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Rapid Defunctionalization of Carbonyl Group to Methylene with Polymethylhydrosiloxane−B(C_6F_5)$_3$[†]

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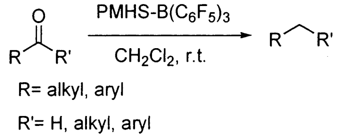
Abstract: The polymethylhydrosiloxane−B(C_6F_5)$_3$ combination is found to be a versatile carbonyl defunctionalization system under mild and rapid conditions. For the first time, B(C_6F_5)$_3$ has been used as a nonconventional Lewis acid catalyst to activate PMHS. Aromatic and aliphatic carbonyl compounds were effectively reduced to give the corresponding alkanes in high yields.

Defunctionalization of organic functional groups is an equally desirable achievement as compared to functionalization. There is a great need to discover new methodologies for defunctionalization especially for conversion of polyfunctional natural products to useful building blocks and bioactive molecules. Available literature speaks of only a few protocols for removal of a certain functional group, viz., the carbonyl group can be defunctionalized to a methylene group by Clemensen[1] or Wolff−Kishner reduction,[2] both of which require very drastic reaction conditions. The hydroxyl group can be removed by a Barton−McCombie procedure,[3] wherein highly malodorous xanthate and Bu_3SnH are required. Some other methods known in the literature include catalytic hydrogenation[4] and reaction involving use of PtO_2,[5] HI−phosphorus,[6] BH_3,[7] Zn/HCl/$HgCl_2$/H_2O,[8] $NaBH_4$−CF_3CO_2H,[9] $NaCNBH_3$−BF_3Et_2O,[10] LAH−$AlCl_3$,[11] Et_3SiH−BF_3Et_2O or CF_3CO_2H[12] besides a few others.[13] The majority of the known procedures used for defunctionalization are nonchemoselective and require harsh reaction conditions.

SCHEME 1



All of these methods, while offering some advantages, also suffer from disadvantages. Most of these methods are generally restricted to aromatic systems, are some times harsh and need a pyrophoric hydride source for reduction, require longer reaction hours with careful workup procedures for quenching the excess reagent, and are often associated with low yields. The usefulness of polymeric hydride source polymethylhydrosiloxane (PMHS), a coproduct of the silicone industry, as an excellent reduction reagent is well demonstrated in several recent publications.[14,15] The quest to find newer activators for this rather inert polymer resulted in identification of tris(pentafluorophenyl)borane as an excellent catalyst for activation of PMHS. B(C_6F_5)$_3$[16] is a relatively unexplored Lewis acid. This combination of PMHS−B(C_6F_5)$_3$ is found to be a versatile carbonyl defunctionalization system with very short reaction times (Scheme 1). Interestingly, this combination establishes a powerful "catalytic switch", viz., our initial studies using $ZnCl_2$ as an activator resulted in reduction of ketone to alcohol,[17] whereas this new catalyst promoted the reduction of the same substrate to methylene group.[18]

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[18] Polymethylhydrosiloxane in the presence of $AlCl_3$ reduced aryl carbonyl group to methylene; see ref 13d.

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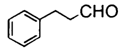
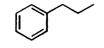
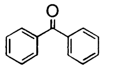
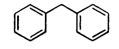
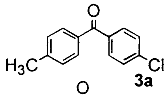
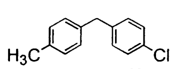
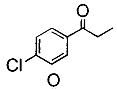
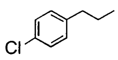
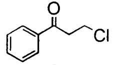
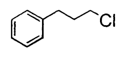
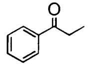
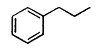
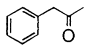
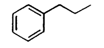
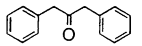
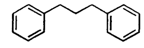
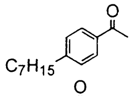
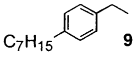
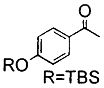
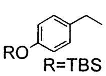
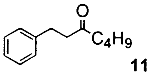
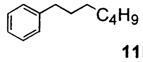
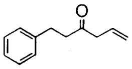
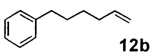
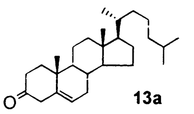
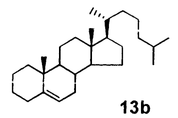
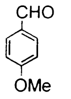
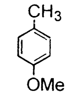
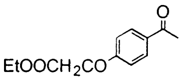
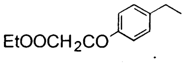
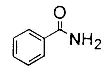
TABLE 1. Defunctionalization of Carbonyl Compounds

