stage, since the unwanted allylic alcohol by-product was destroyed through reaction with methanesulfonyl chloride and pyridine, presumably by pyridinium salt formation, in the next step of the sequence. Mesylate **10** underwent hydrogenolysis of the methanesulfonoxy and benzyl groups in lithium–ammonia–*tert*-butyl alcohol to give the desired *cis*-dimethylbicyclo[4.3.0]nonylcarbinol **11**. The stereochemistry of this intermediate can be assigned on the basis of previous studies with keto ester **1**[10] and the expectation of stereoselective protonation of the enolate derived from aldehyde **8**.[8]

The methanesulfonate **12** was smoothly converted to the hydroazulenyl acetate **13** in refluxing acetic acid buffered with potassium acetate. At this point we were faced with the problem of replacing the acetoxyl grouping of acetate **13** by a 1-methyl-1-hydroxyethyl side chain with retention of stereochemistry. An earlier plan to prepare the related cyano derivative (**13**, X = CN) by conducting the solvolysis of mesylate **12** in liquid HCN had met with failure in a model study[8] and was therefore not pursued. In this previous study we were unable to prepare appropriate Grignard reagents from halides related to **15** and were consequently forced to devise a more circuitous route to the desired substituted hydroazulene. In the present work the onset of cooler and dryer weather encouraged us to reexamine the Grignard route.

To that end the alcohol **14** was converted with phosphorus tribromide in benzene to the bromide **15**. Successful initiation of the Grignard reaction was eventually achieved by adding a portion of the bromide **15** mixed with methyl iodide (neat) to crushed magnesium turnings. Once reaction had been initiated, the remainder of the bromide could be added in tetrahydrofuran solution. Carbonation followed by esterification of the resulting acidic material with diazomethane afforded at 2:1 mixture of esters **17b** and **17a** in 27% yield. The low overall yield of this sequence makes it difficult to draw valid conclusions regarding the stereochemistry of the carbonation reaction. In related cases this reaction was found to be highly stereoselective with retention of configuration.[13] Our isolation of a 2:1 mixture of acids **16b** and **16a** may therefore reflect the isomer composition of the organometallic derived from bromide **15**. We chose not to examine the addition of acetone to this Grignard reagent, a seemingly more direct route to guaiol (**18**), because of the reported low yields for a similar conversion.[13] Furthermore, since the ratio of carbonation products (2:1 **16b** to **16a**) was unfavorable we wished to study the equilibration of esters **17a** and **17b** with a view to increasing the proportion of the former isomer. In fact, this aim

(13) C. H. Heathcock and T. R. Kelly, *Tetrahedron*, **24**, 1801 (1968), and references cited therein.

could be accomplished by treating the aforementioned 1:2 mixture with methanolic sodium methoxide at reflux, whereupon a 1:1 mixture was secured. In an analogous compound, a 70:30 mixture of the related esters **19a** and **19b** (see below) was obtained upon equilibration.[9] These findings underscore the hazards of relying upon equilibration to control stereochemistry in hydroazulene ring systems.



19a (70%) **19b** (30%)

Treatment of the 1:1 ester mixture **17** with ethereal methyllithium afforded a comparable mixture of (±)-guaiol (**18a**) and (±)-7-*epi*-guaiol (**18b**), separated by preparative gas chromatography and identified through comparison with naturally derived material.[6]

Experimental Section[14]

Methyl *cis*-4-Methyl-*cis*-2-methanesulfonoxy-8-octalin-10-carboxylate (4).—A solution of 1.00 g of keto ester 1 (9:1 *cis*:*trans*)[10] in 85 ml of ethyl acetate containing 17 μl of 70% perchloric acid and 8.2 ml of acetic anhydride was allowed to stand at room temperature for 11 min.[11] The solution was washed with saturated sodium bicarbonate and the product was distilled, affording 1.13 g (95%) of enol acetate **2**: bp (bath temperature) 110° (0.03 mm); λ_{max}^{film} 3.32, 5.68, 5.80, 5.98, 6.13 mμ; $\delta_{TMS}^{CCl_4-CDCl_3}$ 5.79 (H-1), 5.56 (H-8 triplet, J = 4 Hz), 3.66 (OCH_3), 2.10 (CH_3CO), 1.08 ppm (CH_3 doublet, J = 6 Hz). Longer reaction times gave rise to an unidentified by-product while shorter reaction times led to varying amounts of recovered starting material.

