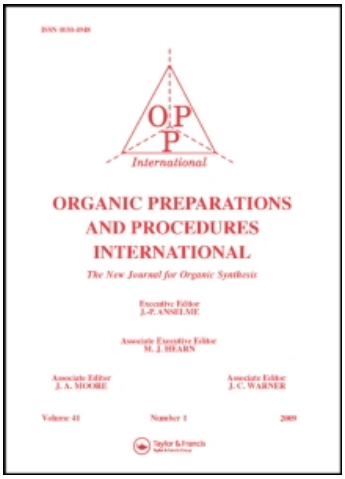

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AN IMPROVED SYNTHESIS OF SUBSTITUTED 1,3,4-THIADIAZOLES

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AN IMPROVED SYNTHESIS OF SUBSTITUTED 1,3,4-THIADIAZOLES

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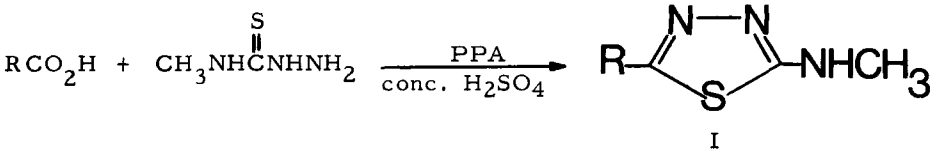
The synthesis of 2-amino- and 2-alkylamino-5-substituted-1,3,4-thiadiazoles is well documented.[1-6] The present paper describes an improved procedure for the one-step preparation of 2-methylamino-5-alkyl-1,3,4-thiadiazoles,[7-9] which affords the desired products in higher purity than previously reported.[10]



I

a) R = C_2H_5(93%); b) R=$(CH_3)_2CH$(97%); c) R=$(CH_3)_3C$(93%)

The reaction of suitable carboxylic acids and 4-methylthiosemicarbazide in the presence of three parts of polyphosphoric acid and one part (w/w) of conc. sulfuric acid gave I which can be reacted without further purification with alkyl isocyanates leading to the corresponding urea. Lower yields are obtained if either conc. sulfuric acid or polyphosphoric

acid is employed alone in the reaction. This procedure has been scaled up with good reproducibility.

EXPERIMENTAL

All mps were determined on a Thomas Hoover capillary melting point apparatus and are uncorrected. NMR spectra were obtained in $CDCl_3$ on an Varian HA 60 spectrometer using TMS as internal standard. Mass spectra were obtained on a CEC 110 mass spectrometer.

General Procedure. - 4-Methylthiosemicarbazide (21 g., 0.2 mole) was added to a solution of polyphosphoric acid and conc. sulfuric acid (72 g., 3:1 by weight) maintained at 10-15° with an ice-water bath. Propionic acid (14.8 g., 0.2 mole) was then added while the temperature was kept between 10-15°. After the addition, the reaction mixture was allowed to warm up to 30° and it was then heated to 100-105° for 3 hrs. Water (50 ml) and toluene (50 ml) were added and the pH of the reaction mixture was adjusted to 7 with conc. ammonium hydroxide. The toluene layer was azeotropically dried and toluene was removed under vacuum to give 27 g., (93.5%) of Ia, mp. 84-87°.

Nmr: δ 1.30 (t, 3, $C\underline{H}_3$), 2.92 (q, 2, $C\underline{H}_2$), 3.00 (s, 3, N-$C\underline{H}_3$); M^+ 143.

Anal. Calcd for $C_5H_9N_3S$: C, 41.93; H, 6.33
Found: C, 41.67; H, 6.09

Ib, liquid; nmr: δ 1.35 (d, 6, $C\underline{H}_3$), 3.20 (m, 1, C-$\underline{H}$), 3.00 (s, 3, N-$C\underline{H}_3$); M^+ 157.

Anal. Calcd for $C_6H_{11}N_3S$: C, 45.83; H, 7.05
Found: C, 45.50; H, 7.00

Ic, mp. 80-82°; nmr: δ 1.38 (s, 9, $C\underline{H}_3$), 300 (s, 3, N-$\underline{CH}_3$); $M^{+\cdot}$ 171.

Anal. Calcd for $C_7H_{13}N_3S$: C, 49.09; H, 7.65.

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