551. *Gibberellic Acid. Part IX.* The Structure of* allo*Gibberic Acid.*

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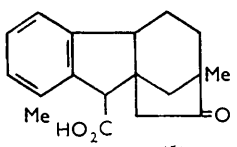
*allo*Gibberic acid, an acid-hydrolysis product of gibberellic acid, is shown to have structure (III).

*allo*Gibberic acid, the unsaturated hydroxy-acid $C_{18}H_{20}O_3$ obtained by mild degradation of gibberellic acid $C_{19}H_{22}O_6$ with mineral acid,[1,2] isomerises under more vigorous conditions to the saturated keto-acid, gibberic acid, for which structure (I) has been proposed.[3,4]



(I)

The present paper details and extends the evidence, described briefly in Part IV,[3] for the formulation of *allo*gibberic acid as (III).

*allo*Gibberic acid $C_{18}H_{20}O_3$ is a tetracyclic monocarboxylic acid containing an alcoholic hydroxyl group, a benzene ring, and an ethylenic bond.[1] The ultraviolet spectrum [1] (see p. 2696) shows that the aromatic ring and the ethylenic bond are not conjugated. Ozonolysis of the acid and its methyl ester yielded 0·4—0·5 mol. of formaldehyde whereas dihydro*allo*gibberic acid [1] (II) gave only a trace and was mainly recovered unchanged. The other products obtained from *allo*gibberic acid and its methyl ester were ketones containing one carbon atom less than the starting material. Thus a terminal methylene group is present in *allo*gibberic acid.

The infrared spectrum of methyl *allo*gibberate in ethylidene chloride showed a strong band near 890 cm.$^{-1}$ (=CH_2). Although methyl dihydro*allo*gibberate also absorbs in this region, the band is much weaker.

Kuhn–Roth estimations on both *allo*- and dihydro*allo*-gibberic acids gave 1·1 *C*-methyl groups; the failure to show the expected difference (cf. ref. 5) was presumably due to isomerisation of *allo*gibberic acid to gibberic acid (which also contains two *C*-methyl groups) under the strongly acid conditions used.

The alcoholic hydroxyl group present in *allo*gibberic acid is considered to be tertiary. *allo*Gibberic acid was acetylated with difficulty. Dihydro*allo*gibberic acid did not give a toluene-*p*-sulphonate or an acetate under normal conditions, although in boiling acetic anhydride a neutral gum was obtained which seemed to be mainly a mixed anhydride acetate. Similarly, attempts to oxidise the hydroxyl group to a carbonyl group in dihydro*allo*gibberic acid with chromic oxide in pyridine [6] and permanganate in acetone failed.

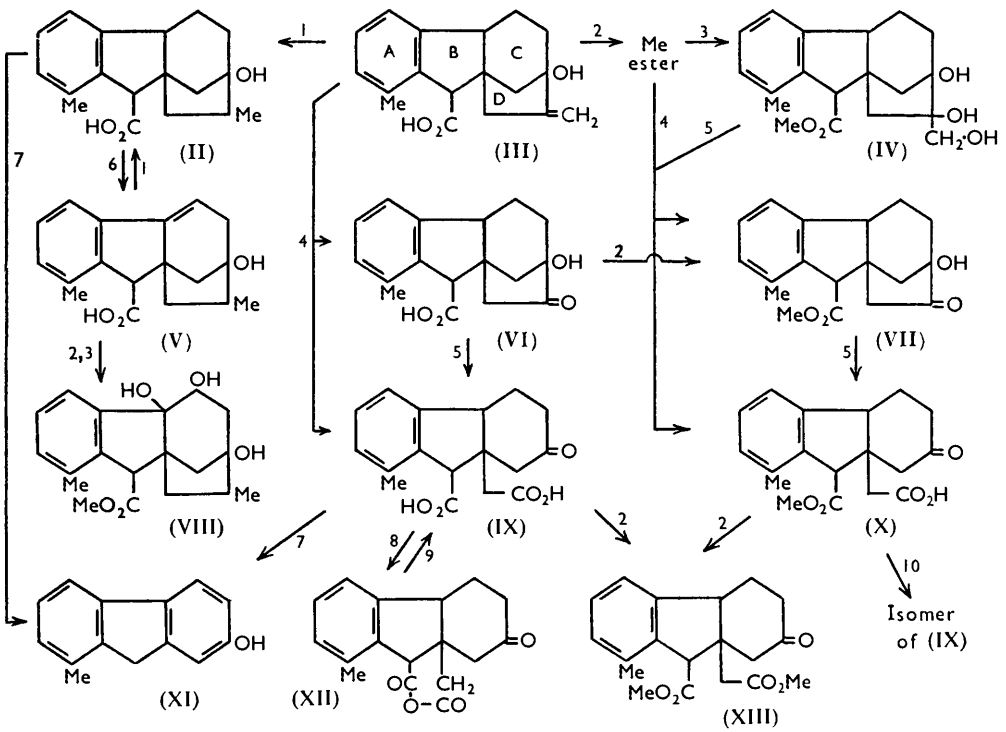
When dihydro*allo*gibberic acid was oxidised with alkaline permanganate the hydroxyl

* Part VIII, *J.*, 1958, 2536.

[1] Cross, *J.*, 1954, 4670.
[2] Brian, Grove, Hemming, Mulholland, and Radley, *Plant Physiol.*, 1958, in the press.
[3] Cross, Grove, MacMillan, and Mulholland, *Chem. and Ind.*, 1956, 954.
[4] *Idem*, *J.*, 1958, 2520.
[5] Adams and Herz, *J. Amer. Chem. Soc.*, 1949, **71**, 2546.
[6] Poos, Arth, Beyler, and Sarrett, *ibid.*, 1953, **75**, 422.

group was not attacked but a dehydro-derivative $C_{18}H_{20}O_3$ (V) was formed, in which an ethylenic bond was introduced in conjugation with the benzene ring. This reaction is analogous to the oxidation [4] of gibberic acid to dehydrogibberic acid. The dehydro-derivative (V) was converted into dihydro*allo*gibberic acid by catalytic hydrogenation and its non-crystalline methyl ester gave a crystalline diol (VIII) with osmium tetroxide.

