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.

Acknowledgments.—We are indebted to the National Institutes of Health for their support of this work through a research grant (National Cancer Institute, 5 R01 CA 11089) and a predoctoral fellowship. A sample of Guaiacum Wood Oil was generously provided by Professor R. B. Bates.

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

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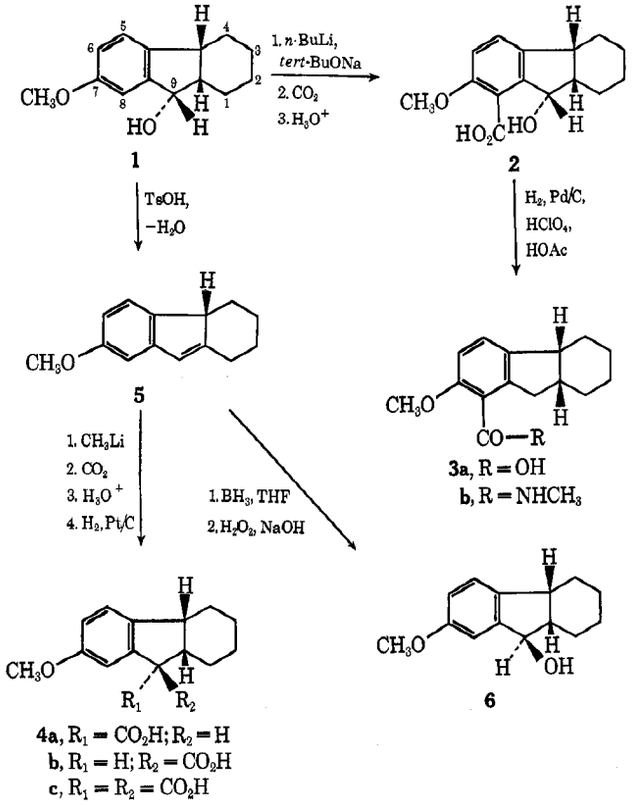
The regiospecific metalation of the methoxy acid **3a** at C-9 has been accomplished by reaction of the corresponding *N*-methylamide with *n*-butyllithium. Carbonation of the organolithium intermediate has provided a useful synthetic route to the epimeric diacid derivatives **9** and **10**. The applicability 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

(1) (a) This research has been supported by Public Health Service Grant R01-CA-12634 from the National Cancer Institute. (b) Department of Chemistry, Georgia Institute of Technology, Atlanta, Georgia 30332. (c) National Institutes of Health Predoctoral Fellow, 1968–1971.

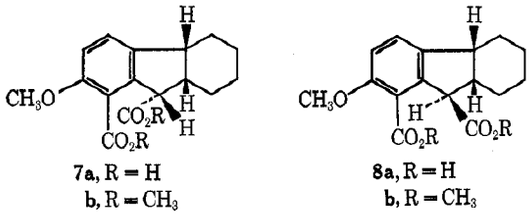
(2) H. O. House, T. M. Bare, and W. E. Hanners, *J. Org. Chem.*, **34**, 2209 (1969).

SCHEME I



malonic acid derivative **4c** yielded a mixture of the epimeric acids **4a** and **4b**.

By the successive use of these two metalation procedures we had been able[2] to convert the alcohol **1** *via* the hydroxy acid **2** and the related olefin to the epimeric dicarboxylic acid derivatives **7** and **8**. However, the

