

Proton-Transfer Reactions. 4. Near-Unity Kinetic Isotope Effects for Hydron Exchange and Dehydrofluorination Reactions

Heinz F. Koch,* Donald B. Dahlberg,* Gerrit Lodder,* Karen S. Root,¹
Nancy A. Touchette,¹ Robert L. Solsky, Robin M. Zuck, Linda J. Wagner,
Nanci H. Koch, and Michael A. Kuzemko²

Contribution from the Department of Chemistry, Ithaca College, Ithaca, New York 14850, the Department of Chemistry, Lebanon Valley College, Annville, Pennsylvania 17003, and the Gorlaeus Laboratories, University of Leiden, The Netherlands. Received December 31, 1981. Revised Manuscript Received November 1, 1982

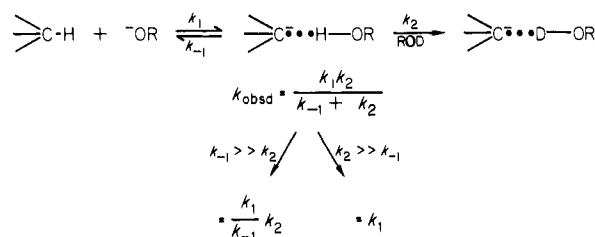
Abstract: Rates and isotope effects are reported for benzylic hydron exchange and dehydrofluorination reactions of $C_6H_5C^HClCF_3$ (I) and $C_6H_5C^H(CF_3)_2$ (II) in alcoholic sodium alkoxide solutions. Reactions of I were studied in ethanol and isotope effects are reported at 75 °C: $(k^H/k^D)_{\text{exch}} = 1.06$, $(k^H/k^D)_{\text{elim}} = 1.04$, and $(k^{\text{EtOD}}/k^{\text{EtOH}}) = 2.3$. Exchange occurs 9–10 times faster than does elimination. Reactions of II were studied in both ethanol and methanol and isotope effects are reported at 25 °C: ethanol (methanol), $(k^H/k^D)_{\text{exch}} = 1.21$ (1.10), $(k^H/k^D)_{\text{elim}} = 1.08$ (1.05), and $(k^{\text{ROD}}/k^{\text{ROH}}) = 2.74$ (2.63). Exchange occurs 4–5 times faster than does elimination in ethanol and 7–8 times faster in methanol. The near-unity primary kinetic isotope effects can be interpreted as arising from a mechanism that features extensive internal return occurring during the first step of the reaction, which forms a strongly hydrogen-bonded carbanion intermediate. We postulate that a second carbanion is formed by the breaking of this hydrogen bond and that both the exchange with solvent and ejection of fluoride occur from this second intermediate. It is suggested that the carbanions generated from both I and II are largely localized on the benzylic carbon and that this dictates the proposed multistep mechanism.

Proton transfer to and from carbon is a basic step of importance to many chemical reactions. When a proton is transferred from oxygen to neutralize a carbanion, a question regarding the nature of the negative charge on carbon can arise. Is that charge localized on one carbon atom, or is it delocalized to other parts of the molecule? Kresge³ has reported on effects that charge delocalization can have on rates of proton transfer and that this effect depends on the identity of the atoms involved in the transfer. In the accompanying paper we report on the effect delocalization can have on partitioning of carbanion intermediates between proton transfer and β -fluoride ion ejection.⁴

Delocalization of negative charge from carbon can also effect the observed rate of proton transfer from carbon to a negatively charged oxygen such as an alkoxide ion.^{5a} A delocalized carbanion will have less internal return (Scheme I), and this will enhance the observed rate of exchange with solvent. On the other hand, a localized carbanion could have extensive internal return, $k_{-1} \gg k_2$, and this can seriously retard the rate of exchange. Since exchange of the alcohol generated by proton transfer with solvent is thought to be a diffusion-controlled process, $k_2 \gg k_{-1}$, the observed rate of exchange is often quoted as the rate of the proton-transfer reaction (see Scheme I); however, when a system has appreciable internal return, the exchange step, k_2 , must have a substantial energy barrier and the process cannot be diffusion controlled.

To illustrate the differences encountered when dealing with delocalized and localized carbanions, one could compare the rates of methoxide-catalyzed exchange of the 9-position of 9-phenylfluorene (PhFl) with those of pentafluorobenzene (PFB). The rate of exchange of PhFl, $k^H = 1.70 \times 10^{-3} \text{ M}^{-1} \text{ s}^{-1}$,^{5a} is about 14 times slower than that of PFB at 25 °C.⁶ The primary kinetic isotope effects for PhFl, $k^H/k^T = 16.0$ and $k^D/k^T = 2.50$ at 25 °C, suggest that the exchange reaction does not have a large amount of internal return, $a^H = k_{-1}^H/k_2$. Values of $a^H = 0.48$, $a^D = 0.048$, and $a^T = 0.015$ can be calculated from the data,⁷ and this suggests that k_{obsd}^H is only 0.68 times k_1^H , which is the true rate constant for the proton-transfer step.^{8,9} On the other hand, k_{obsd}^T is $0.977 \times k_1^T$ and this value would be within the experimental limits of observed rate constants. Therefore, the rate of

Scheme I



detrifitiation of PhFl would represent an accurate value for the hydron-transfer process when comparing tritium exchange rates.

