A REMARKABLE REARRANGEMENT OF LITHIUM DIALKYL-9-BORABICYCLO[3.3.1]NONANE "ATE" COMPLEXES

Gary W. Kramer and Herbert C. Brown*

The Richard B. Wetherill Laboratory of Chemistry

Purdue University, West Lafayette,

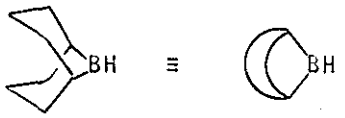
Indiana 47907, U.S.A.

Lithium dialkyl-9-borabicyclo[3.3.1]nonane "ate" complexes react *via* hydride transfer with a variety of reducible organic substrates providing a simple synthesis of the *cis*-bicyclo[3.3.0]oct-1-yldialkylboranes and their derivatives.

CONTENTS

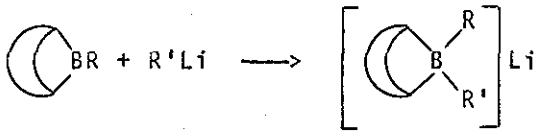
A. INTRODUCTION

The preparation and properties of 9-borabicyclo[3.3.1]-nonane (9-BBN, 1) have been described in the preceding article.[1] The present discussion deals with the unusual



1

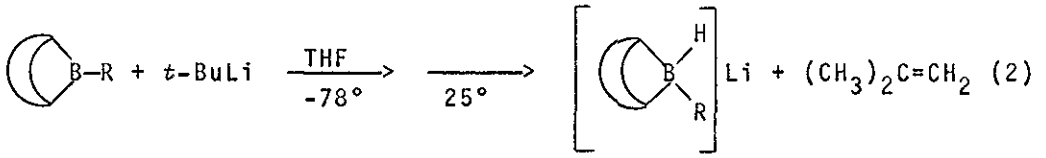
chemistry of the lithium dialkyl "ate" complexes of 9-BBN (2),[2] conveniently prepared by the addition of organolithiums to *B*-alkyl-9-BBN's (eq 1). These tetraalkylborates are formed



(1)

2

quantitatively when the organolithium is primary or aryl. However, if the lithium reagent is secondary or tertiary and contains a β-hydrogen, the dialkyl "ate" complex is not produced. Instead, an interesting hydride transfer occurs, giving the lithium trialkylborohydride (3) (eq 2).[2-5] Indeed,

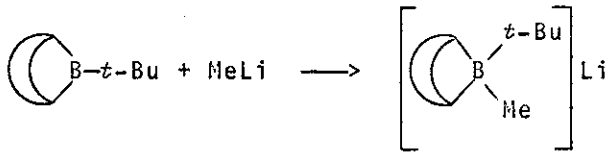


(2)

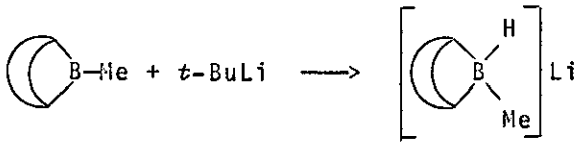
3

with *tert*-butyllithium the formation of 3 is quantitative and nearly instantaneous. These trialkylborohydrides (3) are extremely useful reagents for selective reductions.[5-6] However, a discussion of their characteristics is beyond the scope of this review.

The transfer of hydride from the organolithium to the trialkylborane must be a kinetic phenomenon since it is possible to form tetraalkylborates containing secondary and tertiary moieties, with β-hydrogens, if they are present initially in the trialkylborane (eqs 3, 4).



(3)

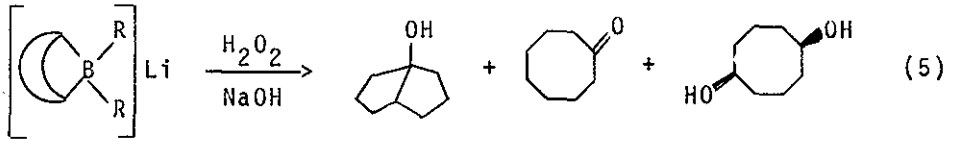


(4)

B. AN ANOMALOUS OXIDATION

In the course of a detailed study of the syntheses of those *B*-alkyl-9-BBN derivatives not available *via* hydroboration,[7] we had occasion to prepare several lithium dialkyl-9-BBN "ate" complexes. We undertook to confirm their structures by the usual oxidation with alkaline hydrogen peroxide. Surprisingly, these oxidations afford major products other than the expected alcohols and *cis*-1,5-cyclooctanediol.[8] The

principal components of this mixture proved to be *cis*-bicyclo-[3.3.0]octan-1-ol (4) and cyclooctanone (eq 5).

