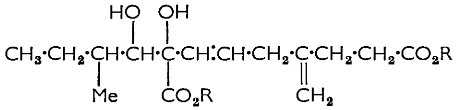
172. *Alternaric Acid. Part II.*[1] *Oxidation.*

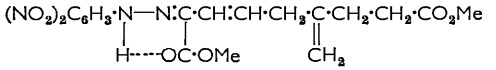
By J. R. Bartels-Keith.

Alternaric acid is oxidised by alkaline hydrogen peroxide to 7,8-dihydroxy-9-methyl-3-methyleneundec-5-ene-1,7-dicarboxylic acid.

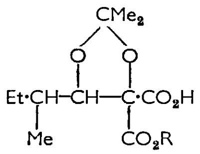
Alternaric acid, the antifungal and phytotoxic metabolite of *Alternari solani* (Ell. and Mart.) Jones and Grout, is oxidised slowly by alkaline hydrogen peroxide at room temperature, giving a crystalline acid $C_{15}H_{24}O_6$, together with formic acid and acetone. The yield of acetone is small, however, and comparative experiments indicate that it arises from concomitant alkaline hydrolysis of alternaric acid.[1] The compound $C_{15}H_{24}O_6$ is an optically active, unsaturated dibasic acid; degradative evidence shows that it is 7,8-dihydroxy-9-methyl-3-methyleneundec-5-ene-1,7-dicarboxylic acid (I; R = H). It follows that alternaric acid is also optically active and that the apparent inactivity[1] is due to internal compensation.



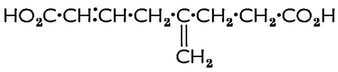
$CH_3{\cdot}CH_2{\cdot}\underset{Me}{CH}{\cdot}\overset{HO}{CH}{\cdot}\underset{CO_2R}{\overset{OH}{C}}{\cdot}CH{:}CH{\cdot}CH_2{\cdot}\underset{\overset{\|}{CH_2}}{C}{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2R$ (I)



$(NO_2)_2C_6H_3{\cdot}\underset{H{\cdots}}{N}{-}N{:}\underset{OC{\cdot}OMe}{C}{\cdot}CH{:}CH{\cdot}CH_2{\cdot}\underset{\overset{\|}{CH_2}}{C}{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2Me$ (II)

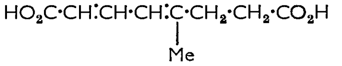


(III)



$HO_2C{\cdot}CH{:}CH{\cdot}CH_2{\cdot}\underset{\overset{\|}{CH_2}}{C}{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H$

(IV)



$HO_2C{\cdot}CH{:}CH{\cdot}CH{:}\underset{Me}{C}{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H$ (V)

Hydrogenation of the acid (I; R = H) indicated the presence of two ethylenic double bonds, which were not conjugated as shown by the absence of a maximum in the ultraviolet absorption spectrum. The infrared absorption and active-hydrogen content of the acid and of its methyl ester, obtained by the action of diazomethane, showed the presence of two hydroxyl groups. Treatment of the ester (I; R = Me) with acetic anhydride and pyridine gave only a monoacetate which showed infrared absorption at 3510 cm.$^{-1}$ (aliphatic OH), while the acid (I; R = H) and its methyl ester both gave liquid *OO*-isopropylidene derivatives. These findings show that the acid $C_{15}H_{24}O_6$ is acyclic and contains a 1,2- or 1,3-diol system in which one hydroxyl is tertiary.

The acid (I; R = H) gave a positive test for the 1,2-diol grouping with potassium triacetoxyosmiate in acetic acid,[2] and rapidly consumed 1 mol. of periodic acid, giving (+)-α-methylbutyraldehyde. The ester (I; R = Me) reacted similarly with periodic acid and gave, in addition to the above aldehyde, a neutral oil which formed a 2,4-dinitrophenylhydrazone, $C_{18}H_{20}O_8N_4$. The ultraviolet absorption in ethanol was characteristic of a C:C·C:N·N grouping in accordance with structure (II), but in chloroform the principal absorption band suffered a bathochromic shift of 19 mμ, which we attributed to intramolecular hydrogen-bonding between the NH group and the neighbouring ester-carbonyl group. The infrared spectrum showed bands at 3140 (bonded NH), 1744 (free ester-carbonyl) and 1700 cm.$^{-1}$ (bonded ester-carbonyl). This compound was also obtained

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[1] Part I, *J.*, 1952, 4056.

