Commercial 2,5-dimethyltetrahydrofuran proved to be a mixture of isomers, from which a greatly enriched sample of lower boiling[19] *cis* isomer was obtained by distillation for gas chromatographic comparison.

Acknowledgment. The picture of halogen "weak participation" presented here bears marked resemblance to one which may be envisioned for phenyl participation as outlined by Professor H. C. Brown in a conversation. Samples of fluoroalkenes were furnished by Professor B. S. Rabinovitch and Professor F. L. M. Pattison. 5-Methoxy-2-pentyl tosylate was prepared and studied by Mr. R. Belloli.

α-Fluoro and α-Alkoxy Substituents as Deactivators in Carbanion Formation[1a]

Jack Hine,[1b] Louis G. Mahone, and Charles L. Liotta

Contribution from the School of Chemistry, Georgia Institute of Technology, Atlanta, Georgia. *Received April 26, 1967*

Abstract: The kinetics of the methoxide ion catalyzed deuterium exchange of the α-hydrogen atoms of several methyl esters in methanol-*d* solution have been investigated. The second-order rate constants observed for the acetate, propionate, butyrate, β-phenylpropionate, and succinate are correlated well by a Taft ρ^* value of 1.78. The β-methoxypropionate and phenylacetate are too reactive to give agreement with the Taft equation, the latter giving a carbanion stabilized by the resonance effect of the phenyl substituent. The methoxyacetate, fluoroacetate, dimethoxyacetate, and difluoroacetate are less reactive (by $10^{2.6}$-, $10^{4.7}$-, 10^{7}-, and 10^{12}-fold, respectively) than expected from the Taft equation. These deviations from the Taft equation are rationalized in terms of the differences in electronegativity between sp^3 carbon (as in the α-carbon atoms of the esters) and sp^2 carbon (as in the negative carbon atoms of the carbanions) and in terms of the stabilization associated with the attachment of several oxygen or fluorine atoms to the same sp^3 carbon atom. Literature data are quoted to show that α-fluoro and α-alkoxy substituents either decrease rate and equilibrium constants for the formation of sp^2-hybridized carbanions or they increase them to a much smaller extent than would be expected from the inductive effects of these substituents. The available data on the formation of sp^3-hybridized carbanions show that α-fluoro and α-aryloxy substituents increase the reactivity by about the amount to be expected from the inductive effect.

According to Pauling's equation[2] the energy of a carbon–halogen bond in a saturated organic halide may be expressed

$$BE_{sp^3C-Y} = \frac{BE_{sp^3C-sp^3C} + BE_{Y-Y}}{2} + 23(X_{sp^3C} - X_Y)^2 \quad (1)$$

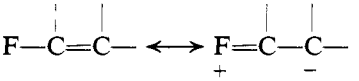
where the *BE*'s are the energies (in kcal/mole) of the bonds denoted by subscripts and the *X*'s are electronegativities. An analogous expression may be written for the energy of an sp^2 carbon–halogen bond and combination of this expression with eq 1 gives an expression for the difference in carbon–halogen bond energies for sp^3 and sp^2 carbon.

$$BE_{sp^2C-Y} - BE_{sp^3C-Y} = \frac{BE_{sp^2C-sp^2C} - BE_{sp^3C-sp^3C}}{2} + 23(X_{sp^2C}^2 - 2X_{sp^2C}X_Y - X_{sp^3C}^2 + 2X_{sp^3C}X_Y) \quad (2)$$

Combination of this with the corresponding expression for hydrogen yields

$$(BE_{sp^2C-Y} - BE_{sp^3C-Y}) - (BE_{sp^2C-H} - BE_{sp^3C-H}) = -46(X_{sp^2C} - X_{sp^3C})(X_Y - X_H) \quad (3)$$

According to this equation, if sp^2 carbon is more electronegative than sp^3 carbon, as has been claimed,[3] when the carbon atom to which a halogen is attached has its hybridization changed from sp^3 to sp^2, the carbon–halogen bond energy will increase less (or decrease more) than the corresponding carbon–hydrogen bond energy. The magnitude of this effect will increase with the electronegativity of the halogen. This effect has been suggested as a possible partial explanation for the deactivating effect of β-fluorine substituents (relative to β-chlorine and bromine) in E2 reactions of β-haloethyl bromides.[4] If olefin stabilities depended only on Pauling electronegativities, a fluorine substituent on a double bond would be expected to act as a destabilizer to a greater extent than any other halogen. However, from a comparison of the Hammett substituent constants for the *meta* and *para* halogens it appears that sp^2 carbon-bound fluorine is capable of resonance electron donation to a π-electron system to a greater extent than any other halogen.



Such resonance interaction should lead to a stabilization of fluoroolefins that will counteract and perhaps overwhelm the destabilization due to the electronegativity effect.

(1) (a) Part XII in the series "Polar Effects on Rates and Equilibria." For part XI see J. Hine, *J. Am. Chem. Soc.*, 88, 5525 (1966). This work was supported in part by Research Grant GP-2002 from the National Science Foundation. Abstracted largely from the Ph.D. Thesis of L. G. Mahone, 1966. (b) Author to whom inquiries may be addressed at the Evans Laboratory of Chemistry, The Ohio State University, Columbus, Ohio 43210.

(2) L. Pauling, "The Nature of the Chemical Bond," 3rd ed, Cornell University Press, Ithaca, N. Y., 1960, pp 85–105.

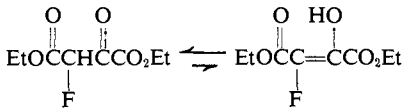
(3) *Cf.* G. W. Wheland, "Resonance in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1955, pp 128–129.

(4) J. Hine and P. B. Langford, *J. Am. Chem. Soc.*, 78, 5002 (1956).

Comparison of enthalpies of formation of saturated and unsaturated organic fluorides and thermodynamic data on reactions in which such compounds are interconverted should yield information on the relative importance of these two opposed effects. Unfortunately, however, few such data appear to be available. Although a number of thermochemical and rate and equilibrium measurements have been made on certain polyfluoroolefins such as tetrafluoroethylene,[5a] the interpretation of such data is complicated by the possibility that the transformation of such polyfluoroolefins to saturated compounds is strongly favored by a stabilization characteristic of compounds with several fluorine atoms attached to the same saturated carbon atom.[5b] No appropriate data on simple monofluoroolefins have been found, but from the enthalpies of formation of isopropyl fluoride,[6,7] propane,[8] benzene,[8] toluene,[8] and the appropriate fluoroaromatics,[9] enthalpy changes may be calculated for the following reactions in the vapor phase at 25°.

	ΔH, kcal/mole
$i\text{-}C_3H_7F + C_6H_6 \longrightarrow C_3H_8 + C_6H_5F$	−2.8
$i\text{-}C_3H_7F + C_6H_5F \longrightarrow C_3H_8 + o\text{-}C_6H_4F_2$	2.3
$i\text{-}C_3H_7F + C_6H_5F \longrightarrow C_3H_8 + m\text{-}C_6H_4F_2$	−2.4
$i\text{-}C_3H_7F + C_6H_5F \longrightarrow C_3H_8 + p\text{-}C_6H_4F_2$	−0.7
$i\text{-}C_3H_7F + C_6H_5CH_3 \longrightarrow C_3H_8 + p\text{-}CH_3C_6H_4F$	−2.4
$i\text{-}C_3H_7F + C_6H_5CF_3 \longrightarrow C_3H_8 + p\text{-}CF_3C_6H_4F$	−1.8

The endothermic character of the reaction in which *o*-difluorobenzene is produced may be due to instability resulting from the interaction of the two juxtaposed carbon–fluorine bond dipoles. Except for this case all these reactions, in which a fluorine atom attached to a secondary sp^3 carbon atom is transferred to a secondary sp^2 carbon atom, are exothermic. On the other hand Kumler, Kun, and Shoolery found that although diethyl oxaloacetate is 79% enolized (as the pure liquid), diethyl fluorooxaloacetate contains no detectable amount of enol,[10] *i.e.*, the transformation



of an sp^3 carbon to which fluorine is attached to an sp^2 carbon is disfavored, relative to the case in which a hydrogen atom is present instead of the fluorine. Perhaps the destabilizing electronegativity effect that accompanied the transformation of an sp^3 carbon–fluorine bond to an sp^2 carbon–fluorine bond is overwhelmed by resonance interaction between the aromatic ring and the unshared electron pairs on fluorine, but in the case of the enol of diethyl fluorooxaloacetate the electron-donating hydroxy substituent increases the electron density of the π system to such an extent that further electron donation from fluorine is minimized (in spite of the two electron-withdrawing carbethoxy groups present) or perhaps the resonance interaction of the hydroxy group with the carbethoxy group with which it is conjugated interferes with resonance interactions between the fluorine atom and the π system to which it is attached.

