group on ASE2 reactions is about the same as the effect of a phenyl group, although the magnitude can vary widely (see Table III). For the four compounds listed, the ratio $k_{C_6H_5}/k_{CH_3}$ varies from 0.2 to 15. Except for $k_{styrene}/k_{propylene}$, the ratio is approximately 0.5. Since the comparisons of styrene to propylene and ethylene had to be made by circuitous and rather extensive extrapolations, these values should be treated with some caution, and it seems safe to say that the effect of a methyl substitution on double bond protonation is very similar to the effect of phenyl substitution.

In contrast, the rates of SN1 solvolyses are enhanced considerably more by phenyl groups than by methyl groups. Streitwieser has generalized,[26] "A rough approximation is that a phenyl group is as effective in stabilizing a carbonium ion as are two methyl groups." Since both types of reactions presumably give identical carbonium ions one might expect similar effects of phenyl and methyl groups on the rates of both types of reaction.

This discrepancy might be partially resolved by taking into consideration the effects of substituents on the ground states of the substrates. In particular, both a methyl group and a phenyl group are known to stabilize double bonds. If the stabilization of the double bond by a phenyl group were *much* greater than by a methyl group, then the relative rate enhancement by a phenyl group should be less. A comparison of the heats of hydrogenation of model compounds will show whether the difference in ground state stabilization can account for the difference in relative rates. Heats of hydrogenation[27] for α-methylstyrene (26.07 kcal), isobutylene (28.11 kcal), and propylene (29.71 kcal) show that the stabilization of the ground state due to a phenyl group is approximately equal to that provided by two methyl groups. Since the same ratio holds for stabilization of carbonium ions, the relative effects of methyl and phenyl groups on double bond protonations should be the same as they are on SN1 solvolyses.

Although the above approximations are rather rough, the authors feel that they fairly represent the true situation. Further evidence for an effect in the ground state due to a phenyl group which is about twice that due to a methyl group is the fact that the phenyl/hydrogen and methyl/hydrogen ratios are similar for all of the compounds in Table III, even though the magnitude of the ratios vary widely.

Thus, it is apparent that the similarity in rates of methyl substituted and phenyl substituted compounds in ASE2 reactions cannot be explained by recourse only to ground state stabilities. Perhaps this result is indicative of substantially different transition states in the ASE2 reactions and corresponding SN1 solvolyses, and that treating both transitions states as like the product carbonium ions is not as good an assumption as is widely believed.

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[26] A. Streitwieser, Jr., "Solvolytic Displacement Reactions," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p 43.

[27] American Petroleum Institute, "Selected Values of Physical and Thermodynamic Properties of Hydrocarbons and Related Compounds," Carnegie Press, Pittsburgh, Pa., 1953.

General Acid Catalysis of Ketal Hydrolysis. The Hydrolysis of Tropone Diethyl Ketal

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Received July 7, 1969

Abstract: The hydrolysis of tropone diethyl ketal has been studied in water at 15°. A pronounced general acid catalysis by the acid species of the buffer can be observed. The rate constant for catalysis by Tris (H^+) is less in D_2O than H_2O ($k_{DA}/k_{HA} = 0.67$). The mechanism undoubtedly involves partially rate-determining protonation by the general acid. Thus, if the carbonium-ion intermediate is of great stability general acid catalysis can be obtained even with ketals of aliphatic alcohols. At pH values greater than 10 the rate of hydrolysis is independent of pH. This pH-independent reaction has a D_2O solvent isotope effect (k_{D_2O}/k_{H_2O}) of 0.86.

It has been generally accepted that the acid-catalyzed hydrolysis of simple acetals and ketals involves an A1 mechanism with preequilibrium protonation of the substrate by hydronium ion followed by a unimolecular, rate-determining breakdown of the protonated intermediate to an alcohol and a resonance-stabilized carbonium ion.[2] Intramolecular participation by a neighboring carboxyl group[3,4] or acetamido group[5] has been postulated to occur in the hydrolysis of phenolic acetals and glycosides. Intramolecular participation was not observed, however, in the hydrolysis of a series of carboxyl-substituted ketals of aliphatic alcohols.[6] General acid catalysis by buffer acids has been found in the hydrolysis of 2-(substituted phenoxy)tetrahydropyrans when the substituent group is electron withdrawing.[7]

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[2] E. H. Cordes, *Progr. Phys. Org. Chem.*, 4, 1 (1967).

