

857. Wessely-Moser Rearrangement with Xanthones.

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1 : 4-Dihydroxy-7-methoxyxanthone (I; R = Me) when treated with hydriodic acid under pressure rearranged to form 1 : 2 : 7-trihydroxyxanthone (IV).

RAO AND SESHADRI¹ found that 1 : 4-dihydroxy-7-methoxyxanthone (I; R = Me) when heated with hydriodic acid did not undergo the Wessely-Moser type of rearrangement² (5 : 8- to 5 : 6-dihydroxyflavone), but gave the normal product, 1 : 4 : 7-trihydroxyxanthone (I; R = H). It has now been found³ that compound (I; R = Me) when demethylated by hydriodic acid under sufficiently drastic conditions yields by rearrangement the corresponding 1 : 2 : 7-trihydroxyxanthone (IV), with, presumably, intermediate formation of the diaryl ketone (II). This is in agreement with the mechanism proposed for this type of rearrangement in flavones.⁴

The structure of the compound (IV) was confirmed by its synthesis from 2 : 3 : 6-trimethoxybenzoyl chloride (VI) and quinol dimethyl ether. Analysis showed the product to be a monohydroxytetramethoxydiphenyl ketone (III; R + R' + R'' = H + 2Me) with a hydroxyl group *ortho* to the carbonyl group (positive ethanolic ferric reaction). The compound was simultaneously demethylated and cyclised by hydriodic acid or by

¹ Rao and Seshadri, *Proc. Indian Acad. Sci.*, 1947, **26**, A, 288.

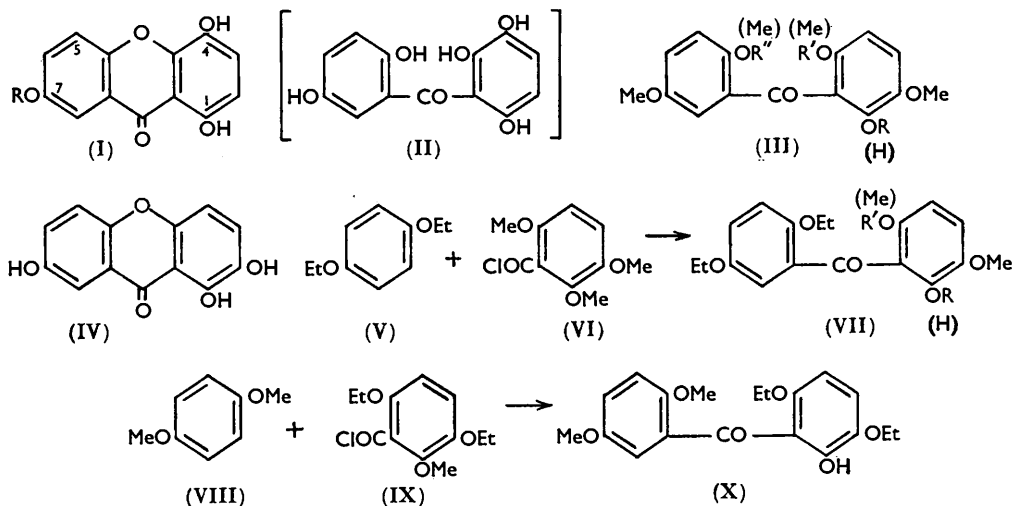
² Wessely and Moser, *Monatsh.*, 1930, **56**, 97.

³ Cf. Philbin, Swirski, and Wheeler, *Chem. and Ind.*, 1955, 445.

⁴ Shah, Mehta, and Wheeler, *J.*, 1938, 1555.

aluminium chloride in benzene to form a trihydroxyxanthone which was not the 1 : 4 : 7-trihydroxy-compound (I; R = H) and could only be the isomer (IV). Efforts to synthesise the latter from 2-formyl-1-hydroxy-7-methoxyxanthone by application of the Dakin reaction were unsuccessful.

The position of the hydroxyl group in the ketone (III), for which there are three possibilities (R or R' or R'' = H), was determined by the following considerations: (a) Condensation of 2 : 3 : 6-trimethoxybenzoyl chloride (VI) with quinol diethyl ether (V) gave a compound



with a positive ethanolic ferric reaction which analysis proved to be a 2 : 5-diethoxyphenyl hydroxydimethoxyphenyl ketone (VII; R + R' = H + Me). This result showed that dealkylation had occurred in the acid chloride nucleus. Again: (b) 3 : 6-Diethoxy-2-methoxybenzoyl chloride (IX) when condensed with quinol dimethyl ether (VIII) gave an isomer of the ketone (VII) which also exhibited an ethanolic ferric reaction, and which could only have structure (X). Compound (III) is, accordingly, 2-hydroxy-3 : 6-dimethoxyphenyl 2 : 5-dimethoxyphenyl ketone (III; R = H; R' = R'' = Me). It is clear that demethylation precedes cyclisation when this compound is converted into the trihydroxyxanthone (IV) by treatment with hydriodic acid or by aluminium chloride.

