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COMMUNICATION

Magnesium-catalysed hydroboration of aldehydes and ketones†‡

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The heteroleptic magnesium alkyl complex [CH{C(Me)NAr}$_2$-Mg^{n}Bu] (Ar = 2,6-^{i}Pr$_2$C$_6$H$_3$) is reported as a highly efficient pre-catalyst for the hydroboration of aldehydes and ketones with pinacolborane.

The reduction of aldehydes and ketones to primary and secondary alcohols is one of the most important transformations in organic chemistry. Brown's discovery of uncatalysed diborane reduction of aldehydes and ketones in 1939, thus, served to direct research from harsh metal hydride reagents with poor selectivity towards catalytic processes using milder silane and borane hydride sources.[1] To this end rather intense attention has been focused upon the metal-catalysed hydrosilylation of carbonyl derivatives[2] while a large body of recent work has been directed toward the enantioselective reduction of prochiral ketones with BH$_3$ in the presence of chiral oxazaborolane organocatalysts.[3] In contrast metal-catalysed hydroboration reactions are relatively uncommon and limited to a handful of catalyses using heavier group 13,[4] titanium[5] or ruthenium precatalysts.[6]

$$\text{(1)}$$

Research in our group and by others has centred around the application of well-defined catalysts of the heavier group 2 elements (Mg, Ca, Sr, Ba) towards a range of catalytic heterofunctionalisation reactions of unsaturated bonds.[7] We have recently shown that the magnesium alkyl complex [CH{C(Me)NAr}$_2$]Mg^{n}Bu] (Ar = 2,6-^{i}PrC$_6$H$_3$), **1**, catalyses the hydroboration-dearomatisation of pyridine derivatives with pinacolborane (HBpin)[8] *via* the likely intermediacy of Jones' previously reported hydridomagnesium species, **2**,[9] which is formed by B–H/C–Mg metathesis (eqn (1)). During the course of this study it was noted that 3-pyridinecarboxaldehyde underwent exclusive hydroboration at the carbonyl functionality.[8]

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Scheme 1 Catalytic benzophenone hydroboration reaction.

In this work we report extensions of this latter reactivity to the efficient magnesium-catalysed reduction of aldehydes and ketones with HBpin. We have also previously described that addition of one equivalent of HBpin to a solution of **1** at room temperature leads to stoichiometric formation of ^{n}BuBpin and a heteroleptic magnesium hydride species reminiscent of compound **2**,[9] which exists in equilibrium with a labile magnesium borohydride species of the anion [^{n}BuHBpin]$^-$.[8]

Repetition of this procedure and addition of one equivalent of benzophenone to the reaction mixture resulted in an orange solution, the ^{1}H NMR spectrum of which suggested the formation of a heteroleptic diphenylmethoxymagnesium species (compound **3** in Scheme 1 and see Supplementary Information†) displaying a characteristic 1H singlet at 5.98 ppm resulting from the insertion of the carbonyl functionality into the magnesium-hydride bond. Addition of further equivalents of HBpin and benzophenone provided complex **4** which was isolated and characterised by NMR spectroscopy and a single crystal X-ray diffraction experiment (Fig. 1).§ This latter analysis revealed compound **4** to be a bis(diphenylmethoxy)borato magnesium complex, which may also be formulated as an adduct between a molecule of compound **3** and the pinacolborate ester hydroboration
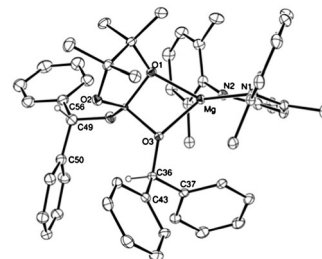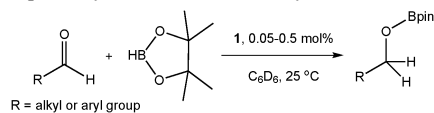

Fig. 1 ORTEP representation of **4**. Thermal ellipsoids at 20% probability. Isopropyl methyl groups and hydrogen atoms omitted except those attached to C(36) and C(49). Selected bond lengths (Å) and angles (°): Mg–N(1) 2.0561(19), Mg–N(2) 2.044(2), Mg–O(1) 1.9789(16), Mg–O(3) 2.0194(16); N(2)–Mg–N(1) 95.31(8), O(1)–Mg–O(3) 70.51(6).

