**746.** " *Citrylidene-malonic Acid* ": cis-1(Me),3(H),4(H)-cis-3(H), α(H)-1,8-*Dihydroxy*-3-p-*menthylmalonic Dilactone.**

By C. E. Berkoff and L. Crombie.

The compound $C_{13}H_{18}O_4$, obtained by condensing citral with malonic acid in the presence of pyridine, is the tricyclic dilactone (VI) named in the title. Each lactone ring has been opened and the products have been degraded to show the sizes and points of attachment of these rings: the skeleton has been established by degradation to (±)menthone, and structural conclusions have been verified by nuclear magnetic resonance spectra. Stereochemical and conformational proposals are made and the mechanism of formation is considered. Pyrolysis of the dilactone gave five products and these are reconciled with the structure proposed. Farnesal yields a similar tricyclic dilactone.

" Citrylidene-malonic acid," $C_{13}H_{18}O_4$, m. p. 191°, is formed when citral is condensed with malonic acid in the presence of pyridine,[1] or when citral is condensed with malonic ester and the product is hydrolysed and acidified.[2] Verley proposed structure (I; R = H), Grünhagen (II), and Kuhn and Hoffer, rejecting both these and the planar projections (III) and (IV), considered (V) to be correct. Structures (II) and (V) have received acceptance,[4-6] despite scepticism in some quarters.[7,8] Structure (VI) is now proposed.[†] Writing this formula (VI) as a non-committal planar projection (IV) shows that it differs from Kuhn and Hoffer's structure (V) only in the size and point of attachment of ring B, but it will emerge that most of Kuhn and Hoffer's degradation products are incorrectly formulated in that when the ring B is removed with retention of the A, or the A ring with retention of ring B, the changes were represented by them as the reverse.
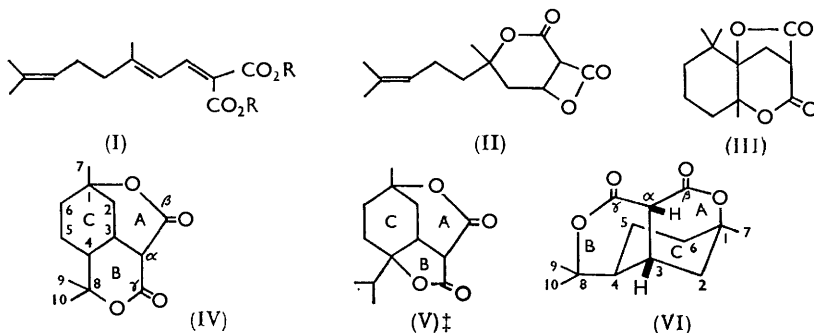
" Citrylidene-malonic acid " is insoluble in sodium carbonate solution, lacks typical carboxylic acid vibrations in the infrared spectrum, and does not react with permanganate, tetranitromethane, bromine in carbon tetrachloride, or hydrogen over Adams catalyst.

* Cf. Berkoff and Crombie, *Proc. Chem. Soc.*, 1959, 400.
† This, and mechanisms for the formation and pyrolysis similar to those given below, were put forward by one of us and J. L. Tayler[9] before detailed experimental backing was available.
‡ In Kuhn and Hoffer's paper[3] letters A and B are interchanged. All racemates are here represented as one enantiomorph.

[1] Verley, *Bull. Soc. chim. France*, 1899, **21**, 414.
[2] Grünhagen, Diss., Heidelberg, 1898.
[3] Kuhn and Hoffer, *Ber.*, 1931, **64**, 1243.
[4] Vulfson and Shemyakin, *J. Gen. Chem. (U.S.S.R.)*, 1943, **13**, 436.
[5] Wotiz and Matthews, *J. Org. Chem.*, 1955, **20**, 155.
[6] de Tribolet, Gamboni, and Schinz, *Helv. Chim. Acta*, 1958, **41**, 1587.
[7] Batty, Burawoy, Heilbron, W. E. Jones, and Lowe, *J.*, 1937, 755.
[8] Simonsen and Owen, " The Terpenes," Cambridge, 1947, Vol. I, p. 99.
[9] Tayler, Thesis, London, 1956.

Acetone is not formed on treatment with ozone. These facts, together with lack of ultra-violet light absorption, rule out structures (I) and (II) and, as claimed,[3] the substance is tricyclic and saturated. Kuhn and Hoffer found that when the " acid " was warmed with one equivalent of alkali a monodecarboxylated " hydroxy-lactone A," $C_{12}H_{20}O_3$, was obtained, whereas refluxing with two equivalents of alkali, followed by acidification, led to an isomeric " hydroxy-lactone B." " Hydroxy-lactone A " can also be transformed into " hydroxy-lactone B " by the above procedure. Their structures will now be derived.

The A hydroxy-lactone is *cis*-3(H),4(H)-1,8-dihydroxy-3-*p*-menthylacetic 1-lactone (VII; R = OH). It shows a δ-lactone band (1712s cm.$^{-1}$) and is resistant to acetylation and benzoylation: oxidation with chromic acid gives no ketonic product and in carbon tetrachloride (<0·005M; LiF) there is a free tertiary hydroxyl band [10] at 3618 cm.$^{-1}$. Further, cold hydrogen chloride in acetic acid converts " hydroxy-lactone A " into

(VII)   (VIII)   (IX)

(X)   (XI)   (XII)
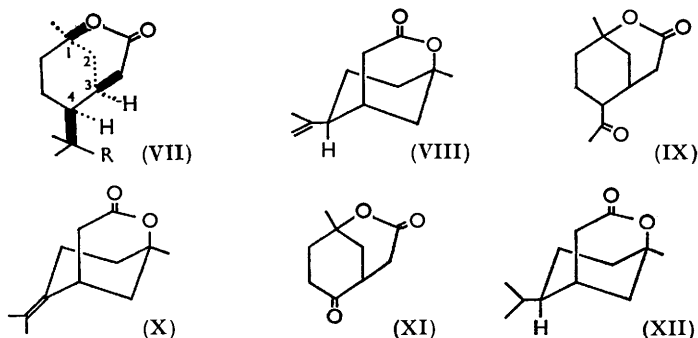
" chloro-lactone A," now formulated as (VII; R = Cl). Pyrolysis of the latter in a vacuum gives the isopropenyl-δ-lactone (VIII), which when ozonised yields formaldehyde and the acetyl compound (IX). The latter has one broad band at 1718s cm.$^{-1}$ which must include both δ-lactone and ketone vibrations, since the 2,4-dinitrophenylhydrazone shows a strong but narrow band at the same wavelength (mull). The acetyl-lactone gave iodoform (66%).


(XIII)   (XIV)   (XV)   (XVI)

(XVII)   (XVIII)   (XIX)
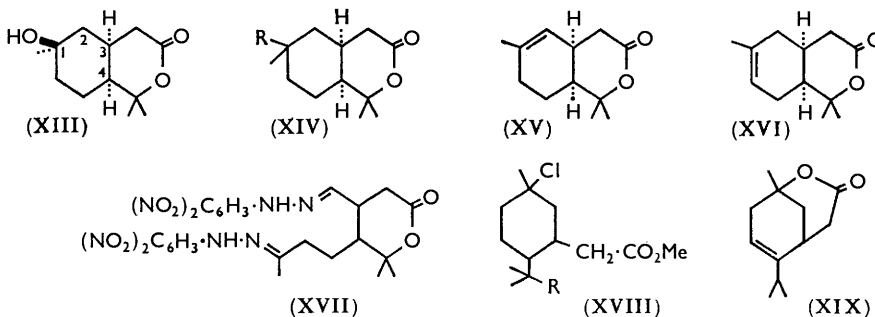
When the chloro-lactone (VII; R = Cl) is dehydrochlorinated in pyridine the iso-propylidene-δ-lactone (X) is obtained [$\nu_{max.}$ (mull) 1717s cm.$^{-1}$]. Ozonolysis yields acetone and the keto-δ-lactone (XI) which gives negative iodoform, Schiff's, and tetranitromethane tests. In the infrared region, the keto-δ-lactone shows only a broad band at 1718s cm.$^{-1}$ in the carbonyl region: this again is compounded of ketone and δ-lactone functions [2,4-dinitrophenylhydrazone, $\nu_{max.}$ 1718s cm.$^{-1}$ (mull)]. The Zimmermann test [11] was still

[10] Cole, Müller, Thornton, and Willix, *J.*, 1959, 1218.
[11] Zimmermann, *Z. physiol. Chem.*, 1935, **233**, 257.

positive after the compound had been heated with alkali.* Dehydration of the hydroxy-lactone (VII; R = OH) with thionyl chloride and pyridine below 30° gave a mixture of both the isopropenyl- (VIII) and the isopropylidene-lactone (X), and hydrogenation of either of these, or of the chloro-lactone (VII; R = Cl), gave the saturated lactone (XII) (for stereochemistry, see below).

" Hydroxy-lactone B," *cis*-1(Me),3(H),4(H)-1,8-dihydroxy-3-*p*-menthylacetic 1-lactone (XIII) is a δ-lactone ($v_{max.}$ 1704s cm.$^{-1}$) containing a tertiary hydroxyl group [$v_{max.}$ 3611 cm.$^{-1}$ (<0·005M; LiF)]. When it is treated with hydrogen chloride in acetic acid, " chloro-lactone B " (XIV; R = Cl) was isolated: there was indication of a little " chloro-lactone A," presumably formed by opening of ring B and reattachment at $C_{(1)}$. Dehydrohalogenation of the chloro-lactone (XIV; R = Cl), or dehydration of the hydroxy-lactone (XIII) with thionyl chloride in pyridine at 20°, gave a crystalline mixture of unsaturated δ-lactones (XV) and (XVI). When ozonised, this mixture gave no volatile ketonic material, but the gummy product yielded a 2,4-dinitrophenylhydrazone which gave analyses for (XVII) or the equivalent from (XVI), indicating that the double bond lies in a ring and that the lactones belong to the 1,2-fused and not the bicyclo-series. Consistent is the fact that the saturated lactone (XII) can be opened by hydrogen chloride in methanol to yield the chloro-ester (XVIII; R = H) which on dehydrohalogenation and ozonolysis again gives no volatile ketone.

(XX)   (XXI)   (XXII)   (XXIII)   (XXIV)
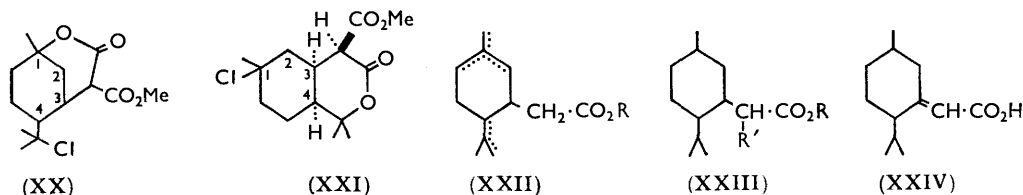
By repeated crystallisation of the mixture of unsaturated δ-lactones, one has been obtained pure and is identical with a δ-lactone, m. p. 64°, isolated by Schinz and his colleagues after a Reformatski reaction between citral and bromoacetic ester.[6] The progenitor and point of origin of this were not clear, and they entertained structures (XV) and (XIX), favouring the former but expressing misgivings that the compound might be skeletally different from either. From our work (see below) the skeletal structure is now certain and the preparation by Schinz and his colleagues suggests that the double bond is as in (XV): if our stereochemical views are correct the lactone is *cis*-fused, and this agrees with the ready re-lactonisation of its acid. Our δ-lactonic mixture gives, as expected, the same dihydro-compound as does the lactone, m. p. 64°. These degradations establish the points of lactonic attachment as $C_{(1)}$ in the A, and $C_{(8)}$ in the B series. What follows defines the skeleton.

When " citrylidene-malonic acid " is treated with methanolic hydrogen chloride a saturated chloro-lactonic ester ($v_{max.}$ 1739s, 1715s cm.$^{-1}$; ester and δ-lactone) giving analyses for (XX) or (XXI) is obtained. Hydrolysis of this, and then acidification, regenerate some " citrylidene-malonic acid." On the other hand, treatment of hydroxy-lactone A or B (VII, R = OH; or XIII) with methanolic hydrogen chloride gives, as reported,[3] a dichloro-ester which is now formulated as (XVIII; R = Cl). Dehydrochlorination of the latter gave a diene-ester showing no high-intensity ultraviolet absorption (only unsaturated methyls detected, τ 8·32 p.p.m.). Although this gave correct analyses and absorbed two mols. of hydrogen over a catalyst, gas–liquid chromatography showed that neither it nor the derived saturated ester [$v_{max.}$ (liq.) 1739 cm.$^{-1}$] was homogeneous.

