A facile and chemoselective conjugate reduction using polymethylhydrosiloxane (PMHS) and catalytic $B(C_6F_5)_3$†

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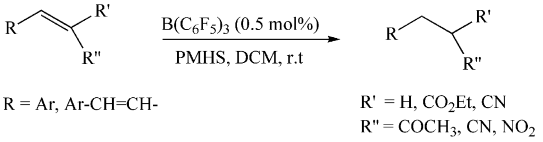
A highly chemoselective conjugate reduction of electron-deficient Michael acceptors, including α,β-unsaturated ketones, carboxylic esters, nitriles and nitro compounds with PMHS in the presence of catalytic $B(C_6F_5)_3$ is described.

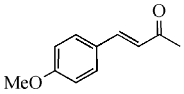
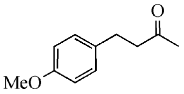
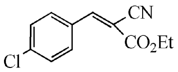
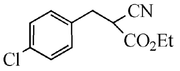
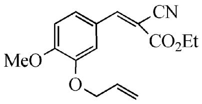
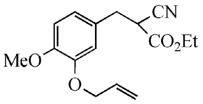
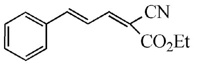
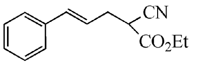
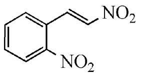
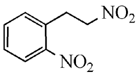
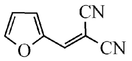
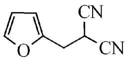
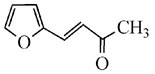
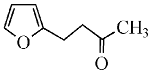
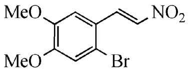
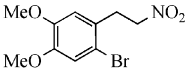
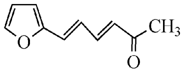
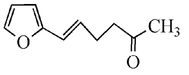
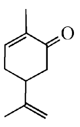
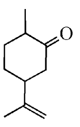
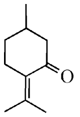
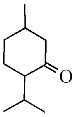
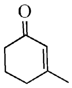
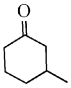
The regioselective reduction of the carbon–carbon double bond in conjugated systems is one of the most desirable transformations in organic synthesis. Despite the fact that a plethora of reducing reagents[1] are available for this operation, new reagents, especially the catalytic versions, are still highly desirable. Most of the procedures reported for the selective reduction of activated (conjugated) olefins involve a pyrophoric hydride source or an expensive catalyst. The metals and metallic hydrides include metals such as iron,[2] tin,[3] zinc,[4] nickel,[5] copper,[6] sodium, boron and aluminium.[7] The expensive catalytic systems include rhodium,[8] molybdenum,[9] cobalt,[10] palladium[11] and platinum.[12] However, the highly hydridic nature of most of these metals (primarily sodium, boron and aluminium and their metal hydrides, but also the platinum or palladium catalysts used for hydrogenation) limits their usefulness when high chemoselectivity is required. Undoubtedly, an eco-friendly, safe and economically viable protocol would be a welcome addition to the repertoire of existing methodologies. We have now made the serendipitous observation that the system based on polymethylhydrosiloxane[13,14] and $B(C_6F_5)_3$,[15,16] which we have thoroughly utilized for the reduction of carbonyl groups to the methylene functionality,[17] is a versatile reagent–catalyst combination for the chemo- and regioselective reduction of various conjugated olefins in excellent yields (Scheme 1). The results pertaining to this very interesting observation are documented herein.



Scheme 1

Initially, compound **1a** was treated with 2 eq. of PMHS and 0.5 mol% of $B(C_6F_5)_3$ and stirred for half an hour, providing the reduced product in 81% yield (Table 1). Encouraged by this result, several other electron-deficient Michael acceptors and

Table 1 Chemoselective reduction with $B(C_6F_5)_3$ using PMHS

Entry no.	Reactant **a**	Product[a] **b**	Time/h	Yield (%)[b]
1			0.5	81
2			3.0	75
3			4.0	82
4			4.0	85
5			10.0	76
6			1.5	89
7			1.0	83
8			12.0	80
9			2.0	85
10			0.5	78
11			0.5	71
12			0.5	74

[a] All new compounds were characterized by ^1H and ^{13}C NMR spectroscopy and mass spectrometry. [b] Isolated yields after column chromatography.

