Article

Fast and Efficient Method for Reduction of Carbonyl Compounds with NaBH$_4$/Wet SiO$_2$ Under Solvent Free Condition

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As reduções de compostos carbonilados estruturalmente diferentes, como aldeídos, cetonas, enais α,β-insaturados e enonas, α-dicetonas e acyloins foram realizadas eficientemente com borohidreto de sódio, na presença de SiO$_2$ úmido (30% m/m), sem solvente. As reações ocorreram em temperatura ambiente ou a 75-80 ºC, tendo-se obtido excelentes rendimentos dos produtos correspondentes. A redução quimiosseletiva de aldeídos na presença de cetonas foi obtida com êxito, usando-se este sistema de redução.

Reduction of structurally different carbonyl compounds such as aldehydes, ketones, α,β-unsaturated enals and enones, α-diketones and acyloins were accomplished efficiently by sodium borohydride in the presence of wet SiO$_2$ (30% m/m) under solvent free condition. The reactions were performed at room temperature or 75-80 ºC with high to excellent yields of the corresponding products. The chemoselective reduction of aldehydes over ketones was achieved successfully with this reducing system.

Keywords: reduction, NaBH$_4$, wet SiO$_2$, solvent free

Introduction

Reduction is one of the frequently used reactions in organic synthesis and a vast variety of reducing agents have been introduced for this achievement.[1] Among the powerful and mild reducing agents which have been developed for the reduction of functional groups, LiAlH$_4$ and NaBH$_4$ are the commonly used reagents in synthetic organic laboratories. Lithium aluminum hydride is an exceedingly powerful reducing agent capable of reducing practically all-organic functional groups. Consequently, it is quite difficult to apply this reagent for the selective reduction of multifunctional molecules. On the other hand, sodium borohydride is relatively mild reducing agent, primarily used for the reduction of reactive functional groups in protic solvents. Consequently the rate of reductions is sometimes slow and a relatively low chemoselectivity is accompanied with the reactions.

To control the reducing power of NaBH$_4$, hundreds of substituted boron hydrides have been reported in chemical literature and many of them are commercially available now. In fact, the progress in this field has been realized by: (*i*) substitution of the hydride(s) with other groups which

may exert marked steric and electronic influences upon the reactivity of the substituted complex ion,[2] (*ii*) variation in the alkali metal cation and metal cation in the complex hydride,[3] (*iii*) concurrent cation and hydride exchange,[4] (*iv*) use of ligands to alter behavior of the metal hydrides,[5] (*v*) combination of borohydrides with metal, metal salts, Lewis acids, mixed solvent systems or some other agents,[6,7] (*vi*) changing of the cation to quaternary and phosphonium borohydrides,[8] and finally (*vii*) use of polymers and solid beds for supporting the hydride species.[9] In this context, we extensively reviewed the applications of modified hydroborate agents in organic synthesis.[5,10] On the other hand, the economical demands and the existing state of environment have generated a need for paradigm shift to perform chemical reactions by using ecologically safe reagents or media. Organic reactions, carried out in dry media, have recently received careful attention with advantages (a simply work-up procedure, energy saving, avoidance of solvent waste, dangers and toxicity) over the solution reactions.[11]

Literature review shows that though the reduction of carbonyl compounds as an important synthetic methodology was usually achieved with NaBH$_4$ in protic solvents, this transformation under solvent free condition has been rarely investigated: e.g., the solid state reduction

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of ketones has been achieved by their mixing with sodium borohydride and storing the mixture in a dry box for five days. 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 $NaBH_4$ (tenfold) is a serious limitation for this method.[12] Reduction of aldehydes and ketones with $NaBH_4$ impregnated on neutral Al_2O_3 under microwave irradiation has also been reported. Though the reported method is fast for reduction of aldehydes, in the case of ketones the need for large amounts of $NaBH_4$ (eightfold); and moderate yields of products are the major limitations.[13] In another report, microwave-assisted reduction of acetophenone and ethyl phenyl ketone with $NaBH_4$ in the presence of celite, SiO_2, $MgSO_4$ and cellulose under solvent free condition was investigated, however, the behavior of other ketones was not further documented.[14]

These days, wet SiO_2 as an inexpensive and readily available reagent has frequently been used in synthetic organic laboratories.[15] Therefore, to expand the above-mentioned strategies and in our continuous efforts to develop modified hydroborate agents,[5,6] herein, we report a mild and convenient method for fast and efficient reduction of carbonyl compounds to their corresponding alcohols with $NaBH_4$/wet SiO_2 under solvent free condition.