entry	substrate	product[a]	yield (%)[b]
1	 **1a**	 **1b**	90
2	 **2a**	 **2b**	88
3	 **3a**	 **3b**	85
4	 **4a**	 **4b**	83
5	 **5a**	 **5b**	84
6	 **6a**	 **1b**	86
7	 **7a**	 **1b**	89
8	 **8a**	 **8b**	88
9	 **9a**	 **9b**	82
10	 R=TBS **10a**	 R=TBS **10b**	90
	R= THP **10a'**	R= THP **10b'**	84
11	 **11a**	 **11b**	90
12	 **12a**	 **12b**	88
13	 **13a**	 **13b**	87
14	 **14a**	 **14b**	65
15	 **15a**	 **15b**	82
16	 **16a**	No Reaction	

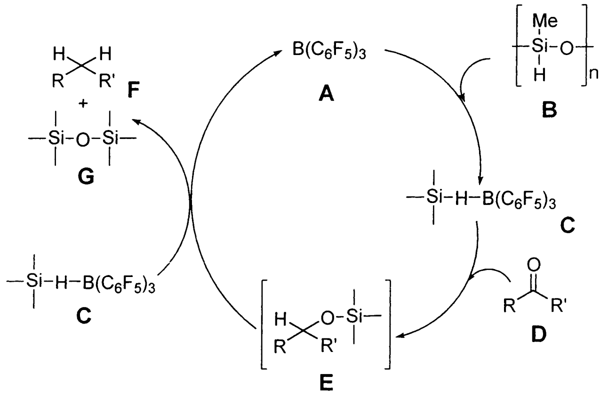
[a] All products were characterized by ^{1}H NMR and mass spectroscopy. [b] Isolated yields.

The procedure is very simple, and the reaction completion is indicated by the termination of effervescence (reaction times ranging from 5 to 20 min).

The earlier procedures involving PMHS as a hydride source for similar transformations required stoichiometric amounts of $AlCl_3$ as an activator[13d] and were limited to aryl carbonyl compounds, whereas in the case of Pd/C as an activator,[13f] double bonds are reduced to saturation instead of carbonyl reduction to a methylene group.

To establish the optimum reaction conditions, the reaction was first studied on readily available benzophenone **2a**, which was reduced to diphenylmethane **2b** in 88% isolated yield (entry 2) in 10 min. Another substrate, phenyl propanaldehyde **1a**, was reduced to *n*-propyl benzene **1b** in 90% yield (entry 1) in 8 min. These two examples demonstrate that not only benzylic ketone (a very easily reducible carbonyl) but also aliphatic aldehyde is suitable for the present protocol (Table 1). The halo-substituted aryl ketones **3a**, **4a**, and **5a** also were reduced to the corresponding methylene compounds **3b**, **4b**, and **5b** without affecting the aryl halide group (entries 3 and 4). The alkyl halide group (entry 5) is also unaffected under the present protocol. Aliphatic keto substrates **7a**, **8a**, **11a**, **12a**, and **13a** were also well suited to the present reaction conditions (entries 7, 8, and 11−13). Substrates **10a** and **10a′** demonstrate the selective reduction of ketone in the presence of TBS and THP ethers (entry 10), and substrate **12a** demonstrates inertness to olefin functionality (entry 12). The steroid substrate **13a** was reduced without isomerization of double bond in 87% yield requiring only 10 min (entry 13). The reduction of anisaldehyde **14a** to 4-methyl anisole **14b** was also achieved, albeit in low yield (65%). In the case of compound **15a** (entry 15), where both carbonyl and ester groups are present in the same substrate, selective reduction of carbonyl group to methylene is observed in 82% isolated yield. Attempts, however, to reduce benzamide **16a** to benzylamine (entry 16) were futile.

SCHEME 2



Hypothetically, we propose that complex **C**, which is formed from $B(C_6F_5)_3$ **A** and PMHS **B**, is responsible for the reduction of the carbonyl functionality.[16a] Complex **C** would react with carbonyl group **D** to form **E** (not isolated), which would produce the reaction product, hydrocarbon **F**, and silyl ether **G** and would regenerate **A** (Scheme 2). Coordination of carbonyl oxygen to boron for facile hydride transfer is also expected. There is literature precedence that Ph_3SiH and Et_3SiH also operate in a more or less similar pathway; the intermediate **E** is isolable when 1 equiv of Ph_3SiH is used,[16b] and longer reaction times (20 h) are required when Et_3SiH is used.[16c] However, in the case of PMHS, even though 1 equiv of reagent is used, the intermediate **E** could not be isolated, and instead 45−50% hydrocarbon conversion was observed within 5−20 min and the remaining starting carbonyl was isolated. This clearly indicates that PMHS is a more powerful reducing agent than Ph_3SiH and Et_3SiH in the presence of $B(C_6F_5)_3$.