The above enol acetate in 30 ml of ethanol was added dropwise to a stirred mixture of 5.3 g of sodium borohydride in 110 ml of ethanol and 16.5 ml of water at 0°.[12] After 30 min, the mixture was stored at 5° for 3 hr and then poured into cold 10% NaOH and extracted with ether–benzene. The entire process was carried out with cold solvents and the solvent was removed below room temperature in order to minimize lactonization of the hydroxy ester **3**. This procedure yielded 1.0 g of **3**: λ_{max}^{film} 2.90, 3.24, 5.80, 5.97 mμ; $\delta_{TMS}^{CCl_4}$ 5.50 (H-8), 4.63 (OCH_3), 0.95 ppm (CH_3 doublet, J = 6 Hz).

The above hydroxy ester in 6 ml of pyridine at 0° was treated with 1.0 ml of methanesulfonyl chloride. After 1 hr at 0° and 3 hr at room temperature, ice chips were added with external cooling and the product was isolated with ether, affording 0.96 g of semisolid material. Recrystallization from methanol at −77° afforded 0.61 g (45% overall) of mesylate **4**: mp 95–100°; λ_{max}^{KBr} 3.30, 5.81, 8.24, 8.58 mμ; $\delta_{TMS}^{CCl_4-CDCl_3}$ 5.65 (H-8), 4.65 (H-2), 3.68 (CH_3O), 3.00 (CH_3SO_3), 0.92 ppm (CH_3 doublet, J = 6 Hz). The analytical sample, mp 102–103°, was obtained after two additional recrystallizations.

Anal. Calcd for $C_{14}H_{22}O_5S$: C, 55.61; H, 7.33; S, 10.60. Found: C, 55.89; H, 7.10; S, 10.50.

***cis*-5-Methyl-10-hydroxymethyl-1(9)-octalin (5).**—To a solution of 5.81 g of lithium in 600 ml of ammonia at −78° was added 3.33 g of mesylate **4** in 50 ml of *tert*-butyl alcohol and 66 ml of tetrahydrofuran. After 1.25 hr at −78° and 2 hr at −33° (reflux) the solution was treated with ethanol to discharge the blue color and solid ammonium chloride was added to neutralize the alkoxides. The ammonia was allowed to evaporate through a mercury trap and the product was isolated with ether, affording 1.79 g (90%) of solid alcohol **5**: bp 100° (bath temperature) (0.1 mm); λ_{max}^{KBr} 3.01 mμ; $\delta_{TMS}^{CCl_4-CDCl_3}$ 5.55 (H-1 triplet, J = 3 Hz), 3.55 (CH_2 AB, J = 10 Hz $\Delta\nu_{AB}$ = 12 Hz), 0.85 ppm (CH_3 doublet, J = 3 Hz). The analytical sample, mp 41–46°, was prepared by sublimation [25° (0.04 mm)].

Anal. Calcd for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 79.70; H, 11.20.

***cis*-5-Methyl-10-benzyloxymethyl-1(9)-octalin (6).**—A solution of 1.79 g of alcohol **5** in 90 ml of dioxane was added to pentane-washed NaH (from 0.96 g of 57% oil dispersion) and the mixture was stirred at reflux for 2 hr. The cooled solution was treated with 1.50 ml of benzyl bromide and the mixture was stirred at reflux for 15 hr. The product was isolated with ether and distilled, affording 2.51 g (94%) of benzyl ether **6**: bp 120° (bath temperature) (0.02 mm); $\delta_{TMS}^{CCl_4-CDCl_3}$ 7.20 (aromatic H's), 5.38 (H-1), 4.39 (benzylic H's), 3.48 (CH_2O), 0.93 ppm (CH_3 doublet, J = 3 Hz).

Anal. Calcd for $C_{19}H_{26}O$: C, 84.39; H, 9.69. Found: C, 84.34; H, 9.59.

