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ORGANOBORANES

XXV *. HYDRIDATION OF DIALKYLHALOBORANES. NEW PRACTICAL SYNTHESES OF DIALKYLBORANES UNDER MILD CONDITIONS **

HERBERT C. BROWN * and SURENDRA U. KULKARNI
Richard B. Wetherill Laboratory, Purdue University, West Lafayette, Indiana 47907 (U.S.A.)

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Summary

Practical methods for the synthesis of dialkylboranes (R_2BH) via the hydridation of dialkylhaloboranes (R_2BX) have been developed. Convenient methods available for the preparation of R_2BX via the hydroboration of alkenes with monohaloborane complexes ($H_2BX \cdot SMe_2$) make this approach valuable for the preparation of various dialkylboranes, R_2BH, many of which are not available by direct hydroboration of alkenes with borane itself. The suitability of various hydriding agents, such as borane derivatives, complex metal hydrides, and alkoxy metal hydrides, for the hydridation of R_2BX was examined, utilizing *B*-halo-9-borabicyclo[3.3.1]nonane as a representative dialkylhaloborane. In this case, the unusual stability of the resulting dialkylborane, 9-BBN, permits direct estimation of the reaction products by ^{11}B NMR spectroscopy. The generality of the procedure has been demonstrated.

Introduction

The hydroboration of unhindered alkenes with diborane affords the corresponding trialkylboranes (R_3B) [1]. In certain cases, the hydroboration of selected alkenes can lead to the synthesis of relatively stable dialkylboranes (R_2BH), although, more generally, the reaction fails to stop at the R_2BH stage, even when the calculated amount of alkene and borane are used. Moreover, attempts to prepare R_2BH by redistribution of R_3B and BH_3 appears to be impractical for the majority of cases. The availability of dialkylboranes by simple routes would have important potential for the rapidly expanding applications of organoboranes [2]. One such application would be the hydroboration

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* For part XXIV see ref. 8.

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of suitable olefins to provide the desired mixed trialkylboranes ($R_2^ABR^B$) for isolation or for transformation into other desired products.

Dialkylboranes, not available by direct hydroboration, have been prepared by the reaction of suitable derivatives (R_2BX, X = OMe, SMe, Br) with various hydriding agents. For example, the borinate esters have been hydrided by $LiAlH_4$ [3], or by AlH_3 [4] (eqs. 1, 2).

$$R_2^ABOMe \xrightarrow{LiAlH_4} [R_2^ABH] \xrightarrow{\text{alkene-}B} R_2^ABR^B \qquad (1)$$

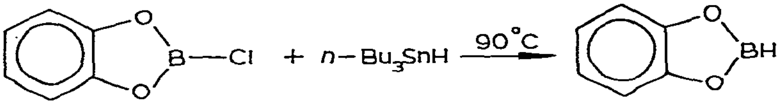
$$R_2^ABOMe \xrightarrow{AlH_3} [R_2^ABH \cdot Al(OMe)_3] \xrightarrow{\text{alkene-}B} R_2^ABR^B \qquad (2)$$

Dialkylboranes can also be generated in high yields by the replacement of thioalkyl groups by hydride (eq. 3) [5].

$$R_2^ABSR \xrightarrow{LiAlH_4} [R_2^ABH] \xrightarrow{\text{alkene-}B} R_2^ABR^B \qquad (3)$$

In some cases, tributyltin hydride has been employed for the replacement of chlorine by hydrogen (eqs. 4, 5) [6].

$$(Me_2N)_2BCl + n\text{-}Bu_3SnH \xrightarrow{90^\circ C} (Me_2N)_2BH \qquad (4)$$



(5)

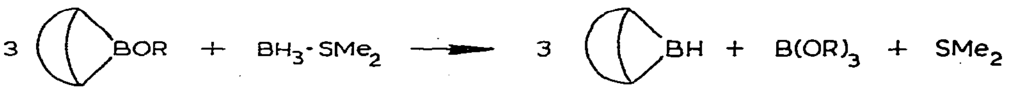
Some of these methods are of limited practical application owing to the harsh reaction conditions employed and the formation of undesirable side-products in the reaction mixture.

