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Dynamics for reactions of ion pairs in aqueous solution: reactivity of tosylate anion ion paired with the highly destabilized 1-(4-methylphenyl)-2,2,2-trifluoroethyl carbocation

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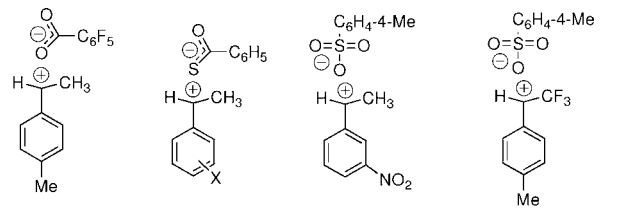
The sum of the rate constants for solvolysis and scrambling of carbon bridging and nonbridging oxygen-18 at 4-MeC$_6$H$_4$CH(CF$_3$)OS(^{18}O$_2$)Tos in 50/50 (v/v) trifluoroethanol/water, ($k_{solv} + k_{iso}$) = 5.4 × 10^{-6} s^{-1}, is 50% larger than k_{solv} = 3.6 × 10^{-6} for the simple solvolysis reaction of the sulfonate ester. This shows that the ion-pair intermediate of solvolysis undergoes significant internal return to form reactant. These data give a value of k_{-1} = 1.7 × 10^{10} s^{-1} for internal return of the carbocation-anion pair to the substrate. This rate constant is larger than the value of k_{-1} = 7 × 10^9 s^{-1} reported for internal return of an ion pair between the 1-(4-methylphenyl)ethyl carbocation and pentafluorobenzoate anion to the neutral ester (4-MeC$_6$H$_4$CH(CH$_3$)O$_2$CC$_6$F$_5$) in the same solvent. The partitioning of ion pairs to the 1-(4-methylphenyl)ethyl carbocation and to the highly destabilized 1-(4-methylphenyl)2,2,2-trifluoroethyl carbocation is compared and contrasted. Copyright © 2010 John Wiley & Sons, Ltd.

Keywords: Solvolysis; Carbocation; Ion-Pair; Dynamics

INTRODUCTION

We are interested in using the experimental protocols developed for the detection of the reaction of ion pair intermediates of solvolysis[1–4] to determine absolute rate constants for the very fast reactions of ion pairs;[5–7] and also to probe changes in reaction mechanism.[8–11] We have prepared several chiral or isotopically labeled substrates for solvolysis reactions, and used these to obtain data that provide estimates of absolute rate constant ratios for partitioning of ion pair intermediates between competing pathways: one pathway that leads to formation of solvolysis products, and the second to the products of racemization of a chiral benzoate ester,[5] isomerization of a thionobenzoate,[7] or exchange of oxygen-16 and oxygen-18 between bridging and nonbridging positions at an isotopically labeled benzoate or tosylate ester.[6,9] These rate constant ratios were combined with the appropriate absolute rate constant for carbocation capture by solvent to obtain estimates of absolute rate constants for reactions of carbocation anion pairs.



1$^+$•C$_6$F$_5$CO$_2^-$ **2$^+$•C$_6$H$_5$COS$^-$** **3$^+$•$^-$O$_3$SC$_6$H$_4$-4-Me** **4$^+$•$^-$O$_3$SC$_6$H$_4$-4-Me**

These earlier experiments focused on the putative ion-pair intermediates of solvolysis of ring-substituted 1-phenylethyl derivatives such as **1$^+$•C$_6$F$_5$CO$_2^-$**,[5] **2$^+$•C$_6$H$_5$CSO$^-$** [7], and **3$^+$•$^-$O$_3$SC$_6$H$_4$-4-Me**.[9,11] We now extend this work and report the results of a study of the reorganization of the ion-pair intermediate **4$^+$•$^-$OSO$_2$C$_6$H$_4$-4-Me** of solvolysis of a ring-substituted 1-phenyl-2,2,2-trifluoroethyl tosylate, where the carbocation is destabilized by the strongly electron-withdrawing α-CF$_3$ substituent.[12–16] This work was initiated for the following reasons.

