General Procedure for the Reductions with Sodium Borohydride.—Ketone, 5.0 mmoles, in 10 ml of ethanol was treated at room temperature with 10 mmoles of sodium borohydride in 10 ml of ethanol. After the exothermic reaction had ended (about 20 min), the mixture was heated on a steam bath for 10 min more. The reaction mixture was hydrolyzed with 25 ml of a 3% sodium hydroxide solution. After the addition of a standard naphthalene solution, the solution was extracted several times with ether, and the ether layer was dried ($MgSO_4$). The solution was concentrated by rotary evaporation and analyzed as before.

General Procedure for the Reductions with Aluminum Hydride.—Into a 50-ml round-bottom flask fitted with a magnetic stirrer and an injection port with a rubber syringe cap, were placed, under nitrogen, 2 mmoles of ketone in enough dry tetrahydrofuran to bring the total volume of the final solution to 10 ml. The solution was brought to 0° by means of an ice bath, and the appropriate amount of a standard aluminum hydride solution in tetrahydrofuran, prepared by the method of Brown and Yoon,[17] was added dropwise (for the normal addition experiments, the ketone was added slowly to the aluminum hydride solution). The mixture was stirred for the appropriate time at 0°. The hydrolysis and analysis procedures were the same as for the lithium aluminum hydride experiments.

General Procedure for the Preparative-Scale Reduction of Δ^2-Cyclopentenones.—The reduction of 3-methyl-2-cyclopenten-1-one is typical of the procedure used. Into a 1-l. round-bottom flask fitted with a magnetic stirrer and an injection port with a rubber syringe cap, was placed, under nitrogen, 10 g (104 mmoles) of 3-methyl-2-cyclopenten-1-one in 400 ml of dry tetrahydrofuran. The solution was brought to 0° by means of an ice bath and 90 ml of a 0.77 *M* aluminum hydride solution in tetrahydrofuran (69.3 mmoles of AlH_3) was added dropwise over a 15-min period. After the addition was complete, the reaction mixture was stirred at 0° for 30 min more and then hydrolyzed by adding successively 2.1 ml of water, 2.1 ml of 15% sodium hydroxide, and 6.3 ml of water. The aqueous layer was salted out with sodium carbonate and the aqueous layer was extracted with ether. The combined organic layers were washed with a saturated sodium bicarbonate solution and dried (K_2CO_3). Removal of the solvent by rotary evaporation afforded 8.5 g of liquid. Distillation of the liquid (12 mm) produced 7.8 g (79.5 mmoles, 76.2% yield) of carbinol. The physical properties of 3-methyl-2-cyclopenten-1-ol and the other Δ^3-cyclopentenols prepared by this procedure are recorded in Table IV.

Registry No.—Aluminum hydride, 1302-30-3.

Perhydroindan Derivatives. XI.[1a] The 7-Methoxyhexahydrofluorene System

HERBERT O. HOUSE, THOMAS M. BARE,[1b] AND WILLIAM E. HANNERS

Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139

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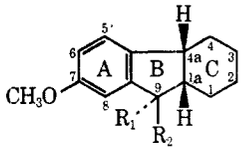
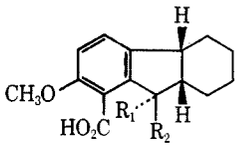
The known methoxyhexahydrofluorenone **6** has been converted into acids **1–4** desired as models for study of transformations in the aromatic ring. Of the various methods used to introduce the carboxyl functions, the selective lithium–hydrogen exchange and subsequent carbonation reactions applied to the olefins **10** and **35** and to alcohol **8** are worthy of special note.

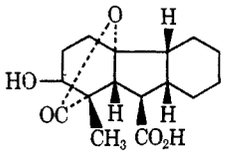
As part of our study of synthetic routes to the gibberellins,[2] we wished to study the acids **1–4** as model compounds for the transformation of the aromatic A ring into the nonaromatic system (*e.g.*, **5**) present in the gibberellins. This paper describes the preparation and interrelation of these model acids **1–4**.



1, $R_1 = CO_2H$; $R_2 = H$
2, $R_1 = H$; $R_2 = CO_2H$



3, $R_1 = CO_2H$; $R_2 = H$
4, $R_1 = H$; $R_2 = CO_2H$



5

The starting material for these acids was the known ketone **6** (Scheme I) prepared by acid-catalyzed cyclization[3] of the unsaturated ketone **7**. The formation of the ketone **6** under equilibrating conditions ensured the formation of the more stable diastereoisomer in which the B and C rings were *cis* fused.[3b] Reduction of the ketone **6** with $LiAlH_4$ yielded a single alcohol believed to have the stereochemistry indicated in structure **8** as a result of attack of the complex metal hydride anion from the less hindered side.[3c,4] Conversion of this alcohol **8** to the crude methanesulfonate ester followed by reaction with sodium cyanide yielded the olefin **9** rather than the desired nitrile. Olefin formation was more easily effected by brief acid-catalyzed dehydration to form the trisubstituted olefin **10** which was readily isomerized to the tetrasubstituted olefin **9**.

The acids **1** and **2** were most efficiently prepared by conversion of the olefin **10** (or mixtures of **9** and **10**) to the allylic lithium reagent which was carbonated to form the unsaturated acid **11** accompanied by small amounts of the isomeric acid **12**. Hydrogenation of the unsaturated acid **11** yielded the acid **1** as a result of the *cis* addition of hydrogen from the less hindered side of the olefin **11**. The methyl ester **13** of acid **1** could be epimerized and then hydrolyzed to yield the more stable C-9 epimer in which the carboxyl function is *trans* to the methylene groups of ring C.

An alternative route (Scheme II) to the acid **2**, although less efficient, provided evidence that the B–C ring fusion in acids **1** and **2** was *cis*. In this sequence the ketone was converted to olefins **15** and **16** by reaction with the appropriate Wittig reagents. Hydrolysis of the enol ether **15** (mixture of geometrical isomers) afforded the aldehyde **17** which was oxidized to the acid **2**. Hydroboration of the olefin **16** proceeded by attack from the less hindered side to yield, after oxidation, the

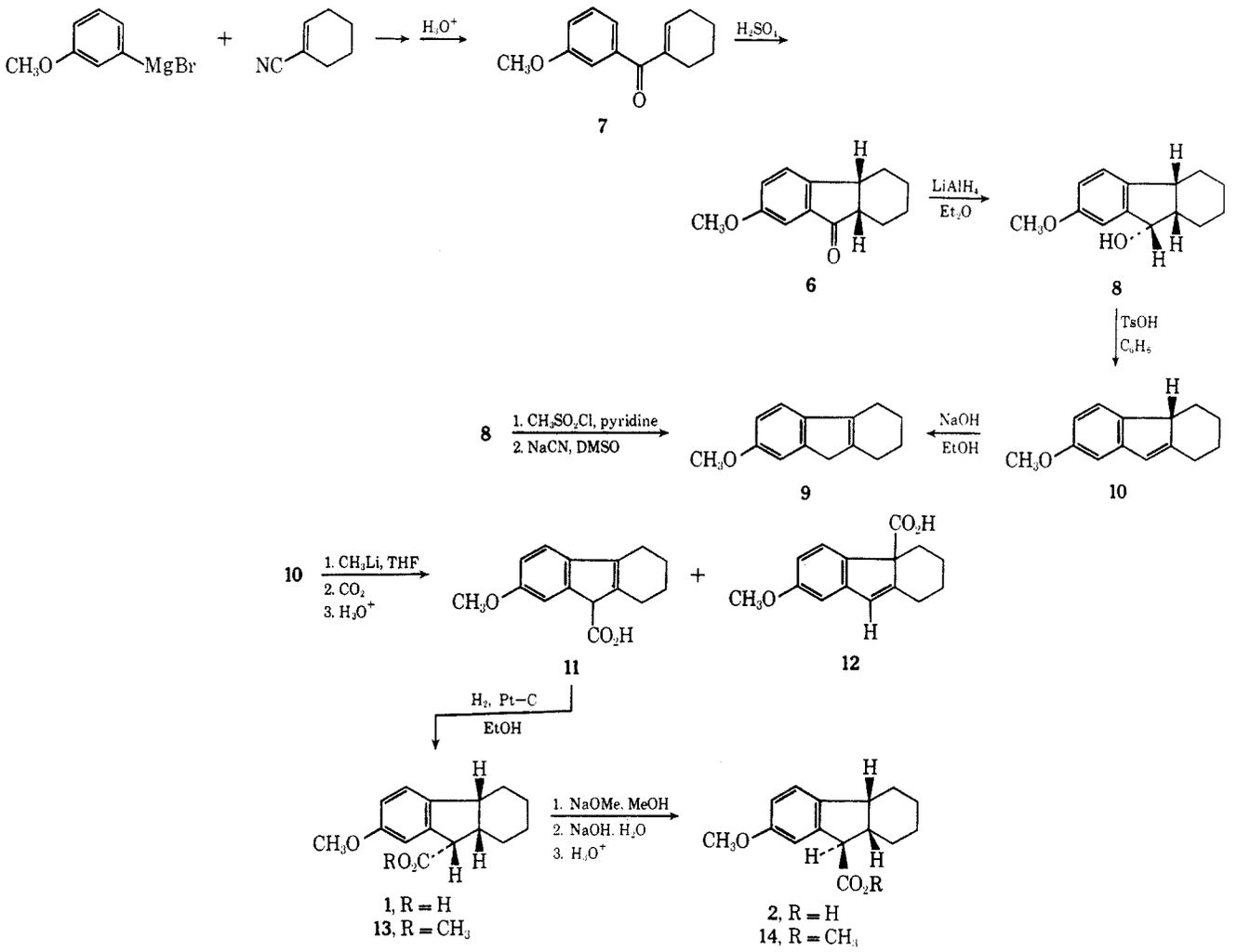
(1) (a) This research has been supported by Research Grant No. GP-5685 from the National Science Foundation and by Public Health Service Grant No. 1-R01-CA10933-01 from the National Cancer Institute. (b) National Institutes of Health Predoctoral Fellow, 1965–1968.

(2) For leading references, see (a) H. O. House, F. J. Sauter, W. G. Kenyon, and J. J. Riehl, *J. Org. Chem.*, **33**, 957 (1968); (b) H. O. House, J. K. Larson, and H. C. Müller, *ibid.*, **33**, 961 (1968).

(3) (a) W. G. Dauben and J. W. Collette, *J. Amer. Chem. Soc.*, **81**, 967 (1959); (b) H. O. House, V. Paragamian, R. S. Ro, and D. J. Wluka, *ibid.*, **82**, 1457 (1960); (c) H. O. House, V. Paragamian, and D. J. Wluka, *ibid.*, **82**, 2561 (1960).

(4) H. O. House, R. G. Carlson, H. Müller, A. W. Noltes, and C. D. Slater, *ibid.*, **84**, 2614 (1962).

