temperature over Pd–carbon. Methylcyclopentane and cyclohexane were produced and identified by the coincidence of their g.l.c. emergence times and mass spectrometric fragmentation patterns with those of authentic materials. *n*-Hexane, which would have resulted from the hydrogenation of any *n*-hexadiene present, could not be detected by g.l.c. techniques.

The remaining unhydrogenated product from the decomposition of IV was distilled and the fraction boiling 20–100° collected. The two product hydrocarbons were isolated in a pure form by preparative g.l.c. techniques. The detailed identity of their infrared, n.m.r., and mass spectra with those of authentic compounds (API samples) proved conclusively that the two monomeric products formed were 3-methylcyclopentene and cyclohexene.

Decomposition of IV in α,α,α-Trichlorotoluene. Eighty-five mmoles (assuming the peroxyester to be of 100% purity) of *t*-butyl Δ^2-cyclopentenylperoxyacetate was decomposed in 170 ml. of α,α,α-trichlorotoluene according to the procedure described above. Thirty-four mmoles or 40.3% of theory of CO_2 was evolved. G.l.c. analysis on a 5-ft. DC-710 column at 100° indicated the presence of two compounds believed to be Δ^2-cyclopentenylmethyl chloride and 4-chlorocyclohexene. From the amounts formed, 10 mmoles (29.4% yield based on CO_2) and 8.8 mmoles (25.9% yield), respectively, it appears that 46.8% of the 3-methylcyclopentenyl radicals rearranged to 4-cyclohexenyl radicals. G.l.c. analyses indicated that 3-methylcyclopentene and cyclohexene were not present.

The two chlorides were isolated in a pure state by preparative g.l.c. One of the compounds, proposed to be Δ^2-cyclopentenylmethyl chloride, has a shorter g.l.c. emergence time (DC-710 column) than either 1-, 3-, or 4-chlorocyclohexene. The mass spectrometric fragmentation pattern of this C_6H_9Cl compound supports the above structure proposal. For example, the fragmentation ion peak at *m/e* 67^+, which is characteristic of the cyclopentenyl structure, is very intense and accounts for ~41% of the total ion current. The 60-Mc./sec. n.m.r. spectrum of this compound showed absorptions centered at δ = ~5.6 p.p.m. from tetramethylsilane for two vinylic hydrogens, ~3.5 for two hydrogens vicinal to the chlorine, and at 3.0 p.p.m. for one hydrogen which is probably allylic and tertiary. Absorption for the remaining four hydrogens extended from δ = 2.6 to ~1.2 p.p.m. which might be expected for two kinds of protons such as the two allylic and two secondary protons of Δ^2-cyclopentenylmethyl chloride. We conclude that the latter is the correct structure for one of the products from the decomposition of IV in α,α,α-trichlorotoluene.

The second product from the decomposition of IV was shown to be the anticipated product of rearrangement, 4-chlorocyclohexene. The infrared, n.m.r., and mass spectra of this compound were all identical in detail with those of 4-chlorocyclohexene which was obtained by the decomposition of III in α,α,α-trichlorotoluene (*vide supra*).

Although 3-chlorocyclohexene has a g.l.c. emergence time (5-ft. DC-710 column) which is greater than that of 4-chlorocyclohexene, it was difficult to exclude it as an additional product from the decomposition of IV by this analysis alone. That is, 3-chlorocyclohexene was shown to undergo some decomposition under the above reaction conditions. However, when a small amount of 3-chlorocyclohexene was heated at 140° in α,α,α-trichlorotoluene in a control experiment, cyclohexadienes were found in the product in ~70% yields. Cyclohexadienes were not produced during the decomposition of IV in α,α,α-trichlorotoluene, which indicates that 3-chlorocyclohexene was not a significant product.

Acknowledgment. The author is grateful to J. W. Forbes and J. L. Jungnickel for several n.m.r. analyses, to C. A. Reilly for n.m.r. spin-decoupling experiments on 4-chlorocyclohexene, and to R. E. Thorpe and P. A. Wadsworth, Jr., for mass spectrometric analyses. Appreciation also is extended to F. D. Mango, J. H. Raley, and R. D. Mullineaux for helpful comments.

Mechanisms of Deboronobromination

Donald S. Matteson and James D. Liedtke[1]

Contribution from the Department of Chemistry, Washington State University, Pullman, Washington. *Received October 13, 1964*

Deboronobromination is a stereospecific trans elimination, dibutyl erythro-2,3-dibromobutane-2-boronate yielding cis-2-bromo-2-butene on treatment with water or base. Rates of ethylene evolution from dibutyl 2-bromoethaneboronate in aqueous ethanol are pseudo-first-order. The Grunwald–Winstein equation is followed in 70–90% ethanol with a slope of 0.40, but the observed rate in 100% ethanol is much slower than predicted. The rate is much slower in aqueous formic acid than in ethanol of similar ionizing power. Second-order kinetics were obtained with several substituted anilines in 100% ethanol, and a plot of log k vs. pK_b for $ArNH_2$ was linear. Dimethylaniline reacted much too slowly to fit the Brønsted correlation and its reaction was not appreciably slowed in O-deuterioethanol, K_H/K_D = 1.06 ± 0.03. We conclude that the general mechanism of deboronobromination is $BrCH_2CH_2B(OR)_2 + X: \rightarrow BrCH_2CH_2B^-X^+(OR)_2 \rightarrow Br^- + C_2H_4 + (RO)_2BX^+$, where X: is a Lewis base such as water or an amine.

