

Unlocking Lewis Acidity *via* the Redox Non-Innocence of a Phenothiazine-Substituted Borane

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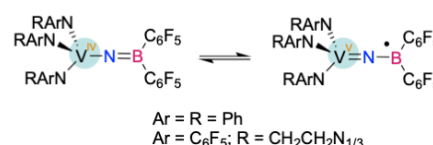
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We describe a new approach to enhancing Lewis acidity, through the single electron oxidation of a borane with a pendant phenothiazine. This results in the formation of a persistent radical cation with increased electrophilicity. Computational and experimental studies indicate this radical cation significantly enhances the Lewis acidity and catalytic activity compared to its neutral analog. These results illustrate the viability of this approach in turning on the Lewis acidity of relatively inert boranes.

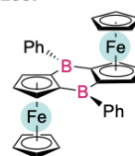
The development of new highly electrophilic main-group Lewis acids has taken additional precedence in recent years with the expansion of practical applications in catalysis, owing to the discovery of frustrated Lewis pairs (FLPs).^{1,2} There are several established methods towards increasing the Lewis acidity of a molecule, including introduction of electron-withdrawing substituents,^{3,4} cationic charges,^{5–7} or geometric perturbation,^{8–10} to name a few; creating a vast library of electrophilic Lewis acids.

A considerably underexplored approach involves the impact of single-electron oxidation on the electrophilicity of main-group Lewis acids. There have been several examples of main-group species that can stabilize open-shell configurations with the assistance of peripheral non-innocent substituents.^{11–14} In many of these examples, the effects of the oxidation state on Lewis acidity were negligible due to coordinative saturation. More recently, there have been some examples of cooperativity between the redox-active functionality and the Lewis acidity at the main-group center. Dobrovetsky and Ménard have reported that vanadium iminoboranes have divergent reactivity depending on the oxidation state of the metal [V(IV)/B(III) vs V(V)/B(II)].¹⁵ The Jäkle group has exploited the reversible redox couple of ferrocene to increase the electrophilicity of ferrocenylboranes.^{16,17} This has been recently built

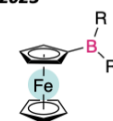
Dobrovetsky & Ménard, 2020



Jäkle, 2007



Paradies, 2023



R = C₆F₅, C₆Cl₅, OC₆Cl₅, catCl

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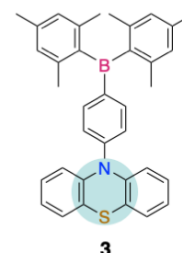
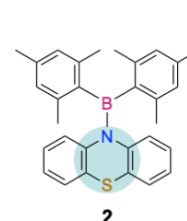
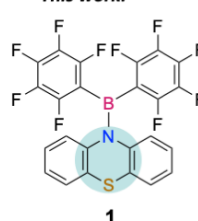


Figure 1. Previously explored Lewis acids with appended redox-active motifs.

upon by Paradies and co-workers, where they have shown that ferrocenylboranes containing electron-withdrawing substituents can be Lewis superacidic upon oxidation to Fe(III), and they applied this toward the activation of C-F and S-F bonds.¹⁸

Intrigued by these results, we sought to expand this approach beyond the realm of transition metal redox chemistry. Phenothiazine is a promising organic alternative that has well-studied redox activity.^{19,20} Furthermore, we were inspired by the work of Okada and co-workers showing that tris(phenothiazinyl)borane can be oxidized by a single electron to yield a persistent radical cation.²¹ Herein, we investigate whether mono-substituted

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phenothiazinylboranes could be chemically oxidized *via* a single-electron process to induce a substantial increase in Lewis acidity.

We began our study with the previously reported bis(pentafluorophenyl)phenothiazinylborane (**1**) and dimesitylphenothiazinylborane (**2**) and explored their redox characteristics.^{22,23} Cyclic voltammograms of aminoboranes **1** and **2** show a quasi-reversible oxidation with half-wave potentials at 0.64 V and 0.66 V, respectively (in CH₂Cl₂ vs Ag/AgCl, Figures S2-S3). Attempts to chemically oxidize these species with NOSbF₆ to the radical cations **1**^{•+} and **2**^{•+} resulted in dark, red-colored solutions. Unfortunately, characterization of these species using X-band continuous wave electron paramagnetic resonance (EPR) spectroscopy were challenging due to inconsistent hyperfine coupling patterns (Figures S5-S6). To elucidate the products of these oxidations, single crystals suitable for X-ray diffraction were obtained, however, the data revealed the structure of a phenothiazinium radical cation in both cases (Figures S22-S23). Thus, it was clear that oxidation of **1** and **2** result in the fragmentation of the B–N bonds.

