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Use of Kinetic Isotope Effects in Mechanism Studies. 5.[1] Isotope Effects and Element Effects Associated with Hydron-Transfer Steps during Alkoxide-Promoted Dehydrohalogenations

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Abstract: The Arrhenius behavior of the primary kinetic isotope effect, $(k^H/k^D)_{Obs}$ and $(k^H/k^T)_{Obs}$, associated with the methanolic sodium methoxide-promoted dehydrohalogenations of $m\text{-}ClC_6H_4C^iHClCH_2Cl$ (**I**), $m\text{-}CF_3C_6H_4C^iHClCH_2Cl$ (**II**) and $p\text{-}CF_3C_6H_4C^iHClCH_2F$ (**III**) has been used to calculate the internal-return parameters, $\mathbf{a} = k_{-1}/k^X_{Elim}$, in a two-step mechanism featuring a hydrogen-bonded carbanion. This carbanion partitions between returning the hydron to carbon, k_{-1}, and the loss of halide, k^X_{Elim}. Isotope effects at 25 °C for **I**, $(k^H/k^D)_{Obs} = 3.40$ and $(k^H/k^T)_{Obs} = 6.20$, and **II**, $(k^H/k^D)_{Obs} = 3.49$ and $(k^H/k^T)_{Obs} = 6.55$, result in similar values for **a**: $\mathbf{a^H} = 0.59$, $\mathbf{a^D} = 0.13-0.14$ and $\mathbf{a^T} = 0.07$. Smaller values of $(k^H/k^D)_{Obs} = 2.19$ and $(k^H/k^T)_{Obs} = 3.56$ for **III** are due to more internal return [$\mathbf{a^H} = 1.9$, $\mathbf{a^D} = 0.50$, and $\mathbf{a^T} = 0.28$] associated with the dehydrofluorination reaction. Calculation of k_1 (= k_{Obs} [$\mathbf{a}$ + 1]) results in similar isotope effects for hydron transfer in these reactions: **I**, $k_1^H/k_1^D = 4.74$ and $k_1^H/k_1^T = 9.20$; **II**, $k_1^H/k^D_1 = 4.91$ and $k_1^H/k_1^T = 9.75$; **III**, $k_1^H/k_1^D = 4.75$ and $k_1^H/k_1^T = 9.17$. Reactions of $m\text{-}ClC_6H_4C^iHBrCH_2Br$ and $m\text{-}ClC_6H_4C^iHClCH_2Br$ have very small amounts of internal return, $\mathbf{a^H} = 0.05$ and $\mathbf{a^D} = 0.01$, and $(k^H/k^D)_{Obs} = 4.95$ results in $k_1^H/k_1^D = 5.11$. The measured isotope effects are therefore due to differences in the amount of internal return and not in the symmetry of transition state structures for the hydron transfer, and the element effect, $(k^{HBr}/k^{HCl}) = 29$, for $m\text{-}ClC_6H_4CHClCH_2X$ is mainly due to the hydron-transfer step, $k_1^{HBr}/k_1^{HCl} = 19$, and not the breaking of the C−X bond. The kinetic solvent isotope effects, $k^{MeOD}/k^{MeOH} \approx 2.5$, are consistent with three methanols of solvation lost prior to the hydron-transfer step. The energetics associated with desolvation of methoxide ion are part of the measured reaction energetics of these systems.

Our interest in alkoxide-promoted dehydrohalogenation reactions began with measuring an extreme element effect, $k^{HCl}/k^{HF} > 10^5$, for the ethoxide-promoted eliminations of $C_6H_5\text{-}CHClCF_2X$, where X = Cl or F. Kinetic studies of primary kinetic isotope effects [PKIE] and Hammett ρ values led to the suggestion that hydrogen-bonded carbanion intermediates are formed on the reaction coordinate.[3] Alkoxide-promoted eliminations of $C_6H_5C^iHXCF_2X$ [X = Br or Cl and ^iH = H or D] resulted in normal element effects, $k^{HBr}/k^{HCl} = 39-48$, and medium sized PKIE, $k^H/k^D = 2.3$ to 4.5. These results could be indicative of a concerted pathway; however, the Arrhenius behavior of the isotope effects is inconsistent with an E2 mechanism.[4] This raises the question about the origin of the element effects associated with alkoxide-promoted dehydrohalogenations in general.

We became aware of the complexities of hydron transfer between carbon and oxygen[5] while studying the formation of a carbanion, $\{C_6H_5C(CF_3)CF_2OCH_2CH_3\}^-$, *via* either a nucleophilic addition of ethoxide to $C_6H_5C(CF_3){=}CF_2$ or a proton abstraction from $C_6H_5CH(CF_3)CF_2OCH_2CH_3$. A mechanism featuring two carbanion intermediates was postulated to explain the hydrogen isotope effects that are associated with these reactions.[6,7] One carbanion is stabilized by a hydrogen bond while the other one has no contact stabilization by either solvent or the counterion.

That mechanism has been a model for our studies of alkoxide-promoted dehydrohalogenations and alkoxide-catalyzed exchange reactions, Scheme 1. The extreme element effect obtained for the ethoxide-promoted eliminations of $C_6H_5\text{-}CHClCF_2Cl$ and $C_6H_5CHClCF_3$ results from the loss of chloride occurring from a hydrogen-bonded carbanion, **HB**, while the loss of fluoride from $−CF_3$ requires the formation of a free carbanion, **FC**. Exchange of hydron from $C_6H_5C^iHClCF_3$ occurring 13 times faster than the loss of HF with a near unity

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(1) Part 4: Koch, H. F.; McLennan, D. J.; Koch, J. G.; Tumas, W.; Dobson, B.; Koch, N.H. *J. Am. Chem. Soc.* **1983,** *105,* 1930.

(2) (a) Summer research student at Leiden from Ithaca College. (b) Summer research student at Ithaca from the University of Leiden. (c) Summer research student at Leiden from Oberlin College.

(3) Koch, H. F.; Dahlberg, D. B.; Toczko, A. G.; Solsky, R. L. *J. Am. Chem. Soc.* **1973,** *95,* 2029.
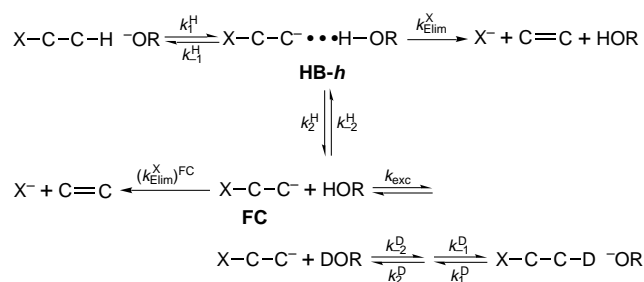
(4) Koch, H. F.; Dahlberg, D. B.; McEntee, M. F.; Klecha, C. J. *J. Am. Chem. Soc.* **1976,** *98,* 1060.

(5) Koch, H. F. *Acc. Chem. Res.* **1984,** *17,* 137.

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

(7) Koch, H. F.; Koch, A. S. *J. Am. Chem. Soc.* **1984,** *106,* 4536.

Scheme 1

isotope effect is consistent with the loss of fluoride ion from **FC**. Since Br$^-$ can leave from a hydrogen-bonded carbanion, k^{HBr}/k^{HCl} values are normal.

Discussion and Results

Distinguishing between Concerted and Nonconcerted Alkoxide-Promoted Dehydrohalogenations. When dehydrohalogenations occur *via* the hydrogen-bonded intermediate in Scheme 1, observed rate constants are defined by

$$k_{Obs} = [k_1 k_{Ellim}^X]/[k_{-1} + k_{Elim}^X] \qquad (1)$$

There are two extremes: (a) $k_{-1} >> k_{Elim}^X$ then $k_{Obs} = [k_1/k_{-1}]$ k_{Elim}^X, and (b) $k_{Elim}^X >> k_{-1}$ then $k_{Obs} = k_1$. For case a second-order kinetics, a near unity PKIE, and a substantial element effect are expected. Case b results in second-order kinetics, a PKIE that obeys the Swain−Schaad relationship,[8] $k^H/k^D = (k^D/k^T)^{2.26}$. For a concerted reaction, both C−H and C−X bonds are partially broken in the transition structure, and could give a variable PKIE, which obeys the Swain−Schaad relationship, as well as a variable element effect, which should be the same for the loss of HX and DX.

When neither extreme for eq 1 is applicable, all three rate constants, k_1, k_{-1}, and k_{Elim}^X, contribute to the experimental rate constants and there is no single rate-determining step. The measured PKIE will vary between the extremes mentioned above; however, the Swain−Schaad relationship would not hold. Streitwieser *et al.* made use of deviations from the Swain−Schaad relationship and single temperature rate constants for all three hydrogen isotopes to calculate an internal-return parameter, $\mathbf{a} = k_{-1}/k_2$ [in our case $k_2 = k_{Elim}^X$].[9] This parameter can be used to calculate k_1 (= k_{Obs} [$\mathbf{a}$ + 1]) for all three isotopic reactions.

The use of eq 2 and a similar one for $(k^H/k^T)_{Obs}$ gives an alternate way to determine the values of $\mathbf{a}$ as well as the energetics associated with internal return by modeling experimental isotope effects obtained over a 25 to 50°C range:[10]

$$\ln(k^H/k^D)_{obs} = [((E_1^D - E_{-1}^D) - (E_1^H - E_{-1}^H))/RT] + \ln\left(\frac{1 + (A_{Elim}^X/A_{-1}) \exp((E_{-1}^D - E_{Elim}^X)/RT)}{1 + (A_{Elim}^X/A_{-1}) \exp((E_{-1}^H - E_{Elim}^X)/RT)}\right) \qquad (2)$$

Three systems were used in our analysis of alkoxide-promoted dehydrohalogenations: $C_6H_5CH_2CH_2X$ and various YC_6H_4-$CHX'CH_2X$ and $YC_6H_4CHX'CF_2X$, where X = Br, Cl, or F and X′ = Br or Cl. Results from reactions of ethanolic sodium

ethoxide with all three systems are in Table 1, while those for the reactions of methanolic sodium methoxide with $YC_6H_4C^i$-$HX'CH_2X$ and $YC_6H_4C^iHX'CF_2X$ are in Table 2. The reactions of $C_6H_5CH_2CH_2X$ were previously reported,[11] and we measured the k^H/k^D associated with $C_6H_5C^iH_2CH_2Cl$ to compare it to that reported for $C_6H_5C^iH_2CH_2Br$.[12] Four systems used three hydrogen isotopes to calculate internal-return parameters: m-$CF_3C_6H_4C^iHClCH_2Cl$, m-$ClC_6H_4C^iHClCH_2Cl$, p-$CF_3C_6H_4C^i$-$HClCH_2F$, and m-$ClC_6H_4C^iHCBrCH_2Br$. Kinetic solvent isotope effects were measured for $C_6H_5CTClCF_2Cl$ and C_6H_5-$CHClCH_2Br$ by using mixtures of CH_3OH and CH_3OD, and the Arrhenius behavior was studied for the dehydrochlorination of p-$CF_3C_6H_4CHClCH_2Cl$ and the protodetritiation of p-$CF_3C_6H_4$-$CTClCF_3$.