The kinetic isotope effect for PFB, $k^D/k^T = 1.00 \pm 0.06$ at 25 °C, suggests that there is extensive internal return occurring during this reaction.⁶ The kinetic expression for an internal return mechanism is given in Scheme I. If the isotope effect is the result of a true equilibrium process, $K = k_1/k_{-1}$, prior to an exchange step, k_2 , then k_{-1} should be at least 10^2 times greater than k_2 . Therefore, even the rate of detrifitiation for PFB would not represent an accurate value for the hydron-transfer reaction. As a result, k_1 for PFB could be at least 1400 times greater than k_1 for PhFl rather than the 14 calculated from the experimentally observed rate constants.

(1) Partially supported by an Ithaca College Provost Grant to work at the University of Leiden during summer of 1976.

(2) Student at Wilkes Barre Campus of the Pennsylvania State University and supported by NSF-URP Grant SPI-7683152 to work at Ithaca College during the summer of 1979.

(3) Kresge, A. J. *Acc. Chem. Res.* 1975, 8, 354–360.

(4) Koch, H. F.; Koch, J. G.; Koch, N. H.; Koch, A. S. *J. Am. Chem. Soc.* (preceding article in this issue).

(5) (a) Streitwieser, A., Jr.; Hollyhead, W. B.; Sonnichsen, G.; Pudjaatmaka, A. H.; Chang, C. J.; Kruger, T. C. *J. Am. Chem. Soc.* 1971, 93, 5096–5102. (b) Boerth, D. W.; Streitwieser, A., Jr. *Ibid.* 1981, 103, 6443–6447.

(6) Streitwieser, A., Jr.; Hudson, J. A.; Mares, F. *J. Am. Chem. Soc.* 1968, 90, 648–651.

(7) Reference 5a does not include a formula to calculate a^H or a^D , but one is given in ref 5b.

(8) The value of k_1^H is a composite of all reactions leading up to and including the proton-transfer process. This would include partial desolvation of methoxide and the formation of an encounter complex.

(9) Murdoch, J. R. *J. Am. Chem. Soc.* 1972, 94, 4410–4418.

* Address correspondence as follows: H. F. Koch, Ithaca College; D. B. Dahlberg, Lebanon Valley College; G. Lodder, University of Leiden.

Table I. Rates and Activation Parameters for Exchange and Dehydrofluorination Reactions with Alcoholic Sodium Alkoxides

compd ^a	solvent	process ^b	$10^7 k, ^\circ\text{C}$ $\text{M}^{-1} \text{s}^{-1}$	$\Delta H^\ddagger, \text{kcal mol}^{-1}$	$\Delta S^\ddagger, \text{eu (25 }^\circ\text{C)}$	temp range, $^\circ\text{C}$	no. of runs
I-h	EtOH	-HF	0.0727	29.3 ± 0.5	11.1 ± 1.5	70 to 110	7
I-d	EtOD	-DF	0.161	28.6 ± 0.7	10.5 ± 2.1	50 to 90	4
I-h	EtOD	H → D	1.65	26.9 ± 0.3	10.1 ± 0.9	35 to 85	8
I-d	EtOH	D → H	0.673	26.8 ± 0.4	8.3 ± 1.3	45 to 82	6
I-t ^d	EtOH	T → H	0.631	26.4 ± 0.5	6.8 ± 1.4	50 to 80	4
I t ^d	EtOD	T → D	1.45	26.4 ± 0.1	8.6 ± 0.4	40 to 80	5
II-h	EtOH	-HF	0.662	25.8 ± 0.3	18.1 ± 1.0	15 to 45	9
II-d	EtOD	-DF	1.67	24.7 ± 0.3	16.0 ± 0.9	0 to 35	5
II-h	EtOD	H → D	8.72	23.3 ± 0.1	14.6 ± 0.2	-20 to 25	6
II-d	EtOH	D → H	2.64	22.6 ± 0.1	10.0 ± 0.4	-20 to 30	7
II-t ^d	EtOH	T → H	2.23	23.0 ± 0.1	10.9 ± 0.2	-5 to 35	9
II-t ^d	EtOD	T → D	6.11	22.6 ± 0.2	11.8 ± 0.6	-15 to 30	9
II-h	MeOH	-HF	0.0298	26.0 ± 0.3	12.5 ± 1.0	20 to 65	9
II-d	MeOD	-DF	0.0748	26.3 ± 0.3	15.5 ± 0.8	20 to 60	7
II-h	MeOD	H → D	0.614	23.9 ± 0.1	11.4 ± 0.3	10 to 50	5
II-d	MeOH	D → H	0.212	24.4 ± 0.1	11.2 ± 0.4	0 to 50	7
II t ^d	MeOH	T → H	0.209	24.1 ± 0.2	9.9 ± 0.7	5 to 50	10
II t ^d	MeOD	T → D	0.549	23.9 ± 0.1	11.1 ± 0.2	5 to 50	9

^a I = PhC^HHClCF₃ and II = PhC^HH(CF₃)₂. ^b Process -HF would be a dehydrofluorination, i.e., I-d, EtOD and -DF is PhCDClCF₃ + EtONa (EtOD) → PhCCl=CF₂.¹¹ Process T → H would be an exchange reaction, i.e., II-t, MeOH and T → H is PhCT(CF₃)₂ + MeONa/MeOH → PhCH(CF₃)₂. ^c Reactions of I reported at 75 $^\circ\text{C}$ and reactions of II reported at 25 $^\circ\text{C}$. ^d Detritiation rates corrected for loss of tritium by competing loss of TF.

