THE PYRIDYLETHYLATION REACTION OF N-ARYLDITHIOCARBAMIC ACIDS

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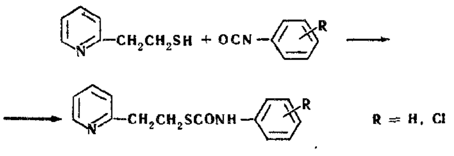
The reaction of 2-(β-mercaptoethyl)pyridine with some aryl isocyanates and aryl isothiocyanates, leading to the formation of β-2-pyridylethyl-N-arylthiocarbamates and -dithiocarbamates has been studied. The latter compounds may also be obtained by the pyridylethylation of N-aryldithiocarbamic acids. The influence of the individual groups on the course of the pyridylethylation reaction has been studied.

In the search for new pesticides, we have studied the reaction of 2-(β-mercaptoethyl)pyridine with phenyl isocyanates. It has been found that β-(2-pyridyl)ethyl N-phenylthiocarbamates are readily formed.



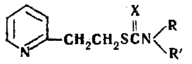
The reaction of 2-(β-mercaptoethyl)pyridine with phenyl, p-methoxyphenyl, and p-ethoxyphenyl isothiocyanates takes place similarly, leading to the corresponding dithiocarbamates. However, in the case of o-tolyl, o-methoxyphenyl, and α- and β-naphthyl isothiocyanates instead of the dithiocarbamates, only the corresponding symmetrical diarylthioureas were isolated, with a yield of 25–40%. It proved possible to obtain these dithiocarbamates by the pyridylethylation of dithiocarbamic acids, in a similar manner to that described for N,N-diethyldithiocarbamic acid [1].

It is known that amines [2], amides [3], phenols [4], and mercaptans [5] having free hydrogen atoms in the corresponding group take part in the pyridylethylation reaction. A comparison of the conditions of the pyridylethylation of amides and of N,N-diethyldithiocarbamic acid shows that the latter reacts incomparably more easily than the former. Consequently, it was possible to expect the predominant pyridylethylation of monosubstituted dithiocarbamic acids at the SH group.

It was first of interest to study whether an N-aryl residue in the dithiocarbamic acid affected the course of this reaction. It was found that ammonium N-methyl-N-phenyldithiocarbamate, which was used in the pyridylethylation reaction in the presence of acetic acid in the usual way, gave a good yield of β-(2-pyridylethyl) N-methyl-N-phenyldithiocarbamate. Thus, the presence of the aromatic radical in the amide group has no adverse effect on the pyridylethylation of N-aryldithiocarbamic acids.

In agreement with the hypothesis, the pyridylethylation of N-monophenyldithiocarbamic acid gave the expected β-(2-pyridylethyl) N-phenyldithiocarbamate, the structure of which was shown by independent synthesis from phenyl isothiocyanate and 2-(β-mercaptoethyl)pyridine. A number of other dithiocarbamates was synthesized similarly, including those not obtained by the reaction of 2-(β-mercaptoethyl)pyridine with aryl isothiocyanates. All the dithiocarbamic acids studied, including those with an OH group in a phenyl ring, which could be obtained in the form of ammonium

Compounds of the General Formula



Compound	R*	Mp, °C	Empirical formula	Found, %		Calculated, %		Yield, %
				N	S	N	S	
I	C_6H_5	114—115	$C_{14}H_{14}N_2OS$	10.94	11.99	10.84	12.41	84
II	C_6H_4Cl-*m*	130—131	$C_{14}H_{13}ClN_2OS$	9.52	10.73	9.57	10.95	91
III	$CH_2C_6H_5$	84—85	$C_{15}H_{16}N_2S_2$	9.77	22.07	9.71	22.23	90
IV	C_6H_5	79—81	$C_{15}H_{16}N_2S_2$	9.51	22.05	9.71	22.23	96
V	C_6H_5	137—138	$C_{14}H_{14}N_2S_2$	10.16	22.94	10.21	23.37	74
VI	$C_6H_4CH_3$-*o*	121.5—122.5	$C_{15}H_{16}N_2S_2$	9.78	22.20	9.71	22.23	75
VII	$C_6H_4CH_3$-*m*	137.5—138.5	$C_{15}H_{16}N_2S_2$	9.46		9.71	22.23	100
VIII	$C_6H_4CH_3$-*p*	153—154	$C_{15}H_{16}N_2S_2$	9.45	22.04	9.71	22.23	95
IX	$C_6H_4OCH_3$-*o*	114.5—115.5	$C_{15}H_{16}N_2OS_2$	9.19	20.76	9.20	21.06	100
X	$C_6H_4OCH_3$-*p*	128—129	$C_{15}H_{16}N_2OS_2$	9.31	21.15	9.20	21.06	93
XI	$C_6H_4OC_2H_5$-*p*	103—104	$C_{16}H_{18}N_2OS_2$	8.61		8.80		85
XII	C_6H_4OH-*o*	134—135	$C_{14}H_{14}N_2OS_2$	9.56	21.97	9.65	22.10	92
XIII	C_6H_4OH-*p*	144—145	$C_{14}H_{14}N_2OS_2$	9.78	22.11	9.65	22.10	90
XIV	$C_{10}H_7$-2	129—131	$C_{18}H_{16}N_2S_2$	8.85	20.00	8.63	19.76	96
XV	C_5H_4N-3	141—142	$C_{13}H_{13}N_3S_2$	15.44	22.90	15.26	23.29	54
XVI	$N(C_6H_5)_2$	155.5—156.5	$C_{20}H_{19}N_3S_2$	11.61	17.84	11.50	17.54	85
XVII	NHC_6H_5	148—149	$C_{14}H_{15}N_3S_2$	14.48	22.06	14.52	22.16	80
XVIII	$NHCOC_6H_5$	124—124.5	$C_{15}H_{15}N_3OS_2$	13.47	19.96	13.24	20.20	70
XIX	$NHCOC_6H_4NO_2$-*m*	132—134	$C_{15}H_{14}N_4O_3S_2$	15.38	17.93	15.46	17.69	87
XX	$NHCOC_5H_4N$-3	126—127	$C_{14}H_{14}N_4OS_2$	17.81	19.73	17.60	20.14	68

