

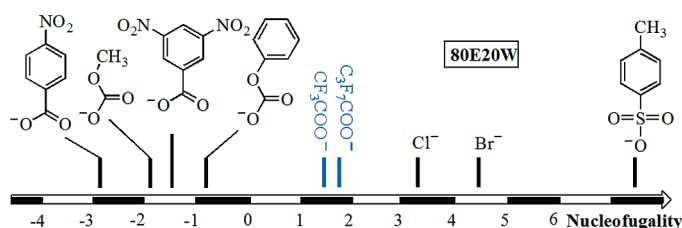
Solvolytic Reactivity of Heptafluorobutyrate and Trifluoroacetates

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A series of X,Y-substituted benzhydryl heptafluorobutyrate (1–6-HFB) and trifluoroacetates (1–6-TFA) were subjected to solvolysis in various methanol/water, ethanol/water, and acetone/water mixtures at 25 °C. The LFER equation $\log k = s_f(E_f + N_f)$ was used to derive the nucleofuge-specific parameters (N_f and s_f) for S_N1 -type reaction. In comparison with TFA, the HFB leaving group is a better nucleofuge for less than 0.5 unit of N_f . X,Y-Substituted benzhydryl trifluoroacetates solvolyze by way of S_N1 reactions unless electron-withdrawing groups are attached to aromatic rings. In such cases the substrates solvolyze faster than predicted for the S_N1 route because of the change in mechanism. X,Y-Substituted benzhydryl heptafluorobutyrate examined here ($E_f \geq -7.7$) solvolyze according to the S_N1 pathway. The almost parallel $\log k$ vs. E_f lines in various solvents for HFBs and TFAs, and the corresponding slope parameters (s_f are in the range of 0.91 and 0.83), indicate early TS with moderately advanced charge separation. NBO charges of HFB and TFA anions and the affinities obtained, all calculated at the PCM-B3LYP/6-311+G(2d,p)//PCM-B3LYP/6-311+G(2d,p) level, revealed that the HFB anion slightly better delocalizes the developing negative charge than TFA, and that the affinity of the benzhydrylium ion is slightly larger toward TFA than toward the HFB anion, which is in accordance with the greater solvolytic reactivity of HFB.

Introduction

Fluorinated esters, particularly heptafluorobutyrate (HFB) and trifluoroacetates (TFA), have been widely used as substrates in solvolytic reactions. For example, in order to investigate the trimethylsilyl group participation in the formation of homoallyl/cyclopropylcarbiny cation, solvolysis of suitable trifluoroacetates was examined recently.¹ The solvolysis rates of adamantyl and *tert*-butyl heptafluorobutyrate and trifluoroacetates in binary aqueous mixtures were measured to examine solvent effects on these leaving groups.² Also, rearrangements of carbocations that arise in solvolysis have been extensively studied by using fluorinated esters as substrates. Thus, the importance of π -conjugative stability in 2-

methylene bicyclic bridgehead compounds was studied by measuring the solvolysis rates of bicyclic compounds with triflates and heptafluorobutyrate as leaving groups.³

However, data about the reactivity HFB and TFA are in discrepancy. Rüchardt et al. stated that heptafluorobutyrate has nucleofugality similar to that of chloride and suggested HFB to be the reagent of choice when reactivity similar to that of chloride was required.⁴ According to data obtained with *tert*-butyl trifluoroacetates,⁵ the authors also estimated HFBs to be about a hundred times more reactive than the corresponding TFAs. On the other hand, Bentley² demonstrated that 1-adamantyl and *tert*-butyl heptafluorobutyrate and trifluoroacetate show relatively low solvolytic reactivity

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TABLE 1. Solvolysis Rate Constants of X,Y-Substituted Benzhydryl Heptafluorobutyrate and X,Y-Substituted Benzhydryl Trifluoroacetates in Various Solvents at 25 °C

