

PYRIDYLETHYLATION OF CYCLIC THIOAMIDES AND AMIDES.

I. PYRIDYLETHYLATION IN THE TETRAZOLE AND 1, 2, 4-TRIAZOLE SERIES

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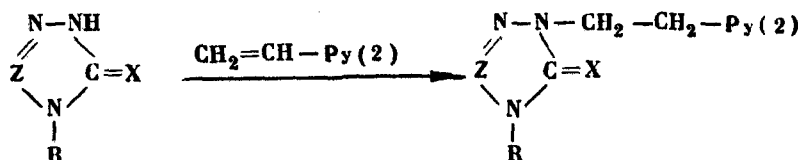
1-Aryltetrazoline-5-thiones and 4-aryl-1, 2, 4-triazolyl-3-thiones which are cyclic amides and potential mercapto compounds have been 2-pyridylethylated for the first time. It is shown that in the compounds prepared the 2-pyridylethyl-2 group is on the nitrogen atom of the thioamide group, so that the above compounds react as thiones.

Previous publications [1, 2] described the cyanoethylation of 1-aryltetrazoline-5-thiones (Ia) and 4-aryl-1, 2, 4-triazoline-3-thiones (IIa), and it was shown that in the case of compounds Ia, reaction takes place at both the nitrogen and the sulfur of the thioamide group. In cyanoethylation of IIa, reaction occurs only at the nitrogen of the thioamide group.

As pyridylethylation has a mechanism similar to that of cyanoethylation [3], it was of interest to bring about pyridylethylation of the cyclic thioamides Ia, IIa, as well as of the corresponding amides Ib, IIb. Pyridylethylation of cyclic thioamides, which are potentially mercapto compounds, has not, as far as is known, so far been investigated. Among other things, effecting this reaction could conceivably lead to physiologically active substances.

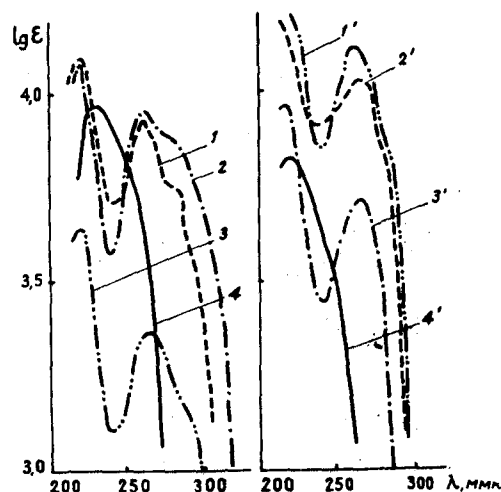
Pyridylethylation is effected by reacting 2-vinylpyridine with compounds Ia and IIa at 105-115° in the presence of glacial acetic acid. In almost all cases the yield of reaction products is about 85%. Pyridylethylation of the tetrazolinone (Ib) and triazolinone (IIb) also takes place smoothly. The resultant compounds crystallize well and readily give hydrochlorides and picrates. The compounds synthesized and their properties are given in the table.

Since the starting compounds Ia and IIa are potential mercapto compounds, pyridylethylation can give compounds of thione or thiol structure. Study of the uv and ir spectra shows that pyridylethylation takes place at the thioamide group, and that the compounds have structures IIIa and IVa.



	Ia, Ib, IIa, IIb	IIIa, IIIb, IVa, IVb
Ia, IIIa	Z=N, X=S	IIa, IVa Z=CH, X=S
Ib, IIIb	Z=N, X=O	IIb, IVb Z=CH, X=O

This conclusion can be drawn from the uv spectra of derivatives Ia and IIa, having thiol structures, differing from those of the starting thiones and their N-derivatives (see figure). On comparing the uv spectra of the compounds obtained



1. 1-phenyl-4-[2-(2-pyridyl)ethyl]tetrazoline-5-thione
2. 1-phenyltetrazoline-5-thione
3. 1-phenyl-4-(β-cyanoethyl)tetrazoline-5-thione
4. 1-phenyl-5-methylmercaptotetrazole
- 1'. 1-phenyl-2[2-(2-pyridyl)ethyl]-1, 2, 4-triazoline-3-thione
- 2'. 4-phenyl-1, 2, 4-triazoline-3-thione
- 3'. 4-phenyl-2-(β-cyanoethyl)-1, 2, 4-triazoline-3-thione
- 4'. 4-phenyl-3-(methylmercapto)-1, 2, 4-triazole

Pyridylethylolation products (III, IV)

