# Nucleofugality and Nucleophilicity of Fluoride in Protic Solvents

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S *Supporting Information*

ABSTRACT: A series of *p*-substituted benzhydryl fluorides (diarylfluoromethanes) were prepared and subjected to solvolysis reactions, which were followed conductometrically. The observed first-order rate constants $k_1(25\ °C)$ were found to follow the correlation equation $\log k_1(25\ °C) = s_f(N_f + E_f)$, which allowed us to determine the nucleofuge-specific parameters N_f and s_f for fluoride in different aqueous and alcoholic solvents. The rates of the reverse reactions were measured by generating benzhydrylium ions (diarylcarbenium ions) laser flash photolytically in various alcoholic and aqueous solvents in the presence of fluoride ions and monitoring the rate of consumption of the benzhydrylium ions by UV–vis spectroscopy. The resulting second-order rate constants $k_{-1}(20\ °C)$ were substituted into the correlation equation $\log k_{-1} = s_N (N + E)$ to derive the nucleophilicity parameters N and s_N for fluoride in various protic solvents. Complete Gibbs energy profiles for the solvolysis reactions of benzhydryl fluorides are constructed.
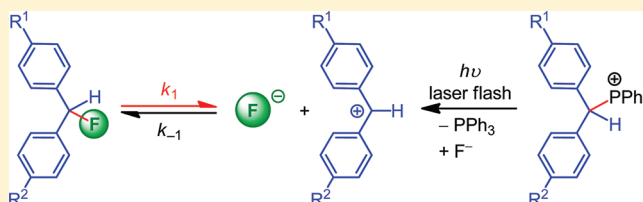
INTRODUCTION

Fluorine is a rare element in organic natural products. Only approximately one dozen organic fluorine compunds are doubtlessly identified.[1–4] More fluorinated compounds that are isolated from natural material, e.g., sponges, probably originate from human sources.[5,6] In contrast, other halides have been detected in several thousand natural products. On the other hand, fluoro-substituted compounds have become highly important in medicinal and agricultural chemistry,[7–13] and 20–25% of the drugs in the pharmaceutical pipeline contain at least one fluorine atom.[12,13] Since the van der Waals radius of fluorine (1.47 Å) is between that of oxygen (1.52 Å) and hydrogen (1.20 Å),[14] incorporation of fluorine into a biologically active substance strongly affects the electronic properties without large changes of its structure. Bioavailability, lipophilicity, blood–brain barrier permeability, and metabolic stability of a pharmaceutically active molecule can, therefore, be customized by incorporation of fluorine. However, incorporation of fluorine into complex organic molecules is often a challenging task for the synthetic chemist.[15–20] Nucleophilic substitutions with [¹⁸F]-fluoride are the key steps in various syntheses of radiopharmaceuticals used in positron emission tomography (PET).[21–26] The low reactivity of the C–F bond has already been recognized by Ingold[27] and Hughes.[28] Consequently, only few quantitative data on the leaving group abilities[29–35] and the nucleophilic reactivities of fluoride are available.[36,37]

In recent years, the Kronja group and we have introduced a novel approach to analyze leaving group abilities in solvolysis reactions.[38–44] By using benzhydrylium ions of variable stabilization as reference electrofuges, we have been able to compare nucleofugalities of anions and neutral leaving groups in different solvents over a wide range of nucleofugality. For the correlation of the solvolysis rate constants k_1 (s⁻¹) we have employed eq 1, where carbocations are characterized by the electrofugality parameter E_f, and combinations of leaving groups and solvents are characterized by the nucleofuge-specific parameters N_f and s_f.

$$\log k_1(25°C) = s_f(N_f + E_f) \qquad (1)$$

So far we had not yet incorporated fluoride into these scales, which presently include parameters for more than 100 leaving group/solvent pairs. In this work, we report on an efficient synthesis of a series of substituted benzhydryl fluorides **2b–f**, the rate constants (k_1) for their solvolyses in various solvents, and the rates (k_{-1}) of the reactions of fluoride ions with benzhydrylium ions (Scheme 1, Table 1) in a variety of solvents.

Scheme 1. Synthesis and Ionization of Benzhydryl Fluorides
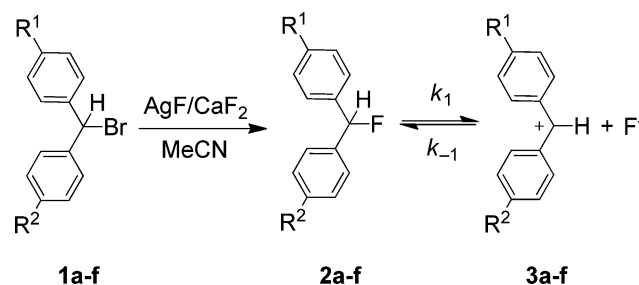
RESULTS

Synthesis of Benzhydryl Fluorides. While Swain and co-workers used hydrogen fluoride for the preparation of trityl

Table 1. Benzhydrylium Ions 3a−l Employed in This Study and Their Electrofugalitites E_f and Electrophilicities E

	R^1	R^2	$E_f{}^a$	E^b
3a	H	H	−6.03	5.90
3b	Me	Me	−3.44	3.63
3c	OMe	H	−2.09	2.11
3d	OMe	Me	−1.23	1.48
3e	OMe	OPh	−0.86	0.61
3f	OMe	OMe	0.00	0.00
3g			0.61	−0.83
3h			1.07	−1.36
3i			1.79	−3.14
3j			3.13	−3.85
3k			3.03	−5.53
3l	NMe₂	NMe₂	4.84	−7.02

