Chemistry of Heterocyclic Compounds, Vol. 36, No. 8, 2000

HALOGEN-CONTAINING PYRIDINES. 7*. SYNTHESIS AND SOME CONVERSIONS OF (3,5-DICHLORO-2-PYRIDYL)HYDRAZINE

K. I. Kobrakov[1], V. K. Korolev[1], I. I. Rybina[1], and V. I. Kelarev[2]

(3,5-Dichloro-2-pyridyl)hydrazine was synthesized by the interaction of 2,3,5-trichloropyridine with hydrazine hydrate. Reaction of the former with carbonyl compounds gave N-(3,5-dichloro-2-pyridyl)hydrazones, and with acid anhydrides N'-acyl derivatives were formed. Azodyestuffs containing 3,5-dichloropyridyl fragments were obtained from some of the hydrazones synthesized.

Keywords: azodyestuffs, hydrazones, pyridylhydrazine, 2,3,5-trichloropyridine.

The development of preparative methods for the synthesis of 2,3,5-trichloropyridine (**1**) by the intramolecular cyclization of δ-oxonitriles [2,3] led to the fact that the compound became an accessible reagent for obtaining various derivatives of chlorine-substituted pyridines.

It is known that the 3,5-dichloropyridyl group is frequently introduced into the structure of organic compounds displaying high biological activity, which at the same time have low toxicity [4]. With the aim of developing 3,5-dichloropyridine derivatives capable for further conversion and enabling the introduction of a 3,5-dichloropyridyl residue into complex molecular structures, we have synthesized (3,5-dichloro-2-pyridyl)hydrazine (**2**) and have studied some of its conversions.

Information on the preparation and properties of hydrazine **2** is extremely limited. According to patent data [5,6] it may be synthesized in up to 70% yield by hydrazinolysis of pyridine **1** in dioxane. As concerning the chemical conversions of hydrazine **2** there is only patent information on its transformation to pyrazole derivatives recommended as herbicides [5-9].

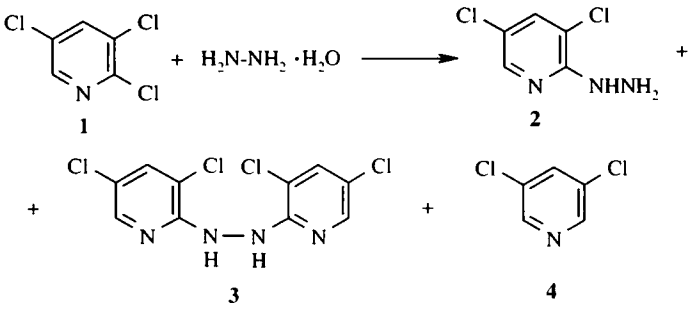
We have established that 2,3,5-trichloropyridine **1** is less reactive than pentachloropyridine or tetrachloronicotinonitrile when reacting with hydrazine hydrate [10]. Boiling pyridine **1** with an excess of hydrazine hydrate in methanol for 70 h did not lead to the formation of the target compound. On heating (80-120°C) pyridine **1** with an excess of hydrazine hydrate in the presence of KOH in DMSO for 4-5 h, the yield of hydrazine **2** did not exceed 10-15%. In boiling DMSO extensive resinification of the reaction mixture occurred, from which only N,N'-bis(3,5-dichloro-2-pyridyl)hydrazine (**3**) (yield 26-28%) and 3,5-dichloropyridine (**4**) (yield 15-18%) were isolated and identified.

The N,N'-disubstituted hydrazine **3** was obtained in 75% yield by the interaction of hydrazine **2** with chloro derivative **1** in pyridine. A yield of 90-96% hydrazine **2** was achieved on boiling trichloropyridine **1** with hydrazine hydrate (molar ratio of **2** to $N_2H_4 : H_2O$ was 1 : 4) for 4 h without solvent.

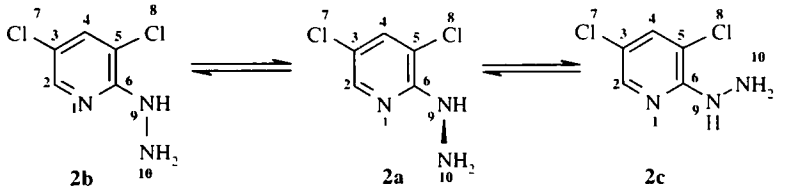
* For Part 6 see [1].

[1] A. N. Kosygin Moscow State Textile University, Moscow 117918, Russia; e-mail: office@msta.ac.ru.
[2] I. M. Gubkin State University for the Oil and Gas Industry, Moscow 117917, Russia. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 8, pp. 1066-1079, August, 2000. Original article submitted April 5, 2000.

0009-3122/00/3608-0931$25.00©2000 KluwerAcademic/Plenum Publishers



In the case of hydrazine **2** it is possible to generate an intramolecular hydrogen bond between the NH_2 group of the hydrazine fragment and the electronegative nitrogen atom of the pyridine ring (structure **2b**) or the chlorine atom in position 3 (structure **2c**).



