Pergamon

Tetrahedron 58 (2002) 10059–10064

TETRAHEDRON

Selective reductions. Part 60: Chemoselective reduction of organyl azides with dichloroborane–dimethyl sulfide

Ashok M. Salunkhe,[†] P. Veeraraghavan Ramachandran* and Herbert C. Brown*

Department of Chemistry, Herbert C. Brown Center for Borane Research, Purdue University, West Lafayette, IN 47907-2038, USA

Received 3 July 2002; revised 8 October 2002; accepted 9 October 2002

Abstract—The rate and stoichiometry of the reduction of an organyl azide with BH_3·THF was examined under standardized conditions at room temperature. Borane derivatives, such as dialkyl-, alkoxy-, and haloboranes were also examined for the reduction of azides. This study revealed $BHCl_2$·SMe_2 to be the most suitable reagent for the reduction of azides. The chemoselectivity of this reagent was also studied by reducing *n*-hexyl azide in the presence of representative series of functional groups, including esters, halides, nitriles, and nitro groups. $BHCl_2$·SMe_2 reduces azides in the presence of all of the above functional groups as well as olefins. Taking advantage of the differences in reactivity of $BHCl_2$·SMe_2 and BH_3·THF or BH_3·SMe_2, it is now possible to reduce selectively an azide in the presence of olefins or to hydroborate an olefin in the presence of azides by a judicious choice of the reagent.

1. Introduction

Nitrogen-containing molecules are extremely important in organic and bio-chemistry.[1] A large majority of pharmaceutical compounds are nitrogen containing molecules. Of the several methods to prepare amines, reduction of azides occupies a prime position.[2] Since numerous methods are available for the preparation of azides with excellent regio-, enantio-, and stereocontrol,[3] the reduction of azides permits a controlled introduction of an amine functionality. A large number of reagents have been reported in the literature for the reduction of azides.[4] However, these reagents suffer from limitations with regard to general applicability, selectivity, operational convenience, and toxicity. For example, the most commonly employed reagent for the reduction of azides, $LiAlH_4$, is used in large excess to achieve the reduction and does not tolerate many functionalities, such as esters, nitro, etc.[5] Catalytic hydrogenation has limitations when applied to molecules with unsaturation, such as olefins or alkynes.[6] Borohydrides and modified borohydride reagents are generally milder reagents, but also face certain disadvantages with regard to the rate and selectivity.[7] Although boranes are highly selective reagents for the reduction of many reducible functional groups,[8] a literature survey reveals that very little attention has been focused on the reduction of azides until our initial report.[9] Although reduction of azide using BH_3·THF is known,[10] several other important borane derivatives, such as halo boranes have not been examined. Consequently, a systematic study of the rate and stoichiometry as well as the chemoselectivity was undertaken of different classes of boranes for the reduction of azides. The results are summarized herein.

2. Results and discussion

The reduction of azides with BH_3–THF has been known for over three decades.[10] However, the rates and stoichiometry of this reaction have not been studied thus far. Such an investigation was undertaken with *n*-hexyl azide as a representative azide.

In order to ascertain whether azides complex with boranes, BH_3·THF, BH_3·SMe_2, BF_3·OEt_2, and $BHCl_2$·SMe_2 were treated with 1 equiv. of *n*-hexyl azide at 0.5 M concentration at 0 °C and examined using ^{11}B NMR spectroscopy. There was no change in their chemical shifts suggesting that there is no coordination of the azides with boron.

2.1. Procedure for rate and stoichiometry studies

n-Hexyl azide was subjected to the reaction with BH_3·THF at room temperature (RT) in different ratios and concentrations with respect to borane and azide. The reactions were followed by (1) ^{11}B NMR spectroscopy, (2) gasimetric analysis of residual hydride,[11] (3) gas chromoatographic (GC) analysis of residual azide with dodecane as an internal standard, and (4) by measuring nitrogen evolution. Both the rate and the stoichiometry (the number of hydrides utilized per mole of the azide) were thus established.

Keywords: azides; reduction; amines; borane; chloroborane.

* Corresponding authors. Tel.: +1-765-494-5316; fax: +1-765-494-6027; e-mail: hcbrown@purdue.edu

† Present address: Pierce Chemical Co., 3747 N. Meridian Rd., P.O. Box 117, Rockford, IL 61105, USA.