* Although this test is generally considered diagnostic for ·CH₂·CO· or ·COMe groups, it has been found that the α-methylene of a number of lactones is activated sufficiently to give a positive reaction. If the lactone ring is opened by preliminary heating with alkali, the test is negative because the methylene grouping in the ion is insufficiently reactive. The matter is summarised in the Table (p. 3748).

The former is therefore non-committally represented as (XXII; R = Me) and the latter as (XXIII; R = Me, R' = H) which is regarded as a mixture of geometrical isomers. Catalytic hydrogenolysis of the dichloro-ester (XVIII; R = Cl) also produced a stereo-isomeric mixture of esters (XXIII; R = Me, R' = H). The saturated ester was α-brominated and the α-bromo-acids (one was crystalline) were dehydrohalogenated. The resulting unsaturated acid, containing (XXIV) (infrared data), though contaminated with β-unsaturated material, was ozonised, and the 2,4-dinitrophenylhydrazone of the product was compared with specimens of (±)-menthone and (±)-isomenthone 2,4-dinitrophenyl-hydrazone. These were presented to us by Professor J. Read, to whom we are most grateful, and were accompanied by the warning that " it is very difficult to prepare pure specimens of the derivatives of these two ketones as they relapse so readily into equilibrium mixtures." Infrared and mixed m. p. data showed that all three 2,4-dinitrophenyl-hydrazones were virtually identical. Our degradation carries only skeletal and no stereo-chemical implication, and only the skeleton is considered to be established. " Citrylidene-malonic acid " has a *p*-menthane skeleton with a malonic residue at position 3: taken with establishment of lactonic attachment at $C_{(1)}$ and $C_{(8)}$, this provides full chemical proof of the planar-projection formula (IV).

Independent support for the structures of " citrylidene-malonic acid " and its degradation products comes from nuclear magnetic resonance spectra.* Confirming the point of lactonic attachment in the saturated lactone (XII), the 1-methyl group appears as a sharp band at τ 8·61 p.p.m. (methyl attached to carbon linked to lactonic oxygen), whilst the saturated CMe_2 grouping is represented as a doublet of twice the area at 9·08 (2·6 c.p.s.) [cf. isopropylcyclohexane τ 9·15 (doublet, 2·8 c.p.s.), 2,3-dimethylbutane 9·15 (doublet, 5 c.p.s.)]. Similarly, the isopropylidene lactone (X) absorbs at τ 8·62 (1-methyl) and 8·33 (=CMe_2), whilst the isopropenyl lactone (VIII) has bands at 8·62 (1-methyl), 8·29 (=CMe), and 5·33 and 5·22 (vinyl-protons probably environmentally distinguished). The ozonolysis product (IX) has the 1-methyl absorption at 8·60 and acetyl-methyl absorption at 7·82. Representing the B-lactone series, compound (XV) has a doublet, τ 8·64 and 8·58 (environmental differentiation of the *gem*-dimethyl on $C_{(8)}$ due to lactonic attachment) of about twice the area of the =CMe group appearing at 8·33 (olefinic C–H, 4·68). As expected, attachment of chlorine to the carbon carrying methyl substituents lowers the τ value still more than attachment of oxygen does. This is apparent in the dichloro-ester (XVIII; R = Cl), for which the 1- and the 8-methyl appear as sharp bands at 8·43 and 8·38 respectively (ester-methyl, 6·30). In the chloro-lactone (VII; R = Cl) the 1-methyl, in agreement with the cases above, appears at 8·61 but the *gem*-dimethyl now at 8·38 (single). The α-methylene absorption of the δ-lactones ranged from 7·40 to 7·60. " Citryl-idene-malonic acid " itself showed three bands, at τ 8·62, 8·58, and 8·54, indicating that the two 8-methyl groups have slight environmental distinction, as in (VI). It follows at once that since the band at 8·62 has the highest τ value in the spectrum, oxygen attachment must be at $C_{(1)}$ and $C_{(8)}$. The $C_α$-hydrogen is represented by the sharp doublet at 6·46 (6·1 c.p.s.). The 4-hydrogen is probably accounted for by the weak, broad multiplet at 6·98 (area the same as that of the $C_α$-hydrogen doublet), whilst the complex of bands in the region τ 8·1 contains methylene resonances and those of the 3-proton. In a recent note Hyne, Mole, and Wailes [12] have independently published a nuclear magnetic resonance spectrum for " citrylidene-malonic acid " and have suggested lactonic attachment at $C_{(8)}$ rather than $C_{(4)}$. They have not, however, applied the above simple and decisive argument based on the chemical shift of methyl groups.

In converting projection (IV) into a stereoformula, the 4-isopropyl grouping is considered to be *cis* to the necessarily 1,3-diaxially fused lactone A. This follows from ready

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[12] Hyne, Mole, and Wailes, *Chem. and Ind.*, 1959, 1446.

re-lactonisation to form lactone B and from the stereospecific catalytic hydrogenation of the isopropylidene lactone (X) into the same saturated lactone (XII) * as results from hydrogenation of the isopropenyl-lactone (VIII) and the chloro-lactone (VII; R = Cl). Adsorption of lactone (X) on the catalyst in the least hindered form (XXV) is assumed. In addition to this evidence, arrangement of the 4-isopropyl group *trans* to the lactone A would lead to bad contortion of all three rings.

Using this information, with ring C in the chair form, leads to models with only minor angular strain if rings A and B are both chair (XXVIII) or both boat forms (XXIX). A model with *trans*-AB-fusion cannot be constructed and those built on a *cis*-relation of lactone A to isopropyl with ring C in the boat form involve considerable strain or steric inter-action. Choice of the formal all-chair (XXVIII) over the A-boat,B-boat,C-chair structure (XXIX) can be made on simple analytic grounds as the former lacks the opposed inter-actions of the α-3-hydrogen atoms and the opposed interactions of the lone-pair electrons of the lactonic-ether oxygen with carbon–carbon bonds. This may not be a final solution because there remains an unfavourable interaction [the same in both (XXVIII) and

(XXV)   (XXVI)   (XXVII)
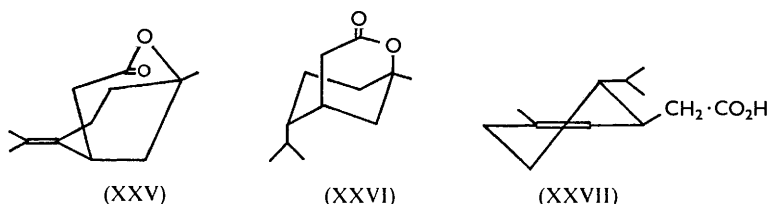
(XXIX)] between one lactonic keto-oxygen atom and the axial 5-hydrogen atom ($\sim$1·85 Å). This interaction is virtually eliminated by flattening the lactonic tip of ring A in (XXVIII) or of ring B in (XXIX), or by flattening both lactonic tips in either model. The doubly flattened conformation, which staggers the trigonal lone-pair orbitals of the ketonic oxygens relative to those of the ether oxygens and which also shows partial staggering of the other non-bonded interactions mentioned, may be the best compromise for it explains the un-usual infrared spectrum of " citrylidene-malonic acid " which, in chloroform, has δ-lactone

(XXVIII)   (XXIX)
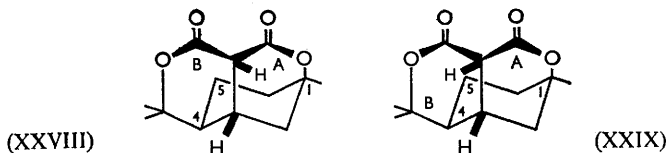
bands at 1750s and 1705m cm.$^{-1}$ (as a mull, at 1739s and 1698m cm.$^{-1}$). There is a fairly large angular separation of carbonyl dipoles in models (XXVIII) and (XXIX), but flat-tening of the tips of one or both lactones reduces this: in the latter event the carbonyl groups are virtually coplanar and vibrational coupling is maximal. Such coupling, which has been reported for malonic esters,[13] satisfactorily explains the large separation of the lactone bands which otherwise has to be accounted for by postulating considerable strain (hybridisation change)[14] in one lactone. It is not, however, intended to imply

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* By treating *p*-menth-1-en-3-ylacetic acid [obtained from ($\pm$)-piperitone] with hydrogen bromide a lactone, m. p. 76°, stated to be 1-hydroxy-3-*p*-menthylacetic lactone, was isolated.[6] It is different from our *cis*-lactone (mixed m. p., and infrared criteria) and is probably the *trans*-isomer (XXVI) derived from the *trans*-precursor (XXVII). A minor lactonic product,[6] m. p. 38°, may, from its infrared spectrum, be a *cis-trans*-mixture. We thank Dr. Schinz for the two specimens.

[13] Abramovitch, *Canad. J. Chem.*, 1958, **36**, 151; 1959, **37**, 361, 1146.
[14] Hall and Zbinden, *J. Amer. Chem. Soc.*, 1958, **80**, 6428.

that the lactones are necessarily identical in this respect, for hydrolysis * of ring B in " citrylidenemalonic acid " is rather faster than that of " hydroxy-lactone B," and it is the B-ring which is decarboxylated when " citrylidene-malonic acid " is pyrolysed.†

Although not discussed by them in stereochemical terms, Kuhn and Hoffer's structure (V) might be represented as in (XXX) and our views differ on two main counts. First, " hydroxy-lactone A " is represented by us as (VII) and not (XXXI), and secondly, " hydroxy-lactone B " as (XIII) rather than (XXXII), and their derivatives similarly. The crux of the difference lies in the dehydrochlorination of the chloro-lactone (VII; R = Cl) according to us and (XXXI; R = Cl) according to Kuhn and Hoffer. At 190—200° under reduced pressure the isopropenyl lactone (VIII) was isolated (above), but at 200—290° under atmospheric pressure as recommended [3] and claimed to give (XXXIII), a liquid mixture of γ- (1768 cm.$^{-1}$) and δ-lactones (1724 cm.$^{-1}$) containing hydrocarbon ($C_{11}H_{18}$) and other impurities was obtained. Perhaps the more severe conditions induce formation of acid (XXII; R = H) and some recyclisation to (XXXIII): decarboxylation of the former would account for the hydrocarbon. Identity of the dihydro-derivative of (XXXIII) with a lactone (XXXIV) prepared by Wallach [15] was claimed,[3] but the criteria used were unsuitable and in addition we have found Wallach's liquid lactone to have both γ- and δ-lactone bands. The final element in the case for structure (XXXI) to represent the A lactonic series was that the two lactones said to be (XXXIV) were each isomerised to the same crystalline lactone by red phosphorus and iodine. This lactone (obtained

(XXX)   (XXXI)   (XXXII)   (XXXIII)   (XXXIV)
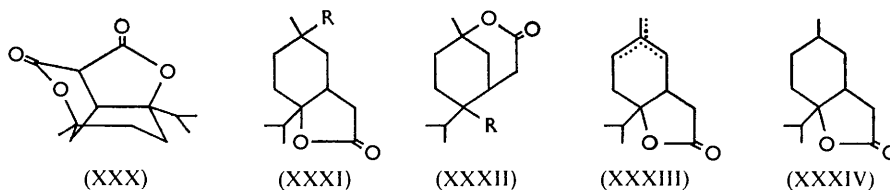
from the " citrylidene-malonic acid " source) is in fact a δ-lactone ($\nu_{max.}$ 1730 cm.$^{-1}$). Unsuspected changes have clearly occurred during Kuhn and Hoffer's degradation, but even though their detail is not understood, the construction [2] that they support a 3-substituted *p*-menthane skeleton appears valid. It is of interest that since one lactone band in " citrylidene-malonic acid " lies at 1750 cm.$^{-1}$, approaching the lower edge of the γ-range, it might be unwise to dismiss structure (V) on this ground only. Consideration of the mechanism of formation and pyrolysis was the best clue that structure (V) was inadequate.