(1) The α-CF$_3$ for α-CH$_3$ substitution has been shown to destabilize ring substituted 1-phenylethyl carbocations by 8–12 kcal/mol relative to neutral substrate.[14–16] We were interested in examining the effect of this strongly electron-withdrawing α-CF$_3$ substituent on the partitioning of ion pair intermediates of solvolysis of 1-(4-methylphenyl)ethyl derivatives.

(2) The ion pair **1$^+$•C$_6$F$_5$CO$_2^-$** has been generated as an intermediate of solvolysis of 1-(4-methylphenyl)ethyl pentafluorobenzoate.[5,6] By comparison, carbocation-anion pairs to the much more unstable 1-(4-methylphenyl)-2,2,2-trifluorethyl carbocation can only be generated using a more weakly basic leaving group anion, such as tosylate anion.[12,14,15] There is little or no data for addition of tosylate anion to carbocations in aqueous solution, so that it is not clear whether addition of this

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Journal of Physical Organic Chemistry

weakly basic anion competes effectively with addition of the relatively nucleophilic solvent water. We were therefore interested in determining whether the ion pair intermediate of the reaction of 1-(4-methylphenyl)- 2,2,2-trifluorethyl tosylate would undergo internal return of the weakly nucleophilic sulfonate anion in the nucleophilic solvent water.

EXPERIMENTAL

All organic and inorganic chemicals were reagent grade from commercial sources and were used without further purification. The oxygen-18 labeled water, 99 atom % excess, was purchased from ISOTEC, Inc. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL AL-400 FT-NMR spectrometer operating at 400 MHz and 100.4 MHz, respectively.

Syntheses

2,2,2-Trifluoro-1-(4-methylphenyl)ethanone was synthesized by the procedure of Stewart and coworkers.[17] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (AB, 2H, $J = 8.0$ Hz, Ar*H*), 7.34 (AB, 2H $J = 8.0$ Hz, Ar*H*), 2.46 (s, 3H, CH_3). 1-(4-Methylphenyl)-2,2,2-trifluoroethanol (**4-OH**) was synthesized by reduction of the ketone with sodium borohydride.[18] The crude alcohol was purified by silica-gel column chromatography eluting with n-hexane: yield 78%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 (AB, 2H, $J = 8.0$ Hz, Ar*H*), 7.22 (AB, 2H, $J = 8.0$ Hz, Ar*H*), 4.98 (dq, 1H, $J = 4.4$ Hz, $^{2}J = 6.4$ Hz, $CHCF_3$), 2.60 (d, 1H, $J = 4.4$ Hz, CHO*H*), 2.37 (s, 3H, CH_3).

[ClS(^{18}O)$_2$]-*p*-Toluenesulfonyl chloride (**ClS(^{18}O)$_2$C$_6$H$_4$-4-Me**) was prepared by bubbling chlorine gas through a mixture of 10 g of *p*-thiocresol and 5 mL of oxygen-18 labeled water for two hours.[19] The reaction products were extracted with ether, purified by silica-gel column chromatography and recrystallized from benzene/n-hexane; yield 27%, mp. 66.0–67.5°C.

1-(4-Methylphenyl)-2,2,2-trifluoroethyl tosylate (**4-OS(O)$_2$C$_6$H$_4$-4-Me)** was synthesized from **4-OH** and *p*-toluenesulfonyl chloride by following a published procedure.[20] The crude reaction product was purified by recrystallization from ether/n-hexane: mp. 81.5-83.0°C. The same procedure was used to synthesize oxygen-18 labeled [(^{18}O$_2$)SO]-1-(4-methylbenzyl)-2,2,2-trifluoroethyl tosylate (**4-OS(^{18}O)$_2$C$_6$H$_4$-4-Me)** from **4-OH** (1g, 5.3 mM) and **ClS(^{18}O)$_2$- C$_6$H$_4$-4-Me** (1g, 5.3 mM); yield 59%, mp. 84-85°C.[20] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65 (AB, 2H, $J = 8.4$ Hz, Ar*H*), 7.22 (d, 4H, $J = 8.0$ Hz, Ar*H*), 7.11 (AB, 2H, $J = 8.4$ Hz, Ar*H*), 5.63 (q, 1H, $^{2}J = 6.4$ Hz, $CHCF_3$), 2.40 (s, 3H, CH_3), 2.33 (s, 3H, CH_3); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 145.14, 140.33, 133.06, 126.66 (1C, quaternary), 129.57, 129.22, 127.95, 127.83 (2C, tertiary), 122.21 (q, $J_{CF} = 280.2$ Hz, CF_3), 78.05 (q, $J_{CF} = 34.2$ Hz, $CHCF_3$).

