[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

Photochemical Reactions. VII.[1] The Intramolecular Cyclization of Carvone to Carvonecamphor[2]

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RECEIVED MARCH 6, 1957

Ciamician[1] and Sernagiotto[9,10] have reported the formation of carvonecamphor by irradiation of carvone (I) with sunlight. From inconclusive evidence structures II and VII were deduced for this tricyclic, saturated ketone. It is shown that the molecule is represented by the unique structure II as suggested by Ciamician. Oxidation of II with permanganate leads to a dicarboxylic acid (III) and a ketocarboxylic acid (IV). Pyrolysis of II at 470° gives VI. On active alumina II is converted to isocarvonecamphor (IX). Two lactones (XII and XIII) are formed when II is allowed to react with perbenzoic acid. Chromatography of XII gives XIII. Reduction of XII and XIII with lithium aluminum hydride yields diols XV and XVI, respectively. Acetylation of XVI gives a monoacetate (XVIII). Upon refluxing in acetic anhydride–pyridine, XVI is converted to an unsaturated monoacetate (XIX). The presence of a cyclopropane ring in XIX is established by conversion to the ketoalcohol XXII. Diols XV and XVI are converted to 1,3-dimethyl-4-ethylbenzene (XXVI) upon treatment with 20% sulfuric acid. The mechanism of formation of II from I is discussed.

Small-ring compounds occur fairly widely distributed in nature and are manifest predominantly in the terpenes. Even within this limited class of natural products the structural variations are manifold and molecules containing three or four-membered carbon rings have been found in all subgroups except the diterpenes.

It seems safe to assume that the small-ring terpenes are formed in nature by cyclization of the appropriate aliphatic precursors.[3] Such cyclizations can in principle occur by two distinctly different mechanisms, one (a) involving ionic and the other (b) radical intermediates. There is ample *in vitro* analogy for the first mode of cyclization leading to alicyclic compounds containing five- and six-membered rings. Recent work on the *in vivo* cyclization of squalene was provided experimental evidence for the soundness of this theory.[4] The biosynthesis of cyclopropanes and cyclobutanes by ionic processes might be viewed with some suspicion because we have very few laboratory analogies for such changes but many for the reverse processes. Biological cyclizations of polyolefins to small-ring compounds involving radical intermediates appear pleasing because many conversions of this type have been realized *in vitro.*

Photoinitiated dimerizations, most probably involving biradical intermediates, are well known to yield cyclobutanes,[5] and recently the formation of cyclopropanes on photoisomerization of bicyclo-[2,2,1]heptadiene-2,3-dicarboxylic acid,[6] β-ionone[7] and santonin[8] have been observed. It therefore seemed attractive to study the photoisomerization of polyolefins which conceivably might be biological precursors of small-ring compounds found in nature. Admittedly, the only point in favor of such a biogenetic theory at this time is the fact that plants do need light for growth and survival.

On searching the chemical literature for intramolecular photochemical cyclizations, we came across the highly interesting conversion of carvone (I) to carvonecamphor (II) first observed by Ciamician and Silber.[9] The isomerization was achieved by irradiating alcoholic solutions of I with Italian sunlight for periods up to one year. The stability of II to bromine and permanganate suggested the presence of a saturated molecule and II should therefore be tricyclic. The ready isomerization of carvonecamphor to the unsaturated isomer, isocarvonecamphor, in the presence of acids was indicative of the presence of a small ring in the molecule. Sernagiotto[10] obtained information concerning the neighborhood of the carbonyl group by vigorous oxidation of II with potassium permanganate which led to a dicarboxylic acid (III), $C_{10}H_{14}O_4$, and a ketocarboxylic acid (IV), $C_9H_{12}O_3$. Further oxidation of III to IV demonstrated that III is merely a precursor of IV. Part structure $R_3CCOCH_2CHR_2$ was thus established, and the evidence discussed above *coupled with the assumption that no skeletal change had occurred in the acid isomerization* led Sernagiotto[10] to reject the Ciamician and Silber structure II and propose structure VII for carvonecamphor. In this paper we shall discuss experimental findings which are in agreement only with structure II proposed by Ciamician.

We now wish to state the facts which eventually confirmed structure II. (1) Carvonecamphor has the molecular formula $C_{10}H_{14}O$ and is definitely monomeric. (2) It contains two C-methyl groups and (3) the infrared carbonyl at 1727 cm.^{-1} indicated a cyclopentanone. (4) No bands characteristic of a CH_2 in a cyclopropane[11] were detectable. (5) The low end absorption in the ultraviolet (λ 210 $m\mu$, ϵ 1800) excludes the presence of double bonds and a cyclopropyl ketone. (6) Ketocarboxylic acid (IV) has $\nu_{\max}$ 1770 cm.^{-1} the ester V has $\nu_{\max}$ 1764 cm^{-1} and λ 210 $m\mu$, ϵ 112. The ketone function therefore must be in a four- or highly strained five-membered ring and *not* in conjugation with a cyclopropane ring. (7)

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[1] Paper VI, G. Büchi and N. C. Yang, THIS JOURNAL, **79**, 2318 (1957).

[2] Part of a program of research supported by a grant from the Godfrey L. Cabot Fund, Publication No. 64, M. I. T. Solar Energy Conversion Project.

[3] A. Eschenmoser, L. Ruzicka, O. Jeger and D. Arigoni, *Helv. Chim. Acta*, **38**, 1890 (1955).

[4] T. T. Tchen and K. Bloch, THIS JOURNAL, **77**, 6085 (1955), and earlier papers cited; W. G. Dauben and J. H. Richards, *ibid.*, **78**, 5329 (1956).

[5] A. Mustafa, *Chem. Revs.*, **51**, 1 (1952) (review article).

[6] S. J. Cristol and R. L. Snell, THIS JOURNAL, **76**, 5000 (1954).

[7] G. Büchi and N. C. Yang, *Chemistry & Industry*, 357 (1955); THIS JOURNAL, **79**, 2318 (1957).

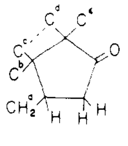
[8] Unpublished observation by G. Büchi and L. J. Krebaum.

[9] G. Ciamician and P. Silber, *Ber.*, **41**, 1928 (1908).

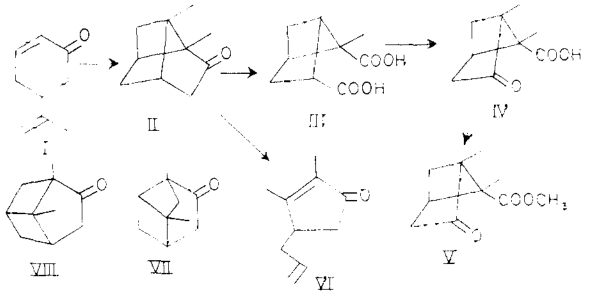
[10] E. Sernagiotto, *Gazz. chim. ital.*, **48**, 52 (1918); **47**, 153 (1917).

[11] A. R. H. Cole, *J. Chem. Soc.*, 3807, 3810 (1954); S. E. Wiberly and S. C. Bunce, *Anal. Chem.*, **24**, 623 (1952).

