References and Notes

(1) B. C. Challis and J. A. Challis, in "The Chemistry of Amides", J. Zabicky, Ed., Interscience Publishers, New York, N.Y., 1970, Chapter 13, p 816 ff.
(2) S. R. Sandler and W. Karo, "Organic Functional Group Preparations", Academic Press, New York, N.Y., 1972, Chapter 9, p 230.
(3) C. Berger and S. C. J. Olivier, *Recl. Trav. Chim. Pays-Bas*, **46**, 600 (1927).
(4) N. O. Sieber, *Z. Physiol. Chem.*, **81**, 185 (1913); *Chem. Abstr.*, **7**, 1028.
(5) J. O. Edwards and R. G. Pearson, *J. Am. Chem. Soc.*, **84**, 16 (1962).
(6) E. Oliveri-Mandala, *Gazz. Chim. Ital.*, **52** (I), 107 (1922); *Chem. Abstr.*, **16**, 2112.
(7) H. Ito, *Chem. Pharm. Bull. Jpn.*, **12** (3), 326–329 (1964).
(8) B. C. Challis and J. A. Challis, ref 1, p 790.
(9) S. A. Hall and P. E. Spoerri, *J. Am. Chem. Soc.*, **62**, 664 (1940).

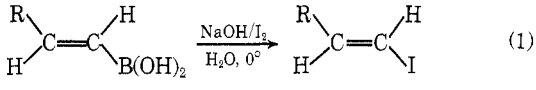
The Procter & Gamble Company **H. L. Vaughn**
Miami Valley Laboratories **M. D. Robbins***
Cincinnati, Ohio 45247

Received January 14, 1975

Reaction of Alkenylboronic Acids with Bromine in the Presence of Sodium Methoxide and Methanol. A Simple One-Stage Synthesis of α-Bromo Acetals

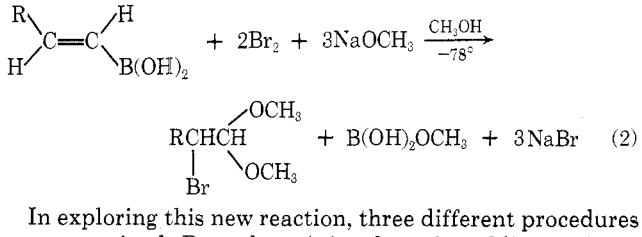
Summary: Alkenylboronic acids add bromine rapidly at −78° in the presence of sodium methoxide in methanol to give the corresponding α-bromo dimethyl acetals in good yield.

Sir: Alkenylboronic acids are readily available via the hydrolysis of the catechol esters produced by the hydroboration of alkynes with catecholborane.[1] We recently reported that such *trans*-1-alkenylboronic acids are converted by iodine under the influence of base into the corresponding *trans*-1-alkenyl iodides of >99% stereochemical purity in almost quantitative yield[2] (eq 1).



(1)

We undertook to prepare the corresponding bromides by an analogous procedure using bromine. However, the results proved unsatisfactory. For example, the addition of bromine to a solution of *trans*-1-octenylboronic acid in aqueous sodium hydroxide at 0° gave a 65:35 mixture of *cis*- and *trans*-1-octenyl bromide in a yield of ~50%, along with 25% *n*-octylaldehyde. A possible route to the aldehyde is oxidation of the vinylboronic acid by sodium hypobromite.[3] Consequently, we examined the use of sodium methoxide in methanol at −78° as a means of avoiding this side reaction.[2] Unexpectedly, the reaction produced 38% new product, the α-bromo dimethyl acetal, together with 8% *cis*-1-octenyl bromide and 10% *trans*-1-octenyl bromide. It seems clear that the formation of the α-bromo dimethyl acetal will require at least 3 equiv of sodium methoxide and 2 equiv of bromine (eq 2).



