sym-TETRACYANOETHANE IN THE SYNTHESIS OF HETEROCYCLES.

3.* SYNTHESIS OF 1-ALKYL(ARYL)-2-AMINO-3,4,4-TRICYANO-4,5-DIHYDROPYRROLES BY THE REACTION OF sym-TETRACYANOETHANE WITH AZOMETHINES

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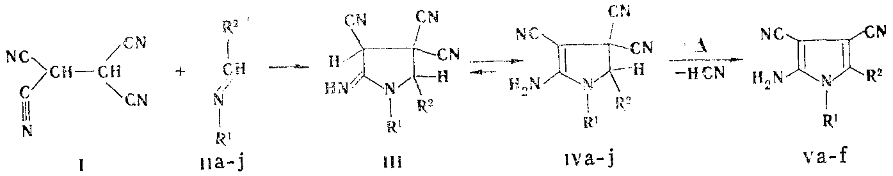
sym-Tetracyanoethane reacts with azomethines to give 1,5-disubstituted 2-amino-3,4,4-tricyano-4,5-dihydropyrroles, which upon heating readily split out HCN to give 1,5-diaryl(hetaryl)-2-amino-3,4-dicyanopyrroles. The structures of the dihydropyrroles and pyrroles were confirmed by the PMR, ^{13}C NMR, and mass spectra.

We have recently reported that sym-tetracyanoethane (I) readily forms 4,5-dihydrofuran derivatives upon reaction with carbonyl compounds [1]. We found that cyanide I in solution in ethanol, aqueous ethanol, or DMSO at no higher than 40°C also reacts smoothly with azomethines IIa-j [2, 3] to give iminopyrrolines III, which, however, exist virtually completely in the tautomeric 2-pyrroline form (IVa-j) in solution (see Table 1).



In fact, in addition to signals of the protons of the substituents, a broad peak of two protons of the NH_2 group at 7.6 ppm, which is shifted to the stronger-field region when the temperature is raised, is observed in the PMR spectra of all of the isolated compounds. In addition, the PMR spectra of IVg,i contain a quartet of a 5-H proton at 4.16 ppm. The ^{13}C

TABLE 1. Properties of 2-Amino-3,4,4-tricyano-3,4-dihydropyrroles (IVa-j)

Compound	R^1	R^2	mp, °C	Found, %			Empirical formula	Calc., %			Synthetic method	Yield, %
				C	H	N		C	H	N		
IVa	C_6H_5	C_6H_5	>100*	73,6	4,6	22,4	$C_{19}H_{13}N_5$	73,3	4,2	22,5	B	93
IVb	4-HO—C_6H_4	C_6H_5	>148*	69,8	4,0	21,4	$C_{19}H_{13}N_5O$	69,7	4,0	21,4	B	80
IVc	4-Cl—C_6H_4	C_6H_5	>185*	66,1	3,6	20,1	$C_{19}H_{12}ClN_5$	66,0	3,5	20,3	B	90
IVd	2-Pyridyl	C_6H_5	>164*	69,4	3,9	26,8	$C_{18}H_{12}N_6$	69,2	3,9	26,9	B	91
IVe	C_6H_5	2-Furyl	>160*	67,8	3,4	23,3	$C_{17}H_{11}N_5O$	67,8	3,7	23,3	B	92
IVf	C_6H_5	2-HO—C_6H_4	>137*	63,5	4,1	21,5	$C_{19}H_{13}N_5O$	69,7	4,0	21,4	B	92
IVg	n-C_5H_{11}	C_2H_5	128—129	65,5	7,6	27,3	$C_{14}H_{19}N_5$	65,3	7,5	27,2	A	96
IVh	n-C_5H_{11}	i-C_3H_7	92—94	66,2	7,7	25,6	$C_{15}H_{21}N_5$	66,4	7,8	25,8	A	86
IVi	n-C_5H_{11}	i-C_4H_9	121—122	67,4	8,1	24,5	$C_{16}H_{23}N_5$	67,3	8,1	24,6	A	92
IVj	t-C_4H_9	n-C_3H_7	159—161	65,5	7,4	27,4	$C_{14}H_{19}N_5$	65,3	7,5	27,2	A	88

*With decomposition.