Further evidence for the structure of *allo*gibberic acid was obtained from oxidation and dehydrogenation, summarised in the scheme. Ozonolysis of *allo*gibberic acid gave a monobasic ketol (VI), also obtained in low yield by oxidation with permanganate. The methyl ester (VII) of the ketol was obtained by ozonolysis of methyl *allo*gibberate. The second product from *allo*gibberic acid was a dibasic keto-acid (IX) whose monomethyl ester (X) was obtained by ozonolysis of methyl *allo*gibberate. Although this ester was not hydrolysed to its acid (IX) with alkali, but gave an isomer (probably owing to a stereochemical change), both the acid and the monomethyl ester (X) gave the same dimethyl ester (XIII). Oxidation of methyl *allo*gibberate with zinc permanganate or *via* the glycol (IV) followed by fission with sodium bismuthate,[7] gave the same products as ozonolysis, though in the former case a trace of a second neutral compound of unknown structure was obtained. Fission of the ketols (VI) and (VII) with sodium bismuthate yielded the corresponding keto-acids (IX) and (X).



Reagents: 1, H_2. 2, CH_2N_2. 3, OsO_4. 4, O_3. 5, $NaBiO_3$. 6, $KMnO_4$–OH^-. 7, Se. 8, Ac_2O or heat. 9, NaOH. 10, KOH.

The keto-acid (IX) formed an anhydride (XII) from which it was recovered by mild alkaline hydrolysis. Dehydration of the acid seemed to be unusually easy, the anhydride also being obtained as a product from oxidation of the ketol (VI) with bismuthate and of *allo*gibberic acid with zinc permanganate.

[7] Rigby, *J.*, 1950, 1907.

Infrared absorption maxima (cm.$^{-1}$) in solution.

Compound	Solvent	CO bands	Compound	Solvent	CO bands
(VI)	Dioxan	1751, 1734	(XIII)	$CHCl_3$	1739, 1712 (no OH)
(VII)	$CHCl_3$	1749, ~1739 (sh)			
	CCl_4	1750	(XII)	Dioxan	1813, 1766, ~1726
	Dioxan	1752, 1736	Succinic anhydride	$CHCl_3$	1871, 1791
(IX)	Dioxan	1735 (broad)	Glutaric anhydride	$CHCl_3$	1815, 1767
(X)	Dioxan	1730, 1715 (sh)			

The ketol (VI) and its ester (VII), which showed reducing properties and were split by sodium bismuthate,[7] must be α-ketols; as expected from the evidence described above they were stable to bismuth oxide in acetic acid [8] and therefore contain a tertiary hydroxyl group.

The infrared spectra in solution (see Table) of the ketols showed a high-frequency band at *ca.* 1750 cm.$^{-1}$. This band was absent from the spectrum of the 2 : 4-dinitrophenylhydrazone of the ketol (VII) and is most reasonably assigned to a carbonyl group present in a saturated five-membered ring, the frequency being raised (cf. gibberone,[4] 1745 cm.$^{-1}$ in CCl_4) by the presence of an adjacent hydroxyl group.[9]

The tertiary hydroxyl group was shown to be situated on a saturated six-membered ring by the oxidation of the ketol (VI), without loss of carbon atoms, to the dibasic keto-acid (IX). The infrared spectrum of the dimethyl ester (XIII) indicated a carbonyl group in a saturated six-membered ring, the bands in the carbonyl-stretching region being at 1712 (*cyclo*hexanone-carbonyl) and 1739 cm.$^{-1}$ (ester-carbonyl).

Dehydrogenation of the dibasic acid (IX) and of dihydro*allo*gibberic acid with selenium established the position of the tertiary hydroxyl group, and hence one point of attachment of the five-membered ring on the hexahydrofluorene skeleton of the ketols and *allo*gibberic acid. While *allo*gibberic acid, like gibberic acid,[10] gave mainly 1 : 7-dimethylfluorene (gibberene), little if any of this compound was obtained from dihydro*allo*gibberic acid. This, and more readily the keto-acid (IX), gave as the main product a fluorenol whose structure was established as 7-hydroxy-1-methylfluorene (XI) by comparison with a specimen prepared by unambiguous synthesis.[11] The fluorenol was also shown to be identical with " phenol C," obtained in low yield by selenium dehydrogenation of gibberic acid.[4] *

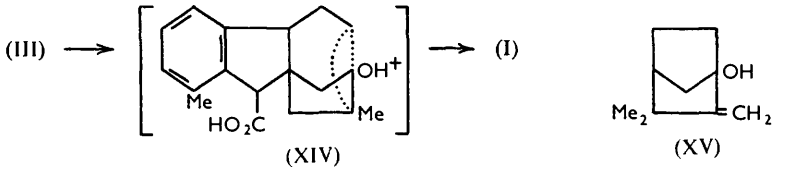
In the dehydrogenation of the acid (IX) to the fluorenol (XI) all the non-skeletal carbon atoms were eliminated except the aromatic *C*-methyl group. Thus the second point of attachment of the five-membered ring in the ketol and in *allo*gibberic acid is angular, as in (VI) and (III) respectively. The alternative angular position does not accommodate either a five-membered ring D or the formation of the dehydro-derivative (V) of dihydro-*allo*gibberic acid. Moreover, the infrared spectrum (Table) of the anhydride (XII) showed it to contain a six-membered anhydride ring. The carboxyl group in *allo*gibberic acid must occupy the same position as in gibberic acid (I) since methyl *allo*gibberate was converted into methyl gibberate by boiling dilute hydrochloric acid. The six-ring anhydride from (IX) can therefore only be formulated as (XII).