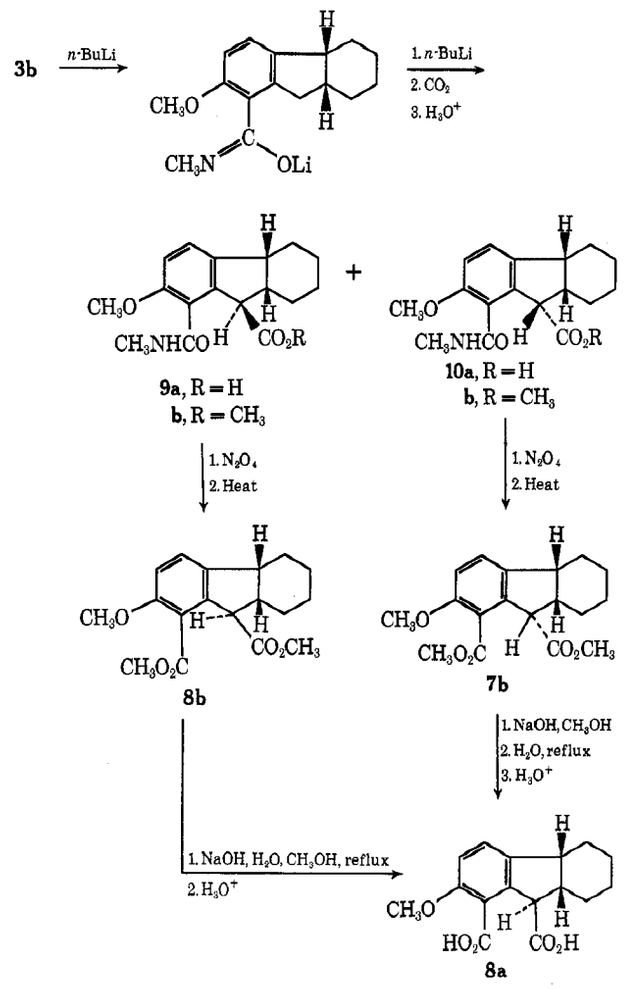


progress of other synthetic work created the need to introduce a second carboxyl function at the benzylic C-9 position in monoacid derivatives such as **3** which contain no additional activating group in the five-membered ring. We have used the compounds **3** as models to explore possible synthetic methods and have found the lithium salt of the *N*-methylamide **3b** to be very effective in directing further metalation at C-9.[3] This conversion to form the epimeric diacid derivatives **9** and **10** is illustrated in Scheme II. Reaction of the amide **9b** with N_2O_4 and subsequent thermal decomposition[4] produced the known[2] diester **8b**, which was further characterized by saponification to the crystalline diacid **8a**. Similarly, the amide **10b** was converted to the known[2] diester **7b**; base-catalyzed epimerization and hydrolysis converted **7b** to the same diacid **8a** which is known[2] to be more stable than its epimer **7a**.

(3) The use of *N*-methylbenzamide as a directing group for ortho metalation has been described by W. H. Puterbaugh and C. R. Hauser, *J. Org. Chem.*, **29**, 853 (1964).

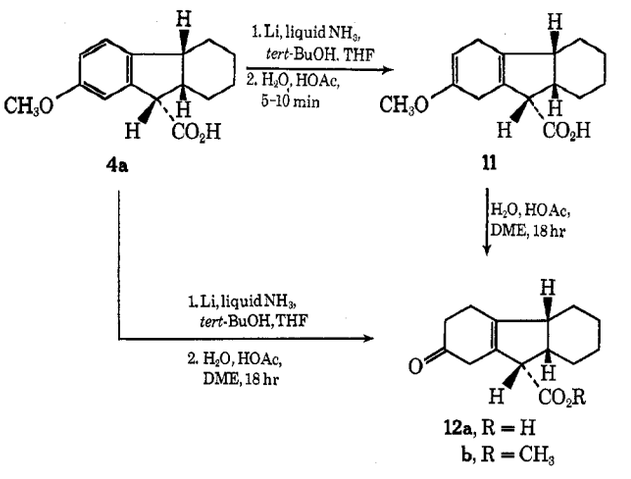
(4) E. White, *Org. Syn.*, **47**, 44 (1967).

