TABLE 1. Characteristics of the Compounds Obtained

Compound	X/Y	R	R′	A	mp, °C (dec.)	Found, %		Empirical formula	Calc., %		Yield, %
						Cl	N		Cl	N	
Ia	O	CH_3	CH_3	ClO_4	249	12,0	9,5	$C_9H_9ClN_2O_7$	12,1	9,6	90
Ib	O	CH_3	CH_3	H_2PO_4	153	—	9,6	$C_9H_{11}N_2O_7P$	—	9,6	67
Ic	O	C_6H_5	C_6H_5	ClO_4	275	8,3	—	$C_{19}H_{13}ClN_2O_7$	8,5	—	37
Id	O	C_6H_5	CH_3	ClO_4	>320	10,3	8,1	$C_{14}H_{11}ClN_2O_7$	10,0	7,9	51
Ie	S	CH_3	CH_3	ClO_4	235	11,6	—	$C_9H_9ClN_2O_6S$	11,5	—	64
If	S	C_6H_5	C_6H_5	ClO_4	229	8,4	—	$C_{19}H_{13}ClN_2O_6S$	8,2	—	18
Ig	S	C_6H_5	CH_3	ClO_4	270	9,9	7,7	$C_{14}H_{11}ClN_2O_6S$	9,6	7,6	56
Ih	O	CH_3	*	ClO_4	>300	8,1	—	$C_{18}H_{18}ClN_3O_7$	8,4	—	96
IIa	NH_2	CH_3	CH_3	ClO_4	226	12,3	14,3	$C_9H_{10}ClN_3O_6$	12,2	14,4	83
IIb	NH_2	CH_3	CH_3	CF_3COO	>300	—	14,1	$C_{11}H_{10}F_3N_3O_4$	—	13,8	50
IIc	NH_2	C_6H_5	C_6H_5	CF_3COO	>300	—	9,7	$C_{21}H_{14}F_3N_3O_4$	—	9,7	90
IId	NH_2	C_6H_5	CH_3	CF_3COO	>300	—	11,6	$C_{16}H_{12}F_3N_3O_4$	—	11,4	79
IIe	NH_2	C_6H_5	CH_3	ClO_4	274	10,0	12,2	$C_{14}H_{12}ClN_3O_6$	10,0	11,9	61
IIf	SCH_3	CH_3	CH_3	ClO_4	232	11,2	—	$C_{10}H_{11}ClN_2O_6S$	11,0	—	57
IIg	SCH_3	C_6H_5	C_6H_5	ClO_4	262	7,9	—	$C_{20}H_{15}ClN_2O_6S$	7,7	—	20
IIh	SCH_3	C_6H_5	CH_3	ClO_4	232	9,2	—	$C_{15}H_{13}ClN_2O_6S$	9,2	—	34
IIIa	O	CH_3	CH_3	ClO_4	266	8,3	—	$C_{15}H_{14}ClN_3O_6 \times$ $\times CH_3COOH$	8,3	—	52
IIIb	O	C_6H_5	C_6H_5	ClO_4	>300	7,2	8,5	$C_{25}H_{18}ClN_3O_6$	7,2	8,5	51
IVa	NH_2	CH_3	CH_3	ClO_4	>300	9,9	15,5	$C_{15}H_{15}ClN_4O_5$	9,7	15,3	75

*p-Dimethylaminostyryl.

5-(p-Dimethylaminostyryl)-7-methylpyrylia[2,3-d]pyrimidin-2,4(1H,3H)dione Perchlorate. A mixture of 0.5 g of salt Ia and 0.25 g of p-dimethylaminobenzaldehyde in 15 ml of acetic anhydride was heated on a water bath for 2 min, after which it was cooled, and the dye crystals were removed by filtration, washed with ether, and recrystallized from acetic anhydride. UV spectrum (in ethanol), λ_{max} (log ε) 570 nm (4.73).

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PREPARATION OF 3-SUBSTITUTED ISOCOUMARINS IN THE REACTIONS OF HOMOPHTHALIC ANHYDRIDE AND ITS DERIVATIVES*

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UDC 547.81

Acetylation of 4-nitrohomophthalic anhydride gave 4-acetyl-7-nitroisochroman-1,3-dione, which was converted to 3-methyl-7-nitroisocoumarin. 3-Benzylisocoumarin derivatives were synthesized by reaction of homophthalic anhydrides with arylacetic acids in acetic anhydride and triethylamine.

The condensation of homophthalic acids and their esters and anhydrides with compounds containing carbonyl groups is the most important method for the synthesis of isocoumarin derivatives [2]. Since homophthalic acid and its derivatives contain carbonyl and active methylene groups, they are also capable of self-condensation to give 3-(2'carboxybenzyl)isocoumarin derivatives [3-6].

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*Communication XXVIII from the series "Condensation of Dicarboxylic Acid Anhydrides with Compounds Containing Active Methylene Groups." See [1] for communication XXVII.