Equilibration of IV with sodium deuteroxide in deuterium oxide results in the introduction of 2.0 D (after conversion of COOD to COOH). The band at 1429 cm.$^{-1}$ due to the deformation frequency of a methylene group adjacent to a carbonyl present in IV had disappeared in the deuterated ketocarboxylic acid, and we could therefore extend the part structure of II to $R_3CCOCH_2CHRCH_2R$. (8) Pyrolysis of II at 470° led to a compound $C_{10}H_{14}O$ (VI) which is a tetrasubstituted cyclopentenone (λ_{max} 237 mμ, ϵ 11400; ν_{max} 1704 cm.$^{-1}$). Bands in the infrared spectrum of VI at 919, 992, 1653 and 3090 cm.$^{-1}$ furthermore suggest the presence of a vinyl group. It is now possible to expand the part structure of II further to

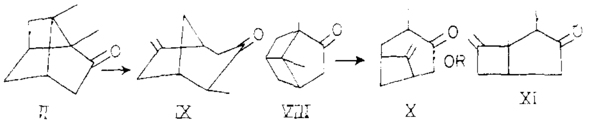


which contains already all carbon atoms present in carvonecamphor. To complete the carbon skeleton two additional carbon–carbon bonds have to be constructed, and to satisfy (4) no bonds can be placed between Cb and Cc nor between Cd and Ce. Because both Cb and Cc and also Cd and Ce are equivalent at this stage, bond formation between any two atoms of the two pairs will result in only one structure (Cc. . .Cd). The second bond to be placed must originate at Ca and can only terminate at either Cc or Cd without violating (2). These considerations thus lead to structure II or VIII for carvonecamphor.



In order to decide between structures II and VIII, it is necessary to consider the possible structures for isocarvonecamphor. It might be pointed out that we have never been able to prepare a pure sample of isocarvonecamphor by the published procedure.[9] Carvonecamphor upon prolonged contact with highly active alumina was partly converted to isocarvonecamphor, $C_{10}H_{14}O$, characterized by a semicarbazone, m.p. 209° (lit.[9] 209°). The infrared spectrum showed bands at 882, 1656, 1710 and 3100 cm.$^{-1}$ attributable to a carbonyl in a six or larger membered ring and a terminal methylene group. The infrared spectrum of isocarvonecamphor is interpretable in terms of a methylenecyclohexane structure but not compatible with a methylene-cyclobutane structure.[12]

Assuming that the isomerization product results from the rupture of a cyclobutane ring at a quaternary carbon atom, then the results can be rationalized in terms of the conversion of II to IX but are incompatible with the conversion of VIII to X or XI.



The bathochromic and hyperchromic effects of the cyclopropane ring adjacent to chromophoric systems are well known. It has been suggested[13] that the cyclobutane ring possesses similar, though less intense, auxochromic properties. The extinctions of the high energy absorptions of carvonecamphor (II) and the ketocarboxylic acid IV measured at 210 mμ are 1800 and 112, respectively. Examination of molecular models of II and IV reveals that the four-membered ring in carvonecamphor (II) is in a more favorable position for conjugation with the carbonyl than in the ketocarboxylic acid IV. The values for the low-energy absorption of II (301 mμ, ϵ 35) and of IV (280 mμ, ϵ 25) are in good agreement with values reported by Mariella[14]: 299 mμ for cyclopentanone and 280 mμ for cyclobutanone. It should be pointed out that the infrared and the ultraviolet spectra of the ketocarboxylic acid were in agreement with either a cyclobutanone or a highly strained cyclopentanone structure, and a definitive differentiation was possible only by chemical methods.

We now wish to discuss a few further findings which provide additional support for II, particularly since they involve a conversion of carvonecamphor to a known compound with retention of all carbon atoms. Oxidation of II with perbenzoic acid followed by rapid chromatography led to an oily neutral substance, $C_{10}H_{14}O_2$ (XII), and an isomeric compound, m.p. 65° (XIII). It was originally assumed that two isomeric lactones were formed by ring cleavage on both sides of the carbonyl group.[15] In order to test this hypothesis, the two compounds were reduced with lithium aluminum hydride giving a diol (XV), m.p. 133°, and an isomeric diol (XVI), m.p. 101°. Because neither of these diols turned out to be identical with a third diol (XVII), m.p. 163°, obtainable by lithium aluminum hydride reduction of the anhydride XIV (infrared bands at 1745 and 1786 cm.$^{-1}$, characteristic of glutaric anhydrides), one of the two lactones must have a rearranged carbon skeleton. Examination of the infrared spectrum of the crystalline lactone XIII, ν_{max} 1776, 3032 and 3064 cm.$^{-1}$, indicated a γ-lactone and a methylene on a cyclopropane ring. The oily lactone (ν_{max} 1739 cm.$^{-1}$), on the other hand, appeared to be a mixture of 80% of the δ-lactone XII and 20% of the γ-lactone XIII. It seemed likely that the γ-lactone is a transformation product of the δ-lactone formed originally in the Baeyer–Villiger oxidation.

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[12] J. D. Roberts and C. W. Sauer, THIS JOURNAL, **71**, 3925 (1949); P. R. Schleyer, Princeton University, private communication.

[13] J. Wren, *J. Chem. Soc.*, 2208 (1956).

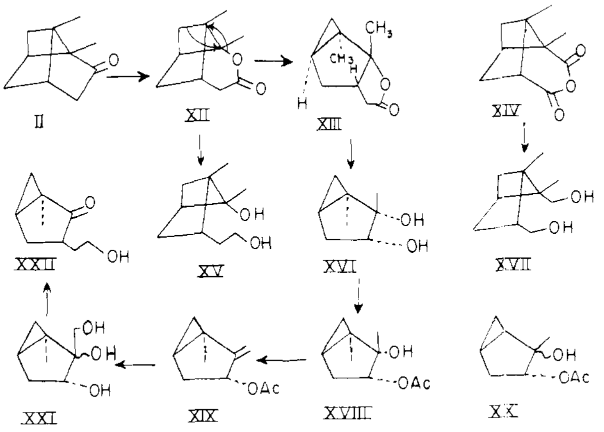
[14] R. P. Mariella and R. Raube, THIS JOURNAL, **74**, 518 (1952).

[15] In all cases studied, with the exception of *camphor*, tertiary alkyl groups migate more readily to oxygen than primary groups. W. von E. Doering and L. Speers, *ibid.*, **72**, 5515 (1950); R. Criegee, *Ann.*, **560**, 127 (1948), and earlier papers cited.

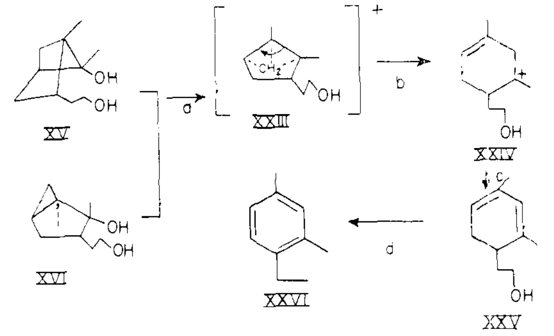
In agreement with this view it was found that XII on prolonged contact with silica gel gave XIII quantitatively, and similarly oxidation of II in the presence of a catalytic amount of mineral acid produced only XIII.