***cis*-7-Methyl-7a-benzyloxymethyl-2,4,5,6,7,7a-hexahydroindene-3-carboxaldehyde (8).**—A solution of 0.63 g of olefin **6** in 27 ml of pentane was treated at −78° with a stream of ozonized oxygen with periodic centrifugation of the solid ozonide. The excess ozone was allowed to evaporate and the pentane was decanted from the solid ozonide. Acetic acid (4.65 ml) and zinc powder (1.16 g) were added at −78° and the mixture was allowed to reach room temperature with stirring. After 11 min, the mixture was filtered and the product was isolated with ether, affording 0.49 g of keto aldehyde **7**: λ_{max}^{film} 3.30, 3.68, 5.80, 5.87 mμ; $\delta_{TMS}^{CCl_4-CDCl_3}$ 9.67 (CHO triplet, J = 2 Hz), 7.20 (aromatic H's), 4.35 (benzylic H's), 3.42 (CH_2O–AB, J = 10 Hz, $\Delta\nu_{AB}$ = 16 Hz), 0.85 ppm (CH_3 doublet, J = 7 Hz).

A 1.48-g sample of the above material was stirred at reflux with 1.30 g of sodium carbonate in 10.6 ml of water and 224 ml of ethanol for 16 hr. The product was isolated with ether–benzene and chromatographed on silica gel to give 0.76 g (38% overall) of aldehyde **8**: λ_{max}^{film} 3.32, 3.67, 6.00 mμ; $\delta_{TMS}^{CCl_4-CDCl_3}$ 10.00 (CHO), 7.15 (aromatic H's), 4.33 (benzylic H's), 3.45 (CH_2O–AB, J = 9 Hz, $\Delta\nu_{AB}$ = 10 Hz), 0.95 ppm (CH_3 doublet, J = 5 Hz). The analytical sample, mp 53–54°, was prepared by crystallization from pentane.

Anal. Calcd for $C_{19}H_{24}O_2$: C, 80.24; H, 8.51. Found: C, 80.21; H, 8.65.

***cis*-3,7-Dimethyl-7a-hydroxymethyl-5,6,7,7a-tetrahydroindan (11).**—Triphenylmethyllithium was prepared from 9.5 ml of 1.5 *M* ethereal methyllithium and 3.85 g of triphenylmethane in 15 ml of 1,2-dimethoxyethane.[15] To this solution was added 1.06 g of aldehyde **8** in 20 ml of DME dropwise over 0.5 hr. After 1 hr this solution was added dropwise to a well-stirred solution of 50 g of sodium borohydride in 50 ml of water and 380 ml of ethanol. After 3.5 hr the solution was poured into 10% NaOH and the product was isolated with ether–benzene and chromatographed on silica gel, affording 0.68 g of alcohol **9**: λ_{max}^{film} 2.94, 3.30 mμ; $\delta_{TMS}^{CCl_4}$ 7.20 (aromatic H's), 5.50 (H-4), 4.33 (benzylic H's), 3.50–3.30 (CH_2OH), 3.25 (CH_2O–), 0.95 ppm (CH_3 doublet, J = 4 Hz). The integration indicated 66% of the desired alcohol **9**. The remaining 34% appeared to consist mainly of the isomeric allylic alcohol.

A 0.60-g sample of the above mixture in 5.5 ml of pyridine at 0° was treated with 1.1 ml of methanesulfonyl chloride. After 0.5 hr at 0° and 2 hr at room temperature, the mixture was cooled and added dropwise to 30 ml of pyridine containing 15 ml of water. Isolation with ether afforded 0.66 g of mesylate **10**: $\delta_{TMS}^{CCl_4-CDCl_3}$ 7.20 (aromatic H's), 5.55 (H-4), 4.36 (benzylic H's), 4.05 and 3.93 (doublets, J = 1.5 Hz), 3.25 (CH_2O–), 2.70 (CH_3SO_3), 0.95 ppm (CH_3 doublet, J = 4 Hz).

The above mesylate in 5.1 ml of *tert*-butyl alcohol and 2.5 ml of tetrahydrofuran was added dropwise to a stirred solution of 0.94 g of lithium in 75 ml of ammonia at −78°. After 1.5 hr at −78° and 1 hr at −33° (reflux) the solution was treated with ethanol dropwise to discharge the blue color and the ammonia was allowed to evaporate through a mercury trap. The product was isolated with ether and distilled, affording 0.26 g (44% overall) of alcohol **11**: bp 110° (bath temperature) (0.05 mm); λ_{max}^{film} 2.93 mμ; $\delta_{TMS}^{CCl_4-CDCl_3}$ 5.55 (H-4), 3.70–3.30 (CH_2OH), 1.15 (CH_3 doublet, J = 7 Hz), 1.00 ppm (CH_3 doublet, J = 3 Hz). The analytical sample was prepared by preparative layer chromatography (95:5 benzene–ether) on silica gel and distillation.