The preceding arguments suggested that reactions involving the transformation of an sp^3 carbon–fluorine bond to an sp^2 carbon–fluorine bond may be slower or less complete at equilibrium than would be expected without consideration of the electronegativity effect, if the sp^2 carbon–fluorine bond produced is part of a π system that is so rich in electrons that electron donation from the unshared electron pairs of fluorine is minimized. Reactions of this type should include the formation of sp^2-hybridized carbanions by removal of a proton from a saturated carbon atom to which fluorine is attached. Hence we have studied the effect of α substituents on the rate of the base-catalyzed deuterium exchange of methyl acetate.

Kinetic Results

The rate of methoxide ion catalyzed deuterium exchange of a number of substituted methyl acetates has been studied in methanol-*d* solution. The rate of reaction was followed by infrared measurements at 3360 cm^{-1} where the protiomethanol formed in the reaction absorbs strongly. The following reaction mechanism was assumed.

$$XCH_2CO_2Me + MeO^- \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} X\bar{C}HCO_2Me + MeOH$$

$$X\bar{C}HCO_2Me + MeOD \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} XCHDCO_2Me + MeO^-$$

$$XCHDCO_2Me + MeO^- \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} X\bar{C}DCO_2Me + MeOH$$

$$X\bar{C}DCO_2Me + MeOD \underset{k_{-4}}{\overset{k_4}{\rightleftharpoons}} XCD_2CO_2Me + MeO^-$$

To permit a simplified treatment we have neglected secondary isotope effects (*i.e.*, assumed that $k_1 = 2k_3$, $k_{-4} = 2k_{-2}$, $k_{-1} = k_{-3}$, and $k_2 = k_4$) and isotope effects on equilibria (*i.e.*, $k_1/k_{-1} = k_{-4}/k_4 = 2k_{-2}/k_2 = 2k_3/k_{-3}$). These two approximations permit us to equate all the primary kinetic isotope effects ($k_1/2k_{-2} = k_{-1}/k_2 = 2k_3/k_{-4} = k_{-3}/k_4 = i$). The net rate of formation of protiomethanol may be expressed

$$\frac{d[MeOH]}{dt} = k_1[MeO^-]([XCH_2CO_2Me] + {}^1/_2[XCHDCO_2Me]) - k_{-1}[MeOH]([X\bar{C}HCO_2Me] + [X\bar{C}DCO_2Me])$$

Expressions obtained from the steady-state approximation for the two intermediate carbanions were substituted into this as were several relationships demanded by the stoichiometry of the reaction. These substitutions and the assumed absence of an equilibrium isotope effect yield the equation

$$\frac{d[MeOH]}{dt} = \frac{k_1}{2}[MeO^-]\left[\frac{d(2a+b) - [MeOH](2a+d)}{d + (i-1)[MeOH]}\right] \quad (4)$$

(5) (a) C. R. Patrick, *Tetrahedron*, **4**, 26 (1958); *Advan. Fluorine Chem.*, **2**, 1 (1961); (b) J. Hine, *J. Am. Chem. Soc.*, **85**, 3239 (1963).

(6) J. R. Lacher, A. Kianpour, and J. D. Park, *J. Phys. Chem.*, 60, 1454 (1956).

(7) J. Hine and R. D. Weimar, Jr., *J. Am. Chem. Soc.*, **87**, 3387 (1965).

(8) F. D. Rossini, K. S. Pitzer, R. L. Arnett, R. M. Braun, and G. C. Pimentel, "Selected Values of Physical and Thermodynamic Properties of Hydrocarbons and Related Compounds," Carnegie Press, Pittsburgh, Pa., 1953.

(9) W. D. Good and D. W. Scott, *Pure Appl. Chem.*, **2**, 77 (1961).

(10) W. D. Kumler, E. Kun, and J. N. Shoolery, *J. Org. Chem.*, **27**, 1165 (1962).

where $a = [XCH_2CO_2Me]_0$, $b = [MeOH]_0$, and $d = [MeOD]_0$. However, we did not use eq 4 since we did not know the value of i, the primary deuterium kinetic isotope effect, and it was not convenient to determine it. Instead we treated the reaction as a simple pseudo-first-order reversible reaction, first order in the concentration of base (constant within any given run) and first order in the term $[MeOH]_{eq} - [MeOH]$.

$$\frac{d[MeOH]}{dt} = k_{obsd}[MeO^-]([MeOH]_{eq} - [MeOH]) \quad (5)$$

When a value for the equilibrium concentration of protiomethanol is substituted into eq 5 from the equilibrium expression

$$[MeOH]_{eq}/(b + d) = (2a + b)/(2a + b + d)$$

and the resulting equation is rearranged, we obtain

$$\frac{d[MeOH]}{dt} = k_{obsd}[MeO^-]\left[\frac{(b + d)(2a + b) - [MeOH](2a + b + d)}{2a + b + d}\right] \quad (6)$$

Equation 6 may be seen to be a form of eq 4 in which d, the initial concentration of methanol-d, has been replaced by $b + d$, the total concentration of methanol, the term $(i - 1)[MeOH]$ has been replaced by $2[XCH_2CO_2Me]_0$, and $k_1/2$ has been replaced by k_{obsd}. The replacement of d by $(b + d)$ has little effect on the magnitude of the term in large brackets because it is made in both the numerator and the denominator and because d was at least forty times as large as b in all our experiments. The replacement of the term $(i - 1)\cdot[MeOH]$ by $2[XCH_2CO_2Me]_0$ may be somewhat more serious, especially when large concentrations of ester are used so that large concentrations of protiomethanol are formed. If i, the primary deuterium isotope effect, is equal to 1.0, the ratio of the magnitude of the term in large brackets in eq 4 to that of the corresponding term in eq 6 will not change significantly during the course of a run. However, if i is equal to 10.0, in the most unfavorable case, the exchange of 0.990 M methyl propionate, the ratio of the bracketed term in eq 4 to that in eq 6 will drop from 0.93 at the beginning of the reaction to 0.67 at 59%, when the last point was taken. Thus the instantaneous first-order rate constants should drop by about $^{26}/_{93}$ or 28% during the part of the reaction studied, and therefore the integrated rate constants should decrease by about 14% during this time. Actually first-order rate plots calculated from the following integrated form of eq 5 (eq 7) in this run and in

$$k_{obsd}t[MeO^-] = 2.303 \log \frac{[MeOH]_\infty - [MeOH]_0}{[MeOH]_\infty - [MeOH]} \quad (7)$$

other runs where protiomethanol was produced in concentrations of 1 M or more seemed to show slopes that decrease slightly with increasing time, but rarely by more than about 5%. For this reason we believe that eq 6 (and hence eq 7) is a satisfactory approximation to eq 4. The values of k_{obsd} obtained from eq 7 may be seen to be equal to $k_1/2$, the rate constant for carbanion formation *per α-hydrogen*. It may be shown that eq 7 will also yield the statistically corrected rate constant in other cases, where the number of α-hydrogen atoms differs from two. If the primary deuterium kinetic isotope effect is 10.0 the carbanion formation rate constants obtained from eq 7 may be as much as 20% too low. Since the kinetic isotope effect is probably smaller than 10.0 the error is probably smaller than this; furthermore, to the extent to which the isotope effect is the same for all the reactants and to which about the same concentrations of protiomethanol are produced in the various runs, the errors resulting from using eq 7 will tend to be the same for the different compounds, and the *relative* magnitudes of the rate constants will not be affected. To help minimize errors owing to the use of eq 7, in those runs in which relatively large concentrations of protiomethanol were formed and some of the last points taken tended to lie below the best straight line described by the earlier points, these last points were ignored.

