The Effect of β-Fluorine Substituents on the Rate and Equilibrium Constants for the Reactions of α-Substituted 4-Methoxybenzyl Carbocations and on the Reactivity of a Simple Quinone Methide

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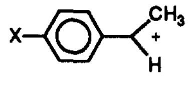
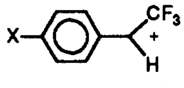
Abstract: The reactions of 4-MeOArCH(R)Cl (R = CH_2F, CHF_2, CF_3) and 4-MeOArC$(CF_3)_2$Y (Y = OTs and Br) with nucleophilic reagents were studied in 50:50 (v/v) trifluoroethanol/water. There is chloride common ion rate depression of the solvolysis of 4-MeOArCH(R)Cl. The large leaving group effect, $k_{OTs}/k_{Br} = 9 \times 10^4$, for the solvolysis of 4-MeOArC$(CF_3)_2$Y suggests that the reaction of the tosylate is accelerated by the relief of ground-state strain. The solvolysis of 4-MeOArC$(CF_3)_2$OTs gives a 33% yield of 4-[bis(trifluoromethyl)methylene]cyclohexa-2,5-dienone which forms by the aromatic substitution reaction of water at 4-MeOArC$(CF_3)_2^+$. This quinone methide reacts slowly with solvent ($t_{1/2} \approx 11$ h) and rapidly with azide ion. All of these compounds react with azide ion by an S_N1 mechanism. Values of k_{az}/k_s and k_{Cl}/k_s (M^{-1}) for the partitioning of the carbocation intermediates between capture by azide or chloride ion and solvent are reported. Absolute rate constants k_s (s^{-1}) and k_Y (M^{-1} s^{-1}, $Y^- = Cl^-, Br^-$) for the capture of 4-MeOArCR^1(R^2)$^+$ were calculated from the values of k_{az}/k_s (M^{-1}) or k_{az}/k_Y and an estimated value of $k_{az} = 5 \times 10^9$ M^{-1} s^{-1} for the diffusion-limited reaction of N_3^-. Values of K_{eq} for the ionization of 4-MeOArCR^1(R^2)Y to give 4-MeOArCR^1(R^2)$^+$ were calculated as the ratio of the microscopic rate constants k_{solv}/k_Y. A single β-fluorine at 4-MeOArCH$(CH_3)^+$ causes a 2-fold increase in k_s, due to a small inductive substituent effect. Additional β-fluorine substituents cause k_s to decrease due to a steric effect; the value of k_s for the capture of 4-MeOArC$(CF_3)_2^+$ is 40-fold smaller than k_s for 4-MeOArCH_2^+. The effect of β-fluorine substituents on log K_{eq} are consistent with steric congestion at the more highly substituted substrates that destabilizes 4-MeOArCR^1(R^2)Y relative to 4-MeOArCR^1(R^2)$^+$. These results support the proposal that the low reactivity of 4-MeOArCH$(CF_3)^+$ toward solvent is due, in part, to a resonance effect.

Introduction

The substitution of an α-CF_3 group for the α-CH_3 group at 4-XArCH$(CH_3)^+$ ($\sigma_X^+ \leq -0.32$) destabilizes the carbocation and causes a (10^7–10^9)-fold decrease in the values of k_{solv} for the formation of the carbocation by an S_N1 solvolysis reaction of a neutral derivative.[1-3] On the other hand, we recently reported that the α-CF_3 for α-CH_3 substitution has no effect on k_{az}/k_s (M^{-1}) for the partitioning of the carbocation between reaction with azide ion and solvent (trifluoroethanol/water).[3] Therefore, there is also no effect on k_s, because both 4-XArCH$(CH_3)^+$[4] and 4-XArCH$(CF_3)^+$[3] are trapped by azide ion in diffusion-limited reactions, with $k_{az} \approx 5 \times 10^9$ M^{-1} s^{-1}.[3-5]



4–XArCH(CH$_3$)$^+$



4–XArCH(CF$_3$)$^+$

These are striking results. Students of organic chemistry are taught that the diarylmethyl cation is more stable and therefore less reactive than the benzyl cation and that the benzyl cation is more stable and therefore less reactive than the methyl cation; i.e., that a decrease in the equilibrium stability of a carbocation is accompanied by a decrease in its kinetic stability.[6] However, the α-CF_3 for α-CH_3 substitution destabilizes the transition state for the formation of 4-MeOArCH(R)$^+$ from the chloride derivatives by about 10 kcal/mol,[7] yet the substitution has *no effect on the reactivity* of the carbocation toward a largely aqueous solvent.

A relatively simple explanation for the small effect of the α-CF_3 group on carbocation reactivity is that the polar effect of the α-CF_3 substituent, which will increase the reactivity of 4-XArCH(R)$^+$ toward solvent, is masked by one or more other effects of the α-CF_3 substituent which *decrease* the reactivity of the carbocation.[3] Two such effects are as follows.

(1) The unexpectedly small value of k_s may be due to destabilization of the transition state for carbocation capture by unfavorable steric interactions between the approaching solvent nucleophile and the β-fluorine substitutents at 4-XArCH$(CF_3)^+$.

(2) The unusual kinetic stability of 4-XArCH$(CF_3)^+$ may be related to the large amount of resonance stabilization in these carbocations.[1-3] This could increase the barrier to carbocation capture, because of the requirement that a large fraction of this resonance stabilization be lost at the reaction transition state.[8,9]

In this work we report the results of experiments that were designed to determine the individual contributions of these two

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(1) Tidwell, T. T. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 20–32. Allen, A. D.; Tidwell, T. T. *Adv. Carbocation Chem.* **1989**, *1*, 1–44.

(2) Allen, A. D.; Ambidge, C.; Che, C.; Michael, H.; Muir, R. J.; Tidwell, T. T. *J. Am. Chem. Soc.* **1983**, *105*, 2343–2350.

(3) (a) Richard, J. P. *J. Am. Chem. Soc.* **1986**, *108*, 6819–6820. (b) Richard, J. P. *Ibid.* **1989**, *111*, 1455–1465.

(4) Richard, J. P.; Rothenberg, M. E.; Jencks, W. P. *J. Am. Chem. Soc.* **1984**, *106*, 1361–1372.

(5) McClelland, R. A.; Banait, N.; Steenken, S. *J. Am. Chem. Soc.* **1986**, *108*, 7023–7027. McClelland, R. A.; Kanagasabapathy, V. M.; Steenken, S. *Ibid.* **1988**, *110*, 6913–6914.

(6) Arnett, E. M.; Petro, C.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1979**, *101*, 522–526. Arnett, E. M.; Hofelich, T. C. *Ibid.* **1983**, *105*, 2889–2895. Diffenbach, R. A.; Sano, K.; Taft, R. W. *Ibid.* **1966**, *88*, 4747–4749.

(7) Calculated from the ratio {[(400 s^{-1})/(3 × 10^{-5} s^{-1})] = 1 × 10^7} of the values of k_{solv} for 4-MeOArCH(CH_3)Cl and 4-MeOArCH(CF_3)Cl at 25 °C in 50:50 (v/v) trifluoroethanol/water (I = 0.50, $NaClO_4$). The value of k_{solv} for 4-MeOArCH(CF_3)Cl is from Table I. The value of k_{solv} for 4-MeOArCH(CH_3)Cl is the average of two different estimates: A value of 230 s^{-1} was calculated from $k_{solv} = 4.6 \times 10^{-4}$ s^{-1} for 4-MeOArCH(CH_3)(3,5-dinitrobenzoate) in 50:50 (v/v) trifluoroethanol/water (Amyes, T. L., unpublished results) and a value of {[(0.65 s^{-1})/(1.32 × 10^{-6} s^{-1})] = 5 × 10^5} for the effect of changing from a 3,5-dinitrobenzoate to a chloride leaving group. This is the ratio of k_{solv} values for 4-MeOArCH_2Cl and 4-MeOArCH_2(3,5-dinitrobenzoate).[18] A value of 570 s^{-1} was calculated from k_{solv} = 0.12 s^{-1} for 3-NO_2, 4-MeOArCH(CH_3)Cl in 20% CH_3CN in water, $\rho^+ = -5.6$ for the solvolysis reaction,[28] and a 2-fold correction for the smaller k_{solv} in 50:50 (v/v) trifluoroethanol/water that was estimated from the ratio of the values of k_{solv} for 4-MeOArCH(CHF_2)Cl in the two solvents.

(8) (a) Kresge, A. J. *Can. J. Chem.* **1974**, *53*, 1897–1903. (b) Jencks, D. A.; Jencks, W. P. *J. Am. Chem. Soc.* **1977**, *99*, 7948–7960.

