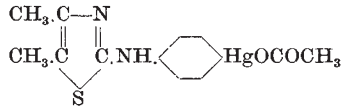
Use of Mercurated Thiazoles as Fungistatic Agents

In the course of our studies on methods of synthesis of thiazole derivatives and their possible useful applications, it appeared of interest to examine their fungicidal properties, since these contain in a cyclic ring structure the grouping N—C—S which is present in known fungicides like tetramethyl thiuram disulphide, thioureas and thioacetamide. Some new mercurated derivatives of thiazoles have also been prepared by us, and since mercury is a powerful fungicidal element, phenyl mercuric acetate being actually used for such diseases as apple scab, it was considered worth while to test these mercurated thiazoles for their fungicidal action.

The thiazole compounds employed were thirteen new 2-substituted-amino 4-5-dimethyl thiazoles prepared by reaction of ethyl methyl ketone with substituted thioureas in presence of iodine by a modified method already reported by us[1]. These compounds have been mercurated by treatment with mercuric acetate in acetic acid. The position taken up by the acetoxy mercuric group has also been fixed by us[2]. The resulting mercurated thiazoles have been assigned the structure :



All the twenty-six new thiazoles (thirteen unmercurated and the rest mercurated) have been tested. For fungicidal assay, the method of Montgomery and Moore[3] was used. *Alternania polanduii* Ayyangar was used as the fungus indicator.

The unmercurated thiazoles completely inhibited spore germination even at a concentration of 100 parts per million. At 250 p.p.m. the percentage of inhibition was only 25–30 per cent.

The mercurated thiazoles were, however, more powerful, being 100 per cent effective in inhibiting spore germination of the fungus even at a concentration of 2 p.p.m.

Detailed investigations will be published elsewhere.

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[2] Pujari, H. K., and Rout, M. K., *J. Ind. Chem. Soc.*, **31**, 257 (1954).
[3] Montgomery and Moore, *J. Pomol. and Hort. Sci.*, **15**, 253 (1938).

Glutathione Breakdown and Transpeptidation Reactions in *Proteus vulgaris*

The enzymic breakdown of glutathione by animal tissues has been extensively studied[1]. Both peptide bonds are split by enzymes of rat kidney homogenates ; the γ-glutamyl bond is first hydrolysed to glutamic acid and cysteinylglycine, the latter being afterwards further broken down to cysteine and glycine[2]. In 1950, Hanes, Hird and Isherwood[3] demonstrated that preparations of sheep kidney not only hydrolysed glutathione, but also catalysed the transfer of the γ-glutamyl residue to the products of hydrolysis and to other added amino-acids. A more detailed analysis of the relative reactivities of various amino-acids with glutathione has recently been carried out[4]. Transpeptidation reactions were also observed between other γ-glutamyl and glycyl peptides and amino-acids in animal and plant tissues[5]. The discovery of such reactions led to speculation on their possible role in the formation of new peptides and of proteins. Although cell-free extracts of *Escherichia coli* synthesize glutathione from its component amino-acids[6], these extracts do not hydrolyse the tripeptide. Breakdown of glutathione and transpeptidation in micro-organisms have not been previously reported ; a study of these reactions in the bacterium *Proteus vulgaris* is described here.

Washed whole-cell suspensions or cell-free extracts of *Pr. vulgaris* (prepared by sonic disintegration) were incubated with glutathione with or without added amino-acids at *p*H 7·4 for 1 hr. at 37°. After deproteinization with ethanol containing N-ethyl maleimide[3], the supernatant was examined for amino-acids and peptides by paper chromatography. Fig. 1 shows a typical chromatogram of the products obtained when *Pr. vulgaris* suspensions or extracts are incubated with glutathione. In addition to the glutamic acid, glycine and small amounts of cysteine expected (cysteine is further metabolized to pyruvate, hydrogen sulphide and ammonia by *Pr. vulgaris*[7]), two new ninhydrin-positive materials with R_F values similar to γ-glutamylglutamic acid and γ-glutamylglycine are produced. The new compounds are increased in amount respectively by the addition of L-glutamic acid or glycine to the original incubation

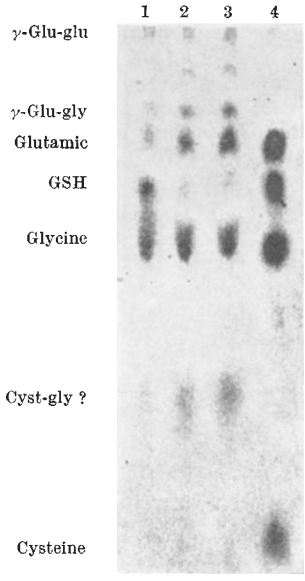

Fig. 1. Descending paper chromatogram showing products of the reaction of *Proteus vulgaris* on glutathione. 1, 2 and 3 represent respectively 7·2, 14·4 and 21·6 mgm. dry weight of organism in phosphate buffer *p*H 7·4 in 0·4 ml. incubation mixture containing 5 μM glutathione. 4 is a control strip of amino-acids and glutathione. Incubations were carried out for 1 hr. at 37°. Whatman No. 3 filter paper developed in propanol–water (80 : 20) for 17 hr. Colour developed by spraying paper with 0·1 per cent ninhydrin in chloroform and heating for 5 min. at 105°