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ELECTROPHILIC SUBSTITUTION OF PRIMARY ALKYLBORANES

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Summary

Electrophilic substitution of a primary alkylborane can proceed with inversion of configuration at carbon. This stereochemical result is obtained even when the electrophile can coordinate to the boron. These results suggest that the stereochemistry of electrophilic cleavage of carbon—metal bonds is affected by the type of carbon attacked as well as by the nature of the electrophile and the metal. The stereochemical results obtained in this system are contrasted with those obtained in other systems.

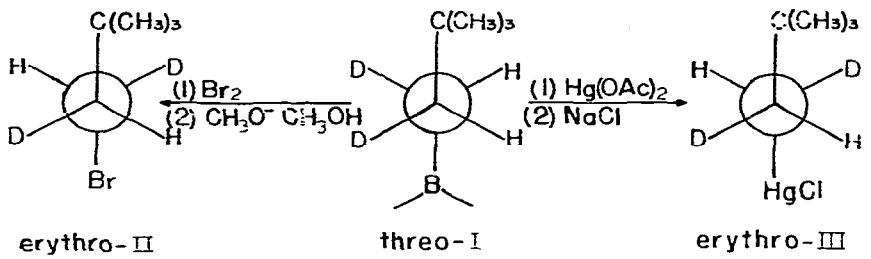
Introduction

Electrophilic substitution is a reaction of widespread importance in organometallic chemistry. In addition to the synthetic importance of this reaction, electrophilic substitution is a topic of current mechanistic interest [1]. Previous mechanistic studies of electrophilic substitution have often concentrated on the stereochemical outcome of such substitution reactions of carbon. In most cases, retention of configuration is observed. Recently Gielen and Fosty [2] reported that mercury(II) cleavage of a tris(*erythro*-3,3-dimethyl-1-butyl-1,2-d_2)borane proceeds with >95% inversion of configuration. Our work confirms this unexpected result and further shows that bromine cleavage of primary diastereomeric alkylboranes also proceeds stereospecifically with inversion. These experimental observations contrast with results in secondary systems and demonstrate that the use of a primary organometallic substrate instead of a secondary organometallic substrate in electrophilic substitution reactions can change the stereochemical result of such reactions. Comparison of the stereochemical result of the cleavage reaction of alkylboranes using bromine and the cleavage reaction of alkylboranes using mercury(II) acetate suggest that the ability of the organometallic reagent to coordinate to the electrophile is not necessarily the determining factor in the stereochemistry of electrophilic substitution at carbon.

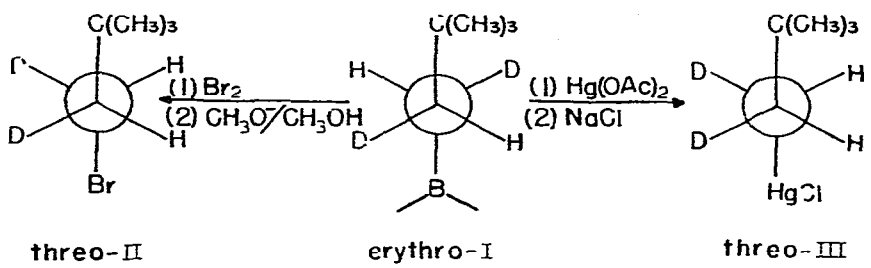
Results and discussion

The primary diastereomeric alkylboranes, tris(*threo*- and *erythro*-3,3-dimethyl-1-butyl-1,2-d_2)borane, *threo*-I and *erythro*-I, were prepared stereospecifically from 3,3-dimethylbutyne-1-d_1 and 3,3-dimethylbutyne by hydroboration with 1,3,2-benzodioxaborole and protonolysis or deuterolysis to a diastereomerically pure alkene [3] followed by deuteroboration with deuteroborane-methyl sulfide [4]. The stereochemistry of the intermediate alkylboranes was determined by alkaline hydrogen peroxide oxidation to the corresponding alcohols [5].

The electrophilic cleavage reactions of *threo*-I and *erythro*-I with bromine and mercury(II) acetate were accomplished according to published procedures [6]. The results of these reactions are detailed in equations 1 and 2. These reactions were carried out with both diastereomers. In every case, the configuration of the product was determined by deuterium-decoupled ^{1}H NMR [7] and by IR (See



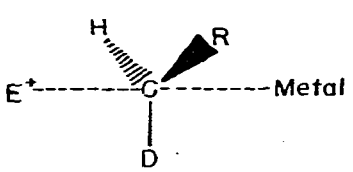
erythro-II threo-I erythro-III (1)



threo-II erythro-I threo-III (2)

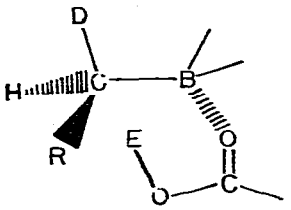
Experimental). The sodium methoxide assisted cleavage of the alkylboranes I with bromine was found to proceed with >95% inversion of configuration at carbon. Predominant inversion of configuration (ca. 90%) was observed in the mercury(II) acetate cleavage of the alkylboranes I. The small amount of retention observed was shown not to be due to epimerization of the organomercurial and probably reflects the presence of an alternative reaction pathway.

