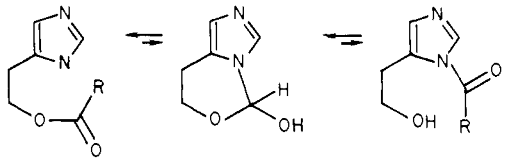
point where it becomes as good or better a leaving group than protonated imidazole.[22]

2. The values of k_{CN} from Table I represent the facility with which the protonated amide acetals undergo C–N cleavage. A Brønsted plot of log k_{CN} vs. pK_a of the parent imidazole (slope −1.0) indicates that the least basic imidazoles undergo C–N cleavage most rapidly.

3. Bicyclic amide acetal **2** at pHs >5 adheres to the general mechanism of hydrolysis common to the acyclic examples **1a–c** with the exception that the ring-opening process is a reversible one such that the rate of hydrolysis of **2** is (1–2) × 10^2-fold slower than that of **1a–c**. The reversibility can be demonstrated by the observation that added nucleophiles such as N_3^- or H_2NOH increase the rate of disappearance of **2** by trapping the intermediate open ion which prevents its reclosure to **2**-H^+.

The additional sigmoidal section to the pH/log k_{obsd} profile of **2** that is observed at pHs <5 is attributable to a second protonation of the imidazole of the open dialkoxymethyl cation (apparent pK_a $\simeq$ 1.8–2) which also effectively prevents the reversal back to **2**-H^+. The net effect is an observed increase in k_{obsd} at low pH to a limiting value dependent on the rate of opening of the protonated imidazole. The observation of buffer catalysis between pH 2 and pH 5 stems from a general-acid catalysis of the protonation of the open ion. Although the overall kinetic behavior is consistent with both H^+-catalyzed C–N and C–O cleavage (the latter being observed in the hydrolyses of some related amide acetals[5]), since no products corresponding to C–O cleavage can be observed, we feel the dominant process is C–N cleavage in both **1** and **2**.

4. Bicyclic **2** can be taken as a model for the tetrahedral intermediate formed from intramolecular attack of imidazole on an ester with an alkoxy group having a high pK_a or intramolecular attack of an alcohol on an acylimidazole as in eq 10. The latter process is of direct relevance to the situation in some serine proteases[4a,c] in which nonideal substrates appear to acylate the histidine N, which subsequently undergoes intramolecular acyl transfer to the adjacent serine OH group. The above study indicates that the ultimate fate of such an intermediate is breakdown to form the ester and furthermore implies that nucleophilic attack by histidine–imidazole on the serine ester is completely reversible such that the process cannot simply be kinetically important in regeneration of the active enzyme. This leaves the role of histidine to be the generally accepted one of general-base catalysis of H_2O attack on the acylserine.[4]



(10)

Acknowledgement is made to the Alberta Heritage Medical Research Fund, Natural Sciences and Engineering Research Council of Canada, University of Alberta, and the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research. In addition, we are grateful to Dr. Z. Frackman for the preparation of **2**. In particular we wish to acknowledge the invaluable advice of Prof. R. A. McClelland for suggesting the mechanism in Scheme I to us.

Registry No. 2, 84802-87-9.

Proton-Transfer Reactions. 3.[1] Differences in the Protonation of Localized and Delocalized Carbanion Intermediates

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Received December 31, 1981. Revised Manuscript Received November 1, 1982

Abstract: Rates, activation parameters, and product distributions are reported for the reaction of methanolic sodium methoxide with $XC_6H_4CH{=}CF_2$ (V) and $C_6F_5CH{=}CF_2$ (IX) and compared to previously reported results for $C_6H_5C(CF_3){=}CF_2$ (I). A ρ = 3.5 was calculated and substituents studied were X = *m*-, *p*-OCH_3, *m*-, *p*-CH_3, H, *o*-, *m*-, *p*-F, *m*-, *p*-Cl, *m*-, *p*-Br, and *m*-, *p*-NO_2. Products obtained for reaction of V (except *p*-NO_2-V) were fairly uniform and varied little with temperature (−15 to 65 °C). A saturated ether, $XC_6H_4CH_2CF_2OCH_3$, was the major product (56 ± 3%). Two vinyl ethers, (*E*)- and (*Z*)-$XC_6H_4CH{=}CFOCH_3$, were formed with *E* at 40 ± 3% favored over *Z* at 5 ± 1%. At higher temperatures slightly more of the saturated ether was observed. However, *p*-NO_2-V showed a large temperature effect on the amount of saturated ether formed, 96% at −77 °C vs. 42% at 28 °C, and yielded equal amounts of *E* and *Z* vinyl ethers. A product isotope effect (PIE) was calculated from product distributions observed when reaction was carried out in MeOD compared to MeOH. Values of PIE (k^H/k^D) are between 1.1 and 1.5 for reaction of I, *m*-NO_2-V, and IX and show little variance with temperature. On the other hand, PIE values for *p*-NO_2-V change in a manner similar to normal primary kinetic isotope effects and range from 15 (−77 °C) to 5.9 (28 °C). The differences in behavior are attributed to the fact that the carbanion *p*-$NO_2C_6H_4C^-HCF_2OCH_3$ is highly delocalized whereas the other carbanions remain largely localized on the benzylic carbon.

When a proton is transferred from oxygen to neutralize a carbanion, a question regarding the nature of the negative charge can arise. Is that charge localized on one carbon, or is it delocalized to other parts of the molecule? Does it matter if that charge is localized or delocalized? Kresge[2] has reviewed the effects that delocalization can have on the rate of proton transfer and concludes that delocalization of charge slows the rate of proton transfer to carbon. We recently proposed a mechanism that features two types of carbanion intermediates along the reaction

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(1) Part 2: Koch, H. F.; Tumas, W.; Knoll, R. *J. Am. Chem. Soc.* **1981**, *103*, 5423–5429.