0040–4020/02/$ - see front matter
PII: S0040-4020(02)01322-4

Table 1. Reduction of *n*-hexyl azide with BH_3·THF (1:1.3) at RT

Time (h)	Hydride used[a]	Azide used[b]	% Reaction[c]
1.0	0.176	0.174	17
2.0	0.39	0.42	42
4.0	0.55	0.55	55
8.0	0.70	0.68	68
12	0.80	0.78	78
24	0.96	0.94	94
32	0.96	0.95	95

12.5 Mmol of azide was added to 16.6 mmol of BH_3·THF.
[a] Mmol of hydride/Mmol of azide.
[b] Determined by GC analysis.
[c] Based on azide consumed during reduction.

2.2. Reaction of *n*-hexyl azide with BH_3·THF

Initially, the reaction was studied using excess borane. The procedure adopted was to add 12.5 mmol of *n*-hexyl azide to 16.6 mmol of BH_3·THF in sufficient THF to make a 50 mL solution. This makes the reaction mixture 0.25 M in the azide and 0.33 M in borane (i.e. 1.00 M in hydride). The reaction was slow at 0°C; hence the solution was maintained at RT and the reaction was monitored as described above. It was observed that the reduction of the azide is very slow and requires 24 h for ~95% completion. During this time, 94% of the azide had reacted as shown by GC analysis. This experiment clearly proved that only one hydride is used per mole of the azide (Table 1).

In order to determine the optimal concentration for the reduction of azide with BH_3·THF, the following experiments were carried out.

The reaction was conducted with a 1:1 molar ratio of the azide and hydride with a concentration of 0.33 M in the reactants. *n*-Hexyl azide (12.5 mmol) was added to 12.5 mmol of BH_3·THF in sufficient THF to make 37.5 mL of solution. The reaction mixture was thus 1.00 M in hydride (three hydrides per BH_3) and 0.33 M in the azide. The solution was maintained at RT and the reaction was monitored as described above. In this case also the rate of the reduction is slow and is only 84% complete in 24 h as was indicated by the consumption of the azide and hydride.

The reaction was repeated with 1 M concentration of the reactants. 25 Mmol of *n*-hexyl azide was added to 25 mmol of BH_3·THF in sufficient THF to make 25 mL of solution (1.00 M in borane as well as in azide). The solution was maintained at RT and the reaction was monitored as described above. As can be seen from Table 2, the rate increased with concentration: 83% reaction complete in 6 h and 95% in 17 h.

Table 2. Reduction of *n*-hexyl azide with BH_3·THF (1:1) at RT

Time (h)	Hydride used[a]	Azide used[b]	% Reaction[c]
1.0	0.4799	0.48	48.0
2.0	0.6695	0.688	68.8
4.0	0.7722	0.788	78.8
6.0	0.8275	0.84	84.0
17	0.938	0.948	94.8

25 Mmol of azide was added to 25 mmol of BH_3·THF.
[a] Mmol of hydride/Mmol of azide.
[b] Determined by GC analysis.
[c] Based on azide consumed during reduction.

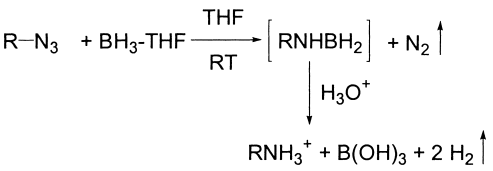
Table 3. Reduction of *n*-hexyl azide with BH_3·THF (1:1) at RT at higher concentration

Time (h)	Hydride used[a]	Azide used[b]	Nitrogen evolved[c]	% Reaction
0.5	0.64	0.64	0.65	65
1.0	0.74	0.73	0.76	75
2.0	0.756	0.76	0.80	80
4.0	0.86	0.88	0.87	87
6.0	0.91	0.91	0.92	92
17	0.935	0.94	0.94	94
32	0.958	0.95	0.95	95

17.12 Mmol of azide was added to 17.12 mmol of BH_3·THF.
[a] Mmol of hydride/Mmol of azide.
[b] Determined by GC analysis.
[c] Based on azide consumed during reduction and mmols of nitrogen evolved during reduction.

To facilitate the reaction, the concentration was increased further. 17.12 Mmol of *n*-hexyl azide was added to 17.12 mmol of BH_3·THF (2.14 M) in sufficient THF to make 11 mL of solution (1.56 M in borane as well as in azide). The solution was maintained at RT and the reaction was monitored as described above. The rate of the reduction increased significantly; 91% in 6 h as indicated by nitrogen evolution, consumed hydride and remaining azide (Table 3).

