Table I. Conversion of Olefins into Ethyl Alkanoates and 2-Haloalkanoates by the Reaction of the Corresponding B-Alkyl-9-borabicyclo[3.3.1]nonanes with Ethyl α-Haloacetates under the Influence of Potassium *t*-Butoxide[a]

Olefin	Ethyl α-haloacetate	Product	Yield, %[c]
Ethene	Br	Ethyl *n*-butyrate[b]	51
1-Butene	Br	Ethyl hexanoate	59
2-Butene	Br	Ethyl 3-methylpentanoate	68
Isobutylene	Br	Ethyl 4-methylpentanoate	53
1-Hexene	Br	Ethyl octanoate	74
1-Hexene	Cl	Ethyl octanoate	74
Cyclopentene	Br	Ethyl cyclopentylacetate	63
1-Methylcyclopentene	Br	Ethyl (*trans*-2-methylcyclopentyl)acetate[d]	57
Cyclohexene	Br	Ethyl cyclohexylacetate	62
Cyclohexene	Br_2	Ethyl α-bromocyclohexylacetate	68
Cyclohexene	Cl_2	Ethyl α-chlorocyclohexylacetate	88
Cyclopentene	Cl_2	Ethyl α-chlorocyclopentylacetate	90

[a] In each experiment, 10 mmol of potassium *t*-butoxide in *t*-butyl alcohol was added to 10 mmol of B-R-9-BBN and 10 mmol of the ethyl α-haloacetate at 0°. [b] 25°. [c] Analysis by glpc. [d] For discussion of stereochemistry, see H. C. Brown, M. M. Rogić, M. W. Rathke, and G. W. Kabalka, *J. Am. Chem. Soc.*, **91**, 2150 (1969).

13.7 g (67% yield) of ethyl α-chlorocyclohexylacetate, bp 119.5° (12 mm), $n^{20}D$ 1.4654.

Hydroboration of 1-hexene with borane produces 94% 1-hexyl and 6% 2-hexyl groups. Since the reaction of trialkylboranes with the ethyl haloacetates exhibits little selectivity between primary and secondary alkyl groups, the products thus obtained are contaminated with small amounts of the isomeric esters. This difficulty is avoided by the use of 9-BBN.

Another major advantage is the apparently much smaller steric difficulties offered by the reagent. Thus, in the reaction of the ethyl dihaloacetates with trialkylboranes we previously experienced difficulties in utilizing relatively hindered organoboranes.[2] For example, tricyclopentylborane gave a product containing 54% ethyl α-chlorocyclopentylacetate and 30% of the corresponding α-*t*-butoxy derivative.[2] Use of B-cyclopentyl-9-BBN gave 90% of the desired ester, essentially free of the α-*t*-butoxy derivative (Table I). Similarly, our initial attempts to achieve the carbethoxymethylation of 1-methylcyclopentene by allowing the organoborane from this hindered olefin to react with ethyl bromoacetate failed. However, B-*trans*-2-methylcyclopentyl-9-BBN reacted readily, yielding the desired ester (Table I).

Recently, Hooz and Linke have reported that diazoacetone, diazoacetonitrile, and ethyl diazoacetate react with trialkylboranes to yield the corresponding ketones, nitriles, and esters.[7] This reaction also utilizes only one of the three alkyl groups on boron. We examined the reaction of B-*n*-butyl-9-BBN with ethyl diazoacetate. A rapid evolution of nitrogen was observed, but the reaction product corresponded to migration of one of the cyclooctylboron bonds, rather than to migration of the *n*-butyl group. Oxidation produced an 80% yield of a product tentatively identified as ethyl (*cis*-5-hydroxycyclooctyl)acetate.

It therefore appears that certain reactions of B-R-9-BBN involve preferential migration of the R-B bond, whereas other reactions take place with preferential migration of the B-cyclooctyl bond.[8] We have developed a tentative explanation, but prefer to defer discussion until it has been subjected to more extended testing.

(7) J. Hooz and S. Linke, *J. Am. Chem. Soc.*, **90**, 5936, 6891 (1968).

(8) A further puzzle is the observation that acrolein, which reacts with remarkable speed even with hindered trialkylboranes,[4] fails to react with B-R-9-BBN. See H. C. Brown, M. M. Rogić, M. W. Rathke, and G. W. Kabalka, *ibid.*, **91**, 2150 (1969).

