tophenone V in 30 ml of methyl formate. After 10-15 min, the mixture was heated to 20-25°, and stirring was continued for 4 h, after which the solvent was evaporated. A mixture of 1 ml of glacial acetic acid, 1.5 ml of concentrated hydrochloric acid, and 1-2 ml of water was added to the dry residue until the pH of the mixture was 0.5-1. The oil that formed initially solidified completely. A solution or suspension of the product in 12 ml of alcohol was refluxed for 40 min with 0.2 ml of concentrated hydrochloric acid, and the solid material was removed by filtration from the cold solution and washed free of acid to give 0.4 g (84%) of product.

2-Trifluoromethyl-3-(1-phenyl-4-pyrazolyl)-5-hexyl-7-alkoxychromones (XVIII, XIX). An acetone solution of 1 mmole of chromone X and 4-5 mmole of dimethyl sulfate or ethyl iodide was stirred at 50-60° with 3 mmole of freshly calcined potassium carbonate for 4-5 h (the end of the reaction was determined by means of TLC), after which the hot solution was filtered. The solvent was evaporated, and the residue was washed with a small amount of alcohol.

3-(1-Phenyl-4-pyrazolyl)-7-acetoxychromones (XX, XXI). A 5-mmole sample of acetic anhydride was added to a warm solution of 1 mmole of the chromone (XVI, XVII) in the minimum volume of pyridine, and the mixture was allowed to stand at room temperature for 24 h, after which the product was removed by filtration and washed on the filter with ether.

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SYNTHESIS OF Δ^2-IMIDAZOLINES IN ETHYLENE GYLCOL

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The use of ethylene glycol as the solvent in the condensation of carboxylic acid and their derivatives with ethylenediamine or its salts makes it possible to obtain various Δ^2-imidazolines in good yields. The ionization constants and the characteristic frequencies of the IR spectra of the synthesized compounds are presented.

Δ^2-Imidazolines have valuable pharmacological properties and are used as starting materials for the preparation of medicinals [1, 2]. However, the physicochemical properties of Δ^2-imidazolines have not been adequately studied. The aim of the present research consisted in the development of a convenient method for the synthesis of these compounds and the determination of their ionization constants and the characteristic frequencies of their IR spectra.

A promising method for the synthesis of Δ^2-imidazolines based on the condensation of carboxylic acids with ethylenediamine (EDA) or its salts has certain disadvantages – the necessity of heating to high temperatures or under pressure and the low yields of final products [3-5]. We have established that these difficulties can be eliminated if the reaction is carried out in ethylene gylcol.

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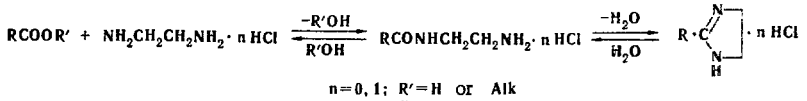


n = 0, 1; R′ = H or Alk

A solution of the carboxylic acid and EDA or its hydrochloride in ethylene glycol is refluxed for several hours, after which the resulting water and part of the solvent are slowly removed by distillation. The yields of the Δ^2-imidazolines are higher if EDA hydrochloride is used, since in this case N,N'-diacylethylenediamines are not formed.

In addition to the carboxylic acids, one can use their esters and, under certain conditions, their nitriles. Thus 2-phenyl-Δ^2-imidazoline is formed in 92% yield when benzonitrile is heated with EDA in ethylene gylcol at 170°C (see [6]). When nitriles of acids that are stronger than benzoic acid are used, imidazolines are obtained in good yields even when the reactants are refluxed in methanol. We were able to synthesize XX in low yield only from 2,4-dichlorobenzoic acid (Table 1). Attempts to use 2,4-dichlorobenzonitrile for this purpose were unsuccessful. This phenomenon is evidently due to steric hindrance, since the similarly constructed 4-chlorophenylimidazoline (X) was obtained in good yield when the corresponding nitrile or acid was used. This method makes it possible to synthesize various Δ^2-imidazolines, including N-substituted derivatives. For example, N-benzylimidazoline XXV was obtained in 91% yield from p-toluic acid and N-benzylethylenediamine.