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*See [1] for communication 2.

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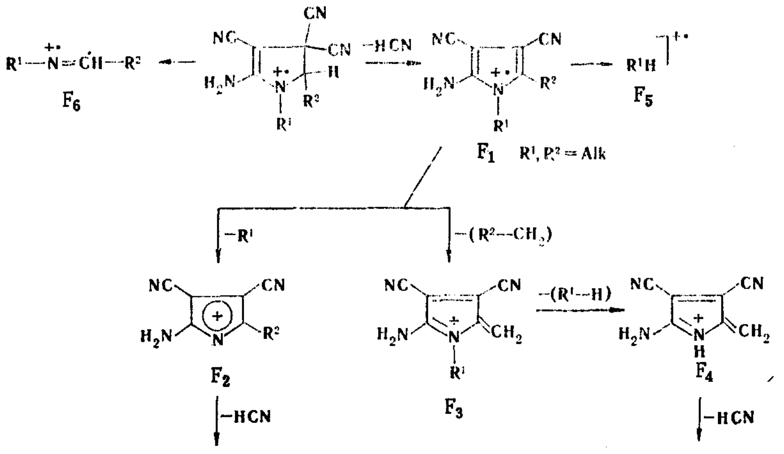
TABLE 2. Chemical Shifts of the Signals of the Carbon Atoms of the Heterocyclic Ring in the ^{13}C NMR spectra of IV and V (ppm)

Compound	$C_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$	CN
IV b	164,12*	50,70	45,26	74,98	116,97; 115,47; 114,09
IV d	162,18	51,49	44,53	69,21	117,75; 116,57; 113,55
IV g	164,06	50,41	42,07	70,09	117,81; 116,41; 114,57
IV i	164,09	50,43	42,53	66,97	118,21; 116,08; 114,57
V a	149,47	71,26	91,29	136,56	115,46; 115,46
V b	150,04	73,01	92,29	137,69	115,89; 115,52
V c	150,23	72,36	92,59	137,44	115,65; 115,54
V d	149,85	71,63	92,21	135,77	115,38; 115,38
V f	148,77	70,50	91,83	134,58	115,70; 115,30

*The $C_{(2)}$ signal was observed at 167-170 ppm in the ^{13}C NMR spectra of similarly constructed 4,5-dihydrofurans [1].

NMR spectra of these compounds give additional information regarding the structures. The assignment of the signals (see Table 2) was made on the basis of the data in [1, 4, 5] and also by comparative analysis of the spectra recorded with the aid of proton decoupling. We established that for all of the isolated compounds there is only one CH group [$C_{(5)}$ signals at 67-75 ppm] in the structure of the heteroring and that the $C_{(3)}$ atom (signal at 50.4-51.5 ppm) is unprotonated.

A relatively unstable (0.1-1.3%) molecular ion, the primary process in the fragmentation of which is elimination of a molecule of hydrocyanic acid to give the F_1 ion, the peak of which is the maximum peak in the spectrum in the case of aromatic substituents, is observed in the mass spectra of all IVa-j (Table 3). The percentage of this ion in the mass spectra of IVa-f reaches 25% (see Table 4). The subsequent fragmentation of this ion is associated with the characteristic (for N-arylpyrroles) loss of substituent R^1 (the F_2 ion) with the subsequent elimination of a molecule of HCN [6].



