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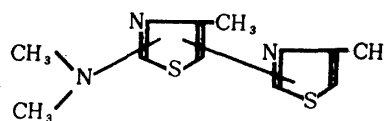
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One Step Synthesis of 5, 2'-Bithiazole Derivatives : Reaction of N,N-Dimethyl-2, 4-dithiobiuret with α -Haloketones

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Thermal reaction of N,N-dimethyl-2, 4-dithiobiuret (1a) with an equivalent of α -haloketone, X-CH₂-C(=O)-R (2a: X=Cl, R=CH₃), in aqueous solution gave 4-methyl-2-(N,N-dimethylthiocarbamoyl)aminothiazole (3a) and structurally unknown substance as pale yellow crystals (4a-HCl) (from 2-PrOH), mp 196-198° in equal amounts (yield, 90%). Neutralization of (4a-HCl) with NaHCO₃ solution gave a free base (4a), mp 85-86° (from hexane). The free base (4a) was also obtained in 90% yield by the reaction of (3a) and (2a). In the NMR spectrum (CDCl₃) of (4a) a signal at δ 3.13 (3H, s) indicated the presence of $\left(\begin{array}{c} \text{CH}_3 \\ \text{CH}_3 \end{array}\right) \text{N}-$, a doublet at δ 2.42 (3H, J=1.0Hz) was due to the signal for 4-CH₃ which undergoes a long-range coupling with 5-H in the thiazole ring appearing at δ 6.72 (1H, d, J=1.0 Hz), and a singlet at δ 2.50 (3H, s) corresponded to the CH₃ in the thiazole ring. These data suggest the following bithiazole structure for (4a).



In order to establish unequivocally the bithiazole structure 4-methyl-2-dimethylamino-5-(4'-methylthiazol-2'-yl)thiazole (4a) was synthesized independently by the condensation of (2a) with 4-methyl-2-dimethylamino-5-thiocarbamoylthiazole (7), as shown in Scheme 1. IR and NMR spectral data of this compound agreed with those of the above-mentioned pale yellow crystals. Therefore, the structure of (4a) was finally established as 5, 2'-bithiazole structure, 4-methyl-2-dimethylamino-5-(4'-methylthiazol-2'-yl)thiazole. The similar reaction of (1a) and (2b) gave only orange yellow precipitates (4b) in 90% yield and (3b) was not obtained.

However, reaction of (1a) and (2b) in dioxane at room temperature gave (3b), mp 168° (from 2-PrOH) in 80% yield. The elemental analysis and mass spectral data gave a molecular formula of C₁₂H₁₃N₃S₂ for 2-(N,N-dimethylthiocarbamoyl)amino-4-phenylthiazole (3b).

In a previous paper, we reported that the reaction of N-methyl-2, 4-dithiobiuret (1b) and (2a) gave 2-(4-methylthiazol-2-yl)imino-3, 4-dimethyl-4-thiazoline (8) *via* route (A), in which a nucleophilic attack of the amide-nitrogen to the carbonyl-carbon in an intermediate (5c) is included. In contrast, (5a) and (5b) may be produced

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by the condensation *via* route (B), in which an active methylene in the intermediate (5a, b) attacks on a carbon at 2-position of the thiazole ring.

