Preparation, NMR Characterization, and Labeling Reactions of Tritiated Borane–THF Complex at High Specific Radioactivity

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Borane–tetrahydrofuran complex is a selective, electrophilic reducing agent. We report a simple and facile synthesis of tritiated borane–THF complex at high specific radioactivity. Li–^{3}H, synthesized from carrier-free tritium gas and dispersed in dry tetrahydrofuran, was treated with boron trifluoride etherate to produce borane–THF complex (*ca.* 3060 GBq/mmol). (The maximum theoretical specific radioactivity of tritium is 1063 GBq/milliatom = 28.76 Ci/milliatom.) This complex was used in an exemplary reduction of 2-naphthoic acid to 2-naphthalenemethanol, in high yield. Both the borane–THF complex and the reduction product were characterized by a combination of ^{1}H, ^{3}H, and ^{11}B NMR techniques, as appropriate. The reduction product was found to have >94% of the maximum theoretical specific radioactivity, and all of the tritium at the reduced position.

Introduction

In tritium-labeling applications borane–tetrahydrofuran (BH_3–THF) complex is valuable in a number of obvious ways: (*i*) the reduction of acids, aldehydes, ketones, epoxides, amides, and nitriles;[1–5] (*ii*) the production of chiral[6] organoboranes for the synthesis of chiral compounds,[7–9] as already demonstrated with deuterium;[10] (*iii*) the selective reduction of acids in the presence of esters or halogenated compounds;[3,6,11] and (*iv*) for the labeling of olefins and olefinic substances which are difficult to label using conventional techniques.[12] These applications, especially the chiral derivatization reactions, are important tools for researchers engaged in tritium-labeling chemistry.

The preparation of tritiated BH_3–THF complex at low to medium specific activity (SA) is well established. Rigden and Koski[13] demonstrated the exchange reaction between diborane and hydrogen gas containing a trace of tritium. Murano *et al.*[14] prepared tritiated diborane by the reaction of tritiated KBH_4 with H_3PO_4, but the chemical yield was only 40% and the product retained only 29% of the theoretical tritium content. The most common synthesis of tritiated BH_3–THF complex relies on the reaction of boron trifluoride etherate (BF_3–$(C_2H_5)_2O$) with labeled $NaBH_4$, according to the reaction in Scheme 1a. This is a robust method, and yields may be as high as 85%.[15,16] In this approach, the tritium content of the borane is controlled by the tritium abundance in the $NaBH_4$, and commercial sources of $NaBH_4$ usually contain ≤50% of the maximum theoretical tritium content.

Scheme 1. Preparation and Use of B^3H_3–THF Complex

(a) $3\,NaB^3H_4 + 4\,BF_3 \longrightarrow 4\,B^3H_3 + 3\,NaBF_4$

(b) $n\text{-Bu-Li} + {}^3H_2 \longrightarrow Li^3H + n\text{-Bu-}{}^3H$

(c) $3\,Li^3H + 4\,BF_3 \longrightarrow B^3H_3 + 3\,LiBF_4$

(d) $R\text{-COOH} + B^3H_3 \longrightarrow R\text{-}C^3H_2\text{-OH}$

(e) $R\text{-COCH}_3 + B^3H_3 \longrightarrow R\text{-}C^3HOH\text{-}CH_3$

[a] Synthesis of B^3H_3–THF complex from NaB^3H_4. Reaction conditions: THF solvent, 1 h at 60 °C. [b] Synthesis of Li^3H. Reaction conditions: 1.1 mol TMEDA, hexanes solvent, 1 h at rt. [c] Synthesis of B^3H_3–THF complex from Li^3H. Reaction conditions: THF solvent, 1 h at 70 °C. [d] Reduction of an acid with B^3H_3–THF complex. Reaction conditions: THF solvent, 50 min at rt. [e] Reduction of a ketone with B^3H_3–THF complex. Reaction conditions: THF solvent, 1 h at rt.

In 1953, Brown *et al.*[17] prepared borane by reducing BF_3–etherate with LiH (as shown in Scheme 1c for Li^3H), and the borane yield was reported to be highly dependent on the reactant stoichiometry[18] and the reactivity of the LiH.[17] Since there have been major advances in the production of finely divided and highly reactive LiH,[19] which we have applied to synthesizing Li^3H (Scheme 1b),[20] we decided to reexamine the synthesis of BH_3 from LiH as a direct path to high specific activity B^3H_3–THF complex.

