THE BENZOYLATION OF 5-HYDROXY-6-ACYL-COUMARINS IN PRESENCE OF PYRIDINE

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Received January 20, 1942
(Communicated by Dr. R. C. Shah, M.Sc., Ph.D.)

In an attempt to prepare its O-benzoyl derivative, 5-hydroxy-6-acetyl-4-methylcoumarin was heated with benzoyl chloride in its pyridine solution; the crystalline product isolated, however, was not the expected benzoyl derivative, 5-O-benzoyl-6-acetyl-4-methyl-coumarin (I). The analytical results for the product closely agreed with those required for 4-methyl-flavono-7':8':6:5-a-pyrene (II, R = H) and the substance was insoluble in alkali but dissolved in conc. sulphuric acid with brownish yellow colour exhibiting bluish-violet fluorescence.

To settle the constitution of the above flavono-coumarin (II, R = H), 5-hydroxy-6-acetyl-4-methylcoumarin was subjected to the Kostanecki benzylation; 4-methyl-3'-benzoyl-flavono-7':8':6:5-a-pyrene (II, R = CO Ph) was obtained (Sethna, Shah and Shah, loc. cit.). Attempts to remove 3'-benzoyl group were unsuccessful. However, the flavono-coumarin (II, R = H) was unambiguously synthesised thus: 5-hydroxy-6-acetyl-4-methylcoumarin on condensation with benzaldehyde in presence of potassium hydroxide gave the coumarino-chalkone, 5-hydroxy-4-methylcoumarino-6-styryl-ketone (III) (unpublished work) which on treatment with selenium dioxide in amyl alcohol gave 4-methyl-flavono-7':8':6:5-a-pyrene, m.p. 251-252° identical with the flavono-coumarin (II, R = H) obtained above (mixed m.p. undepressed).

With regard to the formation of the flavone derivative in the above reaction in presence of pyridine, it appears that the O-benzoyl derivative (I) initially formed undergoes rearrangement with the subsequent ring-formation to give the flavono-coumarin (II, R = H) directly. The above reactions are shown diagrammatically below:
This change is analogous to that undergone by o-benzoyloxy-acetophenones in presence of potassium carbonate as shown by Baker. Recently, such transformations have also been affected by various workers employing sodamide in dry ether, sodium ethylate or alcoholic sodium hydroxide or finely divided sodium. The part played by potassium carbonate and other reagents is carried out by pyridine—an organic base, in the above flavone formation.

Baker (loc. cit.) was able to isolate intermediate o-hydroxy-dibenzoyl-methane derivatives as their potassium salts. In the present case, such a salt formation is not possible, but it is quite plausible that the di-benzoyl-methane derivative may have been formed as an intermediate previous to the flavone-ring formation. 5-Hydroxy-6-propionyl-4-methylcoumarin was similarly treated with benzoic chloride in its pyridine solution. The product obtained gave two types of crystals on crystallisation from alcohol: (I) brownish prismatic crystals, m.p. 159-160°, and (ii) white light needles, m.p. 221°. Both the products were insoluble in alkali and gave no colouration with alcoholic ferric chloride. The former dissolved in conc. sulphuric acid without any fluorescence, while the latter exhibited violet fluorescence in the sulphuric acid solution. By analogy of the previous case, the substance m.p. 221° was assumed to be a flavone derivative, which was settled as follows: 5-hydroxy-6-propionyl-4-methylcoumarin was subjected to the Kostanecki benzoylation; the flavono-coumarin was found identical with substance m.p. 221° (mixed m.p. unchanged): this shows that the substance m.p. 221° has the constitution, 3'-benzo-methyl-4-methyl-flavono-7': 8': 6: 5-a-pyrone (II: R = -CH₂ CO·Ph). Attempts to remove 3'-benzoyl
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Attempts to prepare simple O-benzoyl derivative of the 5-hydroxy-6-propionylcoumarin were unsuccessful. It also gave no derivative characteristic of -CO group. The product melting at 159-160° gave analytical results corresponding to C₂₇H₂₉O₄ indicating that it contained a water molecule more than the flavone obtained above. It was therefore assumed to have the constitution, 5-benzoyloxy-4-methyl-coumarino-6-dibenzoylethane, but the following reactions indicated otherwise: (i) the action of HBr in acetic acid produced the original coumarin, 5-hydroxy-6-propionyl-4-methylcoumarin, (ii) a derivative characteristic of -CO group could not be prepared, and (iii) the action of conc. sulphuric acid according to Sethna and Shah, R.C.⁷ to affect the stepwise elimination of O-acyl and C-acyl groups led to the production of the original coumarin, 5-hydroxy-6-propionyl-4-methylcoumarin, indicating that the -CO-Ph groups were linked through O atom. This shows that the coumarin is also reacting in the enolic form and the product, m.p. 159-160°, is the dibenzoyl derivative of the coumarin in its enolic form.