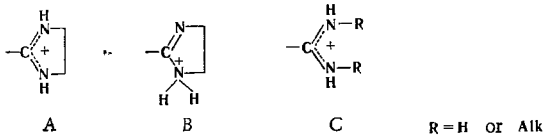
The condensation of EDA with carboxylic acids can also be carried out in nitrobenzene or dichlorobenzene. However, it was experimentally established that the initially formed salt of the carboxylic acid and EDA must dissolve on heating in the indicated solvents and that refluxing and subsequent azeotropic removal of the water by distillation must be effected twice in order to obtain satisfactory results.

The yields and properties of the synthesized Δ^2-imidazolines (I-XXV) and their salts are presented in Table 1.

In a number of cases in the preparation of Δ^2-imidazolines one obtains similar (with respect to the results of elementary analysis and physicochemical properties) N-substituted amidines [6-8]. The characteristic frequencies of the IR spectra of the imidazolines and their salts (Table 2)* make it possible to distinguish two types of compounds (see [2, 8]).

The spectra of the Δ^2-imidazolines contain a strong absorption band of a C=N group at 1585-1625 cm^{-1}. Its position is not changed in the case of salt formation. This distinguishes Δ^2-imidazolines from amidines and other compounds with a C=N group, the conversion of which to salts is accompanied by a characteristic shift of the analogous band of 20-50 cm^{-1} to the high-frequency region [2, 8-11]. For example, the spectra of KBr pellets of 4-chlorophenylimidazolines (X) and its hydrochloride contain absorption bands of a C=N group at 1610 cm^{-1}; similar bands appear at 1675, 1680, and 1665 cm^{-1}, respectively, in the spectra of 4-chlorobenzamidine hydrochloride and its N-methyl and N,N'-dimethyl derivatives. The shift of the band under discussion in the spectra of Δ^2-imidazoline hydrochlorides to the low-frequency region is difficult to explain in terms of the effect of hydrogen bonds, since the position of the bands does not change on passing from the solid state to solution, and Δ^2-imidazoline hexachloroplatinates, which are not inclined to form associated compounds [11, 12], absorb over the same frequency range (Table 2).

The PMR spectra of 2-aryl-Δ^2-imidazolines in trifluoroacetic acid (Table 1, footnote h) provide evidence for the symmetrical structure of imidazolinium ion A.† The decrease in the ν_{as} N⋯C⋯N frequency of salts of Δ^2-imidazolines as compared with salts of amidines is therefore probably not explained by the formation of cation B but rather by the more effective resonance conjugation in imidazolinium cation A as compared with amidinium cation C; this leads to an additional decrease in the double-bond character of the C=N group.



A B C R = H or Alk

* The results of deuteration of Δ^2-imidazolines III and the hydrochlorides of V and X were taken into account in the assignment of the bands.

† A similar conclusion was drawn during a study of the PMR spectrum of 2-alkyl-Δ^2-imidazoline nitrate [13].