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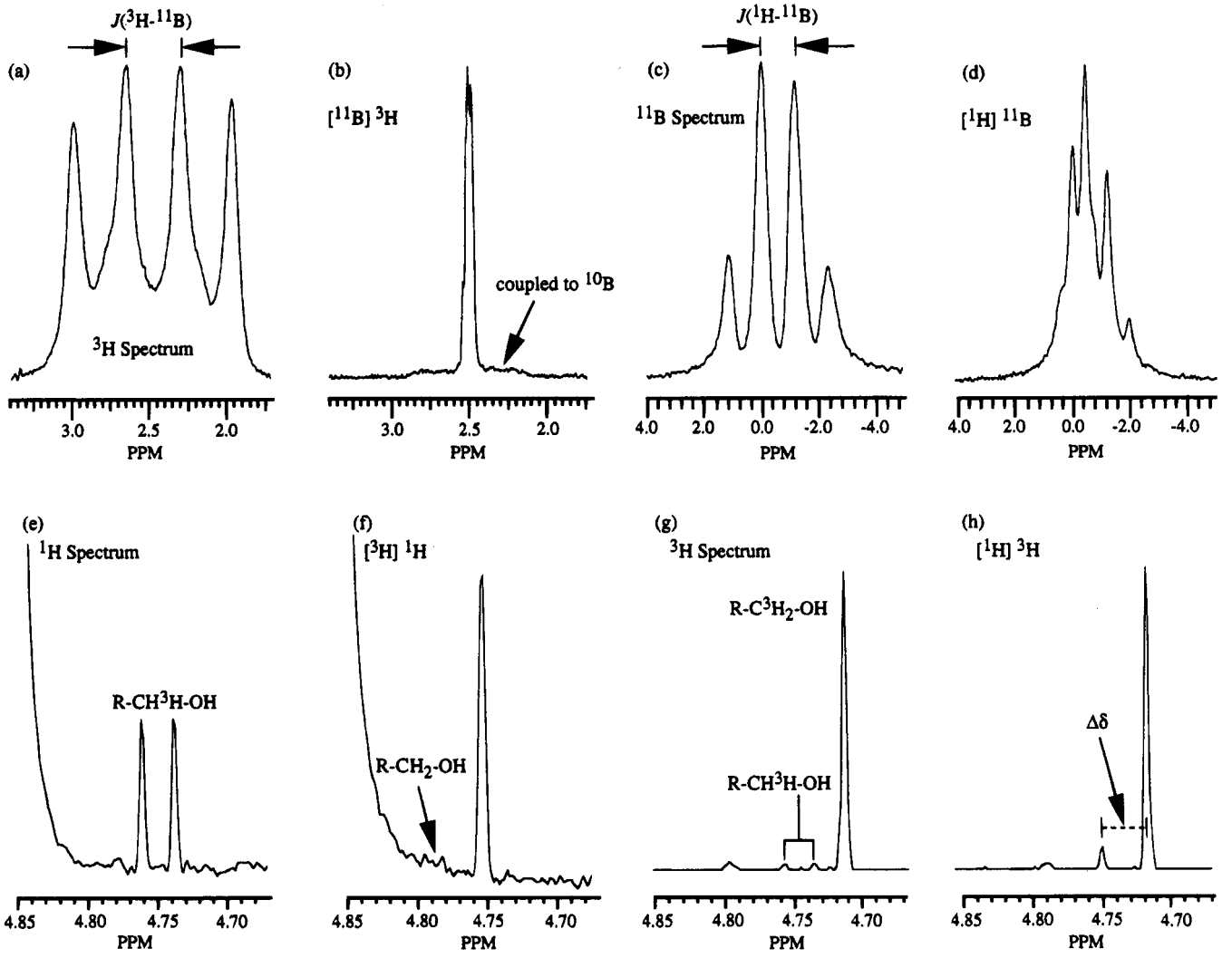

Figure 1. NMR spectra of BH_3–THF complex made from hydrogen gas with 25% tritium content (a–d): (a) 320 MHz ^3H NMR spectrum of the complex (3.40–1.70 ppm); (b) selective ^{11}B-decoupled ^3H NMR spectrum; (c) 96 MHz ^{11}B spectrum (4.00 to −5.00 ppm); (d) ^1H-decoupled ^{11}B spectrum. NMR spectra (4.85–4.67 ppm) of the reduction product (in CD_3OD) given by a B^3H_3–THF complex made from carrier-free tritium gas (R = naphthyl) (e–h): (e) 600 MHz ^1H NMR spectrum; (f) ^3H-decoupled ^1H NMR spectrum; (g) 640 MHz ^3H NMR spectrum; (h) ^1H-decoupled ^3H NMR spectrum.