(2) Kresge, A. J. *Acc. Chem. Res.* **1978**, *8*, 354–360.

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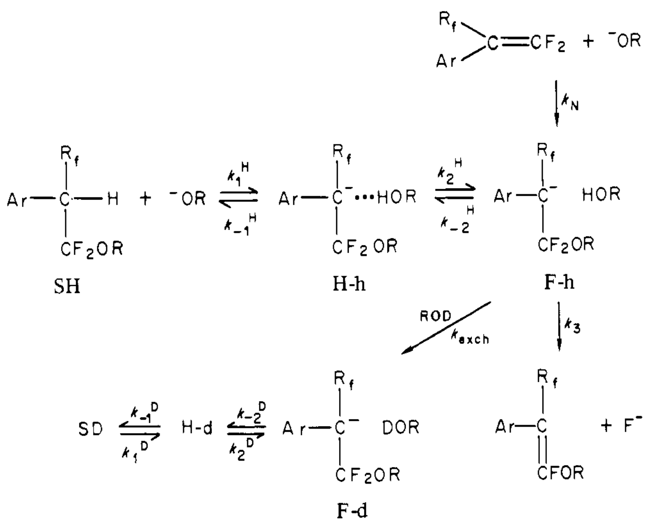
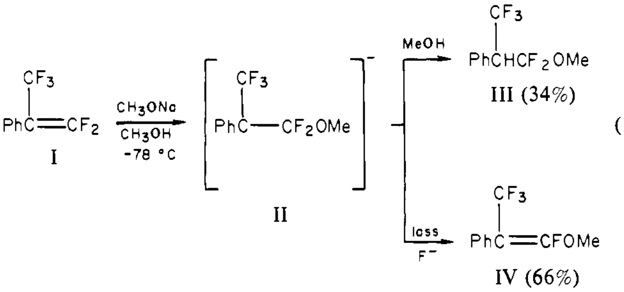
Scheme I



pathway for both the nucleophilic reaction of alkoxide with $PhC(CF_3){=}CF_2$ (I) and the alkoxide-promoted dehydrofluorination and proton-exchange reactions of $PhCH(CF_3)CF_2OMe$ when alcohol is the solvent (Scheme I).[3] What would be the consequence of delocalization of these carbanions?

The hydrogen-bonded carbanion H-h must be a localized species since the proton-transfer reactions, k_1 and k_{-1}, require a tetrahedral carbon. Therefore, delocalization can only affect the reactions of the "free" carbanion F-h. Since these intermediates are only transient species, it would be difficult to obtain values for the individual rate constants; however, observed rates of reaction and the primary kinetic isotope effect (PKIE) would be affected by changes in the relative magnitudes of the various rate constants. Reaction of I with methanolic sodium methoxide at −50 °C would generate F-h (Ar = Ph and $R_f = CF_3$) in a rate-limiting step, and the relationship between k_{-2} and k_3 can be calculated from the product distribution of 66% $PhC(CF_3){=}CFOMe$ (IV) and 34% $PhCH(CF_3)CF_2OMe$ (III).



(1)

A PKIE for the protonation of $PhC^-(CF_3)CF_2OMe$ (II) can be calculated when reaction of methoxide and I occurs in known mixtures of MeOH and MeOD. The calculated k^H/k^D for reaction of II with methanol is 1.22 at −78 °C.[3] The rate-limiting step for protonation must therefore be the formation of H-h, k_{-2}, and the PKIE associated with the proton-transfer reaction, k^{-1}, cannot be observed. This suggests that $k_{-1} > k_2$ and that relationship between the two rate constants would be consistent with an internal-return mechanism when III reacts with alcoholic alkoxide. The near-unity PKIE, $k^H/k^D = 1.3$ at 40 °C,[4] observed for the ethoxide-promoted dehydrofluorination of $PhC^{l}H(CF_3)CF_2OMe$ (SH when Ar = Ph and $R_f = CF_3$) is also consistent with extensive internal return.

Eaborn et al.[5] have reported PKIE values for protonation of various benzylic anions by methanol. The anions are generated in situ by reaction of methanolic sodium methoxide with substituted benzyltrimethylsilanes:

$$MeO^- + Me_3SiCH_2C_6H_4X \rightarrow MeOSiMe_3 + {}^-CH_2C_6H_4X$$

$$XC_6H_4CH_2^- + MeO^{l}H \rightarrow XC_6H_4CH_2{}^{l}H + MeO^- \qquad (2)$$

Isotope effects can be calculated from the known initial ratio of MeOH:MeOD and the observed H:D in $XC_6H_4CH_2{}^{l}H$. They coined the phrase product isotope effect (PIE) for their values even though PIE is the PKIE for proton transfer from oxygen to carbon. We will continue to use PIE when referring to an isotope effect related to the protonation[6] of a carbanion by alcohol and will use PKIE when the proton is transferred in the other direction.

The results reported by Eaborn et al. show small PIE values, $k^H/k^D \sim 1.2$ at 25 °C, for various ring-substituted benzylic anions. These values are similar to the PIE we obtained for reaction of $PhC^-(CF_3)CF_2OMe$ (formed by reaction of I with MeONa) and $MeO^{l}H$, $k^H/k^D = 1.22$ at −78 °C. They also calculated PIE values of ~10 when the benzylic anion has either an ortho or para nitro, and when the anion formed is either fluorenyl or 9-methylfluorenyl. Values of 1.3 were reported for Ph_2CH^- and Ph_3C^-. If these anions enter Scheme I after the rate-limiting step as "free" ions, the differences between the low and high PIE values can be attributed to differences in behavior between localized and delocalized carbanions.

