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Reaction of $InCl_3$ with Various Reducing Agents: $InCl_3$–$NaBH_4$-Mediated Reduction of Aromatic and Aliphatic Nitriles to Primary Amines[§]

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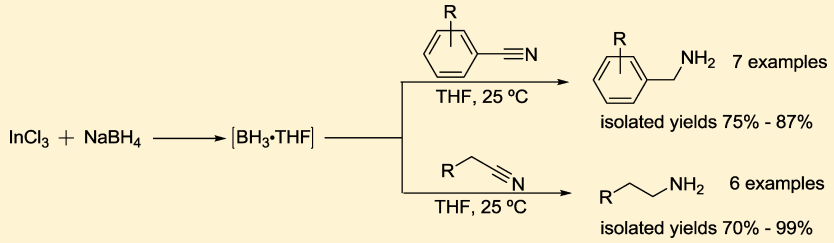
Supporting Information



ABSTRACT: While alternative methods of preparing dichloroindium hydride ($HInCl_2$) via the in situ reduction of $InCl_3$ using lithium amino borohydride (LAB) were explored, generation of $HInCl_2$ from the reduction of $InCl_3$ by sodium borohydride ($NaBH_4$) was also re-evaluated for comparison. The reductive capability of the $InCl_3/NaBH_4$ system was found to be highly dependent on the solvent used. Investigation by ^{11}B NMR spectroscopic analyses indicated that the reaction of $InCl_3$ with $NaBH_4$ in THF generates $HInCl_2$ along with borane–tetrahydrofuran (BH_3·THF) in situ. Nitriles underwent reduction to primary amines under optimized conditions at 25 °C using 1 equiv of anhydrous $InCl_3$ with 3 equiv of $NaBH_4$ in THF. A variety of aromatic, heteroaromatic, and aliphatic nitriles were reduced to their corresponding primary amine in 70–99% isolated yields. Alkyl halide and nitrile functional groups were reduced in tandem by utilizing the reductive capabilities of both $HInCl_2$ and BH_3·THF in a one-pot reaction. Finally, the selective reduction of the carbon bromine bond in the presence of nitriles was achieved by generating $HInCl_2$ via the reduction $InCl_3$ with $NaBH_4$ in CH_3CN or with lithium dimethylaminoborohydride (MeLAB) in THF.

1. INTRODUCTION

The prevalence and extensive use of amines as starting materials for plastics, agrochemicals, and dyes in industry make it an important functional group in organic chemistry.[1] Amines also play important roles in biological processes and in many pharmaceuticals widely used today.[1] The growing interest in and use of amines has necessitated novel and efficient methods for their synthesis.[2] Among the many procedures developed to synthesize amines, the reduction of nitriles is an attractive method because of the ready commercial availability of nitriles and the high atom efficiency of these reductions.[2] A commonly utilized methodology for the conversion of nitriles to primary amines is the hydrogenation of nitriles in the presence of a transition metal at elevated temperature and pressure.[2] Sodium borohydride in combination with various metal salts, such as nickel, cobalt, and aluminum, have been used to reduce nitriles.[3−5] Although some of these methods efficiently reduce nitriles, many require extreme and extended reaction conditions.[3−5] We previously reported that diisopropylaminoborane $[BH_2N(iPr)_2]$ reduces nitriles to primary amines in the presence of a catalytic amount of lithium borohydride in a relatively mild and efficient manner.[6] Although great advances have been made in the reduction of nitriles, the development of novel, mild methods to reduce nitriles remains an attractive endeavor.[7]

Among the many metal hydrides available, $HInCl_2$ is particularly interesting because of its mild reducing properties, which enable it to efficiently and selectively reduce a variety of different functional groups.[8] Dichloroindium hydride was first prepared by reacting tributylstannane (Bu_3SnH) with anhydrous $InCl_3$ at −78 °C in THF.[9] Alternative procedures for the preparation of $HInCl_2$ have since been reported utilizing DIBAL-H/$InCl_3$, Red-Al/$InCl_3$, and triethylsilane/$InCl_3$.[10] Although $HInCl_2$ has great potential as a mild reducing agent, some of the methods used for its synthesis utilize less than ideal conditions and reagents.[10] Herein, we report our results on the preparation of $HInCl_2$ by alternate methods and our attempted use of $HInCl_2$ in the reduction of aromatic, heteroaromatic, and aliphatic nitriles.

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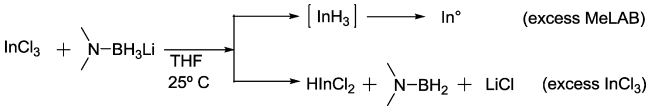
2. RESULTS AND DISCUSSION

2.1. Preparation of $HInCl_2$ from $InCl_3$ and Lithium Aminoborohydride (LAB). Initially, we explored an alternative method of producing $HInCl_2$ by the reduction of $InCl_3$ using LAB reagents previously discovered in our laboratory.[10,11] The experiments were carried out by reacting 1−3 equiv of anhydrous $InCl_3$ with 1−3 equiv of lithium dimethylaminoborohydride (MeLAB) in THF for 1 h at 25 °C. The reactions were then evaluated by determining the ^{11}B NMR spectrum of the supernatant solution under an inert atmosphere. It was discovered that the ratio of $InCl_3$ to MeLAB played a significant role in the formation of the reducing species (Table 1).

