benzene. After refluxing for 1 hr. the product was isolated by the usual procedure. Material with a cinnamon-like odor, b.p. 147–167° (20–18 mm.), was divided by redistillation into a colorless liquid with a flower-like odor (2.3 g.), b.p. 120–155° (23–22 mm.), and a greenish-yellow liquid of similar odor, b.p. 154.5–159° (20–19.5 mm.). A sample of the latter on redistillation was colorless, b.p. 163° (27 mm.), $n^{25}D$ 1.5507, d^{25}_4 1.040, $\lambda_{max}^{ethanol}$ 254 mμ (log ε 4.10) and end absorption.[5]

(5) The shift to shorter wave length when an olefinic bond is conjugated at the 4-position of the veratryl ring system confirms the report on 4-propenylveratole; A. Hillmer and P. Schorning, *Z. physik. Chem.*, **168A**, 81 (1934).

Anal. Calcd. for $C_{12}H_{16}O_2$: C, 74.96; H, 8.39. Found: C, 74.64; H, 8.50.

2-*sec*-Butyl-4,5-dimethoxybenzenesulfonamide.—Catalytic hydrogenation of 1.0 g. of the above olefin with 500 mg. of 5% palladium–carbon in 50 ml. of ethanol consumed 148 ml. of gas; calculated volume 138 ml. After filtration of the catalyst and distillation of the solvent, the residual oil was converted to the sulfonamide (0.63 g.) as indicated in Table III.

SALT LAKE CITY 12, UTAH

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE COLLEGE OF ARTS AND SCIENCES OF THE UNIVERSITY OF LOUISVILLE]

2-Pyrones. XXVI. Alkylidene Methylglutaconic Acids and 3,6-Dialkyl-5-carboxy-5,6-dihydro-2-pyrones from Methyl β-Methylglutaconate and Ethyl Isodehydroacetate and their Isomerization and Decarboxylation

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The condensation of aliphatic aldehydes with methyl β-methylglutaconate gives alkylidene glutaconic acids (III) and carboxy-δ-lactones (IV). Comparable yields are obtained using ethyl isodehydroacetate in place of the glutaconate. Short-chain and branched-chain aldehydes give diacids (III); longer chain and unbranched aldehydes give carboxylactones (IV). Decarboxylation of these products gives the dienonoic acids VI and δ-lactones V. The lactones can be hydrolyzed to the corresponding acids and the preferred route to the isoprenoid acid, 3,7-dimethyl-2,4-octadienoic acid, is *via* decarboxylation of the dipotassium salt to the lactone which is then hydrolyzed. The carboxy isoprenoid acid, γ-isoamylidene-β-methylglutaconic acid, has been obtained in three forms, m.p. 149–150, 163° and 181–184°. The isomer m.p. 149–150° has been assigned the 4-*cis*-2-*trans* structure; the isomer m.p. 181–184° has been assigned the 2-*trans*-4-*trans* structure on the basis of comparisons of their infrared spectra with those of *cis* and *trans* β-methylglutaconic acid. The δ-lactone structure has been established by conversion to the tetrahydro-2-pyrone structure with properties similar to those of other known tetrahydro-2-pyrones.

One of the few known methods for adding an isoprenoid unit to an organic structure involves the base-catalyzed condensation of dimethyl β-methylglutaconate (II) with an aldehyde[1–4] to give γ-arylidene or alkylidene-β-methylglutaconic acids (III). Although previously utilized principally for the synthesis of vitamin A, this method also makes possible the synthesis of acyclic isoprenoid acids of 10 or 15 carbons, which are of current interest as possible intermediates in the biosynthesis of cholesterol[5–8] with varying substituents, notably a 4-carboxyl group. Since previous studies of the reaction have not included comprehensive studies of the scope of the reaction using aliphatic aldehydes, we have undertaken a study of such reactions which we wish to record here along with our observations on the previously unreported accompanying cyclization to lactones (IV), the decarboxylation, and the geometrical isomerism of the γ-alkylidene-β-methylglutaconic acids (III). Particular attention has been directed to 3,7-dimethyl-2,4-octadienoic acid—an isomer of geranic acid and its 4-carboxy derivative.

The condensation reaction previously has been conducted using the aldehyde and dimethyl β-methylglutaconate (II) in methanolic potassium hydroxide. With aliphatic aldehydes the reaction is exothermic and the crystalline potassium salt of the product begins to precipitate shortly after mixing the reactants. The products from aliphatic aldehydes have been isolated in 51–91% yields (Table I). Since the β-methylglutaconate itself is formed readily from ethyl isodehydroacetate (I) by the action of methanolic potassium hydroxide, the utilization of the latter in place of the β-methylglutaconate to give the products directly in one step has been examined and found to be satisfactory. The products obtained by the two processes are comparable in all respects observed. This reaction is also exothermic and gives comparable yields with hexaldehyde (55 as compared to 58%), heptaldehyde (48 as compared to 51%), and pelargonaldehyde (61 as compared to 76%). With isobutyraldehyde (59 as compared to 91%) and isovaleraldehyde (43 as compared to 84%), the yield is noticeably poorer. Allowance for a 75% yield from isodehydroacetate to β-methylglutaconate indicates that the one-step process gives comparable yields with considerable saving of effort by avoiding isolation of the intermediate ester. The combined one-step process has been used with several other aliphatic and aromatic aldehydes listed in Table II. β-Ethoxypropionaldehyde, tiglic aldehyde and acetaldehyde failed to give characterizable products.