The relationship between the lactone grouping and the cyclopropane ring in XIII was established as follows. Acetylation of the corresponding diol XVI afforded a monoacetate (XVIII) which on reduction with lithium aluminum hydride was reconverted to XVI. Treatment of the diol XVI with acetic anhydride in boiling pyridine gave an unsaturated monoacetate (XIX, infrared max. at 866, 1644 and 3000–3100 cm.$^{-1}$, three peaks) rather than a diacetate, a behavior exhibited by many tertiary alcohols. The presence of a terminal methylene group and a CH_2 in a cyclopropane ring was revealed by the infrared spectrum and confirmed by the absence of the methylene vibrations in the dihydroacetate XX obtained by catalytic hydrogenation of XIX. The high end-absorption of XIX in the ultraviolet spectrum (λ 210 mμ, ϵ 8700) suggested a vinylcyclopropane system, and to strengthen the argument XIX was oxidized with osmic acid to the triol XXI, which on cleavage with periodate was converted to formaldehyde and a hydroxyketone $C_9H_{14}O_2$ (XXII), infrared max. at 1717, 3031 and 3068 cm.$^{-1}$; λ 210 mμ, ϵ 3200. The spectral data are in perfect agreement with those reported for dihydroumbellulone.[16] The γ-lactone XIII must therefore contain part structure cyclopropyl–CR(CH_3)OCOR. The properties of the δ-lactone are in agreement with structure XII, and the nature of its conversion to XIII can now be discussed. The most reasonable explanation of this change is that it involves a conversion of the bicyclo[2,1,1]hexane[17] to a bicyclo[3,1,0]hexane. The rearrangement at hand is reminiscent of the cyclobutyl–cyclopropylcarbinyl carbonium ion rearrangement investigated by Roberts.[18] This, however, does not imply that this reaction *must* proceed through a carbonium ion intermediate, and it is possible that the two groups interchange places simultaneously.[19] The molecular model of XII strengthens the feasibility of such a concerted process because the four centers concerned describe a plane (*cf.* XII → XIII arrows).

It seemed to us that the bicyclic diols XV and XVI, both of which contain an acid-sensitive small ring, should be convertible to aromatic hydrocarbons by acid-catalyzed dehydrations. In fact both diols XV and XVI were transformed to the same hydrocarbon XXVI, purified by vapor phase chromatography. The infrared spectrum of this compound was different from that of 1,2-dimethyl-3-ethylbenzene but superimposable on that of 1,3-dimethyl-4-ethylbenzene[20] (see Experimental). Identity was confirmed by comparison of the corresponding trinitro compounds, m.p. 129°.



In our view these two remarkable aromatization reactions proceed as follows: (a) Proton addition to the tertiary hydroxyl function leads to the nonclassical ion XXIII which (b) in the rate-determining step collapses to the most stable planar carbonium ion XXIV. (c) A proton is expelled from XXIV to give the corresponding cyclohexadiene XXV. The final step, (d), involves dehydration of one of the allylic alcohols in equilibrium with XXV.



In conclusion we would like to comment briefly on the mechanism of the cyclization of carvone (I) to carvonecamphor (II). The fact that a sample of I kept in a brown glass bottle for over a year did not contain any II demonstrates that a light-catalyzed reaction is operative in the cyclization. The light-absorbing chromophore undergoing electronic transition in carvone (I) is most probably the α,β-unsaturated carbonyl system containing π–π conjugation. Whether the cyclization occurs in the ionic singlet state or in the biradical triplet state has not been ascertained in this investigation, but an ionic intermediate seems unlikely because the K-band of carvone is at 235 mμ and the Pyrex glass tubes in which the irradiations were carried out are opaque below 285 mμ. One would anticipate a biradical (Ia) to initiate the polymerization[21] of carvone as well as to add to the olefinic bond yielding the most stable biradical.[22] The

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[16] R. H. Eastman, THIS JOURNAL, **76**, 4115 (1954); **77**, 6642 (1955).

[17] The first derivatives of bicyclo[2,1,1]hexane seem to have been obtained by photochemical decomposition of diazocamphor [L. Horner and E. Spietscka, *Ber.*, **88**, 934 (1955)], and several compounds containing this carbon skeleton were described.

[18] J. D. Roberts and R. H. Mazur, THIS JOURNAL, **73**, 2509, 3542 (1951).

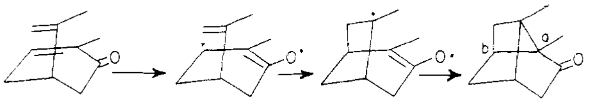
[19] *Cf.* the rearrangement of 9-decalyl hydroperoxide benzoate; D. B. Denney, *ibid.*, **77**, 1706 (1955).

[20] Infrared curve No. 736, American Petroleum Institute.

[21] Compare the photoinitiated polymerization of methyl methacrylate in the presence of benzoin (W. E. Mochel, J. L. Crandall and J. H. Peterson, THIS JOURNAL, **77**, 494 (1955)).

[22] G. Büchi, C. G. Inman and E. S. Lipinsky, *ibid.*, **76**, 4327 (1954).

change is terminated by fusion of the second carbon–carbon bond to give carvonecamphor. It is conceivable that the low yield (10%) of II is partly attributable to the reversibility of the reaction in the presence of ultraviolet light. A photochemical ring fission of II could lead to either I or VI, and the observed pyrolysis of carvonecamphor to the cyclopentenone VI rather than I indicates that the weakest bond in II is between Ca and Cb. The photolysis of carvonecamphor is under investigation.



I Ia Ib II

Experimental[23]

Melting points and boiling points are uncorrected. Ultraviolet spectra were measured in 95% ethanol solution on a Cary recording spectrophotometer, model II. Infrared spectra, unless otherwise indicated, were measured on a Perkin–Elmer recording spectrophotometer, model 21, with a sodium chloride prism. The listings of infrared bands include those bands which are relevant to the structural arguments and other medium and strong bands. The activity of the adsorbents used for chromatograms was determined by the adsorption of dyes according to the procedure of Brockmann.[24]

Carvone (I).—The carvone was obtained from Fritzsche Bros., Inc., New York, and purified by distillation. The fractions used had b.p. 116° at 17 mm., $\alpha^{25}\text{D}$ 55.6 (c 3.07 in ethanol), and $n^{25}\text{D}$ 1.4952–1.4960.

Conversion of Carvone (I) **to Carvonecamphor** (II).—(Modified method of Ciamician and Silber.[9]) A solution of 250 g. of carvone in 2.5 l. of 95% ethanol was placed in a Pyrex tube and irradiated with sunlight in California for 6.5 months. After removal of the ethanol from the yellow reaction mixture by means of distillation under reduced pressure at 35–55°, the residue containing unreacted carvone, carvonecamphor and polymeric material was distilled in a Claisen flask, b.p. 115–126° (36–38 mm.). The distillate (110 g.) was treated with a concentrated aqueous solution of 235 g. of sodium bisulfite which had been neutralized with sodium bicarbonate. The mixture was placed on a shaker at room temperature overnight. After removal of the carvone–bisulfite adduct by filtration, the organic material was extracted into ether, and the extracts were dried over anhydrous sodium sulfate. The ether was removed by distillation through a short column to yield 47 g. of an oil having a camphoraceous odor. Upon cooling, 8.0 g. of carvonecamphor crystallized out and was separated by filtration. The mother liquors were steam distilled three times from dilute, neutral potassium permanganate solutions. During the second and third distillations carvonecamphor crystallized in the condenser. In this way an additional 15.4 g. was obtained, yield 23.4 g. (9.4%).

Carvonecamphor (300 mg.) was purified for analysis by chromatography over 20 g. of silica gel (Davison, activity I). Elution with petroleum ether–chloroform (1:1) yielded 286 mg. Sublimation afforded an analytical sample, m.p. 101–104°, $[\alpha]^{25}\text{D}$ 86.9° (c 1.02 in ethanol). The compound was shown to be homogeneous to vapor phase chromatography over silicone oil and gave no color reaction with tetranitromethane. Infrared spectrum (carbon disulfide solution): 845, 986, 1031, 1091, 1218, 1224, 1275, 1300, 1310(sh), 1380, 1413, 1439, 1727, 2890, 2960 cm.$^{-1}$; no bands in 3000–3100 cm.$^{-1}$ region.[25] Ultraviolet spectrum: end adsorption at 210 mμ (ε 1800), 301 mμ (ε 35).

Anal. Calcd. for $C_{10}H_{14}O$: C, 79.95; H, 9.39; mol. wt., 150. Found: C, 80.07; H, 9.45; mol. wt., in *d,l*-camphor, 536; in exaltone, 153; C-methyl, 1.60.