The results are best explained by a reaction mechanism involving back-side attack of the electrophile on the carbon—boron bond through a transition state like IV. Jensen and Davis have postulated that open transition states such as IV



(IV)

and concomitant inversion of configuration at carbon can be expected when the metal has no low-lying vacant orbitals which could coordinate to the electrophile [8]. While prior coordination of methoxide anion with the alkylborane in the bromination reaction might lead one to predict inversion and a transition state similar to IV for bromination, one would propably predict a priori that mercuration would involve a closed six-membered transition state (V), much like that



(V)

proposed in the protonolysis of alkylboranes with carboxylic acids (a reaction which proceeds with retention at carbon [9]. The experimental observation of inversion in the mercuration reaction suggests that back-side attack of an electrophile can compete favorably with front-side attack, even if the metal has available low-lying empty orbitals which can coordinate to the electrophile.

Previous studies of related reactions provide some interesting comparisons to our results. Brown and Lane have previously inferred predominant inversion of stereochemistry in the bromination of *exo*-norbornylborane [10] in general agreement with our results. However, this previous study was complicated by the fact that Brown and Lane used only one of the two possible diastereomeric alkylboranes and by the observation of substantial amounts (25%) of retention. Analogous results have recently been obtained with iodine [11]. The observation by Matteson and Bowie that mercury(II) chloride cleavage of 1-phenyl-ethaneboronic acid proceeds with predominant retention of configuration [12] and the similar stereochemistry inferred in the mercuric(II) acetate cleavage of *exo*-2-norbornylborane by Brown and Larock [13] contrasts dramatically with our results and those of Gielen and Fosty. The obvious explanation for these discrepancies is that electrophilic substitution may be sensitive to steric factors. Such behavior is perhaps not unexpected in view of the pronounced effects of α-substitution in nucleophilic substitution reactions in organic chemistry. Thus, while a secondary alkylmetal compound may undergo electrophilic substitution with complete or predominant retention a similar primary alkylmetal compound may undergo an analogous reaction with complete or predominant inversion.

Qualitative support for the observed inversion of configuration at carbon in the electrophilic substitution of these primary diastereomeric alkylboranes with mercury(II) acetate is found in the original work by Brown and Larock on mercuration of alkylboranes [14]. In this paper, Brown and Larock have reported reaction times for a variety of substituted primary alkylboranes. The significant differences in reaction times for hydroboration—mercuration observed for 1-butene, isobutylene, and 3,3-dimethylbutene are best accounted for by an S_E2 reaction proceeding with inversion. Such significant steric effects would not be expected for an electrophilic substitution proceeding with retention [8].

Experimental section

All reactions of organometallic compounds were carried out in flame-dried glassware under pre-purified nitrogen or argon using standard techniques [5]. Tetrahydrofuran and other ethereal solvents were distilled from a purple solution of benzophenone dianion prior to use. Methanol was purified by distillation from a methanol-sodium hypoiodate solution. Deuterium-decoupled NMR spectra were obtained using a Varian HA-100 spectrometer at the University of Texas at Austin. High resolution infrared spectra were obtained on a Digilab FTS-20 vacuum infrared spectrometer. Melting points are uncorrected. Solutions of deuteroborane-methyl sulfide complex in tetrahydrofuran were purchased from Aldrich Chemical Company. Other solvents and reagents were purchased from commercial sources in reagent quality.

Tris(threo-3,3-dimethyl-1-butyl-1,2-d_2)boron (threo-I)

To 20 ml of a THF solution containing 3.9 ml (30 mmol, 2.55 g) of (*Z*)-3,3-dimethyl-1-butene-1-d_1 [3] was added dropwise at 0°C 10.5 ml of a 9.5 *M* THF solution of deuteroborane-methyl sulfide complex. The resulting solution was stirred at 0°C for 1 h and at room temperature an additional 5 h. The THF and methyl sulfide were then removed in vacuo. The product *threo*-I was purified by vacuum distillation and isolated in 84% yield; b.p. 105°C (1.8 mmHg); IR (neat) 2150, 1460, 1380, 1355, 1090, 1052, 1035, 924, and 862 cm^{-1}.