Kinetic analyses

The reaction of **4-OS(O)$_2$Tos** in 50/50 (v/v) trifluoroethanol/water ($I = 0.5$, $NaClO_4$) at 25°C was monitored by following the decrease in absorbance at 265 nm. The reaction was initiated by making a 100-fold dilution of a solution of **4-OS(O)$_2$-C$_6$H$_4$-4-Me** in acetonitrile into 3.0 mL of 50/50 (v/v) trifluoroethanol/water ($I = 0.5$, $NaClO_4$) to give a final substrate concentration of 3 mM.

The isomerization reaction of **4-OS(^{18}O)$_2$C$_6$H$_4$-4-Me** was also monitored in 50/50 (v/v) trifluoroethanol/water ($I = 0.5$, $NaClO_4$). The sulfonate ester (100 mg) was dissolved in 1 mL of acetonitrile and mixed with 200 mL of 50/50 (v/v) trifluoroethanol/water ($I = 0.5$, $NaClO_4$) to give a final substrate concentration of 1.4 mM. At specified reaction times the remaining substrate and reaction products were extracted into 500 mL of toluene, the organic layer was washed with water, dried over $MgSO_4$ and the solvent removed on a rotary evaporator. The remaining residue was dissolved in 0.6 mL of C_6D_6 and saved for ^{13}C-NMR analysis.

Product analyses

The products of the solvolysis and of the azide anion nucleophilic substitution reactions of **4-OS(O)$_2$C$_6$H$_4$-4-Me** in 50/50 (v/v) 2,2,2-trifluoroethanol/water ($I = 0.5$, $NaClO_4$) were determined by HPLC analysis, as described in previous work.[15] Published methods were also used to calculate the product rate constant ratio k_{as}/k_s (M^{-1}) from these product yields.[15,21]

^{13}C-NMR analyses

Proton-decoupled ^{13}C-NMR spectra were recorded on a JEOL AL-400 FT-NMR spectrometer operating at 100.4 MHz. The spectra were centered at 78.3 ppm, and collected using a sweep width of 605.4 Hz with 8000 data points (0.076 Hz/pt), an 8 s relaxation delay time, and a pulse angle of 45°. Chemical shifts were measured in ppm relative to the peak at $\delta = 77.0$ ppm for [^{13}C]$CDCl_3$.

RESULTS

The oxygen-18 labeled substrate **4-OS(^{18}O)$_2$C$_6$H$_4$-4-Me** was synthesized by adaptation of published procedures (Experimental section). Earlier studies of the solvolysis and oxygen-18 scrambling of ring-substituted 1-phenylethyl derivatives used substrates enriched in carbon-13 at the benzylic carbon and oxygen-18 at the leaving group.[6,9] The substrate used in this work contains only natural abundance of carbon-13 at the benzylic carbon. This saves time in preparing the solvolysis reaction substrate, but substantially increases the time required for ^{13}C NMR analysis of the distribution of oxygen label at the sulfonate substrate.

A first-order rate constant of $k_{solv} = 3.6 \times 10^{-6}\ s^{-1}$ was determined for solvolysis of **4-OS(O)$_2$C$_6$H$_4$-4-Me** in 50/50 (v/v) trifluoroethanol/water ($I = 0.5$, $NaClO_4$) at 25°C by monitoring the progress of the reaction by UV spectroscopy. The values of k_{solv} remain constant as the azide anion concentration is increased to 0.50 M. A product rate constant ratio of $k_{az}/k_s = 1.1 \pm 0.1\ M^{-1}$ was calculated from the yields, determined by HPLC analysis, of the solvent and azide anion adducts formed in five reactions at [N_3^-] between 0.10 and 0.50 M. These values of k_{solv} and k_{az}/k_s are in fair agreement with $k_{solv} = 3.2 \times 10^{-6}\ s^{-1}$ and $k_{az}/k_s = 0.80\ M^{-1}$ reported in earlier work.

