The Preparation of Carboxylic Amides from Aldehydes by Oxidation

By Norman W. Gilman*

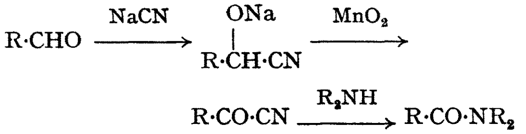
(*Chemical Research Department, Hoffmann-La Roche Inc., Nutley, New Jersey* 07110)

Summary The oxidation of aromatic and αβ-unsaturated aldehydes with manganese dioxide in the presence of sodium cyanide and an amine leads to high yields of the corresponding carboxylic amides.

ACTIVATED manganese dioxide is a selective oxidizing agent for the conversion of primary allylic alcohols into αβ-unsaturated aldehydes.[1] The reaction stops cleanly at the aldehyde stage without further oxidation to the carboxylic acid. However, a recent report[2] described a method for the oxidation of αβ-unsaturated aldehydes to the corresponding methyl esters, using manganese dioxide in the presence of cyanide ion and methanol.

We now report that this type of oxidation procedure is also applicable for the preparation of carboxylic amides. The replacement of methanol with an amine or with an amine in isopropyl alcohol as the solvent leads to amides instead of methyl esters.

Presumably, the mechanism of the reaction involves the formation from the aldehyde of the cyanohydrin, which is oxidized to the acyl cyanide by manganese dioxide. The reaction of the acyl cyanide with an amine yields the amide with displacement of cyanide ion.



$$R\cdot CHO \xrightarrow{NaCN} R\cdot\overset{ONa}{\overset{|}{C}}H\cdot CN \xrightarrow{MnO_2}$$

$$R\cdot CO\cdot CN \xrightarrow{R_2NH} R\cdot CO\cdot NR_2$$

Significantly, in the absence of sodium cyanide, high yields of nitriles are formed from aldehydes, ammonia, and manganese dioxide.[3] The addition of sodium cyanide completely suppresses the formation of the nitrile.

The results for the formation of amides are given in the Table.

The structures of the products were confirmed by a comparison of their physical properties and/or their i.r. spectra with those of authentic samples.

An illustration of the experimental procedure is the preparation of benzamide from benzaldehyde.

To 10 ml of isopropyl alcohol at 0° saturated with ammonia, was added 245 mg (5 mmols) of powdered sodium cyanide. After 5 min, 106 mg (1 mmol) of benzaldehyde was added followed by 1·74 g (20 mmols) of manganese dioxide which was added in two equal portions 10 min apart. After 4 h at 0°, the heterogeneous mixture was diluted with 20 ml of CH_2Cl_2 and filtered through a small bed of Celite. The filtrate was concentrated under reduced pressure and the residue washed with ether to give 78 mg (64%) of benzamide, m.p. and mixed m.p. 124—126°. The i.r. spectrum was identical with that of an authentic sample. There was no evidence for the formation of the isopropyl ester. However, if methanol was used as the solvent, mixtures of benzamide and methyl benzoate resulted.

TABLE

Aldehyde	Amine	Product	Yield (%)
PhCHO	NH_3	$PhCO\cdot NH_2$	64
PhCHO	Et_2NH	$PhCO\cdot NEt_2$	96
2-Furyl·CHO	NH_3	$2\text{-Furyl}\cdot CO\cdot NH_2$	90
2-Furyl·CHO	Et_2NH	$2\text{-Furyl}\cdot CO\cdot NEt_2$	98
PhCH=CH·CHO	NH_3	$PhCH{=}CH\cdot CO\cdot NH_2$	100

(*Received, May 3rd,* 1971; *Com.* 692.)

---

[1] L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis," Wiley, New York, 1967, pp. 637—643.

[2] E. J. Corey, N. W. Gilman, and B. E. Ganem, *J. Amer. Chem. Soc.*, 1968, **90**, 5616.

[3] For a similar synthesis of nitriles using ammonia and $Pb(OAc)_4$ see: K. N. Parameswaran and O. M. Friedman, *Chem. and Ind.*, 1965, 988.