(XXXV)   CO₂H   (XXXVI)   (XXXVII)
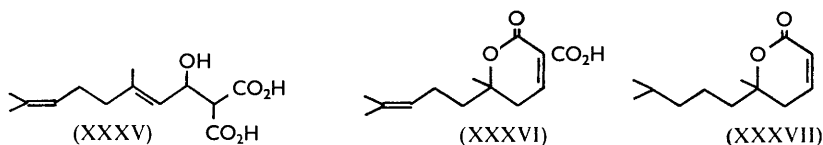
" Citrylidene-malonic acid " is formed by condensing citral and malonic acid in the presence of pyridine, piperidine, or piperidine acetate; yields do not normally reach 50%. The hydroxy-acid (XXXV) initially formed may be envisaged as dehydrating and then lactonising, to give the unsaturated lactone (XXXVI). There is lack of mechanistic

* The A ring, as in " hydroxy-lactone A " (VII; R = OH) and the isopropenyl lactone (VIII) is hydrolysed much more slowly than the B ring in " hydroxy-lactone B " (XIII), the unsaturated lactone (XV), or " citrylidene-malonic acid." Attack by an S_N2 mechanism on the bicyclo-A ring as a boat is hindered by the axially fused cyclohexane ring and if it has the chair conformation steric compression is generated between the axial 5-hydrogen atom and the O⁻ of the tetrahedrally hybridised intermediate formed by OH⁻ attack.

† A point of interest is that intolerable angle-strain would result if the *a*H in (VI) were enolised (cf. Bredt's rule).

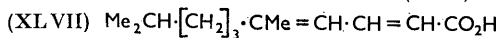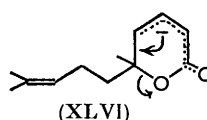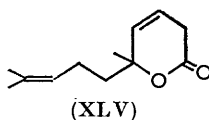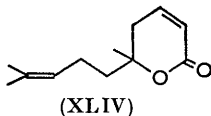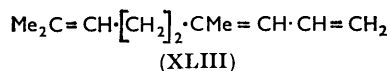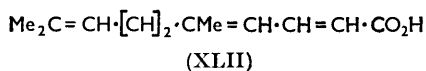[15] Wallach, *Annalen*, 1902, **323**, 135; 1907, **353**, 284.

information [16,17] on the Doebner–Knoevenagel reaction but work on the benzylidene-malonic acid system [17] and Grünhagen's method of preparation [2] from the diester (I; R = Et) support primary dehydration. Formation of lactone (XXXVI) is reasonable as some hex-2-eno-δ-lactone is formed in the Doebner reaction between crotonaldehyde and malonic acid.[18] More relevantly still, we have found that 3,7-dimethyloct-2-enal and malonic acid give more lactone (XXXVII) than acid.* Weak proton sources are available in the medium and it seems likely that the reaction is so catalysed. Ring c may then be envisaged as being formed as in (XXXVIII), and reaction completed as in (XXXIX). This type of cyclisation is to be distinguished from terpenic cyclisation in strongly acidic medium where carbonium ions are formed by protonation of double bonds: it is more akin to the transformation of pseudo-ionone (XL) into the ether (XLI) and related *p*-menthane derivatives.[19] Protonation at the most basic centre initiates reaction.

Some of the variants on this general view are not excluded. Thus, step (XXXVIII) could be written, though less probably, so as to involve the protonated hydroxyl group of an undehydrated lactone formed from (XXXV) and, with the reservation that only *cis*-BC-lactone would cyclise to the final tricyclo-system, ring B might be established before ring A. The effective addition to the isopropylidene double bond is not *trans* in (XXXVIII) and (XXXIX), but there seems a possibility that the carboxyl group participates in a transition state leading to simultaneous closure of rings B and C, *i.e.*, there is some merging of steps indicated in the two ciphers. The isopropenyl lactone (VIII) is a by-product in the formation of " citrylidene-malonic acid " and can be accounted for by competing proton-elimination and decarboxylation of an intermediate related to (XXXIX).

Verley [1] reported that, when " citrylidene-malonic acid " was heated above its m. p.,

(XXXVIII)   (XXXIX)   (XL)   (XLI)
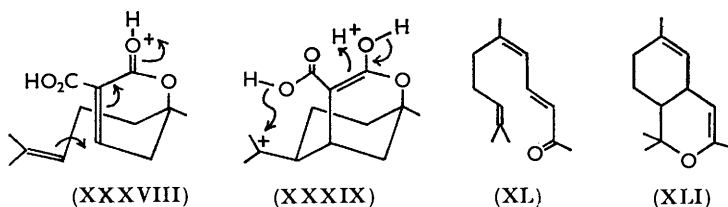
5,9-dimethyldeca-2,4,8-trienoic acid (XLII) was produced: heating at 130—140° in the presence of copper bronze was claimed [3] to give the pure acid, $\lambda_{max.}$ 272 mμ (ε 12,800). From data below, this is less than 60% pure and the pyrolysis range seems to be a misprint. Grünhagen [3] thought the product was a δ-lactone (XLIV). In the present work five

$$Me_2C=CH\cdot[CH]_2\cdot CMe=CH\cdot CH=CH\cdot CO_2H$$

(XLII)

$$Me_2C=CH\cdot[CH_2]_2\cdot CMe=CH\cdot CH=CH_2$$

(XLIII)

(XLIV)   (XLV)   (XLVI)

(XLVII) $Me_2CH\cdot[CH_2]_3\cdot CMe=CH\cdot CH=CH\cdot CO_2H$

* This acid is richer in retro-diene than in conjugated diene [$\lambda_{max.}$ 234 (ε 12,100) and 273 mμ (ε 5200)] and compares with the 5,9-dimethyldecatrienoic acid side product isolated when " citrylidene-malonic acid " is prepared by the pyridine method [$\lambda_{max.}$ 237 (ε 11,600) and 277 mμ (ε 9700)]. This makes it probable that the 5,9-dimethyldecatrienoic acid is a direct outcome of the Doebner reaction rather than a degradation product of " citrylidene-malonic acid."

[16] Corey, *J. Amer. Chem. Soc.*, 1952, **74**, 5897.
[17] Patai, Edlitz-Pfeffermann, and Rozner, *J. Amer. Chem. Soc.*, 1954, **76**, 3446, and references cited there.
[18] Joly and Amiard, *Bull. Soc. chim. France*, 1947, 139.
[19] Naves and Ardizio, *Bull. Soc. chim. France*, 1953, 494; Naves, Wahl, Ardizio, and Favre, *ibid.*, p. 873.

substances were obtained. In what follows, their structures are first cleared up and their formation is then considered.

Brief heating at 190—210° gave 5,9-dimethyldeca-*cis*-2,4,8-trienoic acid (XLII) as the acidic product. This absorbed nearly 3 mols. of hydrogen over a catalyst, to give 5,9-dimethyldecanoic acid, the *p*-bromophenacyl ester of which was identical with that of an authentic specimen.[20] Acetone was obtained on ozonolysis and the ultraviolet absorption $\lambda_{max.}$ 275 mμ (ε 22,500) showed the R·CMe:CH·CH:CH·CO$_2$H chromophore: strong infrared bands at 1684 (conjugated CO$_2$H) and 1624 and 1594 cm.$^{-1}$ (conjugated diene doublet) are in agreement. From the neutral products of the pyrolysis a monocyclic δ-lactone was obtained. This, when treated with sodium methoxide in methanol gave the above acid (XLII), which must therefore have a *cis*-2 grouping (we have no definite stereochemical information on the 4,5-linkage), whilst the δ-lactone itself must have structure (XLIV) or (XLV), giving[21] the ion (XLVI). Structure (XLIV) is preferred for the δ-lactone [$\nu_{max.}$ (liq.) 1718 cm.$^{-1}$] which absorbs 2 mols. of hydrogen to give a saturated δ-lactone [$\nu_{max.}$ (liq.) 1724 cm.$^{-1}$] and has ultraviolet end-absorption greater than that expected of a trisubstituted double bond. The α-olefinic stretching vibration, however, is unexpectedly weak, but this is so also for other α-unsaturated δ-lactones whose structures rest on synthesis,[22] *e.g.*, dec-2-eno-δ-lactone.[23-25a] The strong band at 815 cm.$^{-1}$ (*cis*-CH=CH·CO)[25] favours structure (XLIV).

Further heating of the *cis*-2-acid (XLII) (*p*-bromophenacyl ester, m. p. 77°) causes stereomutation to the *trans*-2-form, as shown by the appearance of pronounced absorption at 980 and 890 cm.$^{-1}$ and decline of the band at 830 cm.$^{-1}$ (*cis*-CH=CH·CO). At the same time the diene doublet (Δ 31 cm.$^{-1}$) closes up (Δ 12—16 cm.$^{-1}$, rather diffuse). A new *p*-bromophenacyl ester, m. p. 100°, derived from the *trans*-2-acid can be obtained and is also isolated directly when " citrylidene-malonic acid " is heated for longer periods. There are expected ultraviolet differences between the derivatives of m. p. 77° and 100°, and whereas the conjugated diene bands of the *cis*-2-ester were at 1636 and 1590 cm.$^{-1}$ (Δ 46), for the *trans*-2-ester they were at 1633 and 1610 cm.$^{-1}$ (Δ 23).* Movement of the conjugated diene doublet to higher frequency (the low-frequency band being mainly concerned) together with reduction of the Δ value when *cis*- is replaced by a *trans*-linkage was first noted in the deca-2,4-dienoic acid series,[24] and has been confirmed.[25a,27]

The other two pyrolysis products were the bicyclic isopropenyl lactone (VIII), separated directly or by chemical means from the neutral fraction, and the hydrocarbon (XLIII) which intrudes particularly on longer pyrolysis. The structure of the latter follows from analysis, ultraviolet data [$\lambda_{max.}$ 234 mμ (ε 23,550)], infrared criteria for the presence of an isopropylidene and a conjugated vinyl grouping, the absorption of 3 mols. of hydrogen over a catalyst, and comparison with synthetic material[28] made by a Wittig reaction

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* Examination of the products obtained (see earlier) when 3,7-dimethyloct-2-enal is condensed with malonic acid, gives support. Thus methoxide-opening of lactone (XXXVII) affords a *cis*-2-acid (XLVII) which lactonises easily and yields a *p*-bromophenacyl ester with conjugated diene bands at 1636 and 1592 cm.$^{-1}$ (Δ 44). As mentioned, the acid formed directly in the condensation contained much retro-diene: its *p*-bromophenacyl derivative showed no strong diene doublet (not conjugated with carboxyl) whilst the ester band was characteristic of an α-saturated (1743 cm.$^{-1}$) rather than an unsaturated (1710—1720 cm.$^{-1}$) grouping. Ultraviolet evidence is to the same effect. Treatment of the mixture of acid-conjugated and retro-diene with phosphorus oxychloride[26] and conversion into the *p*-bromophenacyl ester gave the derivative of the conjugated acid which, from ultraviolet and infrared data, has a *trans*-2-structure ($\nu_{max.}$ 1631 and 1610 cm.$^{-1}$; Δ 21).

[20] Rydon, *J.*, 1939, 1546; Kuhn, Badstubner, and Grundmann, *Ber.*, 1936, **69**, 98.
[21] Cf. Korte and Machleidt, *Chem. Ber.*, 1955, **88**, 136; Eisner, Elvidge, and Linstead, *J.*, 1953, 1372.
[22] Haynes and E. R. H. Jones, *J.*, 1946, 954.
[23] Crombie, *J.*, 1955, 2535.
[24] Crombie, *J.*, 1955, 1007.
[25] (*a*) Wailes, *Austral. J. Chem.*, 1959, **12**, 173; (*b*) Crombie, *J.*, 1952, 2997, 4338; (*c*) Sinclair, McKay, Myers, and Jones, *J. Amer. Chem. Soc.*, 1952, **74**, 2578.
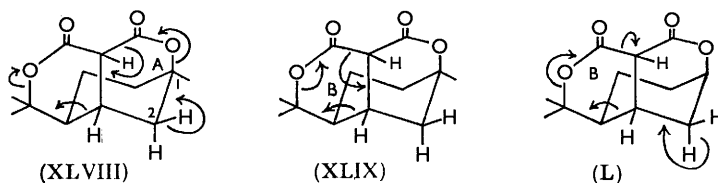[26] Crombie, Harper, and Sleep, *J.*, 1957, 2743.
[27] Crombie, Harper, and Smith, *J.*, 1957, 2754; Clarke and Crombie, unpublished results.
[28] Grignard, *Ann. Chim. (France)*, 1901, **24**, 479.

between citral and methylenetriphenylphosphorane. Except for a band at 965 cm.$^{-1}$ due to impurity in the specimen from the pyrolysis, the spectra of the samples were

(XLVIII)   (XLIX)   (L)

identical. The impurity is thought to have a *trans*-CH=CH structure resulting from bond-migration under the fairly severe conditions.

