mum[26] at 282.5 mμ (ε 2780). The product has n.m.r. absorption[20] at δ 4.87 (1H, partially resolved multiplet, vinyl C–H), 3.13 (2H, partially resolved multiplet, –C=C–CH–C=C–), and 2.52 (3H singlet, CH_3–CO). The latter peak is superimposed on complex absorption in the region δ 1.5–2.8 (4H, aliphatic C–H).

Anal. Calcd. for $C_9H_{10}O_2$: C, 71.98; H, 6.71; mol. wt., 150. Found: C, 71.64; H, 6.64; mol. wt., 150 (mass spectrum).

Reaction of the Triketone 26 with Pyrrolidine.—A mixture of 858 mg. (5.11 mmoles) of the triketone **26**, 1.305 g. (18.4 mmoles) of pyrrolidine, 1.25 g. (10.4 mmoles) of anhydrous magnesium sulfate, and 15 ml. of benzene was heated to 50°, with stirring and under a nitrogen atmosphere, for 46 hr. after which time 20 ml. of 10% aqueous hydrochloric acid was added. The organic phase was diluted with ether, separated, washed with aqueous hydrochloric acid, dried, and concentrated. Chromatography of the residue (276 mg.) on 13.8 g. of Woelm alumina (activity grade III) separated the **pyrrolidylindanone 28** which crystallized from hexane as 41 mg. of yellow crystals, m.p. 97–98°. An additional 207 mg. of this same amino ketone **28**, m.p. 95–97°, was recovered from the aforementioned aqueous acid solution for a total yield of 248 mg. (25%). The amino ketone **28** has infrared absorption[25] at 1715 cm.$^{-1}$ (C=O) with ultraviolet maxima[26] at 246 mμ (ε 30,800) and 287 mμ (ε 2800).[34] The product has n.m.r. absorption[20] in the regions δ 6.9–7.8 (3H, aromatic C–H) and 1.8–3.8 (12H, aliphatic C–H).

Anal. Calcd. for $C_{13}H_{15}NO$: C, 77.58; H, 7.51; N, 6.96; mol. wt., 201. Found: C, 77.54; H, 7.57; N, 6.94; mol. wt., 201 (mass spectrum).

The mother liquors from the chromatographic fractions containing the amino ketone contained[35] a second minor component. An ether solution of the component was repeatedly washed with aqueous hydrochloric acid and then dried and concentrated. Sublimation of the residue afforded 9 mg. (1%) of the crude pyrone **27**, m.p. 105–107°, identified with the previously described sample by comparison of infrared and mass spectra. The later fractions from the chromatography, eluted with hexane–chloroform mixtures, afforded, after distillation in a short-path still, a few milligrams of a third component[35] as a yellow liquid, $n^{25}D$ 1.5430, with infrared absorption[25] at 1720 (C=O in a six-membered ring) and 1745 cm.$^{-1}$ (C=O in a five-membered ring). The mass spectrum of the material has a molecular ion peak at *m/e* 152 corresponding to a molecular formula $C_9H_{12}O_2$. This liquid is believed to be a partially purified sample of the saturated diketone **30**; however, our efforts to obtain enough of this product for characterization were not successful.

Preparation of the Hydroxy Diketone 32.—A solution of 5.10 g. (46.4 mmoles) of cyclohexane-1,2-dione,[36] 3.25 g. (46.4 mmoles) of methyl vinyl ketone, and 3.0 ml. of triethylamine in 20 ml. of ether was stirred at room temperature under a nitrogen atmosphere for 2.5 hr. Distillation of the reaction mixture separated 3.29 g. (40%) of the crude ketol **32** as a straw-colored liquid, b.p. 100–106° (0.01 mm.), $n^{24}D$ 1.5132, which slowly crystallized on standing, m.p. 122–132°. Repeated recrystallization from a hexane–ethyl acetate mixture separated one pure stereoisomer of the **hydroxy diketone 32** as white needles, m.p. 134–135.5°. The product has infrared absorption[19] at 3400 (broad, associated O–H), 1750 (C=O in a five-membered ring), 1705 (C=O), and 1365 cm.$^{-1}$ (CH_3–CO–) with an ultraviolet maximum[26] at 293 mμ (ε 54) and n.m.r. peaks[20] at δ 3.47 (1H, singlet, O–H) and 3.02 (1H, pair of doublets, J = 7 and 11.5 c.p.s., CH–CO–) as well as a singlet at δ 2.38 (3H, CH_3–CO) superimposed on complex absorption in the region δ 1.2–2.8 (9H, aliphatic C–H).

Anal. Calcd. for $C_{10}H_{14}O_3$: C, 65.91; H, 7.74; mol. wt., 182. Found: C, 65.98; H, 7.74; mole wt., 182 (mass spectrum).

(34) The corresponding maxima for *m*-dimethylaminoacetophenone are at 242 mμ (ε 39,900) and 360 mμ (ε 3470): A. E. Lutskiĭ and V. V. Dorofeev, *Zh. Obshch. Khim.*, **27**, 1064 (1957).

(35) A thin layer chromatographic plate coated with aluminum oxide and developed with either chloroform or a mixture of hexane and ethyl acetate was employed for this analysis.

(36) C. C. Hack, C. V. Banks, and H. Diehl, *Org. Syn.*, **32**, 35 (1952).

Perhydroindan Derivatives. V. The Synthesis of Some 3a-Substituted Derivatives[1a]

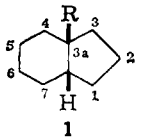
HERBERT O. HOUSE, SHARON G. BOOTS,[1b] AND VERA K. JONES

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

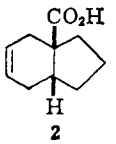
Received March 15, 1965

Several model compounds for ring closure studies have been prepared including 3a-carbomethoxymethyl-5-keto-*cis*-perhydroindan (**25**), 3a-acetyl-5-keto-*cis*-perhydroindan (**35**), and the epoxide of methyl 3-methylenecyclohexylacetate (**39**). The diazo ketones **3** and **27** were converted to the corresponding cyclopropyl ketones **4** and **26** and the reactions of these cyclopropyl ketones with hydrogen bromide and with lithium in ammonia were studied. Application of the Arndt–Eistert reaction to the diazo ketone **3** yielded, in addition to the expected product **5**, the cyclopropyl ketone **4** and two cyclobutanone derivatives **7** and **8**.

This study was prompted by a need for model compounds in the *cis*-fused perhydroindan series **1** which contained appropriate substituents at positions 3a and 5 to permit a study of the construction of a two-carbon bridge between these two positions. As a starting material, we utilized the unsaturated acid **2** which is readily accessible from the Diels–Alder reaction of 1,3-butadiene with cyclopentene-1-carboxylic acid.[2]



1



2

In following our initial plan, the conversion of the acid **2** to the homologous acid **6** *via* an Arndt–Eistert reaction,[3] the diazo ketone **3** was prepared and treated with silver benzoate and triethylamine in methanol.[4] The volatile product of this reaction proved to be a mixture containing only 50% of the desired ester **5** accompanied by 25% of the ketone **4**, as well as a mixture of ketones **7** and **8**.[5]

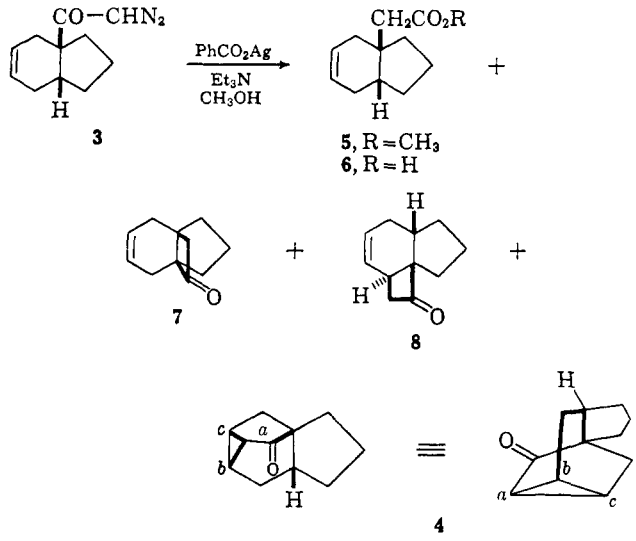
(1) (a) This work was supported by a research grant from the National Science Foundation (No. NSF G-25214); (b) National Institutes of Health Postdoctoral Fellow, 1964–1965.

(2) R. L. Kronenthal and E. I. Becker, *J. Am. Chem. Soc.*, **79**, 1095 (1957).

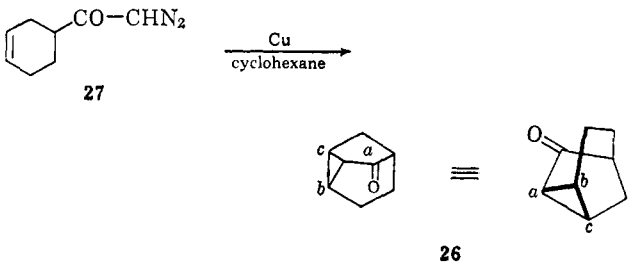
(3) (a) W. E. Bachmann and W. S. Struve, *Org. Reactions*, **1**, 38 (1942); (b) F. Weygand and H. J. Bestmann in "Newer Methods of Preparative Organic Chemistry," Vol. 3, W. Foerst, Ed., Academic Press Inc., New York, N. Y., 1964, p. 451.

(4) M. S. Newman and P. F. Beal, *J. Am. Chem. Soc.*, **72**, 5163 (1950).

(5) We have noted the formation of by-products in a previous application of this modification of the Arndt–Eistert procedure to an γ,δ-unsaturated diazo ketone derived from 3-cyclohexenylacetic acid: (a) H. O. House, R. G. Carlson, and H. Babad, *J. Org. Chem.*, **28**, 3359 (1963). (b) Interestingly, W. von E. Doering, E. T. Fossel, and R. L. Kaye [*Tetrahedron*, **21**, 25 (1965)] have recently reported finding no abnormal products from application of the Arndt–Eistert reaction to the δ,ε-unsaturated diazo ketope derived from 5-cycloheptenylcarboxylic acid.