Hydrogen Isotope Effects Associated with the Ethoxide-Promoted Dehydrohalogenation Reactions. The results in Table 1 show a decrease in k^H/k^D for ethoxide-promoted eliminations of HBr and HCl at 25 °C from the least reactive to the most reactive: $C_6H_5CH_2CH_2Br$ (7.53), $C_6H_5CHClCH_2$-Br (6.10), and $C_6H_5CHBrCF_2Br$ (4.51); and $C_6H_5CH_2CH_2Cl$ (7.43), $C_6H_5CHClCH_2Cl$ (4.24), and $C_6H_5CHClCF_2Cl$ (2.73). According to theory, primary kinetic isotope effects result from differences in C−^iH and/or O−^iH bond zero-point energies in the ground state and the transition structure. Thus the Arrhenius preexponential factors, A, should be equal for isotopically labeled compounds,[13] and k^H/k^D results from ΔE_a^{D-H}, $k^H/k^D = (A^H/A^D) \exp(\Delta E_a^{D-H}/RT)$. The single temperature PKIE values suggest a symmetrical transition structure for eliminations of $C_6H_5C^iH_2CH_2X$ and later transition structures for the other eliminations.[14] However, there are significant differences for the temperature dependence of the isotope effects as A^H/A^D values range from 0.5 to 3.1. Arrhenius parameters associated with $C_6H_5C^iH_2CH_2Cl$ are normal with $\Delta E_a^{D-H} = 1.2$ kcal/mol and $A^H/A^D = 1.1$. Although k^H/k^D is the same for $C_6H_5C^iH_2$-CH_2Br (7.53), the Arrhenius parameters differ with $\Delta E_a^{D-H} = 1.6$ kcal/mol and $A^H/A^D = 0.51$, which halves the k^H/k^D predicted from ΔE_a^{D-H}. The latter results were interpreted as resulting from an E2 mechanism that has quantum-mechanical tunneling.[15]

At the other extreme are the reactions of $C_6H_5C^iHBrCF_2Br$ [$\Delta E_a^{D-H} = 0.3$ kcal/mol and $A^H/A^D = 3.1$] and $C_6H_5C^iHClCF_2$-Cl [$\Delta E_a^{D-H} = 0.1$ kcal/mol and $A^H/A^D = 2.2$], where the calculated A^H/A^D accounts for 69% to 82% of the measured k^H/k^D. High A^H/A^D values of 2.1 to 2.9 were also encountered for reactions of $C_6H_5C^iHClCH_2Cl$, m-$ClC_6H_4C^iHClCH_2Cl$, m-$CF_3C_6H_4C^iHClCH_2Cl$, and $C_6H_5C^iHClCH_2Br$ while those obtained from reactions of m-$CH_3C_6H_4C^iHClCH_2Br$,[16] m-$CH_3C_6H_4C^iHBrCH_2Br$, and $C_6H_5C^iHBrCH_2Br$ are normal with ΔE_a^{D-H} of 0.9 to 1.1, A^H/A^D of 0.8 to 1.4, and k^H/k^D of

(8) Swain, C. G.; Stivers, E. C.; Reuwer, J. T.; Schaad, L. J. *J. Am. Chem. Soc.* **1958**, *80*, 5885.

(9) (a) Streitwieser, A., Jr.; Hollyhead, W. B.; Sonnichsen, G.; Pudjaatmaka, A. H.; Chang, C. J.; Kruger, T. L. *J. Am. Chem. Soc.* **1971**, *93*, 5096. (b) The exponent for the Swain-Schaad relationship used in ref 9a is 2.344.

(10) Koch, H. F.; Dahlberg, D. B. *J. Am. Chem. Soc.* **1980**, *102*, 6102.

(11) DePuy, C. H.; Bishop, C. A. *J. Am. Chem. Soc.* **1960**, *82*, 2535.

(12) Saunders, W. H., Jr.; Edison, D. H. *J. Am. Chem. Soc.* **1960**, *82*, 138.

(13) Schneider and Stern [Schneider, M. E.; Stern, M. J. *J. Am. Chem. Soc.* **1972**, *94*, 1517] considered a variety of model reactions and showed that A^H/A^D was always between 0.7 and 1.2 for a temperature range of 20−2000 K, and had an absolute minimum value of 0.5. Reference 10 includes some calculations where $A^H \neq A^D$.

(14) Since the ρ values of the other reactions are larger than those reported in the phenethyl series, the smaller PKIE values would suggest later rather than earlier transition structures.

(15) Kaldor, S. B.; Saunders, W. H., Jr. *J. Am. Chem. Soc.* **1979**, *101*, 7594.

(16) The A^H/A^D value of 2.1 calculated for $C_6H_5C^iHClCH_2Br$ [Table 3] was obtained from six kinetic points over a 35 °C range for $^iH = H$ and five kinetic points over a 50 °C range for $^iH = D$. The choice of measuring the parameters for m-$CH_3C_6H_4C^iHClCH_2Br$ was made to compare two dehydrohalogenations that occur at almost the same rates: m-$CH_3C_6H_4C^i$-$HClCH_2Br$ (1.2) and $C_6H_5C^iHClCH_2Cl$ (1.0). We plan to redo the $C_6H_5C^i$-$HClCH_2Br$ kinetics.

Table 1. Rate Constants, Activation Parameters, and Hydrogen Isotope Effects for Ethanolic Sodium Ethoxide-Promoted Dehydrohalogenation Reactions

compound	k, M^{-1} s^{-1} (25 °C)	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu (25 °C)	k^{H}/k^{D} or k^{D}/k^{T} (25 °C)	ΔE_a, kcal	A^{H}/A^{D} or A^{D}/A^{T}	temp range, °C [no. of points]
C$_6$H$_5$CH$_2$CH$_2$F^a	4.35×10^{-8}	25.6	-6.4				60 to 80
C$_6$H$_5$CH$_2$CH$_2$Cl	2.95×10^{-6}	22.8 ± 0.1	-7.4 ± 0.2	7.43	1.2	1.1	45 to 85 [10]
C$_6$H$_5$CD$_2$CH$_2$Cl	3.97×10^{-7}	24.0 ± 0.3	-7.4 ± 0.6				50 to 75 [5]
C$_6$H$_5$CH$_2$CH$_2$Br^b	2.32×10^{-4}	20.4 ± 0.3	-6.6 ± 0.9	7.53	1.6	0.5	30 to 50 [3]
C$_6$H$_5$CD$_2$CH$_2$Br	3.08×10^{-5}	22.0 ± 0.2	-5.3 ± 0.5				30 to 50 [3]
C$_6$H$_5$CH$_2$CF$_2$Cl^c	2.47×10^{-4}	20.3 ± 0.1	-7.1 ± 0.5				25 to 70 [5]
C$_6$H$_5$CHClCH$_2$F	2.07×10^{-5}	23.1 ± 0.1	-2.4 ± 0.3	2.20	0.3	1.4	30 to 80 [12]
C$_6$H$_5$CDClCH$_2$F	9.43×10^{-6}	23.4 ± 0.1	-3.0 ± 0.3				45 to 85 [8]
p-CF$_3$C$_6$H$_4$CHClCH$_2$F	4.43×10^{-3}	20.4 ± 0.1	-1.0 ± 0.3	2.59	0.4	1.2	20 to 50 [6]
p-CF$_3$C$_6$H$_4$CDClCH$_2$F	1.71×10^{-3}	20.8 ± 0.1	-1.3 ± 0.4				20 to 50 [6]
C$_6$H$_5$CHClCH$_2$Cl^{d,e}	1.39×10^{-3}	20.7 ± 0.1	-2.3 ± 0.3	4.24	0.3	2.5	-10 to 50
C$_6$H$_5$CDClCH$_2$Cl	3.28×10^{-4}	21.0 ± 0.2	-4.1 ± 0.5				20 to 70
m-ClC$_6$H$_4$CHClCH$_2$Cl	2.64×10^{-2}	19.1 ± 0.1	-1.6 ± 0.2	4.17	0.3	2.5	-15 to 25 [17]
m-ClC$_6$H$_4$CDClCH$_2$Cl	6.33×10^{-3}	19.4 ± 0.1	-3.4 ± 0.4				10 to 50 [6]
m-CF$_3$C$_6$H$_4$CHClCH$_2$Cl	5.79×10^{-2}	18.8 ± 0.1	-1.3 ± 0.4	4.11	0.3	2.9	-10 to 20 [3]
m-CF$_3$C$_6$H$_4$CDClCH$_2$Cl	1.41×10^{-2}	19.0 ± 0.1	-3.4 ± 0.1				-10 to 40 [10]
m-CH$_3$C$_6$H$_4$CHClCH$_2$Br	3.06×10^{-2}	17.9 ± 0.1	-5.4 ± 0.2	5.70	1.0	1.2	-20 to 30 [11]
m-CH$_3$C$_6$H$_4$CDClCH$_2$Br	5.37×10^{-3}	18.9 ± 0.1	-5.7 ± 0.2				0 to 55 [10]
C$_6$H$_5$CHClCH$_2$Br	4.89×10^{-2}	18.0 ± 0.1	-4.3 ± 0.2	6.11	0.7	2.1	-10 to 25 [6]
C$_6$H$_5$CDClCH$_2$Br	8.00×10^{-3}	18.7 ± 0.1	-5.5 ± 0.5				-10 to 40 [5]
m-CH$_3$C$_6$H$_4$CHBrCH$_2$Br^d	2.28×10^{-2}	18.5	-3.8	5.88	0.9	1.4	-10 to 35 [10]
m-CH$_3$C$_6$H$_4$CDBrCH$_2$Br	3.88×10^{-3}	19.4	-4.4				0 to 50 [11]
C$_6$H$_5$CHBrCH$_2$Br^d	3.07×10^{-2}	18.1	-4.8	5.83	1.1	0.8	-20 to 30 [6]
C$_6$H$_5$CDBrCH$_2$Br	5.27×10^{-3}	19.2	-4.5				0 to 45 [6]
C$_6$H$_5$CHClCF$_3$^{f}	4.46×10^{-7}	29.8 ± 0.1	12.2 ± 0.2				70 to 110 [4]
C$_6$H$_5$CHBrCF$_3$	4.64×10^{-7}	29.4 ± 0.3	11.1 ± 0.9				70 to 100 [3]
p-CF$_3$C$_6$H$_4$CHClCF$_3$	3.84×10^{-4}	27.1 ± 0.2	16.6 ± 0.5				20 to 60 [9]
2,6-Cl$_2$C$_6$H$_3$CHClCF$_2$Cl	5.53×10^{-3}	17.0 ± 0.2	-11.8 ± 0.2				10 to 50 [6]
C$_6$H$_5$CHClCF$_2$Cl^e	2.21×10^{-1}	18.6 ± 0.2	0.8 ± 0.5	2.73	0.1	2.2	-20 to 15
C$_6$H$_5$CDClCF$_2$Cl	8.09×10^{-2}	18.7 ± 0.1	-0.8 ± 0.3				-15 to 25
C$_6$H$_5$CHBrCF$_2$Cl	2.14×10^{-1}	18.6 ± 0.2	0.7 ± 0.7				-25 to 15 [9]
C$_6$H$_5$CHBrCF$_2$Br	8.30	14.9 ± 0.1	-4.2 ± 0.4	4.51	0.3	3.1	-55 to -25 [8]
C$_6$H$_5$CDBrCF$_2$Br	1.84	15.2 ± 0.1	-6.5 ± 0.4				-35 to 0 [8]

^{a} Reference 11. ^{b} Reference 12. ^{c} Reworked data from ref 17. ^{d} Corrected for wrong way elimination. ^{e} Reference 1. ^{f} Reference 35.

5.70 to 5.88 at 25 °C. The solvent properties of ethanol are not as good as those for methanol, and for that reason a majority of the more detailed investigations of the YC$_6$H$_4$C^{i}HClCH$_2$X systems use methanolic sodium methoxide. Faster reactions in ethanolic ethoxide are attributed to less internal return for the larger ethanol.[17] The k^{EtOH}/k^{MeOH} at 25 °C are 30 for p-CF$_3$C$_6$H$_4$-CHClCH$_2$F, 11 to 17 for YC$_6$H$_4$CHClCH$_2$Cl, 10 to 11 for YC$_6$H$_4$CHClCH$_2$Br, and 7 for C$_6$H$_5$CHBrCH$_2$Br.