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† Electronic supplementary information (ESI) available: ^1H and ^{13}C NMR, IR, MS and HRMS spectral data for all new compounds. See DOI: 10.1039/b603610b

Table 2 Chemoselective reduction of compounds **1a** and **7a** with different Lewis acids using PMHS. A dash (—) indicates no reaction

	Entry **1**		Entry **7**	
Lewis acid	Time/h	Yield (%)	Time/h	Yield (%)
$B(C_6F_5)_3$	0.5	81	1.0	83
$AlCl_3$	10	—	10	—
$Ti(O^iPr)_4$	10	—	10	—
TMSOTf	10	10	10	20
$BF_3{\cdot}Et_2O$	10	—	10	—
$ZnCl_2$/Pd(0)	10	15	10	0
$ZrCl_4$	10	—	10	—
$CeCl_3{\cdot}7H_2O$	10	—	10	—

α,β-unsaturated ketones were reduced with good yields (Table 1).[18] Surprisingly, the reagent system was found to be highly chemoselective. For instance, the reagent system reduced selectively the α,β-carbon–carbon double bonds in the α,β,γ,δ-diunsaturated compounds **4a** and **9a**. Easily reducible aromatic halides (entries **2** and **8**), nitro compounds (entries **5** and **8**), nitriles (entry **6**) and terminal alkenes (entries **3** and **10**) were also tolerated by this unique reagent, which therefore provides an attractive alternative system for chemoselective reductions.

When attempts were made to improve the yields by increasing the amount of the catalyst $B(C_6F_5)_3$ to 1 mol%, the result was a complex mixture of saturated and unsaturated compounds, with partial reduction of the ketone moiety to the methylene functionality. For comparison, entries **1** and entry **7** were studied with several other Lewis acids [*viz.*, $AlCl_3$, $Ti(O^iPr)_4$, TMSOTf, $BF_3{\cdot}Et_2O$, $ZnCl_2$ (in the presence of 2.0 mol% $Pd(PPh_3)_4$ and 1 eq. $ZnCl_2$), $ZrCl_4$ and $CeCl_3{\cdot}7H_2O$] with PMHS, following a similar protocol (Table 2). The reaction with zinc chloride and TMSOTf looked promising but suffered from lower yields and longer reaction times than the PMHS–$B(C_6F_5)_3$ system. Even when the amount of the catalysts $AlCl_3$, $Ti(O^iPr)_4$, $BF_3{\cdot}Et_2O$, $ZrCl_4$ and $CeCl_3{\cdot}7H_2O$ were increased from 0.5 mol% to 20 mol%, the reactions did not proceed. Thus the PMHS–$B(C_6F_5)_3$ system was found to be superior than other PMHS–Lewis acid combinations.

In conclusion, PMHS along with a catalytic amount of $B(C_6F_5)_3$ was found to be a unique reagent system for the conjugate reduction of Michael acceptors. Currently, development of a chiral version[19] of this novel reagent and further studies on the scope of this reagent system are in progress.

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18 General experimental procedure: To a solution of the α,β-unsaturated ketone (2 mmol) in anhydrous methylene chloride (5 mL) was added $B(C_6F_5)_3$ (5 mg, 0.01 mmol) and PMHS (4 mmol), and the solution was stirred at room temperature for the appropriate time (monitored by TLC). Water was added to the reaction mixture, which was then extracted with methylene chloride (3 × 5 mL). The combined organic layers were washed with brine, dried over anhydrous sodium sulfate, concentrated *in vacuo*, and the crude product purified by flash chromatography.

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