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Aluminum Monohydride Catalyzed Selective Hydroboration of Carbonyl Compounds

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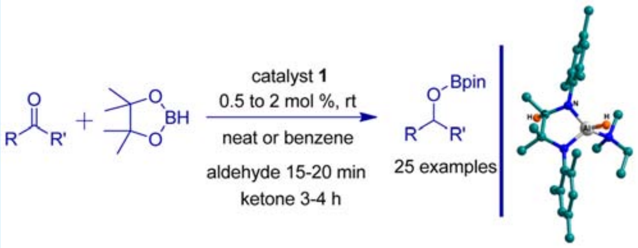
Ⓢ *Supporting Information*

ABSTRACT: The well-defined aluminum monohydride compound $[\{(2,4,6\text{-}Me_3\text{-}C_6H_2)NC(Me)\}_2(Me)(H)]AlH\cdot(NMe_2Et)$ (**1**) catalyzes hydroboration of a wide range of aldehydes and ketones under mild reaction conditions. Moreover, compound **1** displayed chemoselective hydroboration of aldehydes over ketones at rt.

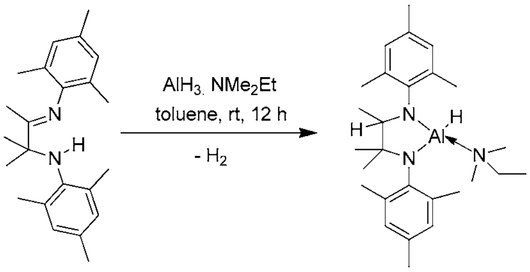


The reduction of aldehydes and ketones to alcohols is one of the most important chemical transformations in organic chemistry.[1] Moreover, selective reduction of aldehyde in preference to the ketone is another synthetically important organic transformation. Originally, reduction of carbonyl compounds was achieved by the use of metal hydride or transition metal catalyzed hydrogenation.[2] The usual methods of hydroboration involve equimolar addition of a borane reagent (BH_3) to carbonyl compounds to form borates, which can be easily hydrolyzed to alcohols. Alkoxyboronate esters have been utilized as borylating agents in Suzuki–Miyaura reactions.[3] Organoborates are convenient nucleophilic reagents due to their stability toward air and moisture and nontoxicity. Therefore, great efforts have been exercised toward the development of organoborane derivatives. In this context, catalytic hydroboration of carbonyl compounds with effective reagents such as catecholborane (HBcat) and pinacolborane (HBpin) has been gaining much attention because of the mild reaction conditions, which avoid flammable and highly pressurized hydrogen gas. In this regard, various transition metal complexes (e.g., Rh,[4] Ru,[5] Mo,[6] Ti,[7] Cu,[8] Zn[9]) have been utilized as catalysts for the hydroboration of carbonyl compounds.[10] However, very few examples of main group metal-catalyzed hydroboration of carbonyl compounds are reported in the literature.[11] In recent years, an attractive area of research involves main group metal (or element) based catalysts for chemical transformations. This is due to being less toxic and inexpensive and the large abundance of main group elements in comparison to transition or lanthanide elements. Thus, the recent trend of main group chemistry is to mimic transition or lanthanide metal chemistry in terms of catalysis and activation of small molecules, etc.[12]

Group 13 metal hydrides have been used for hydrogen storage, different organic transformations, and reduction of unsaturated substrates.[13] Despite numerous reports on synthesis and reactivity studies of molecular aluminum hydride complexes,[14] surprisingly, there have been no reports on aluminum hydride catalyzed hydroboration of carbonyl compounds, except one example (*vide infra*). Moreover, aluminum hydride catalyzed chemoselective hydroboration of aldehydes over ketone is not reported in the literature to date, and it is an important and challenging synthetic transformation.