5-Hydroxy-6-butyryl-4-methylcoumarin (Delwala and Shah, loc. cit.) on similar treatment with benzoyl chloride in pyridine gave only the dibenzoyl derivative of the coumarin reacting in the enolic form as in the previous case. The Kostanecki benzoylation of the 5-hydroxy-6-butyryl-coumarin gave 3'-benzo-ethyl-4-methyl-flavono-7':8':6:5-α-pyrone.

It may be mentioned here that all the above coumarins on treatment with acetic anhydride in pyridine solution afforded only the corresponding 5-acetoxy derivatives. Baker (loc. cit.) was also unable to effect the migration of an aliphatic acid radical in o-acyloxy-acetophenones.

The action of pyridine on resacetophenone dibenzoate and its other simple derivatives was unsuccessful in bringing about the migration of the acid residue. It is thus evident that the reactivity to undergo such transformations in presence of pyridine with the flavone-ring formation in case of 5-hydroxy-6-acyl-coumarins is brought about by the presence of the α-pyrone ring.

Experimental

4-Methyl-flavono-7':8':6:5-α-pyrone (II, R = H)—5-hydroxy-6-acetyl-4-methylcoumarin (Sethna, Shah and Shah, loc. cit.) (1 g.) was dissolved in benzoyl chloride (5 c.c.) by gently heating; pyridine (2 c.c.) was added and the mixture gently refluxed on a small free flame for about 4 hours. It was cooled and mixed with water; sticky red-brown oil separated. It was washed with dil. H₂SO₄ and then with dilute alkali and finally with water. The product obtained slowly solidified on keeping for about 4-5 days.
It was washed with little alcohol which removed coloured impurities; a white solid was collected, which on crystallisation from alcohol gave fine crystalline substance, m.p. 251° (Found: C, 74.9; H, 4.1. C₁₉H₁₂O₄ requires C, 75.0; H, 3.9 per cent.). The flavono-coumarin dissolves in conc. sulphuric acid with brownish yellow colouration exhibiting bluish-violet fluorescence.

**Action of selenium dioxide on 5-hydroxy-4-methylcoumarino-6-styrylketone (III).**—The ketone (1.5 g.) was dissolved in amyl alcohol (30 c.c.) and selenium dioxide (2 g.) added; the mixture refluxed for 11-12 hours at 170–180°. The hot solution was filtered from the ppted metallic selenium when on cooling the crystals began to appear in the filtrate. They were collected and crystallised from alcohol, needles, m.p. 251-252°, the mixed melting point with the flavono-coumarin obtained above was undepressed.

**Action of benzoyl chloride and pyridine on 5-hydroxy-6-propionyl-4-methylcoumarin:** Formation of 3′-benzomethyl-4-methyl-flavono-7′:8′:6′:5′-pyrone (II: R = - CH₃ CO Ph) and di-benzoyloxy derivative of the coumarin.—5-Hydroxy-6-propionyl-4-methylcoumarin (Deliwala and Shah, loc. cit., 1 g.) benzoyl chloride (5 c.c.) and pyridine (2 c.c.) were treated as before and the product obtained similarly. The solid obtained gave two types of crystals on crystallisation from alcohol, brownish prisms and clusters of white light needles side by side. They were mechanically separated.

