

REACTIONS OF CYCLAMMONIUM CATIONS

XXIII.* PYRIDO[1,2-b][1,2,4]TRIAZINIUM SALTS.

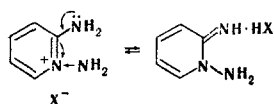
SYNTHESIS AND SOME REACTIONS

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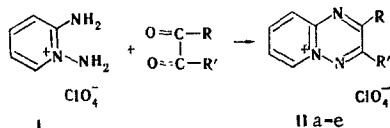
The reaction of 1,2-diaminopyridinium salts with α -dicarbonyl compounds or α -halogeno ketones forms pyrido[1,2-b][1,2,4]triazinium salts. A methyl group present in position 2 of one of these salts condenses with aldehydes, giving styryl derivatives and reacts with orthoesters to give cyanines.

The electron-accepting influence of a pyridinium cation on an amino group present in position 2 or 4 of the ring includes two effects: the negative inductive effect of the quaternary nitrogen atom and a strong negative conjugation effect, which leads to a marked fall in the nucleophilicity of these groups in quaternary 2(4)-aminopyridinium salts. In contrast to this, it is mainly the inductive effect of the pyridinium cation that is transmitted to an N-amino group, as to other substituents attached to the heteroatom [1,2], as a consequence of which in N-aminopyridinium salts the amino group shows a greater nucleophilicity than in the 2(4)-aminopyridines and, all the more, than in their quaternary salts [3]. This explains the relatively high reactivity of the N-amino groups in 1,2-diaminopyridinium salts in reactions with carbonyl compounds that we have observed [3, 4]. The greater protonic activity of the $C-CH_3$ group than of the $\geq N^+-CH_3$ group in the 1,2-dimethylpyridinium cation [5] is one of the closest examples of such an influence. The lowering of the π -electron density in positions 2 and 4 of the pyridinium nucleus and, consequently, a shift of the p-electrons from NH_2 groups present in these positions simultaneously causes a pronounced delocalization of the positive charge of the heteroatom, which leads to a decrease in its -I effect and, as a result, to an even greater increase in the nucleophilicity of the $N-NH_2$ group as compared with an $C-NH_2$ group:



However, such salts can also react at the 2-amino group. For example, with carboxylic acids or acid halides they form sym-triazolo[1,5-a]pyridines [6, 7], which is apparently connected with a reduction in the activation energy of the transition state on intramolecular cyclization.

We have succeeded in showing that 1,2-diaminopyridinium salts which, under various conditions, form Schiff's bases only through one NH_2 group (in reactions with aromatic aldehydes [4]) readily condense with 1,2-dioxo compounds, forming the bicyclic heteroaromatic pyrido[1,2-b][1,2,4]triazinium system (a brief communication on this has been published previously [8]).



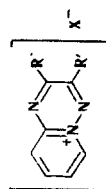
II a $R=R'=CH_3$; b $R=R'=H$, c $R=ClH_3$, $R'=H$, d $R=R'=C_6H_5$; e $R=C_6H_5$, $R'=H$.

* For Communication XXII, see [1].

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TABLE 1



Comp.	R	R'	X	mp, °C (from acetic acid)	R _f	Empirical formula	Found, %			Calculated, %			Yield, %	
							C	H	halogen	N	C	H	halogen	N
IIa	CH ₃	CH ₃	ClO ₄	243—244	0.61	C ₉ H ₁₀ ClN ₃ O ₄	41.9	4.2	13.9	16.2	41.6	3.9	13.6	16.2
IIb	H	H	ClO ₄	225—226	0.61	C ₇ H ₆ ClN ₃ O ₄	36.6	3.0	15.3	18.7	36.3	2.6	15.3	18.1
IIc	CH ₃	H	ClO ₄	198—199	0.67	C ₈ H ₁₂ ClN ₃ O ₄	38.9	3.3	15.0	17.8	39.1	3.2	14.4	17.1
IId	C ₆ H ₅	C ₆ H ₅	ClO ₄	259—260 ^a	0.68	C ₁₃ H ₁₄ ClN ₃ O ₄	59.8	4.0	9.0	11.2	59.4	3.6	9.2	10.9
IIe	CH ₃	CH ₃	HSO ₄ ·I ₂	178 ^a	0.80	C ₉ H ₁₁ I ₂ N ₃ SO ₄	21.3	2.2	50.1	8.5	21.5	2.1	49.6	8.2
II f	CH ₃	CH ₃	I ₃	181—182 ^a	0.78	C ₉ H ₁₀ I ₃ N ₃	20.3	2.2	69.6	7.9	19.9	1.8	70.3	7.7