In Table I are listed the average values (and average deviations from these values) of the rate constants obtained for the various compounds studied. Except where noted, for each compound at least two different runs were made using sodium methoxide concentrations that differed, usually by more than 50%. The sodium methoxide concentrations ranged from 0.004 M for methyl phenylacetate and about 0.01 M for the more reactive of the other esters up to 0.6 M for the less reactive esters.

Table I. Rate Constants for Sodium Methoxide Catalyzed Deuterium Exchange of Methyl Esters in Methanol-d at 35.0°

Ester	k, M^{-1} sec^{-1} [a]
HCH_2CO_2Me	$(1.26 \pm 0.04) \times 10^{-3}$
$MeCH_2CO_2Me$	$(1.64 \pm 0.01) \times 10^{-4}$
$EtCH_2CO_2Me$	$(1.29 \pm 0.04) \times 10^{-4}$
$PhCH_2CO_2Me$ [b]	$>4 \times 10^{-1}$
$PhCH_2CH_2CO_2Me$	$(5.53 \pm 0.21) \times 10^{-4}$
$(CH_2CO_2Me)_2$	$(3.58 \pm 0.12) \times 10^{-3}$
$MeOCH_2CO_2Me$	$(9.24 \pm 0.12) \times 10^{-4}$
$MeOCH_2CH_2CO_2Me$	$(2.59 \pm 0.09) \times 10^{-2}$
$EtOCH_2CH_2CO_2Me$ [b]	$(8 \pm 3) \times 10^{-3}$
$(MeO)_2CHCO_2Me$	$(1.25 \pm 0.15) \times 10^{-5}$
FCH_2CO_2Me	$(2.28 \pm 0.01) \times 10^{-3}$
F_2CHCO_2Me	$(7.55 \pm 0.05) \times 10^{-6}$

[a] Rate constants calculated from eq 7 and essentially equal to the second-order rate constant per α-hydrogen atom for the formation of carbanions from methoxide ions and the given ester. [b] Result of only one run.

Discussion

It might be suggested that the reactions of some of the esters, especially those with strongly electron-withdrawing substituents, may be complicated by transformation of significant fractions of the esters to complexes in which methoxide ions or methanol has added to the carbonyl groups. Bender has shown that in di-*n*-butyl ether sodium methoxide adds to ethyl trifluoroacetate and, to decreasing extents, to ethyl difluoroacetate and fluoroacetate.[11] In methanol solution, however, he found no evidence for the addition of sodium methoxide to ethyl trifluoroacetate. In neither diethyl ether nor the pure alcoholic solvent could he detect any addition of methanol or ethanol to ethyl trifluoroacetate. It therefore seems very unlikely that any of the esters we have studied existed to any sig-

(11) M. L. Bender, *J. Am. Chem. Soc.*, 75, 5986 (1953).

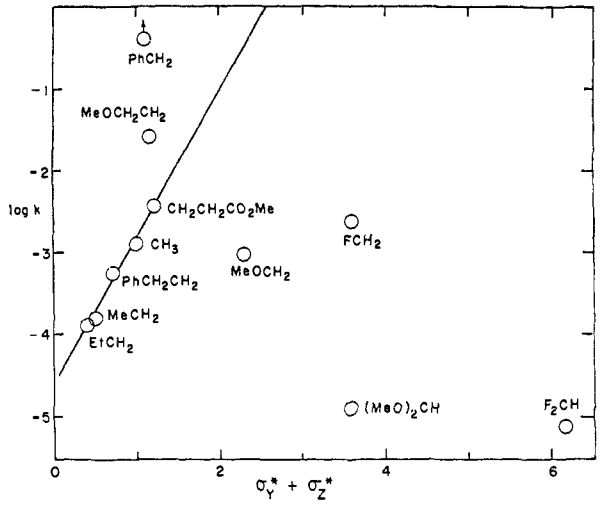


Figure 1. Log of rate constants, per α-hydrogen, for the methoxide ion catalyzed deuterium exchange of esters of the type $YZCHCO_2Me$ *vs.* $\sigma_Y^* + \sigma_Z^*$. Each point is labeled with the appropriate YZCH. The point with an arrow is a minimum value for log k.

nificant extent as complexes under the conditions employed.

We have attempted a Taft equation correlation of our results by plotting log k *vs.* $\sigma_Y^* + \sigma_Z^*$ where Y and Z are the substituents in the reaction

$$YZCHCO_2Me + MeO^- \longrightarrow YZ\bar{C}CO_2Me + MeOH$$

In most cases Y is hydrogen and in one case Z is, too. For most of the substituents σ^* values are directly available, but for three substituents the useful but fallible rule that σ_Y^* is equal to $2.8\sigma^*_{CH_2Y}$ was employed.[12] Thus σ_{OMe}^* and σ_F^* were taken as 2.8 times $\sigma_{CH_2OMe}^*$ and $\sigma_{CH_2F}^*$, respectively, and $\sigma_{CH_2CO_2Me}^*$ was taken as $^1/_{2.8}$ times $\sigma_{CO_2Me}^*$.

Methyl phenylacetate is so reactive that only a minimum value for its rate constant was obtained. This is not important, however, since a point for this compound does not belong in a correlation of inductive effects; the resonance effect of the phenyl substituent would be expected to facilitate carbanion formation markedly in this case.

As seen in Figure 1, the best straight line through the remaining points would have a negative slope. Such a line, corresponding to carbanion formation being slowed by electron-withdrawing groups, would give an implausible picture of the nature of inductive effects in this reaction. Our procedure has instead been to estimate the reactivities that would be expected (from the inductive effect) for the α-fluoro and α-methoxy esters. This was done by consideration of the points for the other six compounds. Five of these points lie within the experimental uncertainty of a straight line, but the point for methyl β-methoxypropionate, which is unexpectedly reactive, deviates markedly. At first it was thought that this might be due to the occurrence of a concerted β-elimination reaction in which the methyl β-methoxypropionate was transformed to methyl acrylate, which would then be expected to undergo base-catalyzed addition of methanol-*d*. It was then assumed that if methanol was eliminated from the β-methoxypropionate by a concerted mechanism, ethanol would probably be eliminated from the β-ethoxypropionate in an analogous fashion. In the latter case the elimination would be much more easily detectable since the net result, after addition of methanol-*d* to the initially formed methyl acrylate, would be to transform the β-ethoxypropionate to β-methoxypropionate.

$$EtOCH_2CH_2CO_2Me \xrightarrow{MeO^-} EtOH + CH_2{=}CHCO_2Me$$

$$MeOD + CH_2{=}CHCO_2Me \xrightarrow{MeO^-} MeOCH_2CHDCO_2Me$$

However, the base-catalyzed D exchange of methyl β-ethoxypropionate in methanol-*d* was found to be accompanied by essentially no exchange of the ethoxy group for methoxy. We have no convincing explanation for the unexpectedly large activating effect of the methoxymethyl substituent. It may be noted that a qualitatively similar but smaller deviation has been reported by Streitwieser, Marchand, and Pudjaatmaka for the effect of a methoxymethyl substituent on the rates of carbanion formation from 9-substituted fluorenes in the presence of methanolic sodium methoxide.[13]

The least-squares line through the best five points is shown in Figure 1. Its slope, the Taft ρ^* for the reaction, is 1.78; if the point for methyl β-methoxypropionate is included, a value of 2.32 is obtained.

