**N-methylacridinium Salts: Carbon Lewis Acids in Frustrated Lewis Pairs for σ Bond Activation and Catalytic Reductions**

Ewan R Clark,*[a] and Michael J Ingleson*[a]

**Abstract:** N-methylacridinium salts are Lewis acids with high hydride ion affinity but low oxophilicity. The cation forms a Lewis adduct with 4-DMAP but a frustrated Lewis pair (FLP) with the weaker base 2,6-lutidine that activates H₂ even in the presence of H₂O. Anion effects dominate reactivity, with both solubility and rate of H₂ cleavage showing marked anion dependency. With the optimal anion, a N-methylacridinium salt catalyzes the reductive transfer hydrogenation and hydrosilylation of aldehydes by amine-boranes and silanes, respectively. Furthermore, the same salt is active for the catalytic dehydrosilylation of alcohols (1°, 2°, 3° and ArOH) by silanes with no over reduction to alkanes observed.

Frustrated Lewis pairs (FLPs), pioneered by Stephan and coworkers,[1] represent a versatile new method for small molecule activations, and have been successfully applied for the catalytic hydrogenation of a range of substrates.[2] Related systems also activate the Si-H bond in silanes, enabling catalytic (de)hydrosilylation.[3, 4] Fluoroboranyls, typified by B(C₆F₅)₃, are the most commonly studied Lewis acids within the field. Despite their clear utility, these boranes are not without drawbacks, with the principal being cost and high oxophilicity which can limit their utility and stability in wet solvents and functional group tolerance.[5] Other main group Lewis acids, including aluminum,[6] silicon[7] and phosphorus,[8] systems have been exploited in FLPs, but these remain extremely oxophilic and in many cases the H₂ activation products are not amenable to further catalytic application. Thus there is a demand for cheaper, less oxophilic Lewis acids for FLP applications.

Softer carbon-centered Lewis acids were shown by Bertrand[9] and Arduengo[10] to be able to activate H₂, but due to the high hydride ion affinity (HIA) of these compounds application in reduction processes are precluded. Alcarazo et al. have used electron deficient allenes as weaker carbon Lewis acids[11] which do activate RS-R′ bonds but are incapable of H₂ activation. The realization of carbon Lewis acid based FLP catalyzed reduction was first reported by Stephan et al. using [(Ph₂PCl)H₂B(n-P₃HPh)]RuCl][B(C₆F₅)₃].[12] This compound whilst able to activate H₂ with an appropriate base still contains a precious metal. Thus the goal of utilizing a metal free, inexpensive carbon Lewis acid for FLP based reductions remains to be realized.

In our prior work, borocation 1[AICl] (scheme 1 center) was found to act in a FLP as a Lewis acid at boron and at the C9 position of the acridine moiety, depending upon reaction conditions.[13] Computational determination of HIA confirmed that C-centered HIA is greater than that at boron by 13.9 kcalmol⁻¹. The high HIA of 1⁺ at carbon is not surprising, as N-alkyl acridinium species have been investigated as model compounds for the biological hydride transfer system NADH / NAD⁺.[14,15] N-Methylacridinium salts (2⁻) are particularly attractive Lewis acids as they: (i) are easy to synthesize, (ii) are indefinitely air and moisture stable[16] and (iii) show little propensity to coordinate H₂O, indicating low oxophilicity. Herein we report the incorporation of 2⁻ into FLPs which activate H-H, Si-H and B-H bonds and are catalysts for the reduction of imines, as well as the dehydrosilylation of alcohols.

Initially the HIA of the 2⁻ ion was quantified[17] and computationally determined to be -53.3 kcalmol⁻¹ (Table 1), 20.5 kcalmol⁻¹ less than the C-centered value for 1⁺. The marked difference is ascribed to the additional stabilization afforded by significant B=N double bond character in 1-H₂. The HIA of 2⁻ was nevertheless found to exceed that of the model compounds of the conjugate Lewis acids of known hydride donors, Hantzsch ester, 3⁺, and NADH, 4⁻. Significantly, 2⁻ has a considerably lower HIA than Ph₃C⁺ (consistent with the experimental observation of hydride abstraction from N-methylacridane by Ph₃C⁺)[14b] essential for transferring a hydride to substrates post H₂ activation. It is however, still 12.3 kcalmol⁻¹ greater than that of B(C₆F₅)₃⁺, indicating that H₂ activation in a FLP with an appropriate base will be thermodynamically favored.[17]