TABLE 1. 2-R-Δ^2-Imidazolines (I-XXV)[a] and Their Hydrochlorides

Compound	R	Imidazolines I-XXV							Imidazoline hydrochlorides			
		preparative method	time, h: refluxing	time, h: distillation	mp, °C	purification method[b]	pK$_a$ in 50% alcohol	yield, %	mp, °C[c]	empirical formula	ionogenic Cl, %[d]: found	ionogenic Cl, %[d]: calc.
I	CH_3	A1	8	8	100—101[17]	Benzene	10,95	91				
II	$(CH_3)_2CH$	A1	14	6	~40	95°(15 mm)	—	74	127—128[e]	$C_6H_{12}N_2 \cdot C_6H_3N_3O_7$	20,6	20,6
III	$1,3\text{-}ClH_2CH_2CH_2$	A1	7	7	162—163	Xylene[f]	10,20	75	202—203	$C_9H_{16}N_4 \cdot 2HCl$	27,9	28,0
IV	C_8H_{17}	A3	6	3	70—71[g]	Benzene	10,65	79	110—111	$C_{11}H_{22}N_2 \cdot HCl$	16,2	16,4
V	$C_{11}H_{23}$	A1	8	6	81—82[23]	The same	—	89	114—115	$C_{14}H_{28}N_2 \cdot HCl$	13,8	13,6
VI	$(\alpha\text{-}C_{10}H_7)CH_2$	A1	5	5	121—122[b]	„ „	10,06	80	249—250[6]			
VII	C_6H_5	B2	5	—	101—102[17]	„ „	9,64	92	243—244[22]			
VIII	$2\text{-}ClC_6H_4$[h]	A1	4	4	69—70	Ether	9,01	85	248—249	$C_9H_9ClN_2 \cdot HCl$	16,4	16,3
IX	$3\text{-}ClC_6H_4$	A3	4	2	136—137[18]	Benzene	8,86	83	221—222	$C_9H_9ClN_2 \cdot HCl$	16,4	16,3
X	$4\text{-}ClC_6H_4$[h]	B1	18	—	186—187[17]	Dichloroeth	9,16	67	284—285	$C_9H_9ClN_2 \cdot HCl$	16,1	16,3
XI	$3\text{-}CH_3OC_6H_4$	A3	2	2	98—99[g]	Benzene[f]	9,51	60	240—241	$C_{10}H_{12}N_2O \cdot HCl$	16,4	16,7
XII	$4\text{-}CH_3OC_6H_4$	A1[i]	5	5	138—139[g]	The same	9,95	46	218—219	$C_{10}H_{12}N_2O \cdot HCl$	16,5	16,7
XIII	$3\text{-}NO_2C_6H_4$	B1	6	—	156—157[20]	50% Alcohol	8,09	91	249—250[26]			
XIV	$4\text{-}NO_2C_6H_4$	B1	10	—	242—243	Dioxane[f]	7,92	88	264—265[20]			
XV	$4\text{-}NH_2C_6H_4$	A1	3	3	146—147[19]	Water[f]	10,84	55	257—258	$C_9H_{11}N_3 \cdot HCl$	17,5	18,0
XVI	$2\text{-}CH_3C_6H_4$[h]	A1	7	4	85—86	Hexane—benzene (1:1)	10,08	64	251—252	$C_{10}H_{12}N_2 \cdot HCl$	18,2	18,0
XVII	$3\text{-}CH_3C_6H_4$	A1[i]	6	2	100—101[g]	CCl_4[f]	9,76	73	232—233	$C_{10}H_{12}N_2 \cdot HCl$	18,0	18,0
XVIII	$4\text{-}CH_3C_6H_4$[h]	A1	7	7	178—179[16]	Benzene—alcohol (14:1)	9,96	94	246—247[22]			
										$C_{12}H_{14}N_4 \cdot 2HCl$	25,2	24,8
XIX	$1,4\text{-}C_6H_4$	A1[i]	1	2	296—297[21]	—	—	92	>360			
XX	$2,4\text{-}Cl_2C_6H_3$	A1	4	4	111—112	156—158° (4 mm)	8,78	33	277—278	$C_9H_8BrN_3O_2 \cdot HCl$	14,2	14,1
XXI	$3\text{-}Br\text{-}5\text{-}NO_2C_6H_3$	B1	10	—	152—153	Benzene	—	80	286—287	$C_9H_8Cl_2N_2 \cdot HCl$	11,7	11,6
XXII	$3,5\text{-}(CH_3O)_2C_6H_3$	A1	3	3	111—112	The same	9,30	62	229—230	$C_{11}H_{11}N_2O_2 \cdot HCl$	14,7	14,6
XXIII	$5\text{-}(m\text{-}NO_2C_6H_4)\text{-}2\text{-}C_4H_3O$	B1	12	—	161—162	70% Alcohol	8,66	86	325—326	$C_{13}H_{11}N_3O_3 \cdot HCl$	12,1	12,1
XXIV	$3\text{-}C_5H_4N$	A1	2	2	101—105[b]	Benzene	8,35	75				
XXV	$4\text{-}CH_3C_6H_4$; $(N\text{-}CH_2C_6H_5)$	A2	2	2	88—89	Ether	9,31	91				

[a]See Table 3 for the microanalytical data.

