A SYNTHESIS OF α-ANHYDROTRIMETHYLBRAZILONE

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WE wish to record a synthesis of α-anhydrotrimethylbrazilone (I) that was carried to the penultimate stage in 1947. Condensation of 1,3-dimethoxybenzene and veratroyl chloride in boiling benzene with aluminium chloride afforded an excellent yield of 2-hydroxy-4,3',4'-trimethoxybenzophenone (II), instead of the tetramethoxy-compound reported [1] to result from this reaction below 40°. This preparation of the phenol (II) appears to be superior to those previously described.[2,3]

Condensation of the phenol (II) with bromoacetone and treatment of the product with alkali gave 2-acetyl-3-(3',4'-dimethoxyphenyl)-6-methoxycoumarone (III), which may be regarded as a dihydro-α-anhydrotrimethylbrazilone. Bromination of this ketone with N-bromosuccinimide proceeded slowly, giving a non-crystalline bromo-compound that afforded α-anhydrotrimethylbrazilone (I) in poor yield on treatment with aluminium chloride in benzene. The low yield of (I) may be attributed at least in part to the production of nuclear as

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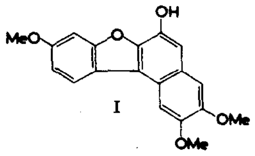
[1] P. C. Mitter and P. K. Paul, J. Indian Chem. Soc. **8**, 271 (1931).

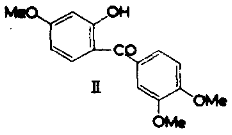
[2] J. N. Ray, S. S. Silooja and P. R. Wadha, J. Indian Chem. Soc. **10**, 617 (1933).

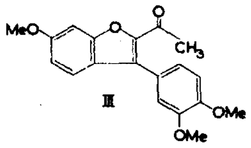
[3] P. C. Johnson and A. Robertson, J. Chem. Soc. 2331 (1950).

well as side-chain brominated derivatives of (III) during the treatment with N-bromosuccinimide, and nuclear bromination appeared to be the main reaction with bromine, since the bromo-compound in that case gave no α-anhydrotrimethylbrazilone on treatment with aluminium chloride.

Friedel-Crafts condensations of α-halogenoketones with aromatic compounds,[4,5] and a synthesis of α-anhydrotrimethylbrazilone,[3] have both previously been reported.


I


II


III

EXPERIMENTAL

2-Hydroxy-4,3',4'-trimethoxybenzophenone. A solution of veratroyl chloride (10.5 g) in dry benzene (30 ml) was added to a boiling mixture of 1,3-dimethoxybenzene (7.0 g), anhydrous aluminium chloride (10 g) and dry benzene (25 ml), and the resulting mixture was heated under reflux for 1½ hr. The benzene was removed and the hard brown aluminium complex was decomposed with ice and hydrochloric acid. The solid product was collected, washed with dilute sodium carbonate and water, and recrystallised from ethanol, when 13 g (87%) of 2-hydroxy-4,3',4'-trimethoxybenzophenone was obtained as very pale yellow needles m.p. 141° (lit. m.p. 141°[2] 140°[3]). The 2:4-dinitrophenylhydrazone was obtained as dark red needles, m.p. 230°

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[4] A. Collet, *Bull. Soc. Chim.* **17**, 506 (1897).

[5] J. P. Mason and L. I. Terry, *J. Amer. Chem. Soc.* **62**, 1622 (1940).

(lit.[3] m.p. 231°). (Found: C, 56.1; H, 4.4; N, 11.7. Calc. for $C_{22}H_{20}O_8N_4$: C, 56.4; H, 4.3; N, 11.9%).

2-Acetyl-3-(3',4'-dimethoxyphenyl)-6-methoxycoumarone. 2-Hydroxy-4,3',4'-trimethoxybenzophenone (5 g), anhydrous potassium carbonate (10 g) and redistilled bromoacetone (12 g) were heated together under reflux in dry ethyl methyl ketone (50 ml) for 2½ hr. The solvent was removed and the residue shaken with warm 10% aqueous sodium hydroxide for 1 hr, to cause internal condensation of the initial phenoxyacetone derivative. During this time the oily product rapidly solidified. The solid was collected, washed well with water and recrystallised from ethanol, when 5 g (88%) of 2-acetyl-3-(3',4'-dimethoxyphenyl)-6-methoxycoumarone was obtained as large canary yellow plates, m.p. 153.5° (Found: C, 69.8; H, 5.6. $C_{19}H_{18}O_5$ requires: C, 69.9; H, 5.5%). This substance was insoluble in aqueous alkalis and gave no colour with ferric chloride.

The 2:4-dinitrophenylhydrazone was obtained as dark red plates, m.p. 192° on recrystallisation from benzene. (Found: C, 59.0; H, 4.1; N, 11.1. $C_{25}H_{22}O_8N_4$ requires: C, 59.3; H, 4.3; N, 11.1%).

This condensation could not be effected with chloroacetone under the same conditions unless sodium iodide was added to the reaction mixture to generate iodoacetone in situ, in which case the product stubbornly retained a brown colour, although the m.p. was easily raised to 153.5°.

α-Anhydrotrimethylbrazilone. 2-Acetyl-3-(3',4'-dimethoxyphenyl)-6-methoxycoumarone (0.150 g), N-bromosuccinimide (0.075 g) and benzoyl peroxide (0.012 g) were boiled under reflux in dry carbon tetrachloride (15 ml) for 24 hr, exposed to ultraviolet light for the first 2 hr. The reaction mixture was cooled and washed four times with equal quantities of water, dried over sodium sulphate and evaporated. The resulting dark yellow resin (which contained reactive bromine, since it reacted with sodium iodide in acetone, with precipitation of sodium bromide) was dissolved in dry benzene (15 ml) and powdered aluminium chloride (0.10 g) was added to the solution. The mixture was heated under reflux on the steam bath for 5 min and allowed to stand at room temperature for 5 hr. The aluminium complex was decomposed with dilute hydrochloric acid, the benzene layer and solid matter were removed, washed with water and then extracted twice with 5 ml portions of 10% aqueous sodium hydroxide. Acidification of the alkaline extract afforded a brown solid (0.025 g) which on crystallisation from ethanol afforded α-anhydrotrimethylbrazilone as yellow-brown plates, m.p. 197° alone or mixed with an authentic specimen prepared from trimethylbrazilone.