REARRANGEMENT OF 2,3,5,6-TETRACHLORO-4-PYRIDYL β-HYDROXYETHYL SULFONE

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A method for the preparation of 4-mercapto-2,3,5,6-tetrachloropyridine was modified. 2,3,5,6-Tetrachloro-4-pyridyl β-hydroxyethyl sulfone was synthesized and converted to 4-hydroxytetrachloropyridine by the action of a base. A mechanism for this rearrangement is proposed.

To carry out the Smiles rearrangement in the polychloropyridine series we accomplished the synthesis of 2,3,5,6-tetrachloro-4-pyridyl β-hydroxyethyl sulfone from 4-mercapto-2,3,5,6-tetrachloropyridine (I). In the case of the preparation of mercapto compound I by reaction of pentachloropyridine with potassium hydrosulfide in alcohol [1] we established that there are two simultaneous competitive processes: reaction with potassium hydrosulfide to give I, and reaction with the alcohol to give 4-ethoxy-2,3,5,6-tetrachloropyridine (IIa). When ethanol is replaced by isopropyl alcohol, the ratio of substitution products does not change. The use of a small amount of water (~5%) in the reaction completely excludes the formation of 4-alkoxy-2,3,5,6-tetrachloropyridines (IIa, b). This is evidently explained by the fact that the water increases the dissociation of KSH and thereby also increases the concentration of SH^- ions. However, in anhydrous solutions potassium hydrosulfide also acts as a base, and this makes the competitive reaction with alcohol possible [2].

The desired 2,3,5,6-tetrachloro-4-pyridyl β-hydroxyethyl sulfide (III) is formed by the action of ethylene chlorohydrin on the sodium salt of mercaptan I. To protect the terminal hydroxy group this sulfide was acetylated thoroughly with acetic anhydride to give 2,3,5,6-tetrachloro-4-pyridyl β-acetoxyethyl sulfide (IV), which we oxidized with trifluoroperacetic acid; however, instead of the expected 2,3,5,6-tetrachloro-4-pyridyl β-acetoxyethyl sulfone, we obtained 2,3,5,6-tetrachloro-4-pyridyl β-hydroxyethyl sulfone (V). We found that sulfone V can also be obtained as a result of oxidation of sulfide II with trifluoroperacetic acid.

The structure of sulfone V was proved by its conversion to the known 2,3,5,6-tetrachloro-4-pyridyl β-chloroethyl sulfone [3]. The IR spectrum of sulfone V contains intense absorption bands at 1170 and 1340 cm^{-1}, which are characteristic for the symmetrical and asymmetrical vibrations of the SO_2 group, and a broad band at 3300-3600 cm^{-1} (OH group with an intermolecular hydrogen bond). When the chloroform solution is diluted, the associates are decomposed, and a single band of medium intensity appears in the spectrum at 3620 cm^{-1}. The PMR spectrum contains two triplets at 4.6 and 4.12 ppm of the methylene protons of the SO_2CH_2 and CH_2O groups and a singlet of an OH group at 2.65 ppm.

4-Hydroxy-2,3,5,6-tetrachloropyridine (VI) rather than the corresponding sulfinic acid – the product of the Smiles rearrangement – was completely unexpectedly obtained when sulfone V was treated with aqueous sodium bicarbonate solution at room temperature. The mechanism of the formation of VI can be conceived of as being the result of intramolecular attack by oxide anion A on the electron-deficient 4-C atom to give a new C–O bond with simultaneous cleavage of the $C-SO_2$ bond. Owing to a shift of the electron density from the carbanion to the strong electron-acceptor tetrachloropyridyl residue, intermediate sulfinic acid B undergoes decomposition to give VI and vinylsulfinic acid.

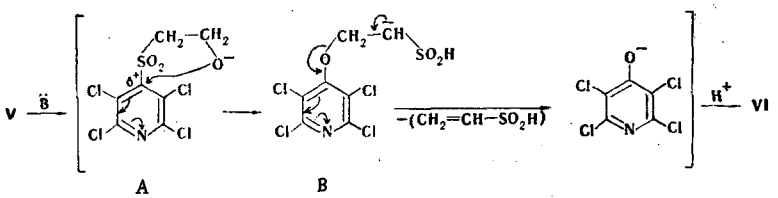

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TABLE 1. Characteristics of the Synthesized Compounds

