

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS, URBANA, ILLINOIS]

Gas Chromatography. IV. The Thermodynamics and Kinetics of the Alcoholysis of Acetals^{1a}BY RICHARD S. JUVET, JR., AND JEN CHIU^{1b}

The two-step, acid-catalyzed methanolysis of diethyl acetal has been investigated by gas chromatography. The reaction proceeds by two consecutive reversible first order reactions corresponding to the stepwise exchange of the acetal ethoxy groups. The rate of both steps shows first order dependence on acid concentration and is independent of alcohol concentration. Gas chromatography is shown to be ideally suited for choosing the reaction period for maximum yield of stable intermediates in consecutive reactions. The equilibrium constants for both of the two consecutive reactions were determined simultaneously from the concentrations of the five components in the equilibrium mixture and are equal to 4.65 ± 0.09 and 1.01 ± 0.04 , respectively. Arrhenius energies and entropies of activation have been obtained from reaction rates measured as a function of temperature. A mechanism analogous to that of the hydrolysis reaction is proposed. No previous thermodynamic or kinetic studies on the alcoholysis of acetals have been reported because of the lack of a suitable analytical method.

As early as 1856 Wurtz² reported the synthesis of the unsymmetrical methyl ethyl acetal by heating a mixture of methanol and ethanol with pyrolusite and sulfuric acid. While Rübenkamp³ was unable to confirm the existence of unsymmetrical acetals, others⁴⁻⁵ claimed successful preparation of several mixed acetals. Because of the lack of an effective analytical tool, no rate or equilibrium studies have been made on the alcoholysis of simple aliphatic acetals. Recently Piantadosi, *et al.*,⁹ prepared cyclic glycerol acetals and determined the equilibrium constant for the interconversion of the 1,2- and the 1,3-benzylidene glycerol acetals by ultraviolet spectrophotometry. This analytical technique may be applied only to those acetals giving distinctive absorption spectra.

During recent years gas chromatography has been employed to an increasing extent in the determination of reaction rates and thermodynamic constants. By taking advantage of this newly developed analytical tool, the two-step, acid-catalyzed methanolysis of diethyl acetal has been investigated. The equilibrium constants for the two consecutive reactions involved have been determined simultaneously from the concentrations of the five components in the equilibrium mixture. Consecutive rate constants and activation energies have also been measured and a reaction mechanism proposed. Gas chromatography is shown to be ideally suited for choosing the reaction period for maximum yield of stable intermediates in consecutive reactions.

Experimental

Materials.—Dimethyl acetal (b.p. 63.5°; d_{25}^{25} 0.8446) and diethyl acetal (b.p. 102.5°; d_{25}^{25} 0.8198) were Eastman white label products purified by distillation over sodium. Methyl ethyl acetal was prepared by a modification of the

Deschamps method.⁸ Diethyl acetal (355 g., 3 moles) and methanol (32 g., 1 mole) were refluxed in the presence of 0.2 ml. of 12 *N* hydrochloric acid for 30 minutes. After cooling, sodium was carefully added in excess to the mixture, and the mixture was refluxed for several hours. A reddish brown precipitate formed which was removed by centrifugation, and the supernatant was distilled over sodium. The fraction collected between 84–85° was further treated with sodium and redistilled. The yield of methyl ethyl acetal (b.p. 84.5°; d_{25}^{25} 0.8325) was ca. 32%. Methanol (Mallinckrodt absolute reagent) was further purified by the magnesium methyllate method.¹⁰ Absolute ethanol (U. S. Industrial Chemical) was purified by treating with sodium, refluxing with ethyl formate¹⁰ and distilling. All volatile reagents were tested for purity by gas chromatography and were shown to be "chromatographically pure." The limit of detection of the apparatus used in the present investigation was of the order of 10^{-8} mole.

Apparatus.—The apparatus used was similar to that described by Bennett, *et al.*,¹¹ and Juvet and Wachi.¹² A silica gel drying tower inserted between the helium cylinder and the preheater was used to remove traces of moisture contained in the carrier gas. The column was 9 feet long and was made from 1/4-inch copper tubing packed with 30% w./w. di-octyl phthalate (Pittsburgh Coke and Chemical Co., PX-138) on 80/100 mesh Johns-Manville acid-washed Chromosorb-W. A column temperature of 80° was used for the equilibrium studies and 97° for the kinetic studies. It is interesting to note that "dinonyl" phthalate and tricresyl phosphate, both with similar polarities, were sufficiently different in solvent properties to prevent adequate resolution of all components. Helium was used as the carrier gas with a flow rate, measured at room temperature and atmospheric pressure, of ca. 40 ml./min.

