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Dynamics of reaction of ion pairs in aqueous solution: racemization of the chiral ion pair intermediate of solvolysis of (*S*)-1-(4-methylphenyl)ethyl pentafluorobenzoate

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ABSTRACT: The chiral ester (*S*)-1-(4-methylphenyl)ethyl pentafluorobenzoate, (*S*)-**1-OC(O)C₆F₅**, was prepared and a value of $k_{\text{rac}} = 8.5 \times 10^{-7} \text{ s}^{-1}$ was determined for the rate constant for its racemization to (*R*)-**1-OC(O)C₆F₅** in 50:50 (v/v) trifluoroethanol–water ($I = 0.50$, NaClO₄). This rate constant is 12 times smaller than $k_{\text{solv}} = 1.06 \times 10^{-5} \text{ s}^{-1}$ for the stepwise solvolysis of **1-OC(O)C₆F₅**, which shows that inversion of the ion-pair intermediate is a relatively rare event during solvolysis in a largely aqueous solvent, and two times smaller than $k_{\text{iso}} = 1.6 \times 10^{-6} \text{ s}^{-1}$ for degenerate isomerization which exchanges the position of the ester bridging and non-bridging oxygens of **1-OC(O)C₆F₅**. A simple relationship is derived between the empirical rate constant ratio $k_{\text{rac}}/k_{\text{iso}}$ and the microscopic rate constants for reaction of the ion-pair intermediate within its solvation shell. Substitution of estimated rate constants for reactions of the 1-(4-methylphenyl)ethyl carbocation–pentafluorobenzoate anion pair into this equation gives $k_i = 1.5 \times 10^{10} \text{ s}^{-1}$ for inversion of the chiral ion pair, which is similar to $k_{-d} = 1.6 \times 10^{10} \text{ s}^{-1}$ for its separation to free ions. Copyright © 2003 John Wiley & Sons, Ltd.

KEYWORDS: reaction dynamics; chiral ion pairs; racemization; solvolysis; (*S*)-1-(4-methylphenyl)ethyl pentafluorobenzoate

INTRODUCTION

The experimental protocols for the detection of the reactions of carbocation–anion pair intermediates of solvolysis reactions are well developed.¹ However, there is still great potential for using these protocols along with modern analytical methods for product analysis to detect ion-pair reactions during solvolysis. These experimental results may then be combined with recent studies of ion pair dynamics to obtain estimates for absolute rate constants for reactions of ion pairs within their solvent cages.^{2–5} For example, we have determined a value of $k_{-d} \approx 1.6 \times 10^{10} \text{ s}^{-1}$ for the rate constant for separation of ion pair intermediates to free ions during solvolysis of ring-substituted 1-phenylethyl derivatives in 50:50 (v/v) water–trifluoroethanol.⁶ This rate constant has served as a ‘clock’ to estimate the following rate constants for

reactions that occur within the solvation shell of ion pair intermediates of solvolysis:

1. a value of $k_r = 1 \times 10^{11} \text{ s}^{-1}$ found for *reorganization* of the ion pair intermediate of solvolysis of ring-substituted 1-phenylethyl thionobenzoates which is a step in the O → S isomerization reaction of this substrate;⁴
2. a value of $k_{-1} = 7 \times 10^9 \text{ s}^{-1}$ found for internal return of the ion pair intermediate of solvolysis of 1-(4-methylphenyl)ethyl pentafluorobenzoate to the neutral ester, which is a step in the degenerate exchange reaction of oxygen-18 label between the ester bridging and non-bridging positions.⁵

Our set of rate constants for reactions of the ion-pair intermediate of solvolysis of 1-(4-methylphenyl)ethyl pentafluorobenzoate in 50:50 (v/v) water–trifluoroethanol within the surrounding solvent cage is nearly complete;^{4–6} all that is missing is the rate constant k_i for inversion of the chiral ion pair intermediate of solvolysis of chiral 1-(4-methylphenyl)ethyl pentafluorobenzoate. We report here the synthesis (*S*)-1-(4-methylphenyl)ethyl pentafluorobenzoate and the results of experiments which show that this compound undergoes

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racemization in 50:50 (v/v) water–trifluoroethanol 12-times slower than solvolysis, but only two times slower than scrambling of the ^{18}O label between ester-bridging and non-bridging positions determined in earlier work.⁵ Combining these rate data with results from earlier work gives a value of $k_i = 1.5 \times 10^{10} \text{ s}^{-1}$ for the rate constant for interconversion of the *S* and *R* forms for the carbocation–anion pair intermediate of solvolysis of (*S*)-1-(4-methylphenyl)ethyl pentafluorobenzoate.

