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ARTICLE

The Role of Ammonia in Promoting Ammonia Borane Synthesis

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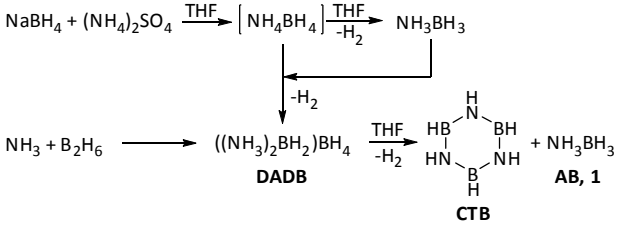
Ammonia promotes the synthesis of pure ammonia borane (AB) in excellent yields from sodium borohydride and ammonium sulfate in tetrahydrofuran under ambient conditions. Examination of the influence of added ammonia reveals that it is incorporated into the product AB, contrary to its perceived function as a catalyst or co-solvent. Mechanistic studies point to a nucleophilic attack by ammonia on ammonium borohydride with concurrent dehydrogenation to yield AB.

Introduction

The ever-growing demand for energy to power the modern world with minimal environmental impact has brought increased attention to renewable energy sources as alternatives to fossil fuels.[1] A robust "hydrogen economy" has been proposed as a viable long-term solution.[2] To realize its full potential, the development and safe transportation of efficient, high-density hydrogen carriers is vital. Ammonia borane (AB, **1**), a solid with excellent stability, high gravimetric hydrogen content (19.6 wt% H_2), and relatively facile hydrogen release has emerged as one of the promising on-board hydrogen-storage materials for automobile applications.[3] Recent reports on the regeneration of AB from spent fuel (dehydrogenation products) have further enhanced its appeal.[4] Moreover, due to its unique reactivity, AB has been successfully utilized as a green alternative to traditional reagents for reduction,[5] reductive amination,[6] and transfer hydrogenation.[7] It has also found application in materials chemistry for the synthesis of metal nanoparticles,[8] as precursor to polyaminoboranes[9] and boron nitride,[10] and as a green hypergolic propellant.[11]

The synthesis of AB remained an elusive endeavor through the first half of the 20th century. The straightforward approach, involving the direct combination of ammonia and diborane, unexpectedly, provided diammoniate of diborane (DADB), an ionic dimer of AB (Scheme 1).[12] Six decades ago, Parry and Shore described in a series of seminal publications that AB could be formed by decomposing DADB in diethyl ether in the presence of catalytic NH_3.[13] During the subsequent decades, efforts from the laboratories of Shore,[14] Mayer,[15] and Manners[16] provided more insight into the synthesis of AB via the displacement of borane-Lewis base complexes with NH_3. Yet, a large-scale synthesis of pure AB directly from NH_3 did not materialize. In a major breakthrough, Shore, Zhao, and coworkers, through an experimental and computational study, elucidated the mechanism of DADB and AB formation via the displacement route.[17] They employed a non-polar solvent (toluene) and a strong Lewis base (dimethyl sulfide (DMS) or dimethyl aniline (DMA) to provide 93-95% pure AB in 91-94% yields (Scheme 2(i)).[18] Kim and coworkers followed up with a low temperature synthesis of AB from ammonia and diborane in 92% yields, containing 5-10% DADB as impurity.[19] Nonetheless, an inherent issue with the displacement approach is the use of pyrophoric reagents and strictly anhydrous conditions.



Scheme 1. DADB formation in AB synthesis.

Salt metathesis of metal borohydrides with ammonium salts remains a preferred approach to AB due to the stability, safety, and handling convenience of the raw materials. Shore and Parry described the preparation of AB, in 45% yield, by adding $LiBH_4$ to a slurry of NH_4Cl or $(NH_4)_2SO_4$ in diethyl ether (Scheme 2(ii)).[13] Building on Parry's work, Geanangel and co-workers[20] described the synthesis of AB from $NaBH_4$ and $(NH_4)_2CO_3$ in 80% yield in 24 h in anhydrous tetrahydrofuran (THF) at 45 °C (Scheme 2(iii)). However, $NaBH_4$ and ammonium salts are sparingly soluble in common ethereal solvents such as THF and diethyl ether. As a result, the primary metathesis product ammonium borohydride (ABH) reacts with the nascent AB to form notable amounts of DADB,[21] which decomposes to cyclotriborazane (CTB) impurity (Scheme 1).[22] Utilizing dilute reaction conditions (0.165 M $NaBH_4$ in THF), we improved upon the Geanangel protocol to provide >98% pure AB in 96% isolated yield (Scheme 2(iv)).[23] Despite the reusability of the solvent after the reaction, the low dilution rendered the process impractical to scale-up. This was overcome by utilizing anhydrous

