CYCLIZATION OF 1-THIOCARBAMOYL-2-PHENYLPYRAZOLIDINES

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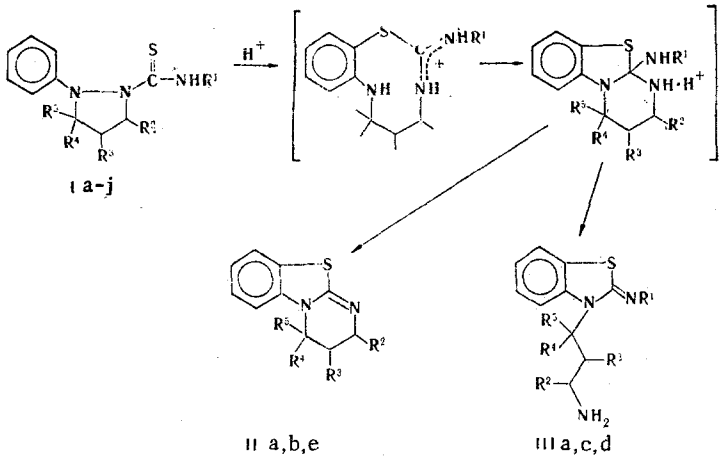
Thiocarbamoyl derivatives of N-phenylpyrazolidines are converted under the influence of acidic agents to mixtures of tetrahydropyrimido[2,1-b]benzothiazoles and 2-imino-3-aminoalkylbenzothiazoles and not only to tetrahydropyrimidobenzothiazoles, as previously assumed. The conditions for the predominant formation of tetrahydropyrimidobenzothiazoles were found.

It has been shown [1] that thiocarbamoyl derivatives of N-phenylpyrazolidines (Ia, b) are converted under the influence of acidic agents to tetrahydropyrimido[2,1-b]benzothiazoles (IIa, b) with splitting out of ammonia. However, as we have previously established [2], two benzothiazoles can be formed in the rearrangement of thiosemicarbazides from the intermediate isothiuronium salt as a result of the elimination of amines. Correspondingly, in the case of 1-thiocarbamoyl-2-phenylpyrazolidines I one should have expected the formation of not one but rather two substances, i.e., heterocycles II and III.



I a-j

II a,b,e

III a,c,d

I—III a $R^1=R^2=R^3=R^4=R^5=H$; b $R^3=CH_3$; c $R^1=Ph$; d $R^1=Ph$, $R^3=CH_3$; e $R^1=R^4=Ph$; f $R^1=Ph$, $R^2=R^4=R^5=CH_3$; g $R^2=R^4=R^5=CH_3$; h $R^4=Ph$; i $R^2=CH_3$; j $R^1=Ph$, $R^2=CH_3$ unindicated R = H

In this connection, we made a detailed study of the transformations of compounds of the I type, including compounds with substituents attached to the amino group. It was found that tetrahydropyrimidobenzothiazoles II are formed almost exclusively in 65-70% yields under mild conditions (at room temperature in trifluoroacetic acid). However, if the reaction mixture is heated with a solution of HCL in ethanol (in which some of the resulting hydrochlorides of amines III are almost insoluble), compounds of the II and III type are formed in approximately equal amounts (25-30%). We have demonstrated by means of special experiments that benzothiazoles II and III do not undergo interconversion under the conditions of the synthesis. Thus, the rearrangement of pyrazolidines I proceeds via the same scheme as the rearrangement of arylthiosemicarbazides through the intermediate formation of an isothiuronium salt to give both possible benzothiazoles.

The constants and spectral characteristics of tetrahydropyrimidobenzothiazoles IIa, b are in agreement with the literature data [1], and the data for IIe are similar to the

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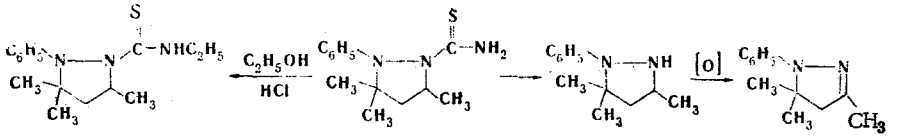
literature data. Benzothiazoles III were isolated from the reaction mixtures in the form of the hydrochlorides or bases; the latter were converted to trifluoroacetyl derivatives. The UV spectra of the derivatives of amines IIIa, c, d are in agreement with the 3-substituted 2-phenyliminobenzothiazole structure (two intense maxima at 221 and 297 nm). Their mass spectra contain molecular-ion peaks with low intensities; this is also characteristic for 3-substituted 2-phenyliminobenzothiazoles [2]. The fragmentation schemes are in agreement with the proposed structures.