Quantum chemical calculations (Table 1) were carried out by the semiempirical SCF MO LCAO method in the PM 3 valence approach [11,12] with full optimization of geometric parameters by the MOPAC program. These data showed that structures **2b** and **2c** are stable systems with intramolecular hydrogen bonds at the nitrogen and chlorine atoms respectively.* Structure **2a** models the transition state for the internal rotation of the NH_2–NH group about the C–N bond. It follows from the results of the calculations that structures **2b** and **2c** are energetically fairly close to one another but structure **2b**, in which a hydrogen bond is formed at the nitrogen atom of the

TABLE 1. Enthalpies of Formation ΔH, kJ/mole, Energies of the Highest Occupied (HOMO) and Lowest Unoccupied (LUMO) Molecular Orbitals, eV, and Charges on the Heavy Atoms Calculated by the PM 3 Method*

Property	2b	2a	2c
ΔH^0_f	168.35	210.85	175.34
E_{HOMO}	-8.92	-9.31	-8.88
E_{LUMO}	-0.56	-0.80	-0.59
Q_{N1}	-0.111	-0.009	-0.079
Q_{C2}	-0.021	-0.066	0.036
Q_{C3}	-0.212	-0.171	-0.195
Q_{C4}	-0.037	-0.072	-0.056
Q_{C5}	-0.209	-0.194	-0.170
Q_{C6}	-0.047	-0.066	-0.029
Q_{C7}	0.096	0.104	0.099
Q_{C8}	0.105	0.109	0.102
Q_{N9}	0.029	-0.050	-0.015
Q_{N10}	-0.033	-0.032	-0.055

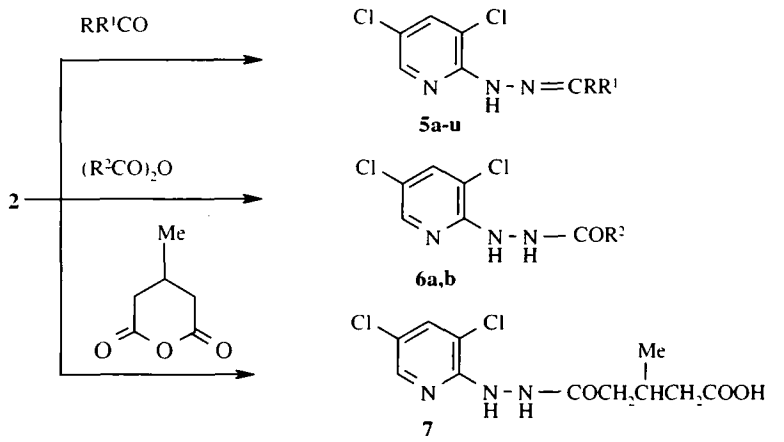
* The numbering of atoms corresponds to that given in the scheme for structures **2a-c**.

*Calculations were carried out by I. A. Abronin.

pyridine ring is 6.99 kJ/mole energetically more favorable. The rotational barrier (the difference in the enthalpies of formation for structures **2a** and **2b**) is relatively small and amounts to 42.5 kcal/mole. All this points to the conclusion that when analyzing the reactivities of these compounds it is necessary to consider the possibility of the presence of these structures in solution. From the data obtained on the electron density distribution (Table 1) it follows that the greatest difference between these structures is in the charges on the nitrogen atoms of the hydrazine fragment. When forming an intramolecular hydrogen bond with the chlorine atom the nucleophilic reactivity of the terminal nitrogen atom of the hydrazine fragment must increase. The data characterizing the energy of the LUMO for structures **2b** and **2c** must lead to an analogous conclusion.

N-(3,5-Dichloro-2-pyridyl)hydrazones **5a-t** or the naphthoquinonimine (**5u**) are formed on boiling equimolar quantities of hydrazine **2** and the appropriate aldehyde, ketone, or 1,2-naphthoquinone in ethanol or 1-propanol. The reaction time and yield of the desired hydrazone depends on the nature and reactivity of the initial carbonyl compound. For example, hydrazones **5a-j,m,n,u** are formed in 68-98% yield after boiling hydrazine **2** with mono- and disubstituted benzaldehydes, acetophenone, 3-chloroacetophenone, and 1,2-naphthoquinone in ethanol or 1-propanol for 15-45 min. On introducing into the reaction 3,5-di-*tert*-butyl-4-hydroxybenzaldehyde, in which the reactivity of the carbonyl group is significantly reduced due to conjugation with the hydroxy group and the shielding influence of the two tert-butyl groups [13], hydrazone **5k** was obtained in 75% yield after boiling the reactants in 1-propanol for 3.5 h. The hydrazones of ketones **5l,o-t** were formed in good yield (Table 2) on boiling the reactants in the solvent for 2-18 h.

The acylation of hydrazine **2** with acid anhydrides (molar ratio 1 : 1) in chloroform at 0-5°C leads in 75-80% yield to the N'-acyl derivatives **6a,b**. The N-substituted monohydrazide **7** was synthesized under analogous conditions from 3-methylglutaric acid anhydride.



5a-k R^1 = H, **a** R = 2-HOC_6H_4, **b** R = 4-HOC_6H_4, **c** R = 4-$MeOC_6H_4$, **d** R = 4-$Me_2NC_6H_4$, **e** R = 4-$O_2NC_6H_4$, **f** R = 4-$HOOCC_6H_4$, **g** R = 4-HO-3-$MeOC_6H_3$, **h** R = 2-HO-5-$MeOC_6H_3$, **i** R = 3-HO-4-$O_2NC_6H_3$, **j** R = 2-HO-5-$O_2NC_6H_3$, **k** R = 4-HO-3,5-(*t*-Bu)$_2C_6H_2$; **5l-q** R^1 = Me, **l** R = *cyclo*-C_3H_5, **m** R = Ph, **n** R = 3-ClC_6H_4, **o** R = 3-$H_2NC_6H_4$, **p** R = 4-$H_2NC_6H_4$, **q** R = 4-HO-2-MeC_6H_3; **5r** R = 4-ClC_6H_4, R^1 = Et; **5s** R = Ph, R^1 = 4-$O_2NC_6H_4$; **5t** R+R^1 = 2-adamantylidene; **5u** R+R^1 = 1-oxo-1,2-dihydro-2-naphthylidene; **6a** R^2 = Me, **b** R^2 = Et

There were intense absorption bands in the IR spectra of hydrazones **5a-u** (Table 2) at 1625-1640 cm^{-1} characteristic of a C=N bond and also bands assigned to other structural elements. A broad band was observed in the IR spectra of compounds **5a,h,j** (0.05 M in acetonitrile) for the stretching vibrations of the OH group at 3350-3340 cm^{-1}. The position of the bands was unchanged on diluting the solution, which indicates the presence in these compounds of a strong intramolecular hydrogen bond.

