REACTIONS OF HETEROCYCLIC CATIONS WITH NITROGEN-CONTAINING NUCLEOPHILES.

11.* REACTION OF 2,6-DIPHENYLPYRYLIUM PERCHLORATE WITH PRIMARY AMINES, HYDRAZINE, AND HYDROXYLAMINE

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The reaction of 2,6-diphenylpyrylium perchlorate with methylamine and various anilines in acetic acid leads to pyridinium salts; 3,4-bispyridinium perchlorates were obtained in dimethylformamide. The reaction of 2,6-diphenylpyrylium perchlorate with hydrazine and the sodium salt of hydroxylamine leads to 3-phenyl-5-phenacyl-2-pyrazoline and -2-isoxazoline.

2,6-Diphenylpyrylium perchlorate (I) was obtained a long time ago [2]. It is known that it reacts with ammonia, benzenesulfonic acid hydrazide, and amidines to give 2,6-diphenylpyridine [3, 4], pyrazoline derivatives [5], and pyrimidine derivatives [6], respectively. The reactions of salt I with primary amines have not been described.

We studied the reaction of salt I with methylamine and found that, like the reaction with 2,4,6-trisubstituted pyrylium salts [7], it takes place in the 2 position of the pyrylium ring to give N-methylpyridinium salt II.

The reaction of salt I with aniline and substituted anilines in acetic acid leads to the synthesis of N-arylpyridinium perchlorates III. However, bisperchlorates IV are isolated in addition to salts III when this reaction is carried out in dimethylformamide (DMF). The formation of the bisperchlorates can be explained by simultaneous hydrolysis of salt I in the presence of DMF, which was studied in detail in [8, 9]. According to the scheme proposed in [8, 9], the initial product is unsaturated ketone V, 2 moles of which undergo Michael condensation to give VI. The latter undergoes cyclization to 4H-pyran VII, which can react with the amines under the reaction conditions to give IV.

The IR spectra of IV do not contain the absorption bands that are characteristic for CO and OH groups, but the absorption of heteroaromatic cations is present. The PMR spectra of IVa,c contain two doublets of the protons in the 4 and 3 positions of the pyridinium ring at 8.81 and 7.96 ppm ($J = 12$ Hz), a singlet (2H) of the protons in the 3 and 5 positions at 7.72 ppm, a multiplet of the remaining aromatic protons at 6.05-7.48 ppm, and a slightly split singlet of six methyl protons of the OCH_3 groups at 3.32 ppm in the case of IVc.

Compounds IV were obtained alternatively by the reaction of 2,2,6,6-tetraphenyl-3,4-bispyrylium bisperchlorate (VIII) with the corresponding anilines. The reaction of salt I with excess amounts of aromatic amines does not suppress the hydrolysis. For example, the same amount of salt IVa is formed with a threefold amount of aniline; however, the yield of perchlorate IIIa is halved.

The reaction of salt I with p-phenylenediamine and p-aminophenol in acetic acid leads to hydroxy- and aminoarylpyridinium perchlorates (IIId,e). The pyridine nitrogen atom in 4-aminopyridine promotes exclusively the hydrolysis of salt I to give previously described diketone IX [8, 9] and 4-aminopyridinium perchlorate (X). (See top, following page.)

Salt I, like 2,4,6-trisubstituted pyrylium salts [10], forms pyrazoline XI upon reaction with hydrazine but under milder conditions. Hydroxylamine does not react with salt I, but its Na salt reacts with perchlorate I to give isoxazoline XII. The cyclic structure of XI and

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*See [1] for Communication 10.

