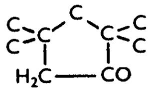
513. *Gibberellic Acid. Part VII.* The Structure of Gibberic Acid.*

By B. E. Cross, John Frederick Grove, J. MacMillan,
and T. P. C. Mulholland.

Gibberic acid is shown to have structure (III), by degradation to the tetramethyl ester (VII; R = Me, R′ = CO_2Me) and to methyl 1 : 7-dimethylfluorene-9-carboxylate (XIV).

Gibberic acid, $C_{18}H_{20}O_3$, an end-product of the acid hydrolysis of gibberellic acid, was shown by Cross [1] to be a benzenoid tetracyclic keto-acid and to possess the partial structure (I) since oxidation with selenium dioxide yielded gibberdionic acid, $C_{18}H_{18}O_4$, a non-enolisable five-membered-ring 1 : 2-diketone. The presence of the hexahydrofluorene nucleus (II) was established by selenium dehydrogenation to 1 : 7-dimethylfluorene [1, 2] and by oxidation to benzene-1 : 2 : 3-tricarboxylic acid in significant yield (ref. 3 and see below). Gibberic acid can also be converted [1] into 1 : 7-dimethylfluorene by mild dehydrogenation of the tricarboxylic acid, $C_{18}H_{20}O_6$, derived from gibberdionic acid by fission of the 1 : 2-diketone grouping. Skeletal rearrangement is therefore unlikely during the selenium dehydrogenation which thus involves the elimination from gibberic acid of a carboxyl group and of the $CH_2{\cdot}CO$ group from the feature (I). The position of these groupings in the hexahydrodimethylfluorene nucleus (II) has now been established, leading to structure (III) for gibberic acid, some of the evidence for which has already been briefly reported.[4]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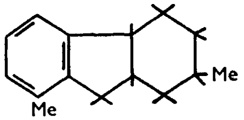
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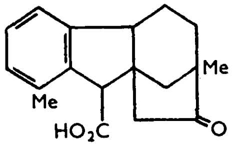
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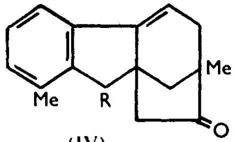
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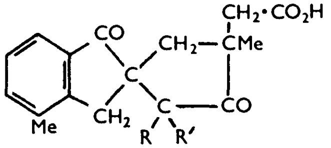
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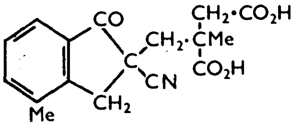
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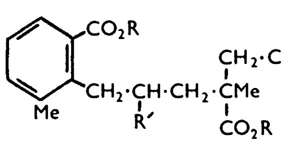
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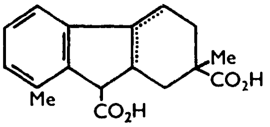
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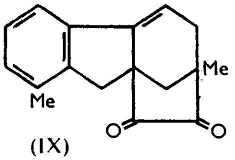
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The position of the methylenecarbonyl bridge has been determined by the following degradative sequence: (III) ⟶ (IV; R = CO_2H) ⟶ (IV; R = H) ⟶ (V; R = R′ = H) ⟶ (V; RR′ = :N·OH) ⟶ (VI) ⟶ (VII; R = H, R′ = CN) ⟶ (VII; R = H, R′ = CO_2H) ⟶ (VII; R = Me, R′ = CO_2Me).

Oxidation of gibberic acid with alkaline potassium permanganate (4 atom-equiv. of oxygen) at 0° gave a 41% yield of dehydrogibberic acid, $C_{18}H_{18}O_3$ (IV; R = CO_2H), in

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* Part VI, *Plant Physiology*, 1958, in the press.

[1] Cross, *J.*, 1954, 4670.

[2] Mulholland and Ward, *J.*, 1954, 4676.

[3] Yabuta, Sumiki, and Aso, *J. Agric. Chem. Soc. Japan*, 1951, **25**, 159.

[4] Cross, Grove, MacMillan, and Mulholland, *Chem. and Ind.*, 1956, 954.

which an ethylenic bond has been introduced in conjugation with the aromatic ring as shown by the ultraviolet spectrum (cf. gibberic acid, Table 1). Dehydrogibberic acid did not undergo either acid or alkaline hydrolysis and regenerated gibberic acid on catalytic reduction. It was rapidly degraded by further alkaline permanganate, a reaction consistent with structure (IV; $R = CO_2H$); attempts to improve the yield of dehydrogibberic acid by reducing the excess of permanganate led to the recovery of unchanged gibberic acid. The formation of dehydrogibberic acid from gibberic acid presumably involves oxidation of the tertiary hydrogen atom to hydroxyl followed by dehydration.

Oxidation at 25° with more potassium permanganate (10 atom-equiv. of oxygen) gave a low yield of a dibasic acid, $C_{17}H_{18}O_4$, m. p. 255—256° (decomp.), possibly identical with the acid of m. p. 245—247° described by the Japanese workers.[5] Like dehydrogibberic acid the dibasic acid had an ethylenic bond in conjugation with the aromatic ring as shown by the ultraviolet spectrum (Table 1), and took up 1 mol. of hydrogen catalytically. The infrared spectrum showed that the five-membered-ring ketone group of gibberic acid had been lost and the dibasic acid must therefore have the structure (VIII) in which the methylenecarbonyl bridge has been ruptured and the tertiary carboxylic acid group $\beta\gamma$ to the ethylenic bond lost as carbon dioxide.

TABLE 1. *Ultraviolet absorption maxima* (*m*μ) *in ethanol.*

Compound	$\lambda_{max.}$	log ε
Gibberic acid	265, 274, 300	2·56, 2·47, 1·49
Dehydrogibberic acid	260, 269, 290, 300	4·14, 4·09, 3·50, 3·44
Acid $C_{17}H_{18}O_4$ (VIII)	265·5	4·01
Gibberone	259·5, 269, 290, 301·5	4·13, 4·07, 3·62, 3·62
Gibberdione	~250, 257, 267, 290, 301	4·14, 4·21, 4·10, 3·65, 3·65
1 : 7-Dimethylfluorene	269, ~275, 293, 297, 304	4·44, 4·37, 3·95, 3·90, 3·95
Methyl 1 : 7-dimethylfluorene-9-carboxylate	~266, 271, ~280, 294, 305·5	4·28, 4·39, 4·25, 3·73, 3·59

Oxidation of gibberic acid at 100° with excess of alkaline permanganate followed by neutral permanganate[6] gave benzene-1 : 2 : 3-tricarboxylic acid (isolated as its methyl ester) in low yield. A low yield (7%) of benzene-1 : 2 : 3-tricarboxylic acid was also obtained by Yabuta *et al.*[3] by means of manganese dioxide in boiling concentrated sulphuric acid. We obtained a better yield (18%) of this acid when the water-soluble gummy by-products from the production of dehydrogibberic acid by alkaline permanganate oxidation of gibberic acid at 0° were re-oxidised with, successively, chromic oxide in acetic acid at 100°, alkaline potassium permanganate at 100°, and neutral permanganate at 20°.

No identifiable product was obtained from the oxidation of gibberic acid with dilute nitric acid, and only acetic acid (isolated as its *p*-bromophenacyl derivative) by oxidation with acid potassium permanganate at 100°. Gibberic acid was largely unaffected by alkaline hydrogen peroxide but a neutral ketone, m. p. 99—101°, was isolated in very low yield.

Decarboxylation of dehydrogibberic acid with palladium–charcoal or charcoal alone at 230° gave the neutral ketone, gibberone (IV; $R = H$); attempted decarboxylation with copper chromite in 1-methylnaphthalene yielded 0·7 mol. of carbon dioxide but no gibberone. Gibberone can however also be prepared by direct dehydrogenation of gibberic acid. Yabuta *et al.*[7] reported the isolation of gibberone in 17% yield on dehydrogenation of gibberic acid with selenium at 300—330° although they wrongly assigned the molecular formula $C_{18}H_{18}O$ to it. We have confirmed that selenium dehydrogenation of gibberic acid at 360° yields gibberone in low yield, together with 1 : 7-dimethylfluorene: in addition three phenolic substances, A, m. p. 207—210°, B, m. p. 198—202°, and C, m. p. 165—169°, a neutral ketonic substance, m. p. 138—139°, and a highly fluorescent material subliming above 300° were isolated in very small yield.

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[5] Yabuta, Sumiki, Aso, Tamura, Igarashi, and Tamari, *J. Agric. Chem. Soc. Japan*, 1941, **17**, 894.

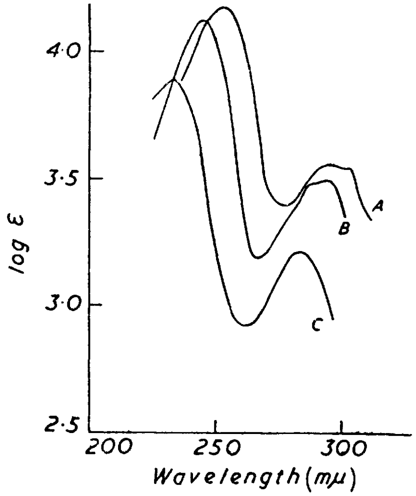
[6] Randall, Benger, and Groocock, *Proc. Roy. Soc.*, 1938, *A*, **165**, 432.

[7] Yabuta, Sumiki, Aso, Tamura, Igarashi, and Tamari, *J. Agric. Chem. Soc. Japan*, 1941, **17**, 975.

Phenol C is shown in a later paper to be 7-hydroxy-1-methylfluorene; phenol A is a hydroxyfluorene of unknown structure—spectroscopic evidence suggests it may be 2-hydroxy-3 : 8-dimethylfluorene; phenol B is possibly a 2-hydroxyfluorene although the ultraviolet spectrum in alkaline solution does not show the expected bathochromic shift compared with the spectrum in ethanol.

The yield of gibberone by selenium dehydrogenation of gibberic acid on a 50 mg. scale was raised to 27% by plunging the reactants into a bath preheated to 360°; on a larger scale, however, the yield of gibberone decreased and that of 1 : 7-dimethylfluorene increased. Milder methods of dehydrogenation were therefore sought.

Gibberic acid was largely unaffected by iodine in chloroform and by chloranil in tetrachloroethane. The best method of preparing gibberone was found to be by heating gibberic acid with 30% palladium-charcoal. At 340° the yields of 1 : 7-dimethylfluorene and gibberone were 10% and 49% respectively: at 300° gibberone was the only neutral product isolated, and at 210° the yield of crude gibberone was 70—80%. At the latter temperature only 0·6—0·7 mol. of carbon dioxide was evolved and an acidic product (10—20%), identified as *epi*gibberic acid,[1] was obtained.



Absorption spectra of (*B*) 2 : 2-*dimethylindan*-1-*one*, (*A*) *the keto-acid* (V; R = R′ = H), *and* (*C*) *the cyano-tricarboxylic acid* (VII; R = H, R′ = CN).