TABLE 2. Characteristics of the Synthesized N-(3,5-Dichloro-2-pyridyl)hydrazones **5a-u**

Compound	Empirical formula	Found, % / Calculated, %			mp, °C*	^{1}H NMR spectrum, δ, ppm (coupling constant, J, Hz)*[2]					Yield, %
		C	H	N		Pyridine ring protons, d (J_{46})		NH, 1H, br. s	–N=CH–, 1H, s	Other protons	
						4-H	6-H				
1	2	3	4	5	6	7	8	9	10	11	12
5a	$C_{12}H_9Cl_2N_3O$	51.04 / 51.09	3.26 / 3.22	15.02 / 14.89	162-164	7.78 (2.5)	8.20 (2.5)	10.04	8.48	6.82-7.02 (2H, m, H_{Ar}); 7.20-7.30 (2H, m, H_{Ar}); 11.76 (1H, s, OH)	70
5b	$C_{12}H_9Cl_2N_3O$	51.20 / 51.09	3.17 / 3.22	14.90 / 14.89	285-287	7.97 (2.4)	8.25 (2.4)	10.12	8.50	6.96 (2H, d, H_{Ar}, J = 7.0); 7.65 (2H, d, H_{Ar}, J = 7.0); 10.47 (1H, s, OH)	90
5c	$C_{13}H_{11}Cl_2N_3O$	52.61 / 52.72	3.68 / 3.74	14.10 / 14.19	142-143	7.55 (2.4)	8.20 (2.4)	8.45	7.98	3.82 (3H, s, MeO); 6.90 (2H, d, H_{Ar}, J = 8.0); 7.69 (2H, d, J = 8.0)	96
5d	$C_{14}H_{14}Cl_2N_4$	54.05 / 54.38	4.58 / 4.56	18.10 / 18.12	160-161	7.73 (2.4)	8.12 (2.4)	9.48	8.21	3.00 (6H, s, Me_2N); 6.75 (2H, d, H_{Ar}, J = 8.5); 7.58 (2H, d, H_{Ar}, J = 8.5)	66
5e	$C_{12}H_8Cl_2N_4O_2$	46.17 / 46.33	2.44 / 2.59	18.11 / 18.01	185-186	7.86 (2.4)	8.23 (2.4)	10.23	8.44	7.98 (2H, d, J = 8.0); 8.28 (2H, d, H_{Ar}, J = 8.0)	75
5f	$C_{13}H_9Cl_2N_3O_2$	50.14 / 50.35	2.87 / 2.93	13.48 / 13.55	289-290 (decomp.)	7.77 (2.2)	8.08 (2.2)	8.44	7.90	6.87 (2H, unsym. d, 2'-H, 6'-H); 7.08 (2H, unsym. d, 3'-H, 5'-H, $J_{2'3'} = J_{5'6'}$ = 2.0 and 3.4, $J_{2'5'} = J_{3'6'}$ = 0.3); 10.32 (1H, s, OH)	75
5g	$C_{13}H_{11}Cl_2N_3O_2$	49.82 / 50.02	3.44 / 3.55	13.66 / 13.46	214-215	7.94	8.02*[1]	8.18	7.87	2.74 (3H, s, MeO); 5.24 (1H, br. s, OH); 7.02 (1H, unsym. d, H_{Ar}, J_{AB} = 7.81); 7.14 (1H, unsym. d, H_{Ar}, J_{AB} = 7.81); 7.24 (1H, m, H_{Ar}, J_{AX} = 2.6)	91

TABLE 2 (continued)

