Lithium Borohydride-catalysed Selective Reduction of Carbonyl Group of Conjugated and Unconjugated Alkenones with Borane in Tetrahydrofuran

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In the presence of a catalytic amount of $LiBH_4$, BH_3 in THF selectively reduced the carbonyl group of conjugated and unconjugated alkenones at −50 °C to quantitatively provide the corresponding alkenols on subsequent hydrolysis.

In the study of the reactivity of BH_3 towards double bonds, it was found that at 25 °C BH_3 favoured reaction with olefinic double bonds rather than with carbonyl double bonds,[1] while it reacted[2] with simple carbonyl compounds, *e.g.* acetaldehyde and acetone, even at −80 °C where the reaction with the olefinic double bond did not occur at all.[3] Here, we report that in the presence of a catalytic amount of $LiBH_4$, BH_3 in THF reduces the carbonyl double bond of conjugated and unconjugated alkenones in a highly selective manner to provide the corresponding alkenols quantitatively on subsequent hydrolysis.

When the unconjugated alkenone **1a** was reacted with $\frac{1}{3}$ equiv. of BH_3 in the absence of $LiBH_4$ at 0 °C for 2 h, GLC analysis of the reaction mixture after hydrolysis showed the presence of unreacted **1a** in 65% yield while the amount of **2a**, formed by preferential reduction of the carbonyl group, was negligible. Alkaline hydrogen peroxide oxidation of the reaction mixture, however, gave **4a** in 35% yield with a trace amount of **3a**, which might be derived by preferential addition of BH_3 to the olefinic double bond (hydroboration). In a similar reaction carried out at −50 °C, 49% of **1a**, 49% of **2a**, and 2% of **4a** were found in the reaction mixture after the oxidation.

However, in a similar reaction carried out in the presence of a catalytic amount (1%) of $LiBH_4$ (Method A), the reduction of the carbonyl group was accelerated to provide **2a** in 85 and 92% yields at 0 °C and at −50 °C respectively.

Where successive addition of 0.5% $LiBH_4$ and $\frac{1}{6}$ equiv. of BH_3 was repeated twice (Method B) or a mixture of 1% $LiBH_4$ and $\frac{1}{3}$ equiv. BH_3 was added (Method C) at −50 °C, the reduction proceeded more effectively to provide **2a** quantitatively, eqn. (1).

These results indicate that the presence of $LiBH_4$† increases the rate of reduction of the carbonyl group even at −50 °C where hydroboration of the double bond does not take place.

A similar accelerated reduction was also occured with **1b** to give **2b** quantitatively, eqn. (2).

The reduction of the carbonyl group of conjugated alkenones with BH_3 was also accelerated by the addition of a catalytic amount of $LiBH_4$. Thus, the reaction of **1c** with $\frac{1}{3}$ equiv. of BH_3 employing Method B or C at −50 °C provided **2c** quantitatively, while in the absence of $LiBH_4$ the reaction gave **2c** in 33% yield at −50 °C, eqn. (3).

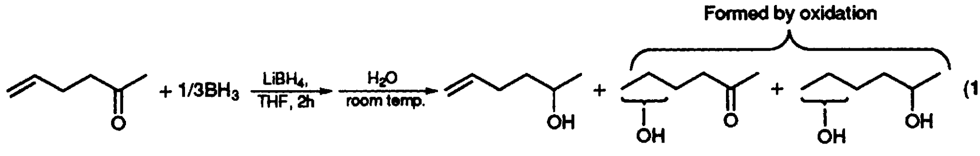
1d and **1e** were converted to the corresponding allylic alcohols, **2d** and **2e**, in high yields by using Method A. Reduction of **1f** and **1g** were a little sluggish under similar reaction conditions. However, the reduction proceeded almost completely with increased amounts of $LiBH_4$ and BH_3 to provide the corresponding allylic alcohols, **2f** and **2g**, in high yields after quenching the reaction mixture with a small amount of methanol at −50 °C‡ and then hydrolysis at room temp.

This reduction and following work-up are carried out under acidic conditions (due to BH_3 in the reduction and to boric

Table 1 The reduction of conjugated alkenones with BH_3 in the presence of $LiBH_4$.[a]

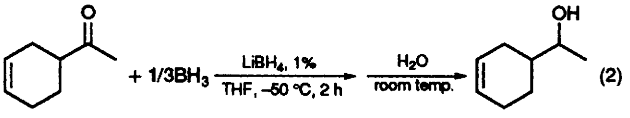
Conjugated alkenone	BH_3/ equiv.[b]	Method	$LiBH_4$/ mol%[c]	Product	Yield of allylic alcohol/%
1c	1/3	A	0	**2c**	61[d]
	1/3	B or C	1		>99[d]
1d	1/3	A	1	**2d**	>99[e] 90[f]
1e	1/3	A	1	**2e**	96[e] 91[f]
1f	1/3	A	3	**2f**	87[d]
	2/3	B	6		98[d] 88[f]
1g	1/3	A	2	**2g**	88[d]
	2/3	C	3		98[d] 92[f]

[a] The analytical reactions were carried out by using 5 mmol of conjugated alkenones in 5 ml of THF. [b] 0.5 mol dm^{-3} solution of BH_3 in THF. [c] 1.0 mol dm^{-3} solution of $LiBH_4$ in THF. [d] Determined by GLC and based on starting amount of conjugated alkenone. [e] Determined by FID/TLC analyser and based on starting amount of conjugated alkenone. [f] Four times amounts of reagents and solvent were used in the reduction and the product was isolated by column chromatography.

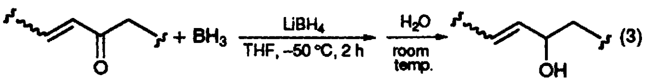


1a **2a** **3a** **4a**

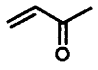
LiBH4		(%)	(%)	(%)
none; 0 °C		0	0	35
" ; −50 °C		49	0	2
1%; 0 °C	Method A	85	0	7
" ; −50 °C	Method A	92	0	0
	Method B or C	>99 (90%, isolated)	0	0



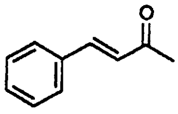
1b **2b** 98%, GLC (92%, isolated)



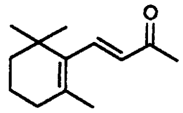
1c–g **2c–g**



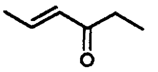
1c



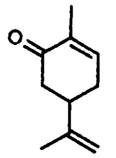
1d



1e



1f



1g

acid in the hydrolysis) in contrast to strong basic conditions in reductions using metal borohydrides[4] suggesting that the present reaction may be effective for the reduction of base-susceptible alkenones. In addition, the work-up is very simple; quenching with a small amount of methanol at −50 °C, hydrolysing and drying. Thus, essentially, there exists no other organic compound than the allylic alcohol and THF in the reaction mixture. The allylic alcohol is easily isolated from the reaction mixture by distillation or column chromatography.

Received, 4th November 1993; Com. 3/06610J

Footnotes

† LiBEt$_3$H and NaBH$_4$ have a similar accelerating effect and may be used instead of LiBH$_4$. LiCl shows a very small effect on the reaction. These results will be appeared elsewhere.

‡ It has been reported that the presence of the lithium borohydride compound accelerated the reaction of BH$_3$ with alcohol, Y. Masuda, Y. Nunokawa, M. Hoshi and A. Arase, *Chem. Lett.*, 1992, 349. Under the conditions employed in the present reduction, BH$_3$ is completely decomposed with methanol.

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