Observation of near-unity kinetic isotope effects for hydron-exchange reactions normally occurs when carbanions that are quite localized on one carbon atom are generated by a reaction of the C-H bond and an oxide base. Kresge³ has discussed the behavior of phenylacetylene and chloroform where the charge must largely remain on a specific carbon and the results for PFB are similar. The systems chosen for our studies, C₆H₅C^HClCF₃ (I) and C₆H₅C^H(CF₃)₂ (II), can generate carbanions that could be localized on the benzylic carbon since the presence of Cl and CF₃ can greatly stabilize a localized negative charge.¹⁰

Results and Discussion

Good pseudo-first-order kinetics were observed for all isotopic exchange and dehydrofluorination reactions. Concentrations of alkoxide were corrected for temperature prior to calculating observed second-order rate constants. Kinetic runs were carried out at different temperatures and activation parameters were calculated (Table I). The rate constants used for the calculation of isotope effects and other correlations were obtained by interpolation from the Arrhenius plots. Elimination reactions were monitored by gas chromatographic analysis.¹¹ Since detritiation reactions were followed by measuring the loss of radioactivity with a liquid-scintillation counter, all tritium exchange rates have been corrected for a loss of tritium by a competitive elimination reaction.¹² A similar correction for hydrogen and deuterium exchange reactions was unnecessary since H:D ratios were obtained by mass spectrometry on samples that had been collected with preparative gas chromatography.

To calculate a primary kinetic isotope effect, k^H/k^D , for hydron-exchange reactions, the observed second-order rate constants were corrected for a kinetic solvent isotope effect (KSIE), which was obtained from corrected detritiation rate constants in light and heavy solvents. Direct measurement of isotope effects for dehydrofluorination reactions is not possible in a common solvent since the corresponding exchange reaction is 4-10 times faster.

$$(\text{KSIE})_{\text{exch}} = (k_{\text{ROD}}^T/k_{\text{ROH}}^T)_{\text{exch}} \quad (1)$$

$$(k^H/k^D)_{\text{exch}} = (k_{\text{ROD}}^H/k_{\text{ROH}}^D)(1/\text{KSIE}) \quad (2)$$

(10) Localized negative charge could mean charge density on that specific carbon. For a benzylic carbon the important criteria is to have charge in an sp³ orbital that is capable of forming a strong hydrogen bond with an alcohol molecule.

(11) The alkene products from a dehydrofluorination reaction cannot be isolated since they will react with alkoxide 10³-10⁵ faster to form secondary products.^{4,17}

(12) For reactions of PhC^HH(CF₃)₂ in ethanol, the exchange of the benzylic hydrogen is only 4-5 times faster than is the dehydrofluorination reaction.

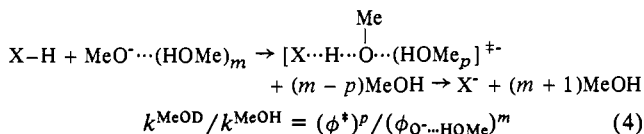
Table II. Solvent and Primary Kinetic Isotope Effects

compd	temp, $^\circ\text{C}$	solvent	KSIE (eq 1)	$(k^H/k^D)_{\text{exch}}$ (eq 2)	$(k^H/k^D)_{\text{elim}}$ (eq 3)
I	75	EtO ^H H	2.30	1.06	1.04
II	25	EtO ^H H	2.74	1.21	1.08
II	25	MeO ^H H	2.63	1.10	1.05

This also makes it impossible to obtain a KSIE for the elimination reaction, and the KSIE for detritiation reactions was used to calculate the primary kinetic isotope effects for the eliminations. Values of the various isotope effects are summarized in Table II.

$$(k^H/k^D)_{\text{elim}} = (k_{\text{ROH}}^H/k_{\text{ROD}}^D)(\text{KSIE})_{\text{exch}} \quad (3)$$

Kinetic Solvent Isotope Effects (KSIE). Gold and Grist¹³ have analyzed possible origins for the KSIE in methanol and conclude that effects are due to a multiple solvated methoxide ion, MeO⁻⋯(HOMe)_m. The deuterium fraction factor, $\phi_{\text{O}^-\cdots\text{HOMe}} = 0.74$, implies that the equilibrium abundance of deuterium in the *m* hydrogen atoms of the solvated methoxide ion is 0.74 times that of bulk solvent. Calculation of a maximum value for KSIE in isotopically pure solvents can be made by using eq 4,