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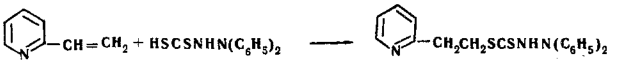
*In compounds I and II, X = O, in III–XX, X = S; in IV, $R_1 = CH_3$; in the others, R_1 = H. Heptane was used for the recrystallization of compounds I and II, acetone for III–VIII, and methanol for IX–XX.

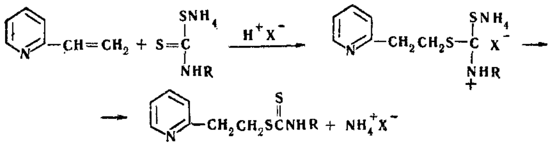
salts from an amine, carbon disulfide, and ammonia, took part in the pyridylethylation reaction with the formation of the corresponding dithiocarbamates. Nitroanilines, p-aminoazobenzene, 2-aminopyridine, and other compounds did not react with carbon disulfide. Nevertheless, 3-aminopyridine yielded β-2-pyridylethyl N-3-pyridyldithiocarbamate.

A study of the possibility of obtaining pyridylethyl dithiocarbazates was also of interest. α,α-Diphenyldithiocarbazic acid reacted like the dithiocarbamic acids with the formation of β-2-pyridylethyl N,N-diphenyldithiocarbazate.



N-Monophenyldithiocarbazic acid also reacted without appreciable complications. As starting material we used carboxylic acid hydrazides, which react with carbon disulfide and alkali in a similar manner to phenylhydrazine, forming salts of N-acyldithiocarbazic acids. The latter are also capable of undergoing the pyridylethylation reaction in the presence of acetic acid. Thus, the corresponding dithiocarbazates were obtained from benzyhydrazide, m-nitrobenzhydrazide, and nicotinic acid hydrazide.

The high rate and ease of performance of the pyridylethylation process (room temperature, pH 5–6) of dithiocarbamic and dithiocarbazic acids combined with the low solubility of their salts in water permits the assumption that the reaction takes place differently from the manner shown in the above schemes. It is most likely that the reaction takes place in the manner of the reaction of 2-vinylpyridine with thiourea in the presence of an acid catalyst.



It is not the free dithioacids that take part in the reaction but their salts. In favor of this is the fact that the comparatively strong dithioacids cannot be displaced from their salts by the weak acetic acid.

EXPERIMENTAL

Reaction of 2-(β-mercaptoethyl)pyridine with arylisocyanates and arylisothiocyanates. Equimolecular amounts (0.02 mole) of 2-(β-mercaptoethyl)pyridine and an aryl isocyanate (or aryl isothiocyanate) were heated in 20 ml of benzene in the water bath for 8–10 hr. Then the benzene was distilled off and the dry residue was recrystallized from heptane or acetone.

Reaction of 2-vinylpyridine with dithiocarbamic and dithiocarbazic acids. The majority of the compounds were obtained without isolation of the ammonium or potassium salts of the dithiocarbamic or dithiocarbazic acids formed as intermediates. Both the free bases and their salts are suitable for the synthesis. If the initial amine or hydrazine is a crystalline substance insoluble in aqueous alkali, to accelerate the reaction with carbon disulfide a small amount of methanol or ethanol must be added. If, in the second stage, i.e., in pyridylethylation, an amount of acetic acid sufficient only to bind the NH_4^+ ions (pH 7) is used, the reaction takes place slowly and a considerable part of the 2-vinylpyridine polymerizes. For the reaction to take place successfully, a pH of 5–6 is necessary.

β-2-Pyridylethyl N-o-methoxyphenyldithiocarbamate. A mixture of 8.3 g (0.067 mole) of o-anisidine, 9 g (0.119 mole) of 25% ammonia, and 6 g (0.079 mole) of carbon disulfide was stirred at room temperature for 45 min. Disregarding the precipitate that had deposited, 30 ml of water, 7.2 g (0.068 mole) of 2-vinylpyridine, and glacial acetic acid to pH 5–6 (~10 ml) were added to the reaction mixture. Immediately after the addition of the acetic acid, a vigorous reaction took place with the evolution of heat. After 30 min, the precipitate that had deposited was filtered off, carefully washed with water, and dried. Yield ~100%. Mp 114–116° C. After recrystallization from methanol, mp 114.5–115.5° C.

β-2-Pyridylethyl N,N-diphenyldithiocarbazate. A mixture of 14.9 g (0.067 mole) of α,α-diphenylhydrazine hydrochloride, 18 g (0.238 mole) of 25% ammonia solution, 6 g (0.079 mole) of carbon disulfide, and 20 ml of methanol was stirred at room temperature for 30 min. Then 30 ml of water and 7.2 g (0.068 mole) of 2-vinylpyridine were added and the mixture was worked up in a manner similar to the preceding experiment.

β-2-Pyridylethyl N-benzoyldithiocarbazate. A mixture of 12.5 g (0.05 mole) of benzoyl dithiocarbazate, 5.3 g (0.05 mole) of 2-vinylpyridine, and 5 ml of glacial acetic acid was stirred at room temperature for 1 1/2 hr. The precipitate that deposited was treated in a similar manner to the preceding experiment.

Summarized information on the preparation of the dithiocarbamates and dithiocarbazates is given in the table.

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