(9) Bernasconi, C. F. *Tetrahedron* **1985**, *41*, 3219–3234.

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effects to the low reactivity of 4-MeOArCH(CF$_3$)$^+$ toward solvent.

Experimental Section

Materials. Reagent grade inorganic salts were used without further purification. Deuterated trifluoroethanol (CF$_3$CD$_2$OD, 99% D) was purchased from Cambridge Isotope Laboratories. DClO$_4$ (99% D) and D$_2$O (99.996% D) were purchased from Aldrich. Commercially available organic chemicals used for syntheses were reagent grade and were not further purified. CF$_3$CH$_2$OH was purchased from Aldrich, and the water used for these studies was distilled and then passed through a Milli-Q water purification system.

Syntheses of Substrates. The following outlines the methods used to prepare the compounds used in this work. Elemental analyses, ^{1}H NMR, and mass spectral data are given in the supplementary material.

The ketones 4-MeOArCOCH$_2$F and 4-MeOArCOCHF$_2$ were prepared by reaction of the Grignard reagent, prepared from 4-bromoanisole, with ethyl fluoroacetate and ethyl difluoroacetate, respectively.[10a]

The alcohols 4-MeOArCH(CH$_2$F)OH and 4-MeOArCH(CHF$_2$)OH were prepared by reduction of the corresponding ketones with NaBH$_4$, in isopropyl alcohol.[10b]

1-(4-Methoxyphenyl)-2-fluoroethyl Chloride. 1-(4-Methoxyphenyl)-2-fluoroethyl alcohol (0.98 g, 5.8 mmol) was dissolved in dry dichloromethane (15 ml) and cooled to 0 °C under argon. Thionyl chloride (12 mmol as 6 mL of a 2.0 M solution in dichloromethane) was added, and the mixture was stirred at room temperature for 16 h. The solvent was evaporated to give a purple residue. This was purified by column chromatography on silica gel (60 g), eluting with 1:1 ether/hexane, to give the chloride (0.82 g, 75%) as an oil.

1-(4-Methoxyphenyl)-2,2-difluoroethyl chloride was prepared as described above for the synthesis of 4-MeOArCH(CH$_2$F)Cl, except that the mixture of the alcohol and thionyl chloride was stirred at 40 °C for 2 days.

1-(4-Methoxyphenyl)-2,2,2-trifluoroethyl chloride was synthesized by an S$_N$1 reaction of chloride ion (0.50 M) with 1-(4-methoxyphenyl)-2,2,2-trifluoroethyl mesylate in 50:50 (v/v) trifluoroethanol/water by the same procedure used to prepare the iodide (4-MeOArCH(CF$_3$)I) and the azide (4-MeOArCH(CF$_3$)N$_3$) adducts.[3b] The ^{1}H NMR spectrum (CDCl$_3$, 400 MHz) of the reaction products showed methine (CHCF$_3$) quartets at δ 4.98 (J = 6 Hz) for 4-MeOArCH(CF$_3$)OH (from the hydrolysis reaction) and at δ 5.08 (J = 7 Hz) for 4-MeOArCH(CF$_3$)Cl in a ratio of 1:4. This mixture was not further purified, because the residual 4-MeOArCH(CF$_3$)OH did not interfere with the measurement of the rate constant for the solvolysis reaction of 4-MeOArCH(CF$_3$)Cl.

1-(4-Methoxyphenyl)-2-fluoroethyl pentafluorobenzoate was prepared by reaction of 4-MeOArCH(CH$_2$F)OH (0.55 g) with 1 equiv of pentafluorobenzoyl chloride (0.74 g) in 2 mL of pyridine for 20 min. The reaction was quenched by the addition of 20 mL of cold (0 °C) saturated NaHCO$_3$. The precipitate was washed with saturated NaHCO$_3$ and water, and the product was recrystallized in 20% yield from ethanol/water.

1-(4-Methoxyphenyl)-1-(trifluoromethyl)-2,2,2-trifluoroethanol and 1-(4-methoxyphenyl)-1-(trifluoromethyl)-2,2,2-trifluoroethyl tosylate were prepared by published procedures.[11]

1-(4-Methoxyphenyl)-1-(trifluoromethyl)-2,2,2-trifluoroethyl bromide was prepared by the reaction of 4-MeOArC(CF$_3$)$_2$OH (1.4 g, 5 mmol) and phosphorus tribromide (1.9 g, 7 mmol) at 150 °C for 2 h. The reaction was quenched with water, and the products were extracted into ether. The ethereal extract was washed (water, NaHCO$_3$, and brine), dried (MgSO$_4$), and evaporated. The resulting oil was purified by column chromatography on Florisil, eluting with 95:5 (v/v) hexane/methylene chloride to give the bromide as an oil.

Kinetic Studies. The kinetic studies were carried out at 25 °C in 50:50 (v/v) trifluoroethanol/water (I = 0.50, NaClO$_4$). The reactions were initiated by making a 100-fold dilution of a solution of the substrate, in acetonitrile, into the reaction mixture to give a final concentration of ~1 mM. The reactions of 4-MeOArCH(CH$_2$F)Cl, 4-MeOArCH(CHF$_2$)Cl, and 4-MeOArCH(CF$_3$)Cl were followed by monitoring the decrease in absorbance at 245, 254, and 254 nm, respectively. The reactions of 4-MeOArCH(CH$_2$F)(pentafluorobenzoate) and 4-MeOArC(CF$_3$)$_2$Br were followed by monitoring the decrease in the peak area for the reactant by HPLC. The reaction of 4-MeOArC(CF$_3$)$_2$OTs was followed spectrophotometrically by monitoring the appearance of the quinone methide **1** at 280 nm (see Results). The subsequent slow reaction of **1** was followed by monitoring the decrease in absorbance at 280 nm. A solution of **1** in 99.5% methanol was prepared by generation of **1** from the reaction of 4-MeOArC(CF$_3$)$_2$OTs (5 mM) in 50:50 (v/v) trifluoroethanol/water for 5 min and then making a 1/200 dilution into 3 mL of methanol.

Pseudo-first-order rate constants for these reactions were calculated from the slopes of linear semilogarithmic plots of reaction progress against time.

Product Studies and HPLC Analyses. The reaction conditions were the same as those for the kinetic studies, except that some of the product studies were at room temperature (22 ± 2 °C) instead of 25 °C.[3b,4] Dilute solutions of HClO$_4$ (0.33 or 1.0 mM) were used in experiments to determine $k_{\mathrm{HOH}}/k_{\mathrm{TFE}}$ for the reaction of 4-MeOArC(CF$_3$)$_2$Y, in order to eliminate the possibility that any products were derived from the reaction of trifluoroethoxide ion.

The products were separated from each other and from the unreacted substrates by HPLC.[3b,4] The products were detected and identified at $\lambda_{\max}$ for the corresponding alcohols: 271 nm for 4-MeOArCH(R)OH and 268 nm for 4-MeOArC(CF$_3$)$_2$OH by methods described in earlier work.[3b,4]

It was not possible to separate the azide and trifluoroethanol adducts to 4-MeOArCH(CHF$_2$)Cl. The contribution of the trifluoroethanol adduct to the area of the peak for the mixture of the azide and trifluoroethanol adducts was estimated as described in previous work.[3b]

Identification of Quinone Methide. The products of the solvolysis of 4-MeOArC(CF$_3$)$_2$OTs were characterized by ^{1}H NMR in the following experiment: 4-MeOArC(CF$_3$)$_2$OTs (6 mg) was dissolved in 0.60 mL of 80:20 (v/v) CF$_3$CD$_2$OD (99% D)/D$_2$O (>99.996% D) at room temperature (22 ± 2 °C) to give a final substrate concentration of 0.023 M. After 20 min, the ^{1}H NMR spectrum (400 MHz) was recorded. Sodium azide (1 mg, solid) was then added to the NMR tube, and a second spectrum was immediately recorded. Finally, ca. 0.3 μL of methanol was added to the NMR tube, and a third spectrum was recorded.

