FORMYLATION OF POLYHYDROXY FLAVONES AND CHROMONES

BY V. V. S. MURTI, T. R. SESHADRI, F.A.SC., V. SUNDARESAN AND B. VENKATARAMANI

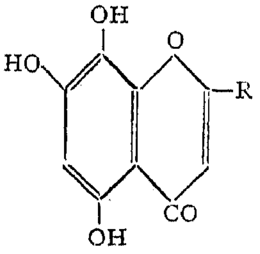
(Department of Chemistry, Delhi University, Delhi)

Received February 5, 1959

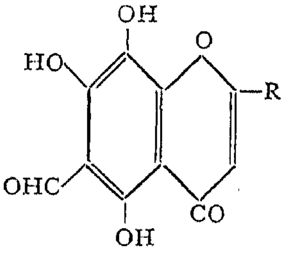
ABSTRACT

In the case of nor-wogonin and 5:7:8-trihydroxy-2-methylchromone, Gattermann method is efficient in yielding the corresponding aldehydes, whereas with their 8-methyl ethers hexamine method works satisfactorily.

IN connection with the synthesis of furano compounds, the preparation of hydroxy aldehydes of flavones and chromones was important. The hexamine method (Duff's method) has been used successfully in a number of cases. With more complex types especially with a larger number of free hydroxyls present in the molecule, it does not work well. For instance, the trihydroxy compounds, nor-wogonin (I *a*) and 5:7: 8-trihydroxy-2-methyl chromone (I *b*) yield only coloured products containing nitrogen and no aldehyde could be obtained. Hence other methods have been investigated; as an alternative the simpler Gattermann reaction using zinc cyanide works very successfully to yield the 6-aldehydes (II *a*, II *b*).



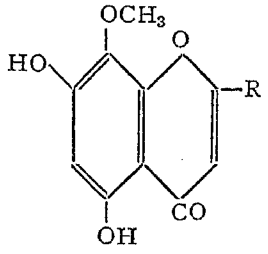
I



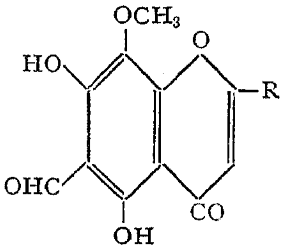
II

(*a*) R=C_6H_5
(*b*) R=CH_3

As examples of 5:7-dihydroxy compounds with the 8-position substituted by a methoxyl group, wogonin (III *a*) and 8-methoxy-5: 7-dihydroxy-2-methyl chromone (III *b*) have now been examined and the hexamine method is found to give satisfactory yields of 6-aldehydes (IV *a*, IV *b*).



III



IV

(*a*) R=C_6H_5
(*b*) R=CH_3

5 : 7 : 8-Trihydroxy-2-methyl chromone-6-aldehyde (II *b*) has also been prepared in good yield in an independent way starting with visnagin which was degraded to 5 : 7-dihydroxy-2-methyl chromone 6-aldehyde according to the method of Schönberg *et al.*,[1] and subjected to oxidation with alkaline persulphate.

EXPERIMENTAL

Nor-wogonin-6-aldehyde (*II a*).—A suspension of nor-wogonin (I *a*) (1·5 g.) in anhydrous ether (200 c.c.) was treated with zinc cyanide (6 g.) and aluminium chloride (5 g.) and the mixture saturated with hydrogen chloride while cooling in ice. In half an hour, a heavy dark liquid separated and the supernatant ether assumed a red colour. The gas was passed for 6 hr. more and the mixture left in the ice-bath overnight. After decanting off the ether layer, the residue was washed with ether and heated with water (100 c.c.) in a boiling water-bath for 20 min. The yellow product that separated was a mixture of nor-wogonin and its 6-aldehyde; the two could be separated by fractional crystallisation from alcohol-acetone mixture in which the aldehyde was less soluble and hence was left behind. From the mother liquor unchanged nor-wogonin (0·5 g.) was isolated. The aldehyde crystallised from alcohol-acetone mixture as golden yellow prismatic needles (0·6 g.), m.p. 270–72° (d.). Mixed m.p. with nor-wogonin (m.p. 254°) was 230° (d.) (Found: C, 64·0; H, 3·1; $C_{16}H_{10}O_6$ requires C, 64·4; H, 3·4%). It gave a green colour with ferric chloride becoming dark with excess of the reagent. The dinitrophenyl hydrazone crystallised as lemon yellow tiny prisms, m.p. 345° (d.).

5: 7: 8-*Trihydroxy-2-methyl-chromone-6-aldehyde* (*II b*).—(i) 5: 7-Dihydroxy-2-methyl chromone-6-aldehyde[1] (1·2 g.) was mixed with potassium hydroxide solution (1·2 g. in 50 c.c. of water) and the resulting mixture treated dropwise with aqueous solution of potassium persulphate (2·4 g. in 100 c.c. of water) during 6 hr. and set aside overnight. It was acidified with hydrochloric acid and the unchanged chromone aldehyde (0·5 g.) extracted with ether. The aqueous solution was heated with more of acid and sodium sulphite at 100°. The product was extracted with chloroform; after evaporating the solvent, the residue was extracted with ether and the ether-soluble portion finally crystallised from methanol-benzene mixture yielding yellow rectangular plates and prisms (0·2 g.) turning brown at 245° and decomposing at 258–60° (Found: C, 56·2; H, 3·6; $C_{11}H_8O_6$ requires C, 55·9; H, 3·4%). The dinitrophenyl hydrazone was obtained as orange yellow small prisms which darkened at 330° and did not melt up to 360°.