[2] Criegee, Marchand, and Wannowins, *Annalen*, 1942, **550**, 99.

from the products of oxidation of the ester (I; R = Me) with lead tetra-acetate or with manganese dioxide in chloroform. Cleavage of the glycol system by the latter reagent is unexpected but may be due to the presence of the tertiary allylic hydroxyl group.

The *OO*-isopropylidene derivative of the ester (I; R = Me), on oxidation with potassium permanganate in acetone, gave an acid, characterised as the *S*-benzylthiouronium salt, $C_{20}H_{30}O_6N_2S$, which contained one methoxyl group and showed infrared absorption at 1736 cm.$^{-1}$ (carboxylic ester). The acid product, $C_{12}H_{20}O_6$, is thus a monomethyl ester and must therefore have structure (III; R = Me). The free monomethyl ester was obtained as a syrup showing infrared absorption at 3240 and 2640 cm.$^{-1}$ (hydrogen-bonded hydroxyl) and at 1747 cm.$^{-1}$ (ester and hydrogen-bonded carboxyl); mild alkaline hydrolysis gave the crystalline hygroscopic diacid (III; R = H).

Further confirmation of the αβ-dihydroxy-acid system in the acid (I; R = H) was afforded by oxidation with lead tetra-acetate in aqueous acetic acid, which gave carbon dioxide, (+)-α-methylbutyraldehyde, and an optically inactive, unsaturated dibasic acid, $C_9H_{12}O_4$. The ultraviolet absorption spectrum indicated the presence of an αβ-unsaturated acid grouping in the dibasic acid. Catalytic hydrogenation resulted in the uptake of 2 mols. of hydrogen, giving an acid, $C_9H_{16}O_4$, the thorium salt of which gave 4-methylcycloheptanone on pyrolysis. The reduction product must therefore be (±)-γ-methylsuberic acid, although its m. p. differs from that reported[3] for the (±)-acid (146°) and is closer to the reported m. p.[4] of the (—)-acid (81°).

Ozonolysis of the dibasic C_9 acid gave formaldehyde, indicating the presence of a terminal methylene group, together with succinic acid and a syrupy mixture from which lævulic acid (isolated as its methyl ester 2,4-dinitrophenylhydrazone) was obtained. Similar results were obtained on ozonolysis of the acid (I; R = H). The presence of a terminal methylene group in the latter was confirmed by the formation of formaldehyde on oxidation with Lemieux and von Rudloff's periodate–permanganate reagent.[5] These results are consistent only with structure (IV) for the acid $C_9H_{12}O_4$ and hence (I; R = H) for the acid $C_{15}H_{24}O_6$. The derivative of methyl lævulate mentioned above presumably arises owing to decarboxylation of the expected ozonolysis product, β-oxoadipic acid.

The presence of a 1,4-diene system in the acid (IV) was confirmed by the action of hot aqueous potassium hydroxide, which gave the isomeric 5-methylocta-2,4-dienedioic acid (V) with the ultraviolet absorption characteristic of a 2,4-dienoic acid.

The 2,4-dinitrophenylhydrazone (II) gives 0·46 *C*-methyl group in the Kuhn–Roth estimation. This must arise from rearrangement of the 1,4-diene system; a similar case of a spurious *C*-methyl value, due to rearrangement of a terminal methylene group, has been noted previously.[6] It is likely that the *C*-methyl value observed for the acid (I; R = H) also includes a contribution from rearrangement of the terminal methylene group.

EXPERIMENTAL

M. p.s are corrected. Unless otherwise stated, ultraviolet absorption spectra were determined for ethanol solutions in a Unicam S.P. 500 spectrophotometer. Infrared absorption spectra were determined on Nujol mulls.

Action of Hydrogen Peroxide on Alternaric Acid.—Isolation of the acid (I; R = H). (*A*) A solution containing alternaric acid (5·02 g.), N-sodium hydroxide (77·6 ml.; 6·35 equivs.), and aqueous hydrogen peroxide (150 ml.; 20-vol.) was made up to 850 ml. with water. After 3 days at room temperature further hydrogen peroxide (100 ml.) was added, and after 6 days the solution was acidified with 3N-sulphuric acid (35 ml.) and continuously extracted with ether for 24 hr. The ethereal extract was washed with 25% aqueous sodium chloride, dried, and evaporated, and the crystalline residue (4·3 g.) triturated with benzene. A solution of the product in ether was diluted with benzene, and the solvent removed under reduced pressure until crystallisation commenced. The crystals (3·2 g.) were separated and recrystallised from benzene (2—4

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[3] Qudrat-i-Khuda and Ghosh, *J. Indian Chem. Soc.*, 1940, **17**, 19.

[4] Ruzicka and Steiger, *Helv. Chim. Acta*, 1927, **10**, 688.

