775. *Chromones and Flavones. Part II.*[1] *Kostanecki–Robinson Acylation of Some Iodo-derivatives of* 2,4- *and* 2,6-*Dihydroxyacetophenone.*

By M. V. SHAH and SURESH SETHNA.

Iodo-derivatives of 2,4- and 2,6-dihydroxyacetophenone have been subjected to Kostanecki–Robinson acetylation and benzoylation and the corresponding iodo-chromones and -flavones synthesised.

No work on the Kostanecki–Robinson " acylation " of the iodo-derivatives of *o*-hydroxyacetophenones has been reported so far. The present work deals with the reaction of some iodo-derivatives of 2,4- and 2,6-dihydroxyacetophenone with acetic and benzoic anhydride. The iodoacetophenones (Ia—c), on reaction with acetic anhydride and sodium acetate, followed by de-esterification with sulphuric acid, gave the corresponding 3-acetylchromones (IIa—c). The di-iodochromone (IIc) in boiling acetic acid gave the monoiodochromone (IIb). The chromones (IIa and c) were also obtained on the iodination of 3-acetyl-7-hydroxy-2-methylchromone. The iodo-ketone (Ia), on reaction with benzoic anhydride and sodium benzoate, followed by de-esterification, gave the 3-benzoylflavone (IIIa), also obtained from 3-benzoyl-7-hydroxyflavone by iodination. The iodo-ketone (Ib) similarly gave the 3-benzoylflavone (IIIb), but the di-iodoketone (Ic) lost an iodine atom and gave the 3-benzoylflavone (IIIb). The di-iodoflavone was, however, obtained by the iodination of 3-benzoyl-7-hydroxyflavone.

2,6-Dihydroxy-3,5-di-iodoacetophenone, obtained on iodination of 2,6-dihydroxyacetophenone and correlated with the known 3,5-di-iodo-2,6-dimethoxyacetophenone, on

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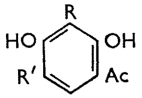
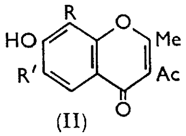
[1] Part I, Shah and Sethna, *J.*, 1959, 2676.

similar treatment gave the corresponding 3-acyl-di-iodo-chromone and -flavone which were also obtained by the iodination of the 3-acyl-5-hydroxy-chromone and -flavone.



(I)



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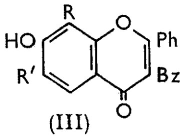

(III)

	a	b	c
R =	I	H	I
R' =	H	I	I

Heating the 3-acyl-hydroxy-chromones and -flavones, except (IIa), with alkali gave impure products, and the methylated 3-acyl-chromones and -flavones gave phenolic ketones, either alone or with phenolic acids, instead of the de-acylated compounds (see Table 2). 7-Hydroxy-8-iodo- and -6,8-di-iodo-flavone and 5-hydroxy-6,8-di-iodoflavone have, however, been prepared by iodination of 7- and 5-hydroxyflavone.

EXPERIMENTAL

Kostanecki–Robinson " Acetylations " (see Table 1).—The iodo-ketone (1 g.) was heated with freshly fused sodium acetate (5 g.) and acetic anhydride (20 ml.) at 155—160° for 6 hr. The mixture was then added to cold water; the *product* crystallised from acetic acid (charcoal) in needles.

Kostanecki–Robinson " Benzoylations " (see Table 1).—The iodo-ketone (2 g.) was heated with freshly fused sodium benzoate (1 g.) and benzoic anhydride (20 g.) at 155—160° for 6 hr. The mixture was then treated repeatedly with hot water and sodium hydrogen carbonate; the residue crystallised from alcohol or the impure *product* was further treated with sulphuric acid as given below. Larger quantities of sodium benzoate lead to decomposition of the iodo-compounds.

Higher reaction temperatures in the acylations lead to deeply coloured unworkable mass.