Figure 1 shows ^{13}C NMR spectra in the region of the benzylic carbon of **4-OS(^{18}O)$_2$C$_6$H$_4$-4-Me** (Fig. 1A) and of the *unreacted* substrate recovered during solvolysis of **4-OS(^{18}O)$_2$C$_6$H$_4$-4-Me** in 50/50 (v/v) trifluoroethanol/water ($I = 0.5$, $NaClO_4$) at 25°C (Figures 1B – 1D). The signal for the benzylic carbon at 78.342 ppm is split into a quartet by fluorines from the α-CF_3 group. Figures 1B – 1D show the appearance of the a second quartet for the isomerization reaction product **4-^{18}OS(^{18}O,^{16}O)C$_6$H$_4$-4-Me**, which is shifted upfield by 0.027 ppm to 78.315 when the oxygen-18 moves from a nonbridging to a bridging position.[22]

Figures 1C and 1D show small peaks for an unknown impurity at ca 78.6 ppm, which is close to the most downfield peak of the

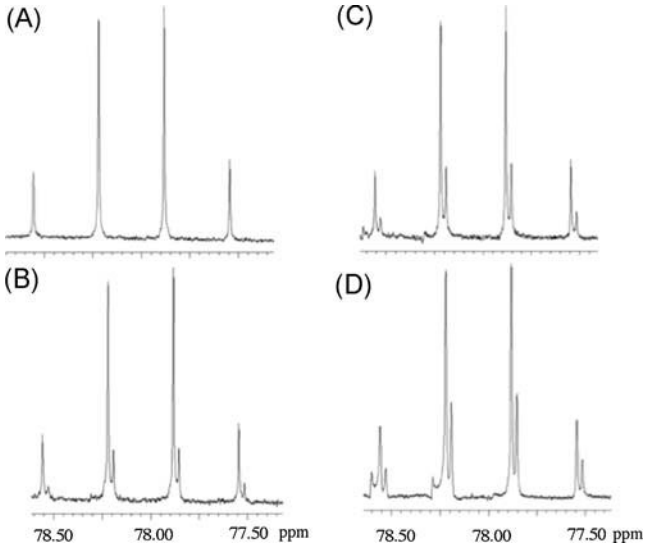


Figure 1. Partial ^{13}C spectra of unreacted substrate in C_6D_6 recovered during the solvolysis of **4-OS(^{18}O)$_2$C$_6$H$_4$-4-Me** in 50/50 (v/v) trifluoroethanol/water ($I = 0.5$, $NaClO_4$) at 25°C. The signal for the benzylic carbon is split by the α-fluorines ($J = 34$ Hz). (A) Initial spectrum of substrate **4-OS(^{18}O)$_2$C$_6$H$_4$-4-Me**. (B) Spectrum of substrate recovered after a 36 hour reaction time (3220 transients). (C) Spectrum of substrate recovered after a 48 hour reaction time (3560 transients). (D) Spectrum of substrate recovered after a 69 hour reaction time (10590 transients). The origin of the small peak at ca 78.6 ppm observed in Figures 1C and 1D is not known