Comparison of the Element and Chlorine 35/37 Isotope Effects Associated with Ethoxide-Promoted Dehydrohalogenations. The element effect was first proposed by Bunnett in a 1957 paper "The 'Element Effect' as a Criterion of Mechanism in Activated Aromatic Nucleophilic Substitution Reactions",[18] and has also been used for studies of dehydrohalogenation mechanisms.[19,20] Use of k^{HBr}/k^{HCl} values replaces the measurement of chlorine isotope effects, and should result from differences of activation enthalpies for reactions with similar activation entropies. Element effects associated with

the ethoxide-promoted dehydrohalogenations of the β-phenethyl halides are good examples as $\Delta S^{\ddagger} = -6 \pm 1$ eu, and values of k^{HCl}/k^{HF} and k^{HBr}/k^{HCl} are due to $\Delta H^{\ddagger}$ differences: $k^{HCl}/k^{HF} = 68$, $\Delta\Delta H^{\ddagger} = 2.8$ kcal/mol [HF $-$ HCl]; $k^{HBr}/k^{HCl} = 79$, $\Delta\Delta H^{\ddagger} = 3.0$ kcal/mol [HCl $-$ HBr].

Values of k^{HBr}/k^{HCl} are similar for C$_6$H$_5$CHClCH$_2$X (35) and C$_6$H$_5$CHBrCF$_2$X (39); however, the k^{HCl}/k^{HF} of 67 for C$_6$H$_5$-CHClCH$_2$X, which is quite normal, differs dramatically from the k^{HCl}/k^{HF} of 1.8×10^5 for C$_6$H$_5$CHBrCF$_2$X. The $\Delta S^{\ddagger}$ values for the C$_6$H$_5$CHClCH$_2$X series are all within 3 eu, and the element effects are largely due to the differences in $\Delta H^{\ddagger}$: $\Delta\Delta H^{\ddagger} = 2.4$ kcal/mol [HF $-$ HCl] and $\Delta\Delta H^{\ddagger} = 2.7$ kcal/mol [HCl $-$ HBr]. In contrast, $\Delta S^{\ddagger}$ values for the C$_6$H$_5$CHBrCF$_2$X series differ significantly, favoring loss of HF [11 eu] over HCl [1 eu] and HBr [-4 eu]. The very large k^{HCl}/k^{HF} for C$_6$H$_5$-CHBrCF$_2$X comes from a much larger $\Delta\Delta H^{\ddagger}$ (10.8 kcal/mol) that is partially offset by a more favorable $\Delta S^{\ddagger}$ for the dehydrofluorination reaction. For k^{HBr}/k^{HCl} the more favorable $\Delta S^{\ddagger}$ for elimination of HCl from C$_6$H$_5$CHBrCF$_2$Cl helps to compensate for the slightly larger $\Delta\Delta H^{\ddagger}$ of 3.7 kcal/mol (HCl $-$ HBr).

The use of element effects to distinguish between an E2 mechanism and a multi-step process with internal return has been questioned.[21] In Table 3 chlorine isotope effects, k^{35}/k^{37},

(17) Koch, H. F.; Tumas, W.; Knoll, R. *J. Am. Chem. Soc.* **1981**, *103*, 5423.

(18) Bunnett, J. F.; Garbisch, E. W.; Pruitt, K. M. *J. Am. Chem. Soc.* **1957**, *79*, 385.

(19) Bartsch, R. A.; Bunnett, J. F. *J. Am. Chem. Soc.* **1968**, *90*, 408.

(20) Gandler, J. R. In The Chemistry of Double-bonded Functional Groups; Patai, Ed.; John Wiley &Sons Ltd.: New York, 1989; p 742−744.

Table 2. Rate Constants, Activation Parameters, and Hydrogen Isotope Effects for Methanolic Sodium Methoxide-Promoted Dehydrohalogenation Reactions

compd	k, M^{-1} s^{-1} (25 °C)	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu (25 °C)	k^H/k^D or k^D/k^T (25 °C)	ΔE_a, kcal	A^H/A^D or A^D/A^T	temp range, °C [no. of points]
p-CF$_3$C$_6$H$_4$CHClCH$_2$F	1.49×10^{-4}	23.4 ± 0.1	2.6 ± 0.3				25 to 65 [10]
p-CF$_3$C$_6$H$_4$CDClCH$_2$F	6.81×10^{-5}	23.9 ± 0.1	2.5 ± 0.3	2.19	0.5	1.1	25 to 60 [6]
p-CF$_3$C$_6$H$_4$CTClCH$_2$F	4.19×10^{-5}	24.2 ± 0.2	2.6 ± 0.6	1.63	0.3	0.93	35 to 63 [9]
C$_6$H$_5$CHClCH$_2$Cl[a]	1.25×10^{-4}	21.7	-3.5				25 to 70
C$_6$H$_5$CDClCH$_2$Cl	3.26×10^{-5}	22.6	-3.4	3.83	0.9	0.95	30 to 75
m-ClC$_6$H$_4$CHClCH$_2$Cl	1.60×10^{-3}	21.1 ± 0.1	-0.5 ± 0.1				0 to 50 [22]
m-ClC$_6$H$_4$CDClCH$_2$Cl	4.71×10^{-4}	21.9 ± 0.1	-0.4 ± 0.5	3.40	0.8	0.96	10 to 60 [9]
m-ClC$_6$H$_4$CTClCH$_2$Cl	2.58×10^{-4}	22.3 ± 0.2	-0.0 ± 0.5	1.83	0.4	0.81	10 to 40 [3]
m-CF$_3$C$_6$H$_4$CHClCH$_2$Cl	3.34×10^{-3}	20.3 ± 0.1	-1.7 ± 0.2				5 to 50 [9]
m-CF$_3$C$_6$H$_4$CDClCH$_2$Cl	9.58×10^{-4}	21.1 ± 0.1	-1.7 ± 0.2	3.49	0.8	1.0	10 to 60 [11]
m-CF$_3$C$_6$H$_4$CTClCH$_2$Cl	5.10×10^{-4}	21.5 ± 0.1	-1.5 ± 0.3	1.88	0.4	0.92	20 to 55 [8]
p-CF$_3$C$_6$H$_4$CHClCH$_2$Cl	8.03×10^{-3}	20.08 ± 0.04	-0.7 ± 0.2				0 to 40 [7]
CH$_3$ONa/CH$_3$OD	1.98×10^{-2}	19.34 ± 0.06	-1.5 ± 0.2				0 to 35 [6]
m-CH$_3$C$_6$H$_4$CHClCH$_2$Br	3.12×10^{-3}	20.1 ± 0.1	-2.5 ± 0.2	5.01	0.9	1.2	5 to 55 [10]
m-CH$_3$C$_6$H$_4$CDClCH$_2$Br	6.23×10^{-4}	21.0 ± 0.2	-2.8 ± 0.6				20 to 70 [9]
C$_6$H$_5$CHClCH$_2$Br	4.38×10^{-3}	19.3 ± 0.1	-4.6 ± 0.2	5.43	1.2	0.67	0 to 50 [12]
C$_6$H$_5$CDClCH$_2$Br	8.07×10^{-4}	20.5 ± 0.1	-3.8 ± 0.2				5 to 60 [11]
p-ClC$_6$H$_4$CHClCH$_2$Br	2.35×10^{-2}	18.6 ± 0.1	-3.4 ± 0.4	5.21	1.0	0.98	-10 to 40 [7]
p-ClC$_6$H$_4$CDClCH$_2$Br	4.51×10^{-3}	19.6 ± 0.1	-3.4 ± 0.4				0 to 50 [11]
m-ClC$_6$H$_4$CHClCH$_2$Br	4.58×10^{-2}	17.8 ± 0.1	-5.0 ± 0.3	4.94	1.0	0.87	-10 to 25 [6]
m-ClC$_6$H$_4$CDClCH$_2$Br	9.28×10^{-3}	18.8 ± 0.1	-4.7 ± 0.3				0 to 40 [6]
p-CF$_3$C$_6$H$_4$CHClCH$_2$Br	1.79×10^{-1}	17.6 ± 0.1	-3.1 ± 0.2	5.39	1.0	0.91	-25 to 20 [8]
p-CF$_3$C$_6$H$_4$CDClCH$_2$Br	3.34×10^{-2}	18.6 ± 0.1	-2.9 ± 0.3				-15 to 30 [8]
C$_6$H$_5$CHBrCH$_2$Br	3.16×10^{-3}	19.9	-3.3	5.27	1.0	0.91	0 to 50 [6]
C$_6$H$_5$CDBrCH$_2$Br	6.00×10^{-4}	20.9	-3.2				15 to 50 [6]
m-ClC$_6$H$_4$CHBrCH$_2$Br	3.27×10^{-2}	18.6	-2.8	4.95	1.0	0.90	-20 to 25 [8]
m-ClC$_6$H$_4$CDBrCH$_2$Br	6.60×10^{-3}	19.6	-2.6	2.02	0.4	1.1	0 to 40 [8]
m-ClC$_6$H$_4$CTBrCH$_2$Br	3.27×10^{-3}	20.0 ± 0.1	-2.8 ± 0.4				20 to 45 [6]
p-CF$_3$C$_6$H$_4$CHClCF$_3$	1.06×10^{-5}	27.9 ± 0.1	12.3 ± 0.3				45 to 70 [7]
p-CF$_3$C$_6$H$_4$CTClCF$_3$[b]	7.91×10^{-4}	25.42 ± 0.08	12.5 ± 0.3				20 to 55 [8]
CH$_3$ONa/CH$_3$OD	2.06×10^{-3}	24.86 ± 0.13	12.5 ± 0.4				20 to 45 [6]
C$_6$H$_5$CHClCF$_2$Cl	1.73×10^{-2}	20.2 ± 0.1	1.2 ± 0.3				-5 to 45 [14]
C$_6$H$_5$CDClCF$_2$Cl	7.60×10^{-3}	20.2 ± 0.1	-0.4 ± 0.3	2.28	0.0	2.3	0 to 50 [13]
C$_6$H$_5$CTClCF$_2$Cl	4.91×10^{-3}	19.6 ± 0.1	-3.5 ± 0.3	1.55	-0.6	4.7	0 to 40 [5]
C$_6$H$_5$CHBrCF$_2$Br	8.19×10^{-1}	16.7 ± 0.1	-3.0 ± 0.2	3.67	0.3	1.6	-40 to -5 [9]
C$_6$H$_5$CDBrCF$_2$Br	2.23×10^{-1}	17.0 ± 0.1	-4.6 ± 0.3	1.76	0.1	1.3	-50 to 20 [19]
C$_6$H$_5$CTBrCF$_2$Br	1.27×10^{-1}	17.1 ± 0.1	-5.1 ± 0.3				-30 to 25 [10]

[a] Reference 1. [b] Kinetics are for methoxide protodetritiation.

Table 3. Chlorine and Hydrogen Isotope Effects and Element Effects Associated with Alcoholic Sodium Alkoxide-Promoted Dehydrochlorination Reactions[a]

compd	solvent	k^{35}/k^{37} [°C]	k^H/k^D [°C]	k^{HBr}/k^{HCl} [°C]
C$_6$H$_5$CH(CH$_3$)CH$_2$Cl	EtOH	1.00590 ± 0.00013 [75]	5.37 [75]	52 [75]
C$_6$H$_5$CD(CH$_3$)CH$_2$Cl		1.00507 ± 0.00036 [75]		55 [75]
C$_6$H$_5$CH$_2$CH$_2$Cl	EtOH	1.00580 ± 0.00034 [75]		
C$_6$H$_5$CHClCH$_2$Cl	EtOH	1.00908 ± 0.00008 [24]	4.24 [25]	35 [25]
C$_6$H$_5$CDClCH$_2$Cl		1.00734 ± 0.00012 [24]		24 [25]
C$_6$H$_5$CHClCH$_2$Cl	MeOH	1.00978 ± 0.00020 [21]	3.83 [25]	35 [25]
C$_6$H$_5$CDClCH$_2$Cl		1.00776 ± 0.00020 [21]		25 [25]
C$_6$H$_5$CHClCF$_2$Cl	EtOH	1.01229 ± 0.00047 [0]	2.77 [0]	66 [0]
C$_6$H$_5$CDClCF$_2$Cl		1.01003 ± 0.00024 [0]		39 [0]
C$_6$H$_5$CHClCF$_2$Cl	MeOH	1.01255 ± 0.00048 [20]	2.28 [25]	47 [25]
C$_6$H$_5$CDClCF$_2$Cl		1.01025 ± 0.00043 [20]		29 [25]

[a] Data from ref 1.

are compared with k^{HBr}/k^{HCl} values for the corresponding eliminations with use of CH$_3$CH$_2$ONa/CH$_3$CH$_2$OH and CH$_3$ONa/CH$_3$OH. There is no correlation between the magnitude of k^{35}/k^{37} and k^{HBr}/k^{HCl}. If these eliminations occur by a concerted mechanism, the chlorine isotope effects should be

(21) Reference 1, pp 1935 and 1936.

the same for loss of HCl or DCl; however, the amount of internal return is different for protium compared to deuterium and this results in $(k^{35}/k^{37})^{HCl} \neq (k^{35}/k^{37})^{DCl}$ for C$_6$H$_5$C^{i}HClCH$_2$Cl and C$_6$H$_5$C^{i}HClCF$_2$Cl.

