COMPARING ISOTOPE EFFECTS AND RATES FOR THE METHANOLIC SODIUM METHOXIDE REACTIONS OF 9-R-FLUORENE TO THOSE FOR p-CF$_3$C$_6$H$_4$CHClR (R = CH$_2$Cl, CH$_2$F AND CF$_3$)

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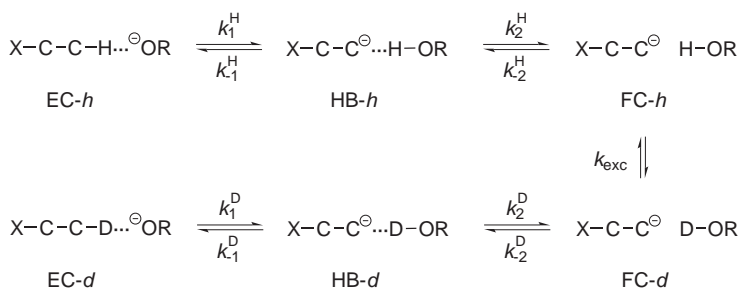
Dedicated to Professor Miloš Hudlický in recognition of his many contributions to the chemistry of organic fluorine compounds.

Kinetic primary isotope effects and activation parameters associated with the methanolic sodium methoxide-promoted dehydrohalogenation reactions of 9-(chloromethyl)fluorene and 9-(fluoromethyl)fluorene are reported and compared to for p-CF$_3$C$_6$H$_4$CHClCH$_2$Cl and p-CF$_3$C$_6$H$_4$CHClCH$_2$F. The element effect, k^{HCl}/k^{HF} = 4 at 25 °C, for the fluorenyl compounds is only a tenth of the value, k^{HCl}/k^{HF} = 54, obtained for the benzylic compounds. Also reported are the activation parameters for the methanolic sodium methoxide reactions of 9-(trifluoro)methylfluorene for deuterium exchange and dehydrofluorination, and are compared to those for p-CF$_3$C$_6$H$_4$CHClCF$_3$. In both cases the exchange reaction is faster than the elimination; however, in the fluorenyl system there is a large difference between the entropies of activation for exchange, $\Delta S^{\neq}$ = –14 eu, and elimination, $\Delta S^{\neq}$ = +10 eu; however, the $\Delta S^{\neq}$ of 12–13 eu are the same for the benzylic systems. The eliminations for 9-(chloromethyl)fluorene and 9-(fluoromethyl)fluorene are 80 to 1,000 times faster than those for p-CF$_3$C$_6$H$_4$CHClCH$_2$X. The reactions of 9-(trifluoromethyl)fluorene are favored over p-CF$_3$C$_6$H$_4$CHClCF$_3$ by 200,000 for the dehydrofluorination and 1,000 for the exchange at 25 °C; however, due to the large differences in activation entropies, the exchange reaction is favored by 10^7 at –50 °C.

Keywords: Reaction kinetics; Isotope effects; Activation parameters; Mechanism; Dehydrohalogenations; Isotope exchange; Carbanions; Fluorinated compounds.

Proton transfer to and from carbon, a basic step of importance to many chemical reactions, has been widely studied using primary kinetic isotope effects (PKIE). When hydron transfer from a carbon acid to methoxide is rate limiting, significant values of k^H/k^D are observed. On the other hand, near unity values of k^H/k^D are attributed to an internal-return mechanism,

where hydron transfer occurs prior to the rate-limiting step[1]. Our working model for hydron exchange reactions of carbon acids with methanolic sodium methoxide is represented in Scheme 1.

After forming an encounter complex, EC-*h*, the proton is transferred from carbon to methoxide, k_1^H, to generate a hydrogen-bonded carbanion, HB-*h*. The reverse of this step, k_{-1}^H, is the internal-return step in the overall process. The hydrogen bond breaks, k_2^H, forming a carbanion, FC-*h*, that still has the CH_3OH in the best position to interact with the lone pair electrons of the carbanion. If k_{-1}^H is much faster than k_2^H, there is an equilibrium for the proton transfer and forming FC-*h*, k_2^H, becomes the rate-limiting step. On the other hand, if $k_2^H \gg k_{-1}^H$ then the actual proton transfer, k_1^H, is rate-limiting. Exchange, k_{exc}, occurs when a CH_3OD replaces the CH_3OH in the most favorable position. This step is usually thought to be much faster than regenerating HB-*h*, k_{-2}^H. When $k_{exc} \gg k_{-2}^H$, the rate law for this mechanism is

$$k_{obs} = k_1 k_2 / (k_{-1} + k_2). \tag{1}$$

Equation (*1*) has two extremes: (i) $k_{-1} \gg k_2$ then $k_{obs} = (k_1/k_{-1})]k_2$, and (ii) $k_2 \gg k_{-1}$ then $k_{obs} = k_1$. For case (i), second-order kinetics and a near-unity PKIE is expected, and for case (ii), second-order kinetics and a PKIE that obeys the Swain–Schaad relationship[2], $k^H/k^D = (k^D/k^T)^{2.26}$, should result. When neither extreme is applicable, all three rate constants, k_1, k_{-1} and k_2, can contribute to the rate constant, k_{obs}. A major contribution to the analysis of isotope effects associated with reactions proceeding by an internal-return mechanism was made by the Streitwieser group in 1971 [3]. Using single-temperature rate constants for all three hydrogen isotopes and the Swain–Schaad relationship, they calculate an internal-return parameter, *a* =