A unique feature of this reaction, which has not been recognized previously, is that not only diacids III but also the isomeric carboxylactones IV are

(1) F. Feist and O. Beyer, *Ann.*, **345**, 117 (1906).
(2) C. D. Hurd and J. L. Abernethy, THIS JOURNAL, **63**, 976 (1941).
(3) V. Petrow and O. Stephenson, *J. Chem. Soc.*, 1310 (1950).
(4) J. D. Cawley, THIS JOURNAL, **77**, 4125 (1955).
(5) H. Rudney, *ibid.*, **76**, 2595 (1954); **77**, 1698 (1955).
(6) J. L. Rabinowitz and S. Gurin, *ibid.*, **77**, 1295 (1955); **76**, 3037, 5168 (1954).
(7) K. Bloch, L. C. Clark and I. Harary, *J. Biol. Chem.*, **211**, 687 (1954).
(8) S. Gurin, *et al.*, *Federation Proc.*, **14**, 752 ff. (1955).

TABLE I

γ-ALKYLIDENE-β-METHYLGLUTACONIC ACIDS AND CARBOXYLACTONES FROM METHYL β-METHYLGLUTACONATE

R of formula III or IV	Yield, %	M.p.,[a] °C.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Neut. equiv. Calcd.	Neut. equiv. Found
Isopropyl	91[b]	157–158 A	60.59	60.64	7.12	7.18	102.1	99.0
Isobutyl	84[b]	149 A	62.25	62.23	7.60	7.78	106.2	105.3
n-Amyl	58[c]	127–129 P	63.70	63.52	8.02	7.99	226.3	229.0
n-Hexyl	52[c]	124–126 P	64.98	64.88	8.39	8.38	240.3	243.6
n-Octyl	76[c]	105–106 P	67.13	67.08	9.02	9.12	268.3	268.8

[a] Recrystallized from A, methanol–water; E, ether–petroleum ether; P, ethyl acetate–petroleum ether. [b] Diacid III. [c] Lactone IV.

TABLE II

γ-ALKYLIDENE-β-METHYLGLUTACONIC ACIDS AND CARBOXYLACTONES FROM ETHYL ISODEHYDROACETATE

R of formula III or IV	Yield, %	M.p.,[a] °C.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Neut. equiv. Calcd.	Neut. equiv. Found
n-Propyl	37[b]	127–128 E	60.59	60.76	7.12	7.36	99.1	105.8
Isopropyl	59[b]	157–158 A	60.59	60.64	7.12	7.26	99.1	100.8
Isobutyl	43[b]	149–150 A	62.25	62.21	7.60	7.82	106.2	105.3
1′-Ethylpropyl	86[b]	216–220 B	63.70	63.66	8.02	8.04	113.1	114.2
1′-Ethylpentyl	60[b]	148 A	66.11	66.23	8.72	8.63	127.2	128.6
Phenyl[d]	48[b]	190–191 A					116.1	115.9
3,4-Dimethoxyphenyl[d]	50[b]	184–185 C						
p-Chlorophenyl[d]	66[b]	193–195 A						
n-Butyl	21[c]	123–124 P	62.26	62.20	7.60	7.62	212.2	214.9
n-Amyl	55[c]	127–129 E	63.70	63.52	8.02	7.99	226.3	229.0
n-Hexyl	48[c]	124–126 A	64.98	64.88	8.39	8.38	240.3	243.6
n-Heptyl	25[c]	115–117 A	66.11	66.42	8.72	8.75	254.3	256.8
n-Octyl	61[c]	105–106 P	67.13	67.08	9.02	9.12	268.3	268.8

[a] Recrystallized from A, methanol–water; B, methanol; C, ethyl acetate; E, petroleum ether–ether; P, ethyl acetate–petroleum ether. [b] Diacid III. [c] Carboxylactone IV. [d] See ref. 4. [e] In cm.$^{-1}$.

formed. It appears that the short chain and branched-chain aliphatic aldehydes and aromatic aldehydes give exclusively the diacid products III and that the longer chain, unbranched aldehydes give principally the carboxylactones IV as products. The contrast in behavior in this respect between valeraldehyde and isovaleraldehyde and between *n*-octaldehyde and 2-ethylhexaldehyde is striking. Assuming that the 2-*cis* form is needed for cyclization and that the 2-*trans* form is customarily obtained[4] in this reaction, isomerization and subsequent lactonization must take place more readily under the conditions used in the reaction with the unbranched types. It is difficult to assign a reason for this in the absence of additional data about the conditions required for geometrical isomerization of these structures. With some of these materials it is possible to lactonize the dibasic acids, although in low yield. Thus, γ-isoamylidene-β-methylglutaconic acid (III, R = isobutyl) is lactonized in 16% yield by treatment with acid. With others it is possible to obtain mixtures of both isomers. Thus, the potassium salt obtained from the hexaldehyde reaction (III, R = *n*-amyl) gives a mixture of the lactone IV and the dibasic acid III when exactly neutralized at 0°. The two types of products formed in this reaction are readily distinguished by their neutral equivalents. The infrared absorption characteristics of the dibasic acids show typical carboxyl carbonyl absorption bands at 1690–1680, at 1455–1445, 1430–1425 and at 950–935 cm.$^{-1}$. The lactones show a strong carbonyl absorption at 1730–1725 cm.$^{-1}$ typical of δ-lactones. The δ-lactone structure is further confirmed by the conversion described in following paragraphs of one derivative to a similar tetrahydro-2-pyrone obtained by another synthetic route. These considerations eliminate the alternative γ-lactone structure.