SCHEME I



hydroxy methyl derivative **18**. This alcohol **18**, also produced from the acid **1**, was the C-9 epimer of the hydroxymethyl derivative **19** formed from the acid **2**. In an attempt to obtain the acid **2** *via* the glycidic ester **20**, the ketone **6** was treated with ethyl chloroacetate under the usual conditions for producing glycidic esters.[5] However, the only material isolated was the C-alkylation product **21** presumed to have the indicated stereochemistry by analogy with earlier studies.[3b,c,4]

To examine the course of electrophilic substitution reactions, the methoxy acid **2** was subjected to the bromination and acetylation reactions summarized in Scheme III. The nmr spectra of the monosubstitution products **22** and **23** and their derivatives **24** and **25** established that substitution had occurred at position C-6 rather than at the desired position C-8. An attempt to acylate the monobromo acid **22** led to acid-catalyzed decarbonylation to yield an olefin. Therefore, these potential routes to C-8 substituted derivatives were abandoned.

We next turned our attention to metallation reactions with the methoxy alcohol **8**. This investigation was prompted by earlier observations that metallation of aromatic hydrocarbons with lithium reagents was accelerated by the presence of *ortho* substituents with unshared electron pairs such as methoxyl, methoxymethyl, and dimethylaminomethyl groups.[6] Presumably the success of these reactions is attributable to reaction of the normally hexameric or tetrameric alkyllithium reagents[7a] to form complexes (*e.g.*, **29**) in which the more reactive monomeric or dimeric form of the lithium reagent is complexed with the *ortho* donor substituents and is in a favorable position for metal–hydrogen exchange.

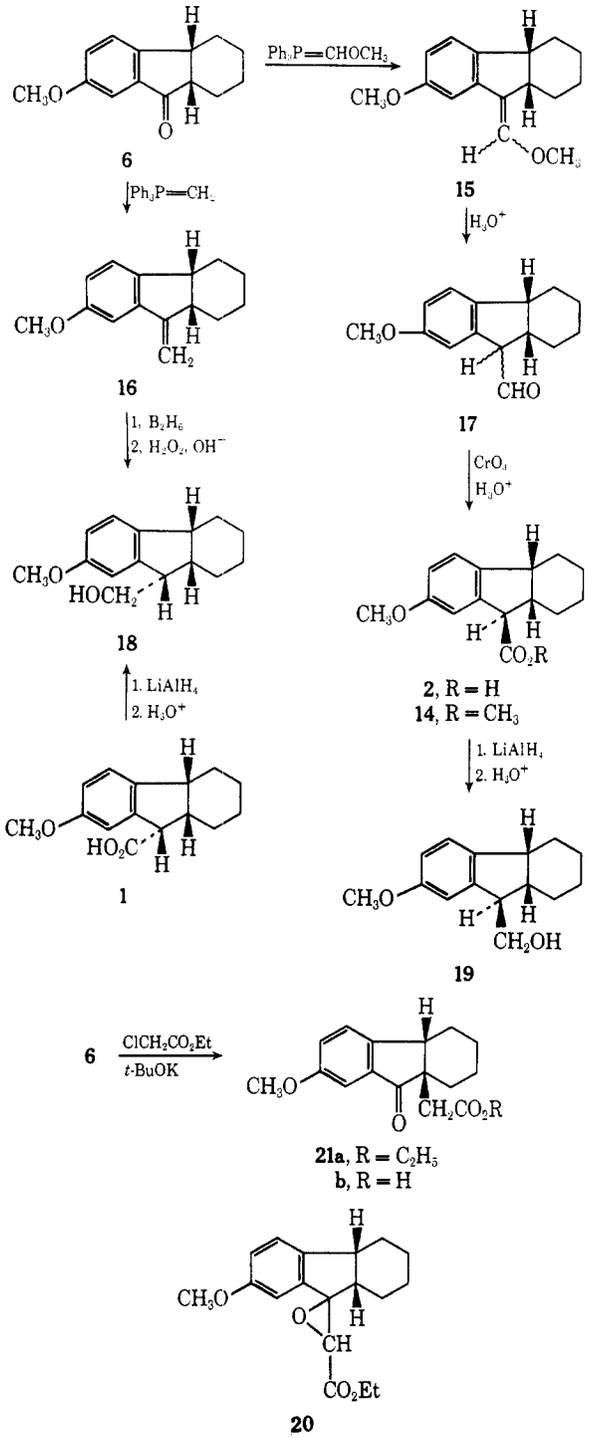
Reaction of the alcohol **8** (Scheme IV) with *n*-butyllithium in a hexane–ether mixture resulted in little if any C metallation and the alcohol **8** was recovered. However, the corresponding reaction with a mixture of *n*-butyllithium and sodium *t*-butoxide in hexane[7b] followed by carbonation produced the desired carboxylic acid **30** in high yield. The structurally specific metallation evidently has rigid requirements for success since the same metallating conditions applied to the homologous alcohol **18** produced a complex mixture of acidic products perhaps caused by competing metallation at the benzylic positions. Activation of the *n*-butyllithium by the addition of N,N,N′,N′-tetramethylethyl-

(5) (a) M. S. Newman and B. J. Magerlein, *Org. Reactions*, **5**, 413 (1949); (b) W. S. Johnson, J. S. Belew, L. J. Chinn, and R. H. Hunt, *J. Amer. Chem. Soc.*, **75**, 4995 (1953).

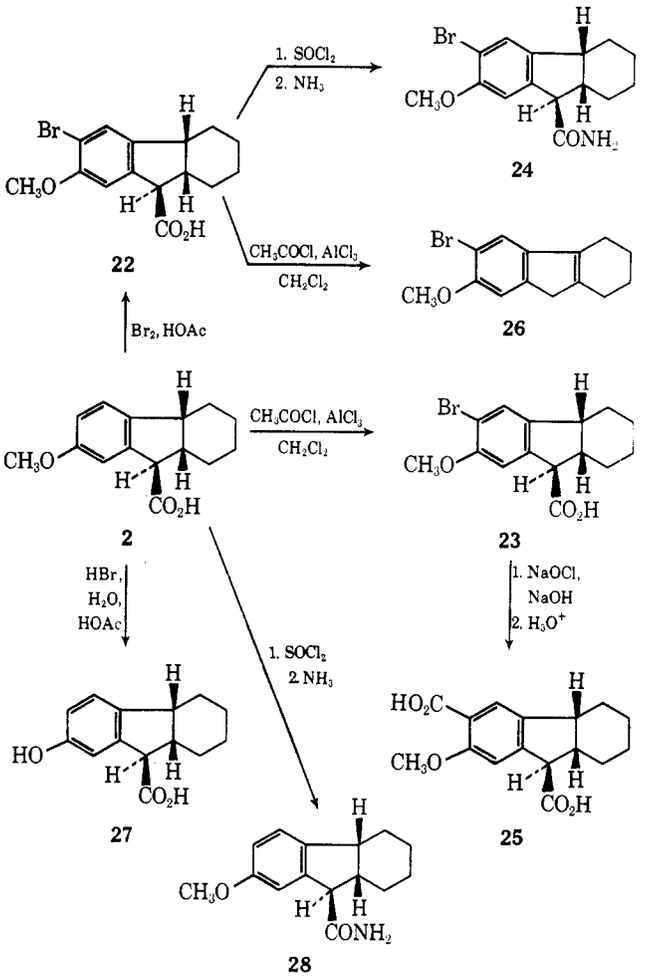
(6) (a) G. Wittig in "Newer Methods of Preparative Organic Chemistry," Vol. 1, Interscience Publishers, Inc., New York, N. Y., 1948, pp 571–591; (b) H. Gilman and J. W. Morton, *Org. Reactions*, **8**, 258 (1954); (c) F. N. Jones, R. L. Vaulx, and C. R. Hauser, *J. Org. Chem.*, **28**, 3461 (1963); (d) R. L. Vaulx, F. N. Jones, and C. R. Hauser, *ibid.*, **30**, 58 (1965); (e) K. P. Klein and C. R. Hauser, *ibid.*, **32**, 1479 (1967); (f) R. L. Gay and C. R. Hauser, *J. Amer. Chem. Soc.*, **89**, 2297 (1967).

(7) (a) T. L. Brown, *Accounts Chem. Res.*, **1**, 23 (1968); (b) this mixture of reactants is reported to form *n*-butylsodium: L. Lochmann, J. Pospisil, and D. Lim, *Tetrahedron Letters*, 257 (1966).

SCHEME II



SCHEME III



enediamine[8] prior to metallation resulted in loss of structural specificity. A mixture of the ester **31** and compounds believed to be the ester **32** and lactone **33** was obtained from the alcohol **18** and both acids **30** and **34** were produced from the alcohol **8**. In these latter cases, we presume that the organolithium–diamine complex is more stable than the alternative alkoxide complex such as structure **29** with the result that the structural specificity resulting from a complex of the type **29** is lost.

The further transformation of the hydroxy acid **30** to the mixture of unsaturated acid derivatives **36** and **37** is illustrated in Scheme V. Hydrogenation of the unsaturated acid **37b** afforded the less stable diacid **3** which could be epimerized at C-9 with potassium hydroxide to form the more stable epimer **4**. These stereochemical results are analogous to the aforementioned hydrogenation of acid **11** to produce the less stable saturated epimer **1**. Hydrogenation of the unsaturated ester **37a** produced the less stable diester epimer **38**. However, the conditions required to saponify this ester also epimerized the acid (or ester) to produce the more stable diacid **4**.