There is an advantage to generating carbanions in situ by the reaction of methoxide with either alkyltrimethylsilanes or β,β-difluorostyrenes (V). Reactions occur at lower temperatures, and the problem of internal return is eliminated. Solvent molecules are excellent trapping agents for carbanions, and only an intramolecular trap appears to be more efficient. The use of difluorostyrenes has the added advantage that the intermediates can partition between the ejection of a β-fluoride and the protonation of the carbanion.

$$\underset{\text{V}}{XC_6H_4CH{=}CF_2} + MeO^- \xrightarrow{MeOH}$$

$$\underset{\text{VI}}{[XC_6H_4CHCF_2OMe]^-} \rightarrow \underset{\text{VII}}{XC_6H_4CH_2CF_2OMe}$$

$$\rightarrow \underset{\text{VIII}}{XC_6H_4CH{=}CFOMe} \qquad (3)$$

We believe that the carbanions generated from the alkoxide-promoted removal of a benzylic proton from fluorinated compounds and from the reaction of alkoxide with fluoroalkenes are largely localized on the benzylic carbon.[3,7] To include an alkene that might result in a delocalized carbanion intermediate, $p\text{-}NO_2C_6H_4CH{=}CF_2$ (p-NO_2-V) was synthesized, and its reactions were compared to other substituted β,β-difluorostyrenes, $C_6F_5CH{=}CF_2$ (IX), and I. We observed a dramatic difference between the product-forming reactions of p-NO_2-V and the other alkenes studied.

Results and Discussion

Good pseudo-first-order kinetics were observed for all reported rate constants. Concentrations of alkoxide ion were corrected for temperature prior to calculating second-order rate constants. Kinetic runs were carried out at different temperatures and ac-

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(3) Koch, H. F.; Koch, J. G.; Donovan, D. B.; Toczko, A. G.; Kielbania, A. J., Jr. *J. Am. Chem. Soc.* **1981**, *103*, 5417–5423.

(4) The k^H was measured in EtOH and k^D in EtOD since there is a competition between elimination and exchange.[3] Correction was made for a kinetic solvent isotope effect, $k^{OD}/k^{OH} = 2$, to give $k^H/k^D = 1.3$. The solvent isotope effect was estimated from other reported values since it cannot be measured directly for this system. Therefore, the PKIE could vary by ±0.3.

(5) (a) Eaborn, C.; Walton, D. R. M.; Seconi, G. *J. Chem. Soc., Perkin Trans. 2* **1976**, 1857–1861. (b) Macciantelli, D.; Seconi, G.; Eaborn, C. *Ibid.* **1978**, 834–838.

(6) Two possible reactions could be referred to as a protonation reaction. When the proton that is transferred to neutralize the carbanion originated as a bulk solvent molecule, we will refer to this as the protonation reaction. Therefore, protonation must first form F-h and then H-h. Proton transfer occurring between the unique alcohol that was formed in the first step of Scheme I, k_1, and the carbanion will be referred to as internal return.

(7) Koch, H. F.; Dahlberg, D. B.; Lodder, G.; Root, K. S.; Touchette, N. A.; Solsky, R. L.; Zuck, R. M.; Wagner, L. J.; Koch, N. H.; Kuzemko, M. A. *J. Am. Chem. Soc.* (following paper in this issue).

Table I. Rates and Activation Parameters for Reactions of $XC_6H_4CH{=}CF_2$ with ~0.3 N Sodium Methoxide in Methanol

X	10^4k, $M^{-1}\,s^{-1}$ 25 °C	10^4k, $M^{-1}\,s^{-1}$ 50 °C	$\Delta H^{\ddagger}$, kcal mol^{-1}	$\Delta S^{\ddagger}$, eu (25 °C)	temp range, °C	no. of runs
m-CH_3O	6.25	67.5	17.3 ± 0.2	−15.1 ± 0.5	35 to 65	6
p-CH_3O	0.423	5.66	19.3 ± 0.2	−13.9 ± 0.5	35 to 65	7
m-CH_3	1.95	25.3	19.0 ± 0.3	−11.7 ± 1.0	35 to 65	5
p-CH_3	1.05	12.9	18.6 ± 0.3	−14.4 ± 0.9	35 to 65	3
H	3.77	41.5	17.8 ± 0.2	−14.6 ± 0.6	20 to 65	8
o-F	54.3	454	15.7 ± 0.1	−16.3 ± 0.4	20 to 50	5
m-F	52.4	463	16.1 ± 0.3	−15.0 ± 1.0	20 to 50	6
p-F	4.26	48.3	18.0 ± 0.3	−13.6 ± 1.0	35 to 65	6
m-Cl	80.5	706	16.0 ± 0.3	−14.3 ± 0.9	15 to 40	6
p-Cl	26.6	266	17.1 ± 0.2	−13.1 ± 0.5	15 to 45	8
m-Br	95.2	807	15.8 ± 0.1	−14.9 ± 0.1	15 to 50	3
p-Br	37.9	351	16.5 ± 0.1	−14.4 ± 0.2	15 to 50	3
m-NO_2	1.26×10^3	9.31×10^3	14.7 ± 0.3	−13.3 ± 1.3	−15 to 15	4
p-NO_2	3.86×10^4	1.89×10^5	11.6 ± 0.3	−17.1 ± 1.2	−50 to −25	6
C_6F_5-[a]	3.10×10^3	1.67×10^4	12.3 ± 0.1	−19.6 ± 0.5	−40 to 0	6

[a] This refers to $C_6F_5CH{=}CF_2$.

