Tetrahedron Letters,Vol.24,No.7,pp 731-734,1983 0040-4039/83/070731-04$03.00/0
Printed in Great Britain

ORGANIC SYNTHESIS USING HALOBORATION REACTION. I. A SIMPLE AND SELECTIVE SYNTHESIS OF 2-BROMO- AND 2-IODO-1-ALKENES

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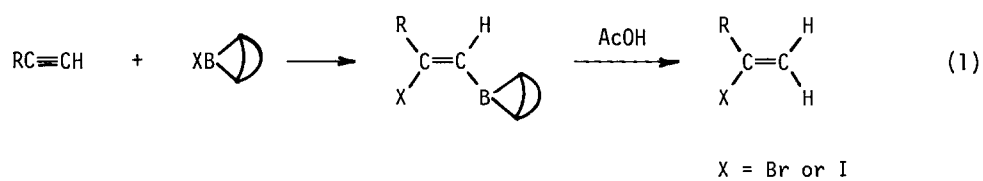
Summary: B-bromo- or B-iodo-9-borabicyclo[3.3.1]nonane reacts readily with 1-alkynes. Such haloboration reactions proceed through the Markovnikov addition of the X-B moiety to C≡C bonds and cis fashion. The bromoboration reaction occurs chemoselectively at terminal C≡C bonds but not at internal C≡C, terminal and internal C=C bonds. The protonolysis of haloboration products with acetic acid gives corresponding 2-bromo- or 2-iodo-1-alkenes in excellent yields.

The recent development of di- or trisubstituted alkene synthesis by cross-coupling reactions between organometallics and alkenyl halides catalyzed by transition metal compounds has increased the importance of starting stereodefined alkenyl halides.[1] The synthesis of 1-halo-1-alkenes has been efficiently achieved by the hydrometallation and carbometallation of 1-alkynes followed by metal-halogen exchange reactions,[2] but these methods are not applicable to the synthesis of 2-halo isomers.[3] Although the halometallation reaction would be a powerful tool for the preparation of 2-halo-1-alkenes, the reaction has not adequately developed for such purposes.[4] We wish to report here that B-bromo-9-borabicyclo[3.3.1]nonane (B-Br-9-BBN) and B-iodo-9-borabicyclo[3.3.1]-nonane (B-I-9-BBN)[5] react with 1-alkynes stereo-, regio- and chemoselectively, and after the protonolysis, 2-halo-1-alkenes are obtained in excellent yields (eq. 1).

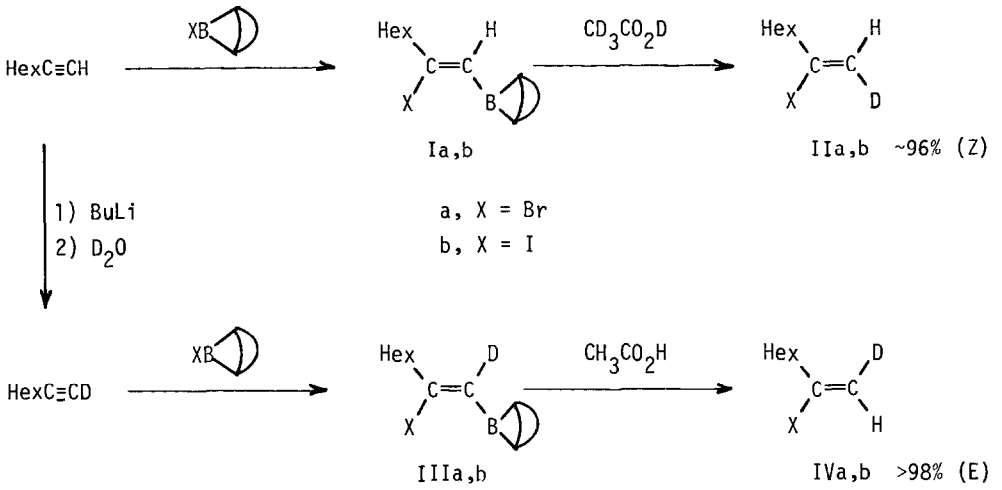


(1)

