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ORGANOBORANES FOR SYNTHESIS. 8. REACTION OF ORGANOBORANES WITH REPRESENTATIVE ORGANIC AZIDES. A GENERAL STEREOSPECIFIC SYNTHESIS OF SECONDARY AMINES AND *N*-SUBSTITUTED AZIRIDINES[1,2]

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Abstract - Reaction of trialkylboranes with organic azides in refluxing xylene, followed by hydrolysis, leads to good yields of secondary amines. This reaction is highly dependent on the steric effects around both boron and the azide moiety. The reaction becomes much slower when the steric bulk of one of the reagents is increased and fails when both are hindered. The dialkylchloroboranes are more reactive than trialkylboranes and provide better yields of the desired secondary amines with all azides tested. The alkyldichloroboranes react with organic azides at temperatures between room temperature and 60°C and produce excellent yields of secondary amines. Furthermore, the stereochemistry of the original carbon-boron bond is retained. The mechanism of these reactions is discussed and the reaction applied to the synthesis of *N*-alkyl- and *N*-arylaziridines.

Applications of organoboranes in organic transformations have been well documented in recent years.[4,5] We previously reported a simple and general synthesis of primary amines *via* the reaction of organoboranes, either with chloramine (eq 1), or with hydroxylamine-*O*-sulfonic acid (eq 2). This has now been improved by utilizing the monoorganyldimethylborane, produced by hydroborating the appropriate alkene with dimethylborane.[1]

$$R_3B + NH_2Cl \longrightarrow 2\ RNH_2 + RB(OH)_2 \qquad (1)$$

$$R_3B + H_2N{\cdot}OSO_3H \longrightarrow 2\ RNH_2 + RB(OH)_2 \qquad (2)$$

We now describe our investigations on the reactions of various organoboranes with a variety of organic azides,[6] thus providing a general, stereospecific synthesis of secondary amines.

$$R'N_3 \xrightarrow[\text{or } h\nu]{\Delta} R'\ddot{N}: + N_2 \qquad (3)$$

$$R'\ddot{N}: + BR_3 \longrightarrow R'RNBR_2 \qquad (4)$$

$$\xrightarrow{MeOH} R'RNH + R_2BOMe$$

Nitrenes are produced in the thermal or photochemical decompositions of organic azides[7] (eq 3). Since the reaction of trialkylboranes with carbenes and carbenoid intermediates are well known,[8] such a nitrene might be expected to react with an organoborane with migration of an alkyl group from boron to nitrogen. Such an intermediate is known to undergo ready solvolysis to the corresponding amines[9] (eq 4).

$$R_3B + R'N_3 \rightleftharpoons \left[\begin{array}{c} R \\ | \\ R_2B{-}N{-}R' \\ | \\ {}^{+}N_2^{-} \end{array}\right] \xrightarrow{-N_2} \begin{array}{c} R \\ | \\ R_2BNR' \end{array} \qquad (5)$$

$$\xrightarrow{\text{hydrolysis}} R'RNH$$

Alternatively, organoboranes may react with organic azides in a Lewis acid fashion to form a tetracoordinated boron species which may ultimately lose nitrogen with migration of an alkyl group from boron to nitrogen. Subsequent hydrolysis would lead to secondary amines (eq 5).

A basic difference in the two modes of reaction is that the first path is expected to exhibit first-order kinetics and the latter path second-order kinetics.

In the present study, results of the reaction of trialkylboranes, dialkylchloroboranes and alkyldichloroboranes with various organic azides are presented. The mechanism of the reaction of the various boranes with azides is considered in light of observed steric effects and rates. Finally, the reaction is applied to the synthesis of stereospecifically defined *N*-substituted aziridines.

RESULTS AND DISCUSSION

Trialkylboranes. The reaction of a 1-*M* solution of triethylborane in tetrahydrofuran (THF) with an equimolar quantity of *n*-butyl azide in an autoclave at 170°C under nitrogen was tried first. After 3 h, the reaction mixture was oxidized with 30% hydrogen peroxide and 3 *M* sodium hydroxide to destroy residual organoborane. Analysis of the dried extract by GC indicated a 55% yield of *n*-butylethylamine (eq 6).

This result was encouraging, but it is far more convenient to carry out reactions on the benchtop. To solve this difficulty, experiments were tried in a number of refluxing solvents and the results of the reaction are summarized in Table 1.

$$Et_3B + n\text{-}BuN_3 \xrightarrow[170°C]{\Delta} \xrightarrow{NaOH/H_2O_2} n\text{-}BuNHEt \qquad (6)$$

Table 1. The reaction of tri-*n*-butylborane with *n*-butyl azide in various solvents

Solvent	Time h	Gas %	$(n\text{-}C_4H_9)_2NH$ %
THF	24	70	33
benzene	30	79	68
toluene	12	94	79
xylene	6	90	80
diglyme	0.75	113	40
decane	0.5	107	50

n-Butyl azide proved to be quite stable in refluxing xylene or diglyme. Over a period of 15 h, no significant nitrogen evolution was observed. Likewise, triethylborane is stable under these conditions. However, addition of an equimolar quantity of triethylborane to the refluxing xylene solution of *n*-butyl azide resulted in immediate evolution of a gas. Over a period of 6 h, 1 mol equivalent of the gas, presumbaly nitrogen, was given off. Hydrolysis of the reaction mixture gave a 72% yield of *n*-butylethylamine (eq 7).