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dioxane as the solvent.[23] Although the reaction could now be conducted at higher concentrations (1 M $NaBH_4$ in dioxane), the carcinogenicity of dioxane remained a major concern (Scheme 2(v)). We then developed a one-pot synthesis of AB in 90% yield and >99% purity from trimethyl borate and NH_4Cl (Scheme 2(vi)) involving *in situ* formation of $LiBH_4$.[24] The use of pyrophoric $LiAlH_4$ as the hydride source and the need for strictly anhydrous reaction conditions were notable disadvantages. Autrey and coworkers synthesized ABH in liquid NH_3 at -78 °C from $NaBH_4$ and NH_4Cl, followed by an anhydrous THF-mediated decomposition (Scheme 2(vii)).[25] Despite the quantitative AB yields, energy-intensive condensation of large quantities of liquid NH_3, coupled with cooling for the reaction (-78 °C) can make scale-up arduous.

Scheme 2. Approaches to AB.

All of the above described routes to AB require anhydrous reaction conditions and heating or cooling, making scale-up inconvenient and adding to the process cost. A detailed comparison of all the known routes to AB is presented in Table 1. With a cost-effective, scalable and high-yielding AB synthesis being a pre-requisite to its success as an effective hydrogen carrier, development in this regard is vital. To this effect, we had recently communicated a facile, large-scale synthesis of high-purity AB from $NaBH_4$ and $(NH_4)_2SO_4$ in ammoniated reagent-grade THF under ambient conditions.[26] Described herein is a full account of our study, including a mechanistic investigation to identify the role of added NH_3.

i) $NH_3 + L{\cdot}BH_3 \xrightarrow[\text{rt}]{\text{Anhydrous Toluene (1 M)}} NH_3BH_3$ Purity: 93-95% Yield: 91-94%
L = Me_2S or Me_2NPh
Chem.-Eur. J., 2012, **18**, 11994-11999.

ii) $LiBH_4 + (NH_4)_2SO_4 \xrightarrow[\text{rt}]{\text{Anhydrous } Et_2O \text{ (0.46 M)}} NH_3BH_3$ Purity: -- Yield: 45%
J. Am. Chem. Soc., 1958, **80**, 8-12.

iii) $NaBH_4 + (NH_4)_2CO_3 \xrightarrow[\text{40-45 °C, 24 h}]{\text{Anhydrous THF (0.67 M)}} NH_3BH_3$ Purity: -- Yield: 80%
J. Inorg. Nucl. Chem., 1977, **39**, 2147-2150.

iv) $NaBH_4 + (NH_4)_2SO_4 \xrightarrow[\text{40 °C, 2 h}]{\text{Anhydrous THF (0.165 M)}} NH_3BH_3$ Purity: 98% Yield: 96%
Inorg. Chem., 2007, **46**, 7810-7817.

v) $NaBH_4 + (NH_4)_2SO_4 \xrightarrow[\text{40 °C, 2 h}]{\text{Anhydrous Dioxane (1 M)}} NH_3BH_3$ Purity: 98% Yield: 95%
Inorg. Chem., 2007, **46**, 7810-7817.

vi) $B(OMe)_3 + NH_4Cl \xrightarrow[\text{Anhydrous THF (0.13 M)}]{\text{LiAlH}_4,\ \text{0 °C, 3 h}} NH_3BH_3$ Purity: 99% Yield: 90%
Org. Lett., 2012, **14**, 6119-6121.

vii) $NaBH_4 + NH_4Cl \xrightarrow[\text{2) Anhydrous THF (0.74 - 1.9 M)}]{\text{1) liq. } NH_3 \text{ (5 M), -78 °C}} NH_3BH_3$ Purity: 99% Yield: 99%
Energy Environ. Sci., 2008, **1**, 156-160.

Ammonia promoted AB synthesis:

$NaBH_4 + (NH_4)_2SO_4 \xrightarrow[\text{0 °C, 2 h}]{\text{5\% } NH_3,\ \text{THF (1 M)}} NH_3BH_3$ Purity: 98% Yield: 92%
rt, 8 h

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Table 1 Detailed comparison of all known routes to AB.