Representative dialkylbromoboranes have been hydrided with alkali metal hydrides (eq. 6) [7].

$$R_2^ABBr \xrightarrow{NaH} [R_2^ABH] \xrightarrow{\text{alkene-}B} R_2^ABR^B \qquad (6)$$

Only some of these methods are practical for the use of the dialkylborane in subseqeunt synthetic sequences. In addition, the starting materials, R_2^ABOR, R_2^ABSR, and R_2^ABBr, themselves have been prepared by relatively difficult procedures.

We recently reported that the exchange reaction between *B*-alkoxy-9-borabicyclo[3.3.1]nonane (*B*-OR-9-BBN) and $BH_3 \cdot SMe_2$ produces 9-borabicyclo-[3.3.1]nonane (9-BBN) in quantitative yield (eq. 7) [8].



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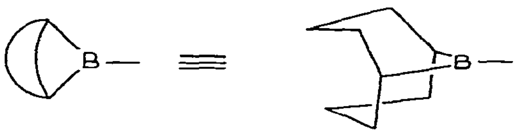


However, this method was unsuccessful for the preparation of other, less stable, dialkylboranes.

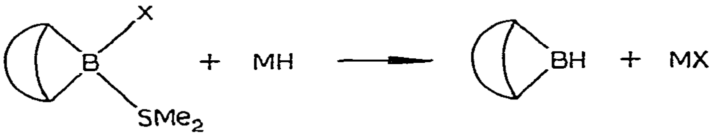
Recent developments in this laboratory have provided simple, general procedures for the synthesis of dialkylhaloboranes (eq. 8) [9].

$$2 \text{ alkene} + H_2BX \rightarrow R_2BX \qquad (8)$$

In view of the availability of dialkylhaloboranes via the simple hydroboration of alkenes with monohaloboranes, we undertook to examine the hydridation of such derivatives to the corresponding dialkylboranes (R_2BH).

Results and discussion

The main objective of this study was to investigate the reaction of a representative R_2BX with a variety of readily available hydride reducing agents under mild conditions. Dialkylboranes, in general, are unstable toward disproportionation, presenting difficulty in direct estimation [10]. Therefore, we chose to emphasize the reaction with *B*-halo-9-borabicyclo[3.3.1]nonane (*B*-X-9-BBN, I) [8], so that the resulting dialkylborane (9-BBN, II), being unusually stable, can be directly estimated. In general, the following reaction was studied (eq. 9).



(9)

(Ia, X = Cl ;
Ib, X = Br)

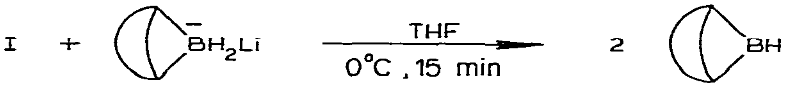
(II)

The analytical procedure consisted of the examination of the ^{11}B NMR spectrum of the reaction mixture from which I (δ 17—19 ppm in THF or Et_2O) and II (δ 27 for the dimer and δ 5 for the SMe_2 complex) can be easily identified and estimated by integration. Any *B*-OR-9-BBN that might result from the cleavage of THF or Et_2O exhibits a ^{11}B resonance around δ 56 ppm.

B-Cl-9-BBN or its SMe_2 complex (Ia) does not cleave ethers at or below 25°C, whereas, *B*-Br-9-BBN cleaves ethers slowly under these conditions. However, the SMe_2 complex (Ib) is relatively stable in ether solvents.

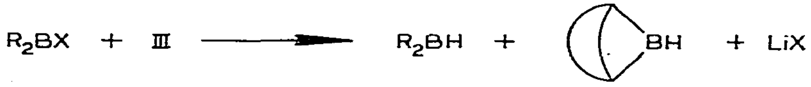
Hydridation with borane derivatives

Among the reagents studied, $BH_3 \cdot SMe_2$, $BH_3 \cdot THF$, $HBCl_2 \cdot SMe_2$ and $HBCl_2 \cdot OEt_2$ fail to reduce Ia at 0—25°C in 24 h. However, lithium 9-borabicyclo[3.3.1]nonane (Li-9-BBNH, III) reduces I cleanly and instantaneously (eqs. 10, 11).