The molecular-ion peak of the base, although it is not very intense, can be recorded in the mass spectrum of the hydrochloride of IIIa recorded at no higher than 160°C. However, if a sample is recorded at 200°C, we obtain a spectrum that is identical to the spectrum of tetrahydropyrimidobenzothiazole IIa. Amine IIIa evidently undergoes cyclization to tetrahydropyrimidobenzothiazole IIa under these conditions (at high temperatures or under the influence of electron impact).

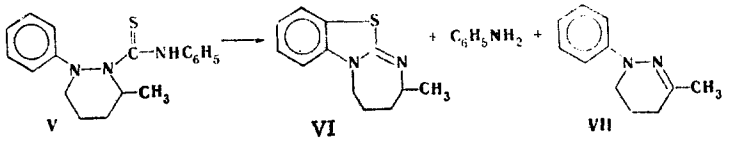
A chromatographic study of the reaction mixtures shows that the reaction in all cases is accompanied by side processes. Hydrolysis of the thioamide bond leads to the formation of 1-phenylpyrazolidines, which are oxidized to 1-phenylpyrazolines. A similar trend in the cleavage of thioureas under the influence of alcohol in acidic media was noted in [3]. When we carried out the reaction in an ethanol solution of HCl, in individual cases we also isolated products of ethylation of thiocarbamoylpyrazolidines I probably at the nitrogen atom of the thiocarbamoyl group, although it is known that thiosemicarbazides [4], thioureas [5], thiohydrazides [6], and thioamides [5] are generally alkylated at the sulfur atom.



IV Ig

The results of elementary analysis of IV are in agreement with the empirical formula $C_{15}H_{23}N_3S$. The PMR spectrum contains additional (as compared with starting Ig) signals of an ethyl group in the form of a quartet at 2.47 ppm (J = 7 Hz) and a triplet at 1 ppm (which is superimposed on the singlets of the protons of the gem-dimethyl groups), and the integral intensity of the signal at 6.30 ppm (the NH_2 group of Ig) is halved (the NH group of IV). The vibrations of the NH group appear in the IR spectrum at 3370 cm^{-1} (solution in CCl_4), while the absorption at 1600-1610 cm^{-1}, which corresponds to vibrations of the C=N group, is absent. The absence of an $[M - C_2H_5]^+$ ion in the mass spectrum of IV constitutes an argument in favor of alkylation at the nitrogen atom. The principal pathways of dissociation ionization of IV are in agreement with the thiosemicarbazide structure [7].

According to the available data [8, 9], the properties of tetrahydropyridazines and pyrazolines sometimes differ appreciably. The possibility of rearrangement of thiocarbamoylphenylhexahydropyridazines V was therefore not obvious. In fact, most of the thiocarbamoyl derivatives of hexahydropyridazine that we obtained were found to be extremely unstable, in contrast to the corresponding pyrazolidine derivatives, and readily undergo cleavage of the C–C and C–N bonds to give tetrahydropyridazine derivatives and ring-cleavage products. Compounds that contain an unsubstituted NH_2 group are particularly unstable. Consequently, although V does undergo rearrangement to give the expected VI, hydrolysis and oxidative processes assume the greatest significance here. A mass-spectral study of the reaction mixture showed that it contains benzothiazole VI, tetrahydropyridazine VII (which is evidently formed in the same way as the pyrazoline in the preceding case), aniline, and substances with unestablished structures, among which dimeric structures (M 440-450) are also present. The formation of the latter constitutes evidence in favor of ion-radical processes that are often accompanied by oxidative reactions.