The latter process in the case of aryl-substituted compounds is also accompanied by the formation of pseudomolecular F_5 ions; it follows from the mass spectra of the deuterium-substituted (at the amino group) Vc and Vd that primary transfer of a hydrogen atom of the amino group is transferred to the leaving R^1 group in this case. In the mass spectra of aryl- and hetaryl-substituted pyrrolines IV F_6 ions are also characteristic. At the same time, the F_1 ions, which are formed in processes involving dissociative ionization of alkyl-substituted pyrrolines IVg-j, undergo the characteristic (for 1- and 2-alkylpyrroles [7, 8]) "benzyl cleavage" of the C–C bond in the aliphatic chain to give stable F_3 fragments with the subsequent loss (or with transfer of a hydrogen atom) of the R^1 group (F_4) and subsequent ejection of a molecule of hydrocyanic acid. The fragmentation pathways worked out above are extremely characteristic, inasmuch as they give from one third to one half of all of the ions of the spectrum. It should be noted that primary loss by either the molecular ions or the fragment (F_1) ions of substituent R^2 is not observed even in the case of alkyl-substituted pyr-

TABLE 3. Mass Spectra* of IVc-j and Va,b†

Compound	m/z (relative intensities, %)
IV c	345* (15), 344* (5), 318* (100), 283 (36), 282 (15), 281 (4), 256 (14), 229 (5), 216 (6), 153 (17), 112* (4)
IV d	312 (3), 285 (100), 284 (30), 259 (6), 257 (7), 220 (10), 207 (12), 79 (34), 78 (23), 51 (11), 45 (34)
IV e	301 (2), 274 (100), 246 (40), 220 (8), 219 (10), 218 (8), 192 (6), 119 (5), 115 (6), 77 (34), 51 (21)
IV f	327 (1,5), 300 (100), 299 (36), 283 (25), 197 (11), 196 (15), 93 (14), 88 (13), 77 (23), 70 (53), 61 (51)
IV g	257 (0,5), 230 (56), 215 (100), 173 (5), 160 (11), 159 (18), 147 (5), 146 (21), 145 (25), 69 (10), 43 (38)
IV h	271 (1), 244 (25), 229 (100), 203 (4), 173 (4), 159 (23), 146 (6), 132 (4), 71 (5), 43 (32), 41 (11)
IV i	285 (0,4), 258 (26), 215 (100), 201 (2), 159 (11), 147 (3), 146 (3), 145 (12), 69 (8), 43 (25), 41 (7)
IV j	257 (7), 230 (25), 201 (36), 174 (100), 173 (13), 146 (29), 145 (87), 132 (23), 131 (12), 57 (65), 56 (28)
V a	284 (100), 283 (14), 256 (6), 229 (3), 207 (7), 180 (17), 154 (8), 104 (12), 78 (8), 77 (26), 51 (10)
V b	300 (100), 272 (5), 223 (6), 207 (5), 196 (13), 180 (9), 170 (6), 120 (10), 100 (9), 94 (9), 77 (10)

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*The molecular-ion peak and the 10 most intense fragment ion peaks are presented. The peaks of the isotope ions are not presented. In the case of IVc the ions that contain the ^{35}Cl isotope are designated by asterisks.

†The mass spectra of Vc,d,f are identical to the mass spectra of the corresponding IV, commencing with the M—27 ion.

TABLE 4. Intensities of the Peaks of the Characteristic Ions in the Mass Spectra of IVc-j (the intensities of the same peaks in the mass spectra of the corresponding V are given in parentheses) (%, Σ_{39})

Compound	W_M	F_1	F_2	F_3	F_4	F_5	F_6
(Va)	(35,1)	—	(2,1)	—	—	(2,4)	(4,8)*
(Vb)							
IVc (Vc)	1,1 (13,4)	25,6	0,4 (0,1)	—	—	0,9 (1,1)	1,6 (1,3)
IVd (Vd)	0,7 (28,3)	21,8	2,6 (1,7)	—	—	7,4 (7,3)	0,8 (0,9)
IVe	0,5	25,5	—	—	—	0,1	—
IVf (Vf)	0,5 (48,5)	14,2	0,3 (0,8)	—	—	0,2 (0,4)	0,4 (1,4)
IVg	0,1 (18,9)	14,0	4,6 (4,8)	25,0 (28,5)	6,3 (6,6)	—	—
IVh	0,3	8,6	1,4	34,5	7,7	—	—
IVi	0,1	10,5	0,2	40,0	5,0	—	—
IVj	1,3	3,8	1,9	5,5	13,1	9,8†	

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*The (F_7-H) ion.