Analysis of the products of the solvolysis of 4-MeOArC(CF$_3$)$_2$OTs in 50:50 (v/v) trifluoroethanol/water by HPLC showed a single major peak, which coeluted with an authentic sample of 4-MeOArC(CF$_3$)$_2$OH, and a second minor peak. The major peak was shown to consist of a mixture of the water adduct and the quinone methide **1** (see Results). The minor peak was assigned to be the trifluoroethyl ether, 4-MeOArC(CF$_3$)$_2$OCH$_2$CF$_3$, because its retention time on HPLC was similar to that for 4-MeOArC(CF$_3$)$_2$N$_3$.[12]

The product yields from the solvolysis of 4-MeOArC(CF$_3$)$_2$OTs were determined in the following experiment. A known concentration of the tosylate was reacted in 50:50 (v/v) trifluoroethanol/water for 10–20 halftimes of the solvolysis reaction. Next, a sufficient volume of aqueous 1.0 M NaN$_3$ was added to give a final azide concentration of 3.3 mM, in order to convert **1** to 4-HOArC(CF$_3$)$_2$N$_3$. The resulting mixture of 4-HOArC(CF$_3$)$_2$N$_3$ and 4-MeOArC(CF$_3$)$_2$OH was then resolved by HPLC. The yield of 4-MeOArC(CF$_3$)$_2$OH was determined by referencing the HPLC peak area of this product from the reaction of 4-MeOArC(CF$_3$)$_2$OTs to a calibration curve of peak areas obtained from the injection of known amounts of a standard solution of 4-MeOArC(CF$_3$)$_2$OH. The yield of trifluoroethanol adduct was calculated from the relative peak areas for the alcohol and trifluoroethyl ethers. The yield of **1** was then calculated as 100% minus the percent yields of 4-MeOArC(CF$_3$)$_2$OH and 4-MeOArC(CF$_3$)$_2$OCH$_2$CF$_3$.

The relative decrease in the yield of **1** obtained from the reaction of a fixed concentration of 4-MeOArC(CF$_3$)$_2$OTs at increasing [Br$^-$] was determined from the decrease in $\Delta A/\Delta A_0$, where ΔA is the change in absorbance at 280 nm at a given [Br$^-$], and ΔA_0 is the change in absorbance at [Br$^-$] = 0.

Calculation of Nucleophile Selectivities. Rate constant ratios $k_{\mathrm{HOH}}/k_{\mathrm{TFE}}$ for the reaction of 4-MeOArCH(R)Y and $k_{\mathrm{az}}/k_{\mathrm{Br}}$ for the reaction of 4-MeOArC(CF$_3$)$_2$OTs were calculated by using eq 1, where $[\mathrm{area}]_{\mathrm{RNu1}}/[\mathrm{area}]_{\mathrm{RNu2}}$ is the ratio of the areas of the peaks for the nucleophile adducts, from HPLC analysis, and $\epsilon_{\mathrm{RNu2}}/\epsilon_{\mathrm{RNu1}}$ is the ratio of the molar extinction coefficients for the two adducts. The ratio of the extinction coefficients for the water and trifluoroethanol adducts to 4-MeOArCR^1(R^2)Y was assumed to be 1.0 (±10%), the same as that determined for these adducts to XArCH(CH$_3$)Y.[4] A value of $\epsilon_{\mathrm{RBr}}/\epsilon_{\mathrm{RN3}}$ = 2.75 was determined for the bromide and azide adducts to 4-MeOArC(CF$_3$)$_2$Y, by using methods described in previous work.[3b,4]

$$k_{\mathrm{Nu1}}/k_{\mathrm{Nu2}} = \frac{\epsilon_{\mathrm{RNu2}}[\mathrm{area}]_{\mathrm{RNu1}}[\mathrm{Nu2}]}{\epsilon_{\mathrm{RNu1}}[\mathrm{area}]_{\mathrm{RNu2}}[\mathrm{Nu1}]} \qquad (1)$$

Nucleophile selectivities for the reaction of 4-MeOArCH(R)Y (Nu = N$_3^-$) and 4-MeOArC(CF$_3$)$_2$OTs (Nu = Br$^-$) were calculated from the slope and the intercept of a double reciprocal plot of product yields

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(10) (a) Creary, X. *J. Org. Chem.* **1987**, *52*, 5026–5030. (b) Stewart, R.; Teo, K. C. *Can. J. Chem.* **1980**, *58*, 2491–2503.

(11) Allen, A. D.; Kanagasabapathy, V. M.; Tidwell, T. T. *J. Am. Chem. Soc.* **1986**, *108*, 3470–3474.

(12) The azide and trifluoroethanol adducts to 4-MeOArCH(CH$_3$)$^{+}$[4] or 4-MeOArCH(CF$_3$)$^{+}$[3b] have similar or identical retention times.

Table I. First-Order Rate Constants, k_{solv}, for the Solvolysis of 4-MeOArCH(R)Cl and Rate Constant Ratios for the Partitioning of 4-MeOArCH(R)$^+$ in 50:50 (v/v) Trifluoroethanol/Water[a]

α-substituent R	k_{solv},[b] s^{-1}	k_{HOH}/k_{TFE}[c]	k_{Cl}/k_s,[d,e] M^{-1}	k_{az}/k_s,[e] M^{-1}	k_{az}/k_{Cl}[c,f]
CH_3	400[g]	1.9[h]		105[h]	
CH_2F	0.32	2.3[i]	8.0	50[i,j]	6.2
CHF_2	9.1×10^{-4}	2.9[k]	12	50[j,k]	4.2
CF_3	3.0×10^{-5}	3.8[l]	15	95[l]	6.3

[a] At 25 °C and ionic strength 0.50 ($NaClO_4$). [b] First-order rate constants for the ionization of 4-MeOArCH(R)Cl to form the free carbocation (Scheme I). [c] Dimensionless ratio of second-order rate constants. [d] The rate constant ratio for partitioning of 4-MeOArCH(R)$^+$ between capture by solvent and chloride ion (Scheme I) determined by analyzing the chloride common ion effect on k_{solv} (eq 2). [e] Treating carbocation capture by solvent as a pseudo-first-order reaction. [f] The product of k_s/k_{Cl} (M) and k_{az}/k_s (M^{-1}). [g] See ref 7. [h] Data from ref 4. [i] Identical product rate constant ratios were obtained for the reaction of compounds with the chloride or the pentafluorobenzoate leaving group. [j] Calculated from the fit of the product yields obtained at five azide ion concentrations between 0.0025 and 0.05 M to a double reciprocal replot of the data: see ref 3b. [k] Data for the reaction of 4-MeOArCH(CHF_2)Cl. [l] Data from ref 3b.

against nucleophile concentration.[3b]

Results

Reaction of 4-MeOArCH(R)derivatives. The decrease in absorbance in the region of 250 nm was monitored for the determination of the first-order rate constants k_{solv} for the reactions of 4-MeOArCH(R)Cl in 50:50 (v/v) trifluoroethanol/water ($I = 0.50$, $NaClO_4$) at 25 °C (Table I). The reaction of 4-MeOArCH(CH_3)Cl is too fast to study by our methods, and the value of k_{solv} for this compound was estimated.[7] A value of $k_{solv} = 1.1 \times 10^{-5}\ s^{-1}$ was determined for solvolysis of 4-MeOArCH(CH_2F)pentafluorobenzoate under the same conditions, by monitoring the disappearance of substrate by HPLC.

There is strong chloride common ion depression of k_{obsd} for the solvolysis of 4-MeOArCH(CH_2F)Cl, 4-MeOArCH(CHF_2)Cl, and 4-MeOArCH(CF_3)Cl. The data (Tables S1–S3 in the supplementary material) show a good fit to eq 2, which was derived for the stepwise solvolysis reaction (Scheme I). The values of k_{Cl}/k_s (M^{-1}) reported in Table I were obtained from the slopes of plots of k_{solv}/k_{obsd} against [Cl^-] (not shown).

Scheme I

$$\text{4-MeOArCH(R)Cl} \underset{k_{Cl}}{\overset{k_{solv}}{\rightleftharpoons}} \text{4-MeOArCH(R)}^+ + Cl^- \xrightarrow{k_s} \text{4-MeOArCH(R)Solv}$$

$$k_{solv}/k_{obsd} = 1 + (k_{Cl}/k_s)[Cl^-] \qquad (2)$$

There is no change in k_{obsd} when [NaN_3] is increased from 0 to 0.50 M for the reaction of 4-MeOArCH(CH_2F)(pentafluorobenzoate) or from 0 to 0.05 M for the reaction of 4-MeOArCH(CHF_2)Cl. Good yields of the respective azide adducts were obtained at these ranges of azide ion concentration. The rate constant ratios k_{az}/k_s (M^{-1}) and k_{HOH}/k_{TFE} for the reaction of nucleophiles with 4-MeOArCH(R)Y, determined from product analysis, are reported in Table I.