k_{-1}/k_2 [4], which is used to calculate the rate constant for the hydron transfer step

$$k_1 = k_{obs} (a + 1). \tag{2}$$

Interesting isotope effects have been reported for hydron transfer from methanol to carbanions generated by the reaction of methanolic methoxide with benzyl(trimethyl)silanes in mixtures of MeOH and MeOD [5]. Values of k^H/k^D range from 10 ($p\text{-}NO_2C_6H_4CH_2^-$) to 1.0 (other $YC_6H_4CH_2^-$) with values of 10 for fluorenyl anions. We reported a similar trend for carbanions $\{YC_6H_4CHCF_2OCH_3\}^-$, generated from the reaction of methanolic methoxide with $YC_6H_4CH=CF_2$, where there is also a dramatic difference between the isotope effects associated with the proton transfer reactions as well as the temperature dependence of these isotope effects[6]. Although benzylic carbanions delocalize the negative charge into the ring, a $p\text{-}NO_2$ group gives additional stabilization due to π-delocalization, and we also find that the competition between proton transfer to make a saturated ether, $YC_6H_4CH_2CF_2OCH_3$, and the ejection of fluoride to give $YC_6H_4CH=CFOCH_3$ as well as the ratio of E/Z isomers for the vinyl ethers differ significantly comparing p-nitro to m-nitro, m-chloro and $m\text{-}CF_3$ [7]. We attributed differences to a $\{p\text{-}NO_2C_6H_4CHCF_2OCH_3\}^-$ that has more π-delocalization of the negative charge into the ring than the other carbanions where charge is largely localized around the benzylic carbon.

In this paper we discuss reactions that generate the highly π-delocalized aromatic fluorenyl anion as intermediates compared to similar results obtained from the reactions of $p\text{-}CF_3C_6H_4CHClCH_2Cl$, $p\text{-}CF_3C_6H_4CHClCH_2F$ and $p\text{-}CF_3C_6H_4CHClCF_3$.

EXPERIMENTAL

Instrumentation

All NMR spectra were measured using a Varian XL 300-MHz FT-NMR with $CDCl_3$ as the lock signal. ^1H and ^{13}C NMR spectra chemical shifts are relative to TMS and ^{19}F chemical shifts are relative to $CFCl_3$. Chemical shifts are given in ppm (δ-scale), coupling constants (J) in Hz. Hewlett Packard 5890 Series II gas chromatographs were used to analyze kinetic mixtures. One was fitted with model 7673 GC/SFC injector autosampler and a hot wire detector. The one used to follow hydron exchange reactions had a 5972 Series mass selective detector. The columns were HP-5 (crosslinked 5% PhMesilane) 30 m × 0.53 mm × 5.0 μm film thickness. The constant temperature baths were NESLAB RTE 111 (to –25 °C) and an FTSSYSTEMS bath (to –80 °C). Water was the bath medium above 0 °C and methanol below 0 °C.

Materials

9-Fluorenemethanol, 9-fluorenecarboxylic acid, diethylaminosulfur trifluoride (DAST) and CH_3OD were purchased from Aldrich Chemical Company. Solutions of methanolic sodium methoxide were made by adding sodium metal directly to anhydrous methanol. We tried to make the concentrations close to 0.3 mol l^{-1} and obtained the actual concentration by titrating with standard HCl. Methyl 9-fluorenecarboxylate was synthesized by conventional methods and reacted several times with CH_3ONa in CH_3OD until more than 98% deuterium was incorporated in the 9 position. The methyl 9-fluorencarboxylate-9-*d* was reduced using $LiAlH_4$ to make 9-fluorenemethanol-9-*d*.

Preparation of 9-Halomethylfluorenes

9-(Fluoromethyl)fluorene. A solution of 1.96 g (10 mmol) of 9-fluorenemethanol in 35 ml CH_2Cl_2 was added to 1.4 ml (1.7 g, 10 mmol) DAST in 5 ml CH_2Cl_2 at –78 °C. The mixture was stirred for 2 h, allowed to warm up to room temperature for a period of 2 h and refluxed for 2 h. The mixture was poured into water. The organic layer was separated, washed with saturated KCl and dried over anhydrous $MgSO_4$. After removing solvent under vacuum, the crude product was dissolved in a pentane/CH_2Cl_2 (60 : 40) mixture, brought onto a silica column and eluted with a pentane/CH_2Cl_2 (85 : 15) mixture. The product was in the first seven fractions: 1.5 g (5.8 mmol; 58% yield). ^1H NMR (300 MHz, CDCl$_3$): 4.30 (CH, d of t, $^3J_{HH} = 11$, $^3J_{FH} = 22$); 4.66 (CH$_2$F, dd, $^3J_{HH} = 11$, $^2J_{FH} = 47$); 7.3–7.8 (CH$_{Ph}$). ^{13}C NMR (75 MHz, CDCl$_3$): 48.40 (CH, d, $^2J_{FC} = 20$); 85.28 (CH$_2$F, d, $^1J_{FC} = 173$); 120.08, 125.18, 127.15, 127.89 (CH$_{Ph}$); 141.37, 142.64 (C$_q$).