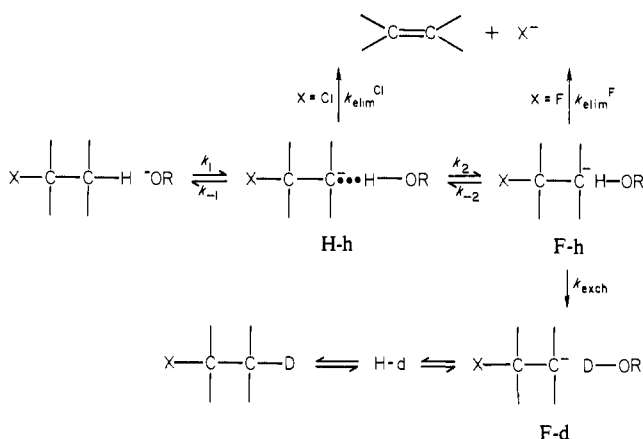
One could predict that ethanol would have a maximum KSIE similar to that calculated for methanol, and the experimental values of 2.74 (25 $^\circ\text{C}$) and 2.30 (75 $^\circ\text{C}$) for ethanol are indeed comparable to the value of 2.63 (25 $^\circ\text{C}$) observed for reaction in methanol. These values suggest that in the rate-determining step of the exchange reactions, alcohol molecules that originally solvated the alkoxide ion now behave like bulk solvent molecules.

Primary Kinetic Isotope Effects (PKIE). The primary kinetic isotope effects observed for both exchange and elimination reactions of I and II are near unity. This suggests extensive amounts of internal return occur with both processes (Scheme I). If $k_{-1} \gg k_2$, the PKIE can be expressed by eq 5, where $K_1 = k_1/k_{-1}$.

$$(k^H/k^D)_{\text{obsd}} = (K_1^H/K_1^D)(k_2^H/k_2^D) \quad (5)$$

An equilibrium isotope effect, K^H/K^D , for the reaction $\text{>C-H} + \text{-OR} \rightleftharpoons \text{>C}^- + \text{HOR}$ can be estimated from zero-point energy

Scheme II



differences between $C-H$ and $O-H$ bonds, which are calculated from stretching frequencies with some allowance made for bending vibrations.¹⁴ This would result in predicted values for $K^H/K^D \approx 0.8$. That value should not be applicable for K_1^H/K_1^D , eq 5, since the intermediate in Scheme I is postulated to have a strong hydrogen bond between the carbanion and the unique alcohol, $>C\cdots^iH-OR$. The zero-point energies for this alcohol molecule in the rate-limiting transition state would not be the same as those for alcohol in bulk solvent and should result in $(k^H/k^D)_{\text{obsd}} > 0.8$.

An alternate approach to predict these values would be to use eq 6, where ϕ_{C-H} is the fractionation factor for the labile hydron

$$(K_1^H/K_1^D) = \phi_{C-H}/\phi_{C\cdots HOR} \quad (6)$$

of the substrate and $\phi_{C\cdots HOR}$ is the fractionation factor for the hydrogen-bonded hydroxyl of the alcohol. Values for ϕ_{C-H} have been reported to be between 0.84 and 1.18 for an sp^3 carbon and 0.78–0.85 for an sp^2 carbon.^{15,16} The fractionation factor of 0.74 for alcohols hydrogen bonded to alkoxide ion could be a reasonable value to estimate the magnitude of $\phi_{C\cdots HOR}$. Making use of eq 6 would allow prediction of K_1^H/K_1^D to be greater than unity, and values of up to 1.5 could be rationalized. To obtain $(k^H/k^D)_{\text{obsd}} = 0.8$, $\phi_{C\cdots HOR}$ would have to be 1.05 to 1.47. Since deuterium content is enhanced in the stronger bonds, one would expect $\phi_{C\cdots HOR}$ to be less than unity, and the experimental value of $\phi_{O\cdots HOMe} = 0.74$ (vide infra)¹³ confirms this expectation.

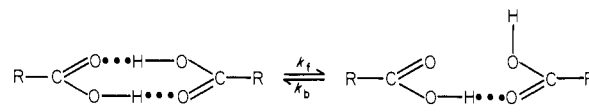
In an attempt to gain information related to k_2^H/k_2^D , both exchange and elimination reactions of I and II were carried out. Using eq 2 and the appropriate $(KSIE)_{\text{exch}}$, $(PKIE)_{\text{exch}}$ values were calculated to be 1.06 (I at 75 °C in ethanol), 1.21 (II at 25 °C in ethanol), and 1.10 (II at 25 °C in methanol). Corresponding $(PKIE)_{\text{elim}}$ values, calculated by using eq 3, are 1.04 (I), 1.08 (II in ethanol), and 1.05 (II in methanol). The PKIE value is slightly greater for any exchange reaction compared to the corresponding elimination, and this fits the proposed mechanism (vide supra) in Scheme II. Larger errors were encountered when calculating activation parameters for reaction of I, and for that reason rate constants were not extrapolated to 25 °C. The isotope effects are, therefore, reported at 75 °C since that was a temperature common to all six studies involving I.

Mechanistic Implications. We have recently proposed a mechanism,¹⁷ which is a refinement of Scheme I, that features two types of carbanions along a reaction pathway common for both nucleophilic reactions of alkenes and elimination and hydron-exchange reactions of saturated compounds (Scheme II).

Initial proton transfer from carbon to alkoxide first forms a strongly hydrogen-bonded carbanion, H, which can return to starting material, k_{-1} , or form a second carbanion, F, by breaking the hydrogen bond, k_2 . The intermediate F is stabilized by a shell of rather loosely attracted alcohol molecules, and any internal return, k_{-2} , at this stage can only occur if the unique alcohol molecule formed by the initial proton-transfer reaction is still in the best position to reprotonate F.