During the process of decarboxylation the dibasic acids and the carboxylactones give either acids such as VI or lactones (5,6-dihydro-2-pyrones) such as V. The dibasic acids (R = isopropyl, isobutyl) decarboxylate in 10–12% yields using 2,4-lutidine and cupric acetate as the catalyst. These products are assumed to have lost the carboxyl groups on the 4-carbon atom, by analogy with previously reported data,[9] to give dienoic acids. These acids are unstable toward oxygen and readily form peroxides. Their purification is difficult and this accounts in part for the low yields in the decarboxylation. Although reactions of these acids with bromine and with maleic anhydride have not given readily characterizable derivatives, the benzylthiuronium salts readily are formed and crystallize nicely.

When the crude dipotassium salts are heated in glacial acetic acid, decarboxylation occurs and the product is the lactone (V, R = isobutyl, *n*-amyl or 2′,6′-dimethyl-5′-heptenyl). Using lutidine and cupric acetate for the decarboxylation, a mixture of lactone V and acid VI results from other dibasic acids (R = propyl, 1′-ethylamyl) and from the carboxylactone (IV, R = butyl). Two of the lactones obtained by decarboxylation (V, R = isobutyl, propyl) have been converted to the open-chain acids by hydrolysis with alcoholic potassium hydroxide. This hydrolysis gave 38% of 3,7-dimethyl-2,4-octadienoic acid (VI, R = isobutyl) and this route *via* dibasic acid salt, decarboxylation to the lactone (71%) and hydrolysis (38%) is pre-

(9) J. D. Cawley and D. R. Nelan, THIS JOURNAL, **77**, 4130 (1955).

ferred to that *via* the decarboxylation of the dibasic acid (12%) since the yield is better and the isolation of the dicarboxylic acid is avoided.

The lactone or 5,6-dihydro-2-pyrone structure assigned to the compounds IV and V has been confirmed by catalytic reduction of 6-butyl-4-methyl-5,6-dihydro-2-pyrone to 6-butyl-4-methyltetrahydro-2-pyrone with infrared absorption characteristics identical in all significant respects with that of 4,6-dimethyltetrahydro-2-pyrone prepared previously.[10] Carbon–hydrogen absorption at 2960 cm.$^{-1}$, a carbonyl doublet at 1735–1710 cm.$^{-1}$ and the ester carbon–oxygen absorption at 1240 cm.$^{-1}$ are the most prominent bands and are at the same location in the spectra of both of these compounds.

The geometric isomerism of acids such as γ-isoamylidene-β-methylglutaconic acid is of considerable significance. This acid is a carboxy isoprenoid acid which by virtue of its structural relation to β-methylglutaconic acid is of interest as a possible intermediate in the biosynthesis of cholesterol. The fact that only *trans*-, not *cis*-, β-methylglutaconic acid is an effective intermediate in this process and that squalene, another apparent intermediate, is of the *trans* configuration, suggest that geometric isomers of the acid should be available for biosynthetic examination.

Attempts to isomerize the acids, m.p. 149–150°, with iodine and ultraviolet light gave an isomer, m.p. 163°, which was also obtained by slow recrystallization of the acid, m.p. 149–150°, from ether–ligroin. The facts that no depression of the melting point of the acid, m.p. 149–150°, is observed with mixtures of the two and that the infrared spectra of the two materials are apparently identical indicates that these two forms may be isomorphic. This does not eliminate the possibility that they are geometric isomers or mixtures thereof.

An isomer of γ-isoamylidene-β-methylglutaconic acid has been obtained by altering the conditions used in the preparation of this acid from methyl β-methylglutaconate. If double the amount of potassium hydroxide is used in a procedure otherwise similar, a product is obtained which melts at 181–184°. This gives a mixed m.p. of 144–151° with the isomer, m.p. 150°. The infrared spectra of the two (Fig. 1) are substantially identical except in the 1285 cm.$^{-1}$ (C–O stretching or O–H deformation) and 1175 cm.$^{-1}$ (band progression) regions where certain minor differences can be correlated with differences in the infrared spectra for *cis*- and *trans*-β-methylglutaconic acid (Fig. 2). There is no substantial difference in the C–H out-of-plane deformation region where disubstituted *cis–trans*-ethylenes show marked differences,[11] but it has previously been noted[12] that trisubstituted ethylenes do not show such differences. *cis*-β-Methylglutaconic acid shows maxima at 1277 and 1148 cm.$^{-1}$ shifted to 1264 and 1167 cm.$^{-1}$, with a shoulder at 1152 cm.$^{-1}$ in the *trans*-acid. The isomer, m.p. 150°, shows maxima at 1289 cm.$^{-1}$ shifted to 1284 cm.$^{-1}$ with shoulders at 1295 and 1310 cm.$^{-1}$ and a new band at 1263 cm.$^{-1}$

(10) R. H. Wiley and A. J. Hart, THIS JOURNAL, **77**, 2340 (1955).
(11) R. N. Jones, *ibid*, **72**, 5322 (1950).
(12) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1954, p. 36.

