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Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information: <u>http://www.tandfonline.com/loi/lsyc20</u>

Speedy and Regioselective 1,2-Reduction of Conjugated α,β -Unsaturated Aldehydes and Ketones Using NaBH_4/I_2

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To cite this article: Jasvinder Singh , Irvinder Kaur , Jasamrit Kaur , Aman Bhalla & Goverdhan L. Kad (2003) Speedy and Regioselective 1,2-Reduction of Conjugated α , β -Unsaturated Aldehydes and Ketones Using NaBH₄/I₂ , Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 33:2, 191-197, DOI: <u>10.1081/SCC-120015699</u>

To link to this article: http://dx.doi.org/10.1081/SCC-120015699

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SYNTHETIC COMMUNICATIONS[®] Vol. 33, No. 2, pp. 191–197, 2003

Speedy and Regioselective 1,2-Reduction of Conjugated α,β-Unsaturated Aldehydes and Ketones Using NaBH₄/I₂

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ABSTRACT

Synthesis of allylic alcohols from α , β -unsaturated aldehydes/ketones has been achieved in excellent yields utilizing NaBH₄ and iodine. This reducing agent is mild and tolerant to a number of functional groups.

Key Words: Regioselective; 1,2-reduction; α , β -unsaturated carbonyl compounds; NaBH₄/I₂.

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DOI: 10.1081/SCC-120015699 Copyright © 2003 by Marcel Dekker, Inc. 0039-7911 (Print); 1532-2432 (Online) www.dekker.com

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The reduction of unsaturated carbonyl compounds (both 1,2- and 1,4-) has attracted a great deal of interest especially those employing metal hydrides. Reduction of such systems involving sodium borohydride, most widely used reducing agent, is highly solvent dependent and does not lead to high regioselectivity. It has already been known that treatment of borohydride with a controlled amount of acetic acid affords a weaker and hence more selective reducing agent. Sodium monoacetoxyborohydride^[1] and Sodium triacetoxyborohydride^[2] has been found to be highly regioselective reagents, leads to the formation of corresponding allylic alcohols (Sch. 1). A variety of other selective reducing agents such as NaBH₄ in the presence of lanthanoid chlorides,^[3] NaBH₄/LnCpCl₂(THF)₃,^[5] 9-BBN,^[6] NiCRA.^[7] NaBH₃CN,^[4] (EtO)₃SiH, Me(EtO)₂SiH,^[8] are available for 1,2-reduction of carbonyl functionality of aldehydes and ketones to the corresponding alcohol.

In continuation with our work on the regioselective 1,2-reduction of α,β -unsaturated carbonyl compounds,^[2] we report herein the use of a highly versatile, selective and cheap reagent namely $NaBH_4/I_2^{[9]}$ for this purpose. This reagent is very effective as regioselective reduction of the conjugated aldehydes and ketones have been brought about in the presence of a number of different functionalities like carbon-carbon double bond, hydroxy, ester, alkoxy, ketal, acetoxy, halide, tosyl, and mesyl groups. This selective addition of borane to the carbonyl moiety may be attributed due to the slow release of borane by controlled addition of iodine to sodium borohydride. The reaction proceeds with excellent yield of the products (as shown in the Table 1), which do not require further purification. Interestingly this reagent is known to bring about the reduction^[10] of amides, nitriles, esters, carboxylic acids and hydroboration of alkenes. However we have observed that in the presence of an isolated carbon-carbon double bond (Entry 3) or an estereal functionality (Entry 2) the reagent preferentially attacks the carbonyl group of conjugated enone. Reduction of neither the isolated (or conjugated double bond), nor of the estereal carbonyl group takes place.



Scheme 1.

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Entry	Reactant (a)	Product (b)	Yield (%)
1	OSO2CH3	OSO2CH3	95
	Сно	Д он	
2	оссн3	O OČCH3	94
3	Сно	с он	94
	Ì		
4	CH3	снз	93
	Цсно	Дон	
5		L°)	92
	Дсно	С	
6	CHO SCHO	Сусон	91
7		Слон	91
8	Сно	ОН	90
9			88
	Дсно	Сн	
10	осн₂сн₃	осн2сн3	88
	СНО	Дон	
11	Сн	СН	88
	Сно	Дон	
12	С	ОН	87
	Сно	ОН	

Table 1. Reduction of conjugated carbonyl compounds using $NaBH_4/I_2$.