Treatment with semicarbazide acetate in methanol gave a semicarbazone, m.p. 239–240° dec., recrystallized from ethanol. Treatment with hydroxylamine hydrochloride and potassium hydroxide in ethanol in the usual manner afforded an oxime which was recrystallized from aqueous ethanol, m.p. 124.8–125.2°.

Dicarboxylic Acid III and Ketocarboxylic Acid IV.—(Modified procedure of Sernagiotto.[9]) A mixture of carvonecamphor (2.64 g., 0.0176 mole), potassium hydroxide (0.53 g.) and potassium permanganate (7.53 g., 0.0478 mole) in 400 ml. of water was heated on a steam-bath with frequent shaking for 2.5 hr. The unreacted carvonecamphor (0.80 g.) was steam distilled out of the reaction mixture, which was then concentrated *in vacuo* to about 100 ml. The residue was acidified to *p*H 3 with dilute sulfuric acid, and the manganese dioxide was reduced by the addition of sodium bisulfite. The mixture was saturated with ammonium sulfate and extracted with ether, and the ether extracts were dried over anhydrous sodium sulfate. Removal of the ether by distillation afforded 1.8 g. of crystalline material which was dissolved in benzene and passed through a column containing 60 g. of silica gel (Davison, activity I). Crystalline ketocarboxylic acid (0.85 g., 40%) was eluted with chloroform–ethyl acetate (4:1) and recrystallized from benzene (needles) to constant m.p. 197–198°; C-methyl. 1.53. Infrared spectrum (carbon disulfide solution): 1702, 1770 cm.$^{-1}$ (potassium bromide pellet): 667, 712, 872(broad), 1015, 1082, 1100, 1138(sh), 1147, 1214, 1232, 1260, 1380, 1394, 1429, 1450, 1487, 2900–3600 (broad doublet) cm.$^{-1}$. Ultraviolet spectrum: 210 mμ (ε 112), 280 mμ (ε 25).

The compound gave a negative color reaction with tetranitromethane and did not give a derivative upon treatment with 2,4-dinitrophenylhydrazine reagent. Treatment with semicarbazide acetate afforded a crystalline semicarbazone, recrystallized from water (small needles), m.p. 246–247° dec.

The same column was eluted with ethyl acetate to give crystalline dicarboxylic acid (0.14 g., 19%), recrystallized from water (lustrous plates) to constant m.p. 177.5–178.0°.

The compound gave a negative color reaction with tetranitromethane.

Conversion of the Dicarboxylic Acid III to the Ketocarboxylic Acid IV.—(Modified method of Sernagiotto.[9]) The dicarboxylic acid (0.565 g., 0.00285 mole), potassium hydroxide (0.565 g.) and potassium permanganate (0.593 g., 0.00375 mole) were dissolved in 30 ml. of water and placed on a steam-bath for 0.5 hr. Work-up and removal of the ether by distillation afforded 0.465 g. of crystalline material which was passed through a column containing 15 g. of silica gel (Davison, activity I). Crystalline ketocarboxylic acid (0.23 g., 70%) was eluted with chloroform–ethyl acetate (4:1) and recrystallized from benzene (needles) to constant m.p. 197–198°.

Elution of the column with ethyl acetate afforded 0.17 g. of unreacted dicarboxylic acid, recrystallized from water (plates) to constant m.p. 177–178°.

Formation of the Anhydride XIV.—The dicarboxylic acid (85 mg., 0.43 mmole) and 1.5 ml. of acetic anhydride were refluxed for 2 hr. The major portion of the acetic anhydride and acetic acid was removed *in vacuo* to yield a semicrystalline material. Recrystallization from hexane (needles) to constant m.p. 170.0–171.0° afforded the anhydride of the dicarboxylic acid (72 mg., 93%). Infrared spectrum (Baird Associates recording spectrophotometer, model B, sodium chloride prism, chloroform solution): 950, 970, 1004, 1022, 1247, 1381, 1447, 1745, 1786, 2830 and 2890 cm.$^{-1}$.

Anal. Calcd. for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71. Found: C, 66.75; H, 6.63.

Methyl Ester V.—To a solution of the ketocarboxylic acid (1.00 g., 0.0060 mole) in a minimum amount of dry ether at 0° was added slowly an ether solution of diazomethane (prepared from 1.2 g. of N-nitrosomethylurea by adding the compound in portions to a cooled, saturated potassium hydroxide solution covered with ether and then drying the ether solution of diazomethane over potassium hydroxide) until the yellow color of the diazomethane persisted. The solution was allowed to stand for 0.5 hr. at room temperature. The small excess of diazomethane was removed by codistillation with the ether, and the resulting oil was distilled through a semimicro distillation apparatus to yield

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[23] Analyses by Dr. S. M. Nagy and associates, Massachusetts Institute of Technology, Microanalytical Laboratory.

[24] H. Brockmann and H. Schodder, *Ber.*, **74**, 73 (1945).

[25] The infrared spectra for the C–H stretching region were run with a Perkin–Elmer single-beam, double-pass recording spectrophotometer, model 112, fitted with a lithium fluoride prism.

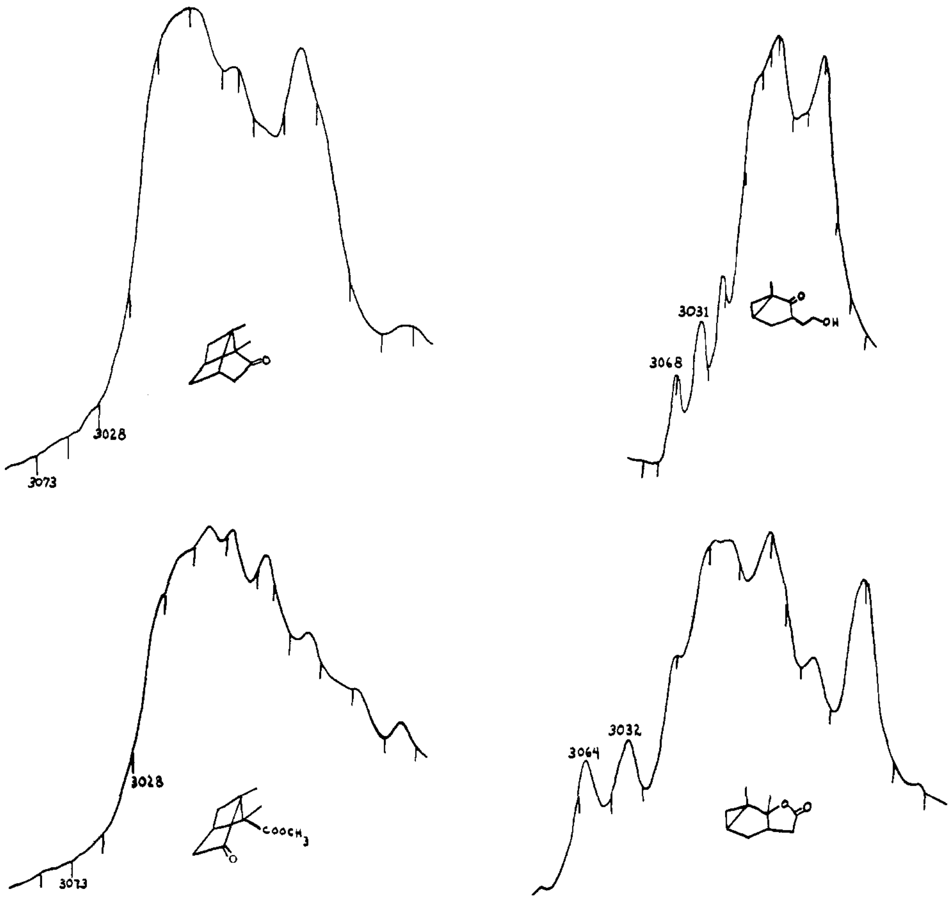

Fig. 1.—Infrared spectra; see ref. 25.

the methyl ester (1.04 g., 95%), $n^{25}D$ 1.4655. Infrared spectrum (carbon disulfide solution): 761, 977, 1010, 1081, 1103, 1133, 1188, 1218, 1228(sh), 1278, 1326, 1376 (sh), 1381, 1428, 1733, 1764 and 2980 cm.$^{-1}$; no bands in 3000–3100 cm.$^{-1}$ region.[25] Ultraviolet spectrum: 210 mμ (ε116), 281 mμ (ε 29).