^{a}From ref 42. ^{b}From ref 45.

fluoride and the parent benzhydryl fluoride (**2a**) from the corresponding alcohols,[35] Ando avoided the use of hydrofluoric acid by treating benzhydryl bromide with silver fluoride dispersed on calcium fluoride (Scheme 1).[46] Following this procedure, the symmetrical benzhydryl fluorides **2b** and **2f** were synthesized, isolated, and characterized. The liquid **2b** was purified by distillation under high vacuum, and **2f** was recrystallized from dichloromethane/diethyl ether. The other benzhydryl fluorides were not isolated because they decomposed during distillation and did not crystallize readily. They were synthesized in acetonitrile solution (0.2 M) and used for kinetic investigations without prior evaporation of the solvent. In general, great care has to be taken to exclude traces of water and acid during synthesis and handling of these compounds, since traces of acid lead to autocatalytic decomposition of the benzhydryl fluorides.[31]

Kinetics of Benzhydryl Fluoride Solvolyses. When compounds **2b−f** were dissolved in aqueous or alcoholic media, an increase of conductance was observed. As the solvolyses (Scheme 2) of alkyl fluorides are prone to autocatalysis,[31] amines were added to trap the protons and to deprotonate the released hydrofluoric acid quantitatively, thus ensuring a linear dependence of the conductance on the reaction progress. Calibration experiments, i.e., stepwise addition of the rapidly solvolyzing benzhydryl fluoride **2e** to

Scheme 2. Simplified Solvolysis Scheme for S_N1 Reactions of Benzhydryl Fluorides
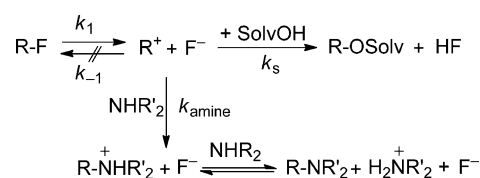
a solution of 80E20W (80% ethanol, 20% water) containing 0.08 M piperidine, showed a linear correlation between the initial concentration of the benzhydryl fluoride **2e** and the conductance at the end of the reaction within the investigated concentration range (see Figure S1 of the Supporting Information). As a consequence, monoexponential increases of the conductance (G) were observed during the solvolysis reactions, and the first-order rate constants k_1 (Table 2) were obtained by

Table 2. Solvolysis Rate Constants k_1 of the Benzhydryl Fluorides 2a−f in Different Solvents (at 25 °C)

solvent^a	ArAr′CHF	k_1 (s^{-1})
methanol (100M)	2f	3.91×10^{-2}
	2e	5.49×10^{-3}
	2d	1.99×10^{-3}
	2c	3.42×10^{-4}
80E20W	2f	7.77×10^{-2}
	2e	1.42×10^{-2}
	2d	4.34×10^{-3}
	2c	7.82×10^{-4}
	2b	5.75×10^{-5}
	2a	2.75×10^{-7b}
ethanol (100E)	2f	4.26×10^{-3c}
	2e	5.63×10^{-4}
	2d	1.63×10^{-4}
60AN40W	2f	8.35×10^{-2}
	2e	9.28×10^{-3}
	2d	4.66×10^{-3d}
	2c	1.01×10^{-3}
	2b	9.98×10^{-5}
80AN20W	2f	7.90×10^{-3}
	2e	1.11×10^{-3}
	2d	4.85×10^{-4}
60A40W	2e	3.55×10^{-3}
	2d	1.87×10^{-3}
	2c	3.80×10^{-4}
	2b	3.28×10^{-5}
80A20W	2f	1.20×10^{-3}
	2e	1.43×10^{-4}
90A10W	2f	9.26×10^{-5}

^{a}Mixtures of solvents are given as (v/v); solvents: A = acetone, AN = acetonitrile, E = ethanol, M = methanol, W = water. ^{b}Rate constant was determined by Swain et al.[35] and not used for the calculation of N_f and s_f parameters. ^{c}Eyring activation parameters: $\Delta H^\ddagger = 62.5$ kJ mol^{-1}, $\Delta S^\ddagger = -81.0$ J mol^{-1} K^{-1}. ^{d}Eyring activation parameters: $\Delta H^\ddagger = 64.1$ kJ mol^{-1}, $\Delta S^\ddagger = -74.7$ J mol^{-1} K^{-1}.

fitting the monoexponential function (eq 2) to the time-dependent conductance G_t.

$$G_t = G_\infty(1 - e^{-k_1 t}) + C \tag{2}$$

The majority of ionization rate constants (k_1) were determined at least at two different concentrations of piperidine (0.08 to 0.16 M, see Supporting Information); for some systems (**2c** and **2e** in 60AN40W and **2d** in 100E) 2,6-lutidine was additionally used as additive for the determination of k_1. In all cases the rate constants varied only within the typical experimental error margin (<13%).

The observation of first-order kinetics and the fact that the observed first-order rate constants are independent of the nature and concentration of the added amines (Figure 1)
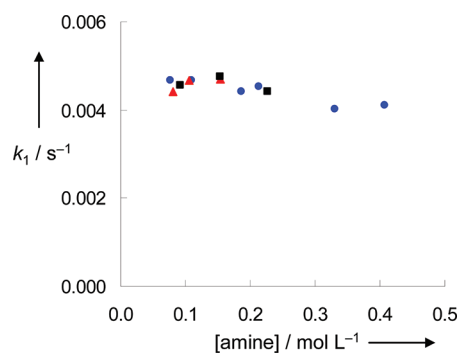

Figure 1. Observed rate constants (k_1) for the solvolysis of **2d** in 60AN40W (60% acetonitrile, 40% water, v/v) at various concentrations of amine (▲, triethylamine; ■, 2,6-lutidine; ●, piperidine).

indicate that the observed first-order rate constants equal k_1. If common-ion return would occur ($k_{-1}[F^-] \approx k_s$), an increase of the piperidine concentration would lead to an increase of the overall rate because trapping of the carbocation by the amine (k_{amine}) would suppress the ion recombination. The second-order rate law for an S_N2 reaction requires a linear increase of k_{obs} with the concentration of the amine, which can be excluded from the data shown in Figure 1.