(1) (a) Abstracted in part from the Ph.D. Thesis of J. D. L. (b) We thank the National Science Foundation for financial support, Grants G-19906 and GP-2953.

Introduction

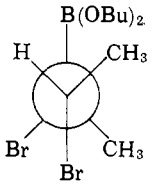
Much of the utility (as well as frustrating instability) of organoboron compounds depends upon the ability of boron to function as a leaving electrophile. We expected that a mechanistic study of deboronobromination would provide information about the nature of boron-containing leaving groups.

A qualitative description of the deboronobromination of dibutyl 2-bromoethaneboronate by mild bases such as water has been reported.[2] Use of an acetylide

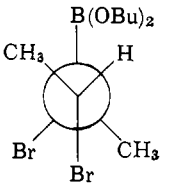
$$(BuO)_2BCH_2CH_2Br + 3H_2O \longrightarrow C_2H_4 + Br^- + H^+ + B(OH)_3 + 2BuOH$$

as the base permits synthesis of relatively unstable acetylenic boronic esters.[3] Other related deborohalogenations have been reported.[4,5]

In order to verify the stereochemistry of deboronobromination, dibutyl *erythro*- (**1**) and *threo*-2,3-dibromobutane-2-boronate (**2**) were selected. It was



1



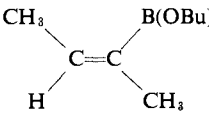
2

expected that the ordinarily stereospecifically *trans* addition of bromine[6] to the corresponding unsaturated boronic esters would provide these compounds, which would undergo deboronobromination in the same fashion as dibutyl 1,2-dibromoethaneboronate.[4]

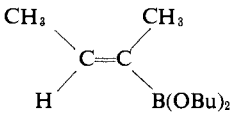
For kinetic studies, the deboronobromination of dibutyl 2-bromoethaneboronate in aqueous ethanol was chosen because it could be followed easily by ethylene evolution.

Results

Stereochemistry. The reaction of either 92% *trans*- or a 50–50 mixture of *cis*- and *trans*-2-bromo-2-butene with magnesium in tetrahydrofuran followed by reaction with methyl borate, acidification, and esterification with butanol led to an almost pure single isomer (97% on the basis of infrared examination) of dibutyl 2-butene-2-boronate. The carbon skeleton was proved by hydrogen peroxide deboronation to methyl ethyl ketone. The *trans* structure **3** was assigned to this isomer on the basis of the following evidence. Carbonation of the Grignard reagent from *trans*-2-bromo-2-butene has been reported to yield angelic acid.[7] Carbonation of our Grignard reagent yielded a mixture judged to be 80% angelic and 20% tiglic acid by n.m.r. This leaves some discrepancy between the behavior of carbon dioxide and methyl borate toward the Grignard reagent. However, n.m.r. observations further confirm the structure assignments. The position of the vinyl proton absorption is at τ 3.82 for angelic acid, 3.03 for tiglic acid,[8] 4.36 for dibutyl *trans*-2-butene-2-boronate (**3**), and 3.73 for the *cis* isomer (**4**), described in the following paragraph.



3



4

Retention of configuration has been reported for the preparation and carbonation of *cis*-2-butenyl-2-lithium in ether at −40°.[9] We failed to prepare the lithium reagent at a temperature low enough to avoid partial isomerization, but preparation of the lithium reagent from 90% *cis*-2-bromo-2-butene at −30° followed by treatment with methyl borate and the usual work-up yielded a small amount of 39% dibutyl *cis*-2-butene-2-boronate (**4**), based on n.m.r. analysis.

The *trans* boronic ester **3** was freed from traces of the *cis* by distillation, then treated with bromine in methylene chloride at −75° to yield dibutyl *erythro*-2,3-dibromobutane-2-boronate (**1**). Mixtures of the *threo* and *erythro* isomers **2** and **1** were also prepared from mixtures of **4** and **3**. For stereochemical studies of the elimination, the bromination products were treated *in situ* with water, 0.1 *N* sodium hydroxide, or pyridine, and the resulting 2-bromo-2-butenes were analyzed by gas chromatography. Dibutyl *trans*-2-butene-2-boronate, free from a detectable amount (1–2%) of *cis*, led to 95.0–96.9% *cis*-2-bromo-2-butene on treatment with each of the reagents at 0 and at 30°, with deviations random. Similarly, 38.6% dibutyl *cis*-2-butene-2-boronate led to 37.5–40.4% *trans*-2-bromo-2-butene at 0°. A sample of diethyl *erythro*-2,3-dibromobutane-2-boronate (**1**, ethyl ester) was isolated and reacted with water to yield 98% *cis*-2-bromo-2-butene.