Table 1. The $InCl_3$/MeLAB System and the Production of $HInCl_2$ and In[a]



entry	$InCl_3$ (equiv)	MeLAB (equiv)	isolated indium (equiv)
1	1	3	0.98
2	1	2	0.99
3	1	1	0.41
4	2	1	0.24
5	3	1	0

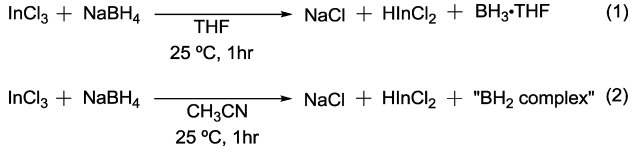
When excess MeLAB was used (Table 1, entries 1 and 2), the reaction mixture quickly turned dark gray and precipitated colloidal indium metal, which aggregated to form a shiny indium nugget. From the weight of the indium metal, it was deduced that indium metal was formed essentially quantitatively in these reactions. Our results indicate that 2 equiv of MeLAB reagent were sufficient to fully reduce $InCl_3$ to indium metal in a quantitative manner (Table 1, entry 2). While other methods of producing $HInCl_2$ undergo a single hydride transfer from the hydride source to the $InCl_3$, our findings indicate that MeLAB can induce multiple hydride transfers.[8−10] It is suspected that the hydride transfers form unstable indium trihydride (InH_3), which subsequently decomposes to produce indium metal (Table 1, entry 2) and hydrogen gas.[12] However, when two or more equivalents of $InCl_3$ were used and 1 equiv of MeLAB was added slowly over 5 min (Table 1, entries 4 and 5), little or no indium metal was generated, and only a slight browning of the reaction mixture was observed. ^{11}B NMR spectroscopy revealed the complete disappearance of the MeLAB quartet at $\delta = -15$ ppm and the appearance of the corresponding aminoborane $[BH_2N(CH_3)_2]_n$ complex that we believe to be a dimer with a triplet at $\delta = 5$ ppm. We believe that the formation of aminoborane is the result of a hydride transfer from the MeLAB reagent to $InCl_3$. The excess $InCl_3$ possibly stabilizes the $HInCl_2$ through a μ-bridge type complex and prevents the loss of hydrogen and the formation of indium metal. It was also found that the $HInCl_2$ produced using the MeLAB/$InCl_3$ reagent system possesses similar reductive capabilities to that of $HInCl_2$ prepared via other methods. For example, we were able to reduce aliphatic halides like (3-bromopropyl)benzene to propylbenzene by reacting it with a 1:2 mol ratio of LAB to $InCl_3$ in THF for 4 h at 25 °C. It is important to note that MeLAB alone is not able to affect the dehalogenation under these reaction conditions.

The efficiency of this new reducing new system was tested by reacting 4-methylbenzonitrile with the MeLAB/$InCl_3$ reagent system. Unfortunately, after several attempts it was found that the MeLAB/$InCl_3$ system does not reduce nitriles. Puzzled by this result, we speculated that $HInCl_2$ itself does not reduce nitriles irrespective of how $HInCl_2$ is prepared. To verify this hypothesis, we attempted the reduction of nitriles using $HInCl_2$ synthesized via known methods, such as the in situ production of $HInCl_2$ from $InCl_3$ and $NaBH_4$.

2.2. Reevaluation of the $InCl_3$/$NaBH_4$ Reagent System. The $InCl_3$/$NaBH_4$ reagent system has received significant attention due to the simple and convenient in situ preparation of $HInCl_2$.[13] $NaBH_4$ is a less expensive and less toxic alternative to the tributyltin hydride originally used to prepare $HInCl_2$.[9,14] Attracted by the simplicity of this $HInCl_2$ generating system, we decided to investigate whether $HInCl_2$ prepared from the $InCl_3$/$NaBH_4$ reagent system was capable of reducing nitriles. Previous studies reported that the solvent utilized in the reaction exerted a significant influence on the reaction rates and yields of various reductions.[13,15] For example, alkyl halides were reduced efficiently (up to 78% reduction) using a catalytic amount of $InCl_3$ along with an equivalent $NaBH_4$ in CH_3CN but very poorly in THF (only 15% reduction) under the same reaction conditions.[13] Similar solvent effects were observed by others working with $HInCl_2$.[14]

Since previous reports had not elucidated the genesis of these solvent effects, we decided to further explore the $InCl_3$/$NaBH_4$ reagent system by monitoring the boron species formed during the reaction via ^{11}B NMR spectroscopy. We consequently reacted a 1:1 molar ratio of $InCl_3$ to $NaBH_4$ in both THF and CH_3CN and analyzed the supernatant solution by ^{11}B NMR spectroscopy to probe the identity of the boron species formed in situ (Scheme 1).

Scheme 1. Reaction of $InCl_3$/ $NaBH_4$ in THF and CH_3CN[a]



[a]Reactions were run for 1 h under argon, from which an aliquot was taken and an NMR sample prepared under an inert atmosphere

^{11}B NMR spectral analysis of $InCl_3$/$NaBH_4$ in THF (Scheme 1, eq 1) revealed a quartet ($J = 105$ Hz) at $\delta = -1$ ppm due to the formation of a borane tetrahydrofuran complex (BH_3·THF).[16] Previous literature in this area has predominantly focused on the formation of $HInCl_2$ rather than the byproduct arising from $NaBH_4$.[8,15] Evidently, the reduction of $InCl_3$ with $NaBH_4$ generates 1 equiv of borane, which then coordinates to THF to give the BH_3·THF complex (Scheme 1, reaction 1). This reaction was also run in dimethyl sulfide (DMS), a known coordinating ligand of borane,[17] and we found that DMS can also trap the generated borane as borane−dimethyl sulfide (BMS). ^{11}B NMR spectral analyses of $InCl_3$/$NaBH_4$ in DMS revealed a quartet ($J = 105$ Hz) at $\delta = -19$ ppm due to the formation of BMS.[17]

When the same reaction was run in CH_3CN (Scheme 1, eq 2), a significantly different ^{11}B NMR spectrum was observed. A triplet ($J = 102$ Hz) at $\delta = -8.5$ ppm indicative of a BH_2 species was observed. We surmised that the initially formed borane reduces the CH_3CN solvent to afford the BH_2-containing complex observed in the ^{11}B NMR spectrum (Scheme 2).

