Mesoionic 1,3,4-Thiadiazole Derivatives

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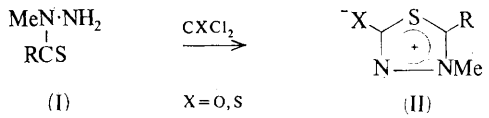
MESOIONIC derivatives of the 1,3,4-thiadiazole ring system (II) have been prepared[1] by reaction of acyl chlorides with potassium 2-aryldithiocarbazinates. Recent interest[2] in the chemical and pharmacological properties of these derivatives makes our results, which provide a convenient, alternative route to these mesoionic compounds, of special interest. This new synthetic route makes available for the first time mesoionic 1,3,4-thiadiazole derivatives with an exocyclic oxygen atom as well as products with alkyl substituents at position 3 which could not be obtained by the earlier procedure.

1-Methyl-1-thioacylhydrazine (I), prepared from methylhydrazine and thioacylthioglycollic acids,[3] readily reacted with thiophosgene in dry chloroform at reflux temperature in the presence of potassium carbonate to form, *e.g.* anhydro-5-mercapto-3-methyl-2-phenyl-1,3,4-thiadiazolium hydroxide (II; R = Ph; X = S) from 1-methyl-1-thiobenzoyl hydrazine (I; R = Ph). Replacement of the thiophosgene in this reaction sequence with phosgene gave the corresponding anhydro-5-hydroxy-3-methyl-2-phenyl-1,3,4-thiadiazolium hydroxide (II; R = Ph; X = O). This procedure complements very effectively the earlier method of Busch and it is now possible to obtain a variety of substituents at positions 2 and 3 of the nucleus (Table).

Analytical† and spectral data clearly showed that cyclization to the mesoionic system had occurred. The absence of NH bands in the i.r. spectrum of (II)



(I) (II)

and the presence of a carbonyl absorption at 1700 cm.$^{-1}$, together with the absence of bands associated with isothiocyanates and isocyanates, indicated that the cyclized products were obtained. The possibility of dimerization of the intermediate isothiocyanate or isocyanate to a tetrazine derivative was eliminated by molecular-weight data (mass spectra).

Results obtained in this laboratory confirm the unresponsiveness of these mesoionic compounds to olefinic and acetylenic dipolarophiles reported recently.[4]

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Some meso-ionic 1,3,4-*thiadiazoles* (II)

R	X	M.p.	% Yield	M^+, *m/e* (rel. abund.)
Ph	O	178—179°	86	192 (52)
p-Cl·C_6H_4	O	149—150°	77	226 (33)
p-MeO·C_6H_4	O	164—165°	59	222 (36)
Ph	S	221° dec.	53	208 (57)
p-Cl·C_6H_4	S	201—202° dec.	63	242 (36)
p-MeO·C_6H_4	S	193—194° dec.	52	238 (43)

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† Satisfactory analytical data were obtained for all compounds described.

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