(continued)

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Tuble 1. Continued.				
Entry	Reactant (a)	Product (b)	Yield (%)	
13	Br	Br	85	
14	H ₃ CO	H ₃ CO	96	
15	OCH3 OCH3	осн ₃ он	95	
16	Haco	OH HaCO	85	
17		OH C	82	
18			80	
19		CI-CI-CI-CI-CI-CI-CI-CI-CI-CI-CI-CI-CI-C	79	

Table 1. Continued.

EXPERIMENTAL PROCEDURE

A typical procedure of reduction is as follows. To a stirred suspension of NaBH₄ (0.45 g, 12 mmol) in dry THF (10 mL) was added slowly a solution of aldehyde (2.48 g, 10 mmol) taken in dry THF (15 mL). The reaction mixture was cooled in an ice-bath and to it was slowly added iodine (1.27 g, 5 mmol) in dry THF (15 mL) in a period of 30 min. Stirring was continued further for 15 min and quenched with 3 N HCl (2×5 mL), followed by extraction with diethyl ether (3×10 mL). The combined organic extracts were washed with 3 N NaOH (3×5 mL), brine and dried over anhyd. Na₂SO₄. Evaporation of the solvent in vacuo afforded the pure alcohol (2.37 g, 95%) (as given in Table 1). The products were identified on the basis of IR and ¹H NMR spectral data.

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In conclusion, the high yields, purity, simplicity alongwith a short reaction time and tolerance towards a number of functional groups, renders this a very attractive procedure for reduction of conjugated aldehydes and ketones.

1b: ¹H-NMR (δ/ppm): 1.0 (d, J = 6 Hz, 3H, -CHC<u>H</u>₃), 1.3 (m, 5H, -CH₂C<u>H</u>(CH₃)C<u>H</u>₂-), 1.7 (s, 3H, CH₃-C=C-), 2.2 (m, 2H, -CH₂-C=), 2.9 (s, 3H, -OSO₂C<u>H</u>₃), 3.3 (bs, 1H, -OH, D₂O exchangeable), 3.8 (s, 2H, -C<u>H</u>₂OH), 4.2 (t, J = 7 Hz, 2H, -C<u>H</u>₂OSO₂-), 5.2 (t, J = 6 Hz, 1H, -C<u>H</u>=C-).

2b: ¹H-NMR (δ /ppm): 1.0 (d, J = 6 Hz, 3H, -CHC<u>H</u>₃), 1.3 (m, 5H, -CH₂C<u>H</u>(CH₃)C<u>H</u>₂-), 1.8 (s, 3H, CH₃-C=C-), 2.2 (m, 5H, -CH₂-C= and -COC<u>H</u>₃), 3.0 (bs, 1H, -OH, D₂O exchangeable), 4.1 (s, 4H, -C<u>H</u>₂OCOCH₃ and -C<u>H</u>₂OH), 5.2 (t, J = 6 Hz, 1H, -C<u>H</u>=C-).

3b: ¹H-NMR (δ /ppm): 1.6 and 1.7 (2s, 9H, =CC<u>H</u>₃ and =C(C<u>H</u>₃)₂), 2.0 (m, 4H, =C(C<u>H</u>₂)₂-), 3.5 (bs, 1H, -OH, D₂O exchangeable), 4.1 (d, J=7.5 Hz, 2H, -C<u>H</u>₂OH), 5.1 (t, J=6 Hz, 1H, =C<u>H</u>CH₂OH), 5.5 (t, J=6 Hz, 1H, -CH₂C<u>H</u>=C-).

