

7-HYDROXYCHROMONE-8-ALDEHYDES AND THEIR CONVERSION INTO CHROMONO-7:8- α -PYRONES

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THE preparation of aldehydes starting from 7-hydroxy-3-methoxyflavone, 7-hydroxy-2-methyl-3-methoxychromone and 7-hydroxy-flavone is described in this paper. The hydroxy compounds undergo condensation with hexamethylene-tetramine in glacial acetic acid solution easily and on subsequent hydrolysis with hydrochloric acid give comparatively good yields of the aldehydes.¹ That the aldehyde group enters the eighth position has been established by reducing the compound derived from 7-hydroxy-3-methoxyflavone using palladium-charcoal and hydrogen. The resulting methyl substituted flavone is found to be identical with 3-methoxy-7-hydroxy-8-methylflavone whose preparation starting from 2-methylresorcinol has already been described.² The reactive position in 7-hydroxy-chromones is therefore the eighth one just as in the case of the 7-hydroxycoumarins.

The hydroxychromones do not undergo condensation with malic acid in the presence of sulphuric acid. The hydroxychromone-aldehydes however react easily with sodium acetate and acetic anhydride (Perkin's reaction) to yield chromono-7 : 8- α -pyrones.

Experimental

7-Hydroxy-3-methoxyflavone-8-aldehyde.—7-Hydroxy-3-methoxyflavone was obtained from ω -methoxyresacetophenone by the method of Allan and Robinson.³ 2 g. of this flavone were heated with hexamethylenetetramine (6 g.) and glacial acetic acid (20 c.c.) for 6 hours in a boiling water-bath. The clear hot solution was then treated with a boiling mixture of fuming hydrochloric acid (10 c.c.) and water (20 c.c.). It rapidly became turbid and began to deposit needle-shaped crystals of the aldehyde in a few minutes. By leaving overnight, a very good yield of the solid was obtained and this was fairly pure. After filtering and washing with water one crystallisation from glacial acetic acid rendered it quite pure. It melted at 222–23°, the yield being 1.3 g. (Found : C, 68.4 ; H, 4.0 ; C₁₇H₁₂O₅ requires C, 68.9, H 4.1%.)

The compound was rather sparingly soluble in alcohol, more easily in glacial acetic acid and readily in pyridine. From acetic acid it came down as shining yellow crystals which appeared as rectangular plates under the

microscope. It was insoluble in cold dilute alkali and only slightly soluble on heating. With alcoholic ferric chloride it gave a brown pink colour. The phenylhydrazone crystallised from alcohol as yellow rectangular rods decomposing at 149–51°. (Found: N, 7.2, loss on drying (at 105°) 4.5; $C_{23}H_{18}O_4N_2$, 1 H_2O requires N, 6.9, loss on drying 4.5%.)

Reduction to 3-methoxy-7-hydroxy-8-methylflavone.—The aldehyde (0.5 g.) was dissolved in glacial acetic acid (120 c.c.), palladium-charcoal (2 g.) added and the mixture shaken in an atmosphere of hydrogen till two molecular proportions of the gas were absorbed. The solution was then filtered and the solvent removed by distillation under reduced pressure. When the residue was crystallised thrice from alcohol colourless rectangular plates of the reduction product were obtained. (Found: C, 71.7; H, 5.2; $C_{17}H_{14}O_4$ requires C, 72.3, H, 5.0%.) The substance melted at 255–56° and a mixture of it with the sample prepared from 2-methylresorcinol² melted at the same temperature.

3-Methoxyflavono-7 : 8- α -pyrone.—The above hydroxyaldehyde (0.3 g.) was heated with anhydrous sodium acetate (1 g.) and acetic anhydride (10 c.c.) for 6 hours in an oil-bath maintained at 175–85°. The mixture was then poured into excess of cold water (30 c.c.) and left overnight. The solid that separated was filtered and crystallised twice from acetic acid. The flavono- α -pyrone was thus obtained as colourless flat needles melting at 254–55°. (Found: C, 70.8; H, 4.0; $C_{19}H_{12}O_5$ requires C, 71.3; H, 3.8%.) The compound was sparingly soluble in alcohol and easily in acetic acid and it gave no colouration with alcoholic ferric chloride. It was almost insoluble in cold dilute alkali, but dissolved rapidly on heating to produce a clear deep yellow solution.