Equilibration Procedure.—Appropriate amounts of acetals were measured into 5-ml. ampoules which had previously been flushed with dried nitrogen. Purified alcohols and alcohols acidified with hydrogen chloride gas were added to give a final acid concentration of ca. 10^{-4} *M*. After sealing, the ampoules were thermostated at $25.00 \pm 0.05^\circ$ for 2 to 16 days. Less than 24 hr. was required to attain equilibrium under these reaction conditions. Although quenching of the hydrogen chloride catalyst prior to gas chromatographic analysis is not necessary in the alcoholysis of esters,^{12,13} quenching is required in the alcoholysis of acetals. The reaction mixture was quenched with concentrated ammonia and analyzed by gas chromatography. The amount of ammonia required to neutralize the catalyst and provide a slight excess was 0.01 microliter per milliliter of sample. This amount was added with sufficient accuracy by means of a 1-mm. diameter solid glass rod wetted on the tip. The presence of a small excess of ammonia had no effect on the chromatogram. Peak areas, measured by a Keuffel and Esser Compensating Polar

(1) (a) Paper III in this series, R. S. Juvet and F. M. Wachi, *Anal. Chem.*, **32**, 290 (1960); (b) Standard Oil Co., Indiana, Fellow, 1959–1960; Minnesota Mining and Manufacturing Co. Fellow, 1960–1961.

(2) A. Wurtz, *Jahresber. Fortschritte Chem.*, 597 (1856).

(3) R. Rübenkamp, *Ann. Chem. Liebigs*, **225**, 267 (1884).

(4) A. Bauchmann, *ibid.*, **218**, 38 (1883).

(5) R. Leimu, *Ann. Acad. Sci. Fennicae*, Ser. A, II, *Chem.*, No. 19 (1946).

(6) M. M. Delepine, *Bull. soc. chim., France*, Ser. 3, **25**, 574 (1901).

(7) R. Alquier, *ibid.*, Ser. 5, **10**, 197 (1943).

(8) J. Deschamps, M. Paty and P. Pineau, *Compt. rend.*, **238**, 911 (1954).

(9) C. Piantadosi, C. E. Anderson, E. A. Brecht and C. L. Yarbrough, *J. Am. Chem. Soc.*, **80**, 6613 (1958).

(10) A. I. Vogel, "Practical Organic Chemistry," Longmans, Green and Co., London, 1957.

(11) C. E. Bennett, S. Dal Nogare, L. W. Safranski and C. D. Lewis, *Anal. Chem.*, **30**, 898 (1958).

(12) R. S. Juvet and F. M. Wachi, *J. Am. Chem. Soc.*, **81**, 6110 (1959).

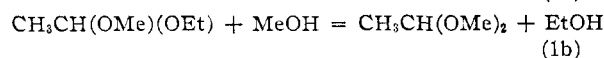
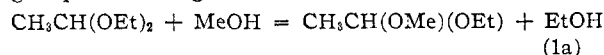
(13) E. V. Kring, G. I. Jenkins and V. L. Buechetta, *J. Phys. Chem.*, **64**, 947 (1960).

Planimeter, were compared with calibration curves made from synthetic blends close in composition to the sample being analyzed. Other experimental details have been described in a previous article.¹²

Kinetic Procedure.—Calculated amounts of acetal were added to acidified methanol contained in a tight-fitting, glass-stoppered 25-ml. flask which previously had been flushed with dry nitrogen. All components were thermostated at the desired temperature for at least 4 hr. before mixing. One milliliter samples were taken at convenient time intervals and quenched with concentrated ammonia as described above. The samples were analyzed gas chromatographically.

Results and Discussion

Equilibrium Constants—The methanolysis of diethyl acetal is a two-step process, the two ethoxy groups being replaced successively by methoxy groups according to the reactions



Five components, three acetals and two alcohols, are present at equilibrium, and the equilibrium constants K_I and K_{II} are given by the relationships

$$K_I = \frac{(\text{Me-Et-Ac})(\text{EtOH})}{(\text{Di-Et-Ac})(\text{MeOH})} \quad (2)$$

and

$$K_{II} = \frac{(\text{Di-Me-Ac})(\text{EtOH})}{(\text{Me-Et-Ac})(\text{MeOH})} \quad (3)$$

where Me, Et and Ac stand for methyl, ethyl and acetal, respectively. The parentheses in equations 2 and 3 refer to concentrations rather than activities; however, the activity coefficients of the acetals would be approximately identical and those of the two alcohols should also be quite similar. Therefore the thermodynamic equilibrium constants and the measured apparent equilibrium constants should be essentially equal. Since the concentrations of all five components of the equilibrium mixture may be obtained from a single gas chromatogram, both equilibrium constants may be determined simultaneously.