(LI)   (LII)   (LIII)

(LIV)   ·CMe=CH·[CH$_2$]$_2$·CMe=CH·CHO
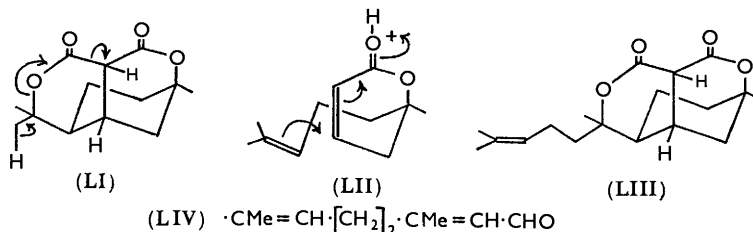
Apart from these structural data, the salient facts about the pyrolysis are as follows. Heating " citrylidene-malonic acid " at 190—210° gives 5,9-dimethyldeca-*cis*-2,4,8-trienoic acid and 5,9-dimethyldeca-2,8-dieno-δ-lactone. These are thermally inter-convertible and this lacto-enoic system recalls Linstead's classical work.[29] But the equili-brium is not stable, for the *cis*-acid is involved in *trans*-2 equilibration and is thermally decarboxylated to 4,8-dimethylnona-1,3,7-triene (cf. geranic acid to geraniolene [30]). 5,9-Dimethyldeca-2,8-dieno-δ-lactone may also be involved in a side reaction (below), but 1-hydroxy-*p*-menth-8,9-en-3-ylacetic lactone is thermally stable for 8 hr. at 200°. Other lactonic degradation products of " citrylidene-malonic acid " such as the monolactones (VII; R = OH), (X), (XII), (XIV; R = H), and (XV) show similar stability, and catenation seems contingent upon the presence of two lactonic rings.

Three types of catenation are considered. In the first type, illustrated by (XLVIII), the carbon dioxide is eliminated from ring A and the hydrogen involved would be at position 2 (or, less probably, 6, necessitating subsequent δε ⟶ γδ equilibration). This type is ruled out, as the trienoic acid produced would be *trans*-2, not *cis*-2. In the cyclic disruption (XLIX), the carbon dioxide comes from ring B. This seems a very acceptable interpretation and leads first to the monocyclic δ-lactone (XLIV) which, when heated, readily forms the *cis*-2-trienoic acid. An alternative (L) involves loss of carbon dioxide from ring B and yields the lactonic ion (XLVI) which would open to give the *cis*-2-trienoic acid or accept a proton to give lactone (XLIV) or (XLV), thermal equilibration then proceeding. The isopropenyl compound (VIII) could arise directly from a competing pyrolytic process (LI) or possibly by re-synthesis (LII) from the lactone (XLIV) followed by proton-loss from the resulting tertiary carbonium ion.

Like citral, farnesal condenses with malonic acid under Doebner conditions and gives a compound, C$_{18}$H$_{26}$O$_4$, m. p. 142°, which absorbs one mol. of hydrogen over a catalyst, gives acetone on ozonolysis, and shows only end-absorption in the ultraviolet region. There were δ-lactonic infrared bands (mull) at 1743s and 1704m cm.$^{-1}$; on pyrolysis at 200° the product had λ$_{max.}$ 274 mμ (ε 15,300). By analogy with " citrylidene-malonic acid " there is little doubt that its structure is (LIII) and its chemistry may provide links

[29] Linstead, *J.*, 1932, 115; Linstead and Rydon, *J.*, 1933, 580.
[30] Tiemann and Semmler, *Ber.*, 1893, **26**, 2724; Bateman, Cunneen, and Waight, *J.*, 1952, 1714.

with lactones isolated after a Reformatsky reaction between farnesal and ethyl bromo-acetate.[31] The reaction to give a tricyclic dilactone under Doebner conditions could be of use in identifying the fragment (LIV) in an unknown structure.

EXPERIMENTAL

Unless stated otherwise, the following apply. Evaporations were conducted under reduced pressure at room temperature, and drying of solutions refers to the use of sodium sulphate. Microhydrogenations were in acetic acid over Adams platinum catalyst and molecular weights were determined ebullioscopically in benzene or chlorobenzene. Ultraviolet spectra refer to ethanol solutions and infrared data to 2% solutions in chloroform: " liq." refers to a film of pure liquid, and " mull " to a paraffin paste. Nuclear magnetic resonance measurements were made on deuterochloroform solutions at 40 Mc. and calibrated against tetramethylsilane as an internal standard. Band positions are given as τ values, defined by Tiers.[32]

" Citrylidene-malonic Acid."—(a) Powdered malonic acid (250 g., 2·4 moles) was added to a mixture of citral (183 g., 1·2 moles) and pyridine (95 g., 1·2 moles), and the mixture was heated at 110° under reflux for 5 hr. Excess of ether was added to the cooled mixture, and the precipit-ated citrylidene-malonic acid was filtered off, washed with ether, and dried (m. p. 188—189°; 102·2 g., 35%). Two crystallisations from ethanol or chloroform–light petroleum (b. p. 60—80°) gave prisms, the m. p. [190—191° (decarboxylation)] of which was unaltered by chromatography on alumina. " Citrylidene-malonic acid " (Found: C, 65·55; H, 7·7%; M, 241. Calc. for $C_{13}H_{18}O_4$: C, 65·55; H, 7·6%; M, 238) is not immediately soluble in cold dilute sodium hydroxide: under mild conditions [3] the equivalent weight is 241, but after 2 hours' refluxing with 0·5N-alcoholic potassium hydroxide the value was 117·4 (two lactone rings). No ultraviolet maximum of $\varepsilon > 2$ was found. Alkaline extraction of the mother-liquors gave an acid (10·75 g., 4·6%), b. p. 119—123°/0·1 mm., n_D^{21} 1·5152, but apart from this and isolation of the isopro-penyl lactone (VIII), other products have not been examined. The citral used was commercial 99—100% material (A. Boake Roberts and Co.); purification by fractional distillation or by Hibbert and Cannon's [33] procedure made little difference to yields. The use of one mol. of malonic acid gives 20% and of three mols. gives 37% yield.

(b) Powdered malonic acid (20·8 g.) was suspended in dry benzene (150 ml.), and citral (30·4 g.) added, followed by piperidine (0·2 ml.). The mixture was shaken for 7 days and when worked up gave " citrylidene-malonic acid " (16%). A similar mixture, heated under reflux for 6 hr., gave a 35% yield. For an experiment of the latter type (modification of Knoevenagel's directions [34]) a yield of 95% was claimed [3] but exact conditions were not given and we have never had yields approaching this.

On dehydrogenation of " citrylidene-malonic acid " with selenium at 280—310° for 25 hr., liquids of b. p. 180—300° were obtained (most 180—190°). Distillation gave a hydrocarbon, b. p. 189°, n_D^{19} 1·4820 (Found: C, 88·55; H, 11·6%), $\lambda_{max.}$ 267 mμ ($E_{1\,cm.}^{1\%}$ 24), $\nu_{max.}$ 815vs cm.$^{-1}$ (two adjacent free hydrogen atoms on an aromatic nucleus). Gas–liquid chromatography showed two closely related components.

cis-3(H),4(H)-1,8-*Dihydroxy*-3-p-*menthylacetic* 1-*Lactone* (" *Hydroxy-lactone A* ") (VII; R = OH).—" Citrylidene-malonic acid " (40 g.) was heated (2 hr.) on a steam-bath with water (117 ml.) and 5N-sodium hydroxide (33·4 ml.). The product was extracted with chloroform, washed, dried, and recovered (m. p. 120—122°; 33·3 g., 94%). Two recrystallisations from benzene(or chloroform)–light petroleum (b. p. 60—80°) gave the *hydroxy-lactone* as prisms, m. p. 123—123·5° (Found: C, 67·8; H, 9·4. $C_{12}H_{20}O_3$ requires C, 67·9; H, 9·5%), $\nu_{max.}$ (mull), 1695 cm.$^{-1}$ (δ-lactone). Tetranitromethane gave no colour with it; attempted acetylation with isopropenyl acetate caused dehydration. Kuhn and Hoffer [3] give m. p. 123—123·5°.

cis-3(H),4(H)-8-*Chloro*-1-*hydroxy*-3-p-*menthylacetic Lactone* (" *Chloro-lactone A* ") (VII; R = Cl).—Dry hydrogen chloride was passed into ice-cold 1,8-dihydroxy-3-p-menthylacetic 1-lactone (13 g.) in glacial acetic acid (65 ml.) for 3½ hr. After the mixture had been kept at 0° for 5 hr., the acetic acid was evaporated and final traces were removed by adding benzene and again

[31] Asselineau and Lederer, *Bull. Soc. chim. France*, 1959, 320.
[32] Tiers, *J. Phys. Chem.*, 1958, **62**, 1151.
[33] Hibbert and Cannon, *J. Amer. Chem. Soc.*, 1924, **46**, 119.
[34] Knoevenagel, G.P. 156,560.

evaporating. The *chloro-lactone* (12·5 g.), after crystallising (charcoal) three times from benzene–light petroleum (b. p. 60—80°), formed needles, m. p. 90·5—91·5° (Found: C, 62·5; H, 8·35; Cl, 15·4. $C_{12}H_{19}O_2Cl$ requires C, 62·45; H, 8·3; Cl, 15·35%), $\nu_{max.}$ (mull) 1709 cm.$^{-1}$ (δ-lactone) (lit.,[3] m. p. 89—90°).

1-Hydroxy-p-*menth*-4(8)-*en*-3-*ylacetic Lactone* (X).—8-Chloro-1-hydroxy-*p*-menthylacetic lactone (8·07 g.) was heated under reflux with anhydrous pyridine (28 ml.) for 1¾ hr. After cooling and addition of ether, pyridinium chloride (3·85 g.) was filtered off, and the filtrate was washed with dilute hydrochloric acid, sodium hydrogen carbonate solution, and brine. The ethereal solution was dried and evaporated, to give 1-*hydroxy*-p-*menth*-4(8)-*en*-3-*ylacetic lactone* (6·22 g.), plates (from pentane), m. p. 59·5—60° (Found: C, 74·45; H, 9·55%; *M*, 191. $C_{12}H_{18}O_2$ requires C, 74·2; H, 9·35%; *M*, 194), absorbing 0·99H_2 on microhydrogenation.

cis-3(H),4(H)-1-*Hydroxy*-p-*menth*-8(9)-*en*-3-*ylacetic Lactone* (VIII).—8-Chloro-1-hydroxy-*p*-menthylacetic lactone (517 mg.) was heated at 190—200° for 8 hr. under water-pump vacuum. The *product*, m. p. 70—71·5° (424 mg.), crystallised from acetone–n-pentane as needles, m. p. 75° (Found: C, 74·1; H, 9·25%; *M*, 198. $C_{12}H_{18}O_2$ requires C, 74·2; H, 9·35%; *M*, 194), microhydrogenation 1·00H_2, $\nu_{max.}$ 1718s (δ-lactone), 1653w, 901m cm.$^{-1}$ (CMe:CH_2), $\nu_{max.}$ (mull) 1710s cm.$^{-1}$ (δ-lactone). A tetranitromethane test was positive.

Dehydration of 1,8-*Dihydroxy*-3-p-*menthylacetic* 1-*Lactone.*—(a) *With thionyl chloride and pyridine.* Thionyl chloride (7·35 g.) was added dropwise in 10 min. to the hydroxy-lactone (10 g.) in pyridine (30 ml.) below 30°. After being stirred for 3 hr. the mixture was set aside overnight and the pyridinium chloride was filtered off and washed with a little pyridine. The filtrate and washings were dissolved in ether, and the solution was washed with 4N-hydrochloric acid, sodium hydrogen carbonate solution, and brine. After drying and evaporation, a gum (6·04 g.) remained which crystallised only after repeated chromatography from benzene on alumina. The more easily eluted component had m. p. 56·5° (softened at 52°) after repeated crystallisations from pentane: the m. p. was not depressed on admixture with 1-hydroxy-*p*-menth-4(8)-en-3-ylacetic lactone. The other component crystallised from acetone–n-pentane in needles, m. p. 73° undepressed on admixture with 1-hydroxy-*p*-menth-8(9)-en-3-ylacetic lactone. Infrared spectra (solution and mull) were identical.