Kinetics. The deboronobromination of dibutyl 2-bromoethaneboronate in aqueous ethanol was followed by the amount of ethylene evolved, pressure change at essentially constant volume being measured. First-order rate constants were reproducible to ±3%. A typical plot is shown in Figure 1.

In 80% ethanol, $\Delta H^* = 12 \pm 1$ kcal./mole and $\Delta S^* = -28$ cal./mole deg. from k values at 0, 16, and 25°; in 70% ethanol, $\Delta H^* = 11$ and $\Delta S^* = -31$.

The effects of changing the medium were investigated. In 80% ethanol at 25°, 0.38 *M* lithium chloride increased k_1 25%, lithium bromide 15%, and sodium iodide 13%. The solvent dependence of the rate followed the Grunwald–Winstein equation[10] over a limited range.

$$\log k = mY + \log k_0$$

Figure 2 shows the plot for 70–90% ethanol at 25°, for which the slope m is 0.40. In 40–70% ethanol at 0°, m is 0.43 and the rate in 80% ethanol is somewhat slower than predicted. The correlation breaks down completely in absolute ethanol. The calculated k at 25° would be 0.67×10^{-3} sec.$^{-1}$ but the observed k was

(2) D. S. Matteson and J. D. Liedtke, *J. Org. Chem.*, **28**, 1924 (1963).
(3) D. S. Matteson and K. Peacock, *J. Organometal. Chem.*, **2**, 190 (1964).
(4) B. M. Mikhailov and P. M. Aronovich, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 927 (1961).
(5) M. F. Hawthorne, *J. Am. Chem. Soc.*, **82**, 1886 (1960).
(6) (a) A. McKenzie, *J. Chem. Soc.*, 101, 1196 (1912); (b) S. J. Cristol, F. R. Stermitz, and P. S. Ramey, *J. Am. Chem. Soc.*, **78**, 4939 (1956); (c) M. J. S. Dewar and R. C. Fahey, *ibid.*, **85**, 2248 (1963), discuss theoretical reasons for *trans* addition of bromine under conditions where chlorine or hydrogen halides may add *cis*.
(7) H. Normant and P. Maitte, *Bull. soc. chim. France*, 1439 (1956).
(8) R. R. Fraser, *Can. J. Chem.*, **38**, 549 (1960).
(9) A. S. Dreiding and R. J. Pratt, *J. Am. Chem. Soc.*, **76**, 1902 (1954).
(10) E. Grunwald and S. Winstein, *ibid.*, 70, 846 (1948).

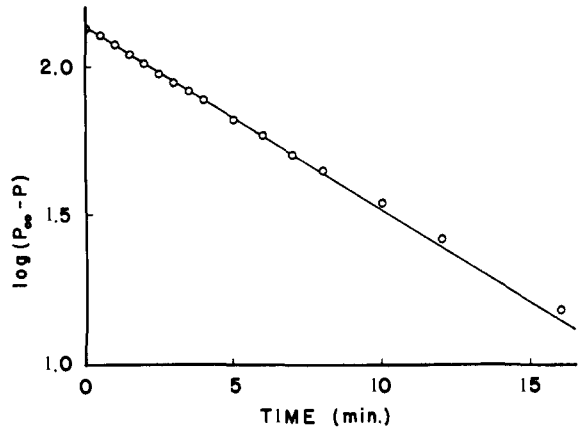


Figure 1. Plot of log $(P_\infty - P)$ *vs.* time for the solvolysis of 0.05 *M* dibutyl 2-bromoethaneboronate in 90% ethanol at 25°.

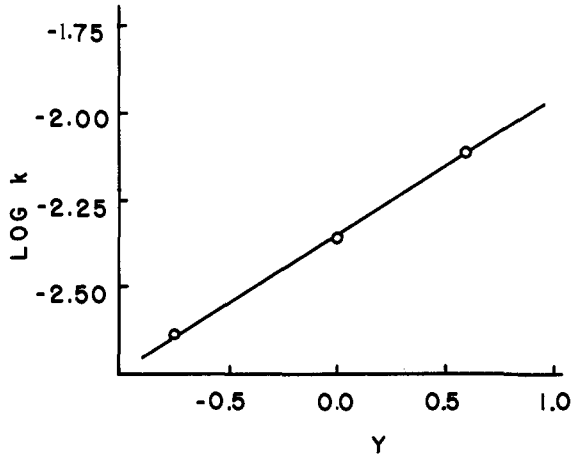


Figure 2. Plot of log *k* *vs.* *Y* for deboronobromination in aqueous ethanol at 25°.

about 0.008×10^{-3}, too slow for accurate measurement with the equipment used.

