

Wet THF as a Suitable Solvent for a Mild and Convenient Reduction of Carbonyl Compounds with $NaBH_4$

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$NaBH_4$ in wet THF can readily reduce varieties of carbonyl compounds such as aldehydes, ketones, conjugated enones, acyloins, and α-diketones to their corresponding alcohols in good to excellent yields. Reduction reactions were performed at room temperature or under reflux condition. In addition, the chemoselective reduction of aldehydes over ketones was accomplished successfully with this reducing system.

Reduction of carbonyl compounds is one of the most ubiquitous reactions in organic synthesis. The discovery of $NaBH_4$ in 1942 brought about revolutionary changes in this area. Although sodium borohydride has been known as a mild reducing agent, it is still a useful reagent for the reduction of aldehydes and ketones in alcoholic solvents.[1] However, it should be pointed out that, in spite of its great convenience, this reagent suffers from certain limitations: e.g., essential need to use polar and protic solvents, limited number of functional groups that can be reduced, the sometimes low reaction rate, and a low selectivity between carbonyl compounds. This situation made it desirable to develop means for controlling the reducing power of such a reagent. Therefore, controlling the reducing power of sodium borohydride has been one of the main interests for organic chemists over many years. In fact, advances in this field have been realized by: a) 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] b) variation in the alkali metal cation and metal cation in the complex hydride which would alter the reducing power of the reagent;[3] c) by concurrent cation and hydride exchange;[4] d) use of ligands to alter behavior of the metal hydrides;[5] e) combination of borohydrides with metal, metal salts, Lewis acids, and some other agents;[6] f) changing the cation to quaternary and phosphonium borohydrides;[7] and finally, g) use of polymers or solid beds for supporting the hydride species.[8] The preparation and application of modified hydroborate agents in organic synthesis have been reviewed extensively.[5d,9]

Performing of the reductions with $NaBH_4$ in protic solvents, especially MeOH, is the commonly used procedure.[1a,b,10a,b] However, the presence of some drawbacks for this reducing agent in protic solvents has led the chemists to use aprotic systems[10c] or mixtures of protic–aprotic solvent systems[10d–i] for different reduction purposes. In addition, to reach the desired selectivity and efficiency in the reductions with $NaBH_4$ while raising the solubility behavior of reaction components, research groups were also attracted to apply wet-protic[10j–l] and wet-aprotic[10m–r] solvent systems as efficient media for reduction of functional groups.

In spite of the convenient selectivity and efficiency of the reductions with $NaBH_4$ in aprotic solvent systems relative to protic ones and the well-known study,[1] performing the reductions under wet-aprotic solvent systems has been less investigated and there are only a few reports in this area, e.g., the kinetic study of reduction of carbonyl compounds was reported with $NaBH_4$ in H_2O, DMSO, or their mixture as a solvent.[10m] The chemoselective reduction of diarydisulfides,[10n] and selective reduction of nitroalkenes[10o] in wet THF and reduction of azides in wet toluene[10q] were also reported with $NaBH_4$. In addition, the reduction of esters in a mixture of H_2O–dioxane[10p] and phenylalanine ethyl ester in H_2O–THF[10r] are other reports which have dealt with this reducing agent. So, in the line of our outlined strategies and our ongoing attention to the development of new modified hydroborate agents in organic synthesis, here we report an extensive and efficient protocol for reduction of varieties of carbonyl compounds with $NaBH_4$ under wet THF conditions.