Hydrolysis with Sulphuric Acid.—For removing the *O*-acyl group the acyloxy-chromones and -flavones were kept with the minimum quantity of concentrated sulphuric acid for 4 hr. (overnight in the case of flavones) at room temperature. The material obtained when the mixture was poured on ice crystallised from acetic acid. These *products* are listed in Table 2.

Preparation of Methyl Ethers.—Acetone solutions of the compounds were refluxed with dimethyl sulphate in presence of anhydrous potassium carbonate. In the case of the 3-acetyl-iodochromones and the 3-benzoyliodoflavones benzene was used as the solvent as some decomposition was observed in acetone. Products are listed in Table 2.

Alkaline Hydrolysis of 3-*Acyl-chromones and -flavones.*—3-Acetyl-7-hydroxy-8-iodo-2-methylchromone was de-acetylated to 7-hydroxy-8-iodo-2-methylchromone by 2% aqueous sodium carbonate on a steam-bath in ¼ hr. In other cases the methylated 3-acetyl-iodochromones were hydrolysed with aqueous-alcoholic 5% sodium carbonate, and the methylated 3-benzoyl-iodoflavones with alcoholic 10% potassium hydroxide on a steam-bath in 2 hr. In all cases a

TABLE 1. *Reactions with* (A) *acetic anhydride and sodium acetate or* (B) *benzoic anhydride and sodium benzoate.*

Ketone	Re-action	Product; Ac deriv. of	M. p.	Found (%) C	H	I	Formula	Required (%) C	H	I
Ia	A	IIa	190—191°	43·8	2·7	32·7	$C_{14}H_{11}O_5I$	43·5	2·8	32·9
,,	B	*	—	—	—	—	—	—	—	—
Ib	A	IIb	149	43·0	3·0	32·6	$C_{14}H_{11}O_5I$	43·5	2·8	32·9
,,	B	*	—	—	—	—	—	—	—	—
Ic	A	IIc	230—231	32·8	1·8	49·6	$C_{14}H_{10}O_5I_2$	32·8	2·0	49·6
,,	B	*	—	—	—	—	—	—	—	—
2,6,3,5-$(HO)_2C_6HI_2Ac$	A	5-Acetoxy-3-acetyl-6,8-di-iodo-2-methylchromone	175—176	32·4	2·1	49·8	$C_{14}H_{10}O_5I_2$	32·8	2·0	49·6
,, ,,	B	3-Benzoyl-5-benzoyloxy-6,8-di-iodoflavone	235	49·6	2·0	36·9	$C_{29}H_{16}O_5I_2$	49·9	2·3	36·4

* The *O*-benzoyl derivative of the flavone was not obtained pure; the crude product was treated directly with sulphuric acid to give the 3-benzoyl-hydroxyflavone (see Table 2).

TABLE 2.

A. Compounds obtained from the products of Table 1 by the action of sulphuric acid.

No.	Product	M. p.*	Found (%) C	Found (%) H	Found (%) I	Formula	Required (%) C	Required (%) H	Required (%) I
1	IIa †	240°	42·4	2·4	36·9	$C_{12}H_9O_4I$	41·9	2·6	36·9
2	IIIa †	246	56·0	3·0	27·0	$C_{22}H_{13}O_4I$	56·4	2·8	27·1
3	IIb ‡	253—254	42·1	2·8	36·4	$C_{12}H_9O_4I$	41·9	2·6	36·9
4	IIIb ¶	303	56·0	2·3	26·6	$C_{22}H_{13}O_4I$	56·4	2·8	27·1
5	IIc	234	30·2	2·0	53·6	$C_{12}H_8O_4I_2$	30·6	1·7	54·0
6	3-Acetyl-5-hydroxy-6,8-di-iodo-2-methylchromone †	219	30·4	1·4	54·6	$C_{12}H_8O_4I_2$	30·6	1·7	54·0
7	3-Benzoyl-5-hydroxy-6,8-di-iodoflavone †	228	44·9	2·2	42·8	$C_{22}H_{12}O_4I_2$	44·5	2·0	42·8