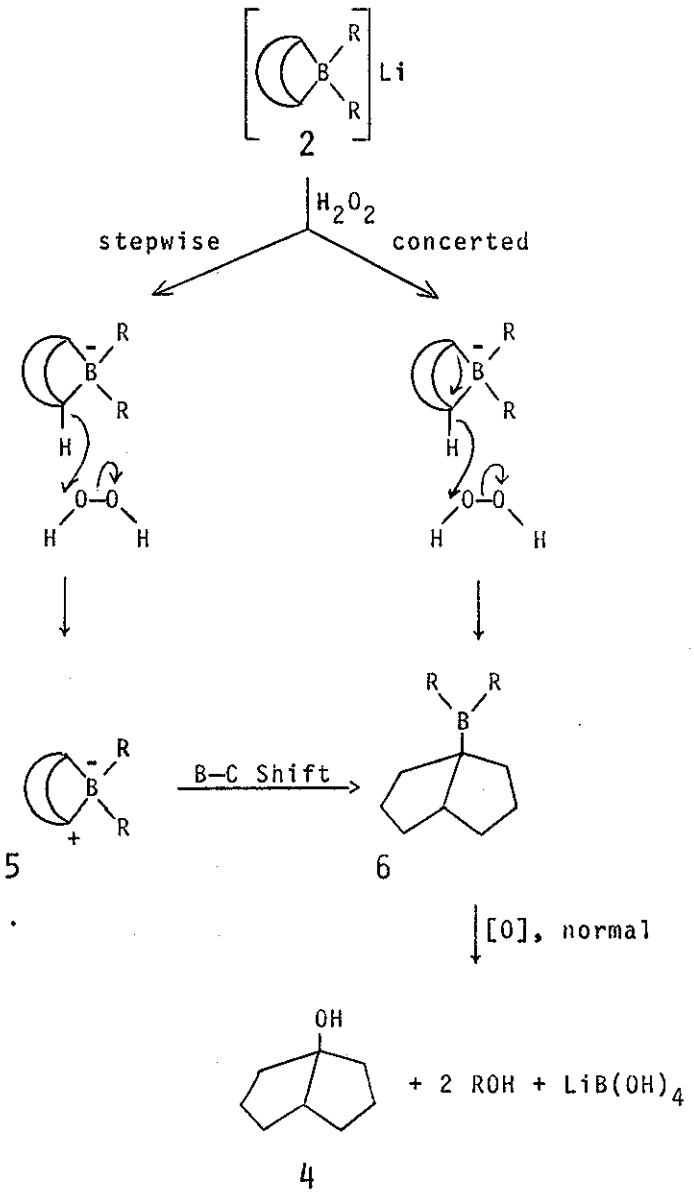


(5)

4 + 2 ROH + other cyclooctyl products

The formation of the bicyclic alcohol, 4, was puzzling. Apparently a hydride had been transferred, but to where? Since no gas evolution accompanies the reaction, the "hydride" is not lost as hydrogen gas; a redox reaction must occur. Accordingly, we proposed that the dialkyl "ate" complex reduces some of the hydrogen peroxide, as shown in Scheme I. The hydrogen peroxide attacks the bridgehead hydrogen of the dialkyl "ate" complex with the concurrent or subsequent migration of the boron-carbon bond. If the migration of this bond is not simultaneous with the loss of the bridgehead hydride, a zwitterionic intermediate, 5, like that originally proposed by Jäger and Hesse, must be implicated.[9] The subsequent migration of a bond from a tetracoordinate boron to an adjacent, electron deficient center is now a well established phenomenon.[10]

Our speculative mechanism led to two important predictions. Since the bridgehead hydrogen transferred easily to the hydrogen peroxide, perhaps it would also transfer to reducible organic substrates. In other words, perhaps these dialkyl-9-BBN "ate"



SCHEME I. Proposed Mechanism for the Formation of *cis*-Bicyclo-[3.3.0]octan-1-ol from a Lithium Dialkyl-9-BBN "Ate" Complex

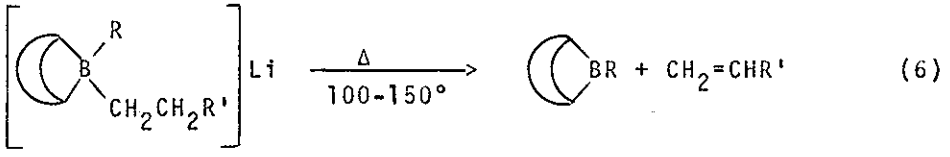
complexes might function as general reducing agents. Secondly, a rearranged organoborane, 6, containing the tertiary *cis*-bicyclo[3.3.0]oct-1-yl moiety, might be formed as an intermediate. If means could be found to prevent the destruction of this intermediate during the reaction, it should be possible to prepare a new family of interesting and perhaps useful organoboranes. We dubbed this novel type of trialkylboranes the "dialkyl butterflyboranes" since molecular models of these structures resemble butterflies when viewed in a certain way.