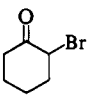
Herbert C. Brown, Milorad M. Rogic
Richard B. Wetherill Laboratory
Purdue University, Lafayette, Indiana 47907
Received December 23, 1968

Reaction of B-Alkyl-9-borabicyclo[3.3.1]nonanes with α-Bromo Ketones under the Influence of Potassium *t*-Butoxide. A Convenient Procedure for the α Alkylation of Ketones

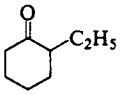
Sir:

Recently we reported that α-bromo ketones, such as phenacyl bromide and α-bromocyclohexanone, react readily with triethylborane under the influence of potassium *t*-butoxide in tetrahydrofuran to produce the corresponding α-ethyl derivatives[1] (1, 2).

$$C_6H_5COCH_2Br + (C_2H_5)_3B + t\text{-BuOK} \xrightarrow{0^\circ} C_6H_5COCH_2CH_2CH_3 + t\text{-BuOB}(C_2H_5)_2 + KBr \quad (1)$$



$$+ (C_2H_5)_3B + t\text{-BuOK} \xrightarrow{0^\circ}$$



$$+ t\text{-BuOB}(C_2H_5)_2 + KBr \quad (2)$$

Attempts to use organoboranes in which the alkyl groups are highly substituted close to the reaction center, organoboranes such as tri-*sec*-butylborane and triisobutylborane, failed. Evidently the α-bromocarbanions from such α-bromo ketones are far more sensitive to the steric environment of the borane acceptor than are the corresponding α-halocarbanions from esters.[2] This represents a serious difficulty, apparently limiting this new alkylation procedure to relatively unhindered alkyl groups. The fact that only one of the three alkyl groups

(1) H. C. Brown, M. M. Rogic, and M. W. Rathke, *J. Am. Chem. Soc.*, **90**, 6218 (1968).

(2) H. C. Brown, M. M. Rogic, M. W. Rathke, and G. W. Kabalka, *ibid.*, **90**, 818, 1911 (1968).

Table I. Alkylation of α-Bromo Ketones with B-Alkyl-9-borabicyclo[3.3.1]nonanes under the Influence of Potassium *t*-Butoxide in Tetrahydrofuran[a]

Olefin	B-R-9-BBN, mmol	α-Bromo ketone[b]	Addn[c]	Product	Yield,[d] %
Ethene	10	A	KOR	Butyrophenone	71
	10	A	SA		82
	20	A	KOR		91
1-Butene	10	A	KOR	Hexanophenone	78
	10	A	SA		80
	20	A	KOR		83
2-Butene	10	A	KOR	β-Methylvalerophenone	45
	10	A	SA		61
	20	A	KOR		65
Isobutylene	10	A	KOR	γ-Methylvalerophenone	33
	10	A	SA		55
	20	A	KOR		65
Cyclopentene	10	A	SA	α-Cyclopentylacetophenone	20
Cyclohexene	10	A	SA	α-Cyclohexylacetophenone	30
4-Vinylcyclohexene	10	A	SA	γ-(3-Cyclohexenyl)butyrophenone	60
1-Butene	10	B	SA	2,2-Dimethyl-3-octanone	78
cis-2-Butene	10	B	SA	2,2,5-Trimethyl-3-heptanone	79
Isobutylene	10	B	SA	2,2,6-Trimethyl-3-heptanone	61
Cyclopentene	10	B	SA	2,2-Dimethyl-4-cyclopentyl-3-butanone	77
Cyclohexene	10	B	SA	2,2-Dimethyl-4-cyclohexyl-3-butanone	60
Ethene	10	C	SA	2-Ethylcyclohexanone	0

[a] 10 mmol of 9-R-9-BBN in tetrahydrofuran was treated with 10 mmol of the α-bromo ketone and 10 mmol of potassium *t*-butoxide. [b] A, phenacyl bromide; B, α-bromopinacolone; C, α-bromocyclohexanone. [c] KOR: addition of potassium *t*-butoxide to the mixture of the other two reactants; SA: simultaneous addition of base and α-bromo ketone to 9-R-9-BBN. Both reactions were carried out at 0°. [d] Glpc analysis.

on boron is utilized in this reaction constitutes another handicap.

We now wish to report that both of these difficulties are largely circumvented by the use of the B-alkyl-9-borabicyclo[3.3.1]nonanes (B-R-9-BBN), readily available from the hydroboration of the appropriate olefins with the new reagent, 9-BBN[3] (3).