These facts establish the structure of *allo*gibberic acid as (III). The isomerisation of *allo*gibberic acid to gibberic acid can be explained by the Wagner–Meerwein mechanism,

* Since the publication of a brief report [3] of the isolation and synthesis of 7-hydroxy-1-methylfluorene, Professor Y. Sumiki of the University of Tokyo has isolated it [12] from gibberellin A_1 methyl ester (methyl α-dihydrogibberellate [13]) by ozonolysis and dehydrogenation, essentially as described above for *allo*gibberic acid.

[8] Rigby, *J.*, 1951, 793.
[9] Jones and Roberts, *Chem. and Ind.*, 1957, 1269.
[10] Mulholland and Ward, *J.*, 1954, 4676.
[11] Morrison and Mulholland, following paper.
[12] Seta, Kitamura, Takahashi, and Sumiki, *Bull. Agr. Chem. Soc. Japan*, 1957, **21**, 73.
[13] Grove, Jeffs, and Mulholland, *J.*, 1958, 1236.

via the intermediate cation (XIV), in the same way that 1-hydroxycamphene (XV) gives camphor.[14]



(XIV) (XV)

Experimental

Some microanalyses are by Messrs. W. Brown and A. G. Olney. Absorption spectra (in ethanol) and alumina for chromatography were obtained as described previously.[10] Unless otherwise stated the infrared spectra were determined on Nujol mulls.

allo*Gibberic Acid.*[2]—The acid (Found: *C*-Me, 5·7; active H, 0·91. Calc. for $C_{18}H_{20}O_3$: 1 *C*-Me, 5·3; 2 active H, 0·70%) had ultraviolet max. at ~259, 264, 273, ~287, ~297 mμ (log ε 2·47, 2·51, 2·35, 1·28, 1·25 respectively).

The *methyl ester*, prepared with diazomethane, crystallised from ether–light petroleum (b. p. 40—60°) in needles, m. p. 98—99° (Found: C, 76·65; H, 7·4; OMe, 10·45. $C_{19}H_{22}O_3$ requires C, 76·5; H, 7·4; OMe, 10·4%), $\nu_{max.}$ 1734 (ester-carbonyl) and 3310 cm.$^{-1}$ (OH).

*allo*Gibberic acid was recovered after treatment with acetic anhydride and pyridine at room temperature for 24 hr. *allo*Gibberic acid (99 mg.) was kept with acetic anhydride (0·6 ml.) in pyridine (1·2 ml.) at 37° for 7 days. The gum obtained by pouring the mixture on ice and dilute hydrochloric acid and recovery in ether crystallised from ether, giving the *acetate* (54 mg.), which recrystallised as prisms, m. p. 200—204° (darkening) (Found: C, 73·7; H, 7·0; Ac, 16·9. $C_{20}H_{22}O_4$ requires C, 73·6; H, 6·8; 1Ac, 13·2%), soluble in cold sodium carbonate solution, $\nu_{max.}$ 1743 (ester), 1691 (CO_2H), 1659, and 3100—3300 (OH) cm.$^{-1}$.

*allo*Gibberic acid was recovered (95%) after being heated with N-sodium hydroxide in nitrogen for 1 hr.

Oxidation.—(i) *allo*Gibberic acid (284 mg.) in sodium hydrogen carbonate (6 ml.) was treated dropwise at 0—5° with 5% aqueous potassium permanganate (12·0 ml.) in 30 min. The clear solution obtained by treatment with sulphur dioxide was acidified with hydrochloric acid and extracted with ether. Evaporation of the extract at room temperature followed by crystallisation of the residue (85 mg.) from ethyl acetate gave colourless needles of the *ketol* (VI) (29 mg.), m. p. 248—250° (decomp.) (Found: C, 71·6; H, 6·5. $C_{17}H_{18}O_4$ requires C, 71·3; H, 6·3%). Purer specimens were obtained by ozonolysis of *allo*gibberic acid (see below).

(ii) *allo*Gibberic acid (284 mg.) in acetone (50 ml.) was treated dropwise at 20° with 6·9% aqueous zinc permanganate (5·0 ml.) in 33 min. After a further 10 min. the precipitate was filtered off, and the weakly pink colour of the filtrate did not fade during a further 30 min. Excess of permanganate was decomposed with ethanol, and the filtered solution was evaporated to dryness *in vacuo* at 25°. The residue was washed with ether–methanol [giving a gum (26 mg.)] and acetone, leaving sparingly soluble crystals (17 mg.) (A). Concentration of the acetone filtrates gave starting material (35 mg.).

Product A crystallised from ethyl methyl ketone in needles and prisms of the *anhydride* (XII), m. p. 279—281° (decomp.) (Found: C, 71·6; H, 5·9. $C_{17}H_{16}O_4$ requires C, 71·8; H, 5·7%). The infrared spectrum was identical with that of a specimen prepared from acid (IX) (see below).

(iii) *Ozonolysis.* (*a*) A current of ozone-enriched oxygen (3 mg. of O_3 per min.) was passed at 100 ml. per min. through a solution of *allo*gibberic acid (284 mg.) in acetic acid (10 ml.) at 22° for 26 min. (estimated ozone absorption 1·1 mol.). The mixture was diluted with water and steam-distilled. Aliquot parts of distillate were treated with an equal volume of saturated aqueous dimedone and kept at room temperature for 48 hr. Crystals of the dimedone derivative of formaldehyde (120 mg., 0·41 mole), m. p. 180—184°, separated from the first 150 ml. of distillate. Recrystallisation from 50% ethanol gave needles, m. p. 186—188°, identical (mixed m. p. and infrared spectrum) with an authentic specimen.