C. SYNTHESES OF *cis*-BICYCLO[3.3.0]OCT-1-YLDIALKYLBORANES

During the time we were investigating the anomalous oxidation of these complexes, our former coworker, Y. Yamamoto, was reinvestigating the work of Jäger and Hesse.[9] He treated several tetraalkylborate complexes with benzyl chloride in hexane.[11] Lithium di-*n*-butyl-9-BBN was among these. After allowing the reaction to proceed 24 hours at room temperature, followed by a normal alkaline hydrogen peroxide oxidation, Yamamoto found essentially quantitative yields of toluene, 1-butanol, and 4. In a similar study using cyclohexanone as the substrate, he observed nearly quantitative reduction to cyclohexanol. Clearly, the dialkyl-9-BBN "ate" complex was behaving as a reducing agent.

Yamamoto's work suggested that treatment of a dialkyl-9-BBN "ate" complex with a reactive halide or carbonyl derivative might allow the isolation of the rearranged organoborane 6.

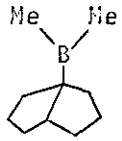
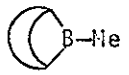
Accordingly, we treated lithium di-*n*-butyl-9-BBN with one equivalent of acetone and were able to isolate the desired di-*n*-butyl butterflyborane in 70% yield.[12] Unfortunately, the same sequence was not as successful during attempts to prepare the dimethyl, the *n*-butylmethyl, and the *tert*-butylmethyl derivatives. The problem was eventually traced to the presence in the reaction mixture of diethyl ether from the methyllithium used to prepare the complex. Attempts to remove the ether completely were unsuccessful, primarily because the ether is strongly held and the complexes cannot be heated since they decompose by elimination of olefin (eq 6).[2]

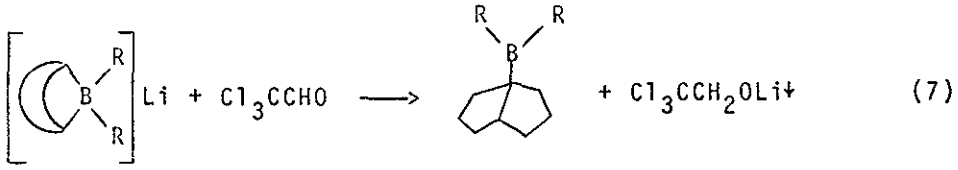


(6)

In view of these difficulties, a more suitable substrate was sought which would cleanly react with the "ate" complex even in the presence of ethers. It appeared that a readily reducible material was required. Consequently, we examined several such substrates for the preparation of dimethyl butterflyborane (Table I). Two promising materials were uncovered: acid chlorides and chloral. The reduction of chloral is rapid and essentially quantitative, but the precipitation of lithium 2,2,2-trichloroethoxide made difficult the isolation of the butterflyborane (eq 7).

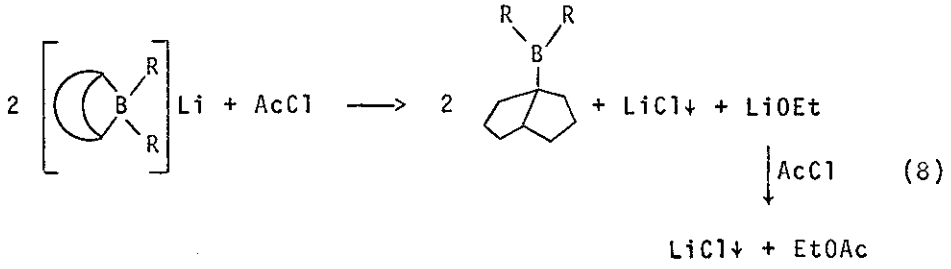
TABLE I. Reaction of Lithium Dimethyl-9-BBN in Ether-Pentane with Various Substrates[2]

