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SYNTHESIS OF 2,5-DISUBSTITUTED 3,3,4,4-TETRACYANOPYRROLIDINES

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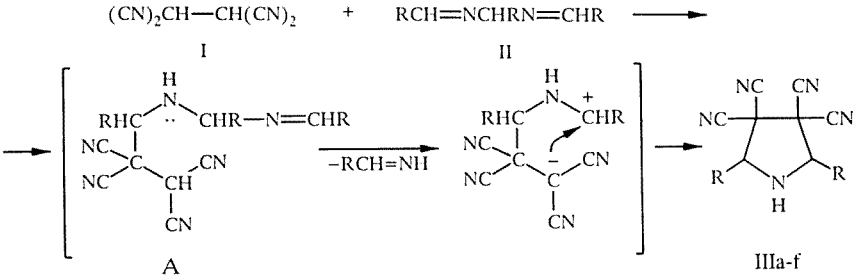
The reaction of 1,1,2,2-tetracyanoethane with 1-R,3-R,5-R-2,4-diazapenta-1,4-dienes leads to 2,5-disubstituted 3,3,4,4-tetracyanopyrrolidines. The conditions for the acylation of the last were selected.

It was previously established that 1,1,2,2-tetracyanoethane condenses with Schiff bases at the C=N bond with the formation of Δ^2-pyrrolines and pyrroles [1, 2] (in the presence of two C=N bonds, bispyrroles are formed [3]) and with azines, the interaction of which proceeds at one of the two existing azomethine fragments [4].

We found an unusual course of the reaction of tetracyanoethane (I) with derivatives of 2,4-diazapenta-1,4-dienes (II) – products of the condensation of aldehydes with ammonia, in which the two C=N bonds are separated by a methylene unit. Under the usual conditions with an aqueous-alcoholic or alcoholic medium [1-4], 2,5-disubstituted 3,3,4,4-tetracyanopyrrolidines (IIIa-t) were synthesized with high yields:



Since the required pyrrolidines (III) are contaminated with initial compounds due to their poor solubility in alcohol or aqueous alcohol when tetracyanoethane reacts with aromatic derivatives of diazadienes (II) under these conditions, acetonitrile was shown to be the most suitable solvent here: the good solubility of tetracyanoethane in acetonitrile allows the reaction to be conducted in 5-10 min and the isolation of the requisite compounds (III), not requiring additional purification, with quantitative yields (Table 1). The aliphatic derivatives (IIIn-t), which are soluble in acetonitrile, are synthesized more conveniently in an alcoholic or aqueous-alcoholic medium, the composition of which is selected according to the solubility of the initial diene (IIn-t) in it.

The reaction probably commences with the addition of tetracyanoethane at one of the C=N bonds. The resulting adduct A eliminates the molecule of the aldimine by analogy with the cleavage of hydrobenzamide by reduction [5, 6] with the subsequent cyclization at the newly formed C=N bond. It was shown in the work [7] using the example of the synthesis of 2,5-diphenyl-3,3,4,4-tetracyanopyrrolidine (IIIa) that the reaction of tetracyanoethane with hydrobenzamide is accomplished with the ratio of 3:2 (or 2:1 in the case where the ammonia released is neutralized by excess tetracyanoethane). This is explained by the fact that the detached aldimine readily undergoes trimerization to the initial hydrobenzamide under the conditions of the reaction. In fact, a decrease in the yield of the requisite compound occurs if the process is carried out in acetic anhydride, when the possibility of the trimerization of the benzaldimine is excluded; that proceeds with the 1:1 ratio of the reagents. Therefore, an increase in the yield of aromatic derivatives of pyrrolidines (IIIa-o) on account of the trimerization of the detached aldimine only occurs in those cases where the initial aldehyde can easily form the diene (II). If this does not occur, the optimal tetracyanoethane:diene (II) ratio is 2:1.