Anal. Calcd. for $C_{10}H_{14}O_3$: C, 65.91; H, 7.74. Found: C, 66.20; H, 7.78.

Treatment with semicarbazide acetate in methanol gave a semicarbazone, m.p. 224.5–225.0° dec., recrystallized from ethanol.

Deuterium Exchange of the Ketocarboxylic Acid III.—To 6 ml. of deuterium oxide was added in small pieces 575 mg. (25 mmoles) of sodium and 100 mg. (0.60 mmole) of ketocarboxylic acid. The solution was left at room temperature for 12 hr. and heated under reflux for 22 hr. The solution was cooled to 25°, adjusted to *p*H 3 with deuterophosphoric acid and extracted with two 25-ml. portions of ether. The ether fractions were combined and dried over anhydrous magnesium sulfate, and the ether was removed *in vacuo.* The crystalline deuterated product was dissolved in 2 ml. of ethanol, and the ethanol was removed *in vacuo.* The product was again dissolved in 2 ml. of ethanol and the ethanol was removed *in vacuo.* The deuterated product was recrystallized from benzene and dried *in vacuo* to yield 55 mg. (55%) of pure deuteroketocarboxylic acid, m.p. 197–198°. Infrared spectrum (potassium bromide pellet): same as undeuterated material in 4–5 μ region but different in the fingerprint region; 1380, 1394, 1451, 1485 cm.$^{-1}$.

Anal. Calcd. for $C_9H_{10}D_2O_3$: D, 16.65. Found: D, 16.80.

Conversion of Anhydride XIV to the Corresponding Diol XVII.—To the anhydride (100 mg., 0.56 mmole) dissolved in 5 ml. of absolute ether was added slowly 2 ml. of ether solution of lithium aluminum hydride (25 mg./ml., 1.3 mmoles). The mixture was heated under reflux for 1.5 hr. Wet ether was added to destroy the excess reagent, and enough water was added to precipitate the lithium aluminate. The ether layer was removed and the precipitate washed with three portions of ether, and the ether removed *in vacuo* from the combined extracts. The residue (51 mg., 55%) was recrystallized from hexane to constant m.p. 162–163° and sublimed to yield the pure diol. Infrared spectrum (Baird Associates recording spectrophotometer, model B, sodium chloride prism, potassium bromide pellet): 1009, 1027, 1059, 1379, 1445, 2874 and 3300 cm.$^{-1}$.

Anal. Calcd. for $C_{10}H_{18}O_2$: C, 70.54; H, 10.66. Found: C, 70.60; H, 10.58.

Conversion of Carvonecamphor (II) to Isocarvonecamphor (IX).—Carvonecamphor (270 mg., 1.80 mmoles) was dissolved in petroleum ether and put on a column containing 30 g. of alumina (Merck, basic, activity I) and left overnight. The first fraction eluted with ether was crystalline carvonecamphor (48 mg., 18%); continued elution with ether afforded an oil, isocarvonecamphor (115 mg., 43%). A small amount was distilled in a Hickman column. Infrared spectrum (carbon disulfide solution): 882, 1200, 1375, 1414, 1656, 1710, 1770(overtone), 2900(sh), 2960 and 3100(strong) cm.$^{-1}$.

The compound gave a positive color reaction with tetranitromethane. Treatment with semicarbazide acetate in methanol afforded a semicarbazone which was recrystallized from ethanol (needles) to constant m.p. 208.5–209.5 and sublimed for analysis.

Anal. Calcd. for $C_{11}H_{17}N_3O$: C, 63.74; H, 8.27. Found: C, 63.61; H, 8.34.

Elution of the same column with ethyl acetate afforded 53 mg. (20%) of oil which formed a semicarbazone only with difficulty and gave a very strong color reaction with tetranitromethane. The material was discarded.

All attempts to prepare isocarvonecamphor by means of acid-catalyzed reactions[9,10] led only to mixtures of unsaturated ketones which did not show absorption in the infrared characteristic of a terminal olefin and which could not be purified by chromatography or careful distillation. Semicarbazones of these mixtures showed strongly-depressed melting points upon admixture with authentic samples of isocarvonecamphor semicarbazone.

Conversion of Carvonecamphor (II) to the Alcohol XXVII.—Carvonecamphor (118 mg. 0.79 mmole) in 5 ml. of absolute ether was treated with 2 ml. of ether solution of lithium aluminum hydride (25 mg./ml., 1.3 mmoles). The mixture was heated under reflux for 5 hr. Wet ether was added to destroy the excess reagent, and enough water was added to precipitate the lithium aluminate. The ether layer was removed and the precipitate was washed with two portions of ether. The ether was removed *in vacuo* from the combined extracts leaving a nearly quantitative yield of the epimeric alcohols. Recrystallization from hexane (needles) and sublimation afforded pure carvoneborneols (mixture of epimers), m.p. 168–171°.

Anal. Calcd. for $C_{10}H_{16}O$: C, 78.89; H, 10.59. Found: C, 78.86; H, 10.45.

Conversion of Carvonecamphor (II) to its Pyrolysis Product VI.—The pyrolysis apparatus consisted of a vertical Pyrex tube (8 mm. inner diameter and 18 cm. long filled $^2/_3$ full with $^3/_{16}''$ Pyrex helices) with a nitrogen inlet and sample inlet capillary at the top and a removable flask in an ice-bath as a receiver at the bottom. The inlet capillary was fitted with a thin wire for adjusting the rate of addition of the compound. Heating was controlled by an external heating jacket (18 cm. long) fitted with a thermocouple. A water-filled inverted graduated cylinder was used to measure the rate of flow of "prepurified" nitrogen through the system.

In a preliminary experiment carvone was shown to pass through the column at 470° unchanged. A sample of pure carvonecamphor (62 mg., 0.41 mmole) in 1 ml. of *n*-hexane was passed through the column (time of addition of the sample, 1 hr.; flow of nitrogen, 38 ml./min.; temperature, 468–470°), and the pyrolysate was taken up in hexane and the hexane was removed *in vacuo* leaving 63 mg. of a colorless oil. A small portion was distilled in a Hickman column. Infrared spectrum (carbon disulfide solution): 919, 992, 1075, 1316, 1328, 1389, 1415, 1435, 1653(strong), 1680(very weak), 1704(strong), 1732(very weak shoulder), 1835(overtone), 2890, 2930, 2980, and 3090(strong) cm.$^{-1}$. Ultraviolet spectrum: $\lambda 237$ mμ (ϵ 11,400).

Treatment of the remainder of the oil with a small amount of semicarbazide acetate in methanol afforded a crystalline semicarbazone. Recrystallization (5 times) from ethanol (plates) followed by sublimation afforded the pure semicarbazone, m.p. 172–174° dec.

Anal. Calcd. for $C_{11}H_{17}N_3O$: C, 63.74; H, 8.27. Found: C, 63.81; H, 8.25.