Substrate	% 	% 	Comments
Benzyl chloride	∿ 90	∿ 10	very slow
Hexanal	∿ 50	∿ 50	
Propanal	∿ 90	∿ 5	
Chloral	96	0	very fast
Acetyl chloride	96	2	very fast
Hexanoyl chloride	88	tr	very fast
Chlorotrimethyl-silane	0	84	fairly slow
Chlorodimethyl-phenylsilane	0	91	fast



(7)

On the other hand, the reaction with acid chlorides proved equally rapid and quantitative. The stoichiometry of this reduction is one acid chloride to two "ate" complexes. The final products are lithium ethoxide and lithium chloride. The lithium ethoxide is effectively removed from the reaction mixture by the utilization of two equivalents of the acid chloride which converts it into an ester and lithium chloride (eq 8).



The lithium chloride precipitates nicely and is easily removed. If acetyl chloride is used as the substrate, the resultant ester, ethyl acetate, is easily removed with the solvents. Acetyl chloride proved to be an excellent substrate (Table II).

Recently, it was reported that lithium tetraalkylborates react smoothly with acid chlorides to give mixed ketones (eq 9).[4,13]

$$LiBR_4 + R'COX \longrightarrow RCOR' + LiX\downarrow + BR_3 \qquad (9)$$

In our studies with 9-BBN derivatives, we observed no evidence for this type of reaction.

On the other hand, the chlorotrialkylsilanes were observed to react with the dimethyl 9-BBN "ate" complex to regenerate *B*-methyl-9-BBN (Table I). Closer examination of the reaction mixtures revealed that the silanes had been methylated (eq 10).

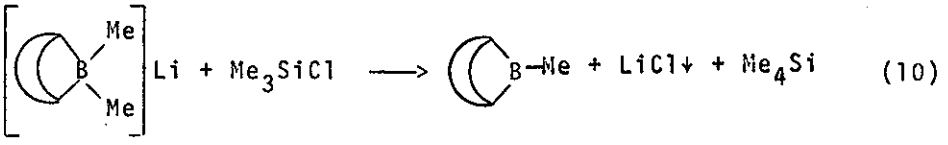


TABLE II. Preparation and Properties of *cis*-Bicyclo[3.3.0]oct-1-yldialkylboranes (6)[12]

Alkyl groups		% yield[c] (GLC)	% yield[d] (Isolated)	% purity[e] (GLC)	Physical data			
							^{11}B NMR	
R[a]	R'[b]				bp, °C	(mmHg)	R_3B[f] δ	"Ate" complex,[g] δ
Methyl	Methyl	96	94	93[h]	76-78	(20)	-81.9	+20
Ethyl	Methyl	99	97	97	28-32	(0.005)	-82.7	+20.4
Isopropyl	Methyl	92	97	94[h]	39-43	(0.005)	-81.3	+18.2
n-Butyl	Methyl	93	—	—	—		-82.7	+20.8
Methyl	*n*-Butyl	—	95	99	53-56	(0.005)	-82.3	+20.8
tert-Butyl	Methyl	91	97	86[h]	46-49	(0.005)	-80.3	+16.7
n-Butyl	*n*-Butyl	—[i]	94	—[i]	65-68	(0.005)	-81.8	+18.5