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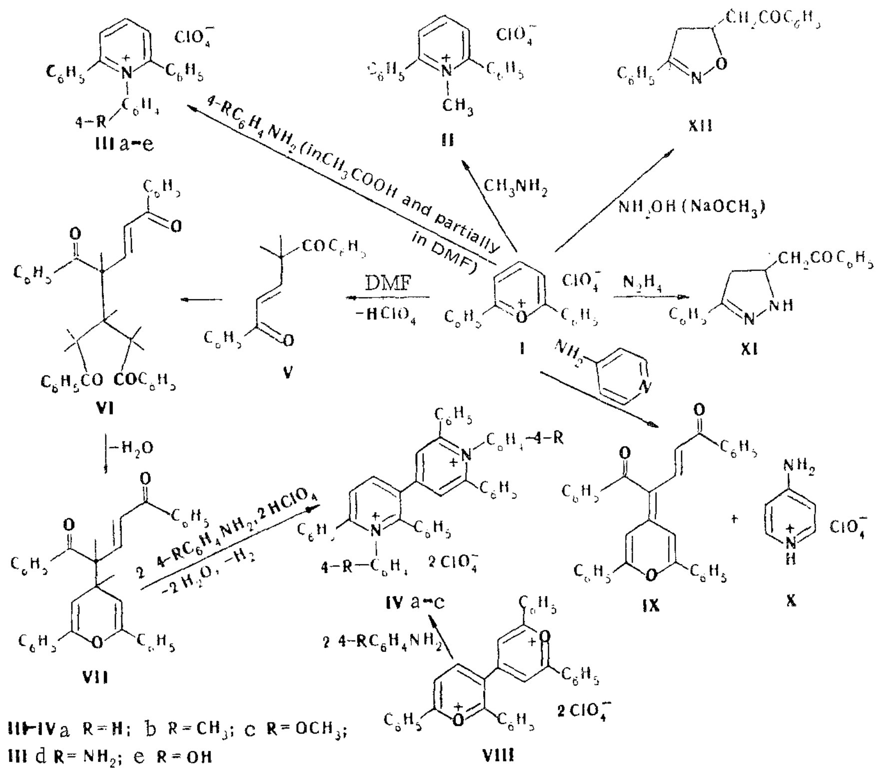

III–IVa R=H; b R=CH_3; c R=OCH_3;
III d R=NH_2; e R=OH

XII is confirmed persuasively by the IR spectroscopic data. Thus the spectrum of the pyrazoline contains an absorption band of the N–H bond of a secondary amino group at 3310 cm^{-1}, while the spectrum of the isoxazoline does not contain the absorption of the hydroxy group of an oxime at 3200–3600 cm^{-1}. The presence of phenacyl groupings is confirmed by intense bands at 1680 cm^{-1}.

EXPERIMENTAL

The IR spectra of mineral oil suspensions of the compounds were recorded with a Specord 71 IR spectrometer. The PMR spectra of solutions of the compounds in CF_3COOH were recorded with a Tesla 467C spectrometer (60 MHz) with hexamethyldisiloxane as the internal standard. The purity of the compounds obtained was monitored by means of thin-layer chromatography (TLC) on plates with silicic acid or aluminum oxide. Data on all of the compounds obtained are presented in Table 1.

Reaction of Perchlorate I with Methylamine. A 0.25-g (3.6 mmole) sample of methylamine hydrochloride and 0.29 g (3.6 mmole) of sodium acetate were pulverized and added to a suspension of 1 g (3 mmole) of perchlorate I in glacial acetic acid, the mixture was heated to the boiling point, and the sodium chloride was removed from the hot solution by filtration. The filtrate was cooled and treated with ether to precipitate 0.87 g of colorless II. PMR spectrum: 3.60 (s, 3H, CH_3), 7.30 (s, 10H, aromatic), 7.50 and 7.62 d (2H, 3-H and 5-H), and 8.17 ppm (t, 1H, 4-H).

Reaction of Perchlorate I with p-Toluidine in Acetic Acid. A mixture of 0.33 g (1 mmole) of perchlorate I and 0.13 g (1.2 mmole) of p-toluidine in 5 ml of glacial acetic acid was heated until the salt dissolved completely. The solution was cooled and treated with ether to precipitate 0.25 g of colorless IIIb. PMR spectrum: 1.78 (s, 3H, CH_3), 6.58 d and 6.88 d (14H, aromatic), 7.65 d and 7.75 d (2H, 3-H and 5-H), and 8.30 ppm (t, 1H, 4-H).

The reactions of perchlorate I with other amines, p-phenylenediamine, and p-aminophenol in acetic acid were carried out similarly.