Results and Discussion

As it was mentioned, the solid state reduction of carbonyl compounds can be achieved by $NaBH_4$ in the presence or absence of mineral solid supports under normal condition or microwave irradiation with some facilities and limitations. However, literature review did not show any application for such reduction in the presence of wet SiO_2 and the subsequent investigation of water influence as a wet species on the rate of reductions. Therefore, we decided to study wet SiO_2 (a convenient and readily available reagent) as a new media to carry out reduction of carbonyl compounds with $NaBH_4$ under solvent free condition.
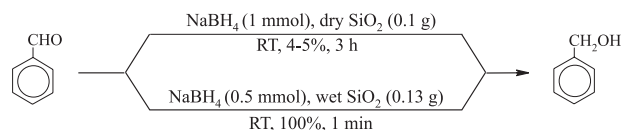
Scheme 1.

Our preliminary experiments showed that reduction of benzaldehyde as a model compound with one molar equivalent of $NaBH_4$ in the presence of dry SiO_2 (0.1 g) under solvent free condition took place with 4-5% conversion after 3 h at room temperature. However, when this reaction was carried out in the presence of wet SiO_2, prepared by simply mixing a small amount of water with SiO_2, the rate of reduction was dramatically accelerated and the reaction was completed in 1 min, while the lower amount of reducing agent was required for the complete conversion without using any solvent, additives or energy sources (Scheme 1) (Table 1).

These results prompted us to investigate the optimum reaction conditions for the influence of water accompanied with SiO_2 on this transformation. We examined a set of experiments on the reduction of benzaldehyde and acetophenone as model compounds with $NaBH_4$ under solvent free condition (Table 1). The results showed that the reduction of benzaldehyde (1 mmol) with 0.5 molar equivalent of $NaBH_4$ in the presence of 10, 20 and 30% m/m wet SiO_2 (0.1 g SiO_2) was efficient. However, the influence of 30% m/m wet SiO_2 showed a faster reduction rate and therefore it was selected as the best for the reduction of aldehydes. We then applied this optimal condition for the reduction of structurally different aliphatic and aromatic aldehydes. The reactions were carried out generally with 0.5 molar equivalent of $NaBH_4$ in the presence of 30% m/m wet SiO_2 in solid state at room temperature. All reactions were completed in less than 3 min with high to excellent yields of the corresponding primary alcohols (93-99%) (Table 2).
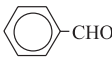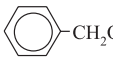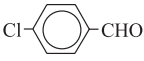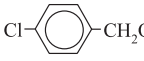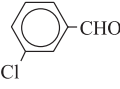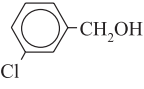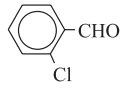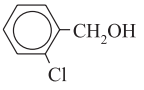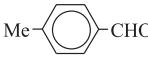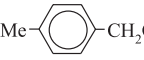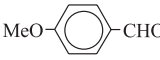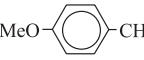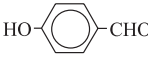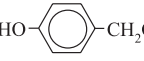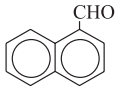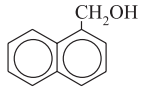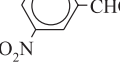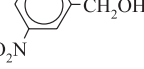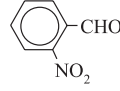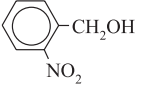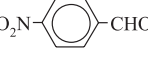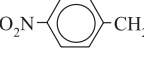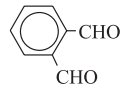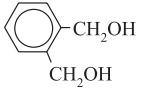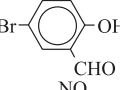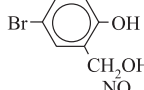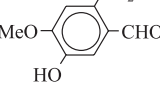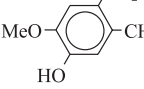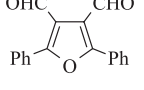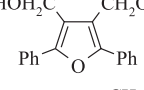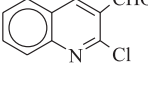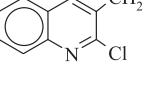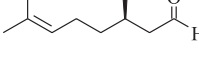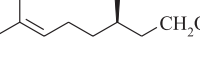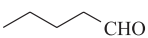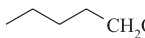
Next, we turned our attention to the reduction of ketones with the experiment in which acetophenone was used as a