Thus, absorption bands of the NH bond are observed in the region of 3350-3280 cm^{-1} in the IR spectra of the 2,5-disubstituted 3,3,4,4-tetracyanopyrrolidines, and the absorption bands of low intensity in the region of 2265 cm^{-1} indicate the

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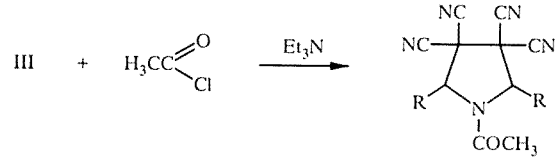
TABLE 1. Properties of the 3,3,4,4-Tetracyanopyrrolidines (III) and (IV)

Compound	R	Empirical formula	mp, °C	Yield, %
IIIa	C_6H_5	$C_{20}H_{13}N_5$	154...155 (decomp.)	92
IIIb	2-Fu	$C_{16}H_9N_5O_2$	135...136 (decomp.)	95
IIIc	2-$H_3COC_6H_4$	$C_{22}H_{17}N_5O_2$	140...141 (decomp.)	91
IIId	4-$H_3COC_6H_4$	$C_{22}H_{17}N_5O_2$	123...125 (decomp.)	95
IIIe	2-ClC_6H_4	$C_{20}H_{11}Cl_2N_5$	178...180 (decomp.)	74
IIIf	4-FC_6H_4	$C_{20}H_{11}F_2N_5$	156...158 (decomp.)	94
IIIg	4-$H_3CC_6H_4$	$C_{22}H_{17}N_5$	154...155 (decomp.)	68
IIIh	3-$O_2NC_6H_4$	$C_{20}H_{11}N_7O_4$	204...205 (decomp.)	80
IIIi	4-$O_2NC_6H_4$	$C_{20}H_{11}N_7O_4$	209...210 (decomp.)	75
IIIj	3-$H_3CC_6H_4$	$C_{22}H_{17}N_5$	144...145 (decomp.)	71
IIIk	3-ClC_6H_4	$C_{20}H_{11}Cl_2N_5$	160...162 (decomp.)	68
IIIl	2-$H_3CC_6H_4$	$C_{22}H_{17}N_5$	154...155 (decomp.)	90
IIIm	4-BrC_6H_4	$C_{20}H_{11}Br_2N_5$	168...169 (decomp.)	65
IIIn	3-BrC_6H_4	$C20H_{11}Br_2N_5$	153...155 (decomp.)	60
IIIo	*i*-C_3H_7	$C_{14}H_{17}N_5$	130...131	78
IIIp	*n*-C_3H_7	$C_{14}H_{17}N_5$	84...85	65
IIIq	C_2H_5	$C_{12}H_{13}N_5$	115...116	82
IIIr	*i*-C_4H_9	$C_{16}H_{21}N_5$	105...106	48
IIIs	*n*-C_4H_9	$C_{16}H_{21}N_5$	81...82	26
IIIt	CH_3	$C_{10}H_9N_5$	135...136	90
IVa	C_6H_5	$C22H_{15}N_5O$	251...252 (decomp.)	57
IVb	2-Fu	$C_{18}H_{11}N_5O_3$	178...179	62
IVc	2-$H_3COC_6H_4$	$C_{24}H_{19}N_5O_3$	195...196	65
IVd	4-$H_3COC_6H_4$	$C_{24}H_{19}N_5O_3$	234...235 (decomp.)	57
IVe	*i*-C_3H_7	$C_{15}H_{19}N_5O$	158...159	69
IVf	*i*-C_4H_9	$C18H_{23}N_5O$	147...149	44

unconjugated character of the cyano groups (Table 2). The symmetrical character of the structure (III) is in accord with the small proportion of signals in the ^{13}C NMR spectra (in each case, there are two signals of the ring carbon atoms at 70-80 and 50-55 ppm, Table 3). Signals at 109-112 ppm are observed for the four C atoms of the cyano groups. The mass spectra of the compounds (III) lack peaks of the molecular ions, and the main direction of the decomposition is associated with the releaseof two molecules of HCN (Table 2). Moreover, the structure of 2,5-diphenyl-3,3,4,4-tetracyanopyrrolidine (IIIa) was demonstrated by the method of x-ray structural analysis [8].