Results and Discussion

Our general approach was to prove the facility and efficiency of borane production with hydrogen or deuterium reactions prior to attempting any tritium synthesis. An initial step was demonstrating the full synthesis of BH_3–THF complex starting with fresh, commercial LiH. Once this was successfully and reproducibly achieved, the same synthesis was then attempted with LiH freshly synthesized from the appropriate hydrogen gas and *n*-butyllithium.[19] The next step in developing a robust labeling methodology was application of the reagent to specific reductions. In Scheme 1b–e we summarize the overall approach to production of high specific radioactivity B^3H_3–THF complex and the reduction and labeling of simple exemplary substrates.

NMR Characterization of Labeled Borane–Tetrahydrofuran Complex. In early studies it became clear that the presence of tetramethylethylenediamine (TMEDA), which serves as a catalyst in producing LiH from *n*-butyllithium, prevents the evolution of borane from the reaction of BF_3 with LiH. After extensive evacuation of the LiH with slow stirring (to ensure that the LiH was free of TMEDA), addition of the exact stoichiometric amount of BF_3–etherate (4/3 mol) led to the formation of BH_3–THF complex at a yield of *ca.* 60%. The chemical yield of BH_3–THF complex was estimated by comparison between the ^{11}B NMR peak integrals of the product and a commercial sample of BH_3–THF complex.

The ^{11}B-coupled ^3H NMR spectrum of BH_3–THF complex from a 25% $^3H/^1H$ synthesis is shown in Figure 1a. A quartet[21,22] centered at $\delta = 2.5$ ppm (BF_3–etherate in THF = 0 ppm) is observed, with an approximate $J(^3H-^{11}B) = 114.3$ Hz (^{11}B, $I = 3/2$, 80.42%). Selective irradiation of ^{11}B leads to the collapse of this quartet, as shown in Figure 1b, and weak, unresolved peaks due to ^{10}B ($I = 3$, 19.58%) coupling were observed around the base of the residual intense multiplet. The ^3H multiplet at the center of this spectrum arises from an overlay of signals from three isotopomers, two of which have ^1H coupling.

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The expected abundance and multiplicity of the three tritium-containing species from a borane synthesis using a mixture of 25% ^3H and 75% ^1H is 73.0% ($B^1H_2{}^3H$, triplet); 24.4% ($B^1H^3H_2$, doublet) and 2.6% (B^3H_3, singlet).

The ^{11}B NMR spectra of the same BH_3–THF sample are shown in Figure 1, parts c and d. The ^1H- and ^3H-coupled ^{11}B spectrum in Figure 1c, shows a quartet centered at $\delta = -0.7$ ppm. The observed splitting is dominated by the most abundant coupling partner (75% ^1H), and the approximate $J(^1H-^{11}B) = 109.9$ Hz. The observed chemical shift and coupling constant $J(^1H-^{11}B)$ are similar to published data[23] and to our own measurements on unlabeled borane, where $J(^1H-^{11}B) = 107.2$ Hz. When ^1H was decoupled from ^{11}B (Figure 1d) a multiplet was observed, attributable to the overlaid spectra of four isotopomers, with the calculated abundances: 42.2% ($^{11}B^1H_3$, singlet), 42.2% ($^{11}B^1H_2{}^3H$, doublet), 14.1% ($^{11}B^1H^3H_2$, triplet), and 1.5% ($^{11}B^3H_3$, quartet). The singlet, doublet, and triplet peaks are clearly discernible (Figure 1d), and the isotope effect ($\Delta\delta = 0.165 \pm 0.013$ ppm at 96.28 MHz) on the ^{11}B chemical shift induced by ^3H substitution may be extracted. This value compares well with a calculated tritium isotope effect, using reported ^2H primary isotope effects on ^{11}B chemical shifts.[24,25]

Reductions Using Labeled Borane–Tetrahydrofuran Complex. The reduction of 2-naphthoic acid was achieved with other preparations of deuterated or tritiated BH_3–THF complex. The reduction product was isolated and analyzed by radio-HPLC followed by both ^1H and ^2H or ^3H NMR spectroscopy. For deuterated products the sample was also analyzed by mass spectrometry to determine the %D in the molecule.