Compound	mp, °C*	Found, %			Empirical formula	Calculated, %			Yield, %
		Cl	N	S		Cl	N	S	
I	159–160	56,9	5,5	12,7	C_5HCl_4NS	57,0	5,6	12,8	97
IIa	58–59	54,1	5,3	—	$C_7H_5Cl_4NO$	54,4	5,4	—	26
IIb	76–77	51,4	5,0	—	$C_8H_7Cl_4NO$	51,6	5,1	—	24
III	97–99	48,1	4,7	10,8	$C_7H_5Cl_4NOS$	48,5	4,8	10,9	89
IV	59–60	42,1	4,3	9,4	$C_9H_7Cl_4NO_2S$	42,4	4,1	9,6	92
V	137–138	43,7	4,2	10,0	$C_7H_5Cl_4NO_3S$	43,7	4,3	9,8	85
VI	227–229	54,3	5,2	—	$C_7H_5Cl_4NO$	54,4	5,4	—	86
VII	52–54	45,9	4,6	10,3	$C_8H_7Cl_4NOS$	46,1	4,5	10,4	62
VIII	131–132	34,2	6,6	7,6	$C_{13}H_8Cl_4N_2O_3S$	34,3	6,8	7,7	83
IX	94–96	41,8	4,0	9,3	$C_8H_7Cl_4NO_3S$	41,9	4,1	9,4	90
X	170–171	32,0	6,2	7,1	$C_{13}H_8Cl_4N_2O_5S$	31,8	6,3	7,1	65
XI	109–110	46,4	4,7	10,5	$C_7H_3Cl_4NO_2S$	46,3	4,6	10,4	80

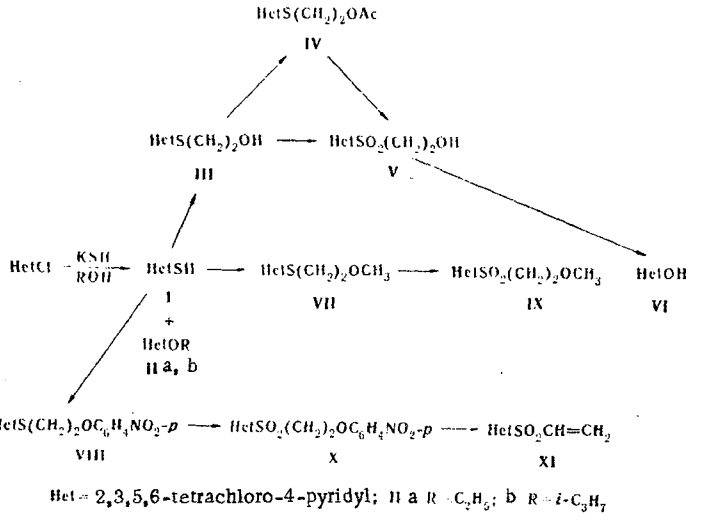
*The compounds were recrystallized: I-III and VI-X from ethanol, IV and XI from heptane, and V from water.

The intramolecular character of the rearrangement [4] is confirmed by the fact that it also takes place when anhydrous alcohol or benzene solutions of sulfone V are treated with triethylamine. In addition, replacement of the alkylsulfonyl group in V by a hydroxy group does not occur when 4-methylsulfonyl-2,3,5,6-tetrachloropyridine is treated with aqueous sodium bicarbonate solution at 20°C for 24 h.

According to the UV-spectral data, the intensity of the absorption band at 320 nm, which is characteristic for sulfone V, decreases to zero with time, and a corresponding increase in the maximum at 285 nm, which is characteristic for VI, is observed. The presence of an isobestic point in the recording of many of the curves and the absence of coloration constitute evidence that this rearrangement does not proceed through a step involving the formation of a Meisenheimer complex but rather via a synchronous addition–cleavage mechanism.

It was also established by means of the UV spectrum that the reaction goes to completion in 10-15 sec in ethanol at 20°C, as compared with 30 min at 10°C and 2.5 h at 2°C.

The reaction rate is reduced by a factor of almost five in 25% aqueous alcohol solution. The inhibiting effect of water is evidently due to a decrease in the nucleophilicity of anion A due to its hydration, as a result of which attack on the electrophilic 4-C atom is hindered.



