

Reduction of Aldehydes and Ketones with $\text{NaBH}_4/\text{Al}_2\text{O}_3$ Under Solvent-Free Conditions

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Aldehydes and ketones are efficiently reduced to the corresponding alcohol using NaBH_4 supported onto alumina under solvent free conditions. It was found that the presence of small amount of methanol in reaction media is essential. Chemoselective 1,2-reduction of α , β -unsaturated carbonyl compounds to the corresponding allylic alcohols are also observed.

Key Words: Reduction, NaBH_4 , Ketone, Aldehyde, Solvent free.

INTRODUCTION

Heterogeneous organic reactions have proven useful to chemists in the laboratory as well as in the industrial context. These reactions are effected by the reagents immobilized on the porous solid supports and have advantages over the conventional solution phase reactions because of the good dispersion of active reagent sites, associated selectivity and easier work-up. The recyclability of some of these solid supports renders these processes into truly eco-friendly green protocols¹. Alumina, an inorganic polymeric material used commonly for column chromatography, is very interesting in organic solids which are used as support in organic reactions, due to its surface properties that suggest a very rich chemistry².

Metal hydrides are valuable reagents in modern organic chemistry. The most frequently used hydride is the NaBH_4 reagent. It is a mild, inexpensive and invaluable reagent for applications in a wide range of reduction processes³. It is widely used as a reducing agent for reduction of aldehydes and ketones in protic or aprotic solvents with Lewis acids or acid resins⁴. NaBH_4 reduction of ketones to alcohols in the solid state has also been reported⁵. However, the drawback of this solid state reaction is that it must be kept in a dry box at room temperature for 5 days and needs to be stirred once a day.

Recently, NaBH_4 supported on inorganic solid supports especially alumina^{6,7} has been reported in literature for the reduction of carbonyl compounds to the corresponding hydroxy derivatives in solution phase⁶ and under solvent free conditions⁷. The remarkable ability of the alumina to promote the reduction of carbonyl groups with NaBH_4 was strongly depended on preloading alumina with the optimum amount of water in solution phase reactions and microwave irradiation in solvent free reactions.

In another report, microwave-assisted reduction of acetophenone and ethyl phenyl ketone with NaBH₄ in the presence of celite, SiO₂, MgSO₄ and cellulose under solvent free condition was investigated; however, the behaviour of other ketones was not further documented⁴.

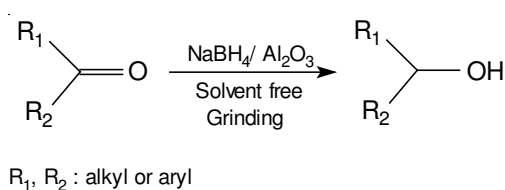
EXPERIMENTAL

All reduction products are known compounds and are identified by comparison of their physical and spectral data with those of authentic samples. Carbonyl compounds, NaBH₄ and Al₂O₃ were purchased from Fluka and Merck. The purity determination of the products and reaction monitoring were accomplished by TLC on silica gel polygram SILG/UV 254 plates.

General procedure for the reduction of aldehydes and ketones using NaBH₄/Al₂O₃: Al₂O₃ (1.4 g) and NaBH₄ (0.38 g, 1 mmol) were crushed together in a mortar so as to form an intimate mixture. A neat carbonyl compounds (1 mmol) and 5 drops of methanol were added to this mixture. The reaction mixture was ground for 5 min. The progress of reaction was monitored by TLC using ether-CCl₄. Then the reaction mixture was poured into ether (10 mL) and filtered through a sintered glass funnel. The filter cake was washed thoroughly with portions of ether. The organic layer was dried over anhydrous sodium sulfate and solvent evaporated under reduced pressure to afford the TLC and ¹H NMR pure products in 53-84 % isolated yields.