The light needles on recrystallisation from alcohol melted at 221° (Found: C, 76.4, 76.3, 75.55; H, 5.7, 5.5, 4.7. C₂₇H₁₇O₆ requires C, 76.8; H, 4.3 per cent.). 3′-Benzo-methyl-4-methyl-flavono-7′:8′:6′:5′-pyrone exhibits violet fluorescence in conc. H₂SO₄ and is insoluble in alkali and gives no ferric chloride colour.

The prismatic crystals were re-crystallised from alcohol, m.p. 159–160° (Found: C, 73.9, 73.7; H, 4.7, 4.6. C₂₇H₁₇O₆ requires C, 73.6; H, 4.5 per cent.). It is insoluble in alkali, gives no ferric chloride colour and dissolves in conc. H₂SO₄ without any fluorescence.

**Kostanecki benzoylation of 5-hydroxy-6-propionyl-4-methylcoumarin.**—The coumarin (1 g.), benzoic anhydride (8 g.) and sodium benzoate (3 g.) were thoroughly mixed and heated for 11 hours at 160–170°. The cooled mass was crushed under water and treated with dilute alkali and finally washed with water. The solid on crystallisation from alcohol gave fine needles, m.p. 222°, the mixed m.p. with the substance (IV) was unaltered.

**Action of benzoyl chloride and pyridine on 5-hydroxy-6-butyryl-4-methylcoumarin.**—The coumarin (Deliwala and Shah, loc. cit.) (1 g.) was refluxed
with benzooyl chloride (5 c.c.) and pyridine (2 c.c.) as in the previous cases. The product crystallised from alcohol, clusters of needles, m.p. 168° (Found: C, 73.9, 73.9; H, 4.9. C_{28}H_{22}O_{8} requires C, 74.0 H, 4.85 per cent.). The substance is insoluble in alkali and dissolves in conc. sulphuric acid with yellowish colour without any fluorescence.

Kostanecki benzyolation of 5-hydroxy-6-butyryl-4-methylcoumarin.—The coumarin (1 g.), benzoic anhydride (7 g.) and sodium benzoate (2 g.) were heated at 170–180° for 12 hours. It was then cooled, treated with alcoholic KOH, filtered and the residue washed with water and crystallised from acetic acid and then from alcohol in which it is sparingly soluble, white lustrous needles, m.p. 220–221° (Found: C, 75.7; H, 5.0. C_{25}H_{20}O_{5} requires C, 75.5; H, 4.7 per cent.). The product is insoluble in alkali and dissolves in conc. H_{2}SO_{4} with violet fluorescence. Attempts to eliminate 3'-benzoyl group were unsuccessful.

The C-H determinations are micro-analysis partly by Dr. A Schoeller and partly by Mr. N. Ghosh, University College of Science, Calcutta. Our best thanks are due to Mr. N. Ghosh and Dr. D. Chakravarti, Calcutta, for micro-analysis.

We express our grateful thanks to Prof. R. C. Shah for his sympathetic interest in the investigation.

Summary

The action of benzooyl chloride on 5-hydroxy-6-acyl-coumarins in pyridine solution has been investigated. The reaction leads to the formation of the flavone derivative instead of the expected benzooyloxy derivative. The constitution of the flavone obtained from 5-hydroxy-6-acetyl-coumarin has been confirmed by unambiguous synthesis from the corresponding chalcone by SeO_{2} reaction. 5-Hydroxy-6-propionyl-coumarin similarly gives the flavone derivative and also reacts in its enolic form, yielding the di-benzooyloxy derivative. 5-Hydroxy-6-butyryl-coumarin gives only the di-benzooyloxy derivative, reacting in its enolic form.

REFERENCES