[14] Forster, *J.*, 1901, **79**, 644.

The yellow emulsion which formed on cooling the fraction not volatile in steam was shaken with benzene. The benzene–aqueous mother-liquors were separated from the resulting sticky solid (115 mg.) which crystallised from ethyl methyl ketone–ethyl acetate, giving (i) needles (43 mg.), m. p. 255° (decomp.), (ii) needles (29 mg.), m. p. 235—245° (decomp.), and (iii) yellowish crystals, decomp. 220—230°. Further crystallisation of fractions (i) and (ii) gave needles, m. p. 258—260° (decomp.), $[\alpha]_D^{19}$ −69° ± 3° (*c* 1·11 in EtOH) of the ketol (VI), identical (infrared spectrum) with the product obtained by oxidation with permanganate (above) [Found: C, 71·5; H, 6·6%; *M* (Rast), 298; equiv., 278, 287. $C_{17}H_{18}O_4$ requires C, 71·3; H, 6·3%; *M*, 286], $\lambda_{max.}$ ~249, 260, ~261, ~268, 290, 301 mμ (log ε 2·90, 3·03, 3·02, 2·98, 2·34, 2·33 respectively). Microhydrogenation did not reveal ethylenic unsaturation. The compound gave a mirror with Tollens's reagent but did not restore the colour to Schiff's reagent or give more than a weak pink colour with 1 : 4-dihydroxynaphthalene in acetic–hydrochloric acid. It did not give a black precipitate with bismuth oxide in acetic acid at 100°.

The *methyl ester* (VII), prepared with diazomethane in ether–methanol, crystallised from ether–light petroleum in prisms and needles, m. p. 130—132°, $[\alpha]_D^{19}$ −57° ± 3° (*c* 0·56 in EtOH) (Found: C, 71·8; H, 6·9; OMe, 10·4; active H, 0·38. $C_{18}H_{20}O_4$ requires C, 72·0; H, 6·7; 1OMe, 10·3; 1 active H, 0·33%), $\lambda_{max.}$ ~260, 265, 274, ~290, 300 mμ (log ε 2·52, 2·57, 2·45, 1·86, 1·86 respectively). The compound was neutral, absorbed no hydrogen in the presence of palladium–carbon in acetic acid, and gave a silver mirror with Tollens's reagent. It did not restore the colour to Schiff's reagent or give a black precipitate with bismuth oxide in hot acetic acid.

The orange-yellow 2 : 4-*dinitrophenylhydrazone* of the ester (VII), obtained in low yield by treatment with Brady's reagent, was absorbed on alumina, eluted with benzene containing 1% of methanol, and crystallised from benzene–ether; it had m. p. 250—254° (Found: N, 11·6. $C_{24}H_{24}O_7N_4$ requires N, 11·7%), $\nu_{max.}$ 1719 cm.$^{-1}$ (ester carbonyl).

Evaporation of the benzene–water mother-liquors from the ozonolysis gave a gum (0·19 g.) from which a small amount of an acid, m. p. 210—220° (decomp.), was isolated, identical with the acid (IX) obtained in the following experiment.

(*b*) *allo*Gibberic acid (500 mg.) was ozonised as described above, giving the crude ketol (VI) [154 mg.; m. p. 235—245° (decomp.)]. The gum recovered from the benzene–aqueous mother-liquors was kept with a little ethyl acetate until no more crystals formed; these gave the *keto-acid* (IX) [37 mg.; m. p. 210—215° (decomp.)] which crystallised from ethyl methyl ketone–ethyl acetate in prisms, m. p. 217—219° (gas evolution) followed by partial solidification and remelting at *ca.* 280° (decomp.), $[\alpha]_D^{23}$ −112° ± 3 (*c* 1·27 in EtOH) [Found: C, 67·0; H, 6·0%; equiv., 150. $C_{17}H_{18}O_5$ requires C, 67·5; H, 6·0%; equiv. (dibasic), 151]. The acid was also obtained by further oxidation of the ketol (VI) (see below). It did not restore the colour to Schiff's reagent or react with bismuth oxide, but slowly reduced Tollens's reagent.

The *dimethyl ester* (XIII), prepared with diazomethane, crystallised from methanol in prisms, m. p. 205—207° (Found: C, 68·7; H, 6·8; OMe, 19·7. $C_{19}H_{22}O_5$ requires C, 69·1; H, 6·7; 2OMe, 18·8%), insoluble in cold sodium hydroxide solution.

Preparation of the Anhydride (XII).—(i) The keto-acid (IX) was heated at 220° until gas evolution ceased and the product crystallised from ethyl methyl ketone, giving the anhydride, m. p. 279—281° (decomp.). (ii) The acid (100 mg.) was heated under reflux for 1 hr. with acetic anhydride (1·2 ml.). On cooling, the *anhydride* (61 mg.) crystallised. Further crystallisation gave needles, m. p. 285—287° (decomp.), identical (infrared spectrum) with material obtained as in (i) and by oxidation of the ketol (VI) (see below) (Found: C, 71·6; H, 5·8. $C_{17}H_{16}O_4$ requires C, 71·8; H, 5·7%), $\lambda_{mxa.}$ 267, ~271, 275 mμ (log ε 2·55, 2·48, and 2·43 respectively).