Table 1. Optimization of reaction conditions and wet SiO_2 in the reduction of benzaldehyde and acetophenone with $NaBH_4$ under solvent free condition

Entry	Reaction components	Molar ratio	Media	Condition	time (min)	Conversion (%)
1	$PhCHO/NaBH_4$	(1:1)	Dry SiO_2	RT	3 h	4-5
2	$PhCHO/NaBH_4$	(1:0.5)	Wet SiO_2 (10% m/m)	RT	20	100
3	$PhCHO/NaBH_4$	(1:0.5)	Wet SiO_2 (20% m/m)	RT	8	100
4	$PhCHO/NaBH_4$	(1:0.5)	Wet SiO_2 (30% m/m)	RT	1	100
5	$PhCHO/NaBH_4$	(1:0.3)	Wet SiO_2 (30% m/m)	RT	40	80
6	$PhCOCH_3/NaBH_4$	(1:2)	Dry SiO_2	Oil bath[a]	12 h	8-10
7	$PhCOCH_3/NaBH_4$	(1:2)	Wet SiO_2 (10% m/m)	Oil bath[a]	3 h	70
8	$PhCOCH_3/NaBH_4$	(1:2)	Wet SiO_2 (20% m/m)	Oil bath[a]	1.5 h	95
9	$PhCOCH_3/NaBH_4$	(1:2)	Wet SiO_2 (30% m/m)	Oil bath[a]	42	100
10	$PhCOCH_3/NaBH_4$	(1:1)	Wet SiO_2 (30% m/m)	Oil bath[a]	3 h	50

[a] Temperature of oil bath was 75-80 °C.

Table 2. Reduction of aldehydes to alcohols with NaBH$_4$ in the presence of wet SiO$_2$[a]

Entry	Substrate	Product	Molar ratio NaBH$_4$ / Substrate	time (s)	Yield (%)[b]	mp or bp (°C) Found	mp or bp (°C) Reported
1			0.5:1	60	97	204-205	205[21]
2			0.5:1	120	95	70-71	70-72[21]
3			0.5:1	50	96	236	237[21]
4			0.5:1	40	95	70-71	69-71[21]
5			0.5:1	180	98	60-61	59-61[21]
6			0.5:1	240	99	259	259[21]
7			1:1	180	93	120-122	118-122[21]
8			0.5:1	40	97	62-63	61-63[21]
9			0.5:1	60	97	31-32	30-32[21]
10			1:1	50	94	70-72	70-72[21]
11			0.5:1	30	95	93-94	92-94[21]
12			0.5:1	60	99	64-65	63-65[21]
13			0.5:1	45	98	111-112	110-112[21]
14			0.5:1	20	95	—	—
15			0.7:1	50	98	—	—
16			0.3:1	10	97	—	—
17			0.5:1	240	93	225-226	225-226[21]
18			0.5:1	60	93	137-138	136-138[21]

[a] All reactions were performed in the presence of wet SiO$_2$ (0.13 g, 30% m/m) under solvent free condition at room temperature. [b] Yields refer to isolated pure products.

model compound. Inherent low reactivity of ketones relative to aldehydes made to perform reduction reactions in drastic conditions: the reductions were performed with 2 molar equivalents of $NaBH_4$ in the presence of 10, 20 and 30% m/m wet SiO_2 at 75-80 °C under solvent free condition. Wet SiO_2 (30% m/m) showed a faster reduction rate and the reaction was completed in 42 min (Table 1). To clarify the influence of water in wet SiO_2 on this reduction, we carried out solid state reduction of acetophenone with 2 molar equivalents of $NaBH_4$ in the presence of dry SiO_2 for 12 h at 75-80 °C. In this case, the progress of reduction was very poor (8-10%) and the unreacted starting material was recovered from the reaction mixture.

The applicability of this reducing system was further explored with the reduction of structurally different aliphatic and aromatic ketones by using 1.5-2 molar equivalents of $NaBH_4$ in the presence of 30% m/m wet SiO_2 under solvent free condition at 75-80 °C. These reductions were also efficient and the reactions were completed within 3-42 min with high to excellent yields of the corresponding secondary alcohols (94-99%) (Table 3). The work-up procedure of reductions was easy: washing the reaction mixture with CH_2Cl_2 and then drying the solvent over anhydrous Na_2SO_4 gave the crude product alcohols for further purification by a short column chromatography on silica gel.

