REACTIONS OF PYRIDYL ISOTHIOCYANATES WITH DIAZOALKANES AND AZOIMIDE

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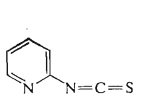
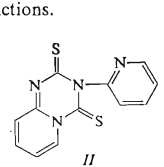
Reaction of 2-, 3- and 4-pyridyl isothiocyanates with diazomethane or diazoethane afforded the corresponding 5-(pyridyl substituted)amino-1,2,3-thiadiazoles or 5-(pyridyl substituted)-amino-4-methyl-1,2,3-thiadiazoles; reaction with azoimide gave 5-(pyridyl substituted)amino--1,2,3,4-thiatriazoles and 5-(2-pyridylamino)tetrazole, which underwent a thermal rearrangement to yield 1-(2-pyridyl)-5-aminotetrazole. The synthesized derivatives are characterized by IR, UV, mass and ^{1}H-NMR spectra.

Reactions of isothiocyanates with 1,3-dipolar reagents offer a convenient one-step approach to various 5-membered heterocyclic compounds[1]. Whereas the 1,3-dipolar cycloaddition reactions of alkyl and aryl isothiocyanates were well studied[1], isothiocyanates having the —NCS group attached to heterocyclic system have been overlooked.

To ensure the successful course of cycloaddition reactions, we chose pyridyl isothiocyanates for the enhanced reactivity of the —NCS group. 2-Pyridyl isothiocyanate (*I*) dimerized at room temperature by a 4 + 2 cycloaddition reaction to furnish 3-(2-pyridyl)-pyrido[1,2-*a*]-1,3,5-triazine-2,4-dithione (*II*), ref.[2,3]. The dimer *II* turned in solution heated to 70°C to the starting monomer *I*, which rapidly cooled to room temperature served (with regard to the thermal stability of the 1,3-dipolar components) for following cycloaddition reactions.



I



II

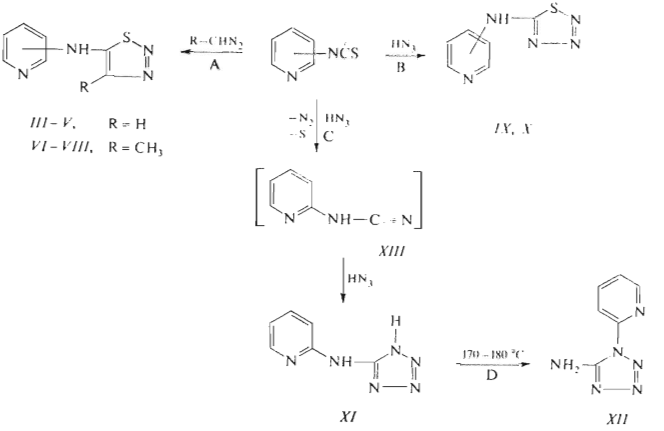
Pyridyl isothiocyanates and diazomethane furnished 5-(2-pyridylamino)1,2,3-thiadiazole (*III*), 5-(3-pyridylamino)-1,2,3-thiadiazole (*IV*) and 5-(4-pyridylamino)-1,2,3--thiadiazole (*V*). With diazoethane analogous 5-(2-pyridylamino)-4-methyl-1,2,3-thiadiazole (*VI*), 5-(3-pyridylamino)-4-methyl-1,2,3-thiadiazole (*VII*) and 5-(4-pyridylamino)-4-methyl-1,2,3-thiadiazole (*VIII*), Table I, Scheme 1*A* were obtained.