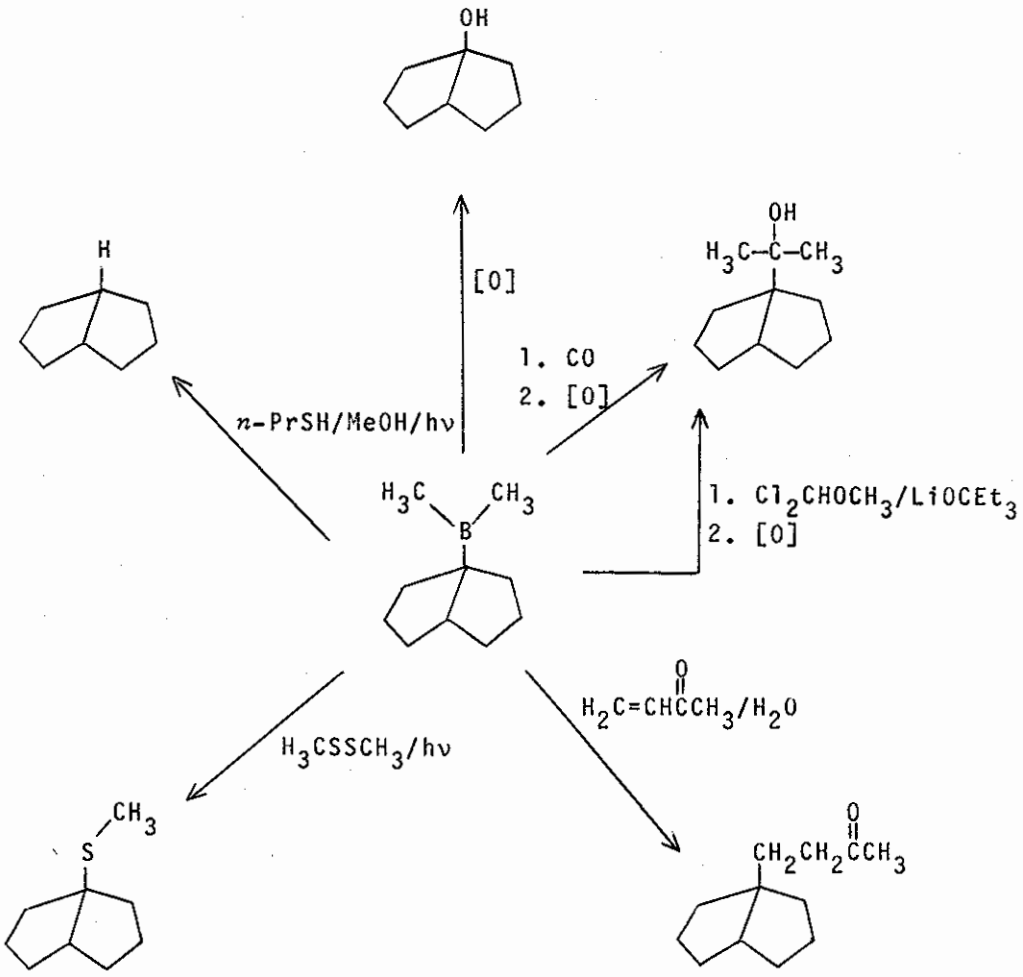
[a] *B*-R-9-BBN. [b] R'Li. [c] Reaction scale 4 mmol. [d] Reaction scales of 15-35 mmol. [e] ^{13}C NMR showed only one set of peaks for the bicyclooctyl ring. [f] ^{11}B NMR shift from BF_3:OEt_2 in ppm for 2. [g] ^{11}B NMR shift from BF_3:OEt_2 for the "ate" complex precursor (2). [h] The major impurity appears to be the *B*-R-9-BBN. [i] The organoborane decomposes in the GLC.

D. SYNTHETIC UTILITY OF *cis*-BICYCLO[3.3.0]-OCT-1-YLDIALKYLBORANES

The acetyl chloride route provided a very simple route to the dialkyl butterflyboranes. We then undertook to explore the synthetic utility of these materials. These organoboranes proved to be valuable intermediates for the preparation of a variety of 1-substituted *cis*-bicyclo[3.3.0]octanes which have heretofore been difficult to synthesize. Employing several common reaction sequences from the organoborane arsenal, we prepared and isolated in high yield several representative 1-substituted *cis*-bicyclo[3.3.0]octanes (Scheme II).[14]

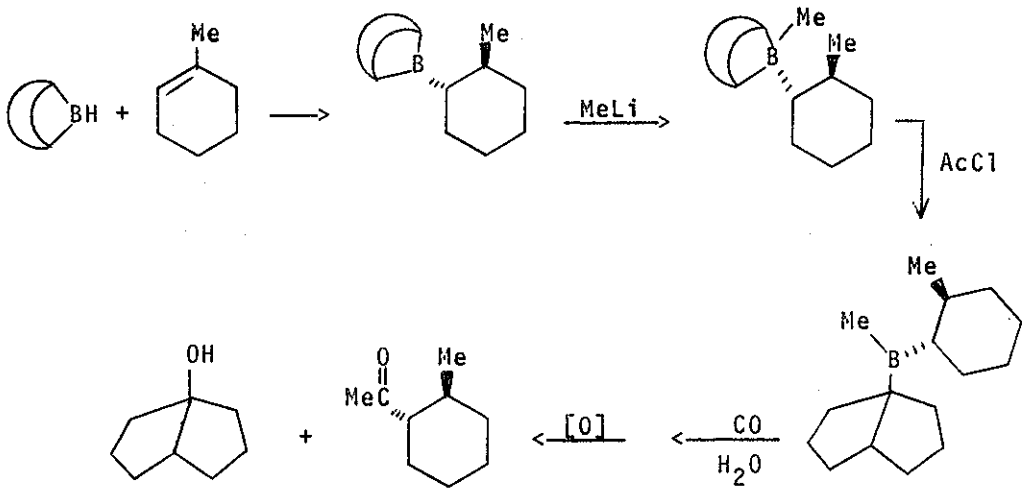
In these preparations, we observed only evidence for the *cis*-bicyclo[3.3.0]octyl moiety. If trans isomers were formed, they were present in concentrations below the detectability of ^{13}C NMR. Although this may at first seem surprising in view of the known free-radical nature of some of the syntheses, the *cis*-bicyclo[3.3.0]octyl moiety is far less strained than the trans isomer. Consequently, it is probable that the bicyclic radical formed is constrained to a pyramidal conformation. The complete retention of stereochemistry is therefore not unreasonable.