The solid state condition, the easy procedure and the availability of reagents prompted us to investigate the applicability of this protocol for large scale purposes. Therefore, as a typical procedure, we examined reduction of benzaldehyde (5.31 g) with $NaBH_4$ (0.95 g) in the presence of wet SiO_2 (6.5 g, 30% m/m) at room temperature under solid state condition. We observed that the reaction was completed in 30 min and benzyl alcohol was obtained in 94% yield. This result obviously shows the general application of this protocol for any practical or industrial purposes.

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[16] and various hydroborate agents have been reported for this achievement.[5,6,17] Since under the defined conditions, reduction of aldehydes and ketones with sodium borohydride in the presence of wet SiO_2 is temperature-dependent, therefore, we thought that this system can have a chemoselectivity towards reduction of aldehydes over ketones. This fact was demonstrated with the selective reduction of benzaldehyde over acetophenone using 0.5 molar equivalent of $NaBH_4$ at room temperature under solvent free condition (Scheme 2).

The chemoselectivity of the reduction was perfect and benzyl alcohol was obtained as the sole product besides
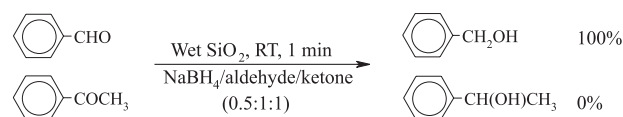
Scheme 2.

acetophenone as an intact material (Table 4). The usefulness of this procedure was further examined with the reduction of benzaldehyde in the presence of benzophenone. We also observed that the aldehyde is reduced exclusively. In the next attempt, we applied this protocol for the reduction of two ketones such as 9-fluorenone or 4-phenyl-2-butanone versus acetophenone; here, it was found that 9-fluorenone and 4-phenyl-2-butanone were reduced in high chemoselectivity (Table 4).

Regioselective 1,2-reduction of α,β-unsaturated aldehydes and ketones is an easy way to obtain allylic alcohols which are important synthetic materials in organic synthesis. This achievement with $NaBH_4$ is highly solvent-dependent and generally the results do not show a useful regioselectivity.[18] Regioselective 1,2-reduction of conjugated carbonyl compounds is usually achieved using modified hydroborate agents, which are formed (*i*) by the replacement of hydride with sterically bulky substituents or electron-withdrawing/releasing groups in order to discriminate between the structural and electronic environments of the carbonyl groups, (*ii*) by changing the metal cation, (*iii*) by combination with metal salts and mixed solvents, and (*iv*) finally immobilization on polymeric supports.[5,6,8,18,19] In addition, the use of non-free hydridic reductants has also been reported for this transformation.[20]
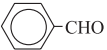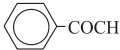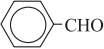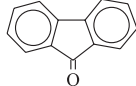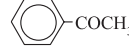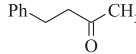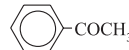
The usefulness of this reducing system was further investigated with the regioselective 1,2-reduction of α,β-unsaturated carbonyl compounds. We first examined reduction of cinnamaldehyde as a model compound with sodium borohydride in the presence of wet SiO_2 (30% m/m). The reduction took place with one molar equivalent of $NaBH_4$ at room temperature under solvent free condition. The reaction was completed in 1 min with a perfect regioselectivity. The product cinnamyl alcohol was obtained in high yield (Table 5). This procedure was also applied for the reduction of citral within 4 min at room temperature and geraniol was obtained regioselectively in 95% yield. In the next attempt, we examined solid state reduction of conjugated enones with $NaBH_4$ in the presence of wet SiO_2. Less reactivity of conjugated ketones relative to aldehydes made to perform reductions with 2 molar equivalents of $NaBH_4$ at 75-80 °C. The results showed that our procedure was also regioselective and efficient. Regioselective 1,2-reductions of benzalacetone, benzalacetophenone and β-ionone were achieved successfully with high to excellent yields of the corresponding allylic alcohols (Table 5). The chemo-

Table 3. Reduction of ketones to alcohols with NaBH$_4$ in the presence of wet SiO$_2$[a]