These experiments showed that palladium-charcoal at 210—300° was effective in bringing about the decarboxylation of gibberic acid but left the methylenecarbonyl bridge intact. However, the methoxycarbonyl substituent was retained on dehydrogenation of methyl gibberate with 30% palladium-charcoal at 220° and (after hydrolysis) dehydrogibberic acid was obtained.

Gibberone was optically active; in accordance with structure (IV; R = H), the infrared spectrum showed five-membered-ring ketone carbonyl absorption at 1745 cm.$^{-1}$ in CCl_4, and the ultraviolet light absorption (Table 1) showed that the ethylenic bond, revealed by catalytic hydrogenation, was conjugated with the benzene ring. Gibberone was stable to hydrolysis by both acid and alkali. It yielded 1 : 7-dimethylfluorene with selenium at 360° and was oxidised by selenium dioxide in ethanol at 140° to a five-membered-ring 1 : 2-diketone gibberdione (IX), which, like gibberdionic acid,[1] had almost identical ultraviolet absorption spectra in ethanol and in sodium hydroxide; the spectra closely resembled that of gibberone (Table 1).

Gibberone, on oxidation with chromic oxide, yielded a monobasic keto-acid, $C_{17}H_{18}O_4$ (V; R = R′ = H), m. p. 155—157°, which is presumably identical with the uncharacterised acid, m. p. 154—155°, obtained in the same way by Yabuta *et al.*[7] Structure (V; R = R′ = H) is assigned to this acid for the following reasons. The four oxygen atoms are contained in a carboxyl group and in two carbonyl groupings: one of the carbonyl groups is present in a saturated 5-membered ring (infrared absorption at 1744 cm.$^{-1}$), while the other is conjugated with the aromatic nucleus as shown by the ultraviolet spectrum (Fig. 1) and is contained in an indanone ring system. The formation of the acid (V; R = R' = H) from gibberone without loss of carbon and with the addition of three oxygen atoms is consistent with the oxidation of a trisubstituted ethylenic double bond to a keto-acid. This acid (V; R = R' = H) was not hydrolysed by dilute mineral acid or alkali and is not therefore a β-keto acid or β-diketone. Like 2 : 2-dimethylindan-1-one it was stable to neutral permanganate at room temperature and to chromic oxide in acetic acid at 75°: under these conditions both 2-methyl- and 2 : 3-dimethyl-indan-1-one are oxidised.

This evidence suggests that the keto-acid is a 2 : 2-disubstituted indan-1-one, and since it retains the partial structure (I), originally present in gibberic acid, the 5-membered ring must be attached at position 2, as in (V; R = R' = H).

Oxidation of the keto-acid with alkaline potassium permanganate gave no identifiable products. However, oxidation of 2 : 2-dimethylindan-1-one with potassium permanganate in the presence of magnesium nitrate [8, 9] yielded 2 : 2-dimethylindane-1 : 3-dione. Application of this method to the keto-acid gave a complex mixture, resolved by crystallisation and chromatography on paper into benzene-1 : 2 : 3-tricarboxylic acid, 3-methylphthalic acid (isolated as the anhydride), a small amount of β-methyltricarballylic acid, traces of an acid having an R_F value corresponding to oxalic acid, and two unidentified acids (one of them probably formed by further oxidation of β-methyltricarballylic acid which was found to be unstable to oxidation under the conditions employed). The isolation of 3-methylphthalic acid and β-methyltricarballylic acid is consistent with the structure (V; R = R' = H), final proof of which was obtained by opening both non-benzenoid rings and by an unambiguous synthesis of the product.

Several methods of opening the saturated 5-membered ring in the keto-acid (V; R = R' = H) were investigated. In contrast to gibberic acid and gibberone, the keto-acid and its ester could not be oxidised to the corresponding 1 : 2-diketones with selenium dioxide. An attempt to prepare hydroxymethylene derivatives of the keto-acid and its ester was likewise unsuccessful. Whilst gibberic acid gave an α-bromo- but no αα-dibromo-derivative, the keto-acid gave an α-bromo-derivative (V; R = H, R' = Br) in ether and an αα-dibromo-compound (V; R = R' = Br) with a large excess of bromine in acetic acid, the former giving the latter on further bromination.

The monobromo-derivative (V; R = H, R' = Br) was resistant to dehydrobromination with collidine, confirming the absence of hydrogen in the α-position to the bromine substituent. Attempted hydrolysis of the bromo-ketones was unsuccessful.

Finally, the keto-acid was treated with butyl nitrite and sodium methoxide [10] to give the desired α-hydroxyimino-compound (V; RR' = :N·OH) in good yield; Beckmann rearrangement of this with polyphosphoric acid gave the isomeric imide carboxylic acid (X): with toluene-*p*-sulphonyl chloride and sodium hydroxide, however, a tricarboxylic acid (VII; R = H, R' = CN) was obtained which contained the expected cyano-group (band at 2250 cm.$^{-1}$). Since all six oxygen atoms in compound (VII; R = H, R' = CN) are present in the three carboxylic acid groups both ketone functions in the acid (V; R = R' = H) must have been eliminated; and this was confirmed by the infrared spectrum (absence of absorption due to the saturated five-membered ring ketone) and by the ultraviolet spectrum (Fig. 1) which showed the absence of the indanone chromophore and was typical of a substituted benzoic acid. The cyano-tricarboxylic acid, which formed an intramolecular 5-membered-ring anhydride when heated with acetic anhydride, must therefore have structure (VII; R = H, R' = CN), formed by alkaline hydrolysis of the

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[8] Riemschneider, *Gazzetta*, 1947, **77**, 607.

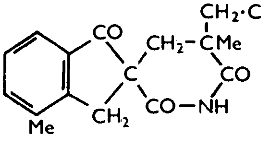
[9] Winkler, *Chem. Ber.*, 1948, **81**, 256.

[10] Koelsch and Le Claire, *J. Org. Chem.*, 1941, **6**, 516.

intermediate β-keto-nitrile (VI). The cyano-tricarboxylic acid (VII; R = H, R' = CN) was not readily oxidised by alkaline potassium permanganate. It was hydrolysed by 50% sulphuric acid to an amorphous tetracarboxylic acid (VII; R = H, R' = CO_2H) which gave two isomeric tetramethyl esters, m. p. 83—84° and 47—48° (VII; R = Me, R′ = CO_2Me), with diazomethane. These esters, which have different optical rotations, must be diastereoisomers arising from racemisation of the $C_{(2)}$ centre during hydrolysis of the β-keto-nitrile (VI). The structure of the two esters was established by the synthesis[11] of their racemates, m. p. 78—80° and 34—36°, respectively. The infrared spectra of the esters obtained by degradation of gibberic acid and the corresponding synthetic racemates were identical in solution.

The synthesis of the tetramethyl esters (VII; R = Me, R' = CO_2Me) finally establishes the structure of the keto-acid (V; R = R' = H) and consequently the structure of gibberone (IV; R = H). It follows that the methylenecarbonyl bridge in gibberic acid must be attached as in (III) and it only remains to prove the position of the carboxyl group.

In an attempt to locate the position of the carboxyl group in gibberic acid by degradation to a substituted 1 : 7-dimethylfluorene wherein the original carboxyl group is retained as a methyl or hydroxymethyl group, the reduction of gibberic acid was studied. Reduction with hydriodic acid and red phosphorus or by the Pondorff method failed: Clemmensen reduction gave deoxogibberic acid (XI; R = R' = R″ = H). Wolff–Kishner reduction gave a mixture of acids isomeric with deoxogibberic acid, separated by fractional crystallisation into α- and β-isomers. The formation of the two isomers is ascribed to racemisation of more than one of the optically active centres present in gibberic acid; it was ascertained that on treatment of gibberic acid with sodium ethoxide alone a significant change took place in the optical rotation. Barbier–Wieland degradation of the methyl ester of the α-acid was unsuccessful.



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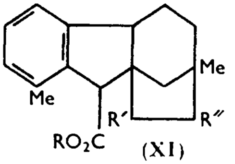

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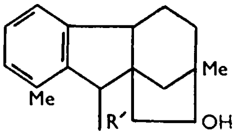

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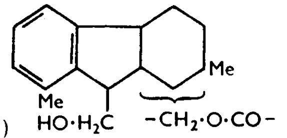

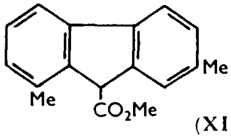

(XIV)

Gibberic acid and methyl gibberate were very resistant to lithium aluminium hydride in ether. Prolonged reduction of gibberic acid with the hydride in boiling tetrahydrofuran gave an amorphous product which was assumed to be the diol (XII; R' = H). Dehydrogenation of the diol with selenium at 360° not unexpectedly gave 1 : 7-dimethylfluorene with loss of the hydroxymethyl substituent. Reduction of methyl gibberate ethylene ketal by lithium aluminium hydride and regeneration of the 5-membered-ring ketone grouping by hydrolysis furnished an intractable neutral product.

Reduction of methyl gibberdionate with lithium aluminium hydride gave two crystalline products, a *cis*-1 : 2-diol (methyl tetrahydrogibberdionate) (XI; R = Me, R' = R″ = OH) (C=O at 1735 cm.$^{-1}$), and a triol (XII; R' = OH), which showed no C=O absorption in the infrared spectrum, gave an inconclusive result with potassium triacetylosmate, and probably contains a *trans*-1 : 2-diol grouping. Attempts to split the triol (XII; R' = OH) with periodate were unsuccessful but oxidation with sodium bismuthate

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[11] Morrison and Mulholland, following paper.

of crude material which contained some of the corresponding *cis*-1 : 2-diol gave an aldehydic gum. Further oxidation of the gum with alkaline silver oxide did not yield the desired alcohol-dicarboxylic acid, but a δ-lactone $C_{18}H_{22}O_3$ of partial structure (XIII).

This approach was abandoned when dehydrogenation of model compounds [12] showed that the conditions necessary for removal of the methylenecarbonyl bridge of gibberic acid by dehydrogenation were sufficiently drastic to eliminate a reduced carboxyl substituent at the 9-position of a fluorene nucleus. Fortunately a convenient method of eliminating the methylenecarbonyl bridge under relatively mild conditions was discovered during an attempt to prepare gibberdione (IX) from gibberdionic acid. With 30% palladium-charcoal at 230° the latter yielded 1 : 7-dimethylfluorene, and treatment of methyl gibberdionate under the same conditions gave the desired methyl 1 : 7-dimethylfluorenecarboxylate and, in low yield, the corresponding ketol $C_{19}H_{22}O_4$. The infrared (C=O at 1736 cm.$^{-1}$ in CCl_4) and ultraviolet spectra (cf. 1 : 7-dimethylfluorene, Table 1) of the 1 : 7-dimethylfluorenecarboxylate indicated that the ester group was unconjugated. The 9-position for the ester substituent was favoured by the fact that alkaline hydrolysis gave a small amount of 1 : 7-dimethylfluorene in addition to the corresponding carboxylic acid.