A chromatogram of the equilibrium mixture is shown in Fig. 1. All five components are well resolved. The equilibrium constants determined at several acetal/alcohol ratios are summarized in Table I. The values of the equilibrium constants were verified by measuring the constant of the reverse reaction, *i.e.*, the ethanolysis of dimethyl acetal. Mean values for K_I of 4.65 and for K_{II} of 1.01 have been obtained with a precision of 2 and 4%, respectively.

Equilibrium constants for reactions 1a and 1b were measured at $0.0 \pm 0.1^\circ$. For an initial ratio of 2:1 diethyl acetal/methanol, equilibrium constants of 4.54 ± 0.04 and 1.07 ± 0.04 have been measured at this temperature for K_I and K_{II} , respectively. Thus, temperature has very little, if any, effect on the equilibrium constant over the range 0 to 25° .

Kinetic Studies.—The acid-catalyzed methanolysis of diethyl acetal involves a consecutive reaction. Two methods, the indirect graphical method and the time-ratio method,^{14a} have been developed to

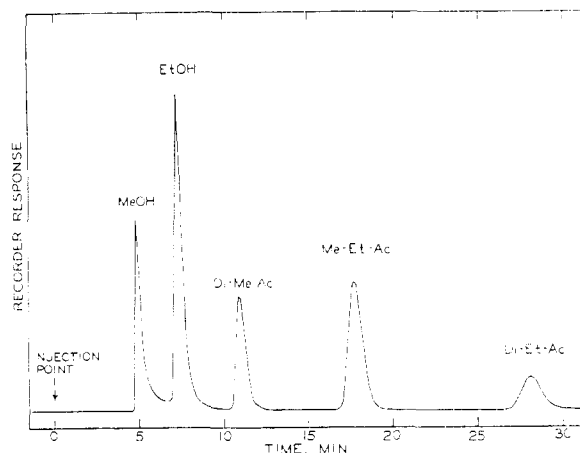


Fig. 1.—Gas chromatogram of the equilibrium mixture in the methanolysis of diethyl acetal: column temperature, 80° ; flow rate of helium, 40 ml./min.; 30% w/w. di-octyl phthalate-Chromosorb-W column; initial mole ratio, Di-Et-Ac/MeOH = 1:2.

evaluate consecutive rate constants. These tedious procedures are often required because of the limitations imposed by the analytical methods available. With gas chromatography, however, the rate constants of both steps may generally be determined directly by following the concentration changes of all the reactants, intermediates and products present in the system. In this investigation it was only necessary to follow concentration variations of the three acetals. The alcohol peaks were not used because of a partial overlapping of the peaks at high ratios of alcohol. A plot of peak height (concentration) *vs.* reaction

TABLE I
EQUILIBRIUM CONSTANTS FOR THE METHANOLYSIS OF DIETHYL ACETAL AT 25.0°

| Initial mole ratio | No. of detns. | K_I | | K_{II} | |
|-----------------------|---------------------|-------|----------|----------|----------|
| | | Mean | σ | Mean | σ |
| Di-Et-Ac/MeOH | | | | | |
| 2:1 | 4 | 4.68 | 0.04 | 1.08 | 0.01 |
| 1.5:1 | 6 | 4.58 | .05 | 1.01 | .02 |
| 1:1 | 5 | 4.57 | .05 | 1.02 | .02 |
| 1:2 | 4 | 4.77 | .06 | 0.95 | .01 |
| Di-Me-Ac/EtOH | | | | | |
| 1:1 | 4 | 4.68 | 0.09 | 0.99 | 0.02 |
| Mean K values: | 23 | 4.65 | 0.09 | 1.01 | 0.04 |

time is shown in Fig. 2. The diethyl acetal rapidly decreases in concentration as methanolysis proceeds and methyl ethyl acetal is formed. The appearance of the dimethyl acetal peak indicates the course of the second step of the methanolysis. Fig. 2 also clearly reveals that the concentration of the intermediate, methyl ethyl acetal, goes through a maximum, the position of which depends on the relative value of the two rate constants. Thus, gas chromatography is ideally suited for choosing the reaction period for maximum yield of stable intermediates in consecutive reactions.