[b]Crystallization solvent or boiling point in vacuo.

[c]Acetone was used to crystallize the hydrochlorides of IV and V, water was used for the hydrochlorides of XV, XIX, and XXIII, 70% alcohol was used for the hydrochloride of XXI, and alcohol was used for the hydrochlorides of the remaining compounds.

[d]This is the percent nitrogen for the picrate of II.

[e]This is the melting point of the picrate of II. The hydrochloride of II was hygroscopic.

[f]This compound was vacuum sublimed at 1-3 mm prior to analysis.

[g]According to the data in [15], IV melts at 52°; according to the data in [16], XII and XVII melt at 109-110° and 97-98.5°, respectively.

[h]In the PMR spectra recorded in CF_3COOH strong signals of protons of the imidazoline ring of VIII, X, XVI, and XVIII appear at, respectively, 4.28, 4.25, 4.24, 4.23 (4H, CH_2CH_2) and 8.24, 8.29, 7.95, and 8.19 ppm (2H, NH).

[i]The methyl ester was used instead of the carboxylic acid.

TABLE 2. Characteristic Frequencies of the IR Spectra of Imidazolines and Their Salts (cm^{-1})[a, b]

Vibrational form	2-Alkyl-Δ^2-imidazolines		2-Aryl-Δ^2-imidazolines			Imidazoline hydrochlorides[c]	X · H_2PtCl_6	V · H_2PtCl_6
	KBr	$CHCl_3$	KBr	$CHCl_3$	CCl_4	KBr	KBr	KBr
$\nu_{C=N}$	1610—1625 vs	1625—1635 vs	1585—1620 vs	1620—1625 vs	1630—1635 vs	1595—1625 vs[d]	1610 vs	1605 vs
$(\nu_{as\,N-C-N})$				1570—1585 i		1560—1575 s[e]	1560 s	—
$\nu_{C=C}$								
δ_{NH}	1500—1510 vs	1490—1495 s	1500—1540 vs	1490—1500 m			—	
δ_{CH_2}	1470—1480 vs	1430—1445 vs	1460—1480 vs	1430—1440 vs	1415—1435 vs	1395—1410 s	1375 s	1385 s
δ_{NH}	1350—1360 w	1350—1375 m	1345—1360 s	1335—1340 s	1330—1335 s	1365—1375 s	1365 s	1355 m
ν_{C-N}	1290—1295 vs		1270—1285 vs	1290 vs		1275—1290 vs	1290 vs	1295 vs
	1265—1275 i		1260—1300 m	1260—1275 m				
δ_{CH_2}	1220—1240 s	1230—1260 s	1240—1260 sh			1240—1255 i	1240 sh	1250 m
			1030—1050 m[f]			1030—1055 s	1050 m	1050 m
δ_{CH_3}	980—995 s[f]			985—990 s		1000—1010 m	1000 m	1000 w
	750—760[g] m br		760—770 m br			740—770 s br	None	
	710—730[g] s		690—740 s			700—740 s	730 vs	725 s
δ_{NH}	660—680 s br		640—680 m br			660—690 s br	590 vs br	610 s, br br
ν_{NH}	3190—3210 vs br	3440—3445 s	3130—3210 vs br	3430—3450 s	3420—3430 s	3040—3100[h] vs, br	3290 vs br	3300 vs br

[a]Arbitrary symbols: v is variable intensity and sh indicates shoulder; the isolated bold-faces arbitrary symbols of the band intensity denote that in some cases its magnitude is reduced somewhat.
[b]These are the ν_{CH_2} values of Δ^2-imidazolines and their salts: 2860-2880 s and 2940-2960 s cm^{-1}.
[c]The IR spectra of the hydrochlorides of IV and V in KBr pellets and chloroform solutions are similar.
[d]Over this range of frequencies the hydrochlorides of 2-aryl-Δ^2-imidazolines often have a second band of medium intensity.
[e]This is not characteristic for the hydrochlorides of 2-alkyl-Δ^2-imidazolines and XIX.
[f]In the spectrum of I: 1030 s, 990 m, and 940 s cm^{-1}.
[g]Over the 710-760 cm^{-1} range the intensities of the bands of imidazolines I and II are reversed.
[h]The presence of two weak or medium broad bands at 2660-2820 cm^{-1}, which are shifted by deuteration to 1930-2020 cm^{-1}, is characteristic for the hydrochlorides of I-XXIII.