Plots of log k_1 for the solvolyses of **2b−f** in various solvents versus the electrofugality parameters E_f of the benzhydrylium ions are linear (Figure 2), indicating the applicability of eq 1.
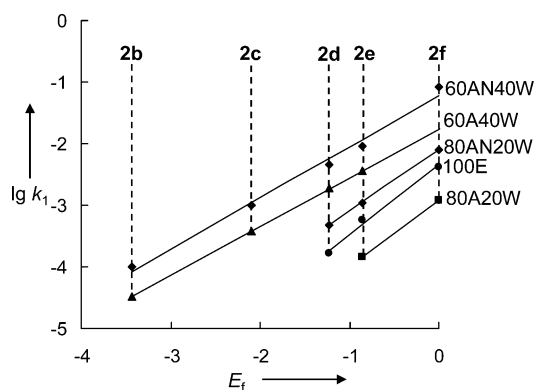

Figure 2. Plots of log k_1 for the solvolysis reactions of various benzhydryl fluorides versus the electrofugalities E_f. The correlation lines for 80E20W and 100M are shown in Figure S8 of the Supporting Information. Mixtures of solvents are given as (v/v); solvents: A = acetone, AN = acetonitrile, E = ethanol, M = methanol, W = water.

From these correlations, obtained for the fluoride leaving group ability in different protic solvents, one can extract the nucleofugality parameters, N_f, as the negative intercepts on

the abscissa (E_f axis) and the s_f parameters as the slopes of the correlation lines (Table 3).

Table 3. Nucleofuge-Specific Parameters N_f and s_f for the Fluoride Anion in Various Solvents

solvent	$N_f{}^a$	$s_f{}^a$
100M	−1.44	0.99
80E20W	−1.24	0.92
100E	−2.08	1.13
60AN40W	−1.47	0.83
80AN20W	−2.13	0.99
60A40W	−2.23	0.79
80A20W	−2.72	1.07

$^a N_f$ and s_f are defined in eq 1.

The rate constant $k_1{}^{calcd} = 2.05 \times 10^{-7}$ s^{-1} for the solvolysis of **2a** calculated by using eq 1, the nucleofugality parameters for fluoride in 80E20W (Table 3), and the electrofugality parameter for the unsubstituted benzhydryl cation **3a** (Table 1) is in excellent agreement with the previously reported experimental rate constant of 2.75×10^{-7} s^{-1},[35] which demonstrates the power of eq 1 and the practicability of these parameters.

Nucleophilicity of Fluoride Anions in Various Solvents. It is well-known that nucleophilicity is not simply the reverse of nucleofugality,[42] and therefore, the nucleophilic reactivity of the fluoride anion has been determined separately. Previously, we determined the nucleophilicity parameters N and s_N of chloride and bromide in various solvents[47] by measuring the rate constants k_{-1} (M^{-1} s^{-1}) of their reactions with benzhydrylium ions and correlation of the data by eq 3. As demonstrated previously, rate constants of the reactions of carbocations with charged and neutral nucleophiles can be expressed by eq 3, where k_{-1} is the second-order rate constant at 20 °C, s_N is a nucleophile-specific slope parameter, N is a nucleophilicity parameter, and E is an electrophilicity parameter.[45]

$$\log k_{-1}(20\,°C) = s_N(N + E) \qquad (3)$$

We now used laser flash photolysis and stopped-flow techniques to characterize the nucleophilic reactivity of fluoride ions by measuring the rates of their reactions with benzhydryl cations **1b−l** in a series of solvents.

The benzhydryltriphenylphosphonium tetrafluoroborates **4b−h** (Scheme 3), which were employed as precursors for

Scheme 3. Precursors 4b−j for the Laser-Flash Photolytic Generation of the Benzhydrylium Ions 3b−j^a
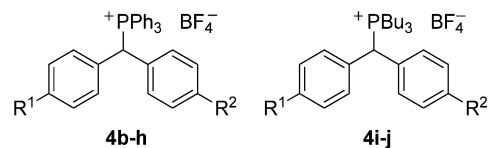
^{a}Substituents R^1 and R^2 are defined in Table 1.

the laser flash-photolytic generation of benzhydryl cations, were prepared by treating the corresponding benzhydrols with equimolar amounts of triphenylphosphane and aqueous tetrafluoroboric acid, followed by heating to 140−180 °C.[48] The benzhydryltributylphosphonium tetrafluoroborates **4i** and **4j** were prepared in acetonitrile solution by adding tributylphosphane to the corresponding benzhydrylium tetrafluoroborates **3i,j**