[3] B. Capon, *Tetrahedron Lett.*, 911 (1963).

[4] B. Capon and M. C. Smith, *Chem. Commun.*, 523 (1965).

[5] D. Piszkiewicz and T. C. Bruice, *J. Amer. Chem. Soc.*, **89**, 6237 (1967).

[6] T. C. Bruice and D. Piszkiewicz, *ibid.*, **89**, 3568 (1967).

[7] T. H. Fife and L. K. Jao, *ibid.*, **90**, 4081 (1968).

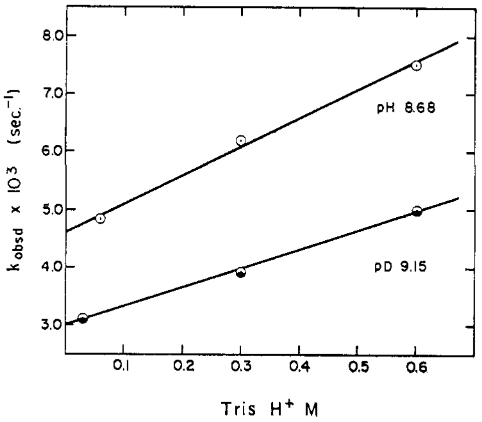
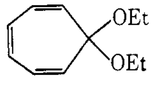


Figure 1. Plot of k_{obsd} *vs.* Tris (H^+) concentration at 15° in H_2O (○) or in D_2O, (●), $\mu = 0.6$ with KCl. Tris (H^+) is the conjugate acid of tris(hydroxymethyl)aminomethane.

In that case the mechanism of both the hydronium ion and general acid-catalyzed reactions most likely involves partially rate-determining protonation of the acetal. Strong electron withdrawal in the leaving group of an acetal will decrease basicity and at the same time facilitate C-O bond cleavage. However, the study of thioacetals, where an oxygen is replaced by a much less basic sulfur, has shown that a simple reduction in basicity of the acetal will not give rise to general acid catalysis.[8,9] This suggests that a critical factor in promoting general acid catalysis is ease of C-O bond breaking. If this is indeed the case, then the hydrolysis of acetals giving an exceedingly stable carbonium ion intermediate should be catalyzed by general acids.

Buffer catalysis has never been conclusively observed in the hydrolysis of acetals or ketals of simple aliphatic alcohols in which the pK_a of the leaving group is high, despite intensive search.[2,10-13] We have, therefore, studied the hydrolysis of the diethyl ketal of tropone **1** since the intermediate carbonium ion will be of extreme stability.[14,15]



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Experimental Section

Materials. Tropone diethyl ketal was prepared by the procedure employed for the preparation of tropone ethylene ketal,[16] substituting ethanol for ethylene glycol. Upon distillation through a Nester-Faust spinning-band column the product was obtained as a colorless liquid boiling at 108° (12 mm), $n^{25}D$ 1.4990. *Anal.* Calcd for $C_{11}H_{16}O_2$: C, 73.29; H, 8.95. Found: C, 73.53; H, 9.22. Infrared and nmr spectra were consistent with structure **1**.

