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Convenient Reduction of Carbonyl Compounds with $NaBH_4$/Wet Al_2O_3 System Under Solvent-Free, Solid-Gel and Microwave Irradiation

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Various carbonyl compounds such as aldehydes, ketones, α,β-unsaturated enals and enones, α-diketones and acyloins were reduced efficiently by $NaBH_4$/wet Al_2O_3 system under solvent-free, solid-gel and microwave irradiation. The chemoselective reduction of aldehydes over ketones was achieved successfully by $NaBH_4$/wet Al_2O_3 system at solvent-free condition.

Key Words: $NaBH_4$, Wet Al_2O_3, Solvent-free, Solid-gel, Microwave.

INTRODUCTION

It is over 50 years that $NaBH_4$ has been widely recognized as the reagent for the reduction of carbonyl compounds in protic solvents[1]. Over the past two decades, the utility of sodium borohydride has been greatly expanded and different techniques and modifications have been reported for this reagent to reduce organofunctional groups in various solvents. These modifications may involve replacement of one or more hydrides with other substituents[2], change of the sodium cation to other metal[3], quaternary ammonium and phosphonium cations[4], a concurrent cation and hydride exchange[5], ligand-metal borohydrides[6,7], combination of borohydrides with Lewis acids, additives and mixed-solvents systems[8,9] and finally use of polymers or solid beds for supporting the borohydride species[10]. In this context, the applications of modified borohydride agents in organic synthesis have been reviewed extensively[6,11].

Nowadays, the simplification of reaction protocols and minimizing the use of auxiliaries is an important paradigm in green chemistry. Working without solvents gives the potential for a simpler process, smaller plants and eliminates the energy costs of removal, recycling and eventual disposal of waste solvents. Several techniques and protocols for the efficient use of solvent-free reactions have been reported in organic synthesis[12]. Literature review shows that the reduction of carbonyl compounds with $NaBH_4$ at solvent-free condition in the presence or absence of mineral solid supports has been rarely investigated: *e.g.*, the solid state reduction of ketones was achieved by mixing the carbonyl compound with sodium borohydride and storing the mixture in a dry box for 5 days[13]. The major shortcoming of this method is that it takes a long time for any practical application. In addition, the need for large amounts of $NaBH_4$ (10-fold) is a serious limitation in this method. Varma and Saini[14] reported that reduction of carbonyl compounds was accomplished in solid state with $NaBH_4$ supported on dry Al_2O_3 under microwave irradiation. Though the method is fast in the reduction of aldehydes, however, in the case of ketones the need for large amounts of $NaBH_4$ (8-fold), moderate yields of products, the slow rate of reductions and low regioselectivity in the reduction of conjugated carbonyl compounds are the major limitations of this protocol. Microwave-assisted reduction of two liquid ketones (acetophenone and ethylphenyl ketone) with $NaBH_4$/dry SiO_2 system was also reported in solid state, however, the behaviour of other carbonyl compounds was not further documented[15]. Recently, $NaBH_4$/wet SiO_2 system was reported by our research group for the reduction of carbonyl compounds under solvent-free condition[16]. This combination system suffers from the acidic surface of silica gel and this condition decomposes $NaBH_4$ vigorously with the evolution of hydrogen gas. In order to overcome the above mentioned limitations specially at $NaBH_4$/wet SiO_2 and $NaBH_4$/dry Al_2O_3/microwave systems and introduce an effective and practical synthetic protocol for the reduction of carbonyl compounds with $NaBH_4$ through minimizing or avoiding of solvents. In this paper, we wish to report wet Al_2O_3 as a perfect media to perform the mild, selective and efficient reduction of carbonyl compounds with $NaBH_4$ under solvent-free, solid-gel and microwave irradiation.

EXPERIMENTAL

All microwave-assisted reactions were carried out in a Yusch household microwave oven (1000 W). All reagents and substrates were purchased from commercial sources with the best quality and they were used without further purification. Al_2O_3 was used in the form of neutral alumina, grade for column chromatography and it was purchased from Merck company. IR and ^1H NMR spectra were recorded on Thermo Nicolet Nexus 670 FT-IR and 300 MHz Bruker Avance spectrometers, respectively. The products were characterized by a comparison with authentic samples (melting or boiling points) and their ^1H NMR or IR spectra. All yields refer to isolated pure products. TLC was applied for the purity determination of substrates, products and reaction monitoring over silica gel 60 F_{254} aluminum sheet.

