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ADDITION COMPOUNDS OF ALKALI METAL HYDRIDES—XIX†

RAPID REACTION OF TRIALKYLBORANES WITH LITHIUM ALUMINUM HYDRIDE IN THE PRESENCE OF TRIETHYLENEDIAMINE. A FACILE AND QUANTITATIVE SYNTHESIS OF LITHIUM TRIALKYLBOROHYDRIDES, INCLUDING DERIVATIVES WITH EXCEPTIONALLY LARGE STERIC REQUIREMENTS

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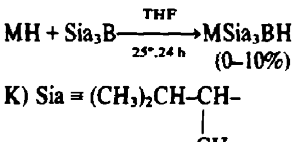
Abstract—Trialkylboranes react rapidly with lithium aluminium hydride (LAH) in diethyl ether in the presence of triethylenediamine (TED) at 0° to form the corresponding lithium triakylborohydrides and aluminum hydride. The aluminum hydride precipitates out of solution as its triethylenediamine adduct. The reaction is applied to a wide variety of triakylboranes. Consequently, the present reaction provides a general, convenient synthesis of lithium trialkylborohydrides including those with exceptionally large steric requirements.

Recent developments[1] in the area of alkali metal trialkylborohydrides have revealed that the trialkylborohydrides are exceptionally powerful nucleophilic reducing agents capable of cleaving cyclic ethers,[2,3] reducing hindered halides,[4] *p*-toluenesulfonate esters of hindered and cyclic alcohols,[5,6] epoxides,[7] and activated olefins,[8] rapidly and quantitatively to the desired products. Investigations in our laboratory and elsewhere have established the ability of hindered and highly hindered trialkylborohydrides to introduce major steric control into the reduction of cyclic and bicyclic ketones.[9] In this respect, these reagents are unequalled by any other reagents currently available. Further, trialkylborohydrides containing an asymmetric alkyl group reduce unsymmetrical ketones to optically active secondary alcohols.[10]

The reactivity of the trialkylborohydrides and the stereochemical course of the reactions involving them are strongly influenced by the steric bulk of the alkyl group on boron.[1] This fact has created immense interest in the exploration of various synthetic routes to the trialkylborohydrides bearing alkyl groups of differing steric requirements. The most direct way to form such hydridoborates is by direct reaction of trialkylboranes and alkali metal hydrides. Such reactions have been carried out using lithium,[11] sodium,[11] and potassium[12] hydrides. The lithium hydride route provides a convenient entry only to the relatively unhindered lithium trialkylborohydrides. Fortunately, potassium hydride, and to a certain extent, sodium hydride, is much more reactive toward organoboranes.[11,12] However, all of the three alkali metal hydrides fail to react satisfactorily in tetrahydrofuran (THF) with highly hindered trialkylboranes, such as trisiamylborane (eqn 1).



$$\mathrm{MH} + \mathrm{Sia_3B} \xrightarrow[25°, 24\,h]{\mathrm{THF}} \underset{(0\text{–}10\%)}{\mathrm{MSia_3BH}} \qquad (1)$$

$$(\mathrm{M} = \mathrm{Li, Na, K})\ \mathrm{Sia} \equiv (\mathrm{CH_3})_2\mathrm{CH{-}}\underset{\underset{\mathrm{CH_3}}{|}}{\mathrm{CH}}{-}$$

Yet these are reagents of exceptional promise.

A general synthesis of lithium trialkylborohydride has been developed using lithium trimethoxyaluminohydride (LTMA)[13] (eqn 2).

$$\mathrm{R_3B} + \mathrm{LiAl(OMe)_3H} \xrightarrow[25°, 0.25\,h]{\mathrm{THF}} \underset{(100\%)}{\mathrm{LiR_3BH}} + \mathrm{Al(OMe)_3}. \qquad (2)$$

However, this suffers from the difficulty of separating the product from the aluminum methoxide formed concurrently. Fortunately, the aluminum salt does not appear to interfere with the use of the borohydrides as reducing agents. The analogous reaction involving tri-t-butoxyaluminohydride (LTBA), while interesting, is not a useful method for borohydride preparation.[14]