To mitigate the decomposition of the aminoboranes upon oxidation, we sought to install a stabilizing bridge between the Lewis acid and the redox-active moiety. Benzophenothiazine-substituted boranes have previously been developed for applications in materials chemistry, and more specifically, (10-phenylphenothiazinyl)dimesitylborane (**3**) is a well-known bench-top stable compound.²⁴ **3** was synthesized following literature procedures in 61 % yield. Cyclic voltammetry showed a reversible oxidation event at 0.76 V (in CH₂Cl₂ vs Ag/AgCl, Figure S4), a slightly higher potential than the aminoboranes **1** and **2**. In attempts to isolate the radical cationic species, chemical oxidation of **3** to **3**^{•+} using NOSbF₆ was undertaken (Figure 2a). Addition of NOSbF₆ to a solution of **3** in CH₂Cl₂ at -78 °C resulted in an immediate formation of a deep, red-colored species. The solvent was removed *in vacuo* yielding a red solid in near quantitative yield. Analysis of this material by EPR spectroscopy at room temperature showed a triplet resonance centered at g=2.0058 with an S=1 nitrogen hyperfine coupling pattern (Figure 2b) and a simulated spectrum agreed with a nitrogen-based radical. Due to the paramagnetic nature of this compound, the ¹H NMR spectrum only exhibited broad resonances corresponding to the protons on the mesityl groups at 6.96, 2.43, and 2.28 ppm, but no resonances corresponding to the phenothiazine protons (Figure S11); both ¹¹B and ¹⁹F NMR spectra did not display any resonances for **3**^{•+} either. Finally, single-crystal X-ray crystallographic studies confirmed the structure of **3**^{•+} (Figure 2c). The phenothiazine fragment shows a planar geometry, where the butterfly angle changes from 159.5° in the neutral species to 173.8°, indicative of radical cation formation.

The Lewis acidity of the neutral and radical cation species was then assessed to confirm our hypothesis. The Gutmann-Beckett method was employed to evaluate the relative Lewis acidities.^{25,26} The reaction of 1 equiv. of Et₃PO with **3** resulted in no observable chemical-shift change in the ³¹P NMR spectrum, highlighting that **3** has no inherent Lewis acid character (Figure S8). Excitingly, the reaction of 1 eq. of Et₃PO with **3**^{•+} resulted in a substantial downfield chemical shift at 65.0 ppm in the ³¹P NMR spectrum (Figure S9), correlating to an acceptor number of ~52 (Table S1). Nevertheless, caution should be taken as this is a paramagnetic compound and the ³¹P NMR chemical shifts were broad. Due to the various

insufficiencies from the Gutmann-Beckett method in assessing the Lewis acidity of **3**^{•+}, several computational approaches were

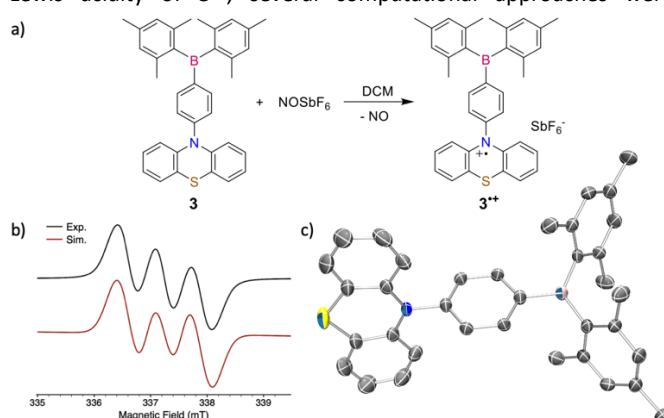


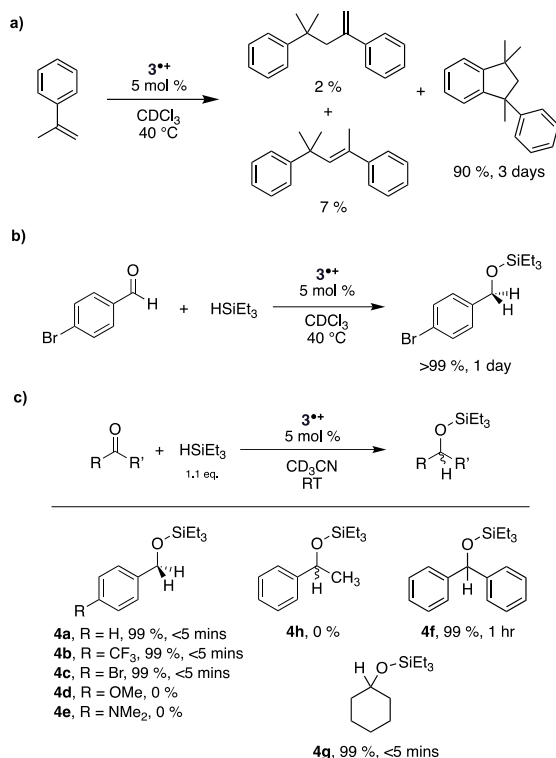
Figure 2. a) Single-electron oxidation of **3** using NOSbF₆ to generate **3**^{•+}, b) Experimental (black) and simulated (red) EPR spectra recorded at 298 K, and c) solid state structure of **3**^{•+} (hydrogen atoms and SbF₆⁻ anion omitted for clarity). Thermal ellipsoids are drawn at 50% probability. N: Blue, S: Yellow, C: Grey, B: Pink.