HPLC analyses showed that the chemical yields of 2-naphthalenemethanol were high (70–90%) and that essentially all radioactivity was in the desired labeled products. Estimates of specific radioactivity were also made by liquid scintillation counting of the isolated HPLC peak effluents, which showed 510 GBq/mmol for the reduction using 25% $^3H_2/^1H_2$, and 2230 GBq/mmol for the carrier-free (100%) tritium experiment. Since the maximum theoretical SA with two tritium atoms per molecule is 2126 GBq/mmol, and the NMR analysis revealed no other labeled positions, we believe the high value (2230 GBq/mmol) in the 100% tritium experiment was due to the combined uncertainties in the calculations from HPLC data (*i.e.* low mass and high radioactivity). The specific radioactivity for both samples was also calculated from the ^1H and ^3H NMR data, as discussed below.

The 600 MHz ^1H- and ^3H-decoupled ^1H NMR spectra of the reduction product from the 100% $^3H_2$ experiment are shown in Figure 1, parts e and f. The (^3H-coupled) ^1H spectrum in Figure 1e shows a doublet [$J(^3H-^1H) = 14.0 \pm 0.9$ Hz] due to the $^1H-^3H$ coupling in the singly tritiated R–CH^3H–OH species. The doublet collapsed into a singlet with double the intensity when ^3H was selectively irradiated (Figure 1f). No signal from the R–CH_2–OH species was observed in these proton spectra, suggesting that the labeled product had a very high incorporation of tritium. If the R–CH_2–OH species was present, a peak would have been detected at the chemical shift indicated in Figure 1f.

The 640 MHz (^1H-coupled) ^3H NMR spectrum in Figure 1g shows a small doublet from the R–CH^3H–OH species, and a large singlet from R–C^3H_2–OH. As expected, the doublet collapsed to a singlet when ^1H was irradiated (Figure 1h). The coupling constant $J(^1H-^3H = 13.9 \pm 0.9$ Hz) and tritium isotope shift ($\Delta\delta = 0.031 \pm 0.001$ ppm) were as expected from previous studies at lower field.[26,27] The calculated specific activity from the peak integrals in Figure 1h gives a value of 2010 GBq/mmol (94.4% of the theoretical maximum of 2126 GBq/mmol). We believe this slightly low SA is due to the loss of tritium through exchange between B^3H_3–THF and the acid hydrogen of naphthoic acid during the reduction. Losses were also observed in deuterium experiments such that the deuterated reduction products incorporated *ca.* 84% of deuterium, as calculated from the mass spectrum. Similar losses were observed in the 25% tritium experiments, as the SA calculated from both HPLC (510 GBq/mmol) and NMR analyses (505 GBq/mmol) are *ca.* 95% of the theoretical SA (532 GBq/mmol). If there is an isotope effect on the exchange between borane and naphthoic acid protons, the rate of tritium exchange would be slower, and the reduced product would therefore incorporate a higher level of tritium than deuterium, as was consistently observed.

The lower than theoretical tritium or deuterium content in reduction products was further investigated by reducing methyl naphthyl ketone, which has no exchangeable hydrogens, with B^2H_3–THF. Mass spectrometric analysis of the reduction product (*ca.* 70% yield) showed 95% deuterium in the molecule, where the product of napthoic acid reductions never exceeded a deuterium content of 84% under similar reaction conditions. We conclude that the BH_3–THF complex has a very similar isotope content to the starting isotopic hydrogen gas (^2H or ^3H).

The selectivity of reductions with BH_3–THF complex was also examined under our reaction conditions. Deuterated B^2H_3–THF complex was used to reduce an equimolar mixture of acid (2-naphthoic acid) and ester (methyl myristate). HPLC analysis of the isolated product mixture showed that only 10% of the methyl myristate was reduced to myristyl alcohol, while the conversion of 2-naphthoic acid to 2-naphthalenemethanol was 75%. Proton and deuterium NMR analyses were used to confirm the ratio of these products, and the conversion of acid to alcohol. This result accords with previous observations that carboxylic acids are rapidly reduced, while the simple esters of aliphatic acids react much more slowly.[3,11]

Conclusions

Highly deuterated or tritiated BH_3–THF has been synthesized at microscale with a yield of *ca.* 60%. The BH_3–THF complex smoothly reduced naphthoic acid to the corresponding alcohol and gave very clean product at excellent yield (70–90%) and very high isotope abundance (≥94% for tritium). The reagent was very effective in ketone reductions and also showed significant selectivity between acid and ester reductions. The reaction

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apparatus employed was simple and compact compared to previous methods,[14,15] and the reagents and reduction products were well characterized by HPLC, NMR, and mass spectrometry.