SCHEME II



We also examined briefly the Birch reduction[5,6] of the methoxy acid **4a** (Scheme III). When the crude reduction product was exposed only briefly to the aqueous acetic acid, the crystalline enol ether acid **11** could be isolated in good yield. However, prolonged exposure

SCHEME III



(5) H. Smith, "Organic Reactions in Liquid Ammonia," Vol. 1, Part 2, Wiley-Interscience, New York, N. Y., 1963, pp 151–285.

(6) M. Smith, "Reduction," R. L. Augustine, Ed., Marcel Dekker, New York, N. Y., 1968, pp 98–126.

of either the crude reduction product or the pure enol ether **11** to aqueous acetic acid resulted in hydrolysis of the enol ether to form the keto acid **12a**.

Experimental Section[7]

Preparation of the Hexahydrofluorene Derivatives 3.—The alcohol **1** was metalated and then carbonated to form the previously described[2] acid **2**, mp 134–135° (lit.[2] mp 136–137°). A solution of 3.00 g (11.5 mmol) of the hydroxy acid **2**, 0.25 ml of aqueous 70% $HClO_4$, and 10 ml of HOAc in 40 ml of tetrahydrofuran was hydrogenated at 1 atm and 25° over 300 mg of a 5% Pd/C catalyst. The absorption of H_2 (305 ml or 12.2 mmol) was complete in 5 min and the reaction mixture was filtered and concentrated. After a solution of the residue in Et_2O had been washed with H_2O, dried (Na_2SO_4), and concentrated, the residue crystallized from hexane as 2.78 g (99%) of the crude acid **3a**, mp 84–93°. Recrystallization from hexane–CH_2Cl_2 mixtures afforded the pure acid **3a** as white prisms: mp 93–94°; ir ($CHCl_3$), 3260 (associated OH) and 1730 cm^{-1} (carboxyl C=O); uv max (95% EtOH) 296 mμ (ε 2900); nmr ($CDCl_3$) δ 10.45 (1 H, broad, OH), 7.28 (1 H d, J = 8 Hz, aryl CH), 6.85 (1 H d, J = 8 Hz, aryl CH), 4.00 (3 H s, OCH_3), and 1.0–3.5 (12 H m, aliphatic CH); mass spectrum m/e (rel intensity) 246 (100, M^+), 228 (31), 203 (22), and 185 (33).

Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.14; H, 7.37. Found: C, 72.96; H, 7.46.

A solution of 800 mg (3.25 mmol) of the acid **3a** in 5.0 ml of $SOCl_2$ was stirred at 25° for 15 hr and then concentrated under reduced pressure. A solution of the residual acid chloride in 10 ml of tetrahydrofuran was added to 40 ml of aqueous 40% CH_3NH_2. The crude product separated and was collected as 755 mg (89%) of a white solid, mp 166–169°. Recrystallization from MeOH afforded the pure amide **3b** as white needles: mp 168–169°; ir ($CHCl_3$) 3430 (NH), 1655 (amide C=O), and 1530 cm^{-1} (amide NH bending); uv max (95% EtOH) 289 mμ (ε 3140); nmr ($CDCl_3$) δ 7.15 (1 H d, J = 8 Hz, aryl CH), 6.75 (1 H d, J = 8 Hz, aryl CH), 7.0 (1 H broad, NH), 3.85 (3 H s, OCH_3), 2.7–3.2 (6 H m, CH_3N and benzylic CH), and 0.9–2.5 (9 H m, aliphatic CH); mass spectrum m/e (rel. intensity), 259 (100, M^+), 229 (22), 216 (43), 185 (50), 127 (68), and 126 (38).

Anal. Calcd for $C_{16}H_{21}NO_2$: C, 74.10; H, 8.16; N, 5.40. Found: C, 74.05; H, 8.06; N, 5.54.