**Scheme 1. Hydride Ion Affinities of 1⁺ (relative to Et₄B)**

<table>
<thead>
<tr>
<th>Lewis Acid</th>
<th>HIA / kcalmol⁻¹</th>
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<tbody>
<tr>
<td>[Ph₃C⁺]⁻</td>
<td>-75.3</td>
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</table>

**Table 1.** HIAs (relative to Et₄B) at the M06-2X/6-311G(d,p), PCM(DCM) level.

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A range of \([2]X\) salts (\(X = I, \text{SbF}_5, \text{BPh}_4\)) tetra(3,5-dichlorophenyl)borate (hereafter BA\(^{Cl}\))\(^{18}\) were readily available in excellent yield by methylation of acridine with methyl iodide followed by anion exchange with the appropriate metathesis reagent. \([2]\text{SbF}_5\), \([2]\text{BPh}_4\) and \([2]\text{BA}\(^{Cl}\)) were crystallographically characterized as well-separated ion pairs, and show good correlation with calculated structural metrics of \(2^+\). The crystal structure of \([2]\text{SbF}_5\) is shown in Figure 1 as exemplar.

Experimental confirmation for the predicted higher HIAs relative to B(C\(_6\)F\(_5\))\(_2\) was obtained by the abstraction of hydride from \([2,6\text{-ludidine}][\text{HB}(\text{C}\(_6\)\text{F}\(_5\))\(_2\)]\) by \([2]\text{BA}\(^{Cl}\)) to yield the corresponding N-methylacridane, 5, and B(C\(_6\)F\(_5\))\(_2\). On combination of 3 equivalents of \([2]\text{BA}\(^{Cl}\)) with Et\(_3\)PO, to determine Lewis acidity by the Gutmann-Beckett method,\(^{19}\) a \(\Delta\delta\)\(^{31}\)P of 4.3 ppm was determined, vastly lower than that of B(C\(_6\)F\(_5\))\(_2\) (at \(\Delta\delta\)\(^{31}\)P 26.8ppm)\(^{20}\). The addition of crotonaldehyde to \([2]\text{BA}\(^{Cl}\)) in DCM (the Childs’ method for assessing Lewis acidity)\(^{21}\) resulted in a minimal downfield shift of the H3 proton with a \(\Delta\delta\)\(^3\)H of 0.02 ppm. Thus, \(2^+\) is a significantly weaker Lewis acid towards Et\(_3\)PO and crotonaldehyde than B(C\(_6\)F\(_5\))\(_2\) in marked contrast to the ordering of the HIAs. These remarkable differences, coupled with the observations that \([2]\text{BA}\(^{Cl}\)) exhibits no observable H\(_2\)O coordination (by \(^1\)H NMR spectroscopy) and that the halide salts, \([2]X\) (\(X = \text{Cl, Br, I}\)), exist as well separated ion pairs\(^{22}\) (closest C9-X contact of 3.896(3) Å for \([2]\text{Cl}_2\text{H}_2\text{O}\)) identifies that the Lewis acidity of these species may be regarded as soft and orbital controlled, and thus hydride selective.

A range of \([2]X\) salts (\(X = I, \text{SbF}_5, \text{BPh}_4\), tetra(3,5-dichlorophenyl)borate (hereafter BA\(^{Cl}\))\(^{18}\) were readily available in excellent yield by methylation of acridine with methyl iodide followed by anion exchange with the appropriate metathesis reagent. \([2]\text{SbF}_5\), \([2]\text{BPh}_4\) and \([2]\text{BA}\(^{Cl}\)) were crystallographically characterized as well-separated ion pairs, and show good correlation with calculated structural metrics of \(2^+\). The crystal structure of \([2]\text{SbF}_5\) is shown in Figure 1 as exemplar.

The FLPs of \([2]\text{Anion}\) and 2,6-ludidine were exposed to 4 atmospheres of \(H_2\) and slow \(H_2\) bond cleavage occurred at 60°C, with significant anion dependency upon rate of reaction observed (Table 2). \([2]\text{SbF}_5\) was found to undergo minimal \(H_2\) activation (entry 1) due to anion decomposition, resulting in a complex and intractable mixture of degradation products. Whilst \([2]\text{BPh}_4\) is almost completely insoluble in \(\text{CH}_2\text{Cl}_2\), it nevertheless displayed the greatest rate of \(H_2\) activation at 60°C (entry 2), albeit still taking over five days to approach completion. From this we conclude that the rate of activation is in fact rapid compared to \([2]\text{BA}\(^{Cl}\))(entry 3), but severely solubility limited. \([2]\text{BA}\(^{Cl}\)) was chosen for further experiments by virtue of its improved solubility, and overall anion and thermal stability. The carbon-centered Lewis acidity was unambiguously confirmed by studies with \(D_2\), with incorporation of \(^2\)D into the C9 position of the resultant 6 by \(^1\)H and \(^2\)D NMR spectroscopy.