The consequences of having a strong hydrogen bond to the initially formed carbanion H has some important mechanistic implications. If a leaving group is ejected from H, the elimination reaction will give experimental results similar to those of a concerted E2 mechanism in almost all aspects. Since k_2 would be rate limiting for the exchange reaction, the leaving group would depart faster than exchange could occur with solvent molecules. Therefore, elimination would not be accompanied by exchange even though it proceeds via a carbanion intermediate. The hydrogen bond would also preserve the stereochemistry at the carbon atom, and elimination would be stereospecific even though a carbanion is formed.

What might one expect for the energetics in going from H to F? Heats of reaction, ΔH , and the activation parameter ΔH_f^\ddagger have been reported for the following equilibrium:¹⁸



The ΔH values for a series of aliphatic carboxylic acids range from 3 to 6 kcal mol⁻¹; however, corresponding ΔH_f^\ddagger values range from 9 to 12 kcal mol⁻¹. This suggests that the breaking of the hydrogen bond of H could require a substantial ΔH^\ddagger . Therefore, k_2 would become the rate-limiting step and the actual rate of exchange, k_{exch} , could be diffusion controlled. With this model, collapse of F-d to form H-d would occur faster than loss of fluoride from CF₃, $k_{-2} > k_{\text{elim}}^F$.

Another approach to estimate the energetics of the transformation of H to F would be to substitute a better leaving group like chloride for one of the fluorines in I. The ethoxide-promoted dehydrochlorination of C₆H₅C(H)ClCF₂Cl (III) occurs without prior exchange with ethanol and has $k^H/k^D = 3.06$ at 25 °C and $k^{35}/k^{37} = 1.01229$ at 0 °C.¹⁹ The hydrogen isotope effects are almost temperature independent with $E_a^H \approx E_a^D$ and $A^H/A^D = 4.8$,²⁰ and the chlorine isotope effect drops to 1.01003 for III-d. The overall isotope effects are therefore inconsistent with a concerted mechanism and suggest that reaction proceeds via a multistep pathway that includes a carbanion intermediate. A similar behavior of the hydrogen isotope effects has been observed for methoxide-promoted dehydrochlorination of III and dehydrobromination of C₆H₅C(H)BrCF₂Br.²⁰ Both loss of HCl and HBr from C₆H₅CHBrCFClBr proceed stereospecifically by a trans elimination,²¹ whereas C₆H₅CH(CF₃)CHFOCH₃ does not undergo methoxide-promoted dehydrofluorination in a stereospecific manner. This has led us to conclude that chloride and bromide can leave from a strongly hydrogen-bonded intermediate like H, but it is easier to form an intermediate similar to F than it is to eject a β -fluoride.

If III is capable of undergoing a proton-transfer reaction to form an intermediate similar to H prior to loss of chloride, then I should be able to form a corresponding carbanion under similar conditions. Therefore, differences in rates and activation parameters for eliminations of III vs. exchange and elimination reactions of I could be attributed to the energetics of going from H to F and any

(14) Bell, R. P. *Chem. Soc. Rev.* **1974**, *3*, 523.

(15) Schowen, R. L. In "Isotope Effects on Enzyme-Catalyzed Reactions"; Cleland, W. W., O'Leary, M. H., Northrop, D. B., Eds.; University Park Press: Baltimore, MD, 1977; p 70.

(16) An excellent paper which deals with theoretically calculated fractionation factors: Hartshorn, S. R.; Shiner, V. J., Jr. *J. Am. Chem. Soc.* **1972**, *94*, 9002–9012.

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

(18) (a) Sano, T.; Tatsumoto, N.; Niwa, T.; Yasunaga, T. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 2669–2673. (b) Sano, T.; Tatsumoto, N.; Mende, Y.; Yasunaga, T. *Ibid.* **1972**, *45*, 2673–2677.

(19) Koch, H. F.; Koch, J. G.; Tumas, W.; McLennan, D. J.; Dobson, B.; Lodder, G. *J. Am. Chem. Soc.* **1980**, *102*, 7955–7956.

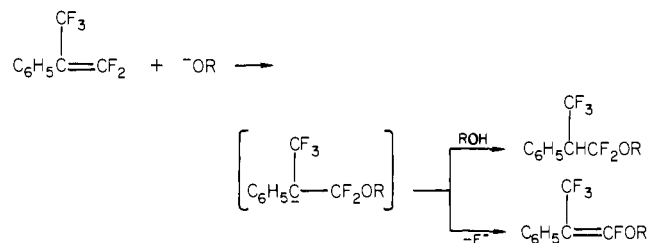
(20) Koch, H. F.; Dahlberg, D. B.; McEntee, M. F.; Klecha, C. J. *J. Am. Chem. Soc.* **1976**, *98*, 1060–1061.