As a consequence of thermal instability of the pyrrolidines (III), we did not manage to acylate them with acid anhydrides, but the reaction with acetyl chloride led to isolation of the N-acetyl-3,3,4,4-tetracyanopyrrolidines (IVa-f) (Table 1).



IVa-f

It should be noted that the acylation may only be performed successfully in the case when triethylamine is added to the solution of the compound (III) and acetyl chloride. The reverse order of the mixing of the reagents leads to the resinification of the reaction mass.

By comparison with the initial pyrrolidines (III), the IR spectra (Table 4) lack the absorption bands of the NH groups, and the region 1700-1680 cm^{-1} has absorption bands of the amide fragment.

By analogy with the compounds (III), the ^{13}C NMR spectra of the acetylpyrrolidines (IV) characterize the symmetrical character of their structure. Only two signals of the pyrrolidine ring are observed (Table 5). In some cases, these are split due to the restrained conformation of the amide fragment: the structure of the compound (IIIa), in which the pseudoequatorially oriented phenyl substituents occur in the cis position, favors the possibility of such a restrained character in the compounds (IVa, d). The splitting of the signals does not occur in the ^{13}C NMR spectra of the pyrrolidines (IVd, e) at the temperature of 80-90°C (Table 5) since the free rotation of the acetyl group becomes possible. The absence of the splitting of the signals

TABLE 2. IR and Mass Spectra of the Compounds (IIIa-t)

Compound	IR spectrum, cm^{-1}		Mass spectrum, m/z (relative intensity, %)*
	ν_{N-H}	$\nu_{C \equiv N}$	
IIIa	3340	2265	323 (–), 296 (4), 269 (100), 195 (5), 194 (19), 193 (27), 165 (20), 139 (15), 128 (41), 103 (49), 76 (56)
IIIb	3350	2265	—
IIIc	3325	2263	—
IIId	3355	2270	—
IIIe	3350	2270	391 (–), 339 (65), 337 (100), 302 (7), 262 (22), 239 (2), 165 (8), 128 (4), 97 (4), 76 (4), 45 (20)
IIIf	3340	2265	359 (–), 306 (20), 305 (100), 257 (2), 256 (13), 230 (10), 183 (4), 157 (4), 134 (62), 95 (4), 76 (2)
IIIg	3342	2270	351 (–), 324 (2), 298 (20), 297 (92), 222 (8), 149 (54), 118 (58), 130 (9), 119 (54), 103 (10), 91 (20)
IIIh	3320	2265	413 (–), 359 (10), 313 (2), 285 (8), 284 (6), 238 (2), 150 (55), 128 (100), 104 (47), 76 (77), 45 (39)
IIIi	3345	2275	—
IIIj	3328	2265	351 (–), 324 (17), 309 (13), 297 (100), 282 (3), 222 (43), 179 (9), 165 (3), 118 (13), 91 (10), 76 (4)
IIIk	3335	2265	391 (–), 364 (30), 339 (63), 337 (100), 302 (22), 263 (35), 226 (14), 228 (14), 138 (33), 128 (19)
IIIl	3330	2265	351 (12), 324 (63), 309 (22), 297 (23), 282 (11), 223 (77), 222 (100), 179 (15), 130 (48), 118 (87), 117 (50)
IIIm	3338	2265	481 (–), 456 (3), 452 (4), 427 (100), 425 (56), 347 (38), 292 (44), 266 (50), 261 (79), 192 (69)
IIIn	3335	2265	481 (–), 456 (48), 454 (100), 452 (60), 429 (42), 427 (80), 425 (44), 379 (16), 346 (13), 267 (34), 169 (34)
IIIo	3293	2260	255 (–), 228 (1), 201 (19), 186 (100), 171 (35), 158 (7), 144 (11), 131 (5), 112 (5), 55 (16), 43 (11)
IIIp	3292	2260	255 (–), 228 (1), 201 (19), 172 (100), 156 (5), 144 (16), 130 (4), 109 (4), 82 (5), 55 (4), 40 (6)
IIIq	3280	2260	227 (–), 200 (1), 185 (4), 173 (28), 172 (14), 171 (12), 158 (100), 156 (27), 143 (22), 131 (13), 44 (15)
IIIr	3300	2260	283 (–), 256 (1), 241 (3), 204 (4), 187 (100), 200 (21), 186 (92), 157 (14), 144 (67), 112 (14), 40 (23)
IIIs	3298	2262	283 (–), 256 (2), 229 (15), 204 (4), 189 (15), 146 (100), 123 (11), 112 (10), 95 (13), 82 (17), 55 (29)
IIIt	3283	2263	199 (11), 184 (14), 171 (23), 158 (16), 145 (28), 144 (48), 130 (23), 107 (16), 71 (100), 56 (86), 42 (73)

*The peak of the molecular ion and the 10 most intense peaks are presented.