| solvent ^a | substrate (X,Y) | E_f^b | k/s^{-1c} | |
|----------------------|-----------------|---------|-----------------------------------|----------------------------------|
| | | | heptafluorobutyrate (HFB) | trifluoroacetate (TFA) |
| 100M | 3 (H, H) | -6.05 | $(8.88 \pm 0.20) \times 10^{-5d}$ | |
| | 4 (4-F, H) | -5.78 | $(1.70 \pm 0.03) \times 10^{-4d}$ | |
| | 5 (4-Me, H) | -4.68 | $(1.62 \pm 0.02) \times 10^{-3d}$ | |
| 90M10W | 2 (4-Cl, H) | -6.52 | $(1.51 \pm 0.05) \times 10^{-4}$ | |
| | 3 (H, H) | -6.05 | $(3.05 \pm 0.06) \times 10^{-4}$ | $(2.56 \pm 0.05) \times 10^{-4}$ |
| | | | $(2.96 \pm 0.09) \times 10^{-4d}$ | |
| | 4 (4-F, H) | -5.78 | $(5.40 \pm 0.09) \times 10^{-4}$ | $(4.65 \pm 0.13) \times 10^{-4}$ |
| | 5 (4-Me, H) | -4.68 | $(5.91 \pm 0.10) \times 10^{-3}$ | $(3.65 \pm 0.07) \times 10^{-3}$ |
| 80M20W | 6 (4-Me, 4-Me') | -3.47 | | $(3.89 \pm 0.09) \times 10^{-2}$ |
| | 1 (3-Cl, H) | -7.74 | $(3.61 \pm 0.01) \times 10^{-5}$ | $(8.64 \pm 0.24) \times 10^{-5}$ |
| | 2 (4-Cl, H) | -6.52 | $(3.63 \pm 0.04) \times 10^{-4}$ | |
| | 3 (H, H) | -6.05 | $(7.10 \pm 0.07) \times 10^{-4}$ | $(5.89 \pm 0.05) \times 10^{-4}$ |
| | 4 (4-F, H) | -5.78 | $(7.14 \pm 0.15) \times 10^{-4d}$ | |
| 70M30W | 5 (4-Me, H) | -4.68 | $(1.36 \pm 0.02) \times 10^{-2}$ | $(8.56 \pm 0.16) \times 10^{-3}$ |
| | 1 (3-Cl, H) | -7.74 | $(7.36 \pm 0.04) \times 10^{-5}$ | $(2.00 \pm 0.01) \times 10^{-4}$ |
| | 2 (4-Cl, H) | -6.52 | $(7.83 \pm 0.13) \times 10^{-4}$ | |
| | 3 (H, H) | -6.05 | $(1.58 \pm 0.02) \times 10^{-3}$ | $(1.29 \pm 0.01) \times 10^{-3}$ |
| | 4 (4-F, H) | -5.78 | $(1.61 \pm 0.05) \times 10^{-3d}$ | |
| 60M40W | 5 (4-Me, H) | -4.68 | $(2.95 \pm 0.01) \times 10^{-3}$ | $(2.37 \pm 0.02) \times 10^{-3}$ |
| | 1 (3-Cl, H) | -7.74 | $(2.72 \pm 0.07) \times 10^{-2}$ | $(1.79 \pm 0.01) \times 10^{-2}$ |
| | 2 (4-Cl, H) | -6.52 | $(1.28 \pm 0.01) \times 10^{-4}$ | $(3.98 \pm 0.06) \times 10^{-4}$ |
| | 3 (H, H) | -6.05 | $(1.58 \pm 0.04) \times 10^{-3}$ | $(1.39 \pm 0.03) \times 10^{-3}$ |
| | 4 (4-F, H) | -5.78 | $(3.16 \pm 0.04) \times 10^{-3}$ | $(2.73 \pm 0.02) \times 10^{-3}$ |
| 100E | 4 (4-F, H) | -5.78 | $(3.03 \pm 0.09) \times 10^{-3d}$ | |
| | 3 (H, H) | -6.05 | $(5.78 \pm 0.09) \times 10^{-3}$ | $(5.08 \pm 0.09) \times 10^{-3}$ |
| | 4 (4-F, H) | -5.78 | $1.20 \times 10^{-5d,e,f}$ | |
| | 5 (4-Me, H) | -4.68 | $3.04 \times 10^{-5d,e,g}$ | |
| | | | $2.84 \times 10^{-4d,e,h}$ | |
| 90E10W | 6 (4-Me, 4'-Me) | -3.47 | $(3.33 \pm 0.08) \times 10^{-3d}$ | |
| | 2 (4-Cl, H) | -6.52 | $(3.92 \pm 0.09) \times 10^{-5d}$ | |
| | 3 (H, H) | -6.05 | $(6.80 \pm 0.01) \times 10^{-5d}$ | |
| | 4 (4-F, H) | -5.78 | $(1.46 \pm 0.01) \times 10^{-4d}$ | |
| | 5 (4-Me, H) | -4.68 | $(1.25 \pm 0.02) \times 10^{-3d}$ | |
| 80E20W | 6 (4-Me, 4'-Me) | -3.47 | $(1.60 \pm 0.03) \times 10^{-2d}$ | |
| | 2 (4-Cl, H) | -6.52 | $(9.06 \pm 0.11) \times 10^{-5}$ | |
| | 3 (H, H) | -6.05 | $(1.70 \pm 0.02) \times 10^{-4}$ | $(1.49 \pm 0.01) \times 10^{-4}$ |
| | 4 (4-F, H) | -5.78 | $(3.69 \pm 0.01) \times 10^{-4}$ | $(3.07 \pm 0.03) \times 10^{-4}$ |
| | 5 (4-Me, H) | -4.68 | $(3.51 \pm 0.01) \times 10^{-4d}$ | |
| 70E30W | 6 (4-Me, 4'-Me) | -3.47 | $(3.13 \pm 0.03) \times 10^{-3}$ | $(2.26 \pm 0.04) \times 10^{-3}$ |
| | 2 (4-Cl, H) | -6.52 | $(3.77 \pm 0.03) \times 10^{-2}$ | $(2.52 \pm 0.01) \times 10^{-2}$ |
| | 3 (H, H) | -6.05 | $(1.63 \pm 0.01) \times 10^{-4}$ | $(2.11 \pm 0.01) \times 10^{-4}$ |
| | 4 (4-F, H) | -5.78 | $(3.11 \pm 0.02) \times 10^{-4}$ | $(2.88 \pm 0.05) \times 10^{-4}$ |
| | 5 (4-Me, H) | -4.68 | $(6.65 \pm 0.06) \times 10^{-4}$ | $(5.83 \pm 0.04) \times 10^{-4}$ |
| 60E40W | 6 (4-Me, 4'-Me) | -3.47 | $(6.62 \pm 0.03) \times 10^{-4d}$ | |
| | 1 (3-Cl, H) | -7.74 | $(5.56 \pm 0.09) \times 10^{-3}$ | $(4.43 \pm 0.03) \times 10^{-3}$ |
| | 2 (4-Cl, H) | -6.52 | $(2.18 \pm 0.02) \times 10^{-5}$ | $(4.49 \pm 0.13) \times 10^{-2}$ |
| | 3 (H, H) | -6.05 | $(2.92 \pm 0.01) \times 10^{-4}$ | $(1.22 \pm 0.01) \times 10^{-4}$ |
| | 4 (4-F, H) | -5.78 | $(5.64 \pm 0.07) \times 10^{-4}$ | $(3.88 \pm 0.05) \times 10^{-4}$ |
| 80A20W | 5 (4-Me, H) | -4.68 | $(5.84 \pm 0.10) \times 10^{-4d}$ | |
| | 4 (4-F, H) | -5.78 | $(1.22 \pm 0.01) \times 10^{-3}$ | $(1.16 \pm 0.00) \times 10^{-3}$ |
| | 5 (4-Me, H) | -4.68 | $(1.20 \pm 0.04) \times 10^{-3d}$ | |
| | 6 (4-Me, 4'-Me) | -3.47 | $(9.55 \pm 0.13) \times 10^{-3}$ | $(8.45 \pm 0.15) \times 10^{-3}$ |
| | 2 (4-Cl, H) | -6.52 | $5.30 \times 10^{-5d,e,i}$ | |
| 70A30W | 3 (H, H) | -6.05 | $(4.86 \pm 0.01) \times 10^{-4d}$ | |
| | 4 (4-F, H) | -5.78 | $(6.26 \pm 0.08) \times 10^{-3d}$ | |
| | 5 (4-Me, H) | -4.68 | $(3.46 \pm 0.03) \times 10^{-5}$ | |
| | 6 (4-Me, 4'-Me) | -3.47 | $(7.64 \pm 0.11) \times 10^{-5}$ | $(6.18 \pm 0.02) \times 10^{-5}$ |
| | 2 (4-Cl, H) | -6.52 | $(1.60 \pm 0.02) \times 10^{-4}$ | $(1.17 \pm 0.02) \times 10^{-4}$ |
| 60A40W | 3 (H, H) | -6.05 | $(1.53 \pm 0.02) \times 10^{-3}$ | $(1.04 \pm 0.02) \times 10^{-3}$ |
| | 4 (4-F, H) | -5.78 | $(1.81 \pm 0.05) \times 10^{-2}$ | $(1.16 \pm 0.01) \times 10^{-2}$ |
| | 5 (4-Me, H) | -4.68 | $(9.24 \pm 0.11) \times 10^{-5}$ | $(1.08 \pm 0.01) \times 10^{-4}$ |
| | 6 (4-Me, 4'-Me) | -3.47 | $(2.02 \pm 0.03) \times 10^{-4}$ | $(1.78 \pm 0.01) \times 10^{-4}$ |
| | 2 (4-Cl, H) | -6.52 | $(4.07 \pm 0.02) \times 10^{-4}$ | $(3.34 \pm 0.03) \times 10^{-4}$ |
| 60A40W | 3 (H, H) | -6.05 | $(3.62 \pm 0.06) \times 10^{-3}$ | $(2.78 \pm 0.06) \times 10^{-3}$ |
| | 4 (4-F, H) | -5.78 | | $(3.04 \pm 0.02) \times 10^{-2}$ |
| | 5 (4-Me, H) | -4.68 | | |
| 6 (4-Me, 4'-Me) | -3.47 | | | |