V VI VII

TABLE 1. Thiocarbamoylpyrazolidines Ia-j

Compound	mp, °C	UV spectrum, λ_{max}, nm (log ε)	IR spectrum, ν, cm^{-1}	Found, %		Empirical formula	Calc., %		Yield, %
				C	H		C	H	
Ia	165—166 [1]	250 (4,28)	3140, 3230, 3340						55[a]
Ib	141—142 [1]	250 (4,24)	3130, 3210, 3370						60[b]
Ic	166—168	237 (4,25), 257 (4,30)	3260	68,5	6,2	$C_{16}H_{17}N_3S$	67,8	6,0	64[b]
Id	104—105	237 (4,24), 259 (4,28)	3280	68,8	6,3	$C_{17}H_{19}N_3S$	68,7	6,4	59[b]
Ie	124—126	257 (4,32)	3320	73,9	5,4	$C_{22}H_{21}N_3S$	73,5	5,9	49[c]
If	160—163	263 (4,37)	3240	70,4	6,9	$C_{19}H_{23}N_3S$	70,2	7,1	35[b]
Ig	179—181	253 (4,30)	3140, 3260, 3400	62,9	7,5	$C_{13}H_{19}N_3S$	62,7	7,6	24[d]
Ih	188—189	251 (4,30)	3150, 3220—3250, 3440	68,1	6,2	$C_{16}H_{17}N_3S$	67,8	6,0	27[c]
Ii	185	253 (4,26)							
Ij	145—148	237 (4,30), 260 (4,27)	3140, 3255, 3360 3300	59,4 68,8	7,2 6,4	$C_{11}H_{15}N_3S$ $C_{17}H_{19}N_3S$	59,7 68,7	6,8 6,4	51[b] 23[b]

[a]Based on the recrystallized thiocarbamoylpyrazolidine. [b]Based on the pyrazolidine hydrochloride. [c]Based on the pyrazolidone. [d]Based on the pyrazoline.

EXPERIMENTAL

The UV spectra of solutions of the compounds in alcohol were recorded with Cary and Specord spectrophotometers. The IR spectra of mineral oil suspensions of the compounds were recorded with IKS-22 and UR-20 spectrometers. The PMR spectra were recorded with a Varian T-60 spectrometer with hexamethyldisiloxane as the internal standard (or as the external standard in the case of solutions in CF_3COOH). The mass spectra were recorded with an MKh-1303 mass spectrometer with introduction of the substances directly into the ion source at an ionizing-electron energy of 50 eV, an emission current of 1.5 mA, and at 30-40°C below the melting points of the investigated compounds.

The pyrazolidines were obtained by reduction of 1-phenyl-3-pyrazolidone and 1-phenyl-4-methyl-3-pyrazolidone with lithium aluminum hydride in ether [10] and reduction of 1,5-diphenyl-3-pyrazolidone in tetrahydrofuran (THF) or by reduction of the C=N bond in salts of Δ^2-pyrazolines by means of lithium aluminum hydride [11]. In view of the ease with which they undergo oxidation, the pyrazolidines were used to obtain the thiocarbamoyl derivatives without additional purification (in the form of the bases or hydrochlorides).

3,5,5-Trimethyl-1-phenylpyrazolidine. A stream of dry HCl was passed into a solution of 13.2 g (0.07 mole) of 3,5,5-trimethyl-1-phenylpyrazoline in absolute ether for 20 min, after which the ether was evaporated, 50 ml of absolute benzene was added, and the benzene was removed by vacuum distillation. A suspension of 8.46 g (0.22 mole) of lithium aluminum hydride in 70 ml of THF was added in portions with vigorous stirring to a suspension of the hydrochloride in 100 ml of THF, and the mixture was refluxed for 4.5 h. It was then decomposed by the addition of 12 ml of water, and the precipitate was removed by filtration and washed with absolute ether and THF. The solution of 3,5,5-trimethyl-1-phenylpyrazolidine was subsequently used without additional purification.

The thiocarbamoyl derivatives (Table 1) were obtained by the general method for the synthesis of thiosemicarbazides [12] from pyrazolidines and phenyl isothiocyanate or from the hydrochlorides of pyrazolidines and ammonium thiocyanate and were recrystallized from alcohol.

