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A simple and convenient method for the preparation of diborane from tetrabutylammonium borohydride and benzyl chloride for application in organic synthesis

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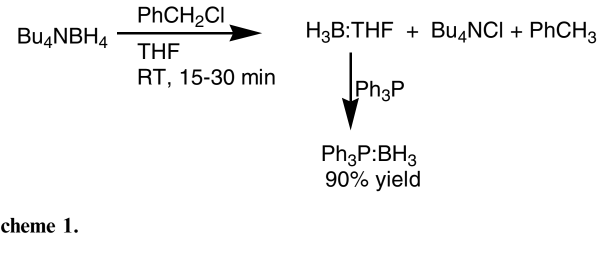
Abstract—Diborane is readily generated in situ at 25 °C in toluene using the $Bu_4NBH_4/PhCH_2Cl$ and Bu_4NBH_4/I_2 reagent systems. The reagent prepared in this way is used for the reduction of carbonyl compounds and hydroboration–oxidation of olefins to obtain the corresponding alcohols in good yields.

The reactive forms of reducing agents such as $LiBH_4$ and diborane require solvents like THF, dioxane and diglyme.[1–4] However, these solvents have a high tendency to form peroxides. Also, it is difficult to recover these solvents after aqueous work-up. Aqueous or alcoholic solvents can be used in the case of $NaBH_4$ but there are some limitations. Raber and Guida[5] reported the reduction of carbonyl compounds by tetrabutylammonium borohydride (Bu_4NBH_4) in dichloromethane. However, an excess of reagent and a long reaction time was required for the completion of the reduction. Recently, it was reported from this laboratory that the CBS (Corey, Bakshi, Shibata) oxazaborolidine catalyst could be easily prepared from borane generated using Bu_4NBH_4/CH_3I and α,α-diphenyl-2-pyrrolidine methanol (DPPM) in THF.[6] We have examined the use of other alkyl halides for the generation of diborane from Bu_4NBH_4, since methyl iodide is toxic. Accordingly, we carried out the reaction of Bu_4NBH_4 with benzyl chloride or iodine in toluene and diborane was readily generated in >90% yield in this way. We report here the reduction of aldehydes, ketones, carboxylic acids, acid chlorides and esters to the corresponding alcohols in good yields using these reagent systems. Also, the $Bu_4NBH_4/PhCH_2Cl$ reagent system is useful for the hydroboration–oxidation of olefins to give the corresponding alcohols in good yields.

The tetraalkylammonium borohydrides are readily soluble in organic solvents and they have low reactivity as reducing agents. It is considerably easier to handle these reagents compared to other metal borohydrides. For instance, they can be recrystallized from ethyl acetate.[7] We have observed that the addition of benzyl chloride to tetrabutylammonium borohydride in THF at 25 °C for 30 min followed by addition of Ph_3P gives $Ph_3P{:}BH_3$ (^{11}B NMR: δ −37.6 ppm) in 90% yield. This indicates the formation of borane in the reaction of Bu_4NBH_4 with $PhCH_2Cl$ (Scheme 1).

The $Bu_4NBH_4/PhCH_2Cl$ system also provides a convenient source of diborane gas. This method can be used for preparing various Lewis acid–BH_3 complexes. For example, $Ph_3P{:}BH_3$ can be prepared in 90% yield by passing B_2H_6, generated by $Bu_4NBH_4/PhCH_2Cl$ in toluene, through a solution of Ph_3P in THF. We have also observed that the diborane generated in this way



Scheme 1.

Keywords: Tetrabutylammonium borohydride; Reduction; Hydroboration; Oxidation.

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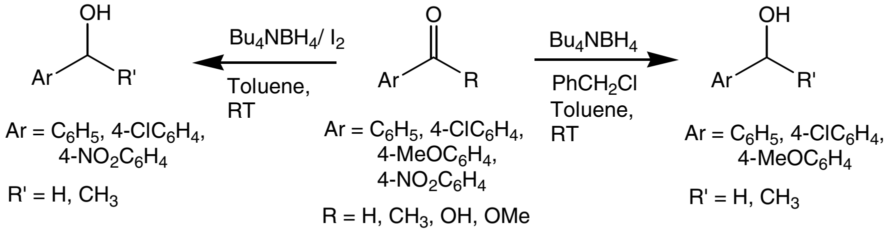
effectively reduces various functional groups such as aldehydes, ketones, carboxylic acids and acid chlorides readily at 25 °C (Scheme 2, Tables 1 and 2). However, esters required 12 h for completion of the reaction. The process is simple and amenable to scale-up.

We also observed that addition of a small amount of THF (2 mL) was advantageous. It is also very important to note that the tetraalkylammonium halide by-product can be readily removed and recovered from the reaction products. The recovered tetraalkylammonium halide can be used directly for the preparation of tetraalkylammonium borohydride, which makes this method economical.