Entry	Substrate	Product	Molar ratio NaBH$_4$/Subs.	time (min)	Yield (%)[b]	mp or bp(°C) Found	mp or bp(°C) Reported
1	Ph–C(=O)–Ph	Ph–CH(OH)–Ph	2:1	17	99	66-67	65-67[21]
2	–COCH$_3$	–CH(OH)CH$_3$	2:1	42	97	203/745 mmHg	204/745[21] mmHg
3	Br–COCH$_3$	Br–CH(OH)CH$_3$	2:1	14	97	35-37	33-37[22]
4	MeO–COCH$_3$	MeO–CH(OH)CH$_3$	2:1	30	98	95/1 mmHg	95/1[23] mmHg
5	–COCH$_3$, Cl	–CH(OH)CH$_3$, Cl	2:1	11	94	123/14 mmHg	121-123/14[22] mmHg
6	Cl–COCH$_3$	Cl–CH(OH)CH$_3$	2:1	15	95	81-82/1 mmHg	80-82/1[22] mmHg
7	–COCH$_3$ (biphenyl)	–CH(OH)CH$_3$ (biphenyl)	2:1	8	99	96-97	95-97[23]
8	fluorenone	fluorenol	2:1	10	99	153-154	153-154[21]
9	1-indanone	1-indanol	2:1	10	97	52-54	50-54[21]
10	benzosuberone	alcohol	2:1	15	95	100-101	100-101[24]
11	Cl, O, OH, CH$_3$	Cl, OH, OH, CH$_3$	2:1	3	94	—	—
12	cyclohexanone	cyclohexanol	1.5:1	3	95	160-161	160-161[21]
13	4-phenylcyclohexanone	4-phenylcyclohexanol	2:1	7	98	57-58	58[25]
14	Ph–CH$_2$CH$_2$–CO–CH$_3$	Ph–CH$_2$CH$_2$–CH(OH)–CH$_3$	2:1	7	97	130/16 mmHg	128-130/16[26] mmHg
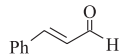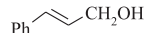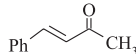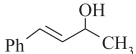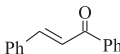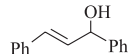
[a] All reactions were performed in the presence of wet SiO$_2$ (0.13 g, 30% m/m) in an oil bath at 75-80 °C under solvent free condition. [b] Yields refer to isolated pure products.

Table 4. Comptetitive reduction of aldehydes and ketones with NaBH$_4$ in the presence of wet SiO$_2$[a]

Entry	Substrate 1	Substrate 2	Molar ratio[b]	Condition	time (min)	Conv.1 (%)[c]	Conv.2 (%)[c]
1	Ph-CHO	Ph-COCH$_3$	0.5:1:1	RT	1	100	0
2	Ph-CHO	Ph$_2$C=O	0.5:1:1	RT	1	100	0
3	fluorenone	Ph-COCH$_3$	2:1:1	Oil bath[d]	10	92	15
4	Ph-CH$_2$CH$_2$-CO-CH$_3$	Ph-COCH$_3$	2:1:1	Oil bath[d]	7	98	3

[a] All reactions were performed in the presence of wet SiO$_2$ (0.13 g, 30% m/m) under solvent free condition. [b] Molar ratio as NaBH$_4$/ Substrate 1/ Substrate 2. [c] Conversions refer to TLC monitoring and isolated pure products. [d] Temperature of oil bath was 75-80 °C.

Table 5. Reduction of α,β-unsaturated carbonyl compounds with NaBH$_4$ in the presence of wet SiO$_2$[a]

Entry	Substrate	Product	Molar ratio NaBH$_4$/Substrate	Condition	time (min)	Yield (%)[b]	mp or bp (°C) Found	mp or bp (°C) Reported
1	Ph-CH=CH-CHO	Ph-CH=CH-CH$_2$OH	1:1	RT	1	96	249-250	250[27]
2	Ph-CH=CH-CO-CH$_3$	Ph-CH=CH-CH(OH)-CH$_3$	2:1	Oil bath[c]	9	97	39-41	39-41[28]
3	Ph-CH=CH-CO-Ph	Ph-CH=CH-CH(OH)-Ph	2:1	Oil bath[c]	15	98	56-57	55-57[27]
4	citral	citral-CH$_2$OH	1:1	RT	4	95	231-232	231-232[27]
5	β-ionone	β-ionol	2:1	Oil bath[c]	16	97	107/3 mmHg	107/3[27] mmHg