Results and Discussion

Reduction of Aldehydes and Ketones. Transformation of aldehydes and ketones to their alcohols is one of the easiest ways for the preparation of alcohols in organic synthesis.[1] Hydride transferring agents such as lithium aluminum hydride and sodium borohydride are the reagents commonly used for these purposes. $LiAlH_4$ as a powerful reducing agent shows poor selectivity for the reduction of multifunctional molecules. On the other hand, $NaBH_4$ is a mild reducing agent and is used for the reduction of a few organic functional groups with some restrictions, which were mentioned above. To overcome the limitations and to facilitate reduction reactions of sodium borohydride with desired selectivity and efficiency, many improvements such as new combination systems of $NaBH_4$ have been announced in the literature.[5d,9] $NaBH_4$ in mixed solvents, especially MeOH-containing systems,[10d–f,h,i,l] has been used for some reduction purposes; however, for the reduction of carbonyl compounds under wet-aprotic solvent systems, as far as we know, there are only two reports.[10m,11] In addition to the kinetic study of reduction of carbonyl compounds in wet DMSO,[10m] very recently, this transformation has been also

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Table 1. Optimization of Reaction Conditions and Water Amount as a Co-solvent in the Reduction of Benzaldehyde and Benzophenone with $NaBH_4$

Entry	Reaction components Molar ratio	Solvent/mL	Condition	Time/min	Conversion/%
1	PhCHO/$NaBH_4$ (1:1)	Dry THF (3 mL)	RT	80	100
2	PhCHO/$NaBH_4$ (1:1)	Dry CH_3CN (3 mL)	RT	90	100
3	PhCHO/$NaBH_4$ (1:0.5)	THF–H_2O (3:0.05 mL)	RT	20	100
4	PhCHO/$NaBH_4$ (1:0.5)	THF–H_2O (3:0.1 mL)	RT	5	100
5	PhCHO/$NaBH_4$ (1:0.5)	THF–H_2O (3:0.2 mL)	RT	4	100
6	PhCHO/$NaBH_4$ (1:0.5)	THF–H_2O (3:1 mL)	RT	2	100
7	PhCHO/$NaBH_4$ (1:0.4)	THF–H_2O (3:0.1 mL)	RT	15	100
8	PhCHO/$NaBH_4$ (1:0.25)	THF–H_2O (3:0.05 mL)	RT	3 h	90
9	PhCHO/$NaBH_4$ (1:0.5)	CH_3CN–H_2O (3:0.1 mL)	RT	10	100
10	PhCOPh/$NaBH_4$ (1:2)	THF–H_2O (3:0.1 mL)	Reflux	50	100

reported with $NaBH_4$ in the presence of a polymeric solid–liquid phase transfer catalyst under wet THF condition.[11]

Our successes in finding new combination systems of $NaBH_4$[5b–g,12] and the lack of systematic information on the reduction of carbonyl compounds with sodium borohydride in a wet-aprotic solvent system without using any other agents, encouraged us to focus on this subject and to investigate the influence of water as a wet species in this transformation. Our preliminary experiments showed that reduction of benzaldehyde as a model compound with one molar amount of $NaBH_4$ took place within 80–90 min in dry THF or CH_3CN at room temperature. When this reaction was carried out in the presence of a small amount of water, however, the rate of reduction was dramatically accelerated and the reaction was completed in 5 min while using lower amounts of reducing agent (Table 1).

These results prompted us to investigate the optimum reaction conditions for the influence of water as a co-solvent. For the selection of appropriate solvent(s) and water amounts in such reductions, we examined a set of experiments on the reduction of benzaldehyde and benzophenone as model compounds with $NaBH_4$ in wet THF or CH_3CN (Table 1). The results showed that the reduction of benzaldehyde at room temperature with 0.5 molar amount of $NaBH_4$ in a mixture of 3:0.1, 3:0.2, and 3:1 mL of THF–H_2O was very efficient. However, we found that the existing of additional amounts of water in the reaction mixture decreased the selectivity in the reductions. Therefore, a mixture of THF–H_2O (3:0.1 mL) was selected as best for reduction of aldehydes (Table 1, entry 4). Reduction reaction in a mixture of CH_3CN–H_2O (3:0.1 mL) was also efficient but wet THF provided faster reaction rate. We then applied this optimal condition for the reduction of structurally different aliphatic and aromatic aldehydes. All the reactions were performed with 0.5–0.8 molar amounts of $NaBH_4$ at room temperature and their primary alcohols were obtained in high to excellent yields (83–99%) (Table 2).