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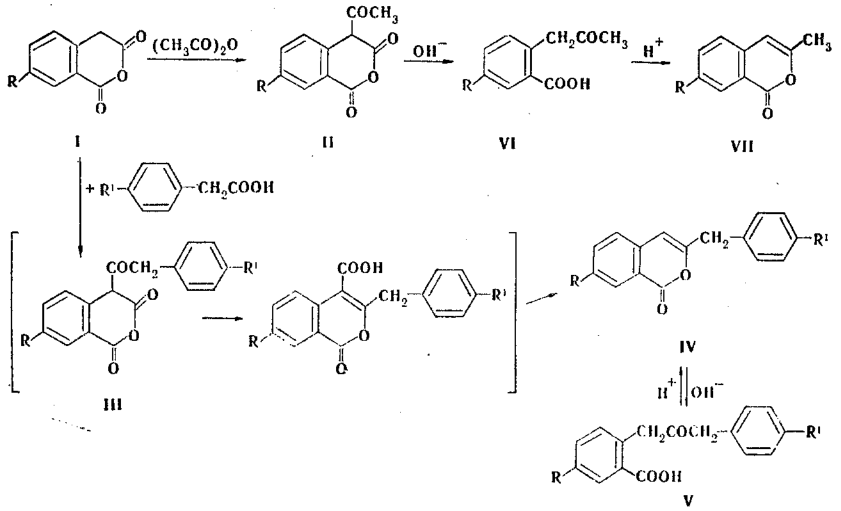
0009-3122/77/1311-1187$07.50

We have established [7] that homophthalic (Ia) and 4-methoxyhomophthalic (Ib) anhydrides do not react with phenylacetic acid as carbonyl components in acetic anhydride in the presence of triethylamine but instead undergo acetylation at C_4. A study of the analogous reaction of 4-nitrohomophthalic anhydride (Ic) showed that at room temperature in the presence of triethylamine Ic is acetylated by acetic anhydride to give 4-acetyl-7-nitroisochroman-1,3-dione (II), which is isolated in the form of the triethylammonium salt. Acetylation of Ic with acetyl chloride in the presence of pyridine at 0-5 deg C leads to pyridinium salt II. The formation of a stable pyridine complex that does not undergo decomposition under the influence of acid was noted in [8] in the synthesis of 4-acetyl-7-methoxy-6,8-dinitroisochroman-1,3-dione.



I a R=H; b R=OCH_3; c R=NO_2; II, VI, VII R=NO_2; IV, V a R=NO_2, R'=H; b R=H, R'=NO_2; c R=OCH_3, R'=NO_2; d R=R'=NO_2

The introduction of an electron-acceptor group in I sharply changes its reactivity. At 90-95 deg C, Ic reacts with phenylacetic acid in acetic anhydride containing triethylamine to give 3-benzyl-7-nitroisocoumarin (IVa). The rather high yield (51%) of IVa indicates that under the acylation conditions (Ic → II and Ic → IVa) phenylacetic acid is more reactive than acetic anhydride. In addition, the introduction of a nitro group in the phenylacetic acid molecule increases its ability to undergo reaction with homophthalic, 4-methoxyhomophthalic, and 4-nitrohomophthalic anhydrides to give 3-benzylisocoumarin derivatives (IV). Our reaction of homophthalic anhydrides Ia-c with arylacetic acids in acetic acid in the presence of triethylamine is a new method for the preparation of the previously unknown 3-benzylisocoumarin derivatives. It may be assumed that the reaction proceeds as acylation with subsequent rearrangement of the intermediate (III) in accordance with the known [9, 10] mechanism of the reaction to give 3-substituted isocoumarins.

With respect to reagents that promote hydrolysis, isocoumarins IV and 4-acetyl-7-nitroisochroman-1,3-dione (II) behave like typical lactones. They are stable with respect to acidic and neutral reagents but react with alkalis to give 2-carboxybenzyl ketones (V, VI), which in acidic media are capable of recyclization to isocoumarins IV and VII.

The band of the stretching vibrations of a carbonyl group in the IR spectra of IV is found in a lower position than in the spectra of aromatic γ-lactones and saturated δ-lactones but has the intensity ratio of the absorption bands that is characteristic for isocoumarins [11]. The most intense band is the $\nu_{C=O}$ band of a lactone ring at 1720-1745 cm^{-1}, followed by the $\nu_{C=C}$ band of the isocoumarin ring in the C_3-C_4 position at 1654-1660 cm^{-1}; the least intense vibrations are those of the benzene ring at 1607-1622 and 1580-1588 cm^{-1}.

The authors sincerely thank Professor N. M. Turkevich for reviewing the manuscript and for his valuable comments.