If the breaking of a C–X bond is not the only reason for the element effect, the ability of β-halide to enhance the hydron-

Table 4. Modeling the Arrhenius Behavior of the Primary Kinetic Isotope Effects Associated with Methanolic Methoxide Promoted Dehydrohalogenation Reactions Based on Eq 2

temp, °C	k^H_{Obs}, M⁻¹ s⁻¹	k^D_{Obs}, M⁻¹ s⁻¹	k^T_{Obs}, M⁻¹ s⁻¹	$(k^H/k^D)_{obs}$	$(k^H/k^D)_{cal}$	$(k^H/k^T)_{obs}$	$(k^H/k^T)_{cal}$	a^H	a^D	a^T
			m-ClC$_6$H$_4$C^{i}HClCH$_2$Cl ($E^D_{-1} - E^H_{-1} = 8.75$; $E^H_{-1} - E^X_{Elim} = -100$ cal/mol; $A_2/A_1 = 2.0$)							
0	5.60×10^{-5}	1.47×10^{-5}	7.46×10^{-6}	3.81	3.82	7.51	7.46	0.60	0.12	0.060
25	1.60×10^{-3}	4.71×10^{-4}	2.58×10^{-4}	3.40	3.37	6.20	6.19	0.59	0.14	0.072
50	2.73×10^{-2}	8.84×10^{-3}	5.15×10^{-3}	3.09	3.04	5.30	5.29	0.58	0.15	0.084
			m-CF$_3$C$_6$H$_4$C^{i}HClCH$_2$Cl ($E^D_{-1} - E^H_{-1} = 900$; $E^H_{-1} - E^X_{Elim} = -100$ cal/mol; $A_2/A_1 = 2.0$)							
0	1.32×10^{-4}	3.37×10^{-5}	1.68×10^{-5}	3.92	3.98	7.86	7.93	0.60	0.11	0.056
25	3.34×10^{-3}	9.58×10^{-4}	5.10×10^{-4}	3.49	3.50	6.55	6.55	0.59	0.13	0.068
50	5.13×10^{-2}	1.62×10^{-2}	9.12×10^{-3}	3.17	3.15	5.63	5.57	0.58	0.14	0.079
			p-CF$_3$C$_6$H$_4$C^{i}HClCH$_2$F ($E^D_{-1} - E^H_{-1} = 850$; $E^H_{-1} - E^X_{Elim} = -850$ cal/mol; $A_2/A_1 = 2.0$ [uses tritium data])							
25	1.49×10^{-4}	6.73×10^{-5}	4.22×10^{-5}	2.21	2.20	3.53	3.55	2.1	0.50	0.27
50	3.44×10^{-3}	1.64×10^{-3}	1.05×10^{-3}	2.10	2.10	3.31	3.27	1.9	0.50	0.28
75	5.06×10^{-2}	2.54×10^{-2}	1.63×10^{-2}	1.99	2.02	3.10	3.04	1.7	0.50	0.30
			m-ClC$_6$H$_5$C^{i}HBrCH$_2$Br ($E^D_{-1} - E^H_{-1} = 925$; $E^H_{-1} - E^X_{Elim} = 1425$ cal/mol; $A_2/A_1 = 2.0$ [uses tritium data])							
0	1.68×10^{-3}	2.89×10^{-4}	1.36×10^{-4}	5.81	5.81	12.4	12.4	0.036	0.0066	0.0032
25	3.26×10^{-2}	6.60×10^{-3}	3.27×10^{-3}	4.94	4.97	9.97	9.97	0.045	0.0095	0.0049
50	4.03×10^{-1}	9.27×10^{-2}	4.82×10^{-2}	4.35	4.36	8.36	8.26	0.054	0.013	0.0070

transfer step must play a partial role. To obtain the effect of β-halide on hydron transfer, kinetics using all three hydrogen isotopes are needed to calculate the amount of internal return, $\mathbf{a} = k_{-1}/k^X_{Elim}$, which can be used to obtain a value for the hydron-transfer step, $k_1 = k_{Obs}[\mathbf{a} + 1]$.

Internal Return Associated with the Hydron-Transfer Step in Methoxide-Promoted Dehydrohalogenation Reactions. When dehydrohalogenations occur by Scheme 1, the use of eq 2 and one for $(k^H/k^T)_{Obs}$ allows the calculation of $\mathbf{a}$ values as well as the energetics associated with internal return by modeling experimental isotope effects obtained over a 25 to 50 °C range.[10] For example, the methanolic sodium methoxide-promoted eliminations of HCl and DCl from m-ClC$_6$H$_4$C^i-HClCH$_2$Cl were studied over a 50 °C range and resulted in $k^H/k^D = 3.40$ (25 °C) with a $\Delta E_a = 0.8$ kcal/mol and $A^H/A^D = 0.96$, Table 2. Although the tritium kinetics were only carried out at three temperatures between 10 and 40 °C, calculated deviations for $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ were similar to those obtained from the deuterium data. Values of k^H/k^D and k^H/k^T at 0, 25, and 50 °C are obtained from the Arrhenius analyses. With use of a set value for A^X_{Elim}/A_{-1} and starting values for $E^D_{-1} - E^H_{-1}$ and $E^H_{-1} - E^X_{Elim}$,[22] a program will systematically change the energy terms to give the best fit for the k^H/k^D data, and calculate the corresponding k^H/k^T. The process is repeated for a best fit for k^H/k^T and calculation of the corresponding k^H/k^D values.[23] With A^X_{Elim}/A_{-1} set at a new value, the process can be repeated.

With use of the data for m-ClC$_6$H$_4$C^{i}HClCH$_2$Cl and $A^X_{Elim}/A_{-1} = 1.0$, calculated k^H/k^D values are within 0.5% of the experimental values; however, corresponding k^H/k^T values are 24−29% high. The best fit for k^H/k^T (-0.4 to -1.3%) gives k^H/k^D values that are low by 8 to 8.4%. When A^X_{Elim}/A_{-1} is changed to 2.0, a best fit for the k^H/k^D (-0.3 to $+0.6$%) still has k^H/k^T values that are high by 8.7 to 10.2%. However, the k^H/k^T fit (-0.2 to -0.7%) gives k^H/k^D values within $+0.3$ to -1.6% of the experimental ones, and results in $E^D_{-1} - E^H_{-1} = $

875 cal/mol,[24] $E^H_{-1} - E^X_{Elim} = -100$ cal/mol, and internal-return parameters of $\mathbf{a^H} = 0.59$, $\mathbf{a^D} = 0.14$, and $\mathbf{a^T} = 0.072$ at 25 °C. If A^X_{Elim}/A_{-1} is set at 3.0, the best fit is the same for the k^H/k^D or k^H/k^T data, with k^H/k^D values that are within 0 to -0.3% and k^H/k^T values within -1.1 to $+1.5$. The value for $E^D_{-1} - E^H_{-1}$ is 875 cal/mol and that for $E^H_{-1} - E^X_{Elim}$ is -325 cal/mol, with $\mathbf{a^H} = 0.58$, $\mathbf{a^D} = 0.13$, and $\mathbf{a^T} = 0.070$ at 25 °C. Since A^X_{Elim}/A_{-1} favors elimination more in the latter case, the $E^H_{-1} - E^X_{Elim}$ favors the return by an additional 225 cal/mol; however, the amounts of internal return are virtually the same for both cases. We use A^X_{Elim}/A_{-1} values of 2.0 for the rest of our calculations.[25]

Although the value of $E^D_{-1} - E^H_{-1}$ seems low, a similar result is obtained for m-CF$_3$C$_6$H$_4$C^{i}HClCH$_2$Cl with $A^X_{Elim}/A_{-1} = 2.0$: $E^D_{-1} - E^H_{-1} = 900$ cal/mol, $E^H_{-1} - E^X_{Elim} = -100$ cal/mol, k^H/k^D within -0.6 to $+1.5$%, k^H/k^T within $+0.9$ to -0.6%, $\mathbf{a^H} = 0.59$, $\mathbf{a^D} = 0.13$, and $\mathbf{a^T} = 0.068$. The data are given for m-CF$_3$C$_6$H$_4$-CHClCH$_2$Cl at nine temperatures between 5.0 and 50 °C, for m-CF$_3$C$_6$H$_4$CDClCH$_2$Cl at ten temperatures between 15 and 60 °C, and for m-CF$_3$C$_6$H$_4$CTClCH$_2$Cl at eight temperatures between 20 and 55 °C. Using the seven common temperatures for all three compounds at 5 °C intervals between 20 and 50 °C gives the same results.

A study with p-CF$_3$C$_6$H$_4$C^{i}HClCH$_2$F at six common temperatures between 35 and 60 °C with A^X_{Elim}/A_{-1} set at 2.0 results in a similar value for $E^D_{-1} - E^H_{-1} = 850$ cal/mol but a higher value for $E^H_{-1} - E^X_{Elim} = -850$ cal/mol. The k^H/k^D values are within -0.5 to $+1.0$% and k^H/k^T are within -0.3 to -1.2%, with $\mathbf{a^H} = 1.9$, $\mathbf{a^D} = 0.50$, and $\mathbf{a^T} = 0.28$ at 35 °C. The larger $E^H_{-1} - E^X_{Elim}$ is consistent with stronger C−F than C−Cl bonds. Since the $E^D_{-1} - E^H_{-1}$ for the three systems are within 50 cal/mol, hydron transfer in the transition structures should be similar for the elimination of hydrogen chloride and hydrogen fluoride.[26] The lower isotope effect is usually attributed to the poorer leaving group having a later transition structure. For our three

(22) The starting point for $E^D_{-1} - E^H_{-1}$ is normally 1300 cal/mol. For loss of ^{i}HF and ^{i}HCl the starting point for $E^H_{-1} - E^X_{Elim}$ is 500 cal/mol and for loss of HBr 1800 cal/mol.

(23) We thank Duncan McLennan, Auckland University in New Zealand, for a copy of his program that models the Arrhenius behavior of primary kinetic isotope effects for a reaction that features an internal-return mechanism. The program makes use of eq 2 and a similar one for protium and tritium. The original program, in Fortran, was converted to Turbo Pascal for use with a PC, and can be obtained from J. G. Koch.

(24) The value of $E^D_1 - E^H_1$ is always 46 cal/mol $[\Delta H^D_f - \Delta H^H_f]$ larger than $E^D_{-1} - E^H_{-1}$. Other values for the equilibrium isotope effects are as follows: $\Delta H^T_f - \Delta H^D_f = 20$ cal/mol and $\Delta H^T_f - \Delta H^H_f = 66$ cal/mol.

(25) Although the best fit is the same when based on either the k^H/k^D or k^H/k^T data for $A^X_{Elim}/A_{-1} = 3.0$, the overall fit with k^H/k^T data with $A^X_{Elim}/A_{-1} = 2.0$ is better.