Conversion of Carvonecamphor (II) to the Lactone XIII.—Freshly sublimed carvonecamphor (1.00 g., 0.0067 mole) was treated with perbenzoic acid (1.91 g., 0.0138 mole) in 36 ml. of dry benzene and 10 mg. of *p*-toluenesulfonic acid, and the mixture was kept in the dark. After three days, addition of iodide to a small aliquot and titration of the liberated iodine with standard thiosulfate showed that the reaction had proceeded to 85% of completion. Titration after four days showed that no further reaction was taking place. The solution was diluted with 100 ml. of ether and the excess perbenzoic acid was reduced by extraction with small portions of a ferrous sulfate solution which had been acidified with acetic acid. The aqueous extracts were washed with ether and the combined ether extracts were washed with bicarbonate solution. The bicarbonate extracts were washed with ether, and the combined ether extracts were dried over anhydrous sodium sulfate. Removal of the ether *in vacuo* left 1.17 g. of brown oil which was taken up in hexane and passed through a column containing 40 g. of alumina (Merck, acid-washed, activity I). Elution with hexane afforded unreacted carvonecamphor (0.19 g.). Continued elution with hexane followed by ethyl acetate afforded crystalline material which was sublimed to give 0.54 g. (60%) of lactone, m.p. 47–57°. Recrystallization from petroleum ether (needles) and sublimation afforded an analytical sample, m.p. 65.0–65.5°. Infrared spectrum (carbon disulfide solution): 676, 923, 933, 1016, 1036, 1081, 1098, 1140, 1158, 1202, 1222, 1256, 1285, 1329, 1365, 1376, 1422, 1776, 2900, 2950 and 2985 cm.$^{-1}$; with lithium fluoride prism[25]: 3032, 3064 cm.$^{-1}$.

Anal. Calcd. for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.36; H, 8.61.

The lactone gave a negative color reaction with tetranitromethane and was hydrolyzed upon refluxing in dilute base. Acidification of the basic solution, extraction into ether and removal of the ether regenerated the lactone.

Conversion of Carvonecamphor (II) to the Lactone XII. A.—Carvonecamphor (3.3 g., 0.022 mole) was treated with perbenzoic acid (3.45 g., 0.025 mole) in 55 ml. of dry benzene and 10 mg. of *p*-toluenesulfonic acid, and the mixture was kept in the dark for 24 hr., at which time titration showed that the reaction was 57% complete. Work-up of the mixture according to the procedure used for the preparation of the lactone XIII afforded 3.78 g. of oil which was quickly passed through a column containing 60 g. of alumina (Merck, acid-washed, activity I). Elution with hexane afforded, after sublimation, 1.27 g. of unreacted carvonecamphor. Elution with increasing amounts of chloroform in hexane afforded 1.53 g. (68%) of material which crystallized slowly on standing for one month. Sublimation of one fraction from the chromatogram afforded a sample of impure lactone, m.p. 49–71°. Infrared spectrum (carbon disulfide solution): 787, 945, 968, 975, 1004, 1045, 1059, 1097, 1135, 1206, 1233, 1248, 1267, 1341, 1365, 1383, 1420, 1739, 2900, 2950 and 2985 cm.$^{-1}$. Also present were minor peaks which could be attributed to about 20% lactone XIII: 676, 923, 933, 1016, 1037, 1081, 1156, 1222, 1284, 1377, 1776 and 3000-3100(doublet, very weak) cm.$^{-1}$.

Anal. Calcd. for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.25; H, 8.43.

B.—Carvonecamphor (1.12 g., 0.0075 mole) was treated with 26 ml. of perbenzoic acid solution (1.38 g., 0.0100 mole) which had been extracted 8 times with water to wash out any mineral acid which might have been present from the preparation. No *p*-toluenesulfonic acid was added. The mixture was set in the dark for 5 days, at which time it was worked up according to the procedure used for the preparation of the lactone XIII. The oil (1.39 g.) was quickly passed through a column containing 80 g. of alumina (Merck, acid-washed, activity I). Elution with hexane–chloroform (11:1) gave 155 mg. of unchanged carvonecamphor, and elution with hexane–chloroform (5:1) afforded 0.83 g. (78%) of lactone XII which crystallized slowly on standing for one month, m.p. 55–77°. Infrared spectrum: identical with that of lactone, m.p. 49–71°, part A. The lactone could not be recrystallized from the usual solvents. All attempts to separate out the lactone XIII impurity by chromatography led to conversion of the lactone XII to the lactone XIII (see below).

Conversion of Lactone XII to the Lactone XIII.—The lactone XII (140 mg., 0.84 mmole) was passed slowly through a column containing 15 g. of silica gel (Davison, activity I). Elution with petroleum ether–chloroform (4:1) afforded 133 mg. (95%) of crystalline material, m.p. 55–62°. Recrystallization from hexane and sublimation afforded the lactone XIII, m.p. 64–65°, pure or mixed with an authentic sample.

Conversion of the Lactone XIII to the Corresponding Diol XVI.—The lactone XIII (100 mg., 0.60 mmole) in 5 ml. of absolute ether was treated with 2 ml. of ether solution of lithium aluminum hydride (25 mg./ml., 1.3 mmoles). The mixture was heated under reflux for 12 hr. Wet ether was added to destroy the excess reagent, and enough water was added to precipitate the lithium aluminate. The ether layer was removed, and the precipitate was washed with two portions of ether and the ether was removed *in vacuo* from the combined extracts leaving a quantitative yield of the diol. Recrystallization from ether (plates) afforded an analytical sample of the diol, m.p. 100–101°. Infrared spectrum (potassium bromide pellet): 920(sh), 930, 951, 1031, 1048, 1061(sh), 1068, 1093, 1140, 1187, 1237, 1270, 1317, 1372, 1386, 1413, 1464, 1476, 1490, 2885, 2960, 3000–3100 (2 peaks) and 3300(broad) cm.$^{-1}$.

Anal. Calcd. for $C_{10}H_{18}O_2$: C, 70.54; H, 10.66. Found: C, 70.66; H, 10.50.

Conversion of Lactone XII to the Corresponding Diol XV.—The lactone XII (135 mg., 0.81 mmole) in 4 ml. of absolute ether was treated with 2 ml. of ether solution of lithium aluminum hydride (25 mg./ml., 1.3 mmoles). The mixture was heated under reflux overnight. Wet ether was added to destroy the excess reagent, and enough water was added to precipitate the lithium aluminate. The ether layer was removed, and the precipitate was washed with two portions of ether and the ether was removed *in vacuo* leaving 140 mg. of crystalline material. Recrystallization from benzene (plates) afforded an analytical sample of the diol, m.p. 133.0–133.5°. Infrared spectrum (potassium bromide pellet): 915, 1017, 1047, 1077, 1157, 1196, 1230, 1279, 1378, 1430, 1452, 2890, 2960 and 3230(broad) cm.$^{-1}$.

Anal. Calcd. for $C_{10}H_{18}O_2$: C, 70.54; H, 10.66. Found: C, 70.37; H, 10.37.

Conversion of the Diol XVI to the Monoacetate XVIII.—The diol XVI (363 mg., 2.14 mmoles) was treated with 4 ml. of reagent pyridine and 4 ml. of acetic anhydride at room temperature overnight. The pyridine and acetic anhydride were removed *in vacuo* leaving 507 mg. of oil which was passed through a column containing 20 g. of alumina (Merck, acid-washed, activity I). Elution with hexane–chloroform (20:1) afforded 449 mg. (92%) of monoacetate. A small amount was distilled in a Hickman column affording an analytical sample, n^{25}D 1.4703. Infrared spectrum (carbon disulfide solution): 917, 933, 1016(sh), 1030, 1053, 1070(sh), 1115, 1135, 1189, 1238(broad), 1363, 1385, 1428, 1738, 2880, 2940, 2965, 3000–3100(2 peaks), 3540 and 3630 cm.$^{-1}$.