\(H_2\) activation by \([2]\text{BA}\(^{Cl}\)) 2,6-ludidine proceeds

\[\text{[2]BA}\(^{Cl}\): \text{F} = \text{F} + \text{LH}_{2}\]

\[\text{[2]BA}\(^{Cl}\): \text{F} = \text{F} + \text{LH}_{2}\]

\[\text{[2]BA}\(^{Cl}\): \text{F} = \text{F} + \text{LH}_{2}\]

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more rapidly at 100°C in ortho-dichlorobenzene (oDCB, entry 4), indicating a significant kinetic barrier to H₂ bond cleavage which, in light of the anion dependence observed, is attributed to anion / cation interactions in solution. Importantly, there is no decomposition of [2]BARCl₂ at 100°C after 2 days, precluding H₂ activation via a B(3,5-C₆H₄Cl₂)₂ / 2,6-lutidine FLP.⁵⁴ Given the utility of N-alkyl acridinium salts as photo-redox catalysts in a wide range of transformations, [2]BARCl₂ / 2,6-lutidine was exposed to dihydrogen and heated in the absence of light, with dihydrogen activation still proceeding in the dark. Pleasingly, the FLP systems are stable to water at room temperature, although slow H₂O activation is observed at raised temperatures (60°C) to form N-Me-9-OH acridane and the 2,6-lutidinium cation. Performing H₂ activation in wet oDCB with [2]BARCl₂ / 2,6-lutidine (entry 5) remarkably still resulted in H₂ activation, however heterolitic O-H cleavage of H₂O was also observed albeit as a minor product. With H₂ activation unequivocally demonstrated, the reduction of the unsaturated substrate N-benzylidene-4-tert-butylamine, 7, was explored in a FLP with [2]BARCl₂. This FLP slowly activated H₂ with reduction of the imine to the corresponding amine observed after heating to 100°C (Table 2, entry 6). To improve reduction kinetics the ability of 2⁺ to activate the inexpensive dihydrogen surrogate Me₂NH·BH₃ was investigated for transfer hydrogenation applications. [2]BARCl₂ reacts with Me₂NH·BH₃ by rapid hydride transfer to generate 5 and catonic boron species. Repeating the reaction in the presence of imine 7 resulted in formation of (Me₂NH·BH₃) and protonated imine, [7H]⁺, which upon heating abstracted hydride from 5 to regenerate [2]BARCl₂ and lead to overall reduction of imine to amine. The observation of 5 and [7H]⁺ indicates it is the hydride transfer step that is the rate limiting step. Catalyst free, direct reduction of 7 with Me₂NH·BH₃ does occur, but this background reaction is slow in CH₂Cl₂ at 60°C, taking 69 h to reach only 78% conversion. In comparison, a 5% loading of [2]BARCl₂ gave complete reduction of imine 7 in the presence of Me₂NH·BH₃ after 18 hours at 60°C (Table 3, entry 1), confirming catalysis of the transfer hydrogenation by the carbon Lewis acid [2]BARCl₂.

Table 3. Catalytic reduction of imidines.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Reductant</th>
<th>Temp. / °C</th>
<th>Conv. / (time)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5</td>
<td>Me₂NH·BH₃</td>
<td>60</td>
<td>&gt;99% (18h)</td>
</tr>
<tr>
<td>2</td>
<td>5b</td>
<td>PhMe₂SiH</td>
<td>60</td>
<td>98% (29h)</td>
</tr>
<tr>
<td>3a,b</td>
<td>5</td>
<td>PhMe₂SiH</td>
<td>100</td>
<td>&gt;98% (4h)</td>
</tr>
<tr>
<td>4a,b</td>
<td>5</td>
<td>PhMe₂SiH</td>
<td>100</td>
<td>&gt;98% (4h)</td>
</tr>
<tr>
<td>5a,b</td>
<td>5</td>
<td>PhMe₂SiH</td>
<td>100</td>
<td>&gt;98% (24h)</td>
</tr>
<tr>
<td>6a,b</td>
<td>5</td>
<td>PhMe₂SiH</td>
<td>100</td>
<td>45% (24h)</td>
</tr>
</tbody>
</table>

