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A COMBINATION OF SODIUM BOROHYDRIDE WITH ANILIDES AS A NEW REAGENT FOR ESTER REDUCTION

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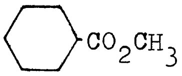
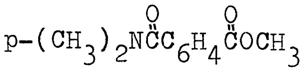
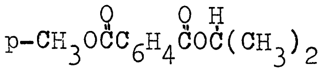
Sodium anilidoborohydrides were synthesized from sodium borohydride and anilides in α-picoline, and these compounds were found to be useful reagents for facile reduction of esters.

Some carboxylic esters, especially pyridinecarboxylic esters, can be reduced with a 10-fold excess of sodium borohydride in refluxing methanol.[1) However, aliphatic and α,β-unsaturated esters cannot be reduced satisfactorily with sodium borohydride for synthetic purpose and it is generally accepted that sodium borohydride does not reduce carboxylic esters in a good yield except in the case of abnormal reduction in which neighboring functional groups are participating.[2a-c)

We synthesized sodium anilidoborohydride[3) by mixing sodium borohydride and an anilide (acetanilide or benzanilide) in α-picoline, by which equimolar amount of hydrogen was evolved and found that methyl esters were reduced in a good yield without affecting other functional groups (amide, nitrile and isopropyl ester) which, with lithium aluminum hydride, would also be reduced. A typical procedure is as follows: A mixture of $NaBH_4$ (7.5 mmol, 285 mg) and benzanilide (5 mmol, 990 mg) in 9 ml of α-picoline was maintained at 100°C for about 40 min. After 5 mmolar hydrogen had evolved, methyl nonanoate (5 mmol, 860 mg) was added and the solution was kept at 100°C for 5 hr. The solvent was distilled off at 70°C/25-30 Torr, 5% HCl (25 ml) was added to the residue with cooling. Benzanilide liberated (about 85% recovery) was collected by filtration and washed with cold $CHCl_3$. The filtrate was extracted with $CHCl_3$ and the combined $CHCl_3$ layer was dried over anhyd. Na_2SO_4. After evaporation of $CHCl_3$, the residual oil was purified by column chromatography (SiO_2, benzene:acetone=6:1) or by distillation.

Results of reduction using anilidoborohydrides are presented in the table. Neither high temperature nor strict anhydrous condition are necessary for this reduction. A 1.5-fold excess of sodium borohydride to ester is adequate for the reduction. This procedure is very simple because benzanilide can be recovered from the work-up solution by filtration due to its low solubility in water and cold organic solvents. As lithium aluminum hydride requires anhydrous conditions and flammable solvents, and reduces various functional groups indiscriminately, reduction with anilidoborohydrides can compensate the limited use of lithium aluminum hydride.

Table. Reduction of Esters with Sodium Anilidoborohydrides in α-Picoline (10-12 ml) at 100°C

Ester	Ester (mmol)	R.A.a) (mmol)	Reaction time (hr)	Isolated alcohol(%)b)
$C_6H_5CO_2CH_3$	5	10	2	71
$C_6H_5CO_2CH_3$	5	15c)	2	6(69)d)
$C_6H_5CO_2CH_3$	10	10	5	85
$C_6H_5CH_2CH_2CO_2CH_3$	10	10	5	97
$CH_3(CH_2)_7CO_2CH_3$	10	10	5	87
$C_6H_5CH{=}CHCO_2CH_3$	7	10	5	71(9:1)e)
o-$CH_3OC_6H_4CO_2CH_3$	5	5*	6	93
p-$CH_3OC_6H_4CO_2CH_3$	5	5*	6	75
	10	10*	6	64
$CH_3(CH_2)_7CO_2CH_3$	5	5*	5	87
$CH_3(CH_2)_6CO_2CH_3$	30	30*	5	74f)
Methyl 2-furoate	5	5*	6	71
p-$NCC_6H_4CO_2CH_3$	5	5*	3	89
 p-$(CH_3)_2N\overset{O}{C}C_6H_4\overset{O}{C}OCH_3$	5	5*	3.5	78
 p-$CH_3O\overset{O}{C}C_6H_4\overset{O}{C}O\overset{H}{C}(CH_3)_2$	5	5*	4	73(85:15)g)

* Asterisks indicate the use of benzanilidoborohydride. Acetanilidoborohydride was used in others. a) Reducing agent. b) All the products gave satisfactory spectral data and/or same retention time as the authentic samples in gas chromatography. c) $NaBH_4$ was employed instead of the complexes for comparison. d) Recovery of the starting ester, 69%. e) Isolated alcohol consisted of 10% of unsaturated and 90% of saturated alcohols. f) Yield after distillation (bp 104-105°C/28 Torr). g) Preferential reduction of methyl ester over that of isopropyl ester, in a ratio of 85 (isopropyl p-hydroxymethylbenzoate):15 (methyl p-hydroxymethylbenzoate).

References

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c) H. Seki, K. Koga, H. Matsuo, S. Ohki, I. Matsuo, and S. Yamada, Chem. Pharm. Bull.(Tokyo), 13, 995(1965).

3) The spectral data of sodium acetanilidoborohydride are as follows: IR ($CHCl_3$) 2250-2400 (B-H), 1604 (N-Ph), 1560-1580 (O-C=N-)cm^{-1}; NMR (δ, $CDCl_3$) 1.75 (3H, s, CH_3), 6.48-6.62 (2H, m, Ph), 7.05-7.12 (3H, m, Ph).

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