The above study established that only one hydride is used per mole of the azide reduced and the rate of the reduction accelerates as the concentration of the reaction mixture increases. The reaction pathway is shown in Eq. (1).[12]



(1)

Table 4. Reduction of *n*-hexyl azide with boranes

Entry	Reagent	Solvent	Time (h)[a]	% Reaction[b]
1	BH_3·THF[c]	THF	6.0	91
2	BH_3·SMe_2	Et_2O	21	5
3	1,4-Oxathiane·borane	Et_2O	24	76
4	Catecholborane[d]	THF	22	40
5	9-BBN	Et_2O	24	–
6	$BHCl_2$·THF/THP[e]	THF	24	49
7	$BHCl_2$·THF/THP	CH_2CI_2	24	70
8	$BHCl_2$·OEt_2	Et_2O	2–3	82
9	$BHCl_2$·SMe_2	Et_2O	24	86
10	$BHCl_2$·SMe_2[e]	CH_2Cl_2	2–3	100
11	$BHBr_2$·SMe_2[e]	CH_2Cl_2	2–3	100

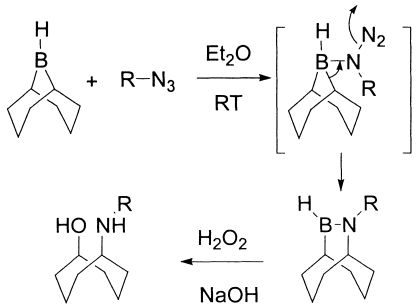
All reactions were carried out at 1.0 M concentration unless otherwise mentioned.
[a] Time after which nitrogen evolution ceased.
[b] % of the reaction based on nitrogen evolution.
[c] Reaction concentration was 1.56 M in boranes and azide.
[d] Reaction concentration is 0.9 M.
[e] 1.5 equiv. of reagent was used and reaction mixture refluxed for 1 h at the end.

2.3. Examination of boranes for reduction of azides

Having established the rate and stoichiometry of the reaction of *n*-hexyl azide with BH_3·THF, our attention was turned to testing different Lewis base complexes of borane and borane derivatives to determine the most efficient reagent for the reduction of organyl azides. BH_3·SMe_2, 1,4-oxathiane·borane,[13] 9-BBN, catechol-borane, and haloboranes, such as $BHCl_2$·THP/THF[14] $BHCl_2$·OEt_2,[15] $BHCl_2$·SMe_2[16] and $BHBr_2$·SMe_2[17] were examined.

The reaction of boranes with azide was followed by measuring the rate of nitrogen evolution after the addition of *n*-hexyl azide to the particular borane at RT. The results are summarized in Table 4. This study revealed that BH_3·SMe_2 is extremely slow in reducing azides, whereas 1,4-oxathiane–borane reduces azides at a faster rate. This may be due to weaker Lewis base complexation with borane. Among the borane complexes tested for the reduction of azide, BH_3·THF gave the best results (Table 4).

Surprisingly, 9-BBN, an excellent reducing reagent for many functional groups,[18] did not reduce *n*-hexyl azide in ethyl ether (Et_2O) at RT. We observed the evolution of 1 equiv. of nitrogen in 24 h. However, the product obtained after alkaline peroxide oxidation was an amino alcohol. The formation of the amino alcohol is illustrated in Eq. (2). Indeed, similar reactions of B-alkyl-9-BBN for the preparation of 2°-amines are known.[19]



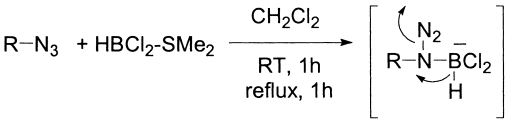
(2)