Structure (XIV) for the ester was confirmed by synthesis. Treatment of the 9-lithium derivative of 1 : 7-dimethylfluorene with solid carbon dioxide [13] afforded 1 : 7-dimethylfluorene-9-carboxylic acid, methylation of which with diazomethane gave the methyl ester identical with the ester obtained by dehydrogenation of methyl gibberdionate.

The isolation of this ester by degradation establishes the position of the carboxyl substituent in gibberic acid which therefore must have structure (III).

Structure (III) for gibberic acid is at variance with the views of the Japanese workers [14] who have advanced the partial structure $C_{16}H_{18}(CO_2H)\cdot COMe$. In support of this structure Seta and Sumiki [15] claimed that the crude product obtained by Beckmann rearrangement of gibberic acid oxime gave a good yield of methylamine on vigorous acid hydrolysis. This experiment has been repeated as the result was inconsistent with the partial structure (I): in our hands a careful examination of the hydrolysis products of the crude mixture from the Beckmann rearrangement (only a portion of which was acidic) failed to reveal the presence of methylamine; about 0·5 mol. of ammonia was produced, estimated as the chloroplatinate. The production of ammonia is not inconsistent with partial structure (I); the remainder of the nitrogen originally present in the oxime was shown to be present, as organic nitrogen, in the other hydrolysis products. An amide-carboxylic acid, isomeric with gibberic acid oxime, $C_{18}H_{21}O_2N$, was isolated from the mixture in low yield.

EXPERIMENTAL

M. p.s are corrected. Microanalyses are by Messrs. W. Brown and A. G. Olney. Light-absorption measurements were obtained as described previously.[2] Unless otherwise stated infrared spectra were determined for " Nujol " mulls and ultraviolet spectra for EtOH solutions.

Gibberic acid [1] was recovered unchanged after 1 hr. in refluxing N-hydrochloric or 2N-sulphuric acid. It did not reduce Tollens's reagent or Fehling's solution and gave no iodoform with iodine and sodium hydroxide.

Bromogibberic Acid.—Gibberic acid (50·4 mg.) was heated under reflux in ether (6·7 ml.) containing bromine (28·9 mg.) until evolution of hydrobromic acid ceased. The residue, after removal of the solvent, was crystallised from ethyl acetate–light petroleum (b. p. 60—80°) and the crystals were separated by hand-picking into needles, m. p. 145—151° (gibberic acid), and aggregates of prisms, m. p. 165—170°. The latter were recrystallised from benzene–light petroleum (b. p. 60—80°), giving *bromogibberic acid*, m. p. 195—196° (Found: C, 59·35; H, 5·35. $C_{18}H_{19}O_3Br$ requires C, 59·5; H, 5·3%). The infrared spectrum showed a carboxylic acid OH band and C=O bands at 1750 (5-membered-ring α-bromo-ketone) and 1709 cm.$^{-1}$ (carboxylic acid).

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[12] Cross and Mulholland, unpublished work.

[13] Burtner and Cusic, *J. Amer. Chem. Soc.*, 1943, **65**, 262.

[14] Yatazawa and Sumiki, *J. Agric. Chem. Soc. Japan*, 1952, **25**, 503.

[15] Seta and Sumiki, *ibid.*, 1952, **26**, 508.

Beckmann Rearrangement of Gibberic Acid Oxime.—Powdered phosphorus pentachloride (0·60 g.) was added in portions during 4 hr. to a stirred solution of the oxime (271 mg.) in dry ether (60 ml.) at 0° ± 1°. After 3·5 hr. at 20°, the mixture was treated with ice, and the ether layer washed with water. The recovered product was heated under reflux with water (5 ml.), giving, on cooling, an amorphous solid (248 mg.), m. p. 80—90° (Found: N, 4·8%). The solid (227 mg., equiv. to 10·9 mg. of N) and 28% hydrochloric acid (4·1 ml.) were heated in a sealed tube at 155—160° for 9 hr. After cooling, the contents of the tube were washed out with water and extracted with methylene chloride. Recovery gave a brown amorphous solid (228 mg.) (Found: N, 2·35% ≡ 5·35 mg. of N).

3N-Sodium hydroxide (20 ml.) was added to the aqueous layer and 16·5 ml. were distilled into concentrated hydrochloric acid (5 ml.) and water (5 ml.). Evaporation yielded a residue (29 mg.) identified as ammonium chloride. No methylamine hydrochloride was detected in the residue by the infrared spectrum. The residue containing ammonium chloride was dissolved in dilute hydrochloric acid, and chloroplatinic acid (150 mg.) in water (1·5 ml.) was added. The ammonium chloroplatinate, determined gravimetrically was equivalent to 6·45 mg. of NH_3 (5·3 mg. of N).

Thus nearly 98% of the nitrogen in the crude Beckmann rearrangement product has been accounted for in the hydrolysis products.

Crystallisation of the brown amorphous solid from ethanol gave an *amide-carboxylic acid* (10 mg.), needles, m. p. 338—343° (decomp.) (Found: C, 71·1; H, 7·2; N, 4·9. $C_{18}H_{21}O_3N$ requires C, 72·2; H, 7·1; N, 4·7%), $\nu_{max.}$ 3260, 3190, ~2600 (broad), 1715, and 1632 cm.$^{-1}$.

Action of Sodium Ethoxide on Gibberic Acid.—Gibberic acid (100 mg.) and ethanol (1·6 ml.) containing sodium (80 mg.) were heated in a sealed tube at 180—190° for 8 hr. The cooled mixture was diluted with water and extracted with ether; the aqueous layer was acidified with concentrated hydrochloric acid and re-extracted with ether giving, on recovery, an intractable gum (78 mg.), $[\alpha]_D^{17}$ −36° (*c* 2·65 in EtOH).

Methyl Gibberate Ethylene Ketal.—Methyl gibberate (108 mg.), ethylene glycol (0·4 ml.), benzene (3 ml.), and toluene-*p*-sulphonic acid (9 mg.) were heated under reflux in a Dean and Stark apparatus for 7 hr. Recovery after washing with aqueous sodium hydrogen carbonate and water furnished a gum (122 mg.) which was chromatographed in light petroleum (b. p. 40—60°) (3 ml.) on alumina (6·5 × 1·3 cm.). Elution with benzene gave a viscous oil (86 mg.) which was distilled at 90°/8 × 10^{-5} mm. giving the oily *ethylene ketal* (Found: C, 73·3; H, 7·8. $C_{21}H_{26}O_4$ requires C, 73·7; H, 7·7%).

Hydrolysis of the ketal (53 mg.) with 90% acetic acid (1 ml.) at 100° for 30 min. and crystallisation of the gummy product from light petroleum (b. p. 60—80°) containing a little benzene gave methyl gibberate, m. p. and mixed m. p. 106—109°.

Reduction of Gibberic Acid.—(1) *Clemmensen method.* Gibberic acid (832 mg.), amalgamated zinc (8 g.), concentrated hydrochloric acid (8 ml.), water (10 ml.), and toluene (10 ml.) were heated under reflux for 72 hr. Portions of concentrated hydrochloric acid (3 ml.) were added after 24 and 48 hr. The toluene was combined with ether extracts of the aqueous layer and washed with dilute hydrochloric acid and water. Recovery gave a gum (830 mg.), separated by Girard's reagent P into a ketonic fraction, which crystallised from ethyl acetate–light petroleum (b. p. 60—80°) in needles of gibberic acid (35 mg.), m. p. 149—152°, and a non-ketonic gum (707 mg.). The gum crystallised from light petroleum (b. p. 40—60°) in prisms of *deoxogibberic acid* (XI; $R = R' = R'' = H$) (416 mg.) m. p. 104—108° raised by further crystallisation to 108—110°, $[\alpha]_D^{23}$ +19° (*c* 1·6 in EtOH) (Found: C, 80·15; H, 8·2%; equiv., 268. $C_{18}H_{22}O_2$ requires C, 80·0; H, 8·2%; *M*, 270), $\lambda_{max.}$ ~259, 265, and 273 mμ (log ε 2·48, 2·57, and 2·48 respectively), $\nu_{max.}$ 1706 cm.$^{-1}$ (C=O). Dehydrogenation of deoxogibberic acid with 30% palladised charcoal at 235—240° afforded 0·9 mol. of carbon dioxide but no crystalline product.

(2) *Wolff–Kishner method.* A mixture of gibberic acid (750 mg.), 100% hydrazine hydrate (1·50 ml.), and sodium ethoxide (0·60 g. of sodium in 12 ml. ethanol) was heated in a sealed tube for 8 hr. at 185—190°. The product was diluted with water and extracted with ether; acidification of the aqueous layer with concentrated hydrochloric acid and extraction with ether afforded, on recovery, an oil which partly solidified. The combined product (1·2 g.) from two experiments was separated by fractional crystallisation from light petroleum (b. p. 40—60) and hand-picking of crystals into (*a*), m. p. 118—126°, $[\alpha]_D$ −33° ± 1° (700 mg.), (*b*), m. p. 138—147°, $[\alpha]_D$ −4° ± 2° (239 mg.), and (*c*) mixed residues (150 mg.). Recrystallisation of material

(*a*) from light petroleum gave a *carboxylic acid* (*α-isomer*), laths or prisms, m. p. 124—126°, $[\alpha]_D^{23}$ −33° (*c* 1·22 in EtOH) (Found: C, 80·2; H, 8·1%; equiv., 269. $C_{18}H_{22}O_2$ requires C, 80·0; H, 8·2%; *M*, 270), $\lambda_{max.}$ ~259, 266, 274 mμ (log ε 2·45, 2·54, 2·42 respectively), $\nu_{max.}$ 1698 cm.$^{-1}$ (C=O). Recrystallisation of material (*b*) from light petroleum gave the less soluble *β-isomer*, microcrystalline nodules, m. p. 147—148°, $[\alpha]_D^{18}$ −2° (*c* 1·46 in EtOH) (Found: C, 79·8; H, 8·2%; equiv., 290), $\lambda_{max.}$ ~259, 266, 274 mμ (log ε 2·46, 2·47, 2·46 respectively), $\nu_{max.}$ 1702 cm.$^{-1}$ (C=O). The α-isomer was dimorphic and sometimes melted at 85—95°. Methylation with diazomethane afforded an oily ester which gave a complex mixture of products on treatment with excess of phenylmagnesium bromide in ether–benzene.

(3) *Lithium aluminium hydride.* Here and below, lithium aluminium hydride reductions were worked up either (*a*) with ether as solvent, by decomposition of excess of hydride with 3N-sulphuric acid followed by ether extraction or (*b*) with tetrahydrofuran as solvent, by addition of water, removal of the solvent by steam-distillation and ether-extraction of the acidified aqueous residue.