The anhydride (38 mg.) was dissolved in warm 3N-sodium hydroxide (0·78 ml.). Acidification of the cooled solution with hydrochloric acid, filtration of the resultant precipitate, and crystallisation from ethyl methyl ketone–light petroleum (b. p. 40—60°) gave prisms (26 mg.), m. p. 216—218° (decomp.), identified as the keto-acid (IX) (mixed m. p. and infrared spectrum) (Found: C, 67·9; H, 6·2. Calc. for $C_{17}H_{18}O_5$: C, 67·5; H, 6·0%).

Oxidation of Ketol (VI) *with Sodium Bismuthate.*—The ketol (250 mg.) was shaken with " AnalaR " sodium bismuthate (600 mg.) and acetic acid (8·0 ml.) at room temperature for 25 hr. After dilution with water the mixture was extracted with ether (A) and then benzene (B). The gummy crystals (0·17 g.) recovered from (A) were extracted with a little hot methanol. The residue [15 mg.; m. p. 279—281° (decomp.)] was combined with the crystals recovered

from (B) [75 mg.; m. p. 275—280° (decomp.)] and crystallised from ethyl methyl ketone, giving prisms of the anhydride (XII), m. p. 285—287° (decomp.).

Fractional crystallisation of the methanol-soluble fraction (above) from ethyl acetate and ethyl methyl ketone gave mixed fractions and the keto-acid (IX) [75 mg.; m. p. 203—215° (decomp.)] which on further crystallisation from ethyl acetate–light petroleum formed prisms, m. p. 218—220° (decomp.), identified by the infrared spectrum.

Degradation of Methyl allo*Gibberate.*—(1) *Acid hydrolysis.* (*a*) Methyl *allo*gibberate (40 mg.) in methanol (1·35 ml.) was heated under reflux in a slow stream of hydrogen chloride for 2 hr. Most of the excess of hydrogen chloride was removed in a stream of dry air, the mixture was diluted, and the neutral product (34 mg.) recovered in ether. Crystallisation from light petroleum gave hexagonal plates of methyl gibberate, m. p. and mixed m. p. 109—111°. (*b*) Methyl *allo*gibberate (124 mg.) was heated in dilute hydrochloric acid (20 ml.; 1 vol. of concentrated acid plus 5 vols. of water) under reflux for 1 hr. The neutral product (112 mg.; m. p. 102—108°), recovered in ether, crystallised in plates of methyl gibberate, m. p. and mixed m. p. 109—111°.

(2) *Oxidation.* (a) *Ozonolysis.* A current of ozonised oxygen (100 ml./min. = 3·1 mg. of O_3 per min.) was passed into a solution of methyl *allo*gibberate (200 mg.) in acetic acid (10 ml.) for 18 min. at 24°, until absorption of ozone became slow. The solution was diluted with water (10 ml.) and steam-distilled. Treatment of the distillate with saturated dimedone solution (cf. above) gave 92 mg. (0·47 mol.) of the dimedone derivative of formaldehyde.

The residue not volatile in steam was extracted with benzene. The extract was washed with sodium carbonate solution and water, dried (Na_2SO_4), and evaporated, giving a gum (101 mg.). This was chromatographed in benzene on alumina (10 × 1·0 cm.) in ultraviolet light. A light blue fluorescent band was eluted with benzene–methanol (50 : 1). The gum recovered crystallised on the addition of a little ether, giving the methyl ester (VII) (31 mg.), m. p. 123—128°, identified by mixed m. p. and infrared spectrum.

The sodium carbonate extract was acidified with hydrochloric acid and extracted with benzene. Recovery gave a gum which crystallised from ether in prisms (43 mg.), m. p. 232—235° (decomp.), raised to 239—241° (decomp.) by further crystallisation from ethyl methyl ketone–light petroleum (b. p. 60—80°), of the *keto-acid* (X), $[\alpha]_D^{21}$ −66° ± 3° (*c* 1·37 in EtOH) (Found: C, 67·8; H, 6·5; OMe, 9·7; active H, 0·41%; equiv., 304, 321. $C_{18}H_{20}O_5$ requires C, 68·3; H, 6·4; 1OMe, 9·8; 1 active H, 0·32%; *M*, 316), $\lambda_{max.}$ ~261, 266, 274 mμ (log ε 2·44, 2·63, 2·34 respectively). The acid was sparingly soluble in cold ethyl acetate; in later experiments gums were removed by washing the crude crystals with ethyl acetate. It dissolved in sodium hydroxide but only slowly in sodium carbonate solution. It did not restore the colour to Schiff's reagent, give a red colour with naphthalene-1 : 4-diol in acetic–hydrochloric acid, or reduce bismuth oxide in acetic acid. It gave a precipitate with Brady's reagent.

The *oxime*, prepared in pyridine, crystallised from ethanol or methanol in needles, m. p. 244° (decomp.) (Found: N, 4·5. $C_{18}H_{21}O_4N$ requires N, 4·4%).

The dimethyl ester (XIII) crystallised from methanol in prisms, m. p. 205—207° (darken), identical (mixed m. p. and infrared spectrum) with material obtained by methylation of acid (IX) (see above).

The keto-acid (X) (50 mg.) was kept in 20% potassium hydroxide solution (2·0 ml.) at room temperature for 4 days. Acidification with hydrochloric acid followed by ether-extraction and recovery from the extract gave a gum (54 mg.). An ethereal solution of the gum deposited crystals; more crystalline material was obtained by gradual addition of light petroleum (b. p. 40—60°). The crystalline product (37 mg.) recrystallised from ethyl methyl ketone–light petroleum (b. p. 60—80°) in prisms, m. p. 247—249° (decomp.), of a *dibasic acid*, $[\alpha]_D^{19}$ −67° ± 3° (*c* 0·54 in EtOH) [Found: C, 67·6; H, 6·1%; equiv., 168. $C_{17}H_{18}O_5$ requires C, 67·5; H, 6·0%; equiv. (dibasic), 151]. The acid was different (infrared spectrum) from the isomer (IX) obtained by oxidation of *allo*gibberic acid and by hydrolysis of the anhydride (XII).