2-Methyl-3-methoxy-7-hydroxychromone.—The 7-acetoxycompound (m.p. 113°) was obtained from ω -methoxyresacetophenone by the method of Allan and Robinson.³ The subsequent hydrolysis has now been effected more quickly and conveniently by heating with 5 per cent. aqueous potash until complete solution is just effected (3–5 minutes), cooling immediately and acidifying the solution. The hydroxychromone crystallised from alcohol as long thin prismatic needles melting at 214–15°.

2-Methyl-3-methoxy-7-hydroxychromone-8-aldehyde.—This was obtained by essentially the same method as was adopted in the case of the methoxyflavone-aldehyde. After hydrolysis by means of boiling hydrochloric acid, the mixture had to be distilled under reduced pressure in order to remove most of the acetic and hydrochloric acids and then treated with water before the required aldehyde could be made to separate as a crystalline solid. When recrystallised from aqueous alcohol it came down as large rectangular prisms melting at 180–81°. (Found: C, 61.2; H, 4.7; $C_{12}H_{10}O_5$ requires C, 61.6;

H, 4.3%.) The yield of the pure aldehyde was 0.8 g. from 2 g. of the chromone. It gave a blood red colour with alcoholic ferric chloride. Its phenylhydrazone crystallised from alcohol as glistening hexagonal plates and melted at 220–22°. (Found: N, 9.0; $C_{18}H_{16}O_4N_2$ requires N, 8.7%.)

2-Methyl-3-methoxychromono-7: 8- α -pyrone—was obtained from the above aldehyde by heating with sodium acetate and acetic anhydride. It was sparingly soluble in alcohol and fairly easily soluble in acetic acid from which it crystallised in the form of pale yellow needles which turned brown at about 250° and melted at 282–84°. (Found: C, 64.8; H, 4.1; $C_{14}H_{10}O_5$ requires C, 65.1; H, 3.9%.) The substance was unaffected by cold dilute alkali but dissolved on heating to give an orange coloured solution.

7-Hydroxyflavone-8-aldehyde.—7-Hydroxyflavone (Robinson and Venkataraman⁴) was condensed with hexamethylenetetramine and the product hydrolysed with boiling hydrochloric acid as described before. The aldehyde slowly separated out as a pale yellow crystalline solid. It was moderately soluble in alcohol and it dissolved easily in hot acetic acid and pyridine. From acetic acid it separated out in the form of large crystals while from alcohol it came out as clusters of fine needles and narrow plates which melted at 223–24°. With alcoholic ferric chloride it gave an orange red colour and it was only slowly dissolved by dilute alkali. (Found: C, 71.7; H, 3.7; $C_{16}H_{10}O_4$ requires C, 72.2; H, 3.8%.) The yield of the pure aldehyde was 0.8 g. from 2 g. of the flavone.

Flavono-7: 8- α -pyrone—was obtained from the above aldehyde by the action of sodium acetate and acetic anhydride. It crystallised from hot glacial acetic acid as colourless fine needles and narrow plates melting at 250°. (Found: C, 74.6; H, 3.9; $C_{18}H_{10}O_4$ requires C, 74.5; H, 3.5%.) In its solubility in alcohol and pyridine and in its reaction towards aqueous alkali it resembled the other α -pyrones described previously.

Summary

Starting from 3-methoxy-7-hydroxyflavone, 2-methyl-3-methoxy-7-hydroxychromone and 7-hydroxyflavone aldehydes have been prepared. In these compounds the aldehyde groups occupy the eighth positions. By the action of sodium acetate and acetic anhydride the corresponding chromono- and flavono- α -pyrones have been synthesised.

REFERENCES

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2. —————. *Ibid.* (A), 1938, **8**, 214.
3. Allan, J., and Robinson, R. *J.C.S.*, 1924, 2192.
4. Robinson, R., and Venkataraman, K. *Ibid.*, 1926, 2344.