552. *Gibberellic Acid. Part X.*[1] 7-*Hydroxy*-1-*methylfluorene.*

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7-Hydroxy-1-methylfluorenone and 7-hydroxy-1-methylfluorene have been synthesised. The latter is identical with the fluorenol obtained by degradation of *allo*gibberic acid.

The fluorenol obtained [1] by dehydrogenation of dihydro- and other degradation products of *allo*gibberic acid has been shown to be 7-hydroxy-1-methylfluorene by comparison with a specimen prepared as follows.

The starting material, 5-methoxy-2-nitrotoluene, is most easily prepared by nitrating *m*-methoxytoluene.[2] The scale of the reaction could be increased safely without much fall in yield although the product was contaminated with a small amount of the 4-nitro-isomer and with 3-hydroxy-2 : 4 : 6-trinitrotoluene. The 5-methoxy-2-nitrotoluene fraction was oxidised [3] with aqueous potassium permanganate to 5-methoxy-2-nitrobenzoic acid which was separated from the 4-nitro-isomer by crystallisation. 5-Methoxy-2-nitrotoluene was less readily oxidised than the 4-nitro-isomer, and when the oxidation of the mixed isomers was carried out in the presence of magnesium sulphate [4] the only acidic product was 3-methoxy-4-nitrobenzoic acid.

5-Methoxy-2-nitrobenzoic acid was more conveniently reduced to the amine by catalytic hydrogenation than by the chemical methods described in the literature. Subsequent reaction of the amine with acetic anhydride gave 6-methoxy-2-methyl-4-oxo-3 : 1-benzoxazine. This with *o*-tolylmagnesium bromide gave 2-acetamido-5-methoxy-2'-methylbenzophenone.[5] Hydrolysis of the acetyl derivative gave the amine, from which 7-methoxy-1-methylfluorenone was obtained by diazotisation and ring closure. Demethylation of the fluorenone gave 7-hydroxy-1-methylfluorenone, and reductive demethylation gave 7-hydroxy-1-methylfluorene. The latter, its acetate, and benzoate were found, by mixed melting point and infrared absorption, to be identical with the fluorenol and corresponding derivatives obtained by degradation of dihydro*allo*gibberic acid.[1] The synthetic fluorenol was also identical with " phenol C " obtained by dehydrogenation of gibberic acid.[6]

Experimental

M. p.s are corrected. The ultraviolet absorption spectrum and alumina for chromatography were obtained as described previously.[7] Microanalyses are by Messrs. W. Brown and A. G. Olney.

5-*Methoxy*-2-*nitrotoluene*.—Nitration [2] of *m*-methoxytoluene was carried out in batches on a maximum scale of 110 g. in 10-l. conical flasks. An ethereal solution of the combined crude product (from 780 g. of starting material) was shaken with aqueous sodium hydrogen carbonate. A yellow sodium salt separated (see below). The ethereal solution was washed with water, dried, and evaporated. Distillation of the residue gave 5-methoxy-2-nitrotoluene (640 g., 58%), b. p. 116—120°/4 mm., m. p. 45—47°. This material, containing some of the 4-nitro-isomer, was used for oxidation without further purification.

Addition of hydrochloric acid to an aqueous solution of the yellow sodium salt (*ca.* 40 g.) gave a precipitate of 3-hydroxy-2 : 4 : 6-trinitrotoluene, which was purified by crystallisation from benzene–light petroleum and from water (charcoal), giving pale yellow needles (31 g.), m. p. 106·5—109° (Found: C, 34·8; H, 2·0; N, 17·4. Calc. for $C_7H_5O_7N_3$: C, 34·6; H, 2·1; N, 17·3%). The recorded m. p. is 109—110°.

[1] Part IX, Mulholland, preceding paper.
[2] Cook, Dickson, Ellis, and Loudon, *J.*, 1949, 1074.
[3] Schiemann, *Ber.*, 1929, **62**, 1794.
[4] Dewar, *J.*, 1944, 619.
[5] Cf. Lothrop and Goodwin, *J. Amer. Chem. Soc.*, 1943, **65**, 363.
[6] Cross, Grove, MacMillan, and Mulholland, *J.*, 1958, 2520.
[7] Mulholland and Ward, *J.*, 1954, 4676.