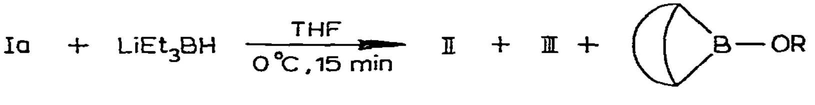
(10)

(III)



(11)

A convenient method for the removal of 9-BBN from the reaction mixture would permit one to use III for the conversion of R_2BX into R_2BH (eq. 11). Lithium triethylborohydride, on the other hand, forms a mixture of products (eq. 12) (Table 1).



(IV)

(12)

Presumably, *B*-OR-9-BBN (IV) arises from the cleavage of THF by some intermediate produced in the course of the reaction.

Hydridation with alkali metal hydrides

While this investigation was underway, a detailed study of the reduction of R_2BBr with LiH, NaH and KH was reported (eq. 13) [11].

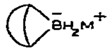
$$R_2^ABX + MH \xrightarrow{\text{alkene-}B} R_2^ABR^B + MX \quad (13)$$

X = Cl, Br M = Li, Na, K

The reaction of R_2BX with lithium hydride in diglyme is slow and proceeds only to the extent of 13% in 17 h. Sodium hydride, however, requires 6—7 h for the completion of reduction, providing 81—99% of the desired product. The use of sodium hydride containing substantial amounts of excess base produced inferior results. Intrinsically more reactive potassium hydride reacts rapidly as expected, but the yields are seldom over 60%. Apparently, potassium bromide, rapidly

TABLE 1

REACTION OF *B*-X-9-BBN WITH HYDRIDE REDUCING AGENTS

B-X-9-BBN	Reagent and stoichiometry	Solvent	Temp. (°C)	Time (h)	Product distribution [a]		
					 (II)	 (IV)	 (III)
Ia, Ib	Li 9-BBNH	THF	0	0.25	100		
Ia	$LiEt_3BH$	THF	0	0.25	30 [b]	35	35
Ia, Ib	$LiBH_4$	THF	0	0.25	100 [c]		
Ia	$NaBH_4$	DG	25	0.25	100 [c]		
Ia, Ib	1/4 $LiAlH_4$	THF	0	0.25	100		
		Et_2O	0	0.25	100		
Ia, Ib	1/2 $LiAlH_4$	Et_2O	0	0.25			100
Ia, Ib	$K(i\text{-}PrO)_3BH$	THF	0	0.25 [d]	>95 [e]	<5	
			25	8.0	80	20	
Ia	2 $K(i\text{-}PrO)_3BH$	THF	0	0.25			100
Ia	$Li(CH_3O)_3AlH$	THF	0	0.25	60	40	
Ib	$Li(t\text{-}BuO)_3AlH$	THF	0	0.25	40	60	

[a] Determined from the relative areas of ^{11}B NMR peaks. [b] By-product of the reaction is Et_3B. [c] One mole of $BH_3 \cdot SMe_2$ was formed. [d] Reaction was complete as soon as it could be examined by ^{11}B NMR. [e] One mole of $(i\text{-}PrO)_3B$, δ 17 ppm, was produced.

formed during the reaction, coats the yet unreacted KH, thus preventing the completion of the reaction. This problem was solved by the use of crown ethers to solubilize KBr [11].

Hydridation with complex metal hydrides

Lithium borohydride converts I to II cleanly and rapidly in both THF and Et_2O solvents (eq. 14).

$$\mathrm{I + LiBH_4 \xrightarrow[0^\circ C,\ 15\ min]{Et_2O/THF} II + BH_3 \cdot SMe_2 + LiX} \tag{14}$$

However, sodium borohydride in these solvents is inert, presumably due to its insolubility. On the other hand, $NaBH_4$ dissolved in diglyme (DG) reacts with I cleanly (eq. 15).

$$\mathrm{Ia + NaBH_4 \xrightarrow[25^\circ C,\ 15\ min]{DG} II + BH_3 \cdot SMe_2 + NaCl} \tag{15}$$

Both of these borohydrides utilize only one hydride for reduction, liberating $BH_3 \cdot SMe_2$, which is inert toward I. Methods available for the selective precipitation of BH_3 as its triethylenediamine or *N,N,N′,N′*-tetramethylethylenediamine complex [12] would permit the use of R_2BH without any interference from BH_3.