Next, we turned our attention to the reduction of ketones with the experiment in which benzophenone was used as a model compound. The low reactivities of ketones relative to those of aldehydes led us to perform reduction reactions in a drastic condition: the reductions were performed with 2 molar amounts of $NaBH_4$ in refluxing wet THF or wet CH_3CN. Because of the faster reaction rate, a mixture of THF–H_2O (3:0.1 mL) was also a suitable solvent; the reaction was completed in 50 min (Table 1, entry 10). To clarify the influence of water in this reduction, we carried out reduction of benzophenone with 3 molar amounts of $NaBH_4$ under refluxing dry THF for 12 h. In this case, the progress of reduction was very poor (5–8%) and the unreacted starting material was recovered from the reaction mixture.

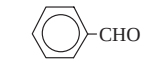
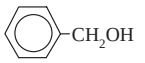
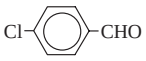
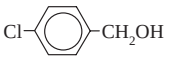
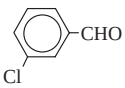
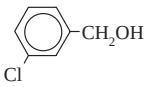
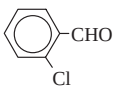
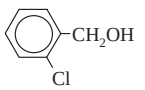
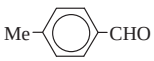
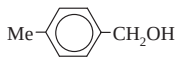
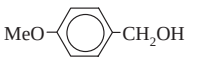
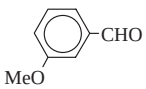
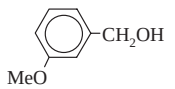
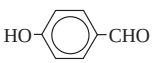
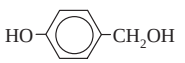
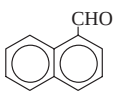
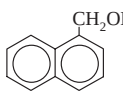
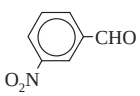
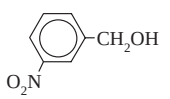
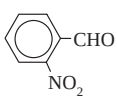
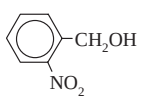
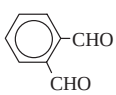
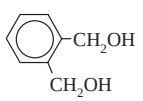
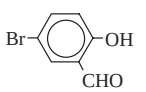
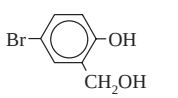
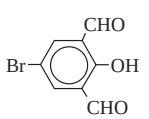
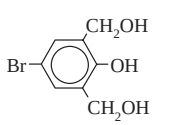
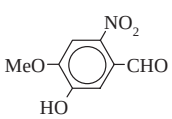
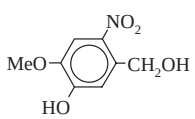
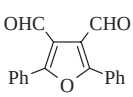
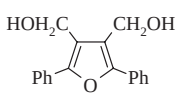
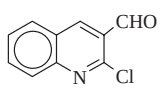
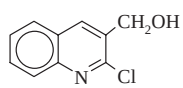
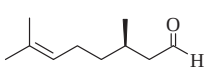
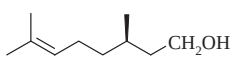
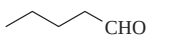
The utility of this reducing system was further explored with the reduction of structurally different aliphatic and aromatic ketones by using 2–3 molar amounts of $NaBH_4$ in THF–H_2O (3:0.1 mL) under reflux condition. Such reductions were also efficient and the corresponding secondary alcohols were obtained in high to excellent yields (85–99%) (Table 3). The work-up procedure of the reductions was simple: adding distilled water to the reaction mixture and then extracting with CH_2Cl_2 afforded the crude product alcohols for further purification by a short column chromatography on silica gel.

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[13] and numerous modified hydroborate systems have been reported for it.[5,7a,b,12–15] Since under the defined conditions, reduction of aldehydes and ketones with sodium borohydride under wet THF condition 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 in the presence of acetophenone using 0.5 molar amount of $NaBH_4$ at room temperature (Scheme 1).