(26) When the observed rate constants are corrected for internal return, the isotope effects associated with the proton transfer step, k_1, are within 7% at 25 °C: m-ClC$_6$H$_4$C^{i}HClCH$_2$Cl, $k^H/k^D = 4.73$; m-CF$_3$C$_6$H$_4$C^{i}HClCH$_2$-Cl, $k^H/k^D = 4.92$; p-CF$_3$C$_6$H$_4$C^{i}HClCH$_2$F, $k^H/k^D = 4.57$.

systems, the lower experimental PKIE is due to greater amounts of internal return for the dehydrofluorination than for the elimination of hydrogen chloride.

Calculations in the $YC_6H_4C^iHClCH_2Br$ systems have been hampered due to the unsuccessful syntheses of pure YC_6H_4-$CTClCH_2Br$. The use of the corresponding dibromides, $YC_6H_4C^i$-$HBrCH_2Br$, also presented experimental problems because of a competing wrong way elimination that forms $YC_6H_4C^iH=$CHBr.[27] The reaction of m-$ClC_6H_4C^iHBrCH_2Br$ resulted in less than 1% of m-$ClC_6H_4CH=CHBr$, but that increases to 3 to 6% for m-$ClC_6H_4CD=CHBr$. Therefore the tritium kinetics could result in 6% to 12% of m-$ClC_6H_4CT=CHBr$ constantly being formed, and require special treatment of the experimental data for m-$ClC_6H_4CTBrCH_2Br$.

Kinetic samples for protium and deuterium compounds are analyzed by using gas chromatography with an internal standard. Experimental rate constants at eight temperatures, -20 to 25 °C, result in a good Arrhenius plot for m-$ClC_6H_4CHBrCH_2Br$ with $E_a^H = 19.26 \pm 0.03$ kcal/mol that shows little change when the rate constants are corrected for wrong way elimination. However, the E_a^D of 20.35 ± 0.05 kcal/mol obtained from the experimental rates for m-$ClC_6H_4CDBrCH_2Br$ decreases slightly to $E_a^D = 20.24$ kcal/mol when corrected for the formation of m-$ClC_6H_4CD=CHBr$. This results in a ΔE_a of 1.0 instead of 1.1 kcal/mol with A^H/A^D increasing from 0.76 to 0.90. Kinetic samples from the reaction of m-$ClC_6H_4CTBrCH_2Br$ will have a growing infinity point due to the formation of m-ClC_6H_4-$CT=CHBr$ in competition with m-$ClC_6H_4CBr=CH_2$. Therefore the experimental counts had to be corrected for the formation of m-$ClC_6H_4CT=CHBr$ using the rate data for the formation of m-$ClC_6H_4CD=CBr$ from m-$ClC_6H_4CDBrCH_2Br$. The corrected rate constants gave a six point Arrhenius plot over a 25 °C range [20 to 45 °C] that resulted in $E_a^T = 20.6 \pm 0.1$ kcal/mol and $A^T = 4.155 \times 10^{12}$.

Rate constants from the Arrhenius analyses are used to calculate k^H/k^D and k^H/k^T at 0, 25, and 50 °C. With A_{Elim}^X/A_{-1} set at 2.0, values for $E_{-1}^D - E_{-1}^H = 925$ cal/mol and $E_{-1}^H - E_{Elim}^X = 1425$ cal/mol are calculated for the best fit of the experimental results.[28] Calculated k^H/k^D values are within 0.0 to +0.4%, k^H/k^T are within 0.0 to -1.2%, and internal-return parameters are $\mathbf{a^H} = 0.045$, $\mathbf{a^D} = 0.0095$ and $\mathbf{a^T} = 0.0049$ at 25 °C. In the absence of tritium data, the Arrhenius behavior of m-$ClC_6H_4CHClCH_2Br$ and m-$ClC_6H_4CDClCH_2Br$ gives a good fit, using eq 2 with $A_{Elim}^X/A_{-1} = 2.0$, $E_{-1}^D - E_{-1}^H = 925$ cal/mol, $E_{-1}^H - E_{Elim}^X = 1350$ cal/mol, $\mathbf{a^H} = 0.05$ and $\mathbf{a^D} = 0.01$.[29] The experimental k^H/k^D values at 25 °C for the two systems are 4.95 and 4.94.

The experimental element effects, k^{Br}/k^{Cl}, associated with methoxide-promoted dehydrohalogenations of m-$ClC_6H_4C^i$-$HClCH_2X$ can now be corrected for internal return. The $(k^{HBr}/k^{HCl})_{exp}$ of 29 results in an element effect for the proton-transfer step of $k_1^{HBr}/k_1^{HCl} = 19$, while $(k^{DBr}/k^{DCl})_{exp}$ of 20 is reduced

slightly to $k_1^{DBr}/k_1^{DCl} = 18$. Therefore the major part of the element effect associated with this dehydrohalogenation is due to a β-bromide enhancing the hydron-transfer step, k_1, more than a β-chloride.[30]

Kinetic Solvent Isotope Effects [KSIE]. It has been proposed that KSIE are due to differences in the number of CH_3O^iH solvating methoxide ion and those solvating the transition structure.[31]

$$R-H + MeO^- \cdots (^iHOCH_3)_m \rightarrow$$
$$\{R\cdot\cdot H\cdot\cdot O(Me)\cdots(^iHOCH_3)_p\}^{\ddagger-} + (m-p)CH_3O^iH$$
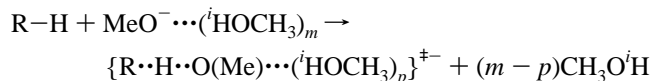
A fractionation factor, $\phi_{OMe} \approx 0.74$,[32] for CH_3OD implies the equilibrium abundance of deuterium in the m hydrogens of a solvated MeO^- is ca. 0.74 times that in the bulk solvent. The value of m is taken as 3 which has methanol at all three possible ligand sites. At least one methanol must be lost to form the encounter complex, $R-H\cdots^-O(Me)\cdots(^iHOCH_3)_p$, prior to proton transfer. Calculation of the KSIE by eq 3 determines the minimum effect, $k^{OD}/k^{OH} \approx 1.3$, when a single methanol is released to solvent ($\phi \approx 1.0$) and the transition structure fractionation factors equal those for methoxide, $\phi_\ddagger = \phi_{OMe}$. A maximum effect has all three methanols released to solvent and results in $k^{OD}/k^{OH} \approx 2.5$.

$$k^{OD}/k^{OH} = (\phi_\ddagger)^p/(\phi_{OMe})^m \tag{3}$$

Reactions of $C_6H_5CTClCF_2Cl$ and $C_6H_5CHClCH_2Br$ are 2.5 times faster in pure CH_3OD than in CH_3OH. A complete study of KSIE should include kinetic runs in mixtures of CH_3OD and CH_3OH as well as in the pure solvents. Equation 4, where n is the mole fraction of CH_3OD, allows calculation of predicted rate enhancement for these mixtures:

$$k_a^{OD}/k^{OH} = 1/[1 - n + 0.74n]^3 \tag{4}$$

The experimental values at 25 °C for the two systems are within 4% of those predicted by eq 4: $[k_n^{OD} \times 10^3 \text{ M}^{-1} \text{ s}^{-1}, (n)]$ $C_6H_5CTClCF_2Cl$, 12.3 (1.0), 8.59 (0.67), 7.31 (0.50), 6.44 (0.33), and 4.91 (0.0); $C_6H_5CHClCH_2Br$, 11.0 (1.0), 8.09 (0.75), 6.67 (0.50), 5.54 (0.25), and 4.38 (0.0).

The temperature dependence of the KSIE for methanol was also measured for the dehydrochlorination of p-$CF_3C_6H_4$-$CHClCH_2Cl$ and the hydrodetritiation reaction of p-$CF_3C_6H_4$-$CTClCF_3$. Values of k^{OD}/k^{OH} are 2.76 [0°], 2.47 [25°], and 2.23 [50°] for p-$CF_3C_6H_4CHClCH_2Cl$, and 2.84 [0°], 2.60 [25°], and 2.42 for p-$CF_3C_6H_4CTClCF_3$. The KSIE in these cases result mainly from $\Delta\Delta H^\ddagger$ of 0.6 kcal/mol with the $\Delta\Delta S^\ddagger$ less than 0.7 eu, Table 2. Therefore the energetics associated with the desolvation of methoxide ion are part of the measured reaction energetics and should be the same for these reactions studied in methanol.

Activation Entropies. To compare rates of bimolecular reactions that differ by several orders of magnitude, we routinely measure kinetics over a 30–50 °C range. To anticipate what to expect for two molecules reacting in the rate-limiting step,

(27) A similar problem was encountered with $C_6H_5CTClCH_2Cl$ where the competitive formation of $C_6H_5CT=CHCl$ interfered with measurement of good tritium kinetics; however, m-$ClC_6H_4C^iHClCH_2Cl$ gave negligible amounts of m-$ClC_6H_4CT=CHCl$ and resulted in good kinetics.

(28) The starting point for $E_{-1}^H - E_{Elim}$ is 1800 cal/mol for the dehydrobrominations. With A_2/A_{-1} ranging from 1.5 to 3.0, $E_{-1}^D - E_{-1}^H$ values are from 925 and 950 cal/mol, $E_{-1}^H - E_{Elim}^X$ values are from 1200 and 1500 cal/mol, and internal-return parameters at 25 °C are $\mathbf{a^H} = 0.046 \pm 0.003$, $\mathbf{a^D} = 0.0097 \pm 0.008$, and $\mathbf{a^T} = 0.0049 \pm 0.0003$.

(29) Using only eq 2 and the temperature dependence of k^H/k^D will give good modeling of the experimental results with a much larger range of A_{Elim}^X/A_{-1} values. Since the measurement of tritium rates is not always convenient, the temptation to use only hydrogen and deuterium data must be suppressed until a consistent value of A_{Elim}^X/A_{-1} is found for several similar systems.

(30) A referee pointed out that the element effect on k_1 suggests negative ion hyperconjugation in the transition structure since the electronegativity of Cl vs Br should give the reverse order. The same would hold true for the case of F vs Cl. A publication that appeared after this manuscript was submitted gives additional computational evidence for negative ion hyperconjugation by a β C–F [Sanuders, W. H., Jr. *J. Org. Chem.* **1997**, *62*, 244].

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

(32) (a) More O'Ferrall, R. A. *Chem. Commun.* **1969**, 114. (b) Gold, V.; Grist, S. *J. Chem. Soc. (B)* **1971**, 1665. (c) Gold, V.; Morris, K. P.; Wilcox, C. F. *J. Chem. Soc., Perkin Trans. 2* **1982**, 1615.