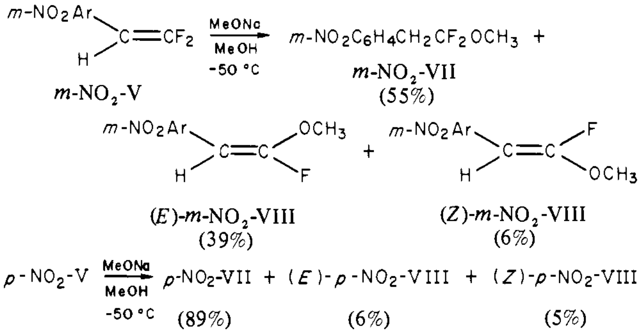
Table II. Relative Rates and Product Distribution for Reactions with Methanolic Sodium Methoxide at −50 °C

compd[a]	relative rate[b]	% saturated ether	%*E* vinyl ether	%*Z* vinyl ether
I	4900	34	7[c]	59[c]
p-NO_2-V	180	89	6	5
IX	10	75	22	3
m-NO_2-V	1.0	55	39	6

[a] $C_6H_5C(CF_3){=}CF_2$(I); *p*-$NO_2C_6H_4CH{=}CF_2$ (*p*-NO_2-V); $C_6F_5CH{=}CF_2$ (IX); *m*-$NO_2C_6H_4CH{=}CF_2$ (*m*-NO_2-V). [b] Rate of *m*-NO_2-V was extrapolated from Arrhenius plot to be 2.14×10^{-5} $M^{-1}\,s^{-1}$. [c] Due to the differences in priority for H and CF_3 vs. C_6H_5, the relationship of the remaining vinyl fluoride and phenyl is the same for (*Z*)-$PhC(CF_3){=}CFOMe$ and (*E*)-$ArCH{=}CFOMe$.

tivation parameters were calculated (Table I). The rate constants used for calculation of relative rates and ρ values were obtained from the Arrhenius plots. Reactions were monitored by following the disappearance of alkene substrate and the appearance of products by gas chromatographic analysis. Structures for compounds were assigned after analysis of the ^{19}F NMR spectra.

The reaction of methanolic sodium methoxide at −50 °C with I occurs 27 times faster than does the reaction with *p*-NO_2-V, which in turn reacts 18 times faster than IX and 180 times faster than *m*-NO_2-V, Table II. The isotope effects for a proton-transfer reaction to neutralize the carbanion intermediates and the partitioning of those intermediates to form the corresponding *E* and *Z* vinyl ethers are quite different for carbanions generated by a reaction of methoxide with *p*-NO_2-V when compared to a reaction with *m*-NO_2-V and other β,β-difluorostyrenes (Table III). Since product distributions for other meta- and para- substituted compounds listed in Table I are quite similar to those obtained for *m*-NO_2-V, discussion of the β,β-difluorostyrenes will be limited to comparisons of *m*-NO_2-V and *p*-NO_2-V. Reaction with IX gives a higher yield of saturated ether (75%), while reaction with I results in a lower amount of the corresponding saturated ether (34%). Both I and IX result in the preferential formation of one vinyl ether over the other.



The fact that *p*-NO_2-V yields about equal amounts of (*E*)-*p*-NO_2-VIII and (*Z*)-*p*-NO_2-VIII is unusual for these reactions. Reaction of I with ethanolic sodium ethoxide at −78 °C gives a mixture of vinyl ethers with a *Z*:*E* ratio of 8:1.[8] When samples

Table III. Product Distribution[a] for Reaction of $XC_6H_4CH{=}CF_2$ with ~0.3 N MeOH and MeOD

X	temp, °C	^iH (MeO^iH)	VII[b] %	ϕ,[c] ppm VII	*E*/*Z*[d] VIII	ϕ,[e] ppm (*E*)-VIII
m-CH_3	65	H	62	77.6	4.6	89.4
H	65	H	59	77.4	6.8	88.4
m-F	50	H	53	77.2	7.3	87.0
p-F	50	H	56	77.7	7.9	89.3
m-Cl	30	H	54	77.1	7.5	86.6
p-Cl	30	H	52	77.4	8.3	87.6
m-NO_2	65	H	59	76.4	3.6	84.6
	65	D	50	76.4	2.8	
	−15	H	56		6.3	
	−15	D	51		6.0	
p-NO_2	28	H	42	76.5	0.9	81.6
	28	D	11		0.9	
	−77	H	96		1.0	
	−77	D	62		0.9	

[a] Obtained by uncorrected gas chromatographic analysis. [b] $XC_6H_4CH_2CF_2OMe$ = VII. [c] ^{19}F chemical shifts (ϕ) relative to $CFCl_3$. J_{HF} values were between 10 and 12 Hz. [d] $XC_6H_4CH{=}CFOMe$ = VIII. *E*/*Z* values calculated by uncorrected GC analysis. [e] (*E*)-$XC_6H_4CH{=}CFOMe$ structure assigned by ^{19}F chemical shift relative to $CFCl_3$ and J_{HF} = 7–8 Hz. The amounts of (*Z*)-VIII are often too small and have a chemical shift in the same region as VII. A ^{19}F spectrum for (*Z*)-*p*-NO_2-VIII gave ϕ 76.7 ppm and J_{HF} = 30.5 Hz, when run with a Brucker WM 300.

of each pure vinyl ether were heated to greater than 150 °C, a mixture of $Z:E = 47:53$ was obtained.[9] This is presumably the equilibrium composition for $C_6H_5C(CF_3){=}CFOC_2H_5$. Therefore, it appears that the mixture of vinyl ethers formed by a reaction of *p*-NO_2-V is close to or equal to the equilibrium composition rather than the kinetically controlled mixtures observed with the other alkenes.

The temperature dependence of the product distribution obtained from reactions of *p*-NO_2-V when compared to all other alkenes studied to date is also different. Normally there is a small increase in the yield of saturated ether when the reaction temperature is increased. Therefore, the carbanion intermediate *m*-NO_2-VI is protonated by methanol to give 55% *m*-NO_2-VII at −50 °C compared to 59% at 65 °C. The opposite occurs for reactions of *p*-NO_2-VI as protonation dominates at lower temperatures (96% *p*-NO_2-VII formed at −77 °C) and ejection of β-fluoride is slightly favored at higher temperatures (42% *p*-NO_2-VII formed at 28 °C).