In Summary, we have demonstrated for the first time, a direct and rapid conversion of carbonyl functionality to methylene group under very mild conditions with high yields. The procedure is very simple, and progress of the reaction can be monitored by visualization without any analytical support. The shorter reaction time in all the cases studied is an added advantage.

Experimental Section

General Methods. Silica gel used was 60−120 mesh. ^{1}H NMR spectra were obtained in $CDCl_3$ at 200 MHz. Chemical shifts are given in parts per million with respect to internal TMS, and J values are given in hertz. Methylene chloride was distilled over CaH_2 prior to use.

General Procedure for Defunctionalization of Carbonyl Group with PMHS−B(C_6F_5)$_3$. To a solution of carbonyl compound (1 mmol) in dry CH_2Cl_2 (5 mL) and tris (pentafluoro phenyl) borane (5 mol %) was slowly added polymethylhydrosiloxane (3 mmol) at room temperature. After 5−20 min, a vigorous effervescence (like foam) was observed. At this point, the solvent was evaporated and reaction mixture was dissolved in hexane and filtered through a silica gel pad using hexane. Evaporation of the volatiles afforded the reduction product in pure form.

Product Data. Spectral data of all products other than **9b**, **10b**, and **10b′** were identical with those of authentic samples.[19] Spectral data for products **9b**, **10b**, and **10b′** are shown below.

1-Ethyl-4-heptyl benzene (9b): ^{1}H NMR ($CDCl_3$) δ 0.82−0.98 (m, 6H), 1.18−1.38 (m, 6H), 1.5−1.68 (m, 4H), 2.2−2.7 (m, 4H), 7.02−7.3 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 14.07, 15.61, 22.68, 28.40, 29.21, 29.36, 31.62, 31.84, 35.57, 127.65, 128.29, 140.11, 141.34.; MS (m/z) 204 (M^+); HRMS (EI) m/z calcd for $C_{15}H_{24}$ 204.1878, found 204.1880.

4-Ethyl(*O-tert*-butyldimethylsilyl)phenol (10b): ^{1}H NMR ($CDCl_3$) δ 0.2 (s, 6H), 0.9 (s, 9H), 1.2 (t, $J = 6.3$ Hz, 3H), 2.6 (q, $J = 6.2$ Hz, 2H), 6.7 (d, $J = 8.3$ Hz, 2H), 7 (d, $J = 8.3$ Hz, 2H); ^{13}C NMR ($CDCl_3$) δ −4.44, 15.77, 18.18, 25.71, 28.04, 119.79, 128.59, 136.88, 153.46; MS (m/z) 236 (M^+); HRMS (EI) m/z calcd for $C_{14}H_{24}OSi$ 236.1596, found 236.1589.

4-Ethyl(*O*-tetrahydropyranyl)phenol (10b′): ^{1}H NMR ($CDCl_3$) δ 1.22 (t, $J = 6.1$ Hz, 3H), 1.50−1.98 (m, 6H), 2.48 (q, $J = 5.6$ Hz, 2H), 3.45 (t, $J = 8$ Hz, 1H), 3.78 (t, $J = 8$ Hz, 1H), 5.25 (s, 1H), 6.78(d, $J = 6.2$ Hz, 2H), 6.98(d, $J = 6.2$ Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 15.73, 18.83, 25.23, 27.99, 30.41, 61.95, 96.53, 116.40, 128.56, 137.32, 155.06; MS (m/z) 206(M^+); HRMS (EI) m/z calcd for $C_{13}H_{18}O_2$ 206.1306, found 206.1305.

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Supporting Information Available: ^{1}H NMR, ^{13}C NMR, and elemental composition data for compounds **9b**, **10b**, and **10b′**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(19) All authentic samples are commercially available except **3b**, **4b**, and **12b**. For **3b**, see: (a) Fukuzawa, S.; Tsuchimoto, T.; Hiyama, T. *J. Org. Chem.* **1997**, *67*, 151. **4b**: (b) Khosrovi, M.; Partchamazad, I.; Fakhrai, H. *Tetrahedron Lett.* **1975**, *16*, 2619. **12b**: (c) Gamage, S. A.; Smith, R. A. J. *Tetrahedron* **1990**, *46*, 2111.