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A Facile and Selective 1,2-Reduction of Conjugated Ketones with $NaBH_4$ in the Presence of $CaCl_2$

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$CaCl_2$ ia an efficient catalyst for the regioselective 1,2-reduction of α-enones with $NaBH_4$ in methanol solution.

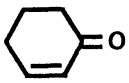
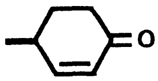
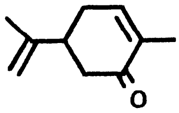
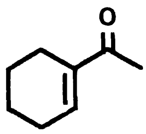
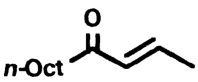
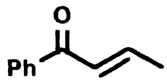
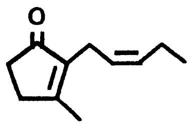
Although alkali metals have received much attention in organic synthesis, there are limited studies on alkaline earth metals except magnesium. In our investigation of pursuing the utility of alkaline earth metals, we have found that α,β-unsaturated ketones could be converted into allylic alcohols selectively with sodium borohydride in the presence of calcium chloride.

Of the alkaline earth metal chlorides tested, $CaCl_2$ appears to offer the best combination of yield and selectivity in the reduction of 2-cyclohexenone with sodium borohydride. Then the reduction of various α,β-unsaturated ketones with $NaBH_4$ in the presence of $CaCl_2$ was examined. The representative results are shown in Table 1.

A typical procedure is described for the reduction of 2-cyclohexenone. Calcium chloride[1)] (0.44 g, 4.0 mmol) was added to a methanol (10 ml) solution of 2-cyclohexenone (0.19 g, 2.0 mmol). The resulting clear solution was stirred for 30 min at 25 °C. The mixture was cooled to 0 °C and $NaBH_4$ (0.11 g, 3.0 mmol) was slowly added with stirring. Vigorous gas evolution occurred. The mixture was stirred for another 1 h. The resulting mixture was poured into 1 M (1 M = 1 mol dm^{-3}) HCl (20 ml) and extracted with ethyl acetate. The ratio of 1,2-reduction product (2-cyclohexen-1-ol):1,4-reduction product (cyclohexanol) was determined (97:3) by the examination of ^1H NMR of the crude product. Purification by silica-gel column chromatography gave 2-cyclohexen-1-ol (0.18 g) in 92% yield.

The $CeCl_3$-$NaBH_4$ system has been widely used for the selective reduction of enones.[2)] This new method provides a simple and cheap alternative procedure for the selective 1,2-reduction of α-enones.[3)]

Table 1. Selective 1,2-Reduction of Conjugated Ketones

Entry	Conjugated ketone	Additive	Product Yield/%	Product Ratio of 1,2:1,4[a)]
1		None	—	51:49[b)]
2		$MgCl_2$	85	95: 5
3		$CaCl_2$	92	97: 3
4		$SrCl_2$	91	81:19
5		$BaCl_2$	86	93: 7
6		None	87	70:30
7		$CaCl_2$	88	>99:<1
8		None	90	70:30
9		$CaCl_2$	97	>99:<1
10		None	72	93: 7
11		$CaCl_2$	81	100: 0
12		None	92	95: 5
13		$MgCl_2$	99	>99:<1
14		$CaCl_2$	98	99: 1
15		None	86[c)]	58:42
16		$CaCl_2$	90[c)]	82:18
17		None	93[c)]	67:33
18		$CaCl_2$	93[c)]	95: 5

a) Determined by NMR and/or capillary gas chromatography of the crude product. b) Ref. 2. c) Products were sensitive to acid and the reaction mixture was quenched with saturated aqueous NaCl instead of 1 M HCl.

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References

1) Calcium chloride was purchased from Wako pure chemical industries, Ltd. and used without further purification.

2) A. L. Gemal and J-L. Luche, J. Am. Chem. Soc., 103, 5454 (1981).

3) The $CaCl_2$-$NaBH_4$ system is not as effective as $CeCl_3$-$NaBH_4$ for the selective reduction of 2-cyclopentenone. Whereas the reduction with $CeCl_3$-$NaBH_4$ gave 2-cyclopenten-1-ol selectively (2-cyclopenten-1-ol (**1**):cyclopentanol (**2**) = 97:3),[2)] the reduction with $CaCl_2$-$NaBH_4$ provided a mixture of **1**:**2** = 6:94.

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