[a] Reactions were performed on a 0.2 mmol scale with 50% excess silane in 0.8cm³ dry DCM except where noted. [b] Reduction in oDCB [c] Calculated by ¹H NMR integration against cyclohexane as internal standard. [d] Consumption of starting imine by ¹H NMR integration against cyclohexane as internal standard. Concomitant transamination occurred under reaction conditions consuming BH₃SiMe₂Ph in to form a range of other amines, see SI for details.

The applicability of [2]BARCl₂ for the activation of Si-H bonds was next investigated. The direct 1:1 combination of [2]BARCl₂ and PhMe₂SiH resulted in no observable reaction and no loss of JSH coupling between the Si-H fragment and the adjacent methyl groups, as observed for analogous systems with B(C₆F₅)₃.⁵³ Nevertheless, mixing Ph₂SiH and Et₂SiD with 5% [2]BARCl₂ resulted in H/D exchange at room temperature, confirming activation of the Si-H bond. Consistent with this, the hydrosilylation of a number of amines was achieved using catalytic [2]BARCl₂. Whilst hydrosilylation of 7 is slow at 60°C it is complete within 4 h at 100°C giving the desired amine post hydrolysis. Hydrosilylation was also observed for the N-Ph and N-Bn imines, 8 and 9, respectively (Table 3, entries 3 and 4). More remarkably, is the hydrosilylation of the unhindered N-Me imine 10, catalyzed by [2]BARCl₂ (entry 6). In contrast, imine 10 is incompatible with B(C₆F₅)₃ catalyzed hydrosilylation due to the formation of a strong Lewis adduct. [2]BARCl₂ shows no significant propensity to bind 10 in DCM (the N-Me resonance of [2]⁺ remains at δ = 4.50 ppm post addition of excess imine 10). Finally, we investigated the utility of this species in other B(C₆F₅)₃ catalyzed reactions. [2]BARCl₂ catalyzes the hydrosilylation of aromatic, 1⁺, 2⁺, and 3⁺ alcohols (Table 4). A range of silanes can be utilized as reductants, though steric bulk precludes the use of trisopropylsilane, whilst triphenylsilane causes anion degradation as a minor competitive pathway (entry 2). Hydrosilylation proceeds unimpeded in the absence of light (entry 3 vs 4). The reaction evolves dihydrogen gas using RH₂SiH (observed via ¹H NMR spectroscopy). When Et₂SiD is used, a mixture of H₂ and HD is evolved, with no D incorporation into the product observed, demonstrating that no carbonyl intermediates derived from alcohol dehydrogenation are involved. This is further supported by the facility with which phenol is silylated, implicating an analogous mechanism to that with B(C₆F₅)₃ involving heterolytic activation of Si-H to form 5 and [RO(H)SiR₃]⁺ which undergoes dehydrocoupling to release H₂ (or mixtures of H₂ and HD when Et₂SiD is used and 5-D formed).¹³ Unlike B(C₆F₅)₃ catalyzed dehydroxylation of alcohols,¹⁰ no over-reduction to alkanes with concomitant siloxane formation is observed, even in the presence of large excess of silane and with prolonged heating, presumably as a result of the lower reducing power of N-methycaracidane vs [HB(C₆F₅)₃]. This allows the reaction to be performed under ambient atmosphere, with no need to pre-dry solvents; the catalyst rapidly converts H₂O to the appropriate siloxane under reaction conditions (confirmed by deliberate siloxane synthesis), and any excess silane poses no threat of R₂Si-OR product over-reduction. This was demonstrated in a bulk synthesis of BrN(SiMe₃)₂Ph using unpurified solvents under air with 64% (unoptimised) conversion despite the use of the challenging silane Ph₃SiH (due to anion decomposition side reactions).