In the case of lithium aluminum hydride ($LiAlH_4$), we observed that all four hydrides are used (eq. 16).

$$\mathrm{4\ I + LiAlH_4 \xrightarrow[0^\circ C,\ 15\ min]{Et_2O/THF} 4\ II + AlX_3 + LiX} \tag{16}$$

Under similar experimental conditions, the hydridation of borinate esters (R_2BOMe) was relatively slow, and utilized only three of the four hydrides in $LiAlH_4$ [3].

Hydridation with alkoxy metal hydrides

Potassium triisopropoxyborohydride, $K(i\text{-}PrO)_3BH$, an extremely mild and highly selective reducing agent [13], converts I into II cleanly and instantaneously (eq. 17).

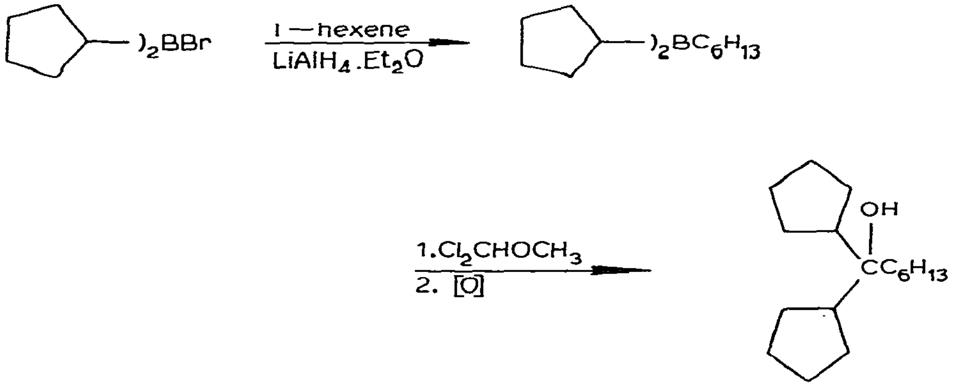
$$\mathrm{I + K(i\text{-}PrO)_3BH \xrightarrow[0^\circ C,\ 5\ min]{THF} II + KX + (i\text{-}PrO)_3B} \tag{17}$$

The exceptional functional group tolerance permits one to use this reagent in the synthesis of mixed organoboranes carrying functionalized alkyl groups. In addition, the by-products of the reaction, $(i\text{-}PrO)_3B$ and KX, largely do not interfere with the further utilization of R_2BH prepared in this manner. However, leaving the reaction mixtures for long periods of time results in the formation of considerable amounts of IV.

Other alkoxy metal hydrides, such as lithium trimethoxyaluminohydride, $Li(MeO)_3AlH$ and lithium tri-t-butoxyaluminohydride, $Li(t\text{-}BuO)_3AlH$, produce considerable amounts of IV during the hydridation of I (Table 1). This could be either via the cleavage of THF by some intermediate species formed during the reaction, or by the exchange of alkoxy groups between aluminum alkoxide and II.

Miscellaneous other agents, such as trichlorosilane (Cl_3SiH), dimethylchlorosilane (Me_2ClSiH), and triethylsilane, failed to react with I under such mild conditions.

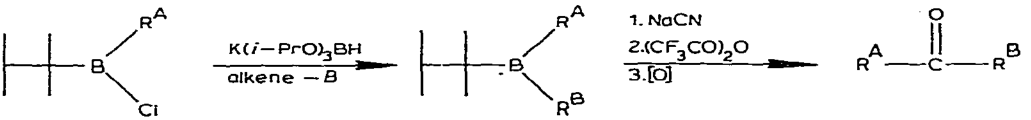
The hydridation procedure developed using *B*-X-9-BBN as a representative example, is generally applicable to any dialkylhaloborane. However, in most cases, the resulting dialkylboranes are unstable toward disproportionation and should be prepared in situ for immediate utilization. Consequently, the hydridation is preferably carried out in the presence of an alkene or alkyne. Thus, dicyclopentabromoborane, when hydrided in the presence of 1-hexene, affords the corresponding mixed organoborane, readily transformed into dicyclopentyl-n-hexylcarbinol via the reaction with α,α-dichloromethyl methyl ether (eq. 18) [14].