Therefore, herein we report a structurally characterized N-donor-supported five-membered aluminum heterocyclic compound (**1**) bearing a terminal Al–H bond, as a catalyst for the hydroboration of a large number of aldehyde and ketone substrates. Furthermore, compound **1** catalysis in both inter- and intramolecular chemoselective hydroboration of aldehydes over ketones under mild reaction conditions has been investigated for the first time.

Aluminum monohydride complex $[\{(2,4,6\text{-}Me_3\text{-}C_6H_2)NC(Me)\}_2(Me)(H)]AlH\cdot(NMe_2Et)$ (**1**) was prepared from the reaction of L [L = $\{(2,4,6\text{-}Me_3\text{-}C_6H_2)NC(Me)\}_2(Me)(H)$][15] with $AlH_3\cdot NMe_2Et$ in toluene with a 1:1 molar ratio at room temperature (see eq 1). Compound **1** was characterized by



(1)

NMR (^1H and ^{13}C), IR, and elemental analyses. Further, the molecular structure of compound **1** was confirmed by X-ray single crystal structural analysis (see Figure 1).[16] Compound **1** exhibits the expected number of signals in the ^1H (except Al–H resonance) and ^{13}C NMR spectra and are consistent with its

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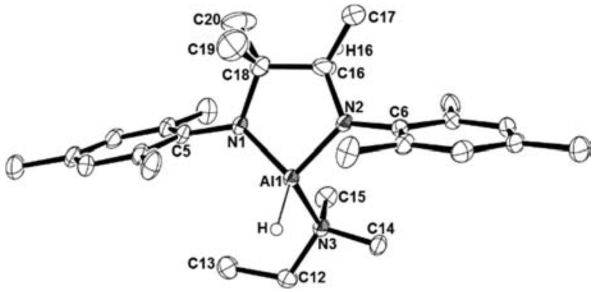


Figure 1. Molecular structure of $C_{27}H_{44}AlN_3$ (**1**) (ORTEP view, 40% probability level). All hydrogen atoms are omitted for clarity (except H and H16). Selected bond lengths (Å) and bond angles (deg): Al1–H 1.510(3), Al1–N1 1.817(2), Al1–N2 1.813(2), Al1–N3 2.037(2), N1–C18 1.504(4), N2–C16 1.469(4), C16–C18 1.504(5), N3–C14 1.484(4); N2–Al1–N1 93.02(10), N2–Al1–H 123.6(12), N1–Al1–H 124.0(12), N3–Al1–H 93.0(12), C16–C18–N1 109.4(3), C20–C18–C19 99.8(4).

composition. The Al–H resonance cannot be detected directly by ^{1}H NMR spectroscopy due to quadrupolar broadening on the ^{27}Al center (nuclear spin = 5/2).[17] However, the presence of an Al–H bond was confirmed by IR spectroscopy, which exhibits one broad band at 1796 cm^{-1}, assigned to the Al–H stretching frequency.

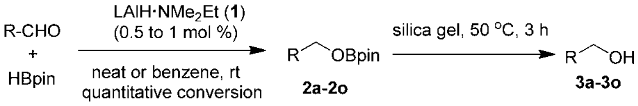
As mentioned earlier, only a handful of well-defined main group metal complexes have been utilized as catalysts for the hydroboration of carbonyl compounds. To the best our knowledge, only one example of an aluminum hydride catalyzed hydroboration of carbonyl compounds has been reported to date, which is Roesky's six-membered aluminum hydride complex bearing a *β*-diketiminate ligand.[18] In view of this, we aimed to test compound **1** as a catalyst for the hydroboration of aldehydes and ketones. We began our investigation with addition of only 1 mol % of catalyst **1** to an equimolar mixture of benzaldehyde and HBpin. We noticed the formation of $PhCH_2OBpin$ in quantitative yield within 15–20 min at room temperature either in benzene or under neat conditions. In contrast, the catalyst-free hydroboration of benzaldehyde displayed little conversion. Further, the same reaction was performed under neat conditions by using lower catalyst loadings (0.1%, 0.2%, and 0.5%). From Table 1, it is clear that a lower catalyst loading leads to a longer reaction time and slightly lower yield when compared to a higher catalyst loading. Therefore, we explored the hydroboration of a wide range of aldehydes by using 0.5–1.0 mol % either in benzene solvent (for solid substrates) or under neat conditions (see Table 2). Progress of the hydroboration reaction was monitored by ^{1}H NMR of the reaction mixture, which confirmed the quantitative formation of boronate esters. Further, hydrolysis of the aromatic and aliphatic boronate esters provided the corresponding alcohols with good to excellent yields (86–96%).