RESULTS AND DISCUSSION

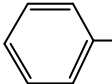
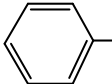
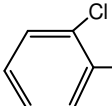
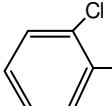
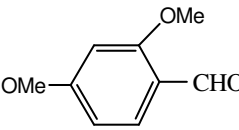
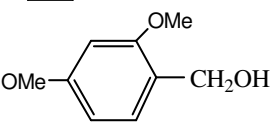
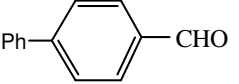
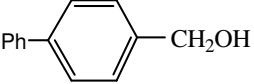
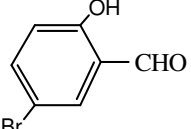
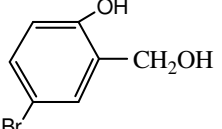
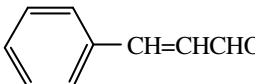
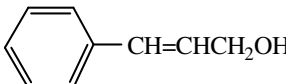
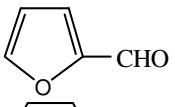
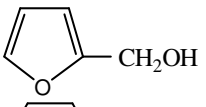
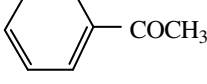
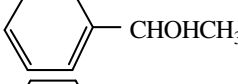
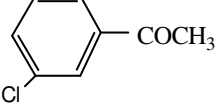
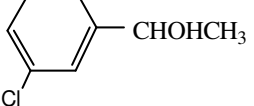
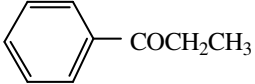
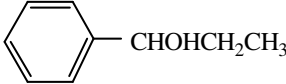
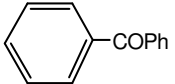
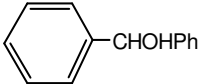
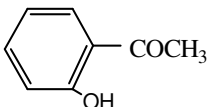
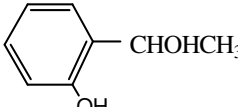
In this work, we report more efficient, simple, practical and milder reduction of aldehydes and ketones using NaBH₄ supported on alumina in solvent free conditions (**Scheme-I**).



Scheme-I

NaBH₄ supported on alumina was prepared by simply cogrinding alumina (1.4 g) with NaBH₄ (1 mmol) in an agate mortar. In this simple and efficient method the starting aldehydes or ketones were reduced to the corresponding alcohols in a mortar with grinding by a pestle in the presence of supported NaBH₄ on alumina and little drops of methanol. The feasibility of the present reduction of carbonyl compounds was first examined using acetophenone as a model substrate. Thus, acetophenone (1 mmol) was thoroughly mixed with NaBH₄/Al₂O₃ (1 mmol based on NaBH₄, 1.438 g) and 5 drops of methanol in a mortar with a pestle and in an ambient air

TABLE-1
 FACILE REDUCTION OF VARIOUS ALDEHYDES AND KETONES
 TO THE CORRESPONDING ALCOHOLS BY $\text{NaBH}_4/\text{ALUMINA}$
 UNDER SOLVENT FREE CONDITIONS

Substrate	Product	Time (min)	Yield (%) ^{a-c}
		8	73
		9	74
		13	68
		8	78
		7	79
		9	53
		7	84
		10	70
		10	71
		11	72
		15	71
		15	67

^aProducts were identified by compares of their physical and spectral data with those of authentic samples. ^bIsolated yields.

environment at room temperature and product was obtained in 70 % yield within 10 min. Filtration, washing of the filter cake with ether, followed by removal of the solvent gave corresponding alcohol. It can be emphasized that the reaction is clean, the work-up is straight forward and from economical and environmental points of view, absence of solvent is favourable.

With the first successful result in hand, reduction of other aldehydes and ketones with NaBH₄/Al₂O₃ were carried out under similar reaction conditions. The results obtained are presented in Table-1. The successful chemoselective 1,2-reduction of α , β -unsaturated ketone (entry 6) to allylic alcohol might extend the utility of the present simple procedure.

The promoting effect of alumina and grinding was definitely confirmed by comparing our results with those previously reported by Toda *et al.*⁵ that applied NaBH₄ in the absence of inorganic support for the reduction of ketones in solvent free conditions at room temperature. For example, the reduction of benzophenone (1 mmol) with NaBH₄ (10 mmol) was completed under solvent free condition after 5 days, while with 1 equivalent of NaBH₄/Al₂O₃ and in the presence of 5 drops of methanol the required time for completion of reduction reaction is only 15 min.

In conclusion, reduction of aldehydes and ketones with NaBH₄/Al₂O₃ in solvent-free conditions is a rapid, simple, selective and environmentally friendly protocol when compared to the conventional solution phase or heterogeneous condition and should utility in contemporary organic synthesis.

ACKNOWLEDGEMENT

Partial support for this work by Islamic Azad University, Omideihe Branch Research Council is gratefully acknowledged.

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(Received: 9 November 2009;

Accepted: 4 June 2010)

AJC-8760