

Selective reduction of mixed anhydrides of carboxylic acids to alcohols using borohydride exchange resin (BER)–nickel acetate†

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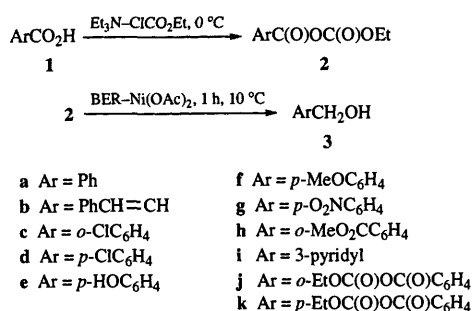
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Mixed anhydrides of carboxylic acids have been selectively reduced to alcohols with borohydride exchange resin–nickel acetate under mild conditions and in good yields.

Introduction

The reduction of carboxylic acids to alcohols, an important synthetic transformation, is brought about in several ways: nickel chloride–diglyme–sodium borohydride,†¹ diborane,² lithium aluminium hydride,³ diisobutylaluminium hydride,⁴ sodium bis(2-methoxyethoxy)aluminium hydride,⁵ sodium borohydride–chlorotrimethylsilane,⁶ benzyl(triethyl)ammonium borohydride–chlorotrimethylsilane,⁷ samarium diiodide–base,⁸ samarium diiodide–acid,⁹ samarium diiodide–water,¹⁰ sodium borohydride–iodine,¹¹ sodium borohydride–catechol¹² and zinc borohydride–trifluoroacetic anhydride.¹³ Recently, selective reduction of aliphatic carboxylic acid in the presence of aromatic carboxylic acid has been achieved with borohydride exchange resin (BER) in methanol at room temperature although it was reported that there was no reduction of aromatic carboxylic acids even after a prolonged reaction period and at reflux temperature.¹⁴ BER is found to be much more stable than NaBH₄ in methanol in the presence of nickel boride and the combination of BER–Ni(OAc)₂ in methanol exhibits enhanced reducing abilities compared with BER.

Recently we reported the facile and direct conversion of aromatic aldehydes into hydrocarbons¹⁵ and aldoximes into amines¹⁶ with the reagent system BER–Ni(OAc)₂. In exploring further the synthetic utility of this reagent system we found that aromatic carboxylic acids, as their mixed anhydrides, are reduced selectively under mild conditions to the corresponding alcohols (Scheme 1). The results of this facile reduction of



Scheme 1

mixed anhydrides of various aromatic carboxylic acids are summarised in Table 1. From our results it is seen that the reduction of cinnamic acid anhydride with BER–Ni(OAc)₂ gives the corresponding α,β -unsaturated alcohol, the olefinic group being unaffected. This contrasts with the substrate's behaviour with LiAlH₄ where it gives 1-phenylpropanol¹⁷ and with zinc borohydride–trifluoroacetic anhydride where there

Table 1 Reduction of mixed anhydrides of carboxylic acids **2** to alcohols **3**

Substrate	Time/h	Product	Yield (%) ^a
2a	1	3a	74
2b	1	3b	80
2c	1.5	3c	91
2d	1.3	3d	88
2e	1	3e	83
2f	1	3f	93
2g	1	3g	75
2h	1	3h	87
2i	2	3i	85
2j	2	3j	74
2k	1.5	3k	62

^a Yield refers to pure isolated products.

was no reduction.¹³ The present reagent system also tolerates a number of other functional groups, *e.g.* chloro, nitro and ester (compounds **2c**, **2d**, **2g** and **2h**) in the molecule.

It has been reported that dicarboxylic acids react with borane reagents to give polymeric insoluble intermediates leading to incomplete reduction.¹⁸ In some cases, however, the corresponding lactone is the major product.¹⁹ In our hands, the present reagent system completely reduces mixed anhydrides of dicarboxylic acids such as phthalic acid and terephthalic acid to the corresponding diols in good yields (entries **2j** and **2k**).

The usefulness of this methodology lies in the fact that the reactions are carried out rapidly under mild conditions with the alcohol, in good yield, as the only product. Easy separation and recyclability of the reagent are noteworthy advantages.

Experimental

All chemicals were of analytical grade. The solvents were distilled before use. Commercially available sodium borohydride was used as received. An ion exchange resin, Tulsion A-27 (chloride form) was obtained from Therman Chemicals, Pune and was used for supporting borohydride anion. All glassware was oven-dried. The products were characterised by their physical constants, spectral characteristics (¹H NMR, IR) and comparison with authentic samples.

Preparation of borohydride exchange resin

Aqueous sodium borohydride (0.5 M; 100 ml) was stirred with the chloride form resin (Tulsion A-27, anion exchange resin; 10 g) for 1 h. The resulting borohydride-bound ion exchange resin was washed thoroughly with distilled water until free of excess sodium borohydride and dried *in vacuo* at 60 °C for 5 h. After this it was analysed for borohydride content by hydrogen evolution on acidification with 0.05 M hydrochloric acid; the average capacity of the ion exchange resin was found to be 3

† Solid supported reactions and reagents. Part 12.

‡ More correctly called sodium boranuide.

mmol $\text{BH}_4^- \text{g}^{-1}$ of dry resin. The dried resin was stored under nitrogen at room temperature. The hydride content was constant over 6 weeks.

Reduction of aromatic carboxylic acids via their mixed anhydrides: general procedure

Ethyl chloroformate (5 mmol) was added to a mixture of the aromatic carboxylic acid (5 mmol), tetrahydrofuran (20 ml) and triethylamine (5 mmol) over a period of 30 min at 0 °C. After being stirred for an additional 30 min at the same temperature, the mixture was filtered and the insoluble salt was washed with THF (3 × 5 ml). BER (15 mmol) was added to $\text{Ni}(\text{OAc})_2$ (100 mg) in methanol (20 ml). When the resin blackened it was filtered off and added to the filtrate of mixed anhydride over a period of 15 min at 10 °C. The mixture was then stirred at the same temperature for the period specified in Table 1. The reaction was monitored by TLC. After completion of the reaction, the resin was filtered off and washed with methanol (2 × 10 ml). Evaporation of the combined filtrates under reduced pressure afforded the almost pure product in good yield.

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