The rate constants were highly sensitive to the basicity of the medium. The rate in the presence of sodium acetate was too rapid to measure. In 80% formic acid, $Y = 2.138$,[11] the rate was only 0.046 times that in 40% ethanol, $Y = 2.196$, or 0.56 that in 80% ethanol, and $Y = 0$, at 0°. Added hydrobromic acid (replacing some of the water in the solvent mixture) decreased the observed rate constants moderately, as shown in Table I.

Table I. Rates of Deboronobromination in 80% Ethanol at 25°

Initial molarity of HBr	$10^3 k_1$, sec.$^{-1}$
0.00	4.22[a]
0.05	3.64[a]
0.20	3.17[a]
0.37	2.93
0.68	2.18
1.36	1.28

[a] Average from two different observers, two or three runs, average deviation 3%.

(11) A. H. Fainberg and S. Winstein, *J. Am. Chem. Soc.*, 78, 2770 (1956).

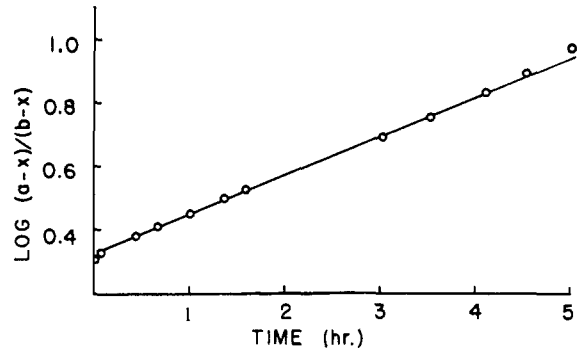


Figure 3. Plot of log $(a - x)/(b - x)$ *vs.* time for the reaction of dibutyl 2-bromoethaneboronate (*b*) with *o*-chloroaniline (*a*) in ethanol at 25°.

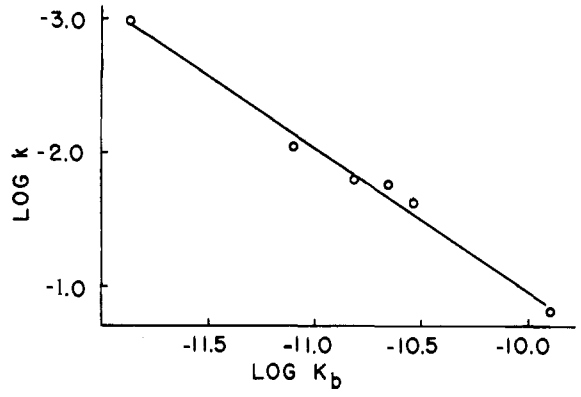


Figure 4. Plot of log k_2 (in 100% ethanol) *vs.* log K_b (in 30% ethanol)[12] for the reaction of dibutyl 2-bromoethaneboronate with *o*-chloro-, *m*-bromo-, *p*-iodo-, *p*-bromo-, *p*-chloroaniline, and aniline, respectively.

The rate was decreased moderately in deuterated solvent. In 80% ethanol–20% deuterium oxide (~62% O–D) at 25°, k_1 was 2.26×10^{-3} (1.9 times slower). In 79% ethanol, k_H/k_D was 1.7 for fully O-deuterated solvent.

Cations which complex bromide ion greatly accelerated deboronobromination. In 80% ethanol at 25° the half-life was estimated to be 15–30 sec. with 0.38 *M* silver nitrate and 1–2 min. with 0.13 *M* mercuric chloride.

Second-order kinetics were observed with aromatic amines in absolute ethanol at 25°, as shown for *o*-chloroaniline in Figure 3. A plot of log k_2 *vs.* log K_b[12] was linear with a slope near 1 for six amines of the series $ArNH_2$, as shown in Figure 4.

Dimethylaniline, $pK_a = 4.76$,[13] yielded a k_2 of only 0.0139, which is about 40 times too slow to fit the Brønsted correlation with $ArNH_2$. In O-deuterioethanol, k_2 was 0.131, or $k_H/k_D = 1.06 \pm 0.03$ (duplicate runs).