(18)

73% yield

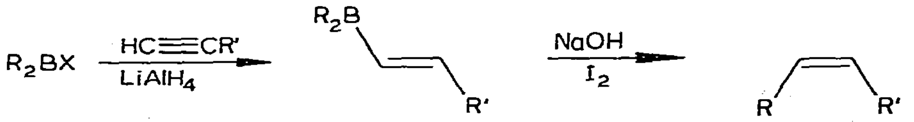
Similarly, the thexylalkylchloroboranes are readily converted into the corresponding mixed organoboranes. The excellent yields and purities of the ketones obtained from such thexyldialkylboranes demonstrate the efficiency of the hydridation step (eq. 19) [15].



(19)

70 – 75 % yield
> 95 % pure

More recently, a series of new dialkylboranes have been prepared and converted into the corresponding *cis*-alkenes (eq. 20) [16].



(20)

65 – 75% yield

These examples prove that the hydridation procedure can be applied for the conversion of a variety of dialkylhaloboranes to the corresponding dialkylboranes.

Conclusions

This study reveals that the dialkylhaloboranes can be conveniently hydrided to the corresponding dialkylboranes by a number of reagents under mild conditions. Two reagents, potassium triisopropoxyborohydride and lithium aluminum hydride ($LiAlH_4$), offer special advantages. The reduction is clean and rapid, even at 0°C. The reaction can be carried out in THF or Et_2O, which are most often used for utilization of the R_2BH produced. The functional group selectivity of $K(i\text{-}PrO)_3BH$ permits the use of this reagent in the synthesis of mixed organoboranes carrying many common functional groups. The methodology developed in this study provides, for the first time, a general synthesis of the dialkylboranes. Consequently, a variety of mixed organoboranes can be prepared by convenient procedures under mild conditions. These intermediates bear great promise for organic syntheses.

Experimental

General comments

The techniques used in handling air-sensitive materials are described elsewhere [17]. All glassware was dried for at least 4 h at 140°C, assembled hot, and allowed to cool under nitrogen. The reaction flasks with sidearms capped with rubber septa were assembled under nitrogen before use. All reactions were carried out under a static pressure of nitrogen. The transfers of liquid and solutions of organometallics were done with hypodermic syringes fitted with stainless steel needles.

Materials

B-X-9-BBN derivatives were prepared according to the literature procedure [8]. Reagent grade ether (Mallinckrodt) was stored over 4 Å molecular sieves under nitrogen. THF was distilled from $LiAlH_4$ and stored under nitrogen. Solutions of active hydride reagents were standardized by hydrolysis [17]. $BH_3 \cdot SMe_2$, $Li(t\text{-}BuO)_3AlH$, $K(i\text{-}PrO)_3BH$ and $LiEt_3BH$ were used as obtained from Aldrich. $LiBH_4$, $NaBH_4$, and $LiAlH_4$ were obtained from Alfa-Ventron. Other reagents like $BH_3 \cdot THF$, $HBCl_2 \cdot SMe_2$, $HBCl_2 \cdot OEt_2$, and $Li(CH_3O)_2AlH$ were prepared as described elsewhere [1]. Li-9-BBNH was prepared from 9-BBN and LiH in THF.

Analyses

The ^{11}B NMR spectra were recorded on Varian FT-80A spectrometer. All chemical shifts are relative to $BF_3 \cdot OEt_2$ (δ 0 ppm); the downfield shifts from the reference are represented by positive signs. Normally the aliquots of the reaction mixture were withdrawn 15 min after the reactants were mixed, for NMR analysis. When the hydridation was not complete, the reaction was allowed to continue at room temperature for longer periods of time.