Even low boiling solvents, such as tetrahydrofuran (THF), produced a reaction, although the rate was exceedingly slow and the yields low. High boiling solvents, such as diglyme or decane, gave very rapid reactions, but low yields of product. Xylene gave the best results and was chosen as the standard solvent for further studies.

$$Et_3B + n\text{-}BuN_3 \xrightarrow[\text{reflux}]{\text{xylene}} \xrightarrow{\text{hydrolysis}} n\text{-}BuNHEt \qquad (7)$$

The reactions of phenyl azide and several representative alkyl azides were examined with triethylborane. The reaction rates for the more hindered azides were somewhat slower. However, all gave 72-80% of the corresponding secondary amines. More hindered boranes gave poor results. The results are summarized in Table 2.

This reaction exhibits many of the features found in the analogous reaction of organoboranes with diazo compounds.[10] Thus, the rate of the reaction is very sensitive to steric effects, both in the azide moiety and in the organoborane. For example, organoboranes derived from terminal olefins react smoothly with *n*-butyl azide (Table 2); however, as the steric effects are increased, either in the organoborane or in the azide, the reactions become more sluggish and the yields drop off. Clearly the reaction does not involve an initial decomposition of the azide into nitrene and nitrogen (eq 3) since steric effects in the organoborane would have no effect on the rate. This conclusion is further supported by the rate data (Table 3), which follow second-order kinetics. The results therefore are in better agreement with a mechanism involving reversible coordination of the azide with the borane, followed by loss of nitrogen with subsequent (or concurrent) migration of the alkyl group from boron to nitrogen (eq 5). Subsequent hydrolysis produces the secondary amines. Apparently with more hindered alkyl groups on either boron or the azide moiety, coordination becomes difficult or impossible and the reaction fails.

Table 2. The reaction of representative organic azides with organoboranes

Organoborane R_3B, R =	Organic Azide[a] RN_3, R =	Time[b] h	Product[c]	Yield[d] %
ethyl	*n*-butyl	6	*n*-butylethylamine	72
ethyl	isobutyl	6	isobutylethylamine	78
ethyl	*sec*-butyl	24	*sec*-butylethylamine	80
ethyl	cyclopentyl	15	cyclopentylethylamine	77
ethyl	cyclohexyl	24	cyclohexylethylamine	73
ethyl	phenyl	9	*N*-ethylaniline	78
n-butyl	*n*-butyl	6	di-*n*-butylamine	80
n-hexyl	*n*-butyl	6	*n*-butyl-*n*-hexylamine	73
isobutyl	*n*-butyl	6	*n*-butylisobutylamine	tr
cyclopentyl	*n*-butyl	24	*n*-butylcyclopentylamine	16
norbornyl	*n*-butyl	36	*n*-butylnorbornylamine	14

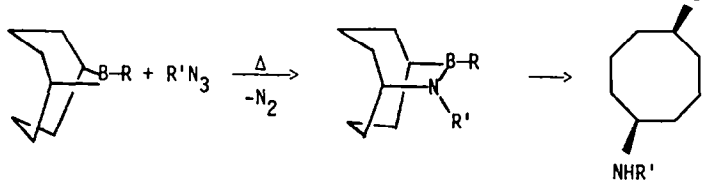
[a]Ten mmol of $R'N_3$ and ten mmol of R_3B in 10 ml of xylene heated under reflux in a nitrogen atmosphere. [b]The time required for greater than 95% of the theoretical amount of nitrogen to be evolved. [c]All products were isolated by GC and exhibited analytical and spectral data in accordance with the assigned structures. [d]GC analysis, based on organic azide.

Although this reaction works well for unhindered trialkylboranes and azides, this procedure suffers from two major disadvantages. 1. Only one of the three alkyl groups on boron is utilized. 2. It is not applicable for more hindered organoboranes.

Table 3. Rate constants for the reaction of alkyl azides with triethylborane in xylene

$R'N_3$	$k \times 10^5$, lm^{-1} sec^{-1}
n-butyl	220
isobutyl	95
sec-butyl	22

The reagent, 9-borabicyclo[3.3.1]nonane (9-BBN),[11] has been extensively used in other systems to overcome such difficulties.[12] Therefore, cyclohexyl and *n*-butyl azides were reacted with *B*-*n*-butyl-9-BBN, and *n*-butyl azide was reacted with *B*-cyclohexyl-9-BBN in refluxing xylene. A gas was rapidly evolved, but analysis revealed none of the expected amine in any of the cases studied. Oxidation produced an amino alcohol resulting from cyclooctyl ring migration (eq 8).



(8)

Similar results have been noted for the reaction of diazoacetone and ethyldiazoacetate with *B*-alkyl-9-BBN.[13] This failure led us to explore the possible applicability of dialkylchloroboranes.