1	2	3	4	5	6	7	8	9	10	11	12
5h	$C_{13}H_{11}Cl_2N_3O_2$	49.84 50.02	3.64 3.55	13.35 13.46	186-187	7.80 (3.0)	8.04 (3.0)	8.42	7.54	3.54 (3H, s, MeO); 6.62 (1H, unsym. d, 3'-H, $J_{3'4'}$ = 8.7, $J_{3'6'}$ = 0.3); 7.03 (1H, unsym. d, 4'-H, $J_{3'4'}$ = 8.7, $J_{4'6'}$ = 2.6); 7.38 (1H, m, 6'-H, $J_{3'6'}$ = 0.3, $J_{4'6'}$ = 2.6); 10.04 (1H, br. s, OH)	89
5i	$C_{12}H_8Cl_2N_4O_3$	44.13 44.06	2.53 2.46	17.29 17.17	169-170	7.80 (2.4)	8.25 (2.4)	10.11	8.42	7.54 (1H, dd, 2'-H, $J_{2'6'}$ = 1.8); 7.67 (1H, dd, 6'-H, $J_{5'6'}$ =7.8, $J_{2'6'}$ = 1.8); 8.20 (1H, d, 5'-H, $J_{5'6'}$ = 7.8); 11.68 (1H, s, OH)	81
5j	$C_{12}H_8Cl_2N_4O_3$	44.18 44.06	2.54 2.46	17.01 17.17	264-265.5	7.90	8.06*[3]	8.44	7.86	5.08 (1H, s, OH); 6.74 (1H, unsym. d, H_{Ar}, J_{AB} = 10.2); 6.98 (1H, unsym. d, H_{Ar}, J_{AB} = 10.2); 7.36 (1H, m, H_{Ar}, J_{AX} = 1.6)	87
5k	$C_{20}H_{25}Cl_2N_3O$	61.08 60.91	6.22 6.34	10.78 10.66	225-226	7.52 (2.7)	7.88 (2.7)	8.38	7.77	1.52 (18H, br. s, 2 *t*-Bu); 5.25 (1H, s, OH); 7.12 (2H, s, H_{Ar})	75
5l	$C_{10}H_{11}Cl_2N_3$	49.15 49.20	4.60 4.54	17.02 17.21	32-33.5*[4]	7.84 (1.8)	7.96 (1.8)	8.58	—	0.52-0.56 (4H, m, *cyclo*-C_3H_5); 0.72-0.64 (1H, m, *cyclo*-C_3H_5); 1.94 (3H, s, Me)	70
5m	$C_{13}H_{11}Cl_2N_3$	55.71 55.73	3.83 3.96	15.06 15.00	121-122	7.57 (2.0)	7.84 (2.0)	8.28	—	1.90 (3H, s, Me); 6.79-6.88 (5H, m, Ph)	92
5n	$C_{13}H_{10}Cl_3N_3$	49.44 49.63	3.08 3.20	13.52 13.36	105-106	7.56 (2.1)	7.88 (2.1)	8.68	—	1.74 (3H, s, Me); 6.84-7.04 (4H, m, H_{Ar})	89
5o	$C_{13}H_{12}Cl_2N_4$	52.99 52.90	4.21 4.10	18.74 18.98	146-146.5	7.92 (3.2)	8.14 (3.2)	8.77	—	2.68 (3H, s, Me); 6.04-6.08 (2H, br. s, NH_2); 6.96-7.12 (3H, m, H_{Ar}); 7.38 (1H, dd, H_{Ar})	90

TABLE 2 (continued)

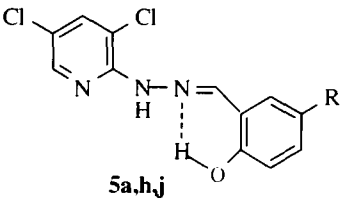
1	2	3	4	5	6	7	8	9	10	11	12
5p	$C_{14}H_{12}Cl_2N_4$	52.72 52.90	3.92 4.10	19.10 18.98	178-180	7.70 (3.0)	7.92 (3.0)	8.48		2.44 (3H, s, Me); 5.58 (2H, br. s, NH_2); 6.89 (2H, m, H_M); 7.37 (2H, m, H_M)	82
5q	$C_{14}H_{11}Cl_2N_3O$	54.31 54.26	4.10 4.05	13.71 13.65	246-247 (decomp.)	7.88 (2.4)	7.96 (2.4)	8.68	—	2.34 (3H, s, Me); 2.59 (3H, s, Me); 5.44 (1H, br. s, OH); 6.84 (1H, d, 5'-H and 6'-H, $J_{5'6'}$ = 9.0); 6.88 (1H, d, 5'-H and 6'-H, $J_{5'6'}$ = 9.0); 7.18 (1H, m, 3'-H)	71
5r	$C_{14}H_{12}Cl_3N_3$	51.28 51.17	3.51 3.68	13.04 12.79	155-156.5	7.77 (3.3)	8.10 (3.3)	8.48	-	1.26 (3H, t, Me); 3.40 (2H, q, CH_2Me); 6.60 (2H, m, 2'-H, 6'-H); 7.07 (2H, m, 3'-H, 5'-H, $J_{2'3'} = J_{5'6'}$ = 9.4, $J_{2'5'} = J_{3'6'}$ = 0.4, $J_{2'6'} = J_{3'5'}$ = 3.2)	83
5s	$C_{18}H_{12}Cl_2N_4O_2$	55.68 55.83	3.02 3.12	14.50 14.47	245-246	7.54 (3.0)	7.70 (3.0)	8.34		6.60 (2H, unsym. d, 2'-H, 6'-H, $J_{2'6'}$ = 2.4 and 3.2, $J_{2'5'} = J_{3'6'}$ =0.4); 6.82-6.94 (5H, m, Ph); 7.18 (2H, unsym. d, 3'-H, 5'-H, $J_{3'5'}$ =3.2 and 2.4)	81
5t	$C_{15}H_{14}Cl_2N_4$	57.90 58.07	5.36 5.52	14.07 13.55	146-147.5	7.72 (2.0)	7.96 (2.0)	8.82	-	1.80-1.96 (12H, m, CH_2 + 3'-H и 7'-H); 2.52 (1H, m, 5'-H); 3.04 (1H, m, 1'-H)	80
5u	$C_{15}H_9Cl_2N_3O$	56.44 56.63	2.88 2.85	13.36 13.21	230.5-233.5	7.52 (2.5)	7.88 (2.5)	8.38	-	6.68-6.84 (4H, m, H_M); 6.97-7.07 (2H, m, H_M); 10.52 (1H, s, OH)	86

* Compounds were recrystallized: **a-c,e,f,j,n,s** from 1-propanol; **d,i** from benzene; **g,h,m,o,p,u** from ethanol; **k** from a hexane–toluene mixture; **q** from toluene; **r** from a 1-propanol–toluene mixture; **t** from aqueous ethanol.

