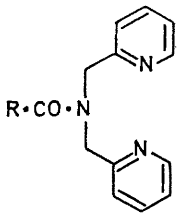
Copper(II)-catalysis of the Methanolysis and Hydrolysis of *NN*-Di-(2-pyridylmethyl)amides

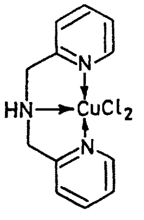
By R. P. HOUGHTON* and R. R. PUTTNER

(*Department of Chemistry, University College, Cathays Park, Cardiff* CF1 1XL)

Summary With cupric chloride, *NN*-di-(2-pyridylmethyl)-amides form 1 : 1 complexes which undergo methanolysis and hydrolysis with remarkable rapidity.

A LARGE number of metal-catalysed nucleophilic substitutions of carboxylic acid derivatives have been described.[1,2] In most of these reactions catalysis occurs because a metal ion is co-ordinated with the oxygen of the carbonyl group, and consequently the metal ion can stabilise the negative charge introduced on to this oxygen when the carbonyl group is attacked by the nucleophile. In some cases, however, *e.g.*, the metal-catalysed hydrolysis of esters of 8-hydroxyquinoline,[3] the leaving group (L) of the derivative (R·CO·L) is co-ordinated to the metal, and this co-ordination not only inhibits the resonance stabilisation of the derivative but also increases the rate at which the leaving group departs from the tetrahedral intermediate of the reaction. We describe some copper(II)-catalysed transformations of *NN*-di-(2-pyridylmethyl)amides which almost certainly involve the second type of catalysis, and which represent some of the most strongly catalysed nucleophilic substitutions of carboxylic acid derivatives reported so far.





(I) a; $R = p\text{-}NO_2\cdot C_6H_4$ (II)

b; $R = Me_3C$

c; $R = Me\cdot CH\overset{t}{=}CH$

When treated with cupric chloride, the amides† (I; a–c) formed pale blue 1 : 1 complexes whose i.r. spectra clearly indicated that in all three cases both pyridine nitrogens and the amide nitrogen were co-ordinated to the copper. The spectrum of the complex of (Ib), for example, showed the two bands[4] at 1575 and 1609 cm^{-1} of the co-ordinated pyridines, and carbonyl absorption at 1656 cm^{-1} (*cf.* 1630 cm^{-1} in the spectrum of the amide). The complexes were not very soluble in cold methanol, but when heated in this solvent they were rapidly converted into the royal blue complex (II) and the methyl ester of the appropriate carboxylic acid. In order for these reactions to proceed to completion it was necessary to heat the mixtures under reflux for 5—10 min. because of the low solubility of the complexes, but it was evident from small-scale experiments that the complexes reacted with the methanol almost immediately they dissolved.

The same transformations were more conveniently achieved by adding the amides to a hot solution of cupric chloride in methanol, but in contrast, both amides were quantitatively recovered and no methyl *p*-nitrobenzoate was detected (t.l.c.) when the amide (Ia) was heated for 24 h in methanol and when *NN*-dibenzyl-*p*-nitrobenzamide was heated for 24 h in methanol with 1 equiv. of cupric chloride.

In hot water the complex of the amide (Ia) was largely dissociated into the two components, and the formation

---

† All new compounds had correct analyses and the expected spectroscopic data.

of *p*-nitrobenzoic acid by hydrolysis of the co-ordinated amide was therefore a much slower reaction than the methanolysis; a 42% yield of the acid was obtained after a reflux period of 15 min.

It is expected that other types of tertiary amides in which the amide nitrogen is one of the internal donors of a polydentate ligand will exhibit metal-ion-catalysed nucleophilic substitutions similar to those described above. This possibility, together with some synthetic uses of the *NN*-di-(2-pyridylmethyl)amide group, is currently being investigated.

We thank S.R.C. for financial support of this work.

(*Received, August* 17*th*, 1970; *Com.* 1393.)

[1] M. L. Bender, Advances in Chemistry Series, No. 37, The American Chemical Society, Washington, D.C., 1962, p. 19.

[2] M. M. Jones, "Ligand Reactivity and Catalysis," Academic Press, London, 1968, p. 42.

[3] C. R. Wasmuth and H. Freiser, *Talanta*, 1962, **9**, 1061.

[4] M. M. da Mota, J. Rodgers, and S. M. Nelson, *J. Chem. Soc.* (*A*), 1969, 2036.