Comparing Neutral (Monometallic) and Anionic (Bimetallic) Aluminum Complexes in Hydroboration Catalysis: Influences of Lithium Cooperation and Ligand Set

Victoria A. Pollard, M. Ángeles Fuentes, Alan R. Kennedy, Ross McLellan,* and Robert E. Mulvey*

Dedicated to Professor Dietmar Stalke on the occasion of his 60th birthday

Abstract: Bimetallic lithium aluminates and neutral aluminum counterparts are compared as catalysts in hydroboration reactions with aldehydes, ketones, imines and alkynes. Possessing Li–Al cooperativity, ate catalysts are found to be generally superior. Catalytic activity is also influenced by the ligand set, alkyl and/or amido. Devoid of an Al–H bond, iBu2Al(TMP) operates as a masked hydride reducing benzophenone through a β-H transfer process. This catalyst library therefore provides an entry point into the future design of Al catalysts targeting substrate specific transformations.

The synthetic value of main-group metal complexes aside from the highly reactive and versatile organolithium and organomagnesium reagents have, from a historical perspective, been overshadowed by the illustrious reputation of transition-metal (notably precious metals) and lanthanide complexes. Emulating the high reactivity, selectivity and versatility of the often toxic and scarce precious metal complexes is a tantalising challenge that needs addressing. In this regard, the pioneering work of Harder, Hill, Jones, Okuda, Power, Roessler, Wright among others, are expanding the vistas of main-group complexes in homegeneous catalysis.[1–2] Since aluminum is the most abundant metal in the earth’s crust, and also benefits from low toxicity, harnessing its reactivity is given high prominence in this main group uprising with longer term sustainability being a key issue. Thus, recently aluminum complexes have made significant strides forward in important stoichiometric and catalytic transformations.[3] For example, they are utilised in C–C cross coupling chemistries, and in deprotonative metalation.[4] Catalytic hydrideelementation reactions have also witnessed impressive progress in the past few years. Roessler and co-workers demonstrated that a β-diketiminato stabilised aluminium hydride complex is an excellent catalyst for hydroboration of alkynes and carbonyl groups.[5] More recently, Cowley, Thomas and Bismuto revealed that DIBAL(H), and Et3Al-DABCO can catalyse hydroboration of alkynes.[6] Our group’s interests lie in exploiting the synergistic reactivity imparted by two distinct metal centros[7,8] installed within a bimetallic complex. In this regard we introduced ate complexes (Figure 1), detailing that heteroleptic lithium diamido-dihydridoaluminates and lithium monoamido-monohydrido-dialkylaluminates implicate that the alkali metal influences the ensuing “aluminum reactivity” in the hydroboration of aldehydes, ketones and terminal alkynes.[9]

Figure 1. Al complexes 1–6 assessed in this study: ates 1–3; neutral 4–6.

Further, the catalytic chemistry of LiAlH4 has recently been explored by Cowley, Thomas and Bismuto in the challenging hydroboration of alkenes, however the role of the alkali metal was not elaborated.[9] Thus, the current state of the field dictates that a systematic analysis of the secondary metal cooperative effects and various ligand factors that

[1] V. A. Pollard, Dr. M. Á. Fuentes, Dr. A. R. Kennedy, Dr. R. McLellan, Prof. Dr. R. E. Mulvey
WestCHEM, Department of Pure and Applied Chemistry
University of Strathclyde
Glasgow G1 1XL (UK)
E-mail: ross.mclellan@strath.ac.uk
r.e.mulvey@strath.ac.uk

Supporting information and the ORCID identification number(s) for the author(s) of this article can be found under:
https://doi.org/10.1002/anie.201806168
The data set underlying this research can be located at https://doi.org/10.15129/9f7efa41-0688-40ea-baf6-c5e4431a4575.

[2] © 2018 The Authors. Published by Wiley-VCH Verlag GmbH & Co. KGaA. This is an open access article under the terms of the Creative Commons Attribution License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.


These are not the final page numbers!
Contribute to efficient hydroboration, is required in order to establish empirical rules for a posteriori design of future catalysts.