9-(Fluoromethyl)fluorene-9-d. A solution of 3.33 g (17 mmol) of 9-fluorenemethanol-9-*d* in 50 ml CH_2Cl_2 was added to 2.5 ml (3.05 g, 18 mmol) DAST in 5 ml CH_2Cl_2 at –78 °C. The remaining procedure as above results in 1.97 g (10.0 mmol; 59% yield). ^1H NMR (300 MHz, CDCl$_3$): 4.64 (CH$_2$F, d, $^2J_{FH} = 47$); 7.3–7.8 (CH$_{Ph}$).

9-(Chloromethyl)fluorene. A mixture of 1.96 g (10 mmol) 9-fluorenemethanol and 10 ml thionyl chloride was refluxed for 2 h. The excess thionyl chloride was removed *in vacuo* and the remaining crude mixture was dissolved in a pentane/CH_2Cl_2 (60 : 40) mixture, brought onto a silica column and eluted with a pentane/CH_2Cl_2 (85 : 15) mixture. The product was in the first seven fractions: 1.59 g (7.4 mmol; 74% yield). ^1H NMR (300 MHz, CDCl$_3$): 3.87 (CH$_2$Cl, d, $^3J_{HH} = 11$); 4.22 (CH, d of t, $^3J_{HH} = 11$); 7.3–7.8 (CH$_{Ph}$). ^{13}C NMR (75 MHz, CDCl$_3$): 46.89 (CH$_2$Cl); 49.28 (CH); 119.98, 124.90, 127.14, 127.98 (CH$_{Ph}$); 141.14, 144.03 (C$_q$).

9-(Chloromethyl)fluorene-9-d. A mixture of 2.15 g (10.9 mmol) 9-fluorenemethanol-9-*d* and 10 ml thionyl chloride was refluxed for 2 h. The remaining procedure as above gave 1.13 g (5.2 mmol; 48% yield). ^1H NMR (300 MHz, CDCl$_3$): 3.88 (CH$_2$Cl); 7.3–7.8 (CH$_{Ph}$).

9-(Trifluoromethyl)fluorene. We used a slight variation of the procedure given in the literature[8]: Polyphosphoric acid (17 g) and 1,1-diphenyl-2,2,2-trifluoromethylethanol (3 g, 12 mmol) were heated with stirring to 120 °C in a 100-ml round-bottom flask for 2 h. The reaction was cooled and terminated by pouring into a slurry of ice water and stirred for 20–24 h. The crude solid was crystalized from a 30 : 70 water/ethanol mixture to give a solid with m.p. 96–97 °C. The reported product was crystalized from petroleum ether giving a m.p. 95.5–96.5 °C. Yields were variable and ranged from 30 to 70%. ^1H NMR (300 MHz, CDCl$_3$): 4.60 (CH, q, $^3J_{FH} = 9$); 7.3–7.7 (CH$_{Ph}$). ^{19}F NMR (282 MHz, CDCl$_3$ + CFCl$_3$): –68.29 (CF$_3$, d, $^3J_{HF} = 9$).

9-(Trifluoromethyl)fluorene-9-d. A mixture of 0.2 g 9-(trifluoromethyl)fluorene and 40 ml CH_3OD was placed in a 50-ml Erlenmeyer flask and sealed with a serum prior to placement in a –50 °C constant temperature. When the mixture had come to temperature (5 to 10 min) 1 ml 0.3 M MeoNa/MeOD was injected into the mixture. After 30 min ($\approx$ 10 half-lives) the mixture was poured into 200 ml dilute HCl and extracted with 2 ml CCl_4. This is similar to the method we use for following kinetics. Since the elimination is 80 times slower than the exchange reaction, this resulted in obtaining 9-(trifluoromethyl)fluorene-9-*d* with less than 5% of the products coming from the elimination of HF. The small amount of impurities did not interfere with the analysis of the H/D content. ^1H NMR (300 MHz, $CDCl_3$): 7.3–7.7 (CH_{Ph}). ^{19}F NMR (282 MHz, $CDCl_3$ + $CFCl_3$): –68.38 (CF_3, s). There is sufficient separation between the CF_3 signal in 9-(trifluoromethyl)fluorene and that in 9-(trifluoromethyl)fluorene-9-*d* to allow following the exchange kinetics using NMR [9]; however, we used the GC/MS to analyze our samples.

