(4) (a) T. Koenig, *Tetrahedron Lett.*, 3127 (1965); (b) T. Koenig, *ibid.*, 2751 (1967).
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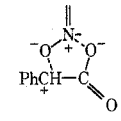
(15) The secondary effects exerted by the benzylic deuterium atoms are indeed long range and may be considered to be negligible here.
(16) R. A. Abramovitch, G. M. Singer, and A. R. Vinutha, *Chem. Commun.*, 55 (1967).
(17) The absolute yields of benzylpicolines were not determined in these experiments since they would be expected to vary in direct proportion to the yields of esters. Unlike reaction II, the relative rates of heterolytic and homolytic fragmentation in reaction III (see below) may be somewhat affected by a secondary isotope effect at the benzylic position. However, assuming a maximum effect of 1.1^{18} and a ratio of esters to benzylpicolines of ca. 2.0,[9] the magnitude of error in the resulting calculation is only 4%. Hence, the yields of benzylpicolines were ignored and the rate of rearrangement was assumed to be directly proportional to the yields of esters.
(18) T. Koenig and R. Wolf, *J. Am. Chem. Soc.*, **91**, 2574 (1969).
(19) Since measuring yield variations in either benzaldehyde or 2-picoline gives similar results, changes in the destruction of benzaldehyde by Perkin condensation must be rather minimal. This is confirmed by the small differences (1–5%) between the yields of 2-picoline and benzaldehyde (Tables I and II).
(20) D. R. Coulson and N. C. Yang, *J. Am. Chem. Soc.*, **88**, 4511 (1966); A. Padwa and R. Gruber, *ibid.*, **90**, 4456 (1968); R. C. Fahey and H.-J. Schneider, *ibid.*, **92**, 6885 (1970).
(21) S. Smith, A. Fainberg, and S. Winstein, *J. Am. Chem. Soc.*, **83**, 618 (1961).
(22) Although the possibility of ion pairing may at first seem remote in sulfolane, it must be remembered that in dipolar aprotic solvents the anion is poorly solvated because it cannot form a hydrogen bond with the solvent. In fact, SN1-like ionization is not common in such solvents.[23]
(23) A. Parker, *Q. Rev., Chem. Soc.*, **16**, 163 (1962).
(24) S. Oae, Y. Kitaoka, and T. Kitao, *Tetrahedron*, **20**, 2685 (1964).
(25) It is also possible that the α-carboxybenzylcarbenium ion **3**, being very acidic, could lose a proton to the phenylacetate anion rather than form a CO bond to it.
(26) The high selectivity of the electrophilic intermediate for pyridine *N*-oxide[8a] might be explained by a 1,3-dipolar interaction of **10** with the *N*-oxide.



(27) Because of an impurity which eluted with either 2-methyl-3-benzylpyridine or 2-methyl-5-benzylpyridine, the yields of those isomers, which represent ca. 20% of the total yield of the three benzylpicoline isomers, were not determined on the VPC. However, it could be estimated from the chromatogram that the yields of the two isomers varied in direct proportion to the yield of the third isomer, 2-(β-phenylethyl)pyridine (**7**). Therefore, the yield of the latter is proportional to the rate of homolysis.
(28) Melting points were determined on a Thomas-Kofler micro hot stage utilizing a stage-calibrated thermometer and are thus corrected. Boiling points are uncorrected. Infrared spectra were determined on Beckman IR-8 or Perkin-Elmer 467 spectrophotometers. Proton magnetic resonance spectra were determined on Varian A-60 or 360 instruments; chemical shifts are relative to internal tetramethylsilane for samples prepared in organic solvents and to the sodium salt of 3-(trimethylsilyl)-1-propanesulfonic acid for samples in aqueous solution. Analytical gas chromatography was performed on Varian 1860-3 (FID) or 920 (TC) instruments equipped with Disc 204 integrators. For determining yields, the responses of authentic samples were calibrated against those of various standards. Isomers were assumed to have identical responses. Isotopic analyses were performed at 20 eV on an LKB 9000 combined gas chromatograph–mass spectrometer equipped with an accelerating voltage alternator.
(29) Sodium phenylacetate slowly exchanges α protons in the presence of 0.05 *M* deuteroxide ion and deuterium oxide.[30] Therefore, to the extent that any sodium deuteroxide remains in the reaction mixture under discussion, redissolving the sodium phenylacetate-d_2 salt in water and washing with ether would dilute the deuterium atom content of the salt.
(30) J. G. Atkinson, J. J. Csakvary, G. T. Herbert, and R. S. Stuart, *J. Am. Chem. Soc.*, **90**, 498 (1968).
(31) It was found that phenylacetic anhydride-d_4 readily exchanges α deuterons in the presence of acidic protons. Therefore, in order to prepare a highly enriched anhydride, all glassware used was oven dried, and the weighings and reagent transfers were performed in a drybox containing phosphorus pentoxide as desiccant. The anhydrous conditions prevent hydrolysis of tosyl chloride to tosyl acid.
(32) D. D. Perrin, W. L. F. Armarego, and D. R. Perrin, "Purification of Laboratory Chemicals", Pergamon Press, Oxford, 1966, p 268.
(33) We are grateful to Dr. J. H. Fager for providing us with an authentic sample of 2-(β-phenylethyl)pyridine.