Perhaps the most elegant synthesis of lithium trialkylborohydrides is the reaction of t-BuLi with trialkylboranes[15] (eqn 3).

$$\mathrm{R_3B} + \mathrm{(CH_3)_3CLi} \xrightarrow[-78°]{\mathrm{THF}} \mathrm{LiR_3BH} + \mathrm{(CH_3)_2C{=}CH_2}. \qquad (3)$$

An extensive study using ^{11}B NMR has shown the generality of this method[16] which has been used to form highly hindered borohydrides[9] and an asymmetric borohydride.[10] However, this suffurs from the cost of t-BuLi for the preparation of the reagent in quantity.

It has been reported that LAH reacts with trimethylborane to give complex products[17] (eqn 4).

$$\mathrm{LiAlH_4} + \mathrm{(CH_3)_3B} \rightarrow \mathrm{LiCH_3BH_3} + \mathrm{(CH_3)_2AlH}. \qquad (4)$$

More recently, LAH was evaluated for its applicability in the hydride-induced carbonylation of organoboranes.[18] The subsequent discovery that other complex hydrides used in this reaction transfer alkali metal hydride to the trialkylborane[13,14,19] generated interest in a systematic investigation of the reaction of LAH with representative trialkylboranes as a potential route to the lithium trialkylborohydrides.

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†Part XVIII in this series; see Ref. 16.

RESULTS AND DISCUSSION

Addition of a THF solution of LAH to triethylborane resulted in a moderately exothermic reaction. Examination of the clear, colorless solution by ^{11}B NMR unexpectedly revealed a triplet (δ −16.7, J = 67 Hz) instead of the anticipated doublet. Other trialkylboranes with primary alkyl groups gave similar results, summarized in Table 1. Evidently, the reaction proceeded as shown in eqn 5.

$$LiAlH_4 + R_3B \xrightarrow[25°, 0.25\ h]{THF} LiR_2BH_2 + RAlH_2. \quad (5)$$

(R = Et, n-Bu, iso-Bu)

Trialkylboranes having secondary alkyl groups behaved somewhat differently. Addition of LAH caused vigorous exothermic reactions and formation of white precipitates. Examination of the supernatant solutions by ^{11}B NMR revealed apparent mixtures of dialkyl- and trialkylborohydrides. The above reaction was carried out at −78° and the solution examined as rapidly as possible by ^{11}B NMR. Initially the resonance attributed to the desired triakylborohydride is observed. This disappears rapidly to give rise to the resonance due to dialkylborohydride. These results established that the reaction proceeds with the initial formation of the desired trialkylborohydride (eqn 6), followed by a transfer of an alkyl group (eqn 7).

$$LiAlH_4 + R_3B \xrightarrow[-78°]{THF} LiR_3BH + AlH_3 \quad (6)$$

$$LiR_3BH + AlH_3 \xrightarrow[25°]{THF} LiR_2BH_2 + RAlH_2. \quad (7)$$

Table 1. Infrared and ^{11}B NMR spectra of the products from reaction of LAH with trialkylboranes having primary alkyl groups

Trialkylborane	IR ν(B–H), cm^{-1}	ν(Al–H), cm^{-1}	^{11}B NMR Chemical shift,[a] δ (multiplicity)	J_{B-H}, Hz
Triethylborane	2100	1750	-16.7(t)	67
Tri-*n*-butylborane	2100	1690	-19.3(t)[b]	69
Triisobutylborane	2120	1760	-21.4(t)	68

[a] All chemical shifts relative to $BF_3 \cdot OEt_2$ with those upfield assigned as negative. [b] There was also a minor resonance at δ -16.2, presumably due to a product arising from di-*n*-butyl-*sec*-butylborane.