5-Methoxy-2-nitrobenzoic Acid.—Oxidation of 5-methoxy-2-nitrotoluene with aqueous potassium permanganate as described by Schiemann [3] gave a 15—20% yield of crude acidic product, m. p. 122—129°. Recovered starting material was recycled until 298 g. of crude acidic product were obtained. The benzene-soluble portion was fractionally crystallised from benzene and benzene containing a little methanol (seeding), giving 5-methoxy-2-nitrobenzoic acid as large prisms and needles (220 g.; m. p. 135—136°; 21 g. of fractions of m. p. 131—136°) and fractions of small needles of 3-methoxy-4-nitrobenzoic acid, m. p. 220—230° (15 g.). The 2-nitro-isomer crystallised from benzene in pale yellow prisms, m. p. 135—136°, which became colourless and opaque on drying at 100—110° (Found: C, 48·8; H, 3·6. Calc. for $C_8H_7O_5N$: C, 48·7; H, 3·6%). Schiemann [3] records m. p. 133°, in agreement with other authors except Hodgson and Beard [8] who give m. p. 255°.

The *methyl ester* formed very pale yellow needles [from light petroleum (b. p. 40—60°)], m. p. 55—57° (Found: C, 51·1; H, 4·3; N, 6·4. $C_9H_9O_5N$ requires C, 51·2; H, 4·3; N, 6·6%).

3-Methoxy-4-nitrobenzoic acid crystallised from ethanol in colourless needles, m. p. 231—233° (Found: C, 48·7; H, 3·6%).

Attempts to improve the yield of acidic products by the use of a higher ratio permanganate : substrate and by gradual addition of the reagent failed. Oxidation in the presence of magnesium sulphate at 75—80° [4] was incomplete and gave 3-methoxy-4-nitrobenzoic acid as the only acidic product. At 100° all the reagent was consumed but the yield of acidic product did not exceed 21%. Oxidation with potassium permanganate in pyridine [7] gave a slightly better yield (26%) but was more tedious on a large scale.

2-Amino-5-methoxybenzoic Acid.—2-Methoxy-5-nitrobenzoic acid (7·6 g.) in ethanol (400 ml.) was hydrogenated at room temperature and pressure in the presence of 5% palladium–charcoal [9] (845 mg.). 3 Mol. of hydrogen were absorbed in 45 min. Evaporation of the filtered solution *in vacuo* at low temperature gave 2-amino-5-methoxybenzoic acid as a pale yellow solid, m. p. 145—147° (6·5 g.). A specimen purified by sublimation *in vacuo* followed by crystallisation from benzene–light petroleum (b. p. 40—60°) and from dilute methanol formed almost colourless needles, m. p. 148—150·5° (Found: C, 57·5; H, 5·3; N, 8·6. Calc. for $C_8H_9O_3N$: C, 57·5; H, 5·4; N, 8·4%). The m. p. has been recorded as 149—150° [10, 11] and 179—180°.[12]

2-Methyl-6-methoxy-4-oxo-3 : 1-benzoxazine.—The above crude amine (99 g.) was added in portions to acetic anhydride (540 ml.) at 130—140°. The mixture was concentrated to *ca.* 90 ml. and cooled, giving the benzoxazine (95 g.; m. p. 116—120°). Recrystallisation from acetic anhydride gave colourless needles, m. p. 119—120° (Found: C, 62·8; H, 4·9; N, 7·3. Calc. for $C_{10}H_9O_3N$: C, 62·8; H, 4·75; N, 7·3%) (lit.,[13] m. p. 124°). Hydrolysis of the benzoxazine with water at 100° gave 2-acetamido-5-methoxybenzoic acid which crystallised from water in needles, m. p. 165—166° (Found: C, 57·5; H, 5·25; N, 6·7. Calc. for $C_{10}H_{11}O_4N$: C, 57·4; H, 5·3; N, 6·7%) (lit.,[12] m. p. 161—162°).

The above acetate and diazomethane gave the *methyl ester*, which crystallised from light petroleum (b. p. 80—100°) in needles and prisms, m. p. 96—97° (Found: C, 59·5; H, 5·9; N, 6·4. $C_{11}H_{13}O_4N$ requires C, 59·2; H, 5·9; N, 6·3%).