*[2] The spectra of compounds **a,b,d,e,i** were recorded in acetone-d_6; **f,g,h,j,m,n,r,s** in DMSO-d_6; **c,k,l,o,p,q,t,u** in $CDCl_3$.

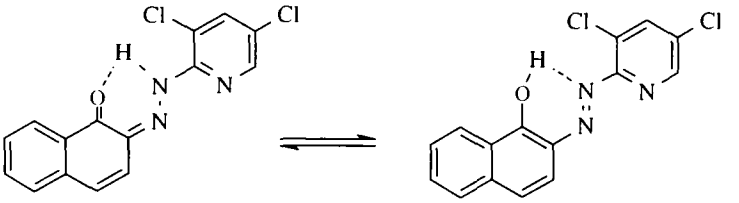
*[3] The signals of the pyridyl protons were observed as multiplets.

*[4] The compound was purified by HPLC.



5a,h,j

It is evident that hydrazone **5u** exists in solution as an equilibrium mixture of the hydrazone ⇌ azoenol type isomers (1,5-prototropic isomerism). In the azo-enol form **5u"** the carbonyl component acquires an aromatic character, which increases the probability of **5u** hydrazone existing in this form stabilized by an intramolecular hydrogen bond.



5u' 5"

The red color of compound **5u** is indirect confirmation of the azo-form existence. A broad absorption band is present at 3390 cm^{-1} in the IR spectrum of compound **5u** taken in a KBr disk, and is assigned to OH and NH groups. Its position is practically unchanged (3420 cm^{-1}) in the spectrum taken for a 5% solution in $CHCl_3$ and also on diluting the solution 5 or 10 times. There are also absorption bands in the spectrum at 1605 (–N=N–), 1635 (–C=N– in hydrazones), and 1670 cm^{-1} (C=O in cyclic α,β-unsaturated systems). In the ^1H NMR spectrum there were signals corresponding to the presence of the isomeric forms indicated. A broadened singlet at 8.38 ppm was assigned by us to the NH group and the fairly narrow singlet at 10.52 ppm to the hydroxyl group located in a quasi-aromatic chelate ring. The ^1H NMR spectra ($CDCl_3$) taken at various temperatures show the change in the ratio of the **5u'** and **5u"** forms. A solution of compound **5u** at -12°C contains 76, at 0°C 72.5, at 10°C 70, at 25°C 64.5, and at 45°C 58% of **5u'** isomer. When determining the melting point (Boetius stage, heating rate 2.5 °/min) it was established that above 105-107°C the color of the compound begins to change from dark red → red-violet → greenish violet → red → dark brown, which indicates the passage of some chemical changes.

The structure analysis for the compounds synthesized shows that some of them (such as **5b,g,k,q**) are of interest for testing as antioxidants. The hydrazones **5a,b,d,g,h,m,p,q** contain hydroxyl and amino groups in the aryl fragment which enable their use as azo and diazo components in the synthesis of dyestuffs. Hydrazones **5c,f,i,j,l,s** contain functional groups capable of further transformation.

It seemed of interest for us to study the reaction of diazonium salts with the hydrazones of substituted benzaldehydes and acetophenones **5a,b,d,g,h,m,p,q** containing hydroxyl, methoxyl, or dimethylamino groups, since such reactions have not been studied previously. It is known [14] that the introduction of a chloropyridyl residue into the molecule of a dye increases its performance properties (in particular, light-fastness of pigments). Diazonium salts obtained from aniline, *p*-aminobenzoic, sulfanilic, and *p*-aminobenzoyl-H-acids were used as diazo components. The azo coupling reactions were carried out by the standard procedure and gave the corresponding azo compounds **8a-j** in high yield (see Table 3).

The synthesized azo compounds **8a-j** did not have clear melting points and decomposed at 150-260°C. Introduction of the 3,5-dichloropyridyl fragment into the azo compound molecule causes a bathochromic shift of the absorption bands in the UV spectra and the appearance of new long wave bands, together with an increase in the intensity of all the absorption bands.

Since azo coupling may occur not only at the aromatic nucleus but also at the –N=CH– bond of the hydrazine fragment, the ^1H NMR spectrum of compound **8d** was recorded. The presence in the spectrum of a singlet at 7.68 ppm, assigned to the resonance of the –N=CH– group proton enabled the conclusion that the coupling reaction occurs in the ring containing activating groups [–OH, $-N(CH_3)_2$].

TABLE 3. Yields and UV Spectra of Compounds **8a-j**

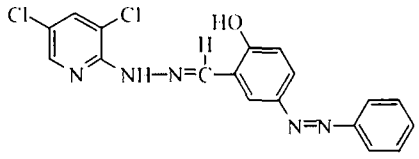
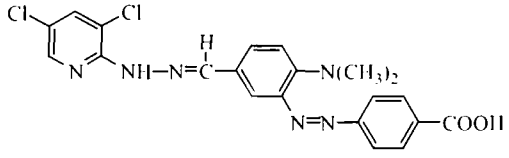
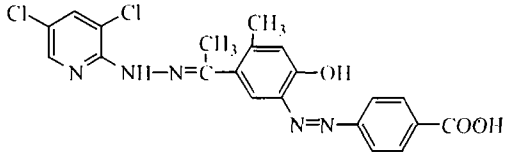
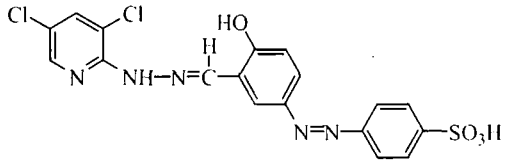
Compound	Formula of compound	λ_{max}, nm (log ε)*[2]	Yield, %
1	2	3	4
8a		476.4 (3.90) *356.4 (4.16) 298.8 (4.53) 269.2 (4.51) *230.0 (4.67) *215.6 (4.81)	91
8b		367.2 (3.93) 340.4 (4.56) 308.0 (4.59) 239.2 (4.27) *227.6 (4.03)	65
8c		329.2 (4.30) 270.8 (4.71) *215.6 (4.72)	70
8d		*534.0 (3.46) *446.4 (3.75) 370.4 (4.02) *314.0 (4.06) 284.0 (4.15) *226.4 (4.04)	76