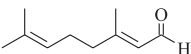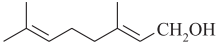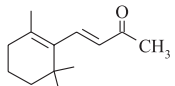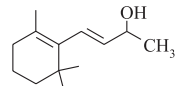[a] All reactions were performed in the presence of wet SiO$_2$ (0.13 g, 30% m/m) under solvent free condition. [b] Yields refer to isolated pure products. [c] Temperature of oil bath was 75-80 °C.

and regioselectivity of this procedure were demonstrated by a competitive reduction of cinnamaldehyde over benzalacetone (Table 6 and Scheme 3). In addition, selective reduction of cinnamaldehyde and citral over β-ionone were achieved successfully with this reducing system at room temperature under solid state condition (Table 6).

Synthetic utilities of vicinal diols are well known and their preparations from reduction of α-diketones and acyloins have attracted a great deal of attention. In this context, we decided to examine solid state reduction of α-

diketones and acyloins with NaBH$_4$ in the presence of wet SiO$_2$. Reduction of α-diketones to their vicinal diols took place by 1.5 molar equivalents of NaBH$_4$ in the presence of wet SiO$_2$ (30% m/m) under solvent free condition at 75-80 °C. The product diols were obtained in excellent yields
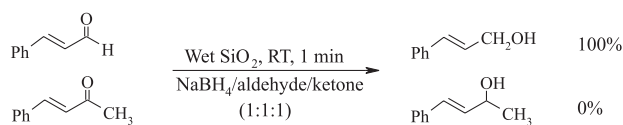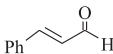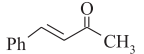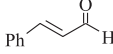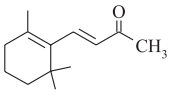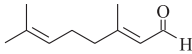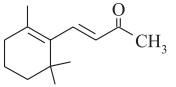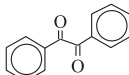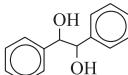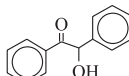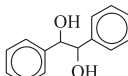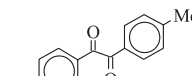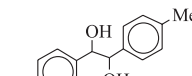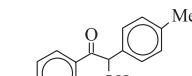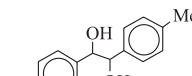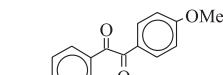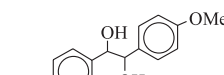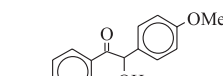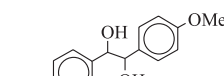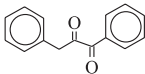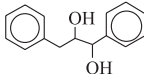
Scheme 3.

Table 6. Comptetitive reduction of conjugated carbonyl compounds with NaBH$_4$ in the presence of wet SiO$_2$[a]

Entry	Substrate 1	Substrate 2	Molar ratio[b]	time (min)	Conv.1 (%)[c]	Conv.2 (%)[c]
1			1:1:1	1	100	0
2			1:1:1	1	100	0
3			1:1:1	4	100	0

[a] All reactions were performed in the presence of wet SiO$_2$ (0.13 g, 30% m/m) at room temperature under solvent free condition. [b] Molar ratio as NaBH$_4$/Substrate 1/Substrate 2. [c] Conversions refer to TLC monitoring and isolated pure products.

Table 7. Reduction of acyloins and α-diketones with NaBH$_4$ in the presence of wet SiO$_2$[a]

Entry	Substrate	Product	Molar ratio NaBH$_4$/Substrate	time (min)	Yield (%)[b]	mp or bp (°C) Found	mp or bp (°C) Reported
1			1.5:1	2	98	135-137	134-137[21]
2			1:1	1.5	98	135-137	134-137[21]
3			1.5:1	3	99	—	—
4			1:1	2.4	98	—	—
5			1.5:1	4	97	—	—
6			1:1	3	95	—	—
7			1.5:1	3	96	63-64	63-64[28]

[a] All reactions were performed in the presence of wet SiO$_2$ (0.13 g, 30% m/m) in an oil bath at 75-80 °C under solvent free condition. [b] Yields refer to isolated pure products without any assumptions of their simple diastereoselectivity (*syn* or *anti*).

and all attempts to reduce α-diketones into acyloins were unsatisfactory by this reducing system (Table 7). Reduction of acyloins to vicinal diols was also achieved successfully by NaBH$_4$/wet SiO$_2$ (30% m/m) in solid state. Using one molar equivalent of NaBH$_4$ at 75-80 °C was the requirement for the excellent yields of the corresponding products (Table 7). No assumptions on the simple diastereoselectivity (syn or anti) of the products were made.