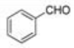
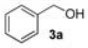
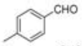
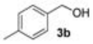
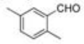
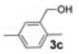
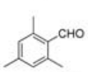
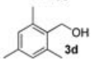
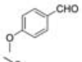
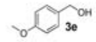
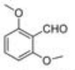
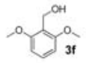
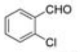
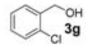
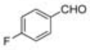
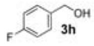
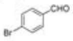
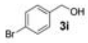
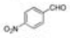
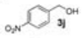
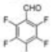
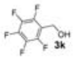
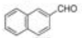
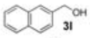
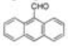
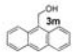
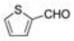
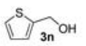
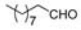
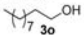
Table 1. Hydroboration of Benzaldehyde Catalyzed by 1[a]

entry	cat. (mol %)	solvent	time (min)	conv (%)[b]
1	0.1	neat	45	96
2	0.2	neat	30	97
3	0.5	neat	20	>99
4	1	neat	15	>99
5	1	benzene	20	99

[a]Benzaldehyde (1 equiv), pinacolborane (1 equiv), LAlH·NMe_2Et (**1**), at rt. [b]Conversion was determined by ^{1}H NMR spectroscopy.

Table 2. Hydroborations of Aldehydes Catalyzed by 1[a]



entry	aldehyde	time (min)	conv (%)[b]	alcohols	yield (%)[c]
1		20	>99	 3a	95
2		20	>99	 3b	96
3		20	>99	 3c	89
4		20	>99	 3d	92
5		20	>99	 3e	90
6		20	>99	 3f	88
7		20	>99	 3g	91
8		15	>97	 3h	87
9		15	>99	 3i	93
10		15	>98	 3j	92
11		20	>98	 3k	90
12		20	>96	 3l	95
13		20	>99	 3m	93
14		20	>99	 3n	86
15		15	>99	 3o	88

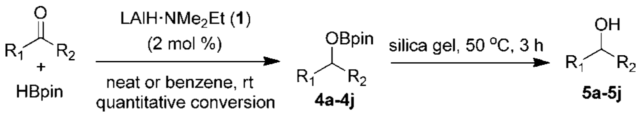
[a]Aldehydes (1 mmol), pinacolborane (1 mmol) and LAlH·NMe_2Et (**1**) (0.5 mol % for liquid substrate and 1 mol % for solid substrate), rt, neat or benzene (1 mL) for the solid substrate. [b]Conversion of aldehydes based on ^{1}H NMR analysis. [c]Isolated yield of 1° alcohol by column chromatography.

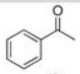
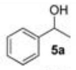
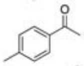
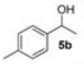
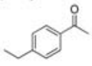
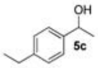
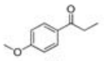
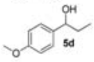
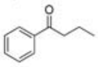
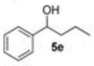
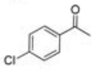
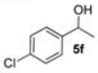
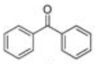
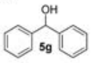
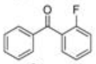
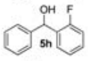
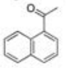
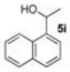
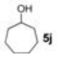
Using aromatic aldehydes with different substituents at different positions that may be electron donating (Table 2; entries 2–6) or electron withdrawing (Table 2; entries 7–11), in both cases quantitative conversion was noticed. Naphthalene and anthracene were independently reacted with an equimolar amount of HBpin and catalyst **1** (1 mol %) in benzene at room temperature. Quantitative conversion of aldehydes was confirmed by ^{1}H NMR analyses (Table 2, entries 12 and 13). Further, anthracene boronate ester (**2m**) (see Scheme S1 in Supporting Information) was characterized by X-ray single crystal analysis (see Figure S1).[19]