Kinetic Measurements. The rates of hydrolysis were measured on a Cary 15 spectrophotometer at 311 mμ. Temperature was maintained constant at 15 ± 0.05° by circulating water from a Precision Scientific Temptrol 154 water bath through a Thelma thermostatted cell. Temperature was measured inside the cuvette. Buffers were maintained at constant ionic strength with KCl. Buffers were made up in 99.8% D_2O using predeuterated Tris and Trisdeuteriochloride. A stock solution of tropone diethyl ketal in acetonitrile (0.01 *M*) was prepared. To initiate the rates 20 μl were added with a Hamilton syringe to 1.4 ml of solution in the cell. Pseudo-first-order rate constants were calculated by a rigorous least-squares procedure on an IBM 360-40 computer. The spectra of the solutions upon completion of the reaction were identical with that of tropone. Also, the hydrolysis product was determined to be solely tropone by isolation followed by infrared and glpc analysis. pH values were determined at 15° with a Radiometer pHM-22 pH meter. To determine pD, the glass electrode correction equation of Fife and Bruice was employed.[17]

Results

Rate constants for hydrolysis of tropone diethyl ketal in phosphate and in Tris-HCl buffers at 15° and $\mu = 0.6$ with KCl are given in Table I. In Figure 1 is shown a plot of k_{obsd} *vs.* Tris (H^+) concentration in H_2O or D_2O as the solvent. It can be seen that a large buffer catalysis is obtained. The slope of the plot is constant as pH is decreased showing the catalysis to be by the acid component of the buffer. It will be noted that the catalytic constant k_{HA} for Tris (H^+) is much less than for $H_2PO_4^-$. The magnitude of the general acid catalysis is less in D_2O than H_2O; $k_{DA}/k_{HA} = 0.67$.

Table I. Rate Constants for Hydrolysis of Tropone Diethyl Ketal in H_2O or D_2O at 15°

Buffer	Concn, total	Solvent	pH or pD	[a] $k_{HA} \times 10^3$, l. mol^{-1} sec^{-1}	[b] $k_0 \times 10^3$, sec^{-1}
Phosphate[c]	(0.015–0.15 *M*)	H_2O	6.75	82.0	30.0
Tris-HCl[c]	(0.06–0.48 *M*)	H_2O	8.52	4.95	4.34
Tris-HCl[d]	(0.12–1.2 *M*)	H_2O	8.68	4.93	4.59
Tris-HCl[e]	(0.095–0.38 *M*)	H_2O	8.10	4.93	4.42
Tris-DCl[d]	(0.06–1.2 *M*)	D_2O	9.15	3.31	2.98
Carbonate[c]	(0.2 *M*)	H_2O	9.84		3.65
Carbonate[c]	(0.02 *M*)	H_2O	9.84		3.65
Carbonate	(0.1 *M* Na_2CO_3)	D_2O	12.0		3.13
NaOH	(0.01 *M*)	H_2O			3.74
NaOH	(0.1 *M*)	H_2O			3.57

[a] Second-order rate constant for general acid catalysis. [b] Rate constant for spontaneous hydrolysis (obtained by extrapolation to zero buffer concentration). [c] $\mu = 0.3$ with KCl. Buffer ratio, HA/A, is 1.0. [d] $\mu = 0.6$ with KCl. Buffer ratio, HA/A, is 1.0. [e] $\mu = 0.3$ with KCl. Buffer ratio, HA/A, is 2.8.

The rate constants at pH values greater than 10 are independent of pH and general acids. The pH independent reaction has a D_2O solvent isotope effect (k_{D_2O}/k_{H_2O}) of 0.86, measured in H_2O and D_2O solutions containing 0.1 *M* Na_2CO_3. At lower pH a hydronium-ion catalyzed reaction is observed. A value of k_{H^+} of 1.5×10^5 l. mol^{-1} sec^{-1} was calculated from the intercept values obtained by extrapolation to zero buffer concentration in plots of k_{obsd} *vs.* buffer concentration.

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(8) T. H. Fife and L. K. Jao, *J. Amer. Chem. Soc.*, **91**, 4217 (1969).

(9) Thioacetals of *para*-substituted thiophenols hydrolyze with no detectable general acid catalysis although the exactly analogous oxygen acetals are susceptible to general acid catalysis. T. H. Fife and E. Anderson, unpublished data.

(10) J. N. Bronsted and W. F. K. Wynne-Jones, *Trans. Faraday Soc.*, **25**, 59 (1929).

(11) M. M. Kreevoy and R. W. Taft, Jr., *J. Amer. Chem. Soc.*, **77**, 3146 (1955).