TABLE III

INFRARED ABSORPTION MAXIMA[a]

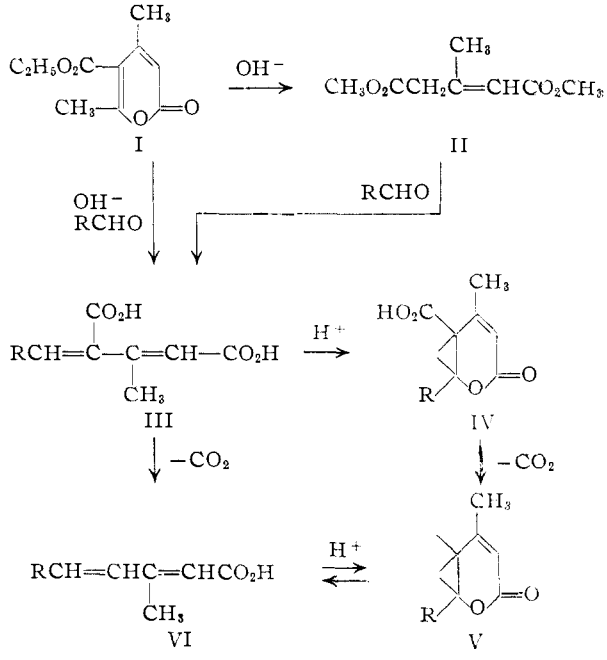
R of formula III	C=O stretching[b]	C=C stretching[c]		Out-of plane deformation[c] OH	CH
γ-Alkylidene-β-methylglutaconic acids					
n-Propyl	1689	1645	1623	935	869
Isopropyl	1689	1650	1623	958	882
Isobutyl	1686	1658	1626	930	877
n-Amyl	1684	1647	1618	936	864
1′-Ethylpentyl	1689	1653	1623	935	866
Phenyl	1684	1639	1608	935	867
3,4-Dimethoxyphenyl	1678	1653	1608	942	871

R of formula IV			
γ-Carboxy-δ-lactones			
Isobutyl	1718/1664	1634	
n-Amyl	1721/1664	1634	
n-Hexyl	1721/1664	1634	
n-Heptyl	1718/1667	1634	

R of formula V			C–O stretching
δ-Lactones			
n-Propyl[d]	1724	1639	1242
Isobutyl[d]	1724	1639	1242
n-Amyl[d]	1727	1642	1252
2,6-Dimethyl-5-heptenyl[d]	1727	1645	1247

[a] In cm.$^{-1}$ as potassium bromide pellets except as noted. [b] All bands of strong intensity. [c] All bands of medium intensity. [d] In carbon tetrachloride.

in the isomer, m.p. 181–184°. The band at 1167 cm.$^{-1}$ in the 150° isomer appears at 1174 cm.$^{-1}$ with a shoulder at 1157 cm.$^{-1}$ in the 181–184° isomer. These differences, although minor in themselves, constitute a total absorption picture in this region which serves to distinguish the isomers rather clearly and, furthermore, resembles the differences in the spectra of *cis*- and *trans*-β-methylglutaconic acids. This would appear to establish the reality of the existence of the isomers and to



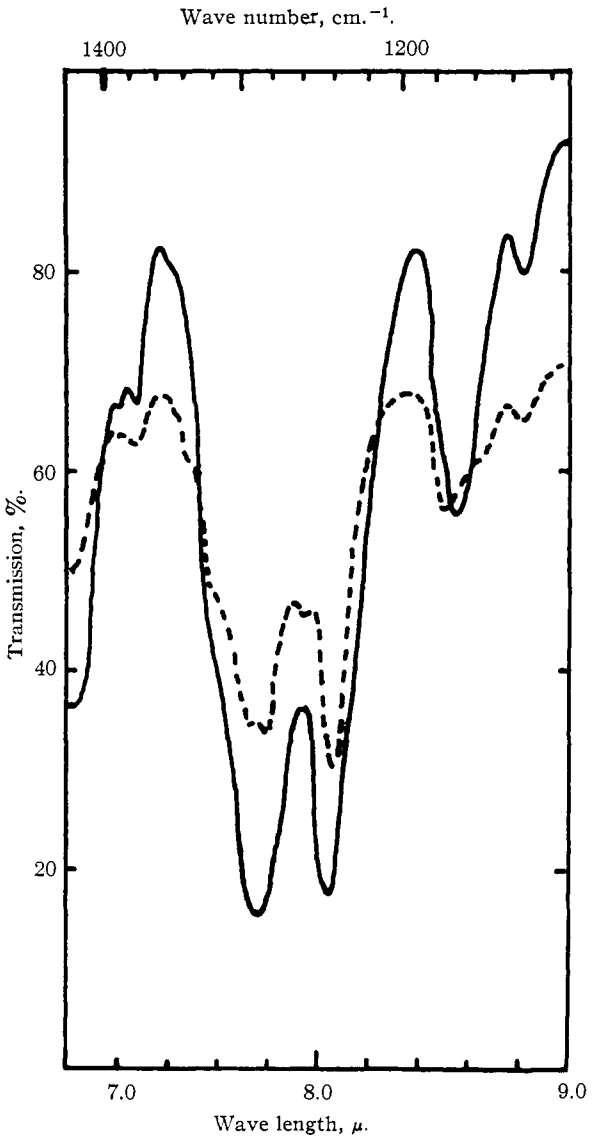


Fig. 1.—Infrared absorption of γ-isoamylidene-β-methylglutaconic acids: m.p. 149–150° (——); m.p. 181–184° (- - - -).