Entry	Reaction Type	Reagents		Reaction Conditions		Yield (%)	Purity (%)	Ref
		NH_3 Source	BH_3 source	Temperature, time	Solvent (molarity)[a]			
1	Metathesis	$(NH_4)_2SO_4$	$LiBH_4$	rt[b]	Anhydrous Et_2O (0.46 M)	45	--	13
2		$(NH_4)_2CO_3$	$NaBH_4$	40-45 ˚C, 24 h	Anhydrous THF (0.67 M)	80	--	20
3		$(NH_4)_2SO_4$	$NaBH_4$	40 ˚C, 2 h	Anhydrous THF (0.17 M)	96	>98	23
4		NH_4HCO_2	$NaBH_4$	40 ˚C, 2 h	Anhydrous Dioxane (1 M)	95	>98	23
5		NH_4Cl	$NaBH_4$	-78 ˚C, 2 h rt, 1 h	Liquid NH_3 and anhydrous THF (0.74-1.9 M)	99	99	25
6		NH_4Cl	$B(OMe)_3$ $LiAlH_4$	0 ˚C, 3 h	Anhydrous THF (0.13 M)	90	>99	24
7		$(NH_4)_2SO_4$	$NaBH_4$	0 ˚C, 2 h rt, 8 h	Reagent-grade THF containing 5% NH_3 (1 M)	92	>98	Current work
8	Displacement	NH_3	$(CH_3)_2O:BH_3$	-78 ˚C	Dimethyl ether	70	--	13
9		NH_3	$THF:BH_3$	-78 ˚C	THF (1 M)	50	--	14
10		NH_3	B_2H_6	-63 ˚C, 1 h	Monoglyme (0.05 M)	68-76	--	15(a)
11		NH_3	$(CH_3)_2S:BH_3$	-20 ˚C, 0.3 h rt, overnight	Anhydrous Et_2O	86	--	16
12		NH_3	$(CH_3)_2S:BH_3$	rt	Anhydrous toluene (2 M)	94	>93	18
13		NH_3	$DMA:BH_3$	rt	Anhydrous toluene (3 M)	91	>95	18
14		NH_3	B_2H_6	-78 ˚C to rt, 20 h	Anhydrous THF (0.36 M)	92	90-95	19
15	Decomposition	$[H_2B(NH_3)_2]BH_4$		rt	Anhydrous Et_2O containing NH_4Cl and catalytic NH_3	80	--	13
16		$[H_2B(NH_3)_2]BH_4$		25 ˚C, 40 h	Diglyme containing catalytic diborane (0.12 M)	80-91	--	15(b)

[a]With respect to the BH_3 source. [b]rt = room temperature.

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Experimental Section

General Information

Unless otherwise noted, all manipulations were carried out in an open-flask. ^{11}B and ^{1}H NMR spectra were recorded at room temperature, on a Varian INOVA 300 MHz NMR spectrophotometer with a Nalorac quad probe. Chemical shifts (δ values) are reported in parts per million (ppm) relative to $BF_3.Et_2O$ for ^{11}B NMR respectively. Differential scanning calorimetry (DSC) was conducted using a TA instruments DSC Q20 calorimeter. AB was weighed (0.5 mg) in an aluminum pan that was then crimped closed. Ramp rates of 5 ^{o}C/min were used with an N_2 purge gas. Thermogravimetric analysis (TGA) was conducted using the TA Instruments TGA Q500 with a ramp rate of 5 ^{o}C/min with 2 mg of AB.

Tetrahydrofuran (THF, ACS grade containing 0.025% BHT) was purchased from Mallinckrodt chemicals and used without purification. Sodium borohydride ($NaBH_4$, powder, 99% pure by hydride estimation[27]) was purchased in bulk from Dow Chemical Co. (Rohm and Haas). Ammonium acetate (ACS reagent, Sigma-Aldrich), ammonium bicarbonate (>99%, Sigma-Aldrich), ammonium fluoride (98%, Sigma-Aldrich), ammonium chloride (ACS reagent, Mallinckrodt), ammonium formate (97%, Sigma-Aldrich), ammonium hydrogen fluoride (95%, Sigma-Aldrich), ammonium phosphate (>98.5%, Sigma-Aldrich), ammonium hydrogen sulfate (98%, Sigma-Aldrich), ammonium sulfate (ACS reagent, Mallinckrodt), and ammonium carbonate (ACS reagent, Sigma-Aldrich) were purchased from the respective commercial sources and powdered prior to use. Prior to conducting ^{11}B NMR experiments, a drop of DMSO was added to the reaction aliquot to solubilize all of the SBH. The purity of AB was determined by both ^{11}B NMR spectroscopy and hydride estimation (hydrolysis reaction).