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Silane</th>
<th>Catalyst Loading</th>
<th>Time / h</th>
<th>Conv.</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>9</td>
<td>R₂SiH</td>
<td>[2]BARCl₂</td>
<td>24</td>
<td>&gt;98%</td>
</tr>
</tbody>
</table>

[2]BARCl₂ / 2,6-lutidine was exposed to dihydrogen and heated in the absence of light, with dihydrogen activation still proceeding in the dark. Pleasingly, the FLP systems are stable to water at room temperature, although slow H₂O activation is observed at raised temperatures (60°C) to form N- Me-9-OH acridane and the 2,6-lutidinium cation. Performing H₂ activation in wet oDCB with [2]BARCl₂ / 2,6-lutidine (entry 5) remarkably still resulted in H₂ activation, however heterolitic O-H cleavage of H₂O was also observed albeit as a minor product. With H₂ activation unequivocally demonstrated, the reduction of the unsaturated substrate N-benzylidene-4-tert-butylamine, 7, was explored in a FLP with [2]BARCl₂. This FLP slowly activated H₂ with reduction of the imine to the corresponding amine observed after heating to 100°C (Table 2, entry 6). To improve reduction kinetics the ability of 2⁺ to activate the inexpensive dihydrogen surrogate Me₂NH·BH₃ was investigated for transfer hydrogenation applications. [2]BARCl₂ reacts with Me₂NH·BH₃ by rapid hydride transfer to generate 5 and catonic boron species. Repeating the reaction in the presence of imine 7 resulted in formation of (Me₂NH·BH₃) and protonated imine, [7H]⁺, which upon heating abstracted hydride from 5 to regenerate [2]BARCl₂ and lead to overall reduction of imine to amine. The observation of 5 and [7H]⁺ indicates it is the hydride transfer step that is the rate limiting step. Catalyst free, direct reduction of 7 with Me₂NH·BH₃ does occur, but this background reaction is slow in CH₂Cl₂ at 60°C, taking 69 h to reach only 78% conversion. In comparison, a 5% loading of [2]BARCl₂ gave complete reduction of imine 7 in the presence of Me₂NH·BH₃ after 18 hours at 60°C (Table 3, entry 1), confirming catalysis of the transfer hydrogenation by the carbon Lewis acid [2]BARCl₂.
Reactions were performed at room temperature on 0.2 mmol scale with 5% excess silane in 0.8cm³ dry DCM except where noted. Yields assessed by 1H NMR spectroscopy. [b] Total consumption of silane observed, but competitive siloxane formation due to H₂O present in PrOH. [c] Heated to 60 °C for reaction; total decomposition of anion observed. [d] Identical conditions to entry 4 but performed in total darkness. [e] Heated to 60 °C. [f] 1-Ad = 1-adamantyl.

In summary, N-alkylated acridinium salts are introduced as simple carbon Lewis acids for FLP based sigma bond activation reactions. They were shown computationally and experimentally to have an appropriate HIA to be useful for carbon-boranes and silane activation, subject to anion dependence upon reactivity. Their application in proof-of-concept catalytic transfer hydrogenation and catalytic hydrosilylation of imines has been demonstrated. Furthermore, the low Lewis acidity of [2+1] towards hard Lewis bases enables the catalytic hydrosilylation of unhindered imines that are incompatible with hydrogenation / hydrosilylation catalyzed by B(C₆F₅)₃. [2+2]BAR is also a cheap, air and moisture stable catalyst for the dehydrosilylation of alcohols, functioning with excellent turnover and good (unoptimized) yield in bench-scale experiments. Current work is extending this family of carbon Lewis acids by developing FLPs containing other N-alkylated pyridium salts with lower HIA and different anionic components.

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**Keywords:** Lewis acids • reduction • frustrated Lewis pairs• dehydrosilylation

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1. PrOH EtSiH 5% >1 86% a
2. PhOH PhSiH 10% 16 75% e
3. BrOH PhMe₂SiH 5% <1 >99%
4. BrOH PhMe₂SiH 5% <1 >99%
5. BrOH PhMe₂SiH 0.5% 2 93% e
6. Cyclic 1-AdOH 1-AdMe₂SiH 5% <1 >99%
8. Phenol PhMe₂SiH 5% <1 >99%

[a] Reactions were performed at room temperature on 0.2 mmol scale with 5% excess silane in 0.8cm³ dry DCM except where noted. Yields assessed by 1H NMR spectroscopy. [b] Total consumption of silane observed, but competitive siloxane formation due to H₂O present in PrOH. [c] Heated to 60 °C for reaction duration; total decomposition of anion observed. [d] Identical conditions to entry 4 but performed in total darkness. [e] Heated to 60 °C. [f] 1-Ad = 1-adamantyl.
**Softly does it:** $N$-methylacridinium salts are shown to be versatile Lewis acids in frustrated Lewis pairs for stoichiometric and catalytic transformations.