(12) T. H. Fife and L. K. Jao, *J. Org. Chem.*, **30**, 1492 (1965).

(13) A very small buffer catalysis was claimed in the hydrolysis of benzophenone ketals: R. H. De Wolfe, K. M. Ivanetich, and N. F. Perry, *ibid.*, **34**, 848 (1969). We have been unable to detect catalysis with benzophenone diethyl ketal and the ethylene glycol ketal of *p,p'*-dimethoxybenzophenone even at very high concentrations of formate and chloroacetate buffers (0.6 *M*). De Wolfe, *et al.*, also reported that no catalysis could be obtained in formate buffer.

(14) N. C. Deno, *Progr. Phys. Org. Chem.*, **2**, 129 (1964).

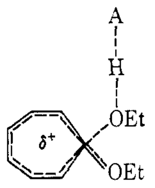
(15) The pK_{R^+} for the cycloheptatrienyl cation is +4.7: G. H. Naville, H. Strauss, and E. Heilbronner, *Helv. Chim. Acta*, **43**, 1221, 1243 (1960).

(16) H. E. Simmons and T. Fukunaga, *J. Amer. Chem. Soc.*, **89**, 5208 (1967).

(17) T. H. Fife and T. C. Bruice, *J. Phys. Chem.*, **65**, 1079 (1961).

Discussion

The hydrolysis of tropone diethyl ketal involves facile catalysis by very weak buffer acids. The mechanism of the general acid-catalyzed reaction undoubtedly involves partially rate-determining protonation by the general acid. Thus, if the intermediate



carbonium ion is of sufficiently great stability, general acid catalysis can be observed even with ketals of aliphatic alcohols where the leaving group is poor.

A free energy-reaction coordinate diagram for the acid-catalyzed hydrolysis of simple acetals might appear as in Figure 2. Decomposition of the protonated acetal is normally the rate-determining step.[2] In order to obtain partially rate-determining protonation by hydronium ion and general acid catalysis, either basicity must be reduced, increasing the height of the peak for the protonation step, and/or the ease of C–O bond breaking must be increased, decreasing the height of the peak for the bond-breaking step. Strong electron withdrawal in the leaving group, which both lowers basicity and facilitates bond breaking, will give rise to general acid catalysis as seen previously in the hydrolysis of 2-(*p*-nitrophenoxy)tetrahydropyran.[7] While reduced basicity is undoubtedly of importance, the predominant feature with the aryloxytetrahydropyrans must be ease of bond breaking, as shown by the increase in the second-order rate constants for formic acid catalysis as electron withdrawal in the leaving group increases ($\rho = +0.9$), in contrast to the negative ρ of -0.9 for hydronium-ion catalysis.[7,18] Therefore, bond breaking is of much greater importance when a weak acid is the catalyst. This results from proton transfer being more difficult with a weak acid catalyst than with hydronium ion. As a consequence, greater C–O bond breaking is necessary in order to attain the transition state. The same factors are probably also influencing the general acid-catalyzed hydrolysis of benzaldehyde methyl phenyl acetal[19] as are important in the hydrolysis of 2-aryloxytetrahydropyrans. In the case of tropone diethyl ketal the leaving group is poor, but bond breaking has been made very facile by the great carbonium-ion stability. Thus, with the acetals and ketals studied to date whose hydrolysis reactions are clearly subject to general acid catalysis involving slow proton transfer, ease of C–O bond breaking appears to be the critical feature in giving rise to these effects.

