

## Mild and Efficient Reduction of $\alpha,\beta$ -Unsaturated Carbonyl Compounds, $\alpha$ -Diketones and Acyloins with Sodium Borohydride/Dowex1-x8 System

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Received August 12, 2002

$\alpha,\beta$ -Unsaturated aldehydes and ketones are regioselectively reduced to the corresponding allylic alcohols with  $\text{NaBH}_4$ /Dowex1-x8 system in THF at room temperature. This system is also efficient for the conversion of  $\alpha$ -diketones and acyloins to the vicinal diols in refluxing THF.

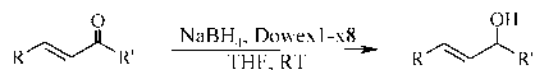
**Key Words :** Sodium borohydride, Dowex1-x8,  $\alpha,\beta$ -Unsaturated carbonyls,  $\alpha$ -Diketones, Acyloins

### Introduction

Reduction of  $\alpha,\beta$ -unsaturated carbonyl compounds by metal hydrides can follow two pathways: addition to carbonyl group (1,2-reduction) to give allylic alcohols or addition to the conjugated double bond (1,4-addition) to give saturated carbonyl compounds. Due to importance of synthetic precursors of allylic alcohols, the regioselective reduction of  $\alpha,\beta$ -unsaturated aldehydes and ketones seems to be a convenient and easy way to obtain these compounds. So, this achievement is synthetically very important.<sup>1</sup> In spite of substantial evidence, the reduction pattern of sodium borohydride for conjugated carbonyl compounds is highly solvent dependent and generally the regioselectivity in these reductions is not useful.<sup>2-4</sup> The regioselective reduction of this system has stimulated considerable interest, leading to the development of new reducing systems for selective 1,4-<sup>5-9</sup> or 1,2-reductions<sup>4,10-19</sup> of  $\alpha,\beta$ -unsaturated aldehydes and ketones.

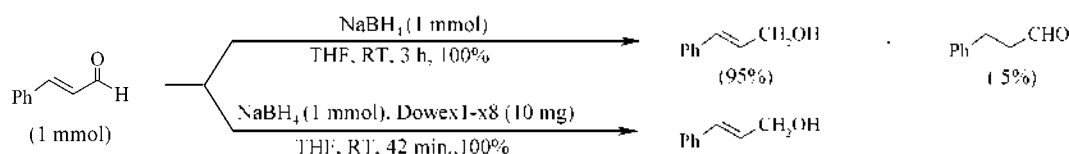
In this context and continuation of our studies for the reduction of functional groups in organic synthesis<sup>20</sup> and application of Dowex1-x8, a highly basic anion exchange resin,<sup>21</sup> we have decided to prepare a new polymeric reducing agent by replacing chlorine anions in Dowex1-x8 with  $\text{BH}_4^-$ . Unfortunately all attempts for such purpose have been failed, but we have found that the presence of small quantity of Dowex1-x8 enhances the reducing power of  $\text{NaBH}_4$  in THF and this system can efficiently reduce cinnamaldehyde with excellent regioselectivity (Scheme 1). Accordingly, we decided to apply this new reducing system for reduction of  $\alpha,\beta$ -unsaturated carbonyl compounds.

Now we wish to report an efficient method for the regioselective reduction of  $\alpha,\beta$ -unsaturated aldehydes and ketones with  $\text{NaBH}_4$ /Dowex1-x8 system.



### Results and Discussion

**Regioselective 1,2-reduction of  $\alpha,\beta$ -unsaturated carbonyl compounds.** Selective 1,2-reduction of  $\alpha,\beta$ -unsaturated carbonyl compounds is usually achieved by using modified tetrahydroborate agents, which are formed: a) by the replacement of hydride(s) with sterically bulky substituents or electron-withdrawing/releasing groups in order to discriminate between the structural and electronic environments of the carbonyl groups,<sup>4,12,22-25</sup> b) combination with Lewis acids<sup>11,26,27</sup> and mixed solvents,<sup>2-4,28</sup> c) using of transition metal tetrahydroborates and its new modifications<sup>13,20,29-33</sup> d) using of quaternary ammonium and phosphonium tetrahydroborates,<sup>34-35</sup> and finally e) immobilization on polymeric supports and anion exchange resin.<sup>36,37</sup> Herewith, our system,  $\text{NaBH}_4$ /Dowex1-x8 system, showed an excellent selectivity. Thus regioselective reductions of  $\alpha,\beta$ -unsaturated carbonyl compounds were easily achieved to give the corresponding allylic alcohols. The reduction proceeds at an efficient rate in THF and room temperature ( $\text{NaBH}_4$ , 1-2 mmols per 1 mmol of compound; Dowex1-x8, 10-20 mg) (Table 1). As shown in Table 1, the regioselectivity achieved by this system is essentially perfect and the yields of allylic alcohols are in high to excellent. In the next attempt, we examined its