Thus far we have examined the utility of the butterflyboranes as precursors for the preparation of *cis*-bicyclo[3.3.0]-oct-1-yl derivatives. However, it may be possible to use the butterflyborane synthesis as a handle in other synthetic schemes. For instance, C. A. Brown has suggested that since the butterfly moiety is attached to boron at the tertiary position, it shculd



SCHEME II. Preparation of *cis*-Bicyclo[3.3.0]oct-1-yl Derivatives from Dialkyl Butterflyboranes

not transfer readily from boron to carbon in either the carbonylation in the presence of water or the cyanidation reactions.[15] If this turns out to be true, we should be able to prepare mixed ketones according to Scheme III. Such a sequence would exploit exceptional regio- and stereoselectivity of hydroborations with 9-BBN in the syntheses of mixed ketones.



SCHEME III. Synthesis of Mixed Ketones *via* Butterflyboranes

E. SELECTIVE REDUCTIONS WITH LITHIUM DIALKYL-9-BORABICYCLO[3.3.1]NONANE "ATE" COMPLEXES

Until now, we have been primarily concerned with the fate of the organoboron moiety in the reactions of the lithium dialkyl-9-BBN "ate" complexes. We now turn attention to the use of these materials as reducing agents. Yamamoto has made several detailed studies in this area.

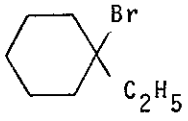
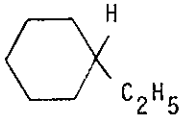
Wittig originally proposed the hydride character of the tetraalkylborates.[16] However, few reports of their reducing properties have been published. Jäger and Hesse reported that lithium tetra-*n*-butylborate reduces benzyl chloride to toluene in 84% yield after heating in an autoclave at 120°.[9] Yamamoto recently reinvestigated this reaction at room temperature (Table III).[11] His results show the 9-BBN derivative to be

TABLE III. Reduction of Benzyl Chloride with Lithium Tetraalkylborates[11]

Tetraalkylborate	% Toluene	% Benzylchloride
$Li(n\text{-}Bu)_4B$	0	100
$Li(n\text{-}Bu)(sec\text{-}Bu)_3B$	75	18
7	100	0

vastly superior to the ordinary tetraalkylborates in reducing ability. Accordingly, he examined the reduction of a number of organic halides with lithium di-*n*-butyl-9-BBN "ate" complex, 7, (Table IV). Tertiary, benzylic, and allylic halides are smoothly reduced while primary, secondary, and aryl halides are nearly inert. This reaction order nicely complements that of the borohydride-type reagents where the primary and secondary halides react readily while the tertiary substrates are inert.[6] This chemoselectivity allows the reduction of tertiary, benzylic, or allylic halides in the presence of primary and secondary halides. For example, 1,2-dibromo-1-phenylethane is reduced

TABLE IV. Reduction of Organic Halides with Lithium Di-*n*-butyl-9-BBN[11]

Substrate	Product	Yield
n-$C_4H_9CBr(CH_3)(C_2H_5)$	n-$C_4H_9CH(CH_3)(C_2H_5)$	98
		90
1-Bromoadamantane	Adamantane	100
1-Bromooctane	Octane	0
2-Bromooctane	Octane	tr
Chlorobenzene	Benzene	0
Benzyl chloride	Toluene	100
1-Bromo-1-phenylethane	Ethylbenzene	81
Cinnamyl bromide	*B*-Methylstyrene	90
1,2-Dibromo-1-phenylethane	1-Bromo-2-phenylethane	60