TABLE 3. Δ^2-Imidazolines

Compound	Empirical formula	Found, %			Calculated, %		
		C	H	N	C	H	N
III	$C_9H_{16}N_4$	60,1	8,8	31,3	60,0	9,0	31,1
IV	$C_{11}H_{22}N_2$	72,3	12,0	15,5	72,5	12,2	15,4
VIII	$C_9H_9ClN_2$	60,0	5,1	15,6	60,0	5,0	15,5
Picrate VIII	$C_9H_9ClN_2 \cdot C_6H_3N_3O_7$	44,2	3,1	17,6	44,0	3,0	17,1
XI	$C_{10}H_{12}N_2O$	68,3	7,0	16,0	68,2	6,9	15,9
XIV	$C_9H_9N_3O_2$	56,5	4,9	22,2	56,5	4,7	22,0
XVI	$C_{10}H_{12}N_2$	74,9	7,5	17,5	75,0	7,6	17,5
XX	$C_9H_8Cl_2N_2$	50,0	3,9	13,4	50,3	3,8	13,0
XXI	$C_9H_8BrN_3O_2$	40,4	3,2	15,8	40,0	3,0	15,6
XXII	$C_{11}H_{14}N_2O_2$	64,3	6,7	13,8	64,1	6,8	13,6
XXIII	$C_{13}H_{11}N_3O_3$	60,5	4,6	16,1	60,7	4,3	16,3
XXV	$C_{17}H_{18}N_2$	81,7	7,6	11,3	81,6	7,3	11,2

TABLE 4. 3-X-5-Nitrobenzamides (XXVII) and Benzonitriles (XXVIII)

Compound	X	mp, °C*	Empirical formula	Found, %			Calculated, %			Yield, %
				C	H	N	C	H	N	
XXVIIa	Cl	176—177	$C_7H_5ClN_2O_3$	42,1	2,7	13,9	41,9	2,5	14,0	85
XXVIIb	Br	189—190	$C_7H_5BrN_2O_3$	34,1	2,0	11,2	34,3	2,1	11,4	92
XXVIIc	I	188—189	$C_7H_5IN_2O_3$	29,1	1,9	9,5	28,8	1,7	9,6	92
XXVIIIa	Cl	82—83	$C_7H_3ClN_2O_2$	46,0	1,6	15,5	46,0	1,7	15,3	90
XXVIIIb	Br	84—85	$C_7H_3BrN_2O_2$	37,0	1,4	12,2	37,0	1,3	12,3	80
XXVIIIc	I	88—89	$C_7H_3IN_2O_2$	30,6	1,1	9,9	30,7	1,1	10,2	97

*The crystallization solvent was 75% alcohol.

The fact that the basicities of Δ^2-imidazolines are lower than the basicities of the similarly constructed amidines evidently constitutes evidence for the greater stabilization of cation A. Thus the pK_a value of 4-chlorophenylimidazoline (X) in 50% alcohol is 9.16, as compared with 11.41 for N,N'-dimethyl-4-chlorobenzamidine (XXVI).

The ionization constants of the Δ^2-imidazolines are presented in Table 1. A linear dependence is observed when the pK_a values of 2-(XC_6H_4)-Δ^2-imidazolines, in which substituent X is incapable of direct polar conjugation, with the corresponding Taft σ° constants [14]. Treatment of the experimental data by the method of least squares gave the following equation: $pK_a = 9.68 - 2.19\sigma^\circ$ ($R = 0.99$; $s_0 = 0.06$).