A typical procedure for reduction of carbonyl compounds with $NaBH_4$/ Wet Al_2O_3 system at solvent-free condition: In a round-bottomed flask (5 mL) charged with Al_2O_3 (0.5 g), H_2O (0.2 g) was added and the mixture was stirred with a magnetic stirrer to produce wet Al_2O_3 (0.7 g, 40 % m/m). To the prepared wet Al_2O_3, benzaldehyde (0.106 g, 1 mmol) was added and the resulting mixture was then stirred for 3 min. Afterward, $NaBH_4$ (0.039 g, 1 mmol) as a fine powder was added to the reaction mixture and the mixture was stirred for 15 min at room temperature. The progress of the reaction was monitored by TLC (eluent; CCl_4/Et_2O: 5/2). At the end of reaction, the mixture was washed three times with CH_2Cl_2 (3 × 8 mL) and the combined washing solvents were dried over anhydrous Na_2SO_4. Evaporation of the solvent and a short column chromatography of the resulting crude material over silica gel (eluent; CCl_4/Et_2O: 5/2) afford the pure colourless liquid benzyl alcohol (0.l04 g, 96 %, Table-1, method A).

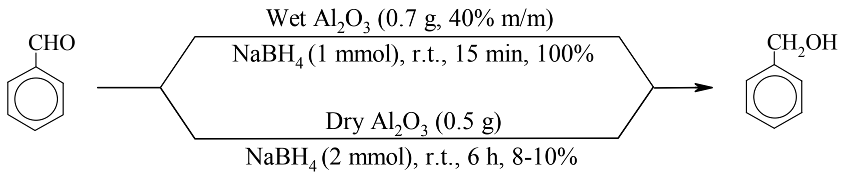
A typical procedure for reduction of carbonyl compounds with $NaBH_4$/Wet Al_2O_3 system in a solid-gel media: In a round-bottomed flask (5 mL) charged with wet Al_2O_3 (0.7 g, 40 % m/m), CH_3CN (0.4 mL) was added and the mixture was stirred with a magnetic stirrer to produce a solid-gel media. To the resulting mixture, benzophenone (0.182 g, l mmol) was added and the mixture was continued to stirring for 3 min. $NaBH_4$ (0.076 g, 2 mmol) as a fine powder was added to the reaction mixture and the mixture was stirred at room temperature for 8 min. TLC was monitored the progress of the reaction (eluent; CCl_4/Et_2O: 5/2). At the end of reaction, the mixture was washed 3 times with CH_2Cl_2 (3 × 8 mL) and the combined washing solvents were dried over anhydrous Na_2SO_4. Evaporation of the solvent and a short column chromatography of the resulting crude material over silica gel (eluent; CCl_4/Et_2O: 5/2) give the pure white crystalline benzhydrol (0.l82 g, 99 %, Table-2, method B).

A typical procedure for competitive reduction of aldehydes over ketones with $NaBH_4$/wet Al_2O_3 system at solvent-free condition: To a round-bottomed flask (5 mL) charged with wet Al_2O_3 (0.7 g, 40 % m/m), benzaldehyde (0.106 g, 1 mmol) and acetophenone (0.12 g, l mmol) was added and the mixture was stirred with a magnetic stirrer for 3 min. $NaBH_4$ (0.039 g, 1 mmol) as a fine powder was added to the reaction mixture and it was stirred at room temperature. After 15 min, the mixture was washed three times with CH_2Cl_2 (8 mL × 3 mL) and the combined washing solvents were dried over anhydrous Na_2SO_4. Evaporation of the solvent and a short column chromatography of the resulting crude material over silica gel (eluent; CCl_4/Et_2O: 5/2) give the pure liquid benzyl alcohol as a sole product and acetophenone as an intact material (Table-4).

A typical procedure for microwave-assisted reduction of carbonyl compounds with $NaBH_4$/Wet Al_2O_3 system: In a round-bottomed flask (5 mL), a mixture of wet Al_2O_3 (1 g, 100 % m/m), acetophenone (0.12 g, 1 mmol) and $NaBH_4$ (0.039 g, 1 mmol) was prepared. The reaction flask was irradiated with microwaves (300 W) for 1 min. The progress of the reaction was monitored by TLC (eluent; CCl_4/Et_2O: 5/2). At the end of reaction, the mixture was washed three times with CH_2Cl_2 (8 mL × 3 mL) and the combined washing solvents were dried over anhydrous Na_2SO_4. Evaporation of the solvent and a short column chromatography of the resulting crude material over silica gel (eluent; CCl_4/Et_2O: 5/2) afford the pure colourless liquid 1-phenylethanol (0.l19 g, 97 %, Table-2).