Preparation of the Diacid 4c.—A sample of the acid **4a**, mp 185–187° (lit.[2] mp 186–187°), was prepared from olefin **5** by previously described procedures.[2] A mixture of 1.0 g (41 mmol) of NaH and 5.00 g (20.4 mmol) of the acid **4a** in 150 ml of tetrahydrofuran was stirred at 55° for 10 min. The resulting solution of the sodium salt was diluted with 250 ml of pentane and cooled in a Dry Ice bath. To the resulting cold suspension was added, dropwise and with stirring over 10 min, 55 ml of a hexane solution containing 88 mmol of *n*-BuLi. The mixture was warmed to 0° and the resulting orange solution was added, with vigorous stirring, to a slurry of 200 g of Dry Ice in 50 ml of tetrahydrofuran. The resulting mixture was concentrated under reduced pressure and a solution of the residue in 500 ml of H_2O was extracted with Et_2O, acidified (HCl), and again extracted with Et_2O. The acidic etheral extract was washed with H_2O, dried, and concentrated. Trituration of the residue with CH_2Cl_2 and with hexane left 5.13 g (87%) of the diacid **4c** as a white solid: mp 175–177° dec; ir (KBr pellet) 3000 (broad, associated OH) and 1705 cm^{-1} (carboxyl C=O); uv max (95% EtOH) 221 mμ (ε 9500), 284 (2920), and 290 (shoulder, 2680); nmr ($CDCl_3$ + pyridine-d_5) δ 13.3 (2 H, OH), 6.7–7.7 (3 H m, aryl CH), 3.75 (3 H s, OCH_3), and 0.9–3.6 (10 H m, aliphatic CH).

Anal. Calcd for $C_{16}H_{18}O_5$: C, 66.19; H, 6.25. Found: C, 66.45; H, 6.24.

A 1.00-g (3.44 mmol) sample of the diacid **4c** was heated to 185° for 5 min under a N_2 atmosphere, at which time decarboxylation appeared to be complete. The residue was crystallized from a CH_2Cl_2–hexane mixture to separate 0.55 g (65%) of the monoacid **4a** as white needles, mp 181–183°. Recrystallization gave the pure monoacid **4a**, mp 185–186°, which was identified with an authentic sample by a mixture melting point and comparison of ir spectra. The mother liquors from this crystallization were concentrated and then crystallized from hexane to separate 0.31 g (36%) of crude monoacid **4b** as white prisms, mp 108–120°. Fractional recrystallization from hexane separated 20 mg (3%) of the pure monoacid **4b**, mp 115–116° (lit.[2] mp 117.5–118.5°), identified with an authentic sample by a mixture melting point determination and comparison of ir spectra.

Preparation of the Alcohol 6.—A 1.00-g (4.58 mmol) sample of the alcohol **1** was dehydrated (TsOH in PhH)[2] to form 890 mg (97%) of the crude olefin **5**. A solution of this olefin **5** in 10 ml of tetrahydrofuran was treated with 4.6 ml of a tetrahydrofuran solution containing *ca.* 5 mmol of BH_3 and the resulting solution was stirred at 25° for 30 min. To the reaction solution were added 1.0 ml of H_2O, 2.0 ml of aqueous 15% NaOH, and 20 ml of aqueous 30% H_2O_2. The resulting solution was partitioned between H_2O and Et_2O and the ethereal layer was washed with aqueous NaCl, dried, and concentrated to leave 940 mg (94%) of the crude alcohol **6**, mp 92–94°. Recrystallization from hexane afforded the pure alcohol **6** as a white solid: mp 98–99°; ir (CCl_4), 3600 and 3450 cm^{-1} (broad) (unassociated and associated OH); uv max (95% EtOH) 217.5 mμ (ε 8000), 225 (shoulder, ε 7600), 281 (2840) and 287 (shoulder, 2520); nmr ($CDCl_3$) δ 6.7–7.4 (3 H m, aryl CH), 4.91 (1 H d, J = 6 Hz, benzylic CHO), 3.82 (3 H s, OCH_3), 2.9–3.3 (1 H m, benzylic CH), and 1.1–2.6 (10 H m, OH and aliphatic CH).

Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 77.05; H, 8.21.

Preparation of the Acid Derivatives 9 and 10.—To a cold (0°) suspension of 5.00 g (19.3 mmol) of the amide **3b** in 10 ml of hexane and 40 ml of tetrahydrofuran was added 32.1 ml of a hexane solution containing 51.3 mmol of *n*-BuLi. When 1 equiv of *n*-BuLi had been added the suspended amide **3b** dissolved to form a yellow solution which became red in color as more *n*-BuLi was added. The resulting solution was stirred at 0° for 1 hr, during which time a yellow precipitate separated. The resulting suspension was refluxed for 30 min. and then cooled and poured into a slurry of 300 g of Dry Ice in 300 ml of Et_2O. The resulting mixture was partitioned between H_2O and Et_2O. Concentration of the ether layer and crystallization of the residue separated 0.22 g (4%) of the starting amide, mp 160–164°. The aqueous layer was cooled in an ice bath and then acidified (HCl, pH 2) and mixed with Et_2O. The mixture was filtered to separate 2.84 g (48%) of the crude acid **10a**, mp 183–195°, which was relatively insoluble in Et_2O. Recrystallization from EtOH afforded the pure acid **10a** as white needles: mp 213–215°; ir (KBr pellet) 3420 (NH), 2940 (broad, associated OH), 1735 (carboxyl C=O with intramolecular H bonding), and 1625 cm^{-1} (amide C=O with intramolecular H bonding); uv max (95% EtOH) 295 mμ (ε 3340) with intense end absorption (ε 27,100 at 210 mμ); nmr (NaOD + D_2O) δ 7.26 (1 H d, J = 9 Hz, aryl CH), 6.95 (1 H d, J = 9 Hz, aryl CH), 3.8–4.4 (4 H m, benzylic CHCO including the CH_3O singlet at δ 3.86), and 1.0–3.5 (13 H m, aliphatic CH including the NCH_3 singlet at δ 2.91); mass spectrum m/e (rel intensity) 303 (0.5, M^+), 272 (29), 259 (100), 242 (24), 229 (43), 228 (32), 227 (22), 216 (48), 185 (67), 128 (21), and 115 (25).

Anal. Calcd for $C_{17}H_{21}NO_4$: C, 67.31; H, 6.98; N, 4.62. Found: C, 67.30; H, 6.97; N, 4.54.

A 560-mg (1.85 mmol) sample of the acid **10a** (mp 209–210°) was esterified with excess CH_2N_2 in an Et_2O–tetrahydrofuran mixture to yield 556 mg (95%) of the crude ester **10b**, mp 158–163°. Recrystallization from MeOH–H_2O afforded the ester **10b** as white needles: mp 158–163°; ir ($CHCl_3$), 3450 (NH), 1730 (conjugated ester C=O), and 1645 cm^{-1} (broad, amide C=O); nmr ($CDCl_3$) δ 6.7–7.3 (3 H m, NH and aryl CH), 4.41 (1 H d, J = 8 Hz, benzylic CHCO), 3.84 (3 H s, OCH_3), 3.63 (3 H s, OCH_3), and 0.7–3.4 [13 H m, aliphatic CH and NCH_3 doublet (J = 5 Hz) at δ 2.92].

Anal. Calcd for $C_{18}H_{23}NO_4$: C, 68.12; H, 7.31; N, 4.41. Found: C, 67.98; H, 7.51; N, 4.25.