EXPERIMENTAL

Materials. Pentafluorobenzoyl chloride, *p*-methylacetophenone, europium tris[3-(heptafluoropropylhydroxymethylene)]-(+)-camphorate and (*S*)-(+)-2,2,2-trifluoro-1-(9-anthryl)ethanol were purchased from Aldrich and used without purification. All other chemicals were of reagent grade and were used without purification.

Chemical syntheses. The chemical shifts of ^1H NMR spectra for routine characterization of the products of chemical synthesis were referenced to CHCl_3 at 7.27 ppm. Racemic 1-(4-methylphenyl)ethyl pentafluorobenzoate was prepared from 1-4-(methylphenyl)ethyl alcohol and pentafluorobenzoyl chloride by adaptation of a published method that is described in greater detail below for the synthesis of the chiral ester.⁷

(*S*)-1-(4-Methylphenyl)ethyl alcohol [(*S*)-**1-OH**] was prepared by reduction of *p*-methylacetophenone with (–)-*B*-chlorodiisopinocampheylborane [(–)-DIP-chloride].⁸ The crude reaction product was purified by silica gel column chromatography eluting with hexane–diethyl ether to give the final product in a yield of 90%. ^1H NMR (400 MHz, CDCl_3), δ 7.26, 7.15 (A_2B_2 , 4H, $J = 8 \text{ Hz}$, $\text{C}_6\text{H}_4\text{Me}$) 4.86 (q, 1H, $J = 6 \text{ Hz}$, CH), 2.34 (s, 3H, ArCH_3), 1.48 (d, 3H, $J = 6 \text{ Hz}$, CH_3).

(*S*)-1-(Methylphenyl)ethyl pentafluorobenzoate [(*S*)-**1-OC(O)C₆F₅**] was prepared by adaptation of a published procedure.⁷ (*S*)-**1-OH** (14.7 mmol) was reacted with 1.7 molar equiv. of pentafluorobenzoyl chloride in pyridine with stirring at 0°C for 30 min, followed by 60 min at room temperature. The reaction was quenched with cold NaHCO_3 (100 ml, 0°C) and the ester was extracted into diethyl ether. The ethereal solution was washed with dilute HCl, 5% aqueous NaHCO_3 and saturated sodium chloride and then dried over MgSO_4 . The crude reaction product was purified by silica gel chromatography eluting with 95:5 hexane–diethyl ether, and then recrystallized twice from diethyl ether–hexane to give a final yield of 7%; m.p. 34–34.2°C; ^1H NMR (400 MHz, CDCl_3), δ 7.31, 7.14 (A_2B_2 , 4H, $J = 8 \text{ Hz}$, $\text{C}_6\text{H}_4\text{Me}$), 6.12 (q, 1H, $J = 6 \text{ Hz}$, CH), 2.35 (s, 3H, ArCH_3), 1.67 (d, 3H, $J = 6 \text{ Hz}$, CH_3). Anal. ($\text{C}_{16}\text{H}_{11}\text{F}_5\text{O}_2$) C, H. Calc: H (3.36%), C (58.19%) Found H (3.35%), C (58.25%).

^1H NMR analyses. ^1H NMR spectra were recorded on a

JEOL AL-400 FT-NMR spectrometer operating at 400 MHz. The chemical shifts are reported relative to a value of $\delta = 7.15 \text{ ppm}$ for the solvent C_6D_6 . The benzylic protons of **1-OC(O)C₆F₅** and **1-OH** were subjected to homonuclear decoupling by irradiation of the corresponding α -methyl protons during data acquisition. Spectra (32 000 data points) were obtained using a sweep width of 4000 Hz centered at the benzylic proton, a 90° pulse angle, an acquisition time of 8 s and a 60 s relaxation delay between pulses (200–400 transients) to ensure complete relaxation of the benzylic proton.

