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Microwave-Assisted Reduction of Carbonyl Compounds in Solid State Using Sodium Borohydride Supported on Alumina

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***Abstract*:** A manipulatively simple and rapid method for the reduction of carbonyl compounds is described that is conducted under solventless 'dry' conditions using $NaBH_4$-Alumina and microwave irradiation.

Heterogeneous reactions that are facilitated by supported reagents on various solid inorganic surfaces have received attention in recent years.[1] The advantage of these methods over conventional homogeneous reactions is that they provide greater selectivity, enhanced reaction rates, cleaner products and manipulative simplicity. Relatively inexpensive sodium borohydride, $NaBH_4$, has been extensively used as a reducing agent in view of its compatibility with protic solvents and safe nature.[2] $NaBH_4$ impregnated on neutral alumina reduces a wide variety of carbonyl compounds to the corresponding hydroxy derivatives in solution phase.[3] The solid state reduction of ketones has also been achieved by mixing with sodium borohydride and storing the mixture in a dry box for five days.[4] The major disadvantage in the heterogeneous reaction with $NaBH_4$ is that solvent reduces the reaction rate while in the solid state reactions time period is too long (5 days) for it to be of any practical utility. Also, the large excess of the hydride reagent requirement (tenfold) in the later case is a serious limitation.[4] Consequently, there is interest in the use of $NaBH_4$ 'doped' supports that are efficient and offer operational advantages.[5]

In continuation of our ongoing program to develop environmentally benign solventless methods using solid supports and microwave activation,[6] we now wish to report a facile reduction of aldehydes and ketones by alumina supported $NaBH_4$[7] that proceeds in the solid state using microwaves. The process in its entirety involves a simple mixing of carbonyl compound with (10%) $NaBH_4$-Alumina in solid state and irradiating the mixture in an unmodified household microwave oven for the time specified in the table. The extraction of the product in dichloromethane affords the corresponding alcohol in high yields. The reduction of aldehydes is completed within seconds on admixing with $NaBH_4$ doped alumina (10%) at room temperature but *p*-nitrobenzaldehyde requires gentle warming for completion of the reaction (Entry 3). The useful chemoselective feature of the reaction is apparent from the reduction of *trans*-cinnamaldehyde (cinnamaldehyde/$NaBH_4$-alumina, 1:1 mol equiv.); olefinic moiety remains intact and only the aldehyde functionality is reduced in a facile reaction that takes place at room temperature. In the case of chalcone (chalcone/$NaBH_4$-alumina, 1:8 mol equiv.), however, two products are formed in the ratio of 60:40 as shown in equation below. The additional examples are summarized in the table.

$$\textit{trans}\text{-PhCH=CH-}\underset{\underset{\displaystyle O}{\|}}{C}\text{-Ph} \xrightarrow[\text{MW}]{NaBH_4\text{-}Al_2O_3} \textit{trans}\text{-PhCH=CH-}\underset{\underset{\displaystyle OH}{|}}{CH}\text{-Ph} + PhCH_2CH_2\text{-}\underset{\underset{\displaystyle OH}{|}}{CH}\text{-Ph}$$

60% 40%

The reduction of acetophenone is representative of the general procedure employed: Freshly prepared $NaBH_4$-alumina[7] (1.13 g, 3.0 mmol of $NaBH_4$) is thoroughly mixed with neat acetophenone (0.36 g, 3.0 mmol) in a test tube and placed in an alumina bath inside the microwave oven and irradiated (30 Sec.).[8] Upon completion of the reaction, monitored on TLC (hexane:EtOAc, 8:2, v/v), the product is extracted into methylene chloride (2x 15 mL). Removal of solvent under reduced pressure essentially provides pure *sec*-phenethyl alcohol in 87% yield. No side product formation is observed in any of the reactions investigated and no reaction takes place in the absence of alumina. Further, the recovered alumina can be recycled by mixing with fresh borohydride and reused for subsequent reductions without any loss in activity. The air used for cooling the magnetron ventilates the microwave cavity thus preventing hydrogen from reaching explosive concentrations. Although we did not encounter any accident during these studies, we recommend extreme caution for reactions on larger scale.

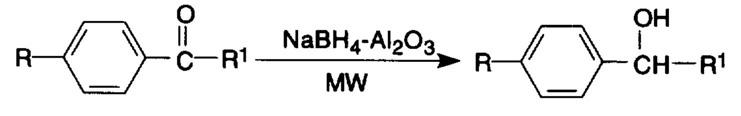
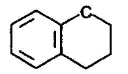


Table: Solid state reduction of carbonyl compounds using $NaBH_4$-Al_2O_3

Entry	R	R^1	Carbonyl Compd/ $NaBH_4$ (equiv.)	Time[a] (sec)	Yield[b] (%)
1	CH_3	H	1:1	RT	90
2	Cl	H	1:1	RT	93
3	NO_2	H	1:2	40	87
4	H	CH_3	1:1	30	87
5	CH_3	CH_3	1:1	90	90
6	H	C_6H_5	1:5	120[c]	92
7	H	$CH(OH)C_6H_5$	1:8	180	79
8	OCH_3	$CH(OH)C_6H_4$-OCH_3-*p*	1:5	120	62
9			1:7	120	85

[a] RT refers to reactions that are completed on simple mixing of the substrates with $NaBH_4$-Al_2O_3 at room temperature.

[b] Unoptimized yields of isolated products that exhibited physical and spectral properties in accord with the assigned structures.

[c] In an oil bath at 130 °C (temperature attained in MW oven, 2 min), the reaction stopped at 40% conversion even after 4 h.

In conclusion, we have developed a facile and practical method for the solid state reduction of carbonyl compounds to alcohols using a solventless system, $NaBH_4$-Al_2O_3, that is accelerated by microwave irradiation.

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7. (10%) $NaBH_4$-Alumina, is prepared by thoroughly mixing $NaBH_4$ (5.0 g) with neutral alumina (45.0 g) in solid state using a pestle and mortar; admixing three components, carbonyl substrate, $NaBH_4$ and alumina together is equally efficient.
8. For a critical evaluation of activation process by microwaves see: Raner, K.D.; Strauss, C.R.; Vyskoc, F.; Mokbel, L. *J. Org. Chem.* **1993**, *58*, 950. The temperature of the alumina bath (heat sink) inside a Sears Kenmore microwave oven (operating at 2450 MHz) equipped with a turntable at full power (900 Watts) found to be ~70 °C after 30 seconds of irradiation.

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