Table 4. Rate Constants for the Reactions of Benzhydrylium Ions 3b−l with Fluoride (k_{-1}) and Pure Solvent (k_s)[a]

solvent (N_1, s_N)	Ar$_2$CH$^+$	E	k_{-1} (M^{-1} s^{-1})	k_s^{exp} (s^{-1})	$k_s^{calcd\ by\ eq\ 1}$ (s^{-1})	k_s^{exp}/k_s^{calcd}
100M (7.54, 0.92)	3h	−1.36	1.56×10^6	7.39×10^5	4.85×10^5	1.5
	3g	−0.83	4.12×10^6	2.44×10^6	1.49×10^6	1.6
	3f	0.00	1.14×10^7	9.91×10^{6b}	8.65×10^6	1.1
	3e	0.61	c	1.97×10^7	3.15×10^7	0.63
80E20W (6.68, 0.85)	3g	−0.83	3.83×10^6	4.87×10^5	9.39×10^4	5.2
	3f	0.00	1.06×10^7	1.66×10^6	4.76×10^5	3.5
100W (5.20, 0.89)	3f	0.00	1.09×10^5	1.79×10^{5d}	4.25×10^4	4.2
	3d	1.48	1.02×10^6	1.02×10^{6d}	8.81×10^5	1.2
10AN90W (5.16, 0.91)	3f	0.00	1.37×10^5	1.40×10^{5e}	4.96×10^{4f}	2.8
	3e	0.61	3.28×10^5	3.15×10^{5e}	1.78×10^{5f}	1.8
	3d	1.48	1.20×10^6	1.04×10^{6e}	1.10×10^{6f}	0.94
60AN40W (5.02, 0.90)	3h	−1.36	1.66×10^5	1.14×10^4	1.97×10^{3g}	5.8
	3g	−0.83	3.94×10^5	3.16×10^4	5.90×10^{3g}	5.4
	3f	0.00	1.82×10^6	9.61×10^4	3.30×10^{4g}	2.9
	3e	0.61	4.36×10^6	2.81×10^5	1.17×10^{5g}	2.4
	3d	1.48	9.04×10^6	1.03×10^6	7.08×10^{5g}	1.5
	3b	3.63	2.0×10^{8h}	3.35×10^7	6.10×10^{7g}	0.55
80AN20W (5.02, 0.89)	3h	−1.36	6.72×10^5	9.38×10^3	1.81×10^3	5.2
	3g	−0.83	1.72×10^6	3.08×10^4	5.36×10^3	5.7
	3f	0.00	5.10×10^6	9.49×10^{4i}	2.94×10^4	3.2
	3e	0.61	9.76×10^6	2.52×10^5	1.02×10^5	2.5
90AN10W (4.56, 0.94)	3h	−1.36	2.89×10^6	7.05×10^{3j}	1.02×10^3	6.9
	3g	−0.83	6.03×10^6	2.12×10^4	3.21×10^3	6.6
	3f	0.00	1.85×10^7	6.78×10^{4j}	1.93×10^4	3.5
98AN2W	3l	−7.02	1.97×10^3	k		
	3k	−5.53	2.95×10^4	k		
	3j	−3.85	4.17×10^5	k		
	3i	−3.14	2.31×10^6	k		
	3h	−1.36	1.12×10^8	k		
	3g	−0.83	1.40×10^8	k		
	3f	0.00	2.69×10^8	k		
	3c	2.11	2.40×10^9	3.85×10^5		
	3b	3.63	8.63×10^9	6.18×10^6		

[a]Mixtures of solvents are given as (v/v); solvents: AN = acetonitrile, E = ethanol, M = methanol, W = water. [b]Calculated from the intercept of plots of k_{obs} vs [F$^-$]. Previously $k_s = 8.4 \times 10^6$ s^{-1} has been reported in ref 52. [c]The rate constant k_{-1} could not be determined because the slope in the plot of [F$^-$] versus k_{obs} was too small. [d]Calculated from the intercept of plots of k_{obs} vs [F$^-$]. In ref 53, $k_s = 1.0 \times 10^5$ and 7.8×10^5 s^{-1} have been reported for 3f and 3d in 100W, respectively. [e]Calculated from the intercept of plots of k_{obs} vs [F$^-$]. In ref 51, $k_s = 9.55 \times 10^4$ and 7.99×10^5 s^{-1} have been reported for 3f and 3d in 9AN91W, respectively. [f]The N_1 and s_N parameters from ref 51 were used for the calculation of k_s^{calcd}. [g]The N and s_N parameters for 67AN33W from ref 51 were used for the calculation of k_s^{calcd}. [h]This value has to be considered approximate due to the low slope of the k_{obs} vs [F$^-$] plot. [i]In ref 51, $k_s = 9.82 \times 10^4$ s^{-1} has been reported for 3f in 80AN20W. [j]In ref 51, $k_s = 7.11 \times 10^2$ and 9.87×10^4 s^{-1} have been reported for 3h and 3f in 90AN10W, respectively. [k]Not determined.

until complete decolorization was achieved. The stabilized benzhydrylium tetrafluoroborates 3i−l were prepared as previously described.[45]

The choice of suitable sources of fluoride anions is not trivial. For the kinetic investigations in methanol, water, and 10AN90W, we used potassium and cesium fluoride, which were sufficiently soluble in these solvents. Methanol was the only anhydrous solvent, where both potassium fluoride and cesium fluoride could be used as fluoride source. In other anhydrous solvents, such as acetonitrile, the solubility of alkali fluorides is too low for kinetic studies. Unlike tetrabutylammonium chloride and bromide, which we used in the previous study,[47] anhydrous tetrabutylammonium fluoride is prone to elimination and is stable for only several hours at room temperature.[49] Therefore, we used the commercially available tetrabutylammonium fluoride trihydrate, which did not allow us to characterize fluoride in anhydrous solvents. Tetrabutylammonium fluoride trihydrate was exclusively used as fluoride source for the investigations in the aqueous solvent mixtures (98AN2W, 90AN20W, 80AN20W, 60AN40W, 80E20W)

because we observed phase separation when trying to dissolve potassium fluoride in these mixtures.