(b) *With osmium tetroxide.* A mixture of methyl *allo*gibberate (92 mg.), pyridine (75 mg.), and osmium tetroxide (105 mg.) in benzene (12 ml.) was kept in the dark at room temperature for 13 days, then evaporated to dryness *in vacuo*. The residue was shaken in methylene chloride (25 ml.) with a 10% solution of mannitol in 1% potassium hydroxide (20 ml.) for 15 min. The organic layer was washed with the mannitol solution and with water, dried (Na_2SO_4), and evaporated, giving a solid (70 mg.), m. p. 186—192°, which crystallised from benzene–light petroleum (b. p. 60—80°) in long needles of the *glycol* (IV) (59 mg.), m. p. 190—194°, raised to

192—194·5° by recrystallisation (Found: C, 68·3; H, 7·3; active H, 0·88. $C_{19}H_{24}O_5$ requires C, 68·65; H, 7·3; 1 active H, 0·90%), $\nu_{max.}$ 3380 and 3500 (OH), 1717 cm.$^{-1}$ (ester).

(c) *Fission of the glycol* (IV). (i) The glycol (100 mg.) in benzene (20 ml.) at 40° was treated with lead tetra-acetate (230 mg.) in benzene (10 ml.). After being heated under reflux for 5 min. and kept for 1 hr. at room temperature (no excess of reagent present) the mixture was filtered. The filtrate was extracted with sodium carbonate solution, washed with water, dried, and evaporated, giving a gum (74 mg.). The alkaline extract was acidified and extracted with benzene and with ether. The water-washed and dried extracts were evaporated, giving a semi-crystalline residue (14 mg.) which crystallised from aqueous ethanol in prisms, m. p. 239—241° (decomp.), of the keto-acid (X). The yield of crystalline material was not increased when more reagent was used.

(ii) A mixture of the glycol (700 mg.) and " AnalaR " sodium bismuthate (1·250 g.) in acetic acid (7·0 ml.) was shaken at room temperature until the solution was almost clear and colourless (5·5 hr.). The mixture was diluted with water and extracted with benzene. The benzene was washed with water, extracted with sodium carbonate solution, washed, dried, concentrated to 5 ml., and chromatographed on alumina (20 × 1·3 cm.). Elution with benzene–methanol in ultraviolet light gave fractions (*x*) (50 : 1) a blue fluorescent band, giving a gum (329 mg.) on recovery, and (*y*) (20 : 1) a diffuse blue band, giving a gum (112 mg.) on recovery. A benzene solution of material from fraction (*x*) was gradually diluted with light petroleum (b. p. 40—60°) at 0°, giving a solid (232 mg.), m. p. 117—123°. Recrystallisation gave needles of the ketol ester (VII), m. p. 129—131°, identified by mixed m. p. and infrared spectrum. The sodium carbonate extract was acidified and the product recovered in benzene as a mixture of gum and crystals (61 mg.) which crystallised from ethyl methyl ketone–light petroleum (b. p. 60—80°) in prisms of the keto-acid (X), m. p. 239—241° (decomp.), identified by analysis, mixed m. p., and infrared spectrum.

(d) *With zinc permanganate.* 6·7% Aqueous zinc permanganate (22·0 ml.) was added in one lot to methyl *allo*gibberate (1·14 g.) in acetone (200 ml.) at 21°. When the reagent was consumed (90 min.) the mixture was filtered. The combined filtrate and acetone washings of the precipitate were concentrated *in vacuo* below 30°. The residue was extracted with benzene and ether. The combined extracts were extracted 3 times with sodium hydrogen carbonate solution, then repeatedly with 2% aqueous sodium hydroxide until the aqueous layer was nearly colourless. The neutral fraction was recovered and treated with ether, giving sticky crystals (0·10 g.) (A) and a gummy residue (0·41 g.) (B). Material (B) was chromatographed in ether on alumina (20 × 2·2 cm.) and eluted in 75 ml. fractions, from which gums were recovered, as follows: 1—5 (ether), 97 mg.; 6—8 [ether–methanol (100 : 1)], 106 mg.; 9—12 [ether–methanol (50 : 1)], 57 mg. On treatment with ether, fractions 9—12 gave crystals (7 mg.) which crystallised from ether–light petroleum in needles, m. p. 126—130°, identified (mixed m. p. and infrared spectrum) as the ketol-ester (VII). Material (A) was crystallised several times from ether–methanol and from ether methyl ketone–light petroleum (b. p. 60—80°), giving a *substance* of unknown structure as needles, m. p. 195—197° (16 mg.) (Found: C, 72·0; H, 7·0; OMe, 10·1; active H, 0·33. $C_{18}H_{20}O_4$ requires C, 72·0; H, 6·7; 1OMe, 10·3; 1 active H, 0·33%), $\nu_{max.}$ 1720 (C=O), 3400 cm.$^{-1}$ (alcoholic OH).

The sodium hydrogen carbonate extract was acidified with hydrochloric acid and extracted with ether and benzene. Recovery gave a gum (186 mg.) which crystallised from ether as prisms, identified (infrared spectrum) as the keto-acid (X) (139 mg.; m. p. 225—230°) which had m. p. 233—236° (decomp.) (104 mg.) on crystallisation from ether–ethyl methyl ketone.