The reduction of *n*-hexyl azide with haloboranes was then investigated. $BHCl_2$·THP/THF and $BHCl_2$·OEt_2 needed for study were prepared according to literature procedures.[14,15] These haloboranes were treated with *n*-hexyl azide at RT and the rate of the reduction was followed by measuring the nitrogen evolved. The reduction of *n*-hexyl azide with $BHCl_2$·THP in THF was very slow; only 49% reaction was observed in 24 h as indicated by nitrogen evolution. This may be due to strong complexation of $BHCl_2$ with THF, the reaction medium. Presumably free $BHCl_2$ is essential for the reduction to occur. Carrying out the reaction in a non-coordinating solvent, such as dichloromethane supports this hypothesis. The rate of the reduction increased to 70% in 24 h as was shown by nitrogen evolution. Since $BHCl_2$·THP/THF did not give the anticipated rate of reduction, attention was turned to other complexes of $BHCl_2$. $BHCl_2$·OEt_2 reduces azide at a faster rate and 80% reduction was achieved in 2–3 h as determined by evolution of nitrogen. $BHCl_2$·SMe_2 and $BHBr_2$·SMe_2 were then examined. $BHCl_2$·SMe_2 in Et_2O reduces azide in 86% yield within 24 h. Initially the rate of reduction was very fast (75% reduction in 1 h), but requires a longer time for complete reduction to occur. However, the reduction was essentially quantitative when carried out in dichloromethane. Thus, among all of the haloboranes tested, $BHCl_2$·SMe_2 in dichloromethane gave the best results.[9] Similar results were obtained with $BHBr_2$·SMe_2 also (Table 4). For procedural convenience and simplicity, $BHCl_2$·SMe_2 in dichloromethane was utilized for further study. In order to achieve complete reduction within a short period, 1.5 equiv. of the reagent was used and the reaction mixture was refluxed for 1 h (Eqs. (3) and (4)).

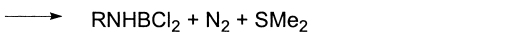
Table 5. Reduction of representative azides with $BHCl_2$·SMe_2 in dichloromethane

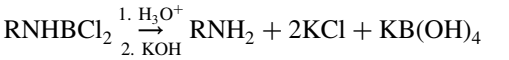
Entry	Azide	Amine	Yield (%)
1	1-Azidohexane	Hexylamine	95[a]
2	1-Azidododecane	Dodecylamine	78[b]
3	2-Azidoundecane	2-Undecylamine	85[b]
4	Azidocyclohexane	Cyclohexylamine	93[a]
5	Azidocycloheptane	Cycloheptylamine	80[b]
6	Phenyl azide	Aniline	94[a]
7	Benzyl azide	Benzylamine	82[b]
8	1-Azidoadamantane	Adamantanamine	75[b]

All reactions were carried out using 1.5 equiv. of $BHCl_2$·SMe_2 in dichloromethane at 1.0 M concentration with respect to $BHCl_2$·SMe_2.
[a] Yield determined by ^1H NMR by adding internal standard.
[b] Yield of the isolated product.



(3)





(4)

Having established the most suitable reagent and the optimum reaction conditions for the reduction of *n*-hexyl azide, our attention was directed in testing the efficacy of this reagent for the reduction of a series of organic azides of varying structural requirements, such as primary, secondary, and tertiary alkyl, cyclic, aromatic, and benzylic azides. As shown in Table 5, $BHCl_2$·SMe_2 in dichloromethane reduces all classes of organyl azides in excellent yields in a relatively short period of time. The reagent is efficient even for the reduction of tertiary alkyl azides (Table 5).

2.4. Chemoselectivity of $BHCl_2$·SMe_2

A search of the current literature reveals several procedures for the reduction of azides.[3] However, chemoselectivity has been a concern for several of these reagents. It has been shown that dichloroborane in THF can be utilized for the selective deoxygenation of sulfoxides in the presence of ketones, esters, nitriles, or a nitro group.[20] This study suggested the possibility of achieving a highly selective reduction of azides with dichloroborane–dimethyl sulfide even in the presence of other readily reducible functional groups. In order to elucidate the selectivity of this reagent, *n*-hexyl azide was reduced in the presence of an equivalent amount of nitropropane, nitrobenzene, ethyl benzoate, bromohexane, and benzonitrile. In all of the cases, the

Table 6. Chemoselective reduction of *n*-hexyl azide with $BHCl_2{\cdot}SMe_2$ at RT

Entry	Reducible compound[a]	% Amine[b]	Recovered reducible compound (%)[c]
1	1-Bromohexane	74	94
2	1-Nitropropane	75	100
3	Nitrobenzene	76	100
4	Benzonitrile	72	93
5	Ethyl benzoate	75	97

All reactions were carried out at RT in dichloromethane at 1.0 M concentration with respect to reducible compound and 1-hexyl azide.
[a] Ratio of reducible compound/azide/$BHCl_2{\cdot}SMe_2$ is 1:1:1.
[b] Amine (%) by nitrogen evolution in 1.0–1.5 h.
[c] Recovery of reducible compounds determined by ^1H NMR by adding suitable internal standard.