Europium tris[3-(heptafluoropropylhydroxymethylene)]-(+)-camphorate (30 mM) and (*S*)-(+)-2,2,2-trifluoro-1-(9-anthryl)ethanol (0.1 M) were used as chemical shift reagents to resolve the enantiomeric protons of **1-OC(O)C₆F₅** and **1-OH**, respectively. The enantiomeric purities of **1-OC(O)C₆F₅** and **1-OH** were determined from the ratio of the integrated areas of the spin-decoupled benzylic protons of the *R*- and *S*-enantiomers determined for spectra in C_6D_6 that contains the appropriate shift reagent.

Kinetic analyses. Solutions of (*S*)-**1-OC(O)C₆F₅** in 50:50 (v/v) trifluoroethanol–water ($I = 0.50$, NaClO_4) were prepared by dissolving 30 mg of substrate in 1 ml of acetonitrile and then adding this to 200 ml of 50:50 (v/v) trifluoroethanol–water ($I = 0.50$, NaClO_4) to give a final substrate concentration of 0.5 mM. At a specified reaction time the remaining substrate and reaction products were extracted into 500 ml of diethyl ether and the ethereal extract was washed with water, dried over MgSO_4 and evaporated. The substrate **1-OC(O)C₆F₅** was separated from products **1-OH** and **1-OTFE** using a Recycling Preparative LC-908 system from Japan Analytical Industry, a JAIGEL-1H styrene polymer HPLC column and eluting with CHCl_3 , and the solvent was stripped from purified **1-OH** and **1-OC(O)C₆F₅**. These compounds were dissolved in C_6D_6 and the appropriate shift reagent was added for NMR analyses.

The rate constant for solvolysis of **1-OC(O)C₆F₅** was determined by monitoring the disappearance of this compound by HPLC.⁹ The pseudo-first-order rate constant for the reaction was obtained from the slope of a linear semi-logarithmic plot of reaction progress against time.

RESULTS

A value of $k_{\text{solv}} = 1.06 \times 10^{-5} \text{ s}^{-1}$ for solvolysis of the ester **1-OC(O)C₆F₅** at 25°C in 50:50 (v/v) trifluoroethanol–water ($I = 0.50$, NaClO_4) was determined by monitoring the disappearance of this compound by HPLC.

Figure 1(A) shows the partial ^1H NMR spectrum in C_6D_6 of the benzylic proton of (*S*)-**1-OC(O)C₆F₅** in which coupling to the methyl protons has been eliminated by using an inverse gated decoupling procedure (see

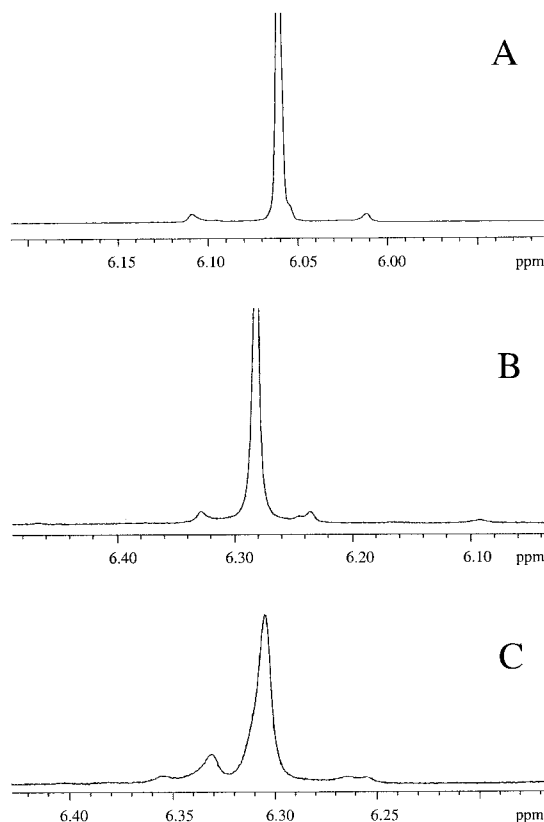


Figure 1. Partial NMR spectra of the benzylic proton of **1-OC(O)C₆F₅** in C₆D₆ in which coupling to the methyl protons has been eliminated by using an inverse gated decoupling procedure. (A) Spectrum of **(S)-1-OC(O)C₆F₅** in the absence of shift reagent. (B) Spectrum of **(S)-1-OC(O)C₆F₅** in the presence of 30 mM europium tris[3-(heptafluoropropylhydroxymethylene)]-(+)-camphorate shift reagent. (C) Spectrum of **1-OC(O)C₆F₅** recovered after solvolysis for 36 h in 50:50 (v/v) trifluoroethanol–water at 25 °C, also in the presence of 30 mM shift reagent