Table 2. Infrared and ^{11}B NMR spectra of the products from reactions of LAH with representative trialkylboranes in the presence of triethylenediamine

Trialkylborane	ν_{B-H}, cm^{-1}	Chemical Shift[a] δ (multiplicity)	J_{B-H}, Hz
Triethylborane	2010	-13.4(d)	61
Tri-*n*-butylborane	2010	-15.4(d)	60
Triisobutylborane	1990	-18.2(d)	61
Tri-*sec*-butylborane	2000	- 6.3(d)	58
Tricyclopentylborane	2050	- 9.3(d)	65
Tricyclohexylborane	2020	- 5.9(d)	59
Tri-*exo*-2-norbornylborane	2030	- 7.9(d)	68
Perhydro-9b-boraphenalene[b]	2050	-10.2(d) -11.1(d)	59 59
Tris(*trans*-2-methylcyclopentyl)borane[c]	2100	-12.4(d) -14.3(d)	75 75
Trisiamylborane[d]	2060	-12.6(d) -13.9(d)	77 78

[a] All chemical shifts relative to $Et_2O \cdot BF_3$ with those upfield assigned as negative. [b] Probably isomeric pair of borohydrides; area δ -10.2/area δ -11.1 is ~ 1/1. [c] Diastereomeric pair of borohydrides; area δ -12.4/area δ -14.3 is ~ 3/1. [d] Diastereomeric pair of borohydrides; area δ -12.6/area δ -13.9 is ~ 3/1.

This study indicated that a new synthesis of lithium trialkylborohydride might be achieved if the aluminum hydride could be trapped as soon as formed so as to avoid the fast subsequent reaction. We had recently observed that triethylenediamine (TED) rapidly and quantitatively precipitates aluminum hydride as TED·AlH_3 from diethyl ether (EE) and THF.[20] Accordingly, the lithium aluminum hydride solution (THF) was added to a THF solution of trialkylborane containing 1.0 equivalent of TED at 0°. A voluminous white precipitate of TED·AlH_3 formed rapidly. The supernatant liquid, examined by ^{11}B NMR and IR, revealed the quantitative formation of the trialkylborohydride. Initially, the precipitate is present as a voluminous gel, difficult to separate from the solution. In THF the precipitate becomes granular only very slowly. However in the EE medium, on standing for approximately 12 h, it becomes granular, easily separated by centrifugation from the reaction mixture. The resulting solution contains the product in pure form. The reaction was applied to a wide variety of trialkylboranes. The results are summarized in Table 2.

Infrared spectra. Alkali metal trialkylborohydrides exhibit a very broad and strong absorption in the infrared region due to the B–H stretch in the borohydride anion. Solutions (1.0 M) of all trialkylborohydrides, prepared by the present procedure, exhibit this characteristic absorption around 2000 cm^{-1}.[11] There were no absorptions attributable to Al–H frequency in the infrared spectrum[21] (Table 2).

^{11}B NMR spectra. Whereas the lithium trialkylborohydrides synthesized by the lithium hydride route exhibit only a singlet in the ^{11}B NMR spectrum,[11] the lithium trialkylborohydrides prepared by the present method exhibit sharp doublets, similar to those realized for the lithium trialkylborohydrides prepared from trialkylboranes and t-BuLi.[16] This is evidence for the completeness of the reaction[22,23] (Table 2).

Stereoselective reduction of 4-t-butylcyclohexanone. The usefulness of the present method as a route for the formation of lithium trialkylborohydrides of high stereoselectivity depends on whether the solutions can be used directly for such stereoselective reductions. Therefore, the reduction of 4-t-butylcyclohexanone was carried out as a test case using lithium trisiamylborohydride prepared by this procedure. The result was a 99 : 1 ratio of the *cis-* and *trans*-4-t-butylcyclohexanols, essentially identical to the ratio realized with lithium trisiamylborohydride prepared by the earlier procedures (eqns 2 and 3).[13,16]

CONCLUSIONS

Lithium aluminum hydride reacts rapidly and quantitatively in the presence of triethylenediamine with all of the trialkylboranes examined including the ones bearing highly hindered alkyl substituents to give the corresponding lithium trialkylborohydrides. The aluminum hydride precipitates out of solution as its triethylenediamine adduct. The reaction is far faster than the corresponding reaction involving lithium hydride. Consequently, the present reaction provides a general, convenient entry into hindered and highly hindered lithium trialkylborohydrides which are especially useful for the stereoselective reduction of ketones.