X = Br or I

The haloboration reaction of 1-alkynes with B-halo-9-BBN is very facile and complete within a few hours. In order to establish the stereochemistry of haloboration reaction, the following experiments were carried out. 1-Octyne was bromoborated with B-Br-9-BBN followed by protonolysis with CD_3CO_2D to give the product, the ^1H NMR spectrum of which showed that the isomeric purity of 1-deuterio-2-bromo-1-octene (IIa) is at least 96% (Z). In the case of iodoboration of 1-octyne, the same result was obtained. On the other hand, the bromoboration of 1-deuterio-1-octyne with

B-bromo-9-BBN followed by treatment with usual acetic acid was found to produce [E]-1-deuterio-2-bromo-1-octene in stereochemical purity more than 98%. Such stereochemical configurations were determined by ^1H NMR spectroscopy.[6] The stereochemistry of the iodoboration reaction is also shown to be >98% by the same method. These results are illustrated in the following scheme, and



definitely indicate that the haloboration involves a cis addition of the halogen-boron bond to the terminal triple bond.

To obtain information on the chemoselectivity of this reaction, the reaction of an equimolar mixture of 1-octyne and 2-octyne with B-Br-9-BBN followed by protonolysis with acetic acid was examined, which indicated that 1-octyne reacts completely to give 2-bromo-1-octene, whereas 2-octyne remains unchanged, as shown in eq. 2. 1-Octene also does not react with B-Br-9-BBN under such reaction conditions (eq. 3). Consequently, it is concluded that the bromoboration using B-Br-9-BBN occurs at terminal triple bonds, and double bonds and internal triple bonds appear capable of tolerating the bromoboration reaction. On the other hand, B-I-9-BBN is a little more reactive than B-Br-9-BBN and less chemoselective for such multiple bonds.

$$\text{HexC}{\equiv}\text{CH} + \text{PenC}{\equiv}\text{CMe} \xrightarrow{\text{B-Br-9-BBN}} \underset{99\%}{\text{HexCBr}{=}\text{CH}_2} + \underset{97\%}{\text{PenC}{\equiv}\text{CMe}} \qquad (2)$$

$$\text{HexC}{\equiv}\text{CH} + \text{HexCH}{=}\text{CH}_2 \xrightarrow{\text{B-Br-9-BBN}} \underset{99\%}{\text{HexCBr}{=}\text{CH}_2} + \underset{96\%}{\text{HexCH}{=}\text{CH}_2} \qquad (3)$$

The following procedure for the preparation of 2-bromo-1-decene is representative. A dry 50-ml flask equipped with a magnetic stirring bar and a septum inlet was flushed with nitrogen. The flask was charged under nitrogen with B-Br-9-BBN (0.36 g, 1.8 mmol) and 10 ml of dichloromethane, and then cooled to 0 °C. To the well-stirred solution, 1-decyne (0.269 ml, 1.5 mmol) was added dropwise and the reaction mixture was stirred for 3 h at 0 °C. Acetic acid (1 ml) was added for protonation and the mixture was stirred for an additional 1 h at 0 °C, followed by the addition of 12 ml of 3M NaOH and 2 ml of 30% hydrogen peroxide. After stirring for 30 min at room temperature, the product was extracted with hexane three times and the combined organic layers were washed with water, aqueous $NaHCO_3$ and water again, and finally dried over $MgSO_4$. The residue concentrated under vacuum was purified by column chromatography (silica gel, hexane) to give 290 mg of 2-bromo-1-decene (88% yield).

The representative results are summarized in Table 1. As expected from the chemoselectivity experiment, 1-ethynylcyclohexene gives only 1-(1-bromoethenyl)cyclohexene as the product in its reaction (entry 11). The haloboration of terminal alkynes containing functional groups such as carbomethoxy (entry 14), propargylic bromo (entries 15 and 16) and acetoxy (entry 17) proceeds without difficulty to give the corresponding products, respectively.