The benzhydrylium ions 3b−j were generated in these solvents by irradiation of 4b−j with a 7 ns laser pulse from the fourth harmonic (266 nm) of a Nd/YAG laser.[48,50] In the absence of added nucleophiles, we typically observed monoexponential decays of the absorbances of 3b−j. Fitting of the single exponential function $A_t = A_0\ e^{-k_{obs}t} + C$ provided the first-order rate constants for the reactions of 3b−j with the solvents, k_s, which are listed in Table 4. When the carbocations were generated in the presence of added fluoride, the observed rate constants increased linearly with the concentration of added fluoride (Figure 3). As expressed by eq 4, the observed pseudo-first-order rate constants k_{obs} are the sum of a second-order term for the reactions of the carbocations with fluoride ions (k_{-1} in Scheme 2) and a first-order term for the reactions of the carbocations with the solvents (k_s).
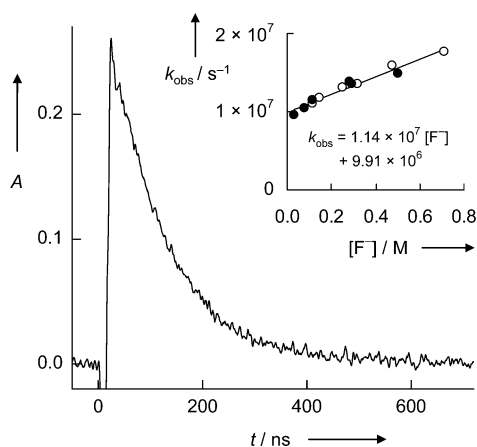
$$k_{obs} = k_{-1}[F^-] + k_s \qquad (4)$$

Figure 3. Decay of the absorption of **3f** in methanol, observed at 500 nm in the presence of 0.3 M CsF. Inset: Determination of k_{-1} from a plot of k_{obs} against the fluoride ion concentration. Alternatively, KF (○) and CsF (●) were used as the fluoride source.

Plots of k_{obs} versus the fluoride concentrations resulted in linear correlations according to eq 4 as exemplified in Figure 3. The second-order rate constants k_{-1} for the reactions with fluoride listed in Table 4 were obtained from the slopes of these plots. The intercepts correspond to the background reaction with the solvent (k_s), which were also determined independently (Table 4). Table 4 demonstrates the good agreement of the experimental data with the values calculated from eq 3 using the previously published N_1 and s_N parameters of the solvents.[51]

As the fluoride anion is a weak base, we had to make sure that fluoride and not hydroxide was the acting nucleophile in aqueous solvents. For the reaction of the bisanisyl carbenium ion (**3f**) with fluoride in water, we used fluoride concentrations ranging from 0.06 to 0.91 M. From pK_b for fluoride in water (10.9), one calculates concentrations of hydroxide from 0.87×10^{-6} to 3.4×10^{-6} M. With eq 3 and the published nucleophilicity parameters for hydroxide in water ($N = 10.47$, $s_N = 0.61$)[54] we can calculate hypothetical pseudo-first-order rate constants $k_{1\Psi}(OH^-) = 2.1$ to 8.3 s^{-1} for the reaction of **3f** with hydroxide at the above-mentioned concentrations of fluoride. As shown in the Supporting Information, rate constants k_{obs} of $(1.84-2.80) \times 10^5$ s^{-1} were observed for the reaction of the bisanisyl carbenium ion (**3f**) with fluoride. Therefore, the nucleophilic reactivity of the hydroxide anion can be neglected for the evaluation of the kinetic experiments.

Further evidence that fluoride, and not hydroxide, was the active nucleophile was obtained by a ^{1}H NMR spectroscopic product analysis. A solution of 4,4′-dimethylbenzhydryl chloride ((tol)$_2$CHCl) in deuterated acetonitrile was combined with a solution of tetrabutylammonium fluoride trihydrate in aqueous acetonitrile to yield a solution of 0.15 M 4,4′-dimethylbenzhydryl chloride and 0.54 M tetrabutylammonium fluoride in 60% aqueous acetonitrile (60AN40W). In line with a calculated solvolysis rate constant of $k_1 \approx 2.4$ s^{-1} at 25 °C,[55] (tol)$_2$CHCl was not observable in a ^{1}H NMR spectrum taken immediately after mixing the two solutions. As depicted in Figure 4, the characteristic doublet at $\delta = 6.46$ (d, 1 H, $^3J_{HF} = 46.0$ Hz, CHF) for **2b** and singlet at $\delta = 5.69$ indicated a 2.4/1 ratio of **2b** and 4,4′-dimethylbenzhydrol. As the benzhydryl fluoride **2b** will solvolyze with a half-life of 1.9 h under these conditions (Table 2), the observed 4,4′-dimethylbenzhydrol cannot arise from hydrolysis of **2b**. Hence, the observed product ratio reflects
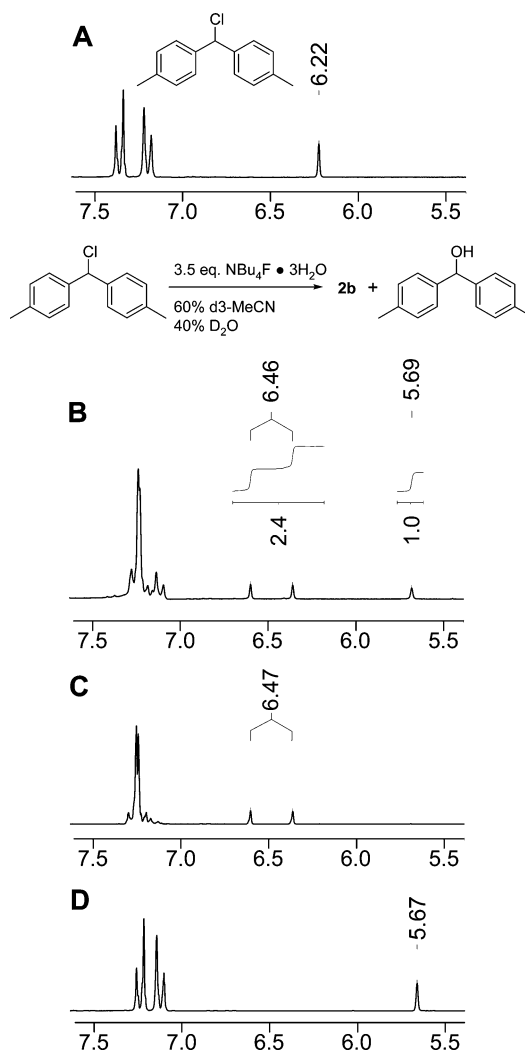

