AN EFFICIENT REDUCTION OF NITRILES AND AMIDES TO THE CORRESPONDING AMINES WITH TETRA-N-BUTYLAMMONIUM BOROHYDRIDE IN DICHLOROMETHANE

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Abstract — The reduction of nitriles and amides to the corresponding amines with tetra-n-butylammonium borohydride in dichloromethane has been reported, in which the other functional groups such as ester, nitro, and halogen attached to the aromatic ring are not affected.

The reduction of nitriles and amides to the amines is a very important, but not so easy organic transformation. The improved methods for the reduction of nitriles[1] and amides[2] with complex metal hydrides have been so far reported.

We wish herein to describe another convenient and efficient method for the reduction of nitriles and amides to the amines with tetra-n-butylammonium borohydride[3-6] in refluxing dichloromethane (eq. 1 and 2), in which the chemospecificity of tetra-n-butylammonium borohydride toward organic cyano and amide compounds was observed. The other functional groups of the ester, nitro, and halogen attached to the aromatic ring are not affected (Table 1, entry No. 6, 7, and Table 2 entry No. 10). The feature of this method is shown by the fact that the above reducing agent is readily soluble in dichloromethane which is a powerful solvent for many organic compounds in contrast with ether as a widespread solvent for alkali metal hydrides. The results are summarized in Table 1 and 2.

$$\mathrm{RCN} \xrightarrow[\mathrm{CH_2Cl_2}]{\mathrm{(n\text{-}Bu)_4NBH_4}} \mathrm{RCH_2NH_2} \qquad \text{(eq. 1)}$$

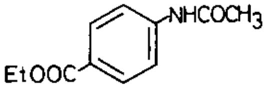
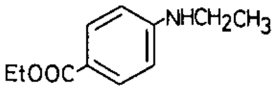
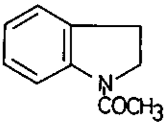
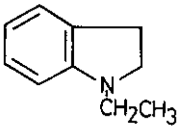
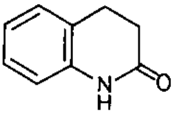
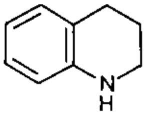
$$\mathrm{RCONR^1R^2} \xrightarrow[\text{"}]{\text{"}} \mathrm{RCH_2NR^1R^2} \qquad \text{(eq. 2)}$$

Table 1 Reduction of nitriles with tetra-n-butylammonium borohydride

No.		Yield(%) of amine HCl	No.		Yield(%) of amine HCl
1	benzonitrile	71	5	diphenylacetonitrile	80
2	phenylacetonitrile	72	6	p-nitrophenylacetonitrile	53
3	p-tolunitrile	87	7	p-chlorophenylacetonitrile	64
4	α-cyanonaphthalene	68			

Table 2 Reduction of amides with tetra-n-butylammonium borohydride

No.		Yield(%) of amine HCl	No.		Yield(%) of amine HCl
1	$PhCONH_2$	70(8)	6	$PhN(CH_3)COCH_3$	53(15)
2	$PhCONHCH_2CH_3$	75(7)	7	$Ph(CH_2)_2CONH_2$	55(16)
3	$PhCON(CH_2CH_3)_2$	51(31)	8	$Ph(CH_2)_2NHCOCH_3$	58(12)
4	$PhNHCOCH_3$	74(1)	9	$Ph(CH_2)_2N(CH_2CH_3)COCH_3$	50(29)
5	PhNHCOPh	70(14)			

No.	Carboxamide	Product	Yield(%) of amine HCl
10			77
11			55*(33)
12			86*

Numbers in parenthesis are yield(%) of recovered carboxamides.

• Yield(%) based on its free amine.

The typical procedure is described in the following:

a) Reduction of p-tolunitrile with tetra-n-butylammonium borohydride to p-tolubenzylamine: To a solution of 298mg(2.55mmol) of p-tolunitrile in 15ml of dichloromethane was added 1.969g(7.65mmol) of tetra-n-butylammonium borohydride. The mixture was vigorously refluxed with stirring for 10h. After removal of the solvent, a solution of 10% hydrochloric acid(15ml) was added to the residue and then refluxed for 1h. An acidic solution was neutralized with solid sodium hydroxide followed by extraction with ether. Evaporation of the solvent dried over anhydrous magnesium sulfate gave the crude amine, which was taken up in dichloromethane and dry hydrogen chloride was bubbled into this solution to afford 320mg(87%) of p-tolubenzylamine hydrochloride, mp 224-226°C(lit.[7] mp 234-235°C).

b) Reduction of acetoanilide with tetra-n-butylammonium borohydride to N-ethylaniline: To a solution of 543mg(4.01mmol) of acetoanilide in 15ml of dichloromethane was added 3.11g(12.1mmol) of tetra-n-butylammonium borohydride. The whole mixture was vigorously refluxed with stirring for 10h. A similar work-up as described above afforded 470mg(74%) of N-ethylaniline hydrochloride, mp 175-177°C(lit.[8] mp 173-175°C).

A further application is described in the following communication.

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