performed to scale Lewis acidity, including fluoride ion affinity, hydride ion affinity, and ammonia affinity (Table S2).^{27,28} All these methods indicated a significant increase in electrophilicity from the neutral species to the radical cation, in some cases approaching the benchmark set by B(C₆F₅)₃.

To experimentally verify the increased Lewis acidity upon oxidation, a stoichiometric reaction with 4-dimethylaminopyridine (DMAP) was undertaken. Addition of 1 equiv. of DMAP to **3**^{•+} in CDCl₃ resulted in a broadening and chemical-shift change for both the DMAP and **3**^{•+} mesityl proton resonances (Figure S12-S13). Furthermore, a sharp singlet was observed in the ¹¹B NMR spectrum at 0.3 ppm (Figure S14), suggesting a tetracoordinate borate species. Encouragingly, when DMAP was added to the neutral **3** in CDCl₃, no changes to the ¹H or ¹¹B NMR spectra were observed (Figure S11). Attempts to unambiguously characterize this adduct proved elusive as single crystals were not obtained and decomposition to an insoluble precipitate was observed in solution over time. Nevertheless, the *in-situ* experiment provides evidence for the formation of the Lewis adduct of DMAP and **3**^{•+} and no adduct formation with the neutral **3**.

Catalytic experiments were performed to further validate the increase in Lewis acidity. It has been well established that strong Lewis acids can dimerize α -methylstyrene, and we sought to explore whether this was possible with **3**^{•+} as well.²⁹ The reaction of 5 mol % **3**^{•+} with α -methylstyrene in CDCl₃ led to the complete conversion to cyclic and linear dimers at 40 °C after 18 h (Scheme 1a). Encouragingly, this reaction did not occur whatsoever when neutral **3** was used as a catalyst. To expand the reactivity scope, we investigated whether **3**^{•+} was Lewis acidic enough to be a catalyst for carbonyl hydrosilylation. To this end we compared the relative activity of **3** vs. **3**^{•+} in the hydrosilylation of 4-bromobenzaldehyde. Using 5 mol% of each catalyst in CDCl₃ at 40 °C resulted in complete conversion to the reduced silyl ether with **3**^{•+} after 24 h, but no reaction was observed with **3** (Scheme 1b).

The initial reactions had to be heated to 40 °C due to the limited solubility of **3**^{•+} in CDCl₃. Therefore, we opted to use a more polar



and donating solvent to further explore the reactivity. To our surprise, catalytic activity was substantially increased in CD₃CN, and **Scheme 1**. a) Dimerization of α -methylstyrene and b) hydrosilylation of 4-bromobenzaldehyde using **3**** in CDCl₃. c) Substrate screening of hydrosilylation using **3**** in CD₃CN.

the reaction completed in less than five minutes at room temperature with full conversion of benzaldehyde to the silyl ether product (Scheme 2c, **4a**). This is contradictory to other known Lewis acids such as B(C₆F₅)₃, where strong Lewis basic solvents hinder electrophilicity.³⁰ Additionally, an EPR spectrum was collected after the reaction was complete and a nitrogen hyperfine coupling pattern was retained (Figure S21). When hydrosilylation was attempted on 4-trifluoromethylbenzaldehyde and 4-bromobenzaldehyde (**4b** and **4c**), the reaction went to completion after less than five minutes at room temperature. No conversion was observed using anisaldehyde (**4d**), 4-dimethylaminobenzaldehyde (**4e**), or acetophenone (**4f**) under the same conditions. We attribute this observation to a less electrophilic carbonyl carbon, making hydride delivery less favorable. Furthermore, reactions with benzophenone and cyclohexanone showed that hydrosilylation was achievable with ketones, and full conversion was rapidly observed at room temperature (**4g** and **4h**). By contrast, neutral **3** was not able to facilitate any reactions under identical conditions, with any of the substrates, again highlighting the increased Lewis acidity of **3****.