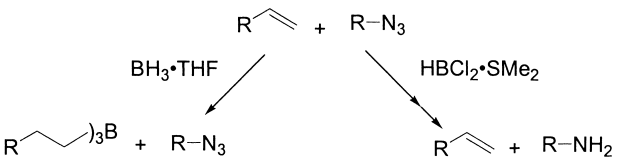
progress of the reduction was monitored by the nitrogen evolution for 1–1.5 h and the reaction mixture was hydrolyzed with water. A suitable internal standard was added to the mixture and GC analysis revealed the percentage of reducible compound remaining in the reaction mixture. In all cases, 72–75% reduction of the azide was observed on the basis of the nitrogen evolution whereas the added reducible compound was recovered almost quantitatively (Table 6). It is evident from the table that the reagent is highly selective and many functional groups survive during the reduction of azide with dichloroborane–methyl sulfide.

Previous studies with dichloroborane have shown it to be a poor hydroborating reagent as a complex with a Lewis base (Me_2S or Et_2O) and olefins are readily hydroborated by free dichloroborane after removing the base with boron trichloride.[15] It was envisaged that even a double bond may survive during the reduction of azide. Accordingly, the reduction of *n*-hexyl azide was carried out in the presence of olefins (Table 7). It was found that this reagent preferentially reduces azides with little effect on the olefin, with ~90% of the olefin was recovered along with 4–7% of the corresponding alkyldichloroboranes.

2.5. Chemoselectivity of $BH_3{\cdot}THF$ or $BH_3{\cdot}SMe_2$

As mentioned earlier, the reduction of azide with $BH_3{\cdot}THF$ at 0°C is slow. This suggested that it should be possible to hydroborate olefins in the presence of azides. Accordingly, we selected a representative series of terminal, di- and trisubstituted, and cyclic olefins and examined their hydroboration in the presence of *n*-hexyl azide. The progress of the hydroboration was followed by ^{11}B NMR spectroscopy. In all cases, the olefins were hydroborated cleanly as indicated by the formation of di- or trialkylboranes and essentially quantitative recovery of the azide (Table 8).

Thus, it is possible to hydroborate an olefin in the presence of an azide or reduce an azide in the presence of an olefin by a judicious choice of the reagent (Eq. (5)).



(5)

3. Conclusions

The rate and stoichiometry of the reduction of azides with boranes has been established. Of the several borane derivatives examined, dichloro- and dibromoborane–methyl sulfide in dichloromethane reduces azides to the corresponding amines in high yields within a short time. We have also established that dichloroborane–methyl sulfide is a chemoselective reducing agent for azides in the presence of several other reducible compounds. It is now possible to

Table 7. Reduction of *n*-hexyl azide in the presence of olefins by $BHCl_2{\cdot}SMe_2$ in CH_2Cl_2 at RT

Entry	Olefin[a]	$RBCl_2$ (%)[b]	% of amine[c]	Recovered olefin[d]
1	1-Decene	4	71	90
2	2-Methyl-1-butene	5	72	90
3	Cyclopentene	6	73	89
4	Norbornylene	7	72	88

All reactions were carried out at 1.0 M concentration with respect to $BHCl_2{\cdot}SMe_2$.
[a] Ratio of olefin/azide/$BHCl_2{\cdot}SMe_2$ is 1:1:1.
[b] Determined by ^{11}B NMR.
[c] % of amine based on nitrogen evolution.
[d] Recovery of the olefin was calculated by ^1H NMR by adding biphenyl as an internal standard.

Table 8. Hydroboration of olefins with $BH_3{\cdot}THF$ or $BH_3{\cdot}SMe_2$ in the presence of *n*-hexyl azide

Entry	Olefin[a]	Reagent	Time (h)[b]	Recovered azide (%)[c]
1	1-Hexene	$BH_3{\cdot}THF$	0.5	100
2	2-Methyl-1-butene	$BH_3{\cdot}THF$	3.0	100
3	2-Methyl-2-butene	$BH_3{\cdot}THF$	4.0	95
4	Cyclopentene	$BH_3{\cdot}THF$	1.5	95
5	Norbornylene	$BH_3{\cdot}THF$	2.0	96
6	1-Hexene	$BH_3{\cdot}SMe_2$	2.0	95
7	2-Methyl-2-butene	$BH_3{\cdot}SMe_2$	1.5	98
5	Norbornylene	$BH_3{\cdot}SMe_2$	4.0	95