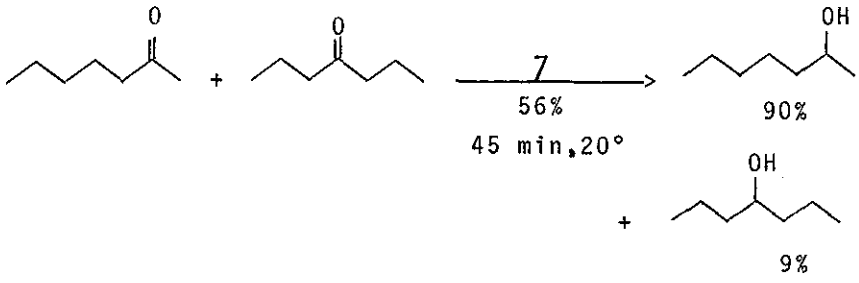
almost exclusively at the benzylic position (eq 11).

$$\phi\text{-}\underset{\displaystyle Br}{\underset{|}{CH}}\text{-}CH_2Br \xrightarrow{7} \phi CH_2CH_2Br \qquad (11)$$

Carbonyl derivatives are also readily reduced by these 9-BBN "ate" complexes.[17] These new reagents exhibit unusual stereo-, chemo-, and regioselectivity in such reductions. For example, aldehydes may be reduced in the presence of ketones (eq 12). Cyclohexenone is reduced to cyclohexanone with

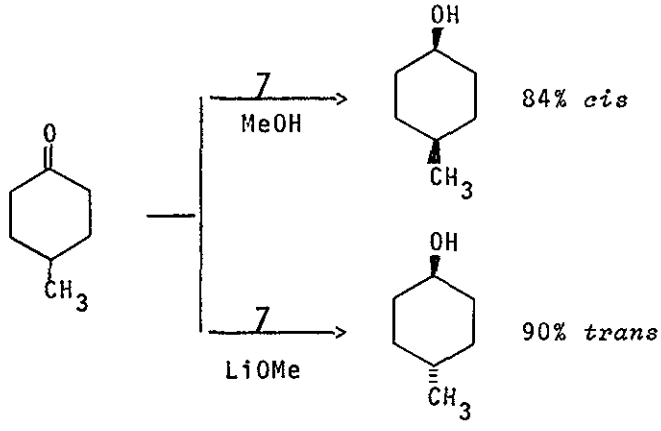
$$n\text{-}C_6H_{13}CHO + n\text{-}C_5H_{11}COCH_3 \xrightarrow[\substack{3\ h,20^\circ \\ MeOH \\ 57\%}]{7} \underset{95\%}{n\text{-}C_6H_{13}CH_2OH} + \underset{5\%}{n\text{-}C_5H_{11}\overset{\displaystyle OH}{\overset{|}{C}}HCH_3} \qquad (12)$$

stoichiometric amounts of the reagent; however if excess of the "ate" complex is employed, cyclohexanol is formed. Methyl benzoate and benzonitrile are not reduced under these conditions. Consequently, these complexes appear to allow the chemoselective reduction of aldehydes in the presence of ketones, esters, and nitriles. Even regio-isomers of ketones can be discriminated (*eq* 13).



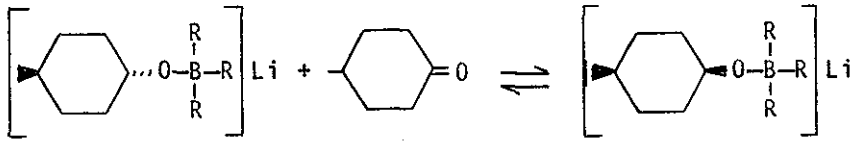
(13)

The stereochemistry of carbonyl reductions can be controlled by the addition of modifiers to the reaction mixture. Thus, 4-methylcyclohexanone gives *cis*-4-methylcyclohexanol in 84% isomeric purity when the reaction is carried out in the presence of methanol. If lithium methoxide is added, *trans*-4-methylcyclohexanol is produced in 90% isomeric purity (eq 14).

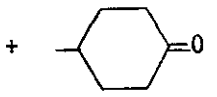


(14)

Apparently the lithium methoxide catalyzes the isomerization of the initially formed *cis* alcohol to the more thermodynamically stable *trans* isomer. Methanol seems to suppress the isomerization which appears to be a Meerwein-Pondorf-Verley type of intermolecular hydride exchange proceeding through the alkoxy "ate" complex 8 (eq 15). Methanol may assist in the

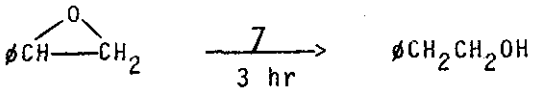


8 8 (15)

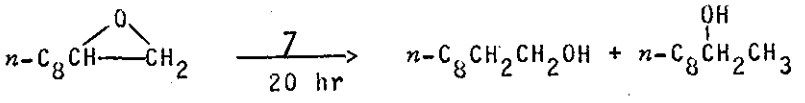


decomposition of 8 minimizing the transfer of hydride.