[5] Lemieux and von Rudloff, *Canad. J. Chem.*, 1955, **33**, 1710.

[6] Mulholland, *J.*, 1958, 2693.

times) and finally from ethyl acetate–light petroleum (b. p. 60—80°), giving pure 7,8-*dihydroxy*-9-*methyl*-3-*methyleneundec*-5-*ene*-1,7-*dicarboxylic acid* as flat needles or leaflets, m. p. 95° (1·92 g., 52%) [Found: C, 60·2; H, 8·0; active hydrogen (Zerewitinoff; in pyridine), 1·33; *C*-Me, 11·6%; equiv., 152. $C_{15}H_{24}O_6$ requires C, 60·0; H, 8·1; 4 active hydrogens, 1·33; 2*C*-Me, 10·0; 3*C*-Me, 15·0%; equiv. (dibasic), 150], $[\alpha]_D^{21}$ +43·5° (*c* 2·01 in acetone), ε 4560 at 210 mμ, $\nu_{max.}$ 3300—3400, 2500, 1718, 1701, 1684, 1669, and 1645 cm.$^{-1}$. On hydrogenation in acetic acid with a palladium catalyst, 4·929 mg. of the substance took up 0·69 ml. of hydrogen at N.T.P., corresponding to 1·9 double bonds. The compound decomposed slowly in air but could be stored indefinitely in a vacuum.

The acid (I; R = H) (299 mg.), on methylation with ethereal diazomethane and chromatography of the product in ether on alumina, gave a product (252 mg.), m. p. 37—43·5°. After recrystallisation from ether–light petroleum (b. p. 40—60°) at −60° this *methyl ester* (I; R = Me) had m. p. 41—43·5° [Found: C, 62·4; H, 8·5; OMe, 18·6; active hydrogen (Zerewitinoff in pyridine), 0·63. $C_{17}H_{28}O_6$ requires C, 62·2; H, 8·6; 2OMe, 18·9; 2 active hydrogens, 0·61%], $[\alpha]_D^{19}$ +48° (*c* 2·01 in ethanol), ε 4440 at 210 mμ, $\nu_{max.}$ 3515, 1720, and 1642 cm.$^{-1}$.

The foregoing methyl ester (198 mg.) with acetic anhydride (4 ml.) and pyridine (4·5 ml.) at room temperature (20 hr.) gave a product (201 mg.) which was chromatographed in benzene–light petroleum (b. p. 40—60°) (1 : 1) on alumina. Elution with benzene gave *methyl* 8-*acetoxy*-7-*hydroxy*-9-*methyl*-3-*methyleneundec*-5-*ene*-1,7-*dicarboxylate* (89 mg.), b. p. 70—80°/10^{-4} mm. (Found: C, 61·7; H, 8·2; OMe, 16·4; Ac, 11·9. $C_{19}H_{30}O_7$ requires C, 61·6; H, 8·2; 2OMe, 16·8; 1Ac, 11·6%), $\nu_{max.}$ 3510w, 1743s, and 1650w cm.$^{-1}$.

The acid (I; R = H) (100 mg.) was dissolved in dry acetone (10 ml.) containing concentrated sulphuric acid (0·05 ml.). After 18 hr. at room temperature sodium hydrogen carbonate (0·63 g.) was added and the mixture shaken for 0·5 hr., cooled to 0°, and shaken with water (20 ml.) and ether (20 ml.). The aqueous layer was acidified at 0° with 3N-sulphuric acid (2·5 ml.) and extracted with ether (3 × 15 ml.), and the combined ethereal extracts were washed with water and evaporated. The resulting syrup (120 mg.) was dissolved in N-sodium hydroxide (0·85 ml.), adjusted to pH 3 with N-hydrochloric acid, and added with stirring to a solution of *S*-benzylthiouronium chloride (135 mg.) in water (1 ml.). After 1 hr. at 0° the solid was collected [m. p. 162—166° (decomp.) (184 mg.)]. Recrystallisation from aqueous ethanol and then from ethanol at −60° gave *di*-(S-*benzylthiouronium*) 7,8-*isopropylidenedioxy*-9-*methyl*-3-*methyleneundec*-5-*ene*-1,7-*dicarboxylate*, m. p. 173·5—174·5° (Found: C, 60·9; H, 7·6; N, 8·1; S, 9·2. $C_{34}H_{48}O_6N_4S_2$ requires C, 60·7; H, 7·2; N, 8·3; S, 9·5%).