1-Phenylthiocarbamoyl-2-phenyl-6-methylhexahydropyridazine (V). This compound, with mp 154-155°C (from ethanol), was obtained in 70% yield from 1-phenyl-3-methylhexahydropyridazine [13] and phenyl isothiocyanate. IR spectrum: 3270 cm^{-1}. UV spectrum: λ_{max} 246 nm (log ε 4.50). Mass spectrum: $[M]^+$ 311. Found, %: C 69.4; H 6.6. $C_{18}H_{21}N_3S$. Calculated, %: C 69.5; H 6.8.

Cyclization of Thiocarbamoylpyrazolidines I. A 2.5-mmole sample of thiocarbamoylpyrazolidine I was heated with 6 ml of a 25-30% solution of HCl in ethanol, and the mixture was allowed to stand at room temperature for several days with 6 ml of CF_3COOH.

A) The solvent was removed by evaporation, and the residue was chromatographed with a

column (30 by 130) filled with alkaline Al_2O_3 (L 40/250) by means of successive elution with benzene, chloroform (tetrahydropyrimidobenzothiazole II), and ethanol (aminoalkyl-2-phenyliminobenzothiazole III).

B) The precipitate was removed by filtration and washed on the filter with hot ethanol, and the mother liquor was worked up as in method A. The precipitate was recrystallized to give the hydrochloride of 3-aminoalkyl-2-iminobenzothiazole III. The yields of benzothiazoles II and III are presented in Table 2. Tetrahydropyrimidobenzothiazoles IIa, b were identical to the samples described in [1] with respect to their IR spectra and the results of mixed-melting-point determinations.

4-Phenyl-2,3,4,5-tetrahydro[2,1-b]pyrimidobenzothiazole (IIe). This compound had mp 156-157°C (from aqueous alcohol). IR spectrum: 1630 cm^{-1}. UV spectrum, λ_{max} (log ε): 222 (4.80), 265 (4.13), 295 nm (3.87). PMR spectrum ($CDCl_3$), δ: 2.1 (2H, m, 3-H), 3.5 (2H, m, 2-H), 5.2 (1H, m, 4-H), and 6.0-7.2 ppm (9H, m, aromatic protons). Mass spectrum, m/e (relative intensity, %): $[M]^+$ 266 (62), 163 (6), 162 (100), 161 (6), 135 (46), 134 (12), 117 (5), 115 (6), 108 (20), 107 (8), 104 (16), 98 (7), 93 (24), 92 (5), 91 (73), 79 (10), 78 (7), 77 (21), 72 (35), 69 (25), 66 (73), 65 (21), 57 (5), 55 (64). Found, %: C 71.9; H 5.4. $C_{16}H_{14}N_2S$. Calculated, %: C 72.2; H 5.3.

3-Aminopropyl-2-iminobenzothiazole (IIIa). This compound was isolated in the form of the hydrochloride, with mp 274°C (from methanol). IR spectrum: 1665, 2040-2090, and 2500-2750 cm^{-1}. UV spectrum (6.06 ml of water, 4 ml of methanol, and 0.1 ml of concentrated HCl), λ_{max} (log ε): 203 (4.78), 212 shoulder (4.71), 250 (4.24), 267 sh (4.10), 277 (4.13), and 285 nm (4.18). PMR spectrum (CF_3COOH), δ: 2.5 (2H, m), 3.5 (2H, m), 4.5 (2H, m), 7.1 (2H, broad s, NH_2), 7.5 (4H, m, aromatic protons), and 8.25 (2H, s, NH_2). Mass spectrum (at 160°C), m/e (relative intensity, %): $[M]^+$ 207 (18), 190 (49), 189 (22), 165 (10), 164 (100), 163 (9), 162 (13), 161 (6), 151 (33), 150 (63), 137 (7), 136 (50), 135 (38), 124 (5), 123 (11), 122 (16), 109 (28), 108 (18), 105 (12), 96 (10), 95 (7), 94 (8), 91 (10), 82 (6), 78 (7), 77 (7), 69 (20), 65 (13), 63 (7), 57 (26), 56 (32), 55 (10). Found, %: C 40.8; H 5.3. $C_{10}H_{13}N_3S \cdot 2HCl \cdot H_2O$. Calculated, %: C 40.5; H 5.7. The picrate had mp 237-238°C (from ethanol). Found, %: C 40.1; H 3.1; N 18.7. $C_{10}H_{13}N_3S \cdot 2C_6H_3N_3O_7$. Calculated, %: C 39.7; H 2.9; N 19.0.

