

SELECTIVE REDUCTION OF ALDEHYDES

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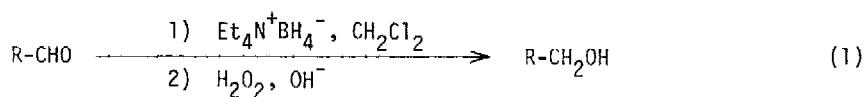
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Tetraethylammonium borohydride performs the selective reduction of aldehydes under mild conditions.

During the course of our investigation on transition metal tetrahydroborate complexes as stoichiometric reducing agents,¹⁻⁴ we recognized that, in organic solvents, the BH_4^- ion reacts preferentially with aldehydes.⁴ We report here on the reactions of tetraethylammonium borohydride.

Alkali-metal borohydride compounds have gained wide use as reducing agents in organic synthesis, in contrast to their tetraalkylammonium analogs which have been known for almost 30 years.⁵ The tetramethyl derivative exhibits solubility and reactivity properties similar to those of the alkali-metal borohydrides, and therefore offers no advantages as a synthetic reagent. Cetyltrimethylammonium and tricaprilmethylammonium borohydrides⁶ reduce aldehydes and carboxylic acid chlorides in non-polar solvents to the corresponding alcohols, although they react with ketones only slowly, even at elevated temperatures. In 1976, Raber⁷ reported the reduction of aldehydes and ketones by tetrabutylammonium borohydride in methylene chloride using four equivalents of hydride in order to get convenient rates in the reduction of ketones. No attempt was made in that work to cultivate the selectivity of the reagent.

Tetraethylammonium borohydride is commercially available⁸ as a stable, white crystalline solid. It is considerably less soluble in non-polar solvents than the longer chain tetraalkylammonium derivatives and for that reason has received little attention as a reagent. However, tetraethylammonium borohydride reduces aldehydes to the corresponding alcohols in methylene chloride at 25° within 20 hr (equation 1), and the isolated yields are high (Table). Ketones



react more slowly with the reagent under similar conditions, and less than 15% disappearance of the ketone is generally observed.⁹ Even unhindered ketones such as 4-*t*-butylcyclohexanone are relatively inert to this reagent, comparable with the best of other reagents that have been used for selective reduction of aldehydes.¹⁰ Tetraethylammonium borohydride offers advantages over other reagents in that it is commercially available, and its use requires no special equipment or conditions.^{11,14}

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REFERENCES AND NOTES

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Table

Starting Material	Product	Yield ^a (%)
benzaldehyde	benzyl alcohol	89
<i>p</i> -chlorobenzaldehyde	<i>p</i> -chlorobenzyl alcohol	87 [71-72°]
<i>p</i> -nitrobenzaldehyde	<i>p</i> -nitrobenzyl alcohol	88 [92-93.5°]
<i>p</i> -anisaldehyde	<i>p</i> -methoxybenzyl alcohol	53 ^b
nonanal	1-nonanol	75
citronellal	citronellol	77
furfural	furfuryl alcohol	83
cyclohexanone	cyclohexanol	10 ^c (80) ^d
acetophenone	α -hydroxyethylbenzene	13 ^c (83) ^d
2-octanone	2-octanol	12 ^c (83) ^d
4- <u>t</u> -butylcyclohexanone	4- <u>t</u> -butylcyclohexanol	12 ^c

a) Yields are for isolated, distilled or recrystallized products (see ref. 12). Mp are in []. b) gc yield; 47% unreacted starting material after 24 hr. c) Number refers to % disappearance of starting material determined by gc; product determined qualitatively by gc. d) Yield of recovered starting material as its 2,4-DNP derivative.

3. T. N. Sorrell and P. S. Pearlman, *J. Org. Chem.*, in press.
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6. E. A. Sullivan, and A. A. Hinckley, *J. Org. Chem.*, **27**, 3731-3733 (1962).
7. D. J. Raber and W. C. Guida, *J. Org. Chem.*, **41**, 690-696 (1976).
8. The reagent was purchased from Alfa Products, Thiokol/Ventron Division, Danvers, Mass.
9. A methylene chloride solution of nonanal and 2-octanone treated with 0.25 equiv of Et₄NBH₄ (1 equiv of hydride ion) for 20 hr at 25° showed 94% reduction of nonanal and 6% loss of 2-octanone.
10. G. H. Posner, A. W. Runquist, M. J. Chapdelaine, *J. Org. Chem.*, **42**, 1202-1208 (1977).
11. The preparation of furfuryl alcohol is representative. To a stirred solution of 0.97 g of furfural in 3 mL of methylene chloride was added, in one portion, 20 mL of 0.15 M Et₄NBH₄ in dichloromethane. After 20 hr, 20 mL of 3% hydrogen peroxide was added to the reaction mixture followed by 10 mL of 10% NaOH. This mixture was stirred for 2 hr, the layers separated, the aqueous layer extracted with three 30-mL portions of methylene chloride, and the combined organic layers washed with saturated sodium sulfite. The organic layer was dried over MgSO₄, filtered, and the solvent was evaporated. The crude furfuryl alcohol was purified by bulb-to-bulb distillation at reduced pressure to give 0.82g (83%) of product, 95% pure by gc (see references 12 and 13).
12. All isolated compounds were at least 95% pure by gc and nmr.
13. Solid alcohols obtained as crystalline products after evaporation of the solvent were greater than 90% pure and were further purified by recrystallization.
14. In alcoholic or aqueous solvents, the reactivity of tetraethylammonium borohydride is similar to the alkali-metal borohydride reagents.

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