TABLE 1. Continued

| solvent ^a | substrate (X, Y) | E_f^b | k/s^{-1c} | |
|----------------------|------------------|---------|----------------------------------|----------------------------------|
| | | | heptafluorobutyrate (HFB) | trifluoroacetate (TFA) |
| 50A50W | 1 (3-Cl, H) | -7.74 | | $(1.29 \pm 0.01) \times 10^{-4}$ |
| | 2 (4-Cl, H) | -6.52 | $(2.52 \pm 0.06) \times 10^{-4}$ | $(3.07 \pm 0.05) \times 10^{-4}$ |
| | 3 (H, H) | -6.05 | $(5.64 \pm 0.07) \times 10^{-4}$ | $(5.40 \pm 0.10) \times 10^{-4}$ |
| | 4 (4-F, H) | -5.78 | $(1.18 \pm 0.03) \times 10^{-3}$ | $(1.01 \pm 0.00) \times 10^{-3}$ |
| | 5 (4-Me, H) | -4.68 | $(9.42 \pm 0.07) \times 10^{-3}$ | $(7.60 \pm 0.15) \times 10^{-3}$ |

^aBinary solvents are on a volume–volume basis at 25 °C. A = acetone, E = ethanol, M = methanol, W = water. ^bElectrofugality parameters are taken from ref 6a. ^cAverage rate constants from at least three runs performed at 25 °C unless otherwise noted. Errors shown are standard deviations. ^dBuffered with 2,6-lutidine. ^eExtrapolated from data at higher temperatures by using the Eyring equation. ^f $\Delta H^\ddagger = 99.8 \pm 4.9 \text{ kJ mol}^{-1}$, $\Delta S^\ddagger = -4.5 \pm 14.7 \text{ J K}^{-1} \text{ mol}^{-1}$. ^g $\Delta H^\ddagger = 91.4 \pm 0.2 \text{ kJ mol}^{-1}$, $\Delta S^\ddagger = -24.9 \pm 0.7 \text{ J K}^{-1} \text{ mol}^{-1}$. ^h $\Delta H^\ddagger = 87.4 \pm 2.5 \text{ kJ mol}^{-1}$, $\Delta S^\ddagger = -19.6 \pm 7.4 \text{ J K}^{-1} \text{ mol}^{-1}$. ⁱ $\Delta H^\ddagger = 91.3 \pm 1.3 \text{ kJ mol}^{-1}$, $\Delta S^\ddagger = -20.6 \pm 4.1 \text{ J K}^{-1} \text{ mol}^{-1}$.

in comparison to chlorides and that the rates of HFBs and TFAs in the same solvent agree within a factor of 2.

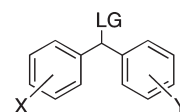
Recently a comprehensive nucleofugality scale has been introduced, developed on benzhydryl derivatives.⁶ According to this approach, because of the linear relationship between logarithms of the rate constants and electrofugalities of substrates in a given solvent, the reaction rate can simply be determined by electrofugality (E_f) of a given electrofuge and nucleofugality (N_f) of the leaving group, according to the following three-parameter LFER eq 1

$$\log k(25^\circ\text{C}) = s_f(E_f + N_f) \quad (1)$$

in which k is the first-order rate constant of the S_N1 reaction, s_f (slope of the correlation line) and N_f (nucleofugality, the negative intercept on the abscissa) are the nucleofuge-specific parameters, and E_f is the electrofugality parameter. Electrofuges are characterized with the E_f parameter only, which is determined with substituents on the benzhydryl system, and nucleofuges are characterized with two parameters, N_f and s_f , which are defined for a combination of the leaving group and a given solvent. The reference E_f values for the series of benzhydrylium ions have been obtained by linear regression of a total of 167 solvolysis rate constants of X,Y-substituted benzhydrylium tosylates, bromides, chlorides, trifluoroacetates, 3,5-dinitrobenzoates, and 4-nitrobenzoates.^{6a} Predefined parameters were $s_f = 1.00$ for chloride nucleofuge in pure ethanol and $E_f = 0.00$ for dianisylcarbenium electrofuge.