Cleavage of Cyclic Ethers by Magnesium Bromide–Acetic Anhydride. SN2 Substitution at a Secondary Site

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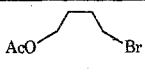
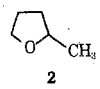
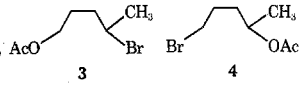
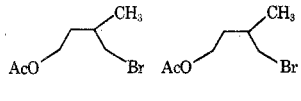
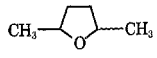
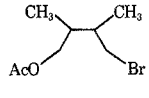
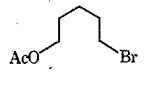
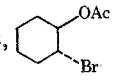
Cyclic ethers are cleaved by magnesium bromide and acetic anhydride in acetonitrile to yield bromoacetates. The reaction occurs readily at room temperature with tetrahydrofuran and substituted tetrahydrofurans. Tetrahydropyrans require higher temperature for cleavage. When *cis*- and *trans*-2,5-dimethyltetrahydrofuran are individually subjected to cleavage conditions a single diastereoisomeric bromoacetate is produced from each. The bromoacetates in turn when exposed to sodium hydroxide in warm ethylene glycol are converted to the specific isomers from which they were formed. Since the reclosure reaction must occur with inversion, the cleavage reaction must also be an inversion process. The mechanism of cyclic ether cleavage with magnesium bromide–acetic anhydride is thus shown to be exclusively an SN2 process.

The ability of Lewis acids and acid anhydrides to cleave ethers has been known since the early part of this century. The reactions have been extensively studied from the standpoints of product composition, mechanism, and stereochemistry, and the subject has been reviewed in detail.[1,2] Despite the "textbook" nature of the process, the search for methods for the formation and cleavage of ethers remains of interest. Ethers serve as effective stable blocking groups for hydroxyl functions and their use in this regard is ubiquitous in organic synthesis. Recently reports of the development of two ether cleavage reagent systems using acid anhydrides have appeared.[3,4]

Table I

Ether	Temp, time, hr	Products	Yield (ratio)
	Ambient, 12		97
 2	Ambient, 15	 3 4	70 (4.1:1)
	Ambient, 15		85 (2.7:1)
	Ambient, 15		88
	85°, 15		50
	Ambient, 12		80

Karger and Mazur[3] have described the cleavage of both cyclic and noncyclic ethers with the mixed anhydride acetyl *p*-toluenesulfonate. In the second recent report, Ganem and Small, using a system originally reported by Knoevenagel, investigated the scope of ether cleavage affected by acetic anhydride and ferric chloride. Both reports also describe efforts to specify the mechanistic aspects of these reactions, whether the cleavage of a specific type of ether with a given reagent is an SN1 or an SN2 reaction or some combination of the two. Unfortunately the results in many of these cases cannot be interpreted unambiguously with regard to a specific mechanism. We wish to describe here a Lewis acid–acid anhydride cleavage reagent for cyclic ethers, and the results of an experiment which clearly define the stereochemical aspect of the mechanism for cleavage of a substituted tetrahydrofuran.