EXPERIMENTAL

The ionization constants of the Δ^2-imidazolines were determined graphically with an automatic recording pH-meter (Radiometr, Denmark) with glass and saturated calomel electrodes. A solution of the substance in 50% alcohol (c 0.021 M) was titrated with 0.1 N hydrochloric acid at 20 ± 0.2°. The IR spectra of KBr pellets or $CHCl_3$ and CCl_4 solutions (cuvette thickness 0.105 mm) were recorded with a UR-20 spectrometer. The hydrochlorides of V and X were deuterated by heating solutions of them in D_2O at 50° for 10 min, after which the solutions were vacuum evaporated. Δ^2-Imidazoline III was deuterated similarly at 20°. The PMR spectra of trifluoroacetic acid solutions of the compounds were recorded with a JNM-4H-100 spectrometer with tetramethylsilane as the internal standard.

Δ^2-Imidazolines (I-XXV, Tables 1 and 3). A1) A mixture of 0.02 mole of the carboxylic acid, 0.011 mole of 100% EDA, 0.011 mole of EDA dihydrochloride, 50 mg of p-toluenesulfonic acid, and ethylene gylcol (3-5 ml of ethylene glycol per gram of carboxylic acid) was refluxed for several hours, after which half of the ethylene glycol was slowly removed by distillation. The residual reaction mixture was evaporated to dryness at reduced pressure, and the residue was mixed with three to eight volumes of water and acidified to pH 3-4. The resulting solution was filtered, shaken with ethyl acetate, cooled with ice, and made strongly alkaline with 50% sodium hydroxide solution. The precipitate was removed by filtration, washed several times with a small amount of ice water, and dried in a vacuum desiccator over potassium hydroxide.

The Δ^2-imidazoline that separated as an oil when the mixture was made alkaline was extracted with chloroform (four 20-ml portions).

The hydrochlorides of 2-aryl-Δ^2-imidazolines were isolated by trituration with acetone of the residue obtained after vacuum evaporation of the reaction mixture. The solid material was removed by filtration, dried at 100-110°, and recrystallized.

A2) An equivalent amount of EDA was used in place of its hydrochloride. The reaction mixture was acidified with concentrated hydrochloric acid to pH 4 prior to vacuum evaporation.

A3) Ethylenediamine was used, but the ethylene glycol was replaced by an equal volume of nitrobenzene or chlorobenzene. A third of the solvent was removed by distillation, after which 0.022 mole of EDA and an amount of solvent equal to the amount removed by distillation were again added to the mixture. The refluxing and distillation operation was repeated, after which the mixture was diluted with ether and extracted with dilute hydrochloric acid solution. The Δ^2-imidazoline was isolated from the solution by method A1.

B1) A mixture of 0.02 mole of the nitrile, 0.021 mole of EDA, 50 mg of p-toluenesulfonic acid, and 50 ml of methanol was refluxed after which the solvent was removed by vacuum distillation, and the Δ^2-imidazoline was isolated in the form of the base or the hydrochloride by method A1.

B2) A mixture of 0.02 mole of the nitrile, 0.021 mole of EDA, 50 mg of p-toluenesulfonic acid, and 10 ml of ethylene glycol was heated at 170°, after which it was evaporated to half its original volume at reduced pressure. The concentrate was acidified to pH 3 with concentrated hydrochloric acid and vacuum evaporated to dryness. The residue was worked up by method A1.

All of the synthesized Δ^2-imidazolines were obtained as white crystalline substances. Compounds containing a nitrophenyl group were yellow. The Δ^2-imidazolines are capable of vacuum sublimation and, except for I-III, are only slightly soluble in water.

The hydrochlorides of the Δ^2-imidazolines (Table 3) obtained from the bases and an alcohol solution of hydrogen chloride, are soluble in water, less soluble in alcohol, and insoluble in acetone. The hydrochlorides of IV and V are appreciably soluble in chloroform.

Platinum Salts of Δ^2-Imidazolines. These salts were obtained by mixing equimolar amounts of a 20% alcohol solution of chloroplatinic acid hexahydrate with a 10% solution of the Δ^2-imidazoline in alcohol. The $V \cdot H_2PtCl_6$ salt had mp 169-170° (from ethanol), and $X \cdot H_2PtCl_6$ had mp 189-190° (from 50% ethanol).