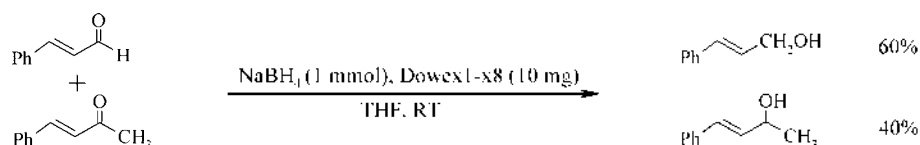
Scheme 1

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**Table 1.** Reduction of  $\alpha,\beta$ -Unsaturated Carbonyl Compounds with NaBH<sub>4</sub>/Dowex1-x8 System<sup>a,b</sup>

Entry	Substrate	Product	Ratio 1.2:1:4	Molar Ratio NaBH <sub>4</sub> Sub.	Dowex1-x8 (mg)	Time (h)	Yield (%) <sup>c</sup>
1			100:0	1:1	10	0.7	96
2			100:0	1:1	10	1.4	98
3			100:0	1:1	10	0.7	95
4			100:0	1:1	10	0.8	89
5			100:0	1:1	10	0.8	90
6			100:0	1:1	10	1.3	94
7			100:0	1:1	10	2.2	91
8			100:0	2:1	10	2.7	87

<sup>a</sup>All reactions were performed in THF at room temperature. <sup>b</sup>Dowex1-x8 which was used as a powder. <sup>c</sup>Yields referred to isolated products.

**Scheme 2**

chemoselectivity toward the reduction of  $\alpha,\beta$ -unsaturated aldehydes over ketones. For example, an equimolar amount of cinnamaldehyde and benzalacetone was reacted with NaBH<sub>4</sub>/Dowex1-x8 system. Due to easily reduction of these substrates at room temperature, all attempts to full clarifying of aldehydes over ketones were unsatisfactory and give a mixture of the corresponding allylic alcohols with low chemoselectivity (Scheme 2).

However, in general, the reaction of unsaturated aldehydes is relatively faster than that of ketones of bulk hindrance. This is due to really activity of aldehydes relative to the ketones and may be also attributed to the bulkiness and polymeric nature of the resin which induces a special steric selectivity in the reduction of carbonyl groups.

To highlight the efficiency of our system, we compared our results with those achieved by other reported reagents such as NaBH<sub>4</sub>, NaBH<sub>3</sub>(OAc),<sup>4</sup> NaBH<sub>3</sub>CN,<sup>28</sup> Li-*n*-BuBH<sub>3</sub>,<sup>12</sup> (*i*-PrO)<sub>2</sub>TiBH<sub>4</sub>,<sup>13</sup> Ph<sub>3</sub>PMeBH<sub>4</sub>.<sup>34</sup> It's clear that in most cases, our new system is more efficient or comparable (Table 2).

**Reduction of  $\alpha$ -diketones and acyloins.** Synthetic applications of  $\alpha$ -hydroxy ketones and  $\alpha$ -diketones are well