All reactions were carried out at 0.5 M concentration with respect to $BH_3{\cdot}THF$ and 1.0 M concentration with respect to $BH_3{\cdot}SMe_2$ unless otherwise mentioned.
[a] In all cases, 3 equiv. of olefin was used except in case of 2-methyl-2-butene where only 2 equiv. of olefin was used.
[b] Time after which all borane was consumed and dialkyl- or trialkylborane was formed. Reactions were followed by ^{11}B NMR.
[c] Recovery of the azide was calculated by ^1H NMR by adding biphenyl as an internal standard.

reduce an azide in the presence of an olefin or vice versa by a judicious choice of the reagent.

4. Experimental

4.1. General methods

All operations were carried out under an inert atmosphere. Techniques for handling air- and moisture-sensitive materials have been previously described.[11]

4.2. Materials

All of the azides used in this study were prepared according to the literature procedure.[21] $BHCl_2{\cdot}OEt_2$ and $BHCl_2{\cdot}THP$ were prepared as reported.[14,15]

4.3. General procedure for the determination of rate and stoichiometry of the reduction of azides with $BH_3{\cdot}THF$ at RT

The following procedure for the reduction of *n*-hexyl azide with $BH_3{\cdot}THF$ in 1:1 molar ratio and at 1.56 M concentration both in azide and borane is representative. A dry 50-mL flask equipped with a magnetic stir bar, septum inlet and reflux condenser was charged with $BH_3{\cdot}THF$ (2.14 M, 17.12 mmol, 8 mL) and dodecane (2.72 mmol, 0.463 g, 0.6 mL) as an internal standard. The reaction flask was connected to a gas buret through a dry ice–acetone trap to measure the evolved nitrogen. To this, *n*-hexyl azide (17.12 mmol, 2.17 g, 2.46 mL) was added slowly at RT and the reaction was monitored by the nitrogen evolved during the reduction. At different intervals, 1 mL aliquots of the mixture were withdrawn, quenched with conc. HCl and the hydrogen evolved was measured volumetrically to determine the consumed hydride. After the reaction was complete, the mixture was treated with conc. HCl, made strongly alkaline, extracted with ether, dried over anhydrous magnesium sulfate and concentrated to provide the product amine which was identified by ^1H NMR. All other experiments using different molar ratios and different concentration were carried out as described above.

4.4. General procedure for the reduction of azides by $BHCl_2{\cdot}SMe_2$ in dichloromethane at RT

The following procedure for the reduction of 2-azidoundecane is representative. $BHCl_2{\cdot}SMe_2$ in dichloromethane (7.5 mL, 7.5 mmol) was added to a dry 25-mL flask equipped with a magnetic stir bar, septum inlet and reflux condenser connected to a gas buret through a dry ice–acetone trap to measure the evolved nitrogen. To this, 2-azidoundecane (0.985 g, 5 mmol) was added slowly at RT and the reaction was monitored by the nitrogen evolved during the reduction (no hydrogen is evolved). The addition of the azide is completed in 35–40 min. During this time, the reaction is ~75% complete and the reaction mixture was refluxed for 1 h to achieve complete reduction. The solvent was removed from the reaction mixture under vacuum and the intermediate was hydrolyzed with conc. HCl at 80°C for 35–40 min. The mixture was then cooled to RT, made strongly alkaline with aqueous potassium hydroxide, extracted with ethyl ether (3×5 mL). The combined ether extracts were washed with water, brine, and dried over anhydrous magnesium sulfate. Removal of the solvent provided an 85% yield of essentially pure 2-undecylamine. The spectroscopic data was in agreement with authentic samples. A similar procedure was adopted for the reduction of all other azides.