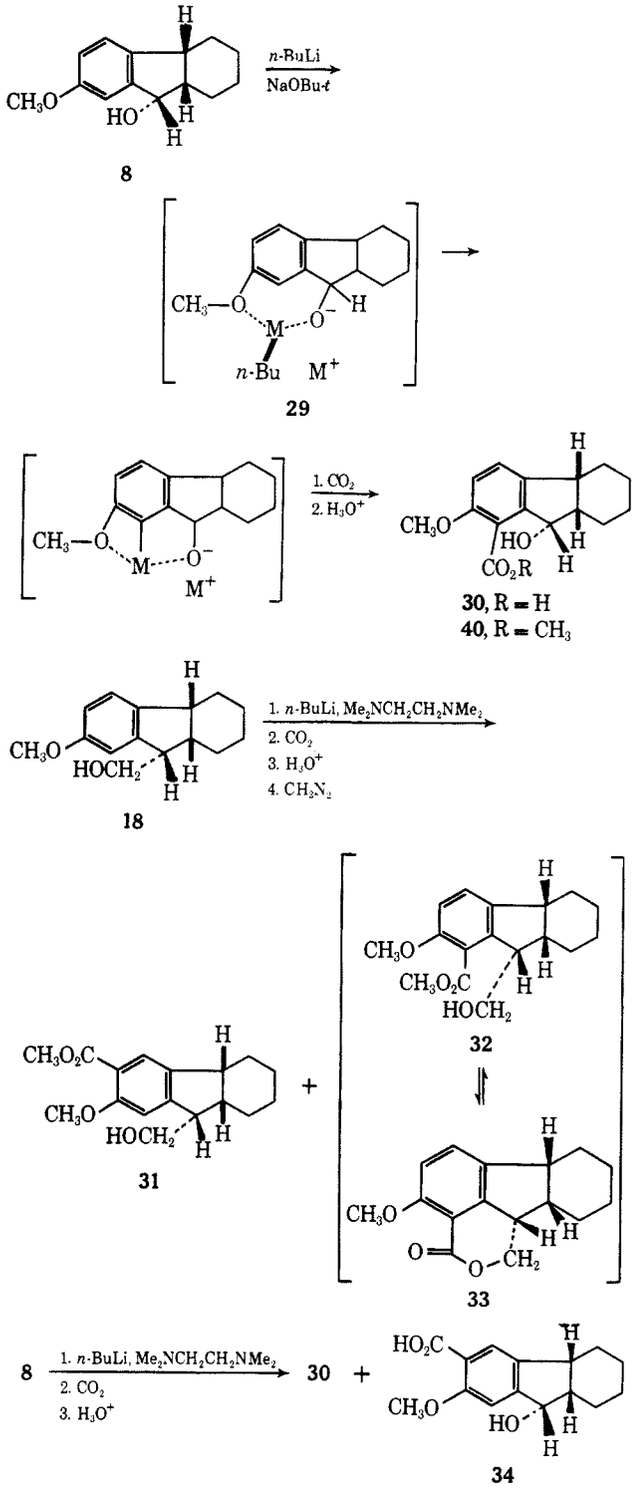
(8) The use of amines to produce reactive monomeric or dimeric complexes with organolithium compounds has been reported by (a) G. G. Eberhardt and W. A. Butte, *J. Org. Chem.*, **29**, 2928 (1964); (b) C. G. Screttas and J. F. Eastham, *J. Amer. Chem. Soc.*, **87**, 3276 (1965).

Experimental Section[9]

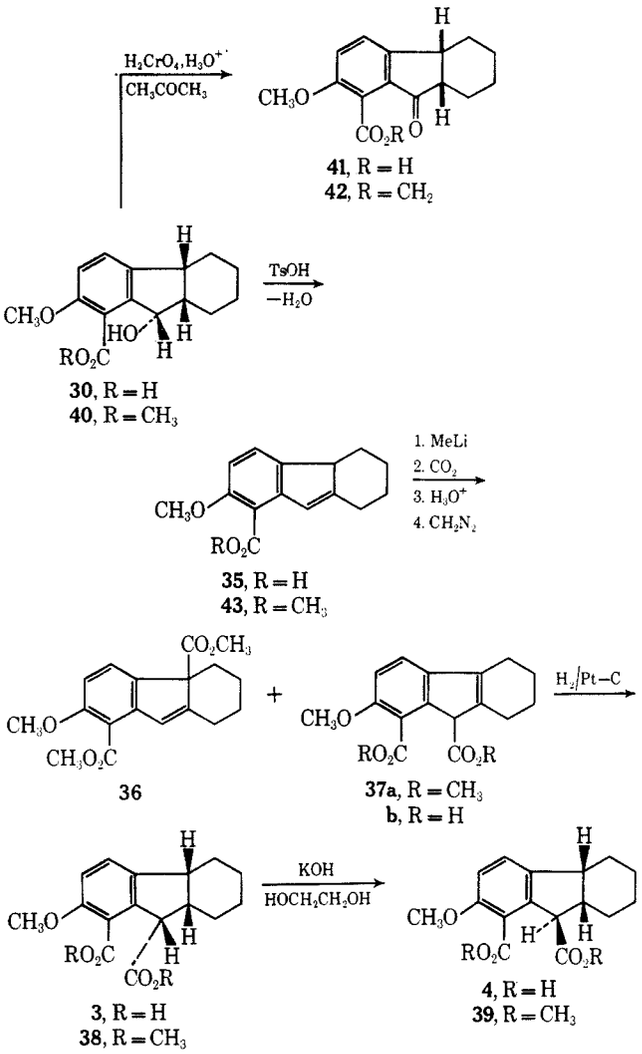
7-Methoxy-*cis*-1,1a,2,3,4,4a-hexahydrofluoren-9-ol (8).—Reaction of 1-cyanocyclohexene with *m*-methoxyphenylmagnesium bromide in Et_2O solution or with *m*-methoxyphenylmagnesium chloride in tetrahydrofuran solution following the general procedures described previously[3b,c,4] produced the unsaturated ketone **7** (52–80% yield) as a pale yellow liquid: bp 129–134° (0.5 mm) [lit.[3a] 164–167° (4 mm)]; ir (CCl_4), 1650 (C=O) and

(9) 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 infrared recording spectrophotometer fitted with a grating. The ultraviolet spectra were determined with a Cary recording spectrophotometer, Model 14. The nmr spectra were determined at 60 Mc with a Varian, Model A-60, nmr spectrometer. The chemical shift values are expressed either in cycles per second or δ values (parts per million) relative to a tetramethylsilane internal standard. The mass spectra were obtained with a CEC, Model 21-130, or with a Hitachi (Perkin-Elmer) mass spectrometer. The microanalyses were performed by Dr. S. M. Nagy and his associates. All reactions involving organometallic or strongly basic intermediates were performed under a nitrogen atmosphere.

SCHEME IV



SCHEME V



1640 cm^{-1} (C=C); uv (95% EtOH), 218 mμ (ϵ 19,600), 247 (11,300), and 301 (2260); nmr (CCl_4), δ 6.7–7.4 (4 H m, aryl CH), 6.43 (1 H br, vinyl CH), 3.76 (3 H s, OCH_3), and 1.4–2.6 (8 H m, aliphatic CH); mass spectrum, molecular ion *m/e* 216, fragments *m/e* 184, 135, 92, 77, 41, 39, and 27. Cyclization of the unsaturated ketone **7** in concentrated H_2SO_4 for 5 min at 60° afforded the ketone **6** as white needles from hexane: mp 99–100°. (lit.[3a] mp 99–100°); yield 69–85%; ir (CCl_4), 1715 cm^{-1} (C=O); uv (95% EtOH), 218 mμ (ϵ 27,700), 248 (9170), and 319 (3930); nmr ($CDCl_3$), δ 7.0–7.5 (3 H m, aryl CH), 3.81 (3 H s, OCH_3), and 1.0–3.7 (10 H m, aliphatic CH); mass spectrum, molecular ion *m/e* 216, abundant fragments *m/e* 188, 187, 175, 174, 173, 162, and 160.

To a cold (0°) suspension of 3.65 g (96.4 mmol) of $LiAlH_4$ in 100 ml of tetrahydrofuran was added, dropwise with stirring, a solution of 50.0 g (231 mmol) of the ketone **6** in 300 ml of tetrahydrofuran. After the resulting mixture had been stirred at 20–25° for 3.5 hr, it was cooled (ice bath), treated successively with 3.65 ml of H_2O, 3.65 ml of aqueous 15% NaOH, and 10.95 ml of H_2O and the filtered to remove the inorganic salts. The residue was washed with CH_2Cl_2 and the combined organic filtrates were concentrated. Recrystallization of the residual solid (hexane–CH_2Cl_2) separated 47.27 g (93.5%) of the alcohol **8** as colorless needles: mp 147–147.5°; ir ($CHCl_3$), 3590 and 3450 cm^{-1} (free and assoc OH); uv (95% EtOH), 220 mμ sh (ϵ 7780), 227 sh (7260), 282 (2750), and 288 (2410); nmr [$(CD_3)_2SO$], δ 6.6–7.2 (3 H m, aryl CH), 4.7–5.3 (1 H m, >CHO), 3.72 (3 H s, OCH_3), and 0.8–3.5 (11 H m, OH and aliphatic CH); mass spectrum, molecular ion *m/e* 218, abundant fragments *m/e* 200, 175, 172, and 121.

Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 77.05; H, 8.40.

Preparation of the Olefins 9 and 10.—A mixture of 781 mg (3.58 mmol) of the alcohol and 501 mg (4.37 mmol) of CH_3SO_2Cl in 4 ml of pyridine was stirred for 1 hr at 0°, allowed to stand overnight in a refrigerator, and then partitioned between Et_2O and cold H_2O. The Et_2O solution was washed successively with cold, dilute, aqueous HCl and with aqueous $NaHCO_3$ and then dried and concentrated. The residual crude sulfonate (and/or olefin), an orange oil, was treated with a solution of 486 mg (9.92 mmol) of NaCN in 9.5 ml of $(CH_3)_2SO$, and then heated to 40° for 2.5 hr, and partitioned between H_2O and Et_2O. The organic layer was washed with H_2O, dried, and concentrated to leave 0.55 g (77%) of the crude olefin **9** as a pale orange solid, mp 40–50°. A warm MeOH solution of the product was decolorized and cooled to separate the pure **olefin 9** as white needles: mp 58–58.5°; ir ($CHCl_3$), 1620 and 1610 cm^{-1} (C=C); uv (95% EtOH), 266 mμ (ϵ 16,200) and 274 sh (13,600); nmr ($CDCl_3$), δ

6.6–7.2 (3 H m, aryl CH), 3.74 (3 H s, OCH_3), 3.13 (2 H br s, benzylic CH_2), 2.1–2.6 (4 H m, allylic CH_2), and 1.4–2.0 (4 H m, aliphatic CH_2); mass spectrum, molecular ion *m/e* 200, abundant fragments *m/e* 199, 172, 171, 129, 128, and 44.

Anal. Calcd for $C_{14}H_{16}O$: C, 83.96; H, 8.05. Found: C, 83.98; H, 8.11.

A solution of 500 mg (2.29 mmol) of the alcohol **8** and 20 mg of TsOH in 20 ml of PhH was refluxed for 5 min and then cooled, washed with aqueous $NaHCO_3$, dried over Na_2SO_4, and concentrated. The residual yellow oil crystallized from EtOH solution as 409 mg (89.5%) of light yellow solid, mp 30–32°. Recrystallization gave the pure olefin **10** as a white solid: mp 31.7–32.7°; ir (CCl_4), 1620 cm^{-1} (C=C); uv (95% EtOH), 226 mμ (ε 25,900), 264 (7220), 293 (3240), and 303 (3030); nmr (CCl_4), δ 7.06 (1 H d, J = 7.7 Hz, C-5 aryl CH), 6.68 (1 H d, J = 2.2 Hz, C-8 aryl CH), 6.48 (1 H, d of d, J = 2.2 and 7.7 Hz, C-6 aryl CH), 6.19 (1 H br s, vinyl CH), 3.68 (3 H s, OCH_3), and 0.8–3.3 (9 H m, aliphatic CH); mass spectrum, molecular ion *m/e* 200, abundant fragments *m/e* 199, 172, 171, 129, 128, and 105.

Anal. Calcd for $C_{14}H_{16}O$: C, 83.96; H, 8.05. Found: C, 83.95; H, 8.21.