(ii) 5:7:8-Trimethoxy-2-methyl chromone[2] was subjected to demethylation using aluminium chloride and benzene.[3] 5:7:8-Trihydroxy-2-methyl chromone crystallised from dilute methanol as yellow rhombic prisms, m.p. 236–38° (Found: C, 57·9; H, 3·8; $C_{10}H_8O_5$ requires C, 57·7; H, 3·9%). With alcoholic ferric chloride it gave a deep green colour changing to brown with excess of the reagent. With aqueous sodium hydroxide it gave a yellow solution which turned purple on shaking with air and then faded. Remethylation with excess of dimethyl sulphate and anhydrous potassium carbonate in acetone solution yielded the original trimethyl ether. The trihydroxy-2-methyl chromone (1·2 g.) was subjected to Gattermann's reaction using zinc cyanide (5 g.) and aluminium chloride (5 g.). The product was worked up as usual and it crystallised from methanol-benzene mixture as rectangular plates and prisms (0·1 g.), m.p. 260–61° (d.) alone or when mixed with the sample obtained by method (i). The mother liquor yielded unchanged original chromone (0·4 g.).

Wogonin-6-aldehyde (*IV a*).—The required 5:8-dimethoxy-7-hydroxy flavone was prepared by the method of Sastri and Seshadri[4] except that pyridine-potash procedure was employed for the conversion of the acetophenone into the diketone. Subsequent partial demethylation was carried out according to Shah *et al.*[5]; it was necessary to use more nitrobenzene in order to get improved yields of wogonin (III *a*).

The aldehyde was obtained by heating a mixture of wogonin (0·35 g.), hexamine (2 g.) and glacial acetic acid (20 c.c.) at 100° for 6 hr. A mixture of concentrated hydrochloric acid and water (1:1, 20 c.c.) was then added and the heating continued for 15 min. more, during which period an yellow crystalline solid separated. The mixture was diluted with water and kept in the refrigerator. The aldehyde that separated was crystallised from benzene or acetic acid yielding pale yellow prismatic needles (0·2 g.), m.p. 257–58° (Found: C, 65·2; H, 4·2; $C_{17}H_{12}O_6$ requires C, 65·4; H, 3·9%). It gave a pink brown colour with alcoholic ferric chloride. The dinitrophenyl hydrazone formed aggregates of orange red tiny prisms, m.p. 290–92° (d.).

8-Methoxy-5:7-dihydroxy-2-methyl chromone (III b).—The intermediate 2-hydroxy-3:6-dimethoxy-4-benzyloxy-ω-acetyl acetophenone was earlier prepared by Geissman[6] but was not characterised. The C-acylation of the corresponding acetophenone has now been carried out in the usual manner using sodium and ethyl acetate; the diketone crystallised from benzene-petroleum ether as stout prisms, m.p. 102–03° (Found: C, 66·2; H, 6·2; $C_{19}H_{20}O_6$ requires C, 66·3; H, 5·8%). It gave a violet-brown colour with ferric chloride which changed to deep violet on standing. The debenzylation of 5:8-dimethoxy-7-benzyloxy-2-methyl chromone was carried out by Geissman by catalytic hydrogenation. In the present work it has been done using a mixture of acetic acid and hydrochloric acid.

5:8-Dimethoxy-7-hydroxy-2-methyl chromone (0·5 g.) was dissolved in dry dioxane (75 c.c.) and allowed to cool. Aluminium chloride (1 g. dissolved in 100 c.c. of dioxane) was added and mixture allowed to stand at room temperature for 48 hr. The complex was decomposed by means of concentrated hydrochloric acid and the mixture extracted with chloroform, and the solvent distilled under diminished pressure. The residue was purified by dissolving in ether which left behind some impurity and finally it crystallised from benzene as colourless aggregates of prisms (0·2 g.), m.p. 190–92° (Found: C, 59·3; H, 4·7; $C_{11}H_{10}O_5$ requires C, 59·5; H, 4·5%). The chromone dissolved in aqueous sodium carbonate and sodium hydroxide giving yellow solutions. With alcoholic ferric chloride, it gave a violet colour which turned green with more of the reagent.

8-Methoxy-5:7-dihydroxy-2-methyl chromone-6-aldehyde (IV b).—A mixture of the foregoing chromone (0·7 g.), hexamine (3 g.) and glacial acetic acid (30 c.c.) was heated in a boiling water-bath for 6 hr. The mixture was worked up as in an earlier case and the aldehyde separated from alcohol as yellow rectangular tablets (0·5 g.), m.p. 188–89° (Found: C, 57·2; H, 3·9; $C_{12}H_{10}O_6$ requires C, 57·6; H, 4·0%). It gave a pink-violet colour with alcoholic ferric chloride. The dinitrophenyl hydrazone was obtained as orange yellow needles, m.p. 290–92° (d.).

REFERENCES

1.	Schönberg *et al.*	.. *J. Amer. Chem. Soc.*, 1953, **75**, 4992.
2.	Chakravorty *et al.*	.. *Proc. Ind. Acad. Sci.*, 1952, **35 A**, 34.
3.	Mukerjee	.. *Ph.D. Thesis* (Delhi University, 1953).
4.	Sastri and Seshadri	.. *Proc. Ind. Acad. Sci.*, 1946, **24 A**, 243.
5.	Shah *et al.*	.. *J. Chem. Soc.*, 1938, 1555.
6.	Geissman	.. *J. Amer. Chem. Soc.*, 1951, **73**, 3514.