^aFrom ethanol. ^bFound, %: S 6.3. Calculated, %: S 6.2.

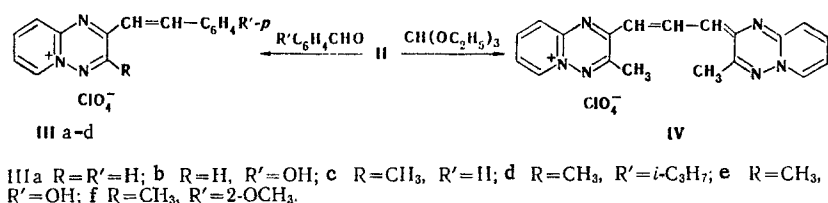
TABLE 2. Styryl Derivatives (III)

Comp.	R	R'	mp, °C (from acetonitrile)	R _f ^a	Empirical formula	Found, %			Calculated, %			Yield, %	
						C	H	Cl	N	C	H	Cl	N
IIIa	H	H	237—238	0.6	C ₁₆ H ₁₂ ClN ₃ O ₄	53.2	3.9	10.8	12.6	53.9	3.6	10.6	12.6
IIIb	H	OH	273—274 ^b	0.62	C ₁₅ H ₁₂ ClN ₃ O ₅	52.1	3.7	10.4	12.4	51.5	3.4	10.1	12.0
IIIc	CH ₃	H	226—227 ^b	0.65	C ₁₆ H ₁₄ ClN ₃ O ₄	55.4	4.4	9.6	12.8	55.2	4.0	10.2	12.1
IIId	CH ₃	<i>i</i> -C ₃ H ₇	220—221	0.69	C ₁₉ H ₂₀ ClN ₃ O ₄	58.3	5.4	9.7	11.2	58.5	5.1	9.1	10.7
III g	CH ₃	2-OCH ₃	219 ^c	0.67	C ₁₇ H ₁₆ ClN ₃ O ₅	—	—	—	11.2	—	—	—	11.2

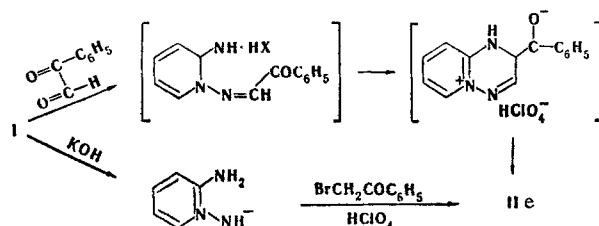
^aResults of chromatography on Al₂O₃. On Leningrad mill paper of type "S" ["fast"] with butanol—acetic acid—water (10:1:3) as the mobile phase it gives R_f 0.42–0.47. ^bFrom ethanol. ^cFrom acetic acid.

The condensation of the salts (I) with unsymmetrical dioxo compounds such as methyl- and phenylglyoxals could be expected to give two isomers. However, the results of paper and thin-layer chromatography have shown the presence of only one isomer, to which, on the basis of its PMR spectrum, we have assigned the structure (IIc,d). In the PMR spectrum of the salt (IIa) there are the signals of the four protons of the pyridine nucleus: doublets of the H atoms in positions 6 and 9 at δ 9.13 and 8.46 ppm ($J = 8$ Hz), triplets of 7-H and 8-H in the 8.15 and 8.68 ppm region ($J = 8$ Hz), and also the singlets of CH_3 groups at 2.91 and 2.97 ppm. The second apparently corresponds to the group in position 2, since it is located in the para position to the quaternary nitrogen atom and in the α position to a tertiary heteroatom, i.e., it is attached to the carbon atom of the triazinium ring having the lowest π -electron density. In the spectrum of substance (IIc) one signal of a CH_3 group is found in the 3.06 ppm region and the singlet of 3-H in the 7.24 ppm region.