TABLE 3. ^{13}C and ^{1}H NMR Spectra of the Compounds (III)

Compound	^{13}C NMR spectrum, δ, ppm			Compound	PMR spectrum, δ, ppm		
	C-1(4)	C-2(3)	C(C ≡ N)		CH	R	NH
IIIa	70,86	51,79	111,50 (broadened	IIIa	5,37	7,54...7,99 (5H, m, C_6H_5)	10,07
IIIb	62,47 62,26	48,20	114,12; 113,01; 111,18; 110,59	IIIh	5,79	7,99...8,76 (4H, m, C_6H_4)	10,25
IIId	66,99	47,99 45,91	118,17; 115,60	IIIk	5,52	7,61...8,02 (4H, m, C_6H_4)	10,09
IIIo	79,19 72,77	51,57 51,36	109,53; 111,23; 111,64; 112,74	IIIo	3,46	2,11 (2H, m, CH); 1,18 (6H, к, CH_3); 1,14 (6H, q, CH_3)	—

in the ^{13}C NMR spectra of the compounds (IVb, c) is probably explained either by the trans disposition of the substituents, or their pseudo-axial orientation.

In one case, with the acylation of compound (IIIa), the elimination of hydrogen cyanide proceeded unexpectedly with the formation of 2,5-diphenyl-3,4,4-tricyano-2-pyrroline (V). The acetyl chloride–triethylamine complex which is formed probably assists the cleavage of the hydrogen cyanide molecule, thereby leading to the Δ^2-pyrroline (V); this agrees with the mass spectral data where the ready elimination of hydrogen cyanide is found. Besides the absorption band of the unconjugated

TABLE 4. IR and Mass Spectra of the Compounds (IV)

Compound	IR spectrum, cm^{-1}		Mass spectrum,* m/z (relative intensity, %)
	$\nu_{C \equiv N}$	$\nu_{C=O}$	
IVa	2270	1670	365 (5), 323 (7), 322 (19), 195 (9), 194 (33), 139 (21), 128 (37), 105 (13), 77 (16), 45 (13), 43 (100)
IVb	2267	1698	345 (5), 302 (5), 201 (46), 175 (54), 174 (56), 159 (14), 118 (5), 94 (5), 78 (6), 52 (12), 43 (100)
IVc	2265	1680	—
IVd	2265	1695	425 (3), 255 (21), 254 (100), 241 (26), 199 (7), 184 (7), 134 (6), 114 (4), 77 (9), 45 (52), 43 (80)
IVe	2265	1672	297 (4), 254 (2), 253 (4), 229 (16), 212 (12), 202 (10), 187 (5), 169 (7), 70 (25), 44 (100), 43 (11)
IVf	2265	1675	325 (2), 310 (5), 282 (3), 243 (17), 154 (44), 135 (10), 112 (31), 111 (32), 86 (21), 44 (8), 43 (100)

*The peak of the molecular ion and the 10 most intense peaks are presented.