B. Methyl ethers of the products in section A.

No.	M. p.	Found (%) C	Found (%) H	Found (%) I	Formula	Required (%) C	Required (%) H	Required (%) I
1	164°	43·1	2·6	35·1	$C_{13}H_{11}O_4I$	43·6	3·1	35·5
2	235—236	57·8	3·1	26·7	$C_{23}H_{15}O_4I$	57·3	3·1	26·3
3	177—178	43·2	2·8	35·8	$C_{13}H_{11}O_4I$	43·6	3·1	35·5
4	273—274	57·6	3·4	25·9	$C_{23}H_{15}O_4I$	57·3	3·1	26·3
5	210—211	32·1	2·4	52·8	$C_{13}H_{10}O_4I_2$	32·2	2·1	52·5
6	213—214	32·1	2·4	52·2	$C_{13}H_{10}O_4I_2$	32·2	2·1	52·5
7	198—199	45·6	2·4	41·4	$C_{23}H_{14}O_4I_2$	45·4	2·3	41·8

* Some of the compounds begin to decompose 15—20° below their m. p.s and melt finally at the temperatures stated. † Also obtained by iodination. ‡ Also obtained by refluxing compound 5 in acetic acid for 10 hr. ¶ From the fourth and the sixth product of Table 1.

TABLE 3. *Iodinations.*

Iodo-compounds

No.	Compound	Product	M. p.*	Formula	Found I (%)	Reqd. I (%)
8	5-Hydroxyflavone	6,8-I_2	252°	$C_{15}H_8O_3I_2$	51·4	51·8
9	7-Hydroxyflavone	8-I	230	$C_{15}H_9O_3I,H_2O$ †	33·5	33·2
		6,8-I_2	282—283	$C_{15}H_8O_3I_2$	52·1	51·8
10	3-Benzoyl-7-hydroxyflavone	6,8-I_2	208	$C_{22}H_{12}O_4I_2$	43·2	42·8
11	2,6-$(HO)_2C_6H_3Ac$	3,5-I_2	133	$C_8H_6O_3I_2$	62·4	62·9

Methyl ethers of iodo-compounds

	M. p.	Formula	Found (%) C	Found (%) H	Found (%) I	Required (%) C	Required (%) H	Required (%) I
8	246°	$C_{16}H_{10}O_3I_2$	37·8	1·6	50·5	38·1	2·0	50·0
9	210—211	$C_{16}H_{11}O_3I$	50·5	2·9	33·8	50·8	2·9	33·6
	198—199	$C_{16}H_{10}O_3I_2$	38·0	1·9	50·1	38·1	2·0	50·0
10	238—239	$C_{23}H_{14}O_4I_2$	45·8	2·6	41·6	45·4	2·3	41·8
11	83—84	$C_{10}H_{10}O_3I_2$	28·0	2·0	58·5	27·8	2·3	58·8

* See first footnote of Table 2. † Decomp. *in vacuo.*

phenolic iodo-ketone, alone or with phenolic iodo-acid was obtained. Variations in heating time or concentration of alkali did not give the desired deacylated chromone or flavone.

Hydrolysis of the Ethers.—Hydrolysis of the ethers listed in Tables 2*B* and 3 gave the following products (described in Part I: Nos. 2 and 9, 2-hydroxy-3-iodo-4-methoxy-acetophenone and -benzoic acid. Nos. 3 and 4, 2-hydroxy-5-iodo-4-methoxy-acetophenone and -benzoic acid Nos. 5, 9, and 10, 2-hydroxy-3,5-di-iodo-4-methoxy-acetophenone and -benzoic acid. Nos. 6 and 8, 2-hydroxy-3,5-di-iodo-6-methoxyacetophenone.

Iodinations (*see Tables* 2 *and* 3).—All the iodinations were carried out with iodine and iodic acid as in Part I.

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