In summary, even though *p*-NO_2-V ($\sigma^- = 1.13$) fits on a Hammett plot ($\rho = 3.5$ at 25 °C) with the other β,β-difluorostyrenes and gives a similar activation entropy (ΔS^*), the product distribution from the reaction of *p*-NO_2-V with methanolic sodium methoxide differs from every alkene that we have investigated.

Product Isotope Effects (PIE). Eaborn et al.[5] calculated near-unity PIE values, $k^H/k^D = 1.1$–1.3, for a number of ring-substituted benzylic anions that were generated by a methoxide displacement reaction with the corresponding benzyltrimethylsilanes in MeOH/MeOD mixtures. We measured a similar PIE[3] for the protonation of a carbanion, II, which was generated by the reaction of methoxide with I in a mixture of MeOH and MeOD.

In the current study, we do not use mixtures of MeOH and MeOD. Instead, product ratios were analyzed for reactions carried out in pure MeOD and compared to product distributions for reactions in MeOH (Table III). A crude k^H/k^D can be calculated by assuming that the rate of fluoride ion ejection from $[NO_2C_6H_4CHCF_2OMe]^-$, (NO_2-VI), is approximately the same in MeOH and MeOD:

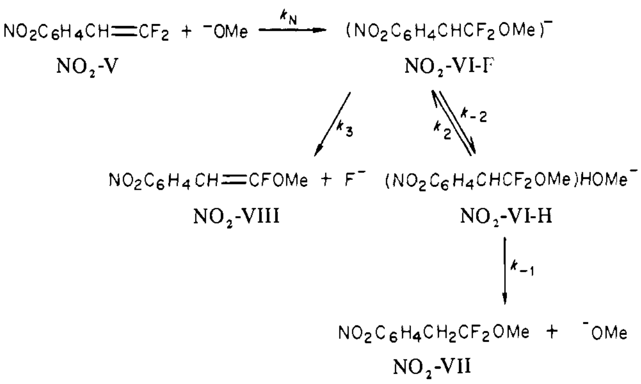
$$\begin{aligned}\text{PIE} = (k^H/k^D) &= (k_{\text{prot}}{}^H/k_{\text{elim}})^{\text{MeOH}}/(k_{\text{prot}}{}^D/k_{\text{elim}})^{\text{MeOD}} \\ &= (\%\ \text{VII}/\%\ \text{VIII})^{\text{MeOH}}/ \\ &\qquad (\%\ \text{VII}/\%\ \text{VIII})^{\text{MeOD}} \quad (4)\end{aligned}$$

Values of PIE calculated by an equation similar to 4 and the previously reported data[10] for reactions of I compare favorably to the measured PIE values obtained with mixtures of MeOH and MeOD: ethanol, 1.2 vs. 1.50 (−78 °C) and 1.5 vs. 1.89 (20 °C), and methanol, 1.1 vs. 1.22 (−78 °C).

When the data for *m*-NO_2-V found in Table III is used in equation 4, PIE values of 1.2 at −15 and 1.4 at 65 °C are calculated. Similar values were obtained for $C_6F_5CH{=}CF_2$ (IX).[11] When the data for *p*-NO_2-V is used, much larger PIE values are obtained, 15 at −77 and 5.9 at 28 °C. Eaborn et al. reported an increase of PIE to 10 at 25 °C for the protonation of *p*-$NO_2C_6H_4CH_2^-$. Therefore, carbanions generated by the reaction of methanolic methoxide with *m*-NO_2-V, *p*-NO_2-V, and IX have an isotope discrimination reaction similar to the corresponding benzylic carbanions that are generated by the reaction of methoxide with *m*-$NO_2C_6H_4CH_2SiMe_3$, *p*-$NO_2C_6H_4CH_2SiMe_3$, and $C_6F_5CH_2SiMe_3$.

A model for the low PIE values could come from the work of Gold and Grist[12] on possible origins for the kinetic solvent isotope effect (KSIE) of alcohols on the reactions of alkoxide ions. They conclude that these effects are due to a multiple solvated methoxide ion which has a deuterium fractionation factor of 0.74. This fractionation factor implies that the equilibrium abundance of deuterium in the *m* hydrogen atoms of the solvated methoxide ion, $MeO^-\cdots({}^iHOMe)_m$, is 0.74 times that of the concentration in bulk solvent. Therefore, MeOH rather than MeOD will preferentially solvate the methoxide ion. If the deuterium fractionation factor for $\gt C^-\cdots{}^iHOMe$ is similar to that for methoxide, then the PIE predicted for reactions of *m*-NO_2-V, I, and IX are close to the observed values.

Scheme II



Mechanistic Implications. Scheme II is a modified version of Scheme I and represents the reactions of *m*-NO_2-V and *p*-NO_2-V. Reaction of *m*-NO_2-V with methoxide forms the intermediate *m*-NO_2-VI-F in the rate-limiting step, k_N. This intermediate can partition between the ejection of β-fluoride to form *m*-NO_2-VIII, k_3, and the formation of a hydrogen-bonded carbanion *m*-NO_2-VI-H, k_{-2}. The formation of *m*-NO_2-VI-H can be viewed as the generation of an encounter complex between a carbanion and an alcohol molecule prior to a formal proton-transfer reaction from oxygen to carbon. This would be analogous to the formation of an encounter complex, $\gt C\text{-}H\cdots{}^-OMe$, prior to proton transfer from carbon to oxygen. The low PIE values suggest that the rate-limiting step for the protonation of *m*-NO_2-VI to form *m*-NO_2-VII is the formation of *m*-NO_2-VI-H, k_{-2}, rather than the proton-transfer reaction, k_{-1}.