The advantage of this method is that it enables measuring of the reaction rates of substrates that have leaving groups of quite different reactivities. This can be achieved by adjusting electrofugality of the substrates with substituents on the aromatic rings, i.e., by combining a weaker benzhydryl electrofuge with a better leaving group or a better electrofuge with a poorer leaving group. Then the nucleofugality parameter can be derived. Since the unit on the N_f scale corresponds to one of order of magnitude in reactivity, comparison of various leaving groups is easy. Useful information about the influence of a given nucleofuge on the transition state can also be deduced from the magnitudes and variations of the reaction constants (s_f values) in different solvents, similarly as from ρ^+ values in the Hammett–Brown correlation. This is because the fundamentals of the E_f

parameters are essentially the same as the fundamentals for σ^+ values in the Hammett–Brown correlation, so the slope parameters (ρ^+ and s_f) measure the same phenomenon.⁷



LG = $\text{CF}_3\text{CF}_2\text{CF}_2\text{CO}_2$ (HFB) and CF_3CO_2 (TFA)

- 1: X = 3-Cl, Y = H
- 2: X = 4-Cl, Y = H
- 3: X = Y = H
- 4: X = 4-F, Y = H
- 5: X = 4Me, Y = H
- 6: X = 4Me, Y = 4Me

To determine the magnitudes of the nucleofugality parameters for fluorinated esters and relate them to N_f values of other commonly used leaving groups, we set out to examine the solvolytic behavior of a series of benzhydryl heptafluorobutyrate and trifluoroacetates kinetically. It turned out that HFBs and TFAs with electrofuges 1–6 have suitable solvolysis rates for conventional methods of measurements. Kinetic data and quantum chemical calculations have been used to gain insight about the relation of their structures to their reactivities.

Results and Discussion

A series of benzhydryl HFBs (1–6-HFB) and benzhydryl TFAs (1–6-TFA) were prepared from the corresponding benzhydrols according to the methods presented in the Experimental Section. The solvolysis rates were measured in various solvents at 25 °C conductometrically (or in a few cases extrapolated from data obtained at higher temperatures). Details are given in the Kinetic Methods in the Experimental Section. The first-order rate constants are presented in Table 1. Quantum chemical calculations were performed to determine the affinity of the TFA and HFB anions toward unsubstituted benzhydrylium carbocation, and also to find structural differences that can account for their relative reactivities.

Kinetic Results. Data in Table 1 show that the reactivities of TFAs and HFBs with the same electrofuges are very similar. Heptafluorobutyrate, whose electrofugality is $E_f \geq -6$, solvolyze somewhat faster than the corresponding trifluoroacetates. However, in a few cases, TFAs that

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generate the least stable carbocations solvolyze faster than the corresponding HFBs.

Logarithms of the first-order rate constants (at 25 °C) measured in a given solvent are plotted against E_f (values of E_f are taken from ref 6a). Plots for HFBs (a) and TFAs (b) are presented in Figure 1 (all other correlation lines can be seen in the Supporting Information). While excellent linear correlation has been obtained with all data collected for HFBs, for TFAs, breakdowns of the $\log k$ vs. E_f plots occur in all solvents studied. Nonlinearity of the $\log k$ vs. E_f plots (similar to the nonlinearity of $\log k$ vs. σ^+ plots in the Hammett–Brown correlation) indicates changes in mechanism of solvolysis of benzhydryl TFAs with weaker electrofuges, i.e., those with electron-withdrawing substituents.

Figure 1 shows that the slopes (s_f) of the $\log k$ vs. E_f correlation lines for TFAs whose electrofugality is $E_f \geq -6$ are similar to those of HFB, while those in the region with E_f below -6 seem to be considerably lower. For the derivation of the nucleofuge-specific parameters for TFA in various solvents, the data for substrates $E_f < -6$ were omitted, since according to definition, s_f is feasible for S_N1 reactions only. The nucleofuge-specific parameters for TFA and HFB in various solvents are shown in Table 2.

Magnitudes of s_f values justify omission of a few data obtained for substrates generating electrofuges with electron-withdrawing groups for TFAs. Thus, the values of the slope parameters obtained for benzhydryl TFAs using the data for substrates with $E_f \geq -6$ ($0.83 \geq s_f \geq 0.87$) only, and that obtained for benzhydryl HFBs using all data available ($0.83 \geq s_f \geq 0.91$), are in the same range as s_f parameters obtained for solvolysis of benzhydryl derivatives with other nucleofuges that solvolyze via the S_N1 path.⁶ On the other hand, the slopes of $\log k$ vs. E_f plots for benzhydryl TFAs with $E_f < -6$ appear to be considerably reduced.