Kinetic Procedures

Kinetics were run under pseudo-first order conditions with a 15 fold excess of methoxide. A 50-ml Erlenmeyer flask was charged with 30 to 40 ml of $\approx$0.3 M methanolic sodium methoxide, sealed with a serum cap and placed in a constant-temperature bath that was held to ±0.1 °C. Substrates were dissolved in toluene and 4-chlorodiphenyl ether was added as an internal standard for elimination kinetics. After the reaction flask had reached the bath temperature (10–20 min), about 150 µl of the sample, standard and toluene was injected by a 1-ml syringe fitted with a 4″ stainless-steel needle and the timer was started. At appropriate intervals (usually four points in the first half-life, three in the second and one in the third), 3 to 4 ml aliquots were taken with a plastic disposable syringe fitted with a 4″ stainless-steel needle and injected into a 125-ml separatory funnel that contained 600 µl CCl_4 and $\approx$100 ml of dilute HCl. Vigorous shaking, followed by a 10-min wait and the lower CCl_4 was separated for analysis by either the GC (elimination kinetics) or GC/MS (exchange kinetics).

RESULTS AND DISCUSSION

The sodium methoxide-promoted dehydrochlorination of m-ClC$_6$H$_4$C^{i}HCl-CH$_2$Cl results in a small isotope effect, $(k^H/k^D)_{obs} = 3.40$ [10], that has normal Arrhenius behavior with $A^H/A^D = 1.0 \pm 0.2$ and ΔE_a^{D-H} accounting for the small value. If the hydron in the transition structure is situated in an asymmetric position between carbon and oxygen, a residual zero-point energy can account for the small isotope effect[11]. However, such Arrhenius behavior can also result from an internal-return mechanism[12]. If the small isotope effects are due to a residual zero-point energy difference between the hydrogen and deuterium in the transition structure, the Swain–Schaad relationship predicts $(k^H/k^T) = (k^D/k^T)^{3.344}$ and $(1.83)^{3.344} = 7.45$ that is 20% larger than the measured $(k^H/k^T)_{obs} = 6.20$ [13]. This suggests internal return with $a^H = (k^H_{-1}/k_2) = 0.59$, $a^D = (k^D_{-1}/k_2) = 0.14$ and $a^T = (k^T_{-1}/k_2) = 0.072$ (Table I). Equation (*2*) allows calculation of the hydron transfer steps occurring dur-

ing the dehydrochlorination: $k_1^H = (1.60 \cdot 10^{-3} \text{ l mol}^{-1} \text{ s}^{-1})1.59 = 2.54 \cdot 10^{-3}$, $k_1^D = (4.71 \cdot 10^{-4} \text{ l mol}^{-1} \text{ s}^{-1})1.14 = 5.37 \cdot 10^{-4} \text{ l mol}^{-1} \text{ s}^{-1}$, and $(k_1^H/k_1^D) = 4.73$ at 25 °C. Reactions of $m\text{-CF}_3\text{C}_6\text{H}_4\text{C}^i\text{HClCH}_2\text{Cl}$ have similar internal-return parameters. If the same is true for the reactions of $p\text{-CF}_3\text{C}_6\text{H}_4\text{C}^i\text{HClCH}_2\text{Cl}$ then $k_1^H = (8.03 \cdot 10^{-3} \text{ l mol}^{-1} \text{ s}^{-1})1.59 = 1.28 \cdot 10^{-2}$ and $k_1^D = (2.25 \cdot 10^{-3} \text{ l mol}^{-1} \text{ s}^{-1})1.14 = 2.57 \cdot 10^{-3}$, resulting in $(k_1^H/k_1^D) = 4.98$ at 25 °C. Therefore isotope effects for the hydron transfer steps for all three compounds are within 5%.

The experimental isotope effects are smaller for the methanolic methoxide-promoted dehydrofluorinations of $p\text{-CF}_3\text{C}_6\text{H}_4\text{C}^i\text{HClCH}_2\text{F}$, $(k^H/k^D)_{obs} = 2.19$ and $(k^D/k^T)_{obs} = 1.63$, and give higher values for the internal-return parameters, $a^H = 2.1$, $a^D = 0.50$ and $a^T = 0.27$ (Table I).

TABLE I
Dehydrohalogention reactions with methanolic sodium methoxide. Data from ref.[10]