(b) *With phosphorus oxychloride and pyridine.* The hydroxy-lactone (3 g.), pyridine (50 ml.) and phosphorus oxychloride (14·4 ml.) were heated together for 1 hr. and the brown product was poured on ice and extracted with ether. The extracts were washed and worked up as above, to give a brown liquid (1·72 g.) which on distillation gave material, b. p. 101—102°/0·1 mm., n_D^{23} 1·5084 (Found: C, 73·95; H, 9·45. Calc. for $C_{12}H_{18}O_2$: C, 74·2; H, 9·35%), microhydrogenation 1·02H_2, $\nu_{max.}$ (liq.) 1727s (δ-lactone) and 1649w cm.$^{-1}$ (C=C). Ozonolysis gave formaldehyde (22% as 2,4-dinitrophenylhydrazone).

Ozonolysis of 1-*Hydroxy*-p-*menth*-4(8)-*en*-3-*ylacetic Lactone* (X).—(a) The lactone (1·0 g.) in ethyl acetate (9 ml.) and " AnalaR " glacial acetic acid (6 ml.) was ozonised at 10° for 2¼ hr. The ozonide was decomposed in the presence of zinc dust (2 g.) at 40—50° for 2 hr. After filtration and evaporation the white residue (746 mg.) was crystallised from ethyl acetate–n-pentane, to give 5-*hydroxy*-5-*methyl*-2-*oxocyclohexylacetic lactone* (XI), plates, m. p. 72—73° (Found: C, 64·4, 64·05; H, 7·35, 7·35%; *M*, 160. $C_9H_{12}O_3$ requires C, 64·25; H, 7·2%; *M*, 168). The 2,4-*dinitrophenylhydrazone* crystallised from methanol in yellow-orange needles, m. p. 193—195·5° (Found: C, 51·85; H, 5·0; N, 16·6. $C_{15}H_{16}O_6N_4$ requires C, 51·7; H, 4·65; N, 16·1%). The furfurylidene derivative, m. p. 148—149·5°, had $\lambda_{max.}$ 322 mμ (ε 16,350), $\nu_{max.}$ (mull) 1712 cm.$^{-1}$, but was not analytically pure.

(b) The lactone (500 mg.) in " AnalaR " glacial acetic acid (7 ml.) was ozonised at 10° for 35 min., an exit trap containing acetic acid being present. The contents of the vessel and trap were united, zinc dust (2 g.) was added, and the mixture was steam-distilled into 2,4-dinitrophenylhydrazine reagent. When chromatographed on bentonite–Celite (4 : 1) and eluted with chloroform, the 2,4-dinitrophenylhydrazone (150 mg.), m. p. 125·5°, was identical with authentic acetone 2,4-dinitrophenylhydrazone (mixed m. p. and infrared spectra).

Ozonolysis of 1-*Hydroxy*-p-*menth*-8(9)-*en*-3-*ylacetic Lactone* (VIII).—(a) The lactone (1·0 g.) was ozonised in ethyl acetate (7 ml.) and " AnalaR " glacial acetic acid (4·5 ml.) for 4 hr. at 10° and the ozonide was decomposed by warming at 60° with zinc dust. The solid (0·94 g.; m. p. 86—90°) obtained on filtration and evaporation was purified by chromatography from chloroform–benzene (10 : 1) on alumina or, more conveniently, by two crystallisations from acetone–n-pentane and gave 2-*acetyl*-5-*hydroxy*-5-*methylcyclohexylacetic lactone* (IX), rods (610 mg.),

m. p. 93·5—94·5° (Found: C, 67·25; H, 8·2%; *M*, 200. $C_{11}H_{16}O_3$ requires C, 67·3; H, 8·2%; *M*, 196). The 2,4-*dinitrophenylhydrazone* formed plates (from methanol), m. p. 189·5—191° (Found: C, 54·35; H, 5·2; N, 14·5%; *M*, 383. $C_{17}H_{20}O_6N_4$ requires C, 54·25; H, 5·35; N, 14·9%; *M*, 376). An iodoform test on the keto-lactone (25 mg.) gave iodoform (33 mg.), m. p. and mixed m. p. 118—119°.

1-*Hydroxy*-3-p-*menthylacetic Lactone* (XII).—(*a*) 1-Hydroxy-*p*-menth-4(8)-en-3-ylacetic lactone (2·25 g.) was hydrogenated in ethanol (30 ml.) over Adams platinum: 0·98 mol. of hydrogen was adsorbed. Kieselguhr was added, the mixture was filtered, and the filtrate and washings were evaporated, to give 1-*hydroxy*-3-p-*menthylacetic lactone* (2·26 g.) which, crystallised from n-pentane, had m. p. 60° (Found: C, 73·5; H, 10·25. $C_{12}H_{20}O_2$ requires C, 73·45; H, 10·25%), $\nu_{max.}$ 1711 cm.$^{-1}$, $\nu_{max.}$ (mull) 1718 cm.$^{-1}$ (δ-lactone). On admixture with starting material the m. p. was below 40°. In another experiment the whole product, before crystallisation, was identical with that of the crystallised product, m. p. 61° (infrared comparison in chloroform).

(*b*) 1-Hydroxy-*p*-menth-8(9)-en-3-ylacetic lactone (150 mg.) was hydrogenated as above, 1·02 mols. being absorbed. Working up gave the same lactone as above (148 mg.), m. p. 59·5°, raised by crystallisation from n-pentane to 61°. Identity was established by mixed m. p. and infrared spectra (solution and mulls).

(*c*) 8-Chloro-1-hydroxy-3-*p*-menthylacetic lactone (2·0 g.) was dissolved in a solution of potassium hydroxide (520 mg.) in dry ethanol (15 ml.) and shaken with hydrogen and 5% palladised charcoal (200 mg.). After 10 hr. 0·96 mol. of hydrogen had been used. Celite was added, the mixture was filtered, and the filtrate and washings were evaporated. The residue was dissolved in ether, washed with brine, and recovered (m. p. 44—49°; 1·49 g.). Three crystallisations from n-pentane raised the m. p. to 58·5°. It was identical (mixed m. p. and infrared mull spectrum) with the above specimens.

cis-1(Me),3(H),4(H)-1,8-*Dihydroxy*-3-p-*menthylacetic 8-Lactone* (*" Hydroxy-lactone B "*) (XIII).—" Citrylidene-malonic acid " (30 g.) was warmed with potassium hydroxide (16·5 g.) in water (63 ml.) and then gently refluxed for 2 hr. After cooling, the clear solution was acidified with 5N-sulphuric acid (effervescence) and extracted with chloroform. The chloroform solution was washed with brine, dried, and evaporated to give, after trituration with n-pentane, a solid of m. p. 104—110° (25·6 g.). Crystallisations from benzene–light petroleum (b. p. 60—80°) (m. p. 106—110°; 24·7 g.), carbon tetrachloride (m. p. 112—115°; 23·8 g.), chloroform–light petroleum (m. p. 117—118°; 13·9 g.) and finally twice from benzene–n-pentane gave the *lactone*, m. p. 121—122° (10·3 g., 39%), as rods (Found: C, 67·95; H, 9·65. $C_{12}H_{20}O_3$ requires C, 67·9; H, 9·5%), $\nu_{max.}$ (mull) 1709 cm.$^{-1}$. Three other experiments gave high yields of crude product with considerable loss on purification though in one case lactone (17 g.) of m. p. 120—121° was isolated after only one crystallisation from benzene–light petroleum. Chromatography from benzene on alumina was not efficient. The lactone gave no ketonic product when oxidised with chromic acid at 10° and was saturated towards tetranitromethane. Kuhn and Hoffer [3] claim an 85% yield of material of m. p. 118—119° in a similar experiment.

Dehydration of " Hydroxy-lactone B ".—The hydroxy-lactone (6·74 g.) in anhydrous pyridine (20 ml.) was treated with thionyl chloride (3 ml.), the temperatire being kept below 22°. The mixture was filtered and the filtrate was washed with 4N-hydrochloric acid, sodium hydrogen carbonate solution, and brine. Drying and evaporation gave a gum (4·16 g.) which solidified when triturated with n-pentane. Chromatography from benzene on alumina gave a mixture of isomers (Found: C, 74·15; H, 9·5%; *M*, 199. Calc. for $C_{12}H_{18}O_2$: C, 74·2; H, 9·35%; *M*, 194), microhydrogenation 0·99H₂, $\nu_{max.}$ (mull) 1715 cm.$^{-1}$, which on repeated crystallisation from pentane gave material of m. p. 58—60°, undepressed on admixture with Schinz's lactone,[6] m. p. 63—64°, and virtually identical with it in its infrared specimen.

Schinz's lactone, isolated according to published directions [6] (Found: C, 73·8; H, 9·55%), crystallised from n-pentane as needles with later crops as plates. They had identical m. p.s and spectra [$\nu_{max.}$ 1706 cm.$^{-1}$ (δ-lactone)]. This absorption differs from the recorded value [$\nu_{max.}$ (mull) 1739 cm.$^{-1}$] but specimens obtained *via* " citrylidene-malonic acid " have been found to have $\nu_{max.}$ (mull) 1736 cm.$^{-1}$. In one case an almost pure sample from this source showed a doublet at 1733 and 1711 cm.$^{-1}$. In these cases the rest of the spectrum is not changed: the carbonyl band in all cases appears composite and in a paraffin spectrum the exact $\nu_{max.}$ may depend on crystal forms and mull conditions.

Unsaturated lactone (mixture of isomers, above) (500 mg.) was hydrogenated over Adams

catalyst (100 mg.) in ethanol (25 ml.); working up in the usual way gave a liquid which despite chromatography on alumina or silica gel, distillation, and storage under pentane at 0°, did not crystallise; it had $\nu_{max.}$ (liq.) 1720 cm.$^{-1}$. Schinz's lactone, m. p. 64°, similarly hydrogenated over Adams catalyst in glacial acetic acid and then distilled, gave a similar product (Found: C, 73·0; H, 10·25. Calc. for $C_{12}H_{20}O_2$: C, 73·45; H, 10·25%), $\nu_{max.}$ (liq.) 1720 cm.$^{-1}$. The infrared spectra of the two specimens were identical and agree with that published by Schinz and his school [6] who report that the dihydrolactone eventually crystallised (m. p. 36°).

cis-3(H),4(H)-1-*Chloro*-8-*hydroxy*-3-p-*menthylacetic Lactone* (XIV; R = Cl).—Dry hydrogen chloride was passed into an ice-cold solution of " hydroxy-lactone B " (27·8 g.) in glacial acetic acid (131 ml.) for $3\frac{1}{2}$ hr. The mixture was set aside at 0° for 7 hr. and evaporated, traces of acetic acid being removed by evaporation with benzene. Chloroform (100 ml.) was added and the solution was washed with sodium carbonate solution and water, and then dried and evaporated to give a viscous liquid which crystallised under light petroleum at 0°. One crystallisation from ether–light petroleum (b. p. 40—60°) gave material (2·7 g.) of m. p. 55—59°. Intrusive bands in the infrared spectrum indicate some 8-chloro-1-hydroxy-3-*p*-menthylacetic lactone and a little γ-lactone ($\nu_{max.}$ 1786w) as impurities. A second crop (3·4 g.) had m. p. 58—59° and contaminants were similar (Found: C, 62·6; H, 8·5; Cl, 15·4%), $\nu_{max.}$ (mull) 1711vs cm.$^{-1}$. Repeated crystallisation of the first crop from benzene–light petroleum (b. p. 60—80°) raised the m. p. of the *chloro-lactone* to 77—77·5° (0·8 g.), plates (Found: C, 62·2; H, 8·3; Cl, 15·3. $C_{12}H_{19}O_2Cl$ requires C, 62·45; H, 8·3; Cl, 15·35%), $\nu_{max.}$ (mull) 1711 cm.$^{-1}$, the γ-lactonic contaminant and the bands attributable to the other impurity having disappeared. Kuhn and Hoffer give m. p. 59·3—60·5°.

The mother-liquors were distilled to give a series of liquid fractions. Material of b. p. 116—118°/1·0 mm., n_D^{20} 1·4973, gave reasonable analyses for a dehydrochlorinated lactone (Found: C, 73·75; H, 9·45%; microhydrogenation 0·98H$_2$) but both γ- and δ-lactone bands were present (1767 and 1725 cm.$^{-1}$).

A second preparation, from " hydroxylactone B " (10 g.), gave material of m. p. 54—56° (9 g.), raised by crystallisations to m. p. 77°.