RESULTS AND DISCUSSION

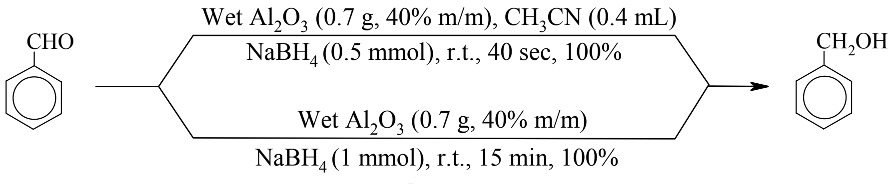
Reduction at solvent-free and solid-gel conditions: Solvent-free reactions promise to be an essential facet of green chemistry. This type of organic reactions possesses some advantages over traditional reactions in organic solvents[12]. In continuation of our research program directed to the application of modified borohydride agents in organic synthesis[6-8] and the lack of information for the use of $NaBH_4$/wet Al_2O_3 system in organic synthesis encouraged us to study the influence of adsorbed water on the surface of alumina on the rate of reduction of carbonyl compound with $NaBH_4$ under solvent-free and solid-gel conditions. We first examined the solvent-free protocol. The room temperature reduction of benzaldehyde with two molar equivalents of $NaBH_4$ and 0.5 g of dry Al_2O_3 was carried out with 8-10 % conversion within 6 h. This reaction in the presence of wet Al_2O_3 (prepared by simply mixing a small amount of water with Al_2O_3) was dramatically accelerated and completed with 1 molar equivalent of $NaBH_4$ within 15 min (**Scheme-I**).



Scheme-I

The optimization experiments showed that using one molar equivalent of $NaBH_4$ in the presence of wet Al_2O_3 (40 % m/m, mass ratio) was the optimal for complete reduction of PhCHO at room temperature. This optimal condition was applied for the reduction of structurally different aliphatic and aromatic aldehydes (method A). The efficiency of reductions was excellent and the corresponding primary alcohols were obtained in 85-99 % yields within 1-40 min (Table-1). The procedure of reduction was easy *i.e.*, a simple mixing and stirring the reaction components (aldehyde, $NaBH_4$ and wet Al_2O_3) at room temperature was produced the product alcohol in the appropriate time.

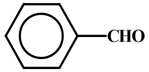
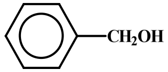
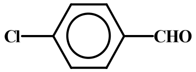
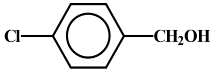
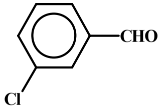
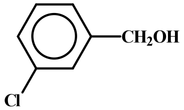
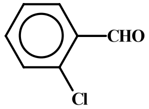
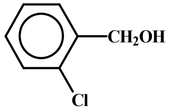
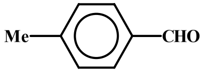
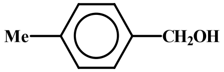
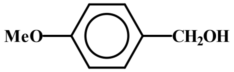
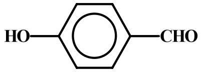
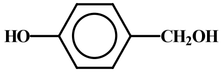
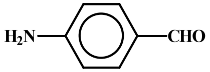
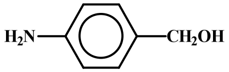
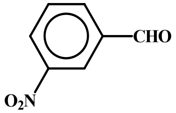
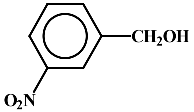
It is also found that by adding a small amount of CH_3CN (0.4 mL) into wet Al_2O_3 (40 % m/m) and performing the reduction of benzaldehyde with 0.5 molar equivalent of $NaBH_4$ in a solid-gel media (method B), the rate of reduction was extremely increased and the reaction was completed in 40 s (**Scheme-II**) (Table-1).

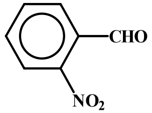
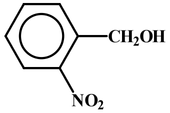
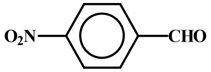
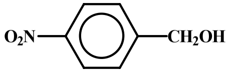
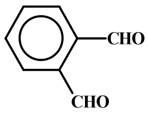
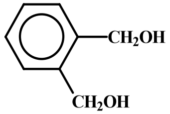
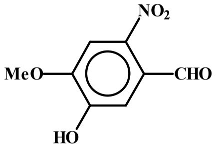
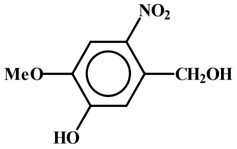
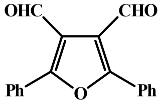
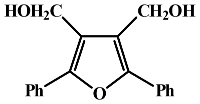
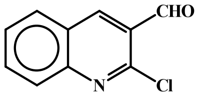
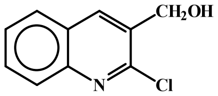
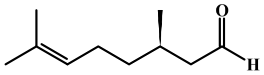
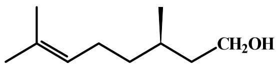
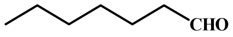
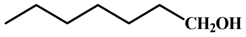


Scheme-II

The efficiency of solid-gel protocol was further examined by the reduction of structurally different aliphatic and aromatic aldehydes with $NaBH_4$/wet Al_2O_3 (40 % m/m) system in 0.4 mL of CH_3CN. All reductions were completed within 3 min (Table-1, method B). Comparison of the results shows that reductions in method B is faster than those in method A, however, the efficiency of both systems is nearly the same.

