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NEW SYNTHESIS OF 4-METHYL-2-METHYLAMINO-5-(N-METHYLTHIOCARBAMOYL) THIAZOLE BY THERMAL ISOMERIZATION

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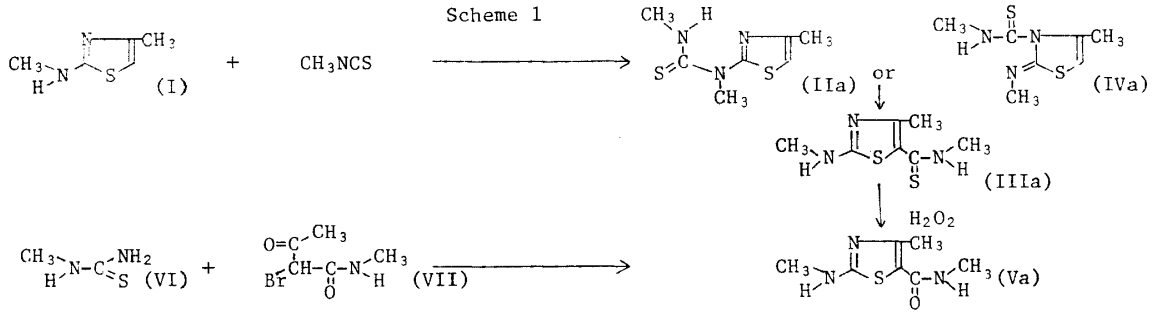
The reaction of 4-methyl-2-methylamionthiazole (I) with methyl isothiocyanate in toluene in the presence of pyridine gave the crystals of mp 56-57°C (IIa) having Rf value of 0.75 (2-propanol : ether, 1 : 1), λ_{max} (2-propanol) 260 (sh.), 291 nm (ε= 19500) and yellow crystals of mp 249-250°C (IIIa) having Rf value of 0.53, λ_{max} (2-propanol) 294 (ε=6310), 340 nm (ε=11500).



The elemental analysis and mass spectral data (MW 201) gave a molecular formula of $C_7H_{11}N_3S_2$ for both (IIa) and (IIIa), isomeric to each other. The thermal isomerization of (IIa) in pyridine gave (IIIa). As the spectral interpretation could not differentiate 1, 3-dimethyl-1-(4-methylthiazol-2-yl) thiourea (IIa) and 4-methyl-2-methylimino-3-(N-methylthiocarbamoyl)-4-thiazoline (IVa), the structure of (IIa) was established by an X-ray analysis.

The NMR spectrum (d_6-DMSO) of (IIIa) showed signals at δ 2.29 (singlet, 3H, =C-CH$_3$), 3.10 (doublet, 3H, J=5.0 Hz, singlet after D_2O exchange, singlet after irradiation at 9.06, -NH), 2.28 (doublet, 3H, J=5.0 Hz, singlet after D_2O exchange, singlet after irradiation at 7.86, -NH), 9.06 (broad, 1H, disappeared after D_2O exchange, -CH$_3$-NH-), and 7.86 δ (broad, 1H, disappeared after D_2O exchange, CH$_3$NH-). The structure of (IIIa) was estimated from the appearance of two doublets for CH$_3$NH and the absence of a singlet due to H at position 5.

The product obtained by the alkaline H_2O_2 treatment of (IIIa) was identified with the product, 4-methyl-2-methylamino-5-(N-methylcarbamoyl)thiazole (Va) from the reaction of (VI) and (VII), by the mixed mp, and from UV, Mass and NMR spectral comparison.

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Table I shows the result of monitoring of the thermal rearrangement of (IIa) to (IIIa), by measuring the absorption at 340 nm due to (IIIa) every 2.5 hr in a different solvent. This result suggests that an essential factor in the rearrangement is the presence of pyridine.

Table I

Solvent	Absorption at 340 nm[b)]	Reflux time (hr)	IIIa Yield (%)
Cyclohexane	—	30	0
Toluene	—	30	0
Toluene-pyridine[a)]	> 5 hr	10	80
Pyridine	>> 5 hr	30	90

a) Ratio 2 : 1

b) Time required for the appearance of the absorption at 340 nm