The stoichiometric reaction of Et₃SiH with **3**** was performed as control experiment and interestingly led to the gradual quenching of the radical cation, as evidenced by EPR spectroscopy (Scheme S19), and the formation of several silicon-containing species, including FSiEt₃ (Figure S15–18). This decomposition and radical quenching led us to consider that a homolytic reaction pathway may be plausible, where the hydrosilylation reaction may proceed through an established hydrogen-atom transfer (HAT) pathway,^{31,32} rather than

the traditional borane-catalyzed route.³³ Therefore we undertook Density Functional Theory (DFT) calculations to better elucidate the

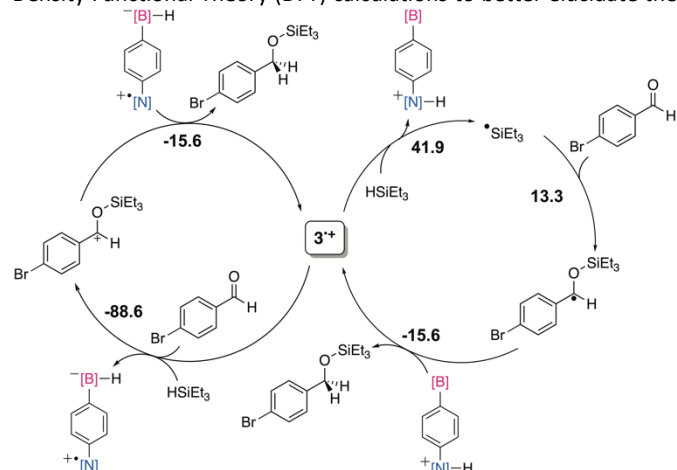


Figure 3. Lewis-acid-mediated pathway (left) and HAT-mediated pathway (right) for the hydrosilylation of 4-bromobenzaldehyde using **3**** in CD₃CN. Numbers in bold are the calculated relative free energy in kcal/mol for each step using B3LYP/6-31+G(d,p) and CPCM solvation model (CH₃CN).

relative energetics of each possible pathway (Figure 3). Calculations were performed at the B3LYP/6-31+G(d,p)^{34–38} of theory employing a continuum solvation model (CH₃CN) using the Gaussian 16 suite of quantum chemistry programs.³⁹ For the Lewis-acid-mediated pathway, a concerted process was considered,³³ where the borane activates the Si–H bond, resulting in a carbonyl carbocation formed from silyl transfer (–88.6 kcal/mol). Delivery of a hydride ion from the borate to the carbocation yields the hydrosilylated product and regenerates the catalyst, **3**** (–15.6 kcal/mol). In the radical pathway, it was found that the HAT from HSiEt₃ to the nitrogen was highly endergonic to generate the SiEt₃ radical (41.9 kcal/mol), and then exergonic to produce the carbonyl radical (13.3 kcal/mol). Formation of the product is also exergonic, resulting from a second HAT step that releases the silyl ether product, and regenerates **3**** (–15.6 kcal/mol).

To further support the computational results, several control experiments were performed. To rule out the possibility photoactivation of phenothiazine, a control experiment focusing on the hydrosilylation of 4-bromobenzaldehyde was performed in the dark, also proceeding to full conversion. Additionally, to probe the potential HAT pathway, a silane with a weaker Si–H bond, tris(trimethylsilyl)silane [HSi(TMS)₃], was used in place of triethylsilane.⁴⁰ Under the same reaction conditions, the hydrosilylation of 4-bromobenzaldehyde did not go to completion, even after three days, compared to Et₃SiH which is complete within 5 minutes. Although the Si–H bond of HSi(TMS)₃ is weaker, the trimethylsilyl groups increase the steric bulk around the hydride, which may preclude activation by the borane. This finding further supports a Lewis-acid-mediated mechanism rather than HAT. To further validate this hypothesis, the reaction of two equivalents of **oC** with 9,10-dihydroanthracene was undertaken. This substrate is known form anthracene via homolytic H₂ loss.⁴¹ After 2 days at room temperature, ¹H NMR spectroscopy indicated only 11% conversion to anthracene, further heating to 40 °C for another 4 days, resulting

in a conversion of 19 % anthracene (Figure S20). This observation suggests that while HAT may be possible, it is unlikely to be occurring under the catalytic conditions.

To summarize, this work highlights how the Lewis acidity of a benzophenothiazine-substituted borane can be increased on-demand through single-electron oxidation of the redox-active motif. The neutral species **3** was not Lewis acidic or catalytically active, however, **3^{•+}** can facilitate the catalytic hydrosilylation of carbonyls in both CDCl_3 or CD_3CN , highlighting the necessity of oxidation to turn on reactivity. Catalytic activity is heightened in CD_3CN compared to CDCl_3 , atypical for boron Lewis acids, and shows complete conversion of electron deficient carbonyls in less than five minutes at room temperature. Computational analysis suggest a Lewis-acid-mediated pathway as opposed to a HAT pathway; however, further mechanistic investigations are underway to solidify this hypothesis. The reported approach provides access to a new class of Lewis acids, potentially unlocking dual modes of reactivity through introduction of both Lewis acidic and radical character.

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Conflicts of interest

There are no conflicts to declare.

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