(14) A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," John Wiley and Sons, Inc., New York, N. Y., 1953: (a) p. 153, (b) p. 172, (c) p. 96.

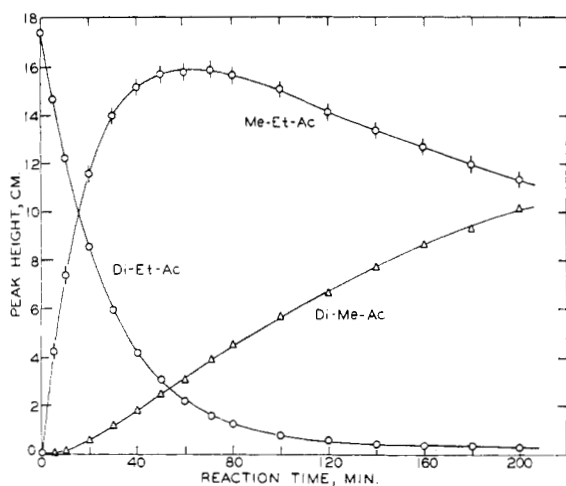


Fig. 2.—Peak height-reaction time curves for the methanolysis of diethyl acetal at 25.1°: initial mole ratio, Di-Et-Ac/MeOH = 1:12; acid concentration, $9.2 \times 10^{-5} M$; sample size, 0.040 ml.

The reaction rates of both steps are shown below to be acid-dependent, first order in acetal, and independent of the concentration of alcohol. The two first order rate constants have been determined at several acid concentrations, initial reactant ratios and temperatures. The methanolysis of diethyl acetal proceeds *ca.* 8 times faster than the methanolysis of methyl ethyl acetal under identical acid concentrations. Typical first order plots for the two steps measured at several acid concentrations are shown in Figs. 3A and 3B. In order to drive the equilibrium toward the formation of dimethyl acetal and to attain a larger change in peak heights during a kinetic run, an initial ratio of diethyl acetal to methanol equal to 1:12 was used. The first order rate constants tabulated in Table II were calculated according

TABLE II
CONSECUTIVE FIRST ORDER RATE CONSTANTS FOR THE
METHANOLYSIS OF DIETHYL ACETAL

| Initial Di-Et-Ac MeOH | Temp., °C. | Acid concn., $\times 10^5$, mole/l. | Rate constants $\times 10^2$, min. ⁻¹ | | | |
|-----------------------------|---------------|---|--|----------|-------------|----------|
| | | | <i>k</i> I | σ | <i>k</i> II | σ |
| 1:12 | 25.1 | 4.6 | 1.02 | 0.06 | | |
| | | 5.8 | 1.78 | .08 | | |
| | | 6.9 | 2.28 | .04 | | |
| | | 9.2 | 3.73 | .04 | | |
| | | 17.3 | 8.36 | .15 | 1.07 | 0.02 |
| | | 23.1 | | | 1.52 | .07 |
| | | 34.6 | | | 2.55 | .03 |
| | | 46.1 | | | 3.21 | .06 |
| 1:12 | 20.3 | 6.9 | 1.36 | 0.02 | | |
| | | 34.6 | | | 1.43 | 0.05 |
| 1:12 | 30.6 | 6.9 | 3.89 | 0.04 | | |
| | | 34.6 | | | 4.47 | 0.10 |
| 1:7 | 25.1 | 4.0 | 1.24 | 0.03 | | |
| | | 6.0 | 2.51 | .05 | | |
| | | 20.0 | | | 1.40 | 0.04 |
| | | 30.0 | | | 2.18 | .05 |
| 1:3 | 25.1 | 5.7 | 1.90 | 0.04 | | |
| | | 7.9 | 3.37 | 0.24 | | |
| | | 34.1 | | | 2.22 | 0.05 |