The ester (I; R = Me) (532 mg.) was dissolved in dry acetone (50 ml.) containing concentrated sulphuric acid (0·25 ml.). After 18 hr. at room temperature an excess of sodium hydrogen carbonate and of anhydrous magnesium sulphate was added. After 3 hr. with occasional shaking, the acetone solution was filtered and evaporated, and the residue (657 mg.) chromatographed in light petroleum (b. p. 40—60°) on alumina. Elution with ether–light petroleum (b. p. 40—60°) gave the *isopropylidene derivative* (530 mg., 89%), $[\alpha]_D^{20}$ +33° (*c* 4·53 in ethanol). For analysis, the chromatography was repeated and the column eluted with light petroleum (b. p. 40—60°). Molecular distillation of the product at 60—75°/0·001 mm. gave the analytical sample (Found: C, 65·4; H, 8·7; OMe, 16·6. $C_{20}H_{32}O_6$ requires C, 65·2; H, 8·75; 2OMe, 16·85%), ε 3248 at 210 mμ, $\nu_{max.}$ 1743 and 1651 cm.$^{-1}$. There were no infrared bands due to the hydroxyl group.

(*B*) Alternaric acid (2·00 g.) was oxidised as above and the acidified mixture distilled to small bulk. The distillate was made alkaline with 0·12N-barium hydroxide, saturated with carbon dioxide, filtered, and distilled to small bulk. Treatment of the distillate with aqueous 2,4-dinitrophenylhydrazine hydrochloride gave a complex mixture of 2,4-dinitrophenylhydrazones (0·11 g.). This mixture was also obtained in an experiment in which the hydrogen peroxide was omitted. Fractional crystallisation from methanol and from light petroleum (b. p. 60—80°) gave a product, m. p. 120—123°, raised to 123—125° on admixture with acetone 2,4-dinitrophenylhydrazone.

The residue from the second distillation, on dilution with acetone, deposited barium formate (228 mg.) (Found: Ba, 60·2. Calc. for $C_2H_2O_4Ba$: Ba, 60·4%), which was converted into *S*-benzylthiouronium formate, m. p. and mixed m. p. 150·5—151·5° (Found: C, 51·05; H, 5·5; N, 13·2. Calc. for $C_9H_{12}O_2N_2S$: C, 50·9; H, 5·7; N, 13·2%).

Oxidation of the Acid (I; R = H) *with Periodic Acid.*—A solution of the acid (152 mg.) in methanol (1 ml.) was treated with 0·12M-periodic acid (4·5 ml.) at room temperature. Volatile products were removed with a current of nitrogen and absorbed in a solution containing 0·5% of 2,4-dinitrophenylhydrazine in 4N-hydrochloric acid (30 ml.) at 5°. After 45 min. the yellow precipitate in the latter solution was collected, chromatographed on alumina, eluted with benzene, and crystallised from methanol, giving plates, m. p. 134—134·5° (64 mg.), $[\alpha]_D^{18}$ +32·6° (*c* 2·50 in chloroform) (Found: C, 49·8; H, 5·6; N, 21·3. Calc. for $C_{11}H_{14}O_4N_4$: C, 49·6; H, 5·3; N, 21·0%), identical (mixed m. p. and infrared absorption spectrum) with (+)-α-methylbutyraldehyde 2,4-dinitrophenylhydrazone.[7] Further material, m. p. 133° (11 mg.), was recovered from the mother-liquors.

Oxidation of Ester (I; R = Me) *with Periodic Acid.*—A mixture of the ester (323 mg.), 0·17M-periodic acid (6·3 ml.), and ethanol containing 5% of ethyl acetate (6 ml.) was kept in the dark for 1 hr., then distilled at 25°/25 mm., the distillate being condensed at −80°. After 1 hr. the distillate was added to 0·2% aqueous dimedone solution (175 ml.) containing acetic acid (2 drops). After 5 days the crystalline product was collected (m. p. 127—130°; 172 mg.). Recrystallisation from aqueous methanol gave plates, m. p. 134—135°, of the *dimedone derivative* of (+)-α-methylbutyraldehyde (Found: C, 72·1; H, 9·2. $C_{21}H_{32}O_4$ requires C, 72·4; H, 9·3%), $[\alpha]_D^{20}$ $\ngtr$ ±2° (*c* 1·88 in ethanol; *l* = 1 dm.), identical (mixed m. p. and infrared absorption spectrum) with a synthetic specimen.