Gibberic acid (250 mg.) in tetrahydrofuran (20 ml.) was added dropwise to a stirred solution of lithium aluminium hydride (230 mg.) in tetrahydrofuran (25 ml.). The mixture was heated under reflux for 18 hr., lithium aluminium hydride (55 mg.) in tetrahydrofuran (5 ml.) added, and heating continued a further 26 hr. The product, a glass (210 mg.), showed no infrared absorption due to C=O but strong alcoholic hydroxyl absorption.

The glass (185 mg.) and selenium powder (188 mg.) were heated in a current of nitrogen at 340°, rising to 360° during 30 min., and then at 360° for 3·75 hr. The cooled mixture was extracted with ether, and the ethereal extract washed with sodium hydroxide. The recovered gum (145 mg.) in benzene–light petroleum (b. p. 40—60°) (1 : 4; 5 ml.) was chromatographed on alumina (pH 4; 12 g.) in ultraviolet light. Elution of a blue fluorescent band gave a sticky solid (96 mg.) which on sublimation at 60°/10^{-1} mm. and crystallisation from methanol yielded 1 : 7-dimethylfluorene (28 mg.), m. p. and mixed m. p. 104—105°.

Reduction of Methyl Gibberate and its Ethylene Ketal.—These reductions, by lithium aluminium hydride in ether, did not yield useful results.

Reduction of Methyl Gibberdionate.—(*a*) Methyl gibberdionate [1] (102 mg.) in tetrahydrofuran (7 ml.) was added dropwise to lithium aluminium hydride (28 mg.) in tetrahydrofuran (10 ml.) and heated under reflux for 6 hr. The gummy product (100 mg.) was chromatographed in benzene–light petroleum (1 : 1; 1·5 ml.) on alumina (5 × 1·2 cm.) in ultraviolet light. After gummy fractions (total 9 mg.) had been eluted with benzene–light petroleum (2 : 1), benzene–ether (98 : 2), and benzene–ether (95 : 5), elution of a weakly fluorescent band with benzene–methanol (99 : 1) yielded a solid (76 mg.), m. p. 139—146°. Crystallisation from benzene–light petroleum and then aqueous methanol gave *methyl tetrahydrogibberdionate* (XI; R = Me, R′ = R″ = OH), needles m. p. 156—158° (Found: C, 72·2; H, 7·6; OMe, 9·9. $C_{19}H_{24}O_4$ requires C, 72·1; H, 7·65; OMe, 9·9%), $\nu_{max.}$ 3320 cm.$^{-1}$ (OH) and 1735 cm.$^{-1}$ (ester C=O), giving a greenish-yellow colour with potassium triacetylosmate.

(*b*) Methyl gibberdionate (1·30 g.) in tetrahydrofuran (35 ml.) was added to lithium aluminium hydride (0·78 g.) in tetrahydrofuran (70 ml.). After 7 hours' heating under reflux, more lithium aluminium hydride (0·24 g.) was added and heating continued for a further 8 hr. The product, an amorphous solid (1·16 g.), was chromatographed in benzene (10 ml.) on alumina (8 × 2 cm.). The following fractions were collected (eluant in parentheses): (i) 30 mg. of yellow gum (benzene), (ii) 131 mg. of amorphous yellow solid showing a strong infrared C=O band (benzene–methanol, 99 : 1), (iii) 576 mg. of amorphous yellow solid (benzene–methanol 99 : 1), (iv) 272 mg., m. p. 187—195° (benzene–methanol, 95 : 5), and (v) 58 mg., m. p. 226—232° (benzene–methanol 9 : 1).

Fraction (v) crystallised from ethanol–light petroleum (b. p. 60—80°) in prisms, m. p. 234—236°, of a *triol* (XII; R′ = OH) (Found: C, 74·7; H, 8·45. $C_{18}H_{24}O_3$ requires C, 75·0; H, 8·4%). The infrared spectrum showed a strong OH band but no absorption band in the C=O region. The triol gave no colour with potassium triacetylosmate.

Fraction (iv) gave prisms, m. p. 198—200°, which gave an inconclusive result with the osmate reagent. The gum from the crystallisation mother-liquors gave a positive test and contained some *cis*-1 : 2-diol.

Fraction (iii) sublimed at 100—120°/8 × 10^{-5} mm. as an amorphous solid (Found: C, 74·5; H, 8·3%), which consisted of a mixture of stereoisomeric triols showing very weak infrared C=O absorption.

The triol (XII; R′ = OH) was recovered after 24 hr. at room temperature with excess of sodium metaperiodate in acidified aqueous methanol.

Oxidation of the Triol (XII; R′ = OH).—The triol (122·5 mg.) in 80% acetic acid (9 ml.) was shaken at room temperature for 5·5 hr. with 80% sodium bismuthate (159 mg., 1·1 mol.). Sufficient 3N-sodium hydroxide to neutralise two-thirds of the acetic acid was added with cooling and the solution extracted with benzene. The benzene extract was washed with aqueous sodium hydrogen carbonate and water; the gum [113 mg.; $\nu_{max.}$ 3360 cm.$^{-1}$ (OH), 2759 cm.$^{-1}$ (CH in aldehyde), 1719 cm.$^{-1}$ (C=O)] obtained on recovery was shaken in dioxan (5·25 ml.) for 3·5 hr. with silver oxide [from silver nitrate (300 mg.) in water (0·3 ml.) and 10% sodium hydroxide (2·7 ml.)], and the solution was filtered. After extraction with ether the filtrate was acidified with concentrated hydrochloric acid. Crystallisation of the precipitate from ethanol gave needles, m. p. 180—181°, of a neutral *lactonic alcohol* (XIII) (Found: C, 75·4; H, 7·7. $C_{18}H_{22}O_3$ requires C, 75·5; H, 7·7%), $\nu_{max.}$ 3510 cm.$^{-1}$ (OH) and 1730 cm.$^{-1}$ (lactone C=O), or in CCl_4 3590 and 1734 cm.$^{-1}$.

Oxidation of Gibberic Acid.—(1) *Alkaline potassium permanganate at* 0°. Gibberic acid (254 mg.) in water (2·5 ml.) and saturated aqueous sodium hydrogen carbonate (2·5 ml.) was treated at −1°, during 5 min., with ice-cold 1% potassium permanganate (40 ml.: 4 atoms-equiv. of O) in three portions. After 10 min. at 0°, the mixture was decolorised with sulphur dioxide, acidified with concentrated hydrochloric acid, and set aside for 12 hr. at 0°. The precipitate [105 mg.; m. p. 205—210° (decomp.)] was crystallised from aqueous methanol, then from benzene–light petroleum (b. p. 60—80°), giving *dehydrogibberic acid* (IV; R = CO_2H) (70 mg.), prisms, m. p. 222—224° (decomp.), $[\alpha]_D^{18}$ +99° (*c* 1·0 in EtOH) (Found: C, 76·95; 76·1; H, 6·55, 6·6%; equiv., 276. $C_{18}H_{18}O_3$ requires C, 76·6; H, 6·4%; *M*, 282). In the infrared spectrum it showed a broad band of weak absorption between 3170 and 2600 (carboxylic acid OH) and C=O absorption at 1730 (5-ring ketone) and 1688 (carboxylic acid) cm.$^{-1}$; these bands were found at 1742 and 1711 cm.$^{-1}$ in $CHCl_3$.

The *semicarbazone*, prepared from semicarbazide acetate in ethanol and crystallised from aqueous ethanol, had m. p. 228—230° (decomp.) (Found: C, 66·7; H, 6·25; N, 12·0. $C_{19}H_{21}O_3N_3$ requires C, 67·2; H, 6·2; N, 12·4%).

Dehydrogibberic acid sublimed at 220°/8 × 10^{-4} mm. but evolved carbon dioxide at the m. p. It did not reduce Fehling's solution or Tollens's reagent, gave no iodoform with sodium hypoiodite, and no colour with concentrated nitric acid. Rigorously purified specimens of dehydrogibberic acid gave no colour with concentrated sulphuric acid but preparative-grade specimens derived from gibberic acid by permanganate oxidation gave an intense royal-blue colour. The impurity was removed by methylation (diazomethane), chromatography of the oily methyl ester on alumina, and hydrolysis. Dehydrogibberic acid was recovered after 2 hours' heating under reflux with 5% aqueous potassium hydroxide and with 2N-hydrochloric acid. In sodium hydrogen carbonate solution at 0° it rapidly decolorised potassium permanganate solution.

Dehydrogibberic acid (25·9 mg.) in methanol (3 ml.) took up 0·95 mol. of hydrogen in 42 min. in the presence of 10% palladium–charcoal (17·8 mg.). Crystallisation of the solid product from aqueous ethanol and then from benzene–light petroleum (b. p. 60—80°) gave gibberic acid (16 mg.), m. p. and mixed m. p. 150—152°.

(2) *Alkaline potassium permanganate at* 25°. Aqueous 5% potassium permanganate (17·5 ml.; 10 atom-equiv. of O) was added with stirring during 70 min. to gibberic acid (250 mg.) in 10% aqueous potassium hydroxide (5 ml.) at 25—30°, and the mixture was set aside for 1 hr. The precipitate (37 mg.), obtained on acidification with concentrated hydrochloric acid of the sulphur dioxide-treated solution, crystallised from aqueous ethanol in needles, m. p. 255—256° (decomp.), of an *acid* (VIII) [Found: C, 71·2; H, 6·3%; *M* (Rast), 293; equiv., 142. $C_{17}H_{18}O_4$ requires C, 71·3; H, 6·3%; *M*, 286], $\nu_{max.}$ 3100—2500 and 1700 cm.$^{-1}$ (carboxylic acid). The acid decolorised potassium permanganate in acetone, and microhydrogenation in acetic acid with a palladium catalyst resulted in the uptake (18 min.) of 0·74 mol. of hydrogen. The fluorescein test for a phthalic acid was negative.

(3) *Isolation of methyl benzene*-1 : 2 : 3-*tricarboxylate.* (*a*) Gibberic acid (2·24 g.) was oxidised in 9 equal portions as described in (1) above. After removal of crude dehydrogibberic acid precipitated by acidification, the filtrate was continuously extracted with ether, giving a gum (1·0 g.). The gum in acetic acid (18 ml.) and water (2 ml.) at 100° was oxidised with chromic oxide (3·2 g.) in 90% acetic acid (27 ml.), added portionwise. After 45 min. the solution was

concentrated *in vacuo* to 10 ml. and continuously extracted with ether for 64 hr. The recovered gum (500 mg.) in aqueous 2% potassium hydroxide (50 ml.) was heated under reflux while 3·5% potassium permanganate solution (52 ml.) was added dropwise during 7 hr., and heating was then continued for a further 2 hr. Excess of permanganate was destroyed with methanol, the hot solution was filtered, and the manganese dioxide was washed with hot water. The combined filtrate and washings, adjusted to pH 5 with 3N-hydrochloric acid, were oxidised at 20° with 3·5% potassium permanganate solution (12 ml.). Excess of permanganate was destroyed as described above and the combined filtrate and washings, after acidification with concentrated hydrochloric acid, were continuously extracted with ether for 83 hr. Methylation of the gum (266 mg.) with diazomethane, followed by sublimation at 100—115°/7 × 10^{-2} mm., afforded crude methyl benzene-1 : 2 : 3-tricarboxylate (158 mg., 18%), identified by the infrared spectrum. Repeated crystallisation from ether–light petroleum gave the pure ester, m. p. 95—97° (26 mg.), identical (mixed m. p. and infrared spectrum) with an authentic specimen.