It may be argued that the good agreement obtained with the substituent hydrogen, *i.e.*, the ester methyl acetate, is merely a coincidence. The hydrogen substituent is notorious for its tendency to deviate in Taft equation correlations. According to Ritchie's argument, if σ^* is considered solely as a measure of the inductive effect of a substituent it should be assigned the value zero for hydrogen and all unsubstituted saturated primary alkyl groups.[14,15] If this procedure is used in the present case, it leaves the four points for methyl butyrate, propionate, β-phenylpropionate, and succinate still very near a straight line with a slope of about 1.8 and the point for hydrogen almost one unit above this line.

In view of these deviations or possible deviations from a correlation of reactivity with the inductive effect, it is worthwhile to point out that the Taft ρ^* value for this reaction would be expected to be of approximately the magnitude observed. For a carbanion formation reaction of the type studied, ρ^* would be expected to be positive and to be smaller than the ρ^* values for the acidity of ammonium ions, which are around 3.2.[16] The smaller ρ^* in the present case would be expected because there is only a partial charge on the carbon atom to which the substituents are attached, partly because in the transition state the carbanion is only partially formed, and partly because much of the charge is distributed onto the carbomethoxy group, whereas in ionization of amines the ammonium ions produced have a full positive charge, largely localized on the atom to which the substituents are attached.

It might be thought that electronegativity effects would be accounted for automatically in a Taft equation correlation. Sager and Ritchie, for example,

(12) J. Hine, "Physical Organic Chemistry," 2nd ed, McGraw-Hill Book Co., Inc., New York, N. Y., 1962, Section 4-4.

(13) A. Streitwieser, Jr., A. P. Marchand, and A. H. Pudjaatmaka, *J. Am. Chem. Soc.*, **89**, 694 (1967).

(14) C. D. Ritchie, *J. Phys. Chem.*, **65**, 2091 (1961).

(15) C. D. Ritchie and W. F. Sager, *Progr. Phys. Org. Chem.*, **2**, 323 (1964).

(16) H. K. Hall, Jr., *J. Am. Chem. Soc.*, **79**, 5441 (1957).

have shown that Pauling's equation may be used to derive a linear free energy relationship of the form of the Hammett and Taft equations in which the substituent constants become group electronegativities.[17] Furthermore, it is known that the replacement of sp^3 carbon atoms in substituent groups by sp^2 carbon atoms and then by sp carbon atoms leads to increasing substituent constants (corresponding to increasing group electronegativity). However, although there are useful correlations between Taft substituent constants and Pauling's electronegativity values that apply for limited numbers of cases, there are major deviations from any general quantitative correlation. Thus, for example, although the Pauling electronegativities stand in the order O > Cl > C = I for the four elements indicated, the values of σ^* for the corresponding XCH_2 (or $HXCH_2$ or H_3XCH_2) groups stand in the order Cl > I > O > C.

In view of the fact that Pauling's electronegativities often parallel Taft substituent constants rather poorly, we have entertained the hypothesis that for the correlation of rates and equilibria one must consider Taft substituent constants and Pauling electronegativities (with the electronegativity being unique for a given element in a given state of hybridization) as two different factors. That is, we have considered that we are dealing with a two-mechanism interaction.[18] Electronegativity effects in terms of Pauling's equation could be written in any reaction in which a bond is broken or formed or in which the hybridization of any atom is changed. However, in most of the reactions for which rate and equilibrium data have been correlated using linear free energy relationships, the electronegativity effects thus calculated would either cancel each other for the individual reactions or would be the same for every reaction in the series. If the equilibrium between the reactants and the transition state for our general reaction is depicted

$$YZCHCO_2Me + MeO^- \rightleftharpoons \left[\begin{array}{c} CO_2Me \\ | \\ YZC\text{--}H\text{--}OMe \end{array}\right]^-$$

and the reaction of methyl acetate is chosen as the standard for comparison, it may be seen that the only difference between the general reaction and the standard reaction is that in the former case bonds from Y and Z to an sp^3 carbon atom have been changed to bonds from Y and Z to the transition-state α-carbon atom (probably nearly sp^2 hybridized), whereas in the latter case two bonds from hydrogen to sp^3 carbon have been changed to bonds from hydrogen to the transition-state α-carbon atom. From the Pauling equation (1) it may be shown that this difference should lead to the activation energy increment[19]

$$E_a^{YZ} - E_a^{HH} = -46(X_C\pm - X_{sp^3C}) \times (X_Y - X_H + X_Z - X_H) \quad (8)$$

where E_a^{YZ} is the activation energy for the YZ-substituted compound, E_a^{HH} is that for methyl acetate, and $X_C\pm$, X_{sp^3C}, X_Y, X_H, and X_Z are the electronegativity values for the transition-state α-carbon atom, sp^3C, Y, hydrogen, and Z, respectively. The electronegativities of Y and Z are simply the electronegativities of the elements in Y and Z that are bonded to the α-carbon atom. The differences in activation energy shown in eq 8 would lead to a rate increment which may be combined with the rate increment calculated from the simple Taft equation to give

$$\log (k_{YZ}/k_{HH}) = \rho^*(\sigma_Y^* + \sigma_Z^* - 2\sigma_H^*) + \rho^E(X_Y + X_Z - 2X_H) \quad (9)$$

where k_{YZ} and k_{HH} are the rate constants for the YZ-substituted compound and methyl acetate and

$$\rho^E = -\frac{46(X_C\pm - X_{sp^3C})}{2.3RT} \quad (10)$$

Since ρ^* has already been evaluated and σ^* and electronegativity values for Y, Z, and H are known, a plot of the left-hand side of the following equation *vs.* $X_Y + X_Z - 2X_H$ should yield a straight line of slope ρ^E.

$$\log (k_{YZ}/k_{HH}) - \rho^*(\sigma_Y^* + \sigma_Z^* - 2\sigma_H^*) = \rho^E(X_Y + X_Z - 2X_H) \quad (11)$$

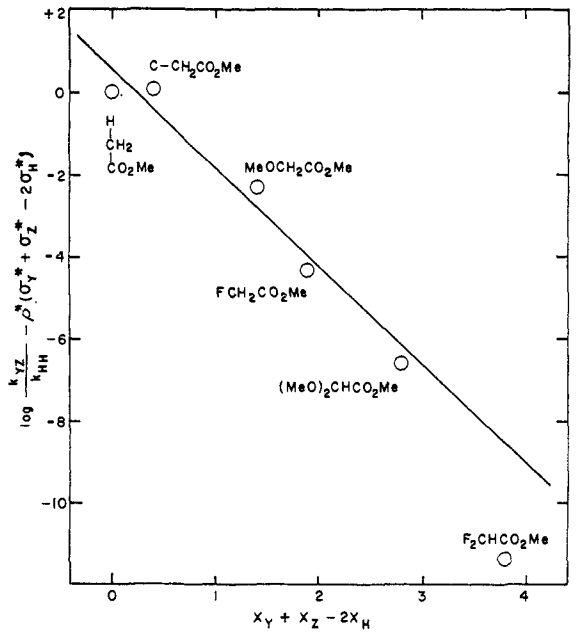


Figure 2. Plot of data from Table I, using eq 11.

Data on all the compounds included in Table I (except methyl phenylacetate and methyl β-methoxypropionate, whose deviations from the Taft plot have already been discussed) are plotted according to eq 11 in Figure 2, using a ρ^* value of 1.78. The points for the four compounds in which the substituent is attached through a carbon atom almost coincided and are labeled C-CH_2CO_2Me collectively. The best straight line has been drawn through the points for the monosubstituted acetates, neglecting the disubstituted acetates for reasons that will be discussed later. The slope of the line, that is, the value of ρ^E, is −2.4. If the hydrogen substituent is given the value zero, as suggested by Ritchie, and ρ^* calculated from the line through the four remaining nearly collinear points in Figure 1, the only

(17) W. F. Sager and C. D. Ritchie, *J. Am. Chem. Soc.*, 83, 3498 (1961).

(18) J. E. Leffler and E. Grunwald, "Rates and Equilibria of Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1963, pp 140–146, 192–194.