General procedure for the hydridation of I with borane derivatives

For the reaction with $BH_3 \cdot THF$ and $BH_3 \cdot SMe_2$, a solution of Ia (5 mmol) in THF was added to the reagent (5 mmol) at 0°C. When no change was observed by ^{11}B NMR, the reaction mixture was stirred at RT for 24 h, examining the aliquots occasionally. No reaction was observed.

In the case of reaction with $HBCl_2 \cdot OEt_2$ and $HBCl_2 \cdot SMe_2$, the respective neat reagents (5 mmol) were added to a solution of *B*-Cl-9-BBN free from SMe_2 in pentane (5 mmol). No reaction was observed in these cases, even after 24 h at room temperature. For the reaction with III and $LiEt_3BH$, a solution of the reagent in THF (5 mmol) was added to a THF solution of Ia (5 mmol) at 0°C. The ^{11}B NMR spectrum of the reaction mixture was recorded (Table 1).

General procedure for the hydridation with complex metal hydrides

A solution of $LiBH_4$ in THF (5 mmol) was added to Ia in THF (5 mmol) at 0°C. When the reaction mixture was examined after 15 min, II and $BH_3 \cdot SMe_2$ were the only boron species present.

For the hydridation with $NaBH_4$, the reagent in diglyme (5 mmol) was added to Ia in diglyme (5 mmol). The reaction of Ia was complete in 15 min. Any excess Ia added was not hydrided.

In the case of $LiAlH_4$, both Ia and Ib were examined in THF and Et_2O. To a solution of I (20 mmol) in THF or Et_2O was added $LiAlH_4$ (5 mmol) in the respective solvents at 0°C. The reaction was fast and the solution showed the presence of II as the only boron species, indicating that all four hydrides of $LiAlH_4$ were utilized. Addition of more $LiAlH_4$ converts II into III.

General procedure for the hydridation with alkoxy metal hydrides

Lithium trimethoxyaluminohydride (5 mmol), prepared by adding a calculated amount of MeOH to a solution of $LiAlH_4$ in THF at 0°C, was mixed with Ia (5 mmol) at 0°C. Lithium tri-t-butoxyaluminohydride from Aldrich was dissolved in THF and standardized by hydrolysis [17]. To a solution of Ia (5 mmol) was added $Li(t\text{-}BuO)_3AlH$ (5 mmol) at 0°C. The results are listed in Table 1.

Potassium triisopropoxyborohydride (5 mmol) in THF was added to I (5 mmol) in THF, Et_2O or CH_2Cl_2 at 0°C. In all cases, the reduction was instantaneous. ^{11}B NMR of the reaction mixture showed the presence of pure II (dimer δ 27 ppm, along with some monomer-SMe_2 complex, δ 5 ppm) apart from $(i\text{-}PrO)_3B$ (δ 17 ppm). When the reaction mixture was allowed to stand for 8 h at room temperature, ~20% of IV was formed.

Preparation of dicyclopentyl-n-hexylcarbinol

To a solution of dicyclopentylbromoborane-methyl sulfide (10 mmol) in CH_2Cl_2 (15 ml), prepared as described elsewhere [9], was added 20 ml of Et_2O at 0°C. To this solution was added 1-hexene (1.38 ml, 11 mmol), followed by a dropwise addition of 4.2 ml solution of $LiAlH_4$ (2.8 mmol, 0.67 *M* solution) in Et_2O. The reaction was allowed to proceed for 2 h, the solvents were removed under the aspirator vacuum, and extracted with pentane. The pentane extract was transferred into another flask, and treated with 2.0 ml of methanol in order to destroy any residual hydrides. Solvents and excess methanol were removed under vacuum and the residue was dissolved in 25 ml of THF. An internal standard, n-$C_{14}H_{30}$ (5.0 mmol) was added and the reaction with α,α-dichloromethyl methyl ether was carried out as described elsewhere [14]. The GC analysis on a 6 ft × 1/8 in SE-30 column indicated a yield of 73% for dicyclopentyl-n-hexylcarbinol, along with some olefinic impurities (presumably arising from the dehydration of the tertiary alcohol).

Acknowledgement

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