

16 $\alpha$ -fluoro-3 $\beta$ -acetoxy-5-androsten-17-one, 2990-52-5; *trans*-2-fluoro-5-*tert*-butylcyclohexene, 23510-86-3; 17-acetoxy-6 $\alpha$ -fluoro-4,16-androstadien-3-one, 108161-28-0; 3-acetoxy-16 $\alpha$ -fluoro-3,5-androstadien-3-one, 108161-30-4; 17-acetoxy-6 $\beta$ -fluoro-4,16-androstadien-3-one, 108161-29-1; (*E*)-20-acetoxy-6 $\alpha$ -fluoro-4,17(20)-pregnadien-3-one, 135663-22-8; 3-acetoxy-17 $\alpha$ -fluoro-3,5-pregnadien-20-one, 135663-23-9; (*E*)-20-acetoxy-6 $\beta$ -fluoro-4,17(20)-pregnadien-3-one, 135663-24-0; 16 $\alpha$ -fluoro-3 $\beta$ -hydroxy-5-androsten-17-one, 1649-27-0; 6 $\beta$ -fluorotestosterone acetate, 2627-94-3; 6 $\beta$ -fluoro-4-androstene-3,17-dione, 1650-83-5; 6 $\beta$ -fluoro-4-pregnene-3,20-dione, 2300-02-9; 6 $\beta$ -fluoro-17 $\beta$ -hydroxy-4-androsten-3-one, 1852-58-0; 16 $\beta$ -fluoro-3 $\beta$ -acetoxy-5-androsten-17-one, 82526-09-8; 16 $\beta$ -fluoro-3 $\beta$ -hydroxy-5-androsten-17-one, 135758-70-2; 2-fluorocyclohexanone, 694-82-6.

### Selective Reduction of Carboxylic Acids into Alcohols Using NaBH<sub>4</sub> and I<sub>2</sub>

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Received March 28, 1991

Reduction of carboxylic acids to alcohols is an important transformation in synthetic organic chemistry. Several methods are available for this purpose that utilize LiAlH<sub>4</sub> and boron reagents.<sup>1-3</sup> Unfortunately, NaBH<sub>4</sub> does not reduce carboxylic acids under ambient conditions.<sup>3</sup> We report here that carboxylic acids can be reduced directly to alcohols with some interesting selectivities by successive addition of NaBH<sub>4</sub> and I<sub>2</sub> to RCOOH and RCOOH to NaBH<sub>4</sub> in THF followed by I<sub>2</sub>.



















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  $\alpha,\beta$ -unsaturated alcohol (entry 8). It is interesting to note that the reduction of this substrate with LiAlH<sub>4</sub> leads to 1-phenylpropanol.<sup>4</sup> Moreover, the olefinic group is not affected when it is away from the carboxylic group. For example, 10-undecenoic acid on reduction with NaBH<sub>4</sub>/I<sub>2</sub> gives 10-undecenol (entry 9). However, the same substrate when treated with insufficient amount of BH<sub>3</sub>-THF gives 1,11-undecanediol as the major product along with a minor amount of 11-hydroxyundecanoic acid.<sup>5</sup>

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

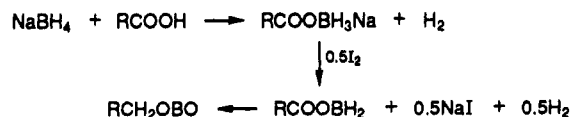
Table I. Selective Reductions of Carboxylic Acids to Alcohols<sup>a</sup>

no.	substrate	product	temp, °C	yield, %
1	C <sub>6</sub> H <sub>5</sub> COOH	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> OH	rt	93
2	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> COOH	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> CH <sub>2</sub> OH	rt	98
3	<i>p</i> -ClC <sub>6</sub> H <sub>4</sub> COOH	<i>p</i> -ClC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> OH	rt	98
4	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>8</sub> COOH	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>8</sub> CH <sub>2</sub> 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

<sup>a</sup> All experiments were carried out by using NaBH<sub>4</sub> (12 mmol), carboxylic acid (10 mmol), and I<sub>2</sub> (5 mmol). Yields are of isolated and purified products.

leading to incomplete reduction.<sup>6</sup> In some cases, however, the corresponding lactone is the major product.<sup>7</sup> 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 NaBH<sub>4</sub>/I<sub>2</sub> system over the borane reagents such as BH<sub>3</sub>-THF deserve an explanation. Hydroboration of olefins with the RCOOH/NaBH<sub>4</sub> system is relatively slow compared to hydroborations using BH<sub>3</sub>-THF.<sup>8,9</sup> Also, the rates of reaction of cyclohexene and caproic acid with diborane are comparable.<sup>10</sup> Presumably, the present reagent system is more selective because the reactive RCOOBH<sub>2</sub> species is produced in the absence of more reactive borane species such as BH<sub>3</sub>-THF.<sup>11-15</sup>



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In conclusion, the high yields of reduced products coupled with the superior selectivity of the simple  $\text{NaBH}_4/\text{I}_2$  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  $\text{NaBH}_4$  (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 ( $3 \times 10$  mL) and brine and dried over  $\text{MgSO}_4$ . 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,  $^1\text{H}$  NMR, and  $^{13}\text{C}$  NMR spectral data, and comparison with data reported in the literature.

**Acknowledgment.** Support of this research work by CSIR (New Delhi) is gratefully acknowledged. We also thank UGC (New Delhi) for Special Assistance and COS-IST support.

(14) Narayana, C.; Periasamy, M. *J. Organomet. Chem.* 1987, 145, 323.

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## Additions and Corrections

Vol. 51, 1986

**Louis D. Quin,\* Jerzy Szewczyk, Krystyna M. Szewczyk, and Andrew T. McPhail.** Synthesis of Phosphonamides in the 5,6-Oxaphosphabicyclo[2.2.2]octene Series as Possible Precursors of Metaphosphoramidates.

Page 3341, title: replace "Phosphinamides" with "Phosphonamides".

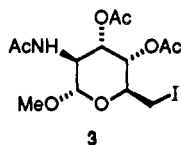
Page 3343, Table I: for 3a, 3b, and 3c, the  $^{31}\text{P}$  NMR shifts for  $\text{P}_a$  and  $\text{P}_b$  should be interchanged.

Vol. 56, 1991

**Alois Fürstner, Denis Jumbam, Judith Teslic, and Hans Weidmann\*.** Metal-Graphite Reagents in Carbohydrate Chemistry. 8. The Scope and Limitations of the Use of Zinc/Silver-Graphite in the Synthesis of Carbohydrate-Derived Substituted Hex-5-enals and Pent-4-enals.

Page 2213, paragraph 2, should read as follows: With the exception of the methyl 6-bromo-6-deoxyhexopyranosides 1d, 9, and 27, which were obtained from 4,6-*O*-benzylidene precursors by reaction with *N*-bromosuccinimide,<sup>10</sup> and compounds 12, 14, 15, 18e, and 18g, which were prepared by the displacement of a sulfonyloxy group by iodide,<sup>11</sup> the starting materials were prepared by iodination of the corresponding 5-*O*- or 6-*O*-unprotected sugars with the triphenylphosphine/imidazole/iodine reagent.<sup>12</sup>

Page 2213, column 2, 3 should be drawn as shown:



Page 2214, column 2, line 26, should read as follows: Interestingly, the reaction of 18e resulted in the reduction of both the carbon-halogen bond and the azido group.