Reaction of 4-MeOArC(CF_3)$_2$derivatives. A value of $k_{solv} = 3.4 \times 10^{-2}\ s^{-1}$ was determined for the solvolysis of 4-MeOArC(CF_3)$_2$OTs in 50:50 (v/v) trifluoroethanol/water ($I = 0.50$, $NaClO_4$) at 25 °C, by following the appearance of the quinone methide **1** (Scheme II) at 280 nm. The ratio of rate constants for the solvolysis of 4-MeOArCH(CF_3)OTs (for which $k_{solv} = 8.7 \times 10^{-2}\ s^{-1}$)[3b] and 4-MeOArC($CF_3$)$_2$OTs in 50:50 (v/v) trifluoroethanol/water, 2.6, is similar to the ratios of 4.6 and 2.4 which can be calculated from the data obtained in earlier studies in 80% and 100% ethanol, respectively.[2,11] A value of $k_{solv} = 3.6 \times 10^{-7}\ s^{-1}$ was determined for the solvolysis of 4-MeOArC(CF_3)$_2$Br under the same condtions, by monitoring the disappearance of the substrate by HPLC.

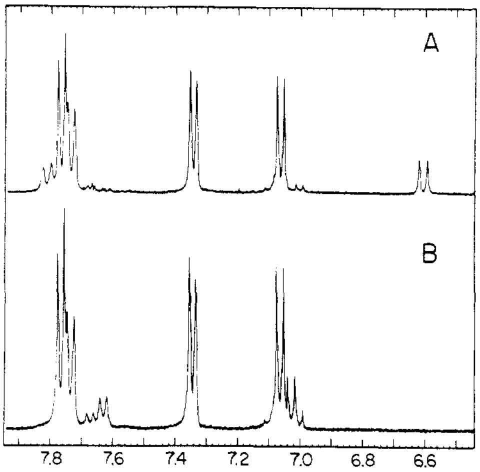
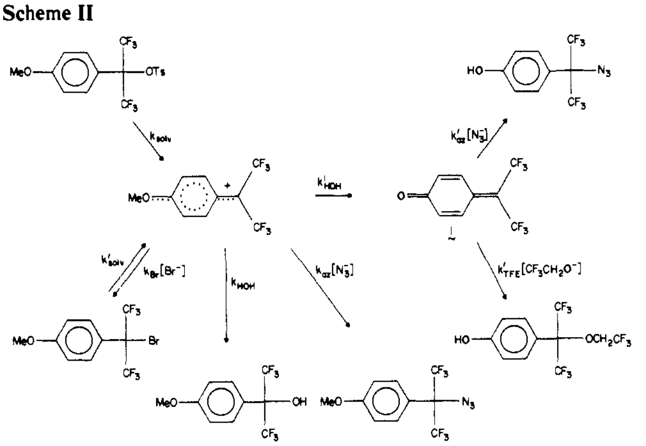


Figure 1. A portion of the ^{1}H-NMR spectra at 400 MHz (16 transients with a 5-s acquisition time) of the products of the reaction of 4-MeOArC(CF_3)$_2$OTs (0.023 M) in 80:20 (v/v) CF_3CD_2OD/D_2O at 22 ± 2 °C. Spectrum A was recorded after a reaction time of 20 min. Spectrum B was recorded after the subsequent addition of 1 mg of solid NaN_3 to the solution.

Scheme II



The solvolysis of 4-MeOArC(CF_3)$_2$OTs in 50:50 (v/v) trifluoroethanol/water gave 4-MeOArC(CF_3)$_2$OH and 4-MeOArC(CF_3)$_2$OCH$_2$CF$_3$ in yields of 65% and 2%, respectively (see Experimental Section). The third product of the reaction (obtained in 33% yield) was identified as the quinone methide **1** in the following experiments.

UV Spectroscopy. The UV absorbance at 283 nm of the product of the reaction in trifluoroethanol/water is more than 20-fold greater than that expected for a mixture of the tosylate anion and the solvent adducts of 4-MeOArC(CF_3)$_2$OTs. Quinone methides such as **1** are known to have intense chromophores.[13] A value of $\epsilon_{283} = 36\,000\ M^{-1}\ cm^{-1}$ was calculated for **1** from the original concentration of 4-MeOArC(CF_3)$_2$OTs, the UV absorbance at 283 nm observed after 10 halftimes for the reaction of this compound, and the yield of 33% for **1**. This extinction coefficient lies within the range of values (26 000–42 000 $M^{-1}\ cm^{-1}$) that have been reported for other quinone methides.[13]

^{1}H NMR. The quinone methide **1** was detected by ^{1}H NMR of the products of the reaction of 4-MeOArC(CF_3)$_2$OTs in 80:20 (v/v) perdeuterated trifluoroethanol/water. The aromatic region of the spectrum is shown in Figure 1A. The pairs of doublets at $\delta = 7.74$, 7.07 ppm ($J = 9$ Hz) and at $\delta = 7.77$, 7.34 ppm ($J = 8$ Hz) were shown by comparison with authentic samples to be the signals for the ring protons of 4-MeOArC(CF_3)$_2$OH and of the *p*-toluenesulfonate anion, respectively. The pair of doublets at $\delta = 7.67$, 7.00 ppm were assigned to be the signals for the ring protons of 4-MeOArC(CF_3)$_2$OCH$_2$CF$_3$. We assigned the pair of doublets at $\delta = 7.82$, 6.61 ppm ($J = 10$ Hz) as the signals for the ring protons of **1**.[14] The addition of 1 mg of solid NaN_3 to the NMR tube resulted in the replacement of the doublets at δ

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(13) Filar, L. J.; Winstein, S. *Tetrahedron Lett.* **1960**, *25*, 9–16.

= 7.82, 6.61 ppm by a new pair of doublets at δ = 7.63, 7.03 ppm (J = 9 Hz); there were no other changes in the spectrum (Figure 1B). We attribute the movement in these doublets to the reaction of **1** with azide ion to form 4-HOArC(CF$_3$)$_2$N$_3$. Further upfield in the spectra in Figure 1A,B there is a singlet at 3.45 ppm, which was shown to be methanol by the addition of authentic material. The methanol is formed from displacement of the methoxy group of 4-MeOArC(CF$_3$)$_2$OTs (Scheme II).

Chemical Reactivity. The chemical reactivity of this product is that expected for **1**.

(1) The first-order rate constant for the disappearance of **1** in 50:50 (v/v) trifluoroethanol/water (I = 0.50, NaClO$_4$) at 25 °C is $k_{obsd} = 1.8 \times 10^{-5}$ s^{-1}. This increases to $k_{obsd} = 4.7 \times 10^{-4}$ s^{-1} for reaction in the more nucleophilic solvent of 99.5:0.25:0.25 (v/v/v) methanol/trifluoroethanol/water.

(2) The reaction of **1** with azide ion in 50:50 (v/v) trifluoroethanol/water is too fast for us to follow under pseudo-first-order conditions. At [N$_3^-$] = 3.3×10^{-5} M, the halftime for the reaction of **1** is less than 2 s, which is consistent with $k_{az} > 10^4$ M^{-1} s^{-1}. The large selectivity, $k_{az}/k_s > 4 \times 10^8$ M^{-1}, is as expected for the reaction of the moderately stable electrophile **1**.[15a,b] The reaction between **1** and 1 mM CF$_3$CH$_2$O$^-$ is also very rapid.

(3) There is no reaction between **1** and bromide ion (up to [Br$^-$] = 0.167 M) in unbuffered solutions of 50:50 trifluoroethanol/water, but in acidic solutions ([HClO$_4$] $\geq$ 0.01 M) a reaction is observed. The products of this reaction break down rapidly at neutral pH on the HPLC column to regenerate **1**. These results are consistent with an acid-catalyzed reaction of **1** with the bromide ion to form 4-HOArC(CF$_3$)$_2$Br, which is stable when protonated, but, which at neutral pH loses a proton from the phenolic oxygen to form 4-$^-$OArC(CF$_3$)$_2$Br and then breaks down rapidly to regenerate **1** and Br$^-$ (eq 3).

$$\mathbf{1} + \mathrm{Br}^- \xrightleftharpoons{K_{eq} \ll 1\ (\mathrm{M}^{-1})} 4\text{-}{}^-\mathrm{OArC(CF_3)_2Br} \qquad (3)$$

The value of k_{obsd} for the reaction of 4-MeOAr(CF$_3$)$_2$OTs in 50:50 (v/v) trifluoroethanol/water (I = 0.50, NaClO$_4$) is constant as [Br$^-$] is increased from 0 to 0.167 M. A good yield of 4-MeOArC(CF$_3$)$_2$Br is obtained (90% at [Br$^-$] = 0.167 M) at the expense of the yields of both **1** and 4-MeOArC(CF$_3$)$_2$OH.