Tritide reducing agents provide an attractive approach for the incorporation of tritium into molecules of biochemical importance, and as the molecules of interest become more complex, the type of chemistry employed in labelling them needs to be more sophisticated and selective. With the recent demand for chiral drugs,[28] advances in tritium-labeling technology are required to ensure the availability of labeled chiral pharmaceuticals for research and clinical studies. Having now developed a simple and robust synthesis of highly tritiated B^3H_3–THF complex, we intend to pursue the development of useful borane derivatives such as borane–dimethyl sulfide complex[29] and other more stereoselective tritiation reagents. The difficulties associated with the generation and use of extremely highly tritiated, reactive, volatile reagents such as B^3H_3–THF complex should be carefully assessed in planning experiments such as those described in this work.

Experimental Section

General. Many preliminary reactions were carried out with deuterium gas to explore the reactant stoichiometry and other critical parameters for tritium reactions. Deuterium gas (99.7%) was purchased from Liquid Carbonic, San Carlos, CA, and tritium gas (97.9%) was purchased from EG&G Mound Applied Technologies, Miamisburg, OH. *n*-Butyllithium (2.4 M in hexanes) was purchased from FMC Lithium Division, Gastonia, NC, and all other starting materials and reagents were purchased from Aldrich Chemical Co., St. Louis, MO. Chemicals were used without further purification, except that tetrahydrofuran was freshly distilled from sodium and stored under dry nitrogen.

Liquid Scintillation Counting. Tritiated samples were analyzed on a Packard 1500 liquid scintillation counter, using AquaFluor cocktail.

Mass Spectrometry. Mass spectra of deuterated products were measured with a VG Prospec mass spectrometer, operating at 70 eV. All mass spectrometric analyses were carried out by the Analytical Laboratory, College of Chemistry, University of California, Berkeley. Mass spectra were corrected for fragmentation and isotope corrected as part of the %D calculations.

High-Pressure Liquid Chromatography. Analytical HPLC was performed on a Waters C-18 radial pak column, using Waters model 510 pumps. The mobile phase was methanol/water (3:2), pumped at 1.5 mL/min. UV detection was at 275 nm on a Hewlett Packard 1040A diode array spectrophotometer, and radioactivity was monitored by an IN/US β-Ram HPLC flow detector, using a lithium glass scintillant cell with an efficiency of *ca.* 0.5%. The specific radioactivity of the reduction products was determined by comparison of UV standards with the analytical sample, combined with liquid scintillation counting of the isolated HPLC peak effluents.

Proton and Tritium NMR Spectroscopy of Tritiated Samples. Proton and tritium NMR spectra were obtained on a Bruker AC-300 NMR spectrometer, or Bruker AMX-600 MHz spectrometer. ^1H (at 300 or 600 MHz) and ^3H (at 320 or 640 MHz) spectra of reduction products were recorded in CD_3OD using 5 mm $^3H/^1H$ dual probes. For analysis on the AC-300 NMR spectrometer, samples were made to a volume of about 250 μL in Teflon tubes (Wilmad, #6005), which were then placed inside 5 mm glass NMR tubes having a screw-cap (Wilmad, 507-TR-8″). A high-quality ^3H band stop-^1H band pass filter (FBT/20-300/3-6/50-3A/3A, Cir-Q-Tel Inc., Indianapolis, IN) was placed in the proton decoupling line of the instrument, and the observe channel had an in-line ^1H band stop-^3H band pass filter (4CH320/8-3-CD, Trilithic Inc., Indianapolis, IN). Samples analyzed on the AMX-600 NMR spectrometer consisted of *ca.* 150 μL of solution, flame-sealed into a 3 mm OD tube. The 3 mm tubes were placed inside a regular 5 mm NMR tube, and kept concentric with Teflon O-rings. The AMX-600 NMR spectrometer was equipped with appropriate filters: ^3H band stop-^1H band pass (X5BE600/9.5-1-CC, Trilithic Inc.), and ^1H band stop-^3H band pass (6CR640/15-3-CC, Trilithic Inc.). Tritium and proton spectra were acquired over approximately 12 ppm, using the following excitation pulses: (AC-300) 5.0 μs (90°, ^3H), 4.0 μs (45°, ^1H); (AMX-600) 10.0 μs (90°, ^3H), 10.0 μs (60°, ^1H). Referencing of tritium chemical shifts was achieved by generation of a ghost ^3H TMS signal from internal TMS in the ^1H NMR spectrum.[30] Spectra were acquired at 298 K without sample spinning.