(3)

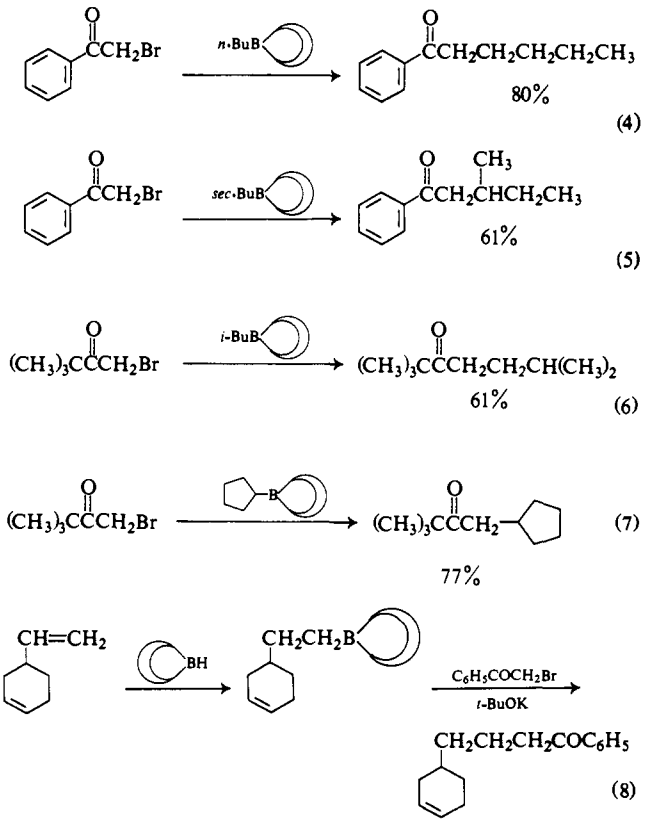
Improved yields were realized by adding the α-bromo ketone and the potassium *t*-butoxide simultaneously to the B-R-9-BBN at 0°. Consequently, this "simultaneous addition" technique was adopted for the later experiments.

The yields could also be improved by using an excess of B-R-9-BBN. However, this is desirable only when the alkyl group represents an easily available reagent and it is desirable to convert as much as possible of a valuable α-bromo ketone to product. Obviously, in cases where it is the alkyl group that is the valuable intermediate, such an excess should be avoided.

In contrast to the earlier procedure, where no product was realized with tri-*sec*-butylborane or triisobutylborane, reasonable yields were realized with B-*sec*-butyl- and B-isobutyl-9-BBN. Typical results are indicated in the following reactions (4–7).

It should be pointed out that attempts to alkylate ketones in the α position by the usual base-catalyzed reaction may fail badly with such halides as isobutyl, *sec*-butyl, and cyclopentyl.[4]

We can also utilize the selectivity of the hydroboration reaction with 9-BBN to achieve selective alkylation with a diene (8).



The results are summarized in Table I.

The following procedure is representative. In the usual hydroboration flask was placed 300 ml of tetrahydrofuran and 80 ml of a 2.5 *M* solution of borane in THF (200 mmol). To this well-stirred solution at room

(3) E. F. Knights and H. C. Brown, *J. Am. Chem. Soc.*, **90**, 5280, 5281, 5283 (1968).

(4) K. B. Wiberg and B. I. Rowland, *ibid.*, 77, 1159 (1955).

temperature was added 24.6 ml (200 mmol) of *cis*-1,5-cyclooctadiene over a period of 15 min. At the end of the addition the temperature of the reaction mixture was 60–65°. The reaction mixture was refluxed for 1.5 hr and then cooled to 0°. *cis*-2-Butene, 11.2 g (200 mmol), was introduced from a cylinder and the reaction mixture stirred for 30 min to complete the hydroboration stage. One of the dropping funnels was charged with 39.8 g of phenacyl bromide in 200 ml of THF and the other with 200 ml of a 1.00 *M* solution of potassium *t*-butoxide in the same solvent. The two solutions were added simultaneously to the solution of B-*sec*-butyl-9-BBN maintained at 0°. Glpc examination of the solution indicated a 65% yield of β-methylvalerophenone. To the reaction mixture was then added 66 ml of 3 *M* sodium acetate, followed by dropwise addition of 45 ml of 30% hydrogen peroxide. The reaction mixture was stirred at room temperature for 1 hr and then diluted with the same volume of pentane. The pentane layer was then washed with 100-ml portions of water and dried, and the solvents were removed. Distillation, 88° at 1 mm, gave 17.6 g, a 50% yield, of β-methylvalerophenone, semicarbazone mp 179–180°.[4]

We have a caution to make. In condensation reactions experience indicates that the reaction conditions must be carefully adjusted to the characteristics of the reagents in order to achieve maximum yield.[5] The present synthesis has many of the characteristics of a condensation reaction. The results indicate that once conditions have been established for satisfactory reaction for a particular α-bromo ketone, such as phenacyl bromide or α-bromopinacolone, these same conditions are applicable to a large variety of alkyl groups in the form of the B-R-9-BBN derivative. However, each α-bromo ketone doubtless has its own characteristic, and it will probably be necessary to vary the reaction conditions (base, solvent, temperature) to achieve maximum yield.[6]