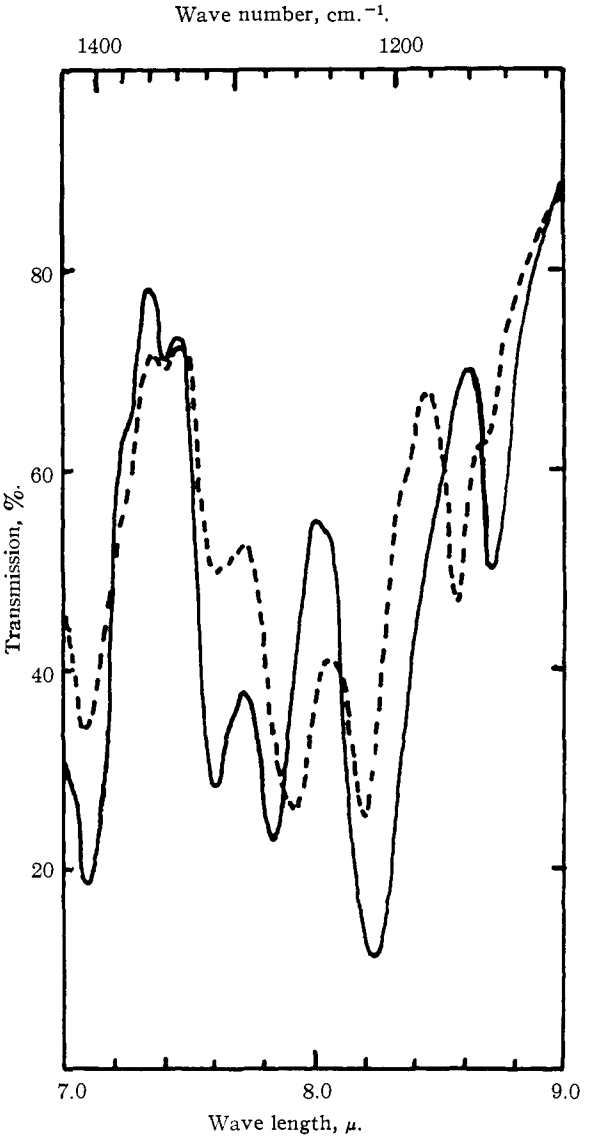


Fig. 2.—Infrared absorption of *cis*- (——) and *trans*- (- - - -) β-methylglutaconic acids.

support a tentative assignment of the *trans–trans* structure to the isomer, m.p. 181–184°, on the basis that the *cis–cis* structure would have undergone lactonization. The 4-*cis*-2-*trans* structure may be tentatively assigned to the isomer, m.p. 150°, on the basis of reasons previously analyzed.[4,9]

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Experimental[13]

The ethyl isodehydroacetate,[14] b.p. 139–142° (5 mm.), and the methyl β-methylglutaconate,[15] b.p. 142° (30 mm.), used in these studies were prepared by the methods previously given. The authors are indebted to the Tennessee Eastman Co. for additional supplies of ethyl isodehydroacetate. The aldehydes were commercial samples and were distilled prior to use. Details of typical reactions will be given. Data on other reactions and characterization of the products are presented in the Tables.

γ-Isoamylidene-β-methylglutaconic Acid (III, R = isobutyl). **From Methyl β-Methylglutaconate. 4-*cis*-2-*trans* Isomer, M.p. 149–150°.**—To a solution of 4.3 g. (0.05 mole) of freshly distilled isovaleraldehyde and 8.6 g. (0.05 mole) of methyl β-methylglutaconate in 10 ml. of methanol was added a filtered solution of 11.2 g. (0.2 mole) of potassium hydroxide in 30 ml of methanol. An immediate exothermic reaction was followed by precipitation of the dipotassium salt of the acid. After six hours the mixture was cooled to 0° and filtered. The salt was washed with cold methanol, dried, and dissolved in water. Acidification with concd. hydrochloric acid precipitated the crude product. Recrystallization from methanol–water gave 8.9 g., 84.6%, of the product, m.p. 149–150°. Analytical data are given in Table I. Slow recrystallization from ether–ligroin gives the acid in a form which has m.p. 163°.

The methyl β-methylglutaconate can be replaced with an equivalent amount of ethyl isodehydroacetate. The crude salt is triturated at 0° first with methanol then with ether before conversion to the acid. Recrystallization of the acid gives 4.6 g. (43.3%) of the product, m.p. 149–150°.

(13) Analysis by Micro Tech Laboratories, Skokie, Ill., m.p.'s are uncorrected.

(14) R. H. Wiley and N. R. Smith, THIS JOURNAL, **74**, 3893 (1952).