(21) Root, K. S., "Abstracts of Papers", EuChem Conference on Mechanisms of Elimination Reactions, Assisi, Italy, September 12–16, 1977.

following product forming steps. Ethoxide-promoted elimination of III at 25 °C occurs $\sim 10^4$ times faster than the exchange reaction of I and $\sim 10^5$ times faster than the corresponding dehydrofluorination.²² Comparing observed ΔH^\ddagger values, one would predict much larger differences in rates: $\Delta H_{-HCl}^\ddagger = 20$, $\Delta H_{\text{exch}}^\ddagger = 27$, and $\Delta H_{-HF}^\ddagger = 29$ kcal mol⁻¹. This compression of rate differences can be attributed to the more favorable ΔS^\ddagger terms observed for reactions of I compared to III: $\Delta S_{-HCl}^\ddagger = 4$, $\Delta S_{\text{exch}}^\ddagger = 10$, and $\Delta S_{-HF}^\ddagger = 11$ eu. If the rate of exchange with solvent to go from F-h to F-d, k_{exch} , is faster than k_{-2} , then the observed rate and activation parameters for the exchange of I with solvent actually describes the formation of F-h.

The fact that the PKIE value for each exchange reaction is slightly larger than that for the corresponding dehydrofluorination is consistent with both reactions proceeding through a common intermediate, F. If the exchange of alcohol molecules, k_{exch} , is faster than the collapse to H, k_{-2} , then the formation of F-h, k_2 , becomes the rate-limiting step for the overall proton-exchange reaction. The transition state for this step could still have a weak hydrogen bond between the carbanion and alcohol and $\phi_{C\dots HOR}$ would be < 1.0 . On the other hand, in the dehydrofluorination reaction the loss of fluoride, k_{elim}^F , is the rate-limiting step, and this occurs from a free carbanion, F. The proton that was abstracted by the alkoxide is now in a bulk solvent alcohol molecule and $\phi_{C\dots HOR}$ would be equivalent to ϕ_{ROH} (1.0). The PKIE observed for the exchange reaction should thus represent a true equilibrium isotope effect for this reaction.

The rate ratio for exchange:elimination can be a measure of the partitioning of F between proton transfer and ejection of fluoride. For reactions carried out in ethanolic sodium, ethoxide, this ratio is 9–10 for I at 75 °C and 4–5 for II at 25 °C. Since II has two CF₃ groups, that rate of elimination should be divided by two as a statistical factor, and this would make $k_{\text{exch}}/k_{\text{elim}}^F$ approximately the same for both compounds when reaction occurs in ethanol. Reactions of II can also give a comparison for reaction occurring in ethanol (4–5) vs. methanol (7–8). This increase in the proton-transfer reaction relative to ejection of fluoride ion when going from ethanol to methanol is consistent with experimental results obtained for the nucleophilic reactions of alcoholic alkoxide with alkenes.¹⁷ For example, reaction of C₆H₅C(CF₃)=CF₂ with alkoxide results in a mixture of a saturated ether (proton transfer) and vinyl ethers (fluoride ejection). At 20 °C, 21% C₆H₅CH(CF₃)CF₂OC₂H₅ is formed in ethanol compared to 44% C₆H₅C(CF₃)CF₂OCH₃ when reaction is run in methanol. Since fluoride has a better leaving ability from CF₂OR than from CF₃, the loss of fluoride from the intermediate is faster than the proton transfer from alcohol to neutralize the carbanion.



Over 10 years ago Ritchie²³ stated that “those carbon acids whose conjugated 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. That is, saturated hydrocarbons, alkenes, alkynes, and cycloalkanes whose conjugate bases are localized are expected to show ‘kinetic acidities’ greater than their thermodynamic acidities”. At the beginning of this paper we pointed out that the rate of proton transfer for methoxide reacting with PFB could be over 1400 times faster than the same reaction with PhFI. Comparing ion-pair pK_a values, obtained by using cesium cy-

clohexylamide in cyclohexylamine, for PhFI (18.49) and PFB (25.81)²⁴ with the corresponding rate factors is an excellent example of Ritchie’s statement. When will a carbanion be localized or delocalized if reactions are carried out in methanol? Clearly fluorenyl derivatives will be delocalized and phenyl derivatives will be localized.

The fate of benzylic carbanions is not at all clear. We feel that carbanions derived from I and II are highly localized benzylic ions that are relatively stable. One reason for this opinion is the fact that PKIE are near unity for alkoxide-catalyzed exchange reactions in alcohols and that this behavior is similar to compounds where the resulting carbanions can not be delocalized. In the accompanying paper we present additional evidence we feel supports our view.⁴ What happens when the substituents that help stabilize the negative charge on the benzylic carbon are removed? When toluene undergoes exchange in the benzylic position with methanolic sodium methoxide, the observed $k^D/k^T \approx 1.0$ at 178 °C.²⁵ This suggests that toluene behaves similar to I, II, and PFB and does not behave like PhFI. This conclusion is made for reactions occurring in methanol and can probably be extended to reactions in water or other alcohols; however, when the exchange is catalyzed by lithium cyclohexylamide in cyclohexylamine, a normal isotope effect, $k^D/k^T = 3.0$ at 50 °C, is observed.²⁶ There are still many unresolved questions in this area of proton-transfer reactions, and we are continuing experimental studies aimed at providing some answers.