4.5. General procedure for chemoselectivity study with $BHCl_2{\cdot}SMe_2$ in dichloromethane at RT

The reduction of *n*-hexyl azide with $BHCl_2{\cdot}SMe_2$ in dichloromethane in the presence of nitrobenzene is representative. To a 25 mL R. B. flask equipped with rubber septum and magnetic stir bar was charged with *n*-hexyl azide (0.381 g, 3 mmol) and nitrobenzene (0.34 mL, 3 mmol) in 2.2 mL of anhydrous dichloromethane. The reaction flask was then attached to a hydride estimation apparatus to measure the evolved gas. $BHCl_2{\cdot}SMe_2$ in dichloromethane (0.3 mL, 3 mmol) was added slowly with stirring and the evolved nitrogen was measured. In 1.5–2.0 h, 76% nitrogen was evolved. The reaction mixture was then hydrolyzed with water and ethyl benzoate was added as internal standard to determine the recovered nitrobenzene. The reaction mixture was extracted with ethyl ether (3×15 mL), washed with water and dried over anhydrous magnesium sulfate. The solvent was removed and the unreacted nitrobenzene was determined by ^1H NMR and found to be almost quantitative. A similar procedure was used for the reduction of *n*-hexyl azide with $BHCl_2{\cdot}SMe_2$ in the presence of other reducible compounds.

4.6. General procedure for the reduction of *n*-hexyl azide in the presence of olefins by $BHCl_2{\cdot}SMe_2$ in dichloromethane at RT

The reduction of *n*-hexyl azide in the presence of 1-decene by $BHCl_2{\cdot}SMe_2$ in dichloromethane is representative. *n*-Hexyl azide (0.381 g, 3 mmol) and 1-decene (0.421 g, 3 mmol) in 2 mL of anhydrous dichloromethane was added to a 25 mL R. B. flask equipped with rubber septum and magnetic stirring bar and attached to a gasimeter to measure the evolved gas. $BHCl_2{\cdot}SMe_2$ (0.34 mL, 3 mmol) was added to the flask, slowly, with stirring and evolved nitrogen was measured. In 1.5 h, 71% nitrogen was liberated. At this stage, the reaction mixture was hydrolyzed with water and biphenyl was added as an internal standard to quantify the recovered olefin. The reaction mixture was extracted with ethyl ether (3×15 mL), washed with water and dried over anhydrous magnesium sulfate. The recovery of the 1-decene was determined by ^1H NMR and found that 90% olefin was recovered. The ^{11}B NMR showed 3–4% formation of alkyldichloroborane–dimethyl sulfide complex. A similar procedure was used for the reduction of *n*-hexyl azide with $BHCl_2{\cdot}SMe_2$ in the presence of other olefins.

4.7. General procedure for the hydroboration of olefins with $BH_3{\cdot}THF$ in the presence of *n*-hexyl azide in tetrahydrofuran at 0°C

The hydroboration of 1-hexene is representative. 1-Hexene (15 mmol, 1.88 mL) and *n*-hexyl azide (5 mmol, 0.635 g) was placed in 2.4 mL of anhydrous THF in a 50 mL R. B.

flask equipped with rubber septum and magnetic stir bar and cooled to 0°C. To this BH_3·THF (5 mL of 1.0 M solution, 5 mmol) was added slowly with stirring and the reaction was monitored by ^{11}B NMR spectroscopy. When all BH_3·THF was consumed (0.5 h) and trialkylborane was formed, the mixture was oxidized with hydrogen peroxide and 3 M sodium acetate by stirring overnight. Biphenyl was added as an internal standard and the recovered azide was estimated using ^1H NMR spectrum, which revealed quantitative recovery. A similar procedure was used for the hydroboration of other olefins in the presence of *n*-hexyl azide with BH_3·THF or BH_3·SMe_2. In the case of BH_3·SMe_2, diethyl ether was used as the solvent.

Acknowledgements

We gratefully acknowledge financial support from the United States Army Research Office (DAAG55-98-1-0405) and the Herbert C. Brown Center for Borane Research (Contribution No. 21).