These results clearly indicate that the unusual solvent effect previously reported in the $InCl_3$/$NaBH_4$ reducing system is

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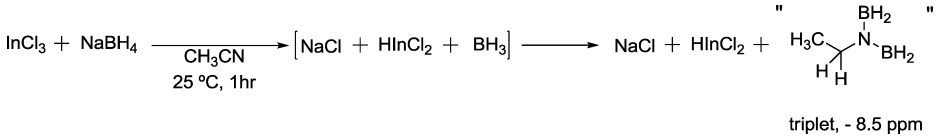
Scheme 2. $InCl_3/NaBH_4$ System in Acetonitrile

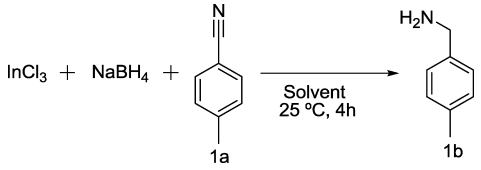


primarily due to the ability of the solvent to either coordinate or scavenge the borane formed during the reaction between $InCl_3$ and $NaBH_4$. Additionally, these results are also consistent with the reported rearrangement of borane−nitrile adducts to the observed aminoborane product.[18]

We suggest that the poor reduction of alkyl halides using a catalytic amount of $InCl_3$ along with 1 equiv of $NaBH_4$ in THF that was previously reported[13] (vide supra) is likely because of the inhibition of the catalytic cycle by the in-situ-generated BH_3·THF. Consequently, when a stoichiometric amount of $InCl_3$ was used along with 3 equiv of $NaBH_4$, (3-bromopropyl)-benzene was fully reduced with an isolated yield of 80%, indicating that BH_3·THF or the solvent THF has little effect on stoichiometric reductions involving $HInCl_2$.

2.3. Reduction of Nitriles Using the $InCl_3/NaBH_4$/THF System. We postulated that on the basis of the ^{11}B NMR spectral data, the $InCl_3/NaBH_4$ system in THF should reduce nitriles efficiently and explored the reduction of 4-methylbenzonitrile under a variety of reaction conditions. The results are summarized in Table 2.

Table 2. The $InCl_3/NaBH_4$ System and the Reduction of 4-Methylbenzonitrile[a]



entry	$NaBH_4$ (equiv)	$InCl_3$ (equiv)	solvent	isolated yield[a] (%)
1	1	1	CH_3CN	*b*
2	1	1	THF	40
3	1	1	DMS	20
4	0	1	THF	*b*
5	1	0	THF	*b*
6	1	2	THF	62
7	1	3	THF	26
8	2	1	THF	72
9	3	1	THF	79
10	1	1	THF/diglyme (3:2)	80

[a]Reactions were carried out on 3 mmol scale in 10 mL of solvent. [b]Starting material was essentially quantitatively recovered.

4-Methylbenzonitrile does not undergo reduction in CH_3CN (Table 2, entry 1), whereas it is reduced to the reduced product amine in THF and in DMS (Table 2, entries 2, 3). Additionally, both $InCl_3$ and $NaBH_4$ are necessary for the reduction of 4-methylbenzonitrile (Table 2, entries 4, 5). Further optimization revealed that 1 equiv of $InCl_3$ and 3 equiv of $NaBH_4$ afforded the best results (Table 2, entry 9). The need for an excess of $NaBH_4$ in the optimized reduction of 4-methylbenzonitrile is possibly due to the lack of solubility of $NaBH_4$ in THF. Additionally, the need for excess $NaBH_4$ is likely due to the coating of the $NaBH_4$ particles with the NaCl byproduct, which likely impedes the efficient formation of BH_3·THF. To improve the solubility of $NaBH_4$ in THF and prevent the coating of the $NaBH_4$ particles with NaCl, varying amounts of diglyme, a known solvent for $NaBH_4$, was added. After some optimizations, it was found that a mixture of THF/diglyme (3:2) was adequate to solubilize $NaBH_4$ and allow the use of $InCl_3$ and $NaBH_4$ in a 1:1 molar ratio to efficiently reduce 4-methylbenzonitrile (Table 2, entry 10). However, it was found that a significant amount of diglyme in the reaction mixture complicated the isolation of product amine because of the increased solubility of the product amines in water. Consequently, 3 equiv of $NaBH_4$ in THF was selected as the optimum ratio to investigate the reduction of other aromatic, heteroaromatic, and aliphatic amines (Table 3).

The results summarized in Table 3 demonstrate that the $InCl_3/NaBH_4$ system was able to reduce a variety of aromatic nitriles, including aromatic nitriles with electron donating groups (Table 3, entries 2, 3), in good to excellent yields (72−98%). A variety of halogen-substituted aromatic nitriles (Table 3, entries 4−7) were also reduced using this simple procedure.[19]

Although benzyl and aliphatic nitriles are typically more challenging to reduce because of the acidity of the α-hydrogens, which tend to be deprotonated under some methods,[20] the $InCl_3/NaBH_4$ system in THF readily reduced these substrates to their corresponding primary amines in good to excellent yields (Table 3, entries 8−13). Nitriles containing heteroaromatic rings such as thiopheneacetonitriles were also reduced exceedingly well using this system (Table 3, entry 12, 13).