known and their reductions to vicinal diols and/or acyloins are the subject of interests in organic synthesis.<sup>38</sup> Reduction of  $\alpha$ -diketones usually gives a mixture of  $\alpha$ -hydroxy ketones and vicinal diols. In spite of this, using of some chemical or biochemical reagents can undergo selective reduction of  $\alpha$ -diketones to only one of the mentioned products. For example Zn/aq.DMF,<sup>39</sup> Zn/H<sub>2</sub>SO<sub>4</sub>,<sup>40</sup> TiCl<sub>3</sub> or VCl<sub>2</sub>/THF,<sup>41</sup> (C<sub>2</sub>H<sub>5</sub>O)<sub>3</sub>P,<sup>42</sup> H<sub>2</sub>S/piperidine/DMF<sup>43</sup> and heating with benzpinacol<sup>44</sup> performed reduction of  $\alpha$ -diketones to acyloins, whereas *Cryptococcus macerans*<sup>45</sup> did this reduction to vicinal diols. Reduction of  $\alpha$ -diketones with modified tetrahydroborate agents is also subject of the interest<sup>20</sup> and easily achieved by NaBH<sub>4</sub>/Dowex1-x8 system. This system efficiently reduces  $\alpha$ -diketones to their vicinal diols in refluxing THF (Table 3).

Our attempts for reduction of  $\alpha$ -diketones to acyloins were unsatisfactory and only vicinal diols were identified as the sole products (93-98%). In addition to reduction of  $\alpha$ -diketones, reduction of acyloins to vicinal diols is also important in organic synthesis. For this transformation using H<sub>2</sub>/CuCr<sub>2</sub>O<sub>4</sub>,<sup>46</sup> *Saccharomyces cerevisiae* (baker's yeast)<sup>47</sup> and modified tetrahydroborate agents<sup>20</sup> have been reported.

**Table 2.** Comparison of Regioselective 1,2-Reduction of  $\alpha,\beta$ -Unsaturated Carbonyl Compounds with  $\text{NaBH}_4$ /Dowex1-x8 System and Other Reported Reagents

Entry	Substrate	Molar Ratio, <sup>a</sup> Time (h) and Yield (%)						
		I	II <sup>b</sup>	III <sup>d</sup>	IV <sup>28</sup>	V <sup>12</sup>	VI <sup>13</sup>	VII <sup>14</sup>
1		I(0.7)(96) (100:0) <sup>c</sup>	I(3)(93) (95:5) <sup>c</sup>	1.67(20)(70) (99:1) <sup>c</sup>	2(1.5)(80) (100:0) <sup>c</sup>	–	I(5 <sup>d</sup> )(90) (>99:<1) <sup>c</sup>	I(–)(95) (100:0) <sup>c</sup>
2		I(1.4)(98) (100:0) <sup>c</sup>	I(2.8)(96) (95:5) <sup>c</sup>	1.67(20)(70) (96:4) <sup>c</sup>	2(1.5)(77) (100:0) <sup>c</sup>	I(2)(98) (100:0) <sup>c</sup>	I(5 <sup>d</sup> )(97) (>99:<1) <sup>c</sup>	I(3.5)(90) (100:0) <sup>c</sup>
3		I(0.7)(95) (100:0) <sup>c</sup>	I(1.7)(95) (90:10) <sup>c</sup>	–	3(2.5)(0)	I(2)(99) (100:0) <sup>c</sup>	–	I(2.6)(90) (100:0) <sup>c</sup>
4		I(1.3)(94) (100:0) <sup>c</sup>	I(2.8)(90) (99:1) <sup>c</sup>	1.67(20)(86) (99:1) <sup>c</sup>	–	–	I(5 <sup>d</sup> )(95) (>99:<1) <sup>c</sup>	–
5		I(2.2)(91) (100:0) <sup>c</sup>	I(3)(80) (95:5) <sup>c</sup>	–	2(2)(88) (100:0) <sup>c</sup>	I(2)(98) (100:0) <sup>c</sup>	–	I(6)(71) (100:0) <sup>c</sup>
6		I(0.8)(89) (100:0) <sup>c</sup>	I(1)(85) (80:20) <sup>c</sup>	1.67(20)(32) (99:1) <sup>c</sup>	–	I(2)(84) (92:8) <sup>c</sup>	–	–

<sup>I</sup> $\text{NaBH}_4$ /Dowex1-x8; <sup>II</sup> $\text{NaBH}_4$ ; <sup>III</sup> $\text{NaBH}_3(\text{OAc})$ ; <sup>IV</sup> $\text{NaBH}_3\text{CN}$ ; <sup>V</sup> $\text{Li-}i\text{-Pr}_2\text{BuBH}_3$ ; <sup>VI</sup> $(i\text{-PrO})_2\text{TiBH}_3$ ; <sup>VII</sup> $\text{Ph}_3\text{PMeBH}_4$ ; <sup>a</sup>Reducing agent/Substrate; <sup>b</sup>Present work and the reactions were performed in THF at room temperature; <sup>c</sup>Ratio of 1,2:1,4; <sup>d</sup>Time in minute; <sup>e</sup>Immediate reaction.