Experimental). Figure 1(B) shows that 30 mM europium tris[3-(heptafluoropropylhydroxymethylene)]-(+)-camphorate causes about a 0.2 ppm downfield shift in the decoupled signal for this benzylic proton. Figure 1(C) shows the spectrum, determined in the presence of the shift reagent, of **1-OC(O)C₆F₅** remaining after solvolysis for 36 h at 25 °C in 50:50 (v/v) trifluoroethanol–water at (*I* = 0.50, NaClO₄). Two signals are now observed, a major peak for the starting substrate **(S)-1-OC(O)C₆F₅** and a minor peak for **(R)-1-OC(O)C₆F₅** which forms by racemization of **1-OC(O)C₆F₅** during the course of its solvolysis reaction.

Table 1 lists the ratio of the peak areas (*A_R/A_S*) for the *R*- and *S*-isomers of **1-OC(O)C₆F₅** determined at four different times during the solvolysis of **(S)-1-OC(O)C₆F₅** in 50:50 (v/v) trifluoroethanol–water (*I* = 0.50, NaClO₄). Table 1 also lists the following normalized areas: (1) the normalized area (*A_{nor}*)_T for total remaining **1-OC(O)C₆F₅** after solvolysis at 25 °C in 50:50 (v/v) trifluoroethanol–water (*I* = 0.50, NaClO₄) at reaction

Table 1. Normalized areas of the ¹H NMR signals due to the benzylic carbon during reaction of **(S)-1-OC(O)C₆F₅** in 50:50 (v/v) trifluoroethanol–water at 25 °C

Time (s)	(<i>A_R/A_S</i>) ^a	<i>A_{nor}</i>		
		(<i>A_{nor}</i>) _T ^b	(<i>A_{nor}</i>) _S ^c	(<i>A_{nor}</i>) _R ^c
		1.00		
43200	0.0274	0.633	0.616	0.0169
81000	0.0846	0.426	0.392	0.034
129600	0.106	0.253	0.229	0.0242
172800	0.14	0.16	0.14	0.0197

^a Ratio of the areas of the peaks for the benzylic protons of **(R)-1-OC(O)C₆F₅** and **(S)-1-OC(O)C₆F₅** determined using a europium tris[3-(heptafluoropropylhydroxymethylene)]-(+)-camphorate shift reagent.

^b Normalized sum (*A_{nor}*)_T = (*A_R* + *A_S*) of the ¹H NMR peak areas due to the benzylic carbon of **(R)-1-OC(O)C₆F₅** and **(S)-1-OC(O)C₆F₅**, calculated as (*A_{nor}*)_T = e^{−*kt*}, where *k* = *k_{solv}* = 1.06 × 10^{−5} s^{−1} for solvolysis of the ester.

^c Normalized areas for the benzylic protons of **(S)-1-OC(O)C₆F₅** [(*A_{nor}*)_S] and **(R)-1-OC(O)C₆F₅** [(*A_{nor}*)_R] calculated from (*A_{nor}*)_T = (*A_R* + *A_S*) and (*A_R/A_S*).

time *t* which is calculated as (*A_{nor}*)_T = e^{−*kt*}, where *k* = *k_{solv}* = 1.06 × 10^{−5} s^{−1}; (2) the normalized areas for **(S)-1-OC(O)C₆F₅** [(*A_{nor}*)_S] and **(R)-1-OC(O)C₆F₅** [(*A_{nor}*)_R], which were determined from the total normalized area (*A*)_T = (*A_R* + *A_S*) and the ratio (*A_R/A_S*).

$$(\mathcal{A}_{\text{nor}})_R = 0.5 \left[e^{-k_{\text{solv}}t} - e^{-(2k_{\text{rac}} + k_{\text{solv}})t} \right] \quad (1)$$

Figure 2 shows the change in (*A_{nor}*)_R with time for the reaction of **(S)-1-OC(O)C₆F₅** at 25 °C in 50:50 (v/v) trifluoroethanol–water. The solid line shows the fit of the data to Eqn. (1) derived for Scheme 1,¹⁰ using *k_{solv}* = 1.06 × 10^{−5} s^{−1} determined by experiment and *k_{rac}* = 8.5 × 10^{−7} s^{−1} determined by non-linear least-squares analysis. The upper and lower dashed lines show the fits obtained using values of *k_{rac}* that are 20% larger