Amine salts appeared to retard the rate moderately. An equimolar quantity of added aniline hydrochloride decreased the apparent k_2 for aniline by 20% (not far outside the experimental error for this inconveniently rapid reaction). Dimethylaniline, the most accurately

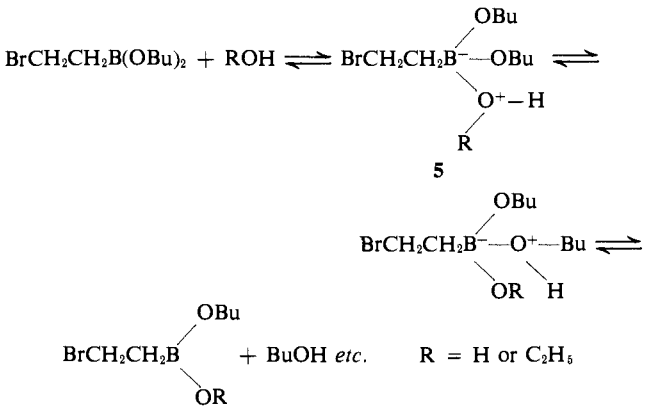
(12) G. M. Bennett, G. I. Brooks, and S. Glasstone, *J. Chem. Soc.*, 1821 (1935), reported pK_b values (we presume $14 - pK_a$) in 30% ethanol at 25°.

(13) In 30% ethanol at 20°; W. C. Davies and H. W. Addis, *ibid.*, 1622 (1937).

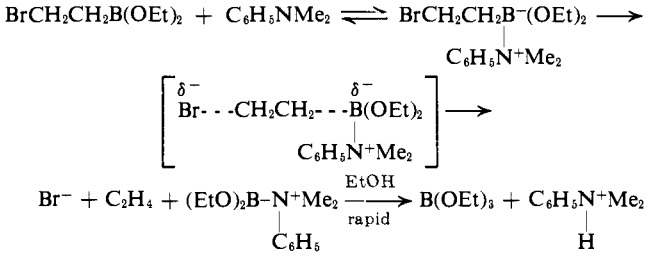
measured of the series, showed curvature in the log $(a - x)/(b - x)$ plots amounting to about 20% reduction in apparent k_2 after 70% reaction.

Discussion

The evidence points to the following mechanism for solvolytic deboronobromination. First, there is a rapid exchange of ligands between boron and the solvent.



Second, the zwitterion intermediates of the type **5** decompose relatively slowly to bromide ion, ethylene, and protonated boric acid or ester. The mechanism of the reaction with amines in ethanol is probably analogous, though our data do not rule out the possibility that the first step instead of the second is rate determining or that the two may be concerted.



The observed stereospecific *trans* elimination shows that the elimination of boron and bromine is concerted, *i.e.*, free carbonium ions or carbanions are not intermediates, under all conditions examined. The 2–4% lack of stereospecificity may be attributed to impurity in the starting material or to the known instability of *cis*-2-bromo-2-butene.[9]

The small effect of acid on the rate of solvolytic deboronobromination indicates that reversible formation of the anion $BrCH_2CH_2B(OR)_3^-$ is not in the major reaction path. Such anions may be involved in the very rapid base-catalyzed deboronobrominations, but there is a strong possibility that the elimination follows immediately after or is concerted with formation of these anions.

Under solvolytic conditions the solvent clearly functions as a base. The low slope m of the Grunwald–Winstein plot (0.40) is similar to those for ethyl bromide (0.34) and methyl bromide (0.26).[14] In view of the equilibria involving ligands on boron, deviation from the Grunwald–Winstein equation such as that in absolute ethanol is not surprising; water and/or hydroxyl groups on boron would have less steric hindrance than ethanol and ethoxy groups. The rate in aqueous formic acid, which is $^1/_{22}$ as fast in aqueous ethanol of the same Y value, is further evidence of the importance of solvent basicity. The accelerating effect of inert salts, like the solvent effects, is consistent with development of some charge separation in the transition state.

Deboronobromination differs from desilicochlorination[15] in the same way that solvolysis of methyl bromide differs from that of *t*-butyl bromide with respect to solvent effects. Sommer has suggested a siliconium ion intermediate.[15]

$$(CH_3)_3SiCH_2CH_2Cl \longrightarrow (CH_3)_3Si^+ + C_2H_4 + Cl^-$$

Deboronobromination clearly does not lead to a boronium ion, $(RO)_2B^+$, but requires a tightly bound solvent molecule, leading to $B(OR)_3H^+$.

The general base catalysis by primary aromatic amines in ethanol suggested the possibility that the rate-determining step might be removal of a proton by the base from a zwitterion intermediate of the type **5**. This is clearly ruled out by the relatively low rate with dimethylaniline, presumably due to steric hindrance to attack at boron, and by the rate depression of only 6% in O-deuterioethanol. The solvolytic deboronobromination conditions seem *a priori* less likely to involve proton transfer. The complexity of the possible equilibria between ligands on boron does not permit unequivocal interpretation, but the isotope effects, 1.7–1.9, are of a magnitude attributable to the lower basicity of deuterated water.[16] These effects are much greater than those found in the solvolysis of methyl halides, k_H/k_D = 1.0–1.1,[17] but this is consistent with the postulated greater positive charge on the attacking solvent molecule in the deboronobromination.