(15) F. R. Goss, C K. Ingold and J. F. Thorpe, *J. Chem. Soc.*, **123**, 327 (1923).

The acids listed in Table II were prepared from ethyl isodehydroacetate by this procedure.

The products obtained from other aldehydes by this procedure are listed in Table I. Acetaldehyde, crotonaldehyde, tiglic aldehyde and β-ethoxypropionaldehyde gave only resins. Citronellal gave a product which, although it was not purified, was used in decarboxylation as described in a following paragraph.

From Methyl β-Methylglutaconate. 2-*trans*-4-*trans* Isomer, M.p. 181–184°.—The procedure described in the preceding paragraph was followed using 22.4 g. (0.40 mole) of potassium hydroxide. The crude acid was dissolved in a minimum amount of ether and an equal volume of ligroin. The acid which crystallizes from this mixture was recrystallized from methanol–water to give 2.1 g., 20%, of the product, m.p. 181–184°; mixed m.p. with the product m.p. 149–150°, 144–151°. The same product, m.p. 181–184°, is obtained when ethyl isodehydroacetate is substituted for the methyl β-methylglutaconate.

Anal. Calcd. for $C_{11}H_{16}O_4$: C, 62.25; H, 7.60; neut. equiv., 106.2. Found: C, 62.27; H, 7.75; neut. equiv., 106.1.

6-Amyl-5-carboxy-4-methyl-5,6-dihydro-2-pyrone (IV, R = *n*-amyl).—The procedure given for the preparation of γ-isoamylidene-β-methylglutaconic acid from methyl β-methylglutaconate was followed using 5.0 g. (0.05 mole) of *n*-hexaldehyde. The lactone is precipitated as a viscous oil which solidifies on washing with dilute acid. Recrystallization from ether–ligroin gives 6.5 g., 58%, of the product as white needles, m.p. 127–129°. Analytical data for this and the other lactones prepared similarly are given in Table I.

The methyl β-methylglutaconate can be replaced by an equivalent amount of ethyl isodehydroacetate in this procedure to give comparable results. The crude salt is purified by trituration with methanol and with ether at 0°. The crude carboxylactone is precipitated as an oil. After solidification it is recrystallized from ether–ligroin to give 6.2 g. (55%) of the product, m.p. 127–129°. Analytical data for the products obtained from this and other aldehydes, by this process are given in Table II.

5-Carboxy-6-isobutyl-4-methyl-5,6-dihydro-2-pyrone (IV, R = isobutyl). **By Lactonization of the Diacid** (III, R = isobutyl).—A solution of 2.0 g. of 4-carboxy-3,7-dimethyl-2,4-octadienoic acid in 40 ml. of C.P. acetone and 10 ml. of 50% aqueous sulfuric acid was refluxed 45 minutes. After removing 30 ml. of acetone by distillation, the residue was diluted with 50 ml. of water and extracted with three 50-ml. portions of ether. The decolorized and dried extracts were combined with 300 ml. of petroleum ether. The product slowly crystallizes from this mixture as a white solid. On standing this solution deposited 0.32 g. (16%) of the product as white crystals, m.p. 133–134°.

Anal. Calcd. for $C_{11}H_{16}O_4$: C, 62.25; H, 7.60; neut. equiv., 212.2. Found: C, 62.75; H, 7.93; neut. equiv., 212.5.

γ-Hexylidene-β-methylglutaconic Acid (III, R = *n*-amyl).—This acid was obtained by careful acidification of the crude salt obtained in the reaction of *n*-hexaldehyde with ethyl isodehydroacetate as described above. The neutralization of the salt is carried out by the dropwise addition of the calculated amount of 0.1 *N* hydrochloric acid. The precipitated product is a mixture of the carboxylactone and dicarboxylic acid. Fractional recrystallization from ether–ligroin gives 27% of the dibasic acid, m.p. 110–112°, as the less soluble fraction.

Anal. Calcd. for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02; neut. equiv., 113.1. Found: C, 63.74; H, 8.07; neut. equiv., 115.6.

3,6-Dimethyl-2,4-heptadienoic Acid (VI, R = isopropyl).—A solution of 5.0 g. of γ-isobutylidene-β-methylglutaconic acid and 0.125 g. of cupric acetate in 25 g. of 2,4-lutidine was heated in a water-bath for one hour. The lutidine was removed under vacuum. Dilution of the residue with 25 ml. of water followed by acidification precipitated the crude acid in 68% yield. Recrystallization gave 0.40 g. (10.4%) of the product, m.p. 82–86°.

Anal. Calcd. for $C_9H_{14}O_2$: C, 70.10; H, 9.15; neut. equiv., 154.2. Found: C, 70.07; H, 9.19; neut. equiv., 157.3.

3,7-Dimethyl-2,4-octadienoic Acid (VI, R = isobutyl).—A solution of 8.0 g. of γ-isoamylidene-β-methylglutaconic acid and 0.25 g. of cupric acetate in 50 ml. of 2,4-lutidine was heated one hour on the water-bath. Most of the lutidine (40 ml.) was removed under vacuum. The residue was dissolved in 100 ml. of ice-water and acidified with 12 *N* hydrochloric acid. The precipitated solid was dissolved in bicarbonate, treated with Norite, extracted with ether, and reprecipitated with acid. Recrystallization from methanol–water, after removal of an insoluble oil, gives 0.80 g. (12.6%) of the product, m.p. 50–53°.