EXPERIMENTAL

Ethanol was employed for crystallisation if no solvent is mentioned.

Formation of 1 : 2 : 7-Trihydroxyxanthone (IV) from 1 : 4-Dihydroxy-7-methoxyxanthone (I; R = Me).—1 : 4-Dihydroxy-7-methoxyxanthone¹ (0.4 g.) was heated with hydriodic acid (10 ml.; *d* 1.7) in a sealed tube at 175—185° for 1 hr., and the product was poured into aqueous sodium hydrogen sulphite. The precipitated 1 : 2 : 7-trihydroxyxanthone [see (a) below], on repeated crystallisation, formed yellow-brown aggregates (0.1 g.), m. p. 270° (decomp.) (Found: C, 64.3; H, 3.5. C₁₃H₈O₅ requires C, 63.9; H, 3.3%). It exhibited a yellowish-green fluorescence in concentrated sulphuric acid and gave a dark greenish-brown colour with ethanolic ferric chloride. The *triacetate*, prepared by the acetic anhydride-sodium acetate method, formed needles, m. p. 215—217° (Found: C, 61.2; H, 3.8. C₁₈H₁₄O₈ requires C, 61.6; H, 3.8%). The mixed m. p. with 1 : 4 : 7-triacetoxyxanthone (m. p. 189—190°) was 160—170°.

The Ullmann condensation between quinol monomethyl ether and 2-chloro-6-methoxybenzoic acid (Ullmann and Panchaud⁵) which is involved in the preparation of 1 : 4-dihydroxy-7-methoxyxanthone proceeded more smoothly when a trace of iodine was added to the copper-bronze catalyst. If moisture was present cyclisation by sulphuric acid of the intermediate diphenyl ether gave 7-hydroxy-1-methoxyxanthone in place of the dimethoxyxanthone. This

⁵ Ullmann and Panchaud, *Annalen*, 1906, **350**, 108.

result confirms the observation by Graebe and Aders⁶ that treatment of 1:7-dimethoxyxanthone with 90% sulphuric acid produced demethylation in the 7-position. Hydriodic acid at 60° has now been found to behave similarly.

2-Formyl-1-hydroxy-7-methoxyxanthone.—1-Hydroxy-7-methoxyxanthone¹ (1 g.), hexamine (3 g.), and glacial acetic acid (10 ml.) were heated together on a boiling-water bath for 6 hr. Hot hydrochloric acid (15%; 10 ml.) was added and heating was continued for $\frac{1}{2}$ hr. The mixture was diluted with an equal volume of water. The precipitated *aldehyde* separated from benzene and from ethyl acetate in yellow needles (0.4 g.), m. p. 203—204° (Found: C, 66.7; H, 3.8. C₁₅H₁₀O₅ requires C, 66.7; H, 3.7%). It was insoluble in alkali and gave a reddish-brown colour with ethanolic ferric chloride. The *phenylhydrazone* formed orange plates, m. p. 198—200° (Found: C, 69.3; H, 4.4; N, 7.7. C₂₁H₁₆O₄N₂ requires C, 70.0; H, 4.5; N, 7.8%). Attempts to replace the formyl group by hydroxyl (Dakin reaction) by use of alkaline hydrogen peroxide at 0°, room temperature, or 100°, or of ethereal hydrogen peroxide, were unsuccessful.

1:2:7-Trihydroxyxanthone (IV).—(a) 2:3:6-Trimethoxybenzoic acid separated from water in plates, m. p. 148—150° (Found: C, 56.1; H, 5.7. Calc. for C₁₀H₁₂O₅: C, 56.6; H, 5.7%). Gilman and Thirtle⁷ give m. p. 145—146°. It was conveniently prepared from 2:3:6-trimethoxyacetophenone⁸ by alkaline hypochlorite oxidation using a method previously employed by Cartwright, Jones, and Marmion⁹ for the preparation of 2:6-dimethoxybenzoic acid. The trimethoxy-acid chloride (b. p. 139°/1.5 mm.) was prepared from the acid and thionyl chloride.

(b) **2-Hydroxy-3:6-dimethoxyphenyl 2:5-dimethoxyphenyl ketone (III; R = H, R' = R'' = Me).** 2:3:6-Trimethoxybenzoyl chloride (9 ml.) was added with stirring to a mixture of aluminium chloride (15 g.), quinol dimethyl ether (5.2 g.), and ether (120 ml.) during $\frac{1}{2}$ hr. After 2 days the mixture was treated with crushed ice and concentrated hydrochloric acid (25 ml.), and the product heated on a steam-bath. Benzene was added and the mixture refluxed for $\frac{1}{2}$ hr. The benzene layer was extracted with 10% aqueous sodium hydroxide. Carbon dioxide precipitated from the alkaline liquid **2-hydroxy-3:6-dimethoxyphenyl 2:5-dimethoxyphenyl ketone** (2.1 g.) which crystallised in yellow needles, m. p. 115—116° (Found: C, 63.7; H, 5.6; OMe, 38.6. C₁₇H₁₈O₆ requires C, 64.1; H, 5.7; OMe, 39.0%). The ethanolic ferric reaction was green.