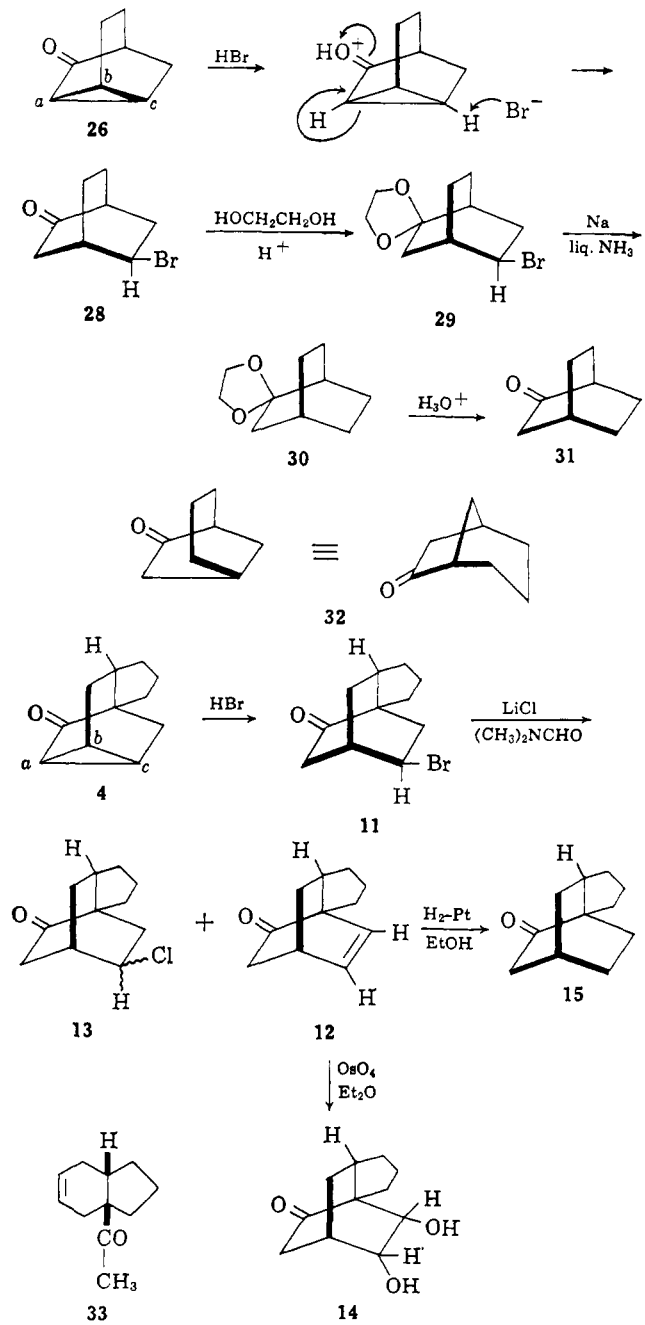


The ketonic products **4**, **7**, and **8** appear to have arisen from insertion of an α-ketocarbene, or a related intermediate,[6] into a carbon–carbon double bond or a carbon–hydrogen bond. The intramolecular addition of the intermediate from diazo ketone and copper to a carbon–carbon double bond has recently become a popular synthetic route to cyclopropyl ketones.[5b,7] In accord with these reports, reaction of the diazo ketone **3** with copper in refluxing cyclohexane produced the cyclopropyl ketone **4**; however, neither of the cyclobutanones **7** and **8** was detected in the mixture from the copper-catalyzed reaction.[8] It was apparent that our general synthetic objective, placing a two-carbon bridge between the 3a- and 5-positions of a *cis*-fused perhydroindan (**1**), could be solved rather neatly if a method could be found to selectively cleave the bond labeled *ab* in the cyclopropyl ketone **4**. Consequently, we examined several reactions of the cyclopropyl ketone **4** as well as its simpler analog **26** prepared from reaction of the diazo ketone **27** with copper.[9]



From the reaction of ketone **4** or **26** with hydrogen bromide in either acetic acid or methylene chloride only a single bromo ketone **11** or **28** was isolated. Although we have no experimental evidence bearing on the stereochemistry of these bromo ketones **11** and **28**, the probable mechanism of their formation (see Scheme I)[10] prompts us to assign tentatively the stereochemistry indicated. The structure of the bromo ketone **28** was established by conversion to the known

SCHEME I



bicyclo[2.2.2]octan-2-one (**31**) rather than the known bicyclo[3.2.1] ketone **32**. Consequently, reaction of the cyclopropyl ketone **26** with hydrogen bromide leads to cleavage of the bond labeled *ac* in structure **26** rather the desired cleavage of the *ab* bond.

The structure of the bromo ketone **11** from cyclopropyl ketone **4** is assigned by analogy to the behavior of simpler analog, the cyclopropyl ketone **26**, with hydrogen bromide; the spectroscopic properties of the

(6) (a) J. Hine, "Divalent Carbon," Ronald Press, New York, N. Y., 1964; (b) D. O. Cowan, M. M. Couch, K. R. Kopecky, and G. S. Hammond, *J. Org. Chem.*, **29**, 1922 (1964); (c) R. Huisgen, G. Binsch, and L. Ghosez, *Chem. Ber.*, **97**, 2628 (1964).

(7) (a) J. Novák and F. Šorm, *Collection Czech. Chem. Commun.*, **23**, 1126 (1958); (b) G. Stork and J. Ficini, *J. Am. Chem. Soc.*, **83**, 4678 (1961); (c) S. Masamune, *ibid.*, **86**, 735 (1964); (d) A. Small, *ibid.*, **86**, 2091 (1964); (e) S. Masamune and N. T. Castellucci, *Proc. Chem. Soc.*, 298 (1964); (f) W. von E. Doering and M. Pomerantz, *Tetrahedron Letters*, **No. 17**, 961 (1964); (g) F. Medina and A. Manjarrez, *Tetrahedron*, **20**, 1807 (1964).

(8) These observations would suggest that a more reactive intermediate, capable of insertion into a carbon–hydrogen bond, is formed in the Arndt–Eistert reaction. We are engaged in further study in an attempt to clarify this point.

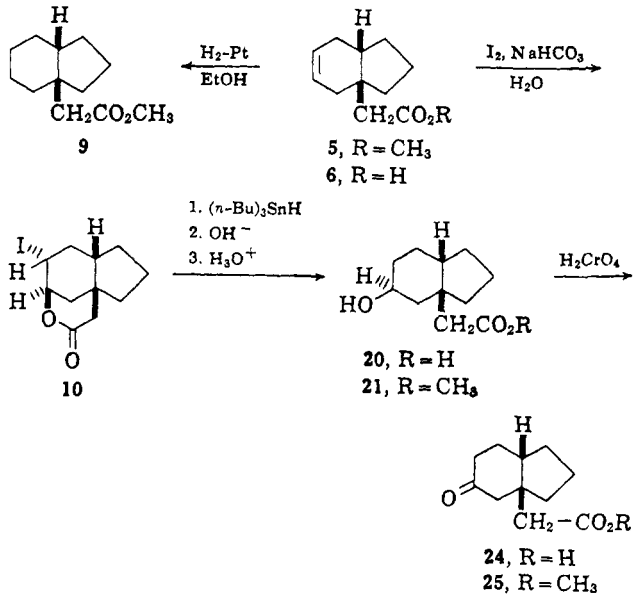
(9) This tricyclic ketone **26**, originally prepared by N. A. LeBel and J. E. Huber [*J. Am. Chem. Soc.*, **85**, 3193 (1963)], has very recently (ref. 5b) been prepared by the same method we employed.

(10) P. de Mayo, *Perfumery Essent. Oil Record*, **49**, 238 (1958).

transformation products **12–15** from the bromo ketone **11** did not permit us to distinguish between the assigned structures **11–15** and an analogous series of structures in which a bicyclo[3.2.1]octane ring system is present. This analogy was strengthened somewhat by the reductive cleavage of each of the cyclopropyl ketones **4** and **26** with lithium in liquid ammonia.[11] In each case a mixture of saturated alcohols and ketones was formed which was treated with chromic acid in acetone[12] to convert the secondary alcohols to the corresponding ketones. From the cyclopropyl ketone **4** we obtained the same saturated ketone **15** produced in Scheme I as well as a small amount (3%) of the unsaturated ketone **33**. This minor product **33** may well have resulted from a minor impurity in the starting ketone **4**. Similarly, reductive cleavage of the simpler analog **26** led to a mixture of ketones **31** and **32** in which the bicyclo[2.2.2]octane derivative **31** was the predominant product. Consequently, we are led to believe that either acid-catalyzed cleavage or reductive cleavage with lithium and ammonia results in predominant breaking of the bond labeled *ac* in cyclopropyl ketones **4** and **26**. This result, of course, is not useful in terms of our general synthetic objective. The cyclopropyl ketone **4** does not appear to be readily susceptible to nucleophilic attack since it was recovered unchanged after removing the ester **5** from a reaction mixture by saponification.