TABLE-1
REDUCTION OF ALDEHYDES WITH $NaBH_4$/Wet Al_2O_3 SYSTEM UNDER SOLVENT-FREE, SOLID-GEL AND MICROWAVE IRRADIATION

Entry	Substrate	Product	Solvent-free and solid-gel				Microwave irradiation[c]			
			Method[a]	Molar ratio $NaBH_4$/subs.	Time	Yield (%)[b]	Molar ratio $NaBH_4$/subs.	Wet (%)	Time (s)	Yield (%)[b]
1			(A) (B)	1:1 0.5:1	15 min 40 s	96 99	0.5:1	40	20	97
2			(A) (B)	1:1 0.5:1	10 min 30 s	99 99	1:1	80	40	98
3			(A) (B)	1:1 0.5:1	8 min 30 s	95 96	1:1	80	40	96
4			(A) (B)	1:1 0.5:1	25 min 30 s	94 97	1:1	80	40	93
5			(A) (B)	1:1 0.5:1	40 min 2 min	98 99	1:1	80	40	97
6			(A) (B)	1:1 0.5:1	30 min 3 min	98 98	1:1	80	40	99
7			(A) (B)	1:1 0.5:1	5 min 10 s	95 95	0.5:1	40	30	93
8			(A) (B)	1:1 0.5:1	1 min 5 s	90 94	1:1	40	40	91
9			(A) (B)	1:1 0.5:1	7 min 20 s	94 97	0.5:1	40	30	97

10			(A) (B)	1:1 0.5:1	5 min 20 s	95 97	1:1	80	30	95
11			(A) (B)	1:1 0.5:1	10 min 20 s	94 97	1:1	80	30	99
12			(A) (B)	1.5:1 0.7:1	3 min 40 s	96 97	1.2:1	40	30	98
13			(A) (B)	1:1 0.5:1	5 min 30 s	94 95	1:1	40	30	95
14			(A) (B)	1.5:1 0.7:1	7 min 40 s	99 98	1.5:1	80	40	88
15			(A) (B)	1:1 0.5:1	3 min 10 s	97 97	1:1	40	30	94
16			(A) (B)	1:1 0.5:1	15 min 2	89 91	1:1	40	30	89
17			(A) (B)	1:1 0.5:1	5 min 10 s	85 88	1:1	40	30	86

[a]Method A: The reactions were carried out in the presence of wet Al_2O_3 (0.7 g, 40 % m/m) at room temperature under solvent-free condition; Method B: The reactions were carried out in the presence of wet Al_2O_3 (0.7 g, 40 % m/m) and 0.4 mL of CH_3CN at room temperature in a solid-gel media; [b]Yield refer to isolated pure products; [c]The reactions were irradiated with microwaves (300 W) in the presence of Al_2O_3 (0.5 g) at the defined wet %.

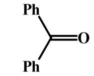
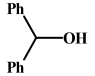
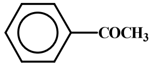
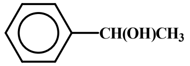
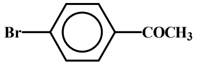
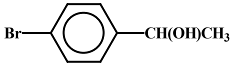
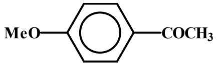
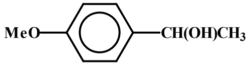
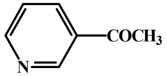
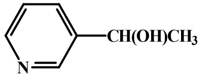
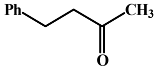
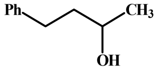
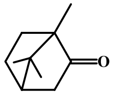
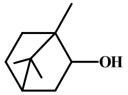
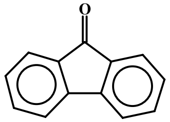
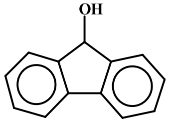
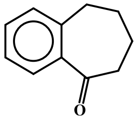
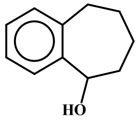
At the next attempt, we turned our attention into solvent-free reduction of ketones, acyloins and α-diketones with sodium borohydride. Less reactivity of ketones relative to aldehydes, led us to perform reductions with two molar equivalents of $NaBH_4$ at room temperature or in an oil bath at 80-85 °C (method A). Table-2 shows that aromatic or more hindered ketones (entries 1-4), acyloins and α-diketones (entries 12,13) exhibited low reactivity towards the protocol even in higher temperature, however, 3-acetylpyridine as the same of aliphatic ketones (entries 7-11) showed a higher reactivity at room temperature. It is thought that less reactivity of ketones and their low interactions with the reducing agent in solid state created the low-moderate efficiency in method A (0-60 %). We enhanced the efficiency of reductions using the solid-gel protocol by adding 0.4 mL of CH_3CN into wet Al_2O_3 (40 % m/m) and performed the reductions with 1-2 molar equivalents of $NaBH_4$ at room temperature (method B). The reactions were completed within 1-8 min in high to excellent yields of products (88-99 %) (Table-2). Method B again showed a faster reduction rates than method A.