Dialkylchloroboranes. The dialkylchloroboranes are readily available[14] *via* hydroboration with monochloroborane diethyl etherate (eq 9). Such compounds are better Lewis acids than the trialkylboranes and might show an increased reactivity in certain reactions. Di-*n*-butylchloroborane was prepared in diethyl ether and *n*-butyl azide added at room temperature. There occurred a surprisingly rapid evolution of a gas. After 1 h, 1 mol of gas per mol of azide had evolved. Upon hydrolysis with water and neutralization with aqueous 40% potassium hydroxide solution, GC examination revealed a 71% yield of di-*n*-butylamine (eq 10).

$$BH_2Cl \cdot OEt_2 + \text{alkene} \xrightarrow[\text{room temperature}]{Et_2O} R_2BCl \qquad (9)$$

$$n\text{-}Bu_2Cl + n\text{-}BuN_3 \xrightarrow[-N_2]{\text{room temperature}} \xrightarrow[OH^-]{H_2O} n\text{-}Bu_2NH \qquad (10)$$

Representative secondary amines were prepared in good yields (Table 4). These dialkylchloroboranes proved to be quite reactive relative to the trialkylboranes. The reaction of di-*n*-butylchloroborane with *n*-butyl azide may be compared to that of triethylborane with *n*-butyl azide. The former is relatively rapid at room temperature while the latter requires 6 h in refluxing xylene. Primary dialkylchloroboranes and primary azides in general react smoothly at room temperature. Others require higher temperatures. These data again support a mechanism involving reversible coordination of the azide with the borane, followed by a transfer from boron to nitrogen (eq 11). The increased reactivity is presumbaly due to the decreased steric bulk around boron as well as the inherent increase in the electrophilicity of boron when attached to a chlorine *versus* an alkyl group.

Table 4. Reaction of dialkylchloroboranes with organic azides for the synthesis of secondary amines

Dialkylchloroborane R_2BCl,[a] R =	Organic Azide $R'N_3$,[b] R' =	Time h	Product[c]	Yield[d] %
n-butyl	*n*-butyl	1[e]	di-*n*-butylamine	71
	cyclohexyl	1	*n*-butylcyclohexylamine	72
	phenyl	1	*N*-*n*-butylaniline	72
isobutyl	cyclohexyl	4	cyclohexylisobutylamine	73
sec-butyl	cyclohexyl	5	*sec*-butylcyclohexylamine	51
cyclopentyl	*n*-butyl	1	*n*-butylcyclopentylamine	80
	cyclohexyl	4	cyclohexylcyclopentylamine	80
	phenyl	4	*N*-cyclopentylaniline	74
cyclohexyl	cyclohexyl	4	dicyclohexylamine	76

[a]Five mmol in 5.5 ml of ether. [b]Five mmol added in 2.5 ml of toluene. [c]All compounds were isolated by GC and exhibited analytical and spectral data in accordance with the assigned structure. [d]Based on azide by GC analysis. [e]This reaction was run at room temperature.

$$R_2BCl + R'N_3 \rightleftharpoons \left[\begin{array}{c} R \\ | \\ RB-N-R' \\ | \\ ClN_2^+ \end{array}\right] \xrightarrow{-N_2} \begin{array}{c} R \\ | \\ RB-N-R' \\ | \\ Cl \end{array} \qquad (11)$$

Thus, the present modification solved the problems to some extent. However, this procedure also suffers from a significant disadvantage--only one of the two alkyl groups on boron is utilized in the synthesis.

Alkyldichloroboranes. These developments suggested that the alkyldichloroboranes might not only give a fast reaction with organic azides, but also provide for complete utilization of the alkyl groups. Alkyldichloroboranes are readily available *via* hydroboration of alkenes with dichloroborane-diethyl etherate[15a] (eq 12).

$$BHCl_2 \cdot OEt_2 + \text{alkene} + BCl_3 \longrightarrow RBCl_2 + BCl_3 \cdot OEt_2 \qquad (12)$$

When *n*-butyldichloroborane (5 mmol) was placed in 5 ml of benzene and *n*-butylazide added dropwise at room temperature, gas was vigorously evolved. The solution was heated briefly to reflux to ensure completion of the reaction, cooled to room temperature, and hydrolyzed with base. Analysis by GC indicated an 84% yield of di-*n*-butylamine (eq 13). In view of these encouraging results, a representative series of alkyldichloroboranes were synthesized[15,16] and their reaction with various organic azides investigated. The results are summarized in Table 5.

$$n\text{-}BuBCl_2 + n\text{-}BuN_3 \xrightarrow[-N_2]{\text{room temperature}} \xrightarrow{H_2O} n\text{-}Bu_2NH \qquad (13)$$

Table 5. The reaction of alkyl- and aryldichloroboranes with organic azides for the synthesis of secondary amines

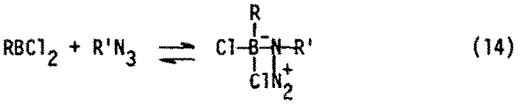
Alkyl- and Aryldichloroborane[a] $RBCl_2$, R =	Organic Azide[b] $R'N_3$, R =	Secondary Amine Product[c] RR'NH	Yield[d] %
n-butyl	*n*-butyl	di-*n*-butylamine	84
	cyclohexyl	*N*-*n*-butylcyclohexylamine	92
	phenyl	*N*-*n*-butylaniline	89
2-methyl-1-pentyl	cyclohexyl	*N*-(2-methyl-1-pentyl)cyclohexylamine	92
3-hexyl	cyclohexyl	*N*-3-hexylcyclohexylamine	85
cyclopentyl	*n*-butyl	*N*-*n*-butylcyclopentylamine	96
	cyclohexyl	*N*-cyclohexylcyclopentylamine	88
	phenyl	*N*-cyclopentylaniline	84
cyclohexyl	*n*-butyl	*N*-*n*-butylcyclohexylamine	95
	cyclohexyl	dicyclohexylamine	92
	phenyl	*N*-cyclohexylaniline	94(91)
trans-2-methylcyclopentyl	cyclohexyl	*N*-(*trans*-2-methylcyclopentyl)-cyclohexylamine	90[e]
exo-norbornyl	*n*-butyl	*N*-*n*-butyl-*exo*-norbornylamine	86
	phenyl	*N*-*exo*-norbornylaniline	92[f]
phenyl	*n*-butyl	*N*-*n*-butylaniline	100
	cyclohexyl	*N*-cyclohexylaniline	96