Het = 2,3,5,6-tetrachloro-4-pyridyl; II a R = C_2H_5; b R = i-C_3H_7

In order to ascertain the effect of some structural factors on the course of the rearrangement, we accomplished the synthesis of methoxy and p-nitrophenoxy derivatives of V. The reaction of the sodium salt of I with 2-methoxy- and 2-(p-nitrophenoxy)ethyl bromides gives 2,3,5,6-tetrachloro-4-pyridyl β-methoxyethyl and 2,3,5,6-tetrachloro-4-pyridyl β-(p-nitrophenoxy)ethyl sulfides (VII and VIII), which upon oxidation with 30% hydrogen peroxide in trifluoroacetic acid give the corresponding sulfones IX and X. At the same time, sulfone IX remains unchanged when it is heated in dimethylformamide (DMF), whereas sulfone X is converted to p-nitrophenol and 2,3,5,6-tetrachloro-4-pyridyl vinyl sulfone (XI). The behavior of sulfone X under these conditions is similar to the behavior of 2,3,5,6-tetrachloro-4-pyridyl β-chloroethyl sulfone [3], which in the presence of tri-

ethylamine readily splits out hydrogen chloride and is converted to the same sulfone (XI). Thus an indispensable condition for the realization of a rearrangement of this type is evidently the presence of a free hydroxy group.

EXPERIMENTAL

The UV spectra of solutions of the compounds ($2 \cdot 10^{-4}$ mole/liter) were recorded with a Specord UV-vis spectrophotometer. The IR spectra were recorded with a UR-20 spectrometer. The PMR spectra were recorded with a Tesla BS-487-B spectrometer (80 MHz) with hexamethyldisiloxane as the external standard. The results of analysis and the melting points of the synthesized compounds are presented in Table 1.

2,3,5,6-Tetrachloro-4-mercaptopyridine (I). A) A mixture of 2.3 g (0.04 mole) of KOH in 150 ml of ethanol was saturated with H_2S at 0°C for 30 min, after which 5 g (0.02 mole) of pentachloropyridine was added, and the mixture was heated at 50°C for 2.5 h while passage of H_2S into the mixture was continued. The alcohol was then partially removed by vacuum distillation, and the residue was treated with water and benzene. The aqueous layer was separated and acidified with HCl, and the mixture was worked up to give I in 72% yield. The benzene solution was washed with water and dried over $NaCO_3$. The yield of IIa was 26%.

B) When ethanol was replaced by isopropyl alcohol, 70% I and 24% 4-isopropoxy-2,3,5,6-tetrachloropyridine (IIb) were obtained.

C) A 2.3-g (0.04 mole) sample of KOH was dissolved in a mixture of 150 ml of ethanol and 5 ml of water, and the solution was saturated with H_2S at 0°C for 30 min. It was then treated with 5 g (0.02 mole) of pentachloropyridine, and the mixture was heated at 50°C for 2.5 h as H_2S passage was continued. The mixture was then poured into water, and the aqueous mixture was acidified with HCl.

2,3,5,6-Tetrachloro-4-pyridyl β-Hydroxyethyl sulfide (III). A mixture of 2.71 g (0.01 mole) of the sodium salt of I in 20 ml of propyl alcohol and 1.3 ml (0.02 mole) of ethylene chlorohydrin was refluxed for 3 h, after which a portion of the solvent was removed by distillation, and the residue was treated with water.

2,3,5,6-Tetrachloro-4-pyridyl β-Acetoxyethyl Sulfide (IV). A 2.9-g (0.01 mole) sample of sulfide II was refluxed in 20 ml of acetic anhydride for 2 h, after which the acetic anhydride was removed by vacuum distillation.

2,3,5,6-Tetrachloro-4-pyridyl β-Hydroxyethyl Sulfone (V). A) A 1.65-g (5 mmole) sample of sulfide III was dissolved in 20 ml of trifluoroacetic acid, 3 ml of 30% H_2O_2 was added, and the mixture was refluxed for 1.5 h. It was then cooled and diluted with 20 ml of water. UV spectrum, λ_{max}: 209 and 315 nm.

B) The oxidation of sulfide III was carried out under similar conditions. The yield was 89%.

4-Hydroxy-2,3,5,6-tetrachloropyridine (VI). A) A 1.6-g (5 mmole) sample of sulfone IV was stirred in 30 ml of a 5% solution of Na_2CO_3 at 20°C for 2 h, during which the solid vanished completely. The solution was acidified with dilute HCl. UV spectrum, λ_{max}: 218 and 280 nm.