The fact that reaction of *p*-NO_2-V with methoxide fits on a Hammett plot and that the activation parameter ΔS^* is in line with values obtained from reactions of the other β,β-difluorostyrenes suggests that the initial reaction of methoxide ion with the *gem*-difluoroethylene group is the same for the entire series. Therefore, the rate-limiting step for the reaction of *p*-NO_2-V with methoxide is also the formation of the intermediate *p*-NO_2-VI-F. However, the relative rates of reactions from *p*-NO_2-VI-F to form products are different than those for *m*-NO_2-VI-F. We believe this is because *p*-NO_2-VI-F is a delocalized anion whereas *m*-NO_2-VI-F has charge mainly localized on the benzylic carbon. The larger PIE obtained from the reaction of *p*-NO_2-VI with methanol suggests that the rate-limiting step for the protonation of *p*-NO_2-VI to give *p*-NO_2-VII is the proton-transfer reaction, k_{-1}, instead of the formation of *p*-NO_2-VI-H. Apparently the delocalization energy of $(p\text{-}NO_2C_6H_4CHCF_2OMe)^-$ is greater than the energy obtained from the formation of a hydrogen bond to the localized carbanion *p*-$NO_2C_6H_4C^-HCF_2OMe$. *Delocalized carbanions can therefore have a "return" reaction that is involved with the formation and destruction of a hydrogen-bonded localized carbanion rather than with a formal proton transfer.* The rate of proton transfer to delocalized carbanions is thought to be slow.[2] This mechanism would slow down the rate of protonation similar to the way internal return slows down the observed rate of a proton-abstraction reaction.

A benzylic anion is generally thought to be delocalized; however, the near-unity PIE suggests that even benzyl anion does not behave in a similar manner to delocalized anions such as 9-fluorenyl. In the accompanying paper,[7] we deal with PKIE obtained from alkoxide-promoted proton-abstraction reactions and come to the same conclusions regarding benzylic anions. The relative amounts of *E* and *Z* vinyl ethers formed are consistent with the delocalized

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(8) Reference 3, p 5418, gives results for reactions of I with sodium ethoxide in ethanol as well as with methanolic sodium methoxide.

(9) Kim, S. W., unpublished results. The ethoxyvinyl ethers were used since they gave good separation on our GC column. There is no reason to believe that the methoxyvinyl ethers would not behave the same.

(10) Reference 3, p 5421.

(11) Preliminary values obtained for $C_6F_5CH{=}CF_2$ are 1.1 at −15 °C and 1.3 at 65 °C.

(12) Gold, V.; Grist, S. *J. Chem. Soc. B* **1971**, 2282–2285.

vs. localized carbanion postulate.

The delocalized para nitro anion apparently does not have a sufficient amount of charge on the benzylic carbon to eject the first β-fluoride to rotate into position, and a free rotation around the C_α–C_β bond results in the formation of approximately equal amounts of (*E*)- and (*Z*)-*p*-NO_2-VIII. On the other hand, *m*-$NO_2C_6H_4C^-HCF_2OMe$ can have a "tetrahedral" configuration and there is enough charge on the benzylic carbon to eject the first β-fluoride to achieve the proper alignment. Therefore *m*-NO_2-VI yields a kinetically controlled mixture of vinyl ethers, and *p*-NO_2-VI gives a thermodynamically controlled mixture of vinyl ethers.

Scheme I can also explain a discrepancy pointed out by Eaborn et al.[13] regarding the PKIE for the methoxide-catalyzed exchange of Ph_3C^iH (TPM) with methanol vs. the PIE for the reaction of Ph_3C^- with mixtures of MeO^iH. Streitwieser et al.[14] report a $k_1{}^{H}/k_1{}^{D} = 4.2$ at 100 °C for hydron exchange of TPM with methanolic methoxide. Eaborn et al. use this value and Schowen's approximate treatment[15] to calculate a C–^{i}H bond order of 0.24 in the transition state of the hydron-transfer step, $k_1{}^{iH}$. Since the transition state for the hydron transfer from methanol to Ph_3C^-, $k_{-1}{}^{iH}$, must be the same, they calculate an expected PIE at 25 °C of ca. 8 rather than the observed value of 1.3. The assumption made was that reaction of TPM and methoxide occurs by a simple internal-return mechanism (eq 5). In eq 5, k_2 represents the

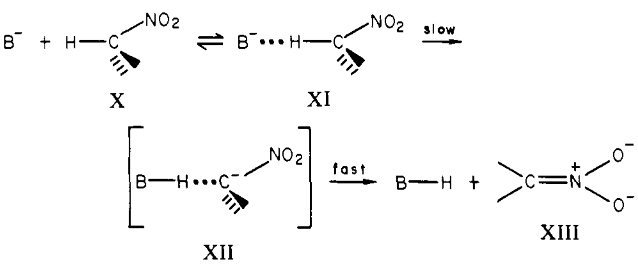
$$\mathrm{Ph_3C{-}H + {}^-OMe \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} Ph_3C^-HOMe \xrightarrow[MeOD]{k_2} Ph_3C^-\ DOMe} \tag{5}$$

exchange step for MeOH to MeOD. The observed PKIE reported by Streitwieser et al. is $(k^H/k^D)_{obsd} = 1.32$ at 97.7 °C ($k^H/k^T = 1.77 \pm 0.005$ and $k^D/k^T = 1.34 \pm 0.03$) and this low value is due to extensive internal return: $a^H = 25$, $a^D = 3.4$, and $a^T = 1.4$.[16] Using the internal return parameters, they were able to convert $(k^H/k^D)_{obsd}$ to the reported value of $k_1{}^H/k_1{}^D$.

If the reactions of TPM with methanolic methoxide and Ph_3C^- with methanol occur by a mechanism similar to that shown in Scheme I, there is no discrepancy between the two reported results. Internal return, $k_{-1}{}^H$, lowers the observed PKIE for reaction of TPM with methoxide, and the methanol generated by the proton-transfer reaction, $k_1{}^H$, can exchange with solvent only after the hydrogen bond, $Ph_3C^- \cdots HOMe$, is broken to generate an intermediate like F-h, $k_2{}^H$. When Ph_3C^- (generated from methoxide and Ph_3CSiMe_3) reacts with methanol, the rate-limiting step becomes the formation of $Ph_3C^- \cdots {}^iHOMe$. Since proton transfer occurs only after the formation of the hydrogen-bonded carbanion, the PIE associated with $k_{-1}{}^{iH}$ cannot be experimentally observed.