(*b*) Oxidation of gibberic acid (250 mg.) in potassium hydroxide at 100° with excess of potassium permanganate during 7 hr. gave methyl benzene-1 : 2 : 3-tricarboxylate (5 mg.), m. p. 98°.

(4) *Acid potassium permanganate at* 100°. Gibberic acid (96·5 mg.) in N-sulphuric acid (10 ml.) at 100° was treated in portions with solid potassium permanganate (1·16 g.) until no further decolorisation took place and the solution was then distilled. Titration of the aqueous acid distillate with 0·1N-sodium hydroxide showed that 0·73 mol. of volatile acid had been liberated. After evaporation to dryness *in vacuo* the residue in water (0·5 ml.) was adjusted to pH 6, *p*-bromophenacyl bromide (77 mg.) and ethanol (1·2 ml.) were added, and the mixture was heated under reflux for 2 hr. On cooling, *p*-bromophenacyl acetate, m. p. and mixed m. p. 82—84°, separated.

(5) *Alkaline hydrogen peroxide.* Hydrogen peroxide (20-vol.; 10 ml.) was added to gibberic acid (240 mg.) in N-sodium hydroxide (5 ml.), and the whole set aside for 20 days. An additional 5 ml. of hydrogen peroxide were added and the mixture was left for 14 days. Needles, m. p. 99—101°, of a neutral ketone (2 mg.) showing C=O bands at 1746 and 1701 cm.$^{-1}$ were deposited and collected. Acidification of the filtrate gave gibberic acid (184 mg.), m. p. and mixed m. p. 149—152°.

Dehydrogenation of Gibberic Acid.—(1) *Selenium at* 360°. (*a*) The neutral product from the experiment described by Mulholland and Ward [2] was chromatographed on alumina in ultraviolet light and the column eluted with light petroleum (b. p. 40—60°)–ether. After removal of the violet fluorescent band, containing 1 : 7-dimethylfluorene,[2] seven blue fluorescent bands were eluted, all of which gave gummy fractions enumerated below (light petroleum : ether ratio and fraction weight in parentheses):

I (50 : 1; 28 mg.), intractable.

II (20 : 1; 379 mg.). This was rechromatographed on alumina in light petroleum–ether (1 : 1). Solid fractions eluted from a very pale blue band were collected (78 mg., 2%) and repeatedly crystallised from methanol, giving plates or needles (10 mg.) of *gibberone* (IV; R = H), m. p. 126—127°, $[\alpha]_D^{21}$ +27° (*c* 1·76 in acetone) (Found: C, 85·4; H, 7·65. $C_{17}H_{18}O$ requires C, 85·7; H, 7·6%), C=O absorption at 1735 cm.$^{-1}$ (1745 cm.$^{-1}$ in CCl_4). The *dinitrophenylhydrazone* crystallised from acetic acid in orange-yellow needles, m. p. 250° (decomp.) (Found: C, 66·1; H, 5·6; N, 12·95. $C_{23}H_{22}O_4N_4$ requires C, 66·0; H, 5·3; N, 13·4%). The *oxime*, prepared from hydroxylamine hydrochloride in pyridine, formed needles (from methanol), m. p. 138—143° (Found: C, 80·2, 81·0; H, 7·6, 7·6. $C_{17}H_{19}ON$ requires C, 80·6; H, 7·6%).

Gibberone sublimed readily at 70°/10^{-4} mm. and gave an intense yellow solution in cold concentrated sulphuric acid. On microhydrogenation in acetic acid with a palladium catalyst it absorbed 0·9 mol. of hydrogen in 7 min. Gibberone was recovered after 5 hours' heating under reflux with 2N-hydrochloric acid and methanol (1 : 1) and after 3 hours' heating under reflux with 3N-sodium hydroxide and methanol (1 : 4).

III (10 : 1; 10 mg.). Rechromatography and elution of the main part of the band with light petroleum–ether (2 : 1) afforded a gum which, after sublimation at 100°/10^{-3} mm. followed by repeated crystallisation from methanol gave prisms, m. p. 138—139°, $\nu_{max.}$ 1730 and 1600 cm.$^{-1}$ in the double-bond stretching region.

IV (5 : 1; 127 mg.), intractable.

V (3 : 1; 52 mg.). Rechromatography and elution of a vivid yellow fluorescent band gave a yellow oil (15 mg.) which solidified under light petroleum (b. p. 60—80°) and thereafter crystallised from acetic acid in yellow prisms (3 mg.), subliming at 300—360° without melting. The infrared spectrum showed C=O absorption at 1687 cm.$^{-1}$ and OH absorption at 3350 and 3150 cm.$^{-1}$. Ultraviolet max. were at 272, 282, 305, 312 mμ ($E^{1\%}_{1\,\text{cm.}}$ 350, 492, 311, 313, respectively).

VI (2 : 1; 105 mg.). This material sublimed at 115°/10^{-3} mm., giving a solid (23 mg.); chromatography and elution of the column with ether–methanol (99 : 1) then yielded a solid (19 mg.), m. p. 178—180° (decomp.), fractional crystallisation of which from benzene afforded phenols A and B.

Phenol A crystallised in stout needles, m. p. 202—205° (decomp.) (Found: C, 84·55; H, 6·8. $C_{15}H_{14}O$ requires C, 85·7; H, 6·7%), $\lambda_{\text{max.}}$ ~270, 277, 307, 315 mμ (log ε 4·24, 4·28, 3·93, 3·95 respectively); 301, 316, 327 mμ (log ε, 4·27, 4·21, 4·20 respectively) in 0·1N-sodium hydroxide; the infrared spectrum showed hydroxyl absorption at 3330 cm.$^{-1}$; bands at 781, 856, and 877 cm.$^{-1}$ suggested 1 : 2 : 3- and 1 : 2 : 4 : 5-substitution patterns respectively on the two benzene rings of a fluorene nucleus. The *acetate* formed plates, m. p. 156—157°, from methanol (Found: C, 80·3; H, 6·4. $C_{17}H_{16}O_2$ requires C, 80·9; H, 6·4%). The infrared spectrum showed an absorption band at 1763 cm.$^{-1}$, characteristic of a phenyl acetate, and no hydroxyl absorption. Hydrolysis of the acetate with methanolic sodium hydroxide regenerated phenol A, m. p. 207—210°.

Phenol A was not soluble in cold 2N-sodium hydroxide but dissolved immediately on being warmed and was recovered unchanged. It was not hydrogenated with palladium in acetic acid, and formed a red substance, m. p. 150—155°, with picric acid. It gave a blue-green solution in concentrated sulphuric acid and gave no ferric chloride colour reaction.

Phenol B crystallised from benzene in long needles, m. p. 199—202° (decomp.), depressed to 175—185° on admixture with phenol A; the acetate (C=O at 1755 cm.$^{-1}$) crystallised from methanol in plates, m. p. 167—169° depressed below 145° on admixture with phenol A acetate. Phenol B was soluble in warm 2N-sodium hydroxide from which it was recovered unchanged. It had $\lambda_{\text{max.}}$ ~264, 271, ~288, ~305, 313 mμ ($E^{1\%}_{1\,\text{cm.}}$ 665, 679, 447, 558, 571 respectively); 245, 252, 277, 328 mμ ($E^{1\%}_{1\,\text{cm.}}$ 1104, 1110, 417, 403, respectively) in ethanol–0·1N-sodium hydroxide (2 : 3).

VII (ether; 215 mg.). This fraction, after sublimation at 120°/10^{-3} mm. and repeated crystallisation of the sublimate from benzene–light petroleum (b. p. 60—80°), gave phenol C in long needles (4 mg.), m. p. 165—169°. Recovery of the crystallisation mother-liquors yielded a solid (41 mg.), m. p. 143—160°, which could not be fractionated by chromatography or sublimation, or through the sodium salt. The crude solid (25 mg.), treated in benzene with picric acid (30 mg.), gave red needles, m. p. 128—134° after several crystallisations from benzene. The solid recovered from the purified picrate afforded phenol C, m. p. and mixed m. p. 163—168°.

The benzene mother-liquors from the picrate were chromatographed on alumina (8 × 1 cm.). Elution of a band fluorescing blue with benzene–methanol (99 : 1) and crystallisation of the recovered solid from benzene gave phenol B, large rosettes of needles, m. p. and mixed m. p. 199—210° (decomp.) (acetate, m. p. and mixed m. p. 166—169°). Further elution yielded a solid, m. p. 150—170°.

(*b*) Gibberic acid (45 mg.) and selenium powder (45 mg.) were mixed in a tube (10 × 1·5 cm.) fitted with a side arm 4 cm. from the top, and a slow stream of nitrogen was passed through the apparatus. The tube was plunged into a metal-bath at 360°: there was immediate evolution of carbon dioxide and hydrogen selenide, and a liquid ring condensed on the cool part of the tube. After 2·25 hr. the cooled mixture was extracted with ether and a little gibberic acid removed by extraction with aqueous sodium hydrogen carbonate. The neutral gum (21 mg.) in light petroleum (b. p. 40—60°) was chromatographed on alumina (15 × 1 cm.) in ultraviolet light. Elution of the band fluorescing pale blue gave a solid (17 mg.) from which crude gibberone (10 mg., 27%), m. p. 119—124°, was obtained by sublimation *in vacuo* and crystallisation from methanol.

Repetition of this experiment on a 100 mg. scale gave a reduced yield of gibberone and some 1 : 7-dimethylfluorene.

(2) *Palladium–charcoal.* (*a*) At 340°. Gibberic acid (104 mg.) and 30% palladium–charcoal (52 mg.; Zelinsky and Turowa-Pollak[16]) were heated in a current of nitrogen from 165° to 320° in 50 min. and then kept at 320—340° for 110 min. The cooled mixture was extracted with ether, and the extract washed with aqueous sodium hydrogen carbonate. The neutral fraction

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[16] Zelinsky and Turowa-Pollak, *Ber.*, 1925, **58**, 1295.