B) A 0.03-g (0.1 mmole) sample of sulfone IV was dissolved in 100 ml of ethanol, two drops of triethylamine were added, and the mixture was stirred for 5 min. It was then treated with 1 ml of concentrated HCl, and the solvent was removed by vacuum distillation.

2,3,5,6-Tetrachloro-4-pyridyl β-Methoxyethyl Sulfide (VII). A mixture of 2.71 g (0.01 mole) of the sodium salt of I, 20 ml of isopropyl alcohol, and 2 g (0.02 mole) of 2-methoxyethyl chloride was refluxed for 2.5 h, after which it was cooled and treated with 40 ml of water.

2,3,5,6-Tetrachloro-4-pyridyl β-Methoxyethyl Sulfone (IX). This compound was obtained by the procedure used to prepare V.

2,3,5,6-Tetrachloro-4-pyridyl β-(p-Nitrophenoxy)ethyl Sulfide (VIII). A mixture of 2.71 g (0.01 mole) of the sodium salt of I, 3.26 g (0.01 mole) of 2-(p-nitrophenoxy)ethyl bromide, and 30 ml of DMSO was heated at 110°C for 2 h, after which it was cooled and poured over ice.

2,3,5,6-Tetrachloro-4-pyridyl β-(p-Nitrophenoxy)ethyl Sulfone (X). This compound was obtained by the procedure used to prepare sulfone V.

2,3,5,6-Tetrachloro-4-pyridyl Vinyl Sulfone (XI). A mixture of 0.44 g (1 mmole) of X and 15 ml of DMF was refluxed for 10 min, after which it was cooled and poured over ice.

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SYNTHESIS AND SPECTRAL CHARACTERISTICS OF 1-(3-PYRIDYL)-3-ARYL-8-NITRO(AMINO)BENZO-[f]QUINOLINES

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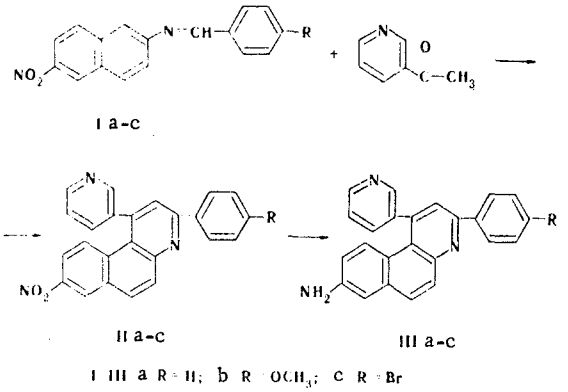
1-(3-pyridyl)-3-aryl-8-aminobenzo[f]quinolines were synthesized by reduction with tin in acidic media of 1-(3-pyridyl)-3-aryl-8-nitrobenzo[f]quinolines obtained by catalytic condensation of arylidene(6-nitro)-2-naphthylamines with acetylpyridine. The structures of the compounds were proved by a set of data from elementary analysis and IR, UV, and mass spectroscopy. The change in the luminescence of 1-(3-pyridyl)-3-aryl-8-aminobenzo[f]quinoline as a function of the solvent was studied.

Continuing our study of the spectral properties of benzo[f]quinoline derivatives [1] we synthesized 1-(3-pyridyl)-3-arylbenzo[f]quinolines containing amino and nitro groups in the 8 position:



I a-c

II a-c

III a-c

I, III a R = H; b R = OCH_3; c R = Br

The 1-(3-pyridyl)-3-aryl-8-nitrobenzo[f]quinolines (II) were obtained by catalytic condensation of arylidene-(6-nitro)-2-naphthylamine (I) with acetylpyridine. The 1-(3-pyridyl)-3-aryl-8-aminobenzo[f]quinolines (III) were synthesized by reduction of the corresponding nitro derivatives (II) with stannous chloride in glacial acetic acid (Table 1).

The structures of the compounds obtained were confirmed by the results of elementary analysis and the data from the IR, UV, and mass spectra. The IR spectra of II and III contain absorption bands characteristic for the stretch ing and deformation vibrations of NO_2 (1520-1530 and 1335-1340 cm^{-1}) and NH_2 (3400-3500 and 1630-1640 cm^{-1} groups, respectively.

Maximally intense molecular-ion peaks are observed in the mass spectra of II and III (Fig. 1). The agreement between the m/e values of the molecular-ion peaks and the molecular weights confirms the proposed

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