The unsaturated acid **6** was carried through the further transformation summarized in Scheme II. The only reaction worthy of note in the transformation of the acid **6** to the keto ester **25** is the use of tributyltin

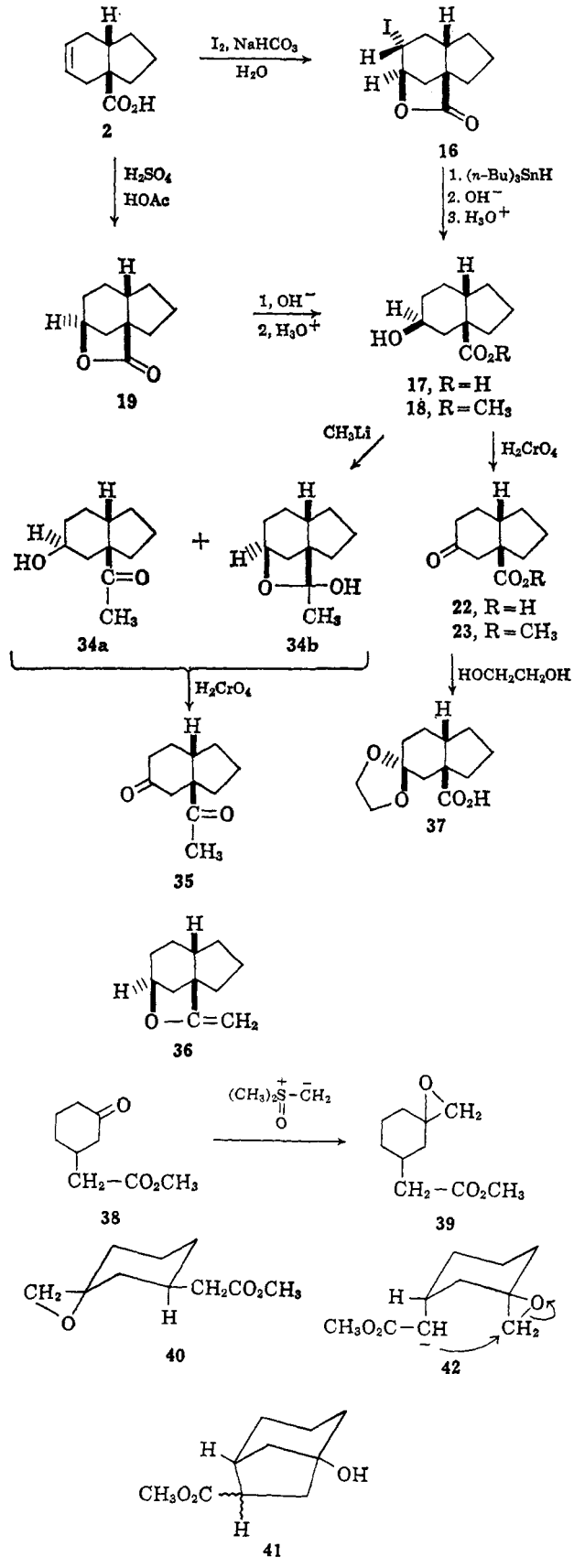
SCHEME II



hydride[13] for the hydrogenolysis of the carbon–iodine bond in the iodo lactone **10**. In our hands, this method was distinctly better than hydrogenolysis of the carbon–halogen bond over a catalyst such as Raney nickel or platinum.

The diketone **35** and the ketal acid **37** were also prepared employing the reaction schemes summarized in Scheme III. The intermediate **34**, obtained from re-

SCHEME III



(11) This reduction of cyclopropyl ketones, which we presume to be mechanistically analogous to the dissolving metal reduction of α,β-unsaturated ketones, has precedent in the previously described reduction of methyl cyclopropyl ketone to a mixture 2-pentanone and 2-pentanol: R. van Volkenburgh, K. W. Greenlee, J. M. Derfer, and C. E. Boord, *J. Am. Chem. Soc.*, **71**, 3595 (1949).

(12) The procedure of A. Bowers, T. G. Halsall, E. R. H. Jones, and A. J. Lemin, *J. Chem. Soc.*, 2548 (1953).

(13) H. G. Kuivila, *Advan. Organometal. Chem.*, **1**, 47 (1964).

action of methyllithium with the hydroxy acid **17**, appeared to be a mixture of tautomeric forms **34a** and **34b**. Since our efforts to separate this mixture were either ineffectual or led to the formation of a compound believed to be the vinyl ether **36**, the mixture was oxidized to the diketone **35**. The epoxy ester **39** was obtained by reaction of the corresponding keto ester **38** with the methylide[14] derived from trimethylsulfoxonium iodide. Although this liquid epoxy ester appears to be homogeneous (gas chromatography and thin layer chromatography), a mixture of stereoisomers would be expected[14a] in which the predominant isomer would have the structure **40** with both carbon substituents equatorial.[14] Various attempts to convert this epoxy ester **39** to the bicyclo[3.2.1]octane derivative **41** by the intramolecular alkylation reaction indicated in structure **42** afforded complex product mixtures from which no pure substance was isolated.

Experimental[15]

The Epoxide of Methyl 3-Methylenecyclohexaneacetate (39).—An ethereal solution of 1.406 g. (9.0 mmoles) of 3-ketocyclohexaneacetic acid[16] was esterified with diazomethane and the crude, neutral product was distilled to separate 1.32 g. (86%) of the **methyl ester 38**, b.p. 87–89° (0.9 mm.) [lit.[16] b.p. 132–133° (9–10 mm.)]. This ester has infrared absorption[17] at 1735 (ester C=O) and 1720 cm.$^{-1}$ (C=O), a molecular ion peak in its mass spectrum at *m/e* 170, and n.m.r. absorption[17] in the region δ 1.2–2.5 (11H, aliphatic C–H) as well as a singlet at δ 3.67 (3H, OCH_3). A 446.8-mg. (2.7-mmoles) sample of the methyl ester was added to a solution of dimethylsulfoxonium methylide prepared[14] from 89.5 mg. (3.7 mmoles) of sodium hydride, 662.4 mg. (3.0 mmoles) of trimethylsulfoxonium iodide, and 15 ml. of dimethyl sulfoxide. The mixture was stirred for 1 hr. at room temperature and for 1 hr. at 40–50°, then cooled, neutralized with acetic acid, and diluted with water. The resulting solution was continuously extracted with pentane for 2.5 days after which time the pentane extract was concentrated and distilled to separate 304 mg. (61%) of the **epoxide 39**, b.p. 70–72° (0.3 mm.). Although this product exhibited only a single spot on thin layer chromatography (silicic acid coating) and a single peak on gas chromatography (silicone fluid no. 710 on firebrick), we have no rigorous evidence that the product is a single stereoisomer. The product has infrared absorption[17] at 1735 cm.$^{-1}$ (ester C=O) with n.m.r.[17] singlets at δ 3.67 (3H, OCH_3) and 2.51 (2H, $\overset{O}{\diagup\diagdown}$ C—CH_2) as well as absorption in the region δ 1.0–2.3 (11H, aliphatic C–H).

Anal. Calcd. for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 65.46; H, 8.85.

3a-Carboxy-*cis*-3a,4,7,7a-tetrahydroindan (2).—Cyclopentanone was converted to the cyanohydrin acetate which was pyrolyzed to form 1-cyanocyclopentene, b.p. 48–48.5° (9 mm.), $n^{27.5}$D 1.4690 [lit.[18b] b.p. 75° (35 mm.), n^{27}D 1.4700], as previously described.[18] The same product was also obtained by dehydration of cyclopentanone cyanohydrin with phosphorus oxychloride in pyridine,[19] a procedure which we found to be more troublesome experimentally. Hydrolysis of the unsaturated nitrile with refluxing, 10% aqueous potassium hydroxide for 20 hr. produced 1-carboxycyclopentene (63–73% yield), m.p. 120–122° (lit.[19] m.p. 121°). A solution of 15.4 g. (0.137 mole) of this unsaturated acid, 0.50 g. of 2,5-di-*t*-butyl-1,4-hydroquinone, and 30 ml. of butadiene in 30 ml. of dimethylformamide was heated to 145–150° in an autoclave for 48 hr. The resulting mixture was diluted with benzene and extracted with aqueous potassium hydroxide. After acidification of the aqueous solution and extraction with ether, the ethereal extract was washed with saturated sodium chloride, dried, and concentrated. A solution of the residue (8.8 g. of white, waxy solid) in acetic acid was poured onto ice to separate 8.626 g. (38%) of the acid **2** as white prisms, m.p. 71–73°. The absence of the starting 1-carboxycyclopentene in this product could be demonstrated by gas chromatography.[20] Repeated recrystallization raised the melting point of this product to 77.5–78.5° (lit.[2] m.p. 80–80.5°). The product has broad infrared absorption[17] in the 3-μ region (associated O–H) with a peak at 1690 cm.$^{-1}$ (carboxyl C=O) and n.m.r. peaks[17] at δ 12.68 (1H, COOH) and 5.68 (2H, partially resolved multiplet, vinyl C–H) as well as broad absorption in the region δ 1.2–3.0 (11H, aliphatic C–H). The mass spectrum of the material has a molecular ion peak at *m/e* 166.

Preparation of the Diazo Ketone 3.—To a cold (5°) suspension of the dry sodium salt from 5.0 g. (0.030 mole) of the acid **2** in 30 ml. of benzene containing 0.7 ml. of pyridine was added, with stirring, 15 g. (0.18 mole) of oxalyl chloride. Immediate gas evolution was observed. The mixture was stirred at 5° for 2 hr. and then concentrated under reduced pressure. After the residue had been mixed with 30 ml. of benzene, the mixture was filtered and the filtrate was added to a cold (0°) ethereal solution containing 0.060 mole of diazomethane. The resulting mixture was stirred at 0° for 1 hr. and at room temperature for 1 hr. and then filtered and concentrated under reduced pressure. The residual crude diazo ketone **3** (5.64 g. of yellow liquid) has infrared absorption[17] at 2120 and 1640 cm.$^{-1}$ (–CO–CHN_2).

Preparation of the Cyclopropyl Ketone 4.—A mixture of 4.372 g. (23 mmoles) of the crude diazo ketone **3**, 260 mg. of copper bronze, and 25 ml. of cyclohexane was refluxed with stirring for 18 hr. at which time the infrared spectrum of the mixture had absorption at 1725 cm.$^{-1}$ but no longer absorbed in the region of 2100 cm.$^{-1}$. The mixture was filtered and concentrated to leave 3.905 g. of a brown liquid which was distilled to separate 2.79 g. of the crude cyclopropyl ketone **4** as a yellow liquid, b.p. 65–90° (1.2–1.4 mm.). This material was chromatographed on 200 g. of Florisil and the product, eluted with ether–hexane mixtures, was distilled in a short-path still (85° at 0.9 mm.) to separate 1.6 g. (41%) of the pure[21] cyclopropyl ketone. This product has infrared absorption[17] at 1725 cm.$^{-1}$ (C=O) with an ultraviolet maximum[22,23] at 277 mμ (ϵ 110) as well as intense end absorption (ϵ 2750 at 210 mμ).[23] The n.m.r. spectrum[17] has a complex pattern of absorption in the region δ 0.9–2.5 with no lower field absorption as would be expected of vinylic protons.