Breakdown of the correlation lines, which indicates that TFAs with weaker electrofuges solvolyze faster than predicted with eq 1, can be rationalized in different ways. First, it can be presumed that fraction of the reaction with such substrates proceeds by nucleophilic attack on the acyl group. The other possible mechanism involves nucleophilic solvent assistance. Thus, while substrates that produce stabilized carbocations solvolyze by the S_N1 route with the expected rate in which only solvation occurs,⁸ solvolysis of the TFAs that produce a less stabilized carbocation is enhanced by nucleophilic participation of the solvent. Similar breakdown of the σ^+, ρ^+ plot has been obtained with benzyl tosylates in aqueous acetone,⁹ in which substrates with electron-donating groups produced considerably steeper σ^+, ρ^+ lines than those with electron-withdrawing groups ($\sigma^+ > 0$). This result was rationalized as switching the mechanism from S_N1 to S_N2 . Even though the mechanism of solvolysis of TFAs with weak electrofuges is yet to be determined, it is more likely that the solvent participation mechanism is operative. It has been shown that trifluoroacetates that have considerable weaker electrofuges than the benzhydrylium ions in the region of the breakdown of the plot follow either k_C displacement reaction (e.g., 1-adamantyl trifluoroacetate) or nucleophilic solvent assisted substitution (e.g., *tert*-butyl

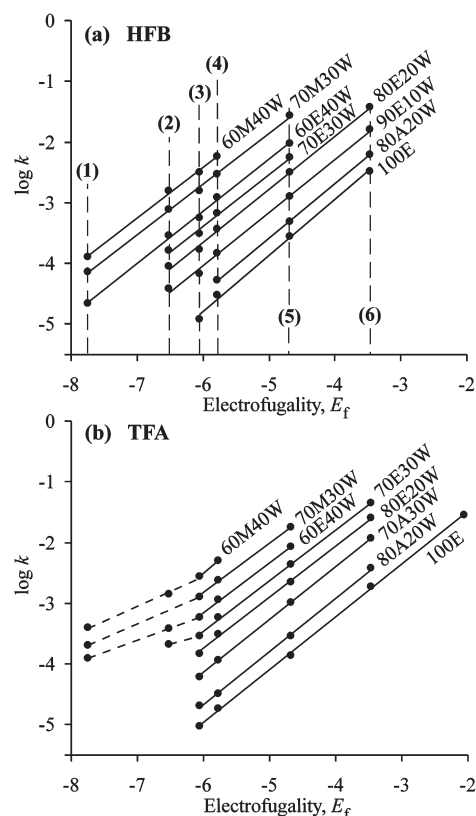


FIGURE 1. Plots of $\log k$ vs. E_f for the solvolysis of X,Y-substituted benzhydryl heptafluorobutyrate (HFB) (a) and benzhydryl trifluoroacetate (TFA) (b) in binary aqueous solvents. Solvent mixtures are given as v/v; solvents: A = acetone, E = ethanol, M = methanol, and W = water.

trifluoroacetate) ($E_f^{\text{adamantyl}} \approx -11$ and $E_f^{t\text{-Bu}} \approx -8$ vs. $E_f \approx -6$),^{6c} and do not solvolyze by nucleophilic attack on the carbonyl group.² The fact that the mechanism of solvolysis of fluorinated esters depends on the structure of the substrate is probably the reason for observed discrepancy of the reactivities.

Having in mind that structures of TFA and HFB leaving groups are similar, one might expect that HFBs which produce less stable carbocations also solvolyze by a different mechanism, which is not the case here. This is probably due to the size of the HFB leaving group, which disables easy approach of the nucleophile to the reaction center. However, it cannot be ruled out that breakdown of the $\log k$ vs. E_f lines for HFBs occurs in the region of lower electrofugality ($E_f < -7.7$).

Once the nucleofugality parameters have been extracted (Table 2), it is easy to compare the abilities of HFB and TFA leaving groups as nucleofuges in various solvents, and also to relate their nucleofugalities to other commonly used leaving groups. Thus, N_f values obtained for HFB and TFA leaving groups are very similar in magnitude, indicating similar reactivities, which is in accordance with Bentley's observation based on solvolysis of the adamantyl derivatives.² According to N_f values, the fluorinated esters ionize approximately 2 orders of magnitude slower than the corresponding chlorides, and approximately 2 orders of magnitude faster than the corresponding phenyl carbonates. Advantageously, the nucleofugalities, and thus the reactivities, of fluorinated

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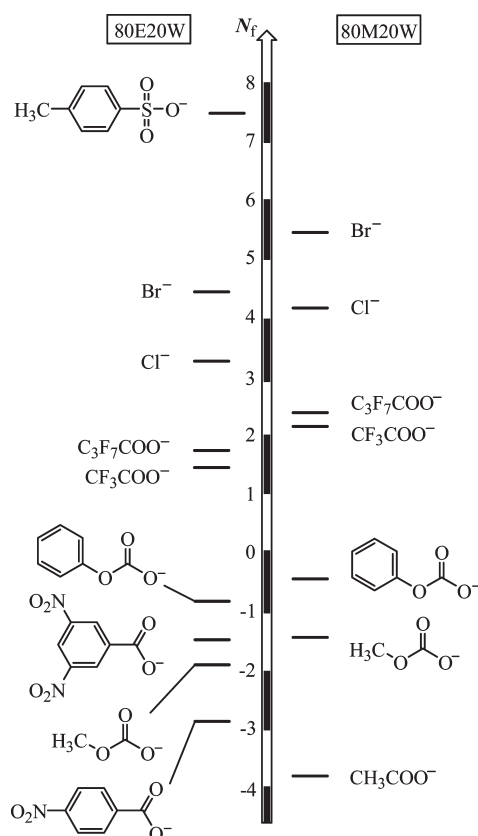
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TABLE 2. Nucleofugality Parameters N_f and s_f for Heptafluorobutyrate and Trifluoroacetate in Various Solvents