(14) Reactions were carried out under a nitrogen atmosphere. The isolation procedure involved adding the reaction mixture to water or saturated brine and extracting thoroughly with the specified solvent. Anhydrous magnesium sulfate or magnesium carbonate was used to dry the combined extracts and the solvent was removed on a rotary evaporator under reduced pressure. Microanalyses were preformed by Microtech Inc., Skokie, Ill.

(15) H. O. House and B. M. Trost, *J. Org. Chem.*, **30**, 1341 (1965).

Anal. Calcd for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 79.86; H, 11.38.

cis-6,10-Dimethylbicyclo[5.3.0]dec-1(7)-en-3-yl Acetate (13).—A solution of 0.16 g of alcohol **11** in 0.95 ml of pyridine was stirred at 0° and 0.4 ml of methanesulfonyl chloride was added dropwise. After 20 min at 0° the mixture was poured into a stirred solution of 6 ml of pyridine and 1 ml of water at 0°. The product was isolated with ether, affording 0.20 g of mesylate **12**.

The above mesylate in 9.5 ml of a solution prepared from 25 ml of acetic acid, 0.5 ml of acetic anhydride, and 0.35 g of potassium carbonate[7] was stirred at reflux for 5.25 hr. The product was isolated with ether and distilled, affording 0.16 g of acetate **13**: bp 100° (bath temperature) (0.05 mm) (80% pure by gas chromatographic analysis); λ_{max}^{film} 5.77, 8.06, mμ; $\delta_{TMS}^{CDCl_3}$ 4.75 (H-3), 2.30 and 2.20 (allylic H's), 1.03 and 0.91 ppm (CH_3 doublets, J = 6 Hz). The analytical sample was obtained by preparative layer chromatography (silica gel, benzene) and distillation.

Anal. Calcd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97. Found: C, 75.50; H, 9.83.

cis-6,10-Dimethylbicyclo[5.3.0]dec-1(7)-en-3-ol (14).—A solution of 158 mg of acetate **13** in 10 ml of ether was added dropwise with stirring to a solution of 0.20 g of lithium aluminum hydride in 100 ml of ether. The mixture was stirred for 8 hr, 0.4 ml of water and 0.32 ml of 10% NaOH were added, and stirring was continued for 1 hr. A small quantity of anhydrous magnesium sulfate was then added and the mixture was filtered, chromatographed on silica gel, and distilled, affording 82 mg of alcohol **14**: bp 100° (bath temperature) (0.05 mm); λ_{max}^{film} 3.02 mμ; $\delta_{TMS}^{CCl_4-CDCl_3}$ 3.60 (CHOH), 2.30 and 2.18 (allylic H's), 1.00 and 0.98 ppm (CH_3 doublets, J = 7 Hz). The analytical sample was prepared by distillation.

Anal. Calcd for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 79.80; H, 11.22.

Methyl *cis*-6,10-Dimethylbicyclo[5.3.0]dec-1(7)-ene 3-Carboxylate (17).—A solution of 92 mg of alcohol **14** and 58 μl of phosphorous tribromide in 0.4 ml of benzene was heated at reflux for 4.5 hr.[13] Ice chips were added to the cooled solution and the product was isolated with benzene, affording 100 mg of bromide **15**, bp 95° (bath temperature) (0.05 mm).

A 10-μl sample of the above bromide and 10 μl of methyl iodide were added under helium to 0.1 g of freshly crushed Mg turnings. After 1 min, the remainder of the bromide in 1 ml of tetrahydrofuran was added dropwise. The mixture was heated at 60° for 45 min, cooled to 10°, and diluted with 1 ml of tetrahydrofuran. Carbon dioxide was slowly bubbled into the solution for 5 min at 10° and 15 min at room temperature. Small chips of Dry Ice were added and the mixture was poured onto crushed Dry Ice. Ether and dilute sulfuric acid were added and the product was isolated with ether. Neutral impurities were removed by extracting with dilute sodium hydroxide, acidifying the basic extracts, and extracting the resulting acid fraction with ether, affording 25 mg of acid **16**. Esterification with diazomethane afforded 28 mg (27%) of methyl ester **17**: bp 100° (bath temperature) (0.1 mm); λ_{max}^{film} 5.75 mμ; $\delta_{TMS}^{CCl_4}$ 3.60 (OCH_3) and 1.2–0.8 ppm (CH_3's). The gas chromatogram showed peaks at 12.7 (55%, **17b**) and 13.6 min (25%, **17a**).[6] The analytical sample was obtained after preparative layer chromatography on silica gel and short path distillation.