Compound	k_{obs} l mol^{-1} s^{-1} 25 °C	k^H/k^D k^D/k^T 25 °C	ΔE_a^{D-H} ΔE^{T-D} kcal mol^{-1}	A^H/A^D A^D/A^T	$a^H =$ k_{-1}^D/k_2 25 °C	$a^D =$ k_{-1}^D/k_2 25 °C	$a^T =$ k_{-1}^D/k_2 25 °C
$m\text{-ClC}_6\text{H}_4\text{CHClCH}_2\text{Cl}$	$1.60 \cdot 10^{-3}$	3.40	0.8	0.96			
$m\text{-ClC}_6\text{H}_4\text{CDClCH}_2\text{Cl}$	$4.71 \cdot 10^{-4}$	1.83	0.4	0.81	0.59	0.14	0.072
$m\text{-ClC}_6\text{H}_4\text{CTClCH}_2\text{Cl}$	$2.58 \cdot 10^{-4}$						
$m\text{-CF}_3\text{C}_6\text{H}_4\text{CHClCH}_2\text{Cl}$	$3.34 \cdot 10^{-3}$	3.49	0.8	1.0			
$m\text{-CF}_3\text{C}_6\text{H}_4\text{CDClCH}_2\text{Cl}$	$9.58 \cdot 10^{-4}$	1.88	0.4	0.92	0.59	0.13	0.068
$m\text{-CF}_3\text{C}_6\text{H}_4\text{CTClCH}_2\text{Cl}$	$5.10 \cdot 10^{-4}$						
$p\text{-CF}_3\text{C}_6\text{H}_4\text{CHClCH}_2\text{Cl}$	$8.03 \cdot 10^{-3}$	3.57	0.7	1.1			
$p\text{-CF}_3\text{C}_6\text{H}_4\text{CDClCH}_2\text{Cl}$	$2.25 \cdot 10^{-3}$						
$p\text{-CF}_3\text{C}_6\text{H}_4\text{CHClCH}_2\text{F}$	$1.49 \cdot 10^{-4}$	2.19	0.5	1.1			
$p\text{-CF}_3\text{C}_6\text{H}_4\text{CDClCH}_2\text{F}$	$6.81 \cdot 10^{-5}$	1.63	0.3	0.93	2.1	0.50	0.27
$p\text{-CF}_3\text{C}_6\text{H}_4\text{CTClCH}_2\text{F}$	$4.19 \cdot 10^{-5}$						
$p\text{-CF}_3\text{C}_6\text{H}_4\text{CHClCH}_2\text{Cl}$	1.58	2.49	−0.2	3.8			
$p\text{-CF}_3\text{C}_6\text{H}_4\text{CDClCH}_2\text{Cl}$	$6.34 \cdot 10^{-1}$						
$p\text{-CF}_3\text{C}_6\text{H}_4\text{CHClCF}_3$	$1.06 \cdot 10^{-5}$						
$p\text{-CF}_3\text{C}_6\text{H}_4\text{CDClCF}_3{}^a$	$8.58 \cdot 10^{-4}$	1.08	−0.4	2.4			
$p\text{-CF}_3\text{C}_6\text{H}_4\text{CTClCF}_3{}^a$	$7.91 \cdot 10^{-5}$						

Equation (*2*) yields k_1^H = (1.49 · 10^{-4} l mol^{-1} s^{-1})3.1 = 4.62 · 10^{-4} and k_1^D = (6.81 · 10^{-5} l mol^{-1} s^{-1})1.50 = 1.02 · 10^{-4} l mol^{-1} s^{-1}, and a (k_1^H/k_1^D) = 4.53, which is within 5–10% of the (k_1^H/k_1^D) calculated for the three dehydrochlorinations. The element effect for the reactions of p-CF$_3$C$_6$H$_4$C^{i}HCl-CH$_2$X, $(k^{HCl}/k^{HF})_{obs}$ = 54, is normal; however, a major portion of that effect is due to the hydron transfer step, (k_1^{HCl}/k_1^{HF}) = 28, and not the step that breaks the halogen bond[14]. An extreme effect, $(k^{HCl}/k^{HF})_{obs}$ = 1.5 · 10^5, for the methoxide-promoted dehydrohalogenations of p-CF$_3$C$_6$H$_4$CHClCF$_2$X are not accounted for by usual explanations on the origins of element effects, but can be rationalized by a possible Gibbs energy diagram for the methanolic methoxide reactions with p-CF$_3$C$_6$H$_4$CHClCF$_3$ (Fig. 1a).

The encounter complex EC-*h* can be about 7 kcal mol^{-1} more stable than the hydrogen-bonded carbanion intermediate HB-*h* which is 7 kcal mol^{-1} more stable than the carbanion FC and (CH$_3$OH)$_2$ [15]. If the elimination of chloride occurs from the hydrogen-bonded carbanion, this would explain the origin of the extreme element effect. Comparing the dehydrofluorination reaction of p-CF$_3$C$_6$H$_4$CHClCF$_3$ (k = 1.06 · 10^{-5} l mol^{-1} s^{-1}) to the exchange of p-CF$_3$C$_6$H$_4$CDClCF$_3$ (k = 8.58 · 10^{-4} l mol^{-1} s^{-1}) suggests that
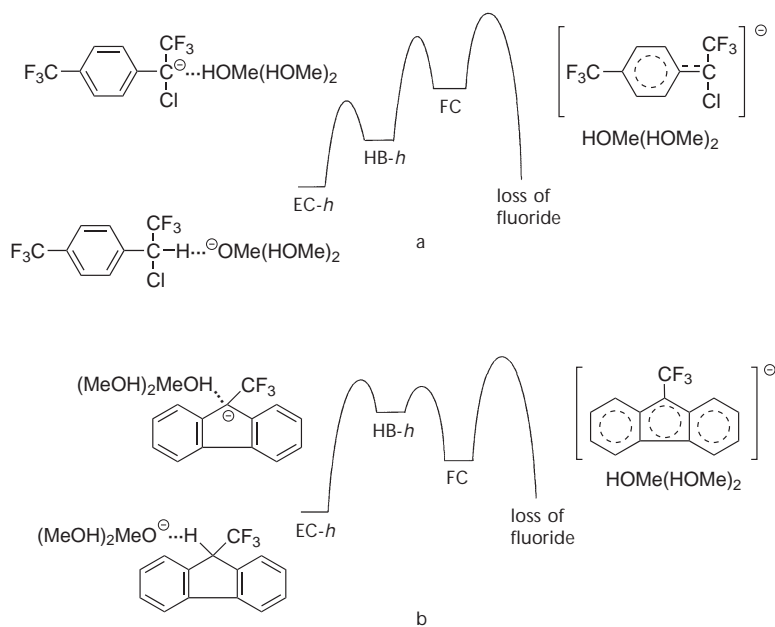