Reaction of Salt I with Aniline in DMF in a Ratio of 1:1.3. A mixture of 1.98 g (6 mole) of perchlorate I and 0.72 g (7.8 mmole) of aniline in 20 ml of DMF was heated to the boiling point, after which it was cooled and treated with ether to precipitate an oil, which was crystallized by trituration with water. The precipitate (1.67 g) was washed repeatedly with warm ethanol to give 0.35 g of colorless IVa. Compound IIIa was precipitated from solution in ethanol by the addition of ether.

TABLE 1. Characteristics of the Synthesized Compounds

Compound	mp, °C	IR spectra, cm^{-1}	Found, %				Empirical formula	Calculated, %				Yield, %	
			C	H	Cl	N		C	H	Cl	N	in CH_3COOH	in DMF
II	218	1620, 1600, 1580, 1100	62,6	4,3	10,4	4,2	$C_{18}H_{16}ClNO_4$	62,4	4,6	10,3	4,1	80	—
IIIa	198—199	1625, 1600, 1580, 1100	67,9	4,7	8,4	3,3	$C_{23}H_{18}ClNO_4$	67,9	4,4	8,5	3,4	60	54
IIIb	210—211	1625, 1600, 1580, 1100	68,8	4,8	7,9	3,4	$C_{24}H_{20}ClNO_4$	68,5	4,8	8,2	3,3	59	49
IIIc	227—228	1625, 1600, 1580, 1320, 1260, 1100	66,0	4,9	7,8	3,3	$C_{24}H_{20}ClNO_5$	65,8	4,6	7,9	3,2	69	51
IIId	181—182	3480, 3390, 3240, 1620, 1600, 1580, 1100	65,6	4,8	8,1	6,6	$C_{23}H_{19}ClN_2O_4$	65,3	4,5	8,4	6,6	67	—
IIIe	227—228	3490, 1630, 1600, 1580, 1100	65,1	4,6	8,7	3,5	$C_{23}H_{18}ClNO_5$	65,2	4,3	8,4	3,3	63	—
IVa	315—316	1635, 1600, 1580, 1560, 1100	67,8	4,5	9,1	3,7	$C_{46}H_{34}Cl_2N_2O_8$	67,9	4,2	8,7	3,4	—	14
IVb	295—296	1635, 1600, 1580, 1560, 1100	68,8	4,9	8,1	3,6	$C_{48}H_{38}Cl_2N_2O_8$	68,5	4,6	8,4	3,3	—	16
IVc	287—288	1635, 1600, 1580, 1560, 1320, 1260, 1100	65,9	4,6	7,8	3,6	$C_{48}H_{38}Cl_2N_2O_{10}$	66,0	4,4	8,1	3,2	—	16
XI	123	3310, 1680, 1590, 1230, 760	76,9	5,9	—	10,9	$C_{17}H_{16}N_2O$	77,2	6,1	—	10,6	77 †	—
XII	129	1680, 1590, 1230, 760	77,3	5,9	—	5,2	$C_{17}H_{15}NO_2$	77,0	5,7	—	5,3	92 ‡	—

*The compounds were purified by crystallization from ethanol (II, IIIa-e, and XII), ethanol–acetonitrile (IVa-c), or benzene–petroleum ether (XI).

† The reaction was carried out in ethanol.

‡ The reaction was carried out in methanol.

The reactions of perchlorate I with the other anilines in DMF were carried out similarly.

Reaction of Perchlorate I with Aniline in DMF in a Ratio of 1:3. A mixture of 1 g (3 mmole) of salt I and 0.9 g (9 mmole) of aniline in 10 ml of DMF was heated to the boiling point, after which it was cooled and treated with ether. The liberated oil was crystallized by trituration with water. The precipitate (0.5 g) was washed repeatedly with warm ethanol to give 0.2 g (16%) of colorless IVa. Compound IIIa (24%) was precipitated from solution in ethanol by the addition of ether.

The reaction of perchlorate I with the other anilines in DMF in a ratio of 1:3 was carried out similarly to give IIIb,c and IVb,c in the same yields.