Compound	R	Z	X	Mp, °C	Formula	N, %		Mp, °C		Yield, %
						Found	Calc.	Hydrochloride	Picrate	
1-Phenyl-4[2-(2-pyridyl)ethyl] tetrazoline-5-thione	C ₆ H ₅	N	S	56—58	C ₁₄ H ₁₃ N ₅ S (a)	24.57	24.73	185—186	171—173	87
1-p-chlorophenyl-4[2-(2-pyridyl)ethyl] tetrazoline-5-thione	<i>p</i> -ClC ₆ H ₄	N	S	117—119	C ₁₄ H ₁₂ ClN ₅ S	22.13	22.04	204—205	164—166	87
1-p-methoxy-4[2-(2-pyridyl)ethyl] tetrazoline-5-thione	<i>p</i> -CH ₃ OC ₆ H ₄	N	S	88—89	C ₁₅ H ₁₅ N ₅ OS	22.04	22.34	180—182	149—151	70
1-p-ethoxy-4[2-(2-pyridyl)ethyl] tetrazoline-5-thione	<i>p</i> -C ₂ H ₅ OC ₆ H ₄	N	S	111—112	C ₁₆ H ₁₇ N ₅ OS	21.67	21.72	191—192	134—136	93
4-Phenyl-2[2-(2-pyridyl)ethyl] 1, 2, 4-triazoline-3-thione	C ₆ H ₅	CH	S	79—80	C ₁₅ H ₁₄ N ₄ S (b)	19.79	19.86	202—204	180—182	97
4-p-chlorophenyl-2[2-(2-pyridyl)ethyl]-1, 2, 4-triazoline-3-thione	<i>p</i> -ClC ₆ H ₄	CH	S	144—145	C ₁₅ H ₁₃ ClN ₄ S	17.45	17.69	217—219	192—193	98
4-p-ethoxyphenyl-2[2-(2-pyridyl)ethyl]-1, 2, 4-triazoline-3-thione	<i>p</i> -C ₂ H ₅ OC ₆ H ₄	CH	S	100—102	C ₁₇ H ₁₈ N ₄ OS	17.32	17.18	189—191	163—165	97
1-phenyl-4[2-(2-pyridyl)ethyl] tetrazolinone	C ₆ H ₅	N	O	50—51	C ₁₄ H ₁₃ N ₅ O (c)	26.59	26.20	167—169	154—155	90
4-phenyl-2[2-(2-pyridyl)ethyl]-1, 2, 4-triazolinone-3-one	C ₆ H ₅	CH	O	117—119	C ₁₅ H ₁₄ N ₄ O (d)	21.14	21.04	167—168	185—187	70

- (a) - Found: C 59.37; H 4.62; S 11.51%, calculated for C 59.35; H 4.63; S 11.32%
 (b) - Found: C 63.75; H 4.98; S 11.15%, calculated for C 63.80; H 4.99; S 11.35%
 (c) - Found: C 62.92; H 5.05%, calculated for C 62.91; H 4.91%
 (d) - Found: C 67.51; H 5.40%, calculated for C 67.64; H 5.30%

with those of the compounds having thione and thiol structures, the pyridylethylation products are seen to have spectra which fully coincide with those of thiones whose structures were previously proved [1, 2, 4]. The ir* spectra of compounds Ia and IIa show bands ascribable to the groups $-N-C=S$ (1430-1440, 1490-1510 cm^{-1} and $C=S$ (1350-1365 cm^{-1} [5, 6]. The ir spectra of the products of pyridylethylation of amides, tetrazolinones (Ib) and triazolinones (IIb) have intense wide bands in the regions 1712 cm^{-1} (for Ib) and 1682 cm^{-1} (for IIb), belonging to valence vibrations of the $C=O$ group.

It is to be assumed that the cases of pyridylethylation of cyclic thioamides here described can be extended to other cyclic thioamides.

Experimental**

1-Aryltetrazoline-5-thiones, 4-aryl-1, 2, 4-triazoline-3-thiones, 1-aryltetrazoline-5-thiones, and 4-aryl-1, 2, 4-triazolin-3-ones are pyridylethylated by the method generally used for all the compounds.

A solution of 0.01 mole Ia, Ib, IIa, or IIb in 0.6 ml glacial acetic acid and 1.16 ml freshly distilled 2-vinylpyridine are heated together for four hours at 110-115°. On cooling, the resultant transparent pale brown oil crystallizes. Yield of unpurified material 70-98%. To remove excess 2-vinylpyridine the precipitate is suspended in petrol ether and filtered. Crystallization from alcohol, using activated carbon, gives a colorless crystalline product.

The hydrochlorides are prepared by passing hydrogen chloride into dry benzene solutions of the bases. Picrates are prepared by mixing alcohol solutions of base and picric acid.

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*The ir spectra were observed with an IKS-14 instrument in a petroleum oil paste. Uv spectra were observed with an SF-4 instrument. We thank I. I. Mudretsova and Yu. N. Ignatov for observing the spectra.

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