A spontaneous rate of hydrolysis is observed for tropone diethyl ketal (Table I), the rate at pH values greater than 10 being independent of pH. It is most likely the occurrence of this fast pH-independent reaction that accounts for the lack of observable catalysis in carbonate buffers, catalysis by HCO_3^- not being able to compete with the spontaneous reaction. The magnitude of the solvent isotope effect ($k_{D_2O}/k_{H_2O} = 0.86$), near unity for spontaneous hydrolysis, indicates that the reaction is very likely a unimolecular decomposition of the unprotonated acetal, although the possibility of a water-catalyzed reaction cannot be conclusively eliminated. In either case bond breaking in the transition state must be important. A pH-independent reaction is also observed in the hydrolysis of 2-(*p*-nitrophenoxy)tetrahydropyran[7] and in the hydrolysis of benzaldehyde methyl S-(2,4-dinitrophenyl)thioacetal[9] with a D_2O solvent isotope effect near unity ($k_{D_2O}/k_{H_2O} = 0.9$) in both cases.[9,18] A fast pH-independent acetal or ketal hydrolysis reaction can therefore be brought about, as is general acid catalysis, either by formation of a very stable carbonium-ion intermediate or by a combination of effects arising from a very good leaving group and a reasonably stable carbonium ion. Increased electron withdrawal in the leaving group would be expected to increase greatly the rate of spontaneous hydrolysis but would decrease the rate of the hydronium-ion catalyzed reaction by decreasing basicity,[20] thereby making the pH-independent reaction relatively easy to detect with these compounds. An enhancement of carbonium-ion stability, however, should increase the rate of both the hydronium-ion catalyzed reaction and the spontaneous reaction although not necessarily to the same extent. It is probably this factor that is responsible for the hydrolysis of tropone diethyl ketal becoming completely pH independent only at pH values greater than 10, whereas this point is reached at pH 4 with 2-(*p*-nitrophenoxy)tetrahydropyran[7,18] and at 0.05 *M* HCl with benzaldehyde methyl S-(2,4-dinitrophenyl)thioacetal.[9]

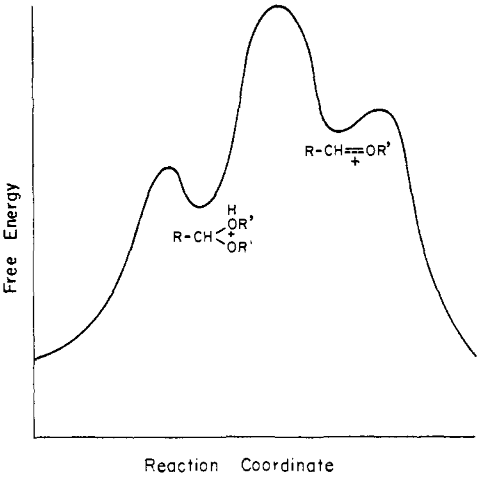


Figure 2. A free-energy *vs.* reaction-coordinate diagram for acid-catalyzed hydrolysis of a simple acetal proceeding by an A1 mechanism.

The elucidation of the structural features responsible for general acid catalysis is of great importance in regard to the insight provided into the factors responsible for the enzymatic hydrolysis of glycosides since general catalysis by functional groups at the active sites is undoubtedly involved. Mechanisms involving general acid catalysis have been suggested for lysozyme.[21] It

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[18] T. H. Fife and L. H. Brod, *J. Amer. Chem. Soc.*, in press.

[19] E. Anderson and B. Capon, *Chem. Commun.*, 390 (1969).

[20] The ρ value for hydronium-ion catalyzed hydrolysis of 2-aryloxytetrahydropyrans[7] is -0.9, and that for hydrolysis of benzaldehyde methyl S-(substituted phenyl)thioacetals[9] is -1.0.

[21] G. Lowe, G. Sheppard, M. L. Sinnott, and A. Williams, *Biochem. J.*, **104**, 893 (1967).

would appear reasonable that the enzyme is making general catalysis possible by enhancing the ease of C–O bond breaking.

