SYNTHETIC EXPERIMENTS IN THE BENZOPYRONE SERIES

Part LV. A New Synthesis of 7-Hydroxy-Chromeno-(3′ : 4′ : 2 : 3)-Chromone

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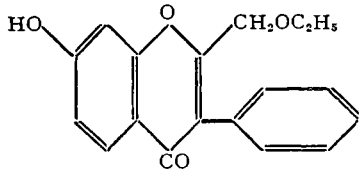
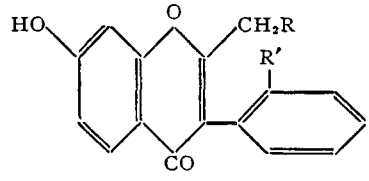
Received October 1, 1955

IN an earlier publication[1] a general method for the synthesis of the four ringed chromeno-chromone unit of the rotenoid skeleton was described based on considerations of possible biogenesis from the related 2-methyl isoflavone. There were a number of stages in this synthesis and the yields were poor. Successful attempts have now been made to simplify the synthesis of such compounds in order to make them available in good yields for further synthetic work.

The new method is based on the earlier findings of La Forge,[2] Baker and co-workers,[3] and Mehta and Seshadri[4] that acid chlorides can be made to condense with desoxy benzoins in presence of pyridine to yield isoflavones. Ethoxy acetyl chloride[5] has now been used as the appropriate reagent. A pilot experiment using ω-phenyl resacetophenone[6] gave a good yield of 2-ethoxymethyl-7-hydroxy isoflavone (I) which on treatment with hydrobromic acid-glacial acetic acid mixture is converted into the 2-bromomethyl derivative which has been reported earlier.[7] When 2 : 4-dihydroxy-2′-methoxy phenyl benzyl ketone[1] is used, 2-bromo-methyl-7 : 2′-dihydroxy isoflavone (II *b*) is obtained through the intermediate (II *a*). It has been

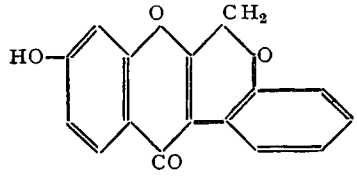


I



II

(*a*) R = OC_2H_5 ; R′ = OCH_3
(*b*) R = Br; R′ = HO



III

found during this work that treatment of 2-ethoxy methyl isoflavones with hydrobromic acid at higher temperature results in considerable resin formation and good results are obtained by employing mild conditions as described in the experimental part. The bromo-methyl-dihydroxy isoflavone (II *b*) readily eliminates a molecule of hydrogen bromide in the presence of anhydrous potassium carbonate in dry acetone giving rise to 7-hydroxy-chromeno-(3′ : 4′ : 2 : 3)-chromone (III).

Experimental

2-Ethoxymethyl-7-hydroxy isoflavone (I)

ω-Phenyl resacetophenone (5 g.) in dry pyridine (30 c.c.) was treated with ethoxy acetyl chloride (10 c.c.) at 0°. The product of condensation was worked up after 24 hours in the manner reported earlier[4] for acetyl chloride. The intermediate diketone could not be obtained crystalline and pure. Hence it was refluxed with 10% aqueous sodium carbonate (200 c.c.) for 2 hours. The solution was cooled, filtered, and the filtrate acidified with dilute hydrochloric acid. The sticky solid that separated out was extracted with ether and the extract dried over anhydrous magnesium sulphate. The residue left after the removal of the solvent crystallised from a mixture of ether and light petroleum and finally from ether as colourless rectangular prisms, m.p. 146–47° (3 g.) (Found: C, 72·9; H, 5·2; $C_{18}H_{16}O_4$ requires C, 73·0 ; H, 5·4%). The mother liquor on concentration yielded the original ketone (1·2 g.).

2-Bromo-methyl-7-hydroxy isoflavone

The above isoflavone (I) (1 g.) was dissolved in glacial acetic acid (10 c.c.) and hydrobromic acid in glacial acetic acid (50%; 10 c.c.) added. After keeping at room temperature for 12 hours a further quantity of hydrobromic acid (50%; 10 c.c.) was added and the mixture refluxed on a water-bath for 45 minutes. Ice-cold water was added and the solid that separated out was filtered and dried. It crystallised from a mixture of ethyl acetate and light petroleum as tiny rectangular prisms, m.p. 246–47° (0·8 g.). Mixed m.p. with an authentic sample[7] was undepressed.

2-Ethoxymethyl-7-hydroxy-2′-methoxy isoflavone (II a)

2 : 4-Dihydroxy-2′-methoxy phenyl benzyl ketone (5 g.) in dry pyridine (30 c.c.) was condensed with ethoxy acetyl chloride (10 c.c.) at 0° and the product worked up as in the previous case. 2-Ethoxymethyl isoflavone (II *a*) crystallised from a mixture of ether and light petroleum and finally from ether as colourless rhombohedral prisms, m.p. 168–70° (3·2 g.) (Found:

C, 69·3; H, 5·7; $C_{19}H_{18}O_5$ requires C, 69·9; H, 5·5%). The mother liquor on concentration gave the original ketone (1 g.).

2-Bromo-methyl-7 : 2′-dihydroxy isoflavone (II b)

The above isoflavone (II *a*) (1 g.) was treated with glacial acetic acid and hydrobromic acid as done in the simpler case. The product crystallised rom a mixture of ethyl acetate and light petroleum and finally from ethyl acetate as colourless stout rectangular prisms, m.p. 213–14° (decomp.) (0·8 g.) (Found: C, 55·4; H, 3·5; $C_{16}H_{11}O_4Br$ requires C, 55·3; H, 3·2%).

7-Hydroxy-chromeno-(3′ : 4′ : 2 : 3)-chromone (III)

The above isoflavone (II *b*) (0·3 g.) was dissolved in dry acetone (100 c.c.), freshly ignited potassium carbonate (3 g.) added and the mixture refluxed for 4 hours. More potassium carbonate (3 g.) was now added and the refluxing continued for 6 hours more. Acetone was distilled off, the residue dissolved in water and acidified with dilute hydrochloric acid. The solid product crystallised from alcohol as colourless needles, m.p. 240–42° (decomp.) (0·2 g.). Mixed m.p. with an authentic sample[1] was undepressed. The acetate obtained by the acetic anhydride-pyridine method also agreed in its melting with the authentic sample.

SUMMARY

By the use of ethoxy acetyl chloride and pyridine at 0°, 7-hydroxy-chromeno-(3′ : 4′ : 2 : 3)-chromone has been synthesised much more conveniently than by the earlier methods reported in the literature.

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