Both these compounds (IIa and IIc) readily condense with aromatic aldehydes forming styryl derivatives with similar UV spectra (III, $\text{R}' = \text{OH}$, λ_{max} 260, 460 nm; $\log \epsilon$ 3.9, 4.4), while the salt (IIa) does not react with a second molecule of aldehyde even under severe conditions. The presence of the isomeric substance could not be detected either chromatographically or spectrophotometrically. The methyl group in position 2 of the salt (IIa) proved to be sufficiently active to react with orthoesters to form cyanine dyes.



Thus, it must be considered that the formation of salts of type (II) takes place as the primary attack of the more nucleophilic $\text{N}-\text{NH}_2$ group on the more electrophilic and sterically accessible center of the methyl- or phenylglyoxal residue — the formyl group — with the subsequent condensation and dehydration of the resulting compound under the influence of the perchloric acid. A 1,2-diaminopyridinium salt apparently reacts with α -halogeno ketones by a similar mechanism, since we also obtained compound (IIe) with phenacyl bromide. The same compound (IIe) was obtained by the reaction of (I) with isonitrosoacetophenone.



1,2-Diaminopyridinium salts also condense readily with some o-quinones; for example, with phenanthrenequinone they form a pyrido[1,2-b]phenanthro[9,10-e][1,2,4]triazinium salt.

When the condensation of 1,2-diaminopyridinium iodide with biacetyl was performed in the presence of sulfuric or hydrochloric acid, the molecular compounds with iodine (IIe,f) of the sulfate or iodide formed were isolated. Under the action of perchloric acid, these salts were readily converted into the perchlorate (IIa). The IR spectra of these compounds, like the other salts (II), lacked the characteristic absorption bands of amino and imino groups.

EXPERIMENTAL

The IR spectra were taken on a UR-10 spectrophotometer in tablets with potassium bromide, and the UV spectra on an SF-4 instrument in ethanol. The PMR spectra were taken on a Bruker H \times 90 instrument in trifluoroacetic acid with TMS as internal standard. Unless stated otherwise, chromatography was performed in a thin layer of alumina of activity grade II in the solvent system isopropanol-chloroform (1:1), and the spots were revealed with iodine vapor.

Pyrido[1,2-b]phenanthro[9,10-e][1,2,4]triazinium Perchlorate. A solution of 0.3 g (1.5 mmole) of (I) in 20 ml of ethanol was treated with 0.3 g (1.5 mmole) of phenanthrenequinone and 1 ml of 70% perchloric acid. The mixture was boiled for an hour, and 0.5 g (90%) of orange crystals were isolated with mp 354°C [from dimethylformamide-isopropanol (1:1)]; R_f 0.67 (Al_2O_3). Found, %: C 59.9; H 3.6; Cl 9.2; N 11.2. $C_{19}H_{12}ClN_3O_4$. Calculated, %: C 59.7; H 3.1; Cl 9.3; N 11.0.