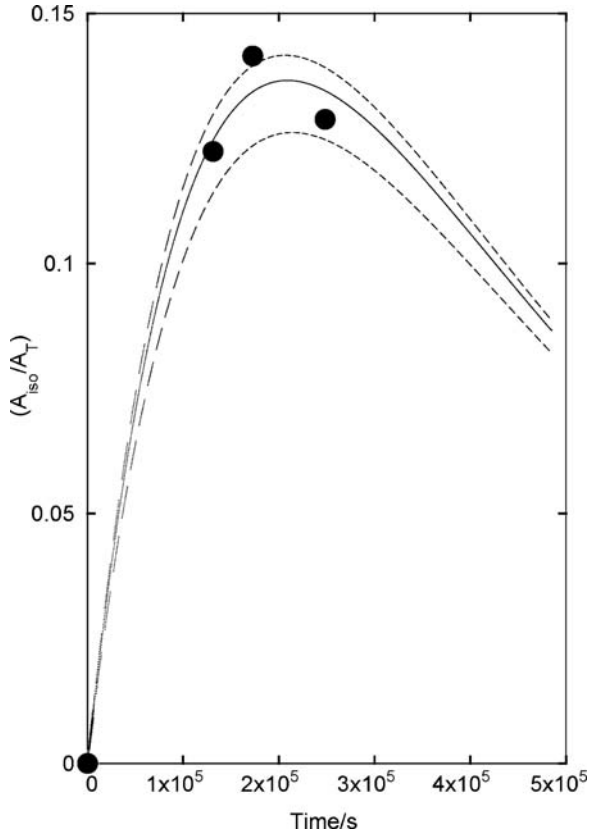


Figure 2. Time course for the formation of isomerized reaction product **4-^{18}OS(^{18}O,^{16}O)C$_6$H$_4$-4-Me** during the solvolysis of **4-OS(^{18}O)$_2$C$_6$H$_4$-4-Me** in 50/50 (v/v) TFE/H_2O at 25°C. The solid line shows the nonlinear least-squares fit of the data to Eqn (1) derived for Scheme 1 using $k_{solv} = 3.6 \times 10^{-6}\,s^{-1}$ and $k_{iso} = 1.8 \times 10^{-6}\,s^{-1}$. The upper and lower dashed lines show the fits obtained using values of k_{iso} that are 10% higher and 10% lower, respectively, than the value from least-squares analysis

quartet for the benzylic carbon. The relative area of the peaks for the isomerization reaction product **4-^{18}OS(^{18}O,^{16}O) C$_6$H$_4$-4-Me** (A_{iso}) and the remaining substrate **4-OS(^{18}O)$_2$C$_6$H$_4$-4-Me** (A_S) was therefore determined from the integrated areas of the two most upfield shifted peaks for the quartet for the benzylic carbon.

Figure 2 shows the fractional conversion of **4-OS(^{18}O)$_2$C$_6$H$_4$-4-Me** to **4-^{18}OS(^{18}O,^{16}O)Tos** [A_{iso}/A_T] at different reaction times t, where A_{iso} is the area of the carbon-13 NMR peak for the benzylic carbon of **4-^{18}OS(^{18}O,^{16}O)C$_6$H$_4$-4-Me** and A_T is the total area of the peak for **4-OS(^{18}O)$_2$C$_6$H$_4$-4-Me** at $t = 0$. Values of A_T were calculated as $A_T = (A_S + A_{iso})/\exp(-k_{solv}t)$, where A_S and A_{iso} are the observed peak areas for the benzylic carbons of **4-OS(^{18}O)$_2$C$_6$H$_4$-4-Me** and **4-^{18}OS-(^{18}O,^{16}O)C$_6$H$_4$-4-Me**, respectively, and $k_{solv} = 3.6 \times 10^{-6}\,s^{-1}$.

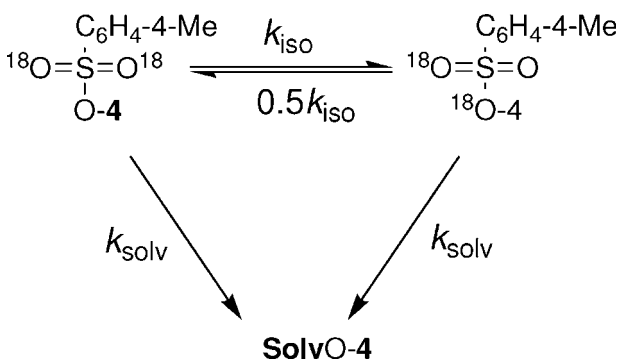
The solid line in Fig. 2 shows the nonlinear least squares fit of the experimental data to eq 1 derived for Scheme 1 using $k_{solv} = 3.6 \times 10^{-6}\,s^{-1}$ determined by monitoring solvolysis by UV spectroscopy and $k_{iso} = 1.8 \times 10^{-6}\,s^{-1}$, which is treated as a variable parameter. The upper and lower dashed lines in Fig. 2 show that the experimental data is accommodated by values of k_{iso} that lie within ±10% of the rate constant determined by least squares analysis.

$$\frac{A_{iso}}{A_T} = \left[\frac{2}{3}\right] e^{-k_{solv}t} - \left[\frac{2}{3}\right] e^{-(1.5k_{iso}+k_{solv})t} \qquad (1)$$