TABLE 3 (continued)

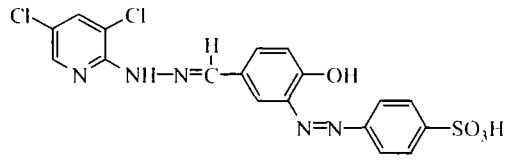
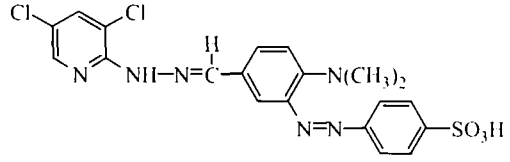
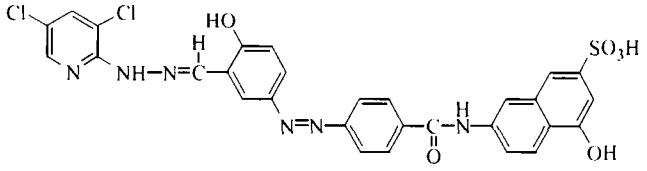
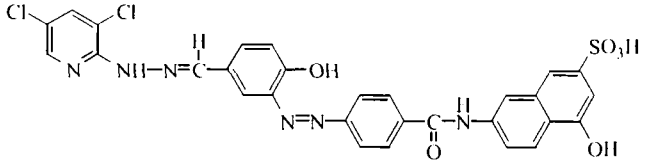
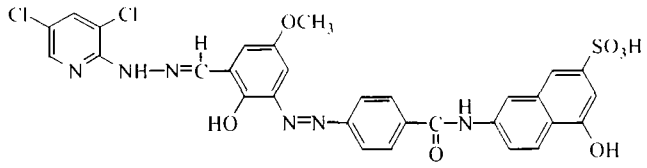
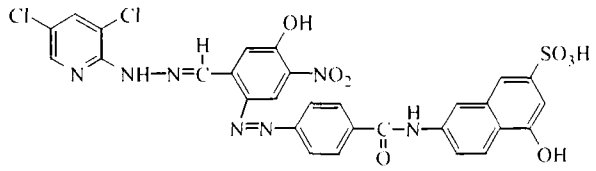
1	2	3	4
8e		*459.2 (3.35) 334.8 (3.58) 265.6 (3.85) *226.8 (3.74)	58
8f		*440.8 (2.89) 324.0 (3.67) 278.0 (3.66) *224.0 (3.62)	60
8g		*509.2 (4.27) 470.0 (4.37) *387.6 (4.12) *304.8 (4.41) 287.2 (4.46) *247.2 (4.41) 206.0 (4.56)	70
8h		*519.2 (3.95) 463.6 (4.14) *385.6 (3.92) 270.0 (4.37) *235.2 (4.33) 201.6 (4.41)	75

TABLE 3 (continued)

1	2	3	4
8i		*520.0 (4.22) 466.4 (4.36) *385.2 (4.13) 278.4 (4.39) *243.6 (4.34) 200.8 (4.42)	77
8j		*521.2 (4.25) 461.2 (4.40) *382.4 (4.20) 284.8 (4.43) 242.0 (4.41) 202.8 (4.46)	66

* Point of inflection.

*[2] The spectra of azo compounds **8a-c** were recorded in ethanol, and of the remaining dyestuffs in water.

Dyestuffs **8b-j** color protein (wool) and polyamide (capron) fiber under standard acid dyeing conditions (shades from yellow-brown to claret), and also dye with subsequent chromizing (wool). A deepening of the color of samples was observed on chromizing. Compounds **8a-c** color polyamide (capron) of a dispersed type (color is claret and terra cotta). In addition we have established that azo compounds **8g-j** may also be used for cellulose fiber (cotton) under direct dyeing conditions (shades in the red ranges).

The introduction into the molecule of the azo dye of a dichloropyridyl fragment confers on the compound biocidal (particularly fungicidal) activity [15], consequently all the dyes obtained and also the samples of tissue dyed with them were submitted to the Research Institute for Restoration for testing. Testing was carried out on the five molds most frequently harmful to textile materials. It was established that all the compounds displayed fungicidal properties (suppressed the spore-carrying of mycelia). The extent of the suppression depends both on the structure of the dye used and on the type of fiber and method of dyeing and varied for different samples within the limits 30-50%.

We noted that suppression of spore-carrying is the first indication of the mutagenicity of the substances applied. However no damage was established on investigating the DNA of the molds, which to a first approximation enables a conclusion to be drawn on some mechanism of action of the compounds studied.