In a second experiment the ester (1·05 g.) gave a distillate which was heated under reflux in a current of nitrogen with semicarbazide hydrochloride (0·4 g.) and sodium acetate trihydrate (0·6 g.). After 1 hr. evaporation under reduced pressure and addition of water gave plates, m. p. 113—117° (240 mg.). After recrystallisation from aqueous ethanol the derivative had m. p. 113—115°, identical (mixed m. p. and infrared absorption spectrum) with the *semicarbazone*, m. p. 115—115·5°, of (+)-α-methylbutyraldehyde (Found: C, 50·45; H, 9·1; N, 29·3. $C_6H_{13}ON_3$ requires C, 50·3; H, 9·15; N, 29·35%), $[\alpha]_D^{22}$ +32° (*c* 1·5 in ethanol). The residue from the distillation was extracted with ether (2 × 20 ml.), and the extracts were washed with 9% aqueous sodium hydrogen carbonate and with 10% aqueous sodium chloride and dried. Evaporation under reduced pressure gave an unstable yellow oil (816 mg.). This product (262 mg.) was added to a solution of 2,4-dinitrophenylhydrazine (225 mg.) in methanol (15 ml.) and concentrated hydrochloric acid (0·5 ml.). After 2·5 hr. at room temperature the mixture was kept overnight at 0°. The red solid (251 mg.) was collected and chromatographed from benzene on alumina. Elution with the same solvent gave a product which on purification from ethyl acetate–light petroleum (b. p. 60—80°) furnished yellow needles, m. p. 149—150° (102 mg.) of the *2,4-dinitrophenylhydrazone* (II) of methyl 6-methylene-2-oxonon-3-enedioate (Found: C, 51·2; H, 4·85; N, 13·1; OMe, 14·5; *C*-Me, 1·7. $C_{18}H_{20}O_8N_4$ requires C, 51·4; H, 4·8; N, 13·3; OMe, 14·8; 1*C*-Me, 3·6%), $\lambda_{max.}$ 217, 253, 257, 375 mμ (ε 20,510, 11,880, 11,570, 23,810), $\lambda_{max.}$ (in $CHCl_3$) 249, 394 (ε 12,230, 25,620), $\lambda_{infl.}$ 403 mμ (ε 25,300).

Oxidation of Ester (I; R = Me) *with Lead Tetra-acetate.*—The ester (101 mg.) in benzene (5 ml.) was treated portionwise with lead tetra-acetate (154 mg.). After 1·5 hr. the lead salts were separated and the filtrate distilled at 20° under reduced pressure into a trap at −80°. The distillate, on treatment with an excess of 0·25% 2,4-dinitrophenylhydrazine in 3N-hydrochloric acid followed by extraction with benzene, gave a product which after purification on alumina and crystallisation from methanol furnished (+)-α-methylbutyraldehyde 2,4-dinitrophenylhydrazone (18 mg.) (mixed m. p. and infrared absorption spectrum). The residue from the distillation on treatment with methanolic 2,4-dinitrophenylhydrazine hydrochloride and isolation as described above gave yellow needles, m. p. 148—148·5° (48 mg., 37%), identical (infrared absorption spectrum) with the 2,4-dinitrophenylhydrazone (II).

Oxidation of Ester (I; R = Me) *with Manganese Dioxide.*—A solution of the ester (492 mg.) in chloroform (25 ml.) was shaken with active manganese dioxide[8] (5 g.) at room temperature for 23 hr. The manganese dioxide was separated and washed with acetone (4 × 10 ml.) and the combined filtrates were evaporated, giving a dark yellow oil (268 mg.). A solution of this product in ether at −80° deposited a yellow oil (55 mg.), $\lambda_{max.}$ 233 and 302 mμ ($E_{1\,cm.}^{1\%}$ 255, 212). The filtrate yielded a second oil (204 mg.), $\lambda_{max.}$ 233 mμ ($E_{1\,cm.}^{1\%}$ 253). The latter product (46 mg.) with 2,4-dinitrophenylhydrazine gave yellow laths (from ethyl acetate), m. p. 146·5—147·5° (14 mg.), identical (mixed m. p. and infrared absorption spectrum) with methyl 6-methylene-2-oxonon-3-ene-1,9-dioate 2,4-dinitrophenylhydrazone (II).

[7] Badin and Pacsu, *J. Amer. Chem. Soc.*, 1945, **67**, 1352.

[8] Mancera, Rosenkranz, and Sondheimer, *J.*, 1953, 2190.