Anal. Calcd. for $C_{12}H_{20}O_3$: C, 67.89; H, 9.50. Found: C, 68.07; H, 9.21.

To show that no rearrangement had taken place in the acetylation reaction, the monoacetate (37 mg., 0.17 mmole) was treated with excess lithium aluminum hydride and worked up in the usual way to give authentic diol XVI (25 mg., 85%).

Conversion of the Diol XV to the Diacetate XXVIII.—The diol XV (101 mg., 0.596 mmole) was treated with 2 ml. of reagent pyridine and 2 ml. of acetic anhydride at room temperature overnight. The pyridine and acetic anhydride were removed *in vacuo* leaving 169 mg. of oil which was passed through a column containing 10 g. of alumina (Merck, acid-washed, activity I). Elution with hexane–chloroform (20:1) afforded 138 mg. (91%) of diacetate. A small sample was distilled in a Hickman column affording an analytical sample, n^{25}D 1.4620. Infrared spectrum (carbon disulfide solution): 945, 1023, 1046, 1106, 1149, 1181, 1241(broad), 1366, 1375(sh), 1431, 1736, 2900 and 2970 cm.$^{-1}$.

Anal. Calcd. for $C_{14}H_{22}O_4$: C, 66.11; H, 8.72. Found: C, 66.17; H, 8.65.

To show that no rearrangement had taken place in the acetylation reaction, the diacetate (108 mg., 0.425 mmole) was treated with excess lithium aluminum hydride and worked up in the usual way to give authenic diol XV (64 mg., 88%).

Conversion of the Diol XVI to the Unsaturated Acetate XIX.—The diol XVI (100 mg., 0.60 mmole) was treated with acetic anhydride (1.23 ml., 6.6 mmoles) and reagent pyridine (0.45 ml.). The mixture was heated under reflux for 5 hr., cooled to room temperature, and the acetic anhydride and pyridine were removed *in vacuo*. The oily residue was taken up in 25 ml. of ether, extracted with a small portion of sodium bicarbonate solution and dried over anhydrous sodium sulfate. Removal of the ether *in vacuo* afforded a sweet-smelling oil which was passed through a column containing 10 g. of silica gel (Davison, activity I). Elution with hexane–chloroform (6:1) afforded 55 mg. (47%) of unsaturated acetate. A small amount was distilled in a Hickman column for analysis, n^{25}D 1.4755. The compound gave a positive color reaction with tetranitromethane. Infrared spectrum (carbon disulfide solution): 866, 1013, 1035, 1057, 1237(broad), 1363, 1386, 1644, 1740, 2880, 2945 and 3000–3100(3 peaks) cm.$^{-1}$. Ultraviolet spectrum: 210 mμ (ε 8730).

Anal. Calcd. for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 73.96; H, 9.27.

Elution of the same column with chloroform afforded 40 mg. (31%) monoacetate (XVIII).

Attempted dehydrations of the monoacetate with phosphorus pentoxide in benzene and iodine in benzene led either to recovery of starting material or small amounts of unsaturated materials which did not show an absorption in the infrared characteristic of a terminal olefin.

When the dehydration using acetic anhydride and pyridine was carried out using a larger quantity of the diol, the yield of unsaturated acetate was increased to 71%.

Hydrogenation of the Unsaturated Acetate XIX.—The unsaturated acetate (17.8 mg., 0.092 mmole) was hydrogenated over 10 mg. of prereduced platinum oxide catalyst in 2 ml. of absolute ethanol at 1 atm. and 26°. The compound took up one mole of hydrogen within 90 minutes and took up no additional hydrogen after 12 hr. Filtration of the reaction mixture, removal of the solvent at reduced pressure and distillation of the oily residue in the Hickman column afforded the dihydro compound XX, 15 mg. (83%). Infrared spectrum (carbon disulfide solution): 1016, 1036, 1055, 1238(broad), 1364, 1375(sh), 1386, 1425, 1737, 2880 and 2940 cm.$^{-1}$; with lithium fluoride prism[25]: 3021 and 3058 cm.$^{-1}$. The compound gave a negative color reaction with tetranitromethane.

Conversion of the Unsaturated Acetate XIX to the Triol XXI.—A solution of the unsaturated acetate (0.764 g., 0.00394 mole) in 5 ml. of reagent pyridine was added slowly to a solution of osmium tetroxide (1.00 g., 0.00394 mole) in 10 ml. of reagent pyridine, and the mixture was allowed to stand for 17 days at room temperature in the dark. Most of the pyridine was removed *in vacuo* and the brown residue taken up in a mixture of 12 ml. of ethanol and 12 ml. of benzene to which was added 7 g. of mannitol and a solution of 7 g. of potassium hydroxide in 12 ml. of water and 22 ml. of ethanol. The mixture was heated under reflux for 7 hr., allowed to cool to 25°, concentrated *in vacuo* to about 10 ml. and extracted with three 50-ml. portions of ether. The combined ether extracts were washed with water and dried over anhydrous magnesium sulfate. Removal of the solvent yielded a viscous oil (0.70 g.) which was dissolved in chloroform and chromatographed on a column of alumina (Woelm, activity IV). Chloroform eluted 0.66 g. (90%) of oil which crystallized slowly on standing. The crystalline material could not be recrystallized from the usual solvents and was distilled in a microdistillation apparatus to give the pure triol. Infrared spectrum (chloroform solution): 982, 1023(broad), 1113, 1225(broad), 1385, 1455, 2880, 2940, 3000–3100(2 peaks), 3420(broad) and 3630(sh) cm.$^{-1}$.

Anal. Calcd. for $C_{10}H_{18}O_3$: C, 64.49; H, 9.74. Found: C, 64.07; H, 9.55.

Conversion of the Triol XXI to the Ketoalcohol XXII.—The triol (213 mg., 1.14 mmoles) in 10 ml. of water was treated with 2 ml. of saturated sodium bicarbonate solution and sodium metaperiodate (470 mg., 2.2 mmoles) in 12 ml. of water at 0°. The solution was stirred and allowed to come to room temperature overnight. After 12 hr. a heavy precipitate had formed, and the mixture was extracted with four 25-ml. portions of ether, and the ether extracts were dried over anhydrous sodium sulfate. The aqueous solution was brought to a boil and 2 ml. of distillate was collected. The presence of formaldehyde was indicated by odor and was confirmed by the isolation of formaldimedon, m.p. 190.0–190.5°, after treatment of the distillate with ethanolic dimedon reagent. The ether was removed *in vacuo* leaving an oil which was dissolved in petroleum ether–ether (2:1) and was passed through a column containing 6 g. of alumina (Woelm, activity IV). Elution with petroleum ether–ether (2:1) afforded 150 mg. (85%) of the ketoalcohol. Distillation in a Hickman column afforded an analytical sample, n^{25}D 1.4870. Infrared spectrum (carbon disulfide solution): 842, 1004, 1014(sh), 1050(broad), 1098, 1368, 1390, 1430, 1705(sh), 1717, 2880, 2935, 3460(broad) and 3640(sh) cm.$^{-1}$; with lithium fluoride prism[25]: 3031 and 3068 cm.$^{-1}$. Ultraviolet spectrum: 210 mμ (ε 8200).

Anal. Calcd. for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 70.31; H, 9.25.