EXPERIMENTAL

General Method for the Preparation of 3-Benzylisocoumarin Derivatives (IV). Equimolar amounts (0.01 mole) of homophthalic anhydride I and arylacetic acid were dissolved in 19 ml (0.2 mole) of acetic anhydride, 4.2 ml (0.03 mole) of triethylamine was added, and the mixture was heated at 90-95 deg C for 15 min, after which it was poured into a mixture of ice and concentrated HCl (100 g/50 ml). After decomposition of the acetic anhydride, the precipitate was removed by filtration and washed with water. The colorless or yellowish products were recrystallized from acetic acid or ethanol.

TABLE 1. 3-Substituted Isocoumarins and Their Derivatives

Compound	mp, °C	Found, %			Empirical formula	Calc., %			IR spectrum, 1500-1800 cm^{-1} region (intensity, %)[a]	Yield, %
		C	H	N		C	H	N		
II[b]	197—198	56,22	4,86	7,05	$C_{28}H_{29}N_3O_{12}$	56,09	4,88	7,01	1735 (80), 1712 (82), 1675 (72), 1608 (86), 1588 (72), 1525 (74)	58,8
II[c]	188—189	56,46	3,30	7,51	$C_{27}H_{19}N_3O_{12}$	56,16	3,32	7,28	1745 (74), 1718 (72), 1668 (61), 1610 (78), 1588 (69), 1530 (66)	44,7
IVa	155—156	67,98	3,86	4,97	$C_{16}H_{11}NO_4$	68,33	3,94	4,98	1742 (82), 1654 (69), 1615 (66), 1585 (66), 1528 (64)	51,0
IVb	175—176	67,90	3,56	4,77	$C_{16}H_{11}NO_4$	68,33	3,94	4,98	1720 (81), 1660 (72), 1610 (65), 1528 (72)	96,0
IVc	216—217	65,85	4,05	4,21	$C_{17}H_{13}NO_5$	65,59	4,21	4,50	1728 (78), 1662 (65), 1607 (60), 1580 (60), 1520 (70)	94,5
IVd	172—173	58,57	3,11	8,28	$C_{16}H_{10}N_2O_6$	58,90	3,09	8,59	1745 (85), 1660 (64), 1622 (71), 1588 (65), 1528 (78)	96,8
VI	143—144	53,55	4,06	6,45	$C_{10}H_9NO_5$	53,82	4,05	6,28	1726 (77), 1700 (81), 1618 (51), 1590 (34), 1530 (63)	80,5
Vb	263—265	64,35	4,37	4,37	$C_{16}H_{13}NO_5$	64,21	4,38	4,68	1674 (56), 1648 (52), 1600 (60), 1518 (66)	73,2
Vc	282—283	62,43	4,73	4,31	$C_{17}H_{15}NO_6$	62,00	4,59	4,25	1715 (48), 1669 (77), 1596 (86), 1519 (75)	81,4
VII	179—180	58,07	3,46	6,39	$C_{10}H_7NO_4$	58,54	3,44	6,83	1745 (80), 1660 (64), 1610 (44), 1588 (66), 1525 (55)	87,5

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[a] The IR spectra of mineral oil suspensions of the solids were obtained with a UR-10 spectrometer. [b] The triethylammonium salt. [c] The pyridinium salt.

2-Carboxybenzyl Ketones (V). Compounds IV were heated in 10% alkali solution until they dissolved completely, after which the solution was cooled and acidified with dilute HCl. The precipitate was removed by filtration and recrystallized from aqueous ethanol or acetic acid.

4-Acetyl-7-nitroisochroman-1,3-dione (II). A) Triethylammonium Salt. A 4.14-g (0.02 mole) sample of Ic was dissolved by gentle heating in 38 ml (0.4 mole) of acetic anhydride, after which the solution was cooled to room temperature and treated with 8.4 ml (0.06 mole) of triethylamine. After 24 h, the mixture was poured over a mixture of 100 g of ice and 50 ml of concentrated HCl. The resulting precipitate was recrystallized from acetic acid or acetone.

B) Pyridinium Salt. A 6.36-ml (0.09 mole) sample of acetyl chloride and 35 ml of absolute pyridine were added at 0-5 deg C in a nitrogen atmosphere to a solution of 6.21 g (0.03 mole) of Ic in 120 ml of absolute dioxane. After 10 min, the yellow precipitate was removed by filtration and recrystallized as in method A.

2-Carboxybenzyl Methyl Ketone (VI). A 0.01-mole sample of salt II was heated at 90 deg C in 40 ml of a 10% NaOH solution for 10 min, during which the liberation of an amine was detected. The solution was cooled and acidified with HCl, and the colorless crystals were recrystallized from water.

3-Methyl-7-nitroisocoumarin (VII). A solution of 2.2 g (0.01 mole) of VI in 10 ml of 90% H_2SO_4 was allowed to stand for 24 h, after which it was diluted with water, and the colorless precipitate was removed by filtration, washed with water, and recrystallized from ethanol. Compound IVb was similarly obtained from Vb.

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