The same olefin **10** (mp 31.5–32.5°) was obtained in 28% yield by reaction of the alcohol **8** with CH_3SO_2Cl in pyridine solution for 4 hr at 25–30°. A solution of 516 mg (2.58 mmol) of this olefin **10** and 100 mg (2.5 mmol) of NaOH in 3 ml of EtOH was stirred for 2 hr at 25–30° and then acidified with aqueous HCl and concentrated. An Et_2O solution of the residual oil was washed with H_2O, dried, and concentrated. Recrystallization of the crude product from EtOH separated 349 mg (67.9%) of the olefin **9**, mp 57–58° (identified with the previously described sample by a mixture melting point and by comparison of ir, uv, and nmr spectra).

Preparation of the Unsaturated Acids 11 and 12.—To a cold (−78°) solution of 791 mg (3.96 mmol) of the tetrahydrofluorene **9** and a few milligrams of Ph_3CH in 10 ml of tetrahydrofuran was added 6 ml (*ca.* 6 mmol) of a solution of MeLi in tetrahydrofuran. The initially yellow solution was allowed to warm to room temperature (during which time it assumed the red color of the Ph_3C^-) and then poured, with stirring into a slurry of 20 g of Dry Ice in 20 ml of tetrahydrofuran. The resulting mixture was acidified with dilute aqueous HCl, filtered, and extracted with Et_2O. The Et_2O solution was extracted successively with aqueous NaCl and aqueous $NaHCO_3$. After acidification of the aqueous $NaHCO_3$ extract, the usual manipulations separated 825 mg (84%) of the crude acids **11** and **12**, mp 133–145°. Recrystallization (CCl_4–hexane) separated 540 mg (55.7%) of the acid **11**, mp 153.5–155° dec. Recrystallization (Et_2O) separated the acid **11** as white prisms: mp 156–157° dec; ir ($CHCl_3$), 1710 (carboxyl C=O) and 1615 cm^{-1} (C=C); uv (95% EtOH), 268 mμ (ε 14,600) and 276 sh (13,200); nmr ($CDCl_3$), δ 10.45 (1 H, COOH), 6.6–7.4 (3 H m, aryl CH), 4.17 (1 H br, benzylic CH), 3.82 (3 H s, OCH_3), 2.2–2.7 (4 H m, allylic CH), and 1.5–2.1 (4 H m, aliphatic CH); mass spectrum, molecular ion *m/e* 244, abundant fragments *m/e* 200, 199, 172, 171, and 44.

Anal. Calcd for $C_{15}H_{16}O_3$: C, 73.75; H, 6.60. Found: C, 73.54; H, 6.60.

In a subsequent preparation, 50.0 g (0.232 mol) of the ketone **6** was reduced, the crude alcohol **8** was dehydrated, and the crude olefin **9** and/or **10** was metallated and carbonated. The crude acidic product was recrystallized (CH_2Cl_2–hexane) to separate 42.2 g (74.6% over-all) of the crude acid **11**, mp 127–149° dec, which was hydrogenated as subsequently described to yield 22.3 g (39.3% over-all) of the saturated acid **1**, mp 185–187°. The nonvolatile portion of the mother liquor remaining after separation of acid **11** was treated with 0.5 g of TsOH in refluxing MeOH for 12 hr. The acidic fraction separated after this treatment was recrystallized (CH_2Cl_2–hexane) to separate 2.0 g (3.5%) of the isomeric unsaturated acid **12** as white crystals: mp 158–159°; ir ($CHCl_3$), 1740 (sh), 1695 (carboxyl C=O), 1625 and 1605 cm^{-1} (C=C); uv (95% EtOH), 230 mμ (ε 32,800), 265 (5970), 294 (2560), and 305 (2370); nmr ($CDCl_3$), δ 12.0 (1 H br, COOH), 6.5–7.5 (3 H m, aryl CH), 6.45 (1 H s, vinyl CH), 3.77 (3 H s, OCH_3), and 0.8–3.2 (8 H m, aliphatic CH); mass spectrum, abundant fragments *m/e* 200, 172, 171, 157, 141, 129, 128, and 44.

Anal. Calcd for $C_{15}H_{16}O_3$: C, 73.75; H, 6.60. Found: C, 73.95; H, 6.67.

Preparation of the Saturated Acid 1.—A solution of 361 mg (1.47 mmol) of the olefinic acid **11** in 8 ml of EtOH was hydrogenated at 25–30° and atmospheric pressure over 36.1 mg of a 5% Pd–C catalyst. After 11 hr the H_2 uptake (37.2 ml or 1.50 mmol) ceased and the mixture was filtered, concentrated, and diluted with water. The crude acidic product (329 mg of pale yellow solid) was recrystallized (Et_2O–hexane) to separate 214 mg (58.8%) of the acid **1** as colorless needles, mp 182–186°. Recrystallization gave the pure acid **1**: mp 186–187°; ir ($CHCl_3$), 1710 cm^{-1} (carboxyl C=O); uv (95% EtOH), 218 mμ (ε 6330), 227 (6780), 281 (2430), and 288 (2140); nmr ($CDCl_3$), δ 10.76 (1 H br, COOH), 6.7–7.4 (3 H m, aryl CH), 4.06 (1 H d, J = 6 Hz, $ArCHCO_2R$), 3.85 (3 H s, OCH_3), and 0.9–3.5 (10 H m, aliphatic CH); mass spectrum, molecular ion *m/e* 246, abundant fragments *m/e* 204, 203, 201, 159, and 115.

Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.14; H, 7.37. Found: C, 73.35; H, 7.18.

Reaction of 920 mg (3.74 mmol) of the acid **1** with excess ethereal CH_2N_2 followed by recrystallization of the crude neutral product from Et_2O yielded 928 mg (95.5%) of the ester **13** as white needles, mp 77.5–78.2°. Recrystallization (H_2O–MeOH) separated the pure **methyl ester 13**: mp 78–79°; ir ($CHCl_3$), 1740 cm^{-1} (ester C=O); uv (95% EtOH), 227 mμ (ε 8190), 282 (2810), and 288 (2470); nmr ($CDCl_3$), δ 6.5–7.2 (3 H m, aryl CH), 3.87 (1 H d, J = 7 Hz, $ArCHCO_2R$), 3.73 (3 H s, OCH_3), 3.69 (3 H s, OCH_3), and 0.8–3.4 (10 H m, aliphatic CH); mass spectrum, molecular ion *m/e* 260, abundant fragments *m/e* 217, 201, 200, 159, and 115.

Anal. Calcd for $C_{16}H_{20}O_3$: C, 73.82; H, 7.74. Found: C, 73.89; H, 7.82.

Gas chromatographic analyses[10] established that ester **14** was eluted more rapidly than ester **13** and that neither ester was contaminated with the other epimer. A solution of 490 mg (1.88 mmol) of the ester **13** and 446 mg of NaOMe in 10 ml of MeOH was refluxed for 12 hr and then 2 ml of H_2O was added and refluxing was continued for 5 hr. The resulting suspension was acidified with aqueous HCl and filtered to separate 382 mg of crude product. Recrystallization (Et_2O–hexane) separated 379 mg (82.2%) of the acid **2** as cubic crystals, mp 116–118°. This sample, mp 117–118° after recrystallization, was identified with the subsequently described sample of acid **2** by a mixture melting point and comparison of ir spectra.

Preparation of the Saturated Acid 2.—To the basic solution[11] prepared from 1.85 g (77.2 mmol) of NaH and 36 ml of $(CH_3)_2SO$ was added a solution of 26.48 g (77.2 mmol) of methoxymethyltriphenylphosphonium chloride,[12] mp 196–200° dec (lit.[12] 201–202° dec), to form a red solution of the ylide. A solution of 9.81 g (45.4 mmol) of the ketone **6** in 34 ml of tetrahydrofuran was added to the ylide solution. The resulting mixture was heated to 50° with stirring for 7 hr and then cooled and partitioned between H_2O and pentane. The pentane extract was concentrated, filtered to separate the Ph_3PO, and further concentrated to leave 13.92 g of the crude enol ethers **15** as an orange oil which exhibited no infrared absorption in the 6-μ region attributable to the starting ketone **6**. From a comparable experiment, the crude product was chromatographed on silicic acid. The fractions eluted with Et_2O–hexane mixtures were liquid with spectral characteristics consistent with the **enol ether 15**: ir ($CHCl_3$), 1675 cm^{-1} (enol ether C=C); uv (95% EtOH), 214 mμ (ε 19,800), 267 (12,900), 274 (11,300), and 309 (8250); nmr ($CDCl_3$), δ 6.0–7.5 (4 H m, aryl and vinyl CH), 3.66, 3.70, 3.76, and 3.78 (6 H total, 4 s, OCH_3, of stereoisomeric enol ethers **15**), and 0.8–3.5 (10 H m, aliphatic CH); mass spectrum, weak molecular ion *m/e* 244, abundant fragments *m/e* 74, 59, 57, 56, 45, 43, and 41.

A comparable reaction was run with 256 mg (10.6 mmol) of NaH, 14.5 ml of $(CH_3)_2SO$, 3.753 g (10.5 mmol) of methyltriphenylphosphonium bromide, 1.732 g (8.02 mmol) of the ketone **6**, and 10 ml of tetrahydrofuran employing a reaction time of 26 hr at 55–60°. The crude product was chromatographed on neutral alumina (activity I) and the fractions (1.57 g) eluted with hexane were combined, concentrated, and distilled in a short-path still (0.01 mm and 88–93° bath) to separate 1.49 g (87%) of the **olefin 16** as a colorless liquid: ir ($CHCl_3$), 1640 and 870 cm^{-1} (C=CH_2); uv (95% EtOH), 213 mμ (ε 23,800), 252 (10,900), 306 (5430), and 314 (4780); nmr ($CDCl_3$), δ 6.6–7.3 (3 H m, aryl CH), 5.38 (1 H d, J = 2 Hz, vinyl CH), 4.93 (1 H

(10) A gas chromatography column packed with silicone gum, SE-30, suspended on Chromosorb P was employed for this analysis.

(11) R. Greenwald, M. Chaykovsky, and E. J. Corey, *J. Org. Chem.*, **28**, 1128 (1963).

(12) G. Wittig and M. Schlosser, *Chem. Ber.*, **94**, 1373 (1961).

d, J = 2 Hz, vinyl CH), 3.77 (3 H s, OCH_3), and 1.0–3.5 (10 H m, aliphatic CH); mass spectrum, molecular ion m/e 214, abundant fragments m/e 199, 186, 185, 160, 128, and 115.

Anal. Calcd for $C_{15}H_{18}O$: C, 84.07; H, 8.47. Found: C, 84.11; H, 8.61.