Cyclic ethers, particularly tetrahydrofuran and alkyl-substituted tetrahydrofurans, are cleaved by acetic anhydride in the presence of zinc chloride.[5] Such reactions have been almost invariably carried out at elevated temperatures, 190–250°C. The yields of cleavage products rarely exceed 60–70%, and other Lewis acids have not been employed to any great extent. In contrast both cyclic and acyclic ethers have been cleaved in the presence of a variety of Lewis acids in conjunction with acetyl chloride[1,2] (a more effective cleavage agent than acetic anhydride). Magnesium salts, however, have been reported to be singularly ineffective as cleavage catalysts.[6] On the basis of previous work, one would expect that the combination of acetic anhydride and magnesium bromide at moderate temperature would be among the least efficacious methods for the cleavage of a cyclic ether. It was surprising, therefore, to find that such a melange provides a mild and effective means of converting tetrahydrofurans and other cyclic ethers to the corresponding ω-bromoacetates.

Treatment of tetrahydrofuran at room temperature with 1 molar equiv of magnesium bromide and 2 equiv of acetic anhydride in acetonitrile affords 4-bromobutyl acetate (1) in 97% yield. Methyl-substituted tetrahydrofurans are similarly cleaved in yields ranging from 70 to 88% as shown in Table I. In contrast to its reactivity with acetic anhydride–zinc chloride, 2-methyltetrahydrofuran (2) affords 70% of the substitution products 3 and 4 when treated with acetic anhydride–magnesium bromide. Under the former conditions a 70% yield of olefinic acetate elimination product is obtained.[7] The finding that the major cleavage product of 2-methyltetrahydrofuran is the secondary bromide 3 suggests that the ring opening reaction is largely an SN1 process. Such a conclusion would be commensurate with the findings of Burwell and coworkers[8] for the cleavage methyl *sec*-butyl ether. The latter affords 2-chlorobutane, the product of displacement at the most substituted carbon, 50% racemized, when exposed to acetyl chloride and zinc chloride, a result suggested to be in accord with a carbonium ion process. We shall show, however, for the case of a methyl tetrahydrofuran, that cleavage of the ring and substitution of a nucleophile at the most substituted carbon is, at least stereochemically, an SN2 process.

As shown in Table I, acetic anhydride–magnesium bromide also cleaves tetrahydropyrans and epoxides. As expected,[1,2] the rate of tetrahydropyran opening is considerably slower than that of the five-membered cyclic ether. Elevated temperature is necessary to affect cleavage in a reasonable time, and a considerable portion of the product from an attempted cleavage of 2-methyltetrahydropyran was unsaturated acetate. The opening of the epoxide ring is relatively unexceptional but for the fact that magnesium bromide alone is known to rearrange epoxides under a variety of conditions.[9] We should also note that simple saturated acyclic ethers are not appreciably cleaved by magnesium bromide–acetic anhydride at room temperature, and that neither reagent by itself affects tetrahydrofuran under the described reaction conditions.

Mechanism and Stereochemistry. The commonly accepted mechanism[1,2] for the cleavage of ethers by acid anhydrides and Lewis acids is illustrated in eq 1–3. A similar

$$(RCO)_2O + MX_n \longrightarrow R\overset{+}{C}O + (RCO_2MX_n)^- \quad (1)$$

$$RCO^+ + R'OR'' \longrightarrow R'-\overset{+}{O}(R'')-COR \quad (2)$$

$$R'-\overset{+}{O}(R'')-COR + (RCO_2MX_n)^- \longrightarrow \begin{Bmatrix} R'OCOR \text{ and/or } R''OCOR \\ R'X \text{ and/or } R''X \end{Bmatrix} \quad (3)$$

sequence may be written for reactions involving acid halides.