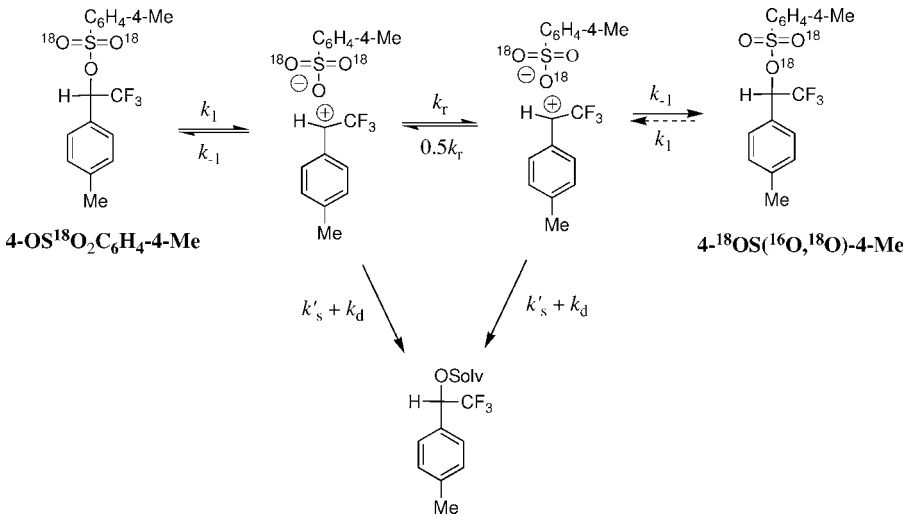
DISCUSSION

It is surprising that the α-CF_3 for α-CH_3 substitution at **1**$^+$, which strongly destabilizes **4**$^+$ towards nucleophile addition, should have little effect on the rate constants for carbocation-nucleophile addition. [14–16] This shows that the increase in the reactivity of **4**$^+$ compared to **1**$^+$ toward nucleophile addition caused by the large effect of the α-CF_3 substituent on the thermodynamic reaction driving force is essentially completely offset by a decrease in reactivity of **4**$^+$ due to an increase in the Marcus intrinsic barrier for carbocation-nucleophile addition.[23–25]

The sum of the rate constants for solvolysis and ^{18}O-scrambling of **4-OS(^{18}O)$_2$C$_6$H$_4$-4-Me**, $k_{solv} + k_{iso} = 5.4 \times 10^{-6}\,s^{-1}$ is larger than $k_{solv} = 3.6 \times 10^{-6}\,s^{-1}$ for solvolysis of the unlabeled ester.



Scheme 1.



Scheme 2.

This scrambling of oxygen-18 label between bridging and nonbridging positions may occur by rearrangement of these oxygen at an ion pair reaction intermediate followed by internal return to reactant (k_r and k_{-1}, Scheme 2), or the reaction may proceed by an uncoupled concerted pathway that avoids formation of a highly unstable reaction intermediate.[8,11,26]

There is good evidence that isomerization of esters that exchanges the position of carbon-bridging and nonbridging oxygen proceeds by a stepwise mechanism (Scheme 2), when the carbocation reaction intermediate has a lifetime of longer than 10^{-11} s.[8,26] The ion pair intermediate of solvolysis of **1-$O_2CC_6F_5$** was shown in earlier work to undergo deprotonation to form alkene,[21] internal return to reform substrate,[6] and racemization followed by internal return to substrate.[5] A similar stepwise mechanism is strongly favored for the isomerization of **4-OS(^{18}O)$_2$$C_6H_4$-4-Me** in 50/50 (v/v) water/trifluroethanol because the lifetimes determined for **1**$^+$ and **4**$^+$ in this solvent are similar.[21,27] The value of $k_s' \approx 6 \times 10^9\ s^{-1}$ for addition of solvent to **1**$^+$ and **4**$^+$ is estimated to be slightly larger than the value of $4 \times 10^9\ s^{-1}$ calculated using the azide ion "clock",[27,28] because a significant fraction of the azide ion adduct is formed by a preassociation mechanism that does not involve diffusion-controlled trapping of the carbocation.[21,27]