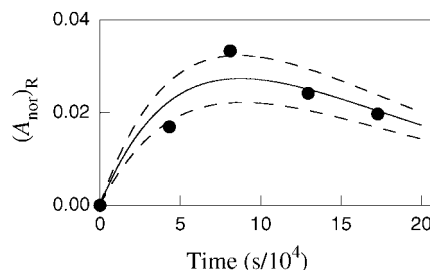
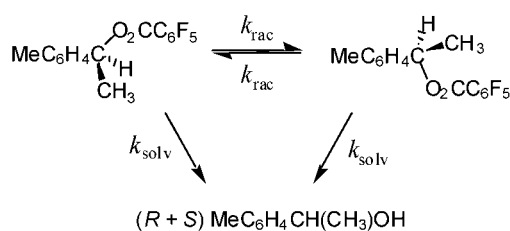


Figure 2. Time course for the appearance of the peak for the benzylic proton of **(R)-1-OC(O)C₆F₅** during solvolysis of **(S)-1-OC(O)C₆F₅** in 50:50 (v/v) trifluoroethanol–water at 25 °C. The peak areas are normalized relative to a value of 1.0 for the benzylic proton of **(S)-1-OC(O)C₆F₅** at *t* = 0. The solid line shows the fit of the data to Eqn. (1) derived for Scheme 1 using *k_{solv}* = 1.06 × 10^{−5} s^{−1} and *k_{rac}* = 8.5 × 10^{−7} s^{−1}. The upper and lower dashed lines show the fits obtained using values of *k_{rac}* that are 20% larger and 20% smaller, respectively, than the best fit value from least-squares analysis



Scheme 1

and 20% smaller, respectively, than the best fit value from least-squares analysis. This shows that the variation in the values of k_{rac} that provide an acceptable fit to these data is $\pm 20\%$.

The partial ^1H NMR spectrum in C_6D_6 of the benzylic proton of (*S*)-**1-OH** is shown in Fig. 3(A). Coupling to the methyl protons was eliminated in this spectrum by using an inverse gated decoupling procedure (see

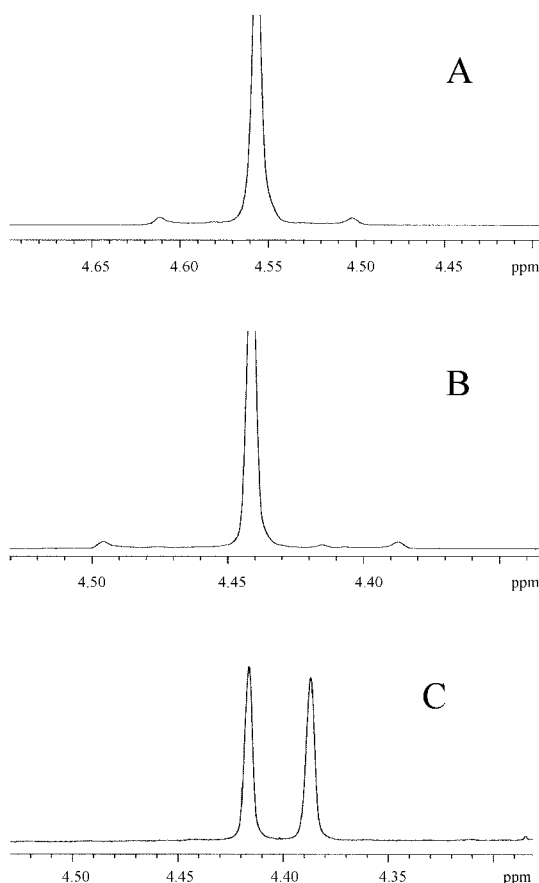


Figure 3. Partial NMR spectra of the benzylic proton of **1-OH** in C_6D_6 in which coupling to the methyl protons has been eliminated by using an inverse gated decoupling procedure. (A) Spectrum of (*S*)-**1-OH** in the absence of shift reagent. (B) Spectrum of (*S*)-**1-OH** in the presence of 0.1 M (*S*)-(+)-2,2,2-trifluoro-1-(9-anthryl)ethanol. (C) Spectrum of **1-OC(O)C₆F₅** recovered after solvolysis for 183 h in 50:50 (v/v) trifluoroethanol–water at 25 °C, also in the presence of the shift reagent

Experimental). Figure 3(B) shows that 0.1 M (*S*)-(+)-2,2,2-trifluoro-1-(9-anthryl)ethanol causes about a 0.1 ppm upfield shift in the decoupled signal for the benzylic proton. Figure 3(C) shows the spectrum of **1-OH** isolated as the major product of a 183 h reaction of (*S*)-**1-OC(O)C₆F₅** (~ 10 half-times) at 25 °C in 50:50 (v/v) trifluoroethanol–water ($I = 0.50$, NaClO_4). Separate signals are observed for (*S*)-**1-OH** and (*R*)-**1-OH** and the ratio of the integrated areas of the signals for the *S*- and *R*- isomers is 1.0.