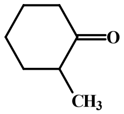
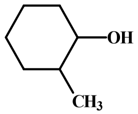
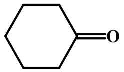
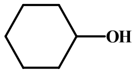
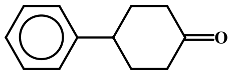
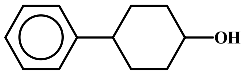
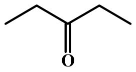
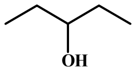
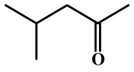
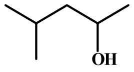
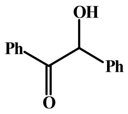
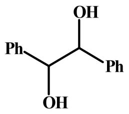
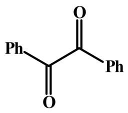
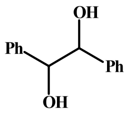
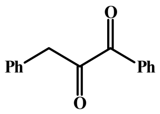
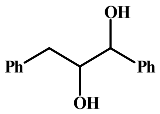
Further utility of $NaBH_4$/wet Al_2O_3 system was investigated with regioselective 1,2-reduction of α,β-unsaturated enals and enones. The selectivity was examined with the reduction of cinnamaldehyde by $NaBH_4$/wet Al_2O_3 (40 % m/m) system. The reduction was carried out with 1.5 molar equivalents of $NaBH_4$ at room temperature under solvent-free condition (method A). The reaction was completed in 15 min and cinnamyl alcohol was obtained with a perfect regioselectivity in 95 % yield (Table-3). This procedure was also applied for the reduction of citral in 15 min and geraniol was obtained in 92 % yield.

The solvent-free reduction of conjugated enones was also examined by $NaBH_4$/wet Al_2O_3 (40 % m/m) system (method A). The reductions were carried out with 2 molar equivalents of $NaBH_4$ in an oil bath at 80-85 ºC. Table-3 shows that though the yields of products in method A were low to moderate, however, only 1,2-reduction manner was observed in the reactions. This situation motivated us to perform the reductions in a solid-gel media (method B). Reduction of conjugated aldehydes and ketones were carried out by $NaBH_4$/wet Al_2O_3 (40 % m/m) system in 0.4 mL of CH_3CN at room temperature. The reactions were completed with 1.0-1.5 molar equivalents of $NaBH_4$ and the corresponding allylic alcohols were obtained within 1-5 min in excellent yields and regioselectivity (Table-3).

The chemoselective reduction of one functional group without affecting the other one is a well-known strategy for preparing of the molecules with ever-increasing complexity in organic synthesis. This subject is of great interest[17] and numerous modified borohydride agents have been reported for this achievement[6-8,18]. Since under the defined conditions, reduction of aldehydes and ketones by $NaBH_4$/wet Al_2O_3 (40 % m/m) system at solvent-free condition was temperature-dependent, it is thought that this system can have a chemoselectivity towards reduction of aldehydes over ketones. This fact was demonstrated with the selective reduction of benzaldehyde in the presence of acetophenone using one molar equivalent of $NaBH_4$ at room temperature (**Scheme-III**).

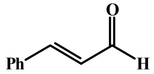
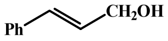
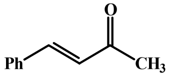
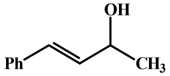
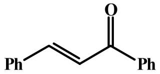
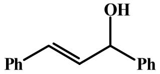
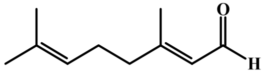
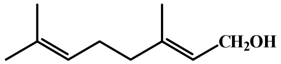
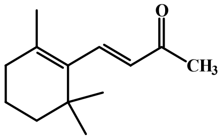
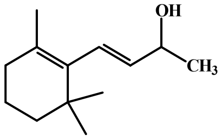
TABLE-2
REDUCTION OF KETONES WITH $NaBH_4$/Wet Al_2O_3 SYSTEM UNDER SOLVENT-FREE, SOLID-GEL AND MICROWAVE IRRADIATION

Entry	Substrate	Product	Solvent-free and solid-gel					Microwave irradiation[d]			
			Method[a]	Molar ratio $NaBH_4$/Subs.	Condition[b]	Time (min)	Yield (%)[c]	Molar ratio $NaBH_4$/Subs.	Wet (%)	Time (min)	Yield (%)[c]
1			(A) (B)	2:1 2:1	Oil bath RT	60 8	0 99	2:1	100	5	30 (99)[e]
2			(A) (B)	2:1 2:1	Oil bath RT	30 5	40 98	1:1	100	1	97
3			(A) (B)	2:1 2:1	Oil bath RT	60 3	10 94	2:1	100	2	97
4			(A) (B)	2:1 2:1	Oil bath RT	30 6	42 95	2:1	100	2	96
5			(A) (B)	2:1 1:1	RT RT	10 1	97 97	1:1	40	0.33	92
6			(A) (B)	2:1 2:1	Oil bath RT	30 2	45 98	1:1	100	2	94
7			(A) (B)	2:1 2:1	Oil bath RT	60 6	35 94	2:1	100	1	98
8			(A) (B)	2:1 2:1	RT RT	20 2	60 97	3:1	100	2	99
9			(A) (B)	2:1 2:1	Oil bath RT	30 3	50 94	2:1	100	1	96

