

CONDENSATION OF 2-AMINOPYRIDINE SALTS WITH β -CHLOROVINYL ALDEHYDES

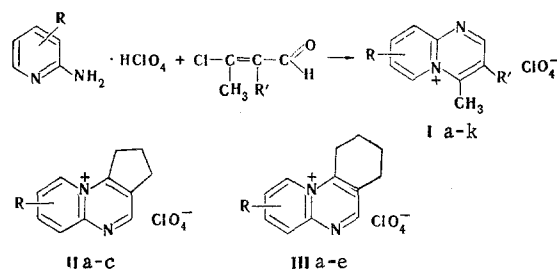
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UDC 547.859'822.7:542.953

2-Aminopyridine perchlorates react with β -chlorovinyl aldehydes to give pyrido[1,2-*a*]-pyrimidinium salts, the structures of which were confirmed by PMR spectra. The reaction products form polymethine dyes through the methyl or methylene group in the α position relative to the bridge nitrogen atom in the pyrimidine ring.

Isomeric products with a substituent in the α [1, 2] or γ [3] position may be formed in the reaction of 2-aminoheterocycles with β -chlorovinyl ketones; as a rule, mixtures of isomers are obtained.

β -Chlorovinyl aldehydes, which are readily obtained via the Arnold-Zemlička method [4], react with 2-aminopyridine salts in alcohol or aqueous alcohol solution to give pyrimidinium salts Ia-k.



1-Formyl-2-chlorocyclopentene and 1-formyl-2-chlorocyclohexane undergo this reaction to give cyclopenta[1',2':4,5]pyrimido[2,3-*a*]pyridinium (IIa-c) and 1,2,3,4-tetrahydropyrido[1,2-*a*]quinazolinium (IIIa-e) derivatives, respectively.

The structure of salts I-III was confirmed by their PMR spectra. The structure was chosen on the basis of the chemical shifts of the methyl and methylene groups bonded to the pyrimidine ring. An additional factor for Ia in the J value of the pyrimidine protons (5 Hz), which is characteristic for $J_{\beta-\gamma}$ in such condensed pyrimidine compounds [3, 6]. The 4-CH₃ chemical shifts are found between 2.7 and 2.8 ppm; this corresponds to finding a methyl group in the α position relative to the bridge nitrogen atom in the pyrimidine ring in pyrido[1,2-*a*]pyrimidinium salts [5]. The chemical shifts for the analogous methylene group are found at 3.4 ppm for II and at 3.0 ppm for III. The 3-methyl groups in I give signals at 2.4 ppm.

The salt of 2,3-diamino-5-bromopyridine reacts with β -chlorovinyl aldehydes in the same way as other 2-aminopyridine derivatives to give pyrido[1,2-*a*]pyrimidinium salts. The reaction proceeds analogously with β -diketones and β -chlorovinyl ketones. 2-Amino-6-methylpyrimidine perchlorate does not give pyridopyrimidinium salts in this reaction as in the reaction with β -diketones, apparently because of steric hindrance created by the methyl group in the 6 position.

Compound Ia is identical to the product obtained in [1] by condensation of 2-aminopyridine with methyl β -chlorovinyl ketone, which is an isomer of 3-chloro-2-butenal. Since methyl β -chlorovinyl ketone and the isomeric 3-chloro-2-butenal form the same product (Ia) under identical conditions, it can be assumed that these two reactions proceed via different mechanisms. The chlorine atom is more active in the chloro

T. G. Shevchenko Kiev State University. Translated from *Khimiya Geterotsiklicheskikh Soedinenii*, No. 2, pp. 242-244, February, 1973. Original article submitted July 19, 1971.

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TABLE 1. Characteristics of the Compounds Obtained

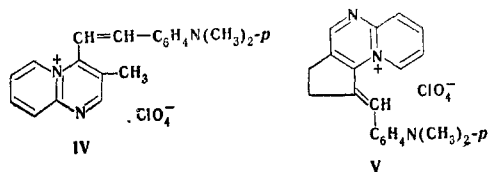
Comp.	R	R'	mp, °C*	Empirical formula	Cl, %		Yield, %
					found	calc.	
Ia	H	H	237	C ₉ H ₉ ClN ₂ O ₄	14,7	14,5	70
Ib	9-CH ₃	H	176	C ₁₀ H ₁₁ ClN ₂ O ₄	13,6	13,7	83
Ic	8-CH ₃	H	164	C ₁₀ H ₁₁ ClN ₂ O ₄	13,7	13,7	79
Id	7,9-Dibromo	H	247	C ₉ H ₇ Br ₂ ClN ₂ O ₄	6,9 †	7,0	53
Ie	H	CH ₃	232	C ₁₀ H ₁₁ ClN ₂ O ₄	13,8	13,7	67
If	9-CH ₃	CH ₃	215	C ₁₁ H ₁₃ ClN ₂ O ₄	13,2	13,0	81
Ig	8-CH ₃	CH ₃	203	C ₁₁ H ₁₃ ClN ₂ O ₄	13,3	13,0	17
Ih	7-Br	CH ₃	248	C ₁₀ H ₁₀ BrClN ₂ O ₄	8,3 †	8,3	76
Ii	7,9-Dibromo	CH ₃	225	C ₁₀ H ₉ Br ₂ ClN ₂ O ₄	6,9 †	6,7	93
Ij	7-Br	CH ₃	263	C ₁₀ H ₉ BrClN ₂ O ₆	11,3 †	11,0	23
Ik	9-NO ₂	CH ₃	188	C ₁₀ H ₁₁ BrClN ₂ O ₄	11,9 †	11,7	74
	7-Br						
IIa	9-NH ₂	—	223	C ₁₁ H ₁₁ ClN ₂ O ₄	13,0	13,1	36
	7-Br						
IIb	8-Br	—	212	C ₁₁ H ₁₀ BrClN ₂ O ₄	8,0 †	8,0	64
IIc	6,8-Dibromo	—	236	C ₁₁ H ₉ Br ₂ ClN ₂ O ₄	6,7 †	6,5	42
IIIa	H	—	248	C ₁₂ H ₁₃ ClN ₂ O ₄	12,7	12,5	65
IIIb	7-CH ₃	—	266	C ₁₃ H ₁₅ ClN ₂ O ₄	12,0	11,8	69
IIIc	9-Br	—	240	C ₁₂ H ₁₂ BrClN ₂ O ₄	7,6 †	7,7	51
IIId	7,9-Dibromo	—	220	C ₁₂ H ₁₁ Br ₂ ClN ₂ O ₄	6,7 †	6,3	68
IIIe	7-NH ₂	—	223	C ₁₂ H ₁₃ BrClN ₂ O ₄	11,0 †	11,1	77
	9-Br	—					