Reaction of Bisperchlorate VIII with Aniline. A 0.33-g (0.5 mmole) sample of bisperchlorate VIII, obtained by the method in [9], was refluxed with 0.14 g (1.5 mmole) aniline in 5 ml of DMF for 2 h, after which it was cooled and treated with ether to precipitate an oil, which was crystallized by trituration with water to give 0.22 g (55%) of a colorless salt with mp 329°C (from ethanol with acetonitrile). No melting point depression was observed for a mixture of this product with IVa.

The reaction of bisperchlorate VIII with the other anilines was carried out similarly; salt IVb was obtained in 60% yield, and salt IVc was obtained in 57% yield.

Reaction of Perchlorate I with 4-Aminopyridine. A 1-g (3 mmole) sample of perchlorate I was heated with 0.34 g (3.6 mmole) of 4-aminopyridine in 15 ml of glacial acetic acid until it dissolved, after which the solution was cooled and treated with ether to give 0.62 g (quantitative yield) of 4-aminopyridinium perchlorate with mp 271°C (from ethanol) (mp 271-272°C [11]). The solvent was evaporated to give 0.5 g (74%) of orange-red diketone IX with mp 216-217°C (mp 220°C [9]).

3-Phenyl-5-phenacyl-2-pyrazoline (XI). A 0.25-ml (4 mmole) sample of hydrazine hydrate was added with stirring to a suspension of 0.67 g (2 mmole) of perchlorate I in alcohol, during which salt I dissolved, and pyrazoline XI subsequently precipitated. The reaction mixture was diluted with an equal amount of water, and 0.4 g of pale-yellow crystals was removed by filtration.

3-Phenyl-5-phenacyl-2-isoxazoline (XII). A mixture of 0.21 g (3 mmole) of hydroxylamine hydrochloride and 0.32 g (6 mmole) of sodium methoxide, obtained from 0.14 g of sodium in 10 ml of methanol, was refluxed until it dissolved completely, after which the solution was cooled. A 0.67-g (2 mmole) sample of perchlorate I was added to the reaction mixture, during which salt I dissolved, and yellow isoxazoline XII subsequently precipitated. The mixture was diluted with an equal amount of water, and 0.49 g of yellow prisms was removed by filtration.

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REACTIONS OF HETEROCYCLIC CATIONS WITH NITROGEN-CONTAINING NUCLEOPHILES.

12.* REACTION OF PYRYLIUM SALTS WITH AZOMETHINES

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The reaction of pyrylium salts with azomethines leads to the formation of styrylpyrylium, styrylpyridinium, and 4-arylbenzylaminopyrylium salts. The reaction of the latter with ammonia and amines gave pyridines and pyridinium salts with a tertiary amino group as a substituent.

We have previously shown that 2,4,6-triarylpyrylium salts react in dimethylformamide (DMF) with azomethines in the 2 position of the ring to give, after ring opening and recyclization, the corresponding pyridinium salts, whereas 2-methyl-substituted salts form 1-aryl-2-styrylpyridinium perchlorates [2, 3].

In the present research in the case of 1,3-dimethyl-6,7-dimethoxy-2-benzopyrylium perchlorate (I) we established that azomethines II initially attack the ring methyl group in the 1 position. (The PMR spectrum of III does not contain the singlet at δ 2.6 ppm that is characteristic for this methyl group.) The liberated aniline then reacts with styrylpyrylium salt III to give isoquinolinium salt IV. In contrast to the reactions of triarylpyrylium salts with azomethines, this reaction takes place in ethanol. In the case of initial attack on the ring the final products would have been the corresponding N-arylisoquinolinium salt and benzaldehyde. However, in separate experiments we showed that methylpyridinium and isoquinolinium salts do not react with benzaldehyde in alcohol. At the same time, salt III and 2-styryl-4,6-diphenylpyrylium perchlorate (V) readily form IV and VI with aniline in alcohol solution.

It is interesting to note that styrylpyrylium salts III and V react with azomethines in the same way as triarylpyrylium salts not only in dimethylformamide (DMF) but also in ethanol (in the latter the degree of conversion is 50% after 1 h).

4-Unsubstituted 2,6-diphenylpyrylium salt VII in acetic acid undergoes attack by azomethines in the 2 position, which leads to the previously described 1,2,6-triarylpyridinium

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*See [1] for Communication 11.
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