As was pointed out earlier, the synthetic application of haloboration reaction is of very recent origin. Nevertheless, it seems to have a number of highly interesting possibilities of considerable value for synthetic chemistry. We are actively exploring the full potentialities of this new chemistry.

REFERENCES AND NOTES

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(2) For carbometallations, see ref. 1d and the references cited therein. For hydrometallation methods, see: H. C. Brown, T. Hamaoka and N. Ravindran, J. Am. Chem. Soc., 95, 5786, 6456 (1973); G. Zweifel and C. C. Whitney, ibid., 89, 2753 (1967); J. Schwartz, ibid., 97, 679 (1975).

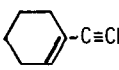
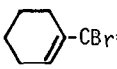
(3) Of course, 2-bromo-1-alkenes are prepared by the reaction of 1-alkynes or their derivatives with HBr. For example, see: a) J. Coussean, Synthesis, 805 (1980); b) R. K. Boeckman, Jr., and D. M. Blum, J. Org. Chem., 39, 3307 (1974). However, these methods cannot be expected more useful applications than halometallation reactions for organic synthesis. Such applications will be discussed in the following papers of this series.

(4) E. Negishi, "Organometallics in Organic Synthesis," Vol. 1, J. Wiley & Sons, New York, 1980.

(5) H. C. Brown and S. U. Kulkarni, J. Organomet. Chem., 168, 281 (1979).

(6) In the ^1H NMR spectrum of the adduct (Ia), there appeared only one kind of vinylic protons at 6.60 ppm attributed to the trans-H to bromine atom, see J. R. Blackborow, J. Organomet. Chem., 128, 161 (1977). ^1H NMR spectra of IIa and IVa were also checked, which showed adequate data in accordance with the assigned structures.

Table 1. The Synthesis of 2-Bromo- and 2-Iodo-1-alkenes

Entry	Alkyne	Method[a]	Product	Yield[b] (%)	Regioselectivity (%)
1	1-Hexyne	A	2-Bromo-1-hexene	99	99
2	"	B	2-Iodo-1-hexene	100	99
3	1-Octyne	A	2-Bromo-1-octene	95	99
4	"	B	2-Iodo-1-octene	100	99
5	1-Decyne	A	2-Bromo-1-decene	(88)	99
6	"	B	2-Iodo-1-decene	100 (83)	99
7	Phenylethyne	A	α-Bromostyrene	95	99
8	"	B	α-Iodostyrene	(85)	99
9	1,6-Heptadiyne	C	2,6-Dibromo-1,6-heptadiene	(82)	98
10	"	D	2,6-Diiodo-1,6-heptadiene	(80)	98
11	 -C≡CH	A	 -CBr=CH_2	81 (65)[c]	98
12	Cyclohexylethyne	A	2-Bromo-2-cyclohexylethene	93 (80)	99
13	"	B	2-Iodo-2-cyclohexylethene	94	99
14	HC≡C$(CH_2)_8$COOMe	E	H_2C=CBr$(CH_2)_8$COOMe	(88)	99
15	Propargyl bromide	F	2,3-Dibromo-1-propene	90	98
16	"	B	3-Bromo-2-iodo-1-propene	88	98
17	HC≡C$(CH_2)_3$OAc	E	H_2C=CBr$(CH_2)_3$OAc	(82)	99

[a]Method A; the amount of B-Br-9-BBN, 1.2 equiv and the reaction was carried out at 0 °C for 3 h in CH_2Cl_2. Method B; B-I-9-BBN, 1.0 equiv and -20 °C for 1 h in pentane. Method C; B-Br-9-BBN, 2.4 equiv and at 0 °C for 3 h in CH_2Cl_2. Method D; B-I-9-BBN, 2.1 equiv and at -20 °C for 1 h in pentane. Method E; B-Br-9-BBN, 2.2 equiv and at 0 °C for 3 h in CH_2Cl_2. Method F; B-Br-9-BBN, 1.5 equiv and at room temperature for 1 h in CH_2Cl_2.

[b]Glc yields based on the alkyne used. The numbers in parentheses are isolated yields.

[c]The product was unstable and gradually decomposed.

(Received in Japan 4 November 1982)