References

1. (a) Gibson, M. S. In *The Chemistry of the Amino Group*; Patai, S., Ed.; Interscience: New York, 1968; p 37. (b) Brown, B. R. *The Organic Chemistry of Aliphatic Nitrogen Compounds*; Oxford University: New York, 1994.
2. (a) Sheradsky, T. In *The Chemistry of the Azido Group*; Patai, S., Ed.; Interscience: New York, 1971; Chapter 6. (b) In *Azides and Nitrenes, Reactivity and Utility*; Scriven, E. F. V., Ed.; Academic: New York, 1984. (c) Scriven, E. F. V.; Turnbull, K. *Chem. Rev.* **1988**, *88*, 298. (d) Kamal, A.; Laxman, E.; Arifuddin, M. *Tetrahedron Lett.* **2000**, *41*, 7743. (e) Lee, J. W.; Fuchs, P. L. *Org. Lett.* **1999**, *1*, 179.
3. (a) Blandy, C.; Choukroun, R.; Gervais, D. *Tetrahedron Lett.* **1983**, *24*, 4189. (b) Caron, M.; Sharpless, K. B. *J. Org. Chem.* **1985**, *50*, 1557. (c) Chong, J. M.; Sharpless, K. B. *J. Org. Chem.* **1985**, *50*, 1650. (d) Onak, M.; Sugita, K.; Izumi, Y. *Chem. Lett.* **1986**, 1327. (e) Sinou, D.; Emziane, M. *Tetrahedron Lett.* **1986**, *27*, 4423. (f) Thompson, A. S.; Hymphrey, G. R.; DeMarco, A. M.; Mathre, D. J.; E, J. J. *J. Org. Chem.* **1993**, *58*, 5886.
4. For recent references, see: (a) Ding, J. C.; Wu, H. Y. *Chin. Chem. Lett.* **2001**, *12*, 659. (b) Malanga, C.; Mannucci, S.; Lardicci, L. *J. Chem. Res. S* **2000**, 256. (c) Pathak, D.; Laskar, D. D.; Prajapati, D.; Sandhu, J. S. *Chem. Lett.* **2000**, 816. (d) Wu, H. Y.; Chen, R.; Zhang, Y. M. *J. Chem. Res. S* **2000**, 248. (e) Fringuelli, F.; Pizzo, F.; Vaccaro, L. *Synthesis* **2000**, 646. (f) Bosch, I.; Costa, A. M.; Martin, M.; Urpi, F.; Vilarrasa, J. *Org. Lett.* **2000**, *2*, 397.
5. (a) Boyer, J. H. *J. Am. Chem. Soc.* **1951**, *73*, 5865. (b) Boyer, J. H.; Canter, F. C. *Chem. Rev.* **1954**, *54*, 1. (c) Hojo, H.; Kobayashi, S.; Soai, J.; Ikeda, S.; Mukaiyama, T. *Chem. Lett.* **1977**, 635. (d) Kyba, E. P.; John, A. M. *Tetrahedron Lett.* **1977**, *18*, 2737.
6. Corey, E. J.; Nicolaou, K. C.; Balanson, R. D.; Machida, Y. *Synthesis* **1975**, 590.
7. Krishnamurthy, S.; Brown, H. C. *Tetrahedron* **1979**, *35*, 567.
8. Lane, C. F. *Aldrichim. Acta* **1975**, *8*, 20.
9. Salunkhe, A. M.; Brown, H. C. *Tetrahedron Lett.* **1995**, *36*, 7987.
10. Fowler, F. W.; Hassner, A.; Levy, L. A. *J. Am. Chem. Soc.* **1967**, *89*, 2077.
11. Brown, H. C.; Kramer, G. W.; Levy, A. B.; Midland, M. M. *Organic Synthesis via Boranes*; Wiley Interscience: New York, 1975; Reprinted as Vol. 1 by Aldrich Chemical Co., 1999; Chapter 9.
12. It has been reported that $RNHBH_2$ exists as a trimer Brown, M. P.; Heseltine, R. W.; Sutcliffe, L. H. *J. Chem. Soc. (A)* **1968**, 612.
13. Brown, H. C.; Mandal, A. K. *Synthesis* **1980**, 153.
14. (a) Brown, H. C.; Tierney, P. A. *J. Inorg. Nucl. Chem.* **1959**, *9*, 51. (b) Zweifel, G. *J. Organometal. Chem.* **1967**, *9*, 215. (c) Pasto, D. J.; Balasubramaniyam, P. *J. Am. Chem. Soc.* **1967**, *89*, 295.
15. Brown, H. C.; Ravindran, N. *J. Am. Chem. Soc.* **1973**, *95*, 2396.
16. Brown, H. C.; Ravindran, N. *J. Org. Chem.* **1977**, *42*, 2533.
17. Brown, H. C.; Ravindran, N. *J. Am. Chem. Soc.* **1977**, *99*, 7097.
18. Brown, H. C.; Krishnamurthy, S.; Yoon, N. M. *J. Org. Chem.* **1976**, *41*, 1778.
19. Brown, H. C.; Midland, M. M.; Levy, A. *Tetrahedron* **1987**, *43*, 4079.
20. Ravindran, N.; Brown, H. C. *Synthesis* **1973**, 42.
21. Brown, H. C.; Salunkhe, A. M.; Singaram, B. *J. Org. Chem.* **1991**, *56*, 1171.