Table 1 Scope of hydroboration of aldehydes with **1**

Entry	R	R′	Cat (mol%)	Time (h)	NMR yield (%)[a]	Isolated yield (%)
1a	Ph	H	—	2	2	—
1b	″	H	0.05	0.25	95	58
2	p-(CH=O)C$_6$H$_4$	H	0.05[b]	<1	>99[c]	97
3	2,4,6-Me$_3$C$_6$H$_2$	H	0.5	1.5	96	75
4	2-OMe-C$_6$H$_4$	H	0.5	1	97	88
5	9-anthracenyl	H	0.5	0.75	96	84
6	1-pyrenyl	H	0.05	0.5	93	57
7	3-pyridine	H	0.05	4.3	97	55
8	Cp$_2$Fe	H	0.05	0.2	98	—
9	Isobutyl	H	0.05	<0.5	>99	—

[a] Obtained by integration of the RCH_2OBpin resonance against an internal tetrakis(trimethylsilyl)silane (TMSS) standard. [b] Two equivalents of HBpin. [c] 7% mono(hydroborated) product.

product of B–H/O–Mg metathesis between HBpin and compound **3** (inset Scheme 1). The stoichiometric formation of compound **4**, thus, demonstrates the viability of the individual B–H/O–Mg metathesis and carbonyl insertion steps of the catalytic benzophenone hydroboration reaction illustrated in Scheme 1. Compound **4** may also be viewed as a model for the likely catalyst resting state in subsequent turnover under catalytic conditions (*vide infra*).

This apparent hydroboration reactivity was then extended to a catalytic regime. While the uncatalysed hydroboration of benzaldehyde showed little reactivity (Table 1, entry 1a) addition of only 0.05 mol% of **1** led to full conversion to [PhCH$_2$OBpin] within less than 30 min at room temperature (Table 1, entry 1b). Encouraged by this result a wide range of aromatic and aliphatic aldehydes and ketones were investigated for hydroboration activity with HBpin at room temperature using catalyst loadings as low as 0.05 mol%. Reactions were monitored by ^{1}H NMR spectroscopy by following the appearance of new upfield resonances between 3.7 and 6.5 ppm corresponding to the α-protons of the borate ester.

Hydroboration of substituted benzaldehyde derivatives such as mesitylaldehyde and 2-methoxybenzaldehyde required an increase in the catalyst loadings to 0.5 mol% to afford the borate ester products in essentially quantitative yield within a few hours at 25 °C (Table 1, entries 3 and 4). The facility of the reaction appears, thus, to be controlled mainly by steric factors as the presence of both electron-withdrawing and -donating substituents impede catalysis. In contrast terephthaldialdehyde, which does not present any steric hindrance *ortho* to the aldehyde functionalities, was smoothly converted at 0.05 mol% catalyst loading within one hour to the bis(hydroborated) product when two equivalents of HBpin were used (Table 1, entry 2). Use of a single equivalent of HBpin invariably led to mixtures of mono- and bis(hydroborated) products independent of reaction conditions. The importance of steric factors was again evidenced through comparison of the hydroboration rates of 1-pyrenecarboxaldehyde and 9-anthraldehyde (Table 1, entries 5 and 6). 1-pyrenecarboxaldehyde, with only one substituent *ortho* to the aldehyde,

underwent essentially quantitative conversion within 30 min with 0.05 mol% of **1**. Conversely, 9-anthraldehyde, having both *ortho* positions blocked, required a ten-fold increase in catalyst loading. Isolation of the crystalline products from the reactions of HBpin with 9-anthraldehyde, 1-pyrenecarboxaldehyde and terephthaldialdehyde before hydrolysis yielded elemental analysis data compatible with the formulation [RR′CHOBpin] (see Supplementary Information†).

As previously reported reaction of 3-pyridine-carboxaldehyde with HBpin led to exclusive hydroboration of the carbonyl functionality instead of pyridine dearomatisation (Table 1, entry 7) as can be expected considering the high oxophilicity of magnesium. Addition of a second equivalent of HBpin did not lead to further hydroboration of the pyridine ring even after prolonged heating, possibly due to preferential coordination of the borate ester to the metal centre *via* the oxygen atoms. Hydroboration of ferrocenaldehyde and the aliphatic substrate isobutyraldehyde proved equally efficient (Table 1, entries 9 and 10). The reaction showed poor functional group tolerance toward NH and OH functionalities: for 2-pyrrolecarboxaldehyde and 3,5-*tert*-butyl-2-hydroxybenzaldehyde reaction with HBpin led to uncatalysed amine-borane and hydroxylborane dehydrocoupling, effectively blocking catalytic C=O hydroboration.

