Metal-assisted Borohydride Reduction of Acid Chlorides to Aldehydes

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Summary Acid chlorides are reduced to aldehydes in good yields by borohydride in suitable solvents at *ca.* 0 °C.

THE direct conversion of readily available acid chlorides into aldehydes is a useful reaction in organic synthesis. Indirect methods, whereby an acid chloride is converted first into an amide[1] or aziridine[2] followed by hydride reduction, are well known. Direct conversion can be achieved as illustrated by the examples of the Rosenmund reduction in boiling solvents[3] and the use of suitably modified aluminium hydrides at −70 °C.[4] The indirect methods are generally not as convenient as the direct in synthesis and the available direct methods require either specially prepared reduction catalysts or greatly modified hydride reagents. Direct reduction of acid chlorides slowly gives primary alcohols with the cheap sodium borohydride[5] but we have found general conditions under which aldehydes may be obtained.

The effect of addition of metal salts to sodium borohydride is generally to increase its reactivity. For example, addition of magnesium chloride to sodium borohydride allows esters to be reduced to alcohols whereas sodium borohydride alone has little or no effect. The subject has been reviewed extensively.[6] Solvents also appear to have a marked effect on the reactivity of sodium borohydride.[7]

We have found that, in the presence of cadmium chloride and dimethylformamide (DMF), acid chlorides are reduced to aldehydes. The cadmium chloride and dimethylformamide are conveniently combined by recrystallization of $CdCl_2.2\frac{1}{2}H_2O$ from dry dimethylformamide to give $CdCl_2.1\frac{1}{2}DMF$. As an example, sodium borohydride (2·0 mmol) was dissolved in acetonitrile (10 ml) and hexamethylphosphoramide (0·5 ml) and then stirred for 5 min with $CdCl_2.1\frac{1}{2}DMF$ (1·25 mmol) at −5 to 0 °C (ice-salt bath). To the slightly opaque solution was added 4-chlorobenzoyl chloride (2 mmol) in acetonitrile (2—3 ml) rapidly with stirring, which was continued for 5 min. Dilute HCl was added slowly to the reaction mixture which was then extracted with ether to give 4-chlorobenzaldehyde, identified as its 2,4-dinitrophenylhydrazone and by ^1H n.m.r. spectroscopy. Some typical yields of aldehydes based on isolated crystalline 2,4-dinitrophenylhydrazones are as follows. Benzaldehydes (RC_6H_4CHO): R=H (76%), 4-Me (89), 4-Cl (74), 4-NO_2 (71), 4-MeO (63), 4-CN (67), 2-Me (60), 2-Br (62), and 2-CO_2Me (52); other aldehydes (R'CHO): R'=CH=CHPh (*trans*) (71%), CH_2Ph (58), n-C_8H_{17} (56), CH=CHMe (*trans*) (54), and Bu^t (32). Indicated yields (^1H n.m.r.) were consistently 5—10% greater and show that most of the organic material, other than aldehyde, is the corresponding alcohol. Typically, the ratio of aldehyde to alcohol in the aromatic series was *ca.* 10:1. Some material was recovered as the acid arising from hydrolysis of acid chloride. As these examples show, other functional groups do not appear to be affected by the reducing agent.

Thus, chloro, cyano, nitro, and ester groups and double bonds are unaffected.

Without dimethylformamide, yields of aldehydes are very low. Without $CdCl_2$, yields of aldehydes are greatly lowered but can be raised again by carrying out the reduction at −70 °C. Other metal ions can be used in this reaction but we have found cadmium to give the most stable reducing solution, so much so that the reducing agent prepared in bulk as above can be kept in a refrigerator at 0 °C for up to 4 days and used as desired.

The authors thank the S.R.C. for a studentship (to R.P.T.)

(*Received*, 23*rd January* 1978; *Com.* 064.)

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