Fig. 1

Possible Gibbs energy diagrams for the reactions of methanolic methoxide: p-CF$_3$C$_6$H$_4$CHClCF$_3$ (a) and 9-(trifluoromethyl)fluorene (b)

return to HB-*d* has a lower barrier than elimination to form
p-CF$_3$C$_6$H$_4$CCl=CF$_2$. The additional stabilization of benzylic anions by tri-
fluoromethyl or chloro groups allows a study of carbanions stabilized by
electronic effects not requiring π-delocalization. For comparison to systems
with extensive π-delocalization, groups attached to the 9 position of
fluorene are made (Table II).

Tᴀʙʟᴇ II
Methanolic sodium methoxide promoted dehydrohalogenation and hydron exchange reactions. Data for *p*-CF$_3$C$_6$H$_4$CHClCF$_2$Cl, *p*-CF$_3$C$_6$H$_4$CHClCF$_3$, *p*-CF$_3$C$_6$H$_4$CHClCH$_2$Cl and *p*-CF$_3$C$_6$H$_4$CHClCH$_2$F from ref.[10]

Compound	MeO^{i}H	*k* l mol^{-1} s^{-1} 25 °C	*k* l mol^{-1} s^{-1} 50 °C	$\Delta H^{\neq}$ kcal mol^{-1}	$\Delta S^{\neq}$ eu
9-CF$_3$-fluorene-9-H	MeOH		$2.18 \cdot 10^{-5}$	19.9 ± 0.1	$+10.1 \pm 0.4$
9-CF$_3$-fluorene-9-D	MeOH		$4.36 \cdot 10^{-3}$	12.2 ± 0.2	-13.8 ± 0.7
9-CF$_3$-fluorene-9-T^a			$1.79 \cdot 10^{-3}$	11.8 ± 0.4	-17.4 ± 1.7
p-CF$_3$C$_6$H$_4$CHClCF$_2$Cl	MeOH	1.58	$4.54 \cdot 10^{-5}$	17.8 ± 0.1	$+2.2 \pm 0.2$
p-CF$_3$C$_6$H$_4$CDClCF$_2$Cl		$6.35 \cdot 10^{-1}$	$2.12 \cdot 10^{-5}$	17.6 ± 0.1	-0.5 ± 0.4
p-CF$_3$C$_6$H$_4$CHClCF$_3$	MeOH	$1.06 \cdot 10^{-5}$		27.9 ± 0.1	$+12.3 \pm 0.3$
p-CF$_3$C$_6$H$_4$CDClCF$_3$	MeOH	$8.58 \cdot 10^{-4}$		25.9 ± 0.1	$+14.3 \pm 0.3$
p-CF$_3$C$_6$H$_4$CTClCF$_3$		$7.91 \cdot 10^{-4}$		25.4 ± 0.1	$+12.5 \pm 0.3$
p-CF$_3$C$_6$H$_4$CTClCF$_3$	MeOD	$2.06 \cdot 10^{-3}$		24.9 ± 0.1	$+12.5 \pm 0.4$
9-CH$_2$Cl-fluorene-9-H	MeOH	$6.52 \cdot 10^{-1}$	$3.05 \cdot 10^{-3}$	15.2 ± 0.1	-8.5 ± 0.1
9-CH$_2$Cl-fluorene-9-D		$1.05 \cdot 10^{-1}$	$3.40 \cdot 10^{-4}$	16.2 ± 0.1	-8.5 ± 0.3
9-CH$_2$F-fluorene-9-H	MeOH	$1.64 \cdot 10^{-1}$	$3.15 \cdot 10^{-4}$	17.8 ± 0.1	-2.8 ± 0.4
9-CH$_2$F-fluorene-9-D		$2.34 \cdot 10^{-2}$	$4.06 \cdot 10^{-5}$	18.1 ± 0.2	-5.3 ± 0.2
p-CF$_3$C$_6$H$_4$CHClCH$_2$Cl	MeOH	$8.03 \cdot 10^{-3}$	$7.09 \cdot 10^{-6}$	20.1 ± 0.1	-0.7 ± 0.2
p-CF$_3$C$_6$H$_4$CDClCH$_2$Cl		$2.25 \cdot 10^{-3}$	$1.58 \cdot 10^{-6}$	20.8 ± 0.1	-1.0 ± 0.3
p-CF$_3$C$_6$H$_4$CHClCH$_2$Cl	MeOD	$1.98 \cdot 10^{-2}$	$2.25 \cdot 10^{-5}$	19.3 ± 0.1	-1.5 ± 0.2
p-CF$_3$C$_6$H$_4$CDClCH$_2$Cl		$5.45 \cdot 10^{-3}$	$5.07 \cdot 10^{-6}$	19.9 ± 0.1	-2.0 ± 0.1
p-CF$_3$C$_6$H$_4$CHClCH$_2$F	MeOH	$1.49 \cdot 10^{-4}$		23.4 ± 0.1	$+2.6 \pm 0.3$
p-CF$_3$C$_6$H$_4$CDClCH$_2$F		$6.81 \cdot 10^{-5}$		23.9 ± 0.1	$+2.5 \pm 0.3$

