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DIRECT RING SYNTHESIS OF 5-HYDROXYISOTHIAZOLES

J.A. Waite

North East London Polytechnic, Romford Road, London E15 4LZ.

K.R.H. Wooldridge

Chemical Research Laboratories, May & Baker Ltd., Dagenham, Essex.

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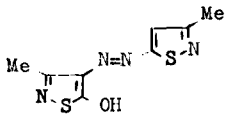
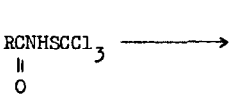
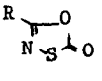
Although many isothiazoles with hydroxyl functions in the 3- and 4-positions have been described, the corresponding 5-substituted compounds have received little attention. Smith[1] was unable to isolate a hydroxy compound from the decomposition of 4-carboxy-3-methylisothiazole-5-diazonium chloride, whilst Goerdeler and Roegler[2] diazotised 5-amino-3-methylisothiazole and obtained the azo-compound (1), presumably by coupling of the initially formed 5-hydroxy-3-methylisothiazole with unreacted diazonium salt. Successful decomposition of 4-substituted isothiazole-5-diazonium salts has recently been reported,[3] together with examples of 5-hydroxyisothiazoles obtained by activated nucleophilic substitution reactions.



(1)



(2)



(3)

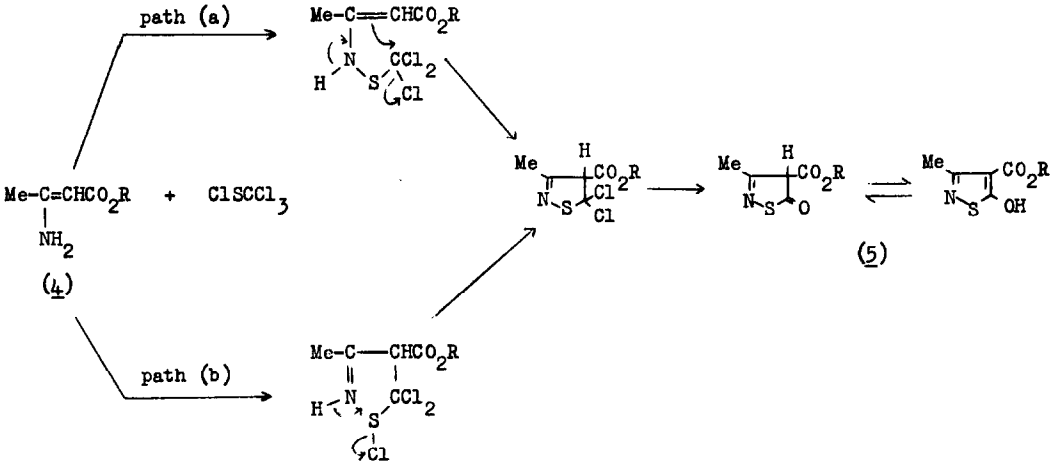
We now wish to report the first direct ring synthesis of a 5-hydroxyisothiazole which was prompted by the facile cyclisation of N-trichloromethylmercaptoamides (2) to yield 1,3,4-oxathiazol-2-ones (3).[4,5] Treatment of β-aminocrotonic ester (4; R=Me and Et) with perchloromethylmercaptan in the presence of base (NaOH or Et_3N) produced the 5-hydroxyisothiazoles[7] (5; R=Me and Et) in 30-40% yield without the isolation of any of the expected intermediates shown in the Scheme. The same products are obtained, but in smaller yield, in the absence of base.

Two possible pathways for the cyclisation process are outlined in the Scheme, but at present we have no evidence to indicate which is the operative mechanism. We favour the

initial N-S bond formation of path (a) because of the analogies with the mercaptoamide intermediates in the original oxathiazolone synthesis.

We are currently investigating the mechanism and extending the scope of this reaction.

SCHEME



*Elemental analysis and spectral data are in accord with the compounds described.

REFERENCES

1. R.E. Smith, Ph.D. thesis, University of N. Carolina, 1966.

2. J. Goerdeler and M. Roegler, Chem.Ber., 1970, 103, 112.

3. I.D.H. Stocks, J.A. Waite and K.R.H. Wooldridge, J.Chem.Soc., (C), 1971, 1314.

4. A. Senning and P. Kelly, Acta Chem.Scand., 21, 1871, 1967.

5. F. Becke and J. Gnad, Annalen, 726, 110, 1969.