| solvent ^a | HFB | | TFA | |
|----------------------|-------------|-------------|--------------------------|--------------------------|
| | N_f^b | s_f^b | N_f^b | s_f^b |
| 100M | 1.63 ± 0.11 | 0.91 ± 0.03 | | |
| 90M10W | 2.12 ± 0.20 | 0.88 ± 0.05 | 1.79 ± 0.04 | 0.84 ± 0.01 |
| 80M20W | 2.38 ± 0.13 | 0.84 ± 0.03 | 2.22 ± 0.10 | 0.84 ± 0.03 |
| 70M30W | 2.76 ± 0.08 | 0.83 ± 0.02 | 2.56 ± 0.11 | 0.82 ± 0.03 |
| 60M40W | 3.11 ± 0.13 | 0.84 ± 0.03 | | |
| 100E | 0.81 ± 0.18 | 0.92 ± 0.04 | 0.30 ± 0.06 ^c | 0.87 ± 0.01 ^c |
| 90E10W | 1.38 ± 0.14 | 0.87 ± 0.03 | | |
| 80E20W | 1.82 ± 0.10 | 0.87 ± 0.02 | 1.58 ± 0.09 | 0.85 ± 0.02 |
| 70E30W | 2.02 ± 0.21 | 0.85 ± 0.05 | 1.87 ± 0.07 | 0.84 ± 0.02 |
| 60E40W | 2.35 ± 0.11 | 0.86 ± 0.02 | 2.20 ± 0.22 | 0.83 ± 0.06 |
| 90A10W | | | 0.12 ± 0.12 ^c | 0.94 ± 0.03 ^c |
| 80A20W | 1.01 ± 0.05 | 0.90 ± 0.01 | 0.70 ± 0.09 ^c | 0.88 ± 0.02 ^c |
| 70A30W | 1.54 ± 0.07 | 0.90 ± 0.02 | 1.26 ± 0.05 | 0.88 ± 0.01 |
| 60A40W | 1.89 ± 0.13 | 0.88 ± 0.03 | 1.70 ± 0.04 | 0.86 ± 0.01 |
| 50A50W | 2.34 ± 0.13 | 0.86 ± 0.03 | 2.12 ± 0.14 | 0.83 ± 0.03 |

^aBinary solvents are v/v at 25 °C. A = acetone, E = ethanol, M = methanol, W = water. ^bErrors shown are standard errors. ^cFrom ref 6a.

**FIGURE 2.** Nucleofugality values (N_f) for some leaving groups in 80% aqueous ethanol and 80% aqueous methanol.

esters fell in the “gap” of ca. four units on the N_f scale between phenyl carbonates and halogens. Figure 2 illustrates the relative reactivities of different leaving groups in 80% aqueous ethanol and in 80% aqueous methanol.

The magnitudes and variations of s_f parameters in S_N1 solvolysis of benzhydryl derivatives are largely defined with

the degree of the solvation of the activated complex, which is, in turn, determined by two major variables, the degree of the charge separation in the transition structure (earlier or later TS)^{9–11} and the degree of the charge delocalization.¹² Clear differentiation between those two influences is difficult, since the net effect is a combination of both. Table 2 shows that the reaction constants s_f for TFAs are slightly but consistently lower than those for HFBs, even though the differences are close to the limits of experimental error. It is likely that somewhat lower s_f values come from the earlier transition state of the slightly more reactive HFBs than that of TFAs.

It has been demonstrated that the variation of the reaction constant s_f of benzhydryl derivatives in various solvents could depend on the leaving group.^{12,13} Thus, while solvolysis of benzhydryl chlorides^{6c} has produced almost parallel lines with s_f close to unity, solvolysis of benzhydryl carbonates and 3,5-dinitrobenzoates¹² has produced log k vs. E_f lines whose slopes decrease as polarity of the solvent increases, i.e., steeper plots were obtained if the fraction of the water in the binary solvent mixture was lower. For example, the s_f values for benzhydryl phenyl carbonates in aqueous ethanol are as follows: $s_f(90EtOH) = 0.93$, $s_f(70EtOH) = 0.83$.¹³ In the later case, the developing negative charge in the TS is almost equally distributed to three carbon atoms of the carbonate moiety, due to resonance and inverse hyperconjugation. Therefore, the importance of solvation is considerably reduced, and the increase of the water fraction in the solvent has less influence on reactivity of such substrates than, e.g., on reactivity of chlorides in which the developed negative charge in the TS is concentrated on the chloride atom only.

Table 2 shows that although the trend of decreasing s_f values exists for both HFBs and TFAs, it is not very pronounced. This indicates charge delocalization to two oxygen atoms only does not diminish the importance of solvation very much. On the other hand, considerably lower slopes for the log k vs. E_f correlation lines of fluorinated esters than that for chlorides indicate that X,Y-substituted benzhydryl TFA and HFB are less sensitive to the substituent change on the benzhydryl rings than X,Y-substituted benzhydryl chlorides. This is probably due to the more reactant-like transition state for the former.

To extract the Grunwald–Winstein m values and get additional information about the sensitivity of different HFBs and TFAs toward solvent polarity, we plotted the logarithms of the rate constants of a given benzhydryl HFB and benzhydryl TFA in a series of aqueous binary solvent mixture against the ionizing power (Y_{OTs}).¹⁴ Table 3 shows m_{OTs} values for 2–6-HFBs and for 3–6-TFAs in the series of aqueous solvents.

For comparison, it should be mentioned that the m_{OTs} values for benzhydryl phenyl carbonates considerably decrease as the electron-donating ability of the substituted benzhydryl rings increases (e.g., $m_{OTs} = 0.83$ for 3-PhCarb, $m_{OTs} = 0.64$ for 6-PhCarb in ethanol/water).¹² For fluorinated esters only a slight decrease in m_{OTs} values occurs, i.e.,

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TABLE 3. Values of m_{OTs} Parameters from the Grunwald–Winstein Correlations for Solvolysis of X,Y-Substituted Benzhydryl Heptafluorobutyrate and Trifluoroacetates

| solvent ^a | $m_{\text{OTs}}^{b,c}$ | | | | | | | | | |
|----------------------|------------------------|----------|----------|----------|----------|----------|----------|----------|---|----------|
| | HFB | | | | | TFA | | | | |
| | 2 | 3 | 4 | 5 | 6 | 3 | 4 | 5 | 6 | |
| M-W | 0.65 (2) | 0.64 (1) | 0.64 (2) | 0.64 (2) | | 0.65 (1) | 0.66 (1) | 0.64 (4) | | |
| E-W | 0.52 (2) | 0.59 (2) | 0.55 (0) | 0.52 (0) | 0.53 (2) | 0.62 (1) | 0.62 (0) | 0.62 (0) | | 0.57 (1) |
| A-W | 0.73 (0) | 0.73 (1) | 0.61 (5) | 0.58 (2) | 0.52 (4) | 0.64 (6) | 0.68 (5) | 0.66 (2) | | 0.58 (3) |