^{a} Data from ref.[8].

Deuterodeprotonation of 9-(trifluoromethyl)fluorene-9-*h* with CH_3ONa in CH_3OD was only measured at –75 °C, $3.36 \cdot 10^{-3}$ l mol^{-1} s^{-1}. Measuring the methanolic methoxide protodedeuteration of 9-(trifluoromethyl)fluorene-9-*d* between –70 and –50 °C allowed an extrapolation of $k^D = 1.13 \cdot 10^{-4}$ l mol^{-1} s^{-1} at –75 °C. Although a kinetic solvent isotope effect, k^{OD}/k^{OH}, has not been measured, it can be estimated to be between 4 and 5 at –75 °C, and this would result in a k^H/k^D of only between 6 and 7 [16]. This suggests internal return with k_1, k_{-1} and k_2 contributing to the experimental rate constant, k_{obs}. The protodedeuteration of 9-(trifluoromethyl)fluorene-9-*d* occurs 200 times faster than the dehydrofluorination of 9-(trifluoromethyl)fluorene-9-*h* at –50 °C; however, this rate difference disappears when extrapolating the rates to 25 °C. The $\Delta H^{\neq}$ favors the exchange reaction by almost 8 kcal mol^{-1}, but the $\Delta S^{\neq}$ of +10 eu for dehydrofluorination compared to the $\Delta S^{\neq}$ of –14 eu for the exchange reaction results in $\Delta G^{\neq}$ values that are the same at 25 °C. Our working hypotheses is that large positive $\Delta S^{\neq}$ values are obtained when the rate-limiting step occurs from intermediates like FC, while lower $\Delta S^{\neq}$ values are due to rate-limiting steps to or from hydrogen-bonded carbanions[17]. The exchange ($\Delta S^{\neq} \approx +13$ eu) and elimination ($\Delta S^{\neq} = +12$ eu) reactions of p-$CF_3C_6H_4C^iHClCF_3$ both have rate-limiting steps occurring from FC. The exchange is associated with near unity isotope effects and is 75–80 times faster than the elimination.

The possible Gibbs energy diagrams associated with these reactions are shown in Fig. 1. Although the reactions for both systems require the formation of carbanion intermediates like FC, the reactions of 9-(trifluoromethyl)fluorene have a barrier from the carbanion HB to FC that is lower than the return barrier to encounter complex EC. The exchange reaction has the formation of HB as rate-limiting and this would result in small amounts of internal return with significant isotope effects that would not obey the Swain–Schaad relationship. The loss of fluoride from the trifluoromethyl group is the rate-limiting step for the elimination reaction and this results in the large positive $\Delta S^{\neq}$ value. On the other hand both reactions of p-$CF_3C_6H_4CHClCF_3$ have large barriers from HB to FC that results in a pre-equilibrium between EC and HB. Even though the barrier for return to HB from FC is lower than the barrier to eject fluoride, formation of FC is rate-limiting.

Figure 2 has possible Gibbs energy diagrams for dehydrohalogenations from CH_2X. Figure 2a is for the methoxide-promoted dehydrochlorination of p-$CF_3C_6H_4CHClCH_2Cl$ where the barrier to eliminate chloride from HB is lower than that returning to an encounter complex. Since there is a much larger barrier to form FC, the reaction would occur faster than predicted

from an anticipated pK_a value of the starting compound. The hydrogen bond also retains any stereochemistry and reaction would proceed with anti-elimination[18]. The case for elimination of HF from p-CF$_3$C$_6$H$_4$CHCl-CH$_2$F is similar except that the barrier to return to the encounter complex is lower than the barrier to eliminate fluoride, and this results in more internal return and a lower isotope effect.