The value of k_{Br}/k_s (M^{-1}) for the reaction of 4-MeOArC(CF$_3$)$_2$OTs, determined from product analysis, is given in Table II. The rate constant k_s (s^{-1}) from this analysis is the sum of all of the pseudo-first-order rate constants for the reaction of 4-MeOArC(CF$_3$)$_2^+$ with solvent, including the addition of water at the C-4 ring position to give **1**. Rate constant ratios for the reactions of 4-MeOArC(CF$_3$)$_2$OTs with other nucleophilic reagents, determined from product analysis, are also given in Table II. The ratio k_{HOH}/k'_{HOH} is for the addition of water at C-α (k_{HOH}) and at the C-4 ring position (k'_{HOH}).

Product analysis by HPLC showed that 4-MeOArC(CF$_3$)$_2$OH is the major product of the solvolysis of 4-MeOArC(CF$_3$)$_2$Br in 50:50 (v/v) trifluoroethanol/water. **1** did not accumulate, because the halftime for its reaction (~11 h) is much shorter than that for 4-MeOArC(CF$_3$)$_2$Br (~22 days). The reaction of N$_3^-$ with 4-MeOArC(CF$_3$)$_2$Br in 50:50 (v/v) trifluoroethanol/water is zero-order in [N$_3^-$]. A greater than 95% yield of the azide adduct was obtained when the products for the reaction at [NaN$_3$] = 0.05 M were sampled after one reaction halftime, but there was a 40% decrease in the ratio of the yields of 4-MeOArC(CF$_3$)$_2$N$_3$ and 4-MeOArC(CF$_3$)$_2$OH when the products were analyzed after two halftimes (45 days) due to the slow reaction of 4-MeOArC(CF$_3$)$_2$N$_3$. The products of this reaction were not characterized.

Discussion

Reaction Mechanism. In 50:50 (v/v) trifluoroethanol/water the reactions of 4-MeOArCH(CH$_2$F)(pentafluorobenzoate) and 4-MeOArCH(CHF$_2$)Cl with N$_3^-$ are zero-order in [N$_3^-$], up to nucleophile concentrations that give a greater than 70% yield of the azide adduct. There is strong inhibition by chloride ion of the solvolysis of 4-MeOArCH(CH$_2$F)Cl, 4-MeOArCH(CHF$_2$)Cl, and 4-MeOArCH(CF$_3$)Cl. These results show that the substrates react by a stepwise S$_N$1 mechanism through carbocation intermediates that can be trapped by azide and chloride ions.

Table II. Nucleophile Selectivities for the Reaction of 4-MeOArC(CF$_3$)$_2$OTs in 50:50 (v/v) Trifluoroethanol/Water[a]

k_{Br}/k_s[b,c]	50 M^{-1}
k_{az}/k_{Br}[d,e]	22
k_{az}/k_s[c,f]	1100 M^{-1}
k_{HOH}/k'_{HOH}[d,g]	2.0
k_{HOH}/k_{TFE}[d,h]	9.0

[a] At room temperature (22 ± 2 °C) and ionic strength 0.50 (NaClO$_4$). [b] Determined from the fit of the product data to a double reciprocal replot: see ref 3b. [c] k_s is the sum of the pseudo-first-order rate constants for the addition of solvent to both C-α and the C-4 ring position of 4-MeOArC(CF$_3$)$_2^+$. [d] Dimensionless ratio of second-order rate constants. [e] Calculated from product ratios (eq 1) and an average of values obtained at a constant [Br$^-$] = 0.0833 M and five different values of [N$_3^-$] between 0.0033 and 0.0833 M. [f] Calculated as (k_{az}/k_{Br})(k_{Br}/k_s). [g] The ratio of the yields of 4-MeOArC(CF$_3$)$_2$OH and **1**. [h] Identical solvent selectivities were observed for reactions at [HClO$_4$] = 0.33 and 1.0 mM.

The following observations are good evidence that 4-MeOArC(CF$_3$)$_2$OTs and 4-MeOArC(CF$_3$)$_2$Br react with nucleophiles by the mechanisms shown in Scheme II.

(1) The reaction of bromide ion with 4-MeOArC(CF$_3$)$_2$OTs to form 4-MeOArC(CF$_3$)$_2$Br and of azide ion with 4-MeOArC(CF$_3$)$_2$Br to form 4-MeOArC(CF$_3$)$_2$N$_3$ are zero-order in the concentration of the respective nucleophiles. We conclude that these are S$_N$1 reactions.

(2) The reaction of water with 4-MeOArC(CF$_3$)$_2$OTs in 50:50 (v/v) trifluoroethanol/water gives a 33% yield of **1** by nucleophilic aromatic substitution. The quinone methide was identified on the basis of its UV spectrum (ϵ_{283} = 36 000 M^{-1} cm^{-1}), its NMR spectrum (Figure 1A), and its reactivity toward nucleophiles (see Results).

(3) The reaction of 4-MeOArC(CF$_3$)$_2$OTs in the presence of increasing [Br$^-$] produces 4-MeOArC(CF$_3$)$_2$Br at the expense of both **1** and 4-MeOArC(CF$_3$)$_2$OH. This result is consistent with the partitioning of a common intermediate, 4-MeOArC(CF$_3$)$_2^+$, to form 4-MeOArC(CF$_3$)$_2$OH, **1**, and 4-MeOArC(CF$_3$)$_2$Br (Scheme II).

Rate and Equilibrium Constants. 4-MeOArCH(CF$_3$)derivatives[3] and 4-MeOArCH(CH$_3$)derivatives[4] react by an S$_N$1 mechanism, through liberated carbocation intermediates that are captured by azide ion in diffusion-limited reactions. The stabilities of 4-MeOArCH(CH$_2$F)$^+$ and 4-MeOArCH(CHF$_2$)$^+$ lie between those of 4-MeOArCH(CH$_3$)$^+$ and 4-MeOArCH(CF$_3$)$^+$; and, 4-MeOArC(CF$_3$)$_2^+$ is thermodynamically the most unstable carbocation that we have studied. Therefore, the capture of all these carbocations by azide ion should be diffusion limited.

The estimated rate constant, $k_{az} = 5 \times 10^9$ M^{-1} s^{-1},[4,5,16] for the diffusion-limited reaction of azide ion and the values of k_{az}/k_s (M^{-1}) (Table I) give the following rate constants for the capture of 4-MeOArCH(R)$^+$ by 50:50 (v/v) trifluoroethanol/water: R = CH$_3$, $k_s = 5 \times 10^7$ s^{-1};[4] R = CH$_2$F, $k_s = 1 \times 10^8$ s^{-1}; R = CHF$_2$, $k_s = 1 \times 10^8$ s^{-1}; R = CF$_3$, $k_s = 5 \times 10^7$ s^{-1}.[3] Rate constants for the capture of 4-MeOArC(CF$_3$)$_2^+$ by nucleophiles, calculated from the product rate constant ratios in Table II, are given in Table III.

Values of k_{Cl} (Table IV) for the capture of 4-MeOArCH(R)$^+$ were calculated from the ratios k_{az}/k_{Cl} in Table I and the above estimate for k_{az}. Rate and equilibrium constants ($K_{eq} = k_{solv}/k_{Cl}$) for the ionization of β-fluorine-substituted substrates 4-MeOArCH(R)Cl to give the free carbocations (Scheme I) are given in Table IV. Rate and equilibrium constants for the ionization of α-CF$_3$ substituted substrates 4-MeOArCR^1(R^2)Y to form the free carbocations are given in Table V.

Steric Effects of β-Fluorine Substituents on Carbocation Reactivity. The very different effects of electron-withdrawing *m*-ring substituents and β-fluorine substituents on carbocation reactivity are illustrated by the plot of log k_s for the reaction of solvent with 3-X,4-MeOArCH(R)$^+$ against log k_{solv} for the solvolysis of 3-X,4-MeOArCH(R)Cl (Figure 2). Electron-withdrawing *m*-ring substituents destabilize 4-MeOArCH(CH$_3$)$^+$ and cause the ex-

Table III. Rate Constants for the Capture of 4-MeOArC$(CF_3)_2^+$ by Nucleophilic Reagents in 50:50 (v/v) Trifluoroethanol/Water[a]

nucleophile	rate constant[b]
Br^-	$k_{Br} = 2 \times 10^8$ M^{-1} s^{-1}
solvent	$k_s = 4.5 \times 10^6$ s^{-1} [c]
H_2O	$k_{HOH} = 1.1 \times 10^5$ M^{-1} s^{-1} [d] $k'_{HOH} = 5 \times 10^4$ M^{-1} s^{-1} [e]
CF_3CH_2OH	$k_{TFE} = 1.1 \times 10^4$ M^{-1} s^{-1}

[a] At room temperature (22 ± 2 °C) and ionic strength 0.50 ($NaClO_4$). [b] Calculated from the nucleophilic selectivity data in Table II and a value of $k_{az} = 5 \times 10^9$ M^{-1} s^{-1}.[5,16] [c] k_s is the sum of the pseudo-first-order rate constants for the addition of solvent to both C-α and the C-4 ring position of 4-MeOArC$(CF_3)_2^+$. [d] Second-order rate constant for the addition of water to C-α of 4-MeOArC$(CF_3)_2^+$. [e] Second-order rate constant for the addition of water to the C-4 ring position of 4-MeOArC$(CF_3)_2^+$.

