Reaction of 5-Chloropyridin-2-yl-thioureas with Phenacyl Bromides: a New Thiazole Synthesis. *X*-Ray Crystal Structure of 5-(5-Chloropyridin-2-yl)-2-diethylamino-4-phenylthiazole

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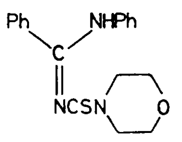
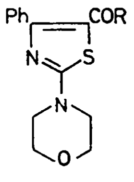
Summary The reaction of *N*-(5-chloropyridin-2-yl)-*N'N'*-dialkylthioureas with phenacyl bromides yields tri-substituted thiazoles *via* a 1,3-pyridyl shift; the *X*-ray crystal structure of one of these, 5-(5-chloropyridin-2-yl)-2-diethylamino-4-phenylthiazole, has been determined.

Ried[1] has recently shown that the reaction of halogenoketones with the benzamidines (**1**) gives the 2-morpholinothiazoles (**2**). This communication reports a similar reaction in which the benzamidine unit is incorporated within a pyridine ring. Thus when phenacyl bromide was treated with *N*-(5-chloropyridin-2-yl)-*N'N'*-diethylthiourea in acetone solution the thiazole (**3**; R^1 = NEt_2, R^2 = H) was isolated as its hydrobromide salt. The free base, obtained by treatment of the salt with water, could not be characterised unequivocally by analysis and spectroscopic examination and the structure was deduced by *X*-ray analysis (Figure) [m.p. 85—86 °C, i.r. ν_{max} (Nujol) 1558 cm^{-1}; u.v.



(1)



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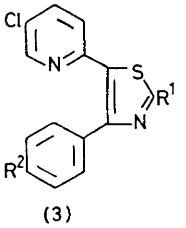

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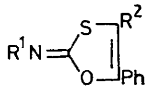

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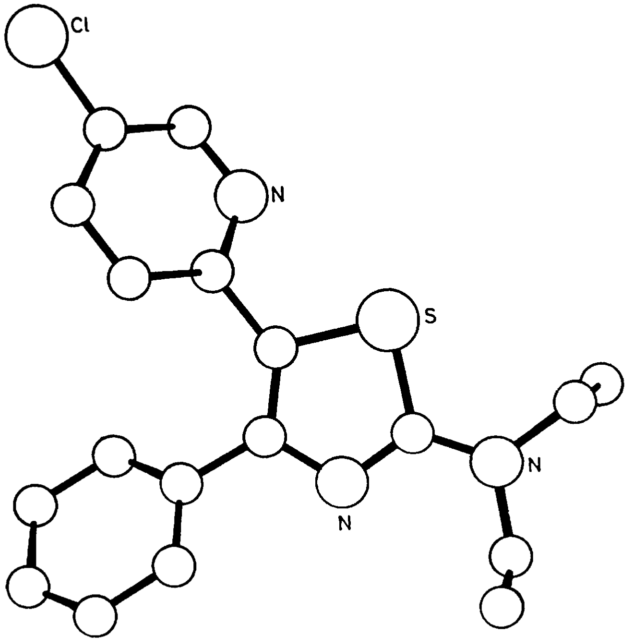


Figure. *X*-Ray structure of 5-(5-chloropyridin-2-yl)-2-diethylamino-4-phenylthiazole.

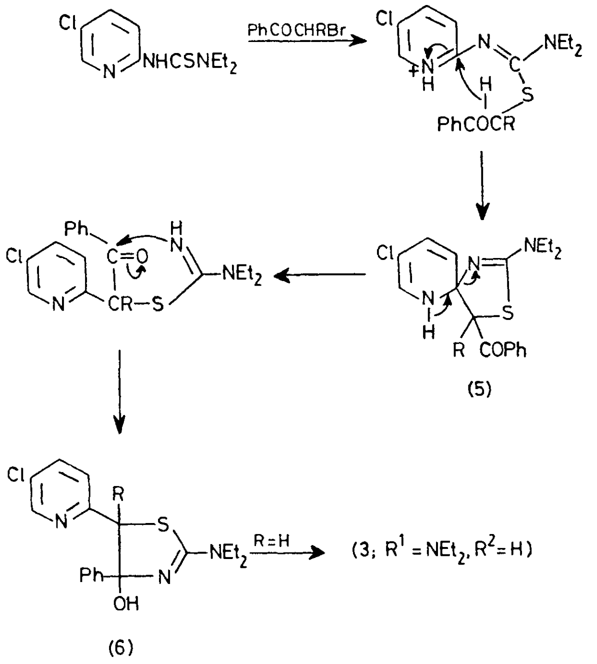
λ_{max} (MeOH) 246 (ϵ 15,098) and 359 nm (19,627); δ ($CDCl_3$) 1·2 (6H, t), 3·45 (4H, q), and 6·98—8·38 (8H, m)].

Crystal data: $C_{18}H_{18}ClN_3S$, $M = 343·9$, monoclinic, $a = 12·67(1)$, $b = 13·98(1)$, $c = 10·43(1)$ Å, $\beta = 105·18(5)°$, space group $P2_1/a$, $U = 1784(2)$ Å^3, $D_c = 1·280$ g cm^{-3} for $Z = 4$, Mo-K_α radiation, Nb filter.

Cell dimensions and full three-dimensional intensity data ($2\theta \leqslant 50°$) were measured on a Picker automatic diffractometer. The structure was solved by direct methods (Multan) and refined with anisotropic temperature factors to $R = 0·068$ for 2359 reflections. Nitrogen atoms were identified by associated bond lengths and isotropic temperature factors. All the peaks on an electron density difference map were less than 0·6 e and were in plausible positions for hydrogen atoms. The phenyl and pyridyl rings are twisted (in the same sense) out of the plane of the thiazole ring by 40 and 30° respectively, though their axes remain very nearly in this plane.†

A similar result was obtained with 4-phenylphenacyl bromide when (**3**; $R^1 = NEt_2$, $R^2 = Ph$), m.p. 131—133 °C, was isolated. These results are in contrast to those obtained with *NN*-dimethyl-*N'*-phenylthiourea when the oxathiole (**4**; $R^1 = Ph$, $R^2 = H$) was obtained.[2] However in the reaction between phenacyl bromide and *N*-(5-chloropyridin-2-yl)morpholinothiourea the major product was (**3**; R^1 = morpholino, $R^2 = H$), m.p. 171—172 °C, but 10% of the isolated product was the oxathiole (**4**; R^1 = 5-chloropyridin-2-yl, $R^2 = H$), m.p. 186 °C; when α-bromopropiophenone was used in place of phenacyl bromide the sole product was (**4**; R^1 = 5-chloropyridin-2-yl, $R^2 = Me$), m.p. 154—156 °C.

The proposed mechanism for this reaction involves the formation of the spiro intermediate (**5**) and in the case of α-bromopropiophenone the methyl group makes this pathway unfavourable possibly since (**6**; R = Me) cannot lose water and the alternative pathway to the oxathiole is taken.



(5)

(6)

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† The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

[1] W. Ried and L. Kaiser, *Annalen*, 1976, 395.
[2] W. Ried and L. Kaiser, *Annalen*, 1975, 958.