TABLE 5. ^{13}C NMR Spectra of the compounds (IV) (δ, ppm)

Compound	C-1(4)	C-2(3)	C(C=O)	C(C ≡ N)
IVa	67,41* 66,76	49,71* 48,09	169,52	110,70; 110,48; 109,13
IVb	61,61	48,12	169,22	109,70; 108,62
IVc	62,58	48,45	171,95	110,32; 108,99
IVd	67,49* 66,87	49,82* 48,23	169,38	110,77*, 109,18 110,56
IVd (80 °C)	67,39	49,13* 47,59	169,39	110,44; 108,93
IVe	72,21* 68,35	48,71* 40,89	172,57	111,64; 110,32
IV e (90 °C)	62,24	47,85	171,46	110,86; 109,51

*Split signals.

cyano groups (2265 cm^{-1}), the IR spectrum of compound (V) contains the absorption band in the region of 2215 cm^{-1}, characteristic of the conjugated cyano group, and the broader absorption band of the NH bond in the region of 3245 cm^{-1}. The mass spectrum of the pyrroline (V) is analogous to the spectrum of the pyrrolidine (IIIa). Its decomposition fully repeats the decomposition of the compound (IIIa) after the elimination of the molecule of hydrogen cyanide.

EXPERIMENTAL

The monitoring of the course of reactions and the purity of the compounds synthesized was performed by the method of TLC on plates of Silufol UV-254 using UV light and iodine vapor for development. The IR spectra were taken on the UR-20 instrument in mineral oil. The ^{13}C NMR spectra were obtained on the WH-90 spectrometer (Bruker) at the working frequency of 22.63 MHz using HMDS as the internal standard. The PMR spectra were registered on the WP 200 SY spectrometer of the firm Bruker using TMS as the internal standard. The mass spectra were obtained on the MS 25 PFA KRATOS and Hitachi M-80 instruments by the method of the direct introduction of the substance at the ion source with ionization energies of 50 and 70 eV correspondingly.

2,5-Disubstituted 3,3,4,4-Tetracyanopyrrolidines (IIIa-n). To the suspension of 0.01 mole of the finely crushed aromatic derivative of the diene (IIa-n) in 15 ml of acetonitrile is added, with stirring, 0.02 mole of 1,1,2,2-tetracyanoethane in one process. The noticeable solution of the initial substances occurs, and the requisite compound crystallizes out after 3-5 min. The reaction mass is maintained with the stirring for 10 min more. The residue is filtered off, and the virtually pure sub-

stance is washed with a small amount of acetonitrile, isopropanol, and then hexane, and dried in air. If required, purification is performed by recrystallization from acetonitrile (Table 1).

2,5-Dialkyl-3,3,4,4-tetracyanopyrrolidines (IIIo-t). To the solution of 0.055 mole of the initial diene (IIo-t) in 50 ml of isopropanol or the mixture of isopropanol–water is added, with stirring, 0.05 mole of 1,1,2,2-tetracyanoethane in one process. Its rapid solution occurs and the residue, which is precipitated in the course of 10-20 min, is filtered off, washed with the 1:1 mixture of isopropanol–water and a small amount of isopropanol, and recrystallized from isopropanol [compound (IIIt) is recrystallized from methanol, Table 1].

2,5-Disubstituted N-Acetyl-3,3,4,4-tetracyanopyrrolidines (IVa-f). To the solution of 0.1 mole of the tetracyanopyrrolidine (III) in 250 ml of anhydrous acetone are added, in one process, 15.7 g (0.2 mole) of acetyl chloride prior to the dropwise addition of the solution of 20.2 g (0.2 mole) of abs. triethylamine in 70 ml of anhydrous acetone while the mixture is cooled with water and stirred. After the addition of the entire amount of triethylamine, the stirring is continued for 30 min at room temperature. The reaction mass is then diluted with water to 1 liter. The isolated oil-forming mass is separated by decantation, washed with water, and then triturated in 70 ml of isopropanol. The substance which thereby crystallized is filtered off, washed with isopropanol, and recrystallized from the 2:1 mixture of isopropanol–methyl cellosolve; the compounds (IVe, f) are recrystallized from isopropanol (Table 1).

The acylation of 2,5-diphenyl-3,3,4,4-tetracyanopyrrolidine is reproduced poorly. In one case, 2,5-diphenyl-3,4,4-tricyano-2-pyrroline (V) was isolated with the yield of 51% and the mp 189-191°C (from acetonitrile) under analogous conditions instead of the acetylpyrrolidine (IVa). The mass spectrum was as follows: 296 (100), 270 (21), 269 (63), 219 (11), 193 (43), 192 (8), 139 (13), 104 (28), 77 (38), and 51 (30).

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