Hydroboration of unsaturated substrates under aluminum catalysis is gaining a foothold in the literature, and a variety of neutral aluminum complexes are displaying excellent potential in this role.\textsuperscript{[2a,3,10]} Previously, we reported that bimetallic lithium \((\text{Bu}_2\text{Al-TMP}(\text{H})\text{Li})\) (1) and \(((\text{HMDMS})_2\text{AlH}(\mu-

\text{H})\text{Li}3\text{THF})\) (2) are both efficient bimetallic \((\text{pre})\)catalysts in the hydroboration of aldehydes and ketones.\textsuperscript{[6]} However, any synthetic advantages/disadvantages of using ate complexes are yet to be fully uncovered, despite their potential. Thus, here, for the first time ate complexes are compared with their neutral aluminum counterparts to fully quantify their value in synthesis, and to glean understanding of their mode of action. Moreover, the complexes chosen vary in their ligand constitution, that is, alkyl versus amido constituents, providing further comparison. Mechanistically a frequently postulated two-step reaction pathway is: 1) insertion of an unsaturated substrate into an \(\text{Al–H}\) bond; 2) \(\beta\)-bond metathesis with a borane, regenerating an active species and liberating product (Scheme 1).

**Table 1:** Hydroboration catalysis results for carbonyls, imines and acetylenes using 1–6 as catalysts.\textsuperscript{[6]}

| Phenylketones | Ph | Me | O
|---------------|---|---|---
| 1\textsuperscript{H} | 99% | 0.5 h | 4 | 94% | 0.5 h
| 2\textsuperscript{H} | 99% | 0.5 h | 5 | 69% | 5 h
| 3\textsuperscript{H} | 79% | 0.5 h | 6 | 17% | 4 h
| 4\textsuperscript{H} | 99% | 0.25 h | 4 | 79% | 1 h
| 5\textsuperscript{H} | 85% | 0.25 h | 2 | 35% | 2 h
| 6\textsuperscript{H} | 99% | 0.25 h | 3 | 53% | 2 h

| Imines | Ph | Me | O
|-------|---|---|---
| 1\textsuperscript{H} | 97% | 2 h | 4 | 40% | 6 h
| 2\textsuperscript{H} | 80% | 3 h | 5 | 55% | 5 h
| 3\textsuperscript{H} | 99% | 0.5 h | 1 | 2 h
| 4\textsuperscript{H} | 80% | 0.25 h | 3 | 98% | 0.25 h
| 5\textsuperscript{H} | 93% | 2.5 h | 4 | 53% | 2 h
| 6\textsuperscript{H} | 91% | 2 h | 5 | 71% | 1 h

| Acetylenes | Ph | Me | O
|----------|---|---|---
| 1\textsuperscript{H} | 62% | 2 h | 4 | 3% | 1 h
| 2\textsuperscript{H} | 35% | 2 h | 5 | 22% | 5 h
| 3\textsuperscript{H} | 78% | 0.75 h | 5 | 56% | 4 h
| 4\textsuperscript{H} | 80% | 0.5 h | 6 | 33% | 4 h
| 5\textsuperscript{H} | 73% | 0.5 h | 4 | 34% | 4 h
| 6\textsuperscript{H} | 71% | 4 h | 4 | 0% | 17 h
| 7\textsuperscript{H} | 80% | 0.25 h | 6 | 83% | 2 h
| 8\textsuperscript{H} | 91% | 2 h | 4 | 10% | 2 h
| 9\textsuperscript{H} | 60% | 2 h | 4 | 40% | 2 h

[a] Aldehyde/ketones: 5 mol % [Al] cat. loading, \(\text{C}_6\text{D}_6\) room temperature. Imines 10 mol % [Al] cat. loading, \(\text{C}_6\text{D}_6\) room temperature. Alkynes 10 mol % [Al] cat. loading, in \(\text{D}_2\text{O}\)toluene at 110 °C. [b, c] Data for 1 from Ref. [8b], [c] data for 2 (1 mol% cat.) from Ref. [8a]. [d] Data for 6 from Ref. [6]. All yields against \(^1\text{H}\) NMR internal standard hexamethylcyclo-trisiloxane.