The chemoselectivity of the reduction was perfect and benzyl alcohol was obtained as the sole product besides acetophenone as an intact material (Table 4). The usefulness of this process was further examined with the reduction of benzaldehyde in the presence of other ketones such as benzophenone or cyclohexanone. We also observed that either aldehyde is reduced exclusively or nearly so. In the next attempt, we applied this procedure 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).

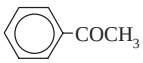
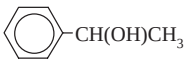
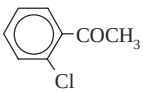
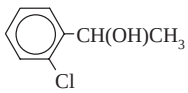
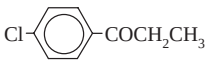
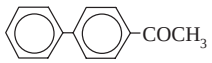
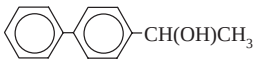
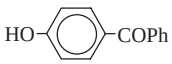
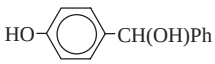
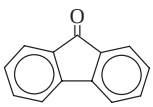
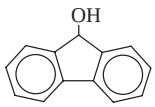
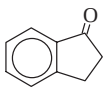
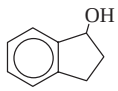
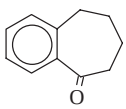
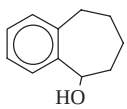
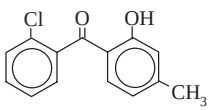
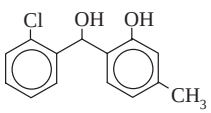
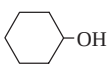
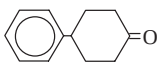
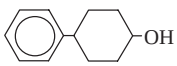
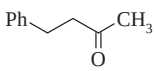
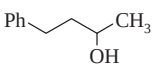
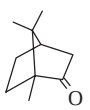
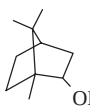
Regioselective 1,2-Reduction of Conjugated Carbonyl Compounds. Regioselective 1,2-reduction of α,β-unsaturated aldehydes and ketones to allylic alcohols is a widely utilized procedure in organic synthesis; considerable interest have

Table 2. Reduction of Aldehydes to Their Alcohols with $NaBH_4$ in Wet THF[a)]

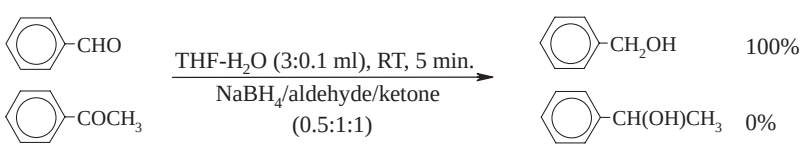
Entry	Substrate	Product	Molar ratio $NaBH_4$/Subs.	Time/min	Yield/%[b)]
1			0.5:1	5	94
2			0.5:1	3	96
3			0.5:1	2	96
4			0.5:1	2	95
5			0.5:1	8	98
6			0.5:1	12	99
7			0.5:1	6	95
8			0.8:1	20	93
9			0.5:1	3	96
10			0.5:1	3	91
11			0.5:1	2	94
12			0.7:1	3	94
13			0.5:1	2	96
14			0.7:1	3	92
15			0.5:1	2	95
16			0.7:1	3	96
17			0.5:1	1	96
18			0.5:1	15	90
19			0.5:1	5	83

a) All reactions were performed in THF–H_2O (3:0.1 mL) at room temperature. b) Yields refer to isolated pure products.