(c) **Demethylation of (III; R = H, R' = R'' = Me).** (i) A mixture of the diphenyl ketone (III; R = H, R' = R'' = Me) (1.5 g.), aluminium chloride (8 g.), and benzene (50 ml.) was refluxed on a steam-bath for 2 hr. The solvent was evaporated and the residue was treated with crushed ice and concentrated hydrochloric acid (25 ml.) and heated on a water-bath for 10 min. The resulting mixture yielded, to ether, 1:2:7-trihydroxyxanthone (IV) which crystallised from ethanol and then from ethyl acetate in yellow-brown aggregates (0.3 g.), m. p. 270° (decomp.) (triacetate, m. p. 215—217°, not depressed by addition of the triacetate of the trihydroxyxanthone obtained by demethylation and rearrangement of 1:4-dihydroxy-7-methoxyxanthone as described above.

(ii) A mixture of the benzophenone (1 g.) in glacial acetic acid (5 ml.) and hydriodic acid (10 ml.) was refluxed for 90 min. and poured into aqueous sodium hydrogen sulphite. The product was identical with that obtained as in (i).

Proof of the Structure of the Diphenyl Ketone (III; R = H, R' = R'' = Me).—(a) **2:5-Diethoxyphenyl 2-hydroxy-3:6-dimethoxyphenyl ketone (VII; R = H, R' = Me).** A mixture of 2:3:6-trimethoxybenzoyl chloride (VI) (1.5 g.), quinol diethyl ether (V) (2 g.), aluminium chloride (7 g.), and ether (100 ml.) was treated as described in the preparation of (III; R = H, R' = R'' = Me). The resulting *diphenyl ketone* formed pale yellow plates (0.15 g.), m. p. 100—101° (Found: C, 66.4; H, 6.6; OMe, 35.5. C₁₉H₂₂O₆ requires C, 65.9; H, 6.4; 2OMe + 2OEt as 4OMe, 35.8%). It gave a green colour with ethanolic ferric chloride.

(b) **3:6-Diethoxy-2-hydroxyphenyl 2:5-dimethoxyphenyl ketone (X).** A mixture of 2-methoxy-3:6-dihydroxyacetophenone⁸ (10 g.), ethyl sulphate (30 ml.), potassium carbonate (50 g.), and acetone (200 ml.) was refluxed for 6 hr. The product was filtered and the solvent evaporated from the filtrate. The residue was dissolved in ether and the solution was washed with 5% aqueous sodium hydroxide. **3:6-Diethoxy-2-methoxyacetophenone** which remained on removal of ether separated from dilute ethanol in needles (5.6 g.), m. p. 45° (Found: C, 65.9; H, 7.7; OMe, 39.7. C₁₃H₁₈O₄ requires C, 65.5; H, 7.6; 2OEt + OMe as 3OMe, 39.1%).

⁶ Graebe and Aders, *ibid.*, 1901, 318, 367.

⁷ Gilman and Thirtle, *J. Amer. Chem. Soc.*, 1944, 66, 858.

⁸ Baker, *J.*, 1939, 956.

⁹ Cartwright, Jones, and Marmion, *J.*, 1952, 3499.

Oxidation of the acetophenone as described above for 2 : 3 : 6-trimethoxybenzoic acid gave 3 : 6-diethoxy-2-methoxybenzoic acid, plates, m. p. 160—161° (Found : C, 60.1; H, 6.7; OMe, 38.6. $C_{12}H_{16}O_5$ requires C, 60.0; H, 6.7; OMe + 2OEt as 3OMe, 38.7%). The acid chloride (IX) which was a solid at room temperature had b. p. 158°/2 mm. A mixture of aluminium chloride (7 g.), quinol dimethyl ether (VIII) (2 g.), and 3 : 6-diethoxy-2-methoxybenzoyl chloride (IX) (4 g.) in ether (70 ml.) was treated as described in the preparation of (III). 3 : 6-Diethoxy-2-hydroxyphenyl 2 : 5-dimethoxyphenyl ketone separated in yellow plates (0.2 g.), m. p. 102—103° (Found : C, 66.2; H, 6.3; OMe, 35.4. $C_{19}H_{22}O_6$ requires C, 65.9; H, 6.4; 2OMe + 2OEt as 4OMe, 35.8%). It gave a green colour with ethanolic ferric chloride.

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