Anal. Calcd. for $C_{11}H_{14}O$: C, 81.44; H, 8.70; mol. wt., 162. Found: C, 81.15; H, 8.73; mol. wt., 162 (mass spectrum).

The Arndt–Eistert Reaction with the Diazo Ketone 3.—To a solution of 435 mg. (2.3 mmoles) of the diazo ketone **3** in 5 ml. of methanol was added, dropwise and with stirring, 0.65 ml. of a solution prepared from 257 mg. of silver benzoate and 2.2 g. of triethylamine.[4] At this time the nitrogen evolution (46 cc. or 0.78 equiv.) ceased. The resulting mixture was stirred at room temperature for 1 hr., treated with decolorizing carbon, heated to reflux, cooled, filtered, and concentrated. The residual oil (242 mg.) contained[20] a group of three or more components (25%, first eluted), the methyl ester **5** (50%, second eluted), and the cyclopropyl ketone **4** (25%, third eluted).

(14) (a) E. J. Corey and M. Chaykovsky, *J. Am. Chem. Soc.*, **84**, 867 (1962); **87**, 1345, 1353 (1965); (b) C. E. Cook, R. C. Corley, and M. E. Wall, *Tetrahedron Letters*, **No. 14**, 891 (1965).

(15) 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 n.m.r. spectra were determined at 60 Mc. with a Varian Model A-60 n.m.r. spectrometer. The mass spectra were obtained with a CEC Model 21-130 mass spectrometer. The microanalyses were performed by Dr. S. M. Nagy and his associates and by the Scandinavian Microanalytical Laboratory.

(16) P. D. Bartlett and G. F. Woods, *J. Am. Chem. Soc.*, **62**, 2933 (1940).

(17) Determined as a solution in carbon tetrachloride.

(18) (a) R. L. Frank, R. E. Berry, and O. L. Shotwell, *J. Am. Chem. Soc.*, **71**, 3889 (1949); (b) S. Dev, *J. Indian Chem. Soc.*, **33**, 769 (1956).

(19) A. H. Cook and R. P. Linstead, *J. Chem. Soc.*, 956 (1934).

(20) A gas chromatography column packed with silicone fluid, no. 550, suspended on ground firebrick was employed.

(21) A gas chromatography column packed with Carbowax, No. 20 M, suspended on ground firebrick was employed.

(22) Determined as a solution in 95% ethanol.

(23) We are indebted to Professor W. G. Dauben and his associates for measuring the ultraviolet absorption of this compound at short wave lengths on a Beckman Model DK-2 ultraviolet spectrophotometer. In cyclohexane solution the compound has an apparent maximum at 187 mμ (ϵ 6600). Attempts to obtain reliable measurements in water and in ethanol were unsuccessful.

A collected[20] sample of the ketone **4** was identified with the previously described sample by comparison of retention times and infrared and mass spectra. A collected[20] sample of the ester **5** was identified with a subsequently described sample by comparison of infrared spectra. In addition, the mass spectrum of the collected ester **5** has a molecular ion peak at *m/e* 194 with fragment peaks at *m/e* 163 (M − OCH_3), 120 (abundant, M − CH_2=C(OH)OCH_3), 74 (CH_2=C(OH)OCH_3), and 59 (CO_2-CH_3). A collected sample[20] of the first group of peaks has a strong infrared band[17] at 1775 cm.$^{-1}$ (cyclobutanone C=O) with a weak bond at 1725 cm.$^{-1}$ (ester C=O).

A 2.6-g. sample of a mixture from a comparable Arndt–Eistert reaction was allowed to react overnight with a solution of 2.0 g. of sodium hydroxide and 5 ml. of water in 20 ml. of refluxing methanol. The resulting mixture was diluted with water, extracted with ether, acidified with hydrochloric acid, and again extracted with ether. After the latter ethereal extract, containing the acidic products, had been dried and concentrated, distillation of the dark-colored, residual liquid (1.2 g.) in a short-path still afforded 561 mg. of colorless distillate which solidified to a waxy solid on standing. In subsequent experiments, the crude acidic product from the saponification was chromatographed on silicic acid, the crystalline acid **6** being eluted with ether–petroleum ether (b.p. 30–60°) mixtures. Recrystallization from a formic acid–water mixture afforded the pure **acid 6** as white needles, m.p. 43–44°, with broad infrared absorption[17] in the 3-μ region (carboxyl associated O–H) and peaks at 1710 (carboxyl C=O) and 1650 cm.$^{-1}$ (weak, C=C). The sample has n.m.r. absorption[17] at δ 11.97 (1H, COOH) and 5.58 (2H, broad, vinyl C–H) with three of the four lines of an AB pattern visible corresponding to absorption at δ 2.16 and 2.46 (positions estimated, 2H, J = 14 c.p.s., $-CH_2-COO-$), and broad absorption in the region δ 1.1–2.2 (11H, aliphatic C–H).

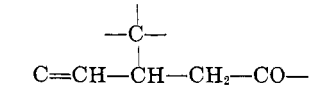
Anal. Calcd. for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95; mol. wt., 180. Found: C, 73.10; H, 9.05; mol. wt., 180 (mass spectrum).

The neutral fraction from the above saponification was concentrated and distilled to separate 410 mg. of colorless liquid, b.p. 72–94° (1.5 mm.), which contained,[20] in order of elution, two closely spaced peaks, component A (21%) and component B (25%), and the cyclopropyl ketone **4** (54%). Collected[20] samples of each of the components A and B have infrared absorption[17] at 1775 cm.$^{-1}$ (cyclobutanone C=O); in addition, component A has a weak band at 1630 cm.$^{-1}$ (C=C) and component B has a weak band at 1640 cm.$^{-1}$ (C=C). The mass spectra of the two components resemble one another closely with very weak molecular ion peaks at *m/e* 162 and very abundant fragment peaks at *m/e* 120 (M − CH_2=C=O) and 91 ($C_7H_7^+$).

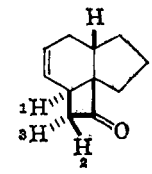
Anal. Calcd. for $C_{11}H_{14}O$: C, 81.44; H, 8.70. Found for component A: C, 81.20; H, 8.64. Found for component B: C, 81.07; H, 8.64.

The n.m.r. spectrum[17] of component A has a partially resolved multiplet centered at δ 5.92 (2H, vinyl C–H) with a singlet at δ 2.63 (2H, >C–CH_2–CO–) superimposed on broad, complex absorption in the region δ 1.1–2.8 (10H, aliphatic C–H). The n.m.r. spectrum of the subsequently described deuterated sample of component A differs only in the absence of the singlet at δ 2.63. These data are, therefore, in agreement with the assignment of structure **7** to component A.

The n.m.r. spectrum[17] of component B has a partially resolved multiplet centered at δ 5.88 (2H, vinyl C–H) with a complex pattern of lines in the region δ 2.3–3.5 (3H) and broad, unresolved absorption in the region δ 1.1–2.3 (9H, aliphatic C–H). The n.m.r. spectrum of the deuterated sample of component B, whose preparation is described below, differs only in the region δ 2.3–3.5 in that the complex pattern present in the nondeuterated sample has collapsed to a single broad peak at δ 2.57 (half-band width 6 c.p.s.) attributable to one proton. The absorption in this region is most readily explicable as the signals from the three protons allylic or α to the carbonyl function in the part structure

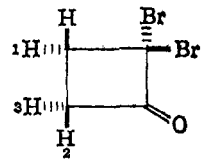


and suggests that component B should be assigned the structure **8**. A detailed analysis[24] of the ABC pattern presented by this absorption in the region δ 2.3–3.5 afforded the chemical shift and coupling constant values listed in Figure 1. The calculated coupling constants compare favorably with values previously reported[25] for 2,2-dibromocyclobutanone (Figure 2).



1-H, δ = 2.57, 2-H, δ = 2.62,
3-H, δ = 3.12
J_{12} = 6.8, J_{13} = 10.3,
J_{23} = −17.1 c.p.s.

Figure 1.



J_{12} = 7.7, J_{13} = 11.1,
J_{23} = −15.3 c.p.s.

Figure 2.

To obtain the aforementioned deuterated ketones, a 500-mg. sample containing[20] component A (15%), component B (28%), and the cyclopropyl ketone **4** (57%) was dissolved in a mixture of 3 ml. of dioxane and 3 ml. of deuterium oxide containing 239 mg. of anhydrous potassium carbonate. The resulting solution was refluxed overnight and then cooled and extracted with pentane. After the pentane extract had been dried and concentrated, the deuterated components A and B were collected from the gas chromatograph.[20] The infrared spectrum of each collected sample resembles closely the spectrum of its nondeuterated analog in the 3- and 6-μ regions. Because of the very weak molecular ion peaks in the mass spectra of these materials, the distribution of deuterium could not be determined; however, the previously described n.m.r. data establish that both components are primarily dideuterated derivatives. It is of interest that the fragmentation pattern of these dideuterated ketones is very similar to the fragmentation pattern of the nondeuterated ketones, indicating that most of the fragment ions are derived from the fragment remaining after loss of ketene (or dideuterioketene) from the molecular ion.