Table IV. Rate and Equilibrium Constants for Heterolytic Bond Cleavage at 4-MeOArCH(R)Cl (Scheme I) in 50:50 (v/v) Trifluoroethanol/Water[a]

α-substituent R	k_{solv},[b] s^{-1}	k_{Cl},[c] M^{-1} s^{-1}	K_{eq},[d] M	Δlog K_{eq}[e]
CH_3	4×10^2	8×10^8 [f]	5×10^{-7}	
CH_2F	3.2×10^{-1}	8×10^8	4.0×10^{-10}	3.1
CHF_2	9.1×10^{-4}	1.2×10^9	7.6×10^{-13}	2.7
CF_3	3.0×10^{-5}	8×10^8	3.8×10^{-14}	1.3

[a] At 25 °C and ionic strength 0.50 ($NaClO_4$). [b] From Table I. [c] Calculated from k_{az}/k_{Cl} (Table I) and $k_{az} \approx 5 \times 10^9$ M^{-1} s^{-1}.[4,5,16] [d] $K_{eq} = k_{solv}/k_{Cl}$. [e] The effect of the β-fluorine for hydrogen substitution on log K_{eq} from the preceding row. [f] Estimated by assuming that the value of k_{az}/k_{Cl} is independent of the number of β-fluorine substituents.[27]

Table V. The Effect of α-CF_3 Substituents on the Rate and Equilibrium Constants for the Formation of 4-Methoxybenzyl Carbocations from Halide Derivatives[a]

$$\text{4-MeOArCR}^1(\text{R}^2)\text{Y} \underset{k_Y}{\overset{k_{solv}}{\rightleftharpoons}} \text{4-MeOArCR}^1(\text{R}^2)^+ + \text{Y}^-$$

substrate	k_{solv},[b] s^{-1}	k_Y,[c] M^{-1} s^{-1}	$K_{eq} = k_{solv}/k_Y$, M	Δlog K_{eq}[d]
$R^1 = R^2 = H$, Y = Cl[e]	0.67	2×10^9	3.4×10^{-10}	
R^1 = H, Y = Cl, $R^2 = CF_3$[f]	3.0×10^{-5}	8×10^8	3.8×10^{-14}	4.0[g]
R^1 = H, Y = Br, $R^2 = CF_3$[h]	6.2×10^{-4}	2×10^9	3.1×10^{-13}	
$R^1 = R^2 = CF_3$, Y = Br[f]	3.6×10^{-7}	2×10^8	1.8×10^{-15}	2.2[i]

[a] In 50:50 (v/v) trifluoroethanol/water at 25 °C and ionic strength 0.50 ($NaClO_4$). [b] The first-order rate constant for the solvolysis reaction. [c] Calculated from k_{az}/k_Y and a value of $k_{az} \approx 5 \times 10^9$ M^{-1} s^{-1}.[4,5,16] [d] The effect of α-CF_3 substituents on log K_{eq} for the formation of the 4-methoxybenzyl carbocation. [e] Data from ref 18. [f] This work. [g] The effect of the first α-CF_3 substituent on log K_{eq}. [h] Data from ref 3b. [i] The effect of the second α-CF_3 substituent on log K_{eq}.

pected decreases in k_{solv} and increases in k_s.[6] Electron-withdrawing β-fluorine substituents also destabilize 4-MeOArCH$(CH_3)^+$ and cause large decreases in k_{solv}, but they cause little change in k_s. The differences between the upper and lower lines in Figure 2 show that the values of k_s for the addition of solvent to 4-MeOArCH$(CH_2F)^+$, 4-MeOArCH$(CHF_2)^+$ and 4-MeOArCH$(CF_3)^+$ are 11-fold, 140-fold, and 1300-fold smaller,[17] respectively, than the values of k_s for the addition of solvent to the hypothetical carbocations 3-X,4-MeOArCH$(CH_3)^+$ which would form at the same rate in solvolysis of the respective chloride derivatives.

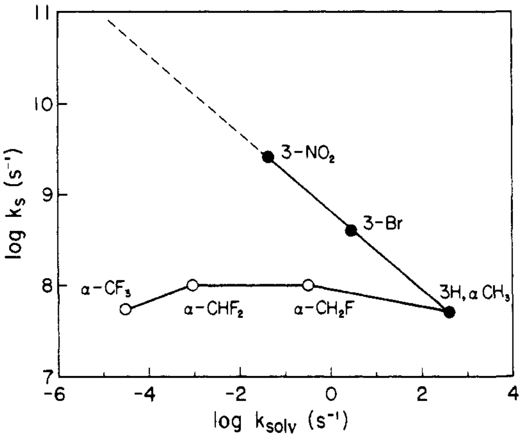

Figure 2. A plot of log k_{solv} for the ionization of 3-X,4-MeOArCH(R)Cl to form 3-X,4-MeOArCH$(R)^+$ against log k_s for the capture of these carbocations by 50:50 v/v trifluoroethanol/water. (●) The correlation obtained upon varying the *m*-ring substituent in 3-X,4-MeOArCH(CH_3)Cl. The values of k_s are from ref 4, and the values of k_{solv} were calculated from $k_{solv} = 400$ s^{-1} for the reaction of 4-MeOArCH(CH_3)Cl (X = H),[7] $\rho^+ = -5.6$ for the solvolysis reaction,[28] and σ values for the *m*-ring substituent (ref 19, p 66). (○) The correlation obtained upon varying the number of β-fluorine substituents in 4-MeOArCH(R)Cl. The values of k_{solv} are from Table I, and the values of k_s were calculated as described in the text.

Figure 2 is consistent with only small steric effects of the β-fluorine substituents on k_s for capture of 4-MeOArCH$(R)^+$. An upper limit for the steric effect of the first β-fluorine substituent is 2-fold, because even if the rate of addition of solvent syn to the fluorine is insignificant, the reaction anti may occur free of steric hindrance. The 2-fold larger value of k_s for the reaction of 4-MeOArCH$(CH_2F)^+$ than 4-MeOArCH$(CH_3)^+$ is due to a small polar effect of the electron-withdrawing fluorine substituent. The second β-fluorine substituent does not further change k_s, which suggests that the polar substituent effect is offset by a steric effect. The third β-fluorine substituent causes a 2-fold decrease in k_s, which is consistent with a still larger steric substituent effect.

The addition of a pair of α-CF_3 groups to 4-MeOArCH$_2^+$ causes a 40-fold decrease in k_s, from 2×10^8 s^{-1} for the capture of 4-MeOArCH$_2^+$,[18] to 5×10^7 s^{-1} for 4-MeOArCH$(CF_3)^+$,[3] to 4.5×10^6 s^{-1} for 4-MeOArC$(CF_3)_2^+$ (Table III). These decreases in k_s also suggest that the α-CF_3 groups sterically hinder the addition of solvent.

Steric Effects of β-Fluorine Substituents on K_{eq} for the Formation of 4-MeOArCR^1(R^2)$^+$. Table IV shows that the β-fluorine substituent effect on log K_{eq} (Δ log K_{eq}) for the formation of 4-MeOArCH$(R)^+$ from 4-MeOArCH(R)Cl decreases with increasing substituents at the β-carbon. Table V shows that the substituent effect of the α-CF_3 group on log K_{eq} for the formation of 4-MeOArCR^1(R^2)$^+$ from 4-MeOArCR^1(R^2)Y decreases with increasing substituents at the α-carbon. These decreasing substituent effects, with increasing crowding at the benzylic carbon, are consistent with steric effects that destabilize 4-MeOArCR^1(R^2)Y relative to 4-MeOArCR^1(R^2)$^+$ and offset the polar substituent effects which destabilize the carbocations relative to the neutral substrates.