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Aromatic Substitution of Olefins. VI. Arylation of Olefins with Palladium(II) Acetate

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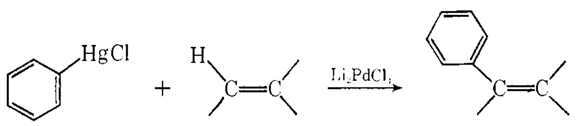
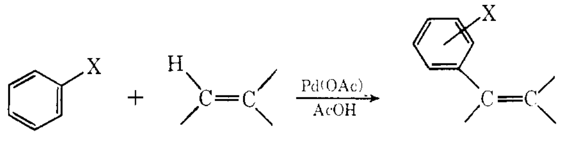
Abstract: Olefins react with benzene derivatives to produce aryl-substituted olefins *via* direct substitution of the aromatic compound for hydrogen on the double bond of the olefin in the presence of palladium salts and reduced palladium metal. The reaction may be made catalytic with respect to the palladium salts by using cupric acetate or silver acetate, and air as reoxidants. The reaction provides an extremely convenient method for the synthesis of a wide variety of olefinic compounds.

Extensive studies on reactions of olefins in the presence of transition metal compounds have been carried out. Much less is known about arylation of olefins with transition metal compounds.

Most recently, Heck described interesting arylation reactions of olefins with arylating agents such as arylmercuric halides in the presence of group VIII metal salts, and showed that palladium salts are the most generally useful, with rhodium and ruthenium salts next best.[2]



We have reported a novel method of synthesizing stilbene derivatives by substitution of aromatic compounds for hydrogen on the double bond of the styrene–palladium chloride complex.[3] In the course of our work, palladium acetate was found to be the most effective for the direct arylation of olefins with aromatic compounds in the presence of acetic acid. The present paper reports a study of substitution reaction of olefins with benzene derivatives by means of palladium salts, especially palladium acetate. A preliminary communication of a portion of this work has been given.[4]



Results and Discussion

In previous papers[3] we described our initial work on the reactions of the styrene–palladium(II) chloride complex with benzene derivatives to give stilbenes. It was noted that for this arylation on a β-carbon atom of styrene, the presence of a carboxylic acid such as acetic is essential because the reactants form a homogeneous solution and the reaction proceeds best in this solvent. Further, it was found that when sodium acetate was added, the yield was greatly increased.

Palladium(II) acetate has been found to be the most generally useful, with palladium(II) chloride–sodium acetate next best for the direct arylation of olefins with benzene derivatives.

The aromatic substitution of olefins takes place in homogeneous solutions of reactant olefin and palladium(II) acetate (equal mole equivalents to olefin) in a solution of the aromatic compound (large excess) and acetic acid. The solution is stirred in the presence of air for a few minutes to several hours (8 hr usually), to give from 10% to *ca.* 90% yield of arylated products, with reduced metallic palladium and a very small amount of acetates. Results are given in Table I.

With unsymmetrical olefins, the aryl group generally adds predominantly to the less substituted carbon atom of the double bond because of steric hindrance of the substituents. This is consistent with that observed in the Heck arylation.[2] Although *cis* and *trans* mixtures are formed, no mixtures resulting from arylation in both directions to unsymmetrical olefins have been found.

Increasing substitution on the olefinic carbons decreases the reactivity of the olefin in the palladium acetate arylation reaction. For example, the reaction of triphenylethylene with benzene and a palladium acetate catalyst gave tetraphenylethylene in low yield (13%),[5] while styrene reacts with benzene to afford *trans*-stilbene in almost quantitative yield.

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[1] On leave of absence from Ube Industries, Ltd., Ube, Japan.

[2] (a) R. F. Heck, *J. Amer. Chem. Soc.*, **90**, 5518 (1968); (b) R .F. Heck, *ibid.*, **90**, 5526 (1968); (c) R. F. Heck, *ibid.*, **90**, 5531 (1968); (d) R. F. Heck, *ibid.*, 90, 5535 (1968); (e) R. F. Heck, *ibid.*, **90**, 5542 (1968).

[3] (a) I. Moritani and Y. Fujiwara, *Tetrahedron Lett.*, 1119 (1967); (b) Y. Fujiwara, I. Moritani, and M. Matsuda, *Tetrahedron*, **24**, 4819 (1968).

[4] Y. Fujiwara, I. Moritani, M. Matsuda, and S. Teranishi, *Tetrahedron Lett.*, 633 (1968).

[5] Yields of arylation products given in this paper are based on the amount of palladium salt utilized.