The ether-soluble fraction from the original carbonation reaction was washed with aqueous NaCl, dried, and concentrated to leave 2.14 g (37%) of the crude acid **9a**, mp 145–147°. Recrystallization from EtOH separated the pure acid **9a** as white

(7) All melting points are corrected and all boiling points are uncorrected. Unless otherwise stated magnesium sulfate was employed as a drying agent. The infrared spectra were determined with a Perkin-Elmer Model 237 or Model 257 infrared recording spectrophotometer fitted with a grating. The ultraviolet spectra were determined with a Cary Model 14 or a Perkin-Elmer Model 202, recording spectrophotometer. The nmr spectra were determined at 60 MHz with a Varian Model A-60 or Model T-60 nmr spectrometer. The chemical shift values are expressed in δ values (parts per million) relative to a tetramethylsilane internal standard. The mass spectra were obtained with an Hitachi (Perkin-Elmer) mass spectrometer. All reactions involving strong bases or organometallic intermediates were performed under a nitrogen atmosphere.

needles: mp 152–153°; ir ($CHCl_3$) 3425 (NH), 2930 (broad, associated OH), 1735 (carboxyl C=O with intramolecular H bonding), and 1615 cm^{-1} (broad, amide C=O with intramolecular H bonding); uv max (95% EtOH) 298 mμ (ε 3430) with intense end absorption (ε 29,100 at 210 mμ); nmr ($CDCl_3$) δ 7.7 (1 H broad, OH or NH), 7.22 (1 H d, J = 9 Hz, aryl CH), 6.86 (1 H d, J = 9 Hz, aryl CH), 3.90 (3 H s, OCH_3), 3.00 (3 H d, J = 5 Hz, NCH_3), and 0.7–4.0 (12 H m, OH or NH and aliphatic CH); mass spectrum m/e (rel intensity), 303 (2, M^+), 259 (100), 216 (29), and 185 (36).

Anal. Calcd for $C_{17}H_{21}NO_4$: C, 67.31; H, 6.98; N, 4.62. Found: C, 67.24; H, 6.90; N, 4.53.

A 1.00-g (3.3 mmol) sample of the acid **9a** (mp 148–150°) was esterified with excess CH_2N_2 in an Et_2O–tetrahydrofuran mixture to yield 918 mg (87%) of the ester **9b**, mp 120–121°, as white plates from Et_2O–hexane. Recrystallization gave the pure ester **9b**: mp 124–125°; ir ($CHCl_3$) 3430 (NH), 1725 (conjugated ester C=O), 1645, 1655, and 1660 cm^{-1} (amide C=O); nmr ($CDCl_3$) δ 6.7–7.4 (3 H m, aryl CH and NH), 4.17 (1 H d, J = 5 Hz, benzylic CHCO), 3.86 (3 H s, OCH_3), 3.67 (3 H s, OCH_3), 2.92 (3 H d, J = 5 Hz, NCH_3), and 1.0–3.4 (10 H m, aliphatic CH).

Anal. Calcd for $C_{18}H_{23}NO_4$: C, 68.12; H, 7.31; N, 4.41. Found: C, 68.15; H, 7.25; N, 4.14.

Attempts to effect equilibration of the esters **9b** or **10b** with NaOMe in MeOH or of the acids **9a** and **10a** with TsOH in PhH produced a crude product which appeared to be a cyclic imide, ir ($CHCl_3$) 1670 and 1710 cm^{-1}.

Birch Reduction of the Acid 4a.—To a mixture of 1.00 g of the acid **4a**, 30 ml of *tert*-BuOH, 40 ml of tetrahydrofuran, and 100 ml of redistilled liquid NH_3 was added 0.40 g (58 mg-atoms) of Li. After the resulting mixture had been stirred under reflux for 4 hr (during which time the blue color was discharged), an additional 0.40 g (58 mg-atom) of Li was added and stirring under reflux was continued for 3 hr. The mixture was treated successively with 30 ml of MeOH and 40 ml of H_2O and then the NH_3 was allowed to evaporate. After the mixture had been filtered and the residue had been washed with H_2O, the combined filtrates and washings were concentrated, and the residue was dissolved in 300 ml of H_2O and acidified with 13 ml of HOAc. The acid **11** which separated was collected as 0.93 g (92%) of white solid, mp 140–141° dec. Recrystallization from CH_2Cl_2–hexane separated 0.63 g (62%) of the pure acid **11** as white needles: mp 147–149° dec; ir ($CHCl_3$) 2920 (broad, associated OH), 1705 (carboxyl C=O), and 1662 cm^{-1} (enol ether C=C); uv (95% EtOH) end absorption (ε 3580 at 210 mμ); nmr ($CDCl_3$ + pyridine-d_5) δ 14.5 (1 H broad, OH), 4.66 (1 H m, vinyl CH), 3.49 (3 H s, OCH_3), and 0.8–3.9 (15 H m, aliphatic CH); mass spectrum, m/e (rel intensity), 204 (100), 177 (21), 162 (55), 161 (83), 123 (24), 91 (22), 83 (28), 81 (26), 79 (24), 73 (46), 55 (27), and 41 (33).