Table 3. Reduction of Ketones to Their Alcohols with $NaBH_4$ in Wet THF[a)]

Entry	Substrate	Product	Molar ratio $NaBH_4$/Subs.	Time/min	Yield/%[b)]
1			2:1	20	96
2			2:1	50	90
3			2:1	20	92
4			2:1	15	98
5			2:1	15	94
6			3:1	25	95
7			2:1	12	99
8			2:1	20	94
9			2:1	15	96
10			2:1	10	93
11			2:1	5	85
12			2:1	10	93
13			2:1	8	96
14			2:1	45	90

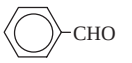
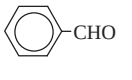
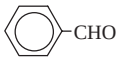
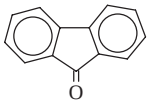
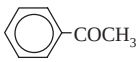
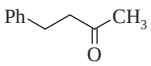
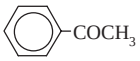
a) All reactions were performed in THF–H_2O (3:0.1 mL) under reflux condition. b) Yields refer to isolated pure products.



Scheme 1.

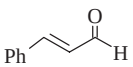
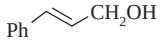
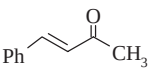
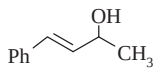
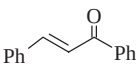
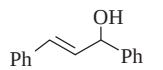
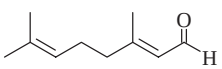
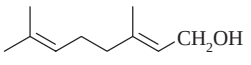
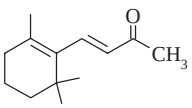
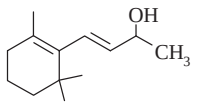
been shown in the development of various hydride transferring agents.[1] Reduction of unsaturated carbonyl compounds with sodium borohydride, one of the most widely utilized reducing agents, is highly solvent dependent and generally does not result in a useful regioselectivity.[10l,16,17] To control the reducing potential and selectivity of $NaBH_4$ into regioselective 1,2-reduction of conjugated enones, numerous hydroborate agents have been developed in the following ways: a) by the replacement of hydride(s) with sterically bulky substituents or electron-withdrawing/releasing groups in order to discriminate be-

Table 4. Competitive Reduction of Aldehydes and Ketones to Their Alcohols with $NaBH_4$ in Wet THF[a)]

Entry	Substrate 1	Substrate 2	Molar ratio[b)]	Condition	Time/min	Conv. 1/%[c)]	Conv. 2/%[c)]
1			0.5:1:1	RT	5	100	0
2			0.5:1:1	RT	5	100	0
3			0.5:1:1	RT	6	100	10
4			2:1:1	Reflux	15	100	12
5			2:1:1	Reflux	10	100	8

a) All reactions were performed in THF–H_2O (3:0.1 mL) at room temperature or under reflux condition. b) Molar ratio as $NaBH_4$/Subs. 1/Subs. 2. c) Conversions refer to TLC monitoring and isolated pure products.

Table 5. Reduction of Conjugated Carbonyl Compounds with $NaBH_4$ in Wet THF[a)]

Entry	Substrate	Product	Molar ratio $NaBH_4$/Subs.	Condition	Ratio 1,2:1,4	Time/min	Yield/%[b)]
1			1:1	RT	100:0	1	92
2			2:1	Reflux	100:0	8	95
3			2:1	Reflux	100:0	12	97
4			1:1	RT	100:0	12	90
5			2:1	Reflux	100:0	15	93

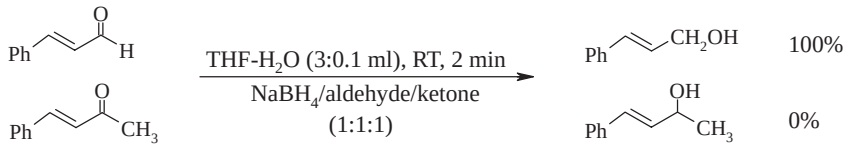
a) All reactions were performed in THF–H_2O (3:0.1 mL) at room temperature or under reflux condition. b) Yields refer to isolated pure products.

tween the structural and electronic environments of carbonyl groups;[17–20] b) combination with Lewis acids[21–23] and mixed solvent systems;[10l,16] c) use of transition metal hydroborates and their new modifications;[5c–e,24] d) use of quaternary ammonium and phosphonium tetrahydroborates;[7] and finally, e) immobilization on an anion exchange resin.[25]