Equations 1–3 give the relationships between the experimental rate constants k_{solv} and k_{iso} and the microscopic rate constants for the individual steps in Scheme 2, where k_s' is the rate constant for direct addition of solvent to the ion pair reaction intermediate, and k_d is rate constant for irreversible diffusional separation of the ion pair to the free carbocation which then undergoes addition of solvent.[6] These rate laws were derived by making the assumption that there is a single rate constant k_{-1} for collapse of the two ion pairs in Scheme 2, and that the reorganization of the ion pair that exchanges any of the three equivalent sulfonate oxygen ($k_r \approx 10^{11}\ s^{-1}$)[7] is much faster than the other reactions of the ion pair, so that $k_r >> (k_s' + k_{-d}), k_{-1}'$. Under these conditions both the steady state concentrations and their rates of internal return of the two ion pairs to give the neutral esters will be equal.

A value of $k_{-1} \approx 1.7 \times 10^{10}\ s^{-1}$ for unimolecular collapse of **4**$^{+\bullet}$ **$^{-18}$OS-(^{18}O,^{16}O)C_6H_4-4-Me** to form **4-^{18}OS(^{18}O,^{16}O)C_6H_4-4-Me** can be calculated (eq 3) from the experimental rate constant ratio $k_{iso}/k_{solv} = 0.50$ and using $k_s' = 6 \times 10^9\ s^{-1}$ and $k_{-d} = 1.6 \times 10^{10}\ s^{-1}$. The estimated rate constant for addition of the tosylate anion to **4**$^+$ is larger than $k_s' = 6 \times 10^9\ s^{-1}$ for addition of the solvent 50/50 water/trifluoroethanol. This suggests that the sulfonate anion should show a modest selectivity towards nucleophile addition to carbocations in aqueous solution.

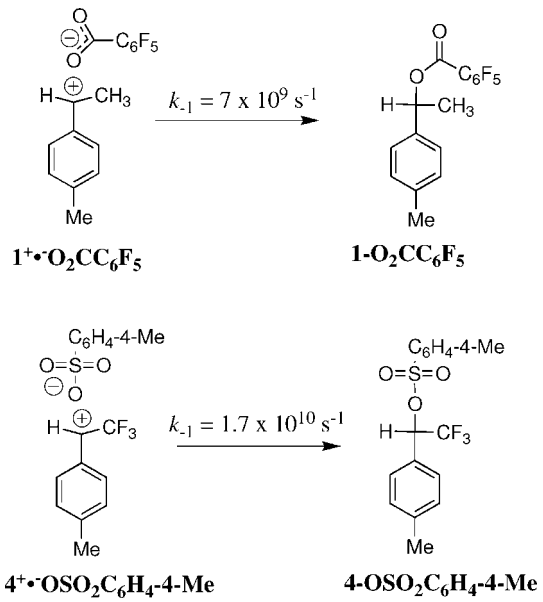
$$k_{solv} = \frac{k_1(k_s' + k_{-d})}{k_s' + k_{-d} + k_{-1}} \quad (1)$$

$$k_{iso} = \frac{k_1 k_{-1}}{1.5(k_s' + k_{-d} + k_{-1})} \quad (2)$$

$$\frac{k_{iso}}{k_{solv}} = \frac{k_{-1}}{1.5(k_s' + k_{-d})} \quad (3)$$

To the best of our knowledge the nucleophilic selectivity of tosylate anion towards addition to carbocations in aqueous solution has not been measured because: (1) Tosylate salts are relatively insoluble in water. (2) Tosylate carbocation anion pairs must be generated by solvolysis of a reactive substrate with a leaving group that is better than tosylate (*e.* g., triflate) in order to give a tosylate ester product that is sufficiently stable to isolate. However, organic triflates are only stable when attached to electron deficient carbon (*e.g.* methyl triflate), and their reactions in water tend to proceed by a concerted-type mechanism that avoids formation of carbocation reaction intermediates.