Anal. Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.56; H, 8.09.

Preparation of the Keto Acid 12. A. From the Enol Ether 11.—A solution of 200 mg (0.81 mmol) of the enol ether **11** and 4.0 ml of aqueous 50% HOAc in 8.0 ml of 1,2-dimethoxyethane was allowed to stand at 25° for 18 hr and then concentrated under reduced pressure. The crude residue (229 mg) was recrystallized from acetone–hexane mixtures to separate 73 mg (29%) of the acid **12a** as white solid, mp 155–156°. The pure acid **12a** crystallized from PhH as white needles, mp 157–158°, identified with the subsequently described sample by comparison of ir spectra.

B. From the Aromatic Acid 4a.—The reduction of 20.0 g (81.5 mmol) of the acid **4a** with 16 g (2.3 g-atoms) of Li, 400 ml of *tert*-BuOH, 400 ml of tetrahydrofuran, and 800 ml of liquid NH_3 was performed as previously described. A solution of the crude product **11** and 350 ml of aqueous 50% HOAc in 450 ml of 1,2-dimethoxyethane was allowed to stand for 18 hr at 25° and then concentrated under reduced pressure. The crude product was partitioned between Et_2O and aqueous HOAc (5:2 v/v) and the ethereal layer was separated, washed with aqueous NaCl, dried (Na_2SO_4), and concentrated. A solution of the residue in 200 ml of toluene was again concentrated to remove water from the crude product **12a** (17.8 g or 94%, mp 105–150°). Recrystallization from CH_2Cl_2–hexane separated 12.9 g (68%) of the acid **12a**, mp 157–158°. This product crystallized from benzene as white needles: mp 157–158°; ir ($CHCl_3$) 2930 (broad, associated OH) and 1710 cm^{-1} (broad, C=O); uv max (95% EtOH) 282 mμ (ε 32) with intense end absorption (ε 3500 at 210 mμ); nmr ($CDCl_3$) δ 11.6 (1 H, broad, OH), 2.0–3.7 (9 H m, aliphatic CH), and 0.9–2.0 (8 H m, aliphatic CH); mass spectrum m/e (rel intensity), 234 (2, M^+), 162 (29), 119 (25), 91 (21), 78 (100), 77 (29), 53 (29), 52 (26), 51 (30), 50 (24), and 39 (38).

Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.62; H, 7.88.

A 5.00-g (21.3 mmol) sample of the acid **12a** was esterified with excess ethereal CH_2N_2. The crude neutral product was obtained as 5.27 g of yellow liquid. A portion of the material was distilled in a short-path still (0.05 mm and 140° bath) to separate the partially purified ester **12b**: $n^{27}D$ 1.5222; ir (neat) 1740 (ester C=O) and 1720 cm^{-1} (C=O); nmr ($CDCl_3$) δ 3.63 (3 H s, OCH_3), 2.0–3.6 (9 H m, aliphatic CH), and 1.0–2.0 (8 H m, aliphatic CH).