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 under wet condition. The reduction reaction took place with one molar amount of $NaBH_4$ in THF–H_2O (3:0.1 mL) at room temperature. The reaction was completed in one minute with a perfect regioselectivity. The product cinnamyl alcohol was obtained in high yield (Table 5, entry 1). This procedure was also applied for the reduction of citral at room temperature and geraniol was obtained regioselectively in 90% yield. In the next attempt, we examined the reductions of conjugated enones with sodium borohydride under wet condition. The results showed that our procedure was also regioselective and efficient, but reduction reactions were performed by using 2 molar amounts of $NaBH_4$ under reflux condition. 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).

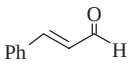
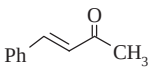
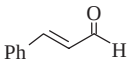
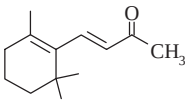
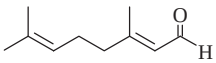
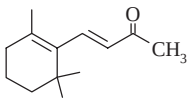
The chemo- and regioselectivity of this procedure were demonstrated by a competitive reduction of cinnamaldehyde over benzalacetone (Scheme 2). In addition, selective reduction of cinnamaldehyde and citral over β-ionone were achieved successfully with this reducing system at room temperature (Table 6).

Reduction of α-Diketones and Acyloins. Synthetic utilities of vicinal diols are well known and their preparations from the reduction of acyloins or α-diketones have attracted a great deal of attention. Reduction of α-diketones usually gives a mixture of α-hydroxy ketones and vicinal diols. Selective reduction of α-diketones to acyloins[26] or vicinal diols[27] can be undergone with some chemical or biochemical reagents. Re-



Scheme 2.

Table 6. Competitive Reduction of Conjugated Carbonyl Compounds with $NaBH_4$ in Wet THF[a)]

Entry	Substrate 1	Substrate 2	Molar ratio[b)]	Time/min	Conv. 1/%[c)]	Conv. 2/%[c)]
1			1:1:1	2	100	0
2			1:1:1	2	100	0
3			1:1:1	15	100	5

a) All reactions were performed in THF–H_2O (3:0.1 mL) at room temperature. b) Molar ratio as $NaBH_4$/Subs. 1/Subs. 2. c) Conversions refer to TLC monitoring and isolated pure products.

duction of α-diketones to vicinal diols with modified hydroborate agents is also a subject of interest[5c–e,12a–c] and this goal was easily achieved by $NaBH_4$ in wet THF. Mixtures of THF–H_2O (3:0.1 mL) are suitable solvents for the reduction of α-diketones to their vicinal diols with $NaBH_4$ (2 molar amounts) under reflux condition. Reduction reactions were performed efficiently in shorter reaction times (1–5 min) (92–98%) (Table 7). Under different conditions, our attempts to reduce α-diketones into acyloins were unsatisfactory and only vicinal diols were identified as the sole products.

In addition, reduction of acyloins to vicinal diols is also a subject of interest in organic synthesis. The applications of non-hydridic reductants[28] and modified hydroborate agents[5c–e,12a–c] have been also reported for such reduction. Using $NaBH_4$ (1 molar amount) in THF–H_2O (3:0.1 mL) also easily provided this transformation under reflux condition. Under the defined condition, conversion of benzoin to hydrobenzoin was efficiently performed in one minute (Table 7). Other acyloin compounds were also reduced readily to their corresponding vicinal diols in high to excellent yields with this reducing system (95–96%) (Table 7).

Conclusion

In this article we have shown that the presence of a small amount of water in THF dramatically accelerates the rates of reduction of carbonyl compounds with $NaBH_4$. Reduction of aldehydes was carried out at room temperature and reduction of ketones under reflux condition. 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 process was further shown with the reduction of acyloins and α-diketones to their vicinal diols in shorter reaction times and excellent yields. Therefore, we think that, in the aspects of high efficiency, chemoselectivity, and a perfect regioselectivity which have been achieved by this reducing system, this procedure can be attractive for a synthetically useful addition to the present methodologies.

