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Preliminary communication

Synthesis of secondary alkyl bromides in the dark reaction of bromine with *B*-sec-alkyl-9-borabicyclo[3.3.1]nonanes. A convenient procedure for the anti-Markovnikov hydrobromination of internal olefins

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It was observed recently that organoboranes react readily in the dark with bromine in methylene chloride solution to give the corresponding alkyl bromide and dialkylboron bromide[1] (Eq.1).

$$R_3B + Br_2 \xrightarrow[25^\circ, \text{dark}]{CH_2Cl_2} R_2BBr + RBr \qquad (1)$$

Unexpectedly, this reaction apparently does not involve the direct rupture of the carbon–boron bond by the bromine molecule. Instead, the reaction apparently proceeds through a free radical substitution of the α position of the organoborane (Eq.2, 3), followed by protonolysis of the intermediate by the hydrogen bromide produced in the bromination stage (Eq.4).

$$R_2B{-}\overset{|}{\underset{|}{C}}{-} + Br\cdot \rightarrow R_2B{-}\overset{|}{\underset{\cdot}{C}}{-} + HBr \qquad (2)$$
$$\quad\ H$$

$$R_2B{-}\overset{|}{\underset{\cdot}{C}}{-} + Br_2 \rightarrow R_2B{-}\overset{|}{\underset{|}{C}}{-} + Br\cdot \qquad (3)$$
$$\qquad\qquad\qquad\quad Br$$

$$R_2B{-}\overset{|}{\underset{|}{C}}{-} + HBr \rightarrow R_2BBr + RBr \qquad (4)$$
$$\quad\ Br$$

While this reaction possesses characteristics that indicate it could be highly useful in certain synthetic applications, it suffers from the disadvantage in utilizing only one of the three alkyl groups in the organoborane.

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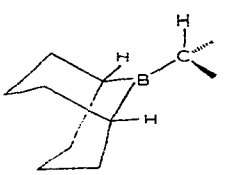
Many of the new reactions of trialkylboranes are limited in their synthetic utility for the same reason: only one of the three alkyl groups on boron participates in the reaction[2] Thus, when a valuable olefin is to be converted into the desired product, the maximum yield obtainable is only 33%. However, hydroboration via 9-borabicyclo[3.3.1]nonane (9-BBN) to give *B*-alkyl-9-BBN[3] has solved this problem for a number of cases. Carbonylation in the presence of metal hydrides[4], reaction with α-halo carbanions[5], and cyclization of γ-chloropropyl derivatives[6] all show a large preference for B–alkyl bond migration as opposed to B–cyclooctyl bond migration. Consequently, maximum utilization of the olefin is possible in these cases.

Unfortunately, the use of 9-BBN could not be applied to all of the new reactions. The *B*–alkyl–9-BBN derivative from the hydroboration of 1-methylcyclopentene failed to undergo a 1,4-addition reaction with acrolein[7]. In general, the migration of the B–cyclooctyl bond appears to be the preferred pathway for the reaction of B–alkyl–9-BBN derivatives with α,β-unsaturated carbonyl compounds[8]: The reaction of α-diazo derivatives[2j,k] with B–alkyl–9-BBN compounds also shows preferential reaction at the B–cyclooctyl bond[5a,9], and we have found that the same is true for the base-induced bromination[10] and amination[11] reactions.

As was pointed out earlier, the dark reaction of trialkylboranes with bromine in a methylene chloride solution also results in the utilization of only one alkyl group[1]. However, the reaction is extremely dependent upon the degree of substitution and steric environment of the α-carbon, *e.g.*, the half-lives of the reaction of bromine with tri-n-butyl, tri-sec-butyl and triisobutylborane were observed to be ~ 30 min, < 5 min, and ~ 20 h, respectively. This indicates that a high degree of selectivity should be possible in this reaction.

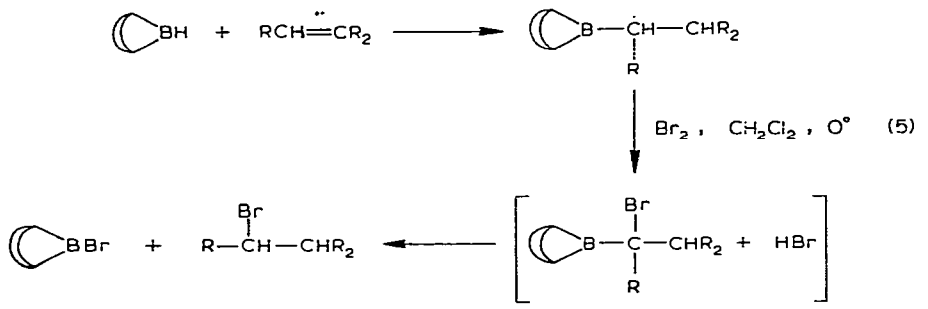
The B–alkyl–9-BBN derivatives appeared to be uniquely structured for the desired selectivity. The α-hydrogen on the alkyl group should be more susceptible to free radical abstraction than the bridge-head hydrogens (I) because the resulting α-boro free radical can