Table 5. Rate Constants and Activation Parameters for Methanolic Sodium Methoxide-Promoted Dehydrochlorination Reactions

compd	k, M^{-1} s^{-1} (0 °C)	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu (25 °C)	temp range, °C [no. of points]
o-CH$_3$C$_6$H$_4$CHClCF$_2$Cl	1.60×10^{-5}	21.81 ± 0.08	-0.5 ± 0.2	25 to 65 [8]
o-CF$_3$C$_6$H$_4$CHClCF$_2$Cl	4.21×10^{-5}	18.90 ± 0.03	-9.2 ± 0.1	20 to 60 [9]
2,6-Cl$_2$C$_6$H$_3$CHClCF$_2$Cl	8.78×10^{-5}	18.60 ± 0.03	-8.8 ± 0.1	10 to 60 [8]
2-Cl-6-FC$_6$H$_3$CHClCF$_2$Cl	1.74×10^{-4}	19.25 ± 0.05	-5.1 ± 0.2	10 to 45 [8]
o-ClC$_6$H$_4$CHClCF$_2$Cl	1.94×10^{-4}	19.44 ± 0.06	-4.2 ± 0.2	15 to 40 [6]
p-CH$_3$C$_6$H$_4$CHClCF$_2$Cl	2.28×10^{-4}	20.94 ± 0.03	1.6 ± 0.1	5 to 45 [12]
m-CH$_3$C$_6$H$_4$CHClCF$_2$Cl	4.01×10^{-4}	20.48 ± 0.07	1.1 ± 0.3	0 to 40 [8]
o-FC$_6$H$_4$CHClCF$_2$Cl	7.03×10^{-4}	19.43 ± 0.04	-1.6 ± 0.2	0 to 40 [6]
C$_6$H$_5$CHClCF$_2$Cl	7.15×10^{-4}	20.04 ± 0.07	0.6 ± 0.2	0 to 45 [10]
2,6-F$_2$C$_6$H$_3$CHClCF$_2$Cl	8.21×10^{-4}	18.27 ± 0.07	-5.6 ± 0.3	-5 to 30 [6]
p-FC$_6$H$_4$CHClCF$_2$Cl	1.16×10^{-3}	20.16 ± 0.07	2.0 ± 0.3	-10 to 30 [6]
2,4-Cl$_2$C$_6$H$_3$CHClCF$_2$Cl	1.64×10^{-3}	18.24 ± 0.08	-4.3 ± 0.3	-5 to 25 [7]
2,4-F$_2$C$_6$H$_3$CHClCF$_2$Cl	1.75×10^{-3}	19.03 ± 0.10	-1.3 ± 0.3	-10 to 20 [8]
p-ClC$_6$H$_4$CHClCF$_2$Cl	5.47×10^{-3}	19.00 ± 0.04	0.8 ± 0.1	-20 to 20 [15]
m-FC$_6$H$_4$CHClCF$_2$Cl	1.25×10^{-2}	18.71 ± 0.03	1.4 ± 0.1	-25 to 5 [7]
m-ClC$_6$H$_4$CHClCF$_2$Cl	1.60×10^{-2}	18.21 ± 0.02	0.1 ± 0.1	-25 to 10 [9]
3,4-F$_2$C$_6$H$_3$CHClCF$_2$Cl	1.79×10^{-2}	18.41 ± 0.09	1.0 ± 0.3	-30 to 5 [6]
m-CF$_3$C$_6$H$_4$CHClCF$_2$Cl	3.71×10^{-2}	18.37 ± 0.09	2.4 ± 0.3	-25 to 0 [6]
p-CF$_3$C$_6$H$_4$CHClCF$_2$Cl	9.14×10^{-2}	17.84 ± 0.06	2.2 ± 0.2	-30 to 0 [8]
m-NO$_2$C$_6$H$_4$CHClCF$_2$Cl	2.10×10^{-1}	16.67 ± 0.10	-0.4 ± 0.4	-45 to -20 [3]
p-CNC$_6$H$_4$CHClCF$_2$Cl	7.67×10^{-1}	15.77 ± 0.03	-1.2 ± 0.1	-61 to -20 [4]
3,5-(CF$_3$)$_2$C$_6$H$_3$CHClCF$_2$Cl	2.88	15.77 ± 0.04	1.5 ± 0.2	-65 to -30 [6]

the $\Delta S^{\ddagger}$ values obtained from the reactions of methanolic sodium methoxide with ring-substituted β,β-difluorostyrenes, YC$_6$H$_4$-CH=CF$_2$ + CH$_3$O$^-$ → {YC$_6$H$_4$CHCF$_2$OCH$_3$}$^-$, were used.[33] The average $\Delta S^{\ddagger}$ for ten ring substituents used to calculate $\rho = 3.56 \pm 0.03$ (25 °C) is -14.3 ± 0.8 eu, the average $\Delta S^{\ddagger}$ for seven compounds not used to calculate rho is slightly lower, -15.7 ± 0.8 eu, and the average $\Delta S^{\ddagger}$ for ten compounds with ortho substituents is -17.3 ± 1.2 eu. Experimental $\Delta S^{\ddagger}$ values calculated from the Arrhenius plots routinely have a standard deviation of less than 0.3 eu. Although methoxide-promoted dehydrochlorinations of YC$_6$H$_4$CHClCF$_2$Cl are bimolecular reactions, the average $\Delta S^{\ddagger} \approx 1$ eu for the non-ortho substituted compounds is much larger than that for the alkene reactions, Table 5.

It was suggested that $\Delta S^{\ddagger}$ values vary with the amount of internal return and more favorable activation entropies occur as the amount of internal return increases.[34] The k^H/k^D of 1.1 to 1.2 for alkoxide-catalyzed exchange and elimination reactions of C$_6$H$_5$C^{i}HClCF$_3$ and C$_6$H$_5$C^{i}H(CF$_3$)$_2$ suggest a very large amount of internal return associated with these reactions, and result in $\Delta S^{\ddagger}$ values greater than 10 eu.[35] On the other hand, ethoxide-promoted dehydrohalogenations of C$_6$H$_5$CH$_2$CH$_2$X [X = Br or Cl] have substantial k^H/k^D values, no internal return, and $\Delta S^{\ddagger}$ values of about -7 eu. The stereochemistry of the elimination can play a major role in determining $\Delta S^{\ddagger}$. Cristol and co-workers measured values of $\Delta S^{\ddagger}$ for the elimination of four isomers of benzene hexachloride, C$_6$H$_6$Cl$_6$—1.0, 3.6, 6.5, and 20.2 eu.[36] The 20.2 eu value is for the only isomer unable to undergo antielimination as all the chlorines are trans to each other.

We have been unable to model the temperature behavior for the isotope effects associated with eliminations from C$_6$H$_5$C^i-HClCF$_2$Cl or C$_6$H$_5$C^{i}HBrCF$_2$Br. The major conformer of C$_6$H$_5$-CHBrCF$_2$Br (>98%) has the bromine atoms anti to each other, and the H−C−C−Cl is not antiperiplanar in either of the two

major conformers of C$_6$H$_5$CHClCF$_2$Cl.[37] Therefore the leaving halogen might not be anti to the encounter complex, CH$_3$O$^-$··H-C, and would require a 60° rotation to obtain the proper alignment.[38] Rotational barriers in highly halogenated compounds are between 9 and 14 kcal/mol,[39] and this could lead to a third step.[40] Elimination from C$_6$H$_5$CH$_2$CF$_2$Cl, which has two benzylic hydrogens, results in a decrease of ca. 8 eu in $\Delta S^{\ddagger}$ compared to C$_6$H$_5$CHClCF$_2$Cl. This is attributed to dehydrochlorination occurring with substantially less or no internal return.

The presence of bulky ortho substituents could hinder internal return, and cause a decrease in the values of $\Delta S^{\ddagger}$. Seven substituents were used to determine $\rho = 3.69 \pm 0.05$ at 0 °C,[41] and the average $\Delta S^{\ddagger}$ equals 1.0 ± 1.0 eu for the 13 non-ortho-substituted YC$_6$H$_4$CHClCF$_2$Cl or Y$_2$C$_6$H$_3$CHClCF$_2$Cl in Table 5. This changes dramatically for the nine compounds with one or two ortho substituents as $\Delta S^{\ddagger}$ values range from -0.5 to -9.2 eu. Values for o-CF$_3$C$_6$H$_4$CHClCF$_2$Cl [-9.2 eu] and 2,6-Cl$_2$C$_6$H$_3$CHClCF$_2$Cl [-8.8 eu] are lowest, while 2,4-F$_2$C$_6$H$_3$-CHClCF$_2$Cl [-1.3 eu] and o-CH$_3$C$_6$H$_4$CHClCF$_2$Cl [-0.5 eu] result in the highest values. There is internal consistency: two o-F compounds [-1.6 and -1.3 eu] and two o-Cl compounds [-4.3 and -4.2 eu]. Values are larger with two ortho substituents: 2,6-difluoro [-5.6 eu], 2-chloro-6-fluoro [-5.1 eu], and 2,6-dichloro [-8.8 eu]. The trifluoromethyl group [-9.2 eu] is the largest and the only problem seems to be the o-methyl [-0.5 eu].[42] Further work is in progress dealing with the effects of ortho substituents.

(33) The measurement of kinetic solvent isotope effect for these reactions has not been as extensive. However, the few that we have measured are about 2.0.
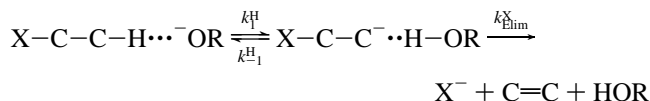
(34) See ref 17, pp 5425−27.

(35) 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.* **1983**, *105*, 2394.

(36) Cristol, S. J.; Hause, N. L.; Meek, J. S. *J. Am. Chem. Soc.* **1951**, *73*, 674.

(37) Drysdale, J. J.; Phillips, W. D. *J. Am. Chem. Soc.* **1957**, *79*, 319.

(38) The methoxide-promoted dehydrohalogenation of C$_6$H$_5$C^{i}HBrCFClBr gives only anti-eliminations of ^{i}HCl and ^{i}HBr [Koch, H. F. In *Comprehensive Carbanion Chemistry*, Part C; Buncel, E., Durst, T., Eds.; Elsevier: Amsterdam, 1987; pp 333 and 334.]

(39) (a) Thompson, D. S.; Newmark, R. A.; Sederholm, C. H. *J. Chem.Phy.* **1962**, *37*, 411. (b) Weigert, F. J.; Winstead, M. B.; Garrels, J. I.; Roberts. J. D. *J. Am. Chem. Soc.* **1970**, *92*, 7359.

(40) One of the referees commented that this would be at odds with the Curtin−Hammett principle. Although this is true, the energetics of the rotational barriers and the competition with internal return may well be an example of the breakdown of this principle, which does not have a large amount of experimental backing.

(41) Substituents used were as follows: p-CH$_3$, m-CH$_3$, H, p-Cl, m-F, m-Cl, and m-CF$_3$. The ρ value for the reaction of YC$_6$H$_4$CH=CF$_2$ increases to 3.92 ± 0.04 at 0 °C.

(42) We are at a loss to explain the $\Delta S^{\ddagger}$ of -0.5 for o-methyl. The compound has been synthesized three times by different students and always results in virtually the same value for $\Delta S^{\ddagger}$.

Conclusions. Our working model for alkoxide-promoted dehydrohalogenation and hydron-exchange reactions is Scheme 1. For reactions with methanolic methoxide, the process starts after methoxide ion loses one molecule of solvation which allows it to form an encounter complex with the carbon acid.

$$MeO^- \cdot\cdot (HOCH_3)_2 + H-C-C-X \rightarrow$$
$$(CH_3OH)_2 \cdot\cdot (Me)O^- \cdot\cdot H-C-C-X$$
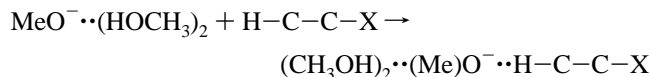
The KSIE associated with the reaction, $k^{OD}/k^{OH} \approx 2.5$ at 25 °C, suggests the two remaining methanols are lost before reaching the transition structure leading to a hydrogen-bonded carbanion, k_1^H. This intermediate partitions between losing β-halide, k_{Elim}^X, or returning hydron to a negatively charged carbon, k_{-1}^H:

$$X-C-C-H \cdot\cdot\cdot {}^-OR \underset{k_{-1}^H}{\overset{k_1^H}{\rightleftharpoons}} X-C-C^- \cdot\cdot H-OR \xrightarrow{k_{Elim}^X}$$
$$X^- + C{=}C + HOR$$

The hydrogen-bonded carbanion not only has the original C−H bond broken, but also has an elongated C−X bond. The latter conclusion comes from the analysis of chlorine isotope effects associated with elimination reactions of $C_6H_5C^iHClCH_2Cl$ and $C_6H_5C^iHClCF_2Cl$.[43]

