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Solid-phase Catalysis of the Hydrolysis of Nitriles to Amides

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The hydrolysis of nitriles to amides usually requires strongly acidic or alkaline conditions and these may be sometimes quite drastic. The hydrolysis may sometimes be effected at room temperature by alkaline hydrogen peroxide[1] but yields are variable and solubility is often a problem. We now report a reaction which takes place at room temperature under ostensibly neutral conditions which gives good yields of amides and no other product.

Manganese dioxide has frequently been used to oxidise alcohols to carbonyl compounds in a variety of solvents.[2] Recently, Harrison has advocated acetonitrile as a more generally useful solvent.[3] In our hands the oxidation was accompanied by the formation of large quantities of acetamide even when the manganese dioxide (several different preparations) had been dried at 100° for 2—3 hours. The presence of the alcohol, in whose oxidation we were interested, was shown to be unnecessary. For practical purposes the hydrolysis could most usefully be carried out in methylene chloride with agitation using a 10% solution of the nitrile and a ratio of substrate to manganese dioxide of 1 : 5—10 by weight. These represent the conditions for the reactions tabulated below and for many others.

Yields of amides are variable, but ease of separation from starting materials and the mild conditions employed commend the method in suitable cases. The high yield of amide obtained from *p*-methoxymandelonitrile *O*-benzoate (and others in this series) suggest that the steric requirements for this reaction are much less than for the normal mode of hydrolysis. The selectivity of the method was tested further with γ-bromobutyronitrile. Here however the intermediate (probably the amide) displaces the bromine to yield γ-bromobutyrolactone in good yield.[4]

Table

	Reaction time (hrs.)	Yield % of corresponding amide
Acetonitrile	80	40
Phenylacetonitrile	70	22
Benzonitrile	70	72
Acetone cyanohydrin	22	53
p-Methoxymandelonitrile *O*-benzoate	45	60*
Acrylonitrile	26	22
cis-3-Bromo-4-methoxycinnamonitrile	96	35*
trans-3-Bromo-4-methoxycinnamonitrile	18	90*

The yields quoted above are of analytically pure material.

* New compounds have given satisfactory analytical and spectroscopic data.

The most probable mechanism for the reaction is a solid-phase catalysed hydrolysis involving water on the surface of the solid. Manganese dioxide retains moisture tenaciously and specimens, after drying at 100° for 2—3 hours, analysed for quantities of water in excess of a mole per mole of nitrile, under the reaction conditions stated. Support for this type of mechanism is forthcoming in the hydrolysis of Schiff bases. Thus we find that benzaldehyde and aniline can be isolated in over 70% yield from a reaction involving benzylideneaniline.

The reaction times involved are longer than those normally required for the oxidation of allylic and benzylic alcohols. But clearly the use of acetonitrile as a solvent for manganese dioxide oxidations will introduce complications for the slower reactions. Further studies are in progress to elucidate the mechanism and extend the scope of the hydrolytic reaction.

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[1] K. B. Wiberg, *J. Amer. Chem. Soc.*, 1953, **75**, 3961; 1955, **77**, 2519.

[2] R. M. Evans, *Quart. Rev.*, 1959, **13**, 61.

[3] I. T. Harrison, *Proc. Chem. Soc.*, 1964, 110.

[4] See C. J. M. Stirling, *J. Chem. Soc.*, 1960, 255, for a similar reaction induced thermally.