Azoimide reacted with 3- and 4-pyridyl isothiocyanates to yield 5-(3-pyridylamino)-1,2,3,4-thiatriazole (*IX*) and 5-(4-pyridylamino)-1,2,3,4-thiatriazole (*X*), Scheme 1*B*, whereas the reaction products of 2-pyridyl isothiocyanate and azoimide were 5-(2-pyridylamino)tetrazole (*XI*) and elemental sulfur, Scheme 1*C*. The different reaction course might be due to a low thermal stability of the 5-(2-pyridylamino)-1,2,3,4-thiatriazol. The latter underwent decomposition at room temperature to give the intermediate *XIII* (ref.[4]), which afforded tetrazole *XI* with azoimide present in the reaction medium. The product of isomerization at 200°C of the tetrazole derivative *XI* is 5-amino-1-(2-pyridyl)tetrazole (*XII*), isolated in a 75% yield, Scheme 1*D*.

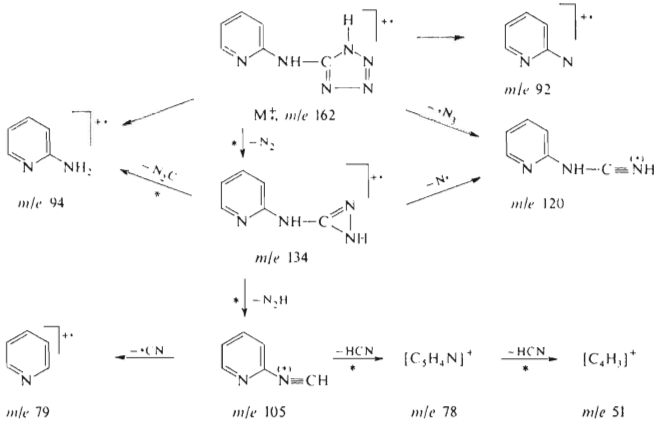
TABLE I
Diagnostic Data of Compounds *III*—*XII*

Compound	Formula (mol. weight)	Calculated/Found		M.p., °C (yield, %)	UV λ_{max}, nm (log ε)	
		% N	% S			
III	$C_7H_6N_4S$ (178·2)	31·44 31·23	17·99 17·73	239—41 (58·3)	241 (3·89)	317 (4·27)
IV	$C_7H_6N_4S$ (178·2)	31·44 31·12	17·99 17·78	166—7 (45·7)	246 (3·66)	322 (4·09)
V	$C_7H_6N_4S$ (178·2)	31·44 31·32	17·99 17·83	208—10 (42·4)	250 (3·79)	317 (4·34)
VI	$C_8H_8N_4S$ (192·2)	29·15 29·27	16·68 16·46	252—3 (58·8)	247 (3·94)	324 (4·30)
VII	$C_8H_8N_4S$ (192·2)	29·15 29·18	16·68 16·49	140—3 (38·6)	247 (3·84)	329 (4·13)
VIII	$C_8H_8N_4S$ (192·2)	29·15 29·23	16·68 16·51	193—5 (45·4)	249 (3·83)	326 (4·19)
IX	$C_6H_5N_5S$ (179·2)	39·08 39·01	17·89 17·64	157—8 (73·2)	241 (3·96)	297 (4·20)
X	$C_6H_5N_5S$ (179·2)	39·08 38·92	17·89 17·61	164—6 (76·4)	241 (3·82)	293 (4·29)
XI	$C_6H_6N_6$ (162·1)	51·83 51·58	— —	171—80 (51·5)	254 (3·99)	271 (3·99)
XII	$C_6H_6N_6$ (162·1)	51·83 51·65	— —	242—4 (75·0)	248 (4·28)	290 (3·75)

The structure of the synthesized substances was proved on the basis of spectral evidence. Mass spectra of all compounds revealed peaks of molecular ions, the relative intensity of which varied within 7·2 and 40·7%. The main direction of the molecular ion fragmentation was the elimination of neutral molecule of nitrogen leading to the base peak of the spectrum corresponding to the radical ion $(M-N_2)^+$.