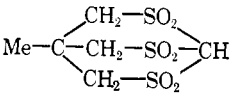
(19) We have neglected entropy effects in this connection and assumed that differences in bond energies will lead to identical differences in activation energies and that rate differences arising from electronegativity effects will be due entirely to activation energy differences.

significant change in Figure 2 is to raise the point for hydrogen by almost one unit, making the four points for monosubstituted compounds more nearly collinear and leading to a ρ^E value of -2.6.

An estimate of the value that would be expected for ρ^E may be based on the differences in electronegativity between sp^2 and sp^3 carbon. According to the calculations of Hinze and Jaffé the electronegativities of the σ orbitals of sp^3, sp^2, and sp carbon are 2.48, 2.75, and 3.29.[20] On the basis of an empirical correlation of force constants, Gordy has assigned sp^3 and sp carbon the electronegativity values 2.55 and 2.83,[21] a much smaller difference than that calculated by Hinze and Jaffé. The change in orbital electronegativity that accompanies changing hybridization calculated by Hinze and Jaffé is much larger than that required to explain our results. However, from Gordy's estimate of 0.28 as the difference in electronegativities of sp and sp^3 carbon and the assumption that such electronegativity differences are proportional to the fraction of s character in the σ orbitals, we may estimate that sp^2 carbon is more electronegative than sp^3 carbon by 0.093 unit. In the transition state for formation of the relatively unstable carbanions that arise in the present study, the hybridization of the α-carbon atom must change from sp^3 almost, but not entirely, to sp^2. Hence, according to eq 10, ρ^E should be negative with an absolute magnitude somewhat smaller than $46(0.093)/2.3RT$ or 3.0. The observed value of ρ^E, -2.4, is that which would be expected if the transition state occurred at 80% carbanion formation. Thus although the magnitude of ρ^E is certainly not predictable it appears to be rationalizable.

It has been pointed out earlier[5b] that the strong tendency of tetrafluoroethylene to undergo addition reactions suggests that at least part of the particular stability associated with the attachment of two (or more) fluorine atoms to the same saturated carbon atom is absent when the two fluorine atoms are attached to the same unsaturated carbon atom. Thus the formation of a carbanion from methyl difluoroacetate should be accompanied by a loss of the stabilization due to the attachment of two fluorine atoms to the sp^3 α-carbon atom of the reactant. For this reason the reactivity of methyl difluoroacetate would be expected to be less than anticipated from eq 11, as it is found to be. The attachment of two oxygen atoms to the same sp^2 carbon atom results in a stabilization of about the same magnitude as that found with two fluorine atoms.[5b] There is less evidence available as to whether part or all of this stabilization is absent when two oxygen atoms are attached to sp^2 carbon, but it is possible that the reactivity of methyl dimethoxyacetate is also decreased by a loss of such stabilization as the hybridization of the α-carbon is changed from sp^3 to sp^2.

We have suggested that although the inductive effect of α-fluoro and α-alkoxy substituents will tend to facilitate the formation of carbanions, there may be an opposing electronegativity effect if the carbon atom to which these substituents are attached changes its hybridization from sp^3 to sp^2. Since this opposing effect would be absent in the formation of an sp^3-hybridized carbanion, it is desirable to compare the effect of α-fluoro and α-alkoxy substituents on rates and equilibria in the formation of sp^3-hybridized carbanions with analogous data on the formation of sp^2-hybridized carbanions. Although clearly relevant data are scarce, observations on the formation of carbanions at the bridgeheads of bicyclic ring systems may be used as evidence for the states of hybridization of various types of carbanions. Oae, Tagaki, and Ohno have found that the base-catalyzed deuterium exchange of such bicyclic orthothioformates as 4-methyl-2,6,7-trithiabicyclo[2.2.2]octane is considerably faster than that of analogous acyclic compounds, such as triethyl orthothioformate.[22] Although decreased steric hindrance may contribute to the large rate of carbanion formation by the bicyclic orthothioformates, we believe that the negatively charged carbon atom of a tris(alkylthio)methyl anion is preferentially not in the same plane as the three sulfur atoms attached to it and that its hybridization is probably near sp^3. By analogy we assume that di- and trihalomethyl anions are also nonplanar with hybridization near sp^3. This assumption is supported by the observations that such isoelectronic species as the nitrogen trihalides are nonplanar. The fact that the bicyclic trisulfone **1** has a pK of 3.3,



1

whereas tris(ethylsulfonyl)methane is too strongly acidic to measure, may be due to a preference by sulfone carbanions for a coplanar geometry.[23] However the fact that **1** is still a rather strong acid suggests that even though the optimum hybridization of a sulfone carbanion is not purely sp^3 it may be intermediate between sp^2 and sp^3.

For the formation of carbanions (as measured by deuterium exchange) by reaction with sodium methoxide in methanol-*d* at 36°, Duke has determined rate constants (per hydrogen atom) of 3.1×10^{-6} and 18×10^{-6} M^{-1} sec^{-1} for methylene bromide and methylene iodide.[24] The effect of α-fluorine substituents on the reactivity may be estimated from the rates of hydroxide ion catalyzed deuterium exchange of dibromofluoromethane-*d* and diiodofluoromethane-*d* in water at 0–25°.[25] Extrapolation of these data to 36° (by use of the Arrhenius equation) gives rate constants of 2.9 and 6.0 M^{-1} sec^{-1}, respectively. Chloroform-*d* exchanges deuterium 11 times as rapidly in the presence of aqueous sodium hydroxide as in the presence of methanolic sodium methoxide, and 2,2-dichloro-1,1,1-trifluoroethane, 2-bromo-2-chloro-1,1,1-trifluoroethane, 2,2-dibromo-1,1,1-trifluoroethane, and 2,2-diiodo-1,1,1-trifluoroethane exchange from 5 to 13 times as rapidly in the presence of aqueous sodium hydroxide.[26] On this basis we assume that dibromofluoromethane-*d* and diiodofluoromethane-*d* would be one-tenth as reactive toward methanolic sodium methoxide as toward

(20) J. Hinze and H. H. Jaffé, *J. Am. Chem. Soc.*, **84**, 540 (1962).
(21) W. Gordy, *J. Chem. Phys.*, **14**, 305 (1946).
(22) S. Oae, W. Tagaki, and A. Ohno, *J. Am. Chem. Soc.*, **83**, 5036 (1961); *Tetrahedron*, 20, 417, 427 (1964).
(23) W. von E. Doering and L. K. Levy, *J. Am. Chem. Soc.*, 77, 509 (1955).
(24) R. B. Duke, Ph.D. Thesis, Georgia Institute of Technology, 1967.
(25) J. Hine, R. Butterworth, and P. B. Langford, *J. Am. Chem. Soc.*, 80, 819 (1958).
(26) J. Hine, R. Wiesboeck, and R. G. Ghirardelli, *ibid.*, **83**, 1219 (1961).

aqueous sodium hydroxide. The resultant estimated rate constants for methoxide ion catalyzed deuterium exchange in methanol, 0.29 and 0.60 M^{-1} sec^{-1}, respectively, would be smaller for the protium compounds because of a primary deuterium kinetic isotope effect. However, k_H/k_D for carbanion formation by haloforms has been found to be in the range 1.4–1.7.[27,28] Furthermore, methoxide ions in methanol-*d* are around 50% more nucleophilic than in protiomethanol,[24,29] just as deuterioxide ions in deuterium oxide are more nucleophilic than hydroxide ions in protium oxide.[30] We have assumed that the solvent kinetic isotope effect and the primary kinetic isotope effect will cancel each other and therefore that 0.29 and 0.60 M^{-1} sec^{-1} are also the rate constants for the formation of carbanions from methoxide ions and dibromofluoromethane and diiodofluoromethane in methanol-*d*. Comparison with the data on the methylene halides then shows that an α-fluoro substituent increases the rate of carbanion formation, per hydrogen atom, by 90,000-fold and 33,000-fold in the cases of methylene bromide and methylene iodide, respectively. If an α-fluoro substituent had increased the rate of carbanion formation of methyl acetate by 38,000-fold, the point for FCH_2 in Figure 1 would lie on the line. Thus, the extent to which α-fluorine increases the rate of carbanion formation by methylene bromide and iodide is in the vicinity of that which would be expected from the inductive effect of fluorine.