Synthetic Methods

Caution: *All of the reactions were carried out in a well-ventilated hood with the reaction vessel outlet directly leading into the hood exhaust due to the hazards associated with escaping toxic and corrosive ammonia and the liberation of large quantities of highly flammable hydrogen.*

Preparation of AB using $NaBH_4$ and ammonium salts with NH_3 as the promoter (Table 1):

Condensed liquid ammonia (2.5 mL) was transferred via cannula to reagent-grade THF (97.5 mL) contained in an indented 250 mL three-neck round bottom flask fitted with an overhead stirrer, stopper, and a cold finger. The flask was cooled in an ice-water bath. Sodium borohydride (3.78 g, 100 mmol) and ammonium salt were transferred to the reaction flask after addition of ammonia. The mixture was stirred carefully at 0 °C and then at room temperature for desired period of time. Upon completion of the reaction, as monitored by ^{11}B NMR spectroscopy (prior to conducting ^{11}B NMR experiments, a drop of DMSO was added to the reaction aliquot to solubilize all of the $NaBH_4$), THF (50 mL) was added to the reaction mixture, stirred for 30 min, filtered through celite, and washed with THF. The filtrate was concentrated *in vacuo* to obtain ammonia borane.

Optimization of reaction conditions with $NaBH_4$ and ammonium sulfate with NH_3 as the promoter (Table 2):

Condensed liquid ammonia was transferred via cannula to reagent-grade THF contained in an indented 250 mL three-neck round bottom flask fitted with an overhead stirrer, stopper, and a cold finger. The flask was cooled in an ice-water bath. Sodium borohydride (3.78 g, 100 mmol) and ammonium sulfate (13.21 g, 100 mmol) were transferred to the reaction flask after addition of ammonia. The mixture was stirred carefully at 0 °C and then at room temperature for the desired period of time to complete the reaction, as monitored by ^{11}B NMR spectroscopy (prior to conducting ^{11}B NMR experiments, a drop of DMSO was added to the reaction aliquot to solubilize all of the $NaBH_4$). In workup A, THF (50 mL) was added to the reaction mixture, whereas, in workup B, 1 M ammoniated THF (50 mL) was added to the reaction mixture and stirred for 30 min, filtered through celite, and washed with THF. The filtrate was concentrated *in vacuo* to obtain ammonia borane.

Optimized large-scale synthesis of AB with NH_3 as the promoter:

Condensed liquid ammonia (500 mL) was transferred via cannula to 10 L reagent-grade THF contained in an indented 22 L three-neck round bottom flask fitted with an overhead stirrer, stopper, and a cold finger. The flask was cooled in an ice-water bath. Sodium borohydride (378.3 g, 10 mol) and powdered ammonium sulfate (1.32 Kg, 10 mol) were transferred to the reaction flask after addition of ammonia. The mixture was stirred carefully for 2 h at 0 °C and then at room temperature for 8 h. Upon completion of the reaction, as monitored by ^{11}B NMR spectroscopy, 1 M ammoniated THF solution (5 L) was added to the reaction mixture, stirred for 30 min, filtered through celite, and washed with THF. The filtrate was concentrated *in vacuo* to obtain ammonia borane (283.9 g, 92%) at >98% chemical purity, as was determined by both ^{11}B NMR spectroscopy (δ -22.37 (q, J = 94.9 Hz)) and hydride analysis. Most of the solvent THF was recovered and re-used.

Deuterium labeling study:

Sodium borohydride (0.19 g, 5 mmol) and ammonium chloride-d_4 (0.57 g, 10 mmol) were added to a 50 mL round bottom flask with a magnetic stir-bar. The reaction contents were cooled in an ice-water bath, followed by addition of THF (5 mL). Condensed liquid ammonia (0.25 mL) was then transferred via cannula to the reaction mixture and reaction careful stirred at 0 ^{o}C for 2 h and room temperature (rt) for 8 h. The contents were then filtered through celite, washed with THF, and the filtrate concentrated *in vacuo* to obtain the product.

The effect of amines on salt metathesis (Table 3):

Sodium borohydride (0.19 g, 5 mmol) and ammonium sulfate (0.66 g, 5 mmol) were added to a 50 mL round bottom flask with a magnetic stir-bar. The corresponding amine was then added to

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the reaction mixture, followed by THF (5 mL). The heterogeneous reaction contents were stirred vigorously at rt till all of the sodium borohydride was consumed, following which a reaction aliquot was analyzed by ^{11}B NMR spectroscopy to gauge the ratio of the amine-borane to ammonia borane.