*Compounds Ia-d, g, i, j, IIa-c, IIIa-c,e were recrystallized from methanol; Ie,h were recrystallized from water; If was recrystallized from aqueous methanol, and Ik and IIId were recrystallized from ethanol.

† N, %.

ketone; the initial reaction is alkylation either at the cyclic nitrogen atom or at the amino group, after which the carbonyl group reacts with the evolution of a water molecule and closing of the pyrimidine ring. This sort of mechanism explains the formation of two isomers. In β -chlorovinyl aldehydes, on the other hand, the carbonyl group is apparently more active and reacts with the amino group to form an azomethine, after which the intermediate undergoes intramolecular alkylation with closing of the pyrimidine ring. In this case, the formation of one isomer with an unsubstituted γ position with respect to the bridge nitrogen atom is possible.

Salts I-III contain active methyl or methylene groups in the α position relative to the bridge quaternary nitrogen atom and can give polymethine dyes. For example, styryl dyes IV and V, respectively, were obtained from Ie and IIa and p-dimethylaminobenzaldehyde.



EXPERIMENTAL

The PMR spectra of trifluoroacetic acid solutions were recorded with a Varian A-60A spectrometer; the chemical shifts are presented on the δ scale with respect to a hexamethyldisiloxane internal standard.

Condensation of 2-Aminopyridine Perchlorates with β -Chlorovinyl Aldehydes. The appropriate 2-aminopyridine perchlorate was dissolved by heating in the minimum amount of alcohol, and a 10-20% excess of β -chlorovinyl aldehyde was added to the solution. (One can use the 2-aminopyridine base and add an equimolecular amount or excess of an aqueous solution of 57% perchloric acid.) The mixture was refluxed on a water bath for a few minutes and allowed to stand overnight at room temperature. The precipitate was removed by filtration and washed with alcohol and ether (Table 1).

4-(p-Dimethylaminostyryl)-3-methylpyrido[1,2-a]pyrimidinium Perchlorate (IV). A solution of 0.2 g (0.78 mmole) of Ie and 0.13 g (0.87 mmole) of p-dimethylaminobenzaldehyde in 5 ml of acetic anhydride was refluxed for 20 min. The precipitated dye was removed by filtration and washed with alcohol and ether to give 0.20 g (71%) of red crystals with mp 255° (from ethanol), λ_{\max} 480 nm, $\log \epsilon$ 4.68 (in alcohol). Found, %: Cl 9.7. C₁₂H₂₀ClN₃O₄. Calculated, %: Cl 9.7.

1-(p-Dimethylaminostyryl)cyclopenta[1',2':4,5]pyrimido[2,3-*a*]pyridinium Perchlorate (V). A solution of 0.3 g (1.1 mmole) of IIa and 0.24 g (1.6 mmole) of p-dimethylaminobenzaldehyde in 3 ml of acetic anhydride was refluxed for 10 min. The precipitated dye crystals were removed by filtration and washed with ether to give 0.3 g (68%) of a product with mp 154° (from alcohol), λ_{max} 530 nm, log ϵ 4.21 (in alcohol). Found, %: Cl 8.5. $\text{C}_{20}\text{H}_{20}\text{ClN}_3\text{O}_4$. Calculated, %: Cl 8.8.

LITERATURE CITED

1. A. N. Nesmeyanov, M. I. Rybinskaya, and N. K. Bel'skii, Dokl. Akad. Nauk SSSR, 113, 343 (1957).
2. A. N. Nesmeyanov and M. I. Rybinskaya, Dokl. Akad. Nauk SSSR, 118, 297 (1958).
3. S. I. Shul'ga and V. A. Chuiguk, Ukr. Khim. Zh., 37, 257 (1971).
4. Z. Arnold and J. Zemlička, Coll. Czech. Chem. Commun., 24, 2385 (1959).
5. A. M. Khmaruk, Yu. M. Volovenko, and V. A. Chuiguk, Ukr. Khim. Zh., 38, 262 (1972).
6. L. W. Werbel, A. Curry, E. F. Elslager, C. A. Gess, M. P. Hutt, and C. Gonstron, J. Heterocycl. Chem., 6, 787 (1969).