Hochberg and Bonhoeffer found that the rate constant for carbanion formation from dimethyl sulfone and deuterioxide ions in deuterium oxide at 0° is 8×10^{-5} M^{-1} sec^{-1} per hydrogen atom.[31] The rate constant for the formation of carbanions from phenyl difluoromethyl-*d* sulfone and hydroxide ions in protium oxide at 0° is 6000×10^{-5} M^{-1} sec^{-1}.[32] A little of the greater reactivity of the latter compound is probably due to the presence of a phenyl group instead of a methyl group (benzoic acid is almost four times as strong as acetic acid). In the absence of a reported primary deuterium kinetic isotope effect for the formation of carbanions from sulfones, it is difficult to tell very accurately the effect of the two α-fluorine substituents, but they appear to increase the rate of carbanion formation by at least 1000-fold. This is in sharp contrast to the 170-fold deactivating effect of two α-fluoro substituents on the rates of methoxide ion catalyzed deuterium exchange of methyl esters. However, in view of the $10^{4.6}$-fold activating effect per α-fluorine that may be calculated from the ρ^* value of 1.78 observed for the deuterium exchange of methyl esters, and the $10^{4.9}$- and $10^{4.5}$-fold activating effects of α-fluoro substituents observed for methylene bromide and methylene iodide, two α-fluorine atoms would have been expected to increase the reactivity of phenyl methyl sulfone by about 10^9-fold in the formation of sp^3-hybridized carbanions. The smaller effect actually observed may be rationalized in terms of our suggestion that the hybridization of the negative carbon atom in a sulfone carbanion is intermediate between sp^2 and sp^3. However, the possibility of changes in the amount of stabilization due to the attachment of two fluorine atoms to the same carbon atom complicates any interpretation of the rates of formation of carbanions from phenyl difluoromethyl sulfone.

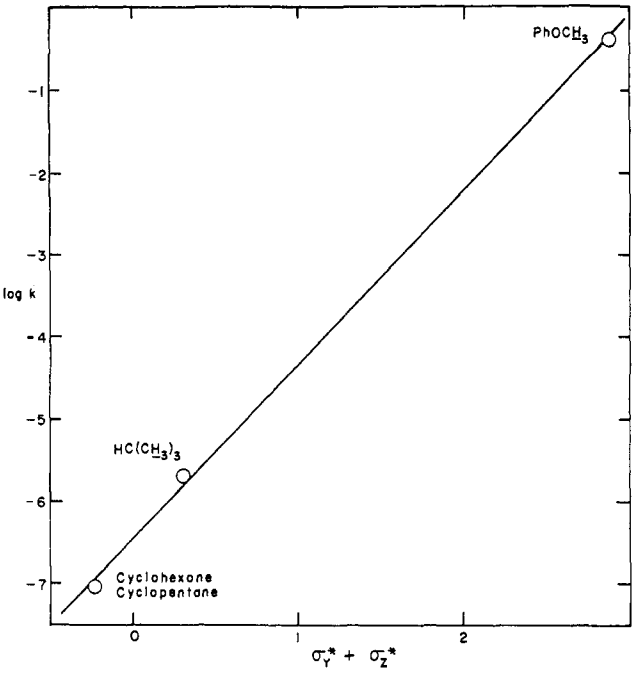


Figure 3. Log of rate constants, per α-hydrogen, for the potassium amide catalyzed deuterium exchange of the underlined hydrogen atoms in compounds of the type $YZC\underline{H}_2$.

We have found no reports of the effect of α-alkoxy substituents on the rates of formation of sp^3-hybridized carbanions. However, Shatenshtein and co-workers have made relevant observations on the effect of aryloxy substituents. From the data of these workers and the assumption that the reaction is first order in potassium amide and first order in hydrocarbon, second-order rate constants of 8.9×10^{-8} and $9.3 \times 10^{-8} M^{-1}$ sec^{-1} may be calculated for the deuterium exchange of cyclopentane and cyclohexane, respectively, and 2×10^{-6} M^{-1} sec^{-1} for the dedeuteration of the methyl groups of isobutane in liquid ammonia at 120°.[33] A similar assumption gives a rate constant of 5.2×10^{-4} M^{-1} sec^{-1} for the dedeuteration of methyl-d_3 phenyl ether at 25°.[34] In order to allow for the difference in temperature we have assumed that the rate of *meta* dedeuteration of diphenyl ether, which has been studied at −20, −10, and 0°,[35] differs from that of $C_6H_5OCD_3$ only because of differences in the Arrhenius activation energy. This leads to an activation energy of 16.3 kcal/mole, from which a rate constant of 0.42 M^{-1} sec^{-1} may be calculated for the dedeuteration of methyl-d_3 phenyl ether at 120°. We then made a Taft equation correlation of the ratio of potassium amide catalyzed deuterium exchange of compounds of the type $YZCH_2$ at 120°. For cyclopentane and cyclohexane it was assumed that the reaction rate was the same as it would be if Y and Z were both *n*-propyl groups. A plot of log *k* *vs.* $\sigma_Y^* + \sigma_Z^*$ is shown in Figure 3.

(27) J. Hine and N. W. Burske, *J. Am. Chem. Soc.*, 78, 3337 (1956).
(28) J. Hine, N. W. Burske, M. Hine, and P. B. Langford, *ibid.*, 79, 1406 (1957).
(29) S. Andreades, *ibid.*, 86, 2003 (1964).
(30) *Cf.* S. H. Maron and V. K. La Mer, *ibid.*, 60, 2588 (1938).
(31) J. Hochberg and K. F. Bonhoeffer, *Z. Physik. Chem.*, A184, 419 (1939).
(32) J. Hine and J. J. Porter, *J. Am. Chem. Soc.*, 82, 6178 (1960).
(33) A. I. Shatenshtein, *Advan. Phys. Org. Chem.*, 1, 155 (1963).
(34) A. I. Shatenshtein and A. V. Vedeneev, *J. Gen. Chem. USSR*, 28, 2672 (1958).
(35) A. I. Shatenshtein, A. N. Talanov, and Yu. I. Ranneva, *ibid.*, 30, 604 (1960).

Although the data are statistically corrected, no correction has been made for primary deuterium kinetic isotope effects or deuterium solvent kinetic isotope effects. The points fall very near a straight line, whose slope, 2.1, is plausible for a carbanion formation reaction, especially when it is considered that if the differences in reaction rate are due to differences in activation energies, the slope (ρ^*) would be 2.8 at 25°. Thus the effect of the phenoxy substituent is about that which would be expected from its inductive effect.

There are several reports, most of which have appeared since this work was begun, of the effects of α-alkoxy and α-fluoro substituents on the rate and equilibrium constants for formation of carbanions with probable concomitant change in the hybridization of carbon from sp^3 to sp^2. From Cram, Kingsbury, and Rickborn's runs 16 and 21, methyl α-phenylethyl ether may be estimated to form carbanions in the presence of potassium *t*-butoxide and dimethyl sulfoxide–*t*-butyl alcohol at about three times the rate that 2-phenylbutane does.[36] This difference in reactivity between corresponding α-methoxy- and α-ethyl-substituted compounds is even smaller than we have observed and strongly suggests that in the case of methyl α-phenylethyl ether carbanion formation is considerably slower than would be expected from the inductive effect of the methoxy substituent. Recent studies of the deuterium exchange of methoxyacetone[37,38] have shown that carbanion formation at the methoxylated methylene carbon atom is from 0.15 to 1.3 times as fast as at the methyl carbon atom, depending on the nature of the base. This corresponds to rates from 3 to 10 times those of acetone,[37,39] an effect considerably smaller than the 200-fold activating effect that would be expected from a ρ^* of 1.78 and the σ^* value we have used for the methoxy substituent.