(68 mg.) in light petroleum (b. p. 60—80°) (4 ml.) was chromatographed on alumina (5 × 1 cm.) in ultraviolet light. Elution of a weakly fluorescent band with light petroleum-ether (99 : 1) gave 1 : 7-dimethylfluorene (7·5 mg.) (from methanol), m. p. and mixed m. p. 104—106°. Further elution of a blue fluorescent band with light petroleum-ether (9 : 1) gave a solid (4·3 mg., 49%), m. p. 85—107°. Crystallisation from methanol afforded gibberone, m. p. and mixed m. p. 116—122°.

At 300° (6 hr.) gibberic acid (105 mg.) with 30% palladium-charcoal evolved carbon dioxide (1 mol.) and gave gibberone (35 mg.), m. p. 120—122°.

(*b*) At 210°. Gibberic acid (140 mg.) and the above catalyst (90 mg.) were heated in the apparatus described above for 80 min. at 210°. 0·73 Mol. of carbon dioxide was evolved. The neutral fraction (84 mg., 72%) consisted of crude gibberone. The acid fraction (27 mg.) recovered from the sodium hydrogen carbonate washings crystallised from methanol in needles, m. p. 250—253°, of *epi*gibberic acid[1] (Found: C, 75·8; H, 7·1. Calc. for $C_{18}H_{20}O_3$: C, 76·0; H, 7·1%).

The yields from ten similar experiments fell in the range: carbon dioxide, 0·6—0·85 mol.; *epi*gibberic acid, 10—20%; crude gibberone 80—70%. Pure gibberone (1·34 g.) was obtained from the crude gibberone (4·59 g.) by chromatography on alumina followed by repeated crystallisation from methanol. Crude gibberone was used directly in the oxidation with chromic oxide described below.

Decarboxylation of Dehydrogibberic Acid.—(a) *Palladium-charcoal.* A mixture of dehydrogibberic acid (56·2 mg.) and 30% palladium-charcoal (30 mg.) was heated in a slow stream of nitrogen at 190°, rising to 230° during 30 min., and then at 230—240° for 1·5 hr. (1·0 mol. of carbon dioxide evolved). The charcoal was extracted with ether, and the extract washed with aqueous sodium hydrogen carbonate. Recovery furnished a yellow solid (42 mg.) which was chromatographed in light petroleum (b. p. 60—80°)-ether (20 : 1) on alumina (2·5 × 1·0 cm.) in ultraviolet light. A semi-solid forerun (7 mg.) was rejected: elution of a blue fluorescent band gave a solid (33 mg.) which crystallised from methanol in plates of gibberone, m. p. and mixed m. p. 125—127°.

(b) *Charcoal.* The experiment was carried out as in (a), except that charcoal (30 mg.) was used and the temperature was raised from 190° to 230° during 10 min. 0·94 Mol. of carbon dioxide was evolved. Chromatography of the neutral fraction gave crude gibberone (25 mg.).

(c) *Copper chromite.* Dehydrogibberic acid (56·4 mg.) and copper chromite (58 mg.) in 1-methylnaphthalene (1·0 ml.) were heated in a current of nitrogen under reflux for 1·5 hr. 0·70 Mol. of carbon dioxide was evolved but the product was intractable.

Fusion of dehydrogibberic acid at 235° in the presence of copper chromite yielded carbon dioxide (0·58 mol.), some unchanged dehydrogibberic acid, and an intractable neutral gum.

Dehydrogenations with 30% *Palladium-Charcoal.*—(1) *Methyl gibberate.* The ester (266 mg.) and the catalyst (100 mg.) were heated at 220—230° for 1·5 hr. in a slow stream of nitrogen. The filtered ether extract of the reaction mixture was washed with aqueous sodium hydrogen carbonate and water, and the recovered neutral gum (264 mg.) was chromatographed in light petroleum (b. p. 40—60°) on alumina (14 × 1 cm.). Fractional elution (25 ml. portions) with ether-light petroleum (1 : 4) afforded a gum (152 mg.) which was hydrolysed by heating it in methanol (5 ml.) and 20% aqueous potassium hydroxide (0·8 ml.) for 2 hr. Removal of the methanol *in vacuo*, acidification of the residue, and crystallisation of the crude acidic product from methanol yielded prisms (76 mg.), m. p. and mixed m. p. with dehydrogibberic acid 217—220° (decomp.).

(2) *Gibberdionic acid.* The acid (85 mg.) and the catalyst (29 mg.) were heated as described in (1) above. The recovered neutral gum (33 mg.) crystallised from methanol in needles (20 mg.), m. p. and mixed m. p. with 1 : 7-dimethylfluorene 104—106°. The acidic fraction (22 mg.) was intractable.

(3) *Methyl gibberdionate.* The ester (250 mg.) and the catalyst (100 mg.) were heated as described in (1). The recovered neutral yellow gum (196 mg.) was triturated with ether (10 ml.), and insoluble starting material filtered off (5 mg.). The ether solution was passed through a column of alumina (13 × 1 cm.) in ultraviolet light. After elution of a pale blue fluorescent band which furnished a yellow gum (*A*) (105 mg.) on recovery, elution with benzene of a band, pale yellow in daylight, furnished a yellow gum (*B*) (31 mg.).

Crystallisation of *B* from methanol gave needles, m. p. 195—205° (22 mg.), which on further crystallisation from ethyl acetate afforded hexagonal plates (10 mg.) of a ***ketol***, m. p. 208—215°

(Found: C, 72·6; H, 7·05. $C_{19}H_{22}O_4$ requires C, 72·6; H, 7·05%), $\lambda_{max.}$ ~260, 266, 273·5 mμ (log ε 2·53, 2·62, 2·58 respectively), $\nu_{max.}$ 3140 (OH) and 1740 cm.$^{-1}$ (C=O) (1745 cm.$^{-1}$ in $CHCl_3$; intensity equivalent to two C=O groups).

Crystallisation of *A* from methanol gave *methyl* 1 : 7-*dimethylfluorene*-9-*carboxylate* (XIV) (52 mg.), needles, m. p. 121—122°, $[\alpha]_D^{21}$ −5° ± 3°, $[\alpha]_{5461}^{21}$ −0·5° ± 3° (*c* 1·92 in EtOH) (Found: C, 80·7; H, 6·6; OMe, 12·9. $C_{17}H_{16}O_2$ requires C, 80·9; H, 6·4; OMe, 12·3%), $\nu_{max.}$ 1731 cm.$^{-1}$ (C=O) (1736 cm.$^{-1}$ in CCl_4). This ester was identical (mixed m. p. and infrared spectrum) with a synthetic specimen (see below).

Hydrolysis of the ester (33 mg.) in hot methanol (2 ml.) and 40% aqueous potassium hydroxide (2 ml.) for 3 hr. gave 1 : 7-dimethylfluorene (3 mg.), m. p. 102—105° (identified by mixed m. p. and infrared spectrum), and 1 : 7-*dimethylfluorene*-9-*carboxylic acid* (30 mg.), which crystallised from acetic acid in needles, m. p. 221—223° (decomp.), $[\alpha]_D^{18}$ +3° ± 3°, $[\alpha]_{5461}^{18}$ +1° ± 3° (*c* 1·32 in 0·1N-NaOH) (Found: C, 80·0, 80·0; H, 6·1, 5·95%; equiv., 238. $C_{16}H_{14}O_2$ requires C, 80·6; H, 5·9%; *M*, 238), $\lambda_{max.}$ ~260, 271, ~280, 306 mμ (log ε 4·19, 4·33, 4·18, 3·65, 3·60 respectively), $\nu_{max.}$ 1691 (C=O) and 3100—2500 cm.$^{-1}$ (OH) (identical with the synthetic specimen described below).

1 : 7-*Dimethylfluorene*-9-*carboxylic Acid.*—Lithium (0·32 g.) in ether (12 ml.) was treated with a few drops of a solution of butyryl chloride (1·84 g.) in ether (6·0 ml.). When the reaction started, the mixture was cooled to −40° during the addition (30 min.) of the rest of the reagent. The temperature of the stirred solution was allowed to rise to 20° during 4 hr. and, after the addition of 1 : 7-dimethylfluorene (2·90 g.) in portions, the mixture was heated under reflux for 1 hr., diluted with ether (8 ml.), cooled to −40°, and poured on freshly crushed solid carbon dioxide. When the temperature of the mixture reached 20°, water was added and the aqueous layer was separated, washed with ether, and acidified with concentrated hydrochloric acid. The precipitate (2·85 g.), m. p. 214—217° (decomp.), crystallised from acetic acid in needles m. p. 221—222° (decomp.), of 1 : 7-dimethylfluorene-9-carboxylic acid (Found: C, 80·0; H, 6·0%), identical (infrared spectrum) with the acid obtained above by dehydrogenation of methyl gibberdionate.

The methyl ester (XIV) crystallised from methanol in needles, m. p. 119—120° (Found: C, 81·0; H, 6·3%). It was identical (mixed m. p. and infrared spectrum) with the ester derived from methyl gibberdionate.

The *ethyl ester* crystallised from light petroleum (b. p. 40—60°) in prisms, m. p. 69—70° (Found: C, 80·95; H, 7·0. $C_{18}H_{18}O_2$ requires C, 81·2; H, 6·8%).

Dehydrogenation of Gibberone.—Gibberone (45 mg.) and selenium powder (45 mg.) were heated at 360° in a stream of nitrogen in the apparatus described above for the selenium dehydrogenation of gibberic acid. Carbon dioxide was evolved but no volatile carbonyl compounds (2 : 4-dinitrophenylhydrazine trap) were detected. After 1 hr. the cooled mixture was extracted with ether, and the ether extracted with aqueous sodium hydrogen carbonate (no acidic material recovered). The recovered neutral gum (27 mg.) in light petroleum (b. p. 40—60°) was chromatographed on alumina (15 × 1 cm.) in ultraviolet light. Elution of a band fluorescing violet gave 1 : 7-dimethylfluorene (5 mg.), m. p. and mixed m. p. 105—107°. A band fluorescing pale blue, eluted with light petroleum–ether (50 : 1), gave gibberone (11 mg.).

Oxidation of Gibberone.—(1) *Chromic oxide.* To gibberone (47 mg.) in acetic acid (1·0 ml.) was added portionwise chromic oxide (80 mg., 6 atom-equiv. of O) in acetic acid (0·5 ml.) and water (0·2 ml.). After each addition the mixture was heated at 100° until the oxidant was consumed and the process continued until excess of chromic oxide was present (1 hr.). After the addition of water (10 ml.) continuous extraction with benzene afforded a gum which was extracted with aqueous sodium hydrogen carbonate. The acid fraction, recovered in ethyl acetate, solidified when rubbed with ether and crystallised from benzene–light petroleum (b. p. 60—80°) in needles (20 mg., 35%), m. p. 155—156°, $[\alpha]_D^{18}$ +27° (*c* 0·93 in acetone), of 4-*methyl*-1-*oxoindane*-2-spiro-1′-(*4′-methyl-3′-oxo*cyclo*pentane-4′-acetic acid*) (V; R = R′ = H) (Found: C, 71·5; H, 6·5%; equiv., 268. $C_{17}H_{18}O_4$ requires C, 71·3; H, 6·3%; *M*, 286), $\lambda_{max.}$ ~248, 254, 293, ~302 mμ (log ε 4·16, 4·18, 3·55, 3·54 respectively), $\lambda_{max.}$ (in 0·1N-NaOH) ~250, 256, 288, 298, ~305 mμ (log ε 4·08, 4·13, 3·34, 3·42, 3·38 respectively). The infrared spectrum showed broad OH absorption at 3130 cm.$^{-1}$ and C=O bands at 1740 and 1713 cm.$^{-1}$: in dioxan it showed C=O bands at 1744 (5-membered-ring ketone), 1738 (monomeric carboxylic acid), and 1715 cm.$^{-1}$ (indanone-carbonyl).