Dehydrochlorination of " Chloro-lactone B " (XIV; R = Cl).—The chloro-lactone (2·6 g.; m. p. 66°) was refluxed in dry pyridine (20 ml.) for $2\frac{1}{2}$ hr. After cooling, the whole was filtered and the filtrate was dissolved in ether (50 ml.) and washed with brine, 6N-hydrochloric acid, sodium hydrogen carbonate solution, and brine. The ethereal solution was evaporated, to give crystals, m. p. 45—46° (1·6 g.). Seven crystallisations from light petroleum (b. p. 40—60°)– benzene gave 8-hydroxy-*p*-menth-1-en-3-ylacetic lactone, plates, m. p. 62—63° ($\nu_{max.}$ 1718 cm.$^{-1}$), undepressed on admixture with Schinz's lactone, m. p. 63—64°. The infrared spectra (mulls) were superimposable.

Ozonolysis of cis-3(H),4(H)-8-*Hydroxy*-p-*menth*-1-*en*-3-*ylacetic Lactone.*—Material of m. p. 45·5—46·5° was used and is therefore not free from contaminant containing a 1,6-double bond. The lactone (103 mg.) was ozonised in glacial acetic acid (5 ml.) for 30 min. at 10° (acetic acid trap). Working up as above gave no 2,4-dinitrophenylhydrazone of a volatile aldehyde or ketone. The aqueous steam-distillation residue was extracted with chloroform, and the extracts were washed with brine, dried, and evaporated. The gum gave a 2,4-*dinitrophenyl-hydrazone* which after chromatography from chloroform on bentonite–kieselguhr (4 : 1) and crystallisation from methanol formed orange crystals, m. p. 136—139° (Found: C, 49·45; H, 4·9. $C_{24}H_{26}O_{10}N_8$ requires C, 49·25; H, 4·5. $C_{18}H_{22}O_8N_4$ requires C, 51·2; H, 5·25%).

Methyl 1-*Chloro*-3-p-*menthylacetate* (XVIII; R = H).—1-Hydroxy-3-*p*-menthylacetic lactone (650 mg.) was dissolved in dry methanol (8 ml.) and hydrogen chloride was passed in for $3\frac{1}{2}$ hr. at 5°. The mixture was set aside at 0° for 3 days, then evaporated to a gum (730 mg.) which solidified when triturated at −10° with n-pentane. Low-temperature crystallisation from n-pentane gave the *ester* as needles, m. p. 30—31° (Found: C, 63·1; H, 8·95; Cl, 13·9. $C_{13}H_{23}O_2Cl$ requires C, 63·3; H, 9·4; Cl, 14·35%), $\nu_{max.}$ 1727s cm.$^{-1}$, $\nu_{max.}$ (mull) 1736 cm.$^{-1}$ (ester).

The monochloro-ester (1·51 g.) was refluxed in anhydrous pyridine (10 ml.) for 2 hr. Ether was added and pyridinium chloride (630 mg.) was filtered off. Working up the filtrate gave a liquid (1·11 g.) which did not crystallise after chromatography but had b. p. 63·5°/0·1 mm., n_D^{22} 1·4698 (Found: C, 74·55; H, 10·55. Calc. for $C_{13}H_{22}O_2$: C, 74·25; H, 10·55%). This is presumably a mixture of methyl *p*-menth-1- and -1(6)-en-3-yl acetate, $\nu_{max.}$ 1727s cm.$^{-1}$ (ester), microhydrogenation 1·01H$_2$. Two ozonolyses showed that no volatile ketonic material was formed (as detected by 2,4-dinitrophenylhydrazine).

Methyl 1,8-*Dichloro*-3-p-*menthylacetate* (XVIII; R = Cl).—1,8-Dihydroxy-3-*p*-menthyl-acetic 1-lactone (101·3 g.) was dissolved in methanol (262 ml.), cooled to 0°, and dry hydrogen chloride was passed in for 5 hr. After 3 days at 0° the crystals (99·2 g.; m. p. 122—123·5°) were filtered off, washed with cold methanol, water, and cold methanol, and then twice crystallised from boiling methanol. This ester formed needles, m. p. 123·5—124·5° (lit.,[6] m. p. 123·5—124°) (Found: C, 55·5; H, 7·65; Cl, 25·4%; M, 282. Calc. for $C_{13}H_{22}O_2Cl_2$: C, 55·5; H, 7·9; Cl, 25·2%; M, 281), $\nu_{max.}$ 1728 cm.$^{-1}$ (ester). The same substance (m. p. 123—124° and mixed m. p.) was similarly obtained from " hydroxy-lactone B."

Lactonic Ester (XX) *or* (XXI) *from* " *Citrylidene-malonic Acid.*—" Citrylidene-malonic acid " (9·0 g.) in methanol (200 ml.) was cooled in ice and treated with hydrogen chloride for 3 hr. and then left at 0° for 3 days. Evaporation gave a liquid from which a little unchanged " citrylidene-malonic acid " separated on dissolution in ether (300 ml.). The ethereal solution was evaporated and chromatographed from chloroform on alumina. The gum produced was extracted liberally with boiling light petroleum (b. p. 60—80°) and on crystallisation from the extracts the *chloro-lactonic ester*, m. p. 84—85·5° (850 mg.), was isolated (Found: C, 58·7; H, 7·55; Cl, 12·5%; M, 287. $C_{14}H_{21}O_4Cl$ requires C, 58·25; H, 7·35; Cl, 12·3%; M, 289), $\nu_{max.}$ 1739s (ester), 1715s cm.$^{-1}$ (δ-lactone).

The chloro-lactonic ester (220 mg.) was refluxed with potassium hydroxide (150 mg.) in methanol (2 ml.) and water (5 ml.) for 1 hr. The methanol was evaporated and the product acidified to give, on working up, a gum (100 mg.) which crystallised when triturated with ether to give " citrylidene-malonic acid," m. p. 186—188° (mixed m. p. and infrared spectrum).

Methyl 3-p-*Menthylacetate.*—(*a*) Methyl 1,8-dichloro-3-*p*-menthylacetate (95 g.) was refluxed in anhydrous pyridine (271 ml.) for 3 hr. On cooling, filtering, and working up in the usual way an oil (64·6 g.) was isolated which distilled as one main fraction, methyl 3-*p*-menthadienyl-acetate, b. p. 95·5—96°/0·25 mm., n_D^{21} 1·4886 (61·8 g.) (Found: C, 75·2; H, 9·8. Calc. for $C_{13}H_{20}O_2$: C, 74·95; H, 9·7%; microhydrogenation 1·97H_2), $\nu_{max.}$ (liq.) 1730 cm.$^{-1}$ (ester). There was no significant ultraviolet absorption between 215 and 360 mμ but gas–liquid chromatography showed that more than one compound was present. The ester (48 g.) in glacial acetic acid (230 ml.) was hydrogenated over Adams catalyst (1 g.) and absorption ceased when 1·98 mol. had been absorbed. Filtration, evaporation, and distillation gave *methyl* 3-p-*menthylacetate*, b. p. 64·5°/0·3 mm., n_D^{20} 1·4573 (Found: C, 73·5; H, 11·5%; M, 211. $C_{13}H_{24}O_2$ requires C, 73·55; H, 11·4%; M, 212), $\nu_{max.}$ (liq.) 1739s cm.$^{-1}$. Gas–liquid chromatography indicated that it was not stereochemically homogeneous.

(*b*) Methyl 1,8-dichloro-3-*p*-menthylacetate (1 g.) was dissolved in methanol (10 ml.) containing potassium hydroxide (0·45 g.) and hydrogenated over 5% palladised charcoal (200 mg.). Absorption ceased after 4 hr. and the mixture was filtered and evaporated. The residue was dissolved in ether, washed with brine, dried and evaporated, giving a liquid, b. p. 63°/0·1 mm., $n_D^{23.5}$ 1·4559 (420 mg.) (Found: C, 73·2; H, 11·55%).

Degradation of 3-p-*Menthylacetate to Menthone.*—The ester (7 g.) from route (*a*) above was added to phosphorus tribromide (0·3 ml.) and bromine (3 ml.), heated at 65—70° for 5½ hr. and then to 110° for 1½ hr., dissolved in ether, and extracted with sodium hydrogen carbonate solution. Acidification of the bicarbonate extract, saturation with ammonium chloride, and extraction with chloroform gave a gum (5·50 g.). Chromatography of a portion from chloroform–benzene (3 : 1) on alumina gave α-bromo-3-p-*menthylacetic acid*, m. p. 128·5—130° (from n-pentane; plates) (Found: C, 51·5; H, 7·55. $C_{12}H_{21}O_2Br$ requires C, 52·0; H, 7·65%), $\nu_{max.}$ (mull) 1709 cm.$^{-1}$ (α-halogeno-acid). Comparison of the infrared spectrum of the acidic gum (liquid) and the paraffin mull of the crystalline acid indicated that the former consisted largely of the latter. Degradation was continued on the gum.

The bromo-acid gum (900 mg.) was refluxed with pyridine (8 ml.) for 1¾ hr. Ether was added. The crude dehydrobromination product showed infrared bands at 1695s cm.$^{-1}$ (α-unsaturated acid) and 1639m cm.$^{-1}$ (conjugated C=C). This (365 mg.) was ozonised in ethyl acetate (6 ml.) and glacial acetic acid (4 ml.) at 5° for 1 hr. Zinc dust (1 g.) was added and the suspension was warmed, under reflux, on the steam-bath for 20 min. Solvents were removed by distillation under reduced pressure directly into 2,4-dinitrophenylhydrazine reagent: no derivative was formed. The residue, smelling of menthone, was diluted with methanol and treated with Brady's reagent. The 2,4-dinitrophenylhydrazone, m. p. 135—143°, was chromatographed first through bentonite–kieselguhr and then through Woelm neutral alumina from chloroform. After rejection of a small amount of material, m. p. 155—162° (plates), orange

needles contaminated with a little of the former were isolated. Crystallisation from chloroform, in which the contaminating plates were relatively insoluble, gave orange needles, m. p. 139—143°. This m. p. was not depressed on admixture with Professor Read's specimen of ($\pm$)-menthone 2,4-dinitrophenylhydrazone (m. p. 140—145°) or with that labelled ($\pm$)-isomenthone 2,4-dinitrophenylhydrazone (m. p. 145·5—147°). A mixture of the two authentic specimens had m. p. 140·5—142°. The infrared spectra (mulls) of all three samples were identical.

Hydrolysis of Diethyl 4,8-*Dimethylnona*-1,3,7-*triene*-1,1-*dicarboxylate.*—The diester, prepared according to Grünhagen's best conditions,[2] had b. p. 142—143·5°/0·35 mm., n_D^{21} 1·5058 (Found: C, 69·05; H, 9·2%; M, 289·5. Calc. for $C_{17}H_{26}O_4$: C, 69·35; H, 8·9%; M, 294, microhydrogenation 3·00H_2), $\lambda_{max.}$ 287 (ε 20,600), $\nu_{max.}$ (liq.) 1724s (α-unsaturated ester), 1631s and 1600m cm.$^{-1}$ (conjugated diene). The barium salt ($\lambda_{max.}$ 274·5 mμ) was prepared by Grünhagen's method[2] and on acidification " citrylidene-malonic acid " (15%), m. p. 190—191° and mixed m. p., was isolated.

The Zimmermann Test.—The substance (2 mg.) in ethanol (0·2 ml.) was added to saturated ethanolic potassium hydroxide (0·2 ml.), and a 1% solution of *m*-dinitrobenzene in ethanol (0·2 ml.) was added. A control test was performed. If, after 1—2 min., a violet colour not dispersed by ten-fold dilution with water, was observed in the test solution but not in the control, the reaction was recorded as positive. No colour, or any other colour, was recorded as negative. A second test was also carried out by pre-heating the substance to 80° for 5—10 min. with ethanolic alkali before adding *m*-dinitrobenzene solution to the cooled mixture. Results are collected in the Table.

Lactones and the Zimmermann test.

	Usual	Pre-heated
Acetone	pos.	pos.
γ-Valerolactone	pos.	neg.
1,8-Dihydroxy-3-*p*-menthylacetic 1-lactone (VII; R = OH)	pos.	neg.
8-Chloro-1-hydroxy-3-*p*-menthylacetic lactone (VII; R = Cl)	pos.	neg.
1-Hydroxy-*p*-menth-4(8)-en-3-ylacetic lactone (X)	pos.	neg.
1-Hydroxy-*p*-menth-8(9)-en-3-ylacetic lactone (VIII)	pos.	neg.
1-Hydroxy-3-*p*-menthylacetic lactone (XII)	pos.	neg.
1,8-Dihydroxy-3-*p*-menthylacetic-8-lactone (XIII)	pos.	neg.
8-Hydroxy-*p*-menth-1-en-3-ylacetic lactone (XV)	pos.	neg.
5-Hydroxy-5-methyl-2-oxocyclohexylacetic lactone (XI)	pos.	pos.
2-Acetyl-5-hydroxy-5-methylcyclohexylacetic lactone (IX)	pos.	pos.
" Citrylidene-malonic acid " (VI)	neg.	neg.
" Farnesylidene-malonic acid " (LIII)	neg.	neg.