The PIE value measured for protonation of 9-methylfluorenyl anion does agree quite well with the reported PKIE for reaction of 9-methylfluorene-*9-^{i}H* (9-MeFl) with methanolic methoxide.[14] When Scheme I is applied to delocalized carbanions, the intermediate F becomes more stable than the intermediate H. The delocalized carbanion generated by a proton-transfer reaction, 9-MeFl with methoxide, has little or no internal return[17] since $k_2{}^H > k_{-1}{}^H$ and $k_{exch}{}^H > k_{-2}{}^H$. For the overall reaction, the rate-limiting step is proton transfer, $k_1{}^H$. Since $k_2{}^H > k_{-1}{}^H$, the proton-transfer step, $k_{-1}{}^H$, becomes rate limiting when the delocalized carbanion is generated by other means. Since the proton-transfer step is postulated to be rate limiting in both directions for delocalized carbanions, it is not surprising that PIE and PKIE values observed for the fluorenyl systems are in close agreement.

Scheme III



Thibblin and Jencks[18] suggest the Eaborn data is consistent with a preassociation mechanism when the departing carbanion is unstable, and this would result in the low PIE observed for some of the benzylic anions. When the leaving carbanion is stable enough to diffuse into the mixture of MeOH and MeOD, it can discriminate among solvent molecules prior to protonation and thus give a larger PIE. We cannot rule out a preassociation mechanism for the reactions of alkoxide with the *gem*-difluoroalkenes; however, we see no need to postulate that mechanism to explain our results. Our current working model is that the carbanion initially generated in alcohol is free of contact stabilization by either solvent or gegenion. There are three avenues open for stabilization: (1) ejection of a leaving group to yield the more stable alkene, (2) interaction with an alcohol molecule to form a more stable hydrogen-bonded species, and (3) delocalization of negative charge to give a more stable "free" carbanion intermediate.

A hydrogen-bonded carbanion (assumed to be pyramidal) can have a normal proton transfer occur from oxygen to carbon to form a saturated product. Although the overall sequence from "free" carbanion to saturated compound is fast, the ejection of a halide can be faster. An exception to this is the loss of fluoride from trifluoromethyl.[3,19] Since the observed PIE is near unity for the protonation, we conclude that the rate-limiting step for this process is the formation of a hydrogen-bonded intermediate. When the delocalization energy is large enough, the carbanion gains stability by losing the hydrogen bond to the lone pair localized on the benzylic carbon. In this case, the hydrogen-bonded intermediate can return to the "free" delocalized ion or can accept a proton from the alcohol molecule in what now becomes the rate-limiting step for the protonation.

The reaction of methoxide with ring-substituted benzyltrimethylsilanes (eq 2) has a $\rho = 4.7$,[20] which is larger than the 3.5 calculated for the reaction of the ring-substituted β,β-difluorostyrenes (eq 3). The benzylic anions that were displaced from the silanes were originally in a pyramidal geometry, while the potential carbanion site in the styrene reactions was trigonal. Since *m*-NO_2-V, *m*-$NO_2C_6H_4CH_2SiMe_3$, $C_6F_5CH{=}CF_2$, and $C_6F_5CH_2SiMe_3$ give similar near unity PIE values, the original hybridization of the carbon does not appear to be significant. The same relationship occurs when comparing *p*-NO_2-V and *p*-$NO_2C_6H_4CH_2SiMe_3$.

Seven years ago Bordwell and Boyle[21] suggested that a localized pyramidal nitrocarbanion, XII, is the initial intermediate resulting from a base-promoted proton removal from a nitroalkane, X (Scheme III). Therefore, rehybridization of the carbanion and electron delocalization to form the more stable planar nitronate ion, XIII, would lag behind proton transfer. Although we do not

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(13) Reference 5b, p 836.

(14) Streitwieser, A., Jr.; Hollyhead, W. B.; Sonnichsen, G.; Pudjaatmaka, A. H.; Chang, C. J.; Kruger, T. L. *J. Am. Chem. Soc.* **1971**, *93*, 5096–5102.

(15) Schowen, R. L. *Prog. Phys. Org. Chem.* **1972**, *9*, 286–288.

(16) The definition of $a^{iH} = k_{-1}{}^{iH}/k_2$, and k_2 is assumed to have a negligible isotope effect. There are slight differences in the a^{iH} values calculated by us and those reported by Streitwieser et al.[14] This arises from the use of slightly different values for K_T'. Our value has been assigned from the observed values of k^H/k^D in systems believed to be proceeding by a mechanism that has a carbanion intermediate formed in a preequilibrium prior to the rate-limiting step.[3] Reference 14 does not include an equation to calculate a^H and a^D; however, this is given in a recent paper by Boerth and Streitwieser (Boerth, D. W.; Streitwieser, A., Jr. *J. Am. Chem. Soc.* **1981**, *103*, 6443–6447.

(17) The calculated internal return values are $a^H = 0.66$, $a^D = 0.09$, and $a^T = 0.04$.

(18) Thibblin, A.; Jencks, W. P. *J. Am. Chem. Soc.* **1979**, *101*, 4963–4971.

(19) This discussion is limited to benzylic carbanions. Relative rates change when the phenyl group is replaced by a chlorine or fluorine. Reaction of $CF_2{=}CCl_2$ with methanolic methoxide results in $MeOCF_2CHCl_2$ as the only reported product and $CF_2{=}CFCF_3$ reacts to form over 90% of the corresponding saturated ether.

(20) Alexander, R.; Asomaning, W. A.; Eaborn, C.; Jenkins, I. D.; Walton, D. R. M. *J. Chem. Soc., Perkin Trans. 2*, **1974**, 490–494.