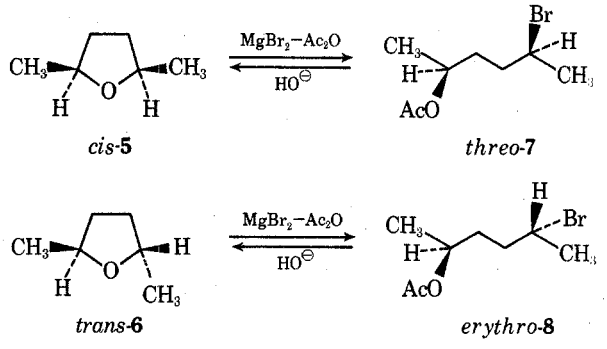
Most investigations of the details of this sequence have focused on step 3, the actual substitution reaction, in order to determine if concerted displacement or stepwise formation of a cation followed by attack of a nucleophile occurs. In their recent work on cleavages promoted by acetic anhydride–ferric chloride Ganem and Small[4] followed the stereochemical course of the reaction of optically active methyl and benzyl 2-octyl ethers. Since ferric chloride is used in these reactions in only catalytic amount, all of the products are acetates. As a consequence the position of substitution (primary vs. secondary) cannot be specified on the basis of product structure. They did observe that the resulting 2-octyl acetate was largely racemized: 96% for the methyl compound and 85% for the benzyl case. Net inversion was also found in the cleavage of the methyl ether and net retention of configuration for the benzyl compound. A variety of pathways for the substitution step of the mechanism (eq 3) may be envisioned to explain such results. For example, in the case of benzyl 2-octyl ether, racemization could result from a relatively equal mix of SN2 substitution occurring at both oxygen-bearing carbons, from SN1 reaction

at the secondary position, or from some combination of both types. Net retention would only require some excess of cleavage at the benzyl position, either concertedly or nonconcertedly. Ganem and Small quite reasonably concluded that the cleavage step occurred by SN1 and/or SN2.

In the case of the cleavage of 2-methyltetrahydrofuran with acetic anhydride–magnesium bromide it is clear that, regardless of specific mechanism, the preferred position for substitution is the secondary carbon. Further insight into the details of the substitution step may be gained from an examination of the stereochemical outcome of the cleavage. One may employ, however, as a substrate, not the optically active material, but the epimerically different compounds, *cis*- and *trans*-2,5-dimethyltetrahydrofuran. Loss of configurational integrity in the cleavage of either of these ethers can be observed as a diastereoisomeric change rather than as an enantiomeric one. To whatever extent either of these ethers yields a mixture of diastereoisomeric products one may invoke the intermediacy of a planar cationic intermediate.

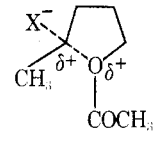
The isomeric ethers *cis*- and *trans*-2,5-tetrahydrofuran were separated from a commercial mixture by spinning band distillation. As little as 10% of one isomer could be detected in the presence of the other by GLC analysis on either an SE-30 or Carbowax 20M liquid phase. The ^{13}C chemical shifts of the methyl and methine carbons of each ether are also readily distinguished and both analytical methods showed that the lower boiling cis compound used for subsequent experiments contained less than 10% of the trans isomer. Each isomer when exposed to anhydrous magnesium bromide–acetic anhydride in acetonitrile produced a *single* bromoacetate. The latter compounds, though undistinguishable by normal spectroscopic methods, are readily separable by GLC.

The production of a single bromoacetate from each of the isomeric dimethyltetrahydrofurans demands that the cleavage reactions occur with either complete retention or complete inversion of configuration. Thus *cis*-**5** must open either with inversion to give *threo*-**7** or with retention to yield *erythro*-**8**. Similarly *trans*-**6** must yield *erythro*-**8** by inversion or *threo*-**7** by retention. The identification of the



configurations of the bromoacetates was made by reconstituting the original ethers from the cleavage products. Each of the isomeric bromoacetates was treated with potassium hydroxide in ethylene glycol. The resulting 2,5-dimethyltetrahydrofurans (ca. 40% yield in each case) were isolated by distillation. The bromoacetate from *cis*-**5** gave only *cis*-**5** again after base treatment, and the one obtained from *trans*-**6** similarly afforded only *trans*-**6**. Since re-formation of the ethers from the bromoacetates must be a simple SN2 inversion reaction, *the initial cleavage reaction must also occur cleanly with inversion.* If, for example, *cis*-**5** had undergone either SN1 cleavage or some combination of concerted and nonconcerted opening a mixture of both *cis*-**5** and *trans*-**6** would have been obtained on reclosure. In the event that cleavage had occurred with retention of configuration *trans*-**6** would have been the ultimate product from the opening and reclosure of *cis*-**5**. Our results show therefore that the cleavage of a *secondary* cyclic ether is stereochemically an SN2 process.