Relative Speeds of Lactonic Hydrolysis.—All operations were at 35·9°. The lactone (2 × 10⁻³ mole) was dissolved in 50% aqueous ethanol (40 ml.). N-Potassium hydroxide (5 ml.) was added and the volume of the solution was adjusted to 50 ml. with water. At intervals portions (5 ml.) were titrated with 0·02N-acetic acid to phenolphthalein. A blank experiment was run. The times at which one-half and three-quarters of one lactonic function had been hydrolysed were, for " citrylidene-malonic acid " 2½ and 7 min., and for " hydroxy-lactone B " 5 and 12½ min. The times at which one-tenth of one lactonic function had hydrolysed were, for " citrylidene-malonic acid " ¾ min., for " hydroxy-lactone B " 1¼ min., for "hydroxy-lactone A " 45 min., for *cis*-3(H),4(H)-*p*-menth-1-enylacetic lactone (XV) 1 min. ($t_{\frac{1}{2}}$ 13½ min.), and for *cis*-3(H),4(H)-1-hydroxy-*p*-menth-8(9)-en-3-ylacetic lactone 29 min.

Pyrolytic Degradation of " Citrylidene-malonic Acid."—(a) *For* 3 *hr.* " Citrylidene-malonic acid " (20 g.) was heated at 190—210° under water-pump vacuum in the presence of a little copper bronze. Ether was added and, after refrigeration, unchanged material (1·1 g., 6%) was filtered off. The ethereal solution was repeatedly extracted with 2N-sodium hydroxide, the alkaline extracts were extracted with ether and these ether extracts were rejected. Evaporation of the ethereal solution after alkaline extraction gave neutral product (3·14 g., 20·4%), whilst acidification (Congo Red) of the alkaline extract (under ether; cold) gave acidic product (9·5 g., 61·6%). Neutral : acid ratio = 1 : 3·31.

The acid was distilled fairly rapidly and was collected as five fractions, b. p. 125·5—127°/0·1 mm., n_D^{26} 1·5268—1·5361. Infrared examination of these and the material before distillation showed them all to be closely similar and lactonic contaminant was not detected. The main fraction, n_D^{26} 1·5361, 5,9-*dimethyldeca*-cis-2,4,8-*trienoic acid* (with a little *trans*-2 contaminant) was used for analysis (Found: C, 74·35, 74·1; H, 9·15, 9·40. $C_{12}H_{18}O_2$ requires C, 74·2;

H, 9·35%), $\lambda_{max.}$ 275 mμ (ε 22,500), $\nu_{max.}$ (liq.) 1684s (conjugated CO_2H), 1624s and 1595s (conjugated *cis*-2-diene), 980mw (*trans*-·CH:CH·?), 890mw, 828m cm.$^{-1}$ (*cis*-·CH:CH·CO·). The *cis*-2 acid crystallised from light petroleum, m. p. 53°, and its p-*bromophenacyl ester* formed plates (from ethanol), m. p. 77·5° (Found: C, 61·1; H, 6·0. $C_{20}H_{23}O_3Br$ requires C, 61·35; H, 5·9%), $\lambda_{max.}$ 280 mμ (ε 42,600) with intrusion of a second max. of similar ε at 263 mμ, $\nu_{max.}$ (mull) 1712m (unsaturated ester), 1629s (C=O), 1636m, 1590m (conjugated *cis*-2-diene; the latter overlies an aromatic band), 1437m, 1276w, 1233w, 1203m, 1172s, 1071m, 1010m, 975m, 895m, 830m, 817s, and 726w, br. On hydrogenation over palladium–barium sulphate in ethyl acetate the acid absorbed 2·61 mols. of hydrogen. The hydrogenated acid was converted into its p-bromophenacyl ester, m. p. 60—61°, undepressed by p-bromophenacyl 5,9-dimethyl-decanoate (below). When ozonised, the acid yielded acetone isolated as the 2,4-dinitrophenyl-hydrazone, m. p. and mixed m. p. 126°.

The neutral product from the pyrolysis was distilled and, after elimination of a little material of low b. p. (probably 4,8-dimethylnona-1,3,7-triene), was collected as five fractions, b. p. 103—104°/0·2 mm., n_D^{23} 1·4886—1·4921 (Found, for the fraction of n_D^{23} 1·4901: C, 74·55; H, 9·45%; microhydrogenation 1·8H$_2$. For the fraction of n_D^{23} 1·4913: C, 74·1; H, 9·45; O, 16·45. Calc. for $C_{12}H_{18}O_2$: C, 74·2; H, 9·35; O, 16·45%). Scrutiny of the infrared spectra (liq.) showed that the first fraction was pure 5,9-dimethyldeca-2,8-dieno-δ-lactone and that contamination with 1-hydroxy-p-menth-8(9)-en-3-ylacetic lactone increased with increasing refractive index (see also chemical proof below). For the fraction of n_D^{26} 1·4901: no ultraviolet max., ε at 210 and 220 mμ 6300 and 3350 respectively.

A portion (1·23 g.) of the united neutral fractions from the above distillation was added to sodium (0·16 g.) dissolved in dry methanol, and set aside (2 hr.). After evaporation, water was added and neutral material was extracted with ether. The acid (0·875 g.) was isolated with the precautions above and, after evacuation at 0·1 mm., the infrared spectrum (liq.) was closely similar to that of the compound obtained directly from the pyrolysis except (*a*) that it contained a trace of δ-lactone and (*b*) the bands at 980 and 890 cm.$^{-1}$ were very weak relative to that at 828 cm.$^{-1}$. On distillation more lactonisation was induced: the product, b. p. 127°/0·1 mm., n_D^{22} 1·5250—1·5270, gave a p-bromophenacyl ester, m. p. 77°; mixed m. p. and infrared comparison with the derivative above established identity. The neutral fraction from the methoxide fission crystallised when triturated with n-hexane at 0°; recrystallisation from hexane containing a little acetone gave 1-hydroxy-p-menth-8(9)-en-3-ylacetic lactone, m. p. and mixed m. p. 75—76°. In a control experiment to check the stability of the latter to sodium methoxide, the menthene lactone (200 mg.) was added to sodium (30 mg.) in methanol (2 ml.) and was set aside for 2½ hr. On working up, recovered lactone (153 mg.) was obtained together with an acidic compound (25 mg.), m. p. 175° (Found: C, 68·05; H, 9·35. $C_{12}H_{20}O_3$ requires C, 67·9; H, 9·5%). As the infrared spectrum (mull) contains bands at 3310 (OH), 1712 (saturated CO_2H), 1650 and 900 cm.$^{-1}$ (CMe:CH$_2$), together with the typical acid-hydroxyl absorption, the compound appears to be 1-*hydroxy*-p-*menth*-8(9)-*en*-3-*ylacetic acid*.

(*b*) *For* 90 *min.* " Citrylidene-malonic acid " (17·5 g.) was heated as above for 90 min. to give recovered material (2·24 g., 13%), neutral product (2·77 g., 19·5%), and acid product (7·8 g., 55%). Neutral : acid ratio = 1 : 3·2. Distillation of the neutral product gave, after elimination of a little 4,8-dimethylnona-1,3,7-triene, 5,9-*dimethyldeca*-2,8-*dieno*-δ-*lactone*, b. p. 98°/0·01—0·05 mm., $n_D^{23·5}$ 1·4880—1·4886 (Found: C, 74·5; H, 9·25. $C_{12}H_{18}O_2$ requires C, 74·2; H, 9·35%). Subsequent fractions of the same b. p. had refractive indices rising to $n_D^{23·5}$ 1·4920 and infrared examination showed contamination with 1-hydroxy-p-menth-8(9)-en-3-ylacetic lactone. 5,9-Dimethyldeca-2,8-dieno-δ-lactone showed end absorption of λ 216 mμ (ε 3200) and $\nu_{max.}$ (liq.) 1718s (α-unsaturated-δ-lactone) and 814s cm.$^{-1}$ (*cis*-·CH:CH·CO·). On hydrogenation in ethyl acetate over palladium–barium sulphate, 2·1 mols. of hydrogen were absorbed. The resulting lactone had $\nu_{max.}$ 1724s cm.$^{-1}$ and no appreciable absorption at 814 cm.$^{-1}$. 5,9-Dimethyldeca-2,8-dieno-δ-lactone was heated at 190—210° under water-pump vacuum. A specimen recovered after 10 min. had been largely converted into 5,9-dimethyl-deca-*cis*-2,4,8-trienoic acid. Prolonged heating (2 hr., 4 hr., and 5½ hr.) resulted in characteristic spectral changes showing *cis*-2 ⟶ *trans*-2 stereomutation (see below).

The acid fraction from this pyrolysis of " citrylidene-malonic acid " had an infrared spectrum closely similar to that of the acid from experiment (*a*) and it was spectrally unchanged after ultraviolet irradiation in light petroleum (b. p. 60—80°) containing a trace of iodine (quartz vessel). Portions of the acid were heated to 190—210° for ¾, 1⅓, and 5½ hr. under water-pump

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vacuum and then examined spectroscopically. Progressive change ensued, the definition of the diene doublet becoming reduced and eventually it appeared merged near 1629 and 1613 cm.$^{-1}$; the band at 830 cm.$^{-1}$ declined greatly in intensity, whilst the bands at 980 and 890 cm.$^{-1}$ were much strengthened. There were also indications of lactone formation. A larger portion was heated with a little copper bronze for 18 hr. as above and the product was separated into neutral (0·53 g.) and acidic (3·47 g.) material. Neutral : acid ratio = 1 : 6·55. The acidic product had b. p. 124—124·5°/0·1—0·2 mm., n_D^{22} 1·5364—1·5376 (Found: C, 74·4; H, 9·35. Calc. for $C_{12}H_{18}O_2$: C, 74·2; H, 9·35%), $\lambda_{max.}$ 274 mμ (ε 23,500). Its infrared spectrum showed the changes noted above and indicates that large amounts of 5,9-dimethyldeca-*trans*-2,4,8-trienoic acid are present ($\nu_{max.}$ 1625s, 1613s, 978ms, 888ms, 828mw cm.$^{-1}$). The *p*-bromophenacyl ester was a mixture of *cis*-2- and *trans*-2-components but by repeated crystallisation from ethanol p-*bromophenacyl 5,9-dimethyldeca*-trans-2,4,8-*trienoate* was isolated as the less soluble component, m. p. 100° (Found: C, 61·0; H, 5·9. $C_{20}H_{23}O_3Br$ requires C, 61·35; H, 5·9%), $\lambda_{max.}$ 275 mμ (ε 39,600). In the infrared (mull) there were bands at 1723m (unsaturated ester), 1698m (C=O), 1633m, 1610m (conjugated *trans*-2-diene), 1585m (Ph), 1420m, 1307m, 1279m, 1252w, 1230w, 1212m, 1160s, 1131s, 1105w, 1070m, 1011w, 987i, 980s, 893m, 837w, 813m, 727m, and 722m. The infrared spectrum of the neutral fraction indicated that it contained 5,9-dimethyldeca-2,8-dieno-δ-lactone together with other lactonic impurity. Thus treatment with sodium methoxide gave spectrally impure 5,9-dimethyldeca-*cis*-2,4,8-trienoic acid: the neutral lactonic residue [$\nu_{max.}$ (liq.) 1712s with bands at 1645w, 1590m, and hydroxyl absorption near 3390 cm.$^{-1}$] is an obvious mixture but bands at 1093 and 980 cm.$^{-1}$ are strong and comparison suggests the presence of 1-hydroxy-*p*-menth-8(9)-en-3-ylacetic lactone. In a similar experiment with 9 hours' heating, the acid (3·4 g.) gave acidic product (2·78 g.) containing much *trans*-2 material and a neutral fraction (0·31 g.) whose spectrum simulated that of 5,9-dimethyldeca-2,8-dieno-δ-lactone very closely and indicated that much less extraneous material was present than in the product from the 18 hr. experiment.

