2-BENZOPYRYLIUM SALTS

XIV.* SYNTHESIS OF 3-ALKOXYCARBONYL-2-BENZOPYRYLIUM SALTS BY THE ACYLATION OF ESTERS OF 3,4-DIMETHOXYPHENYLPYRUVIC ACID

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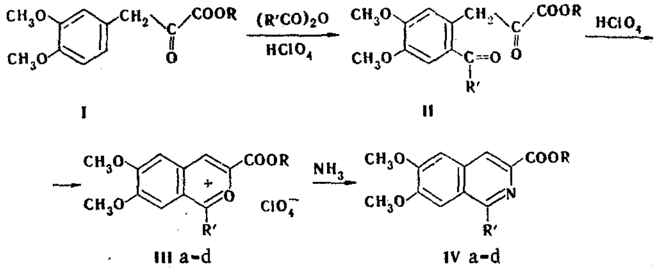
The acylation of esters of 3,4-dimethoxyphenylpyruvic acid with anhydrides of aliphatic acids in the presence of 70% $HClO_4$ leads to the formation of 3-alkoxycarbonyl-1-alkyl-6,7-dimethoxy-2-benzopyrylium salts which, on being boiled with sodium acetate in glacial acetic acid, are converted into 3-alkoxycarbonyl-1-alkyl-6,7-dimethoxyisoquinolines.

The study of the acylation of esters of aryl-substituted pyruvic acids is of interest within the framework of the development of a method for obtaining the previously almost unknown 3-alkoxycarbonyl-2-benzopyrylium salts, which are the starting materials for the synthesis of isoquinoline bases forming close analogs of some natural alkaloids.

It has recently been shown that 3-alkoxycarbonyl-2-benzopyrylium salts can be obtained in low yield by the acylation of ethyl 3,4-dimethoxyphenylglycidate [2].

We have performed the acylation of esters of 3,4-dimethoxyphenylpyruvic acid (I) with anhydrides of aliphatic acids in the presence of 70% $HClO_4$, which passes through the intermediate stage of the formation of the dicarbonyl compound (II), which then cyclizes under the action of the perchloric acid to the 2-benzopyrylium salt (III):



I II III a-d IV a-d

III, IV a $R=R'=CH_3$; b $R=CH_3$, $R'=C_2H_5$; c $R=C_2H_5$, $R'=CH_3$; d $R=R'=C_2H_5$

In attempts to acylate 3,4-dimethoxyphenylpyruvic acid under similar conditions, the reaction took place with pronounced resinification and it was impossible to isolate benzopyrylium salts.

The IR spectra of the salts obtained show strong absorption bands in the 1745-1730 cm^{-1} region (ν_{COOR}) and the 1630-1620 and 1550-1520 cm^{-1} regions, which correspond to the stretching vibrations (8a, 8b) of the pyrylium cation [3, 4]. It must be mentioned that in 2-benzopyrylium salts when the 3-CH_3 group is replaced by an alkoxycarbonyl group the main absorption bands of the pyrylium cation (8a, 8b) shift into the lower-frequency region. At the same time, the absorption bands of the aromatic ring in the 1600-1585 cm^{-1} region remain unchanged.

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*For Communication XIII, see [1].

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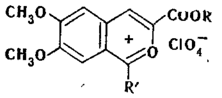
TABLE 1



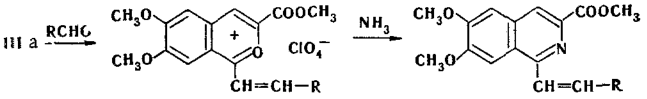
Compound	R	R¹	Decomp. point, °C	Empirical formula	Found, %			Calc., %			Yield, %
					C	H	Cl	C	H	Cl	
IIIa	CH_3	CH_3	198	$C_{14}H_{15}ClO_9$	46,8	4,4	9,9	46,3	4,1	9,8	41
IIIb	CH_3	C_2H_5	195*	$C_{15}H_{17}ClO_9$	47,6	4,8	9,6	47,8	4,5	9,4	22
IIIc	C_2H_5	CH_3	260	$C_{15}H_{17}ClO_9$	48,0	4,4	9,3	47,8	4,5	9,4	40
IIId	C_2H_5	C_2H_5	159*	$C_{16}H_{19}ClO_9$	48,8	4,7	9,8	49,2	4,9	9,1	16
Va	CH_3	$3,4(CH_3O)_2C_6H_3CH{=}CH$	246	$C_{23}H_{23}ClO_{11}$	53,9	4,9	7,0	54,1	4,5	7,0	98
Vb	CH_3	$3,4(CH_2O_2)C_6H_3CH{=}CH$	299	$C_{22}H_{19}ClO_{11}$	53,0	3,6	7,4	53,4	3,8	7,2	74
Vc	CH_3	$C_6H_5CH{=}CH$	272	$C_{21}H_{19}ClO_9$	57,9	4,6	7,8	58,2	4,4	7,9	80

*Correspond to literature figures [2].