The finding that 2-methyltetrahydrofurans are opened at a secondary position with clean inversion of retention cannot necessarily be extended to the cleavage reactions of other ethers. Five-membered heterocycles are in general more easily opened than their higher homologues. Harley-Mason[10] has found, for example, that substituted pyrrolidines are cleaved by anhydrides under conditions where the corresponding piperidines are inert. Tetrahydrofuran cleavage may more closely resemble epoxide opening than the cleavage of an acyclic ether. As a consequence the transition state for opening of the ring of the intermediate acyl oxonium ion in a concerted displacement may display considerable positive character at carbon. Bond breakage may to a large extent precede bond cleavage but without the actual formation of a symmetric intermediate. The finding that concerted displacement occurs preferentially at a secondary site is compatible with such a pathway.[11]



Experimental Section

Gas chromatographic analyses were performed on an F & M 720 chromatograph. Infrared spectra were determined with Perkin-Elmer spectrometers, Models 137-B and 257. Proton NMR spectra were recorded in the indicated solvent with either a Varian T-60 or a Jeol 100-MHz spectrometer and ^{13}C spectra on a Varian CFT-20 instrument. Tetramethylsilane was used as internal reference for both nuclei. Chemical shifts are given in parts per million downfield from Me_4Si. Elemental analyses were performed by Atlantic Microlab, Inc., Atlanta, Ga. Solvents were purified according to standard procedures.[12]

4-Bromobutyl Acetate (1). General Procedure for the Cleavage of Tetrahydrofurans. Anhydrous magnesium bromide was prepared by the addition, under an argon atmosphere, of 2.16 ml (26 mmol) of 1,2-dibromoethane to 0.63 g (26 mmol) of magnesium turnings suspended with stirring in 25 ml of dry ether. When formation of the salt was complete the ether was removed under vacuum and replaced with 25 ml of dry acetonitrile. To this stirred suspension, cooled in an ice–water bath, was added 2.05 ml (26 mmol) of dry tetrahydrofuran and 5.2 ml (52 mmol) of acetic anhydride. The reaction mixture was brought to room temperature and stirred for 12 hr. Saturated sodium bicarbonate solution was then added and the mixture was stirred to destroy excess acetic anhydride. Ether extraction followed by drying of the extract over sodium sulfate and evaporation of the solvent under reduced pressure afforded a dark brown oil. Evaporative distillation of the oil yielded 4.89 g (96.5%) of 4-bromobutyl acetate: bp 85–87° (1.8 mm) [lit.[13] 92–93° (12 mm)]; ir ($CHCl_3$) 1742 cm^{-1}; ^1H NMR (CCl_4) 1.6–2.2 (m, 4 H, CH_2), 2.02 (s, 3 H, $COCH_3$), 3.46 (t, 2 H, CH_2Br, J = 6 Hz), 4.08 ppm (t, 2 H, CH_2O–, J = 6 Hz).

Anal. Calcd for $C_6H_{11}BrO_2$: C, 36.95; H, 5.69; Br, 40.97. Found: C, 36.95; H, 5.68; Br, 40.89.

Cleavage of 2-Methyltetrahydrofuran. 4-Bromopentyl Acetate (3) and 5-Bromo-2-pentyl Acetate (4). Cleavage of 2.6 ml (26 mmol) of 2-methyltetrahydrofuran under the previously described conditions gave, after distillation, 3.79 g (70% yield) of a mixture of **3** and **4**. Analysis of the mixture by GLC on a 10 ft × 0.25 in, 10% diisodecyl phthalate column at 145° showed the ratio **3** to **4** to be 4.1:1: ir (mixture) (CCl_4) 1730 cm^{-1}; ^1H NMR (mixture) (CCl_4) 1.22 (d, 3 H, CH_3CHOAc, J = 6 Hz), 1.74 (d, 3 H, CH_3CHBr, J = 7 Hz), 1.7–2.0 (m, 4 H, CH_2CH_2), 2.02 (s, 3 H, $OCOCH_3$), 3.42 (t, 2 H, CH_2Br, J = 6 Hz), 3.98–4.30 (m, 3 H, BrCHC– and $–CH_2O$), 4.96 ppm (m, 1 M, –CCHOAc).

