# Copper(II) Ion-assisted Hydrogen Ion-catalysed Hydrolysis of Thioamides

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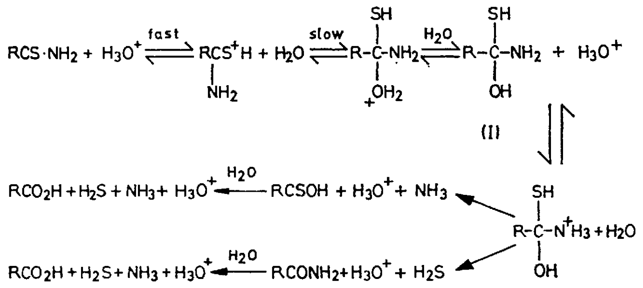
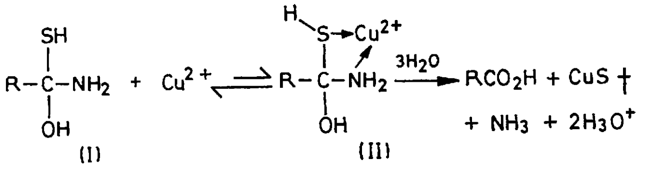
*Summary* The hydrogen ion-catalysed hydrolysis of thioamides is accelerated by $Cu^{2+}$ ions which probably form a complex with the usual tetrahedral intermediate and thereby assist leaving group departure.

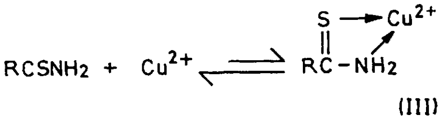
As we have recently shown,[1] the kinetics of the hydrogen ion-catalysed hydrolysis of thioamides ($10^{-4}$M) in aqueous solution are similar in outline to those of amides, the observed rate constant passing through a maximum value as $[H_3O^+]$ rises. For thioamides the observed facts, including the formation of both the thiocarboxylic acid and the amide as initial products, can be satisfactorily rationalised[1] on the basis of the formation of a carbonyl addition intermediate (I) whose steady-state concentration passes through a maximum as [$H_3O^+$] rises. For thiobenzamide and *N*-cyclohexylthiobenzamide this maximum occurs at *ca.* 5M $HClO_4$, and for thioacetamide[2] at *ca.* 3·5M-$HClO_4$.



We now find that the velocity of this catalysed hydrolysis is increased by the presence of relatively low concentrations (*e.g.* $10^{-3}$—$10^{-2}$ M) of copper(II) ions and, at any given value of [$H_3O^+$], that the reaction order in $Cu^{2+}$ is close to unity At any fixed value of [$Cu^{2+}$], as in the absence of $Cu^{2+}$, the observed rate constants pass through a maximum value as [$H_3O^+$] is increased. The position of this maximum on the [$H_3O^+$] scale is largely unaffected by the presence of the $Cu^{2+}$ ions, and the percentage acceleration provided by any given value of [$Cu^{2+}$] is roughly independent of [$H_3O^+$]. For aromatic thioamides the acceleration is *ca.* 100% at 60 °C when [$Cu^{2+}$] = *ca.* $3{\cdot}5 \times 10^{-3}$ M; for aliphatic thioamides the effect is smaller.

These results suggest that $Cu^{2+}$ is facilitating the removal of the leaving group(s) SH and/or $NH_2$ from (I), so that less of (I) returns to the thioamide. We suggest that the formation of (II) from (I), and its subsequent decomposition to the non-thio-acid, underlies the observed copper(II) ion promotion. The effects are not easy to explain in terms of an entirely separate mechanism for the copper reaction and are distinct from the copper(II) ion promotion of thioamide decomposition observed at low concentrations (< 0·1 M) of $H_3O^+$. This latter reaction,[3] which resembles the similar process involving $Hg^{2+}$ ions,[4] probably proceeds *via* complexes like (III) and for primary amides leads directly to the nitrile. It contributes negligibly to the effects observed at high acid concentrations, and these effects can hardly arise from the protonation of (III).





The involvement of both protons and metal ions as kinetically important acid catalysts within a single mechanism, which our results suggest, has to date been rarely implicated in homogeneous, non-enzymatic systems and in the few examples known the role of the H-acid has been taken to be the protonation of a pre-formed substrate–metal ion complex. Our results cannot be explained in this way and require the existence of a novel mechanism such as that we propose.

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[†] The CuS remains in solution at the concentrations and temperature used.

[1] A. J. Hall and D. P. N. Satchell, *J.C.S. Perkin II*, 1974, 1077.
[2] D. Rosenthal and T. I. Taylor, *J. Amer. Chem. Soc.*, 1957, **79**, 2684.
[3] A. J. Hall and D. P. N. Satchell, to be published.
[4] A. J. Hall and D. P. N. Satchell, *Chem. and Ind.*, in the press; *J.C.S. Perkin II*, in the press.