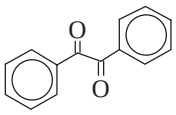
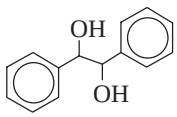
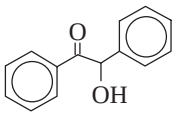
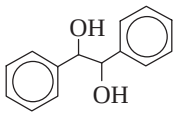
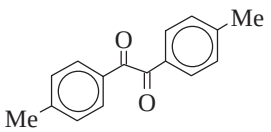
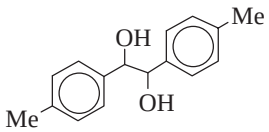
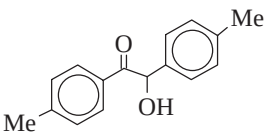
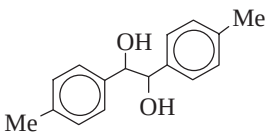
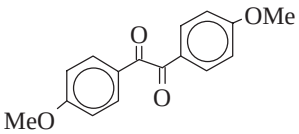
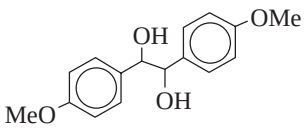
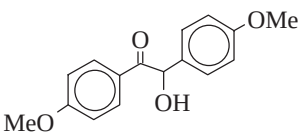
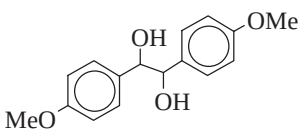
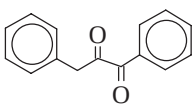
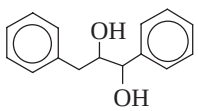
Experimental

General. All substrates and reagents were obtained from commercial sources with highest quality and were used without further purification. The products were characterized by a comparison with authentic samples (melting or boiling points) and their ^1H NMR or IR spectral data. Organic layers were dried with anhydrous sodium sulfate before concentration in vacuo. All yields refer to isolated pure products. TLC was applied for reaction monitoring and for the purity determination of substrates or products over silica gel PolyGram SILG/UV-254 plates.

A Typical Procedure for Reduction of Aldehydes to Alcohols with $NaBH_4$ in Wet THF. In a round-bottomed flask (10 mL) equipped with a magnetic stirrer and charged with a solution of benzaldehyde (0.106 g, 1 mmol) in THF–H_2O (3:0.1 mL), $NaBH_4$ (0.019 g, 0.5 mmol) was added. The resulting mixture was stirred magnetically at room temperature for 5 min. TLC monitored the progress of the reaction (eluent; CCl_4/Et_2O: 5/2). After completion of the reaction, distilled water (3 mL) was added to the reaction mixture and this solution was then stirred for an additional 5 min. The mixture was extracted with CH_2Cl_2 (3×8 mL) and dried over anhydrous sodium sulfate. Evaporation of the solvent and short column chromatography of the resulting crude material over silica gel (eluent; CCl_4/Et_2O: 5/2) afforded the pure liquid benzyl alcohol (0.102 g, 94% yield, Table 2).

A Typical Procedure for Reduction of Ketones to Alcohols with $NaBH_4$ in Wet THF. In a round-bottomed flask (10 mL) equipped with a magnetic stirrer and a condenser, a solution of 9-fluorenone (0.18 g, 1 mmol) in THF–H_2O (3:0.1 mL) was prepared and $NaBH_4$ (0.076 g, 2 mmol) was then added. The resulting mixture was heated magnetically to gentle reflux. TLC moni-

Table 7. Reduction of α-Diketones and Acyloins with $NaBH_4$ in Wet THF[a)]