Figure 4. ^{1}H NMR spectra (200 MHz) recorded for product analysis: (A) (tol)$_2$CHCl in CD$_3$CN; (B) ^{1}H NMR spectrum recorded 5 min after combining (tol)$_2$CHCl with 3.5 equiv of tetrabutylammonium fluoride trihydrate in 60AN40W (deuterated solvents); (C) (tol)$_2$CHF (**2b**) in CD$_3$CN; (D) (tol)$_2$CHOH in 60AN40W (deuterated solvents).

the relative reactivities of the benzhydryl cation **3b** toward F$^-$ and H$_2$O (OH$^-$ negligible as discussed above). This ratio shall be compared with the ratio of the absolute rate constants for the reaction of **3b** with F$^-$ and H$_2$O. The second-order rate constant for the reaction of **3b** with fluoride in 60AN40W has been determined ($k_{-1} = 2.0 \times 10^8$ M^{-1} s^{-1}).[56] The rate constant for the reaction of **3b** with 60% aqueous acetonitrile is 3.35×10^7 s^{-1} (see Table 4). According to the ^{1}H NMR spectrum, 70% of (tol)$_2$CHCl ($c_0 = 0.15$ M) are converted into the benzhydryl fluoride **2b**. Thus, the average concentration of fluoride $[F^-]_{av}$ during the reaction is 0.49 M (eq 5).

$$[F^-]_{av} = [F^-]_0 - 0.5[2b]$$
$$= (0.54 - 0.5 \times 0.70 \times 0.15) \ M = 0.49 \ M \quad (5)$$

Multiplication of the second-order rate constant (k_{-1}) for the reaction of **3b** with $[F^-]_{av}$ yields the pseudo-first-order rate constant for the reaction of **3b** with F$^-$, which is divided by k_s

to yield an expected product ratio of 2.9/1 (eq 6), in fair agreement with the product ratio observed by ^1H NMR (2.4).

$$\frac{[2b]}{[(tol)_2CHOH]} = \frac{k_{-1}[F^-]_{av}}{k_s} = \frac{2.0 \times 10^8 \times 0.49}{3.4 \times 10^7} = 2.9$$

(6)

A more accurate comparison of the kinetic results with the ^1H NMR product analysis is provided in the Supporting Information.

When plotting log k_{-1} for the reactions of F^- with benzhydryl cations against the electrophilicities E of the corresponding benzhydryl cations, linear correlations according to eq 3 were obtained (Figure 5). In 98AN2W solution, we could determine
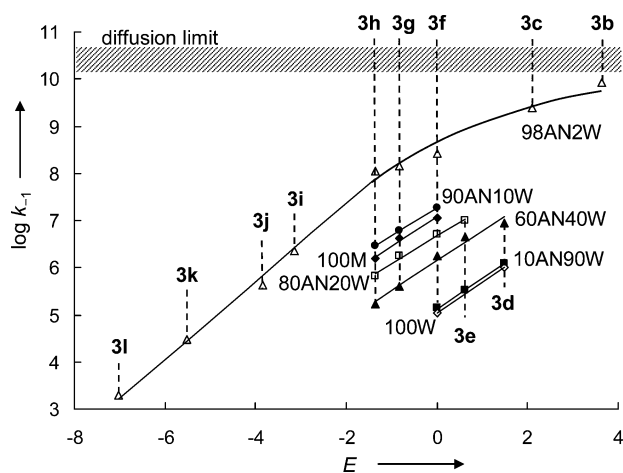
Figure 5. Plot of log k_{-1} for the reactions of benzhydrylium ions with fluoride ions versus their electrophilicity parameters E. Mixtures of solvents are given as (v/v); solvents: AN = acetonitrile, M = methanol, W = water.

absolute rate constants for the reactions of fluoride with a wide variety of benzhydrylium ions. The rate constants for the reactions of fluoride with **3k** and **3l**, determined by the stopped-flow method, lie on the same graph as the rate constants for the reactions of **3b–j**, which were determined by the laser flash photolysis technique, demonstrating the consistency of the results obtained by the different methods (Figure 5). The linear correlation for the rate constants for **3 h–l** bends downward as k_{-1} exceeds 10^8 M^{-1} s^{-1} due to the proximity of the diffusion limit (ca. 2×10^{10} M^{-1} s^{-1}). An analogous behavior was observed for numerous other nucleophiles.[57]