Preparation of the Ester 9.—An ethereal solution of 107 mg. (0.59 mmole) of the crude unsaturated acid **6** was esterified with excess diazomethane to give, after concentration, 156 mg. of a liquid containing[20] 80% of the ester **5** and 20% of an unidentified component. A collected[20] sample of the ester **5** has infrared bands[17] at 1740 (ester C=O) and 1650 cm.$^{-1}$ (weak, C=C). A 140-mg. portion of this mixture in 7 ml. of ethanol was hydrogenated at room temperature and atmospheric pressure over the catalyst from 40 mg. of platinum oxide. The hydrogen uptake (9.0 cc. or 0.69 equiv.) ceased after 10 min. and the mixture was filtered and concentrated. The saturated ester **9**, the main component in the residual liquid, was collected from the gas chromatograph.[20] The product has infrared absorption[17] at 1740 cm.$^{-1}$ (ester C=O) with an n.m.r. singlet[17] at δ 3.61 (3H, O–CH_3) as well as an AB pattern (J = 14 c.p.s.) corresponding to absorption at δ 2.12 and 2.43 (positions estimated, 2H, $-CH_2-COO-$) and unresolved absorption in the region δ 1.1–1.8 (15H, aliphatic C–H).

Anal. Calcd. for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27; mol. wt., 196. Found: C, 73.53; H, 10.30; mol. wt., 196 (mass spectrum).

Preparation of the Iodo Lactone 10.—To a solution of 772 mg. (4.3 mmoles) of the unsaturated acid **6** in 40 ml. of 0.5 *M* aqueous sodium bicarbonate was added a solution of 3.3 g. (13 mmoles) of iodine and 7.0 g. (42 mmoles) of potassium iodide in 20 ml. of water. The resulting solution was allowed to stand in the dark for 40 hr. and then was extracted with methylene chloride. After the organic extract had been washed with aqueous sodium thio-

(24) We are indebted to Professor George M. Whitesides for these calculations.

(25) K. L. Servis and J. D. Roberts, *J. Phys. Chem.*, **67**, 2885 (1963).

sulfate, dried, and concentrated, the crude crystalline iodo lactone (1.0754 g. of 82%) was recrystallized from an ethyl acetate–petroleum ether mixture to separate the iodo lactone **10** as pale yellow crystals, m.p. 65–68°. After the sample had been chromatographed on silicic acid, the white solid eluted with ether–petroleum ether mixtures was recrystallized from an ether–petroleum ether mixture to separate the pure iodo lactone as white prisms, m.p. 70.5–71°. The product was infrared absorption[17] at 1745 cm.$^{-1}$ (δ-lactone C=O) and broad n.m.r. peaks[17] at δ 4.46 and 4.88 (2H, >CH–O– and CH–I) as well as broad, complex absorption in the region δ 1.3–2.8 (13H, aliphatic C–H).

Anal. Calcd. for $C_{11}H_{15}IO_2$: C, 43.15; H, 4.94; I, 41.47. Found: C, 42.91; H, 4.95; I, 41.31.

Preparation of the Bromo Ketone 11. A. In Acetic Acid.—A solution of 200 mg. (1.24 mmoles) of the cyclopropyl ketone **4** in 10 ml. of acetic acid containing 4% (by weight) of hydrogen bromide was allowed to stand for 24 hr. at room temperature and then poured onto ice. The resulting mixture was neutralized with potassium hydroxide and extracted with ether. After this ethereal extract had been washed with water, dried, and concentrated, the residual white solid (295 mg.) was recrystallized from an ether–petroleum ether mixture to separate 230 mg. (77%) of the bromo ketone **11**, m.p. 79–82°. An additional recrystallization afforded the pure bromo ketone as white needles, m.p. 80–82°, with infrared absorption[17] at 1730 cm.$^{-1}$ (C=O) and an ultraviolet maximum[22] at 287 mμ (ε 43) as well as end absorption (ε 470 at 210 mμ). The highest peak in the mass spectrum of the material is at *m/e* 162 (M − HBr). The sample has n.m.r. absorption[17] in the region δ 0.9–2.7 (14H, aliphatic C–H) with a triplet (separation = 7.5 c.p.s., further splitting is apparent but not resolved) at δ 4.30 (1H, >CH–Br).

Anal. Calcd. for $C_{11}H_{15}BrO$: C, 54.34; H, 6.22; Br, 32.87. Found: C, 54.31; H, 6.27; Br, 33.15.

B. In Methylene Chloride.—A cold (0°) solution of 145 mg. (0.895 mmole) of the cyclopropyl ketone **4** in 20 ml. of methylene chloride was saturated with hydrogen bromide over a 5-min. period. After the resulting mixture had been allowed to stand at 0° for 2 hr., it was poured onto ice and the methylene chloride layer was separated, washed successively with water, aqueous sodium hydroxide, and water, dried, and concentrated. The residual semisolid (216 mg.) was recrystallized from an ether–petroleum ether mixture to separate 133 mg. (61%) of the bromo ketone **11**, m.p. 78–81°, which was identified with the previously described sample by comparison of infrared spectra and a mixture melting point determination.

Preparation of the Unsaturated Ketone 12.—A solution of 600 mg. (2.5 mmoles) of the crude bromo ketone **11** and 429 mg. (10 mmoles) of lithium chloride in 10 ml. of dimethylformamide was refluxed for 18 hr. and then cooled, diluted with water, and extracted with pentane. Drying and concentration of the pentane extract left 500 mg. of pale yellow liquid containing,[20] in addition to a small amount of dimethylformamide, the olefin **12** (*ca.* 70%, first eluted) and the cyclopropyl ketone **4** (*ca* 30%, second eluted). A collected[20] sample of the cyclopropyl ketone **4** was identified with the previously described sample by comparison of retention times, mass spectra, and infrared spectra. A collected[20] sample of the unsaturated ketone **12** has infrared absorption[17] at 1740 (C=O) and 1625 cm.$^{-1}$ (weak, C=C) with a broad ultraviolet maximum[22] at 289 mμ (ε 29) and end absorption (ε 776 at 210 mμ).[26,27] The sample has n.m.r. absorption in the region δ 1.1–2.9 (12H, aliphatic C–H) with two sets of four lines centered at δ 5.64 (J = 2 and 9 c.p.s.) and 6.10 (J = 6 and 9 c.p.s.) attributable to the two vinyl protons H_A and H_B, respectively, in the following part structure.

$$-\overset{|}{\underset{|}{C}}-CH_A=CH_B-CH<$$

Anal. Calcd. for $C_{11}H_{14}O$: C, 81.44; H, 8.70; mol. wt., 162. Found: C, 81.46; H, 8.73; mol. wt., 162 (mass spectrum).

A solution of 35 mg. of the unsaturated ketone **12** and 129 mg. of anhydrous potassium carbonate in a mixture of 1 ml. of dioxane and 2 ml. of deuterium oxide was refluxed for 2.5 days and then cooled and extracted with pentane. After the pentane extract had been dried and concentrated, the residual liquid (35 mg.), that exhibited only a single peak on gas chromatography,[20] was collected from the gas chromatograph and analyzed by mass spectrometry. The sample contained 96% d_2 species and 4% d_1 species and had infrared absorption[17] in the 3- and 6-μ region comparable to the nondeuterated sample with an additional weak band at 2200 cm.$^{-1}$ (C–D) and a number of differences from the spectrum of the nondeuterated sample in the fingerprint region.

In a subsequent dehydrohalogenation reaction, a solution of 705 mg. (2.9 mmoles) of the bromo ketone **11** and 430 mg. (10 mmoles) of lithium chloride in 10 ml. of dimethylformamide was heated to 100° for 2 days. The crude product (460 mg.), isolated as in the previous example, contained[20] the olefin **12** (10%, first eluted), the cyclopropyl ketone **4** (22%, second eluted), and a new component believed to be the chloro ketone **13** (68%, third eluted). A collected sample of this component has infrared absorption[17] at 1730 and 1745 cm.$^{-1}$ (C=O) with molecular ion peaks at *m/e* 198 and 200 in the mass spectrum and n.m.r. absorption[17] in the region δ 0.9–2.9 (14H, aliphatic C–H) with a triplet (separation = 8 c.p.s., further splitting not resolved) at δ 4.22 (1H, >CH–Cl).

Preparation of the Diol 14.—A solution of 85 mg. (0.52 mmole) of the unsaturated ketone **12** and 125 mg. (0.49 mole) of osmium tetroxide in 10 ml. of ether was allowed to stand for 2 days. After the supernatant liquid had been decanted, the residual osmate ester was mixed with a solution of 2 g. of sodium sulfite and 5 ml. of ethanol in 20 ml. of water and the resulting mixture was refluxed for 2 hr. and then allowed to stand overnight. After a chloroform extract of this mixture had been dried and concentrated, the crude residual diol (86 mg. or 85%) was sublimed (80–100° at 0.1 mm.) to separate the pure diol as white crystals, m.p. 131–132°. The product has infrared absorption[28] at 3530 (broad, associated O–H) and 1725 cm.$^{-1}$ (C=O) with complex n.m.r. absorption in the region δ 1.0–3.0 (12H, aliphatic C–H) with broad peaks at δ 4.56 (2H, O–H) and 3.81 (2H, >CH–O).

Anal. Calcd. for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.10; H, 8.34.

Preparation of the Ketone 15. A. From the Unsaturated Ketone 12.—A solution of 60 mg. (0.37 mmole) of the unsaturated ketone **12** in 5 ml. of ethanol was hydrogenated at 27° and atmospheric pressure over the catalyst from 26 mg. of platinum oxide. The hydrogen uptake (8.1 ml. or 1.06 equiv.) ceased after 5 min. and the reaction mixture was filtered and concentrated. The residual liquid (55 mg.), which exhibited only one peak on gas chromatography,[20] was purified by distillation in a short-path still. The sample has infrared absorption[17] at 1740 cm.$^{-1}$ (C=O) with complex n.m.r. absorption[17] in the region δ 0.9–2.7 (aliphatic C–H).

Anal. Calcd. for $C_{11}H_{16}O$: C, 80.44; H, 9.83; mol. wt., 164. Found: C, 80.23; H, 9.87; mol. wt., 164 (mass spectrum).