As expected, hydroboration of more sterically hindered ketonic carbonyl functions generally required slightly higher catalyst loadings than that of aldehydes to achieve similar results. Contrary to hydrosilylation reactions of ketones with the hydrido-calcium analogue of the magnesium β-diketiminate complex **2**, no enolisation or aldol condensation side reactions were observed in any case.[10] Benzophenone was cleanly converted in less than two hours at 25 °C and 0.1 mol% catalyst loading to the corresponding borate ester while 9-fluorenone proved only slightly less reactive (Table 2, entries 1–2). The reaction showed tolerance towards fluoride groups, as demonstrated by the clean hydroboration of 4,4′-difluorobenzophenone (Table 2, entry 3). The presence of the fluoride groups in the *para* positions also led to a slight increase in reactivity compared to the parent benzophenone. Under the same reaction conditions benzil underwent double hydroboration in

Table 2 Scope of hydroboration of ketones with **1**
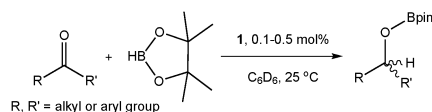
Entry	R	R′	Cat (mol%)	Time (h)	NMR yield (%)[b]	Isolated yield (%)
1	Ph	Ph	0.1	2	98	92
2	9-fluorenyl		0.1	3	95	82
3	4-FC$_6$H$_4$	4-FC$_6$H$_4$	0.1	<1.2	>99	78
4	Ph	PhC=O	0.1[a]	<2	>99[c]	72
5	Ph	Me	1	4	94	
6	2,4,6-Me$_3$C$_6$H$_2$	Me	1	1.25	91	77
7	2-indanyl		1	3	90	93
8	CH$_2$=CH(CH$_2$)$_2$	Me	0.1	1.2	97	66

[a] Two equivalents of HBpin. [b] Obtained by integration of the RR′CHOBpin resonance against an internal TMSS standard. [c] Less than 2% mono(hydroborated) product.

the presence of two equivalents of HBpin. The bis(borate ester) showed poor solubility in C_6D_6 and crystallised over the course of the reaction. An X-ray diffraction experiment was performed on crystals of the (R,S)/(S,R) diastereomer, the results of which demonstrated unambiguously that the carbonyl double bonds had been reduced (see Supplementary Information†).

Comparison of the reactivity of acetophenone and 2′,4′,6′-trimethylacetophenone once again highlighted the importance of steric factors in these hydroboration reactions (Table 2, entries 5 and 6). Reduction of aliphatic ketones such as indanone and 5-hexen-2-one with HBpin also proceeded with equal efficiency (Table 2, entries 7 and 8). In the case of the latter enone substrate no hydroboration of the alkene moiety was observed, an observation which is consistent with the results of a recently reported attempt to carry out the calcium-catalysed hydroboration of alkenes.[11] In this latter case, any observed reactivity of 1,1-diphenylethylene with HBpin was reasoned to be a consequence of a group 2-centred redistribution to BH_3 and uncatalysed olefin addition rather than an alkaline earth-catalysed hydroboration process.[11] For all of the current cases, the reactions were readily scaled up to allow isolation of the resulting primary and secondary alcohols in good yields after acid hydrolysis. It is noteworthy that in many cases the intermediate borate esters proved surprisingly air and moisture stable and could only be hydrolysed under forcing conditions (see Supplementary Information†).

In summary we have demonstrated that the easily prepared and inexpensive magnesium alkyl **1** may be applied to the efficient hydroboration of a variety of aromatic and aliphatic aldehydes and ketones under extremely mild conditions and at low catalyst loadings. Catalytic turnover most likely proceeds *via* formation of a catalytically active magnesium hydride species, insertion of the carbonyl moiety into the Mg–H bond and subsequent σ-bond metathesis with pinacolborane. We are continuing to study the scope, selectivity and mechanism of these reactions and will report our findings in subsequent publications.

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