(21) Bordwell, F. G.; Boyle, W. J. *J. Am. Chem. Soc.* **1975**, *97*, 3447–3452.

include an encounter complex (XI), Scheme I is quite similar to Scheme III.

Streitwieser et al.[22] report small amounts of internal return occurring in the methoxide-catalyzed exchange reactions of 9-MeFl.[17] Removal of the proton in the 9 position of 9-MeFl by methoxide would generate a hydrogen-bonded pyramidal carbanion, which can partition between an internal-return reaction and the rehybridization of that carbon to generate the delocalized planar 9-methylfluorenyl anion. The transition state for the rate-limiting proton transfer for the reaction of 9-MeFl would be similar to that of other proton-transfer reactions involving an sp^3 C–H and alkoxide. Over a dozen years ago Ritchie[23] stated that "those carbon acids whose conjugate bases have localized charge are predicted to have proton transfer rates considerably greater than acids of the same thermodynamic strength whose conjugate bases have delocalized charges". Therefore, if the rate-limiting transition state is closer in energy to a localized 9-MeFl carbanion than to a delocalized 9-methylfluorenyl anion, the rate of proton exchange would be much slower than anticipated. This point is discussed in greater detail in the accompanying paper.[24]

Other studies have recently appeared that explore the large stabilizing effects of a nitro group conjugated with an anion. Jencks and co-workers[25] have been investigating elimination reactions of *p*-nitrophenethyl compounds, and Bernasconi et al.[26] are studying the rates of proton transfer to delocalized carbanions, making use of the fast kinetic techniques pioneered by Eigen. The latter work is mainly concerned with proton transfer between nitrogen and carbon. We are continuing our investigations using systems that can generate carbanions by both the nucleophilic reactions of alkenes and base-promoted proton abstraction.

Experimental Section

Materials. Compounds V (excluding *p*-NO_2-V) and IX were obtained by using a procedure similar to that reported by Herkes and Burton for the synthesis of 2-(*p*-chlorophenyl)pentafluoropropene (method II).[27] This procedure calls for a reaction of the substituted benzaldehyde, CF_2ClCO_2Li, and triphenylphosphine in a molar ratio of 1:2:2 with anhydrous DMF as the reaction solvent. After reaction is complete, the alkene is codistilled with water from the reaction mixture. The lower layer is separated and dried over Drierite. The yields are usually between 40 and 60% and the alkenes were pure enough to use without further treatment. Synthesis of *p*-NO_2-V proved more difficult, and when DMF was used as a reaction solvent, only trace quantities or no *p*-NO_2-V was observed. When anhydrous diglyme was used in place of DMF, *p*-NO_2-V was usually obtained in <10% yield. We are still working on a better synthesis for *p*-NO_2-V. Methanolic sodium methoxide solutions were made from a reaction of sodium with methanol. The small chunks of freshly cut sodium were washed with alcohol prior to placing them into the reaction solution. Deuterated methanol was purchased from Aldrich and used with further purification. Nuclear magnetic resonance spectra were recorded using a Varian HA-60 IL spectrometer.

Kinetics. Kinetics were carried out under pseudo-first-order conditions with ratios of alkoxide:alkene of better than 10:1. The procedure for kinetic runs is described in detail in the following paper.[7] Since kinetic samples were analyzed by gas chromatography, we were able to monitor product formation as well as substrate disappearance.

Acknowledgment. We are grateful to the donors of Petroleum Research Fund, administered by the American Chemical Society, and the Research Corporation for a Cottrell College Science Grant, for support of this research. We thank William Jencks, Jerry Kresge, Rory More O'Ferrall, and William Tumas for helpful suggestions and discussions.

Registry No. *m*-$CH_3OC_6CH=CF_2$, 84750-90-3; *p*-$CH_3OC_6H_4CH=CF_2$, 1608-24-8; *m*-$CH_3C_6H_4CH=CF_2$, 84774-73-2; *p*-$CH_3C_6H_4CH=CF_2$, 28321-07-5; $C_6H_5CH=CF_2$, 405-42-5; *o*-$FC_6H_4CH=CF_2$, 61317-65-5; *m*-$FC_6H_4CH=CF_2$, 63082-37-1; *p*-$FC_6H_4CH=CF_2$, 1743-00-6; *m*-$ClC_6H_4CH=CF_2$, 84750-91-4; *p*-$ClC_6H_4CH=CF_2$, 28321-09-7; *m*-$BrC_6H_4CH=CF_2$, 84750-92-5; *p*-$BrC_6H_4CH=CF_2$, 84750-93-6; *m*-$NO_2C_6H_4CH=CF_2$, 84750-94-7; *p*-$NO_2C_6H_4CH=CF_2$, 1742-99-0; $C_6F_5CH=CF_2$, 653-19-0.

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(22) Reference 14, p 5099.

(23) Ritchie, C. D. *J. Am. Chem. Soc.* **1969**, *91*, 6749–6753.

(24) Reference 7.

(25) Alunni, S.; Jencks, W. P. *J. Am. Chem. Soc.* **1980**, *102*, 2052–2060. Keeffe, J. R.; Jencks, W. P. *Ibid.* **1981**, *103*, 2457–2459. Gandler, J. R.; Jencks, W. P. *Ibid.* **1982**, *104*, 1937–1951.

(26) Bernasconi, C. F.; Hibdon, S. A.; McMurray, S. E. *J. Am. Chem. Soc.* **1982**, *104*, 3459–3471. Bernasconi, C. F.; Carre, D. J. *Ibid.* **1979**, *101*, 2698–2707. Bernasconi, C. F.; Kanavarioti, A. *J. Org. Chem.* **1979**, *44*, 4829–4832.

(27) Herkes, F. E.; Burton, D. J. *J. Org. Chem.* **1967**, *32*, 1311–1318.