Fragmentation pathway of the molecular ion of tetrazole derivative *XI* is shown in Scheme 2. Compounds *III*–*X* have in their UV spectra two characteristic regions of absorption at 240–250 nm (log ε 3·66–3·96) and 290–330 nm (log ε 4·09–4·34). Thiatriazoles *IX*, *X* displayed, when compared with thiadiazoles *III*–*VIII* a hypsochromic shift due to a higher electronegativity of the thiatriazole ring. Tetrazoles *XI* and *XII* showed a more pronounced absorption in the 250 nm region, whilst the maximum at higher wavelength was less pronounced. IR spectra revealed absorption bands in the 746 ± 58 and 1065 ± 65 cm^{-1} regions ascribable to out-of plane bending vibrations of pyridine and thiazole rings, some strong absorption bands of skeletal vibrations between 1190–1486 cm^{-1} and absorptions of stretching vibrations at 1543–1655 cm^{-1} associated with C=C and C=N bonds in rings.



EXPERIMENTAL

Melting points were determined on a Kofler block, IR spectra were measured with UR 20 (Zeiss, Jena), UV spectra with UV VIS Specord (Zeiss, Jena) spectrophotometers, mass spectra with an MS 902 S (AEI Manchester) apparatus and ^{1}H-NMR spectra in hexadeuteriodimethyl sulfoxide with a Tesla BS 487 C instrument operating at 80 MHz. The starting 2-, 3 and 4-pyridyl isothiocyanates were prepared according to[2,5,6].

Reaction of Pyridyl Isothiocyanates with Diazomethane

A mixture of pyridyl isothiocyanate (1·36 g, 10 mmol) and diazomethane (0·462 g, 11 mmol) in ether was left to stand at room temperature for 24 h. The solvent was evaporated under diminished pressure and the residue was crystallized from methanol. Compounds *IV*, *V* were prepared according to this procedure, *VII*, *VIII* from diazoethane and *IX*, *X* from azoimide.

5-(2-Pyridylamino)-1,2,3-thiadiazole (*III*)

A solution of dimeric 2-pyridyl isothiocyanate (1·36 g, 5 mmol) in dioxane (50 ml) was refluxed for 5 min, cooled to room temperature and added to a solution of diazomethane (0·462 g, 11 mmol) in ether. This mixture was allowed to stand at room temperature for 24 h, the solvent removed *in vacuo* and the residue crystallized from methanol. Compound *VI* was prepared in an analogous way from diazoethane.

Reaction of 2-Pyridyl Isothiocyanate with Azoimide

A solution of dimeric 2-pyridyl isothiocyanate (1·36 g, 5 mmol) in dioxane (50 ml) was refluxed for 5 min and cooled to room temperature. Solution of azoimide (0·473 g, 11 mmol) in benzene was added to this solution what caused the reaction to start immediately under liberation of nitrogen. After 24 h standing at room temperature the solvent was distilled off under reduced pressure and the residue dissolved in boiling ethanol (20 ml) was filtered thus leaving 0·11 g of sulfur. 5-(2-Pyridylamino)tetrazole (*XI*, 0·57 g) crystallized from the filtrate. ^{1}H-NMR spectrum (δ, ppm): 8·52 (m, 1 H) $C_{(6)}$—H, 8·19—7·82 (m, 2 H) $C_{(4)}$—H, $C_{(3)}$—H, 7·66 (s, broad, 1 H) N—H, 7·44 (m, 1 H) $C_{(5)}$—H.

Thermal Rearrangement of Tetrazole *XI*

Compound *XI* (0·16 g, 1 mmol) was fused at 200°C for 1 h and the melt crystallized from ethanol. Yield 0·12 g of 1-(2-pyridyl)-5-aminotetrazole (*XII*). ^{1}H-NMR spectrum: 8·24 (m, 1 H) $C_{(6)}$—H, 7·69 (m, 1 H) $C_{(4)}$—H, 7·11—6·84 (m, 2 H) $C_{(3)}$—H, $C_{(5)}$—H, 5·41 (s, broad, 2 H) NH_2.

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