Preparation of ammonium borohydride (ABH):

ABH was synthesized as described in the literature[28] with minor modifications. $NaBH_4$ (0.19 g, 5 mmol) and powdered NH_4F (0.2 g, 5.5 mmol) were transferred to a 50 mL round bottom flask. The reaction flask was purged with N_2 gas to maintain an inert atmosphere and cooled to -60 ^{o}C using a chloroform/dry ice bath. Liquid NH_3 (3 mL) was added to the flask followed by vigorous stirring for ~6 h at -60 ^{o}C. NH_3 was then evaporated *in vacuo* at -60 ^{o}C to yield a mixture of ABH and NaF, that was used as is for further experiments.

Representative procedure for hydride analysis (Hydrolysis reaction) of AB:

An aqueous solution of AB (1 mmol in 1 mL H_2O) was transferred to a glass vial with a septum inlet fitted with a connecting tube. The connecting tube was attached to an analytical gas burette filled with $CuSO_4$ solution. 3 M HCl was syringed into the vial, dropwise, till no further gas evolution was observed. The gas evolved was measured using the analytical gas burette maintained at 25˚C.

Results and Discussion

Our aim was to achieve a convenient synthesis of high purity AB in near quantitative yields at high concentration of reactants and, if possible, in reagent-grade solvents under open-flask and ambient conditions. We envisioned that achieving facile salt metathesis would necessitate a reaction environment wherein the ionic reagents ($NaBH_4$ and ammonium salts) are soluble. The high solubility of $NaBH_4$ in NH_3[29] and the reported facile decomposition of DADB by NH_3 in ether[13b] prompted the use of NH_3 as an additive to THF. Indeed, a reaction with an equivalent each of $NaBH_4$ and $(NH_4)_2SO_4$ in anhydrous THF at 1 M concentration containing 2.5% NH_3 provided AB under ambient conditions in 77% isolated yield and >99% purity by ^{11}B NMR spectroscopy (Figure 1(c); Table 2, Entry 1, highlighted in boldface). Computational studies from the Dixon laboratory have described the role of NH_3 as a Lewis base catalyst for AB dehydrogenation.[30] Gratifyingly, no AB dehydrogenation products were observed in our protocol and a hydride analysis revealed >98% chemical purity. A reaction without added NH_3 under similar conditions was found to be extremely sluggish (Figure 1(a): ^{11}B NMR spectra of aliquot at 0 ^{o}C after 2 h) and provides impure AB only after 16 h at rt (Figure 1(b)).

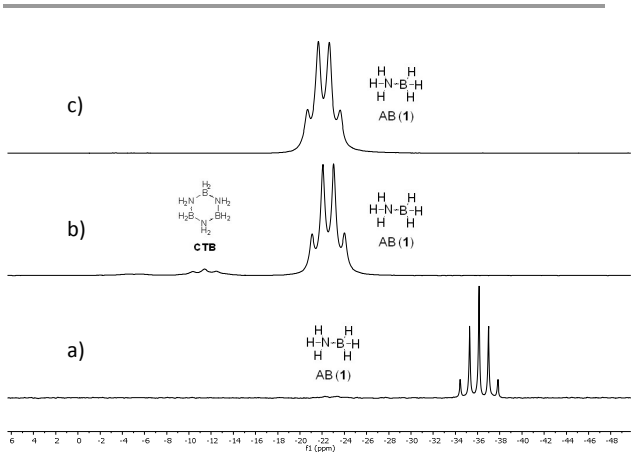

Figure 1. (a) ^{11}B NMR spectrum of $NaBH_4$ and $(NH_4)_2SO_4$ (1:1) at 0 ^{o}C after 2 h in THF. (b) ^{11}B NMR spectrum of AB prepared from $NaBH_4$ and $(NH_4)_2SO_4$ (1:1) at rt after 16 h in THF. (c) ^{11}B NMR spectrum of AB prepared from $NaBH_4$ and $(NH_4)_2SO_4$ (1:1) in THF containing 2.5% NH_3.

Delightfully, when the NH_3-promoted AB synthesis was repeated in reagent-grade THF, no drop in yield or chemical purity was observed. We then proceeded to screen a variety of ammonium salts with the hope of improving the reaction yield (Table 2). Ammonium acetate, fluoride, and formate provided AB in respectable yields, but lower chemical purity than with ammonium sulfate (entries 2-4). Switching to ammonium chloride resulted in marginally faster reactions, but lower yields of AB (entry 5). Amongst the other salts screened (entries 6-10), only ammonium bisulfate gave high purity AB, but in significantly lower, 58% yield. Reactions with ammonium bicarbonate and carbonate led to excessive frothing, rendering stirring and filtration difficult. Overall, none of the screened ammonium salts provided results superior to $(NH_4)_2SO_4$. Notably, utilizing lower equiv. of $(NH_4)_2SO_4$ led to the formation of small amounts of CTB byproduct. Substituting THF with diethyl ether resulted in slower reactions with considerable amounts of unreacted $NaBH_4$ present, even after 12 h.