Cram and Lorand's report that each of the four nonring hydrogen atoms of *m*-methylbenzal fluoride undergoes deuterium exchange with potassium *t*-butoxide in *t*-butyl alcohol-*d* at about the same rate[40] provides evidence that the hydrogen atom with two α-fluoro substituents is removed much more slowly than would be expected from the rate of exchange of the other hydrogens and the inductive effect of fluorine. Cram's explanation in terms of the large p character of the carbon–fluorine bonds is related to the reason why sp^2 carbon has a higher electronegativity than sp^3 carbon. In the case of *m*-methylbenzal fluoride it seems probable that loss of stabilization associated with the attachment of two fluorine atoms to the same saturated carbon atom will also tend to decrease the rate of carbanion formation at the difluorinated carbon atom.

Recently Subrahmanyan, Malhotra, and Ringold have reported that both axial and equatorial 4-fluoro substituents in androst-4-ene-3,17-dione increase the rate of removal of the 4-hydrogen atoms by potassium *t*-butoxide, and the equatorial substituent also increases the equilibrium constant for this proton removal reaction.[41] This activating influence of fluorine was attributed to the inductive effect *and* to resonance interactions of the fluorine atom with the extended π system. It was noted that such resonance interaction may be encouraged by the existence of the carbanion as part of an ion pair and by the large size of the π system, which could thus more easily accommodate two negative charges. The activating effects of fluorine, 13-fold and 90-fold, are much smaller than would be expected from an inductive and a resonance stabilization effect in the absence of any deactivating effect.

Other observations relevant to the present work have also appeared, in the form of data on the ionization constants of α-fluoronitroalkanes. Adolph and Kamlet have found that the ionization constants of ethyl nitroacetate, α-nitroacetamide, chloronitromethane, and dinitromethane[42] are all decreased by the introduction of an α-fluoro substituent, although they are all increased by the introduction of α-chlorine.[43] The increases in pK_a (per α-hydrogen) brought about by the fluorine substituent were 0.23, 0.41, 2.64, and 3.83, respectively. The application of equilibrium data rather than rate data to the study of the effect of α-fluorine substituents on carbanion formation has the advantage of eliminating the uncertainties concerning the nature of the transition state. A satisfactory Taft equation correlation of these data on the acidity of aliphatic nitro compounds would permit a more quantitative discussion. A Taft correlation has been reported but the only α-substituents present were hydrogen, chlorine, nitro, and saturated primary alkyl groups.[44] The σ^* constants for saturated primary alkyl groups differ very little from each other, as α-substituents on a carbanion, both nitro and chlorine, are believed to be capable of important resonance effects; and hydrogen is particularly prone to deviations from the Hammett equation.[14,15]

According to all the available data α-alkoxy and α-fluorine substituents either decrease the rate and equilibrium constants for formation of carbanions believed to be sp^2 hybridized or they increase them to a much smaller extent than would be expected from the inductive effect. The deviations of the observed values from rate and equilibrium constants to be expected from the inductive effect are larger for fluorine than for alkoxy substituents. In the smaller number of observed cases where the negatively charged carbon atom is significantly or completely sp^3 hybridized, α-fluoro and α-phenoxy substituents increase the reactivity to a much greater extent, an extent that in some cases is about as large as would be expected from the inductive effect. These observations are in qualitative agreement with the hypothesized effect of the difference in electronegativity between sp^2- and sp^3-hybridized carbon.

Experimental Section

Reagents. All the methyl esters were obtained from commercial sources or prepared by standard procedures; all except the succinate (which was purified by fractional freezing) were purified by

(36) D. J. Cram, C. A. Kingsbury, and B. Rickborn, *J. Am. Chem. Soc.*, 83, 3688 (1961).
(37) A. A. Bothner-By and C. Sun, *J. Org. Chem.*, 32, 492 (1967).
(38) J. Hine, K. G. Hampton, and B. C. Menon, *J. Am. Chem. Soc.*, 89, 2664 (1967).
(39) J. R. Jones, *Trans. Faraday Soc.*, 61, 95 (1965).
(40) D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press Inc., New York, N. Y., 1965, p 59.
(41) G. Subrahmanyan, S. K. Malhotra, and H. J. Ringold, *J. Am. Chem. Soc.*, 88, 1332 (1966).
(42) *Cf.* V. I. Slovetskii, L. V. Okhobystina, A. A. Fainzilberg, A. I. Ivanov, L. I. Biryukova, and S. S. Novikov, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 2063 (1965).
(43) H. G. Adolph and M. J. Kamlet, *J. Am. Chem. Soc.*, 88, 4761 (1966).
(44) V. I. Slovetskii, A. A. Fainzilberg, and S. S. Novikov, *Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 924 (1962).

Table II. Kinetics of the Deuterium Exchange of Dimethyl Succinate in the Presence of NaOMe–MeOD[a]

Time, sec	Absorbance	ϵ[MeOH]	$\log \frac{\epsilon[MeOH]_\infty - \epsilon[MeOH]_0}{\epsilon[MeOH]_\infty - \epsilon[MeOH]_t}$
105	0.366	5.56	0.023
408	0.406	6.14	0.048
820	0.433	6.54	0.066
1130	0.459	6.90	0.083
1432	0.493	7.40	0.108
2030	0.547	8.18	0.149
3166	0.622	9.27	0.215
3500	0.655	9.72	0.245
4300	0.708	10.47	0.300
4650	0.734	10.81	0.328
5500	0.780	11.48	0.389
6760	0.839	12.32	0.479
8142	0.887	12.96	0.563
9820	0.976	14.20	0.794

[a] Initial concentrations: dimethyl succinate, 0.210 *M*; MeOH, 0.365 *M*; NaOMe, 0.0431 *M*.

fractional distillation through a spinning-band column. Analysis by gas–liquid partition chromatography showed no impurities in the difluoroacetate, acetate, butyrate, 3-ethoxypropionate, β-phenylpropionate, methoxyacetate, and propionate. Methanol-*d* was prepared from deuterium oxide and trimethyl borate by a procedure based on that of Bunnett and Reinheimer.[45] Solutions of sodium methoxide in methanol-*d* were prepared by washing metallic sodium with a little methanol-*d* and then dissolving the metal in methanol-*d*.

Drying of Methanol. The kinetics of the drying of methanol by use of sodium methoxide and dimethyl phthalate were studied in a manner analogous to that described for the drying of isopropyl alcohol.[46]

$$MeO^- + H_2O \overset{K}{\rightleftharpoons} MeOH + OH^-$$

$$OH^- + RCO_2Me \xrightarrow{k} RCO_2^- + MeOH$$

Inasmuch as water is a weaker acid than methanol[47] and is present in much smaller concentrations, the steady-state approximation may be made for the hydroxide ion. The drying reaction will then be a simple third-order process.

$$-(dW/dt) = dB/dt = KkEWB$$

where E, W, and B are the concentrations of ester, water, and base (methoxide ions), respectively. In this derivation it is assumed that only one carbomethoxy group of the ester (which is used in excess) is hydrolyzed, the negative charge on the *o*-carboxylate anion substituent minimizing further hydrolysis of the half-ester. Using 0.16 *M* sodium methoxide, 0.19 *M* water, and 0.200 *M* dimethyl phthalate a value of $(2.5 \pm 0.5) \times 10^{-3}\ M^{-1}\ sec^{-1}$ was obtained for Kk at 64.5 ± 0.5°. From this value it may be calculated that at base and ester concentrations of 0.5 *M* the concentration of water in a sample of methanol will be reduced by 1000-fold after 3 hr at 64.5°. This calculation and our kinetic treatment depend on the assumption that the drying reaction is irreversible. The equilibrium constant for the reaction might be estimated as follows. The equilibrium expression for the reaction may be written

$$K_e = \frac{[RCO_2^-][MeOH]^2}{[RCO_2Me][H_2O][MeO^-]} = \left(\frac{[RCO_2H][MeOH]}{[RCO_2Me][H_2O]}\right)\left(\frac{[H^+][RCO_2^-]}{[RCO_2H]}\right)\left(\frac{[MeOH]}{[H^+][MeO^-]}\right) = \frac{K_hK_a}{K_m}$$

where K_h is the equilibrium constant for the neutral hydrolysis of the ester, a number that would be expected to be within a power of ten of unity,[48] K_a is the ionization constant of the acid (about 10^{-3}, like phthalic acid), and K_m is the ionization constant of methanol (about 10^{-15} since it is slightly stronger than water). It follows then that K_e is about 10^{12}. This is large enough so that reversibility would not invalidate any of the statements made so far in this paragraph. However, with several tenths molar carboxylate anion, ester, and methoxide ions in methanol the water concentration would drop to an equilibrium value of around 10^{-11} *M* (after about 12 hr). It would not drop to the level of one molecule per liter as erroneously claimed in the paper on isopropyl alcohol, in which the reversibility of the reaction was ignored.[46]