2-Acetamido-5-methoxy-2'-methylbenzophenone.—A Grignard reagent prepared from *o*-bromotoluene (10·6 g.) and magnesium (1·6 g.) in ether (40 ml.) was filtered and added dropwise in 60 min. to a well-stirred, ice-cold solution of the benzoxazine (11·7 g.) in benzene (250 ml.). A solid separated. The mixture was heated at 30° for 1 hr., cooled, and decomposed with ice (300 g.) and 3N-sulphuric acid (180 ml.). The organic layer and ether-washing of the aqueous layer were combined, washed with water, sodium hydrogen carbonate and with water, and evaporated. The residue was steam-distilled A solution of the non-volatile fraction in ether was washed with water, dried, and evaporated, giving a solid (14·5 g.), m. p. 85—95°. In the best preparations this was pale yellow but sometimes was orange. The product in ether (700 ml.) was chromatographed on alumina (26 × 4·0 cm.). Elution with ether in ultraviolet light removed a blue fluorescent band and then a band appearing brown. Recovery of the

[8] Hodgson and Beard, *J.*, 1926, 147.
[9] Vogel, " Practical Organic Chemistry," Longmans Green & Co., London, 1948, p. 990.
[10] Pschorr, *Annalen*, 1912, **391**, 23.
[11] Smith, Elisberg, and Sherrill, *J. Amer. Chem. Soc.*, 1946, **68**, 1301.
[12] Friedlaender, *Ber.*, 1916, **49**, 955.
[13] Heilbron, Kitchen, Parkes, and Sutton, *J.*, 1925, **127**, 2167.

latter gave a pale yellow solid (10 g.) which crystallised from light petroleum (b. p. 80—100°) and from methanol as colourless prisms (7·5 g.), m. p. 121—122°, of *2-acetamido-5-methoxy-2'-methylbenzophenone*. Further crystallisation raised the m. p. to 123—124° (Found: C, 71·7; H, 6·1; N, 4·9. $C_{17}H_{17}O_3N$ requires C, 72·1; H, 6·05; N, 4·9%).

In later preparations the combined crude acetate (155 g.) was crystallised twice from methanol, giving 64 g., of m. p. 118·5—121°. 23 g. were recovered from the mother-liquors.

2-Amino-5-methoxy-2'-methylbenzophenone.—The above amide (1·00 g.) was heated under reflux with ethanol (10 ml.) and concentrated hydrochloric acid (3 ml.) for 3·5 hr. The solution was made alkaline with dilute ammonia solution and kept at 0°, giving crystals (885 mg.) of the *amine*, m. p. 52—54·5°. Recrystallisation from dilute methanol gave prisms, m. p. 62—63° (Found: C, 74·4; H, 6·3; N, 5·9; OMe, 12·9. $C_{15}H_{15}O_2N$ requires C, 74·7; H, 6·3; N, 5·8; OMe, 12·9%). It regenerated the acetyl derivative, m. p. and mixed m. p. 120°.

7-Methoxy-1-methylfluorenone.—A solution of the above crude amine (2·0 g.) in 25% hydrochloric acid (250 ml.) was diazotised at 0—5° with sodium nitrite (0·70 g.) in water (5 ml.). The solution was allowed to warm to room temperature, then heated at 100° for 2 hr. and under reflux for 2·5 hr. An ethereal extract of the cooled mixture was washed with dilute sodium hydroxide and with water, treated with charcoal, dried, and evaporated. A solution of the residue (1·15 g.) in ether–light petroleum (b. p. 40—60°, 6 : 1) was chromatographed on alumina (1·5 × 12 cm.). Elution with the same solvent in ultraviolet light removed a brown band from which a solid was recovered (642 mg.; m. p. 80·5—83°). Crystallisation from methanol gave the *fluorenone* as orange-yellow needles (538 mg.), m. p. 83—84° raised to 84—84·5° by recrystallisation (Found: C, 80·45; H, 5·5; OMe, 14·1. $C_{15}H_{12}O_2$ requires C, 80·3; H, 5·4; OMe, 13·8%). The *oxime*, prepared in pyridine, crystallised from light petroleum (b. p. 80—100°) in pale greenish-yellow needles, m. p. 185—186° (Found: C, 74·9; H, 5·3; N, 5·8. $C_{15}H_{13}O_2N$ requires C, 75·3; H, 5·5; N, 5·85%). The 2 : 4-*dinitrophenylhydrazone* crystallised from nitrobenzene–acetic acid in red needles, m. p. 275·5—276·5° (Found: C, 62·7; H, 4·2; N, 14·3. $C_{21}H_{16}O_5N_4$ requires C, 62·4; H, 4·0; N, 13·9%).