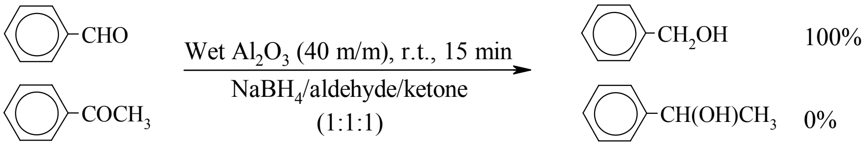
10			(A) (B)	2:1 1:1	RT RT	10 2	87 92	1:1	40	0.67	90
11			(A) (B)	2:1 1:1	RT RT	10 2	81 90	1:1	40	0.67	92
12			(A) (B)	2:1 1:1	RT RT	15 2	96 97	1:1	100	1	94
13			(A) (B)	2:1 1:1	RT RT	60 2	83 91	1:1	40	0.67	85
14			(A) (B)	2:1 1:1	RT RT	10 2	83 88	1:1	40	0.67	83
15			(A) (B)	2:1 1:1	Oil bath RT	10 1	88 98	2:1	100	2	98
16			(A) (B)	2:1 2:1	Oil bath RT	15 2	90 97	4:1	100	3	99
17			(A) (B)	2:1 2:1	Oil bath RT	30 3	48 96	4:1	100	3	98

[a]Method A: The reactions were carried out in the presence of wet Al_2O_3 (0.7 g, 40 % m/m) under solvent-free condition; Method B: The reactions were carried out in the presence of wet Al_2O_3 (0.7 g, 40 % m/m) and 0.4 mL of CH_3CN at room temperature in a solid-gel media; [b]The temperature of oil bath was 80-85 ºC; [c]Yield refer to isolated pure products; [d]The reactions were irradiated with microwaves (300 W) in the presence of Al_2O_3 (0.5 g) at the defined wet %; [e]The reaction was irradiated in the presence of wet Al_2O_3 (0.7 g, 40 % m/m) and 0.4 mL of CH_3CN for 2 min.

TABLE-3
REDUCTION OF CONJUGATED CARBONYL COMPOUNDS WITH $NaBH_4$/Wet Al_2O_3 SYSTEM UNDER SOLVENT-FREE, SOLID-GEL AND MICROWAVE IRRADIATION

Entry	Substrate	Product	Solvent-free and solid-gel					Microwave irradiation[d]			
			Method[a]	Molar ratio $NaBH_4$/subs.	Condition[b]	Time (min)	Yield (%)[c]	Molar ratio $NaBH_4$/subs.	Wet (%)	Time (min)	Yield (%)[c]
1			(A)	1.5:1	RT	15	95	1:1	40	0.67	98
			(B)	1:1	RT	1	97				
2			(A)	2:1	Oil bath	25	70	2:1	100	3	99
			(B)	1.5:1	RT	3	96				
3			(A)	2:1	Oil bath	20	35	3:1	100	3	93
			(B)	1.5:1	RT	5	98				
4			(A)	1.5:1	RT	15	92	1:1	40	0.5	92
			(B)	1:1	RT	2	94				
5			(A)	2:1	Oil bath	20	43	2:1	100	3	96
			(B)	1.5:1	RT	3	96				

[a]Method A: The reactions were carried out in the presence of wet Al_2O_3 (0.7 g, 40 % m/m) under solvent-free condition; Method B: The reactions were carried out in the presence of wet Al_2O_3 (0.7 g, 40 % m/m) and 0.4 mL of CH_3CN in a solid-gel media; [b]The temperature of oil bath was 80-85 ºC; [c]Yields refer to isolated pure products; [d]The reactions were irradiated with microwaves (300 W) in the presence of Al_2O_3 (0.5 g) at the defined wet %.