The influence of water in wet SiO$_2$ for the dramatic acceleration in reduction reactions with sodium borohydride is not clear, but we think that the following factors may play a role in this acceleration: (*i*) The adsorbed water on the surface of SiO$_2$ can solubilize sodium borohydride and therefore lead to fine dispersion of reducing agent on the surface of silica gel to do more interaction with the substrate; (*ii*) SiO$_2$ in the presence of water with shows a Lewis acidity character and then more interaction with the carbonyl group, make this functional group susceptible for the hydride attack; (*iii*) In our experiments we observed that wet SiO$_2$ in the

presence of $NaBH_4$ extremely reacts with the liberation of hydrogen gas. Therefore, we think that the generated molecular hydrogen synergistically with the hydride attack or with the formation of active new species on the surface of SiO_2 as silica-borohydride accelerates the rate of reduction; (*iv*) The borate intermediate which is produced by the reaction of borohydride and the carbonyl group can be hydrolyzed by the adsorbed water on the surface of silica gel and subsequently shows acceleration on the rate of reduction.

Conclusions

In this investigation, we have shown that the presence of small amounts of water accompanied with SiO_2 as wet SiO_2 (30% m/m) dramatically accelerates the rate of reduction of structurally different carbonyl compounds such as aldehydes, ketones, α,β-unsaturated enals and enones, α-diketones and acyloins with sodium borohydride under solvent free condition. Reduction of aldehydes was carried out at room temperature and reduction of ketones at 75-80 ºC. The chemoselective reduction of aldehydes over ketones was achieved successfully with this reducing system. Regioselectivity of this system was also investigated with exclusive 1,2-reduction of conjugated carbonyl compounds to their corresponding allylic alcohols in high to excellent yields. The usefulness of this protocol was further shown with the reduction of α-diketones and acyloins to their vicinal diols in shorter reaction times and excellent yields. Therefore, we think that in considering high efficiency, chemoselectivity and a perfect regioselectivity which have been achieved by this reducing system as well as the advantages of solid state reactions such as a simply work-up procedure, saving of energy, avoidance of solvent waste, dangers and toxicity, this procedure can be attractive for a synthetically useful addition to the present methodologies.

Experimental

All reagents and substrates were purchased from commercial sources with the best quality and were used without further purification. SiO_2 was used in the form of silica gel 60 (70-230 mesh ASTM) and was purchased from Merck company. IR and ^{1}H NMR spectra were recorded on Thermo Nicolet Nexus 670 FT-IR and Bruker Avance DPX-300 MHz spectrometers, respectively. The products were characterized by a comparison with authentic samples (melting or boiling points) and their ^{1}H 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 aldehydes with $NaBH_4$ in the presence of wet SiO_2

In a round-bottomed flask (5 mL) charged with SiO_2 (0.1 g), H_2O (0.03 g) was poured into SiO_2 and the mixture was stirred with a magnetic stirrer to produce wet SiO_2 (0.13 g, 30% m/m). Benzaldehyde (0.106 g, 1 mmol) was then added to the prepared wet SiO_2 and the resulted mixture was stirred for an additional 5 min. Afterward $NaBH_4$ (0.019 g, 0.5 mmol) as a fine powder was added to the mixture and was stirred for 1 min at room temperature. The progress of 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 (3×6 mL) and the combined washing solvents were dried over anhydrous Na_2SO_4. Evaporation of the solvent and a short column chromatography of the resulted crude material over silica gel (eluent; CCl_4/Et_2O: 5/2) gave the pure colorless liquid benzyl alcohol (0.l05 g, 97%, Table 2).

A procedure for large scale reduction of benzaldehyde with $NaBH_4$ in the presence of wet SiO_2

In a round-bottomed flask (50 mL) charged with SiO_2 (5 g), H_2O (1.5 g) was poured into SiO_2 and the mixture was stirred with a magnetic stirrer to produce wet SiO_2 (6.5 g, 30% m/m). Benzaldehyde (5.31 g, 0.05 mol) was then added to the prepared wet SiO_2 and the resulted mixture was stirred for an additional 5 min. Afterward $NaBH_4$ (0.95 g, 0.025 mol) was added to the mixture and was stirred for 30 min at room temperature. The progress of reaction was monitored by TLC (eluent; CCl_4/Et_2O: 5/2). After completion of the reaction, the mixture was washed three times with CH_2Cl_2 (3×25 mL) and the combined washing solvents were dried over anhydrous Na_2SO_4. Evaporation of the solvent and a short column chromatography of the resulted crude material over silica gel (eluent; CCl_4/Et_2O: 5/2) gave the pure colorless liquid benzyl alcohol (5.08 g, 94%).