The *methyl ester*, prepared with diazomethane, crystallised from benzene–light petroleum (b. p. 40—60°) in needles, m. p. 129—130° (Found: C, 71·9; H, 6·75; OMe, 11·0. $C_{18}H_{20}O_4$ requires C, 72·0; H, 6·7; OMe, 10·3%), $\lambda_{max.}$ ~249, 254, ~295, 300 mμ (log ε 4·14, 4·16, 3·49, 3·50 respectively), $\nu_{max.}$ (C=O) 1735 and 1702 cm.$^{-1}$ (1744 and 1717 cm.$^{-1}$ in CCl_4).

The keto-acid (V; R = R′ = H) gave a precipitate with dinitrophenylhydrazine in 2N-hydrochloric acid. It gave colourless solutions in concentrated sulphuric acid or ferric chloride. It was recovered unchanged after 4 hours' heating with 2N-hydrochloric acid and after 3 hours' heating with 3N-sodium hydroxide. Both the acid and its methyl ester were saturated to potassium permanganate in acetone and were not oxidised by chromic oxide in aqueous acetic acid at 70—80°. Neither the acid nor its methyl ester gave crystalline hydroxymethylene derivatives with ethyl formate and sodium methoxide.

When the oxidation was repeated with crude gibberone the yield of pure keto-acid was 23%.

(2) *Selenium dioxide.* Gibberone (80 mg.) in ethanol (0·3 ml.) was heated with selenium dioxide (44 mg.) in a sealed tube at 140° for 4 hr. Filtration of the cooled mixture and recovery gave an orange gum (90 mg.) which was chromatographed in ether (50 ml.) on alumina (pH 4; 12 × 1 cm.) in ultraviolet light. Elution with ether gave (*a*) a yellow gum (30 mg.) from a greenish-yellow fluorescent band (several crystallisations from methanol afforded gibberone), (*b*) a yellow gum (8 mg.) from an interband, and (*c*) an orange gum (33 mg.) from a dull greenish-brown band. Several crystallisations of (*c*) from benzene–light petroleum (b. p. 60—80°) gave orange-yellow needles (12 mg.) of *gibberdione* (IX), m. p. 181—182° (Found: C, 80·3; H, 6·4. $C_{17}H_{16}O_2$ requires C, 80·9; H, 6·4%), $\lambda_{max.}$ in EtOH–0·1N-sodium hydroxide, 250, 257·5; 267, 290, 301 (log ε 4·12, 4·18, 4·07, 3·66, 3·62 respectively), $\nu_{max.}$ (C=O) 1745 cm.$^{-1}$, shoulder at 1757 cm.$^{-1}$.

The yield of gibberdione was lower when heating was continued for 8 hr. No oxidation of gibberone took place with selenium dioxide at 110° in ethanol in a sealed tube; in boiling acetic acid only gums were obtained.

Bromination of the Keto-acid (V; R = R′ = H).—(a) *In ether.* A solution of bromine (170 mg., 5 mol.) in ether (10 ml.) was added to a suspension of the keto-acid (57 mg.) in ether (4 ml.) until the yellow colour persisted for 15 min. After 12 hr. the solution was washed with water and the solute recovered. The gummy product solidified on trituration with benzene and crystallised from ethyl acetate–light petroleum (b. p. 60—80°) in rods (16 mg.) of the *2′-bromo-ketone* (V; R = H, R′ = Br), m. p. 178—182° or 199—203° (Found: C, 56·0; H, 4·7; Br, 21·7. $C_{17}H_{17}O_4Br$ requires C, 55·9; H, 4·7; Br, 21·9%). The two forms were interconvertible by seeding with the appropriate crystalline modification, and had $\lambda_{max.}$ ~250, 256, 292, 300 mμ (log ε 4·03, 4·06, 3·30, 3·32 respectively). Infrared spectra: high-m. p. form, C=O bands at 1756, 1749, ~1729, 1722, and 1708 cm.$^{-1}$: low-m. p. form, C=O bands at 1748 1728, 1705 cm.$^{-1}$. In dioxan both forms had identical spectra (C=O bands at 1766, 1734, and 1719 cm.$^{-1}$). The bromo-ketone was recovered after being heated under reflux for 4 hr. with collidine.

(b) *In acetic acid.* Bromine (128 mg., 8 mol.) was added to the keto-acid (29 mg.) in acetic acid (2 ml.) containing 48% hydrobromic acid (0·03 ml.), and the solution was set aside in the dark for 8 days. The solid obtained by evaporation of the solvent *in vacuo* crystallised from benzene–light petroleum (b. p. 60—80°) in needles (26 mg.), m. p. 205—207° (decomp.), of the *2′ : 2′-dibromo-ketone* (V; R = R′ = Br) (Found: C, 45·5; H, 3·75; Br, 36·2. $C_{17}H_{16}O_4Br_2$ requires C, 46·0; H, 3·6; Br, 36·0%), $\nu_{max.}$ (C=O) 1764 and 1707 cm.$^{-1}$.

Bromination of the monobromo-ketone (48 mg.) in acetic acid at room temperature in the dark during 14 days afforded the dibromo-ketone (44 mg.), m. p. and mixed m. p. 203—205°.

The dibromo-ketone (41 mg.) in collidine (0·5 ml.) was heated under reflux for 1 hr. After removal of collidine hydrobromide (22 mg.) acidification of the filtrate with 3N-hydrochloric acid gave a dark-red oil which slowly solidified. Recovery of a filtered ether solution gave the monobromo-ketone (8 mg.), m. p. and mixed m. p. 199—203°.

Nitrosation of the Keto-acid (V; R = R′ = H).—The keto-acid (120 mg.) in methanol (0·5 ml.) was treated with sodium (30 mg.) in methanol (0·5 ml.), followed by butyl nitrite (0·1 ml.). After 6 days the yellow solution was diluted with water (0·5 ml.). Acidification with 3N-hydrochloric acid afforded needles (130 mg.), m. p. 224—226° (decomp.), which after being washed with benzene followed by recrystallisation from acetic acid gave prisms, m. p. 238—240° (decomp.), of the *2′-hydroxyimino-derivative* (V; RR′ = :N·OH) (116 mg.) (Found: C, 64·7; H, 5·5; N, 4·6. $C_{17}H_{17}O_5N$ requires C, 64·75; H, 5·4; N, 4·4%), $\lambda_{max.}$ 228, 234, 277·5 mμ (log ε

4·01, 3·99, 4·43 respectively), $\lambda_{max.}$ (in 0·1N-NaOH) ~280, 320 mμ (log ε 4·01, 4·34 respectively), $\nu_{max.}$, OH at 3260 cm.$^{-1}$ and double-bond stretching region at 1746, 1730, 1677, 1610, and 1595 cm.$^{-1}$ (in dioxan 1724 and 1625 cm.$^{-1}$).

Beckmann Rearrangement of the 2′-Hydroxyimino-keto-acid (V; RR′ = :N·OH).—(a) *With toluene*-p-*sulphonyl chloride.* The above 2′-hydroxyimino-derivative (265 mg.) of the keto-acid, toluene-*p*-sulphonyl chloride (270 mg.), and 10% aqueous sodium hydroxide (1·0 ml.) were heated at 110—130° for 15 min. with vigorous stirring. Acidification of the cooled mixture gave a solid which was washed with benzene, followed by ether. The product (221 mg.; m. p. 180—182°) crystallised from 20% aqueous methanol in needles, m. p. 188—189° (decomp.), of 3-*carboxy*-6-(2-*carboxy*-6-*methylphenyl*)-5-*cyano*-3-*methylhexanoic acid* (VII; R = H, R′ = CN) [Found: C, 61·4; H, 5·8; N, 4·6%; equiv., 113. $C_{17}H_{19}O_6N$ requires C, 61·25; H, 5·75; N, 4·2%; equiv. (tribasic), 111], $\lambda_{max.}$ 233, 284, ~293 mμ (log ε 3·89, 3·21, 3·08 respectively), $\nu_{max.}$ ~1660 (shoulder), 1696 (broad), 2250 and ~2400 – ~3150 cm.$^{-1}$ (broad) [in dioxan ~1730 –1721 cm.$^{-1}$ (broad)].

The nitrile gave no colour with ferric chloride or with concentrated sulphuric acid; it did not give a precipitate with Brady's reagent and was only very slowly oxidised by alkaline potassium permanganate at room temperature.

The nitrile, heated under reflux for 1 hr. with acetic anhydride, gave a glassy anhydride which regenerated the nitrile in hot water. The anhydride after sublimation at 10^{-3} mm. showed infrared bands at 3100—2500 (broad, carboxylic acid OH), 2240 ($C{\equiv}N$), 1860 and 1775 (5-membered-ring anhydride), and 1700—1630 cm.$^{-1}$ (broad, carboxylic acid $C{=}O$).

(b) *With polyphosphoric acid.* The hydroxyimino-compound (180 mg.) and polyphosphoric acid (6·5 g.) were stirred at 130° for 15 min. After cooling and dilution with water the resulting precipitate was filtered off and extracted with cold sodium hydrogen carbonate solution. Acidification of the extract with hydrochloric acid and filtration gave an *imide-carboxylic acid* (X) (105 mg.), m. p. 242—243° (decomp.), which crystallised from acetic acid in prisms, m. p. 243—245° (decomp.) (Found: C, 64·4; H, 5·7; N ,4·4%; equiv., 328. $C_{17}H_{17}O_5N$ requires C, 64·75; H, 5·4; N, 4·4%; *M*, 315), $\nu_{max.}$ 3360, ~3140, 1739, 1722, 1691, 1593 cm.$^{-1}$.