The third β-fluorine substituent has a significantly smaller effect on log K_{eq} than either the first or second β-fluorines (Table IV). The smaller effect is probably due to unfavorable interactions between the chlorine and the flanking gauche fluorines at 4-MeOArCH(CF_3)Cl, which are relieved upon ionization of the

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(14) To the best of our knowledge this is the first report of the NMR spectrum for a simple quinone methide with no substituents at the ring carbons. There is NMR spectral data for quinone methides with a pair of alkyl or bromo substituents ortho to the carbonyl oxygen. Mare, P. B. D.; Newman, P. A. *J. Chem. Soc., Perkin Trans. 2* **1984**, 231–238. Dyall, L. K.; Winstein, S. *J. Am. Chem. Soc.* **1972**, *94*, 2196–2199.

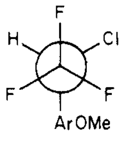
(15) (a) Ritchie, C. D.; Virtanen, P. O. I. *J. Am. Chem. Soc.* **1972**, *94*, 4966–4971. (b) Bunton, C. A.; Huang, S. K. *Ibid.* **1972**, *94*, 3536–3544. (c) Ta-Shma, R.; Rappoport, Z. *J. Am. Chem. Soc.* **1983**, *105*, 6082–6095.

(16) Diffusion-limited rate constants of (4–7) × 10^9 M^{-1} s^{-1} have been measured directly for the reaction of azide ion with unstable carbocations in water or predominately aqueous solutions.[5]

(17) The hypothetical values of k_s were calculated from the values of k_{solv} for the reaction of the respective β-fluorine-substituted chlorides and log k_s = 8.86 − 0.433log k_{solv} which describes the least-squares line through the data for the reactions of 3-X,4-MeOArCH$(CH_3)^+$ (Figure 2).

(18) Amyes, T. L.; Richard, J. P., preceding paper in this issue.

substrate to form 4-MeOArCH(CF_3)$^+$. The destabilization associated with each interaction between gauche (see 2) halogens at 4-MeOArCH(CF_3)Cl is more severe than that for the simple interaction between a pair of gauche halogens. For example, the difference in the stabilities of 3 and 4 (2.6 kcal/mol)—which is due largely to the additional interaction between gauche chlorines at 3—is larger than the difference in the stabilities of the gauche and anti conformations of 1,2-dichloroethane (1.2 kcal/mol).[19] This is because the interaction between gauche substituents can normally be relieved by increasing the dihedral bond angle to >60°; but, in the case of 3, a change in the dihedral angle to relieve one gauche interaction would aggravate the second interaction.



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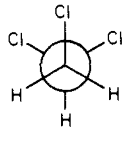

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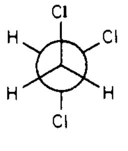

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The value of $K_{eq} = 3.8 \times 10^{-14}$ M for the ionization of 4-MeOArCH(CF_3)Cl (Table IV) is 140-fold larger than $K_{eq} = 2.7 \times 10^{-16}$ M, which can be calculated with the assumption that the polar effect of each β-fluorine substituent on K_{eq} is additive and is equal to that observed for the addition of the first β-fluorine (1200-fold, Table IV). The factor of 140 is a rough estimate of the extent to which the relief of interactions between the gauche α-Cl and β-F substituents which occurs on moving from 4-MeOArCH(CF_3)Cl to the carbocation offsets the destabilization of the carbocation by the polar substituent effect.

The small (160-fold) effect of the second α-CF_3 group on log K_{eq} for the ionization of 4-MeOArCR^1(R^2)Y (Table V) is consistent with extreme congestion at the benzylic carbon of 4-MeOArC(CF_3)$_2$Br. The increase in k_{OTs}/k_{Br} from 140, for the solvolyses of 4-MeOArCH(CF_3)OTs and 4-MeOArCH(CF_3)Br,[3] to 9×10^4, for the solvolyses of 4-MeOArC(CF_3)$_2$OTs and 4-MeOArC(CF_3)$_2$Br, suggests that the second α-CF_3 for H substitution introduces an even greater amount of steric strain into the substrate with the bulkier tosylate leaving group.[20] An even larger value of $k_{OTs}/k_{Br} = 1.6 \times 10^6$ has been reported for the reactions of $Ph_2C(CF_3)OTs$ and $Ph_2C(CF_3)Br$.[21] The unusual reactivity of 4-MeOArC(CF_3)$_2$OTs was first noted by Tidwell,[11] and X-ray crystallographic analysis of this compound revealed deformation of bond angles and bond lengths from ideal tetrahedral geometry, consistent with the proposal that its great reactivity might be due to relief of strain at the transition state.[22]

Resonance Effects and Transition-State Imbalance. The following observations show that the steric inhibition by β-fluorine substituents of the capture of 4-MeOArCH(R)$^+$ by solvent is insufficient to account for the low reactivity of these carbocations toward solvent.

(1) The rate constant k_s for the reaction of 4-MeOArCH(CH_2F)$^+$ is 11-fold smaller than that for the reaction of a hypothetical cation 3-X,4-MeOArCH(CH_3)$^+$ which forms at the same rate as 4-MeOArCH(CH_2F)$^+$ in the solvolysis of the respective chlorides (Figure 2). Only a small part of this difference can be attributed to a steric effect, because the approach of the solvent molecule anti to the β-fluorines is free of steric hindrance.

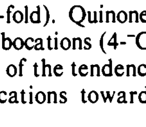
(2) The rate constant k_s for the reaction of 4-MeOArCH(CF_3)$^+$ is 1300-fold smaller than that for the reaction of 3-X,4-MeOArCH(CH_3)$^+$ which forms at the same rate as 4-MeOArCH(CF_3)$^+$ in the solvolysis of the respective chlorides (Figure 2). Not all of this difference can be caused by the *partial* development of steric interactions between solvent and the β-fluorines at the transition state, because the *full* loss of similar interactions is estimated to increase K_{eq} by only ≈140-fold for the ionization of 4-MeOArCH(CF_3)Cl, compared to K_{eq} for the ionization of 4-MeOArCH(CH_3)Cl (see above).

The addition of β-fluorine substituents to 4-MeOArCR^1(R^2)$^+$ results in increased electron delocalization from the 4-methoxyphenyl ring to C-α.[1-3] This leads to an increase in the stabilization of the carbocation by resonance and may be accompanied by an increase in the "intrinsic barrier" to carbocation capture by solvent, in the same sense that the intrinsic barriers to thermoneutral protonation of carbanions increase with increasing stabilization of the carbanion by resonance.[8a] Both results can be explained by an "unbalanced" transition state in which the loss of resonance stabilization of the intermediate has progressed further than has the change in intramolecular electrostatic interactions between the CF_3 dipole and the cationic center.[8,9]

There is evidence of an imbalance in the change in resonance and inductive interactions at the transition state for the capture of ring-substituted 1-phenylethyl carbocations,[4] oxocarbenium ions,[23] and for diarylmethyl and triarylmethyl carbocations.[24] An imbalance in the expression of the β-fluorine substituent effects on k_s for the capture of 4-MeOArCR^1(R^2)$^+$, in which the carbocation-stabilizing resonance effect is largely lost and the (larger) destabilizing inductive effect is only slightly lost, could lead to a cancellation of the two effects.[3]

These ideas are the basis for the principle of nonperfect synchronization, which states that a reactant stabilizing factor (e.g., resonance) will increase the intrinsic barrier for a reaction (e.g., carbocation capture), if the stabilizing factor is largely lost on moving from the reactant to the transition state.[9]

Nucleophilic Aromatic Substitution Reactions. There have been a number of previous reports of nucleophilic aromatic substitution reactions at α-CF_3-substituted 4-methoxybenzyl carbocations.[11,25] Nucleophilic aromatic substitution reactions at 4-MeOArC(CF_3)$_2^+$ are favored by resonance electron delocalization and by steric effects (see above), both of which decrease the reactivity of C-α relative to the C-4 ring carbon. The product of the reaction with water is a quinone methide 1 of unusual stability. In methanol at 25 °C, 1 ($k_{obsd} = 4.7 \times 10^{-4}$ s^{-1}) is 85-fold less reactive than 5 ($k_{obsd} = 4.0 \times 10^{-2}$ s^{-1}).[13] The effect of the pair of α-CF_3 substituents on the reactivity of 5 toward MeOH (>85-fold)[26] is similar in magnitude to the effect of a pair of α-CF_3 groups on k_s for the reaction of 4-MeOArCH$_2^+$ with 50:50 (v/v) trifluoroethanol/water (40-fold). Quinone methides are, in one sense, resonance-stabilized carbocations (4-$^-$OArCR^1(R^2)$^+$), so that this is still another example of the tendency of α-CF_3 substituents to stabilize benzyl carbocations toward capture by nucleophilic solvents.