Although other metal halide/sodium borohydride systems are known to reduce nitriles,[3−5] the $InCl_3/NaBH_4$ system presented here is fundamentally distinct from these other methods. We have shown that $InCl_3$ generates BH_3·THF from $NaBH_4$, which effects the reduction of nitriles. In the case of nickel chloride, it is reported that nickel boride is generated from $NaBH_4$, and this boride catalyzes the reduction of nitriles via a hydrogenation method.[5] The $InCl_3/NaBH_4$ system is unique in that it generates BH_3·THF in situ, making this reagent combination distinct from other methods.

2.4. Tandem Reductions Using $HInCl_2$ and BH_3·THF. While the previous study demonstrated the $InCl_3/NaBH_4$ system's ability to reduce nitriles to primary amines utilizing the in-situ-generated BH_3·THF, we also sought to explore the reductive capabilities of the mixture of $HInCl_2$ and BH_3·THF. This was achieved by investigating a tandem reduction reaction that would utilize both the $HInCl_2$ and BH_3·THF generated in situ from the $InCl_3/NaBH_4$ system.

Since $HInCl_2$ is known to reduce alkyl halides,[15] 4-(bromomethyl)benzonitrile was selected as a probe to demonstrate the tandem reduction of both the halide and nitrile using the $InCl_3/NaBH_4$ system in THF. 4-(Bromomethyl)benzonitrile underwent the expected tandem reduction to afford 4-methylbenzylamine in an isolated yield of 61% (Scheme 3). 6-Bromohexanenitrile also underwent a similar tandem reduction to afford hexylamine in an isolated yield of 68%, clearly demonstrating the reductive potential of $HInCl_2$ and BH_3·THF generated in situ from the $InCl_3/NaBH_4$ system in THF.

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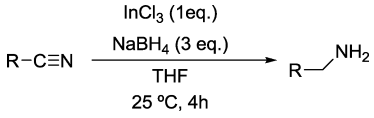
2.5. Selective Reduction of Halides in the Presence of Nitriles. The selective reduction of halides in the presence of nitriles using the $InCl_3/NaBH_4$ system was also investigated. The main obstacle envisioned for this reaction was the selective scavenging of BH_3·THF from the mixture of $HInCl_2$ and BH_3·THF. It was reported that tetramethylethylenediamine (TMEDA) readily complexes with BH_3 to form $(BH_3)_2$·TMEDA.[21] It was thus anticip run "i:/template/macmillan/npgeqn.3mated that TMEDA would selectively coordinate to BH_3·THF and allow the selective dehalogenation utilizing only $HInCl_2$. Upon addition of 1 equiv of TMEDA to the mixture of $HInCl_2$ and BH_3·THF, a clear shift was observed in the ^{11}B NMR spectra from the quartet at −1 ppm corresponding to BH_3·THF to a quartet at −10 ppm indicating the formation of $(BH_3)_2$·TMEDA (Scheme 4).

Table 3. $InCl_3/NaBH_4$ Reduction of Aromatic, Heteroaromatic and Aliphatic Nitriles to Primary Amines[a]



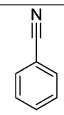
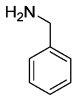
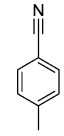
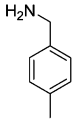
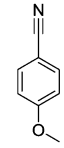
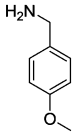
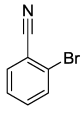
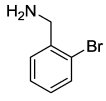
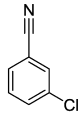
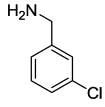
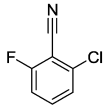
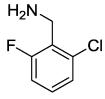
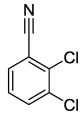
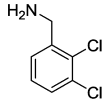
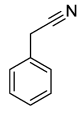
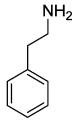
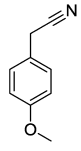
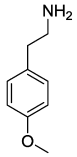
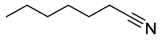
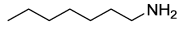
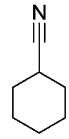
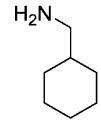
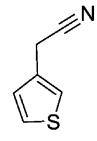
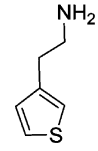
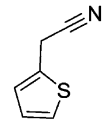
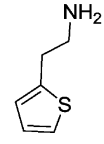
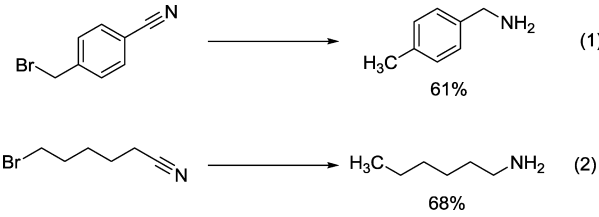
Entry	Substrate	Product	Isolated Yield (%)
1			75
2			79
3			83
4			80
5			87
6			75
7			75
8			70
9			80
10			86

Table 3. continued

Entry	Substrate	Product	Isolated Yield (%)
11			72
12			97
13			98

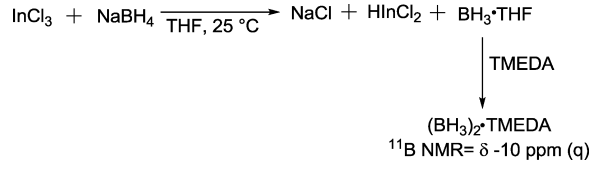
[a]Reactions were carried out on 3 mmol scale with 1 equiv of InCl3 and 3 equiv of NaBH4 in 10 mL of THF. Reaction progress was monitored by TLC and IR.