**Table 3.** Reductions of  $\alpha$ -Diketones and Acyloins with  $\text{NaBH}_4$ /Dowex1-x8 System<sup>a,b</sup>

Entry	Substrate	Product	Molar Ratio $\text{NaBH}_4$ /Subs.	Time (min)	Yield (%) <sup>c</sup>
1			2	10	96
2			2	7	95
3			2	6	97
4			2	6	98
5			2	6	94
6			2	6	93
7			2	7	95
8			2	7	90

<sup>a</sup>All reactions were performed with 20 mg of Dowex1-x8 in THF under reflux conditions. <sup>b</sup>Dowex1-x8 which was used as a powder. <sup>c</sup>Yields referred to isolated products.

We also found that this goal easily achieved by this system: we observed that benzoin is efficiently reduced to hydrobenzoin in refluxing THF ( $\text{NaBH}_4$ , 2 mmols; Dowex1-x8, 20 mg) (Table 3).

In conclusion, we have shown that  $\text{NaBH}_4$ /Dowex1-x8 system reduces  $\alpha,\beta$ -unsaturated aldehydes and ketones regioselectively to its corresponding allylic alcohols. This

system is also efficient for the reduction of  $\alpha$ -diketones and acyloins to its corresponding vicinal diols. Excellent regioselectivity, convenient procedure, mild reaction condition, high yields of the products and also easy work-up of the reaction mixture could be make this system as an attractive method and a synthetically useful addition to the present methodologies.

### Experimental Section

**General.** The products were characterized by a comparison with authentic samples (mp or bp) and their  $^1\text{H-NMR}$  or IR spectra. All yields referred to isolated products. TLC accomplished the purity determination of the substrates, products and reactions monitoring over silica gel PolyGram SILG/UV 254 plates.

**Regioselective 1,2-reduction of  $\alpha,\beta$ -unsaturated carbonyl compounds with  $\text{NaBH}_4/\text{Dowex1-x8}$  system.** *A Typical Procedure.* In a round-bottom flask (15 mL) equipped with magnetic stirrer a solution of cinnamaldehyde (0.132 g, 1 mmol) and Dowex1-x8 (10 mg) in THF (8 mL) was introduced. To this mixture  $\text{NaBH}_4$  (0.037 g, 1 mmol) was added and the resulting mixture was stirred at room temperature. TLC monitored the progress of the reaction (eluent:  $\text{CCl}_4/\text{Et}_2\text{O}$ : 5/2). After 42 min reaction, methanol (3 mL) was added to the mixture and stirred for 10 min. The solvent was evaporated and the resulting crude material was purified by silica gel column chromatography using  $\text{CCl}_4/\text{Et}_2\text{O}$ : 5/2 as the eluent. Evaporation of the solvent affords pure liquid cinnamyl alcohol (0.127 g, 95% yield, Table 1).

**Reduction of  $\alpha$ -diketones with  $\text{NaBH}_4/\text{Dowex1-x8}$  system.** *A Typical Procedure.* In a round-bottom flask (15 mL) equipped with magnetic stirrer and condenser, a solution of benzil (0.21 g, 1 mmol) and Dowex1-x8 (20 mg) in THF (8 mL) was introduced. To this mixture  $\text{NaBH}_4$  (0.075 g, 2 mmol) was added and the reaction mixture was stirred for 10 min under reflux. TLC monitored the progress of the reaction (eluent:  $\text{CCl}_4/\text{Et}_2\text{O}$ : 5/2). After completion of the reduction, methanol (3 mL) was added to the reaction mixture and was stirred for 10 min. The solvent was evaporated and the resulting crude material was purified by a silica gel column chromatography using  $\text{CCl}_4/\text{Et}_2\text{O}$ : 5/2 as the eluent. Evaporation of the solvent affords hydrobenzoin as pure crystals (0.20 g, 96% yield, Table 3).

**Acknowledgment.** We gratefully acknowledge partial support of this work by the research councils of Urmia and Guilan Universities.

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