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[19] Hine, J. *Structural Effects on Equilibria in Organic Chemistry*; Wiley-Interscience: New York, 1975; p 107.

[20] Bingham, R. C.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1971**, *93*, 3189–3199.

[21] Liu, K.-T.; Kuo, M.-Y. *Tetrahedron Lett.* **1985**, *26*, 355–358.

[22] Kanagasabapathy, V. M.; Sawyer, J. F.; Tidwell, T. T. *J. Org. Chem.* **1985**, *50*, 503–509.

[23] Young, P. R.; Jencks, W. P. *J. Am. Chem. Soc.* **1977**, *99*, 8238–8248. Amyes, T. L.; Jencks, W. P. *J. Am. Chem. Soc.* **1989**, *111*, 7888–7900.

[24] McClelland, R. A.; Kanagasabapathy, V. M.; Steenken, S. *J. Am. Chem. Soc.* **1989**, *111*, 3966–3972.

[25] Richard, J. P. *J. Am. Chem. Soc.* **1989**, *111*, 6735–6744. Richard, J. P. *Tetrahedron Lett.* **1989**, *30*, 23–26.

[26] This is a lower limit for the α-CF_3 substituent effect on the reactivity of 4-$^-$OArCH$_2^+$, because 5 should be stabilized by the weakly electron-donating *o*-methyl substituents.

[27] The difference between the values for k_{az}/k_{Cl} for these two carbocations is not expected to be larger than the 2-fold difference in the observed ratios k_{az}/k_{AcO} for the capture of 4-MeOArCH(CH_3)$^+$ by azide and the anionic nucleophile acetate [$k_{az}/k_{AcO} = 60$ (Richard, J. P.; Jencks, W. P. *J. Am. Chem. Soc.* **1984**, *106*, 1373–1383)] and 4-MeOArCH(CF_3)$^+$ (k_{az}/k_{AcO} = 30).[3b]

[28] Richard, J. P.; Jencks, W. P. *J. Am. Chem. Soc.* **1984**, *106*, 1383–1396.

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Supplementary Material Available: Analytical data for the compounds whose synthesis is described in the Experimental Section (^{1}H NMR, exact molecular weights, and elemental analyses) and tables of kinetic data for the reaction of 4-MeOArCH(R)Cl (R = CH_2F, CHF_2, CF_3) at increasing concentrations of chloride ion (5 pages). Ordering information is given on any current masthead page.

How Far Can a Carbanion Delocalize? ^{13}C NMR Studies on Soliton Model Compounds[1]

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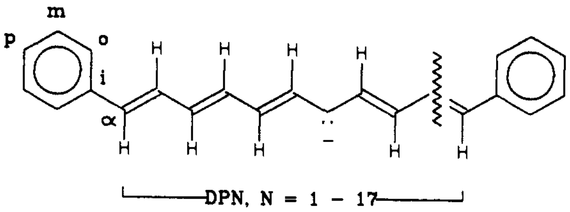
Abstract: For well-defined π systems, ^{13}C chemical shifts are correlated with π-electron density. We have used this correlation to develop models for charge carriers in *n*-doped polyacetylene ("solitons") that allow us to determine if the charge density distribution predicted by the soliton theory is correct. In this investigation, a linear chemical shift/charge density relationship is obtained for anions of the general structure $Ph(CH)_nPh^-$, $n = 1, 3, 5, 7, 9, \ldots$ (DP*N*), if the average chemical shift (δ_C) of all carbons is plotted against the average charge density (ρ_{av}). Such a plot has allowed us to develop the empirical relationship $\rho_C = (\delta_C - 132.7)/187.3$ and thus to calculate the charge density at each carbon atom. Moreover, comparison with neutral compounds of formula $Ph(CH{=}CH)_nPh$ allows us to define the soliton length, that is, the point at which carbanion delocalization in a linear chain ceases.

Introduction

Although many of the qualitative aspects of charge transport in conductive polymers[2] have their counterparts in classical organic chemistry, the concept of a mobile charge carrier ("soliton") is one of the most difficult to reconcile with the conventional understanding of resonance. According to the soliton theory, the charge carrier in reductively (or oxidatively) doped polyacetylene is a resonance-stabilized carbanion (or carbocation) of finite width with maximum charge at the center of the defect and diminishing amplitude away from the center.[3] Charge transport is thus associated with migration of the charge density wave down the polymer chain (see Figure 1). Such migration will be isoergic only if the solitonic charge density wave has finite width relative to the unsaturation length. Although increased charge density at the center of an odd-alternant hydrocarbon anion has been a familiar aspect of the chemistry of polyenyl anions since the pioneering work of Kloosterziel,[4] less widely understood is the requirement that what would ordinarily be static resonance forms become only dynamically equivalent at long chain length. Figure 1 thus represents the centers of delocalized finite domains as they migrate down the chain. The relevance of the *intra*chain charge-transport mechanism to the overall mechanism of conductivity in bulk polymers, for which *inter*chain charge migration ("intersoliton hopping") is apparently rate limiting, is still the subject of controversy[3e] and is not addressed here.

In order to relate this conclusion from solid-state theoretical physics to the organic chemistry of conductive polymers, we undertook an examination of the effect of increasing chain length on the spectral properties of polyenyl anions, using as our main analytical technique ^{13}C NMR spectroscopy.[1] Use of O'Brien's implementation[5] of the Spiesecke–Schneider relationship,[6] which relates the charge density at individual carbon atoms to the ^{13}C chemical shift, would in principle allow us to determine the charge density at each site of a polyenyl anion of discrete length and extrapolate those charge densities to their limiting values. For reasons of convenience, we chose α,ω-diphenylpolyenyl anions (DP1, DP3, DP5, ...), asking at what chain length the properties of these anions and *n*-doped polyacetylene converge. In addition to providing precursors that are relatively stable toward polymerization, examination of the chemical shifts as a function of chain length, and comparison with neutral compounds, has allowed us to draw conclusions about the point at which the carbanion ceases delocalization into the aryl ring and thus directly to measure the soliton width. Inasmuch as the use of charge density/chemical shift correlations is still the subject of much controversy, we now report experimental details, analysis of the experimental and



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(1) For a preliminary communication, see: Tolbert, L. M.; Ogle, M. E. *J. Am. Chem. Soc.* **1989**, *111*, 5958.

(2) A number of excellent monographs on the subject of conducting polymers are now available: (a) Skotheim, T. J., Ed. *Handbook of Conducting Polymers*; Marcel Dekker: New York, 1986; Vols. 1 and 2. (b) Chien, J. C. W. *Polyacetylene: Chemistry, Physics, and Materials Science*; Academic Press: New York, 1984. (c) Seanor, D. A., Ed. *Electrical Properties of Polymers*; Academic Press: New York, 1982. (d) For an excellent "layman's guide", see: Kaner, R. B.; MacDiarmid, A. G. *Scientific American* **1988**, February, 106–111.

(3) (a) Su, W. P.; Schrieffer, J. R.; Heeger, A. J. *Phys. Rev. Lett.* **1979**, *42*, 1698. (b) Su, W. P.; Schrieffer, J. R.; Heeger, A. J. *Phys. Rev., Sect. B.* **1980**, *22*, 2099. (c) Su, W. P. In *Handbook of Conducting Polymers*; Skotheim, T. J., Ed.; Marcel Dekker: New York, 1986; pp 757–794. (d) Heeger, A. J.; Kivelson, S.; Schrieffer, J. R.; Su, W.-P. *Rev. Mod. Phys.* **1988**, *60*, 781. (e) Roth, S. *Mater. Sci. Forum* **1989**, *42*, 1.

(4) (a) Kloosterziel, H.; Werner, M. A. *Recl. Trav. Chim. Pays-Bas* **1975**, *94*, 124. (b) Kloosterziel, H. *Recl. Trav. Chim. Pays-Bas* **1974**, *93*, 215. (c) Bates, R. B.; Gosselink, D. W.; Kaczynski, J. A. *Tetrahedron Lett.* **1967**, 205.

(5) O'Brien, D. H.; Hart, A. J.; Russell, C. R. *J. Am. Chem. Soc.* **1975**, *97*, 4410.

(6) Spiesecke, H.; Schneider, W. G. *Tetrahedron Lett.* **1961**, 468.

0002-7863/90/1512-9519$02.50/0