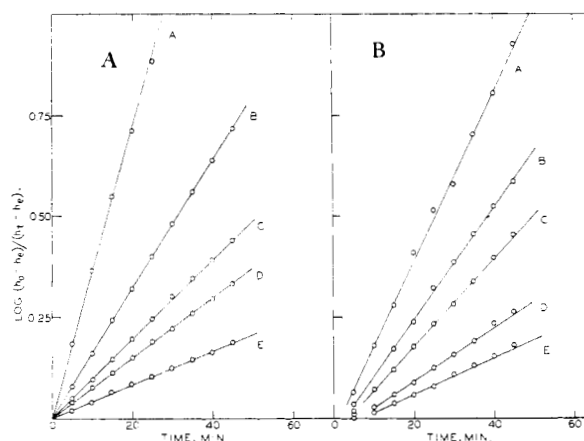


Fig. 3.—First order plots.—Set A: methanolysis of diethyl acetal at acid concentrations: A, $17.3 \times 10^{-5} M$; B, $9.2 \times 10^{-5} M$; C, $6.9 \times 10^{-5} M$; D, $5.8 \times 10^{-5} M$; E, $4.6 \times 10^{-5} M$ HCl. Set B: methanolysis of methyl ethyl acetal at acid concentrations: A, $6.92 \times 10^{-4} M$; B, $4.61 \times 10^{-4} M$; C, $3.46 \times 10^{-4} M$; D, $2.31 \times 10^{-4} M$; E, $1.73 \times 10^{-4} M$ HCl.

to the equation^{14b}

$$k = k_{+1} + k_{-1} = \frac{2.303}{t} \log \frac{h_0 - h_e}{h_t - h_e}$$

where h_0 , h_t and h_e are peak heights at time $t = 0$, t and ∞ and k , k_{+1} and k_{-1} are the effective rate constant, and the first order rate constants for the forward and reverse reactions, respectively.

In the ideal situation the rate constants for both reactions may be determined from a single run (*cf.* the values measured at an acid concentration of $1.73 \times 10^{-4} M$ in Table II). With the system under investigation, however, this can only be done accurately over a narrow range of acid concentration because of the sizable difference in rates of the two reactions.

Plots of $\log k$ vs. \log (acid concentration) for initial mole ratios of diethyl acetal to methanol ranging from 1:3 to 1:12 are shown in Fig. 4. Linear curves with slopes of 1.3 and 1.1, corresponding to the first and second steps in the methanolysis, respectively, were obtained. This suggests that both rates are first order with respect to the acid catalyst concentration and are independent of the concentration of methanol.

It may be seen from Fig. 2 and Fig. 3B that an induction period is present in the second reaction. This often occurs in the case of consecutive reactions when the rate of the reaction is determined from the rate of formation of the product rather than from the rate of disappearance of the reactant.¹⁵

The variation of rate with temperature has been studied at 20.3, 25.1 and 30.6° for reactions 1a and 1b at acid concentrations of $6.9 \times 10^{-5} M$ and $3.46 \times 10^{-4} M$, respectively. The variation of rate with temperature follows the Arrhenius equation, $\log k = \log A - E_a/2.303 RT$, as shown in Fig. 5. The activation energies, E_a , of reactions

(15) S. L. Friess and A. Weissberger, "Technique of Organic Chemistry," Vol. VIII, Interscience Publishers, Inc., New York, N. Y., 1953, p. 287.

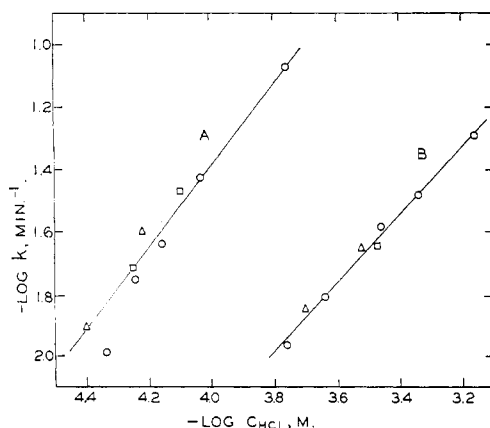


Fig. 4.—Acid and alcohol dependence: A, methanolysis of diethyl acetal; B, methanolysis of methyl ethyl acetal; initial mole ratio, diethyl acetal/methanol: O, 1:12; Δ , 1:7; \square , 1:3.