†Also m/z 57 ($C_4H_9^+$).

TABLE 5. Properties of 2-Amino-3,4-dicyanopyrroles (Va-g)

Compound	mp,* °C	Found, %			Empirical formula	Calc., %			Yield, %
		C	H	N		C	H	N	
Va	235—236	76,1	4,3	19,9	$C_{18}H_{12}N_4$	76,0	4,3	19,7	98
Vb	198—200	72,0	4,1	18,7	$C_{18}H_{12}N_4O$	72,0	4,0	18,7	90
Vc	239—240	67,9	3,3	17,6	$C_{18}H_{11}ClN_4$	67,8	3,5	17,6	95
Vd	220—222	71,4	3,6	24,6	$C_{17}H_{11}N_5$	71,6	3,9	24,5	97
Ve	211—212	70,1	3,7	20,7	$C_{16}H_{11}N_4O$	70,0	3,7	20,4	98
Vf	213 (dec.)	72,0	4,1	18,4	$C_{18}H_{12}N_4O$	72,0	4,0	18,7	88
Vg	162—164	67,4	8,1	24,2	$C_{13}H_{18}N_4$	67,8	7,9	24,3	96

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*From aqueous dimethylformamide.

rolines. This indicates that tautomeric form III is also apparently absent in the gas phase.

We found that aryl-substituted IVa-f, as well as IVg, readily lose HCN even upon brief heating in solution in dimethylformamide (DMF), as a result of which pyrroles Va-f are formed in high yields (see Table 5). A broad singlet of protons of the amino group is present in their PMR spectra, and the signal of the 5-H proton vanishes. In contrast to the spectra of IV, signals of only two CN groups are observed in the ^{13}C NMR spectra of these pyrroles (see Table 2), while the $C_{(5)}$ signal is shifted markedly (by 60-65 ppm) to weak field. The signals of the $C_{(3)}$ and $C_{(4)}$ atoms undergo a similar shift, but it amounts to only 20-50 ppm. The assignment of the signals was made by means of structural analogs (pyrrole and phenol [4]), and the chemical shifts of the pyrrole and benzene rings were calculated by an additive scheme [9], as well as by a comparative analysis of the spectra recorded with decoupling.

Highly stable molecular ions (W_M = 13-48%), the fragmentation of which resembles the fragmentation of the F_1 ions in the mass spectra of IVa-f, thereby confirming the structures proposed for them, are characteristic for the mass spectra of Va-f (Tables 3 and 4).

Attempts to realize the thermal (or photochemical) dehydrocyanation of most of alkylpyrrolines IVa-j invariably led to pronounced resinification of the reaction mixtures, from which we were unable to isolate any individual reaction products. Facile opening of the pyrroline ring and the formation of polymeric products probably occur in the presence of these aliphatic groups and in the absence of the stabilizing effect of aromatic substituents. Thus the reaction of tetracyanoethane with azomethines can serve as a convenient preparative method for the synthesis of 2-pyrroline and pyrrole derivatives that contain reactive functional substituents such as cyano and amino groups.

EXPERIMENTAL

The PMR and ^{13}C NMR spectra were recorded with a Brucker H-90 spectrometer with hexamethyldisiloxane as the internal standard. The mass spectra were recorded with a Varian MAT-212 spectrometer at an ionization energy of 70 eV.

2-Pyrrolines (IVa-j). A) Azomethine II (50 mmole) was added at 10-15°C in a nitrogen atmosphere to a solution of 50 mmole of cyanide I in 20 ml of DMSO. At the end of the reaction (determined from the disappearance of spots of the starting reagents on the thin-layer chromatogram), the mixture was diluted with water, and the resulting precipitate was removed by filtration, dried, and precipitated from solution in cold ethyl acetate by means of n-hexane.