EXPERIMENTAL

The reaction flasks and other glass equipment used for experiments were oven-dried and assembled in a stream of dry N_2. The special techniques for the manipulation of air-sensitive materials are described elsewhere.[24]

Tetrahydrofuran, diethyl ether and organoboranes were stored under N_2 in Teflon stopcock protected ampoules. THF and diethyl ether were distilled from excess LAH. The standard soln of LAH was prepared, filtered and stored as described earlier.[25] Triethylborane (Callery) was used as received; the isomeric tributylboranes were distilled before use. All other trialkylboranes were prepared by the hydroboration of corresponding olefins.[24]

Spectra were obtained under inert atmosphere using apparatus and techniques described elsewhere.[24] The IR spectra were obtained for 1.0 M solns with Perkin–Elmer 700 spectrometer using sealed liquid cells and the two-syringe technique.[24] ^{11}B NMR and ^{27}Al NMR spectra were recorded on Varian FT-80A instrument. The ^{11}B NMR chemical shifts are in δ ppm relative to EE·BF_3 with chemical shifts downfield from EE·BF_3 assigned as positive. Glc analyses were carried out with Hewlett–Packard 5752B chromatograph with thermal conductivity detector.

Reaction of lithium aluminum hydride with trialkylborane. The following procedure using triisobutylborane is representative. A dry, 20-ml flask with a magnetic stirring bar and a septum inlet was fitted with a dry condenser connected to a mercury bubbler. The apparatus was flushed with N_2 until cool, then 3.8 ml of THF and 1.2 ml (5 mmol) of triisobutylborane were introduced. To the well-stirred soln was added 2.5 ml of a 1.99 M THF soln of LAH (5 mmol), causing a moderately exothermic reaction. Stirring was continued for 0.5 h at room temp resulting in a clear colorless soln. ^{11}B NMR (THF): δ -21.4 (t, J = 68 Hz). IR (THF): 2120, B–H; 1760, Al–H; cm^{-1}.

The above reaction was carried out at −78° and the soln examined as rapidly as possible by ^{11}B NMR. Initially, the ^{11}B NMR exhibited a broad singlet at δ -11.2. This signal disappeared fast to give rise to a triplet at δ -21.2 (J = 68 Hz).

Reaction of lithium aluminum hydride with trialkylboranes in the presence of triethylenediamine. The following procedure in EE is representative. An oven-dried, 50-ml centrifuge tube was charged with 10 ml of a 1.0 M soln of trisiamylborane and 10 ml of a 1.0 M soln of triethylenediamine. The clear soln was then cooled to 0° and 10 ml of a 1.0 M soln of LAH was added slowly with vigorous stirring. A voluminous ppt of TED·AlH_3 separated out. The mixture was stirred as efficiently as possible. The mixture was then set aside for 12 h at 25° and centrifuged to remove the granulated TED·AlH_3. A 1.0-ml aliquot of clear soln gave on hydrolysis 0.33 mmol (100%) of H_2. The supernatant liquid (27 ml, 90%) was withdrawn for further examination. By washing the ppt with cold EE, essentially quantitative lithium trisiamylborohydride was recovered. ^{11}B NMR (THF); δ -12.6 (d, J = 77 Hz); -13.9 (d, J = 78 Hz). IR (THF): 2060, B–H; cm^{-1}. No signals attributable to AlH_3 could be detected in ^{27}Al NMR.

Reduction of 4-t-butylcyclohexanone. In a 50-ml flask, fitted with a septum inlet and magnetic stirring bar and connected to a mercury bubbler was placed 15.0 ml of lithium trisiamylborohydride (5 mmol) soln. The flask was cooled to −78°, followed by addition of 4-t-butylcyclohexanone (4.2 mmol) in EE. After the usual workup, glc analysis indicated the presence of *cis*-4-t-butylcyclohexanol, $\geq 99\%$ isomerically pure.[9b,13] The volatile solvent and the siamyl alcohol were removed under reduced pressure to give 0.6 g, a yield of 90%, of pure *cis*-4-t-butylcyclohexanol, m.p. 80–81° (recrystallized from 40% EtOH) [lit.[26] m.p. 82°].

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