B. From the Cyclopropyl Ketone 4.—To a solution of 33 mg. (4.6 mg.-atoms) of lithium in 40 ml. of liquid ammonia and 20 ml. of ether was added, dropwise over a 5-min. period, 206 mg. (1.27 mmoles) of the cyclopropyl ketone **4**. The resulting mixture was stirred under reflux for 1 hr. and then the excess lithium was destroyed by the addition of ammonium chloride. After the ammonia had been allowed to evaporate, the residue was diluted with water and ether and the ethereal layer was separated, washed with water, dried, and concentrated. The residual yellow liquid (186 mg.) had relatively weak infrared absorption[17] at 1730 cm.$^{-1}$ (C=O) with absorption at 3620 and 3450 (broad) cm.$^{-1}$ (unassociated and associated O–H). From each of two runs the crude product contained[21] four components listed in order of increasing retention time: A (2–3%, 5.6 min.), B (7%, 8.8 min.), C (77–79%, 12.2 min.), and D (11–14%, 18 min.). Since the product contained more alcoholic than ketonic products, it was oxidized without further characterization. A cold (0°) solution of 171 mg. of the crude reduction product in 5 ml. of acetone was treated with 0.3 ml. of an aqueous 8 *N* chromic acid solution[12] and the resulting mixture was stirred for 5 min. After the excess oxidant had been destroyed by the addition of isopropyl alcohol, the mixture was filtered and the residue was washed with isopropyl alcohol. The combined filtrates were concentrated and then diluted with water and ether. After the ethereal layer had been separated, washed with water, and dried, concentration afforded 123 mg. of colorless liquid with infrared absorption at 1740 and 1710 (sh) cm.$^{-1}$

(26) The simpler analog, bicyclo[2.2.2]oct-5-en-2-one, is reported to have maxima in cyclohexane solution at 190 mμ (ε 3000), 202 (3000), and 290 (110).[27]

(27) (a) H. Labhart and G. Wagniere, *Helv. Chim. Acta*, **42**, 2219 (1959); (b) S. F. Mason, *Quart. Rev.* (London), **15**, 287 (1961).

(28) Determined as a solution in chloroform.

(C=O) but no absorption in the 3-μ region attributable to a hydroxyl function. The crude product contained,[21] in order of increasing retention time, the methyl ketone **33** (3%), the ketone **15** (74%), and the starting ketone **4** (22%). Identification of a collected sample of the ketone **4** with the previously described sample was accomplished by comparison of infrared spectra and retention times, and a collected sample of the ketone **15** was identified with the previously described sample by comparison of infrared and mass spectra. A collected sample of the minor product, the methyl ketone **33**, was identified with the subsequently described sample by comparison of retention times and infrared and mass spectra. To obtain a sample of this methyl ketone **33**, a solution of 363 mg. (2.27 mmoles) of the unsaturated acid **2** in 10 ml. of ether was added to 5 ml. of an ether solution containing 7.5 mmoles of methyllithium. After the reaction mixture had been stirred for 1 hr. it was poured into ice water and the organic phase was separated, washed with water, dried, and concentrated. The residual colorless liquid (329 mg.) contained,[21] in order of elution, the methyl ketone **33** (75%) and a second component presumed to be the corresponding tertiary alcohol (25%). A collected sample of the ketone **33** has infrared absorption[17] at 1705 (C=O), 1660 (C=C), and 1355 cm.$^{-1}$ (CH_3–CO–) with peaks in the mass spectrum at *m/e* 164 (M^+), 149 (M − CH_3), 121 (abundant, M − $COCH_3$), and 43 (abundant, CH_3—C≡O^+).[29,30]

Preparation of the Iodo Lactone 16.—To a solution prepared from 1.88 g. (11.3 mmoles) of the unsaturated acid **2** and 100 ml. of 0.5 *M* aqueous sodium bicarbonate was added a solution of 9.1 g. (36 mmoles) of iodine and 19.6 g. (118 mmoles) of potassium iodide in 55 ml. of water. The mixture was allowed to stand at room temperature in the dark for 48 hr. and then was extracted with ether. The organic phase was washed successively with aqueous sodium thiosulfate, water, aqueous sodium hydroxide, and aqueous sodium chloride and then dried and concentrated. The residual orange oil (2.970 g.) was filtered through a column of silicic acid (50 g.), the iodo lactone being eluted with ether–petroleum ether mixtures, to separate 2.687 g. of the colorless crystalline lactone. Recrystallization from an ether–petroleum ether mixture afforded 2.523 g. (76.5%) of the iodo lactone **16** as white prisms, m.p. 48–50°. The product has infrared absorption[17] at 1790 cm.$^{-1}$ (γ-lactone C=O) with n.m.r. peaks at δ 5.05 (1H doublet with J = 5 c.p.s., >CH–O–CO–) and 4.23 (1H, a broad triplet with apparent separations of 9 c.p.s. and further splitting apparent but not resolved, >CH–I) as well as complex absorption in the region δ 1.2–2.9 (11H, aliphatic C–H). The highest peak in the mass spectrum of the compound is at *m/e* 165 (M − I).

Anal. Calcd. for $C_{10}H_{13}IO_2$: C, 41.07; H, 4.45; I, 43.53. Found: C, 41.07; H, 4.52; I, 43.59.

Preparation of the Hydroxy Acid 17.—To a cold (5°) solution of 4.943 g. (17 mmoles) of the iodo lactone **16** in 5 ml. of benzene was added, dropwise and with stirring under a nitrogen atmosphere over a 15-min. period, 5.8 g. (20 mmoles) of tri-*n*-butyltin hydride. The resulting solution was stirred at room temperature under nitrogen for 24 hr. and then concentrated under reduced pressure. The residual colorless liquid (a mixture of the crude lactone **19**, $\nu_{max}^{CCl_4}$ 1760 cm.$^{-1}$, and the tributyltin iodide) was stirred with 50 ml. of 10% aqueous potassium hydroxide for 24 hr. and the mixture was then extracted with ether. The aqueous phase was acidified with hydrochloric acid and then extracted with ethyl acetate. After the organic phase had been washed successively with water, aqueous sodium thiosulfate, and water and then dried and concentrated, recrystallization of the residual white solid (2.90 g.) from an ethyl acetate–petroleum ether mixture afforded 2.766 g. (86.7%) of the hydroxy acid **17** as white needles, m.p. 127–130°. Further recrystallization raised the melting point of the acid to 130–131°. The product has infrared absorption[31] at 3400, 2950 (broad, associated O–H), and 1710 cm.$^{-1}$ (carboxyl C=O).

Anal. Calcd. for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 65.15; H, 8.67.

A sample of the hydroxy acid **17** was esterified with excess ethereal diazomethane to form the crude liquid **hydroxy ester 18**. Attempts to purify this ester by distillation lead to at least partial formation of the lactone **19**. The crude ester has infrared absorption[17] at 3620, 3470 (unassociated and associated O–H), and 1740 cm.$^{-1}$ (ester C=O) with n.m.r. absorption[17] at δ 3.67 (4H, singlet superimposed on other absorption, CH_3O– and >CH–O) and 2.98 (1H, singlet, shifted by adding pyridine, O–H) as well as complex absorption in the region δ 1.2–2.5 (13H, aliphatic C–H).

Preparation of the Lactone 19.—To a cold solution of 510 mg. (3.07 mmoles) of the unsaturated acid **2** in 17.5 ml. of acetic acid was added, dropwise with stirring, 7 ml. of concentrated sulfuric acid.[32] The resulting solution was allowed to stand at 0° for 24 hr. and then poured onto ice and extracted with ether. The ethereal extract was washed successively with aqueous potassium hydroxide and water and then dried and concentrated to leave 158 mg. (31%) of the crude lactone **19** as a yellow liquid. The same lactone **19**, identified by comparison of infrared spectra, was also formed as a neutral by-product in certain of the Diels–Alder reactions (see previous description) used to prepare the unsaturated acid **2**. A collected[33] sample of the lactone **19** has infrared absorption[17] at 1780 cm.$^{-1}$ (γ-lactone C=O) with an n.m.r. peak[17] at δ 4.72 (1H, broad with coupling unresolved, >CH–O–CO–) as well as complex absorption in the region δ 1.0–2.7 (13H, aliphatic C–H).

Anal. Calcd. for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49; mol. wt., 166. Found: C, 72.09; H, 8.71; mol. wt., 166 (mass spectrum).

A 158-mg. sample of the lactone **19** was stirred with a solution of 116 mg. of potassium hydroxide in 5 ml. of water for 12 hr. at room temperature and the resulting solution was extracted with ether. The aqueous phase was acidified with hydrochloric acid and extracted with ethyl acetate to separate 125 mg. of the crude hydroxy acid **17**. Recrystallization from an ethyl acetate–petroleum ether mixture afforded 97 mg. of the hydroxy acid **17**, m.p. 127–129°, which was identified with the previously described sample by a mixture melting point determination.

Preparation of the Hydroxy Acid 20.—A solution of 443 mg. (1.46 mmoles) of the iodo lactone **10** in 1 ml. of benzene was reduced with 500 mg. (1.72 mmoles) of tri-*n*-butyltin hydride as previously described. The colorless residual liquid from the reduction was allowed to react at room temperature with a solution of 0.50 g. of potassium hydroxide in a mixture of 10 ml. of water and 5 ml. of methanol for 24 hr. The mixture was diluted with ether and the basic aqueous phase was separated, acidified, and extracted with ethyl acetate. After the organic extract had been washed with water, dried, and concentrated, the residual solid (222 mg.) was filtered through silicic acid and then recrystallized from an ethyl acetate–hexane mixture to separate 156 mg. (54%) of the acid **20** as white needles melting within the range 126–135°. Recrystallization afforded the pure hydroxy acid **20**, m.p. 133.5–134.5°. The product has infrared absorption[31] at 3440, 2950 (broad, associated O–H), and 1715 cm.$^{-1}$ (carboxyl C=O).

Anal. Calcd. for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.44; H, 9.08.

After reaction of a sample of the hydroxy acid **20** with excess ethereal diazomethane, the resulting crude ester was distilled in a short-path still (150° at 0.25 mm.) to give the pure **hydroxy ester 21** as a colorless liquid with infrared absorption[17] at 3630, 3500 (unassociated and associated O–H), and 1740 cm.$^{-1}$ (ester C=O). The product has n.m.r. absorption[17] at δ 3.65 (4H, singlet superimposed on a broad peak, CH_3–O– and >CH–O), 2.79 (1H, shifted when pyridine added, O–H), and 2.19 and 2.49 (2H, AB pattern with J = 14 c.p.s., –CH_2–CO–O–) as well as complex absorption in the region δ 1.0–2.0 (13H, aliphatic C–H).