We attribute the small decelerating effect of amine salts to lowering of the activity coefficient of the amine, which has been previously noted,[12] and the similar effect of hydrobromic acid under solvolysis conditions to lowered activity of the water by proton solvation. The first-order solvolysis plots show less curvature than might be expected from the acid generated, but a compensating error may be operating.

The mechanism of ligand exchange on boron in neutral or acid solution is also elucidated by the foregoing observations. Dibutyl 2-bromoethaneboronate can be transesterified without deboronobromination,[2] and ligand exchanges on boron are generally very rapid.[18] Proton loss from the zwitterion **5** to solvent is too slow to observe, and proton acceptance by **5** in dilute acid should be even slower. Therefore the proton transfer necessary for ligand exchange must be intramolecular.

The information about boron-containing leaving groups obtained in the present study is consistent with previous interpretations of electrophilic displacements of boron,[19] for which the kinetics tend to be complex and leave considerable ambiguity about the structure of the leaving electrophile.

(14) S. Winstein, E. Grunwald, and H. W. Jones, *J. Am. Chem. Soc.*, **73**, 1120 (1951).

(15) L. H. Sommer and G. A. Baughman, *ibid.*, **83**, 3346 (1961).

(16) K. B. Wiberg, *Chem. Rev.*, **55**, 713 (1955).

(17) C. G. Swain, R. Cardinaud, and A. D. Ketley, *J. Am. Chem. Soc.*, **77**, 934 (1955).

(18) H. Steinberg and D. L. Hunter, *Ind. Eng. Chem.*, **49**, 174 (1957).

(19) (a) D. S. Matteson and J. O. Waldbillig, *J. Am. Chem. Soc.*, **86**, 3778 (1964). (b) K. V. Nahabedian and H. G. Kuivila, *ibid.*, **83**, 2167 (1961).

Experimental

Dibutyl trans-2-Butene-2-boronate (**3**). An 88-g. sample of 92% *trans*-2-bromo-2-butene[20] was converted to the Grignard reagent in tetrahydrofuran. The usual reaction with methyl borate and subsequent work-up[21] led to a 56% yield of dibutyl 2-butene-2-boronate, b.p. 34–38° (0.1 mm.). From the height of the peak at 6.13 μ the *cis* isomer was estimated to be about 3%. Careful fractionation through a packed column yielded pure *trans* isomer, b.p. 27° (0.05 mm.), infrared C=C peak at 6.06 μ, n.m.r. vinyl proton quartet at τ 4.36.

Anal. Calcd. for $C_{12}H_{25}BO_2$: C, 67.94; H, 11.88; B, 5.10. Found[22]: C, 68.00; H, 12.01; B, 5.36.

Dibutyl erythro-2,3-Dibromobutane-2-boronate (**1**). To a stirred solution of 2.60 g. of dibutyl *trans*-2-butene-2-boronate in 20 ml. of methylene chloride at −75° under nitrogen was added dropwise 1.96 g. of bromine. Distillation yielded 3.93 g. (88%) of dibutyl *erythro*-2,3-dibromobutane-2-boronate, b.p. 95–98° (0.1 mm.).

Anal. Calcd. for $C_{12}H_{25}BBr_2O_2$: C, 38.77; H, 6.77; B, 2.90; Br, 42.97. Found: C, 38.89; H, 6.92; B, 2.81; Br, 43.06.

Dibutyl cis- and trans-2-Butene-2-boronate (**4** *and* **3**). A 78.6-g. sample of 92% *cis*-2-bromo-2-butene[17] was added dropwise under argon to 8.1 g. of lithium (surface prepared by scraping under mineral oil) in 600 ml. of anhydrous ether at −30°. The shiny lithium surface became dull after 1 hr., presumably indicating that the reaction had stopped. The mixture was cooled to −60° and 60 g. of methyl borate in 250 ml. of ether was added in 10 min. After stirring for 0.5 hr. the mixture was worked up in the usual manner used for Grignard syntheses.[21] Distillation yielded 17.3 g. (14%) of dibutyl 2-butene-2-boronates, b.p. 29–33° (0.1 mm.). The infrared spectrum showed a medium *trans* C=C band at 6.06 and a strong *cis* C=C band at 6.13 μ. The n.m.r. spectrum showed two quartets due to vinyl protons, 38.6% *cis* at τ 3.73 and 62.4% *trans* at 4.36.

Anal. Found: C, 67.72; H, 11.66; B, 5.19.

Diethyl erythro-2,3-Dibromobutane-2-boronate. Dibutyl *trans*-2-butene-2-boronate, 30 g., was converted to the boronic acid by treatment with water and fractional distillation of the butanol–water azeotrope at 20 mm. The residue was treated with 85 ml. of absolute ethanol and 150 ml. of benzene and the azeotrope was distilled through a 30-cm. packed column. Distillation yielded 46% of impure diethyl 2-butene-2-boronate, b.p. 50° (20 mm.), C=C peak at 6.09 μ. Bromination under the same conditions used with the butyl ester yielded diethyl *erythro*-2,3-dibromobutane-2-boronate, b.p. 42–43° (0.05 mm.).