EXPERIMENTAL

The IR spectra were recorded on Perkin-Elmer 983 and Perkin-Elmer 993 instruments in KBr disks, in Nujol, in thin films, or in solution in acetonitrile or chloroform. The ^{1}H NMR spectra were recorded on Bruker WP 250 and WM 360 spectrometers for 10-15% solutions at 22-24°C, internal standard was TMS. The UV spectra were obtained on a Uvidec 610 instrument in water and ethanol, layer thickness was 0.5-1.0 cm. A check on the progress of reactions and the purity of the compounds obtained was effected by TLC on Brockmann activity grade III Al_2O_3 in the solvent system benzene–acetone 15 : 1, on Silufol UV 254 plates in benzene or chloroform, and also on plates with a bound layer of Merck LU 074 Al_2O_3. Visualization was with iodine vapor. Paper chromatography on Filtrak 20 paper was used for compounds **8b-j**, eluent was water–ethanol–NH_4OH 1 : 1 : 1. Preparative high performance liquid chromatography was carried out on a Waters model 590 instrument, fitted with a Gilson model 116 UV detector with sensitivity range 0.1 and with stainless steel columns (1100 × 4.6 mm), packed with Lichrosorb RP-18 (5-10 μ) or Silasorb C_{18} (10 μ). Mobile phases were the solvent systems heptane–chloroform–methanol 70 : 20 : 10, benzene–chloroform–methanol 80 : 15: 5, ethyl acetate–hexane from 50 : 50 to 85 : 15, benzene–methanol from 95 : 5 to 75 : 25, flow rate was 1.2 ml/min, wavelength 255 nm. Melting points were determined with a Boetius PHMK-05 microinstrument, heating rate was 2-4°/min.

(3,5-Dichloro-2-pyridyl)hydrazine (2). A mixture of 2,3,5-trichloropyridine **1** (2.45 g, 13.4 mmol), 30% $N_2H_4 \cdot H_2O$ (2.6 ml, 46.9 mmol), and 1-propanol (1 ml) was boiled with stirring for 4 h. The reaction mixture was cooled to 20°C and an aqueous solution of NaOH (0.53 g, 13.4 mmol) in H_2O (10 ml) was added with stirring and the mixture was stirred for 20 min. The resulting white crystals were filtered off, washed with water, dried at 80°C, and crystallized from ethanol. Yield 90%; mp 180-182°C. After additional purification by HPLC mp 185-186.5°C (179-182°C [5], 172-174°C [6]). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm, J (Hz): 6.38 (1H, br. s, NH); 6.58 (2H, br. s, NH_2); 7.38 (1H, d, J_{46} = 2.3, 4-H pyridine); 7.88 (1H, d, 6-H pyridine). Found, %: C 33.81; H 2.85; N 23.57. $C_5H_5Cl_2N_3$. Calculated, %: C 33.73; H 2.83; N 23.60.

N,N'-Bis(3,5-dichloro-2-pyridyl)hydrazine (3). A mixture of hydrazine **2** (4.45 g, 25.0 mmol), pyridine **1** (5.019 g, 27.5 mmol), and pyridine (20 ml) was boiled for 12 h. The reaction mixture was poured into cold water (30 ml), and extracted with benzene. The benzene extract was evaporated in vacuum. The residue was purified by HPLC. Yield 75%; mp 105-106°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm, J (Hz): 6.48-6.52 (2H, m, 2NH); 7.29 (1H, d, J_{46} = 2.2, 4-H pyridine); 7.94 (1H, d, J_{46} = 2.2, 6-H pyridine); 7.37 (1H, J_{46} = 2.6, 4-H pyridine); 8.08 (1H, d, J_{46} = 2.6, 6-H pyridine). Found, %: C 36.52; H 2.08; N 15.02. $C_{10}H_6Cl_4N_4$. Calculated, %: C 36.38; H 1.82; N 15.15.

N-(3,5-Dichloro-2-pyridyl)hydrazones 5a-u (General Procedure). A mixture of pyridylhydrazine **2** (5.0 mmol), the appropriate aldehyde or ketone (5.25 mmol), in solvent (10 ml) (ethanol or 1-propanol) was boiled until disappearance of the initial hydrazine **2** from the reaction mixture (check with TLC, 15-45 min when

obtaining **5a-j,m,n,u**, 3.5 h when obtaining **5k**, 2-18 h when obtaining **5l,o-t**). After cooling the reaction mixture the precipitate was filtered off, dried, and recrystallized from a suitable solvent or purified by HPLC.

Acylation of (3,5-Dichloro-2-pyridyl)hydrazine 6a,b, 7 (General Procedure). A mixture of pyridylhydrazine **2** (5.0 mmol), mono- or dicarboxylic anhydride (5.0 mmol), and chloroform (10 ml) was stirred for 5-10 min. The solvent was evaporated, the residue treated with aqueous $NaHCO_3$ solution (5.0 mmol in 10 ml water), filtered off, washed with distilled water, dried over P_2O_5, and recrystallized from a suitable solvent, or purified by HPLC.

Acetic Acid (3,5-Dichloro-2-pyridyl)hydrazide (6a). Yield 80%; mp 116-118°C (heptane–chloroform). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm, *J* (Hz): 2.89 (3H, s, Me); 5.38 (1H, br. s, NH); 7.12 (1H, s, 4-H pyridine); 7.45 (1H, s, 6-H pyridine); 7.84 (1H, s, NHCO). Found, %: C 38.15; H 3.27; N 18.99. $C_7H_7Cl_2N_3O$. Calculated, %: C 38.21; H 3.21; N 19.10.