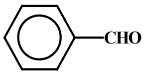
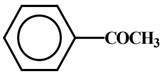
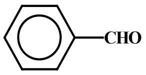
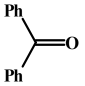
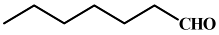
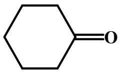
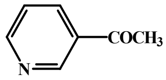
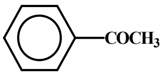
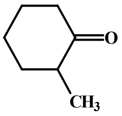
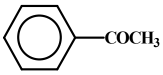
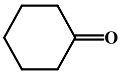
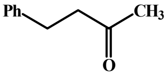
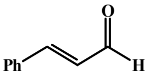
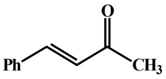
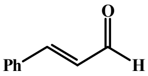
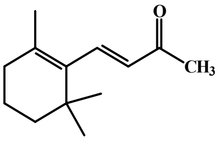
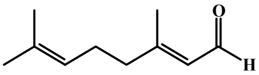
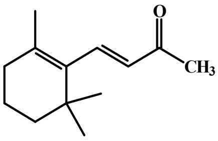
Scheme-III

Chemoselectivity of the reduction was excellent and benzyl alcohol was obtained as a sole product besides acetophenone as an intact material (Table-4, entry 1). The usefulness of this protocol was further examined with the reduction of benzaldehyde over benzophenone and heptanal *versus* cyclohexanone (entries 2,3). It is again observed that the chemoselectivity was perfect or nearly the so. In the next attempt, we applied this procedure for the reduction of 2 ketones such as 3-acetylpyridine or 2-methylcyclohexanone *versus* acetophenone and cyclohexanone over 4-phenyl-2-butanone (entries 4-6). It was found that 3-acetylpyridine, 2-methylcyclohexanone and cyclohexanone were reduced in a perfect selectivity. The chemoselective reduction of α,β-unsaturated enals and enones was investigated successfully with the selective reduction of cinnamaldehyde *versus* benzalacetone or β-ionone and citral over β-ionone (entries 7-9). Investigation of the results exhibited an excellent chemoselectivity for $NaBH_4$/wet Al_2O_3 (40 % m/m) system under solvent-free condition.

Reduction under microwave irradiation: Nowadays, microwave irradiation as an unconventional energy source has been widely used to accomplish many kinds of chemical reactions and numerous reviews and papers demonstrated its importance[19]. In this context and to explore the synthetic utility of $NaBH_4$/wet Al_2O_3 system in the reduction of carbonyl compounds, it is decided to couple the solvent-free protocol with microwave irradiation in order to study the influence of adsorbed water on the surface of alumina for transferring the electromagnetic energy to perform reduction reactions.

In this investigation, a household domestic microwave oven is used to perform reduction of benzaldehyde with 0.5 molar equivalent of $NaBH_4$ in the presence of wet Al_2O_3 (40 % m/m). The reduction was taken place effectively in 20 s under microwave irradiation (300 W). This observation led us to investigate the reducibility of aliphatic and aromatic aldehydes with $NaBH_4$/wet Al_2O_3 system under microwave irradiation. The reactions were carried out with 0.5-1.5 molar equivalents of $NaBH_4$ in the presence of wet Al_2O_3 (40-80 % m/m) under microwave irradiation (300 W). Completion of the reactions was taken place within 20-40 s and the corresponding primary alcohols were obtained in 86-99 % yields (Table-1). The reducibility of ketones including acyloins and α-diketones with $NaBH_4$/wet Al_2O_3 system was also examined under microwave irradiation. The reduction of acetophenone was taken place with one molar equivalent of $NaBH_4$ in the presence of wet Al_2O_3 (100 % m/m) under microwave irradiation (300 W). The reaction was completed

TABLE-4
CHEMOSELECTIVE REDUCTION OF ALDEHYDES AND KETONES WITH $NaBH_4$/Wet Al_2O_3 SYSTEM[a]

Entry	Substrate 1	Substrate 2	Molar ratio[b]	Time (min)	Conv. 1 (%)[c]	Conv. 2 (%)[c]
1			1:1:1	15	100	0
2			1:1:1	15	100	0
3			1:1:1	5	85	15
4			1.5:1:1	10	100	0
5			1.5:1:1	10	100	0
6			1.5:1:1	10	100	0
7			1.5:1:1	15	100	0
8			1.5:1:1	15	100	0
9			1.5:1:1	15	100	0

[a]The reactions were carried out in the presence of wet Al_2O_3 (0.7 g, 40 % m/m) at room temperature under solvent-free condition; [b]Molar ratio as $NaBH_4$/substrate 1/substrate 2; [c]Conversion refer to TLC monitoring and isolated pure products.

in 1 min and 1-phenylethanol was obtained in 97 % yield. The reduction of structurally different ketones was achieved perfectly with $NaBH_4$/ wet Al_2O_3 under microwave irradiation (Table-2). The results shows that generally using 1-2 molar equivalents of $NaBH_4$ in the presence of wet Al_2O_3 (40-100 % m/m) were the requirements for the complete reduction of ketones to their corresponding secondary alcohols in 83-99 % yields. Benzophenone probably because of its bulk hindrance had low efficiency after 5 min irradiation (Table-2, entry 1). When the mixture was irradiated under microwaves in a solid-gel media, benzhydrol was obtained in 99 % yield within 2 min. Acyloins and α-diketones were also reduced to *vicinal* diols using 2-4 molar equivalents of $NaBH_4$ in the presence of wet Al_2O_3 (100 m/m) under microwave irradiation within 2-3 min (Table-2).