Conversion of the Amide Esters 9 and 10 to the Diesters 7 and 8. A. The More Stable Epimer 9b.—A solution of 830 mg (2.62 mmol) of the amide ester **9b** and 450 mg (5.5 mmol) of NaOAc in 21 ml of HOAc was cooled to the freezing point and then treated with 0.70 ml (*ca.* 11 mmol) of liquid N_2O_4. The resulting green suspension was stirred for 15 min and then partitioned between cold H_2O and CCl_4. After the organic layer had been washed with aqueous $NaHCO_3$ and with H_2O, it was dried (Na_2SO_4) and concentrated. A mixture of the residual yellow oil, 55 mg of anhydrous Na_2CO_3, and 100 ml of methylcyclohexane was refluxed with stirring for 36.5 hr and then cooled, diluted with Et_2O, and washed successively with aqueous 5% NaOH and with H_2O. The organic phase was dried and concentrated to leave 518 mg of the crude product as a brown liquid. The aqueous NaOH wash was acidified and extracted with EtOAc to separate 200 mg of crude acid product, which was esterified with excess ethereal CH_2N_2. The combined neutral products were distilled in a short-path still (0.15 mm and 160° bath) to separate 505 mg (64%) of the diester **8b** as a pale yellow liquid, which was identified with an authentic sample by comparison of ir and nmr spectra. For further characterization, a mixture of 446 mg (1.4 mmol) of the diester **8b**, 4.5 ml (9 mmol) of methanolic 2 *M* NaOMe, and 4.5 ml of H_2O was refluxed for 2 hr and then partitioned between H_2O and CH_2Cl_2. After the aqueous phase had been acidified and extracted with CH_2Cl_2, the organic extract was dried and concentrated. The residual crude product was recrystallized from CH_2Cl_2–PhH to separate 314 mg (77%) of the diacid **8a** as tan prisms, mp 189–190° dec. Recrystallization afforded the pure acid **8a** as white prisms, mp 189.5–191° dec, which was identified with an authentic sample (lit.[2] mp 190–191° dec) by a mixture melting point determination and by comparison of ir spectra.

B. The Less Stable Epimer 10b.—The same reaction procedure was used with 785 mg (2.48 mmol) of the amide ester **10b**, 427 mg (5.28 mmol) of NaOAc, 22 ml of HOAc, and 0.75 ml (*ca.* 12 mmol) of N_2O_4. The crude *n*-nitroso amide, a yellow liquid, and 85 mg of anhydrous Na_2CO_3 in 100 ml of methycyclohexane was refluxed with stirring for 51 hr and then subjected to the previously described isolation procedure. The crude neutral product (503 mg of orange liquid) was distilled in a short-path still (0.15 mm and 160° bath) to separate 377 mg (48%) of the diester **7b** as an orange liquid. The ir and nmr spectra of this product indicated the presence of the known[2] diester **7b** accompanied by small amounts of the more stable epimer **8b**. For further characterization, a solution of 377 mg (1.18 mmol) of the diester product and 8 mmol of NaOMe in 10 ml of MeOH was refluxed for 22 hr and then treated with 4 ml of H_2O and refluxed for an additional 2 hr. The reaction mixture was subjected to the previously described isolation procedure to separate 90 mg (27%) of the diacid **8a**, mp 179–188° dec. Recrystallization (acetone–hexane) afforded a sample of the pure diacid **8a**, mp 188–189° dec, which was identified with an authentic sample by a mixture melting point determination and by comparison of ir spectra.

Registry No.—**3a**, 33495-50-0; **3b**, 33495-51-1; **4a**, 19765-79-8; **4c**, 33495-53-3; **6**, 33495-54-4; **7b**, 33495-55-5; **8a**, 19765-82-3; **8b**, 19766-02-0; **9a**, 33495-58-8; **9b**, 33495-59-9; **10a**, 33495-60-2; **10b**, 33495-61-3; **11**, 33537-16-5; **12a**, 33495-62-4; **12b**, 33495-63-5.