To a cold (0°) solution of the 13.9 g of the crude enol ether **15** in 480 ml of tetrahydrofuran was added, dropwise and with stirring over a 15-min period, 47 ml of aqueous 70% $HClO_4$. The resulting solution was stirred for 2 hr at 25–30° and made basic with aqueous NaOH and concentrated under reduced pressure. The residue was extracted with Et_2O and the extract was dried and concentrated to leave 13.7 g of the crude aldehyde **17** as an orange oil which contained no enol ether (infrared analysis). From a comparable hydrolysis of 294 mg of the enol ether **15**, the crude product (396 mg) was distilled in a short-path still (0.04 mm and 120–130° bath) to separate 226 mg (81%) of the **aldehyde 17** as a pale yellow liquid: ir ($CHCl_3$), 2720 (aldehyde CH) and 1720 cm^{-1} (C=O); uv (95% EtOH), 281 mμ (ε 2790) and 287 sh (2510); nmr ($CDCl_3$), δ 9.70 (1 H d, J = 3 Hz, CHO, a barely discernible doublet, J = 3 Hz, centered at 9.80 suggests the presence of a small amount of the second aldehyde stereoisomer **17** epimeric at C-9), 6.6–7.3 (3 H m, aryl CH), 3.77 (3 H s, OCH_3), 3.57 (1 H, d of d, J = 3 and 6 Hz, ArCHCO), and 1.0–3.3 (10 H m, aliphatic CH); mass spectrum, molecular ion m/e 230, abundant fragments m/e 201, 159, 121, and 115.

Anal. Calcd for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88. Found: C, 78.38; H, 8.07.

To a cold (3°) solution of 13.7 g of the crude aldehyde **17** in 1700 ml of acetone was added, dropwise and with stirring over 7 min, 15.8 ml of aqueous 2.67 M H_2CrO_4.[13] After the resulting solution had been stirred for 4 min, excess i-PrOH was added and the solution was concentrated and then partitioned between H_2O and Et_2O. The Et_2O extract was dried and concentrated to leave a crude product (7.48 g of dark oil) which was crystallized (Et_2O–hexane) to separate 5.333 g (46.7% based on the ketone **6**) of crude acid **2** as tan prisms, mp 113–116°. Decolorization (carbon) and recrystallization afforded 4.20 g of the acid **2** (mp 116–118°) as pale tan prisms: mp 117.5–118.5° after further recrystallization; ir ($CHCl_3$), 1705 cm^{-1} (carboxyl C=O); uv (95% EtOH), 218 mμ sh (ε 8670), 282 (2850), and 287 (2580); nmr ($CDCl_3$), δ 11.15 (1 H, COOH), 6.6–7.4 (3 H m, aryl CH), 3.77 (3 H s, OCH_3, superimposed on a second 1 H signal, $ArCHCO_2R$), and 1.0–3.4 (10 H m, aliphatic CH); mass spectrum, molecular ion m/e 246, abundant fragments m/e 203, 201, 159, 115, 91, and 44.

Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.14; H, 7.37. Found: C, 73.23; H, 7.51.

Reaction of 1.05 g (4.27 mmol) of the acid **2** with excess ethereal CH_2N_2 afforded 1.178 g of crude neutral product. Distillation in a short-path still (0.05 mm and 115–117° bath) separated 1.04 g (93.8%) of the **methyl ester 14** as a colorless liquid: ir (CCl_4), 1740 cm^{-1} (ester C=O); uv (95% EtOH), 218 mμ (ε 8120), 282 (2940), and 287 sh (2720); nmr ($CDCl_3$), δ 6.5–7.2 (3 H m, aryl CH), 3.70 (3 H s, OCH_3), 3.64 (3 H s, OCH_3), and 1.0–3.7 (11 H m, aliphatic CH); mass spectrum, molecular ion m/e 260, abundant fragments m/e 217, 201, 200, 157, and 115.

Anal. Calcd for $C_{16}H_{20}O_3$: C, 73.82; H, 7.74. Found: C, 74.07; H, 7.91.

After a mixture of 506 mg (2.05 mmol) of the acid **2** and 1.2 ml (17 mmol) of $SOCl_2$ had been stirred at 25–30° for 5 hr, the resulting solution was added to excess aqueous NH_3 and then extracted with CH_2Cl_2. The crude amide (514 mg, mp 176–177.5°) obtained from the organic extract was recrystallized (H_2O–EtOH) to separate 433 mg (86.1%) of the **amide 28** as white needles: mp 178.5–179°; ir ($CHCl_3$), 1670 cm^{-1} (amide C=O); uv (95% EtOH), 218 mμ (ε 8320), 282 (2890), and 287 (2590); nmr [$(CD_3)_2SO$], δ 6.4–7.6 (5 H m, NH and aryl CH), 3.64 (3 H s, OCH_3), and 1.0–3.7 (11 H m, aliphatic CH); mass spectrum, molecular ion m/e 245, abundant fragments m/e 201, 200, 159, and 43.

Anal. Calcd for $C_{15}H_{19}NO_2$: C, 73.44; H, 7.81; N, 5.71. Found: C, 73.30; H, 7.95; N, 5.68.

A mixture of 1.005 g (4.08 mmol) of the methoxy acid **2**, 11.5 ml of aqueous 48% HBr, and 11 ml of HOAc was refluxed for 5 hr and then partitioned between water and CH_2Cl_2. The organic phase was dried, concentrated, and crystallized (CH_2Cl_2–hexane) to separate 787 mg (83%) of the **hydroxy acid 27** as tan needles: mp 177–178°; ir (KBr pellet), 3400 (broad, OH) and 1710 cm^{-1} (carboxyl C=O); uv (95% EtOH), 222 mμ sh (ε 7050) and 283 (3050); nmr [$(CD_3)_2SO$], δ 6.3–7.2 (3 H m, aryl CH), 3.58 (1 H d, J = 7 Hz, $ArCHCO_2R$), and 1.0–3.2 (10 H m, aliphatic CH); mass spectrum, abundant fragments m/e 86, 84, 49, 43, and 40.

Anal. Calcd for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.19; H, 6.90.

Reaction of the Ketone 6 with Ethyl Chloroacetate.—To a cold (10°), stirred suspension of 1.998 g (9.24 mmol) of the ketone **6**, 1.131 g (9.23 mmol) of ethyl chloroacetate, and 1.5 ml of t-BuOH was added, dropwise and with stirring, a solution of t-BuOK prepared from 395 mg (10.1 mg-atom) of K and 8 ml of t-BuOH.

The reaction mixture was stirred at 15–20° for 2 hr and then concentrated under reduced pressure and extracted with Et_2O. After the Et_2O solution had been washed successively with H_2O and aqueous NaCl and then dried, concentration left 2.687 g of residual pale yellow oil. The thin layer chromatogram[14] of this material showed two spots corresponding in R_f value to the starting ketone **6** and a component believed to be the ester **21a**. The crude product had infrared absorption (CCl_4) at 1735 (ester C=O) and 1715 cm^{-1} (ketone C=O) with prominent nmr peaks (CCl_4) at δ 3.80 and 2.63 attributable to OCH_3 and CH_2CO_2R functions.

A mixture of 1.106 g of this crude product, 710 mg of NaOH, and 7.1 ml of H_2O was refluxed with stirring for 4 hr and then partitioned between H_2O and Et_2O. Concentration of the Et_2O layer separated 201 mg of crude unchanged starting ketone **6**. After the aqueous phase had been acidified and extracted with CH_2Cl_2, the organic extract was dried and concentrated to leave 768 mg of the crude acid **21b**, mp 145–148°. Recrystallization (EtOAc–hexane) separated 593 mg of the **keto acid 21b** as pale tan plates, mp 151–152°. An additional crystallization raised the melting point to 152–153°; ir ($CHCl_3$), 1715 cm^{-1} (br, C=O of ketone and carboxyl group); uv (95% EtOH), 220 mμ (ε 26,700), 249 (8190), and 320 (3650); nmr ($CDCl_3$), δ 10.75 (1 H, COOH), 6.9–7.7 (3 H m, aryl CH), 3.84 (3 H s, OCH_3), 3.38 (1 H m, benzylic CH), 2.86 (2 H s, CH_2CO_2R), and 0.8–2.4 (8 H m, aliphatic CH); mass spectrum, molecular ion m/e 274, abundant fragments m/e 186, 144, 116, 115, 57, 56, 45, 44, 43, and 41.

Anal. Calcd for $C_{16}H_{18}O_4$: C, 70.05; H, 6.61. Found: C, 70.07; H, 6.67.

From a comparable reaction employing 1,2-dimethoxyethane as the reaction solvent, the crude product obtained corresponded closely in ir and nmr absorption to the crude product obtained with t-BuOH as the reaction solvent.

Preparation of the Hydroxymethyl Derivatives 18 and 19.—A mixture obtained from 180 mg (4.75 mmol) of $LiAlH_4$, 958 mg (3.89 mmol) of the acid **2**, and 10 ml of Et_2O was stirred at 25–30° for 5 hr, the excess hydride reagent was destroyed with H_2O, and the resulting mixture was partitioned between Et_2O and aqueous 10% H_2SO_4. After the Et_2O extract had been dried and concentrated, the residual oil (933 mg) was distilled in a short-path still (0.07 mm and 130–135° bath) to separate 840 mg (92.8%) of the **alcohol 19** as a pale yellow viscous liquid: ir ($CHCl_3$), 3600 and 3440 cm^{-1} (free and assoc OH); uv (95% EtOH), 219 mμ (ε 7070), 227 (7320), 281 (2930), and 287 sh (2540); nmr ($CDCl_3$), δ 6.7–7.3 (3 H m, aryl CH), 3.82 (3 H s, OCH_3), an overlapping doublet in the region 3.7–3.9 (2 H, CH_2OR), 2.05 (1 H s, disappears with added D_2O, OH), and 1.0–3.5 (11 H m, aliphatic CH); mass spectrum, molecular ion m/e 232, abundant fragments m/e 201, 196, 139, 112, 57, 43, and 41.

Anal. Calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found: C, 77.58; H, 8.71.

A comparable reduction employing 1.022 g (27.0 mmol) of $LiAlH_4$, 5.009 g (20.4 mmol) of the acid **1**, and 140 ml of tetrahydrofuran yielded 4.779 g of neutral product as a white solid. Recrystallization from hexane separated 3.821 g (80.8%) of the epimeric **alcohol 18** as white crystals, mp 94–95°, identified with the subsequently described sample by a mixture melting point and comparison of ir and nmr spectra.

A solution containing 4.701 g (21.9 mmol) of the olefin **16** and 13.9 mmol of B_2H_6 in 20 ml of tetrahydrofuran was stirred at 25–30° for 2 hr and then treated with 2.6 ml of water. The resulting mixture was heated to 45–50°, treated successively with

(13) D. C. Kleinfelter and P. von R. Schleyer, *Org. Syn.*, **42**, 79 (1962).

(14) A plate coated with silicic acid and eluted with a hexane–Et_2O mixture was employed for this analysis.