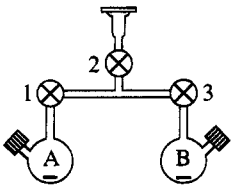

Figure 2. Glassware used for preparation of deuterium- or tritium-labeled BH_3–THF complex, and subsequent reduction of acids or ketones. Flasks A and B had a nominal volume of 5 mL. Valves 1, 2 and 3 were Teflon vacuum valves. Connections between the portions of the apparatus, and to the vacuum line, were made by #9 O-ring joints, using Teflon O-rings. The side-arm connections on each flask consisted of an "electrode adaptor" including a Teflon septum, which allowed injection of materials into the evacuated flasks.

Proton and Deuterium NMR Spectroscopy of Deuterated Samples. All spectra were obtained on a Bruker AC-300 NMR spectrometer, using a 5 mm $^3H/^1H$ dual probe, and observing ^2H on the lock coil. The spectra of reduction products were recorded by taking *ca.* 10% of the product for ^1H analysis (300 MHz, CD_3OD lock), and the remaining 90% for ^2H measurement (46 MHz, CH_3OH lock). Samples were made to a volume of about 500 μL in 5 mm glass NMR tubes. For deuterium experiments, the observe channel had an in-line ^1H band stop-^2H band pass filter (4BE46/5-3-DC, Trilithic Inc., Indianapolis, IN), and spectra were acquired over approximately 22 ppm, using a 35 μs (45°) excitation pulse. Referencing of deuterium chemical shifts was achieved by setting the natural abundance CDH_2OH resonance of the solvent to 3.30 ppm. All spectra were acquired at 298 K with sample spinning.

Boron NMR Spectroscopy. ^{11}B NMR spectra (96 MHz) of tritiated BH_3–THF complex were recorded in THF-d_8 using a 5 mm $^{11}B/^1H/^3H$ probe on a Bruker AC-300 NMR spectrometer. A ^{11}B pass filter (6BE96/7-3-DC, Trilithic Inc.) was placed in the ^{11}B observe channel. No ^1H pass filter was used in the ^1H decoupling line for ^{11}B NMR. ^{11}B spectra were acquired over 135 ppm, using a 4.0 μs (90°) excitation pulse. Boron spectra were acquired at 298 K without sample spinning. ^{11}B chemical shifts were referenced to a THF solution of BF_3–etherate (=0 ppm).

Borane Synthesis. Deuterations were performed on several different chemical scales. Tritiations generally required 0.4 mmol of Li^3H, yielding 0.08 mmol of B^3H_3–THF complex (*ca.* 60% yield), which was used to reduce 0.04 mmol of substrate. The apparatus developed for these syntheses (Figure 2) allowed isolation of the 5 mL side-arm pyrex flasks A and B by closing Teflon vacuum valves 1 and 3. Flasks A and B could also be isolated from the vacuum line by closing Teflon valve 2, thus allowing short-path vapor transfer of materials between the two flasks.

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Typical reaction conditions for the production of deuterated or tritiated BH_3–THF complex were as follows: Deuterium or tritium gas was admitted to a final pressure of *ca.* 100 kPa to one flask of the reaction apparatus, which was connected to a high vacuum line during the entire reaction. A solution of *n*-butyllithium in hexanes (typically 2.4 M, 0.4 mmol, 165 μL) was injected and rapidly stirred. Slow injection of TMEDA (0.44 mmol, 66 μL) to the vigorously stirred solution gave a creamy white precipitate (Li^2H or Li^3H) immediately. The uptake of deuterium or tritium gas was monitored with a Wallace & Tiernan gauge. After 1 h, the excess gas and solvent were removed by evacuation, and the solid hydride was slowly ground by a magnetic stirrer under vacuum for a further hour. Dry nitrogen gas was then introduced into the flask to 80 kPa, and THF (500 μL) was added and the solution outgassed. Nitrogen gas was again admitted to 80 kPa and BF_3–etherate (0.54 mmol, 66 μL) was then injected dropwise into the flask at room temperature, after which the solution was warmed and kept at 70 °C with constant stirring. After 1 h the generation of BH_3–THF complex was considered complete.