In spite of these difficulties, it is evident that this new alkylation procedure has many promising possibilities. Thus it has proven possible to alkylate with *sec*-butyl, isobutyl, cyclopentyl, and cyclohexyl groups, groups that are difficult to introduce by the usual reaction of alkyl halides with carbanions. We are currently exploring the introduction of aryl groups with the aid of B-aryl-9-BBN. Consequently, this new alkylation procedure is not merely an alternative to the procedures presently available for the alkylation of ketones, but it promises to make possible the introduction of groups which cannot be handled by the other processes currently available.

(5) See H. O. House, "Modern Synthetic Reactions," W. A. Benjamin, Inc., New York, N. Y., 1965, Chapter 7, for a discussion of the alkylation of active methylene compounds.

(6) For example, in one experiment with α-bromocyclohexanone and B-ethyl-9-BBN (Table I) no yield of α-ethylcyclohexanone was realized although we had previously realized a yield of 68% using triethylborane[1] for the alkylation. Yet with phenacyl bromide and α-bromopinacalone our yields with B-R-9-BBN were invariably higher than with the corresponding R_3B.

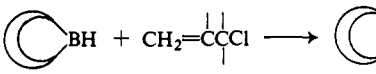
(7) Visiting scholar on funds provided by the Mitsui Petrochemical Co., Tokyo, Japan.

Herbert C. Brown, Milorad M. Rogic
Hirohiko Nambu,[7] Michael W. Rathke
Richard B. Wetherill Laboratory
Purdue University, Lafayette, Indiana 47907
Received December 23, 1968

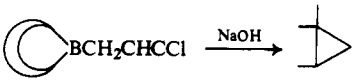
Facile Cyclization of B-(γ-Chloropropyl)-9-borabicyclo[3.3.1]nonanes. An Improved Synthesis of Cyclopropane Derivatives *via* Hydroboration

Sir:

We wish to report that B-(γ-chloropropyl)-9-borabicyclo[3.3.1]nonanes, readily available by the reaction of the parent borane, 9-BBN,[1] with appropriate allylic chlorides (1), undergo cyclization with aqueous sodium hydroxide, to form the corresponding cyclopropane derivatives (2).

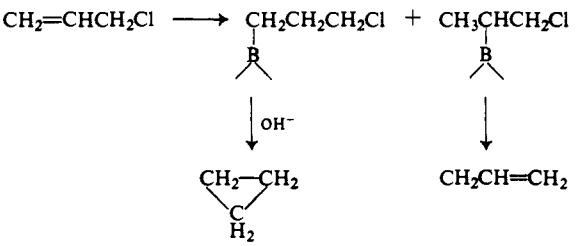


(1)



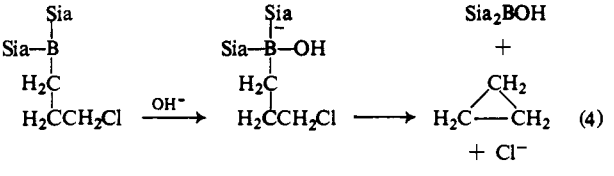
(2)

The cyclization of hydroborated allylic chlorides to form the corresponding cyclopropanes was discovered by Hawthorne and Dupont[2] and subsequently applied to the synthesis of a variety of cyclopropanes.[3] A major difficulty with this procedure is revealed by the parent compound, allyl chloride. The powerful directive effect of the substituent directs hydroboration with diborane to give roughly 50:50 of the two isomeric boron derivatives (3). Consequently, in such cases the maximum yield of cyclopropane derivative cannot be greater than approximately 50%.



(3)

This difficulty was circumvented by the use of the more selective hydroborating agent, disiamylborane.[4] It was subsequently observed that the use of this highly hindered borane introduced difficulty, especially when the chlorine substituent is relatively reactive.[5] The cyclization reaction apparently requires prior coordination of the base with the boron atom to produce a quaternary derivative which then undergoes cyclization (4). In the



(4)

case of highly reactive chlorides, loss of the substituent is competitive with the slow coordination and cyclization.

(1) E. F. Knights and H. C. Brown, *J. Am. Chem. Soc.*, **90**, 5280, 5283 (1968).
(2) M. F. Hawthorne and J. A. Dupont, *ibid.*, **80**, 5830 (1958).
(3) M. F. Hawthorne, *ibid.*, **82**, 1886 (1960).
(4) H. C. Brown and K. A. Keblys, *ibid.*, **86**, 1791 (1964).
(5) Research in progress.