2.5 ml of aqueous 3 *M* NaOH and 2.7 ml of aqueous 30% H_2O_2 and then stirred at 40° for 1.5 hr. After the resulting mixture had been partitioned between aqueous NaCl and Et_2O, the organic layer was dried and concentrated to leave 5.248 g of the crude alcohol, mp 83.5–88°. Recrystallization (hexane) separated 4.18 g (81.9%) of the **alcohol 18** as white crystals, mp 94–94.5°. Recrystallization raised the melting point to 95–95.5°; ir ($CHCl_3$), 3590 and 3440 cm^{-1} (free and assoc OH); uv (95% EtOH), 228 mμ (ε 7820), 282 (3010), and 288 (2610); nmr ($CDCl_3$), δ 6.4–7.2 (3 H m, aryl CH), 3.6–4.2 (2 H m, CH_2OR), 3.71 (3 H s, OCH_3), and 0.8–3.4 (12 H m, OH and aliphatic CH); mass spectrum, molecular ion *m/e* 232, abundant fragments *m/e* 202, 201, 159, 121, and 115.

Anal. Calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found: C, 77.58; H, 8.68.

Bromination of the Acid 2.—A solution of 199 mg (0.81 mmol) of the acid **2** in 2 ml of HOAc was treated with 0.05 ml (*ca.* 1 mmol) of Br_2 and the resulting solution was stirred at 25–30° for 1 hr and then concentrated under reduced pressure. Attempts to recrystallize the residual crude **acid 22** (267 mg of viscous orange oil) were unsuccessful; ir ($CHCl_3$), 1710 cm^{-1} (carboxyl C=O); nmr ($CDCl_3$), δ 7.23 (1 H s, aryl CH), 6.85 (1 H s, aryl CH), 3.80 (3 H s, OCH_3), 3.62 (2 H d, J = 6 Hz, $ArCHCO_2R$), and 0.8–3.5 (*ca.* 11 H m, aliphatic CH). A mixture of 173 mg (0.5 mmol) of the crude acid **22** and 1 ml (14 mmol) of $SOCl_2$ was stirred for 4 hr and the resulting solution was poured into aqueous NH_3 and extracted with CH_2Cl_2. The organic extract was dried and concentrated to leave 198 mg of the crude amide **24**, mp 167–170°. Recrystallization (H_2O–EtOH) separated 135 mg (78.5%) of the **bromo amide 24** as white needles, mp 172–173.5°. After recrystallization the material melted at 173.5–174.5°; ir ($CHCl_3$), 1680 cm^{-1} (amide C=O); uv (95% EtOH), 288 mμ (ε 4620) and 294 (4210); nmr [$(CD_3)_2SO$], δ 7.23 (1 H s, aryl CH), 6.85 (1 H s, aryl CH), 7.42 and 6.87 (2 H, br, NH_2), 3.72 (3 H s, OCH_3), 3.52 (1 H d, J = 6 Hz, $ArCHCONR_2$), and 1.0–3.3 (10 H m, aliphatic CH); mass spectrum, abundant fragments *m/e* 186, 144, 116, and 115.

Anal. Calcd for $C_{15}H_{18}BrNO_2$: C, 55.56; H, 5.59; N, 4.32; Br, 24.65. Found: C, 55.75; H, 5.74; N, 4.33; Br, 24.61.

To a cold (0°) solution prepared from 248 mg (1.86 mmol) of $AlCl_3$, 283 mg (3.61 mmol) of AcCl, and 0.6 ml of CH_2Cl_2 was added, dropwise and with stirring, a solution of 252 mg (*ca.* 0.7 mmol) of the crude bromo acid **22** in 1.2 ml of CH_2Cl_2. Gas evolution was observed during the addition. The resulting mixture was stirred at 0° for 15 min and at 25–30° for 45 min and then partitioned between aqueous HCl and CH_2Cl_2. The organic extract was dried and concentrated and the residual yellow solid (205 mg) was recrystallized (H_2O–EtOH) to separate 90.2 mg (44%) of the **bromo olefin 26** as pale yellow plates, mp 130.5–132°. Recrystallization raised the melting point to 131–133°; ir ($CHCl_3$), 1630 cm^{-1} (C=C); uv (95% EtOH), 217 mμ (ε 27,900), 269 (13,400), 280 sh (10,600), 306 (2750), and 316 sh (1950); nmr ($CDCl_3$), δ 7.17 (1 H s, aryl CH), 6.88 (1 H s, aryl CH), 3.81 (3 H s, OCH_3), 3.09 (2 H, br, benzylic CH_2), 2.1–2.5 (4 H m, allylic CH_2), and 1.5–2.0 (4 H m, aliphatic CH_2); mass spectrum, molecular ion *m/e* 280 (^{81}Br isotope), abundant fragments *m/e* 252, 250, 199, 171, and 128.

Anal. Calcd for $C_{14}H_{15}BrO$: C, 60.23; H, 5.42; Br, 28.59. Found: C, 60.22; H, 5.27; Br, 28.80.

Acetylation of the Acid 2.—To a cold (0°) solution prepared from 752 mg (5.63 mmol) of $AlCl_3$, 773 mg (9.83 mmol) of AcCl, and 1.6 ml of CH_2Cl_2 was added a solution of 492 mg (2.00 mmol) of the acid **2** in 2.6 ml of CH_2Cl_2. The resulting solution was stirred at 0° for 20 min and at 25–30° for 40 min and partitioned between aqueous HCl and CH_2Cl_2. After the CH_2Cl_2 solution had been dried and concentrated, the crude **keto acid 23** was obtained as a viscous oil (634 mg) which could not be induced to crystallize; ir ($CHCl_3$), 1710 (carboxyl C=O) and 1660 cm^{-1} (conjugated ketone C=O); nmr ($CDCl_3$), δ 9.27 (1 H s, COOH), 7.43 (1 H s, aryl CH), 6.93 (1 H s, aryl CH), 3.82 (3 H s, OCH_3), 3.69 (1 H d, J = 6 Hz, $ArCHCO_2R$), 2.55 (3 H s, CH_3CO), and 1.0–3.5 (10 H, aliphatic CH).

A solution of 289 mg (1 mmol) of the crude keto acid **23** and 1.8 ml of an aqueous solution containing 2.7 mmol of NaOCl in 5 ml of aqueous 10% NaOH was stirred at 25–30° for 5 min and at 40° for 30 min. The resulting solution was successively treated with aqueous $NaHSO_3$, extracted with CH_2Cl_2, acidified with aqueous HCl, and extracted with CH_2Cl_2. After the final extract had been dried and concentrated, an Et_2O solution of the residual solid (231 mg) was decolorized (carbon) and diluted with hexane. The **diacid 25** separated as 221 mg (76.3% based on acid **2**) of white needles: mp 211–212°; ir (KBr pellet), 1740 (intramolecularly H-bonded carboxyl C=O) and 1710 cm^{-1} (carboxyl C=O); uv (95% EtOH), 212 mμ (ε 30,400), 243 (8540), and 304 (4480); nmr ($CDCl_3$), δ 10.6 (2 H s, COOH), 7.81 (1 H s, aryl CH), 7.05 (1 H s, aryl CH), 3.98 (3 H s, OCH_3), 3.75 (1 H d, J = 6 Hz, $ArCHCO_2R$), and 1.0–3.5 (10 H m, aliphatic CH); mass spectrum, abundant fragments *m/e* 58, 57, 56, 44, and 43.

Anal. Calcd for $C_{16}H_{18}O_5$: C, 66.19; H, 6.25. Found: C, 66.17; H, 6.28.

Preparation of the Hydroxy Acids 30 and 34.—To a vigorously stirred mixture of 31.73 g (0.330 mol) of sublimed (220–250° at 0.05 mm), powdered *t*-BuONa, 34.7 g (0.159 mol) of the alcohol **8**, and 500 ml hexane was added, dropwise over a 15-min period, 230 ml of a hexane solution containing 0.356 mol of *n*-BuLi, while the reaction mixture was kept at approximately 30°. The resulting dark red solution was stirred at 25–30° for 1 hr and then siphoned, with stirring, into a flask containing powdered Dry Ice. The reaction mixture was diluted with 450 ml of H_2O and then 30 g of Na_2CO_3 was added with stirring and the resulting mixture was allowed to stand overnight. The relatively insoluble sodium salt of acid **30** was collected. From the remaining organic layer, 2.32 g of the crude unchanged alcohol **8** was recovered. The sodium salt of acid **30** was acidified with aqueous HCl and extracted with CH_2Cl_2. After the CH_2Cl_2 extract had been dried and concentrated, the residual acid (36.90 g) was recrystallized (CH_2Cl_2–hexane) to separate 33.8 g (88.0% based on unrecovered alcohol) of the acid **30**, mp 133–137°. The pure **hydroxy acid 30** crystallized (CH_2Cl_2–hexane) as white needles: mp 136–137°; ir ($CHCl_3$), 3240 (broad, OH) and 1725 cm^{-1} (carboxyl C=O); uv (95% EtOH), 291 mμ (ε 2860) with intense end absorption; nmr ($CDCl_3$), δ 7.4–8.8 (2 H br, OH and COOH), an AB pattern with J = 9 Hz and estimated line positions of 7.38 and 6.97 (2 H, aryl CH at C-5 and C-6), 5.35 (1 H d, J = 6.5 Hz, ArCHOR), 4.05 (3 H s, OCH_3), and 1.0–3.1 (10 H m, aliphatic CH); mass spectrum, abundant fragments *m/e* 258, 244, 226, 213, 212, 198, and 184.

Anal. Calcd for $C_{15}H_{18}O_4$: C, 68.68; H, 6.92. Found: C, 68.49; H, 6.89.

Reaction of 2.758 g (10.5 mmol) of the acid **30** with excess ethereal CH_2N_2 yielded 2.70 g (92.8%) of the **methyl ester 40** as white needles (mp 120.5–121.5°) from hexane. Recrystallization raised the melting point to 121–122°; ir ($CHCl_3$), 3570, 3400 (OH), 1735, and 1705 cm^{-1} (ester C=O, partial intramolecular H bonding); uv (95% EtOH), 292 mμ (ε 3190); nmr ($CDCl_3$), AB pattern with J = 8.5 Hz and estimated line positions of δ 7.27 and 6.87 (2 H, aryl CH at C-5 and C-6), 5.17 (1 H br t, collapsed to d, J = 6 Hz, upon addition of D_2O, ArCHOR), 3.92 (3 H s, OCH_3), 3.83 (3 H s, OCH_3), and 1.0–3.3 (11 H m, OH and aliphatic CH); mass spectrum, molecular ion *m/e* 276, abundant fragments *m/e* 248, 243, 216, 201, 165, 115, 44, and 41.

Anal. Calcd for $C_{16}H_{20}O_4$: C, 69.54; H, 7.30. Found: C, 69.54; H, 7.34.