Borane NMR. The BH_3–THF complex was vapor transferred to the empty adjoining flask of the apparatus, and subsequently transferred by syringe to an NMR tube for analysis.

Borane Reduction of 2-Naphthoic Acid. The BH_3–THF complex (assumed 60% yield, 0.08 mmol) was vapor transferred to the adjoining second flask, which contained a degassed THF solution (150 μL) of 2-naphthoic acid (6.8 mg, 0.04 mmol) for reduction. The reaction was allowed to proceed in that flask at room temperature, with stirring, for 50 min. At the end of the reaction, methanol (1 mL) was injected to quench the excess borane reagent, the pressure rose significantly, and both solvent and gas was removed in *vacuo*. The reaction flask was then removed from the vacuum line, the product was dissolved in ethyl acetate (1 mL), and the borate salts were removed by extraction with NaOH (1 N, 1 mL, 2×). Ethyl acetate was removed by lyophilization, and the residual solids were dissolved in CD_3OD for ^1H and ^2H or ^3H NMR, radio-HPLC, and liquid scintillation counting analyses. For deuterated products the sample was also analyzed by mass spectrometry to determine the deuterium content (%D) of the molecule. Deuterium Experiment: yield 70%; 84%D; *m*/*z* 161 (10.8%), 160 (63.7%), 159 (19.8%), 158 (5.7%); ^2H NMR (CH_3OH) δ 4.68 (C^2H_2). Tritium (25%) Experiment: yield 89%; specific activity (by 300 MHz NMR, CD_3OD) 505 GBq/mmol; δ 4.80 (CH_2, 57.4%), δ 4.75 (CH^3H, 38.1%), and δ 4.72 (C^3H_2, 4.6%). Tritium (100%) Experiment: yield 73%; specific activity (by 640 MHz ^3H NMR, CD_3OD, ^1H decoupled) 2010 GBq/mmol; δ 4.75 (CH^3H, 12.7%) and δ 4.72 (C^3H_2, 87.3%).

Reduction of Acetonaphthone. B^2H_3–THF (assumed 60% yield, 0.16 mmol, 1 mL THF) was synthesized using the method described above and was vapor transferred to the adjoining second flask, which contained a degassed THF solution (300 μL) of acetonapthone (13.4 mg, 0.08 mmol). After reduction for 1 h with stirring, the reaction was quenched by addition of methanol (1 mL). A mixture of NaOH (1 M, 500 μL) and 30% H_2O_2 (500 μL) was injected (to destroy the dialkoxyborane). The solvent was evaporated and the residue was extracted in the same manner as in the naphthoic acid reduction: yield 70%; 95%D; *m*/*z* 175 (1.0%), 174 (12.1%), 173 (80.2%), 172 (6.7%); ^2H NMR (CH_3OH) δ 4.92 (C^2H).

Reduction of Naphthoic Acid and Methyl Myristate Mixture. B^2H_3–THF (assumed 60% yield, 0.16 mmol, 1 mL THF) was synthesized, using the method described above, and was vapor transferred to the adjoining second flask, which contained a degassed THF solution (300 μL) of 2-naphthoic acid (7.2 mg, 0.04 mmol) and methyl myristate (9.9 mg, 0.04 mmol). The reaction mixture was stirred for 1 h and was quenched by addition of methanol (1 mL), after which the solvents were removed under vacuum and the solid residue was dissolved in CH_3OH. HPLC analysis showed the product 2-naphthalenemethanol in 75% yield [87%D; *m*/*z* 161 (10.9%), 160 (69.1%), 159 (14.6%), 158 (5.4%); ^2H NMR (CH_3OH) δ 4.68 (C^2H_2)] and myristyl alcohol in 10% yield [68%D; *m*/*z* 246 (10.0%), 245 (60.0%), 244 (30.0%); ^2H NMR (CH_3OH) δ 3.46 (C^2H)].

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