3-Aminopropyl-2-phenyliminobenzothiazole (IIIc). This compound was isolated in the form of the base (as a colorless oil). The picrate had mp 202-204°C. Found, %: C 51.5; H 4.0. $C_{16}H_{18}N_3S \cdot 2C_6H_3N_3O_7$. Calculated, %: 51.5; H 4.1. The trifluoroacetyl derivative had mp 130°C (from 2-butanol). IR spectrum: 1610, 1725, 3070, and 3200 cm^{-1}. UV spectrum, λ_{max} (log ε): 221 (4.65) and 298 nm (4.19). PMR spectrum (d_6-DMSO), δ: 2.0 (2H, m), 3.3 (m, CH_2, DMSO), 4.15 (2H, m), 6.9-7.6 (9H, m, aromatic protons), and 9.5 (1H, s, NH). Mass spectrum, m/e (relative intensity, %): $[M]^+$ 379 (42), 287 (19), 253 (10), 240 (43), 239 (30), 227 (13), 226 (100), 225 (80), 173 (5), 154 (6), 150 (36), 149 (14), 136 (19), 135 (8), 134 (7), 128 (7), 126 (6), 123 (6), 115 (12), 109 (48), 106 (19), 104 (6), 96 (9), 93 (24), 92 (7), 91 (81), 83 (6), 81 (7), 78 (21), 77 (81). Found, %: C 56.2; H 4.0. $C_{18}H_{16}F_3N_3O_3S$. Calculated, %: C 57.0; H 4.2.

3-(3-Amino-2-methylpropyl)-2-phenyliminobenzothiazole (IIId). This compound was isolated in the form of the hydrochloride with mp 252-254°C (from ethanol). IR spectrum: 1620, 2050, 2090, and 2400-2750 cm^{-1}. UV spectrum, λ_{max} (log ε): 221 (4.54) and 298 nm (4.12). PMR spectrum (CF_3COOH), δ: 1.13 (3H, d, J = 5 Hz, CH_3), 2.6-3.6 (3H, m, CH, CH_2), 4.5 (2H, m, CH_2), and 6.8-7.8 ppm (11H, m, aromatic protons, NH_2). Found, %: C 55.4; H 5.8. $C_{17}H_{17}N_3S \cdot 2HCl$. Calculated, %: C 55.4; H 5.2. The trifluoroacetyl derivative had mp 128-130°C. IR spectrum: 1620, 1730, 3070, and 3200 cm^{-1}. UV spectrum, λ_{max} (log ε): 221 (4.19) and 297 nm (3.75). PMR spectrum (d_6-DMSO), δ: 0.9 (3H, d, J = 6 Hz, CH_3), 2.5-3.5 (m, CH, CH_2) 4.0 (2H, m, CH_2), and 6.9-7.6 ppm (9H, m, aromatic protons). Mass spectrum: $[M]^+$ 393.

Cyclization of 1-Phenylthiocarbamoyl-2-phenyl-3,3,5-trimethylpyrazolidine (If). A 762-mg (2.3 mmole) sample of pyrazolidine If was heated in a sealed ampul with 6 ml of a 30% solution of HCl in ethanol at 100°C for 9 h, after which the solvent was removed by evaporation, and the residue was chromatographed with a column (30 by 140 nm) filled with alkaline Al_2O_3 (L 40/250) by means of successive elution with benzene, benzene–chloroform (from 1:1 to 3:10), chloroform, and alcohol. Workup of the eluate gave 40 mg (9%) of 3,5,5-trimethyl-1-phenylpyrazoline, which was chromatographically identical to an authentic sample. According to thin-layer chromatography (TLC), the chloroform fraction contained 2,4,4-trimethyl-2,3,4,5-tetrahydropyrimido[2,1-b]benzothiazole (IIf) (R_f 0.2-0.4 on Al_2O_3 in chloroform) and a few

TABLE 2. Reaction Conditions and Yields of Benzothiazoles II and III with HCl in Ethanol As the Catalyst at 100-110°C (or with CF_3COOH at 20°C)