Aromatization of the Diol XVI.—To 198 mg. (1.16 mmoles) of diol, m.p. 100–101°, was added 5 ml. of 20% (by volume) sulfuric acid, and the mixture was heated under reflux for 10 minutes. The mixture was cooled to 25° and extracted with three 25-ml. portions of ether, and the ether extracts were washed with bicarbonate solution. The ether fractions were combined and dried over anhydrous magnesium sulfate, and the ether was removed *in vacuo* leaving 168 mg. of brown oil. The oil was taken up in ether and passed through a column containing 5 g. of silica gel (Davison, activity I). Elution with ether afforded 130 mg. of yellow oil which was distilled in a Hickman column giving 60 mg. of colorless oil. The material gave a strong tetranitromethane color reaction. Infrared spectum (carbon disulfide solution): 718, 771, 786, 814, 870, 890, 920, 944, 972, 1010, 1030, 1085, 1105, 1130, 1157, 1255, 1329, 1369, 1430, 1613, 1664, 1730, 1810, 1880, 2720, 2880, 2920, 2960 and 3000–3100(sh) cm.$^{-1}$. Ultraviolet spectrum: end absorption at 210 mμ (ε 9300), 245 mμ (ε 345), 267 mμ (ε 260), 276 mμ (ε 224). Analysis of a small sample by means of vapor phase chromatography on a column containing silicone oil on fire-brick indicated that the sample was composed of three components in the ratio of 7:2:1.

Anal. Calcd. for $C_{10}H_{14}$: C, 89.49; H, 10.51. Found: C, 83.51; H, 10.74.

Aromatization of the Diol XV.—To 84 mg. (0.50 mmole) of diol, m.p. 133–133.5°, was added 5 ml. of 20% (by volume) sulfuric acid, and the mixture was heated under reflux for 10 minutes. After cooling to 25° the mixture was worked up according to the procedure used for the aromatization of the diol XVI above. Distillation of the ether eluate in a Hickman column afforded 30 mg. of oil. Infrared spectrum (carbon disulfide solution): identical with that of product obtained in aromatization of diol XVI, except for minor differences in intensities of peaks in the 1000–1150 cm.$^{-1}$ region. A small sample was passed through a silicone-on-fire-brick column in the vapor phase at 200°, and the main component (70%) was collected in a small receiver in a Dry Ice trap. The chromatographed sample was taken up in ether and distilled in a small Hickman column at 190°, 1 atm., and the distillate was taken up in ethanol. Ultraviolet spectrum (concentration not determined): peaks at 247, 253, 259, 263, 265, 270 and 276 mμ.

Aromatization of Mixture of Diols XV and XVI.—To 559 mg. (3.30 mmoles) of diols XV and XVI, m.p. 82–101°, was added 6 ml. of 20% (by volume) sulfuric acid, and the mixture was heated under reflux for 2 hr. The mixture was worked up according to the procedure used for the aromatization of the diol XVI above. Infrared spectrum (carbon disulfide solution): identical with that of 1,3-dimethyl-4-ethylbenzene, except for intensities of peaks in the 1000–1150 cm.$^{-1}$ region.

The chromatographed sample was passed through the column in the vapor phase for a second time, as above. Distillation of the product in a small Hickman column afforded a sample of 1,3-dimethyl-4-ethylbenzene. Infrared spectrum (carbon disulfide solution): identical with that of 1,3-dimethyl-4-ethylbenzene described below.

Anal. Calcd. for $C_{10}H_{14}$: C, 89.49; H, 10.51. Found: C, 88.79; H, 10.56.

To 55 mg. of material from the vapor phase chromatogram was added 0.5 ml. of concentrated sulfuric acid and dropwise, 0.5 ml. of fuming nitric acid. The mixture was heated on a steam-bath for 10 minutes and poured over 5 g. of ice. The yellow precipitate (90 mg.) was recrystallized from ethanol (fine needles) to constant m.p. 126.8–129°; no depression in m.p. after mixing with a synthetic sample of the trinitro compound described below.

One drop of hydrocarbon was added to one drop of synthetic 1,3-dimethyl-4-ethylbenzene. Analysis of the mixture by means of vapor phase chromatography on a column containing silicone oil on fire-brick indicated that only one molecular species was present.

1,3-Dimethyl-4-ethylbenzene (XXVI).—A solution of *m*-xylene in carbon disulfide was treated with aluminum chloride and acetic anhydride according to the procedure of Adams and Noller.[26] The 2,4-dimethylacetophenone was reduced by means of amalgamated zinc in hydrochloric acid according to the procedure of Martin.[27] A small quantity of the crude product was passed through a column of silica gel. The material eluted with petroleum ether was distilled in a Hickman column at 195°, 1 atm., affording a pure sample of 1,3-dimethyl-4-ethylbenzene, $n^{25}D$ 1.5008, the infrared spectrum of which was identical with Infrared Spectrum No. 736, American Petroleum Institute. Infrared spectrum (carbon disulfide solution): 690, 725, 734, 772, 784, 814, 871, 922, 940, 962, 975(sh), 1015, 1030, 1059, 1113, 1155, 1207, 1227, 1280, 1305, 1318, 1336, 1375, 1428, 1613, 1684, 1737, 1811, 1880, 2380, 2720, 2880, 2930, 2960, 3000(sh) and 3120 cm.$^{-1}$.

A small amount of the synthetic material was nitrated as described above. The crystalline material was recrystallized from ethanol (small needles) to constant m.p. 127.4–129.5° (lit.[28] for trinitro derivative of 1,3-dimethyl-4-ethylbenzene).

Acknowledgments.—We are indebted to the National Institutes of Health for a fellowship to I. M. Goldman and to Mr. Monroe Evans for the high resolution infrared spectra.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF BARNARD COLLEGE]

Dissociation Constants of Acids and Rates of Alkaline Hydrolysis of Esters in the Benzylidenepyruvic Acid Series

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RECEIVED MARCH 1, 1957

The dissociation constants of *m*- and *p*-substituted benzylidenepyruvic acids (pK_0 2.58) have been determined in 48 volume per cent. methanol–0.2 *M* lithium chloride and compared with those of substituted benzoic acids in the same solvent (pK_0 4.99). The ρ-value for the former is +0.106, for benzoic acids ρ = +1.260. The first-order rates of hydrolysis of substituted methyl benzylidenepyruvates have been determined spectroscopically at 24.8° in 11.8 volume per cent. methanolic buffers and compared with those of substituted methyl benzoates. The ρ-value for methyl benzylidenepyruvates is +0.484; for methyl benzoates it is +1.672. The rate for methyl benzylidenepyruvate is estimated as 47,400 times that of methyl benzoate. Data are included for *o*-methoxy- and *o*-nitrobenzylidenepyruvic acids and esters. Taft's polar substituent constant, σ^*, for $C_6H_5CH{=}CHCO$ relative to CH_3 is estimated as +1.9 (or +1.6) depending on the method of calculation.

In a series of substituted benzoic acids the inductive and resonance effects of the substituent groups are reflected in a predictable manner in the ionization constants of the acids. These group effects have been generalized and treated quantitatively by Hammett[1] and more recently by Jaffe.[2] Any grouping (Y in formula I) intervening between the benzene ring and the carboxyl group reduces the electronic effect of a substituent X—less however, if the group is unsaturated and conjugated with the ring. Thus β-phenylpropionic acids show smaller group effects than cinnamic acids, though in both cases Y contains two atoms.

$$\underset{\text{I}}{XC_6H_4{-}Y{-}COOH}\qquad \underset{\text{II}}{XC_6H_4CH{=}CHCOCOOH}$$

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[1] (a) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, Chapter VII; (b) *Chem. Rev.*, **17**, 125 (1935); (c) THIS JOURNAL, **59**, 96 (1937).

[2] (a) H. H. Jaffé, *Chem. Revs.*, **53**, 191 (1953); (b) **53**, 253 (1953); (c) *J. Chem. Phys.*, **21**, 415 (1953).