(c) *For 45 min.* " Citrylidene-malonic acid " (20 g.), pyrolysed in the usual way, gave unchanged material (3·75 g.), acid (9·40 g.), and neutral product (3·14 g.). Neutral : acid ratio = 1 : 2·99. The acid had a spectrum closely similar to that from experiments (a) and (b) above and the neutral fraction was again a mixture of 5,9-dimethyldeca-2,8-dieno-δ-lactone and 1-hydroxy-*p*-menth-8(9)-en-3-ylacetic lactone.

(d) *For 8 hr.* " Citrylidene-malonic acid " (200 g.) and copper bronze (0·6 g.) were heated as before for 8 hr. Ether-insoluble material (6·8 g.) was recovered and the neutral (25·5 g.) and the acidic fraction (121·3 g.) were isolated. On distillation, the neutral fraction gave 4,8-dimethylnona-1,3,7-triene (2·95 g.), b. p. 41°/0·5 mm., n_D^{25} 1·4841 (Found: C, 87·95; H, 12·1. Calc. for $C_{11}H_{18}$: C, 87·9; H, 12·1%; microhydrogenation 3·0H$_2$), $\lambda_{max.}$ 234 mμ (ε 23,550), $\nu_{max.}$ (liq.) 1675w and 815w (Me$_2$C:CH·), 1650m, 1600w, 987s, and 898vs cm.$^{-1}$ (·CMe:CH·CH:CH$_2$). The spectrum was identical with that of the synthetic specimen below except that it contained a medium-weak band at 965 cm.$^{-1}$ (*trans*-·CH:CH·). Continued distillation gave fractions of b. p. 122—129°/0·5 mm., n_D^{25} 1·4945—1·4997 (18·4 g.). Infrared examination showed large amounts of 1-hydroxy-*p*-menth-8(9)-en-3-ylacetic lactone and by trituration with n-pentane at −77° it was isolated (m. p. and mixed m. p. 74·5—75°). Attempted distillation of the acid fraction through a Stedman column gave 4,8-dimethylnona-1,3,7-triene (4·2 g.) and then mixtures of acid and lactone. Only after repeated distillation of the upper fractions was 5,9-dimethyldeca-2,4,8-trienoic acid obtained apparently lactone-free (Found: C, 73·8; H, 9·4%; microhydrogenation 2·85H$_2$), $\lambda_{max.}$ 274·5 mμ (ε 23,320). The *p*-bromophenacyl ester, after repeated crystallisation, had m. p. 99·5—100·5° and was identical with the *trans*-2-derivative, m. p. 100°, described above. The *isobutylamide*, b. p. 142—148°/2 × 10^{-3} mm., n_D^{21} 1·5291 (Found: N, 5·4. $C_{16}H_{27}NO$ requires N, 5·6%), was not appreciably toxic to *Tenebrio molitor*. The saturated acid produced on preparative hydrogenation (2·93 mol. absorbed) gave a *p*-bromophenacyl ester, m. p. 59—60°, identical (mixed m. p.) with *p*-bromophenacyl 5,9-dimethyldecanoate.

5,9-Dimethyldecanoic Acid.—Citral was catalytically hydrogenated to tetrahydrocitral and the latter was condensed with malonic acid to give 5,9-dimethyldec-2-enoic acid (containing some 5,9-dimethyldec-3-enoic acid), b. p. 120—128°/0·3 mm., n_D^{24} 1·4690—1·4713. Hydrogenation of the mixture over palladium–carbon in ethanol gave 5,9-dimethyldecanoic acid, b. p. 104—108°/0·5 mm., n_D^{17} 1·4400—1·4404, $\nu_{max.}$ 1706 cm.$^{-1}$ (saturated CO$_2$H) [*p*-bromophenacyl ester, m. p. 60—61°, from ethanol (Found: C, 60·3; H, 7·45. Calc. for $C_{20}H_{29}O_3Br$:

C, 60·45; H, 7·3%), $\lambda_{max.}$ 255 mμ (ϵ 18,000), $\nu_{max.}$ (mull) 1742s (saturated ester), 1706s (C=O), 1590w (Ph), 1160w, 1072w, 1010w, 973w and broad, 828m, and 816m cm.$^{-1}$].

4,8-Dimethylnona-1,3,7-triene.—Methyltriphenylphosphonium bromide (58·2 g.) was added in portions and with stirring to phenyl-lithium in ether [from bromobenzene (28·2 g.) and lithium (2·58 g.)]. After 3 hours' stirring, citral (24·5 g.) in ether (40 ml.) was added and stirring continued for 3 hr. The product was heated under reflux for 1 hr., water (200 ml.) was added, and the ethereal layer was separated and washed with 6N-hydrochloric acid, 40% aqueous sodium pyrosulphite, and then water. After drying and evaporation the product (31·2 g.) was distilled (12·9 g.) and after redistillation from sodium gave 4,8-dimethylnona-1,3,7-triene, b. p. 102°/22 mm., n_D^{22} 1·4835 (Found: C, 87·45; H, 12·1. Calc. for $C_{11}H_{18}$: C, 87·9; H, 12·1%; microhydrogenation 3·0H$_2$), $\lambda_{max.}$ 235 mμ (ϵ 22,950), $\nu_{max.}$ (liq.) 1675, 815 (Me$_2$C:CH·), 1647, 1600, 997, 897 cm.$^{-1}$ (·CMe:CH·CH:CH$_2$).

Doebner Condensation between 3,7-Dimethyloct-2-enal and Malonic Acid.—Malonic acid (3·5 g.) was added to pyridine (5·5 g.) and 3,7-dimethyloct-2-enal (4·88 g.). The mixture darkened rapidly and was set aside at 20° for 7 hr., then heated for 6 hr. at 70° and extracted with 2N-sodium hydroxide. These extracts were extracted with ether before acidification and collection of the acid (2·22 g.) with ether. After removal of pyridine with dilute sulphuric acid a neutral fraction (3·1 g.) was obtained. Distillation of the acid gave four fractions, b. p. 119—142°/0·2 mm., n_D^{25} 1·4762—1·4890 (some resinification). Attention was concentrated on the main material, b. p. 134—142°/0·2 mm., n_D^{25} 1·4847—1·4890 (Found: C, 72·9; H, 10·35. Calc. for $C_{12}H_{20}O_2$: C, 73·4; H, 10·25%), $\lambda_{max.}$ 234 mμ (ϵ 12,100) and 273 mμ (ϵ 5200). The p-*bromophenacyl ester* had m. p. 69° (from ethanol) and is the derivative of the retro-acid component (Found: C, 59·85; H, 6·25. $C_{20}H_{25}O_3Br$ requires C, 61·1; H, 6·4%), $\lambda_{max.}$ 245 mμ (ϵ 25,500) [subtracting from the curve obtained, that for the p-bromophenacyl ester of 5,9-dimethyldecanoic acid, gives $\lambda_{max.}$ 232 mμ (ϵ 22,000)]. In the infrared spectrum were $\nu_{max.}$ 1743s (α-saturated ester), 1708s (C=O), 1592m (Ph), 1235m, 1217m, 1170m, 1157m, 1067mw, 1049w, 1010w, 978i, 970s, 839m, 826m, 816m, 810i, 729m, and 720m cm.$^{-1}$. A portion of the acid (550 mg.) was heated under reflux with phosphorus oxychloride (0·2 ml.) in benzene (8 ml.) for 40 min. The black solution was poured into water and extracted with ether. Drying and evaporation of the extract gave an oil which was distilled at 0·1 mm. [$\nu_{max.}$ 1686s (α-unsaturated acid), 1631s and 1616s (*trans*-2-diene), 980m and 890m cm.$^{-1}$: no absorption near 830 cm.$^{-1}$] and converted into p-*bromophenacyl 5,9-dimethyldeca-trans-2,4-dienoate,* m. p. 100° (Found: C, 61·05; H, 6·65%), $\lambda_{max.}$ 275 mμ (ϵ 44,900), $\nu_{max.}$ 1712i (α-unsaturated ester), 1695s (C=O), 1631m, 1610m (conjugated *trans*-2-diene), 1586(Ph), 1412m, 1318m, 1282m, 1238w, 1208m, 1167s, 1145s, 1104w, 1070m, 1009m, 982w, 978s, 892s, 856w, 830w, 820i, 813m, 729m, and 721m cm.$^{-1}$.

The neutral fraction, b. p. 93—99°/0·2 mm., n_D^{20} 1·4680 (Found: C, 73·4; H, 10·4. $C_{12}H_{20}O_2$ requires C, 73·4; H, 10·25%), had ultraviolet end absorption ϵ 1600 at 216 mμ, $\nu_{max.}$ 1720s (α-unsaturated lactone), 1634w (·C:C·), 813m (*cis*-CH:CH·CO), and 724m cm.$^{-1}$. Lactone (870 mg.) was added to sodium (112 mg.) in dry methanol (5 ml.) and after 2 hr. the acidic product was isolated in the usual way. The infrared spectrum before distillation showed partial lactonisation, $\nu_{max.}$ 1712 very broad (merged acid and δ-lactone bands), 1637m and 1602m (*cis*-2-diene) and 828m (*cis*-CH:CH·CO). Distillation (b. p. 120°/0·03 mm.) apparently caused more lactonisation and the product, n_D^{26} 1·4730, had $\lambda_{max.}$ 275 mμ (ϵ 4250) with infrared bands as above. The p-bromophenacyl ester, m. p. 78°, had $\lambda_{max.}$ 280 mμ (ϵ 28,600) with intrusion of a strong inflexion near 260 mμ due to the phenacyl residue: $\nu_{max.}$ 1714 (α-unsaturated ester), 1695s (C=O), 1636m, 1592m (*cis*-2-diene; latter band overlies the Ph vibration), 1439m, 1277w, 1235w, 1206m, 1175s, 1071m, 1010m, 975m, 897w, and 822s.

" Farnesylidene-malonic Acid."—(a) Malonic acid (10·4 g.) was added to a mixture of farnesal (11 g.) and pyridine (3·95 g.), and the whole was heated at 110° for 5 hr. Ether was

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* From the two pairs of p-bromophenacyl esters of *cis*- and *trans*-2-acids with the chromophore ·C(Me):CH·CH:CH·COR it was noted that, whereas all the esters have a fairly strong doublet at 1203—1212m cm.$^{-1}$ and 1160—1175s cm.$^{-1}$, the *trans*-2-compounds also have a band at 1130—1145 ms cm.$^{-1}$ and one at 1410—1420 cm.$^{-1}$: both are absent in the *cis*-series, where there is an extra band at 1438 cm.$^{-1}$. An expected band at 978—980 cm.$^{-1}$ is present in the *trans*-2-compounds, but as the *cis*-2 also have a band at 975 cm.$^{-1}$, its utility is limited. Similarly, there is the expected band at 817—822 cm.$^{-1}$ (*cis*-CH:CH·CO·) in the *cis*-2-series, but in each case there is interfering absorption in the other series. Both *trans*-2-isomers, however, show a clear doublet at 728 and 722 cm.$^{-1}$, whereas the *cis*-2 have a single broad band here.

added and the mixture was set aside at 0° for 18 hr. Recrystallisation of the product from ethanol gave " *farnesylidene-malonic acid* " (2·8 g.), m. p. 141—142°. (*b*) Powdered malonic acid (5·2 g.) was added to a mixture of farnesal (11·0 g.) and pyridine (3·95 g.), and the suspension was shaken for 24 hr., then set aside for 5 weeks. The product was warmed to 55—60° for 15 min., then cooled, and the crystals were collected and united with further product obtained from the mother-liquors (3·77 g.; m. p. 138·5—140°): crystallisation from ethanol (needles) raised the m. p. to 140·5—141·5°. " Farnesylidene-malonic acid " (Found: C, 70·65; H, 8·55%; M, 291; microhydrogenation 0·99H_2. $C_{18}H_{26}O_4$ requires C, 70·55; H, 8·55%; M, 306) reacted neutral, gave a positive test with nitromethane, and showed no ultraviolet absorption maximum. On ozonolysis " farnesylidene-malonic acid " (950 mg.) in " AnalaR " acetic acid (10 ml.) gave acetone 2,4-dinitrophenylhydrazone (202 mg.), m. p. and mixed m. p. 126°. " Farnesylidene-malonic acid " (0·7 g.) was heated at 190—200° for 4 hr. under water-pump vacuum: the yellow acidic oily product showed $\lambda_{max.}$ 274 mμ (ε 15,300) with a less prominent maximum at 233 mμ (ε 5900).

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