Anal. Calcd. for $C_{12}H_{20}O_3$: C, 67.89; H, 9.50. Found: C, 68.14; H, 9.47.

Preparation of the Keto Ester 23.—To a cold (0°) solution of 510 mg. (2.77 mmoles) of the hydroxy acid **17** in 10 ml. of acetone was added, dropwise and with stirring, 2.0 ml. of an aqueous 8 *N* chromic acid solution.[12] The reaction mixture was stirred at 0° for 30 min. and then the excess oxidant was consumed by the addition of isopropyl alcohol. After the resulting mixture had been filtered, concentrated, diluted with water, and extracted with ethyl acetate, the organic extract was washed with water, dried, and concentrated. A portion of the residual liquid (485 mg. or 96%) was distilled in a short-path still (170° at 0.25 mm.) to separate the pure **keto acid 22** as a colorless liquid with infrared absorption[17] at 2950 (broad, associated O–H), 1735

(29) The ketone **33**[30] is reported to boil at 78–78.2° (2.4 mm.).[2]

(30) Lit.[2] $n^{25}D$ 1.4890.

(31) Determined as a suspension in a potassium bromide pellet.

(32) The procedure of D. B. Bigley, N. A. J. Rogers, and J. A. Barltrop, *J. Chem. Soc.*, 4613 (1960).

(33) A gas chromatography column packed with silicone fluid, no. 710, suspended on ground firebrick was employed.

(C=O of an intramolecularly hydrogen-bonded carboxyl group), and 1705 cm.$^{-1}$ (C=O).

Anal. Calcd. for $C_{10}H_{14}O_3$: C, 65.91; H, 7.74. Found: C, 65.55; H, 7.80.

Esterification of 125 mg. (0.686 mmole) of the keto acid **22** with excess ethereal diazomethane afforded, after short-path distillation (150° at 0.25 mm.), 97 mg. (72%) of the keto ester **23** as a colorless liquid with infrared absorption[17] at 1730 cm.$^{-1}$ (broad, ester and ketone C=O). The product has n.m.r. absorption[17] at δ 3.67 (3H, singlet, O–CH_3) with three of the four lines resolved of an apparent AB pattern for absorption at δ 2.18 and 2.52 (2H, J = 15.5 c.p.s., CO—CH_2—C<) as well as complex absorption in the region δ 1.2–2.5 (11H, aliphatic C–H).

Anal. Calcd. for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22; mol. wt., 196. Found: C, 67.12; H, 8.24; mol. wt., 196 (mass spectrum).

Preparation of the Keto Ester 25.—A solution of 50 mg. (0.253 mmole) of the hydroxy acid **20** in 2 ml. of acetone was oxidized with 0.2 ml. of aqueous 8 *N* chromic acid[12] for 15 min. following the reaction and isolation procedures described in the previous experiment. The crude acidic product, 35 mg. of the **keto acid 24** as a colorless oil, was esterified with excess ethereal diazomethane. The resulting neutral product (33 mg.) was distilled in a short-path still (150° at 0.25 mm.) to separate 25 mg. of the keto ester **25** as a colorless liquid with infrared absorption[17] at 1735 (ester C=O) and 1715 cm.$^{-1}$. The sample has n.m.r. absorption[17] at δ 3.61 (3H, singlet, O–CH_3) with complex absorption in the region δ 1.2–2.7 (15H, aliphatic C–H).

Anal. Calcd. for $C_{12}H_{18}O_3$: C, 68.54; H, 8.63; mol. wt., 210. Found: C, 68.20; H, 8.69; mol. wt., 210 (mass spectrum).

Preparation of the Cyclopropyl Ketone 26.—To a cold (5°) suspension of the anhydrous sodium salt from 3.775 g. (30 mmoles) of Δ^3-cyclohexene-1-carboxylic acid in 30 ml. of benzene containing 0.8 ml. of pyridine was added, with stirring, 15 g. (0.12 mole) of oxalyl chloride. The resulting mixture was stirred at 5° for 2 hr. and then filtered and concentrated. A solution of the residual crude acid chloride in 30 ml. of benzene was added to a cold (0–5°) ethereal solution containing 60 mmoles of diazomethane, and the solution was stirred for 2 hr. at 0–5° and for 12 hr. at room temperature. The resulting solution was filtered, dried, and concentrated to leave 4.88 g. of the crude diazo ketone **27** as a yellow liquid with infrared absorption[28] at 2100 and 1620 cm.$^{-1}$ (–CO–CH–N_2).

To a mixture of 250 ml. of refluxing cyclohexane and 400 mg. of copper bronze was added, dropwise over a 1-hr. period, a solution of 3.791 g. (25 mmoles) of the diazo ketone **27** in 50 ml. of cyclohexane. After the mixture had been refluxed, with stirring, for 24 hr., it was filtered and concentrated to leave 2.951 g. of yellow liquid. Short-path distillation [120–130° (20–25 mm.)] separated 2.337 g. of yellow liquid which was chromatographed on 60 g. of Florisil. The product, eluted with ether–petroleum ether mixtures, was distilled to separate 1.854 g. of the cyclopropyl ketone **26** as a colorless liquid, b.p. 100–103° (17 mm.), n^{25}D 1.5086, which solidified on standing, m.p. 41–43° (lit.[9] m.p. 41–44°). Short-path distillation (150° at 25 mm.) of the residue from the above distillation afforded an additional 300 mg. of the cyclopropyl ketone **26**, n^{25}D 1.5067, for a total yield of 2.154 g. (57%). The product has infrared absorption[17] at 1735 cm.$^{-1}$ (C=O) with complex n.m.r. absorption in the region δ 1.4–2.4 and a molecular ion peak in its mass spectrum at m/e 122.[34] Comparison of infrared, mass, and n.m.r. spectra established the identity of our sample with the previously reported[9] sample of the cyclopropyl ketone **26**.

Preparation of the Bromo Ketone 28.—A 233-mg. (1.91 mmoles) sample of the cyclopropyl ketone **26** was dissolved in 10 ml. of acetic acid containing 4% (by weight) of hydrogen bromide and the resulting solution was allowed to stand at room temperature for 24 hr. After the reaction mixture had been poured onto ice, neutralized with potassium hydroxide, and extracted with ether, the organic phase was washed with water, dried, and concentrated. Recrystallization of the residual white solid (316 mg.) from an ether–petroleum ether mixture afforded 204 mg. (52%) of the crude bromo ketone **28** which softened at 68° and melted over the range 85–95°. Additional recrystallizations separated the pure bromo ketone **28** as white prisms, m.p. 99–100°. Comparison of the infrared and mass spectra of the crude and pure samples of the bromo ketone **28** suggests that the crude bromo ketone is not contaminated with any substantial amount of a second component. The material has infrared absorption[17] at 1740 cm.$^{-1}$ (C=O) with n.m.r. absorption[17] at δ 4.42 (1H, triplet with J = 7 c.p.s., further splitting apparent but not resolved, >CH–Br) and broad, complex absorption in the region δ 1.4–2.8 (10H, aliphatic C–H).

Anal. Calcd. for $C_8H_{11}BrO$: C, 47.31; H, 5.46; Br, 39.35; mol. wt., 202, 204. Found: C, 47.16; H, 5.51; Br, 39.41; mol. wt., 202, 204 (mass spectrum).

In a subsequent experiment, a cold (0–5°) solution of 240 mg. (1.97 mmoles) of the cyclopropyl ketone **26** in 20 ml. of methylene chloride was saturated with hydrogen bromide over a period of 5 min. and the resulting mixture was allowed to stand at 0° for 2 hr. After the reaction mixture had been poured onto ice, the organic phase was separated, washed successively with aqueous sodium hydroxide and water, dried, and concentrated. Recrystallization of the residual yellow oil (323 mg.) from an ether–petroleum ether mixture separated 174 mg. of the crude bromo ketone **28**, m.p. 60–94°. Two additional recrystallizations afforded 117 mg. (29%) of the bromo ketone **28**, m.p. 97–99°, identified with the previously described sample by a mixture melting point determination and by comparison of infrared and n.m.r. spectra.

Dehalogenation of the Bromo Ketone 28.—A solution of 270 mg. (1.32 mmoles) of the bromo ketone **28**, 10 mg. of *p*-toluenesulfonic acid, and 0.1 ml. (1.8 mmoles) of ethylene glycol in 20 ml. of benzene was refluxed, with stirring and continuous separation of water, for 18 hr. The reaction mixture was cooled, diluted with ether, washed successively with aqueous sodium hydroxide and water, dried, and concentrated. Short-path distillation (110–130° at 0.2 mm.) of the residual yellow liquid (371 mg.) separated 303 mg. (93%) of the crude **bromo ketal 29** as a colorless liquid. This material has no infrared absorption in the 6-μ region attributable to a carbonyl function and exhibits broad n.m.r. absorption[17] centered at δ 4.32 (1H, >CH–Br) with a partially resolved multiplet at δ 3.82 (4H, –CH_2–O) and complex absorption in the region δ 1.3–2.9 (10H, aliphatic C–H).

To a solution of 200 mg. (0.81 mmole) of the crude bromo ketal **29** in 20 ml. of ether and 40 ml. of liquid ammonia was added 35 mg. (1.52 mg.-atoms) of sodium and the resulting blue solution was stirred under reflux for 4 hr. After the excess sodium had been destroyed by the addition of ammonium chloride, the ammonia was allowed to evaporate and the residue was added to a mixture of water and ether. The organic phase was separated, washed with water, dried, and concentrated. Distillation of the colorless liquid residue (130 mg.) in a short-path still (130° at 25 mm.) separated 107 mg. (79%) of the crude **ketal 30** as a colorless liquid. This product has no infrared absorption in the 3- or 6-μ region attributable to hydroxyl or carbonyl groups and has n.m.r. absorption[17] at δ 3.86 (4H, partially resolved multiplet, –CH_2–O) with complex absorption in the region δ 1.1–2.3 (12H, aliphatic C–H). The mass spectrum of the sample has a molecular ion peak at m/e 168.