To a stirred solution prepared from 2.010 g (9.22 mmol) of the alcohol **8**, 50 ml of hexane, 5.95 ml of a hexane solution containing 9.22 mmol of *n*-BuLi, and 1.12 g (9.62 mmol) of $(Me_2NCH_2-)_2$ was added 6.10 ml of a hexane solution containing 9.45 mmol of *n*-BuLi. The resulting mixture from which a tan precipitate began to separate after 2 min, was refluxed with stirring for 30 min and then siphoned into a stirred mixture of Dry Ice and hexane. The resulting mixture was extracted with aqueous Na_2CO_3 and the remaining hexane solution was concentrated to separate 525 mg of the unchanged alcohol **8**. After the aqueous extract had been acidified and extracted with CH_2Cl_2, the organic layer was dried and concentrated to leave 1.836 g of the crude acidic products as a yellow oil. Fractional crystallization (CH_2Cl_2–hexane and CH_2Cl_2) separated 1.4713 g (82.3%) of crystalline fractions containing various proportions of the acids **30** and **34**. Recrystallization of the more soluble fractions separated a sample of the pure **hydroxy acid 30** as white needles, mp 136–137°, identified with the previously described sample by comparison of ir spectra. From the less soluble fractions, recrystallization (CH_2Cl_2–hexane) separated the pure **hydroxy acid 34** as white needles: mp 154–156°; ir ($CHCl_3$), 3570, 3260 (OH), and 1730 cm^{-1} (carboxyl C=O); uv (95% EtOH), 213 mμ (ε 28,200), 244 (7920), and 304 (4170); nmr (pyridine-d_5), δ 11.2 (2 H br, OH and COOH), 8.07 (1 H s, aryl CH), 7.43 (1 H s, aryl CH), 5.43 (1 H d, J = 6 Hz, ArCHOR), 3.81 (3 H s, OCH_3), and 0.9–3.4 (10 H m, aliphatic CH); mass spectrum,

abundant fragments *m/e* 200, 172, 171, 141, 129, 128, 115, and 44.

Anal. Calcd for $C_{15}H_{18}O_4$: C, 68.68; H, 6.92. Found: C, 68.45; H, 6.84.

Preparation of the Keto Acid Derivatives 41 and 42.—After reaction of 1.002 g (3.82 mmol) of the hydroxy acid **30** with 1.2 ml (3.2 mmol) of aqueous 2.67 *M* H_2CrO_4[13] in 100 ml of acetone at 2–4° for 5 min, the excess oxidant was destroyed with *i*-PrOH and the solution was concentrated and partitioned between H_2O and CH_2Cl_2. The organic layer was dried and concentrated to leave 917 mg (92.3%) of the crude keto acid **41** as a tan solid, mp 211–215°. An EtOH solution of the product was decolorized (charcoal) and diluted with hexane. The pure **keto acid 41** crystallized as pale yellow prisms: mp 214–216°; ir ($CHCl_3$), 1715 cm^{-1} (br, carboxyl and ketone C=O); uv (95% EtOH), 218 mμ (ε 23,200), 248 (6490), and 323 (4060); nmr (pyridine-d_5), δ 14.4–15.4 (1 H, COOH), AB pattern with J = 8.5 Hz and line positions estimated to be 7.43 and 7.30 (2 H, aryl CH at C-5 and C-6), 3.79 (3 H s, OCH_3), and 0.8–3.5 (10 H m, aliphatic CH).

Anal. Calcd for $C_{15}H_{16}O_4$: C, 69.21; H, 6.20. Found: C, 69.19; H, 6.24.

The same reaction procedure was followed with 989 mg (3.59 mmol) of the hydroxy ester **40** and 1.15 ml (3.07 mmol) of aqueous 2.67 *M* H_2CrO_4[13] in 60 ml of acetone. The crude product (1.177 g of pale yellow oil) was distilled in a short-path still (0.07 mm and 160–170° bath) to separate 966 mg of the **keto ester 42** as a viscous yellow liquid: ir ($CHCl_3$), 1720 cm^{-1} (broad, ester and ketone C=O); uv (95% EtOH), 220 mμ (ε 23,700), 244 (6650), and 323 (4280); nmr ($CDCl_3$), AB pattern with J = 8.5 Hz and estimated line positions of δ 7.48 and 7.20 (2 H, aryl CH at C-5 and C-6), 3.95 (3 H s, OCH_3), 3.85 (3 H s, OCH_3), and 0.9–3.5 (10 H m, aliphatic CH); mass spectrum, molecular ion *m/e* 274, abundant fragments *m/e* 259, 243, 241, 115, 104, 77, 59, 55, 45, 44, 43, 41, and 39.

Anal. Calcd for $C_{16}H_{18}O_4$: C, 70.05; H, 6.61. Found: C, 69.92; H, 6.59.

Preparation of the Unsaturated Acid Derivatives 35 and 43.—A solution of 4.857 g (18.6 mmol) of the hydroxy acid **30** and 436 mg of TsOH in 125 ml of PhH was refluxed with continuous separation of H_2O for 1 hr and then washed with H_2O, dried, and concentrated. The residual unsaturated acid **35**, mp 155–157°, amounted to 4.468 g (98.8%). A portion of the material was recrystallized (CH_2Cl_2-hexane) to give the pure **unsaturated acid 35** as pale yellow prisms: mp 161.5–162.5°; ir ($CHCl_3$), 1730 cm^{-1} (ester C=O); uv (95% EtOH), 232 mμ (ε 21,800), 264 (11,500), and 318 (4140); nmr ($CDCl_3$), δ 11.20 (1 H s, COOH), 7.38 (1 H s, vinyl CH), 7.40 (1 H d, J = 8 Hz, aryl CH), 6.73 (1 H d, J = 8 Hz, aryl CH), 4.00 (3 H s, OCH_3), and 0.8–3.2 (9 H m, aliphatic CH); mass spectrum, molecular ion *m/e* 244, abundant fragments *m/e* 226, 212, and 198.

Anal. Calcd for $C_{15}H_{16}O_3$: C, 73.75; H, 6.60. Found: C, 73.74; H, 6.55.

A 119-mg (0.487 mmol) sample of the unsaturated acid was esterified with excess ethereal CH_2N_2 and the crude product was recrystallized (hexane) to separate 74.5 mg (59.5%) of the **unsaturated ester 43** as pale yellow plates: mp 95–96°; ir ($CHCl_3$), 1720 (ester C=O) and 1615 cm^{-1} (C=C); uv (95% EtOH), 235 mμ (ε 21,200), 262 (11,300), and 316 (4300); nmr ($CDCl_3$), δ 7.31 (1 H d, J = 8.5 Hz, aryl CH), 6.68 (1 H d, J = 8.5 Hz, aryl CH), 6.60 (1 H s, vinyl CH), 3.92 (3 H s, OCH_3), 3.83 (3 H s, OCH_3), and 0.8–3.2 (9 H m, aliphatic CH); mass spectrum, molecular ion *m/e* 258, abundant fragments *m/e* 227, 226, 199, 198, 141, 128, and 115.

Anal. Calcd for $C_{16}H_{18}O_3$: C, 74.40; H, 7.02. Found: C, 74.29; H, 7.05.

Preparation of the Unsaturated Diesters 36 and 37a.—To a solution of 4.051 g (16.6 mmol) of the unsaturated acid **35** in 100 ml of tetrahydrofuran was added, dropwise and with stirring, 23 ml of an Et_2O solution containing 37.3 mmol of MeLi. During the initial phase of the addition a white precipitate separated and then largely redissolved as the addition continued to give a deep red solution. After the solution had been stirred at 35–40° for 15 min it was siphoned onto Dry Ice with thorough mixing. The resulting mixture was diluted with Et_2O and extracted with aqueous Na_2CO_3. The aqueous extract was acidified (HCl) and the crude acid mixture which separated was collected, dissolved in 100 ml of tetrahydrofuran, and esterified with excess ethereal CH_2N_2. The neutral product, a mixture[14] of esters **36** and **37a**, amounted to 5.289 g of a pale orange oil which partially crystallized on standing. The material was chromatographed (SiO_2). The early fractions eluted (1% Et_2O in PhH) were recrystallized (EtOH) to separate 1.60 g (30.5%) of the **diester 36** as white prisms: mp 105.5–106°; ir ($CHCl_3$), 1725 cm^{-1} (ester C=O); uv (95% EtOH), 235 mμ (ε 28,800) and 317 (3850); nmr ($CDCl_3$), δ 7.45 (1 H d, J = 8.5 Hz, aryl CH), 6.73 (1 H s, vinyl CH), 6.69 (1 H d, J = 8.5 Hz, aryl CH), 3.93, 3.85 3.61 (three 3 H s, OCH_3), and 0.8–3.2 (8 H m, aliphatic CH); mass spectrum, molecular ion *m/e* 316, abundant fragments *m/e* 284, 257, 256, 225, 46, 45, 43, and 31.

Anal. Calcd for $C_{18}H_{20}O_5$: C, 68.34; H, 6.37. Found: C, 68.28; H, 6.44.

The later fractions eluted (2–4% Et_2O in PhH) were combined and recrystallized (EtOH) to separate 2.00 g (38%) of the **diester 37a** as white needles: mp 91–91.5°; ir ($CHCl_3$), 1730 cm^{-1} (ester C=O); uv (95% EtOH), 273 mμ (ε 14,000) with intense end absorption (ε 22,900 at 210 mμ); nmr ($CDCl_3$), δ 7.22 (1 H d, J = 8.5 Hz, aryl CH), 6.89 (1 H d, J = 8.5 Hz, aryl CH), 4.44 (1 H br, $ArCHCO_2R$), 3.86 (6 H s, OCH_3), 3.64 (3 H s, OCH_3), 2.1–2.7 (4 H m, allylic CH_2), and 1.5–2.1 (4 H m, aliphatic CH_2); mass spectrum, molecular ion *m/e* 316, abundant fragments *m/e* 257, 256, 225, 44, and 31.

Anal. Calcd for $C_{18}H_{20}O_5$: C, 68.34; H, 6.37. Found: C, 68.49; H, 6.52.

A mixture of 485 mg (1.54 mmol) of the diester **37a**, 156 mg (3.89 mmol) of NaOH, and 7 ml of H_2O was refluxed under N_2 for 45 min. The resulting solution was acidified to separate the crude acidic product which was collected and recrystallized (H_2O–MeOH). The diacid **37b** separated as 329 mg (74%) of white needles, mp 187° dec (dependent on rate of heating). Recrystallization raised the decomposition point of the **diacid 37b** to 200° (dependent on rate of heating); ir (KBr pellet), 1720 (carboxyl C=O) and 1640 cm^{-1} (C=C); uv (95% EtOH), 273 mμ (ε 13,400) and 333 (2220); nmr (pyridine-d_5), AB pattern (J = 8 Hz) with estimated line positions at δ 7.32 and 7.03 (2 H, aryl CH), 5.05 (1 H br s, $ArCHCO_2R$), 3.81 (3 H s, OCH_3), 2.0–3.0 (4 H m, allylic CH_2), and 1.3–2.0 (4 H m, aliphatic CH_2).

Anal. Calcd for $C_{16}H_{16}O_5$: C, 66.66; H, 5.59. Found: C, 66.68; H, 5.66.

