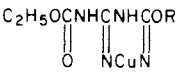
COMMUNICATIONS

Metabolic Decomplexation of [1-(Carbethoxyamidino)-*O*-alkylisourea]copper(II) by Four Fungi

[1-(Carbethoxyamidino)-*O*-alkylisourea]copper(II), where R = hydrogen, methyl, ethyl, isopropyl,



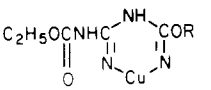
ethoxyethyl, and benzyl, is synthesized and evaluated for fungicidal activity. None of the compounds was found to be active even up to a concentration of 2000 μg/mL against *Curvularia*, *Aspergillus niger*, *Fusarium*, and *Alternaria solani*. This is plausibly attributed to their metabolic decomplexation.

In continuation of our earlier study of the synthesis and fungicidal activity of bis(1-amidino-*O*-ethylisourea)copper(II) carbamates (Medhekar and Boparai, 1981), which seem to be capable of transporting copper(II) to a susceptible site in fungus, thereby hindering some enzyme systems, [1-[(ethoxycarbonyl)amidino]-*O*-alkylisourea]-copper(II) was synthesized and evaluated for fungicidal activity. Two active moieties, i.e., guanido and carbamate, encompassed in these compounds were expected to confer enhanced biological activity.

Carbethoxydicyandiamide required for the above synthesis was prepared by the method of Kaiser and Thurston (1952) and was purified by recrystallization from ethanol. On heating it with copper acetate and an alcohol or water in the presence of sodium carbonate, we obtained the complexes. Sodium carbonate is required to neutralize the acetic acid, liberated during the reaction. Although, owing to their insolubility in most of the common solvents, it was not possible to purify the products by recrystallization, pure products could directly be obtained by employing scrupulously purified precursors and washing the products with acetone and water to remove any unreacted reactants.

METHODS AND MATERIALS

[1-(Carbethoxyamidino)-*O*-akylisourea]copper(II). Carbethoxydicyandiamide (0.1 mol), copper acetate (0.1 mol), sodium carbonate (0.05 mol), and water or a dry alcohol are heated on a water bath, under moisture exclusion, until copper acetate is consumed (generally 2–8 h are required). A blue to violet complex starts precipitating within a few minutes of heating and indicates the progress of the reaction. The complex is filtered from the hot solution and repeatedly washed with hot acetone and water. After a final washing with acetone, it is dried in the oven at about 60 °C. In case of water, sodium carbonate is initially left out of the reaction mixture and later added intermittently so as to keep the pH of the mixture always below 6 in order to suppress the hydrolysis of copper acetate. In the case of benzyl alcohol, a thick slurry is obtained as the final reaction mixture, which is diluted with ethanol before filteration. For analysis of copper, about 0.2 g of a complex, thus obtained, is weighed accurately into an iodine flask and decomplexed by heating with 5 mL of 50% aqueous acetic acid. Ten milliliters of a 10% solution of potassium iodide is then added, and the iodine, thus liberated, is titrated against 0.04 N sodium thiosulfate solution. The copper content of the complexes corresponds to the probable structure where R = hydrogen,



methyl, ethyl, isopropyl, ethoxyethyl, and benzyl.

Evaluation of Fungicidal Activity. The fungicidal activity of these compounds is evaluated against *Curvularia*, *Aspergillus niger*, *Fusarium*, and *Alternaria solani* by employing the method of Lindenfelser (1967). The fungal cultures are grown in Petri dishes containing a peptone–glucose–agar medium (pH 6.4) and examined visually for purity and growth after 72 h.

RESULTS AND DISCUSSION

The chelates do not completely inhibit the growth of any of the fungi even up to a concentration of 2000 μg/mL. This may be ascribed to their insolubility, like that of bis(1-amidino-*O*-ethylisourea)copper(II) sulfate, due to which they seem to lack adequate transport capability (loc. cit.). In 72 h the color of the chelates changes from violet-blue to blue (the original color of the compounds also observed in uninoculated control) as is observed with acid decomplexation. This is suggestive of decomplexation of the compounds, by acidic metabolites of the fungi, which goes on unabated in the absence of counteracting carbamate ion (loc. cit.).

LITERATURE CITED

Kaiser, D. W.; Thurston, J. T. *J. Org. Chem.* **1952**, *17*, 185.
Lindenfelser, L. A. In "Source Book of Laboratory Excercises in Plant Pathology"; Kelman, A., Ed.; W. H. Freeman: London, 1967; p 301.
Medhekar, S.; Boparai, K. S. *J. Agric. Food Chem.* **1981**, *29*, 421.

Sharad D. Medhekar*
Aziz Bhai
K. S. Boparai

School of Studies in Chemistry
Vikram University
Ujjain 456010, India

Received for review April 21, 1981. Accepted August 4, 1982. S.D.M. was awarded a research fellowship from C.S.I.R.

0021-8561/83/1431-0442$01.50/0