Reaction illustrated with an aldehyde/ketone

![Scheme 1. Postulated insertion mechanism in Al-catalysed hydroboration.](image)

Catalytic activities were screened with aldehydes, ketones, imines and alkynes, providing reaction scope to determine key divergences in catalytic reactivity. We previously reported key divergences in catalyst reactivity. We previously reported

\(\text{R} = \text{H, alkyl, aryl} \)

hexane and \(\text{C}_6\text{D}_6\) where clear, facile quantitative reaction occurs rapidly at room temperature (isobutene, the coproduct of \(\beta\)-hydride elimination, is seen in the \(^1\text{H}\) NMR spectra). X-ray diffraction studies of colourless crystals grown from the hexane solution revealed formation of \([[\text{TMP}]\text{Ph}_2(\text{H})\text{CO}][\text{Al}(\mu-\text{OC}(-\text{H})\text{Ph}_3)]\) (7) in a 45 % isolated yield (Scheme 2). It is germane to note that Et\(_4\text{Al-DABCO} can catalyse hydroboration of alkynes due to a redistribution reaction with HBpin generating the active Et\(_4\text{AlIH} species.\textsuperscript{[6]}

The structure of 7 (Figure 2, left) reveals a dimer wherein both \text{iBu} groups of 4 have been replaced, by \text{Ph}(_3\text{H})\text{CO}.
Catalytic hydroboration reactions of N-benzylidenemethylamine, using 1–6 showed lower reactivity at room temperature than with aldehydes and ketones, however the same reactivity pattern emerges, in that the bimetallic complexes are superior to monometallic counterparts. After two hours, conversions are with 1 (42%), 2 (35%), 3 (53%), 4 (3%), 5 (22%) and 6 (5%). Nevertheless, these results with 1–3 constitute the first use of Al complexes in imine hydroboration. Stoichiometric reactions between 1, 3, 4 and 6 with the imine provide further insight. Compound 4 forms only a coordination adduct with the imine in contrast to the β-hydride elimination product with benzophenone, whereas, 1, 3 and 6 add across the C=N double bond, with 6 displaying higher insertion reactivity (see Supporting Information). Notably Stephan and co-workers reported a dimeric structure of an analogous reaction between 6 and a related imine.[14c] However, faster substrate insertion does not translate into fast catalytic transformation. Thus we infer that the α-bond metathesis step with HBpin is greatly facilitated by the additional polarity imposed by the bimetallic ate constitution. Reinforcing this hypothesis, Harder and co-workers’ imine hydrogenation using catalytic LiAlH4, illuminates the important role of the alkali metal, via DFT studies, wherein Al-H-Li interactions are retained throughout the proposed catalytic cycle.[14c]

We next screened benzophenone imine in the catalysis with 1, 3, 4 and 6 (10 mol%), since this substrate has an acidic N-H atom amenable to deprotonation and therefore provides the possibility of reaction proceeding via an alternative deprotonation pathway. Furthermore, amido groups in 1 and 4 can directly compared with alkyl groups in 3 and 6. 1 and 3 achieve 73% and 80% conversion after 2 h or 30 minutes, respectively. Compounds 4 and 6 perform poorly, showing no catalytic activity at room temperature, prompting further consideration. Two stoichiometric reactions between benzophenone imine and 1, and 4 were conducted, wherein both exhibit amido basicity. In the reaction with 4 [tBu2Al([µ-N=CPh2])2] (8; Figure 2, right), was isolated as single crystals in a 24% yield (1H NMR yield of 86% against hexamethylcyclotrisiloxane as internal standard). In contrast to the benzophenone case where catalysis proceeds after a β-hydride process step, the reactivity here ceases after an initial deprotonation by the TMP basicity. Interestingly, both 3 and 6 display trace amounts of H2 evolution in their catalytic reactions as evidenced by a low intensity singlet resonance in the respective 1H NMR spectra at δ 4.47 ppm.

The catalytic results with benzophenone imine merit further comment. Both 1 and 4 exhibit deprotonation, suggesting that in a catalytic regime, reaction (using 1) may proceed in the pathway outlined in Scheme 3, that is, deprotonation followed by hydroboration then protonolysis to liberate product and generate a catalytically active species.

That 1 is active and 4 is not, may be assigned to the nature of deprotonation products, which clearly demonstrates the key role of bimetallic (Li–Al) cooperativity. 1 is the proposed deprotonation intermediate using 1 and 1’ using 4, which corresponds to the crystallographically authenticated 8. In 1 the alkali metal would instil a different molecular charge distribution to that in 1’. This scenario clearly facilitates the
phenylacetylene (PhCCH) in C₆D₆, reveal deprotonation of reactions of TMP-containing

1 (85% conversion after 2 hours), [6] reveal that only very slowly hydroaluminates PhCCH, at room temper-

hydroboration of PhCCH with a key step.[8b] Alternatively, the increased steric demand of TMP may slow reactivity. Moreover, it is apparent that even when the deprotonation pathway is available (catalyst 1 with benzophenone imine), the pathway that follows, insertion (catalyst 3 with benzophenone imine) is favoured, albeit marginally.