Oxidation of Methyl 7,8-*Isopropylidenedioxy*-9-*methyl*-3-*methyleneundec*-5-*ene*-1,7-*dicarboxylate with Potassium Permanganate*.—A solution of the isopropylidene derivative (1·047 g.) in dry acetone (50 ml.) was treated portionwise with powdered potassium permanganate (4·0 g.) during 1 hr. at 24°. After a further 3 hr. the mixture was cooled to 0°, decolorised by sulphurous acid, and quickly extracted with ether (4 × 30 ml.). The combined ethereal extracts were washed with 9% aqueous sodium hydrogen carbonate (6 × 10 ml.), and the combined aqueous washings were cooled in ice, acidified with 3N-sulphuric acid, and rapidly extracted with ether (3 × 50 ml.). The combined ethereal extracts were washed with water, dried, and evaporated. The resulting syrup (631 mg.) was dissolved in N-sodium hydroxide (2·5 ml.), adjusted to pH 3 with N-hydrochloric acid, and added with stirring to a solution of *S*-benzylthiouronium chloride (589 mg.) in water (3 ml.). After 1 hr. at 0° the precipitate of S-*benzylthiouronium methyl* 2,2-*dimethyl*-5-*s*-*butyl*-1,3-*dioxolan*-4,4-*dicarboxylate* was collected (m. p. 141—141·5°; 446 mg.). Recrystallisation from 50% aqueous ethanol raised the m. p. to 146° (Found: C, 56·7, 56·6; H, 7·3, 7·5; N, 6·6, 6·6; S, 7·2, 7·3; OMe, 7·5, 7·7. $C_{20}H_{30}O_6N_2S$ requires C, 56·3; H, 7·1; N, 6·6; S, 7·5; 1OMe, 7·3%), $[\alpha]_D^{23}$ +64° (*c* 1·00 in EtOH).

This salt (1·37 mg.) was shaken with ether (10 ml.) and 3N-sulphuric acid (5 ml.) at 0°. The aqueous layer was quickly extracted with further ether (2 × 10 ml.), and the combined ethereal solutions were washed with water, dried, and evaporated under reduced pressure. The residue when dried over phosphoric oxide *in vacuo* gave *methyl hydrogen* 2,2-*dimethyl*-5-*s*-*butyl*-1,3-*dioxolan*-4,4-*dicarboxylate* as a viscous syrup (Found: C, 53·1; H, 7·6%; equiv., 281. $C_{12}H_{20}O_6,\frac{1}{2}H_2O$ requires C, 53·5; H, 7·9%; *M*, 269).

A solution of the monomethyl ester (190 mg.) in 0·4N-potassium hydroxide (12 ml.) was left for 20 hr. at room temperature, then washed with ether, cooled in ice, acidified with 3N-sulphuric acid, and extracted with ether (3 × 15 ml.). The combined ethereal extracts on evaporation gave the intensely hygroscopic *diacid*, m. p. 87—94° (171 mg.), which could be handled only in a dry-box in the presence of a ^{204}Tl static eliminator. Recrystallisation from methylene chloride–light petroleum (b. p. 40—60°) gave shining prisms, m. p. 88·5—94° [Found: C, 53·2; H, 7·2%; equiv., 113. $C_{11}H_{18}O_6$ requires C, 53·65; H, 7·4%; equiv. (dibasic), 123], $[\alpha]_D^{19}$ +40·5° (*c* 0·97 in acetone), $\nu_{max.}$ 3100—2500, 1728 and 1715 (shoulder) cm.$^{-1}$. The *silver salt* decomposed above 150° (Found: C, 28·8; H, 3·8; Ag, 45·95. $C_{11}H_{16}O_6Ag_2$ requires C, 28·7; H, 3·5; Ag, 46·9%).

Ozonolysis of the Acid (I; R = H).—(A) *In acetic acid.* A stream of ozonised oxygen was passed into a solution of the dihydroxy-acid (143 mg.) in acetic acid (15 ml.) at 19° for 14 min. After addition of magnesium powder and water (70 ml.) the mixture was distilled to small bulk and the distillate added to 0·2% aqueous dimedone (150 ml.). After 6 days the precipitate was collected (m. p. 179·5—186·5°; 83 mg.). Recrystallisation from methanol gave needles (71 mg.), m. p. 189—191°, alone or mixed with formaldehyde dimethone. After a further 15 days the aqueous filtrate deposited further solid from which additional material (10 mg.) was obtained having m. p. 189—190°. The pure derivative so obtained represents a 58% yield of formaldehyde.

(B) *In methyl acetate.* A stream of ozonised oxygen was passed into a solution of the acid (144 mg.) in methyl acetate (12 ml.) at −50° for 14 min. After removal of the solvent at 0°/2 mm. the ozonide was decomposed with water (25 ml.) and steam-distilled. The distillate was added to 0·2% aqueous dimedone (100 ml.). After 3 days the solid was collected (58 mg.); recrystallisation from methanol gave formaldehyde dimethone (31 mg., 22%), m. p. and mixed m. p. 187°.