7-Hydroxy-1-methylfluorene.—7-Methoxy-1-methylfluorenone (908 mg.) was heated with acetic acid (7·5 ml.), red phosphorus (100 mg.), and hydriodic acid (6 ml.; *d* 1·66) for 96 hr. A filtered ethereal extract of the crude mixture was washed with water, sodium carbonate solution, dilute sodium dithionite solution, and water, dried, and evaporated, giving a solid (868 mg.). This was chromatographed in 1 : 1 ether–light petroleum (b. p. 40—60°) on alumina (1·6 × 22 cm.). Elution with the same solvent removed a light blue fluorescent band, from which an almost colourless solid (509 mg.; m. p. 150—165°) was recovered. Sublimation *in vacuo* followed by crystallisation from benzene–light petroleum (b. p. 80—100°) gave needles of 7-hydroxy-1-methylfluorene (402 mg.), m. p. 161—165°, raised to 166—168° by recrystallisation (Found: C, 85·45, 86·1; H, 6·5, 6·0. Calc. for $C_{14}H_{12}O$: C, 85·7; H, 6·2%), $\lambda_{max.}$ (in EtOH) 274, ~283, 304, ~313 mμ (log ε 4·26, 4·17, 3·70, 3·66 respectively). The acetate crystallised from methanol in plates, m. p. 131—132° (Found: C, 80·5; H, 5·8. $C_{16}H_{14}O_2$ requires C, 80·6; H, 5·9%). The benzoate (cf. ref. 14) crystallised from dilute acetic acid or light petroleum (b. p. 80—100°) in plates, m. p. 159—160·5° (Found: C, 83·8; H, 5·5. Calc. for $C_{21}H_{16}O_2$: C, 84·0; H, 5·4%).

The *methyl ether* crystallised from ethanol in colourless plates, m. p. 111—112·5° (Found: C, 85·7; H, 6·9; OMe, 14·6. $C_{15}H_{14}O$ requires C, 85·7; H, 6·7; 1OMe, 14·8%). The 1 : 3 : 5-*trinitrobenzene adduct* of the methyl ether crystallised from ethanol in red needles, m. p. 97—98° (Found: C, 59·2; H, 4·3; N, 10·3. $C_{15}H_{14}O,C_6H_3O_6N_3$ requires C, 59·6; H, 4·05; N, 9·9%). The *adduct* of the methyl ether with 3-hydroxy-2 : 4 : 6-trinitrotoluene crystallised from ethanol in bronze needles, m. p. 128·5—130° (Found: C, 58·1; H, 4·4; N, 9·7. $C_{15}H_{14}O,C_7H_5O_7N_3$ requires C, 58·3; H, 4·2; N, 9·3%).

7-Hydroxy-1-methylfluorenone.—7-Methoxy-1-methylfluorenone (1·00 g.) was heated with 48% hydrobromic acid (40 ml.) and acetic acid (10 ml.) for 3·5 hr., then cooled. The red precipitate was washed with water, dried, and chromatographed in ether on alumina (20 × 3·0 cm.). Elution with ether removed a yellow band from which starting material was recovered, and further elution with ether–methanol (99 : 1) removed a red band. Recovery of the latter gave a solid (720 mg.) which crystallised from ethanol in red needles (640 mg.) of the *hydroxyfluorenone*, m. p. 178·5—180°, raised to 183—184° by recrystallisation (Found: C, 79·7; H, 4·65. $C_{14}H_{10}O_2$ requires C, 80·0; H, 4·8%). The *acetate* crystallised from methanol in

[14] Kliegl, Wunsch, and Weigele, *Ber.*, 1926, **59**, 631.

yellow needles, m. p. 138—140° (Found: C, 76·4; H, 4·9. $C_{16}H_{12}O_3$ requires C, 76·2; H, 4·8%). The *oxime* of the hydroxyfluorenone crystallised from toluene in yellow-green needles, m. p. 228·5—230° (Found: C, 74·8; H, 5·15; N, 6·7. $C_{14}H_{11}O_2N$ requires C, 74·65; H, 4·9; N, 6·2%).

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