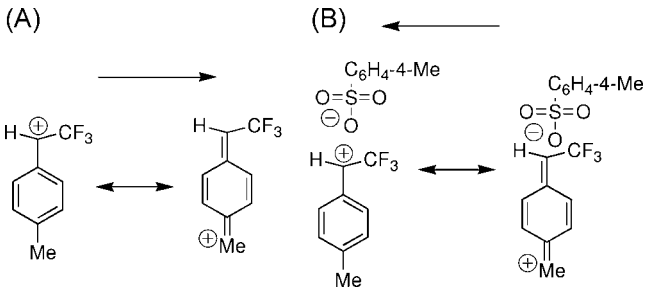
There is less internal return of the ion-pair intermediate during solvolysis of **1-^{18}OC(O)C_6F_5** in 50/50 trifluoroethanol/water ($k_{iso}/k_{solv} = 0.13$)[6] compared with internal return during solvolysis of **4-OS(^{18}O)$_2$$C_6H_4$-4-Me** in the same solvent ($k_{iso}/k_{solv} = 0.50$). The two carbocations **1**$^+$ and **4**$^+$ show similar reactivity ($k_s' = 6 \times 10^9\ s^{-1}$) toward addition of solvent.[15,21,27] The smaller rate constant ratio of $k_{iso}/k_{solv} = 0.13$ for the reaction of **1-^{18}OC(O)C_6F_5** compared with the reaction of **4-OS(^{18}O)$_2$$C_6H_4$-4-Me** requires a smaller rate constant k_{-1} for internal return of the pentafluorobenzoate anion to form rearranged product **1-OC(^{18}O)C_6F_5**. Combining the rate constant ratio $k_{iso}/k_{solv} = 0.13$ determined for the isomerization and solvolysis reactions of the pentafluorobenzoate ester **1-^{18}OC(O)C_6F_5** with $k_s' = 6 \times 10^9\ s^{-1}$ and $k_{-d} = 1.6 \times 10^{10}\ s^{-1}$ gives $k_{-1} = 7 \times 10^9\ s^{-1}$ for unimolecular collapse of the ion pair intermediate of solvolysis to the neutral benzoate ester, which is ca. 2-fold smaller than $k_{-1} \approx 1.7 \times 10^{10}\ s^{-1}$ estimated in this work for collapse the intermediate of solvolysis of **4-OS(^{18}O)$_2$$C_6H_4$-4-Me** (Scheme 3).[6]



Scheme 3.

The similar rate constants for collapse of the ion pairs shown in Scheme 3 is interesting. The two carbocations show the same intrinsic reactivity towards addition of nucleophlic solvent ($k_s' = 6 \times 10^9$ s^{-1}).[15,21,27] However, tosylate anion is *ca* 10^8-more reactive as a leaving group than pentafluorobenzoate anion in solvolysis reactions with rate determining bond cleavage of α-substituted 4-methoxybenzyl derivatives.[23] This leaving group is therefore expected to show a smaller nucleophilicity for reaction in the reverse bond synthesis direction. The observed similar reactivity of tosylate and pentaflurobenzoate towards addition to carbocations **1**$^+$ and **4**$^+$ which show similar intrinsic electrophilic reactivity almost certainly reflects a Hammond-type leveling in the selectivity of these anions in nucleophilic addition to reactive carbocations.[29]

We have made the simplifying assumption that $k_s' \approx k_s$ for addition of aqueous/trifluoroethanol to the ion pair **4**$^+$•$^-$^{18}**OS-(**^{18}**O,**^{16}**O)C$_6$H$_4$-4-Me** and to free carbocation **4**$^+$. We note, however, that there is good evidence that addition of the strongly electron-withdrawing α-CF$_3$ group to benzylic carbocations is accompanied by an increase in delocalization of charge into the phenyl ring (Scheme 4A).[15,30] This attenuates the destabilizing inductive substituent effect by moving the center of positive charge away from the electron-withdrawing α-CF$_3$ dipole. This increased delocalization in charge is the underlying cause of the large Marcus intrinsic barriers for nucleophile addition to ring-substituted phenyl 2,2,2-trifluoroethyl carbocations.[23,24] It is interesting to speculate that placement of a leaving group anion next to the carbocation might favor partial relocalization of charge onto the benzylic carbon (Scheme 4B). This would reduce the Marcus intrinsic reaction barrier and cause an increase in the rate constants for carbocation nucleophile addition that could partly explain the high observed reactivity of the tosylate anion in internal return to neutral substrate.



Scheme 4.

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