[a]Five mmol in 5 ml of benzene. [b]Five mmol added dropwise. [c]All compounds exhibited analytical and spectral data in accordance with the assigned structures. [d]Analysis by GC. [e]The product was pure trans amine by GC. [f]The product was pure exo amine by NMR.

With less hindered boranes or azides, the reaction is rapid, evolving gas at room temperature. In the more hindered cases, such as cyclohexyl, the reaction is slower, requiring 3-4 h for completion at room temperature. Gradually raising the temperature of the benzene solution to reflux brings the reaction to completion in 30-40 min. Nearly quantitative yields of the amines were obtained in all cases.

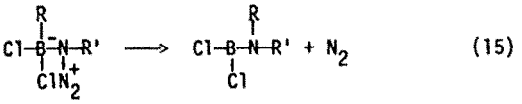
The reaction is much faster and proceeds under milder conditions than the corresponding reaction with dialkylchloroboranes. However, the use of a complexing solvent, such as ethyl ether or tetrahydrofuran, stops the reaction, again suggesting that the crucial factor in the rate is the electrophilicity of boron.

The data for the reactions of the organoboranes discussed is consistent with a mechanism involving Lewis acid complexation (eq 14). This may be followed by transfer of an alkyl group (eq 15), or chloride (eq 16), from boron to nitrogen with loss of nitrogen gas.



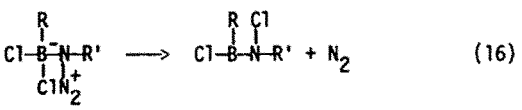
(14)

Chloride migration leads to an intermediate, which, upon attack by a nucleophile, X^-, can undergo alkyl group migration, as may occur in the reaction of trialkylboranes with chloramine.[1]



(15)

In an attempt to determine which pathway is followed (*e.g.*, eq 15 or 16), *n*-butyl- and phenyldichloroboranes were allowed to react with phenyl and *n*-butyl azides respectively (eqs 17 and 18).



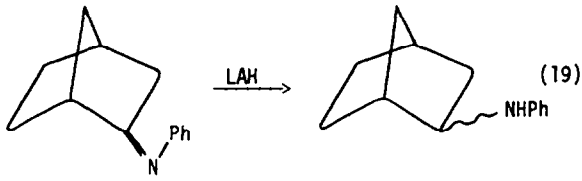
(16)

The proton NMR of the intermediates were identical. Furthermore, both products gave a single ^{11}B NMR absorption at +31 ppm from boron trifluoride etherate characteristic of *N,N*-dialkylaminodichloroboranes[17] suggesting the two intermediates are identical. This supports the conclusion that the reaction follows the pathway indicated in eq 15.

$$n\text{-BuBCl}_2 + \text{PhN}_3 \xrightarrow{-N_2} \text{Cl}_2\text{B–N}(n\text{-Bu})(\text{Ph}) \quad (17)$$

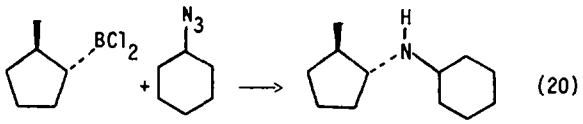
$$\text{PhBCl}_2 + n\text{-BuN}_3 \xrightarrow{-N_2} \text{Cl}_2\text{B–N}(n\text{-Bu})(\text{Ph}) \quad (18)$$

With the successful development of this new synthesis, the stereochemistry of the resultant amines becomes important. The stereochemistry of *N-exo*-norbornylaniline prepared by the above procedure was established by comparison with the mixture of *exo*- and *endo*-amines produced by the reduction of phenylnorbornylimine with LAH (eq 19).[18] Consequently, this corresponds to retention in the reaction of the *exo*-norbornylboron moiety, produced in the hydroboration step, with the phenyl azide. Similarly, *trans*-2-methylcyclopentyldichloroborane reacts stereospecifically with cyclohexyl azide to give pure *N*-(*trans*-2-methylcyclopentyl)cyclohexylamine (eq 20).



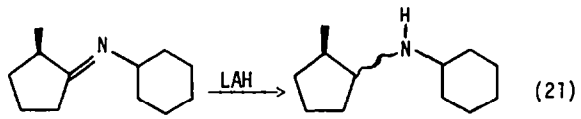
(19)

In contrast, reduction of *N*-cyclohexyl-2-methylcyclopentylimine with LAH gave a 78:22 mixture of *trans*- and *cis*-amines (eq 21).