The effect of microwave irradiation on the regioselective 1,2-reduction of α,β-unsaturated carbonyl compounds was examined with the reduction of cinnamaldehyde by $NaBH_4$/wet Al_2O_3 system. The reduction was carried out with one molar equivalent of $NaBH_4$ in the presence of wet Al_2O_3 (40 % m/m) within 40 s (Table-3). Cinnamyl alcohol was obtained in a perfect regioselectivity and yield. The possibility of this protocol was further examined with the 1,2-reduction of structurally different conjugated enals and enones. The reductions were accomplished by 1-3 molar equivalents of $NaBH_4$ in the presence of wet Al_2O_3 (40-100 % m/m) under microwave irradiation within 3 min. Table-3 shows that the corresponding allylic alcohols were obtained in a perfect regioselectivity and efficiency (92-99 %).

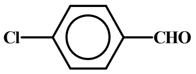
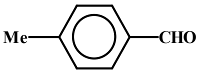
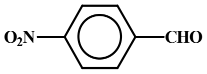
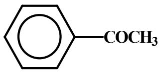
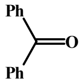
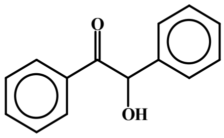
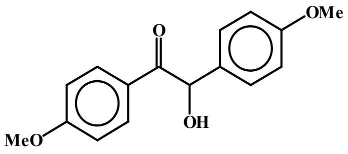
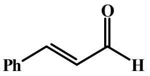
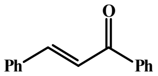
Comparison of present results with those reported by $NaBH_4$/dry Al_2O_3/microwave system[14] shows that in view points of the molar equivalents of $NaBH_4$, efficiency, rate and regioselectivity of reductions, present protocol is more efficient (Table-5).

The exact mechanism for the influence of water in wet Al_2O_3 is not clear. However, we think that the following factors may play a role in this acceleration: (i) The adsorbed water on the surface of Al_2O_3 can solubilize $NaBH_4$ and therefore fine dispersion of the reducing agent on the surface of alumina and subsequently more interaction with the substrate makes an acceleration; (ii) Al_2O_3 in the presence of water by showing a Lewis acidity character for the carbonyl group, makes this functional group susceptible for the hydride attack; (iii) The formation of an active new species on the surface of Al_2O_3 as aluminato-borohydride may be promote the reduction; (iv) Hydrolysis of the generated alkoxy-borate intermediate by the adsorbed water on the surface of alumina exhibits an acceleration.

Conclusion

In this paper, it is shown that the presence of water on the surface of alumina (wet Al_2O_3) effectively accelerates reduction of carbonyl compounds with $NaBH_4$ under solvent-free, solid-gel and microwave irradiation. At solvent-free condition reduction of aldehydes with $NaBH_4$/wet Al_2O_3 system was taken place fast and efficiently at room temperature. However, reduction of ketones was accomplished with low-moderate yields of products at 80-85 ºC. Aliphatic ketones showed higher efficiency at room temperature. In a solid-gel media reduction of carbonyl compounds was extremely accelerated using lower amounts of $NaBH_4$. The solvent-free reduction of carbonyl compounds by $NaBH_4$/wet Al_2O_3 system was investigated successfully under microwave irradiation (300 W). In the case of conjugated carbonyl compounds, the reductions were accomplished by $NaBH_4$/wet Al_2O_3 with excellent regioselectivity and efficiency under solvent-free, solid-gel and microwave irradiation. We think that in view points of high efficiency, chemo- and regioselectivity of the

TABLE-5
COMPARISON OF THE REDUCTION OF CARBONYL COMPOUNDS
WITH $NaBH_4$/Wet Al_2O_3 AND $NaBH_4$/DRY Al_2O_3 SYSTEMS
UNDER MICROWAVE IRRADIATION

		$NaBH_4$/Wet Al_2O_3[a]			$NaBH_4$/Dry Al_2O_3[14]		
Entry	Substrate	Molar ratio $NaBH_4$/ Subs.	Time (s)	Yield (%)	Molar ratio $NaBH_4$/ Subs.	Time (s)	Yield (%)
1		1:1	40	98	1:1	–	93
2		1:1	40	97	1:1	–	90
3		1:1	30	99	1:1	40	87
4		1:1	60	97	1:1	30	87
5		2:1	300	99	5:1	120	92
6		2:1	120	98	8:1	180	79
7		2:1	120	99	5:1	120	62
8		1:1	40	98[b]	1:1	–	90[b]
9		3:1	180	93[b]	8:1	–	60[b] 40[c]

[a]The present method; [b]1,2-Reduction; [c]1,4-Reduction.

reductions as well as the benefits of solid state reactions, $NaBH_4$/wet Al_2O_3 system could be a synthetically useful method for the reduction of carbonyl compounds.

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