Anal. Calcd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97. Found: C, 75.81; H, 9.93.

A combined sample of 86 mg of ester **17** (2:1 **17b** and **17a**) in 12 ml of 0.4 *M* methanolic sodium methoxide was heated at reflux for 40 hr. Acidic material was esterified with diazomethane and the combined ester sample was distilled, affording 48 mg of a 53:47 mixture of esters **17b** and **17a** according to gas chromatography.[6]

(±)-Guaiol (18a) and (±)-7-Epiguaiol (18b).—To 4 ml of 1.5 *M* ethereal methyllithium was added 26 mg of the above 1:1 ester mixture in 6 ml of ether. After 3.5 hr the mixture was poured onto ice and the product was isolated with ether, affording 26 mg of a 1:1 mixture of guaiol and 7-epiguaiol, bp 120° (bath temperature) (0.1 mm). The two epimers separated by preparative gas chromatography had the following properties. (1) (±)-Guaiol: mp 55–60°; λ_{max}^{KBr} 3.00, 6.90, 7.38, 7.67, 7.88, 8.04, 8.18, 8.30, 8.52, 8.70, 8.80, 10.05, 10.33, 10.81, 11.00, 11.38, 12.20 mμ; $\delta_{TMS}^{CDCl_3}$ 1.18 (CH_3's), 0.98 (CH_3 doublet, J = 7.5 Hz), 0.96 ppm (CH_3 doublet, J = 7 Hz). The spectral and chromatographic characteristics exactly matched those of natural guaiol.[6] (2) (±)-7-Epiguaiol: λ_{max}^{film} 2.97, 6.89, 7.32, 7.60, 8.85, 9.18, 10.36, 10.79, 11.12, 12.22 mμ; $\delta_{TMS}^{CDCl_3}$ 1.19 (CH_3's), 1.04 (CH_3 doublet, J = 7 Hz), 1.03 ppm (CH_3 doublet, J = 6 Hz). The spectral and chromatographic characteristics exactly matched those of material obtained from natural sources.[6]

Registry No.—**2**, 33536-32-2; **3**, 33536-33-3; **4**, 33536-34-4; **5**, 32667-68-8; **6**, 33536-36-6; **7**, 33536-37-7; **8**, 32667-69-9; **9**, 32667-70-2; **10**, 33536-40-2; **11**, 33536-41-3; **13**, 33536-42-4; **14**, 33536-43-5; **15**, 33536-44-6; **17a**, 33536-45-7; **17b**, 33536-46-8; **18a**, 33496-08-1; **18b**, 33536-48-0.

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Perhydroindan Derivatives. XIII. Selective Metalation of a 7-Methoxyhexahydrofluorene Derivative[1a]

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The regiospecific metalation of the methoxy acid **3a** at C-9 has been accomplished by reaction of the corresponding *N*-methylamide with *n*-butyllithium. Carbonation of the organolithium intermediate has provided a useful synthetic route to the epimeric diacid derivatives **9** and **10**. The applicability of the Birch reduction to the conversion of the methoxy acid **4a** to either the enol ether **11** or the keto acid **12a** has also been demonstrated.

In previous model studies with 7-methoxyhexahydrofluorene derivatives[2] we developed selective metalation procedures that allowed us to introduce carboxyl functions at either C-8 or C-9. The use of these methods to prepare acids **3a** and **4a** is illustrated in Scheme I. Also illustrated is the hydroboration of the intermediate olefin **5** from the less hindered side to form alcohol **6**, an epimer of the previously described alcohol **1**; this sequence confirms our earlier tentative assignment of stereochemistry to alcohol **1**.[2] Further reaction of the sodium salt of acid **4a** with *n*-BuLi formed a benzylic anion which reacted with carbon dioxide to form the 9,9-dicarboxylic acid **4c**; thermal decarboxylation of this

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(2) H. O. House, T. M. Bare, and W. E. Hanners, *J. Org. Chem.*, **34**, 2209 (1969).