Anal. Calcd for $C_7H_{13}BrO_2$: C, 40.21; H, 6.27; Br, 38.22. Found: C, 40.35; H, 6.28; Br, 38.14.

Cleavage of 3-Methyltetrahydrofuran. The title compound exposed to the standard reaction conditions afforded, after distil-

lation, 4.63 g (85%) of a mixture of 3-methyl-4-bromobutyl acetate and 2-methyl-4-bromobutyl acetate in a ratio of 2.7:1. The proportions of the isomers were obtained from the integrated intensities of the NMR signals for the methylene protons of the acetate-bearing carbons in the two compounds; ir ($CHCl_3$) 1730 cm^{-1}; NMR (CCl_4) 0.98 (d, 3 H, CH_3, J = 6 Hz), 1.07 (d, 3 H, CH_3, J = 7 Hz), 1.5–2.2 (m, 3 H, –CH and CCH_2C), 2.04 (s, 3 H, $OCOCH_3$), 3.35–3.6 (t, 2 H, CH_2CH_2Br and d, 2 H, $-CHCH_2Br$), 3.96 (d, 2 H, $-CHCH_2O$, J = 6 Hz), 4.12 ppm (t, 2 H, CH_2CH_2O-, J = 7 Hz).

Anal. Calcd for $C_7H_{13}BrO_2$: C, 40.21; H, 6.27; Br, 38.22. Found: C, 40.31; H, 6.31; Br, 38.16.

Cleavage of 2,5-Dimethyltetrahydrofuran. A mixture of *cis*- and *trans*-2,5-dimethylfuran (2.6 g, 26 mmol) under the standard conditions afforded 5.22 g (88%) of the diastereoisomeric 2-methyl-4-bromopentyl acetates: ir ($CHCl_3$) 1730 cm^{-1}; NMR (CCl_4) 1.20 (d, 3 H, CH_3CH-O, J = 6 Hz), 1.60–1.95 (m, 4 H, CH_2), 1.69 (d, 3 H, CH_3CHBr, J = 7 Hz), 2.00 (s, 3 H, CH_3CO_2-), 4.13 (m, 1 H, CHBr), 4.9 ppm (m, 1 H, –CHO).

Anal. Calcd for $C_8H_{15}BrO_2$: C, 43.07; H, 6.77; Br, 35.82. Found: C, 43.10; H, 6.78; Br, 35.85.

Cleavage of Tetrahydropyran. Application of the usual conditions with the exception of the reaction temperature, 85° in the present case, to tetrahydropyran (2.53 ml, 26 mmol) yielded 3.32 g (50%) of 5-bromopentyl acetate:[13] ^1H NMR (CCl_4) 1.4–1.8 (m, 6 H, CH_2) 2.0 (s, 3 H, $OCOCH_3$), 3.45 (t, 2 H, CH_2Br, J = 6 Hz), 4.08 ppm (t, 2 H, CH_2O, J = 7 Hz).

Cleavage of Cyclohexene Oxide. The title compound (2.55 g, 26 mmol) after treatment with magnesium bromide–acetic anhydride and subsequent distillation gave 4.58 g (80%) of *trans*-2-bromocyclohexyl acetate:[14] ^1H NMR (CCl_4) 1.15–2 (m, 8 H), 2.05 (s, 3 H), 3.87–4.16 (m, 1 H, CHBr), 4.74–5.0 ppm (m, 1 H, CHOAc).

***cis*-2,5-Dimethyltetrahydrofuran (*cis*-5).** Distillation of commercial 2,5-dimethyltetrahydrofuran at atmospheric pressure through a Nester–Faust annular Teflon spinning band column operating at a reflux ratio of 30:1 afforded *cis*-2,5-dimethyltetrahydrofuran: bp 90–91° (lit.[15] 90–91°); ^1H NMR (CCl_4) 1.15 (d, 3 H, CH_3, J = 6 Hz), 1.28–2.24 (m, 4 H, CH_2), 3.81–4.41 (m, 2 H, CH); ^{13}C NMR ($CDCl_3$) 21.60 (CH_3), 33.38 (CH_2), 75.36 ppm (CH). Both GLC analysis on SE-30 silicone rubber and Carbowax 20M and peak height measurements of the ^{13}C NMR spectrum of the cis compound indicated the presence of no more than 10% of the trans isomer *trans*-2,5-dimethyltetrahydrofuran (*trans*-6).