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Table 2: Preparation of AB using $NaBH_4$ and ammonium salts with NH_3 as the promoter.[a]

Entry	Ammonium salt	Reaction Condition	Yield (%)[b]	Purity (%)[c]
1	**$(NH_4)_2SO_4$**	**0 °C, 4 h; rt, 5 h**	**77**	**98**
2	NH_4OAc	0 °C, 2 h; rt, 2 h	70	94
3	NH_4F	0 °C, 2 h; rt, 9 h	74	96
4	NH_4HCO_2	0 °C, 2 h; rt, 2.5 h	74	97
5	NH_4Cl	0 °C, 2 h; rt, 2 h	71	98
6	NH_4HCO_3	0 °C, 2 h; rt, 2 h	75	96
7	NH_4HF_2	0 °C, 2 h; rt, 3 h	73	95
8	$(NH_4)_3PO_4$	0 °C, 2 h; rt, >16 h	Incomplete	ND[d]
9	NH_4HSO_4	0 °C, 2 h; rt, 8 h	58	98
10	$(NH_4)_2CO_3$	0 °C, 4 h; rt, 6 h	76	97

[a]All reactions were performed in THF (1 M with respect to $NaBH_4$) containing 2.5% NH_3. [b]Isolated yields with respect to $NaBH_4$. [c]Determined by hydride analysis. [d]ND = Not determined (AB was not isolated due to slow reaction).

Surprisingly, the best protocol (Table 3, entry 1) provided AB in varying yields (70-85%) with different batches. To understand this discrepancy, the filter cake was dissolved in DMSO and analysed by ^{11}B NMR spectroscopy, which revealed the presence of residual AB. To avoid this loss of AB, THF containing 1 M NH_3 was added to the reaction mixture prior to filtration, improving the isolated yield of AB to a consistent 87% (Table 3, entry 2, Workup B). Unsatisfied with the less than quantitative yields of AB, we further optimized the reaction conditions for molarity, ammonia content, and reaction temperature (Table 3). Conducting the entire protocol at room temperature (rt) led to longer reaction times and lower AB yields, presumably due to the loss of dissolved NH_3 (entry 3). Increasing the quantity of added NH_3 to 5% led to a rise in AB yields (92%, entry 4, highlighted in boldface). Raising the reaction concentration beyond 1 M provided inferior outcomes (entries 5-6). Thus, the conditions in Table 3, entry 4 was selected as optimal. The robustness and scalability of this optimized NH_3-promoted AB synthesis was demonstrated with a 10-mole scale reaction with no loss in yield or purity.

Thermal analysis of the product AB by DSC displayed melting with exothermic decomposition with an extrapolated onset temperature of 110 °C and a peak melting temperature of 112 °C. TG analysis revealed an onset dehydrogenation temperature of 117 °C, which is in excellent agreement with the literature value.[31]

Table 3: Optimization of reaction conditions with $(NH_4)_2SO_4$ for AB synthesis with NH_3 as the promoter.

Entry	Molarity[a]	NH_3 (%)	Reaction condition	Workup[b]	Yield[c]
1	1	2.5	0 °C, 4 h, rt, 5 h	A	77%
2	1	2.5	0 °C, 4 h, rt, 5 h	B	87%
3	1	2.5	rt, 15 h	B	70%
4	**1**	**5**	**0 °C, 2 h, rt, 8 h**	**B**	**92%**
5	1.5	5	0°C, 2 h, rt, 10 h	B	69%
6	2	5	0°C, 2 h, rt, 18 h	B	43%

[a]Molarity of $NaBH_4$ in THF containing NH_3. [b]A: No addition of ammoniated THF prior to isolation. B: Additional 1 M solution of NH_3 in THF was added to the reaction mixture prior to isolation. [c]Isolated yield with respect to $NaBH_4$.