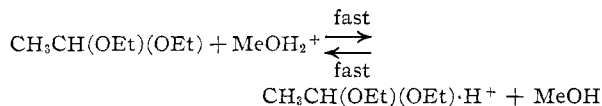
1a and 1b were calculated to be 18.1 ± 0.4 and 19.6 ± 0.9 kcal./mole, respectively. Accordingly, enthalpies of activation ΔH^* and entropies of activation ΔS^* were found to be 17.5 kcal./mole and -16.3 cal./mole-deg. for reaction 1a and 19.0 kcal./mole and -11.1 cal./mole-deg. for reaction 1b at 25.1° from the equations^{14c}

$$\Delta H^* = E_a - RT$$

$$k = (RT/Nh)e^{(T\Delta S^*/\Delta H^*)}$$

where N is Avogadro's constant; h , the Planck constant; and the other symbols maintain their conventional meanings.

Mechanism.—Although the mechanism of the acid-catalyzed alcoholysis of acetals has not been previously reported, that of the hydrolysis of acetals is well established. Experimental evidence¹⁶ confirms that hydrolysis of acetals proceeds according to a unimolecular mechanism involving a fission of the aldehyde carbon-to-oxygen bond, as originally suggested by Ingold.¹⁷ In view of the fact that the methanolysis of diethyl acetal is first order in acetal, first order in acid concentration and independent of alcohol concentration, it seems probable that the alcoholysis reaction has a mechanism analogous to that of the hydrolysis reaction. Accordingly, the scheme proposed for reaction 1a is



(16) M. M. Kreevoy and R. W. Taft, Jr., *J. Am. Chem. Soc.*, **77**, 3146 (1955); F. Stasiuk, W. A. Sheppard and A. N. Bourns, *Can. J. Chem.*, **34**, 123 (1956); E. Whalley and J. Koskikallio, *Trans. Faraday Soc.*, **55**, 809 (1959).

(17) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, New York, 1953, p. 334.

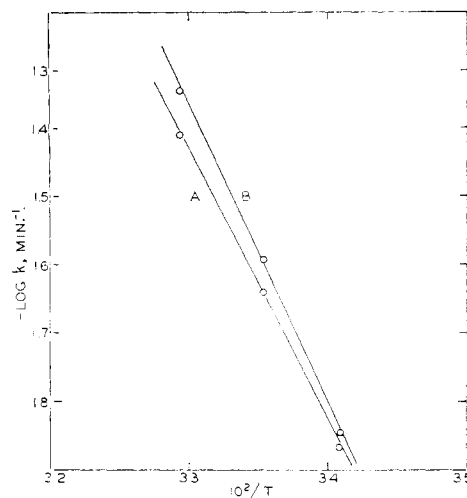
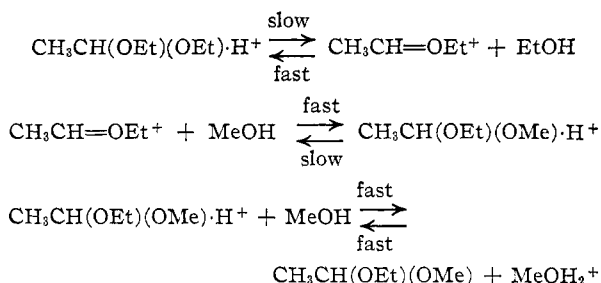


Fig. 5.—Temperature dependence: A, methanolysis of diethyl acetal, CHCl_3 , $6.9 \times 10^{-4} M$; B, methanolysis of methyl ethyl acetal, CHCl_3 , $3.46 \times 10^{-4} M$.



A similar scheme can be drawn for the second step in the methanolysis.

It has been shown that the methanolysis of diethyl acetal is *ca.* 8 times faster than that of methyl ethyl acetal. It is interesting to point out that the hydrolysis of diethyl acetals is also *ca.* 8 times that of the corresponding dimethyl acetals.¹⁸ Since the equilibrium constant for reaction 1b is essentially equal to unity, it can be deduced that the rate of the first step in the ethanolysis of dimethyl acetal is about equal to that of the methanolysis of methyl ethyl acetal. Likewise, from the equilibrium constant of reaction 1a, the rate of the methanolysis of diethyl acetal is *ca.* 5 times that of the ethanolysis of methyl ethyl acetal. It is readily seen that the alcoholysis rate depends on the remaining alkoxy group rather than on the leaving group or the attacking group. This is consistent with the assumed operation of the inductive effect on unimolecular substitution.

(18) A. Skrabal and H. H. Eger, *Z. physik. Chem.*, **122**, 349 (1926), report a hydrolysis rate ratio of 8.5 between diethyl and dimethyl formal; A. Skrabal and I. Sawiuk, *ibid.*, **122**, 357 (1926), report a rate ratio of 7.3 for diethyl and dimethyl acetals in general.