Starting compound	Reaction time, h, (days)	Method of isolation	Yield, %	
			II	III
Ia	4,5	B	35	23
Ib	(7)	(A)	(65)	
Ic	5 (9)	A (A)	29 (70)	35
Id	4,5 (3)	B (A)	30 (71)	37 (15)
Ie	(10)	(A)	(69)	

other substances, including aniline. In the mass spectrum, the peaks of ions with m/e (relative intensity, %): 232 (12), 217 (19), 202 (26), 201 (11), 200 (27), 199 (14), 198 (10), 165 (15), 144 (10), 100 (100), 98 (10), 96 (34), 94 (24), 93 (100), 92 (47), 91 (160) correspond primarily to IIf. IR spectrum (of a film): 1680 (vibrations of an unconjugated C=N bond); 3070, 3195, and 3320 cm^{-1} (admixed aniline).

Reaction of 1-Thiocarbamoyl-2-phenyl-3,3,5-trimethylpyrazolidine (Ig) with an Alcohol Solution of HCl. A 690-mg (2.75 mmole) sample of Ig was heated in a sealed ampul with 6 ml of a 30% solution of HCl in ethanol at 100°C for 5 h, after which the solvent was removed by evaporation, and the residue was separated preparatively in a thick layer of neutral aluminum oxide (L 40/250) in a chloroform–methanol system (19:1). The fraction with R_f 0.83-1 was collected and worked up to give 390 mg (34%) of an orange oil that solidified when petroleum ether was added. The solid was recrystallized from benzene–petroleum ether to give colorless crystals of 1-ethylthiocarbamoyl-2-phenyl-3,3,5-trimethylpyrazolidine with mp 80°C. IR spectrum (in CCl_4): 3370 cm^{-1}. UV spectrum: λ_{max} 244 nm (log ε 4.02). PMR spectrum (CCl_4), δ: 0.93-2.1 (14H, m, four CH_3 groups, 4-H), 2.47 (2H, q, J = 7 Hz, NCH_2), 4.23 (1H, m, 3-H), 6.30 (1H, s, NH), and 7.07 ppm (5H, m, aromatic protons). Mass spectrum, m/e (relative intensity, %): $[M]^+$ 227 (16), 190 (28), 189 (100), 175 (11), 134 (46), 133 (25), 118 (10), 105 (9), 92 (8), 91 (16), 77 (53), 69 (8), 65 (6), 60 (7), 56 (9), 55 (14). Found, %: C 64.9; H 8.4; N 15.4. $C_{15}H_{22}N_3S$. Calculated, %: C 65.0; H 8.3; N 15.2.

Cyclization of 1-Phenylthiocarbamoyl-2-phenyl-6-methylhexahydropyridazine (V). A 740-mg (2.4 mmole) sample of V was heated in a sealed ampul with 7 ml of a 25% solution of HCl in ethanol at 100°C for 11 h, after which the solvent was removed by evaporation, and the residue was chromatographed with a column (30 by 135 mm) filled with alkaline aluminum oxide (L 40/250) by successive elution with benzene, benzene–chloroform (from 2:1 to 1:2), chloroform, and alcohol. According to the mass spectrum, the fraction eluted with benzene–chloroform contained the expected 2-methyl-2,3,4,5-tetrahydro-1,3-diazepino[2,1-b]benzothiazole (VI) (M^+, $[M-15]^+$, and $[M-HCN]^+$), as well as 1-phenyl-3-methyltetrahydropyridazine (VII) (M^+ 174). Aniline was subsequently eluted; higher-molecular-weight compounds (M^+ 440-450) predominated in the more polar fractions (those eluted with chloroform and alcohol).