(2)

In exploring this new reaction, three different procedures were examined. Procedure A involves the addition of two equivalents of bromine in dichloromethane to a solution of *trans*-1-octenylboronic acid and 3 equiv of sodium methoxide in methanol at −78°. Procedure B involves the addition of *trans*-1-octenylboronic acid to a solution of 2 equiv of bromine and 3 equiv of sodium methoxide in methanol at −78°. Procedure C involves the addition of a cold solution of *trans*-1-octenylboronic acid and a 1 *M* equiv of sodium methoxide in methanol to a solution of 2 equiv of bromine and 2 equiv of sodium methoxide in methanol at −78°. The results are summarized in Table I.

Table I
Reaction of *trans*-1-Octenylboronic Acid with Bromine in the Presence of Sodium Methoxide at −78°

Procedure	α-Bromo acetal, %	*cis*-1-Octenyl bromide, %	*trans*-1-Octenyl bromide, %
A	80	2	16
B	63	19	16
C	92	0	4

Bromination of a series of *trans*-1-alkenylboronic acids was carried out by procedure C to produce the corresponding α-bromo dimethyl acetals. The results are summarized in Table II.

Table II
Preparation of α-Bromo Acetals by the Bromination of *trans*-1-Alkenylboronic Acids in the Presence of Sodium Methoxide at −78°

Alkyne	Alkenylboronic acid, %[a]	α-Bromo dimethyl acetal, %[b]
1-Hexyne	90	92,[c] 82[d]
1-Octyne	90	92,[c] 82[d] (72,[c] 55[d])
3-Chloro-1-pentyne	92	90,[c] 82[d]
Cyclohexylethyne	93	88,[c] 81[d]
3,3-Dimethylbutyne	94	52,[c] 49[d]

[a] See ref 1. Isolated yields. [b] The yields are by GLPC analysis. The values in parenthesis are isolated yields. [c] Based on alkenylboronic acid. [d] Based on alkyne.

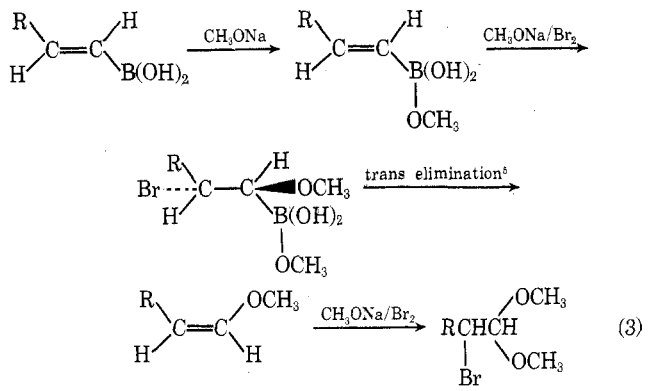
One exception to the generality of this procedure was observed. *trans*-2-Phenyl-1-ethyleneboronic acid was converted by procedure C to give a product which was not the 2-bromo acetal. This product is under investigation.

The following experimental procedure (procedure C) was used. In a 250-ml flask were placed 100 mmol of *trans*-1-octenylboronic acid[1] and 100 ml of absolute methanol; 100 mmol of a solution of sodium methoxide in methanol (33.4 ml of 3.0 *M*) was added at 0°. The solution was maintained at 0°. In another 500-ml flask were placed 200 ml of absolute methanol and 200 mmol of sodium methoxide solution in methanol (66.8 ml, 3.0 *M*). The mixture was cooled to −78°, 200 mmol of bromine (10.4 ml) was added over 30 min, and the pale yellow colored solution was stirred for 15 min. To this solution was added through a double-ended needle under nitrogen pressure over 30 min the solution of *trans*-1-octenylboronic acid and sodium methoxide in methanol previously prepared. The reaction mixture was stirred for 30 min at −78° and then brought to room temperature. The product was extracted with 400 ml of *n*-pentane and 200 ml of water saturated with sodium chloride. The water layer was further extracted with *n*-pentane (200 ml × 2). The combined pentane extract was washed with 100 ml of water and dried over anhydrous magnesium sulfate. Following removal of the solvent, pure α-bromooctylaldehyde dimethyl acetal, bp 68° (0.15 mm), was obtained in 72% yield. The identification of the compound was carried out by a comparison of its ir, ^{1}H NMR, and mass spectra with those of an authentic sample.[4]

An attempt to use the catechol ester directly resulted in a very poor yield of the product (16%).