The condensation with ninhydrin took place similarly, forming a single substance with the composition $C_{13}H_8ClN_3O_5$, mp 295–296°C [from dimethylformamide-isopropanol (1:1)]; R_f 0.68. The IR spectrum has the bands of a carbonyl group in the 1750 cm^{-1} region, of C=C and C=N bonds at 1622 and 1658 cm^{-1} , of a ring at 1590 cm^{-1} , and of the ClO_4^- anion at 1100 cm^{-1} . Found, %: C 50.4; H 2.8; Cl 10.5; N 12.0. $C_{13}H_8ClN_3O_5$. Calculated, %: C 50.4; H 2.4; Cl 10.6; N 12.6. Semicarbazone, mp 274–275°C (from water). Found, %: N 21.9. $C_{15}H_{11}ClN_6O_5$. Calculated, %: N 21.5. On the basis of the fact that in the salt (I) it is apparently the more active 1-amino group that reacts first, and in ninhydrin it is the carbonyl group in position 2 [9], we assigned to the compound obtained the structure of a dihydropyrido[1,2-b]indeno[1,2-e]-[1,2,4]triazinium perchlorate. The structure of this compound was not established in more detail.

2-Phenylpyrido[1,2-b][1,2,4]triazinium Perchlorate (IIe). A. Similarly, 0.6 g (3 mmoles) of (I) and 0.5 g (3 mmoles) of phenylglyoxal hydrate in the presence of perchloric acid gave 0.45 g (45%) of substance (IIe), mp 302°C (from glacial acetic acid); R_f 0.65. Found, %: N 13.7. $C_{13}H_{10}ClN_3O_4$. Calculated, %: N 13.6. Substance (IIe) was also obtained with a yield of 27% by boiling (I) with isonitrosoacetophenone in ethanol in the presence of perchloric acid. The other pyrido[1,2-b][1,2,4]triazinium salts (Table 1) were obtained similarly. The chromatography of these salts on type KSK silica gel with ethanol-chloroform-acetic acid (1:1:2) as the stationary phase showed the presence of a single spot with R_f 0.34 \pm 0.03.

B. With cooling to 0 to –5°C and stirring, 0.22 g (4 mmoles) of potassium hydroxide was added to a solution of 0.84 g (4 mmoles) of (I) in 15 ml of methanol, the mixture was stirred for an hour, the precipitate of potassium perchlorate that had deposited was filtered off, and with cooling and stirring a solution of 0.79 g (4 mmoles) of phenacyl bromide in 15 ml of ethanol was added dropwise to the filtrate. After 2 h, 1.5 ml of perchloric acid was added to the reaction mixture and the solvent was distilled off to give 0.25 g (20%) of substance (IIe), mp 302°C. A mixture with a known sample gave no depression of the melting point, and their IR spectra were identical: 1616 cm^{-1} ($\nu_{C=N}$), 1580 cm^{-1} (ν_{ring}), 1100 cm^{-1} ($\nu_{ClO_4^-}$).

2-(p-Hydroxystyryl)-3-methylpyrido[1,2-b][1,2,4]triazinium Perchlorate (IIIe). To a solution of 0.3 g (1.1 mmole) of the salt (IIa) in 5 ml of acetonitrile were added 0.15 g (1.2 mmole) of p-hydroxybenzaldehyde and 1–2 drops of 70% perchloric acid. The mixture was boiled on the water bath for 1 h. The red crystals that had deposited were filtered off to give 0.2 g (50%) of compound (IIIe), mp 266°C (from acetonitrile). Found %: C 53.3; H 4.2; Cl 10.1; N 11.7. $C_{19}H_{14}ClN_3O_5$. Calculated, %: C 52.8; H 3.8; Cl 9.7; N 11.5.

The other styryl derivatives (III) (Table 2) were obtained similarly.

Bis(3,3-dimethylpyrido[1,2-b][1,2,4]triazine)trimethinecyanine Perchlorate (IV). To a solution of 0.5 g (2 mmoles) of the salt (IIa) in 15 ml of glacial acetic acid was added 3 ml of orthoformic ester, and the mixture was boiled for 40 min. Blue-green crystals with mp 223–224°C (from ethanol) separated out in an amount of 0.35 g (42%). UV spectrum: λ_{max} 305, 620 nm; log ϵ 4.1, 4.4. Found, %: C 52.8; H 4.6; Cl 8.4; N 19.3. $C_{19}H_{17}ClN_6O_4$. Calculated, %: C 53.1; H 4.2; Cl 8.2; N 19.5.

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