The residue from the steam-distillation was extracted continuously with ether (24 hr.). Evaporation of the ethereal extract gave a product (111 mg.) which partly dissolved in methylene chloride. The undissolved solid, m. p. 176—183° (9 mg.), on sublimation at 150/12 mm. gave succinic acid (5·8 mg., 10%), m. p. and mixed m. p. 187° (correct infrared spectrum).

Evaporation of the methylene chloride solution gave an oil which was heated under reflux with 2,4-dinitrophenylhydrazine (0·20 g.) and concentrated hydrochloric acid (3 ml.) in methanol (20 ml.). After 1·5 hr. the mixture was evaporated to half bulk and kept at 0° for 5 days. The dark precipitate (62 mg.) was collected and a solution in benzene chromatographed on alumina. Elution with benzene gave an orange solid (44 mg.). Crystallisation from methanol gave orange leaflets, m. p. 140° (32 mg., 21%), of methyl lævulate 2,4-dinitrophenylhydrazone, identical (mixed m. p. and infrared spectrum) with a synthetic specimen.

Periodate–Permanganate Oxidation of the Acid (I; R = H).—A solution of the acid (30·5 mg.) in water (10 ml.) containing 4N-sodium carbonate (0·3 ml.) and N-sodium hydroxide (2 ml.) was treated with sodium metaperiodate (0·56 g.) and 0·034M-potassium permanganate (1 ml.) in water (20 ml.). After 1 min. N-hydrochloric acid (2 ml.) was added and after 3 hr. a solution of arsenic trioxide (2·0 g.) in 3N-sodium hydroxide (8 ml.), followed by 3N-sulphuric acid (15 ml.). Steam-distillation gave a distillate from which formaldehyde dimethone was isolated as above, having m. p. and mixed m. p. 187·5—188·5° (7·3 mg., 25%).

In a parallel experiment titrimetric analysis showed that the acid consumed 9·0 atoms of oxygen per mol. in 1·5 hr. Thereafter oxidation was slow, 10·7 atoms being consumed after 18 hr.

Oxidation of the Acid (I; R = H) *with Lead Tetra-acetate.*—(*a*) A current of nitrogen was passed successively through a vessel containing lead tetra-acetate (1·59 g.), a trap containing a 0·33% solution of 2,4-dinitrophenylhydrazine in 4N-hydrochloric acid (160 ml.), an empty trap cooled to −80°, and two traps which contained in all 100 ml. of 0·147N-barium hydroxide. A solution of the dihydroxy-acid (479 mg.) in 60% aqueous acetic acid (25 ml.) was admitted, whereupon rapid reaction occurred with effervescence. After 2 hr. the contents of the barium hydroxide traps were made up to 200 ml. with boiled-out water. 20 ml. of this solution neutralised 11·6 ml. of 0·100N-hydrochloric acid, equivalent to the formation of 0·98 mole of carbon dioxide per mole of the dihydroxy-acid.

The reaction mixture was then distilled at 20°/2 mm. into the cooled (−80°) trap, and the distillate added to the contents of the 2,4-dinitrophenylhydrazine trap. The mixture was kept overnight at 0°, after which the precipitate was collected (265 mg.) and purified in benzene on alumina. Crystallisation of the product from methanol gave leaflets, m. p. 134—135° (227 mg., 53·5%), identical (mixed m. p. and infrared spectrum) with (+)-α-methylbutyraldehyde 2,4-dinitrophenylhydrazone.

The residue from the above distillation was treated with 3N-sulphuric acid (2 ml.) and extracted with ethyl acetate (3 × 10 ml.), and the combined extracts were washed with 25% aqueous sodium chloride, dried, and evaporated. The semicrystalline residue (264 mg.), on sublimation at 90—100°/10^{-4} mm., gave a sticky sublimate which on crystallisation from acetone–carbon tetrachloride yielded a product, m. p. 115·5—119·5° (57 mg.). Further purification gave *5-methyleneoct-2-enedioic acid* as prisms, m. p. 120—122° (37 mg., 12·5%) [Found: C, 58·3, 58·3; H, 6·7, 6·5%; equiv., 91, 94. $C_9H_{12}O_4$ requires C, 58·7; H, 6·6%; equiv. (dibasic), 92], $[\alpha]_D^{20} \not> \pm 1°$ (*c* 2·0 in acetone). $\lambda_{max.}$ (in 90% EtOH) 208 mμ (ε 12,860); $\nu_{max.}$ 1700, 1685, and 1648 cm.$^{-1}$. The compound sublimed at 150—180°/15 mm. with only slight decomposition and was recovered unchanged after treatment with boiling acetyl chloride for 1 hr.