Similarly, quantitative conversion of 2-thiophene-carboxaldehyde was noted upon reaction with HBpin in the presence of catalyst **1** (entry 14). Further, we tested the catalytic activity of compound **1** by choosing an aliphatic aldehyde as a substrate, i.e., 1-decanal. Reaction of equimolar amounts of decanal and HBpin led to the formation of boronate ester in quantitative yield (entry 15).

As expected, a higher catalyst loading is required for the hydroboration of ketones when compared to aldehydes due to their steric nature. Initial investigation for hydroboration of phenyl acetone catalyzed by **1** under different conditions was carried out (Table S1). We observed that 2 mol % of catalyst at rt provided the best result. Therefore, under these optimized reaction conditions, further hydroboration of ketones to give their corresponding boronate ester was briefly examined, which resulted in a quantitative yield for all the cases within 3−4 h. The conversion was determined by ^{1}H NMR spectroscopy. All the secondary alcohols were isolated by column chromatography with good to excellent yields (Table 3, entries 1−10).

Table 3. Hydroborations of Ketones Catalyzed by **1**[a]



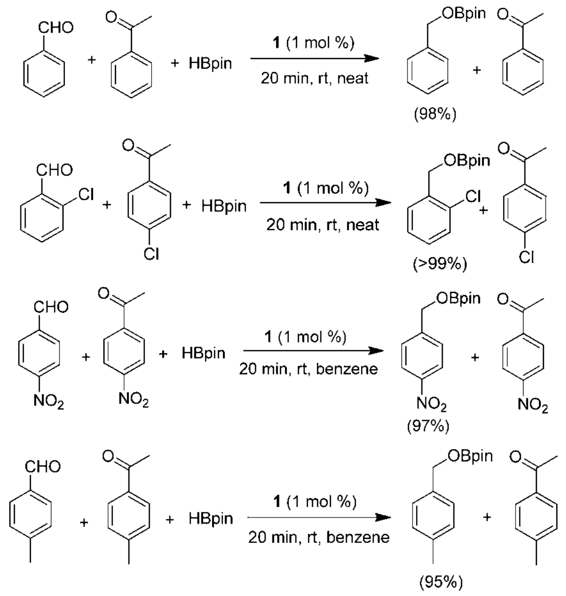
entry	ketones	time (h)	alcohols	yield (%)[b]
1		3	 5a	93
2		4	 5b	90
3		4	 5c	86
4		4	 5d	91
5		4	 5e	88
6		3	 5f	87
7		4	 5g	92
8		4	 5h	95
9		4	 5i	90
10		3	 5j	89

[a]Ketone (1 mmol), pinacolborane (1 mmol), LAlH·NMe$_2$Et (**1**) (2 mol %), rt, neat or benzene (1 mL) used for the solid substrate. [b]Isolated yield of 2° alcohol by column chromatography.