(20)

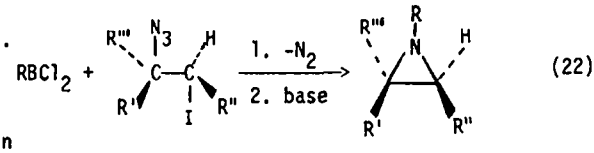
The ready availability[19] of 2-iodoalkylazides suggested the possibility that they might react with organodichloroboranes to give the corresponding 2-iodo-*sec*-amines. Subsequent treatment of these amines with base should lead *via* ring closure to the corresponding *N*-substituted aziridines (eq 22).



(21)

trans/cis = 78/22

Dropwise addition of 1-azido-2-iodoethane to phenyldichloroborane in benzene results in vigorous evolution of nitrogen, complete within 30 min. Hydrolysis of the intermediate with aqueous base at room temperature gives the secondary amine. If the organic phase is separated, dried and treated with *n*-butyllithium, *N*-phenylaziridine is isolated in a yield of 73%. Depending on the nature of the organoborane and the 2-iodoazide ring closure can be effected by a number of convenient bases. Heating with aqueous potassium hydroxide is suitable as is heating a benzene solution with excess anhydrous potassium carbonate. Alternatively, treatment of the intermediate at room temperature with *n*-butyllithium provides a method for the synthesis of thermally sensitive aziridines. Because of the sensitivity of *N*-phenylaziridines to aqueous base and heat, this is the preferred procedure for the synthesis of these derivatives. The results for a representative series of organodichloroboranes are summarized in Table 6.



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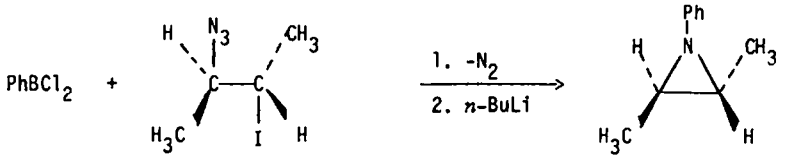
The well established *anti*-addition of iodine azide to olefins suggests this synthesis should allow complete stereochemical control around the aziridine ring. In order to firmly establish that the stereochemistry of the original *anti*-addition of iodine azide is maintained in the product, we have studied by 100 MHz NMR *N*-phenyl-*cis*- and -*trans*-2,3-dimethylaziridine (eqs 23 and 24) in carbon disulfide at -89°C. At this temperature, the phenyl group is frozen into one conformer rather than rapidly equilibrating. Thus, the *trans*-isomer shows two absorptions (2 *m*, 1.79 and 2.09) for the ring protons and two broadened doublets (0.85 and 1.26) for the methyl groups. This strongly suggests that hydrogen and methyl exist both *syn* and *anti* to the phenyl (conformer 1). In accordance with expectations, the *cis*-isomer showed only one absorption (multiplet, 2.07) for the

Table 6. The reaction of organodichloroboranes with 2-iodoalkyl azides for the synthesis of *N*-alkyl- or *N*-phenylaziridines

$RBCl_2$,[a] R =	$R'N_3$[b]	Product	Yield,[c,d] %
n-hexyl	*erythro*-2-azido-3-iodobutane	*N*-*n*-hexyl-*trans*-2,3-dimethyl-aziridine	92
	trans-1-azido-2-iodocyclo-hexane	*N*-*n*-hexyl-7-azabicyclo-[4.1.0]heptane	92,86,[e]94[f]
	1-azido-2-iodohexane	*N*-*n*-hexyl-2-*n*-butylaziridine	91(83)
2-methyl-1-pentyl	*trans*-1-azido-2-iodocyclo-hexane	*N*-(2-methyl-1-pentyl)-7-azabicyclo[4.1.0]heptane	87
3-hexyl	*trans*-1-azido-2-iodocyclo-hexane	*N*-3-hexyl-7-azabicyclo-[4.1.0]heptane	86
cyclopentyl	*trans*-1-azido-2-iodocyclo-hexane	*N*-cyclopentyl-7-azabicyclo-[4.1.0]heptane	94
cyclohexyl	*trans*-1-azido-2-iodocyclo-hexane	*N*-cyclohexyl-7-azabicyclo-[4.1.0]heptane	86(81)
phenyl	2-iodoethylazide	*N*-phenylaziridine	73[e,g]
	trans-1-azido-2-iodocyclo-hexane	*N*-phenyl-7-azabicyclo-[4.1.0]heptane	73[e]
	threo-2-azido-3-iodocyclo-butane	*N*-phenyl-*cis*-2,3-dimethyl-aziridine	83[e]
	erythro-2-azido-3-iodobutane	*N*-phenyl-*trans*-2,3-dimethyl-aziridine	76(72)[e]

[a]Five mmol in 5 ml of benzene. [b]Five mmol added dropwise. [c]Analysis by GC (isolated yields in parentheses were run on a 10-mmol scale). [d]All compounds exhibited analytical and spectral data in accordance with the assigned structure. [d]Ring closure, unless otherwise noted, by heating with 5 ml of 40% potassium hydroxide for 1-3 h. [e]Ring closure with 5 mmol of *n*-butyllithium at room temperature for 15 min in benzene. [f]Ring closure by heating with 25 mmol of potassium carbonate in refluxing benzene for 1-2 h. [g]Yield by NMR.