DISCUSSION

Reaction conditions

The high instability and short lifetimes of carbocation–anion pairs in aqueous solution create difficult problems for the design of experiments to determine rate constants for their reorganization in this solvent:

1. The products of reorganization of ion pairs can be observed experimentally when the product is ‘trapped’ by internal return to reactant, but this requires that trapping be very fast and competitive with separation of the ion pair to free ions ($k_{\text{-d}} = 1.6 \times 10^{10} \text{ s}^{-1}$). We have presented strong evidence in earlier work that internal return of the 1-(4-methylphenyl)ethylpentafluorobenzoate ion intermediate of solvolysis of (*S*)-**1-OC(O)C₆F₅** occurs at a rate similar to its separation of free ions.^{5,6}
2. It is difficult to determine rate constants of $>10^{10} \text{ s}^{-1}$ by direct methods. However, it is possible to use the value of $k_{\text{-d}} = 1.6 \times 10^{10} \text{ s}^{-1}$ for ion separation as a clock for other reactions of these ion pairs which are steps in the degenerate isomerization and racemization reactions of neutral substrates.^{2,4,5}
3. The neutral organic substrates used as precursors to carbocation–anion pairs generally show low solubility in aqueous solution. The good sensitivity of modern high-resolution NMR spectroscopy in comparison with polarimetric methods allowed us to work at a low initial concentration 0.5 mM (*S*)-**1-OC(O)C₆F₅**, which is soluble in 50:50 (v/v) water–trifluoroethanol at 25 °C. By comparison, a substrate concentration of ~ 40 mM was used in earlier studies in 60–90% aqueous acetone of the reactions of ion pair intermediates of chiral and O^{18} -labeled 1-(4-methoxyphenyl)ethyl 4-nitrobenzoate.¹¹

Racemization of (*S*)-**1-OC(O)C₆F₅** during solvolysis

Solvolysis of **1-OC(O)C₆F₅** in 50:50 (v/v) trifluoroethanol–water proceeds by a stepwise reaction mechanism.⁹ Figure 1(C) shows the partial NMR spectrum determined in the presence of a chemical shift reagent of the substrate

Scheme 2, except that inversion step (k_i) has been substituted by ion-pair 'reorganization' ($k_r = 1 \times 10^{11} \text{ s}^{-1}$), is given by Eqn. (3).⁵ Equation (3) was derived with the assumption that $k_r \gg k'_s + k_{-d}$.⁵ Equation (4) gives the relationship between the rate constant ratio $k_{\text{rac}}/k_{\text{iso}} = 0.53$ and the rate constants for partitioning of the ion pair reaction intermediate from Scheme 2. Equation (4) shows that racemization and isomerization would have proceeded at similar rates if inversion of the ion pair were very much faster than other reactions of the ion pair ($2k_i \gg k'_s + k_{-d} + k_{-1}$). Our observation that $k_{\text{rac}}/k_{\text{iso}}$ drops to a value of about 0.50 requires that $2k_i \approx k'_s + k_{-d} + k_{-1}$.

Substitution of $k_{-d} = 1.6 \times 10^{10} \text{ s}^{-1}$ (Ref. 6), $k'_s = 6 \times 10^9 \text{ s}^{-1}$ (Ref. 6) and $k_{-1} = 7 \times 10^9 \text{ s}^{-1}$ (Ref. 5) into Eqn. (4) gives $k_i = 1.5 \times 10^{10} \text{ s}^{-1}$ for inversion of the ion pair in 50:50 (v/v) water–trifluoroethanol. In other words, the rate constant for separation of this ion pair to free ions, which involves complete loss of intermolecular ionic interactions ($k_{-d} \approx 1.6 \times 10^{10} \text{ s}^{-1}$),⁶ is similar to the rate constant for inversion of the ion pair, which involves substantial reorganization of the ions but maintains the intermolecular interactions between these ions.