Chloride and bromide can leave from the hydrogen-bonded intermediate as can fluoride when it leaves from a −CH$_2$F; however, when fluoride is part of a trifluoromethyl group, each C−F bond is stronger than that in a −CH$_2$F. This requires the formation of the free carbanion before F$^-$ can depart to form an alkene. The near unity isotope effect for the exchange reactions of p-CF$_3$C$_6$H$_4$C^{i}HCF$_3$, $k^D/k^T = 1.08$ at 25 °C,[44] [similar values are reported for $C_6H_5C^iH(CF_3)_2$ and $C_6H_5C^iHCClCF_3$],[34] means that hydron transfer is not occurring in a rate-limiting step for the exchange reaction. Since the exchange is over 60 times faster than the elimination reaction, the barrier for the formation of a hydrogen-bonded intermediate is lower than that for loss of fluoride. The acidity of the benzylic C−H bonds should be about the same for p-CF$_3$C$_6$H$_4$CHClCF$_3$ and p-CF$_3$C$_6$H$_4$CHClCF$_2$Cl,[45] and result in similar rates of formation for the respective hydrogen-bonded intermediates. The element effect, k^{HCl}/k^{HF} of 1.5×10^5,[46] has a $\Delta\Delta G^\ddagger$ of 7 kcal/mol, and this is not an unreasonable value for the breaking of a hydrogen bond.[47]

For reactions of m-ClC$_6$H$_4$C^{i}HClCH$_2$X, a β-bromine accelerates the formation of the hydrogen-bonded carbanion by a factor of ≈ 19 over β-chlorine. The experimental element effect, $k^{HBr}/k^{HCl} = 29$, is largely due to the proton-transfer step, $k_1^{HBr}/k_1^{HCl} = 19$, rather than the formal breaking of the carbon−halogen

bond. The competition between a loss of β-Cl and internal return has an activation energy slightly favoring internal return and an A factor slightly favoring the loss of chloride, and this results in the moderate amounts of internal return, $k_{-1}^H \approx 0.6$ k_{Elim}^{Cl}. Dehydrobromination has a much more favorable activation energy for loss of β-Br as well as the favorable A factor which results in a negligible amount of internal return, $k_{-1}^H \approx 0.05$ k_{Elim}^{Br}. Since the internal return does not affect the overall rate of dehydrobromination, the reactions of m-ClC$_6$H$_4$CHClCH$_2$-Br and m-Cl$_6$H$_4$CHBrCH$_2$Br could be classified as E2 mechanisms by at least one operational definition: *that the transition structure for the rate-limiting step has the β-hydrogen partially but not completely transferred and the C−X bond partially but not completely broken. This allows for the formation of some intermediates along the reaction pathway; however, the intermediates would not contribute to the kinetics or rate of the overall process.*[48]

Since a β-Br is more effective than a β-chloride in accelerating the hydron-transfer step, it should carry more of the negative charge and has a weaker bond to carbon.[49] Removing the benzylic halide would place more charge on β-bromide and could result in even less internal return. The Arrhenius behavior of the isotope effect obtained for ethoxide-promoted dehydrobrominations of $C_6H_5C^iH(CH_3)CH_2Br$ was shown to be consistent with a reaction proceeding by Scheme 1. Swain−Schaad does not hold, $(k^H/k^T) \neq (k^D/k^T)^{3.26}$, and the temperature dependence was modeled by using $A_{Elim}^{Br}/A_{-1} = 0.1$, $E_{-1}^D - E_{-1}^H = 1340$ cal/mol, and $E_{-1}^H - E_{Elim}^{Br} = 1950$ cal/mol.[50] The fit is good with $\mathbf{a^H} = 0.39$ at 25 °C; however, the A_{Elim}^{Br}/A_{-1} favoring internal return is inconsistent with the A_{Elim}/A_{-1} used for the analyses in this study. The Arrhenius behavior, $A^H/A^D = 0.4$, has been attributed to quantum-mechanical tunneling occurring during an E2 mechanism.[15] Some preliminary studies with $C_6H_5C^iH(CH_3)CH_2Cl$ did not give satisfactory kinetics over a reasonable temperature range to see if this system behaves similar to $C_6H_5C^iH_2CH_2Cl$. Work is in progress with $YC_6H_4C^iH(CH_3)CH_2Cl$ compounds with electron withdrawing groups to enhance reactivity and obtain better rate measurements.

Experimental Section

Materials. All starting materials were purchased from Aldrich. Solutions of alcoholic sodium alkoxide were made from the reaction of sodium with anhydrous alcohol. Deuterated alcohols were purchased from Aldrich and used without further purification. NMR spectra were recorded with several instruments. Early 60-MHz ^{19}F spectra were obtained from a Varian HA-60 IL and ^{1}H spectra were obtained with a Varian T-60. Recent spectra have been obtained by using a Varian XL 300-MHz FT-NMR. A Varian VISTA system with 6 ft 0.25 or 0.06 in. packed columns with 15−20% SE-30 or OV 101 on 60/80 Chromasorb W was initially used to analyze kinetic samples. A HP 4600 with a 30 m RSL-150 polydimethylsiloxane (OV 101) with 0.53 mm i.d. and 1.2 μm film thickness is currently being used and gives much better results.

Synthesis of $YC_6H_4C^iHClCH_2F$. A three-step synthesis started with YC_6H_4MgBr and $FCH_2C{\equiv}N$ to give a ketone, $YC_6H_4COCH_2F$, which was reduced by NaB^iH_4 after purification by column chromatography. The $YC_6H_4C^iHOHCH_2F$ was converted to $YC_6H_4C^iHClCH_2F$ by reaction with $(C_6H_5)_3P$ and CCl_4. Yields for the first step ranged from 60% to 80%. Although yields for the last two steps were variable, they can each be carried out in >90% yield.

(43) Reference 1, p 1934, has a full discussion of this with additional references.

(44) The rate of exchange for p-CF$_3$C$_6$H$_4$CDClCF$_3$ with methanolic sodium methoxide at 25 °C is 8.58×10^{-4} with activation parameters of $\Delta H^\ddagger = 25.90 \pm 0.08$ and $\Delta S^\ddagger = 14.3 \pm 0.3$. Justin C. Biffinger, unpublished results.

(45) Relative rates of methoxide-promoted dehydrobromination of C_6H_5-CHBrCF$_2$Br, C_6H_5CHBrCFClBr, and C_6H_5CHCFBr$_2$ vary by a factor of 4, with the slowest being one diastereomer of C_6H_5CHBrCFClBr and the fastest being the other diastereomer [Koch, H. F. In *Comprehensive Carbanion Chemistry: Ground and Excited State Reactivity*; Buncel, E., Durst, T., Eds.; Elsevier: Amsterdam, 1987; Part C, Chapter 6, p 330−335].

(46) The rate of dehydrofluorination of p-CF$_3$C$_6$H$_4$CHClCF$_3$ at 25 °C and activation parameters are given in Table 2. The activation parameters for p-CF$_3$C$_6$H$_4$CHClCF$_2$Cl and rate at 0 °C are given in Table 5. The rate at 25 °C is 1.58 M^{-1} s^{-1}.

(47) Sano, T; Tatsumoto, N.; Niwa, T.; Yasunaga, T. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 2669. (b) Sano, T.; Tatsumoto, N.; Mende, Y.; Yasunaga, T. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 2673.

(48) Saunders, W. H., Jr. *Acc. Chem. Res.* **1976**, *9*, 19.

(49) A referee states: "It is assumed that the faster reaction with β-Br than β-Cl is a result of more bond breaking to halogen at the transition state: it seems at least possible that much of this rate effect could come from relief of two serious gauche interactions as the α-carbon moves from sp^3 to sp^2 hybridization."

(50) Reference 11, p 6106.

1. p-CF$_3$C$_6$H$_4$COCH$_2$F. 4-Bromobenzotrifluoride (12.4 g, 55 mmol) in 100 mL of ether was added dropwise to 1.3 g (55 mmol) of Mg in 25 mL of ether. After the addition was completed, the reaction mixture was refluxed for 30 min and then allowed to cool to room temperature prior to the dropwise addition of 2.95 g (50 mmol) of fluoroacetonitrile in 50 mL of ether. The reaction mixture was cooled to 0 °C before adding 50−75 mL of 1 M HCl, which dissolves the precipitate formed during the reaction. After separation, the aqueous layer was extracted twice with 50 mL of ether. The combined ethereal layers were washed with water until neutral and 50 mL of saturated CaCl$_2$ and the dried over MgSO$_4$. Ether was removed by a rotary evaporator. The remaining organic material was purified by using a column of silica gel and 20% ether/hexane to yield 6.6 g (32 mmol, 64%) of a yellow oil that was used in the next step. The ^{1}H MNR at 60 MHz has a doublet due to the −CH$_2$F at 5.5 ppm with a $J_{H−F}$ of 47 Hz, and the usual pattern for para substitution in the aromatic region.

2. p-CF$_3$C$_6$H$_4$CHOHCH$_2$F. 2-Fluoro-4′-trifluoroacetophenone (3.0 g, 14.6 mmol, 1.0 equiv) in 10 mL of ethanol was added dropwise to a solution of 0.3 g (7.3 mmol, 2.0 equiv) of NaBH$_4$ in 50 mL of ethanol and warmed to 50 °C for 30 min. Addition of 25 mL of 3 M HCl dissolved the precipitate formed during the reaction, and the resulting mixture was added to 200 mL of ice water and extracted four times with 50 mL of CH$_2$Cl$_2$. The combined methylene chloride layers were washed three times with ice water and dried over MgSO$_4$. Removal of the CH$_2$Cl$_2$ by a rotary evaporator left 3.7 g of residue that consisted of ≈3 g of product and ≈0.7 g of ethanol. This mixture was used in the last step, and the amount of (C$_6$H$_5$)$_3$P used was adjusted for any ethanol in the sample.

3. p-CF$_3$C$_6$H$_4$CHClCH$_2$F. The 3.7-g product from the previous reaction was refluxed with 6.5 g (24.8 mmol) of (C$_6$H$_5$)$_3$P and 50 mL of CCl$_4$ for 4 h. A precipitate formed and a GC of the CCl$_4$ layer showed no residual alcohol.[51] The CCl$_4$ was removed by distillation, and the remaining mixture was codistilled with water. The two layers of the distillate were separated after adding 10 mL of CH$_2$Cl$_2$, and the aqueous layer was extracted twice with 10 mL of CH$_2$Cl$_2$. The combined CH$_2$Cl$_2$ layers were dried over MgSO$_4$ prior to removal of the CH$_2$Cl$_2$ by a rotary evaporator. The remaining 3.0 g of colorless liquid were used for kinetics. The ^{1}H MNR at 60 MHz has a doublet of doublets for the −CH$_2$F at 4.6 ppm with a $J_{H1−H2}$ of 6 Hz and a $J_{H2−F}$ of 47 Hz, and a multiplet for the benzylic proton at ≈5.0 ppm, which overlaps with the upfield part of the −CH$_2$F signal. The ^{19}F NMR at 200 MHz has a doublet of triplets at 211.7 ppm with a $J_{H2−F}$ of 47 Hz and $J_{H1−F}$ of 13 Hz. The ^{1}H 60-MHz spectrum of p-CF$_3$C$_6$H$_4$-CDClCH$_2$F is much cleaner with −CH$_2$F at 4.6−4.7 ppm and d with $J_{H−F}$ = 47 Hz.

Synthesis of Styrenes. Substituted styrenes and β,β-difluorostyrenes are the precursors of the dichloro, dibromo, and bromochloro compounds used in this study. β,β-Difluorostyrenes were made by following a procedure similar to that reported for the synthesis of 2-(p-chlorophenyl)pentafluoropentene (method II).[52] This is a Wittig type reaction of (C$_6$H$_5$)$_3$PCF$_2$CO$_2$Li [made *in situ* from ClCF$_2$CO$_2$Li and (C$_6$H$_5$)$_3$P] and the substituted benzaldehyde with dimethylformamide as solvent. The phosphonium salt is used in n excess [from 1.3 to 2.0] to ensure complete reaction of the aldehyde. After the reaction is complete, the alkene is codistilled with water from the dark reaction mixture. The lower layer is separated and dried over CaSO$_4$. The yields range from 40% to 60%, and the alkenes are pure enough for the next step without further purification.