Entry	Substrate	Product	Molar ratio $NaBH_4$/Subs.	Time/min	Yield/%[b)]
1			2:1	2	97
2			1:1	1	95
3			2:1	5	96
4			1:1	3	96
5			2:1	4	95
6			1:1	3	96
7			2:1	4	93

a) All reactions were performed in THF–H_2O (3:0.1 mL) under reflux condition. b) Yields refer to isolated pure products.

tored the progress of the reaction (eluent; CCl_4/Et_2O: 5/2). After completion of the reaction within 12 min, distilled water (3 mL) was added to the reaction mixture and it was then stirred for an additional 5 min. The mixture was extracted with CH_2Cl_2 (3 × 8 mL) and dried over anhydrous sodium sulfate. Evaporation of the solvent and short column chromatography of the resulting crude material over silica gel (eluent; CCl_4/Et_2O: 5/2) afforded the pure crystals of 9-fluorenol (0.18 g, 99% yield, Table 3).

A Typical Procedure for Competitive Reduction of Aldehydes and Ketones with $NaBH_4$ in Wet THF. In a round-bottomed flask (10 mL) equipped with a magnetic stirrer, a solution of benzaldehyde (0.106 g, 1 mmol) and acetophenone (0.12 g, 1 mmol) in THF–H_2O (3:0.1 mL) was prepared. $NaBH_4$ (0.019 g, 0.5 mmol) was then added and the mixture was stirred magnetically at room temperature. TLC monitored the progress of reaction. After 5 min, the reaction mixture was quenched by addition of distilled water (3 mL) and this mixture was then stirred for an additional 5 min. The mixture was extracted with CH_2Cl_2 (3 × 8 mL) and dried over anhydrous sodium sulfate. Evaporation of the solvent and short column chromatography of the resulting crude materials over silica gel (eluent; CCl_4/Et_2O: 5/2) afforded the pure liquid benzyl alcohol as a sole product, besides acetophenone as an intact material (Table 4).

A Typical Procedure for Regioselective 1,2-Reduction of Conjugated Carbonyl Compounds with $NaBH_4$ in Wet THF. In a round-bottomed flask (10 mL) equipped with a magnetic stirrer and a condenser, a solution of benzylideneacetone (0.146 g, 1 mmol) in THF–H_2O (3:0.1 mL) was prepared and $NaBH_4$ (0.076 g, 2 mmol) was then added. The resulting mixture was heated magnetically to gentle reflux. TLC monitored the progress of the reaction (eluent; CCl_4/Et_2O: 5/2). After completion of the reaction within 8 min, distilled water (3 mL) was added to the reaction mixture and this mixture was then stirred for an additional 5 min. The mixture was extracted with CH_2Cl_2 (3 × 8 mL) and dried over anhydrous sodium sulfate. Evaporation of the solvent and short column chromatography of the resulting crude material over silica gel (eluent; CCl_4/Et_2O: 5/2) afforded the pure liquid 4-phenyl-3-buten-2-ol (0.141 g, 95% yield, Table 5).

A Typical Procedure for Reduction of α-Diketones and Acyloins with $NaBH_4$ in Wet THF. In a round-bottomed flask (10 mL) equipped with a magnetic stirrer and charged with a solution of benzil (0.21 g, 1 mmol) in THF–H_2O (3:0.1 mL), $NaBH_4$ (0.076 g, 2 mmol) was added. The resulting mixture was stirred under reflux condition for 2 min. TLC monitored the progress of the reaction (eluent; CCl_4/Et_2O: 5/2). After completion of the reaction, distilled water (3 mL) was added to the reaction mix-

ture and this combination was then stirred for an additional 5 min. The mixture was extracted with CH_2Cl_2 (3×8 mL) and dried over anhydrous sodium sulfate. Evaporation of the solvent and short column chromatography of the resulting crude material over silica gel (eluent; CCl_4/Et_2O: 5/3) afforded the pure crystals of hydrobenzoin (0.21 g, 97% yield, Table 7).

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