The value of $k_{\text{rac}}/k_{\text{iso}} = 0.54$ reported for the reaction of chiral and ^{18}O -labeled 1-(4-methoxyphenyl)ethyl 4-nitrobenzoate in 90% aqueous acetone is similar to the value $k_{\text{rac}}/k_{\text{iso}} = 0.53$ determined here for the reaction of a different chiral and ^{18}O -labeled substrate in a different solvent. By comparison, the same change in substrate and reaction conditions results in about a 12-fold decrease in the values of both $k_{\text{rac}}/k_{\text{solv}}$ (see above) and $k_{\text{iso}}/k_{\text{solv}}$ for the reaction of the **1-OC(O)C₆F₅** in 50:50 (v/v) trifluoroethanol–water. A detailed analysis of the significance of these results is not possible because of uncertainties about the absolute rate constants for reactions of the ion pair intermediate of solvolysis of 1-(4-methoxyphenyl)ethyl 4-nitrobenzoate in 90% aqueous acetone. However, they suggest that the relative values of the absolute rate constants for the reactions of ion pairs that lead to ^{18}O scrambling and inversion show a low sensitivity to these specific changes in solvent and substrate structure.

Inversion of the ion pair becomes more difficult and then impossible to detect as the carbocation is stabilized and k_{-1} becomes very much smaller than $k_{-d} = 1.6 \times 10^{10} \text{ s}^{-1}$. Similarly, inversion of the ion pair becomes more difficult and then impossible to detect as the carbocation is *destabilized* and k'_s increases to the point where the ion pair undergoes quantitative addition of solvent before significant inversion can occur ($k'_s \gg k_i$). This is the case for solvolysis of (*R*)-1-phenylethanol, which proceeds by a stepwise mechanism, through a 1-phenylethyl carbocation intermediate which is captured by water with an estimated rate constant of $k'_s \approx 1 \times 10^{11} \text{ s}^{-1}$.^{9,15} This 1-phenylethyl carbocation is so reactive that nearly all of the products of its formation from unlabelled

(*R*)-1-phenylethanol in ^{18}O -labeled water result from direct addition of ^{18}O -labeled water, and only a barely detectable 1–3% result from migration of the ^{16}O -labeled water leaving group from the *re* to the *si* face of the carbocation followed by collapse of the ion–dipole pair to form (*S*)-1-phenylethanol.¹⁶ Similarly, internal return to reactant that accompanies the stepwise solvolysis of 1-phenylethyl 4-nitrobenzoate in 70% aqueous acetone does not result in detectable racemization of the remaining ester.¹¹

Stereochemical course of solvolysis

The selectivity for reaction of **1-OC(O)C₆F₅** with methanol and trifluoroethanol, $k_{\text{MeOH}}/k_{\text{TFE}} = 5.3$, in a solvent of 50:45:5 water–trifluoroethanol–methanol is significantly smaller than the selectivity determined for the acid-catalyzed reaction of **1-OH**, $k_{\text{MeOH}}/k_{\text{TFE}} = 7.5$,⁶ under the same conditions. This result shows that partitioning of the ion pair is influenced by the presence of the pentafluorobenzoate leaving group. The smaller value of $k_{\text{MeOH}}/k_{\text{TFE}}$ for reaction of **1-OC(O)C₆F₅** compared with reaction of **1-OH** is consistent with more effective general base catalysis by the pentafluorobenzoate leaving group of addition of trifluoroethanol than addition of methanol to the 1-(4-methylphenyl)ethyl carbocation reaction intermediate, which was observed in earlier studies on bimolecular catalysis by alkyl carboxylate ions of the addition of methanol and trifluoroethanol to the 1-(4-methoxyphenyl)ethyl carbocation.^{17,18} This pentafluorobenzoate leaving group is also expected to provide steric hindrance to frontside addition of solvent.^{19,20} Therefore, the observation that essentially racemic **1-OH** is obtained from the reaction of (*S*)-**1-OC(O)C₆F₅** in 50:50 (v/v) water–trifluoroethanol suggests that steric hindrance by the pentafluorobenzoate leaving group to frontside addition of solvent water to form products of retained configuration is balanced by pentafluorobenzoate leaving group catalysis of the frontside water, so that there are similar values for the rate constants for these reactions.

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