Experimental Section

Materials. The synthesis of the two alkenes required to make I (C₆H₅CCl=CF₂)²⁷ and II (C₆H₅C(CF₃)=CF₂)²⁸ are reported in the literature. Reaction of the appropriate alkene with CsF (3-fold excess) in DMF resulted in the formation of the protio-saturated compound. Greater than 93% deuterium incorporation into the benzylic position could be realized when the reaction mixture was spiked with a 10-fold excess of D₂O. Likewise the incorporation of tritium was accomplished by adding HOT. A detailed synthesis will be reported elsewhere.²⁹ Alcoholic alkoxide solutions were made from a reaction of sodium with alcohol. The small chunks of freshly cut sodium were washed with alcohol prior to placing them into the reaction solution. Deuterated alcohols were purchased from Aldrich and used without further purification. Mass spectra were recorded with an MS-9 mass spectrometer at sufficiently low eV to exclude the P-1 peak. Detritiation runs were monitored with a Nuclear of Chicago Unilux III two-channel liquid scintillation counter. Proton NMR spectra were recorded with a Varian T-60 and ¹⁹F NMR spectra were run with a Varian HA-60IL.

Kinetics. Dehydrofluorination kinetics were carried out under pseudo-first-order conditions with ratios of alkoxide:substrate of better than 15:1. For a typical run, a 50-mL Erlenmeyer was charged with 30–40 mL of a ~ 0.3 N alcoholic alkoxide solution, capped with a serum stopper, and allowed to reach temperature in a constant-temperature bath. The reactant, 100–150 μ L, and a suitable standard, 75–100 μ L, were mixed and then injected into the reaction Erlenmeyer by means of a 1-cm³ glass Luer-lok syringe equipped with a 4-in. stainless steel needle. To assure mixing, the syringe was pumped 10–20 times and this was taken as $T = 0$. Disposable glass syringes (5 cm³) fitted with a 4-in. stainless steel needle were used to take 3–4-mL aliquots which were immediately syringed into ca. 100 mL of dilute aqueous HCl kill solution. The kill solution and 0.25 cm³ of CCl₄ were contained in a 125-mL separating funnel which had a Teflon stopcock. After vigorous shaking for about 1 min, the solutions were allowed to separate, and the CCl₄ layer was carefully removed and analyzed by gas chromatography. A 6-ft SE-30 (20% on 60/80 Chromasorb W) was used. Normally care must be taken since the saturated compound and the corresponding alkene have similar retention times under these conditions; however, the alkene reacts ca. 10³ faster than the corresponding substrate and there-

(24) Streitwieser, A., Jr.; Scannon, P. J.; Niemeyer, H. M. *J. Am. Chem. Soc.* **1972**, *94*, 7936–7937.

(25) Keevil, T. A. Doctoral Dissertation, University of California, Berkeley, 1972.

(26) Streitwieser, A., Jr.; Langworthy, W. C.; Van Sickle, D. E. *J. Am. Chem. Soc.* **1962**, *84*, 251–254.

(27) Burton, D. J.; Anderson, A. L.; Takei, R.; Koch, H. F.; Shih, T. L. *J. Fluorine Chem.* **1980**, *16*, 229–235.

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

(29) Koch, H. F.; Schwab, C. W.; Donovan, D. B.; Frank, J. W., to be submitted to *J. Fluorine Chem.*

(22) Koch, H. F.; Dahlberg, D. B.; Toczko, A. G.; Solsky, R. C. *J. Am. Chem. Soc.* **1973**, *95*, 2029–2030.

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

fore did not interfere with the analysis. A typical run consisted of eight to nine points plus an infinity sample.

Deuterium exchange reaction kinetics were run with 250–300 mL of substrate in 10 mL of alcoholic alkoxide solution. Aliquots (~1 cm³) were syringed into a separatory funnel containing 50 mL of ca. 1 N aqueous HCl and 0.5 mL of CCl₄. The substrate was isolated from the CCl₄ by preparative gas chromatography and then submitted for mass spectral analysis. A typical run consisted of six to eight points plus an infinity sample.

Detritiation kinetics were run with 10–40 μL of substrate in 15 mL of alcoholic sodium alkoxide. Aliquots were taken by a 1-cm³ glass Luer-lok syringe equipped with a 4.5-in. stainless steel needle. Nine points and an infinity sample was taken for each run. The same size sample (0.90–1.00 mL) was taken with a separate syringe for each point. The aliquot was syringed into a 125-mL separatory funnel (with a Teflon stopcock) that contained 50.0 mL of 0.2–0.3 N aqueous HCl and 15.0 mL of toluene. The funnel was shaken for a set time for each run (usually 30–60 s) and then allowed to sit for ca. 10 min prior to draining the lower water layer. The toluene layer was then poured into a 25-mL Erlenmeyer containing Drierite. After the solution dried, 10.0 mL of the toluene solution was added to a scintillation vial containing 10.0 mL of scintillation cocktail (4 g of PPO, 1 g of POPOP in 1.0 L of toluene).

After dark adapting for 30–60 min, the samples were counted.

The results and calculated activation parameters are reported in Table I. The temperature range and number of total runs used for the calculations are also given. Normally we would measure rate constants at 10-deg intervals and a reported range of 50–80 °C with 4 runs would translate to single kinetic runs at 50, 60, 70, and 80 °C. Occasionally a kinetic run would be off the Arrhenius plot and was therefore not included in the calculations.

Acknowledgment. We are grateful to the donors of Petroleum Research Fund, administered by the American Chemical Society, and to the Research Corporation for a Cottrell College Science Grant for support of this research. We thank Jerry Kresge and William Tumas for helpful suggestions and discussions, and J. van Thuijl, W. C. M. M. Luyten, and J. J. van Houte for the mass spectral data used to calculate the hydrogen and deuterium exchange rates.