Scheme 3. Tandem Reduction of Bromonitriles[a]



[a]Reactions were carried out on 3 mmol scale with 1 equiv of nitrile, 1 equiv of $InCl_3$, and 3 equiv of $NaBH_4$ in 10 mL of THF at 25 °C for 4 h under argon.

Scheme 4



However, 4-(bromomethyl)benzonitrile was not selectively reduced to 4-methylbenzonitrile when reacted with $InCl_3/NaBH_4$/TMEDA

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in THF. Instead, the starting material was quantitatively recovered. It was suspected that TMEDA complexed to both BH_3·THF and $HInCl_2$, rendering the reducing agents unreactive. Similarly, $InCl_3$/$NaBH_4$/TMEDA in CH_3CN also resulted in the recovery of starting material, further demonstrating TMEDA's ability to complex $HInCl_2$ and render it unreactive.

Continued exploration of the selective reduction of halides prompted us to revisit the MeLAB/$InCl_3$ system, which was found to reduce (3-bromopropyl)benzene to the corresponding propylbenzene. It was speculated that this system was also capable of effecting selective reductions utilizing the generated $HInCl_2$ because other hydride sources like BH_3 are not generated in this system and would not interfere with the reduction. After some optimization, the MeLAB/$InCl_3$ system was found to selectively reduce alkyl halides in the presence of nitriles as evidenced by the reduction of 4-(bromomethyl)-benzonitrile to 4-methylbenzonitrile in 70% yield. Lastly, as noted earlier, CH_3CN was found to be an excellent borane scavenger. This property of CH_3CN, along with $HInCl_2$'s ability to reduce halides, was utilized to selectively reduce 4-(bromomethyl)benzonitrile to 4-methylbenzonitrile in an isolated yield of 65% as well as the full conversion 6-bromohexanenitrile to hexanenitrile.[13] The results of these selective reductions are summarized below in Scheme 5.

3. CONCLUSION

In summary, the reaction of $InCl_3$ with MeLAB in a 2:1 ratio produces $HInCl_2$, which was unsuitable for nitrile reduction. Use of excess MeLAB reduced $InCl_3$ to indium metal, presumably through the intermediate formation of InH_3. Reinvestigation of the previously reported $InCl_3$/$NaBH_4$ system by ^{11}B NMR spectroscopy revealed the formation of BH_3·THF and $HInCl_2$ upon reduction of $InCl_3$ with $NaBH_4$ in THF. Both BH_3·THF and $HInCl_2$ were found to be capable of effecting selective and/or tandem reductions. $InCl_3$/$NaBH_4$ in THF was found to reduce nitriles to the corresponding primary amines in a simple, efficient, and mild manner at 25 °C using the in-situ-generated BH_3·THF. Aromatic, heteroaromatic, benzylic, and aliphatic nitriles were reduced to their corresponding primary amine in good to excellent yields (72−98%). Additionally, it was demonstrated that halides and nitrile functionalities can be reduced in tandem by making use of the reductive capabilities of both $HInCl_2$ and BH_3·THF reducing agents. This was demonstrated by reducing 4-(bromomethyl)benzonitrile to the corresponding 4-methylbenzylamine with an isolated yield of 85%. Selective reduction of halides in the presence of nitriles was achieved by using either $InCl_3$/$NaBH_4$ in CH_3CN or MeLAB/$InCl_3$ in THF (Scheme 6).

4. EXPERIMENTAL SECTION

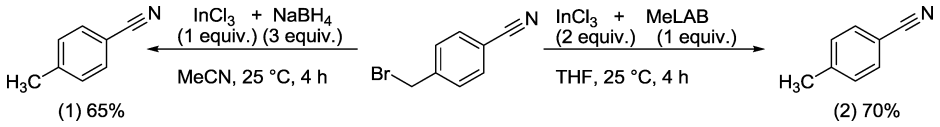
4.1. General Methods. All reactions were carried out in oven-dried glassware under an argon atmosphere with magnetic stirring. All air and moisture-sensitive compounds were introduced via syringe or cannula through a rubber septum. Reactions were analyzed by nuclear magnetic resonance (NMR) spectroscopy measured in ppm and were obtained on a 500 MHz spectrometer using $CDCl_3$ (δ = 7.26) as an internal standard for ^1H and 125.7 MHz using $CDCl_3$ (δ = 77.0) as an internal standard for ^{13}C spectra, as well as 160 MHz using BF_3·Et_2O (δ = 0) as an external standard for ^{11}B spectra. NMR data are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad, dd = doublet of doublets; coupling constants (J) are given in Hertz (Hz).

4.2. Materials. Materials were purchased commercially and used without further purification unless otherwise noted. CH_3CN and THF were transferred from a solvent purification system to an ampule under an argon atmosphere and stored for no more than 4 weeks before use.