Analysis for Protiomethanol in Methanol-*d*. The concentration of protiomethanol in methanol-*d* solutions was determined by infrared measurements, using a Perkin-Elmer spectrophotometer, Model 21, on the O–H stretching band at 3360 cm^{-1}. The method used is based on one devised by Duke.[24] The extinction coefficient of protiomethanol at 3360 cm^{-1} was determined by adding known amounts of protiomethanol to methanol-*d* solutions. It was found to decrease with increasing concentration of sodium methoxide in the solution, following the equation

$$\epsilon = 137.3 - 13.1[CH_3ONa]$$

The methanol solutions slowly dissolved the windows of the sodium chloride cells used so that it was necessary to redetermine the length of the light path (by measurements on the 1960-cm^{-1} band of benzene as described by the manufacturer of the spectrophotometer) rather frequently and, less frequently, to disassemble the cell and refinish the windows.

Kinetic Procedure. The following procedure used in the case of dimethyl succinate is typical of that used for the deuterium exchange of methyl esters in methanol-*d*. A 25-ml erlenmeyer flask was dried in an oven, cooled under dry nitrogen, and capped with a rubber septum that had been boiled in acetone, dried, and stored in a desiccator. Using dry syringes, 1.1760 g of 0.34 *M* sodium methoxide in methanol-*d* and 8.248 g of methanol-*d* were added to the flask, which was vented during the addition. Then 0.3667 g of dimethyl succinate was added by syringe and within 1 min the flask was weighed, placed in a 35.0° constant temperature bath, and shaken. A timer was started when the flask was placed in the bath and at recorded times samples were removed, placed in ~0.05-mm cells, and analyzed within 2 min by infrared measurements as indicated in the previous section. Some of the samples taken were titrated acidimetrically for their sodium methoxide content. The concentration of ester in the reacting solution was calculated from the known density of the ester, the density of the solution of sodium methoxide in methanol-*d*, and the assumption that the volume of the solution is equal to the sum of the volumes of the ester and the sodium methoxide solution. The initial concentration of protiomethanol was estimated, by extrapolation from the first points, to

(45) J. F. Bunnett and J. D. Reinheimer, *J. Am. Chem. Soc.*, **84**, 3285 (1962).
(46) J. Hine and K. Tanabe, *J. Phys. Chem.*, **62**, 1463 (1958).
(47) J. Hine and M. Hine, *J. Am. Chem. Soc.*, **74**, 5266 (1952).
(48) *Cf.* N. Menshutkin, *Ann.*, **195**, 334 (1879); **197**, 193 (1879).

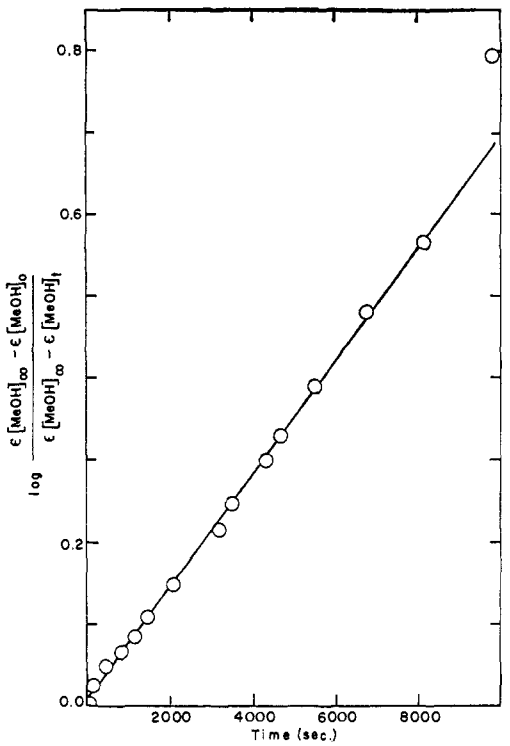


Figure 4. Kinetic plot for the deuterium exchange of dimethyl succinate.

be 0.365 *M*. According to the Beer–Lambert law

$$A = \epsilon[\mathrm{MeOH}]l$$

where A is the absorbance, ϵ the extinction coefficient, and l the path length. At the beginning of the reaction the path length was found to be 0.0657 mm, at 3500 sec it was 0.0674 mm, and at 9820 sec, 0.0687 mm. At intermediate points the path length was calculated from the assumption that it was a linear function of the number of points that had been taken. From these path lengths and the absorbances determined, a value of ϵ[MeOH] was calculated at each point. The value of $\epsilon[\mathrm{MeOH}]_\infty$ was calculated by assuming that there is no isotope effect on the equilibrium constant for deuterium exchange. This assumption leads to the equation

$$[\mathrm{MeOH}]_\infty = [\mathrm{MeOH}]_0 + \frac{24n[\mathrm{ester}]}{n[\mathrm{ester}] + [\mathrm{MeOH}]_0 + 24}$$

since the total concentration of methanol (both isotopic forms) in all cases is very near to 24 *M*. In the above equation n is the number of exchangeable hydrogen atoms in the ester. The equation

$$kt = 2.303 \log \frac{\epsilon[\mathrm{MeOH}]_\infty - \epsilon[\mathrm{MeOH}]_0}{\epsilon[\mathrm{MeOH}]_\infty - \epsilon[\mathrm{MeOH}]_t}$$

was then used to determine the first-order rate constant for the reaction, by plotting the log term *vs.* time. The data obtained in the run described above are listed in Table II and plotted in Figure 4. From the slope of the line in Figure 4 a first-order rate constant of 1.57×10^{-4} sec^{-1} was calculated. Division by the average concentration of sodium methoxide present during the reaction gave the second-order rate constant $3.65 \times 10^{-3}\ M^{-1}$ sec^{-1}. The concentration of sodium methoxide decreased during the kinetic run because of a side reaction, perhaps the hydrolysis of the ester by small amounts of water present. In no case did this decrease amount to more than 3%, however.

Reaction of Methyl β-Ethoxypropionate with Sodium Methoxide in Methanol-*d*. Three milliliters of 0.14 *M* sodium methoxide and 0.45 *M* methyl β-ethoxypropionate was maintained at 35.0° for 560 sec and then added to 0.50 ml of 0.92 *M* hydrochloric acid. The resultant solution was concentrated to about 2 ml under a nitrogen stream, combined with 5-ml of pH 7 buffer solution, and extracted with three 1.0-ml portions of chloroform. The combined chloroform extract was concentrated under a nitrogen stream and analyzed by glpc. A large amount of methyl β-ethoxypropionate was found but no methyl β-methoxypropionate was detected. From the results it was estimated that the amount of the β-methoxypropionate present was less than 0.2% that of the β-ethoxypropionate.

A rough measurement of the rate of deuterium exchange of methyl β-ethoxypropionate was carried out by a method based on that used for the other esters except that the reaction was carried out in the infrared cell, at 32 ± 2°. The first-order rate constant obtained using 0.31 *M* ester in the presence of 0.40 *M* sodium methoxide was 2.3×10^{-3} sec^{-1}, from which a second-order rate constant of $5.7 \times 10^{-3} M^{-1}$ sec^{-1} was calculated. From this a second-order rate constant of $(8 \pm 3) \times 10^{-3}\ M^{-1}$ sec^{-1} at 35° is estimated.