***trans*-2,5-Dimethyltetrahydrofuran (*trans*-6).** The higher boiling fraction from spinning band distillation afforded the title compound: bp 91–92° (lit.[15] 92–94°); ^1H NMR (CCl_4) 1.13 (d, 3 H, CH_3, J = 6 Hz), 1.28–2.41 (m, 4 H, CH_2), 3.81–4.41 (m, 2 H, CH); ^{13}C NMR ($CDCl_3$) 21.48 (CH_3), 34.31 (CH_2), 74.55 ppm (CH).

Cleavage and Reconstitution of the Isomeric 2,5-Dimethyltetrahydrofurans. Each of the above isomers was subjected to the cleavage conditions described previously. The distilled products were analyzed on a Carbowax 20M column at a programmed temperature rate increase of 2°/min from an initial temperature of 110°. The retention time for *threo*-7 (from *cis*-5) was 10.3 min and that for *erythro*-8 (from *trans*-6) was 11.5 min. Analysis of mixtures of the isomers indicated that 10% of one isomer was detectable in the presence of the other. The bromoacetate *threo*-7 (2.26 g, 10 mmol) was dissolved in 25 ml of ethylene glycol containing 0.7 g of potassium hydroxide. The solution was heated at 60° for 6 hr. Distillation through a Vigreaux column at 92° and atmospheric pressure followed by separation of water and drying yielded *cis*-5 (0.44 g, 44%). Gas chromatographic and spectroscopic analysis as described above indicated the presence of 10% or less of the trans isomer. Application of the same procedure to *erythro*-8 (2.26 g, 10 mmol) afforded pure *trans*-6 (0.42 g, 42%).

Registry No.—**1**, 4753-59-7; **2**, 96-47-9; **3**, 26923-92-2; **4**, 26923-93-3; **5**, 2144-41-4; **6**, 2390-94-5; **7**, 56761-56-9; **8**, 56761-57-0; tetrahydrofuran, 109-99-9; 3-methyltetrahydrofuran, 13423-15-9; 3-methyl-4-bromobutyl acetate, 56761-58-1; 2-methyl-4-bromobutyl acetate, 56761-59-2; 5-bromopentyl acetate, 15848-22-3; tetrahydropyran, 142-68-7; cyclohexene oxide, 286-20-4; *trans*-2-bromocyclohexyl acetate, 5837-71-8.

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An Unusual Rate Law for Vinyl Ether Hydrolysis. Observation of H_3PO_4 Catalysis at High pH

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An unusual rate law has been observed for hydrolysis of several vinyl ethers in phosphate buffers in the pH range 5.5–7.6. In addition to the expected terms in $[H^+]$ and $[H_2PO_4^-]$ alone, a term in $[H^+][H_2PO_4^-]$ was also observed. After determination of the pK'_a of H_3PO_4 (1.62 ± 0.06) in the 5% dioxane, μ = 1.0 M (KCl), solvent system used for the kinetics, and evaluation from a Brønsted correlation of the contribution expected from H_3PO_4 catalysis, it has been shown that the unusual rate law does not represent a new mechanism, but rather direct observation of H_3PO_4 catalysis at pH values *more than four units higher than its* pK'_a. The consequences of this observation are listed.

In the study of the hydrolysis of vinyl ethers to their corresponding ketones, we[1,2] and others[3a] have shown repeatedly that these species undergo hydrolysis by the rate law

$$k_\psi = k_H[H^+] + \sum_i k_{HA_i}[HA_i] \quad (1)$$

where k_ψ is the observed, pseudo-first-order rate constant, and HA_i is a general acid catalyst. We were therefore rather surprised when, while studying the hydrolysis of compounds **1** and **2** in phosphate buffers,[4] we observed apparent conformity to the rate law