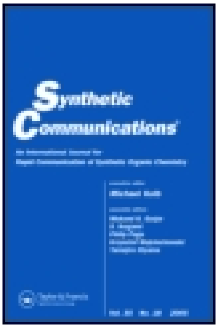

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Reduction of Carboxylic Acids by Tetraalkyl Ammonium Borohydride

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REDUCTION OF CARBOXYLIC ACIDS BY TETRAALKYL AMMONIUM BOROHYDRIDE

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Abstract: Tetraalkylammonium borohydride reduces carboxylic acids to the corresponding alcohols in good yields utilizing only stoichiometric quantities of hydride and also in the absence of any Lewis acids.

Selective conversion of acids to alcohols is a very useful transformation and is generally effected by reagents such as borane-dimethylsulphide,[1] borane-tetrahydrofuran,[2] or sodium borohydride in the presence of Lewis acids such as aluminium chloride[3] or iodine.[4] Recently zinc borohydride has been shown to reduce acids without the need for the addition of Lewis acids, indicating the "Borane" like nature of this reagent.[5] Interestingly, in our study on tetraalkylammonium borohydrides, we found that a borane like species can be produced in these borohydrides

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in chlorinated solvents. This prompted us to study the utility of these reagents in the reduction of carboxylic acids without involving addition of any Lewis acids.

Tetrabutylammonium borohydride and benzyltriethylammonium borohydride were prepared as reported in the literature by the metathesis reaction of sodium borohydride with the corresponding tetraalkylammonium salts.[6]

The reagents are obtained as solids and are very easy to handle. The reagents are ineffective in THF but reduced acids easily in common solvents like dichloromethane, chloroform etc. In view of its facile removal, dichloromethane is used as the solvent in the present study. In a preparative study a number of carboxylic acids were reduced to the corresponding alcohols by both tetrabutylammonium borohydride and benzyltriethylammonium borohydride in good yields in refluxing dichloromethane. The results are presented in table 1. Curiously, unlike other metal borohydrides ester group was not reduced during the reduction of acids. Hence a selective reduction of carboxylic group can be achieved in the presence of an ester group. A representative reduction of methylhydrogen phthalate resulted in the formation of methyl(2-hydroxymethyl)benzoate.

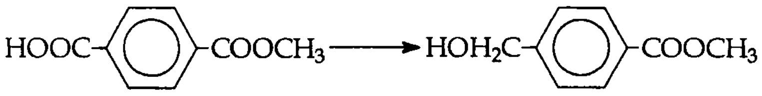


Table 1 Reduction of Carboxylic acids by Benzyltriethylammonium borohydride, (BTEAB) and Tetrabutylammonium borohydride, (TBAB) at reflux temperature.

Substrate	Product	MP/BP (°C)	Yield (%)	
			BTEAB	TBAB
Palmitic acid[a]	Cetyl alcohol	54 (54)	80	83
Valeric acid[a]	Amyl alcohol	130 (130) /760mm	70	70
Pivalic acid[a]	Neopentyl alcohol	56 (55)	70	70
Azelaic acid[b]	1,9-nonane diol	47 (47)	75	77
Methylhydrogen phthalate[c]	methyl(4-hydroxy methyl)phthalate	49 (48)	72	70
monomethyl ester of azelaic acid[c]	methyl 9-hydroxy azelate	---	70	69
Benzoic acid[a]	benzyl alcohol	205 (205) /760mm	74	74
2-chloro benzoic acid[a]	2-chlorobenzyl alcohol	70 (69)	67	71
4-nitro benzoic acid[a]	4-nitrobenzyl alcohol	93 (92)	78	79
Acetyl salicylic acid[a]	Salicyl alcohol	83 (83)	67	69
Undecenoic acid[ic]	1,11-undecanediol[d]	60	75	75
Cinnamic acid[c]	Cinnamyl alcohol[e] and diol	250 (250) 760mm	78	78.9

[a] [acid] : [H^-]= 5:16 ; [b] [acid] : [H-] = 1 : 7 ; [c] [acid] : [H-] = 1 : 3 [d] mixture of undecenol and diol in the ratio 1 : 9 [e] mixture ratio of cinnamyl alcohol : 1,2-diol : 1,3 - diol = 36 : 28 : 36 in $BzEt_3N^+BH_4^-$ and 25 : 15: 60 in $Bu_4N^+BH_4^-$, [e] The MP and BP data given in the brackets are from the literature.

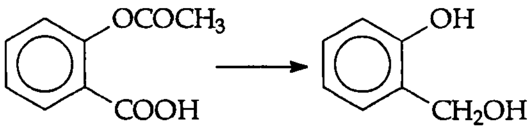
Similarly the reduction of monomethyl ester of azelaic acid resulted in the formation of the corresponding hydroxy ester. This selective conversion has been utilized in the preparation of pheromones with Z-9—olefinic configuration.

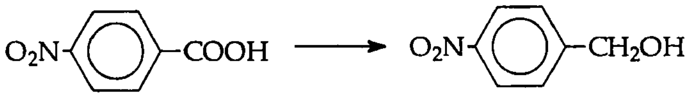
$$\mathrm{HOOC(CH_2)_7COOCH_3} \longrightarrow \mathrm{HO(CH_2)_8COOCH_3}$$

However, double bonds are hydroborated. For example, 10-undecenoic acid produced 1,11-undecanediol diol after oxidative work-up. Cinnamic acid produced a mixture of cinnamyl alcohol and 1,2 and 1,3-diols.

$$\mathrm{H_2C{=}CH(CH_2)_8COOH} \longrightarrow \mathrm{HO(CH_2)_{11}OH}$$

The ratio of 1,2 and 1,3 diol was 1:4 indicating the higher preference for benzylic positions. Reduction of salicylic acid stopped with the liberation of hydrogen. But acetyl salicylic acid was reduced to yield 2-hydroxybenzyl alcohol. Nitro group was also tolerated during the reduction.





In conclusion tetrabutylammonium borohydride and benzyltriethylammonium borohydride offer a simple convenient method for the conversion of carboxylic acids to the corresponding alcohols with good selectivity utilizing only stoichiometric quantities of hydride and also with out any Lewis acids. The method is very useful in the selective reduction in the presence of esters for the preparation of pheromones.

Experimental :

All the reactions were carried out under nitrogen atmosphere.

Reduction of palmitic acid: To 1.02g (4mmol) of tetrabutylammonium borohydride was added 1.3g (5mmol) of palmitic acid dissolved in 10 mL of CH_2Cl_2. The reaction mixture was stirred under reflux conditions for 5 - 6h. The flask was then cooled to room temperature and the excess hydride was quenched by adding 1mL of 3N H_2SO_4. The alcohol formed was extracted in CH_2Cl_2 and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure. The tetraalkylammonium salt present along with the product, cetyl alcohol was removed by passing through a silica gel column (Yield 80%)

Reduction of 10-undecenoic acid: To 1.28g of tetrabutylammonium borohydride (5mmol), was added 1 mL of 10-undecenoic acid dissolved in 10 ml of CH_2Cl_2 and the reaction mixture was refluxed for 4 - 5 h. The excess hydride was quenched by adding 1 mL of 3N dilute H_2SO_4 and then made alkaline with NaOH solution followed by oxidation with 30% H_2O_2.

The organic layer was separated, washed with NaOH and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure. The tetraalkylammonium salt present along with the product, 1,11-undecane diol was removed by passing through a short silica gel column. (Yield 75%)

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