Propionic Acid (3,5-Dichloro-2-pyridyl)hydrazide (6b) was synthesized analogously. Yield 75%; mp 115-116°C (hexane–benzene). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm, *J* (Hz): 1.18 (3H, t, Me); 1.98 (2H, q, CH_2); 5.68 (1H, br. s, NH); 7.04 (1H, s, 4-H pyridine); 7.28 (1H, s, 6-H pyridine); 7.92 (1H, s, NHCO). Found, %: C 40.97; H 3.90; N 18.01. $C_8H_9Cl_2N_3O$. Calculated, %: C 41.05; H 3.88; N 17.95.

3-Methylglutaric Acid (3,5-Dichloro-2-pyridyl)-hydrazide (7) was synthesized analogously. Yield 83%; mp 128-129.5°C (HPLC). IR spectrum (KBr), ν, cm^{-1}: 3350 (broad band, NH), 3255 (NH), 2750-2765 (group of bands, dimerized OH), 1725 (C=O in COOH group), 1680 (C=O in CONH group, amide I band), 1575 (deformation vibrations of NH group, amide II band). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm, *J* (Hz): 1.14 (3H, d, Me); 1.64-1.81 (1H, m, CH); 2.20 (2H, unsymm. d, CH_2); 2.38 (2H, unsymm. d, CH_2); 5.02 (1H, br. s, NH); 7.67 (1H, d, J_{46} = 2.8, 4-H pyridine); 7.88 (1H, d, J_{46} = 2.8, 6-H pyridine); 9.38 (1H, br. s, CONH); 11.30 (1H, br. s, COOH). Found, %: C 43.04; H 4.16; N 13.56. $C_{11}H_{13}Cl_2N_3O_3$. Calculated, %: C 43.14; H 4.25; N 13.73.

General Procedure for Synthesis of Azocompounds 8a-j. Diazonium salt (as a solution or suspension) prepared from aniline (4.0 mmol) (when obtaining **8a**), *p*-aminobenzoic (**8b-c**), sulfanilic (**8d-f**), or *p*-aminobenzoyl-H-acid (**8g-j**) and $NaNO_2$ (4.0 mmol) was added with stirring to a solution of hydrazone **5a** (or **5b,g,h,m,p,q** respectively) (4.0 mmol) in 1 : 1 ethanol–water (30 ml) with the addition of alkali (when obtaining **8a,c-e,g-j**) or **5d** in 1 : 1 acetic acid–ethanol (30 ml) (when obtaining **8b,f**) at 3-5°C following the reaction temperature and its pH (pH 7.5-8.5 for **8a,c-e,g-j**; pH 4.0-5.5 for **8b,f**). The mixture was stirred until the end of the reaction of the azocompound at 3-5°C (negative test for discharge with R salt), the reaction mixture was heated to 60-80°C, and neutralized to pH 7.0 with sodium carbonate solution or with 30% acetic acid solution. The precipitated dyestuff was filtered off, washed with several small volume portions of distilled water, dried, and azocompounds **8a-j** were obtained (Table 3).

Azocompound **8e** was purified by HPLC, yield 76%; mp >220°C (decomp.). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm, *J* (Hz): 5.64 (1H, br. s, OH); 6.84-7.18 (7H, m, H arom); 7.68 (1H, s, CH=N); 7.90-7.98 (2H, m, 4-H and 6-H pyridine); 9.18 (1H, br. s, NH); 11.38 (1H, br. s, SO_3H).

REFERENCES

1. D. M. Gafarov, V. A. Shul'chishin, V. K. Korolev, and K. I. Kobrakov, *Izv. Vyssh. Uchebn. Zaved., Khim. Khim. Tekhnol.*, **40**, No. 2, 69 (1997).
2. E. Steiner, P. Martin, and D. Bellus, *Helv. Chim. Acta*, **65**, No. 3, 983 (1982).
3. M.-G. A. Shvekhgeimer, K. I. Kobrakov, S. S. Sychev, and V. K. Promonenkov, *Khim. Geterotsikl. Soedin.*, No. 8, 1082 (1987).
4. N. N. Mel'nikov, *Pesticides* [in Russian], Khimiya, Moscow (1987).
5. Ger. Offen. 3520327; *Chem. Abstr.*, **106**, 119882 (1987).
6. Ger. Offen. 3443308; *Chem. Abstr.*, **105**, 153057 (1986).
7. Ger. Offen. 3520328; *Chem. Abstr.*, **106**, 8460 (1987).
8. Ger. Offen. 3520330; *Chem. Abstr.*, **106**, 156458 (1987).
9. Ger. Offen. 3917469; *Chem. Abstr.*, **114**, 164251 (1987).

10. Z. G. Aliev, V. G. Kartsev, E. M. Gizatullina, S. V. Chapyshev, and L. O. Atovmyan, *Chemistry of Biologically Active Nitrogen Heterocycles. Reports*, Part 1, Chernogolovka (1990), p. 28.
11. J. J. P. Stewart, *J. Comput. Chem.*, **10**, No. 2, 209 (1989).
12. J. J. P. Stewart, *J. Comput. Chem.*, **10**, No. 2, 221 (1989).
13. Yu. A. Bruk, D. Yu. Rachinskii, L. V. Zolotova, and M. Z. Borodulina, *Zh. Obshch. Khim.*, **42**, 1603 (1972).
14. K. I. Kobrakov, G. S. Stankevich, and A. A. Makarov, *Vestnik MGTA*, Moscow (1995), p. 88.
15. K. I. Kobrakov, G. S. Stankevich, V. T. Kondratkov, and M. B. Dmitrieva, *Khim. Volokna*, No. 4, 38 (1999).