Registry No. D₂, 7782-39-0; H₂, 1333-74-0; T₂, 10028-17-8; EtOD, 925-93-9; MeOD, 1455-13-6; C₆H₅CHClCF₃, 384-65-6; C₆H₅CH(CF₃)₂, 3142-78-7.

Photolytic Cleavage of Remote Functional Groups in Polyfunctional Molecules. Photolysis of *exo*- and *endo*-2-Benzonorbornenyl Chlorides and Methanesulfonates^{1a,b}

Harry Morrison,*^{1c} Alan Miller,^{1c} and B. Bigot^{1d}

Contribution from the Department of Chemistry, Purdue University West Lafayette, Indiana 47907, and Laboratoire de Chimie Organique Théorique, Université Pierre et Marie Curie, Paris Cedex 75230, France. Received July 12, 1982

Abstract: The photochemistry and photophysics of the title compounds are reported. The *exo* chloride exhibits a facile cleavage of the C–Cl bond upon excitation of the aryl chromophore (eq 1–3). The reaction has a rate >700-fold larger than that observed with the *endo* isomer, derives from the singlet excited state, and leads to the formation of “hot” carbocations as well as free radicals. The *exo* mesylate shows similar characteristics (eq 4). A mechanism (Scheme II) is suggested which incorporates both heterolytic fission as well as sequential homolytic fission (to a polarized radical pair), followed by electron transfer to form an ion pair. The stereoelectronically controlled activation of the C–Cl and C–OMs moieties is explained by a correlation diagram (Figure 5) which depicts the π, π^* state as correlating with the diradical product state through an avoided crossing with the C–X σ, σ^* state. Calculations indicate that this avoided crossing is considerably larger (and the barrier to reaction therefore considerably smaller) when the C–X unit in the 2-benzonorbornenyl series is *exo*.

Introduction

The photochemical and spectroscopic consequences of intramolecular interactions between nonconjugated functionalities remains a subject of considerable interest.² There is now ample evidence that only by a systematic investigation of model bifunctional substrates can the organic photochemist expect to understand and utilize the diverse chemistry to be found in complex multifunctional compounds. Toward these ends we have earlier

presented a preliminary report³ on an unusual, stereoelectronically controlled, photolytic cleavage of the chloro and methanesulfonyl (mesyl) groups in the benzonorbornenyl series. In this paper, we summarize our detailed studies on these interesting examples of the photoactivation of remote functional groups.

Results

A. Photochemistry and Spectroscopy of *exo*-2-Benzonorbornenyl Chloride (*exo*CIBNB). Photochemistry of *exo*CIBNB in Cyclohexane. The title compound was prepared by hydrochlorination of benzonorbornadiene.⁴ Irradiation of a 0.02 M solution in cyclohexane at 254 nm produces HCl and two volatile photoproducts which have been identified as benzonorbornene (**1**) and bicyclohexyl (**2**) by comparison of spectra with authentic samples.⁵ Quantum efficiencies were determined in low conversion runs and are given in eq 1.⁶

(1) (a) Organic Photochemistry. 54. Part 53: Morrison, H.; Giachero, D.; Pandey, G. *Tetrahedron Lett.* 1982, 3437. Part 52: Morrison, H.; Miller, A.; Pandey, B.; Pandey, G.; Severance, D.; Strommen, R.; Bigot, B. *Pure Appl. Chem.* 1982, 54, 1723. Part 51: Morrison, H.; Giachero, D. *J. Org. Chem.* 1982, 47, 1058. (b) Abstracted, in part, from the Doctoral Dissertation of A. M., Purdue University, 1980. (c) Purdue University. (d) Université Pierre et Marie Curie.

(2) (a) For a review and leading references, see: Morrison, H. *Acc. Chem. Res.* 1979, 12, 383. (b) Additional examples include Lin, C-I; Singh, P.; Maddox, M.; Ullman, E. F. *J. Am. Chem. Soc.* 1980, 102, 3261. Studebaker, J.; Srinivasan, R.; Ors, J. A.; Baum, T. *Ibid.* 1980, 102, 6872. McCullough, J. J.; MacInnis, W. K.; Lock, C. J. L.; Faggiani, R. *Ibid.* 1980, 102, 7782. Manning, T. D. R.; Kropp, P. J. *Ibid.* 1981, 103, 889. Calcaterra, L. T.; Schuster, D. I. *Ibid.* 1981, 103, 2460. Castellan, A.; Desvergne, J.-P.; Bouas-Laurent, H. *Chem. Phys. Lett.* 1980, 76, 390. Cristol, S. J.; Opitz, R. J.; Bindel, T. H.; Dickenson, W. A. *J. Am. Chem. Soc.* 1980, 102, 7977.

(3) Morrison, H.; Miller, A. *J. Am. Chem. Soc.* 1980, 102, 372.

(4) Wilt, J. W.; Gutman, G.; Ranus, W. J., Jr.; Zigman, A. R. *J. Org. Chem.* 1967, 32, 893.

(5) Several high molecular weight products are also detectable, the principal two being tentatively assigned as *exo*- and *endo*-2-cyclohexylbenzonorbornene on the basis of ¹H NMR and mass spectral data.