B) A 50-mmole sample of azomethine II was added at 35-40°C in a nitrogen atmosphere to a solution of 50 mmole of cyanide I in 20 ml of ethanol, and the mixture was allowed to stand until the reaction was complete (TLC). It was then poured into water, and the precipitate was recrystallized from aqueous alcohol (1:1).

Pyrroles (Va-f). A solution of pyrroline IV in the minimum amount of DMF was refluxed for 5-25 min, after which it was cooled, and the solid was removed by filtration and recrystallized from DMF. The synthesis of Vc,d which contain an ND_2 group, was accomplished by twofold dissolving of the samples in CH_3OD with subsequent evaporation of the solvent; the preparations obtained were 95% pure.

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sym-TETRACYANOETHANE IN THE SYNTHESIS OF HETEROCYCLES.

4.* SYNTHESIS OF 1-ALKYLIDENEIMINO-2-AMINO-3,4,4-TRICYANO-4,5-DIHYDROPYRROLES BY THE REACTION OF sym-TETRACYANOETHANE WITH AZINES

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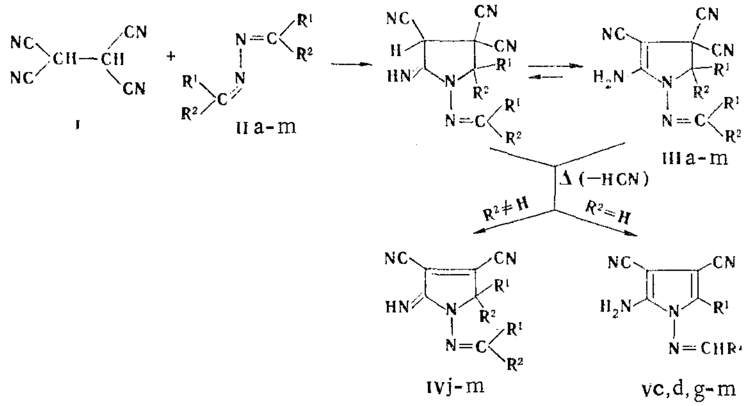
sym-Tetracyanoethane reacts with aldazines and ketazines to give 1-alkylideneimino-2-amino-3,4,4-tricyano-4,5-dihydropyrroles, some of which are thermally converted to 1-alkylideneimino-2-amino-3,4-dicyanopyrroles or to 5,5-disubstituted 1-alkylideneimino-2-imino-3,4-dicyano-2,5-dihydropyrroles. The structures of the compounds were confirmed by the PMR, ^{13}C NMR, and mass spectra.

In a previous communication [1] we showed that azomethines, like carbonyl compounds [2, 3], react with sym-tetracyanoethane (I) via a scheme involving aldol addition, which ultimately leads to the formation of 4,5-dihydropyrrole derivatives. Inasmuch as azines contain two azomethine groupings that are capable of such reactions, the reaction of cyanide I with aldazines and ketazines II could lead to cyclization of the primary intermediate addition products to favor the formation of derivatives of piperidazine, pyrrolines, or dipyrrolines.



We have found that the reaction of cyanide I with aldazines, as well as with azomethines, takes place in aqueous alcohol or alcohol and also leads to 4,5-dihydropyrrole derivatives IIIa-m in high yields (see Table 1). The reaction with ketazines similarly leads to pyrrolines IIIj-m; however, the yields of final products do not exceed 45-48%, evidently as a consequence of steric hindrance. The results of elementary analysis, as well as the mass-spectrometric determination of the molecular masses, make it possible to exclude the possibility of the formation of dipyrrolines IX.

A broad singlet of two protons, which undergo a strong-field shift when the temperature is raised, is observed in the PMR spectra of III at weak field (7.6 ppm); this indicates the

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*See [1] for communication 3.

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