Finally, we turned to acetylene hydroboration comparing reactivity once more between 1, 3, 4 and 6. Stoichiometric reactions of TMP-containing 1 and 4 with terminal alkyne phenylacetylene (PhCCH) in C₆D₆ reveal deprotonation of PhCCH at room temperature, in agreement with the fact that hydroboration of PhCCH with 1 implicated deprotonation as a key step.[8b] Alternatively 3 is unreactive with PhCCH, and 6 only very slowly hydroaluminates PhCCH, at room temper-

tature. Catalysis, using 10 mol% loadings in [D₆]toluene at 110°C, in line with the reported reaction conditions using 6 (85% conversion after 2 hours),[8d] reveal that 1 and 3 catalyse the transformation to the anti-Markovnikov vinylboronate ester in yields of 71% and 83% respectively. Conversely, 4 as expected, does not function as a catalyst. Thus 3 is compa-

able to 6 however, for the first time we note that a clear ate effect is not in operation. Furthermore, 3 is a better catalyst than 1 underlying that increased hydride nucleophilicity is more important, mechanistically, than deprotonation, though reduced steric effects may also be a factor.

A similar picture is seen with the internal alkyne diphenylacetylene. 6 (10 mol%) is reported to convert diphenylacetylene to the boronic ester in 40% yield after 2 hours at 110°C in [D₆]toluene,[9b] whereas 1 is completely inactive, and 3 only reaches conversions of approximately 10% after 2 hours, which is surprising given our preceding observations. One potential rationale for this marked reduc-

tion in ate reactivity with diphenylacetylene may be attribu-

ted to a steric effect (Scheme 4).

Considering the required initial insertion step at the sp-C of diphenylacetylene, insertion into the Al-H bond of 3 (three iBu groups, one hydride) is likely to be slower than for 6 (two iBu groups, one hydride) due to the inherently more sterically demanding ate constitution, even given the trimeric solution constitution of 6 (via DOSY NMR spectroscopy, see Supporting Information). Clearly, with ketones and imines any insertion step at the sp² O/N would be considerably less congested, thus facile insertion would occur, thereby facilitating the ate enhancement seen in the ensuing hydroboration catalysis. Elaborating further, we attempted one further substance in comparative catalytic experiments with 6 and 3. With 6, 1-phenyl-propyne is only hydroborated in trace amounts, despite the intrinsically smaller CH₃ group with respect to diphenylacetylene.[6b] On the other hand, 3 catalyses the transformation to a mixture of regio-isomers (60% conversion overall) in favour of borylation at the least sterically hindered alkine carbon atom, demonstrating once more the advantage of ate complexes in these catalytic transfor-

mations.

This study into hydroboration of aldehydes, ketones and imines reveals that anionic ate complexes are important additions to the main-group catalyst toolbox, providing higher conversions in shorter timescales. We attribute this superiority to the greater polarisation of key reaction intermediates induced by the heterobimetallic complexes. Moreover, a novel new catalytic activation pathway was elucidated for ketone hydroboration involving a β-hydride process. With internal alkynes the scenario is different and mononuclear species are the catalysts of choice when steric constraints override the ate effect. Overall this study illum-

inated that while ate complexes are beneficial in most cases, the mononuclear species are more effective in others. Thus, in the field of aluminum-catalysed hydroelementation, there is a high degree of substrate dependence, governing the appropriate choice of catalyst.

**Acknowledgements**

The referees are thanked for excellent suggestions. Support is duly acknowledged from the EPSRC (DTP award EP/M508159/1 to VAP) and the Alexander von Humboldt foundation (Humboldt Research Award to REM: host Universität Regensburg, Germany).
Conflict of interest

The authors declare no conflict of interest.

Keywords: aluminum · bimetallic synergy · homogeneous catalysis · hydroboration · lithium


Manuscript received: May 29, 2018
Accepted manuscript online: June 15, 2018
Version of record online: ■■■■■■■■■■
Comparing Neutral (Monometallic) and Anionic (Bimetallic) Aluminum Complexes in Hydroboration Catalysis: Influences of Lithium Cooperation and Ligand Set

Team mATES: Aluminum works better as a hydroboration catalyst when teaming up with lithium in ate complexes, for reactions with aldehydes, ketones, imines and alkynes. Catalytic activity is also influenced by the ligand set, whether alkyl and/or amido.