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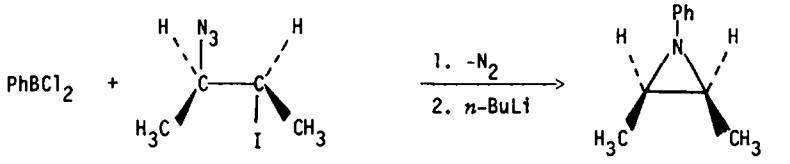
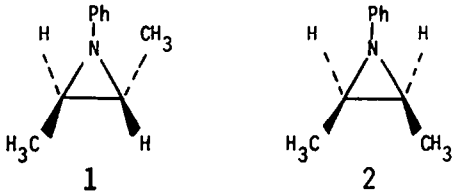
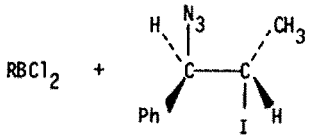


(24)

ring protons and one absorption (*d* 1.24) for the methyl group (conformer 2) at -80°C. The resultant stereochemistry is in accord with prediction and with similar reactions of this type.

We encountered one failure. No nitrogen was evolved upon treatment of *erythro*-1-azido-2-iodo-1-phenylpropane with an organodichloroborane. Instead, the solution became purple in color. GC analysis of the organic phase after workup showed the presence of β-methylstyrene and the absence of aziridine (eq 25). Reductive elimination of the elements of iodine azide by





(25)

lithium aluminum hydride has previously been observed.[20] Such eliminations appear to be favored by electrophilic reducing agents, by phenyl groups vicinal to the azide and by compounds in which the *anti*-conformation of azide and iodine are preferred.

The reaction of organoboranes and especially alkyldichloroboranes provides a highly useful stereospecific synthesis of secondary amines. The application of this reaction to 2-iodoalkyl azides provides for the first time a convenient synthesis of ring substituted *N*-phenyl- and *N*-alkylaziridines in which the stereochemistry of the ring substituents may be easily defined. The fact that the *N*-alkyl groups retain the original stereochemistry of the group attached to boron provides a relatively simple route to aziridines with well defined stereochemistry. Consequently, the present procedure provides a simple synthetic route for the synthesis of many amine derivatives.

EXPERIMENTAL SECTION

All solvents used were dried and distilled under a nitrogen atmosphere. The organoboranes were always handled under nitrogen.[4] PMR, ^{11}B NMR and IR spectra were obtained with a Varian T-60, a Varian XL-100, and a Perkin-Elmer 700 respectively. The organoboranes, dialkylchloroboranes and alkyldichloroboranes were prepared by hydroboration with borane-THF,[4] monochloroborane diethyl etherate,[14] and dichloroborane diethyl etherate.[15a]

Trialkylboranes. A dry, 50-ml flask equipped with a septum inlet, reflux condenser and magnetic stirrer was flushed with nitrogen. The flask was charged with 10 ml of xylene and 0.98 g, 1.42 ml (10 mmol), of triethylborane. The solution was then heated to reflux and attached to a gas buret. Then, 1.11 g (10 mmol) of cyclopentyl azide[20,21] was added and the gas evolution followed. After completion of the evolution of nitrogen, the solution was cooled, 30 ml of diethyl ether added, and the amine was extracted with 6 *N* hydrocyloric acid (2 x 20-ml portions). The aqueous phase was washed with ether to remove residual borinic acid. The solution was made strongly alkaline with potassium hydroxide and the amine was extracted with ether. Analysis by GC (10% SE-30 column) revealed a 77% yield of cyclopentylethylamine of > 99% purity. All amines were isolated by preparative GC and exhibited satisfactory spectroscopic data.

Rate Data. Solutions of 1.0 *M* organoborane and alkyl azide were heated to reflux in a 50-ml flask and the nitrogen evolution followed with a gas buret.[4] A plot of $1/[RN_3]$ (from nitrogen evolution) *versus* time gave a straight line, while kinetic plots of other orders gave curvature. The rate was calculated from the slope of the line.

Reaction of *B*-Alkyl-9-BBN Compounds with Alkyl Azides. *B*-*n*-Butyl-9-BBN (10 mmol) was prepared in 10 ml of THF in a 50-ml flask and the solution brought to reflux. *n*-Butyl azide, 10 mmol, was added and gas evolution followed with a gas buret. After 3 h, 73% of the theoretical amount of gas had evolved. GC analysis after hydrolysis indicated the absence of the expected di-*n*-butylamine. Oxidation produced butanol (80%) and a second product, which was characterized by IR, NMR and mass spectra as 5-(*N*-butylamino)cyclooctanol. *n*-Butyl-9-BBN was reacted with cyclohexyl azide. The reaction required 4 h in refluxing xylene for 95% gas evolution. Hydrolysis gave none of the expected *n*-butylcyclohexylamine.