A solution of 50 mg. (0.30 mmole) of the ketal **30** in a mixture of 10 ml. of ether and 10 ml. of 1 *M* aqueous hydrochloric acid was stirred at room temperature for 20 hr. after which the ether layer was separated and the aqueous phase was extracted with ether. The combined ether solutions were washed with water, dried, and concentrated to leave 30 mg. of white solid which was sublimed (120° at 25 mm.) to separate 24 mg. (65%) of the **ketone 31** as a volatile white solid with infrared absorption[17] at 1735 cm.$^{-1}$ (C=O), two broad n.m.r. peaks[17] at δ 2.15 (4H) and 1.74 (8H), and a mass spectrum exhibiting a molecular ion peak at m/e 124 with a very abundant fragment peak at m/e 80 (M − CH_2=C=O − 2H). This product was identified with an authentic sample of the ketone **31**[35] by comparison of retention times,[21] infrared spectra, and mass spectra.

Reduction of the Cyclopropyl Ketone 26.—To a solution of 49.5 mg. (7.0 mg.-atoms) of lithium in 40 ml. of liquid ammonia and 20 ml. of tetrahydrofuran was added 184 mg. (1.55 mmoles) of the cyclopropyl ketone **26**. The resulting blue solution was stirred under reflux for 10 min. and then the excess lithium was destroyed by the addition of ammonium chloride and the ammonia was allowed to evaporate. Water and ether were added

(34) Measurements of the ultraviolet absorption of the ketone **26** at short wave lengths gave apparent maxima at 182 mμ (ϵ 6500) in cyclohexane solution and at 205 mμ (ϵ 5300) in water solution.[23] An ethanol solution of the ketone **26** is reported[9] to have a weak maximum at 281 mμ (ϵ 63).

(35) We are indebted to Professor Norman A. LeBel for providing us with an authentic sample of the ketone **31**.

to the residue and the organic phase was separated, washed with water, dried, and concentrated. Sublimation (150° at 25 mm.) of the residue afforded 150 mg. of white solid which had infrared absorption at 3630, 3450, and 1735 cm.$^{-1}$ indicating the presence of both alcoholic and ketonic components. The gas chromatogram[21] of the product exhibits five peaks: the ketone **32** (<1%, 17.0 min.), the ketone **31** (2%, 20.2 min.), a peak apparently attributable to a mixture of alcohols (84%, 22.4 min.), an unidentified component (1%, 26.4 min.), and the starting ketone **26** (13%, 32.2 min.).

A comparable reaction employed less lithium (16.5 mg., 2.3 mg.-atoms, in 40 ml. of liquid ammonia and 12 ml. of tetrahydrofuran) with 238 mg. (1.92 mmoles) of ketone **26**. After a reaction time of 15 min. some excess lithium still remained. The product (186 mg. of white solid) obtained after sublimation exhibited infrared absorption attributable to both hydroxyl and carbonyl functions and contained[21] an unknown component (<1%, 13.8 min.), the ketone **32** (9%, 19.0 min.), the ketone **31** (25%, 22.4 min.), a peak believed attributable to an alcohol mixture (16%, 25.2 min.), and the starting ketone **26** (50%, 36.3 min.). Repeated efforts to reduce the amounts of alcoholic products by use of various drying procedures for the solvents and apparatus had no apparent effect.

A solution of 84 mg. of the above product mixture (from reduction of the ketone **26** with excess lithium) in 5 ml. of cold (0°) acetone was treated with 0.3 ml. of 8 *N* aqueous chromic acid[12] and the resulting solution was stirred for 5 min. After the excess oxidant had been destroyed by the addition of isopropyl alcohol, the mixture was filtered and the residue was washed with isopropyl alcohol. The combined filtrates were diluted with ether, washed with water, dried, and concentrated to leave 67 mg. of white solid containing[21] the ketone **32** (37%, 14.6 min.), the ketone **31** (42%, 17.4 min.), and the cyclopropyl ketone **26** (21%, 28.2 min.). Collected[21] samples of ketones **31** and **26** were identified with previously described samples by comparison of infrared spectra and retention times. A collected[21] sample of **ketone 32** has infrared absorption[17] at at 1745 cm.$^{-1}$ (C=O) with broad, complex n.m.r. absorption[17] in the region δ 1.3–2.8, and a molecular ion peak in the mass spectrum at *m/e* 124 as well as abundant fragment peaks at *m/e* 81, 80, 67, 55, 54, 41, and 39. This product was identified with an authentic sample of the ketone **32**[36] by comparison of retention times and infrared and mass spectra.

Preparation of the Diketone 35.—To a cold (0°) suspension of 552 mg. (3.0 mmoles) of the hydroxy acid **17** in 20 ml. of dry ether was added, dropwise and with stirring, 12 ml. of an ether solution containing 18.0 mmoles of methyllithium. The resulting mixture was stirred at 0° for 1 hr. and at room temperature for 3 hr. and then was poured onto ice and extracted with ether. The organic solution was washed with water, dried, and concentrated to leave 576 mg. of neutral product as a yellow liquid which was chromatographed on 30 g. of Florisil. Earlier fractions, eluted with petroleum ether containing less than 10% ether, consisted of 85 mg. of a colorless oil whose infrared spectrum[17] lacked absorption in the 3- or 6-μ regions attributable to hydroxy or carbonyl functions. Latter fractions, eluted with 20–50% ether in petroleum ether, afforded 432 mg. of the **hydroxy ketone 34** as a colorless oil with infrared absorption[17] at 3680, 3450 (OH), 1700 (C=O), and 1350 cm.$^{-1}$ (CH_3–CO–). The n.m.r. spectrum has a broad peak at δ 3.95 (1H, >CH–O), a sharp peak (shifted by the addition of pyridine) at δ 3.02 (1H, O–H), and a singlet at δ 2.19 (3H, CH_3–CO) superimposed on broad complex absorption in the region δ 0.7–2.5 (13H). The mass spectrum of the product showed no molecular ion peak but had abundant fragment peaks at *m/e* 164 (M − H_2O), 121, 110, 79, and 43 (CH_3—C≡O$^+$).[37] Attempts to purify this material by collection from a gas chromatography column[21] resulted in the formation of a new substance with no infrared absorption[17] in the 3-μ region attributable to a hydroxy function and two sharp peaks at 1675 and 1710 cm.$^{-1}$ attributable to an enol ether. The mass spectrum of this product has a molecular ion peak at *m/e* 164 with a very abundant fragment peak at *m/e* 42 (CH_2=C=O$^+$). Thus, this material appears to be the enol ether **36** derived from dehydration of the tautomer **34b** of the hydroxy ketone.

To a solution of 700 mg. of the crude hydroxy ketone **34** described above in 10 ml. of acetone was added 1 ml. of 8 *N* aqueous chromic acid[12] and the resulting solution was stirred at room temperature for 30 min. After the excess oxidant had been destroyed by the addition of isopropyl alcohol, the mixture was filtered and the residue was washed with hot isopropyl alcohol. The combined filtrates were concentrated and then mixed with ether and water. The organic phase was separated, washed with water, dried, and concentrated to leave 541 mg. of yellow liquid. Short-path distillation (150° at 0.6 mm.) afforded 470 mg. of a pale yellow liquid which contained[21] 94% of the diketone **35** (second eluted) accompanied by 4% of an unknown component (eluted third) and 2% of an unknown component (first eluted). Chromatography on silicic acid separated fractions, eluted with 20% ether in petroleum ether, which were subjected to short-path distillation (110–120° at 0.2 mm.). The pure[21] **diketone 35** was obtained as a colorless liquid with infrared absorption[17] at 1720 cm.$^{-1}$ (broad, C=O) and n.m.r. peaks[17] centered at δ 2.52 and 2.23 (2H, AB pattern with J = 15 c.p.s., $-CH_2$–CO–) as well as a singlet at δ 2.11 (3H, CH_3–CO–) superimposed on broad absorption in the region δ 1.2–2.2. The mass spectrum has a molecular ion peak at *m/e* 180 with abundant fragment peaks at *m/e* 137, 95, 55, and 43 (CH_3—C≡O$^+$).

Anal. Calcd. for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.13; H, 8.86.

Preparation of the Ketal Acid 37.—A solution of 480 mg. (2.64 mmoles) of the keto acid **22**, 10 mg. of *p*-toluenesulfonic acid, and 333 mg. (5.4 mmoles) of ethylene glycol in 25 ml. of benzene was refluxed for 13 hr. with continuous separation of water. The resulting solution was cooled, diluted with ether, washed with water, dried, and concentrated to leave 587 mg. of the crude ketal as a white solid. Recrystallization from an ether–hexane mixture afforded 1.210 mg. (46%) of the ketal **37**, m.p. 113–115°, and further crystallization gave the pure ketal **37** as white prisms, m.p. 117–118°. The product has infrared absorption[28] at 2950 (broad, associated O–H) and 1700 cm.$^{-1}$ (carboxyl C=O) with n.m.r. peaks at δ 11.85 (1H, –COOH) and 3.92 (4H, $-CH_2$–O–) as well as broad absorption in the region δ 1.1–2.5 (13H).

Anal. Calcd. for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02. Found: C, 63.61; H, 7.92.

Acknowledgment.—We are indebted to Professor Norman A. LeBel for providing us with an authentic sample of bicyclo[2.2.2]octan-2-one (**31**) and for comparing samples of the related cyclopropyl ketone **26.** We are also grateful to Professor Harlan Goering for providing us with an authentic sample of bicyclo-[3.2.1]octan-6-one (**32**).

(36) We are indebted to Professor Harlan Goering for providing us with an authentic sample of the ketone **32**.

(37) It is probable that the subsequently described dehydration of the hydroxy ketone **34** was occurring to some extent in the inlet system of the mass spectrometer.