Only a narrow range of carbocations could be investigated in solvent mixtures containing a higher percentage of water or alcohols. The reactions of fluoride with the more stabilized benzhydrylium ions ($E < -2$) do not proceed quantitatively, and the fast reversible reactions with F^- have to compete with the slower but irreversible reactions with water or methanol giving rise to kinetics that are difficult to evaluate. On the other hand, the reactions of fluoride with the less stabilized benzhydrylium ions ($E > 2$) are difficult to follow, because for highly electrophilic carbocations the major fraction of k_{obs} (eq 4) is due to the reaction of the benzhydrylium ion with the solvent. As shown for the example of methanol in Figure 6 the rate constants for the reactions of **3** with the solvents are more sensitive toward variation of the electrophiles than those of the reactions of **3** with fluoride (fluoride has a lower s_N parameter
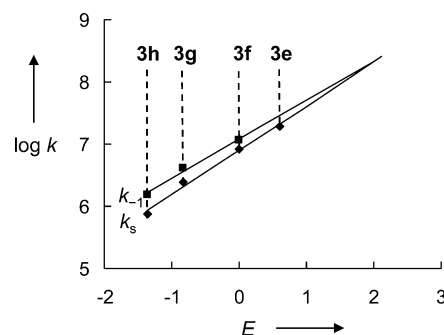

Figure 6. Plot of log k_{-1} (■) and log k_s (◆) for the reactions of benzhydrylium ions with fluoride ions and methanol versus their electrophilicity parameters E.

in eq 3, see below), with the consequence that the accurate determination of the small contribution of the $k_{-1}[F^-]$ term becomes difficult.

Another limitation of the laser flash photolytic technique is the recombination of the benzhydrylium ions with the phosphine photoleaving group. For that reason, we could not determine rate constants $k_{obs} < 10^5$ s^{-1} in 100W and in 10AN90W.

Plots of the second-order rate constants k_{-1} for the reactions of **3** with fluoride (Table 4) against the electrophilicity parameters E of the benzhydrylium ions were linear (Figure 5) for rate constants k_{obs} up to 1×10^8 s^{-1} and yielded the s_N parameters and the nucleophilicity parameters N of fluoride in methanol and aqueous solvents (Table 5). Rate constants log

Table 5. Nucleophilicity Parameters N and s_N for Fluoride in Various Solvents

solvent[a]	N	s_N
100M	11.31	0.63
80E20W	(13.2)[b]	(0.53)[b]
100W	(7.7)[b]	(0.66)[b]
10AN90W	8.05	0.64
60AN40W	9.75	0.63
80AN20W	11.40	0.59
90AN10W	12.27	0.59
98AN2W	10.88	0.83

[a]Mixtures of solvents are given as (v/v); solvents: AN = acetonitrile, E = ethanol, M = methanol, W = water. [b]Correlation based on only two data points.

$k_{obs} > 8.0$ were not used for the determination of reactivity parameters N and s_N as these reactions approach the diffusion limit (see above).

■ DISCUSSION

With the nucleofugality parameters (N_f, s_f) listed in Table 3, it now becomes possible to directly compare the leaving group abilities of fluoride and those of other common leaving groups in different solvents. As $s_f \approx 1$, a general overview can be derived from the N_f parameters,[42] some of which are compared in Table 6. Depending on the solvent, fluoride is a slightly weaker or better leaving group than 3,5-dinitrobenzoate.[42]

Replacing fluoride by chloride accelerates the solvolysis reactions approximately by 4–5 orders of magnitude, while replacing fluoride by bromide results in an acceleration of approximately 5–6 orders of magnitude. Thus the unsubstituted

Table 6. Comparison of Nucleofugalities N_f of Important Leaving Groups in Different Solvents and Solvolysis Half Lives of Ph$_2$CHX in 80E20W at 25°C

solvent	leaving group X			
	DNB[a]	F	Cl	Br
80A20W	−2.34	−2.72	2.03	3.01
100E	−2.05	−2.08	1.82	2.93
80E20W	−1.43	−1.24	3.24	4.36
$\tau_{1/2}$[b]	164 d	39 d	7 min	27 s

[a]DNB = 3,5-dinitrobenzoate. [b]Solvolysis half-life of Ph$_2$CHX in 80% aqueous ethanol (80E20W) at 25 °C calculated by eq 1 by using E_f(3a) = −6.03 from Table 1, N_f from this table, and s_f = 0.98 (for DNB), 0.92 (for F), 0.99 (for Cl), and 0.95 (for Br); s_f for DNB, Cl, and Br from ref 42.

benzhydryl fluoride will solvolyze in 80E20W with a half-life of 1 month, whereas the half-life is 7 min for benzhydryl chloride, 27 s for benzhydryl bromide, and only 50 ms for the parent benzhydryl tosylate (not shown in Table 6). These findings are in agreement with previous results by Swain and Scott who reported chloride/fluoride ratios of 10^6 and 10^5 for the couples trityl chloride/trityl fluoride (85% aq acetone) and *tert*-butyl chloride/*tert*-butyl fluoride (80% aq ethanol).[19] The poor nucleofugality of F$^−$ is commonly attributed to the high C−F bond energy. Table 7 shows a further reason: The

