

Selective Reduction of Carboxylic Acids into Alcohols Using NaBH₄ and I₂

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Reduction of carboxylic acids to alcohols is an important transformation in synthetic organic chemistry. Several methods are available for this purpose that utilize LiAlH₄ and boron reagents.¹⁻³ Unfortunately, NaBH₄ does not reduce carboxylic acids under ambient conditions.³ We report here that carboxylic acids can be reduced directly to alcohols with some interesting selectivities by successive addition of NaBH₄ and I₂ to RCOOH and RCOOH to NaBH₄ in THF followed by I₂.

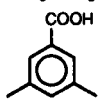
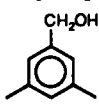
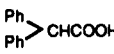
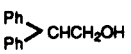
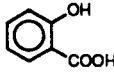
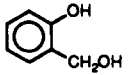
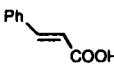
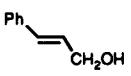
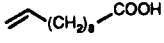
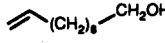
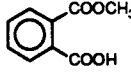
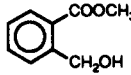
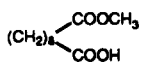
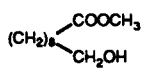
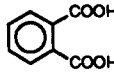
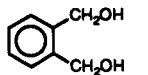
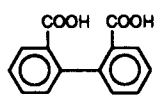
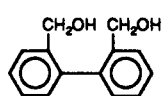
In a typical procedure, the carboxylic acid in THF is added slowly to the suspension of sodium borohydride in THF and the mixture stirred until gas evolution ceases. Iodine in THF is then added slowly at the temperature mentioned in Table I and the contents are stirred for 1 h at the same temperature. After the usual workup, the alcohol is obtained. The results are summarized in Table I.

Simple carboxylic acids (entries 1 to 7 in Table I) are reduced to the corresponding alcohols in very good yields. Reduction of cinnamic acid gives the corresponding α,β -unsaturated alcohol (entry 8). It is interesting to note that the reduction of this substrate with LiAlH₄ leads to 1-phenylpropanol.⁴ Moreover, the olefinic group is not affected when it is away from the carboxylic group. For example, 10-undecenoic acid on reduction with NaBH₄/I₂ gives 10-undecanol (entry 9). However, the same substrate when treated with insufficient amount of BH₃-THF gives 1,11-undecanediol as the major product along with a minor amount of 11-hydroxyundecanoic acid.⁵

The present reagent system is also effective in reducing an acid group, leaving behind an ester group unaffected when both groups are present in the compound. This is so even when the ester group is near the acid group (entry 10).

It has been reported that dicarboxylic acids react with borane reagents to give polymeric insoluble intermediates

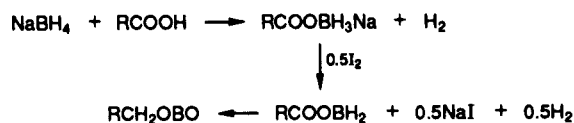
Table I. Selective Reductions of Carboxylic Acids to Alcohols^a

no.	substrate	product	temp, °C	yield, %
1	C ₆ H ₅ COOH	C ₆ H ₅ CH ₂ OH	rt	93
2	C ₆ H ₅ CH ₂ COOH	C ₆ H ₅ CH ₂ CH ₂ OH	rt	98
3	<i>p</i> -ClC ₆ H ₄ COOH	<i>p</i> -ClC ₆ H ₄ CH ₂ OH	rt	98
4	CH ₃ (CH ₂) ₈ COOH	CH ₃ (CH ₂) ₈ CH ₂ OH	rt	95
5			rt	92
6			rt	96
7			rt	92
8			0	97
9			0	89
10			0	82
11			0	89
12			rt	86
13			rt	87

^a All experiments were carried out by using NaBH₄ (12 mmol), carboxylic acid (10 mmol), and I₂ (5 mmol). Yields are of isolated and purified products.

leading to incomplete reduction.⁶ In some cases, however, the corresponding lactone is the major product.⁷ On the other hand, the present reagent system completely reduces diacids such as phthalic acid and diphenic acid to the corresponding diols in very good yields (entries 12 and 13).

The selectivities realized with the NaBH₄/I₂ system over the borane reagents such as BH₃-THF deserve an explanation. Hydroboration of olefins with the RCOOH/NaBH₄ system is relatively slow compared to hydroborations using BH₃-THF.^{8,9} Also, the rates of reaction of cyclohexene and caproic acid with diborane are comparable.¹⁰ Presumably, the present reagent system is more selective because the reactive RCOOBH₂ species is produced in the absence of more reactive borane species such as BH₃-THF.¹¹⁻¹⁵



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In conclusion, the high yields of reduced products coupled with the superior selectivity of the simple NaBH_4/I_2 system should make this procedure valuable for applications in synthetic organic chemistry.

Experimental Section

General Procedure for Reduction. A solution of the carboxylic acid (10 mmol) in THF (20 mL) was slowly added to a suspension of NaBH_4 (12 mmol) in THF (20 mL) at room temperature (10 min). The mixture was stirred until evolution of gas ceases. Iodine (5 mmol) in THF (20 mL) was added slowly (10

min) at the temperature mentioned in Table I. Additional hydrogen evolved. The contents were further stirred for 1 h. Dilute HCl (5 mL, 3 N) was added carefully and the mixture extracted with ether. The combined ether extract was washed with 3 N NaOH (3×10 mL) and brine and dried over MgSO_4 . Evaporation of the organic layer gives the alcohol product, which is essentially pure. It was further purified by distillation (or) column chromatography on silica gel. The products were identified by the physical constants data, IR, ^1H NMR, and ^{13}C NMR spectral data, and comparison with data reported in the literature.

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