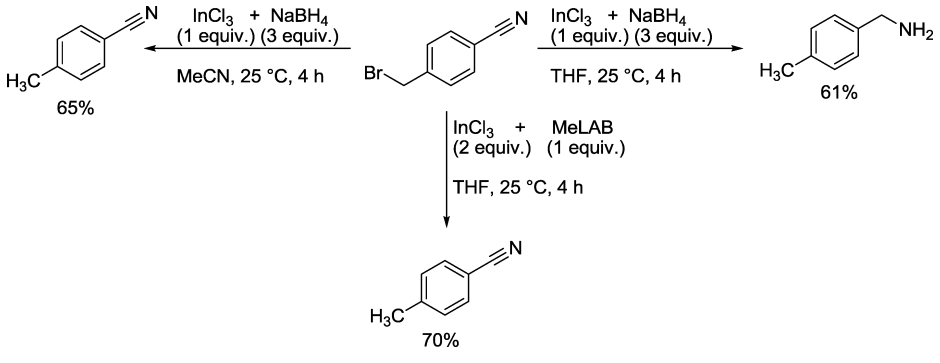
4.3. General Procedure for the $InCl_3$/MeLAB Studies (Table 1). The following procedure for the reaction of $InCl_3$/MeLAB is representative. An oven-dried round-bottom flask (25 mL) was cooled under argon and charged with a stir bar, anhydrous $InCl_3$ (0.663 g, 3 mmol), and anhydrous THF (10 mL), and then fitted with a rubber septum. The mixture was stirred vigorously for 5 min, followed by the slow addition of MeLAB (3 mL of a 1 M solution in THF, 3 mmol) over 5 min via syringe. The reaction was then stirred at 25 °C for 1 h under argon. An aliquot was taken and analyzed by ^{11}B NMR spectroscopy. The metal nugget formed during the reaction was collected, dried, and weighed. See Table 1.

4.4. $InCl_3$/LAB Reduction of the Carbon Bromine Bond. An oven-dried round-bottom flask (25 mL) was cooled under argon and charged with a stir bar and anhydrous $InCl_3$ (1.327 g, 6 mmol), and then fitted with a rubber septum, followed by the addition of anhydrous THF (10 mL). (3-Bromopropyl)benzene (0.456 mL, 3 mmol) was then added dropwise to the reaction flask, followed by the dropwise addition of MeLAB (3 mL of a 1 M solution in THF, 3 mmol) over 5 min while stirring. The reaction mixture was allowed to stir at 25 °C, and after 4 h, thin layer chromatography analysis

Scheme 5. Selective Reductions



Scheme 6



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indicated completion of the reaction. The reaction mixture was quenched with deionized water (10 mL), and the mixture was extracted with Et_2O (3 × 10 mL). The combined organic layers were dried with anhydrous $MgSO_4$, filtered, and evaporated in vacuo (25 °C, 1 Torr) to afford the reduced propylbenzene product as a colorless oil (0.278 g, 77% yield).

Propylbenzene.[22] Colorless oil (0.278 g, 77% yield): ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.01 (t, 3H, J = 7.5), 1.72 (m, 2H), 2.65 (t, 2H, J = 7.5), 7.24 (m, 3H), 7.34 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.9, 24.7, 38.2, 125.8, 128.3, 128.5, 142.7.

4.5. General Procedure for the $InCl_3/NaBH_4$ Studies (Scheme 1). The following procedure for the reaction of $InCl_3/NaBH_4$ is representative. An oven-dried round-bottom flask (25 mL) cooled under argon was fitted with a rubber septum and charged with a stir bar, anhydrous $InCl_3$ (0.663 g, 3 mmol), anhydrous THF (10 mL), and $NaBH_4$ (0.11 g, 3 mmol). The reaction was then stirred at 25 °C for 1 h, and an aliquot was taken and analyzed by ^{11}B NMR spectroscopy. A similar procedure was followed when using CH_3CN and dimethyl sulfide as a solvent (see Scheme 1).

4.6. $InCl_3/NaBH_4$ Reduction of the Carbon Bromine Bond. An oven-dried round-bottom flask (25 mL) cooled under argon was fitted with a rubber septum and charged with a stir bar, anhydrous $InCl_3$ (0.663 g, 3 mmol), anhydrous THF (10 mL), and $NaBH_4$ (0.34 g, 9 mmol). The reaction was stirred at 25 °C for 1 h. (3-Bromopropyl)benzene (0.456 mL, 3 mmol) was then added dropwise, and the mixture was stirred at 25 °C. After 4 h, thin layer chromatography analysis indicated completion of the reaction. The reaction was quenched with deionized water (10 mL), and the mixture was extracted with Et_2O (3 × 10 mL). The combined organic layers were dried with anhydrous $MgSO_4$, filtered, and evaporated in vacuo (25 °C, 1 Torr) to afford the reduced propylbenzene product as a colorless oil (0.289 g, 80% yield).

Propylbenzene.[22] Colorless oil (0.289 g, 80% yield).

4.7. General Procedure for the Reduction of Aromatic, Benzyl, and Aliphatic Nitriles (Table 3, Entries 1−13). The following procedure for the reduction of benzonitrile by $InCl_3/NaBH_4$ is representative. An oven-dried round-bottom flask (25 mL) cooled under argon was fitted with a rubber septum and charged with a stir bar, anhydrous $InCl_3$ (0.663 g, 3 mmol), anhydrous THF (10 mL), and $NaBH_4$ (0.34 g, 9 mmol). The reaction was stirred at 25 °C for 1 h, followed by the dropwise addition of benzonitrile (0.306 mL, 3 mmol), and the mixture was stirred at 25 °C. After 4 h at 25 °C, thin layer chromatography analysis and infrared spectroscopy indicated completion of the reaction. The solution was quenched with 3 M hydrochloric acid (10 mL), and the solution was refluxed for 1 h to dissolve remaining metal salts. The reaction mixture was cooled to 25 °C, methanol (5 mL) was added, and the mixture was again refluxed for 1 h. The reaction mixture was then cooled to 25 °C and filtered, and the methyl borate/methanol was removed from the filtrate by evaporation. The remaining acidic solution was extracted with Et_2O/THF (3 × 10 mL), and the organic layers were discarded. The acidic aqueous layer was then basified with NaOH pellets to pH ∼ 10 and again extracted with a 1:1 mixture of Et_2O/THF (3 × 10 mL). The combined organic layers were dried with anhydrous $MgSO_4$, filtered, and evaporated in vacuo (25 °C, 1 Torr) to afford the benzylamine product as a yellowish oil (0.242 g, 75% yield).