^aBinary solvents are A = acetone, E = ethanol, W = water. ^bObtained from $\log k$ vs. Y_{OTs} plots. ^cThe uncertainties of the last reported figure (standard error) are shown in parentheses.

the sensitivity toward the solvents is almost independent of the benzhydryl structure. The decrease of m_{OTs} as the electrofugality of the substrate increases was taken as an indication of diminished solvation due to charge delocalization in the nucleofuge. Therefore, almost invariant m_{OTs} values indicate that delocalization in the carboxylate moiety does not diminish the importance of solvation very much in HFBs, which is in agreement with the above drawn conclusions based on practically invariant s_f values for HFB. On the basis of the trends of m_{OTs} values and on the above s_f , the same can be concluded for TFAs.

Somewhat higher reactivity of HFBs than TFAs in solvolysis may come from back strain due to the size of HFB, and/or also from different charge distribution in the TS. It has been shown that relief of back strain leads to an early transition state with little charge separation, and therefore an unusually small ρ value.^{10,11} Even though s_f values obtained are almost equal, indicating that the relief of the back strain is probably not a very important parameter that determines the relative reactivities of HFBs and TFAs, it cannot be ruled out that the size of the fluorinated alkyl group does at least partially influence the relative reactivities. Solvolytic reactivity is also in accordance with experimental findings that heptafluorobutyric acid is slightly more acidic than trifluoroacetic acid ($\Delta pK \approx 0.1$),¹⁵ i.e., that the less basic HFB anion is a better leaving group.

Quantum Chemical Calculations. To identify the structural features that are responsible for slightly different nucleofugalities of TFA and HFB, we carried out quantum chemical calculations using the Gaussian 03 program suite.¹⁶ Geometries of **3-TFA** and **3-HFB**, and those of the corresponding anions (trifluoroacetate and heptafluorobutyrate anions, respectively), were fully optimized at B3LYP/6-31G(d,p) levels. For benzhydryl heptafluorobutyrate 14 energy minimum structures were located on the PES, while two structures were located for benzhydryl trifluoroacetate (all

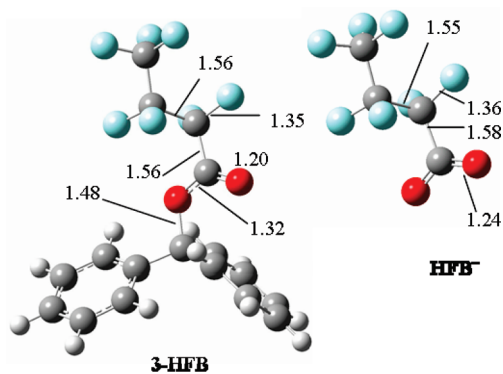
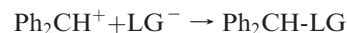


FIGURE 3. Optimized PCM-B3LYP/6-311+G(2d,p) geometries of the most stable conformers of benzhydryl heptafluorobutyrate and heptafluorobutanoate anion with selected bond lengths (angstroms).

presented in the Supporting Information). For the most stable conformers, the geometries were optimized and the frequencies were calculated at the B3LYP/6-311+G(2d,p) level. NBO charges in the gas phase and in ethanol were calculated at the B3LYP/6-311+G(2d,p) level (for complete data see the Supporting Information). The most stable optimized B3LYP/6-311+G(2d,p) structures of benzhydryl heptafluorobutyrate and the HFB anion are presented in Figure 3, along with some parameters.

By using the polarizable continuum model (PCM), the geometries of the most stable conformers of **3-TFA** and **3-HFB** and the corresponding anions, and the benzhydrylium ion in ethanol were optimized at the PCM-B3LYP/6-311+G(2d,p) level.

The affinity of the benzhydrylium cation toward a given leaving group, presented with the following process (LG = TFA and HFB)



is calculated according to eq 2, taking the calculated energies for the most stable conformers:

$$\Delta E_{\text{aff}} = E_{\text{calcd}}(\text{Ph}_2\text{CH-LG}) - [E_{\text{calcd}}(\text{Ph}_2\text{CH}^+) + E_{\text{calcd}}(\text{LG}^-)] \quad (2)$$

The affinities (ΔE_{aff}) are presented in Table 4, along with NBO charge distributions between the carboxylate moiety and the fluorinated alkyl group (R).

Both theoretical results and the charge distribution and affinities of the benzhydrylium ion toward the leaving groups are consistent with experimental findings that HFBs are somewhat more reactive in $S_{\text{N}}1$ reactions. Interestingly, the

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TABLE 4. Calculated Affinities of Benzhydrylium Cation toward Heptafluorobutyrate and Trifluoroacetate Leaving Groups and Group NBO Charges

| leaving group | level of theory | $-\Delta E_{\text{aff}}^a/\text{kJ mol}^{-1}$ | group NBO charges | |
|---------------|--------------------------------------|---|-------------------|--------------------|
| | | | R ^b | carboxylate moiety |
| TFA | PCM-B3LYP/6-311+G(2d,p) ^c | 74.6 | -0.15 | -0.85 |
| | B3LYP/6-311+G(2d,p) | 461.0 | -0.20 | -0.80 |
| HFB | PCM-B3LYP/6-311+G(2d,p) ^c | 72.5 | -0.19 | -0.81 |
| | B3LYP/6-311+G(2d,p) | 445.0 | -0.25 | -0.75 |

^a $\Delta E_{\text{aff}} = E_{\text{calc}}(\text{Ph}_2\text{CH-LG}) - [E_{\text{calc}}(\text{Ph}_2\text{CH}^+) + E_{\text{calc}}(\text{LG}^-)]$. ^bR represents trifluoromethyl group for TFA and the heptafluoropropyl group for HFB. ^cPolarizable continuum solvent model for ethanol.