When the salts (III) were treated with aqueous ammonia, and also when they were boiled with anhydrous ammonium acetate in glacial acetic acid, the 3-alkoxycarbonyl-1-alkyl-6,7-dimethoxyisoquinolines (IV) were formed in 70-85% yield. The IR spectra of the isoquinolines (IV) contained absorption bands in the following regions (cm^{-1}): 1730-1720 (ν_{COOR}), 1630-1620, 1550-1520 (ν of the pyridine ring of an isoquinoline), and 1275-1230, 1080-1020 (ν_{OCH_3}).

The perchlorate (IIIa) condenses with aromatic aldehydes to form in high yield intensely colored styryl derivatives of pyrylium salts (V). The IR spectra of the styryl derivatives (V) contain strong absorption bands in the following regions (cm^{-1}): 1720 (ν_{CO}), 1640-1630, 1520-1510 (ν of a pyrylium cation), 1600-1580 (ν of an aromatic ring), 1270-1280, 1050-1020 (ν_{OCH_3}), and 1100-1090 ($\nu_{ClO_4^-}$).

On being boiled with ammonium acetate in glacial acetic acid, the perchlorates (V) were converted into the corresponding isoquinolines (VI).



V VI

EXPERIMENTAL

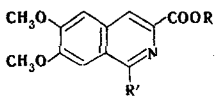
Esters of 3,4-Dimethoxyphenylpyruvic Acid (I). A mixture of 10 g of 3,4-dimethoxyphenylpyruvic acid [5], 150 ml of dry methanol, and 0.7 ml of concentrated H_2SO_4 was boiled for 5 h. The bulk of the methanol was slowly distilled off, the residue was poured onto ice, and the mixture was left in the refrigerator for 24 h. Then the precipitate that had deposited was filtered off and dried, and after a further day the mother liquor yielded a further small amount of the methyl ester in the form of a colorless low-melting amorphous substance. The total yield was 6.75 g (63%). Ethyl 3,4-dimethoxyphenylpyruvate was obtained similarly with a yield of 66%.

6,7-Dimethoxy-3-methoxycarbonyl-1-methyl-2-benzopyrylium Perchlorate (IIIa, Table 1). To 1.2 g of the ester (I) were added 3 ml of acetic anhydride and, carefully, in drops, 0.5 ml of 70% $HClO_4$. After a day, 5 ml of dry ether was added to the solution and the resulting precipitate was filtered off, washed with glacial acetic acid and with ether, and dried. Yield 0.75 g (41%), mp 198°C (from glacial acetic acid).

1-(3,4-Dimethoxystyryl)-6,7-dimethoxy-3-methoxycarbonyl-2-benzopyrylium Perchlorate (Va, Table 1). A mixture of 0.5 g (1.2 mmole) of (IIIa) and 0.32 g (2.4 mmoles) of veratraldehyde in 4 ml of glacial acetic acid was heated for 15 min. A dark red crystalline precipitate deposited; yield 0.69 g (98%), mp 246°C (decomp., from a mixture of glacial acetic acid and nitromethane). The other perchlorates (Table 1) were obtained similarly.

6,7-Dimethoxy-3-methoxycarbonyl-1-methylisoquinoline (IVa, Table 2). A mixture of 1 g of the perchlorate (IIIa) and 3 g of anhydrous ammonium acetate in 4 ml of glacial acetic acid was heated for 1 h. After cooling, the mixture was diluted with water and the precipitate that deposited was filtered off and dried; yield 0.6 g (85%), light-yellow crystals, mp 224°C (decomp., from ethanol). The isoquinolines (IVb-d and VI) (Table 2) were obtained similarly.

TABLE 2



Compound	R	R′	mp, °C	Empirical formula	Found, %			Calc., %			Yield, %
					C	H	N	C	H	N	
IVa	CH_3	CH_3	224*	$C_{14}H_{15}NO_4$	64,7	5,5	5,1	64,4	5,7	5,3	85
IVb	CH_3	C_2H_5	258	$C_{15}H_{17}NO_4$	66,0	6,1	5,0	66,2	6,2	5,1	70
IVc	C_2H_5	CH_3	146	$C_{15}H_{17}NO_4$	66,3	6,0	4,8	66,2	6,2	5,1	81
IVd	C_2H_5	C_2H_5	152	$C_{16}H_{19}NO_4$	66,2	6,5	4,6	66,4	6,6	4,8	66
IVe	H	CH_3	217	$C_{13}H_{13}NO_4$	63,2	5,4	5,1	63,2	5,3	5,7	90
VI	CH_3	$3,4(CH_3O)_2C_6H_3CH{=}CH$	175*	$C_{23}H_{23}NO_6$	67,5	5,7	3,5	67,5	5,6	3,4	92

*With decomposition.

6,7-Dimethoxy-1-methylisoquinoline-3-carboxylic Acid (IVe, Table 2). A mixture of 0.5 g of the isoquinoline (IVa) and 5 ml of a 20% ethanolic solution of caustic potash was boiled for 10 min. After cooling, the reaction mixture was neutralized with concentrated acetic acid to pH 7. A yellow precipitate deposited; yield 0.4 g (90%), mp 217°C (from ethanol).

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