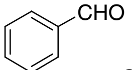
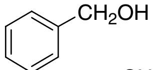
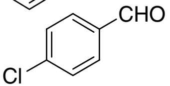
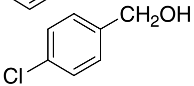
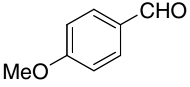
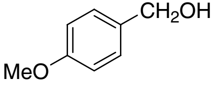
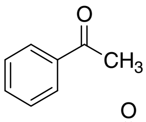
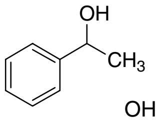
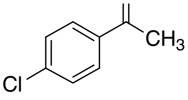
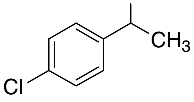
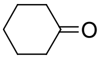
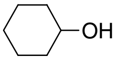
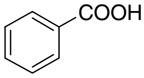
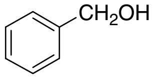
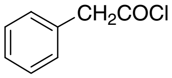
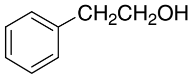
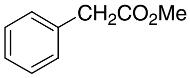
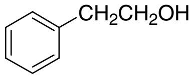
Diverse hydroborating agents such as BH_3:THF, BH_3:$S(CH_3)_2$, 9-BBN and thexylborane are available commercially. However, each has limitations and all are air sensitive.[11] Previously, hydroboration of olefins has been reported using tetrabutylammonium borohydride in chloroform under refluxing conditions.[12] The $R_4N^+BH_4^-/Me_3SiCl$ system has been used for the conversion of olefins to alcohols without any oxidizing agent.[13] We have observed that the $Bu_4NBH_4/PhCH_2Cl$ reagent system can be used for hydroborating olefins under ambient conditions in toluene/THF mixture and the corresponding alcohols were obtained in good yields after H_2O_2/OH^- oxidation (Scheme 3, Table 3).

In conclusion, the $Bu_4NBH_4/PhCH_2Cl$ and Bu_4NBH_4/I_2 reagent systems were used for reduction of various carbonyl compounds to the corresponding alcohols under mild conditions and in good yields (82–94%). These reagents are also useful for the hydroboration of



Scheme 2. Reduction of representative carbonyl compounds with $Bu_4NBH_4/PhCH_2Cl$ and Bu_4NBH_4/I_2.

Table 1. Reduction of representative carbonyl compounds with $Bu_4NBH_4/PhCH_2Cl$[8]

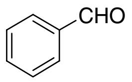
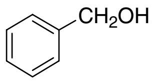
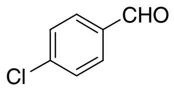
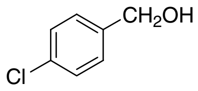
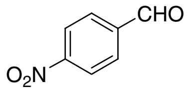
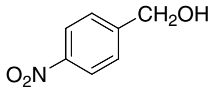
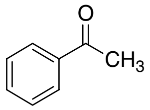
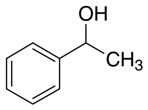
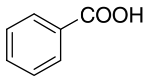
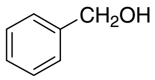
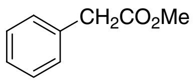
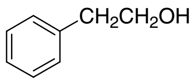
Entry	Substrate[a]		Time (min)	Product[b]		Yield[c] (%)
1		**1a**	15		**6a**	86
2		**1b**	15		**6b**	92
3		**1c**	30		**6c**	91
4		**2a**	15		**7a**	91
5		**2b**	15		**7b**	94
6		**2c**	90		**7c**	82
7		**3**	120		**6a**	89
8		**4**	15		**8**	90
9		**5**	720		**8**	82

[a] All the reactions were carried out on 5 mmol scale with 7 mmol of the $Bu_4NBH_4/PhCH_2Cl$ reagent.

[b] Products were characterized by IR, ^1H NMR, ^{13}C NMR and by comparison with reported data.[9]

[c] Yields of isolated products.

Table 2. Reduction of representative carbonyl compounds with Bu_4NBH_4/I_2[10]

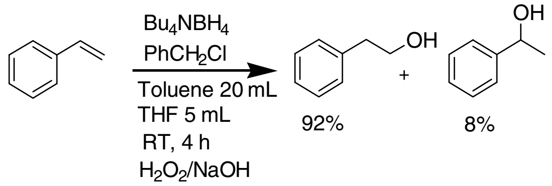
Entry	Substrate[a]		Time (min)	Product[b]		Yield[c] (%)
1		**1a**	15		**6a**	90
2		**1b**	15		**6b**	94
3		**1d**	15		**6d**	89
4		**2a**	15		**7a**	91
5		**3**	30		**6a**	89
6		**5**	720		**8**	86

[a] All the reactions were carried out on 5 mmol scale with 6 mmol of the Bu_4NBH_4/I_2 reagent.