inductive effect of the seven fluorine atoms on the heptafluoropropyl group (C₃F₇⁻) are somewhat stronger than that of the three fluorine atoms on the trifluoromethyl group (CF₃⁻), although in the later three fluorine atoms are all in the vicinity of the carboxylate group. Thus, the fluorinated propyl group carries slightly more negative charge (-0.19) than the fluorinated methyl group (-0.15) in pure ethanol. Somewhat more intense charge delocalization stabilizes the HFB anion, so the affinity of the benzhydrylium ion toward HFB anion is about 2 kJ mol⁻¹ less than that toward the TFA anion in ethanol (16 kJ mol⁻¹ in vacuum). Therefore, TFAs solvolyze via a slightly higher barrier than HFBs producing a less stabilized anion (for example, in 80% ethanol the rate constants for unsubstituted benzhydryl derivatives indicate that $\Delta\Delta G^\ddagger = 0.5$ kJ/mol at 25 °C).

On the basis of experimental findings, particularly on almost equal s_f parameters for HFBs and TFAs, and on charge distribution obtained computationally, it seems that HFBs are slightly more reactive than TFAs mainly because of more efficient negative charge delocalization rather than relief of back strain.

Experimental Section

Substrate Preparation. Benzhydryl Heptafluorobutyrate (3-HFB). A solution of heptafluorobutyryl chloride (2.5 g, 10.8 mmol) in dry benzene (20 mL) was added dropwise to the previously prepared stirring solution of benzhydrol (1.5 g, 8.1 mmol) and pyridine (1.7 g, 21.5 mmol) in benzene (30 mL). The reaction mixture was stirred for 15 h under an atmosphere of argon at ambient temperature. The solid pyridinium chloride was then removed by filtration, while the excess of pyridine was removed by 5% aq hydrochloric acid (vigorous stirring). The benzene layer was separated and washed with water (2×). After drying over anhydrous sodium sulfate, benzene was evaporated in vacuo to give a pale yellow oil (2.2 g; 5.8 mmol; yield = 71%). Additional purification (column chromatography, preparative chromatography, vacuum distillation) resulted in decomposition of the product. According to the NMR spectrum (see the Supporting Information), the crude product did not contain starting materials or other noticeable impurities.

3-Chlorobenzhydryl heptafluorobutyrate (1-HFB), 4-chlorobenzhydryl heptafluorobutyrate (2-HFB), 4-fluorobenzhydryl heptafluorobutyrate (4-HFB), 4-methylbenzhydryl heptafluorobutyrate (5-HFB), and 4,4'-dimethylbenzhydryl heptafluorobutyrate (6-HFB) were prepared as pale yellow oils according to the procedure described for 3-HFB, yielding 70–81% of the desired products. According to the NMR spectra (see the Supporting Information), the crude products did not contain the starting materials and other noticeable impurities.

Benzhydryl Trifluoroacetate (3-TFA). Benzhydrol (2.0 g; 10.9 mmol) and pyridine (2.5 g; 31.6 mmol) were dissolved in dry benzene (20 mL). A solution of trifluoroacetic anhydride (4.0 g;

19.0 mmol) in dry benzene (30 mL) was then added dropwise. The reaction mixture was heated at 50 °C for 2 h under an atmosphere of argon. After cooling slowly to ambient temperature, 20 mL of water was added, and stirring was continued for 1 h. The aqueous phase was separated and an excess of pyridine in the benzene phase was removed by 5% hydrochloric acid. The organic phase was then washed with water (2×). After drying over anhydrous sodium sulfate, the solvents were evaporated in vacuo yielding a pale yellow oil. After 2 days of standing at 5 °C, the oil was converted into the white solid (2.4 g; 8.6 mmol; yield = 79%).

3-Chlorobenzhydryl trifluoroacetate (1-TFA), 4-chlorobenzhydryl trifluoroacetate (2-TFA), 4-fluorobenzhydryl trifluoroacetate (4-TFA), 4-methylbenzhydryl trifluoroacetate (5-TFA), and 4,4'-dimethylbenzhydryl trifluoroacetate (6-TFA) were prepared as pale yellow oils according to the procedure described for 3-TFA yielding 75–85% of the desired products. According to the NMR spectra (see the Supporting Information), the crude products did not contain the starting materials and other noticeable impurities.

Kinetic Methods. Solvents were purified and dried according to the standard procedures. Freshly prepared solvents (30 mL) were thermostated (± 0.01 °C) at 25 °C for several minutes prior to addition of the substrate. Typically, 20–40 mg of substrate was dissolved in 0.10–0.15 mL of dichloromethane and injected into the solvent. Solvolysis rate constants (± 0.1 °C) were measured conductometrically. An increase of the conductivity during solvolysis was monitored automatically by means of a WTW LF 530 conductometer, using a Pt electrode LTA 1/NS. Individual rate constants were obtained by the least-squares fitting of the conductivity to the first-order kinetic equation for 3–4 half-lives. Rate constants were averaged from at least three measurements.

Calibration showed a linear response of the conductivity toward concentrations of trifluoroacetic and heptafluorobutyric acids. To check the influence of the liberated acids on the solvolytic rate constants, some kinetic runs were repeated in the presence of 2,6-lutidine. The values of the rate constants determined in buffered and unbuffered solutions were identical within experimental error (Table 1).

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Supporting Information Available: Correlations of $\log k$ (25 °C) versus E_f for solvolyses, Grunwald–Winstein correlations for solvolyses, and NMR spectra (¹H, ¹³C, ¹⁹F) of substituted benzhydryl heptafluorobutyrate and benzhydryl trifluoroacetates, quantum chemical calculations, and solvolysis rate constants of substituted benzhydryl heptafluorobutyrate in different solvents at various temperatures. This material is available free of charge via the Internet at <http://pubs.acs.org>.