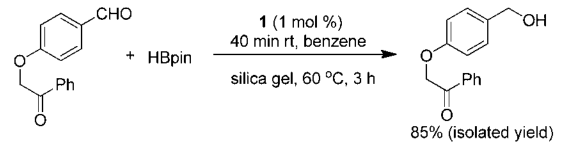
More importantly, we have demonstrated that compound **1** catalyzed both inter- and intramolecular chemoselective hydroboration of aldehydes over ketones for the first time (see, Scheme 1). Reaction of equimolar amounts of benzaldehyde, acetophenone, and HBpin were reacted together with catalyst **1** (1 mol %) under neat conditions at room temperature, which produced the corresponding boronate ester in 98% conversion of benzaldehyde, in preference to the ketone. Similarly, reaction of 2-chlorobenzaldehyde gives 99% boronate ester in preference to the ketone (see Scheme 1A). Additionally, reaction of equimolar amounts of 4-nitrobenzaldehyde, 4-nitroacetophenone, and HBpin proceeded with catalyst **1** (1 mol %) in benzene at room temperature. The ^{1}H NMR spectrum indicated 97% conversion of aldehyde. Similarly, 4-methylbenzaldehyde gives the corresponding boronate ester (95%) in preference to the ketone. Furthermore, we have investigated the intramolecular chemoselective hydroboration reaction by choosing 4-(2-oxo-2-phenylethoxy)-benzaldehyde, as an example.

Scheme 1. Chemoselective Hydroboration of Aldehydes Catalyzed by Aluminum Monohydride Complex

A. Intermolecular Chemoselective Reactions



B. Intramolecular Chemoselective Reaction

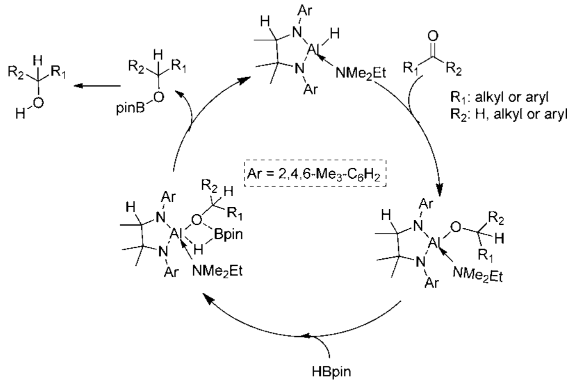


Reaction of 4-(2-oxo-2-phenylethoxy)benzaldehyde with an equimolar quantity of HBpin and catalyst **1** (1 mol %) in benzene at room temperature was carried out. ^{1}H NMR analysis of this reaction mixture indicated the chemoselective hydroboration of aldehyde with 98% conversion over ketone. The corresponding alcohol was isolated in 85% yield (see Scheme 1B) after hydrolysis of the boronate ester, and ^{1}H NMR of the alcohol confirmed that the ketone functional group remained intact.

The mechanism of main group catalyzed hydroboration of carbonyl compounds (i.e., insertion/σ-bond metathesis type) was previously investigated by the Hill,[11d] Jones,[11c] Roesky,[18] and Kinjo[10,11b] research groups, independently. Accordingly, herewith we are also proposing an insertion/σ-bond metathesis type mechanism (see Scheme 2). First, insertion of the Al−H bond into the carbonyl substrate (C═O functional group) occurs, which leads to the formation of the corresponding aluminum alkoxide intermediate. Second, reaction of the metal alkoxide with HBpin via σ-bond metathesis to yield the alkoxyboronate ester product regenerates the aluminum monohydride catalyst for further reaction. Hydrolysis of alkoxyboronate esters leads to the formation of corresponding alcohols.

In summary, we have demonstrated that aluminum monohydride complex **1** acts as an efficient catalyst for the hydroboration of carbonyl compounds with HBpin. More importantly, we have shown main group metal catalyzed intermolecular chemoselective hydroboration of aldehydes over ketones for the first time.

Scheme 2. Proposed Mechanism for Hydroboration of Carbonyl Compounds Catalyzed by Aluminum Monohydride Complex (1)



■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b02310.

Experimental procedures and characterization data (PDF)

Crystallographic data for the new compounds (CIF, CIF)

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Author Contributions

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Notes

The authors declare no competing financial interest.

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