LITERATURE CITED

1. A. N. Kost, G. A. Golubeva, and L. A. Sviridova, Khim. Geterotsikl. Soedin., No. 4, 495 (1973).
2. A. N. Kost, N. Yu. Lebedenko, L. A. Sviridova, and V. N. Torocheshnikov, Khim. Geterotsikl. Soedin., No. 4, 467 (1978).
3. N. B. Galstukhova, I. M. Berzina, and M. N. Shchukina, Zh. Org. Khim., 9, 1070 (1973).
4. E. E. Reid, The Organic Chemistry of Bivalent Sulfur, Vol. 5, New York (1963), p. 194.
5. M. J. Janssen, in: Sulfur in Organic and Inorganic Chemistry, Vol. 3, New York (1972), p. 373.
6. W. Walter and K. I. Reubke, in: The Chemistry of Amides, Interscience Publ., London (1970), p. 501.
7. P. A. Sharbatyan, N. Yu. Lebedenko, and A. N. Kost, Zh. Org. Khim., 14, 116 (1978).
8. Yu. S. Shabarov, N. I. Vasil'ev, N. K. Mamaeva, and R. Ya. Levina, Dokl. Akad. Nauk SSSR, 135, 879 (1960).
9. M. A. Lapitskaya, A. N. Kost, and G. A. Golubeva, Vestn. Mosk. Univ., Khim., No. 2, 105 (1969).

10. G. A. Golubeva, Yu. N. Portnov, A. N. Kost, and L. A. Sviridova, Khim. Geterotsikl. Soedin., No. 1, 118 (1971).
11. G. A. Golubeva, L. A. Sviridova, N. Yu. Lebedenko, and A. N. Kost, Khim. Geterotsikl. Soedin., No. 4, 547 (1973).
12. Houben-Weyl, Methoden der organischen Chemie, Vol. 9, Georg Thieme Verlag, Stuttgart.
13. A. N. Kost, A. V. Dovgilevich, and L. A. Sviridova, Zh. Org. Khim., 16, (1980).

REACTION OF 1,4-DIAZINES WITH INDOLES IN THE PRESENCE OF ACYLATING AGENTS*

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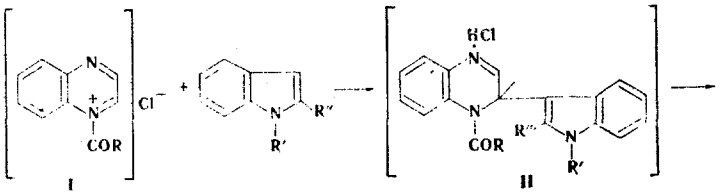
2,3-Diindolyl-1,4-diacyl-1,2,3,4-tetrahydropyrazines and 2,3-diindolyl-1,2,3,4-tetrahydroquinoxalines with acyl residues attached to one or both nitrogen heteroatoms were obtained by the reaction of pyrazines and quinoxalines with indole and 1-methyl- and 2-methylindoles in the presence of acyl chlorides or acetic anhydride.

In the reaction of monoazines and acylating agents with indoles the latter undergo hetarylation by the intermediately formed N-acyl azinium cations [3].

It seemed extremely tempting to attempt to extend this reaction also to 1,4-diazines, since the participation of these N-heteroaromatic systems, which are the least basic diazines [4], in hetarylation would imply the possibility of its extension to other diazines. One example of such a reaction with the participation of a phthalazine with a basicity that is higher by a factor of five than the basicities of 1,4-diazines is known [5]. This reaction involves the formation of Reissert compounds by the reaction of phthalazine with potassium cyanide in the presence of benzoyl chloride.

We first attempted to preparatively synthesize N-acyl salts of 1,4-diazines by the reaction of pyrazine and quinoxaline with acylating agents. It was found that the N-acyl salts of these N-heteroaromatic systems are not formed either under the conditions for the preparation of N-acylpyridinium chlorides [6] or under the conditions described for the preparation of stable N-acylimmonium [7] and N-acylazolium [8] stibnates. However, we obtained hetarylation products, viz., 1-acyl-2,3-diindolyl-1,2,3,4-tetrahydroquinoxalines (III) and 1,4-diazyl-2,3-diindolyl-1,2,3,4-tetrahydropyrazines (IV), in the reaction of pyrazine and quinoxaline with indoles in the presence of acyl halides.

Nevertheless, the process evidently takes place through the intermediate formation of N-acyl salts I, which attack the indoles electrophilically to give monosubstituted adducts II, as described for N-alkylquinoxalinium salts [9]. However, in our case when an oxidizing



I II

*See [1, 2] for our preliminary communications.

Donetsk State University, Donetsk 340055. Dnepropetrovsk Construction-Engineering Institute, Dnepropetrovsk 320631. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 2, pp. 234-238, February, 1980. Original article submitted March 19, 1979.

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