4b: ¹H-NMR (δ /ppm): 1.0 (d, J = 6 Hz, 3H, -CHC<u>H</u>₃), 1.3 (m, 5H, -C<u>H</u>₂C<u>H</u>(CH₃)C<u>H</u>₂-), 1.7 (s, 3H, C<u>H</u>₃-C=C-), 2.3 (m, 2H, -C<u>H</u>₂-C=), 2.5 (s, 3H, ArC<u>H</u>₃), 4.0 (s, 4H, -C<u>H</u>₂OTs and -C<u>H</u>₂OH), 4.1 (bs, 1H, -OH, D₂O exchangeable), 5.2 (t, J = 6 Hz, 1H, -C<u>H</u>=C-), 7.3 (d, J = 6 Hz, 2H, Ar<u>H</u>), 7.6 (d, J = 6 Hz, 2H, Ar<u>H</u>).

5b: ¹H-NMR (δ /ppm): 1.2 (s, J = 6 Hz, 3H, $\underline{\text{H}}_{3}\text{C} \xrightarrow{\mathbf{O}}$), 1.6 (s, 3H, C<u>H</u>₃-C=C-), 2.3 (m, 4H, -C<u>H</u>₂C(CH₃)- and -C<u>H</u>₂C=), 3.0 (bs, 1H, -OH, D₂O exchangeable), 4.0 (s, 6H, -OC<u>H</u>₂C<u>H</u>₂O- and -C<u>H</u>₂OH), 5.2 (t, J = 6 Hz, 1H, -C<u>H</u>=C-).

(i, J = 0 HZ, HI, $-C\underline{H} = C^{-}$). **6b**: ¹H-NMR (δ /ppm): 3.5 (bs, 1H, -OH, D₂O exchangeable), 4.5 (s, 2H, $-C\underline{H}_2OH$), 6.1 (m, 2H, H, H, -OH, D₂O exchangeable), 4.5 **7b**: ¹H-NMR (δ /ppm): 3.5 (bs, 1H, -OH, D₂O exchangeable), 4.5 (s, 2H, $-C\underline{H}_2OH$), 6.1 (m, 2H, H, H, -OH, D₂O exchangeable), 4.5 (s, 2H, $-C\underline{H}_2OH$), 6.1 (m, 2H, H, H, -OH, D₂O exchangeable), 4.8 **8b**: ¹H-NMR (δ /ppm): 3.5 (bs, 1H, -OH, D₂O exchangeable), 4.8

(d, J = 6 Hz, 2H, -CH₂OH), 6.8 (m, 2H, -CH=CH-), 7.1 (s, 5H, ArH).

9b: ¹H-NMR (δ /ppm): 1.0 (d, J = 6 Hz, 3H, -CHC<u>H</u>₃), 1.5 (bs, 14H, -C<u>H</u>₂C<u>H</u>(CH₃)C<u>H</u>₂-, ring protons and C<u>H</u>₃C=C-), 2.3 (m, 2H, -C<u>H</u>₂-C=), 3.3 (bs, 1H, -OH, D₂O exchangeable), 3.5 (m, 4H, 2 × -OC<u>H</u>₂-), 3.8 (s, 2H, -C<u>H</u>₂OH), 4.9 (s, 1H, -O-C<u>H</u>^O), 5.2 (t, J = 6 Hz, 1H, -C<u>H</u>=C-). **10b:** ¹H-NMR (δ /ppm): 1.0 (t, J = 6 Hz, 3H, -OCH₂C<u>H</u>₃), 1.2

10b: ¹H-NMR (δ /ppm): 1.0 (t, J = 6 Hz, 3H, -OCH₂C<u>H</u>₃), 1.2 (d, J = 6 Hz, 3H, -CHC<u>H</u>₃), 1.4 (m, 5H, -C<u>H</u>₂C<u>H</u>(CH₃)C<u>H</u>₂-), 1.7 (s, 3H, C<u>H</u>₃-C=C-), 2.2 (m, 2H, -C<u>H</u>₂-C=), 3.4 (m, 4H, -C<u>H</u>₂OC<u>H</u>₂CH₃),

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3.8 (s, 2H, $-CH_2OH$), 4.0 (bs, 1H, -OH, D₂O exchangeable), 5.2 (t, J = 6 Hz, 1H, -CH=C-).