Anal. Calcd. for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59; neut. equiv., 168.2. Found: C, 71.26; H, 9.71; neut. equiv., 169.2.

The benzylthiouronium salt, m.p. 143–144°, was prepared from the salt and benzylthiouronium chloride.

Anal. Calcd. for $C_{18}H_{26}O_2N_2S$: C, 64.65; H, 7.81 Found: C, 64.62; H, 7.92.

6-(2′,6′-Dimethyl-5′-heptenyl)-4-methyl-5,6-dihydro-2-pyrone.—Ten grams of crude 4-carboxy-3,7,11-trimethyl-2,4,10-dodecatrienoic acid, obtained from citronellal and methyl β-methylglutaconate, was heated with 0.1 g. of copper powder at 165° for one hour. The residue was fractionated to give 3.2 g. (38.2%) of an oil, b.p. 155° (3 mm.). The infrared absorption data show a band at 1727 cm.$^{-1}$ characteristic of the γ-lactone structure.

Anal. Calcd. for $C_{15}H_{24}O_2$: C, 76.22; H, 10.24; sapn. equiv., 236.3. Found: C, 76.09; H, 10.41; sapn. equiv., 226.4.

6-Isobutyl-4-methyl-5,6-dihydro-2-pyrone by Decarboxylation of the Dipotassium Salt.—A solution of 10 g. of the dipotassium salt of γ-isoamylidene-β-methylglutaconic acid in 10 ml. of glacial acetic acid was heated on a water-bath for two hours. The reaction mixture was diluted with 300 ml. of water to separate a water-insoluble layer which was separated, dried, and fractionated to give 4.3 g. (71.5%) of the product, b.p. 130–133° (8 mm.), $n^{26}D$ 1.4754.

Anal. Calcd. for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59; sapn. equiv., 168.1. Found: C, 71.27; H, 9.71; sapn. equiv., 167.7.

3,7-Dimethyl-2,4-octadienoic Acid by Hydrolysis of Its Lactone.—A solution of 3.0 g. of 6-isobutyl-4-methyl-5,6-dihydro-2-pyrone in 45 ml. of 20% alc. potassium hydroxide is refluxed for six hours, diluted with 100 ml. of water, cooled to 0°, and acidified. The precipitated solids were collected, dried, and extracted with hot methanol to separate the insoluble potassium sulfate. Water is added to the methanol solution and the solid which crystallizes on cooling was recrystallized to give 1.1 g. (38%) of the product, m.p. 50–53°, identical with that obtained by decarboxylation.

6-Amyl-4-methyl-5,6-dihydro-2-pyrone was prepared by the process given above for the 6-isobutyl analog. Fractionation gave 66.7% of the product, b.p. 134° (5 mm.), $n^{25}D$ 1.4705.

Anal. Calcd. for $C_{11}H_{18}O_2$: C, 72.49; H, 9.96; sapn. equiv., 182.2. Found: C, 72.30; H, 10.16; sapn. equiv., 176.

4-Methyl-6-propyl-5,6-dihydro-2-pyrone.—A solution of 20 g. of γ-butylidene-β-methylglutaconic acid and 0.25 g. of cupric acetate in 45 ml. of 2,4-lutidine was heated at 100° for 45 minutes. Addition of ice and acidification precipitates an oil which was taken up in ether. The crude product obtained from these ether extracts was fractionated to give 7.5 g. of material, b.p. 112–135° (6 mm.), which showed the infrared carbonyl absorption characteristics of a mixture of the δ-lactone and unsaturated acid (1738 and 1680 cm.$^{-1}$). The mixture was dissolved in water, neutralized, and extracted with ether to obtain 2.1 g. (13.5%) of the pure 2-pyrone, b.p. 124° (7 mm.), $n^{30}D$ 1.4821.

Anal. Calcd. for $C_9H_{14}O_2$: C, 70.09; H, 9.15; sapn. equiv., 154.2. Found: C, 70.05; H, 9.23; sapn. equiv., 154.

3-Methyl-2,4-octadienoic Acid Benzylthiouronium Salt.—A solution of 0.5 g. of 4-methyl-6-propyl-5,6-dihydro-2-pyrone in 10 ml. of methanol is refluxed for one hour with a solution of 0.2 g. of potassium hydroxide in 5 ml. of water. Neutralization precipitated the 3-methyl-2,4-octadienoic acid as a crude oil which could not be purified by crystallization or distillation. Addition of a slight excess of benzyl-

thiouronium chloride in methanol precipitated the salt. Recrystallization gave 0.75 g. (68%) of the product as white needles, m.p. 150°.

Anal. Calcd. for $C_{17}H_{24}O_2N_2S$: N, 8.74. Found: N, 8.98.

6-Butyl-4-methyl-5,6-dihydro-2-pyrone.—5-Carboxy-6-butyl-4-methyl-5,6-dihydro-2-pyrone was decarboxylated in 2,4-lutidine with cupric acetate by the procedure given above for the 6-propyl analog given above. The mixture of lactone and acid, b.p. 115–117° (4 mm.), obtained from 20 g. of starting material was dissolved in alkali and extracted with ether to obtain 6.7 g. (42.5%) of the product, b.p. 124° (4 mm.), $n^{11}D$ 1.4935. The pure acid could not be obtained from the alkaline solution.

