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Base-induced Bromination of Tri-*exo*-norbornylborane: an Electrophilic Substitution with Predominant Inversion of Configuration

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Summary The reaction of bromine with tri-*exo*-norbornylborane under the influence of methanolic sodium methoxide results in inversion of configuration at carbon during the electrophilic substitution to give predominantly *endo*-bromonorbornane (75 ± 5% *endo*).

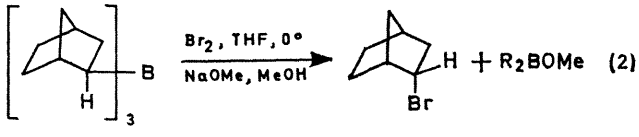
We recently reported[1] that organoboranes prepared *via* hydroboration of terminal olefins react rapidly at 0° with bromine under the influence of sodium methoxide [reaction (1)]. All three alkyl groups on boron are converted into

$$3\,RCH{=}CH_2 \xrightarrow[THF]{BH_3} (RCH_2CH_2)_3B \xrightarrow[NaOMe]{Br_2} 3\,RCH_2CH_2Br \qquad (1)$$

the corresponding alkyl bromide to give an essentially quantitative yield based on starting olefin. Consequently, this hydroboration–bromination reaction provides a convenient procedure for the anti-Markovnikov hydrobromination of terminal olefins.

We have since studied the mechanism of this base-induced bromination. A detailed kinetic study of the reaction rate could not be accomplished because of the rapid side reaction of bromine with sodium methoxide. However, we could analyse (by g.l.c. and n.m.r. spectroscopy) the stereochemistry of the product from the base-induced bromination of tri-*exo*-norbornylborane, which, under these mild conditions,[1] converts only one norbornyl group into the bromide. Surprisingly, the 2-bromonorbornane obtained was predominantly *endo*, indicating that inversion of configuration had occurred at the carbon atom undergoing reaction (2). The procedure was repeated a number of times and the norbornyl bromide formed was always 75 ± 5% *endo* by either g.l.c. or n.m.r. analysis.

This result is unexpected since most reported electrophilic substitution reactions proceed with retention of configuration.[2] However, a few electrophilic substitution reactions have been reported to proceed with inversion of configuration. Thus, the reaction of bromine with *exo*- or *endo*-norbornyl-lithium,[3] with menthyl-lithium,[4] or with 4-t-butylcyclohexyl-lithium[4] results in predominant, though not stereospecific, inversion.



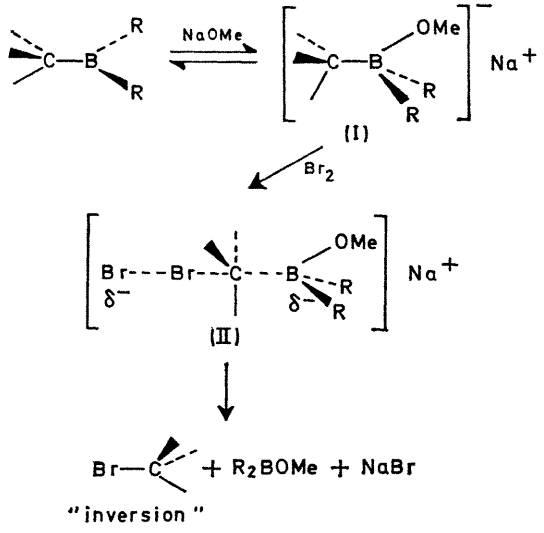
(2)

This inversion of configuration for the base-induced bromination is even more unusual when compared to the highly consistent behaviour of other reactions of organoboranes.[5] Essentially all the non-free-radical reactions of organoboranes, *e.g.* protonolysis with carboxylic acids, oxidation with alkaline hydrogen peroxide, amination with hydroxylamine-*O*-sulphonic acid, carbonylation, and ethoxycarbonylmethylation, are highly stereospecific reactions with complete retention of configuration at the carbon atom undergoing reaction.[6]

The sodium methoxide used in this bromination has a pronounced effect upon both the rate of reaction and the stereochemistry. The reaction of bromine in the dark at 20° with an equimolar quantity of tri-n-butyl- or tri-s-butylborane in tetrahydrofuran in the absence of added base was quite slow, being only 30—40% complete after 8 h. Similar reactions in the presence of base were virtually 100% complete as fast as the analysis could be made following addition of the methoxide. The bromination of tri-*exo*-norbornylborane in the absence of base under analogous conditions was also quite slow and the small amount of bromide formed was > 99% *exo* by g.l.c. analysis.

A mechanism which can account for this remarkable inversion is shown in the Scheme. The tremendous acceleration in rate upon addition of base is presumably due to "ate" complex formation (I). This should increase

the electron density on carbon, and increase the ease of bond scission upon back-side attack by bromine. Most electrophilic substitutions which result in retention of configuration are thought to involve four-centre transition states.[2] In the "ate" complex, such a four-centre transition state is not possible, so the reaction takes a different mechanistic course resulting in inversion.



SCHEME

The small amount of the *exo*-norbornyl bromide formed may arise from a competing mechanism proceeding through a free-radical substitution[7] or through a typical electrophilic substitution of a small amount of tri-*exo*-norbornylborane in equilibrium with the "ate" complex. We are not yet able to define the precise path for the minor product.

Although the mechanistic implications of this study are interesting, the synthetic importance may be even greater because this base-induced bromination of tri-*exo*-norbornylborane provides a convenient means of preparing *endo*-bromonorbornane† and, presumably, related bicyclic derivatives. The simultaneous addition procedure described previously[1] followed by selective solvolysis of the more reactive *exo*-form in 80% aqueous ethanol[9] gave after distillation pure *endo*-bromonorbornane (> 99% *endo* by g.l.c. and n.m.r. analysis, n_D^{20} 1·5158).

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† A reported attempt at obtaining this compound *via* a nucleophilic displacement was unsuccessful.[8] The only known alternate procedure is that reported by Roberts and his co-workers.[9]

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