The success of NH_3 as an additive to accelerate AB synthesis (Scheme 3) posed a fundamental question on its role in the reaction. Interestingly, Parry and Shore had identified anhydrous NH_3 as a "catalyst" for the decomposition of DADB in diethyl ether during the preparation of AB.[13b] To delineate whether NH_3 is a catalyst in our AB synthesis, a deuterium labeling study was conducted aiming to access ND_3BH_3 from ND_4Cl and $NaBH_4$ in THF with 5% NH_3 as the promoter. Ideally, if NH_3 is accelerating the reaction by catalysis or solvation, it should not be incorporated into the product. When such a reaction was performed, unexpectedly, NH_3BH_3 was the major product with ND_3BH_3 as a minor constituent,[32] pointing to the probable role of NH_3 as a reagent.

The observed NH_3BH_3 formation could alternately be rationalized either by a NH_3-ND_3 or H-D exchange from ND_3BH_3. However, the NH_3-ND_3 exchange was ruled out since previous work from this laboratory[33] has shown that amine exchange with NH_3BH_3 occurs extremely slowly at room temperature (rt). To evaluate the possibility of a H-D exchange, a control experiment involving the addition of NH_3 to preformed ND_3BH_3[7b] in THF at 0 °C/rt was conducted. Indeed NH_3BH_3 was obtained as the major product corroborating a fast H-D exchange. Thus, NH_3BH_3 formation from ND_4Cl and $NaBH_4$ in ammoniated THF could be either due to NH_3 being the reagent or a H-D exchange, rendering the isotope labeling study inconclusive and further experiments to delineate the role of ammonia were sought.

$$2\ NaBH_4 + (NH_4)_2SO_4 \xrightarrow[\text{0 °C, 2 h}\ \rightarrow\ \text{rt, 8 h}]{\text{5\% } NH_3,\ \text{THF (1 M)}} 2\ NH_3BH_3 + Na_2SO_4 + 2\ H_2$$
Yield: 92%
Purity: 98%

Scheme 3. AB synthesis in THF with NH_3 as the promoter.

Amines were considered as an appropriate surrogate for NH_3 to ascertain its role due to their similar $NaBH_4$ solvation capabilities.[29] If NH_3 was indeed acting as a reagent in AB synthesis, the amines also should act as reagents and be incorporated in the product providing the corresponding

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amine-boranes. Thus, we embarked upon an investigation on the influence of amines on the metathesis between $NaBH_4$ and $(NH_4)_2SO_4$ in THF at rt at 1 M concentration (Table 4).

Table 4: Effect of added nucleophiles on salt metathesis.

Entry	Nucleophile (Nu)	Time (h)	Product ratio[a] (%)		
			Nu-BH_3	AB	CTB
1	None	16	00	94	06
2	Cyclohexylamine	2	82	18	00
3	Piperidine	2	93	07	00
4	Piperidine (20 mol%)	16	32	67	01
5	Triethylamine	2	85	15	00
6	Pyridine	2	84	16	00
7	Diisopropylamine	2	62	38	00
8	Triisobutylamine	16	09	85	06
9	Diisopropylethylamine	24	03	96	01
10	2,2,6,6-Tetramethylpiperidine	16	00	97	03
11	Dimethyl sulfide	16	00	98	02
12	Triphenylphosphine	2	70	30	00

[a]Ascertained by ^{11}B NMR spectroscopy.

A control experiment, without an amine, had yielded a product mixture containing 94% AB and 6% CTB after 16 h (*vide supra*, Figure 1(b); Table 4, entry 1). Repeating the above reaction in the presence of an equiv. of cyclohexylamine, however, led to significant rate enhancement providing a mixture of cyclohexylamine-borane and AB in 82:18 ratio within 2 h (entry 2). The incorporation of cyclohexylamine in the final product corroborated, indirectly, the role of NH_3 as a reagent. The formation of minor quantities of AB could be explained via a THF-mediated ABH decomposition.[25] Notably, no CTB was detected similar to the results obtained when NH_3 was the additive. Piperidine, a secondary amine, also provided rate acceleration and a mixture of piperidine-borane and AB in 93:7 ratio, within 2 h, with no CTB (entry 3). The rate acceleration was neutralized when only catalytic amounts of piperidine were used (entry 4), stressing the necessity for stoichiometric quantities of additive, further ruling out the role of NH_3 (indirectly) as a catalyst. Screening tertiary and heteroaryl amines, such as triethylamine and pyridine, respectively, also provided the corresponding amine-boranes predominantly, within 2 h (entries 5-6).