When the CH$_2$Cl is in the 9 position of fluorene (Fig. 2c) we anticipated that the barrier to lose chloride would be about the same as the one to form the highly π-delocalized FC intermediate. On the other hand, the barrier to lose fluoride should be larger than that to form FC, and elimination of fluoride would occur from FC. An element effect, k^{HCl}/k^{HF}, of 4 is ten times lower than expected for a concerted elimination reaction. A k^{HBr}/k^{HCl} of 6 was reported for the methoxide-promoted elimination rates of 9-(bromomethyl)fluorene and 9-(chloromethyl)fluorene[19,20]. A kinetic run of 9-(fluoromethyl)fluorene with CH$_3$ONa/CH$_3$OD resulted in a faster rate, $k_{obs} = 6.77 \cdot 10^{-3}$ l mol^{-1} s^{-1} at –10 °C, with no deuterium incorporation into the unreacted starting compound. The rate enhancement is due to a kinetic solvent isotope effect, $k^{OD}/k^{OH} = 2.56$. The lack of deuterium incorporation
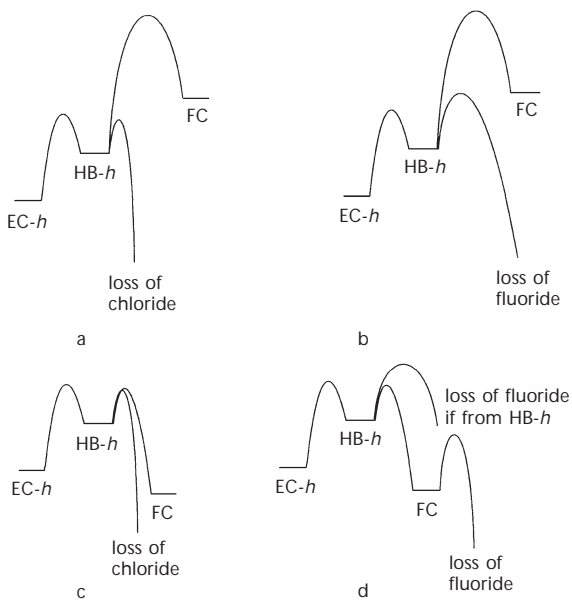

F$_{IG}$. 2

Possible Gibbs energy diagrams for the reactions of methanolic methoxide with p-CF$_3$C$_6$H$_4$CHClCH$_2$Cl (a), p-CF$_3$C$_6$H$_4$CHClCH$_2$F (b), 9-(chloromethyl)fluorene (c) and 9-(fluoromethyl)fluorene (d)

suggests the barrier to eliminate fluoride from FC is lower than the one to return to HB. Isotope effects at 0 °C are the same, $(k^H/k^D)_{obs} = 7.35$, for 9-(chloromethyl)fluorene and 9-(fluoromethyl)fluorene[21], and this is not so for the reactions of p-CF$_3$C$_6$H$_4$CHClCH$_2$Cl $((k^H/k^D)_{obs} = 3.95$ at 0 °C) and p-CF$_3$C$_6$H$_4$CHClCH$_2$F $((k^H/k^D)_{obs} = 2.34$ at 0 °C). We have been unsuccessful in attempts to make 9-(chlorodifluoromethyl)fluorene, but predict it would undergo dehydrochlorination from FC instead of HB at a rate similar to that for the exchange for 9-(trifluoromethyl)fluorene with a larger isotope effect than the one measured for p-CF$_3$C$_6$H$_4$CHClCF$_2$Cl.

In conclusion, organic compounds with carbon–fluorine bonds are ideal to investigate carbanion chemistry. Carbonyl and nitro compounds form stable anions; however, charge is mainly on the hetero atoms due to a π-delocalization of the electrons. Compounds containing β-C–Cl bonds to stabilize any negative charge are unstable and eliminate chloride ion with such ease that they are thought to undergo a concerted elimination reaction. The C–F bond can act as a C–Cl bond that has "glue" to keep it in place, and allows a study of carbanions that are stabilized by halogens. Comparing the chemistry of groups in the 9 position of fluorene to those attached to a benzylic carbon offers an opportunity to see the difference between an anion that is aromatic compared with one that is capable of delocalizing charge through a π-network, does not form an aromatic anion and has charge mainly on carbon atoms.

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13. We use 3.344 for the Swain–Schaad exponent as recommended in ref.[3b].

14. For a discussion of this, see ref.[10], p. 9967.

15. Calculations using B3LYP/6-31+G(d,p) on the reactions of $C_6H_5CHClCF_3$ and methoxide ion with two methanol molecules of solvation result in the encounter complex 7.8 kcal mol^{-1} more stable than the hydrogen-bonded carbanion. To form the free carbanion and $(HOCH_3)_3$ requires another 7.3 kcal mol^{-1}. Koch H. F., DeTuri V. F.: Unpublished results.

16. The methanolic sodium methoxide protodetritiation of 9-(trifluoromethyl)fluorene-9-*t* was reported in ref.[8] between –45 and –31 °C. The temperature dependence plot has sufficient error not to allow extrapolation to –75 °C. The $k^D/k^T = 2.44$ at –50 °C, which would have the Swain–Schaad relationship predict a k^H/k^D value of 8.1 at –50 °C and should be even larger at –75 °C.

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