Hydrogenation of the Diester 37a.—A solution of 324 mg (1.03 mmol) of the diester **37a** in 7.5 ml of MeOH was hydrogenated at 25° and atmospheric pressure over 62.5 mg of a 5% Pt-C catalyst. After 2.75 hr the H_2 uptake (25 ml or 1.0 equiv) ceased and the mixture was filtered and concentrated. The residual crude diester **38** amounted to 339 mg of colorless liquid [ir ($CHCl_3$), 1730 cm^{-1} (ester C=O)] which has three nmr peaks ($CDCl_3$) attributable to methoxyl groups at δ 3.85, 3.77, and 3.68. A mixture of this crude diester with 294 mg (7.35 mmol) of NaOH and 20 ml of H_2O was refluxed for 1.75 hr and the resulting solution was acidified and extracted with CH_2Cl_2.

After the organic extract had been dried and concentrated, a solution of the crude acidic product in PhH–CH_2Cl_2 deposited 258 mg (86.3%) of the crystalline diacid **4**, mp 190–191° dec. Recrystallization (acetone–hexane) afforded the **diacid 4** as white needles: mp 189.5–190.5° dec; ir (KBr pellet), 1735 and 1690 cm^{-1} (carboxyl C=O); uv (95% EtOH), 299 mμ (ε 3280) with intense end absorption; nmr (pyridine-d_5), δ 14.80 (2 H s, carboxyl OH), AB pattern (J = 8.5 Hz) with estimated line positions at 7.29 and 6.93 (2 H, aryl CH), 4.45 (1 H d, J = 4 Hz, $ArCHCO_2R$), 3.73 (3 H s, OCH_3), and 1.0–3.9 (10 H m, aliphatic CH).

Anal. Calcd for $C_{16}H_{18}O_5$: C, 66.19; H, 6.25. Found: C, 66.18; H, 6.22.

A 149-mg sample of the diacid **4** was esterified with ethereal CH_2N_2 to yield 170 mg of the crude diester **39** as a pale yellow oil. The crude product was distilled in a short-path still (0.05 mm and 140–150° bath) to separate 143 mg (88%) of the **diester 39** as a pale yellow liquid: ir ($CHCl_3$), 1730 cm^{-1} (ester C=O); uv (95% EtOH), 300 mμ (ε 3470) with intense end absorption (ε 25,500 at 210 mμ); nmr ($CDCl_3$), AB pattern (J = 9 Hz) with estimated line positions at δ 7.27 and 6.88 (2 H, aryl CH), 3.84 (6 H s, OCH_3), 3.65 (3 H s, OCH_3), and 0.9–4.0 (11 H m, aliphatic CH); mass spectrum, weak molecular ion *m/e* 318, abundant fragments *m/e* 258, 220, 206, 205, and 57.

Anal. Calcd for $C_{18}H_{22}O_5$: C, 67.91; H, 6.97. Found: C, 68.33; H, 7.14.

Hydrogenation of the Diacid 37b.—A solution of 422 mg (1.45 mmol) of the diacid **37b** in a mixture of 20 ml of HOAc and 20 ml of tetrahydrofuran was hydrogenated at 25° and atmospheric pressure over 81.7 mg of a 5% Pt-C catalyst. After 2.75 hr when the H_2 uptake was 37.0 ml (1.04 equiv), the mixture was

filtered and concentrated. The residual solid was recrystallized (acetone–hexane) to separate 343.6 mg (81.2%) of the **diacid 3** as white needles, mp 196.5–198.5° dec. Recrystallization raised the decomposition point to 201–203°; ir (KBr pellet), 1705 cm^{-1} (carboxyl C=O); uv (95% EtOH), 300 mμ (ε 3390) with intense end absorption; nmr (pyridine-d_5), δ 12.8–14.2 (2 H br, carboxyl OH), AB pattern (J = 8.5 Hz) with estimated line position at 7.28 and 6.95 (2 H, aryl CH), 4.71 (1 H d, J = 7 Hz, $ArCHCO_2R$), 3.78 (3 H s, OCH_3), and 0.8–3.5 (10 H m, aliphatic CH).

Anal. Calcd for $C_{16}H_{18}O_5$: C, 66.19; H, 6.25. Found: C, 66.52; H, 6.44.

A solution of 120 mg (0.415 mmol) of the diacid **3** and 574 mg (8.7 mmol) of KOH in 3.5 ml of $HOCH_2CH_2OH$ was refluxed under N_2 for 2.5 hr and then poured into H_2O, acidified, and extracted with CH_2Cl_2. After the organic extract had been dried and concentrated, the residual crystalline diacid **4** (95.9 mg or 79.8%, mp 184.5–186° dec) was recrystallized (acetone–hexane) to separate the diacid **4**, mp 187–188° dec, identified with the previously described sample by a mixture melting point and comparison of ir spectra.

A 166-mg sample of the diacid **3** was esterified with ethereal CH_2N_2 and the crude neutral product was distilled in a short-path still (0.05 mm and 140–150° bath) to yield 168 mg (92%) of the **diester 38** as a colorless liquid: ir ($CHCl_3$), 1735 cm^{-1} (ester C=O); uv (95% EtOH), 302 mμ (ε 3750) with intense end absorption (ε 27,700 at 210 mμ); nmr ($CDCl_3$), AB pattern (J = 8.5 Hz) with estimated line positions at δ 7.27 and 6.90 (2 H, aryl CH), 4.22 (1 H d, J = 6 Hz, $ArCHCO_2R$), 3.86, 3.79, 3.68 (three 3 H s, OCH_3), and 0.8–3.5 (10 H m, aliphatic CH); mass spectrum, molecular ion m/e 318, abundant fragments m/e 220, 206, 205, 126, 84, 83, 55, and 43.

Anal. Calcd for $C_{18}H_{22}O_5$: C, 67.91; H, 6.97. Found: C, 67.73; H, 7.06.

Metallation of the Alcohol 18.—A suspension of 2.501 g (10.8 mmol) of the alcohol **18** in 55 ml of hexane was treated with a hexane solution containing 11.9 mmol of n-BuLi. A solution was formed from which a new precipitate slowly separated. To this stirred suspension was added 1.443 g (12.4 mmol) of $(Me_2NCH_2-)_2$ and 12.4 mmol of n-BuLi in hexane solution. The resulting suspension was refluxed for 45 min and then added to excess Dry Ice with thorough agitation. The usual isolation procedure separated 981 mg of crude starting material in the neutral fraction and 2.077 g of crude acid product as an oil. This acidic product was esterified with ethereal CH_2N_2 to give 2.119 g of orange oil which contained[14] three components. Chromatography on SiO_2 separated an additional 326 mg of the starting alcohol **18** (eluted with Et_2O–PhH) followed by 245 mg of a liquid fraction (eluted with Et_2O–PhH) with ir and nmr absorption suggesting it to be a mixture of the ester **32** and the lactone **33**. Our efforts to obtain either of these components pure were unsuccessful.

Later chromatographic fractions (eluted with Et_2O–PhH) afforded 328 mg of crude ester **31** which was recrystallized (CH_2Cl_2–hexane). The pure **ester 31** separated as 246 mg of white needles: mp 115.5–116°; ir ($CHCl_3$), 3590, 3470 (OH), and 1720 cm^{-1} (ester C=O); uv (95% EtOH), 215 mμ (ε 34,500), 244 (9300), and 304 (4750); nmr ($CDCl_3$), δ 7.58 (1 H br s, aryl CH), 7.05 (1 H br s, aryl CH), 4.05 (2 H d, J = 3.5 Hz, CH_2OR), 3.88 (6 H s, OCH_3), and 0.7–3.5 (12 H m, OH and aliphatic CH); mass spectrum, abundant fragments m/e 57, 45, 44, 43, 41, 31, 29, 28, 18, and 17.

Anal. Calcd for $C_{17}H_{22}O_4$: C, 70.32; H, 7.64. Found: C, 70.38; H, 7.64.

Registry No.—**1**, 19765-79-8; **2**, 19765-80-1; **3**, 19765-81-2; **4**, 19765-82-3; **6**, 19765-83-4; **8**, 19765-84-5; **9**, 19766-18-8; **10**, 19765-85-6; **11**, 19766-19-9; **12**, 19766-20-2; **13**, 19765-86-7; **14**, 19765-87-8; **15**, 19765-88-9; **16**, 19765-89-0; **17**, 19765-90-3; **18**, 19765-91-4; **19**, 19765-92-5; **21b**, 19765-93-6; **22**, 19765-94-7; **23**, 19765-95-8; **24**, 19779-41-0; **25**, 19765-96-9; **26**, 19766-21-3; **27**, 19779-42-1; **28**, 19765-97-0; **30**, 19765-98-1; **31**, 19765-99-2; **34**, 19766-00-8; **35**, 19766-22-4; **36**, 19766-23-5; **37a**, 19766-24-6; **37b**, 19766-01-9; **38**, 19779-43-2; **39**, 19766-02-0; **40**, 19766-03-1; **41**, 19766-04-2; **42**, 19766-05-3; **43**, 19766-25-7.

Notes

Effects of Solvent on the Cyclopropylidene–Allene Conversion[1]

W. M. JONES[2] AND JOHNNY M. WALBRICK

Department of Chemistry, University of Florida, Gainesville, Florida 32601

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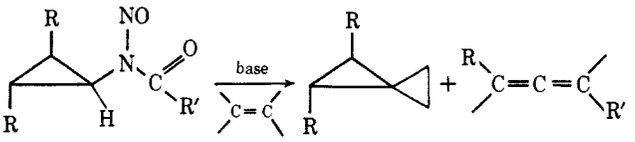
In previous investigations in these laboratories on the chemistry of substituted diazocyclopropanes and cyclopropylidenes, it was found that treatment of the N-nitrosourea or N-nitrosocarbamate of a cyclopropane with base in the presence of an alkene gives a very clean reaction yielding primarily two products, a spiropentane and an allene.[3–5] In an attempt to gain insight into the precursors of these products, the reaction using the 2,2-diphenylcyclopropyl system was studied in some



detail. From a variety of observations, it was concluded that both the spiropentane and the allene have the carbene as a common precursor. However, if this were the sole progenitor to both products, it was reasoned that a plot of the ratio of spiropentane to allene *vs.* the concentration of alkene should be linear. In fact, when such a plot was made (Figure 1), it showed a strong curvature.[5] Furthermore, although it was recognized that the curvature could arise from a solvent effect as a result of the large change in alkene concentration (1.14–11.35 M) the exceptionally good fit to

(1) Based partly upon a dissertation submitted by J. M. Walbrick to the Faculty of the University of Florida in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(2) Alfred P. Sloan Fellow, 1963–1967.

(3) W. M. Jones, M. H. Grasley, and D. G. Baarda, *J. Am. Chem. Soc.*, **86**, 912 (1964); D. L. Muck and W. M. Jones, *ibid.*, **88**, 74 (1966); W. M. Jones, D. L. Muck, and T. K. Tandy, Jr., *ibid.*, **88**, 68 (1966); W. M. Jones and D. L. Muck, *ibid.*, **88**, 3798 (1966); for additional work on cyclopropylidenes, see P. S. Skell and R. R. Engel, *ibid.*, **89**, 2912 (1967), and references included therein.

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(5) W. M. Jones and M. H. Grasley, *Tetrahedron Letters*, 927 (1962).