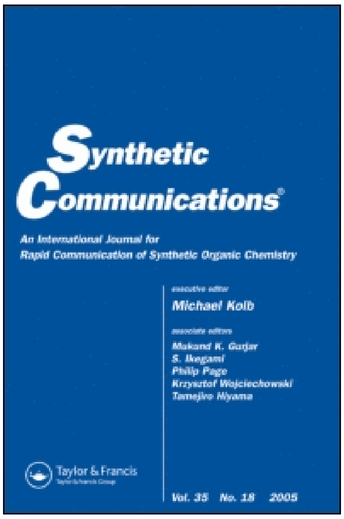

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# A Convenient Methodology for the Selective Reduction of Carboxylic Acids With Benzyltriethyl-Ammonium Borohydride—Chlorotrimethylsilane

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# A CONVENIENT METHODOLOGY FOR THE SELECTIVE REDUCTION OF CARBOXYLIC ACIDS WITH BENZYLTRIETHYLAMMONIUM BOROHYDRIDE - CHLOROTRIMETHYLSILANE

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A combination of benzyltriethylammonium borohydride and chlorotrimethylsilane (1:1) in dichloromethane (0-25°C) has been found to be a convenient reagent system for the selective reduction of carboxylic acids to alcohols.

Metal borohydrides are important reducing agents in organic chemistry[1] and reducing agents formed by a combination of transition metal halide and $NaBH_4$ have been used for the reduction of various functional groups and these reactions have attracted considerable attention in organic synthesis.[2]

Recently we reported our results on the facile and direct conversion of alkenes to alcohols with a new reagent system consisting of benzyltriethylammonium borohydride-chlorotrimethylsilane.[3] In exploring further the synthetic utility of this reagent system we

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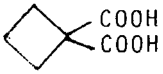
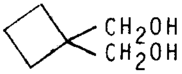
find that carboxylic acids are reduced selectively in dichloromethane under very mild reaction conditions to the corresponding alcohols. The results of this facile reduction of a wide variety of aliphatic and aromatic carboxylic acids are summarised in the Table. As it is evident from the table the reagent system tolerates a number of other functional groups like nitro, chloro, thiol and carbomethoxy (entries 3,5,9 and 12) in the molecule. The usefulness of this methodology lies in the fact that the reactions are done at room temperature in a short period of time, alcohols are formed as the only product in high yields and dichloromethane as a solvent offers distinct advantage as the reaction medium.

The mechanism of this reaction and active species responsible for the reduction remain unclear. We have earlier shown that this reagent system behaves differently from borane.[3] Additionally, free borane generated in situ in dichloromethane by the reaction of quaternary ammonium borohydride-methyliodide[4] very readily reduces p-nitro methyl benzoate in 80% yield whereas with our reagent system even after prolonged reaction time (8h) at 28°C more than 70% of starting material could be recovered unchanged (entry 13). Unlike borane this reagent system reduces benzoyl chloride to the alcohol at 0°C (entry 14). $\delta$ -

## TABLE

| Entry | Substrate | Time(h) | Product[a] | yield[b] |
|---|---|---|---|---|
| 1 | $C_6H_5COOH$ | 5 | $C_6H_5CH_2OH$ | 92 |
| 2 | p-tBu-$C_6H_4COOH$ | 4 | p-tBu-$C_6H_5CH_2OH$ | 95 |
| 3 | p-$NO_2$-$C_6H_4COOH$ | 2.5 | p-$NO_2C_6H_4CH_2OH$ | 94 |
| 4 | p-MeO-$C_6H_4COOH$ | 4.5 | p-MeO-$C_6H_4CH_2OH$ | 97 |
| 5 | m-Cl-$C_6H_4COOH$ | 4.5 | m-Cl-$C_6H_4CH_2OH$ | 94 |
| 6 | Ph-$CH_2COOH$ | 4 | Ph-$CH_2CH_2OH$ | 88 |
| 7 | $C_6H_{11}COOH$ | 4 | $C_6H_{11}CH_2OH$ | 96 |
| 8 |  | 6 |  | 78 |
| 9 | $HSCH_2COOH$ | 6 | $HSCH_2CH_2OH$ | 96 |
| 10 | $H_3C(CH_2)_{16}$ COOH | 4 | $H_3C(CH_2)_{16}CH_2OH$ | 97 |
| 11 | $H_3C(CH_2)_3COOH$ | 4 | $H_3C(CH_2)_3$ $CH_2OH$ | 85 |
| 12 | $H_3COOC(CH_2)_7COOH$ | 2.5 | $H_3COOC(CH_2)_7CH_2OH$ | 92 |
| 13 | p-$NO_2$-$C_6H_4$-$COOCH_3$ | 8 | p-$NO_2$-$C_6H_4CH_2OH$ | 25 |
| 14 | Ph-COCl[c] | 3 | Ph-$CH_2OH$ | 95 |
| 15 | δ-Valerolactone[c] | 5 | NO REACTION | -- |
| 16 | Ph-$COOC_2H_5$[c] | 6 | NO REACTION | -- |

a) The products exhibited expected spectral data and were compared with authentic samples.

b) Yield refers to pure isolated products.

c) The reaction was performed at 0°C.

Valerolactone (entry 15) and ethyl benzoate (entry 16) remain largely unaffected by this reagent system.

While this work was in progress a report appeared in the literature on the use of sodium borohydride-chlorotrimethylsilane in THF for the reduction of a number of organic substrates.[5] Our methodology using benzy triethylammonium borohydride-chlorotrimethylsilane in dichloromethane appears to be milder and more selective.

## Experimental

### General Procedure for the reduction of carboxylic acids

To a stirred solution of benzyltriethylammonium borohydride (4 mmol) in dichloromethane (6 mL) cooled to 0°C was added chlorotrimethylsilane (4 mmol) in dichloromethane (2 mL). After stirring for 0.15h, a solution of the carboxylic acid (2 mmol) in dichloromethane (4 mL) was added. The reaction was allowed to come to room temperature (25°C) and stirred for 3-6h. A solution of 10% sodium bicarbonate (15 mL) was added and the reaction mixture was extracted with ether (3x25 mL). The combined organic extract was washed with saturated sodium bicarbonate solution, water and brine. After drying over anhydrous $Na_2SO_4$ the solvent was evaporated and the residue was purified by flash chromatography to reveal the product.

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