The synthesis of YC$_6$H$_4$C^{i}H=CH$_2$ [^{i}H = D or T] started with a reduction of YC$_6$H$_4$COCH$_3$ with NaB^{i}H$_4$ to make YC$_6$H$_4$C^{i}HOHCH$_3$, which was dehydrated using KHSO$_4$ to give the substituted styrene, YC$_6$H$_4$C^{i}H=CH$_2$.[53] When ^{i}H = H, a Grignard reaction of YC$_6$H$_4$MgBr and CH$_3$CHO yielded YC$_6$H$_4$CHOHCH$_3$ directly. The dehydration occurred with variable yields, but was favored for deuterium or tritium incorporation over our old procedure *via* a dithiane to obtain the YC$_6$H$_4$C^{i}HO followed by a Wittig reaction.[1] When possible, YC$_6$H$_4$-

CH=CH$_2$ was purchased. Deuterium and tritium incorporation for β,β-difluorostyrenes still made use of dithianes.

1. m-ClC$_6$H$_4$CD(OH)CH$_3$. m-Chloroacetophenone (24.8 g, 161 mmol, 1.0 equiv) was added dropwise to a solution of 1.97 g (47 mmol, 1.17 equiv) of NaBD$_4$ dissolved in 30 mL of 95% ethanol at a rate to keep the reaction below 50 °C. A white solid is formed during the addition. After 45 min of stirring, 60 mL of 3 M HCl was added to dissolve the precipitate. The solution was heated (to evaporate ethanol) until two distinct layers formed. After the layers separated, the aqueous layer was washed twice with 25 mL of CH$_2$Cl$_2$. The combined organic layers were washed four times with 25 mL of cold water to remove any remaining ethanol and dried over MgSO$_4$. The CH$_2$Cl$_2$ was removed by a rotary evaporator, and the resulting 18.6 g (118 mmol, 73% yield) of m-ClC$_6$H$_4$CD(OH)CH$_3$ was 99% pure according to gas chromatography. The proton MNR at 60 MHz had signals at 1.3 (3H, s), 4.2 (1H, s), 7.1 (3H), and 7.2 ppm (1H) for the aromatic protons.

2. m-ClC$_6$H$_4$CD=CH$_2$. m-ClC$_6$H$_4$CD(OH)CH$_3$ (4.48 g, 28 mmol, 1.0 equiv), 2.61 g of KHSO$_4$, 0.05 g of 4-*tert*-butylcatechol, and a magnetic stir bar were placed in a 50-mL single neck 24/40 round bottom flask fitted with a Claisen head that had a vacuum takeoff with a 50-mL round bottom flask receiver. Heat was applied by a 100 mL heating mantle filled with sand around the reaction flask. Maximum voltage was applied to rapidly raise the temperature of the sand to >200 °C over a period of 8−10 min. A vacuum of 160 to 180 mmHg was applied and the receiver was immersed in a Dewar with liquid nitrogen. Distillate came over between 60 and 75 °C. The 2.85 g (20 mmol) of m-ClC$_6$H$_4$CD=CH$_2$ was separated from the codistilled water, and the GC gave the purity of 98%. The proton MNR at 60 MHz had signals for the vinyl hydrogens at 5.1 (1H), 5.5 (1H), 7.1 (3H), and 7.2 ppm (1H) for the aromatics. A second run started with 7.04 g of m-ClC$_6$H$_4$-CD(OH)CH$_3$ and 5.42 g of KHSO$_4$ and resulted in a yield of only 48%. It has been our experience that the best yields are obtained when under 5 g of starting alcohol is used.

Synthesis of YC$_6$H$_4$C^{i}HClCH$_2$Cl. Initially the chlorination of styrenes was carried out in CCl$_4$; however, this method can form up to 30% YC$_6$H$_4$CHClCHCl$_2$ as an impurity.[1] An alternate method with dimethylformamide, DMF, as the solvent was used for most of the YC$_6$H$_4$C^{i}HClCH$_2$Cl in this study.[54] This gave a significant reduction in the amount of the trichloride (2−5%). These small amounts of YC$_6$H$_4$CHClCHCl$_2$ did not interfere with the kinetics since YC$_6$H$_4$-CCl=CHCl and YC$_6$H$_4$CH=CCl$_2$ formed by dehydrohalogenation had different retention times in the gas chromatographic analysis of kinetic samples. Since it is 30 times more reactive, the trichloride does not interfere with the dichloride tritium kinetics and only results in a slightly higher infinity point activity due to the small amount of YC$_6$H$_4$-CT=CCl$_2$ formed.

m-ClC$_6$H$_4$CDClCH$_2$Cl. m-ClC$_6$H$_4$CD=CH$_2$ (2.8 g, 20 mmol) was dissolved in 15 mL of DMF in a 50 mL round-bottom flask with a stir bar and placed in an ice bath. Chlorine (1.4 g, 20 mmol) was condensed into the reaction flask. The reaction mixture was stirred for 30 min at room temperature before a short path distillation head replaced the reflux condenser prior to vacuum distillation. m-ClC$_6$H$_4$CDClCH$_2$Cl (2.9 g, 14 mmol, 69% yield) was collected between 108 and 120 °C at 7 mmHg. The 300 MHz ^{1}H MNR has an AB pattern for the −CH$_2$Cl at 3.9 ppm with $J_{A−B}$ = 11 Hz. The −CH$_2$Cl of m-ClC$_6$H$_4$CHClCH$_2$Cl has an ABX pattern at 3.9 to 4 ppm with $J_{A−X}$ = 6 Hz, $J_{B−X}$ = 8 Hz, and $J_{A−B}$ = 11 Hz, and the benzylic proton has a d of d at 5.0 ppm. m-ClC$_6$H$_4$CDClCHCl$_2$ has a singlet at 5.95 ppm, and m-ClC$_6$H$_4$-CHClCHCl$_2$ has two doublets at 5.2 and 6.0 ppm with a $J \approx 8$ Hz.

Synthesis of m-ClC$_6$H$_4$CHBrCH$_2$Br. m-ClC$_6$H$_4$CH=CH$_2$ (3.5 g, 27 mmol) and 35 mL of CCl$_4$ were placed in a 125 mL Erlenmeyer flask with a magnetic stir bar. A solution of 4.3 g (27 mmol) of Br$_2$ and 2 mL of CCl$_4$ was added dropwise, and the resulting mixture was stirred overnight. After the CCl$_4$ was removed the product was purified by column chromatography by using a silica gel column and a 1:1 ratio of hexanes:CH$_2$Cl$_2$. The 4.0 g (49% yield) of m-ClC$_6$H$_4$CHBrCH$_2$-Br had a mp of 42.5 to 44 °C. The 300 MHz NMR has an ABX pattern for the non-aromatic protons: H$_X$ at 5.1 ppm ($J_{A−X}$ = 5 Hz, $J_{B−X}$ = 11 Hz); H$_A$ at 4.0 ppm ($J_{A−B}$ = 11 Hz); H$_B$ at 3.9 ppm. The m-ClC$_6$H$_4$-

(51) The extent of reaction has also been followed by the disappearance of the OH proton using proton NMR.

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

(53) Roberts, R. M.; Gilbert, J. C.; Rodewald, L. B.; Wingrove, A. S. *An Introduction to Modern Experimental Organic Chemistry*, 2nd ed.; Holt, Rinehart and Winston, Inc.: New York, 1974; pp 323 and 324.

(54) De Roocker, A.; De Radzitzky, P. *Bull. Soc. Chim. Belges* **1970**, *79*, 531.

CDBrCH$_2$Br resulted in the absence of the signal at 5.1 ppm, with an AB pattern at 4.0 ppm (2H, J_{A-B} = 11 Hz).

Synthesis of *m*-ClC$_6$H$_4$CDClCH$_2$Br. A 250 mL Erlenmeyer flask was charged with 26 mL of water, 26 mL of 12 M HCl, and a magnetic stir bar and placed in an ice/water bath. While the solution was stirred small portions of 17.5 g (126 mmol) of *m*-chlorostyrene and 17.3 g (126 mmol) of *N*-bromosuccinamide were added alternately and formed a second layer.[55] The aqueous layer was washed three times with 25 mL of CH$_2$Cl$_2$ and combined with the original organic layer. This was washed once with 25 mL of 5% NaHCO$_3$, twice with 25 mL of 20% NaS$_2$O$_5$, and three times with water and dried over MgSO$_4$. The CH$_2$-Cl$_2$ was removed by a rotary evaporator prior to vacuum distillation. After preliminary distillation, the combined cuts were carefully redistilled and a center cut, 138−140 °C at 12−13 mmHg, was still found to contain about 17% of the dibromide, *m*-ClC$_6$H$_4$CDBrCH$_2$Br. The 60 MHz ^{1}H NMR had the −CH$_2$Br at 3.9 for *m*-ClC$_6$H$_4$CDClCH$_2$-Br and at 4.0 for *m*-ClC$_6$H$_4$CDBrCH$_2$Br.

Since neither the *m*-ClC$_6$H$_4$CDBrCH$_2$Br nor the reaction products, *m*-ClC$_6$H$_4$CBr=CH$_2$ or *m*-ClC$_6$H$_4$CD=CHBr, interfere with the GC analysis, this sample was used for kinetic runs. The product ratios for the synthesis of *m*-ClC$_6$H$_4$CHClCH$_2$Br was similar to that for the deuterium compound.

Synthesis of YC$_6$H$_4$CHClCF$_2$Cl. The chlorination reaction of C$_6$H$_5$-CH=CF$_2$ dissolved in CCl$_4$ has been described in detail.[56] The ^{19}F 60 MHz NMR spectra of all the YC$_6$H$_4$CHClCF$_2$Cl shows a clear ABX pattern: F$_A$ at 57−58 ppm, F$_B$ at 61−62 ppm, $J_{A-H} \approx$ 7 Hz, $J_{B-H} \approx$ 10 Hz, and J_{A-B} = 162−164.

Kinetics of Hydrogen and Deuterium Compounds. Dehydrohalogenation kinetics were carried out under pseudo-first-order conditions with ratios of alkoxide to substrate larger than 15 to 1. A solution of alcoholic sodium alkoxide solution [30−40 mL ≈ 0.3 M] in a 50-mL Erlenmeyer capped with a serum stopper was allowed to reach temperature in a bath held to ± 0.1 °C. The reactant, 25−75 μL, and a standard, 15−50 μL, were mixed and injected into the solution by a 1-mL glass Luer-lok syringe equipped with a 4 in. stainless steel needle. Disposable glass or plastic 5-mL syringes fitted with 4-in. stainless steel needles were used to take 3−4-mL samples that were injected into about 100 mL of dilute aqueous HCl and extracted with 0.25 to 1 mL of CCl$_4$ with use of a 125 mL separatory funnel with a Teflon stopcock. After vigorous shaking for about a minute, the layers were allowed to separate [usually waiting 15−20 min] and the CCl$_4$ layer was analyzed with an automated gas chromatographic instrument. A typical run consisted of nine samples and an infinity point. The advantage of using gas chromato-graphy to analyze the samples is that both the disappearance of substrate and the appearance of products can be followed.

Kinetics of Tritium Compounds. The detritiohalogenation and exchange reactions were run with <10 μL substrate in 12−15 mL methanolic sodium methoxide. Aliquots were taken with a 1 mL glass or plastic syringe fitted with a 4-in. stainless steel needle. Nine points and an infinity sample were taken. Samples for a given run were of the same size [0.85 to 0.95 mL] and were injected into 75 mL of dilute aqueous HCl and extracted with 10.0 mL of toluene by using a 125 mL separatory funnel with a Teflon stopcock. The mixture was shaken for the same length of time [30−60 s] and allowed to stand for 20 min before the layers were separated. The toluene layer was dried for 20 min with Drierite. A 5.0-mL sample of the dried toluene was mixed with 5 mL of a scintillation cocktail [INSTA-FLUOR (TM) or OPTI-FLUOR (R)] and counted with a Packard Tri-Carb 4640.

(55) Buckles, R. E.; Long, J. W. *J. Am. Chem. Soc.* **1951**, *73*, 998.

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