[b] Products were characterized by IR, ^1H NMR, ^{13}C NMR and by comparison with reported data.[9]

[c] Yields of isolated products.

olefins to afford the corresponding alcohols in good yields (80–86%) after oxidation. Hence, this reagent system has considerable potential for further synthetic exploitation.



Scheme 3.

Acknowledgements

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References and notes

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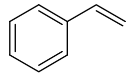
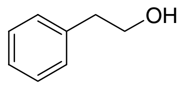
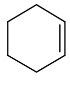
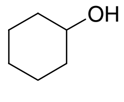
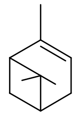
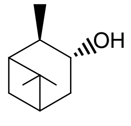
Table 3. Hydroboration of alkenes using $Bu_4NBH_4/PhCH_2Cl$[14]

Entry	Substrate[a]		Time (h)	Product[b]		Yield[c] (%)
1		**9**	3		**8**	86
2		**10**	4		**7c**	82
3		**11**	4		**12**	80

[a] All the reactions were carried out on 7.5 mmol scale with 9 mmol of the $Bu_4NBH_4/PhCH_2Cl$ reagent.

[b] Products were characterized by IR, ^1H NMR, ^{13}C NMR and by comparison with reported data.[9]

[c] Yields of isolated products.

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7. Brandstorm, A.; Junggren, U.; Lamm, B. *Tetrahedron Lett.* **1972**, *31*, 3173–3176.
8. *General procedure for the reduction of carbonyl compounds utilizing the* $Bu_4NBH_4/PhCH_2Cl$ *reagent system (Table 1)*: Bu_4NBH_4 (1.79 g, 7 mmol) in toluene (25 mL) at 25 °C, was treated with benzyl chloride (0.84 mL, 7 mmol) followed by slow addition of the substrate (5 mmol) to be reduced and the reaction mixture was stirred until the starting material had disappeared (TLC analysis). The mixture was carefully quenched with 2 N HCl (5 mL) and extracted with ether (3 × 25 mL). The combined organic extracts was washed with brine (25 mL) and dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure and the residue purified on a silica gel column to obtain the pure product using hexane/ethyl acetate (97:3) as eluent.
9. (a) De Vries, J. G.; Van Bergen, T. J.; Kellogg, R. M. *Synthesis* **1977**, 246–247; (b) Santaniello, E.; Farachi, C.; Manozcchi, A. *Synthesis* **1987**, 912–914; (c) Lane, C. F.; Daniels, J. J. *Org. Synth.* **1972**, *52*, 59; (d) Basavaiah, D.; Reddy, J. G.; Rao, K. V. *Tetrahedron: Asymmetry* **2004**, *15*, 1881–1888; (e) *CRC Handbook of Chemistry and Physics*, 85th ed., The Chemical Rubber Co.: Boca Raton, Florida, 2004.
10. *General procedure utilizing the* Bu_4NBH_4/I_2 *reagent system (Table 2)*: A mixture of Bu_4NBH_4 (1.54 g, 6 mmol) in toluene (15 mL) and THF (2 mL) in a two-neck RB flask was stirred at 25 °C for 5 min under an N_2 atmosphere and then cooled to 0 °C. I_2 (0.76 g, 3 mmol) dissolved in toluene (10 mL) was added slowly over 10 min. The substrate to be reduced (5 mmol) was added and the reaction mixture was warmed to 25 °C and stirred until the starting material had disappeared (TLC analysis). The mixture was carefully quenched with 2 N HCl (5 mL) and extracted with ether (3 × 25 mL). The combined organic extracts was washed with brine (25 mL) and dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography to afford the corresponding alcohol using hexane/ethyl acetate (97:3) as eluent.
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14. *General procedure for the hydroboration of olefins with the* $Bu_4NBH_4/PhCH_2Cl$ *reagent system (Table 3):* A mixture of Bu_4NBH_4 (2.31 g, 9 mmol) in toluene (20 mL) and THF (5 mL) was treated with benzyl chloride (1.1 mL, 9 mmol) and the mixture stirred for 5 min at 25 °C. Styrene (0.9 mL, 7.5 mmol) was added and the reaction mixture was further stirred for 4 h. Excess hydride was destroyed by the dropwise addition of 2 mL of water, followed by the addition of aqueous NaOH (5 mL). The reaction flask was cooled to 5 °C and the borinic acid was oxidized at 25 °C by slow addition of H_2O_2 (5 mL). The mixture was extracted with ether (3 × 25 mL) and the combined organic extracts washed with brine (25 mL) and dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography to afford the corresponding alcohol using hexane/ethyl acetate (97:3) as eluent.