A typical procedure for reduction of ketones with $NaBH_4$ in the presence of wet SiO_2

According to the previous procedure, in a round-bottomed flask (5 mL) charged with wet SiO_2 (0.13 g, 30% m/m), benzophenone (0.182 g, l mmol) was added to wet SiO_2 and the resulted mixture was stirred with a magnetic stirrer for an additional 5 min. $NaBH_4$ (0.076 g, 2 mmol) as a fine powder was then added to the mixture and was continued to stirring in an oil bath at 75-80 ºC for 17 min. TLC was monitored the progress of reaction (eluent; CCl_4/Et_2O: 5/2). At the end of reaction and cooling to room temperature, the mixture was washed three times with

CH_2Cl_2 (3×6 mL) and the combined washing solvents were dried over anhydrous Na_2SO_4. Evaporation of the solvent and a short column chromatography of the resulted crude material over silica gel (eluent; CCl_4/Et_2O: 5/2) gave the pure white crystalline benzhydrol (0.182 g, 99%, Table 3).

A typical procedure for competitive reduction of aldehydes over ketones with NaBH₄ in the presence of wet SiO₂

In a round-bottomed flask (5 mL) charged with wet SiO_2 (0.13 g, 30% m/m), benzaldehyde (0.106 g, 1 mmol) and acetophenone (0.12 g, l mmol) were added to wet SiO_2 and the resulted mixture was stirred with a magnetic stirrer for 5 min. $NaBH_4$ (0.019 g, 0.5 mmol) as a fine powder was then added to the mixture and was continued to stirring at room temperature. After 1 min, the mixture was washed three times with CH_2Cl_2 (3×6 mL) and the combined washing solvents were dried over anhydrous Na_2SO_4. Evaporation of the solvent and a short column chromatography of the resulted crude material over silica gel (eluent; CCl_4/Et_2O: 5/2) gave the pure liquid benzyl alcohol as a sole product of reduction and acetophenone as an intact material (Table 4).

A typical procedure for regioselective 1,2-reduction of conjugated carbonyl compounds with NaBH₄ in the presence of wet SiO₂

To a round-bottomed flask (5 mL) charged with wet SiO_2 (0.13 g, 30% m/m), cinnamaldehyde (0.132 g, 1 mmol) was added to wet SiO_2 and the resulted mixture was stirred with a magnetic stirrer for 5 min. $NaBH_4$ (0.037 g, 1 mmol) as a fine powder was then added to the mixture and was stirred for an additional 1 min at room temperature. The progress of reaction was monitored by TLC (eluent; CCl_4/Et_2O: 5/2). After completion of the reaction, the mixture was washed three times with CH_2Cl_2 (3×6 mL) and the combined washing solvents were dried over anhydrous Na_2SO_4. Evaporation of the solvent and a short column chromatography of the resulted crude material over silica gel (eluent; CCl_4/Et_2O: 5/2) gave the pure yellowish liquid cinnamyl alcohol (0.l29 g, 96%, Table 5).

A typical procedure for reduction of α-diketones and acyloins with NaBH₄ in the presence of wet SiO₂

To prepared wet SiO_2 (0.13 g, 30% m/m) in a round-bottomed flask (5 mL), benzil (0.21 g, l mmol) was added and the resulted mixture was stirred with a magnetic stirrer for 5 min. $NaBH_4$ (0.056 g, 1.5 mmol) as a fine powder was then added to the mixture and was stirred for an additional 2 min in an oil bath at 75-80 ºC. TLC was monitored the progress of reaction (eluent; CCl_4/Et_2O: 5/2). After completion of the reaction and cooling to room temperature, the mixture was washed three times with CH_2Cl_2 (3×6 mL) and the combined washing solvents were dried over anhydrous Na_2SO_4. Evaporation of the solvent and a short column chromatography of the resulted crude material over silica gel (eluent; CCl_4/Et_2O: 5/3) gave the pure white crystalline hydrobenzoin (0.21 g, 98%, Table 7).

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