The lithium dialkyl-9-BBN "ate" complexes exhibit a "reversed" regioselectivity in the reduction of epoxides.[18] For example, aromatic epoxides are reduced from the most hindered position while aliphatic epoxides are attacked at the least hindered site (eqs 16, 17).



3 hr
100% 99% (16)



20 hr
100% 7% 93% (17)

These results contrast with the reductions of epoxides using complex metal hydrides such as $LiAlH_4$ or $LiEt_3BH$, which show Markovnikov ring opening (attack from the least hindered side), or the mixed hydrides, such as $LiAlH_4$:$AlCl_3$ or BH_3:BF_3, which show *anti*-Markovnikov ring opening (attack from the most hindered side).[19-21]

F. CONCLUSION

The lithium dialkyl "ate" complexes derived from the addition of organolithium reagents to *B*-alkyl-9-BBN's are a most unusual type of tetraalkylborate. Their facile reaction with reducible organic substrates was unexpected. However, the initial identification of a mysterious peak in the GLC trace of an oxidation mixture has led to the development of a new branch in the tree of organoborane chemistry, providing a general synthesis of *cis*-bicyclo[3.3.0]oct-1-yldialkylboranes and their derivatives, as well as the discovery of a novel class of reducing agents possessing highly desirable characteristics.

Acknowledgement:

The support of the National Institutes of Health (GM 10937) and the National Science Foundation (CHE 76-20846) in the studies of the remarkable rearrangement of these 9-BBN "ate" complexes is gratefully acknowledged.

REFERENCES

1 H. C. Brown and C. F. Lane, *Heterocycles*, 1977, preceding paper.

2 G. W. Kramer, Ph.D. Thesis, Purdue University, West Lafayette, Indiana, 1976.

3 E. J. Corey, K. R. Becker, and R. K. Varma, *J. Am. Chem. Soc.*, 1972, 94, 8618.

4 E. Negishi, K.-W. Chiu, and T. Yoshida, *J. Org. Chem.*, 1975, 40, 1676.

5 S. Krishnamurthy and H. C. Brown, *J. Am. Chem. Soc.*, 1976, 98, 3383.

6 S. Krishnamurthy, *Aldrichimica Acta*, 1974, 7, 55.

7 G. W. Kramer and H. C. Brown, *J. Organometal. Chem.*, 1974, 73, 1.

8 G. W. Kramer and H. C. Brown, *J. Organometal. Chem.*, 1975, 90, C1.

9 H. Jäger and G. Hesse, *Chem. Ber.*, 1962, 95, 345.

10 H. C. Brown, "Boranes in Organic Chemistry," Cornell University Press, Ithaca, New York, 1972.

11 Y. Yamamoto, H. Toi, S.-I. Murahashi, and I. Moritani, *J. Am. Chem. Soc.*, 1975, 97, 2558.

12 G. W. Kramer and H. C. Brown, *J. Am. Chem. Soc.*, 1976, 98, 1964.

13 E. Negishi, A. Abramovitch, and R. E. Merrill, *J. C. S. Chem. Comm.*, 1975, 138.

14 G. W. Kramer and H. C. Brown, *J. Org. Chem.*, in press.

15 H. C. Brown, G. W. Kramer, A. B. Levy, and M. M. Midland, "Organic Syntheses via Boranes," Wiley-Interscience, New York, 1975.

16 G. Wittig, *Angew. Chem.*, 1958, 70, 65.

17 Y. Yamamoto, H. Toi, A. Sonoda, and S.-I. Murahashi, *J. Am. Chem. Soc.*, 1976, 98, 1965.

18 Y. Yamamoto, H. Toi, A. Sonoda, and S.-I. Murahashi, *J. C. S. Chem. Comm.*, 1976, 672.

19 E. L. Eliel and M. N. Rerick, *J. Am. Chem. Soc.*, 1960, 82, 1362.

20 S. Krishnamurthy, R. M. Schubert, and H. C. Brown, *J. Am. Chem. Soc.*, 1973, 95, 8486.

21 H. C. Brown and N. M. Yoon, *J. C. S. Chem. Comm.*, 1968, 1550.

Received, 30th May, 1977