Anal. Calcd. for $C_8H_{17}BBr_2O_2$: C, 30.41; H, 5.42; B, 3.43; Br, 50.61. Found: C, 30.44; H, 5.64; B, 3.20; Br, 50.47.

Stereochemistry of Eliminations. The *cis–trans* ratios of dibutyl 2-butene-2-boronate samples were determined by n.m.r. A 0.03-g. portion was cooled to −75° and a solution of bromine in ~0.2 ml. of methylene chloride was added until the bromine color persisted. The solution was warmed to 0° and treated with about 3 drops of either water, 0.1 *M* sodium hydroxide, or pyridine. The mixture was allowed to stand for 5–10 min. at 0° in the dark with occasional shaking. The ratio of *cis*- to *trans*-2-bromo-2-butene was determined by gas chromatography on a 5-ft. × 0.125 in. SE 30 silicone rubber on Chromosorb W column at 30°. With a nitrogen flow rate of 22 ml./min. the retention time of the *trans* isomer was 2.3 min., the *cis* 2.9 min.

Kinetics. A 100-ml. side-arm flask was fitted with a rubber septum for injection of samples and connected to a mercury manometer made from 4-mm. glass tubing. A bath controlled to ±0.05° was used at 25°. Ice and water controlled the temperature of the reaction mixture at 0.0–0.2°, as measured with an Anschütz thermometer. The three runs at 15.5–16° were ±0.2°. Solvents (20 ml. total before mixing) were measured from burets. Uncertainty in solvent composition is a potential source of error in the rates, since an error of 0.1 ml. in the water content at 80% ethanol would change the rate 3–4%. The reaction mixture was stirred magnetically; the apparent rate of reaction slowed if rapid stirring was not maintained. For the solvolytic runs, the internal pressure was adjusted to about 200 mm. below atmospheric (700 mm.) and a 0.25-ml. sample of redistilled dibutyl 2-bromoethaneboronate[2] was injected. The manometer was tapped gently to prevent lagging of the mercury level. Reactions were followed to 75–90% completion (little deviation occurred even after 5 half-lives) and then

Table II. First-Order Rate Constants for Solvolysis of Dibutyl 2-Bromoethaneboronate

Organic solvent, % by vol.[a]	Temp., °C.	$10^3 k_1$, sec.$^{-1}$
Ethanol, 90	25.1	2.35
Ethanol, 80	25.1	4.32
Ethanol, 80 + 0.38 *M* LiCl	25.1	5.40
0.38 *M* LiBr	25.1	4.97
0.38 *M* NaI	25.1	4.90
Ethanol, 80	16	2.30
	0	0.59
Ethanol, 70	25.1	8.07
	15.5	5.42
	0	1.44
Ethanol, 60	15.5	8.46
	0	2.30
Ethanol, 50	0	4.17
Ethanol, 40	0	7.15
t-Butyl alcohol, 80	25.1	3.86
Acetic acid, 50	0	2.94
Formic acid, 80	0	0.33

[a] Remainder water.

Table III. Second-Order Rate Constants for Reactions of Substituted Anilines with Dibutyl 2-Bromoethaneboronate in Absolute Ethanol at 25.1°

Substituent	k_2, l. mole^{-1} sec.$^{-1}$
None	0.154
None[a]	0.124
p-Chloro	0.0243
p-Bromo	0.0178
p-Iodo	0.0163
m-Bromo	0.00896
o-Chloro	0.00106

[a] With added aniline hydrochloride and lower concentrations of reactants; see text.

(20) F. G. Bordwell and P. S. Landis, *J. Am. Chem. Soc.*, **79**, 1593 (1957).
(21) D. S. Matteson, *ibid.*, **82**, 4228 (1960).
(22) Microanalyses by Galbraith Laboratories, Knoxville, Tenn.

allowed to run until the pressure became constant (10 half-lives) to provide the infinity pressure. The gas volume change in a typical run was 0.2%; the pressure change was 140 mm. First-order reactions were generally slow the first min., good to ±5% in succeeding 1 min. intervals, reproducible to ±3% average deviation. The second-order runs with amines of the class $ArNH_2$ were carried out under similar conditions with 2.9 mmoles of amine and 0.38 ml. of boronic ester, except that in the run with aniline hydrochloride 2.06 mmoles of aniline, 2.32 mmoles of aniline hydrochloride, and 0.25 ml. of boronic ester were used. Rate constants are summarized in Tables II and III.