Anal. Calcd. for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 70.88; H, 9.73.

6-Butyl-4-methyltetrahydro-2-pyrone.—A solution of 4.5 g. of the crude dihydro-2-pyrone obtained as described in the preceding paragraph in 50 ml. of ether was hydrogenated over palladium-on-charcoal catalyst. The crude product was neutralized and extracted with ether. The ether extracted oil was fractionated to give 1.6 g. (35%) of the product, b.p. 114° (4 mm.), $n^{10}D$ 1.4517. This compound shows infrared absorption bands in carbon tetrachloride at 2959 (C–H stretching), 1712 (carbonyl stretching), 1381 (unassigned) and 1238 cm.$^{-1}$ (C–O stretching) as does also 4,6-dimethyltetrahydro-2-pyrone.[10]

Anal. Calcd. for $C_{10}H_{18}O_2$: C, 70.54; H, 10.66; sapn. equiv., 170.2. Found: C, 70.37; H, 10.64; sapn. equiv., 169.

6-(1′-Ethylamyl)-4-methyl-5,6-dihydro-2-pyrone.—Four grams of 4-carboxy-6-ethyl-3-methyl-2,4-dodecanoic acid was decarboxylated in 10 ml. of 2,4-lutidine with 0.01 g. of cupric acetate at 100°. The lutidine was removed by distillation. The residue was acidified and extracted with ether. The ether-extracted oil on fractionation gave 2.6 g. of a mixture of the lactone and acid. The acid was extracted from an ether solution of the mixture with dilute alkali. The ether extracts were evaporated and the residue fractionated to give 1.7 g. (51%) of the product, b.p. 141–143° (5 mm.), $n^{25}D$ 1.4641.

Anal. Calcd. for $C_{18}H_{32}O_2$: C, 74.24; H, 10.54; sapn. equiv., 210.3. Found: C, 74.38; H, 10.48; sapn. equiv., 205.

The infrared absorption spectra were determined using potassium bromide pellets, except as otherwise noted, and a Baird double beam recording infrared spectrometer with sodium chloride optics.

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[CONTRIBUTION FROM THE CHARLOTTE DRAKE CARDEZA FOUNDATION, JEFFERSON MEDICAL COLLEGE]

Synthesis of Acids Containing Hydrophenanthrene and Hydroacephenanthrylene Rings

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The Reformatsky reaction with methyl 3-carbomethoxy-2-keto-3-methyl-6-phenylcyclohexane-1-acetate yields an unsaturated acid which can be cyclized either to a keto-anhydride (IV) or to an acephenanthrylene phenol (VI). The structure of the latter was shown by an independent synthesis from the α-form of 2-methyl-2-carbomethoxy-9-methoxy-1,2,3,4-tetrahydrophenanthrene-1-acetic acid. The β-stereoisomer of the acephenanthrylene also was prepared.

The cyclic keto-ester I described previously[1] was allowed to react with ethyl bromoacetate in the Reformatsky reaction. The principal crystalline material obtained from this reaction was the lactone ester II. The presence of the lactone ring was indicated by the infrared spectrum $\lambda_{max}^{CS_2}$ 5.56, 5.75 μ. This is similar to the result obtained by Johnson and Christiansen[2] in a similar reaction.

Hydrolysis of the lactone II with alcoholic potassium bicarbonate gave the unsaturated acid III. The ultraviolet absorption spectrum of this acid showed a band at 209 mμ (ε 16520), supporting the structure indicated[3] containing a conjugated double bond. The infrared spectrum of the methyl ester of the acid showed a band at 5.75 μ but no absorption at 5.56 μ and a new weak band, not present in the lactone, at 6.12 μ and probably caused by the double bond. The double bond was resistant to oxidation by permanganate under the conditions described by Johnson and Hunt,[4] a method which proved successful with unhindered double bonds.[1] When III was hydrogenated in acetic acid in the presence of Adams catalyst and hydrochloric acid, a product was obtained in which the aromatic ring was reduced but not the hindered double bond.

The acid III was cyclized with polyphosphoric acid, and the product was not an ester, but instead the keto-anhydride IV. Since the product is not phenolic, the double bond must be exocyclic as indicated in the structural formula. This is confirmed by the ultraviolet absorption spectrum, which shows the characteristics of the phenyl and carbonyl chromophores in conjugation,[5,6] and deviates from the spectrum of 9-keto-1,2,3,4,4a,-9,10,10a-octahydrophenanthrene[7] only at the lower minimum where the molecular extinction is greater, reaching 21000 at 212 mμ, the limit of measurement.

The anhydride IV was recovered unchanged after boiling with alcoholic alkali and acidifying. If the double bond were in the nucleus, the substance might be expected to isomerize to a phenol under these conditions. Another substance that exists only in anhydride form and not as the free acid has been obtained in the α-amyrin series by Ruzicka's group.[8,9] It seems probable that the anhydride IV belongs to the same stereochemical series as the major products described by Johnson and Christiansen[2] and it is of interest that it would then conform to the stereochemical arrangement in the Ruzicka anhydride.

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