(*b*) The crude non-volatile oxidation product (1·18 g.) (from 2·00 g. of the dihydroxy-acid) was subjected to 100 transfers in a counter-current apparatus, with acetic acid–benzene–water (4 : 4 : 1). Evaporation of the contents of tubes no. 25—41 at 20°/2 mm. gave crystals which were purified from acetone–carbon tetrachloride to yield 5-methyleneoct-2-enedioic acid, m. p. 121—123° (464 mg., 38%).

Hydrogenation of 5-*Methyleneoct*-2-*enedioic Acid.*—A solution of 5-methyleneoct-2-enedioic acid (118 mg.) in ethyl acetate (10 ml.) was hydrogenated over Adams platinic oxide catalyst (28 mg.). Uptake (1·99 mol. of hydrogen) ceased after 0·5 hr. Isolation gave (±)-γ-methylsuberic acid, m. p. 53—63° (112 mg.). Crystallisation from benzene–light petroleum (b. p. 60—80°) and then from water gave prisms, m. p. 64·5—67° [Found: C, 57·75; H, 8·8%; equiv., 101. $C_9H_{16}O_4$ requires C, 57·4; H, 8·6%; equiv. (dibasic), 94].

Pyrolysis of γ-Methylsuberic Acid.—A solution of (±)-γ-methylsuberic acid (112 mg.) in N-sodium hydroxide (1·20 ml.) was added to thorium nitrate tetrahydrate (180 mg.) in water (1 ml.). After 1 hr. the precipitate was collected, washed cautiously with water, and dried at 110° for 1 hr. The dried salt (194 mg.) was placed in a small tube connected to a trap cooled to −80° and heated at 340—350°/1 mm. After 0·5 hr. the temperature was raised slowly to 390°. The contents of the cold trap gave a semicarbazone as prisms, m. p. 153—155° (49 mg.). Recrystallisation from ethanol raised the m. p. to 156·5—157·5°, alone or mixed with synthetic 4-methylcycloheptanone semicarbazone.[9] The infrared absorption spectra of the natural and the synthetic specimen were identical.

Ozonolysis of 5-*Methyleneoct*-2-*enedioic Acid.*—Ozonised oxygen was passed through a solution of the acid (62 mg.) in methyl acetate (8 ml.) at −50° for 14 min. Water (120 ml.) was added and the mixture distilled. The aqueous distillate (100 ml.), treated as above, gave formaldehyde

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[9] Adamson and Kenner, *J.*, 1939, 181.

dimethone, m. p. and mixed m. p. 190·5—191·5° (66·5 mg., 67·5%) (infrared spectrum). The residue from the distillation was extracted continuously with ether for 20 hr. Evaporation of the ethereal extract gave a semi-solid product (39 mg.), which with methylene chloride gave a solid. Sublimation at 130°/12 mm. then gave succinic acid (4·4 mg., 11%) identical (infrared spectrum) with an authentic specimen. The methylene chloride-soluble fraction on evaporation gave an oil which was converted into the 2,4-dinitrophenylhydrazone as above. The crude product (56 mg.), after purification in benzene on alumina and elution with benzene, gave a solid (42 mg.) which crystallised from methanol to give methyl lævulate 2,4-dinitrophenylhydrazone (37 mg., 35%) (mixed m. p. and infrared spectrum).

Isomerisation of 5-*Methyleneoct*-2-*enedioic Acid.*—The acid (37·5 mg.) was heated in N-potassium hydroxide (4 ml.) under reflux in nitrogen for 4 hr. The cooled mixture was cautiously acidified with concentrated hydrochloric acid, and the precipitate collected (m. p. 181·5—185°; 22 mg.). Recrystallisation from ethyl methyl ketone gave 5-*methylocta*-2,4-*dienedioic acid*, feathery needles, m. p. 195—196·5° (10 mg.) [Found: C, 58·5; H, 6·6%; equiv., 97. $C_9H_{12}O_4$ requires C, 58·7; H, 6·6%; equiv. (dibasic), 92], $\lambda_{max.}$ (in 90% EtOH) 271 mμ (ε 26,780), $\nu_{max.}$ 1695 (shoulder), 1685, 1630, and 1610 cm.$^{-1}$.

Extraction of the foregoing aqueous filtrate with ethyl acetate (2 × 10 ml.) and evaporation of the extracts gave further material, m. p. 120—150° (16 mg.). Attempts at further purification were unsuccessful, but ultraviolet absorption measurements indicated the presence in the material of 60% of 5-methylocta-2,4-dienedioic acid.

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