Isotope Effects. In 80% ethanol (4:1 by syringe) at 25.0 ± 0.05°, k_1 was 4.22 and 4.12 × 10^{-3}. Substitution of 99.8% deuterium oxide for the water reduced k_1 to 2.26 × 10^{-3}. In 79% ethanol (2 ml. of water and 10 ml. of 95% ethanol, 0.20 ml. of dibutyl 2-bromoethaneboronate) k_1 was 4.29 × 10^{-3}. Substituting deuterium oxide and 95% O-deuterioethanol (98 atom % of D, Merck Sharpe and Dohme of Canada) reduced k_1 to 2.53 × 10^{-3}. For second-order runs, the solvent and reactants were weighed to 0.1% in syringes and injected into the closed, nitrogen-filled apparatus. In 12 ml. of absolute ethanol, 0.20 ml. (0.83 mmole) of dibutyl 2-bromoethaneboronate and 0.20 ml. (1.54 mmole) of dimethylaniline yielded k_2 = 0.0138 and 0.0141 (calculated assuming initial volumes additive). In absolute O-deuterioethanol, 98 atom % of D, k_2 = 0.0133 and 0.0129.

Mechanisms of Cleavage of Heteroaromatic Ethers. II. The Acid-Catalyzed Cleavage of 2-Methoxypyrimidine-O^{18} [1,2]

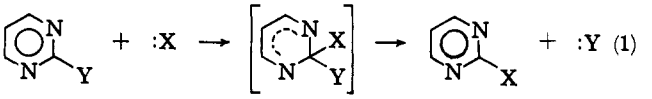
Ralph Daniels, Lee T. Grady,[3] and Ludwig Bauer

Contribution from the Department of Chemistry, College of Pharmacy, University of Illinois at the Medical Center, Chicago, Illinois 60612.
Received November 5, 1964

Cleavage of 2-methoxypyrimidine-O^{18} in an aqueous acid medium has been determined as proceeding predominantly via an aromatic nucleophilic substitution (SNAr) reaction. In addition, it has been shown that an SN2 mechanism makes a minor contribution to the overall cleavage of 2-methoxypyrimidine in an aqueous acid medium.

It is well known that the cleavage of a typical alkyl aryl ether proceeds with great difficulty and requires the use of a concentrated mineral acid or a strong Lewis acid; by contrast, certain alkyl heteroaromatic ethers may be cleaved under relatively milder conditions such as dilute aqueous acids.[4] The experiments described in this paper represent part of a study designed to elucidate the mechanisms by which alkyl heteroaromatic ethers were cleaved.

It has been long assumed[5-7] that the facile, acid-catalyzed cleavage of α- and γ-alkoxypyrimidines proceeds *via* a mechanism closely related to the nucleophilic displacement of other functional groups attached to *suitably substituted* aromatic or heteroaromatic rings. Such displacement reactions involve an attack by a nucleophile X at the carbon atom bearing the functional group Y; an intermediate is formed which undergoes loss of Y to afford the substitution product (eq. 1).



However, for the cleavage of heteroaromatic ethers, at least three general mechanisms may be written. Chart I depicts these mechanisms portraying as the substrate the 2-alkoxypyrimidinium cation **1**, the subject of this research.

Mechanism A. Nucleophilic attack of a water molecule at the *aromatic* carbon atom carrying the ether linkage would lead to the formation of an SNAr intermediate (**2**) of the type described above. Subsequently this intermediate would decompose to form an alcohol (**3**) and the 2-hydroxypyrimidinium cation **4**.

Mechanism B. Conversely, an SN2 attack of a water molecule at the *aliphatic* carbon atom of the ether linkage would lead to the same products (**3** and **4**) but these would proceed through a transition state (**5**) rather than an intermediate–complex (**2**).

Mechanism C. These same products could arise *via* an SN1 mechanism involving prior, unimolecular cleavage of the alkyl-to-oxygen bond of the cation **1** to produce a carbonium ion intermediate **7**, which among other reactions could react with water to form the alcohol **3** and a proton. The 2-hydroxypyrimidinium cation **4** would then arise by protonation of the 2-pyrimidone **6** formed by the original cleavage reaction.

(1) This research was supported by National Science Foundation, Cooperative Graduate Fellowship, Oct. 1, 1959–Sept. 30, 1961, and by the Research Board of the Graduate College of the University of Illinois, Grant No. 56-92-62.

(2) A preliminary account of part of this work has been published: R. Daniels, L. T. Grady, and L. Bauer, *J. Org. Chem.*, **27**, 4710 (1962).

(3) This paper is abstracted from the thesis submitted by L. T. Grady to the Graduate College of the University of Illinois at the Medical Center, 1963, in partial fulfillment of the requirements for the Ph.D. Degree.

(4) J. Sauer and R. Huisgen, *Angew. Chem.*, **72**, 294 (1960).

(5) B. Lythgoe, *Quart. Rev.* (London), **3**, 181 (1949).

(6) J. F. Bunnett and R. E. Zahler, *Chem. Rev.*, **49**, 273 (1951).

(7) J. Hine, "Physical Organic Chemistry," 2nd Ed., McGraw-Hill Book Co., Inc., New York, N. Y., 1962, 384 ff.