Although we have not yet attempted to make a specific study of the mechanism of this synthesis of α-bromo acetals, it is evident that the reaction possesses highly interesting characteristics. For example, if the sodium methoxide is omitted, only traces of the α-bromo dimethyl acetal are produced.

It seems probable that the reaction proceeds via (a) the trans addition of the elements of methyl hypobromite, (b) the formation of the alkenyl methyl ether by trans elimination of boron and bromine, and (c) addition of the elements of methyl hypobromite to the methyl ether (eq 3).



(3)

The synthesis of α-bromo acetals has been achieved by a variety of procedures. These may be summarized briefly as follows: (a) direct bromination of the aldehyde, followed by the treatment with alcohol;[6] (b) addition of bromine to the enol acetate in alcohol;[7] (c) 1,4 addition of organoboranes to 2-bromoacrolein, followed by conversion of the product to the acetal;[8] (d) halogenation of the aldehyde with cupric halides in alcohol.[4,9]

The reaction of terminal alkenylboronic acids with bromine in the presence of sodium methoxide in methanol provides a new simple route to the α-bromo dimethyl acetals from the corresponding acetylenes.

References and Notes

(1) H. C. Brown and S. K. Gupta, *J. Am. Chem. Soc.*, **94,** 4370 (1972).
(2) H. C. Brown, T. Hamaoka, and N. Ravindran, *J. Am. Chem. Soc.*, **95,** 5786 (1973).
(3) (a) H. C. Brown and C. F. Lane, *J. Am. Chem. Soc.*, **92,** 6660 (1970); (b) H. G. Kuivila, L. E. Benjamin, C. J. Murphy, A. D. Price, and J. H. Dolevy, *J. Org. Chem.*, **27,** 825 (1962).
(4) C. E. Castro, E. J. Gaughan, and D. C. Owsley, *J. Org. Chem.*, **30,** 587 (1965).
(5) (a) D. S. Matteson and J. D. Liedtke, *J. Am. Chem. Soc.*, **87,** 1526 (1965); (b) H. C. Brown, D. H. Bowman, S. Misumi, and M. K. Unni, *ibid.*, **89,** 4531 (1967); (c) D. J. Pasto and Sr. R. Snyder, O.S.F., *J. Org. Chem.*, **31,** 2773 (1966); (d) H. C. Brown, T. Hamaoka, and N. Ravindran, *J. Am. Chem. Soc.*, **95,** 6456 (1973).
(6) (a) R. Kuhn and C. Grundmann, *Ber.*, **70,** 1894 (1937); (b) R. G. Jones, E. C. Kornfeld, K. C. McLaughlin, and R. C. Anderson, *J. Am. Chem. Soc.*, **71,** 4000 (1949); (c) P. Duhamel, L. Duhamel, and J. Y. Valnot, *Bull. Soc. Chim. Fr.*, 1465 (1973).
(7) S. M. McElvain and D. Kundiger, *Org. Syn.*, **23,** 8 (1943), or "Organic Syntheses", Coll. Vol. III, Wiley, New York, N.Y., 1960, p 123; (b) E. M. Filachione, *J. Am. Chem. Soc.*, **61,** 1705 (1939); (e) P. Z. Bedoukian, *ibid.*, **66,** 1325 (1944).
(8) H. C. Brown, G. W. Kabalka, M. W. Rathke, and M. M. Rogic, *J. Am. Chem. Soc.*, **90,** 4165 (1968).
(9) C. E. Castro, *J. Org. Chem.*, **26,** 4183 (1961).
(10) Visiting Scholar on funds provided by the Fuji Photo Film Co., Ltd., Tokyo, Japan.

Richard B. Wetherill Laboratory **Tsutomu Hamaoka**[10]
Purdue University **Herbert C. Brown***
West Lafayette, Indiana 47907

Received February 11, 1975