Dialkylchloroboranes. A dry, 200-ml flask equipped with a septum inlet, distilling head and magnetic stirrer was flushed with nitrogen and maintained under positive nitrogen pressure. The flask was cooled to 0°C and charged with 55 ml of a 0.91-*M* chloroborane (50 mmol) solution in ether. Then, 7.5 g of cyclopentene (110 mmol) was added dropwise. The solution was stirred at 0°C for 1 h. Finally, 6.25 g of cyclohexyl azide[23] (50 mmol) was added, followed by 25 ml of dry toluene. The resulting solution was heated to remove the diethyl ether and maintained at gentle reflux once the ether was removed. After 4 h, nitrogen evolution had ceased. The reaction mixture was cooled and cautiously hydrolyzed with 20 ml of water. The amine was extracted with 20 ml of 6 *N* hydrochloric acid. The combined aqueous phases were washed with 50 ml of ether to remove residual boronic acid. The solution was made strongly basic with 40% aqueous potassium hydroxide and the amine extracted with ether. The ether layer was dried (K_2CO_3) and distilled. There was obtained 6.2 g (74%) of cyclohexylcyclopentylamine: bp 83.0-83.5° (2.4 mm); n^{20}D 1.4796 [lit.[24] bp 118-120° (17 mm)].

Alkyldichloroboranes. A dry, 250-ml flask equipped with a septum inlet, reflux condenser and magnetic stirrer was flushed with nitrogen. The flask was charged with 100 ml of benzene and 15.9 g (100 mmol) of phenyldichloroborane.[16] Cyclohexyl azide,[23] 12.5 g (100 mmol), was added dropwise over 30 min at 20°C (water bath). The solution was stirred an additional 15 min, then slowly heated to 80°C over a 45-min period. Gas evolution had ceased at this point. The solution was cooled to 0°C and very carefully hydrolyzed by slowly adding 10 ml of water (exothermic!). An additional 90 ml of water was added and the precipitate removed by filtration. The organic phase was separated and washed with 100 ml of 3 *N* hydrochloric acid. The combined aqueous layers and precipitate were made strongly basic with 40% potassium hydroxide. The amine was extracted with ether. The ether solution was dried (K_2CO_3) and the ether removed under vacuum. Upon

distillation, there was collected 15.9 g (91%) of *N*-cyclohexylaniline, bp 82-84° (0.1 mm), $n^{20}D$ 1.5600 [lit.[25] bp 87-89° (0.21 mm); $n^{20}D$ 1.5614].

Stereochemistry. A mixture of *N-cis-* and *N-(trans-*2-methylcyclopentyl)cyclohexylamine was prepared by the following method. A 100-ml flask equipped with a Dean-Stark trap was charged with 30 mmol of 2-methylcyclopentanone (3.2 ml), 30 mmol of cyclohexylamine (3.44 ml), 25 ml of benzene and a few small crystals of *p*-toluene sulfonic acid. The solution was refluxed for 4 h and the water collected in the trap. The solution was cooled and the benzene concentrated to about 5 ml on a rotovac. Lithium aluminum hydride (30 mmol, 1.14 g) in 15 ml of ether and 10 ml of THF was added to the solution and the reaction refluxed for 1 h. The solution was cooled and cautiously hydrolyzed with 40% potassium hydroxide until the aluminum salts separated. The organic phase was separated and extracted with 3 x 10 ml of 6 *N* hydrochloric acid. The acid was neutralized with 40% potassium hydroxide and the amine extracted with ether. Analysis of the amine by GC on a 6 ft x 0.25 in 10% Carbowax 20M plus 1% Armac column revealed two isomers in a 78:22 ratio.[26] The major component corresponded to the product from the azide reaction. None of the minor components were detected in the azide reaction. In a similar manner, a mixture of *exo-* and *endo-N*-norbornylaniline was prepared from LAH reduction of the amine. The product was a single component by GC (6 x 0.25 in in SE-30). The NMR of the product revealed two multiplets at δ 3.7 and 3.6, corresponding to a mixture of 84% endo and 16% exo amine. No endo amine was detected by NMR analysis of the product from the azide reaction.

N-Substituted Aziridines. The following procedure for the preparation of *N*-cyclohexyl-7-azabicyclo[4.1.0]heptane is representative. A dry, 50-ml flask equipped with a septum inlet, reflux condenser and magnetic stirring bar was flushed with nitrogen. The flask was charged with 10 ml of benzene and 1.67 g (10 mmol) of cyclohexyldichloroborane.[15] *trans*-1-Azido-2-iodocyclohexane,[19] 2.50 g (10 mmol) was added dropwise. After the addition was complete, the reaction was brought to 80°C over 1 h. Gas evolution had ceased at this point. The solution was cooled to 0°C and carefully hydrolyzed with 10 ml of 10% hydrochloric acid (exothermic). To ensure complete precipitation of the salt, 15 ml of hexane was added. The organic layer was separated and washed with 30 ml of 10% hydrochloric acid. The combined aqueous layer and precipitate were made strongly basic with 40% potassium hydroxide. The amine was extracted with 30 ml of benzene and the resultant solution heated under reflux with 30 ml of potassium hydroxide for 1 h. The organic layer was separated, dried ($CaSO_4$), and the benzene removed under vacuum. Distillation in a Kugelrohr oven gave 1.46 g (81%) of *N*-cyclohexyl-7-azabicyclo[4.1.0]heptane, bp 80-82° (41 mm), $n^{20}D$ 1.4835. Anal. Calcd. for $C_{12}H_{21}N$: C, 80.44; H, 11.72; N, 7.82. Found: C, 80.46; H, 11.65; N, 8.00.