Hydrolysis of the Nitrile (VII; R = H, R′ = CN).—Hydrolysis of the nitrile (260 mg.) with boiling 50% sulphuric acid (4·0 ml.) in nitrogen for 7·5 hr. gave a clear solution. Only a trace of carbon dioxide was evolved. On cooling, an oil separated which appeared to solidify. Ether-extraction of the mixture and recovery gave a gum, which on trituration with light petroleum gave an amorphous solid, α + β-3 : 5-*dicarboxy*-6-(2-*carboxy*-6-*methylphenyl*)-3-*methylhexanoic acid* (VII; R = H, R′ = CO_2H) (268 mg.), m. p. 175—179° [Found: C, 58·1; H, 5·8%; equiv., 90. $C_{17}H_{20}O_8$ requires C, 57·95; H, 5·7%; equiv. (tetrabasic), 88].

The crude methyl ester, prepared from the above acid (77 mg.) and ethereal diazomethane, was passed through alumina (1 × 1·5 cm.) in ether. Fractional crystallisation of the recovered gum (77 mg.) by dilution of an ethereal solution with light petroleum (b. p. 40—60°) gave *A*, needles (48 mg.), and *B*, a gum. Crystallisation of *A* from ether–light petroleum (b. p. 60—80°) gave long needles of α-*methyl* 3 : 5-*dimethoxycarbonyl*-6-(2-*methoxycarbonyl*-6-*methylphenyl*)-3-*methylhexanoate* (VII; R = Me, R′ = CO_2Me), m. p. 83—84°, $[\alpha]_D^{23}$ –6° ± 3° (*c* 1·65 in EtOH) (Found: C, 61·9; H, 6·8; OMe, 30·1. $C_{21}H_{28}O_8$ requires C, 61·75; H, 6·9; OMe, 30·4%).

Repeated recrystallisation of *B* from ether–light petroleum at 0° gave the β-*ester* (21 mg.), small needles, m. p. 47—48°, $[\alpha]_D^{23}$ +12° ± 3° (*c* 1·25 in EtOH) (Found: C, 61·8; H, 7·1; OMe, 29·6%). A mixture of the α- and β-ester had m. p. 50—70°. They could not be interconverted by seeded crystallisation, and the m. p.s were not depressed by mixture with the synthetic α- and β-racemate respectively.[11] The infrared spectra of the natural esters and the corresponding synthetic racemates were identical in carbon tetrachloride.

Oxidation of the Keto-acid (V; R = R′ = H).—(1) A mixture of the acid (700 mg.), potassium permanganate (3·88 g., 15 atom-equiv. of O), magnesium nitrate hexahydrate (7·0 g.), and water (100 ml.) was heated at 80—85° with stirring until the permanganate was consumed and gas evolution ceased (20 min.). After cooling, the precipitate was filtered off and washed with water and dilute aqueous ammonia. Recovery of the product in ether from the combined acidified filtrates gave a gum (0·53 g.). Extraction of the gum with chloroform (*ca.* 4 ml.) gave a semi-solid residue (*A*) (0·15 g.) and a soluble gum (0·3 g.) (*B*). Material *A* was dissolved in a little ether and diluted with chloroform, giving crystals (63 mg.) which were washed with ether. The product (44 mg.), m. p. 181—187°, crystallised from saturated aqueous potassium acetate solution in glistening flakes (25 mg.). Recrystallisation from water gave potassium benzene-1 : 2 : 3-tricarboxylate, identical (infrared spectrum) with an authentic specimen. The ether and ether–chloroform mother-liquors from *A* were evaporated, giving a gum *C* (73 mg.).

This gum *C* (60 mg.) was spotted on to Whatman's no. 3 MM. paper in 31 spots. The paper was developed for 20 hr. in the phenol–water–formic acid solvent system of Opieńska-Blauth, Saklawska-Szmonowa, and Kański.[17] Very light spraying with bromophenol-blue revealed spots with the R_F values listed below [values for reference acids (100 μg.) in parentheses]: (1) 0·45 (benzene-1 : 2 : 3-tricarboxylic acid and tricarballylic acid, 0·45); (2) 0·54 (β-methyltricarballylic acid 0·55); (3) 0·64; (4) 0·71 (3-methylphthalic acid, 0·71); (5) 0·87. (The crude oxidation product gave an additional weak spot with R_F 0·3, corresponding to oxalic acid.) The spots were cut out and each series was extracted with sodium hydrogen carbonate solution and water. The extracts were concentrated, acidified, and continuously extracted with ether for 22 hr.

Product (1) (9 mg.) was dissolved in ether, filtered from yellow material, and allowed to evaporate, giving crystals, m. p. 182—192° not depressed on admixture with benzene-1 : 2 : 3-tricarboxylic acid. Product (2) (3·5 mg.) was dissolved successively in a little acetone and ether, yellow material being filtered off. Slow evaporation of the ethereal solution gave prisms which were washed with ether and crystallised by dilution of an ethereal solution with carbon tetrachloride, giving (i) prisms, m. p. 157—160° (0·4 mg.), and (ii) prisms, m. p. 151—157° (1·9 mg.). Product (i) recrystallised as prisms, m. p. 158—161°, identified as β-methyltricarballylic acid by mixed m. p. and infrared spectrum.

Product (4) (3 mg.) was combined with a similar fraction (2·8 mg.) from the following experiment. Heating at 100—140°/760 mm. gave a sublimate (1·6 mg.) consisting of long needles, m. p. 110—112°, of 3-methylphthalic anhydride, identical (infrared spectrum) with an authentic specimen.

Products (3) (3 mg.) and (5) (11 mg.) were intractable.

Material *B* was sublimed at 135°/10^{-2} mm. for 2 hr. and the sublimate (104 mg.) in potassium hydroxide was extracted with ether. Recovery of the acidic fraction in ether gave a gum which was heated at 120°/700 mm. for 28 min. and then sublimed at 100—130°/10^{-2} mm., giving a solid (55 mg.). The ether-soluble portion was resublimed at 90°/10^{-2} mm., giving crystals (27 mg.), m. p. 80—100°. Three crystallisations from light petroleum (b. p. 80—100°) gave needles of 3-methylphthalic anhydride m. p. and mixed m. p. 111—114° (Found: C, 66·3; H, 3·8. Calc. for $C_9H_6O_3$: C, 66·7; H, 3·7%).

(2) The acid (143 mg.) was oxidised with magnesium nitrate hexahydrate (770 mg.) and potassium permanganate (420 mg., 8 atom-equiv. of O) in water (5 ml.) for 30 min. at 70° until the reagent was consumed and no more gas was evolved. Of the gummy product (0·12 g.), isolated as described above, 108 mg. was applied to Whatman's no. 3 MM. paper in 54 spots. Development in the same way as before gave spots with the following R_F values: (1) 0·30; (2) 0·46; (3) 0·54; (4) 0·70; (5) 0·87 from which gums were isolated; (2) 3·3 mg.; (3) 1·7 mg.; (4) 2·8 mg.; (5) 43·2 mg.

Crystallisation of fraction (3) from ether–carbon tetrachloride gave prisms (0·8 mg.), m. p. 158—160°, identified as β-methyltricarballylic acid. Fraction (4) was added to a similar fraction from the preceding experiment (see above).

β-*Methyltricarballylic Acid.*—The acid [18] crystallised from ether–light petroleum (b. p. 40—60°) or from ether–carbon tetrachloride in prisms, m. p. 166—167·5° (lit., m. p. 156—158°,[18] 162—164° [19]) (Found: C, 44·2; H, 5·2. Calc. for $C_7H_{10}O_6$: C, 44·2; H, 5·3%), $\nu_{max.}$ in the double-bond stretching region at 1738, 1712, and 1650 cm.$^{-1}$ and carboxylic acid hydroxyl absorption at ~3100 – ~2500 cm.$^{-1}$. The anhydride crystallised from chloroform in prisms, m. p. 138—140° (Found: C, 48·5; H, 4·6. Calc. for $C_7H_8O_5$: C, 48·8; H, 4·7%); $\nu_{max.}$ (C=O) 1850, 1780, and 1706 cm.$^{-1}$.

Chromatography of the acid on Whatman's no. 3 MM. paper and recovery by the method described for the degradation products (above) resulted in a 68% yield of material of m. p. 155—158°, raised to 160—162° by crystallisation from ether–carbon tetrachloride.

A mixture of the acid (190 mg.), potassium permanganate (948 mg., 9 atom-equiv. of O), and magnesium nitrate hexahydrate (1·80 g.) in water (5·0 ml.) was stirred at 80—85° for 1 hr.

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[17] Opieńska-Blauth, Saklawska-Szymonowa, and Kański, *Nature*, 1951, **168**, 511.

[18] Jeger, Rüegg, and Ruzicka, *Helv. Chim. Acta*, 1947, **30**, 1294.

[19] Hope, *J.*, 1912, 892.

After destruction of the excess of oxidant with ethanol, the crude product (70 mg.) was isolated as described for the degradative experiments (above). 500 μg. were spotted on Whatman's no. 1 paper and developed in the usual way, giving four spots, with R_F 0·24 (trace, tails), 0·46 (20—30%) 0·58 (40—60%), and 0·67 (5—10%), and corresponding to oxalic acid (0·24 tails), tricarballylic acid (0·47), and starting material (0·57). The fourth spot was not identified but may represent the spot (R_F 0·64) which arises in the first degradative oxidation described above.

3-*Methylphthalic Acid.*—(i) Oxidation of 4-methylindan-1-one (1·00 g.) with dilute nitric acid [20] gave a gum which was heated at 160°/760 mm. for 15 min. Repeated sublimation at at 75—90°/10^{-2} mm. gave 3-methylphthalic anhydride (198 mg.), m. p. 104—111°. The free acid crystallised from ethyl acetate–light petroleum in needles (78 mg.), m. p. 151—152° (decomp.) (Found: C, 59·8; H, 4·65. Calc. for $C_9H_8O_4$: C, 60·0; H, 4·5%).

(ii) The indanone (588 mg.), potassium permanganate (1·234 g.), and magnesium nitrate hexahydrate (3·1 g.) in water (10·0 ml.) were heated at 75—85° (stirring) until gas evolution ceased and the oxidant was consumed. Filtration and recovery of the neutral fraction in ether gave starting material (353 mg.). Acidification of the aqueous fraction and recovery of the acidic product in ether followed by sublimation as described above gave 3-methylphthalic anhydride (51 mg.), m. p. 113—115° [from light petroleum (b. p. 80—100°)] (Found: C, 66·4; H, 3·9. Calc. for $C_9H_6O_3$: C, 66·7; H, 3·7%).

2 : 2-*Dimethylindane*-1 : 3-*dione.*—2 : 2-Dimethylindan-1-one (533 mg.), potassium permanganate (1·06 g.), and magnesium nitrate hexahydrate (1·95 g.) in water (8·5 ml.) were heated at 60—75° (stirring) for 4 hr. Filtration and recovery of the neutral product (476 mg.) in ether afforded 2 : 2-dimethylindane-1 : 3-dione (200 mg.), plates, m. p. 104—105° [from light petroleum (b. p. 40—60°)] (Found: C, 75·95; H, 5·8. Calc. for $C_{11}H_{10}O_2$: C, 75·8; H, 5·8%).

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