11b: ¹H-NMR (δ /ppm): 1.2 (d, J = 7 Hz, 3H, -CH(OH)CH₃), 1.6 (s, 3H, CH₃-C=C-), 2.2 (m, 4H, -CH₂-C=, CH₂C(CH₃)-), 2.2 (bs, 2H, 2×-OH, D₂O exchangeable), 3.7 (m, 1H, -CHOH), 3.8 (s, 2H, -CH₂OH), 5.2 (t, J = 6 Hz, 1H, -CH=C-).

12b: ¹H-NMR (δ /ppm): 1.0 (d, J = 6 Hz, 3H, -CHC<u>H</u>₃), 1.3 (m, 5H, -C<u>H</u>₂C<u>H</u>(CH₃)C<u>H</u>₂-), 1.7 (s, 3H, C<u>H</u>₃-C=C-), 2.2 (m, 2H, -C<u>H</u>₂-C=), 3.5 (t, J = 7 Hz, 2H, -CH₂C<u>H</u>₂OH), 3.8 (s, 2H, =C(CH₃)C<u>H</u>₂OH), 3.9 (bs, 2H, 2 × -OH, D₂O exchangeable), 5.2 (t, J = 6 Hz, 1H, -C<u>H</u>=C-).

13b: ¹H-NMR (δ /ppm): 1.0 (d, J = 6 Hz, 3H, -CHC<u>H</u>₃), 1.3 (m, 5H, -C<u>H</u>₂C<u>H</u>(CH₃)C<u>H</u>₂-), 1.7 (s, 3H, C<u>H</u>₃-C=C-), 2.2 (m, 2H, -C<u>H</u>₂-C=), 3.0 (bs, 1H, -OH, D₂O exchangeable), 3.3 (t, 2H, -C<u>H</u>₂Br), 3.9 (s, 2H, -CH₂OH), 5.2 (t, J = 6 Hz, 1H, -CH=C-).

14b: ¹H-NMR (δ /ppm): 3.5 (bs, 1H, -OH, D₂O exchangeable), 3.7 (s, 6H, 2 × -OC<u>H</u>₃), 5.1 (d, J = 6 Hz, 1H, -C<u>H</u>OH), 6.3 (m, 2H, -C<u>H</u>=C<u>H</u>-), 7.3 (m, 8H, Ar<u>H</u>).

15b: ¹H-NMR (δ /ppm): 1.2 (d, J = 6 Hz, 3H, -C<u>H</u>₃), 3.5 (bs, 1H, -OH, D₂O exchangeable), 4.3 (m, 1H, -C<u>H</u>OH), 6.3 (m, 2H, -C<u>H</u>=C<u>H</u>-), 7.3 (m, 5H, Ar<u>H</u>).

16b: ¹H-NMR (δ /ppm): 3.7 (s, 3H, -OC<u>H</u>₃), 4.4 (bs, 1H, -OH, D₂O exchangeable), 5.1 (d, J = 6 Hz, 1H, -C<u>H</u>OH), 6.3 (m, 2H, -C<u>H</u>=C<u>H</u>-), 7.2 (m, 9H, Ar<u>H</u>).

17b: ¹H-NMR (δ /ppm): 2.5 (bs, 1H, -OH, D₂O exchangeable), 5.2 (d, J = 6 Hz, 1H, -CHOH), 6.3 (m, 2H, -CH=CH-), 7.3 (m, 14H, ArH).

18b: ¹H-NMR (δ /ppm): 3.3 (bs, 1H, -OH, D₂O exchangeable), 4.6 (d, J = 6 Hz, 1H, -C<u>H</u>OH), 6.3 (m, 2H, -C<u>H</u>=C<u>H</u>-), 7.3 (m, 8H, Ar<u>H</u>).

19b: ¹H-NMR (δ /ppm): 3.4 (bs, 1H, -OH, D₂O exchangeable), 5.1 (d, J = 6 Hz, 1H, -C<u>H</u>OH), 6.3 (m, 2H, -C<u>H</u>=C<u>H</u>-), 7.3 (m, 9H, Ar<u>H</u>).

ACKNOWLEDGMENTS

The authors wish to thank CSIR and UGC, New Delhi for funding this piece of research work.

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Received in the Netherlands December 10, 2001



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