Tris(erythro-3,3-dimethyl-1-butyl-1,2-d_2)boron (erythro-I)

This isomer was prepared in 84% yield from (*E*)-3,3-dimethyl-1-butene-1-d_1 [3] by the procedure described above for *threo*-I; b.p. 105°C (1.8 mmHg); IR (neat) 2150, 1460, 1380, 1355, 1015, 924, and 898 cm^{-1}. The IR spectra of *erythro*-I and *threo*-I differ in the 1100—1010 and 905—855 cm^{-1} regions.

Erythro-1-bromo-3,3-dimethylbutane-1,2-d_2 (erythro-II)

Erythro-II was prepared by a slight modification of the procedure of Brown and Lane [15]. To a solution of 2.0 ml (5.7 mmol, 1.58 g) of *threo*-I and 10 ml of THF was added dropwise at 0°C 1.2 ml (22.8 mmol, 3.64 g) of bromine. This addition was followed by the dropwise addition of 5.0 ml (28.5 mmol) of a 5.69 *M* methanol solution of sodium methoxide. After following the work-up procedure described by Brown and Lane [15], *erythro*-II was isolated in 49.8% yield by vacuum distillation (64.5% by GPC); b.p. 137—138°C (lit. [16] b.p. 138°C); IR (CS_2) 2955, 2900, 2865, 1398, 1368, 1304, 1290, 1250, 1238, 1213, 1161, 1076, 1049, 1040, 990, 918, 820, and 626 cm^{-1}; deuterium-decoupled ^1H NMR ($CDCl_3$) δ (ppm) 3.31 (d, 1, *J* 12.3 Hz), 1.82 (d, 1, *J* 12.3 Hz), 0.95 (s, 9).

Threo-1-bromo-3,3-dimethylbutane-1,2-d_2 (threo-II)

Threo-II was prepared in 51.2% yield (64.5% by GPC) from *erythro*-I by the same procedure used to prepare *erythro*-II; b.p. 137—138°C (lit. [16] b.p. 138°C); IR (CS_2) 2955, 2900, 2865, 1395, 1368, 1321, 1313, 1295, 1250, 1237, 1204, 1190, 1168, 1040, 980, 865, 808, and 627 cm^{-1}; deuterium-decoupled ^1H NMR ($CDCl_3$) δ (ppm) 3.31 (d, 1, *J* 5.0 Hz), 1.87 (d, 1, *J* 5.0 Hz), 0.95 (s, 9). The IR spectra of *erythro*-II and *threo*-II differ in the fingerprint region.

Erythro-3,3-dimethyl-1-butyl-1,2-d_2-mercuric chloride (erythro-III)

Erythro-III was prepared according to the general procedure of Larock and Brown [14]. To a solution of 1.0 ml (2.9 mmol, 0.79 g) of *threo*-I and 10 ml of THF was added 2.72 g (8.6 mmol) of mercuric acetate. The resulting white suspension was stirred 2 h at 25°C and then poured into 100 ml of 1 *M* aqueous sodium chloride. The resulting white suspension was stirred overnight and then diluted to twice its volume with water. The resulting white precipitate was collected by suction filtration to yield 2.44 g (7.6 mmol, 88%) of *erythro*-III after one recrystallization from 95% ethanol; m.p. 131.5—132°C (lit. [17] m.p. 132—132.5°C); IR (CS_2) 2950, 2895, 2867, 1390, 1368, 1295, 1262, 1238, 1191, and 1108 cm^{-1}; deuterium-decoupled ^1H NMR ($CDCl_3$) δ (ppm) 1.94 (d, 1, *J* 12.3 Hz), 160(d, 1, *J* 12.3 Hz) 0.92 (s, 9).

Threo-3,3-dimethyl-1-butyl-1,2-d_2 mercuric chloride (threo-III)

Threo-III was prepared in 88% yield from *erythro*-I by the procedure described above for *erythro*-III; m.p. 131.5—132°C (lit. [17] m.p. 132—132.5°C); IR (CS_2) 2950, 2885, 2853, 1388, 1362, 1302, 1242, 1201, and 1129 cm^{-1}; deuterium-decoupled ^1H NMR ($CDCl_3$) δ (ppm) 1.92 (d, 1, *J* 5.5 Hz), 1.61 (d, 1, *J* 5.5 Hz), 0.92 (s, 9). The IR spectra of *erythro*-III and *threo*-III differ mainly in the 1100—1270 cm^{-1} region.

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