(I)

interact with the vacant *p*-orbital on boron, while a bridge-head free radical would not be able to interact with the boron atom. This is because the odd electron in the bridge-head free radical would necessarily occupy an orbital which is orthogonal to the vacant *p*-orbital on boron, and the rigid bicyclic structure prevents the bond rotation required for maximum interaction.

The experimental results proved quite satisfactory. The *B*-sec-alkyl-9-BBN's, readily available via hydroboration of internal olefins with 9-BBN, readily undergo the α-bromination–HBr cleavage reaction[1] to give the corresponding alkyl bromides in good yields (Eq.5).



This provides a convenient procedure for the anti-Markovnikov hydrobromination of internal olefins and nicely complements the base-induced bromination reaction[10], which provides an alternative convenient procedure for the anti-Markovnikov hydrobromination of terminal olefins.

A wide range of internal olefins can be accommodated, as indicated by the results summarized in Table 1.

TABLE 1

DARK REACTION OF *B*-sec-ALKYL-9-BORABICYCLO[3.3.1]NONANES WITH BROMINE [a]

B-alkyl-9-BBN from olefin	Product	Yield (%) [b]
Butene-2	2-Bromobutane	85
2-Methylbutene-2	2-Bromo-3-methylbutane	88
2,3-Dimethylbutene-2	2-Bromo-2,3-dimethylbutane	0 [c]
4-Methylpentene-2	2-Bromo-4-methylpentane	88
Cyclohexene	Bromocyclohexane	84
Norbornene	2-*exo*-Bromonorbornane [d]	90
1-Methylcyclopentene	1-Bromo-2-methylcyclopentane [e]	80

[a] Reactions were allowed to proceed for 30 min at 0–5° then one hour at 20–25° in a closed system using a 10% excess of bromine and methylene chloride as solvent. [b] By GLPC analysis. The yields are based on the amount of starting olefin. [c] The alkyl group does not contain an α-hydrogen, therefore, α-bromination cannot occur. [d] The absence of the *endo* isomer was indicated by GLPC analysis (<1%). [e] Stereochemistry was not established.

The following procedure for the conversion of 4-methyl-2-pentene into 2-bromo-4-methylpentane is representative. A dry 500-ml flask equipped with septum inlet, gas outlet tube with stopcock, reflux condenser, and magnetic stirrer was flushed with nitrogen and then maintained under a positive nitrogen pressure. The flask was charged with 190 ml of a 0.57 *M*-solution of 9-BBN (108 mmol of hydride) in tetrahydrofuran. 4-Methyl-2-pentene (12.5 ml, 100 mmol) was added and the solution was heated to reflux and maintained at reflux for one hour★. The THF was then removed via reduced pressure and replaced with 100 ml of methylene chloride. The solution was cooled to 0° and the outlet tube stopcock

★In the present reaction it is desirable to avoid the presence of an excess of 9-BBN. Consequently, more vigorous reaction conditions are necessary to achieve complete conversion of the olefin than in the original study involving this reagent which utilized the reagent in ~100% excess[3].

was closed. The entire reaction flask was covered with aluminum foil and 5.6 ml (110 mmol) of bromine was added through the septum inlet over a period of 1 min using an all glass syringe equipped with a Teflon needle. The reaction was then allowed to stir for 30 min at 0° followed by 1 h at 25°. After removal of the aluminum foil and venting the flask (HBr gas) to a trap containing alkali, the *B*-bromo-9-BBN and any excess bromine was destroyed by the dropwise addition of 75 ml of a 3 *M* sodium hydroxide solution at 0°. After 15 min stirring, the lower organic layer was removed, dried over anhydrous potassium carbonate, and filtered through Celite. Following removal of the methylene chloride on a rotary evaporator, vacuum distillation gave 12.2 g (74%) of 2-bromo-4-methylpentane, b.p. 58–60° (54 mm), n_D^{21} 1.4415 (lit. [12] n_D^{24} 1.4406).

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