REFERENCES AND NOTES

1. For Part 7 in this series, see: H. C. Brown, K-W. Kim, M. Srebnik and B. Singaram preceding paper in this issue.
2. For preliminary reports, see: a) A. Suzuki, S. Sono, M. Itoh, H. C. Brown and M. M. Midland, *J. Am. Chem. Soc.*, 93, 4329 (1971). b) H. C. Brown, M. M. Midland and A. B. Levy, *Ibid.*, 94, 2114 (1972). c) *Idem., Ibid.*, 95, 2394 (1973).
3. a) National Science Foundation Predoctoral Fellow, 1968-1972. b) Postdoctoral research associate on grant GM 10937 from the National Institutes of Health.
4. H. C. Brown, G. W. Kramer, A. B. Levy and M. M. Midland, "Organic Syntheses via Boranes," Wiley-Interscience, New York, 1975.
5. H. C. Brown, *Pure & Appl. Chem.*, 47, 49 (1976).
6. The organic azides can now be easily prepared from organoboranes: A. Suzuki, M. Ishidoya and M. Tabata, *Synthesis*, 687 (1976).
7. W. Wowski, Ed., "Nitrenes," John Wiley & Sons, New York, 1970.
8. a) D. Seyferth and B. Prokai, *J. Am. Chem. Soc.*, 88, 1834 (1966). b) G. Köbrich and H. R. Merkle, *Angew. Chem. Int. Ed. Engl.*, 6, 74 (1967). c) *Idem., Chem. Ber.*, 100, 3371 (1967). d) A. Suzuki, S. Nozawa, N. Miyaura, M. Itoh and H. C. Brown, *Tetrahedron Lett.*, 2955 (1969). e) H. C. Brown, B. A. Carlson and R. H. Prager, *J. Am. Chem. Soc.*, 93, 2070 (1971).
9. H. Steinberg and R. J. Brotherton, "Organoborane Chemistry," Vol. II, John Wiley & Sons, New York, 1966, p. 27.
10. a) H. C. Turner, *Chem. & Indust.*, 1405 (1958). b) J. E. Leffler and B. G. Ramsey, *Proc. Chem. Soc.*, 117 (1961). c) A. G. Davies, D. G. Hare, O. R. Kahn and J. Sikora, *Ibid.*, 172. d) H. Meerwein, *Angew. Chem.*, 60, 78 (1948). e) J. Hooz and S. Linke, *J. Am. Chem. Soc.*, 90, 5936, 6891 (1968). f) J. Hooz and D. M. Gunn, *J. Chem. Soc. Chem. Commun.*, 139 (1969). g) J. Hooz and G. F. Morrison, *Can. J. Chem.*, 48, 868 (1970).
11. a) E. F. Knights and H. C. Brown, *J. Am. Chem. Soc.*, 90, 5280, 5281 (1968). b) J. A. Soderquist and H. C. Brown, *J. Org. Chem.*, 46, 4599 (1981).
12. H. C. Brown, M. M. Rogić, M. M. Nambu and M. W. Rathke, *J. Am. Chem. Soc.*, 91, 2147 (1969).
13. J. Hooz and D. M. Gunn, *Tetrahedron Lett.*, 3455 (1969).
14. H. C. Brown and N. Ravindran, *J. Am. Chem. Soc.*, 98, 1785 (1976).
15. a) H. C. Brown and N. Ravindran, *J. Am. Chem. Soc.*, 98, 1798 (1976). b) H. C. Brown and A. B. Levy, *J. Organometal. Chem.*, 44, 233 (1972).
16. Phenyldichloroborane is available from Ventron Corporation; others may be prepared by the method of Hooz: J. Hooz and V. G. Calzada, *Org. Prep. Proced. Int.*, 4, 211 (1972).

17. H. Nöth and H. Vahrenkamp, *Chem. Ber.*, 99, 1049 (1966).
18. R. S. McDaniel and A. C. Oehlschlager, *Tetrahedron*, 25, 1381 (1969).
19. F. W. Fowler, A. Hassner and L. A. Leby, *J. Am. Chem. Soc.*, 89, 2077 (1969).
20. A. Hassner, G. J. Mathews and F. W. Fowler, *J. Am. Chem. Soc.*, 91, 5046 (1969).
21. Prepared from cyclopentyl bromide and sodium azide: J. H. Boyer and J. Hamer, *J. Am. Chem. Soc.*, 77, 951 (1955). The other azides were prepared similarly.
22. Phenyl azide was prepared by the method of R. O. Lindsay and C. F. H. Allen, "Organic Synthesis," Coll. Vol. III, Wiley, New York, 1955, p. 710.
23. Cyclohexyl azide was prepared from cyclohexylbromide and excess sodium azide in DMF in analogy with A. J. Parker, *J. Chem. Soc.*, 1328 (1961).
24. K. Jewers and J. McKenna, *J. Chem. Soc.*, 2209 (1958).
25. Universal Oil Products Company, Netherlands Application for Patent 6,410,987, 1966. *Chem. Abstr.*, 65, 3766d, (1966).
26. LAH reduction of 2-methylcyclopentanone gives *trans*- and *cis*-2-methylcyclopentanol in 76:24 ratio: H. C. Brown and R. H. Deck, *J. Am. Chem. Soc.*, 87, 5620 (1965).