Benzylamine (Table 3, Entry 1).[6] Yellowish oil (0.242 g, 75% yield): ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.85 (s, 2H), 3.86 (s, 2H), 7.25−7.36 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 46.5, 126.9, 127.3, 128.7, 143.3.

4-Methylbenzylamine (Table 3, Entry 2).[6] Colorless oil (0.287 g, 79% yield): ^{1}H NMR (500 MHz,$CDCl_3$) δ 1.73 (bs, 2H), 2.35 (s, 3H), 3.80 (s, 2H), 7.16 (d, 2H, J = 8), 7.21 (d, 2H, J = 8.5); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.0, 46.3, 127.2, 129.4, 136.5, 140.4.

4-Methoxybenzylamine (Table 3, Entry 3).[6] Yellowish oil (0.344 g, 83% yield): ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.54 (bs, 2H), 3.80 (s, 5H), 6.87 (d, 2H, J = 9 Hz), 7.23 (d, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 46.0, 55.4, 114.1, 128.4, 135.7, 158.7.

2-Bromobenzylamine (Table 3, Entry 4).[6] Yellowish oil (0.439 g, 80% yield): ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.79 (s, 2H), 3.89 (s, 2H), 7.10 (t, 1H, J = 7.5), 7.28 (t, 1H, J = 7.5), 7.35 (d, 1H, J = 7.75), 7.54 (d, 1H, J = 8); ^{13}C NMR (125 MHz, $CDCl_3$) δ 47.1, 123.6, 127.9, 128.6, 129.2, 132.9, 142.3.

3-Chlorobenzylamine (Table 3, Entry 5).[23] Yellowish oil (0.371 g, 87% yield): ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.52 (s, 2H), 3.82 (s, 2H), 7.18−7.30 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 46.0, 125.3, 126.9, 127.3, 129.9, 134.4, 145.4.

2-Chloro-6-fluorobenzylamine (Table 3, Entry 6).[6] Yellowish oil (0.361 g, 75% yield): ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.74 (bs, 2H), 3.96 (s, 2H), 6.96 (m, 1H), 7.15 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 37.5, 114.3, 125.5, 128.8, 134.9, 160.4, 162.4.

2,3-Dichlorobenzylamine (Table 3, Entry 7).[6] Yellowish oil (0.395 g, 75% yield): ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.75 (bs, 2H), 3.86 (s, 2H), 7.19 (m, 1H), 7.29 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 43.9, 127.4, 129.4, 129.8, 133.3, 133.9 139.2.

Phenethylamine (Table 3, Entry 8).[6] Yellowish oil (0.255 g, 70% yield): ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.44 (s, 2H), 2.74 (t, 2H, J = 6.5), 2.96 (t, 2H, J = 6.5) 7.21 (m, 3H), 7.30 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 40.0, 43.5, 126.2, 128.5, 128.9, 139.9.

2-(4-Methoxyphenyl)ethanamine (Table 3, Entry 9).[6] Yellowish oil (0.362 g, 80% yield): ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.26 (bs, 2H), 2.67 (t, 2H, J = 7), 2.91 (t, 2H, J = 7), 3.76 (s, 3H), 6.83 (d, 2H, J = 6.5), 7.10 (d, 2H, J = 8.5); ^{13}C NMR (125 MHz, $CDCl_3$) δ 39.1, 43.7, 55.2, 113.9, 129.8, 131.9, 158.1.

Heptylamine (Table 3, Entry 10).[24] Yellowish oil (0.297 g, 86% yield): ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.87 (t, 3H, J = 7), 1.28 (m, 8H), 1.41 (m, 2H) 1.51 (bs, 2H), 2.67 (t, 2H, J = 6.5); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.1, 22.6, 26.9, 29.2, 31.8, 33.6, 42.1.

Cyclohexanemethylamine (Table 3, Entry 11).[25] Yellowish oil (0.248 g, 72% yield): ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.85 (m, 2H), 1.2 (m, 4H), 1.30 (s, 2H), 1.70 (m, 5H), 2.49 (d, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 26.1, 26.7, 30.8, 41.3, 48.9.

2-(3-Thienyl)ethanamine (Table 3, Entry 12).[26] Yellowish oil (0.372 g, 97% yield): ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.59 (bs, 2H), 2.75 (t, 2H, J = 6.5), 2.93 (t, 2H, J = 6.5), 6.93 (m, 1H), 6.97 (m, 1H), 7.26 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 34.4, 42.7, 121.2, 125.8, 128.3, 140.2.

2-(2-Thienyl)ethanamine (Table 3, Entry 13).[27] Yellowish oil (0.375 g, 98% yield): ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.42 (bs, 2H), 2.98 (m, 4H, J = 8), 6.85 (m, 1H), 6.95 (m, 1H), 7.16 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 33.2, 40.4, 126.8, 128.3, 128.5, 136.6.