Oxidation of the Ketol-ester (VII).—(1) *With zinc permanganate.* The compound (150 mg.) in acetone (20 ml.) was treated with 6·7% zinc permanganate solution (1·1 ml.) and kept at room temperature until the reagent was consumed (3·5 hr.). The mixture was filtered and the filtrate and acetone washings were evaporated *in vacuo*. An ethereal solution of the residual gum was extracted with sodium carbonate solution. Recovery of the neutral fraction gave starting material (41 mg.), m. p. 130—132°, identified by the infrared spectrum. The neutral compound, m. p. 195—197° (obtained by the oxidation of methyl *allo*gibberate with zinc permanganate), was not obtained. Recovery from the sodium carbonate extract gave the keto-acid (X) (12 mg.) which crystallised from acetone–ether in prisms, m. p. 235—239° (decomp.).

(2) *With sodium bismuthate.* The compound (25 mg.) was shaken with " AnalaR " sodium bismuthate (50 mg.) in acetic acid (0·6 ml.) at room temperature for 3 hr. The mixture was diluted with water and extracted with benzene. The benzene extract was extracted with

sodium carbonate solution. Recovery of the neutral fraction gave a gum (4 g.). Recovery of the acid fraction gave the keto-acid (9 mg.), which crystallised from acetone–ether in prisms (8 mg.), m. p. 235—238° (decomp.), identified by infrared spectrum and mixed m. p.

*Dihydro*allo*gibberic Acid.*—The following preparation gave a product of higher m. p. than that previously described.[1] *allo*Gibberic acid (3·00 g.) in methanol (120 ml.) was hydrogenated at room temperature and pressure in the presence of Adams catalyst (200 mg.). Uptake of hydrogen ceased after the absorption of 1·05 mol. in 30 min., and crystals of the product separated. The mixture was filtered. Evaporation of the combined filtrate and acetone washings gave a solid which was dried by distillation with toluene and crystallised from toluene–methanol as prisms (2·61 g.) of dihydro*allo*gibberic acid, m. p. 200—203°. Further crystallisation raised the m. p. to 204—207°. This product had $[\alpha]_D^{21}$ −67° ± 3° (*c* 0·96 in EtOH) (Found: C, 75·4; H, 7·8; *C*-Me, 5·6; active H, 0·79. Calc. for $C_{18}H_{22}O_3$: C, 75·5; H, 7·7; 2 *C*-Me, 10·5; 2 active H, 0·70%). Concentration of the mother-liquors gave a further crop (0·38 g., m. p. 199—202°). Dihydro*allo*gibberic acid crystallised from water in needles of the *hydrate*, m. p. 204—207° (shrinking at *ca.* 130—144°) (Found, after drying at 20°: C, 71·2; H, 8·0. $C_{18}H_{22}O_3,H_2O$ requires C, 71·0; H, 7·95%). Like *allo*gibberic acid,[2] anhydrous dihydro-*allo*gibberic acid showed a double peak in the carbonyl stretching region at 1715 and 1687 cm.$^{-1}$, whereas the hydrate showed a sharp band at 1700 cm.$^{-1}$. Ultraviolet max. were at ~260, 264, 273 mμ (log ε 2·18, 2·24, 2·08 respectively). The methyl ester did not crystallise.

Dihydro*allo*gibberic acid was recovered (86%) after 1 hour's heating with N-hydrochloric acid.

*Acylation of Dihydro*allo*gibberic Acid.*—(*a*) The compound was stable to acetic anhydride in pyridine during 40 hr. at room temperature.

(*b*) The compound (104 mg.) was kept at 35° wth acetic anhydride (0·60 ml.) in pyridine (1·20 ml.) for 7 days Treatment with ice and hydrochloric acid and recovery of the *acetate* in ether gave a glass (101 mg.) (Found: C, 73·05; H, 7·6; Ac, 17·4. $C_{20}H_{24}O_4$ requires C, 73·1 H, 7·4; 1Ac, 13·1%). The glass dissolved readily in cold sodium carbonate solution. The infrared spectrum showed hydroxyl bands (3100—3400 cm.$^{-1}$), strong bands at 1738 and 1706 cm.$^{-1}$, and very weak absorption at *ca.* 1800—1810 cm.$^{-1}$.

(*c*) The compound (150 mg.) was heated under reflux with acetic anhydride (10 ml.) for 6 hr. The product obtained by evaporation was passed through a column of alumina in ether and recovered as a glass (136 mg.) (Found: Ac, 21·4. Calc. for $C_{22}H_{26}O_5$: 2Ac, 23·2%). The glass did not dissolve readily in cold sodium carbonate solution. An infrared spectrum showed C=O absorption at 1813 and 1737 cm.$^{-1}$ and no hydroxyl absorption. Treatment of the glass with boiling water or cold 1% sodium hydroxide solution gave an acidic glass whose infrared spectrum approximated to the above acetate but a very weak band at *ca.* 1810 cm.$^{-1}$ persisted.

(*d*) Treatment of the compound with toluene-*p*-sulphonyl chloride in pyridine for 68 hr. at room temperature gave starting material.

*Oxidation of Dihydro*allo*gibberic Acid.*—(*a*) The compound (100 mg.) in pyridine (1·0 ml.) was added to chromium trioxide (100 mg.) in pyridine (1·0 ml.). The mixture was kept at room temperature for 18 hr. Only starting material (74 mg.) was recovered.

A solution of the compound (28·6 mg.) in acetone (1 ml.) was treated with potassium permanganate (11 mg.) in water (0·50 ml.). After 18 hr. at room temperature, recovery gave starting material (11 mg.).