N,N'-Dimethyl-4-chlorobenzamidine (XXVI). An 8.5-g (0.05 mole) sample of 4-chlorobenzoic acid methylamide was added in portions to a refluxing solution of 9.5 g (0.046 mole) of PCl_5 in 50 ml of benzene, and the mixture was refluxed for 6 h. It was then cooled, and filtered, and the filtrate was evaporated at reduced pressure. The residual oil was vacuum distilled to give 7.6 g (81%) of the N-methyl-4-chlorophenylimidochloride [bp 100-103° (2 mm) and n_D^{20} 1.5810], which was dissolved in 50 ml of benzene and added with stirring to 40 ml of ice-cooled 25% aqueous methylamine solution. The heterogeneous mixture was shaken for 2 h, after which the organic layer was separated, and the aqueous layer was extracted with two 5-ml portions of benzene. The combined benzene extracts were washed with saturated sodium chloride solution (two 10-ml portions), dried with anhydrous Na_2SO_4, and evaporated to give 5.8 g (65%) of amidine XXVI with mp 163-164° (from benzene). Found: C 58.8; H 6.2; N 15.4%. $C_9H_{11}ClN_2$. Calculated: C 59.2; H 6.1; N 15.3%. The hydrochloride of XXVI had mp 283-284° (from ethanol), and $XXVI \cdot H_2PtCl_6$ had mp 200-201° (from 30% ethanol); these compounds were obtained in the same way as the corresponding Δ^2-imidazoline salts.

Like the other 3-X-5-nitrobenzonitriles (XXVIII) (Table 4), the starting 3-bromo-5-nitrobenzonitrile (XXVIIIb) was synthesized from 3,5-dinitrobenzoic acid, which was reduced to 3-amino-5-nitrobenzoic acid by means of ammonium sulfide. Hydrogen sulfide is less convenient for the reduction [24]. The 3-halo-5-nitrobenzoic acids obtained from 3-amino-5-nitrobenzoic acid [25] were converted to amides XXVII by heating with sulfamic acid and fuming sulfuric acid [26]. The use of phosphorus oxychloride for the dehydration of amides XXVII to nitriles XXVIII gave better results than thionyl chloride.

3-Amino-5-nitrobenzoic Acid. A total of 180 ml of 16-17% aqueous ammonium monosulfide was added with stirring in the course of 3 h to a heated (to 80°) suspension of 71 g of 3,5-dinitrobenzoic acid in 300 ml of water, after which the mixture was allowed to stand for 1 h. It was then cooled and filtered, and the filtrate was acidified with concentrated hydrochloric acid to pH 3.5. The resulting precipitate was separated, washed on the filter with 100 ml of cold water, and dissolved in a mixture of 250 ml of concentrated hydrochloric acid and 800 ml of water. The solution was decolorized with charcoal and filtered, and the filtrate was neutralized to pH 3.5 with sodium carbonate. The precipitate was removed by filtration, washed with two 100-ml portions of water, dried at 100-110°, and recrystallized from a 25-fold amount of water to give 48 g (79%) of a product with mp 209-210° (mp 200-202° and 211-213° [24]).

3-Halo-5-nitrobenzamides (XXVIIa-c, Table 4). A mixture of 0.1 mole of 3-halo-5-nitrobenzoic acid [25], 0.15 mole of sulfamic acid, and 80 ml of 20-30% fuming fulfuric acid was heated at 80-100° For 1.5 h, after which it was cooled and poured into 400 g of ice. The resulting precipitate was removed by filtration, washed successively with water, 8% ammonium hydroxide, and water, and dried at 100-110°.

3-Halo-5-nitrobenzonitriles (XXVIIIa-c, Table 4). A 0.01-mole sample of amide XXVII was heated with 3-5 ml of phosphorus oxychloride at 100° for 2-3 h, after which the excess phosphorus oxychloride was removed by distillation at reduced pressure. The residue was triturated with ice water, and the mixture was filtered. The solid material was vacuum dried over P_2O_5 and crystallized.

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