To gauge the effect of the nucleophilicity of the amines on reaction outcome, a hindered amine, diisopropylamine, was employed when the reaction was complete within 2 h at rt; however the ratio of the diisopropylamine-borane to AB altered to 62:38 (entry 7). Utilizing even bulkier non-nucleophilic amines, such as triisobutylamine, diisopropylethylamine, and 2,2,6,6-tetramethylpiperidine was revealing (entries 8-10). They provided AB as the predominant product but with concurrent formation of CTB and no enhancement of the reaction rate, similar to the control experiment. Summarizing the above results, it is clear that the presence of a stoichiometric nucleophilic amine is essential to promote the reaction with its concurrent incorporation into the product and suppression of CTB. To further support this theory, dimethyl sulfide, a poor nucleophile, and triphenylphosphine, a strong nucleophile, were utilized as additives. As expected, the reaction with dimethyl sulfide provided no rate acceleration and AB was formed along with CTB, whereas that with triphenylphosphine was complete within 2 h yielding a mixture consisting only of triphenylphosphine-borane and AB in 7:3 ratio (entries 11-12).

With the knowledge that nucleophilic attack on AB occurs extremely slowly at ambient conditions,[33] the incorporation of nucleophiles in the final product could be rationalized on the basis of two distinct reaction pathways (Scheme 4). Path A describes a tandem nucleophile-ammonium salt equilibration-metathesis sequence. Although this justifies the synthesis of amine- and phosphine-boranes at rt from $NaBH_4$,[34] it does not explain the observed rate acceleration and complete suppression of CTB. In addition, the facility of AB synthesis with NH_3 as the nucleophile is not explained since the exchange will provide an identical ammonium salt and offer no rate enhancement. As a result, the possibility of a tandem nucleophile-ammonium salt equilibration-metathesis sequence can be discounted.

A) Tandem Nucleophile-Ammonium Salt Equilibration-Metathesis

$$(NH_4)_2SO_4 + :Nu \underset{\text{rt, THF}}{\overset{-:NH_3}{\rightleftharpoons}} \left[(NuH)_2SO_4\right] \xrightarrow[-H_2,\ \text{THF}]{NaBH_4} Nu{\rightarrow}BH_3$$

B) Tandem Nucleophilic Attack-Dehydrogenation

$$(NH_4)_2SO_4 + NaBH_4 \xrightarrow{THF} \left[NH_4BH_4\right] \xrightarrow[:NH_3 + H_2]{:Nu} Nu{\rightarrow}BH_3$$

Scheme 4. Possible rationale for nucleophile incorporation into the product

Path B illustrates an *in situ* synthesis of ABH from ammonium salts and $NaBH_4$ via salt metathesis, followed by a tandem nucleophilic attack-dehydrogenation sequence, resulting in the incorporation of the nucleophile in the final product. This could be envisioned via an attack of the nucleophile on the boron center of ABH with concurrent dehydrogenation and ammonia release. The rate enhancement observed with strong nucleophiles may be explained via a nucleophile accelerated dehydrogenation of ABH. Furthermore, the byproduct CTB, formed by the reaction between ABH and nascent AB, is circumvented due to the direct nucleophilic attack on ABH. Thus, all of the experimental observations could be reasoned by the mechanistic rationale in Path B.[35] For additional support of

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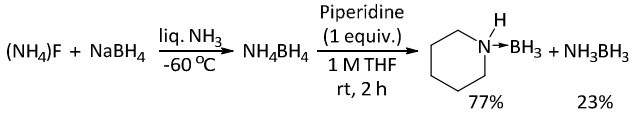
our premise, ABH isolated from a reaction of $NaBH_4$ and NH_4F in liquid NH_3,[28] was treated with THF containing 1 equiv. of piperidine at -40 °C. Upon warming to rt and stirring for 2 h, the reaction mixture revealed the presence of 77% piperidine-borane and 23% AB, substantiating the occurrence of a nucleophilic attack on ABH (Scheme 5). Increasing the equiv. of piperidine (2 equiv.) improved the proportion of piperidine-borane to 86%.



Scheme 5. Reaction of ABH with piperidine in THF.

Conclusions

In conclusion, a convenient and scalable synthesis of pure AB from sodium borohydride and ammonium sulfate in reagent-grade THF with added NH_3 has been developed. The presence of ammonia is critical for the reaction to proceed at ambient temperature and pressure and under open-flask conditions. The role of ammonia in accelerating AB synthesis has been examined. On the basis of amines as surrogates, we hypothesize that, contrary to its presumed function as catalyst or co-solvent, the added NH_3 is incorporated into the product AB. Ammonium borohydride, the primary metathesis product of $NaBH_4$ and ammonium salts, is believed to undergo a tandem nucleophilic attack-dehydrogenation sequence to furnish the product. We believe that this convenient synthesis of AB should aid in its development as a reliable hydrogen carrier.

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