(*b*) The compound (572 mg.), dissolved in sodium hydrogen carbonate solution (12 ml.), was treated dropwise at 0—3° with 5% aqueous potassium permanganate (12·5 ml.) during 19 min. After 5 min. sulphur dioxide was passed into the mixture, and the solution was acidified with hydrochloric acid. The precipitate (254 mg.) was filtered off. Crystallisation from dilute methanol gave prisms (198 mg.) of the *dehydro-derivative* (V), which softened at *ca.* 115—125° (loss of solvent), giving a gum which partly resolidified and remelted at 170—172° (Found, after drying at room temperature over P_2O_5: C, 72·1; H, 7·5%; equiv., 321. $C_{18}H_{20}O_3,CH_3{\cdot}OH$ requires C, 72·1; H, 7·65%; *M*, 316). Infrared bands included broad carboxylic OH absorption, alcohol OH (3360 cm.$^{-1}$), and a C=O band (1703 cm.$^{-1}$). Ultraviolet max. were at ~250, 259, 268, 290, 300 mμ (log ε 3·98, 4·13, 4·07, 3·50, 3·46 respectively).

Crystallisation from water gave needles of a *hydrate*, softening at *ca.* 110°, becoming gummy at 118—120°, and liquid at *ca.* 150° (Found, after drying over P_2O_5 at room temperature: C, 72·9; H, 7·3. $C_{18}H_{20}O_3,\frac{2}{3}H_2O$ requires C, 73·0; H, 7·3%). The acid was soluble in cold

sodium carbonate solution and was unsaturated to permanganate in acetone. With concentrated sulphuric acid it gave a yellow colour changing to reddish purple and finally to pink.

The methyl ester, prepared with diazomethane in ether, was a gum. This (146 mg.) was kept with osmium tetroxide (142 mg.) and pyridine (154 mg.) in benzene (8 ml.) in the dark at room temperature for 13 days. After evaporation *in vacuo* a solution of the residue in methylene chloride (30 ml.) was shaken with a 10% solution of mannitol in 1% potassium hydroxide (25 ml.). The organic layer was washed with water, dried, and evaporated, giving a gum which crystallised on trituration with ether as prisms (78 mg.) of the *glycol* (VIII), m. p. 162—165°. Further crystallisation from benzene–light petroleum (b. p. 60—80°) gave needles, m. p. 169—171° (Found: C, 68·65; H, 7·3. $C_{19}H_{24}O_5$ requires C, 68·65; H, 7·3%), $\nu_{max.}$ 1708 (C=O), 3320, 3400, and 3520 cm.$^{-1}$ (alcoholic OH).

Reduction of the Dehydro-derivative (V).—The compound (29 mg.) in methanol (6 ml.) was hydrogenated in the presence of Adams platinum catalyst (33 mg.) at room temperature and pressure. 1 mol. of hydrogen was absorbed and the product (29 mg.; m. p. 192—194°) crystallised from toluene in prisms, m. p. 200—202°, of dihydro*allo*gibberic acid (mixed m. p. and infrared spectrum).

Dehydrogenation.—(1) allo*Gibberic acid.* A mixture of *allo*gibberic acid (100 mg.) and selenium (100 mg.) was heated in a stream of nitrogen for 2 hr. at 360°. The product (38 mg.) collected by distillation at 15—20 mm. was chromatographed in light petroleum (b. p. 40—60°; 4 ml.) on alumina (10 × 1·0 cm.) and eluted in ultraviolet light. It afforded 1 : 7-dimethylfluorene (26 mg.), m. p. 102—105°, as sole identified product.

(2) *The keto-acid* (IX). The acid (50 mg.) and selenium (50 mg.) were heated in a stream of nitrogen at 350—360° for 200 min., then distilled at 20 mm. The distillate (18 mg.) in ether–light petroleum (b. p. 40—60°; 1 : 3) was chromatographed on alumina (10 × 0·8 cm.) in ultraviolet light, giving four fractions. Only a fraction (6 mg.) eluted with ether was tractable. It crystallised from light petroleum (b. p. 60—80°) in needles (3·5 mg.), m. p. 166—168°, of *7-hydroxy-1-methylfluorene*, identical (mixed m. p. infrared and ultraviolet spectra) with an authentic specimen of the same m. p. prepared by synthesis [11] and with " phenol C " obtained by dehydrogenation of gibberic acid [4] (Found: C, 85·0, 85·7; H, 6·2, 6·8. $C_{14}H_{12}O$ requires C, 85·7; H, 6·2%). More was obtained by dehydrogenation of the gums recovered from the crystallisation mother-liquors of the keto-acid (IX) and the ketols (VI) and (VII).

The *benzoate* crystallised from dilute acetic acid or light petroleum (b. p. 80—100°) in plates, m. p. 160—161° (Found: C, 84·0; H, 5·4. $C_{21}H_{16}O_2$ requires C, 84·0; H, 5·4%), and the *acetate* from methanol in plates, m. p. 130—131° (Found: C, 80·0; H, 5·9. $C_{16}H_{14}O_2$ requires C, 80·6; H, 5·9%), respectively identical (mixed m. p. and infrared spectra) with authentic specimens of m. p. 159—160·5° and 131—132°.

(3) *Dihydro*allo*gibberic acid.* The compound (430 mg.) was heated with selenium for 2 hr. at 360° in a stream of nitrogen, and then distilled as described above. The distillate (180 mg.) was chromatographed in ether on alumina (24 × 1·5 cm.). Two fractions gave defined products. Fraction (ii), eluted with light petroleum containing 5—10% of ether, crystallised from methanol but the m. p. was not raised above 75—90°. Fraction (iv) (27 mg.), obtained with 20 : 3 light petroleum–ether, crystallised from dilute ethanol in small needles, m. p. 159—161°, not depressed on admixture with 7-hydroxy-1-methylfluorene. Fractions (v)—(vii) (122 mg.), eluted with light petroleum containing 20—50% of ether and with ether–methanol (20 : 1), were rechromatographed giving more (51 mg.) of the fluorenol; sublimation at 100—120°/10^{-2} mm. and several crystallisations from light petroleum gave needles, m. p. and mixed m. p. 165—168°.

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