4.8. Tandem Reduction of 4-(Bromomethyl)benzonitrile Using $InCl_3/NaBH_4$ in THF (Scheme 3). An oven-dried round-bottom flask (25 mL) cooled under argon was fitted with a rubber septum and charged with a stir bar, anhydrous $InCl_3$ (0.663 g, 3 mmol), anhydrous THF (10 mL), and $NaBH_4$ (0.34 g, 9 mmol). The reaction was then stirred at 25 °C for 1 h, at which time 4-(bromomethyl)benzonitrile (0.588 g, 3 mmol) was added to the reaction mixture and stirred. After 4 h, thin layer chromatography analysis and infrared spectroscopy indicated completion of the reaction. The reaction was quenched with 3 M hydrochloric acid (10 mL), and the solution was refluxed for 1 h. The reaction mixture was cooled to 25 °C, methanol (5 mL) was added, and the mixture was again refluxed for 1 h. The reaction mixture was again cooled to 25 °C and then filtered, and the methyl borate was removed from the filtrate by evaporation. The remaining acidic solution was extracted with a 1:1 mixture of Et_2O/THF (3 × 10 mL), and the organic layers were discarded. The acidic aqueous layer was then basified with NaOH pellets to pH ∼ 10 and again extracted with a 1:1 mixture of Et_2O/THF (3 × 10 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and evaporated in vacuo (25 °C, 1 Torr) to afford the tandem reduction 4-methylbenzylamine product as a slightly yellowish oil (0.287 g, 61% yield). 6-Bromohexanenitrile also underwent a similar tandem reduction under the same reaction conditions to afford hexylamine as a colorless oil (0.206 g, 68% yield).

4-Methylbenzylamine.[6] Colorless oil (0.287 g, 61% yield): ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.73 (bs, 2H), 2.35 (s, 3H), 3.80 (s, 2H), 7.16 (d, 2H, J = 8), 7.21 (d, 2H, J = 8.5); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.0, 46.3, 127.2, 129.4, 136.5, 140.4.

Hexylamine.[24] Colorless oil (0.206 g, 76% yield): ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.84 (m, 3H), 1.25 (m, 6H), 1.38 (m, 2H), 1.64 (bs, 2H),

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2.63 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.9, 22.5, 26.5, 31.6, 33.6, 42.1.

4.9. $InCl_3$/$NaBH_4$/TMEDA Studies (Scheme 4). An oven-dried round-bottom flask (25 mL) cooled under argon was fitted with a rubber septum and charged with a stir bar, anhydrous $InCl_3$ (0.663 g, 3 mmol), anhydrous THF (10 mL), and $NaBH_4$ (0.34 g, 9 mmol). The reaction was then stirred at 25 °C for 1 h, at which time TMEDA (0.45 mL, 3 mmol) was added, and the mixture was stirred vigorously at 25 °C for 1 h. An aliquot was taken and analyzed by ^{11}B NMR spectroscopy. A similar procedure was followed using CH_3CN as a solvent. Results are summarized in Scheme 4.

4.10. Selective Reduction of the Carbon Bromine Bond in the Presence of Nitriles Using $InCl_3$/LAB in THF (Scheme 5). An oven-dried round-bottom flask (25 mL) fitted with a rubber septum was cooled under argon and charged with a stir bar, anhydrous $InCl_3$ (0.663 g, 3 mmol), and anhydrous THF (10 mL). 4-(Bromomethyl)-benzonitrile (0.588 g, 3 mmol, 3 mmol) was then added dropwise to the reaction flask, followed by the dropwise addition of MeLAB (3 mL of a 1 M solution in THF, 3 mmol) over 5 min with constant stirring. The reaction mixture was then stirred at 25 °C, and after 4 h, thin layer chromatography analysis indicated completion of the reaction. The reaction was quenched with deionized water (10 mL), and the mixture was extracted with Et_2O (3 × 10 mL). The combined organic layers were dried with anhydrous $MgSO_4$, filtered, and evaporated in vacuo (25 °C, 1 Torr) to afford the selectively reduced 4-methylbenzonitrile product as a colorless oil (0.246 g, 70% yield).

4-Methylbenzonitrile.[28] Colorless oil (0.246 g, 70% yield): ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.41 (s, 3H), 7.28 (d, 2H), 7.52 (d, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.9, 109.4, 119.3, 130.0, 132.2, 143.9.

4.11. Selective Reduction of Carbon Bromine Bond in the Presence of Nitriles Using $InCl_3$/$NABH_4$ in CH_3CN (Scheme 5). An oven-dried round-bottom flask (25 mL) fitted with a rubber septum was cooled under argon and charged with a stir bar, anhydrous $InCl_3$ (0.663 g, 3 mmol), anhydrous CH_3CN (10 mL), and $NaBH_4$ (0.34 g, 9 mmol). The reaction was then stirred at 25 °C for 1 h, at which time 4-(bromomethyl)benzonitrile (0.588 g, 3 mmol) was added to the reaction mixture. The reaction mixture was stirred at 25 °C, and after 4 h, thin layer chromatography analysis indicated completion of the reaction. The reaction was quenched with deionized water (10 mL), and the mixture was extracted with Et_2O (3 × 10 mL). The combined organic layers were dried with anhydrous $MgSO_4$, filtered, and evaporated in vacuo (25 °C, 1 Torr) to afford the selectively reduced 4-methylbenzonitrile product as a colorless oil (0.246 g, 68% yield). 6-Bromohexanenitrile also underwent a similar selective reduction under the same reaction conditions to afford hexanenitrile as a colorless oil (0.262 g, 90% crude yield).

4-Methylbenzonitrile.[28] Colorless oil (0.227 g, 65% yield): ^{1}H NMR (500 MHz,$CDCl_3$) δ 2.41 (s, 3H), 7.28 (d, 2H), 7.52 (d, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.9, 109.4, 119.3, 130.0, 132.2, 143.9.

Hexanenitrile.[29] Colorless oil (0.262 g, 90% crude product yield): ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.91 (t, 3H), 1.35 (m, 4H), 1.62 (m, 2H), 2.34 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.7, 17.1, 21.9, 25.1, 30.7, 119.6.

■ ASSOCIATED CONTENT

Supporting Information

^{11}B NMR spectra of boron complexes along with ^{1}H and ^{13}C NMR spectra of all compounds characterized. This material is available free of charge via the Internet at http://pubs.acs.org.

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