Table 7. Eyring Activation Parameters for the Solvolyses of Benzhydryl and *tert*-Butyl Halides in Different Solvents

entry	substrate	solvent[a]	$\Delta H^{\ddagger}$ (kJ mol^{-1})	$\Delta S^{\ddagger}$ (J mol^{-1} K^{-1})
1	Ar$_2$CHF (**2d**)	60AN40W	64.1	−74.7
2	(3-FC$_6$H$_4$)PhCH-Cl[b]	60AN40W	83.0	−34.6
3	(3-FC$_6$H$_4$)PhCH-Br[b]	60AN40W	86.5	0.55
4	*tert*-butyl chloride[c]	80A20W	90.3	−51.6
5	*tert*-butyl bromide[c]	80A20W	85.1	−35.0

[a]Mixtures of solvents are given as (v/v); solvents: A = acetone, AN = acetonitrile, W = water. [b]This work (Supporting Information). [c]Data from ref 58.

activation entropies for the solvolysis reactions of benzhydryl fluorides are considerably more negative than those of benzhydryl chlorides and bromides. Thus, entries 1−3 show that in 60% aqueous acetonitrile, $\Delta S^{\ddagger}$ becomes more negative in the series Ar$_2$CHBr to Ar$_2$CHCl and Ar$_2$CHF. The same trend, more negative entropy of activation for R-Cl than for R-Br, has also been observed in the *tert*-butyl series (entries 4 and 5). The higher degree of solvent orientation needed for the solvation of fluoride ions is in line with the relative hydration energies for halide ions (−$\Delta H_h°$), which increase from I$^−$ (294 kJ mol^{-1}), Br$^−$ (335 kJ mol^{-1}), Cl$^−$ (366 kJ mol^{-1}) to F$^−$ (502 kJ mol^{-1}).[26]

As illustrated for the 4,4'-dimethyl-substituted benzhydryl derivatives tol$_2$CH-X in Figure 7, the leaving group abilities increase significantly in the series F$^−$ ≈ DNB ≪ Cl$^−$ < Br$^−$, but the exact ranking depends on the solvent.

As previously reported for several other leaving groups,[42,59] the sensitivity parameters s_f of fluoride decrease slightly with increasing water content of the solvents. Since the carbocation character is not fully developed in most of the benzhydryl fluoride solvolyses investigated in this work (see below), the trend in s_f might be explained by a smaller degree of charge separation in the transition states in solvents with a high percentage of water. As analogous trends in s_f are also observed
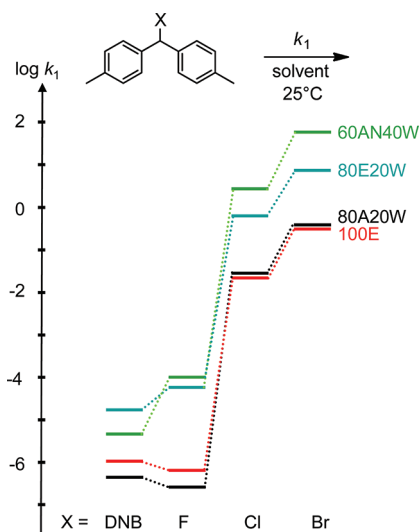

Figure 7. Comparison of the solvolysis rates (at 25 °C) for the reactions of the 4,4'-dimethyl-substituted benzhydryl derivative tol$_2$CH-X with different leaving groups X (DNB = 3,5-dinitrobenzoate). Mixtures of solvents are given as (v/v); solvents: A = acetone, AN = acetonitrile, E = ethanol, W = water.

in solvolyses of benzhydryl chlorides and bromides, where the ion combination is diffusion-limited, i.e., where the transition states correspond to the carbocations, other factors must contribute.[42]

Fluoride is not only a poorer nucleofuge than the other halide ions but also a poorer nucleophile in protic solvents. As shown in Figure 8, nucleophilicity increases in the series
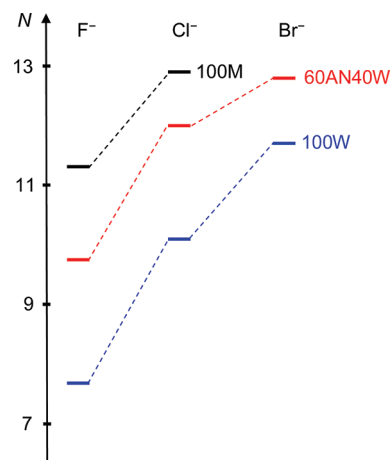

Figure 8. Comparison of the nucleophilic reactivities of fluoride with those of other halide anions in different solvents. Mixtures of solvents are given as (v/v); solvents: AN = acetonitrile, M = methanol, W = water.

F$^−$ < Cl$^−$ < Br$^−$ in water, aqueous acetonitrile, and methanol.[47] The variable sensitivities s_N for fluoride in different solvents (Table 5) imply that the relative reactivities depend slightly on the nature of the electrophile, which is also illustrated in Figure 5. The bis-dihydrofuranyl annelated benzhydrylium ion **3h**, for example, reacts 10^4 times faster with F$^−$ in 98% acetonitrile/2% water than in 100% water. One can extrapolate that in a solution containing 15% water F$^−$ has a reactivity in between that of 98% acetonitrile/2% water and 100% water. Because of the problems obtaining anhydrous F$^−$,[49] we refrain to present a number for

anhydrous acetonitrile. A strong reduction of the nucleophilic reactivity of fluoride ions by water molecules has also been observed in S_N2 reactions.[36]

The low nucleophilicity of fluoride in protic solvents compared to chloride and bromide accounts for the fact that common-ion return is rarely encountered in S_N1 reactions of alkyl fluorides. As a result, deviations from the first-order rate law, due to reversible ionization toward the end of the kinetic experiments, have not been observed in any of the benzhydryl fluoride solvolyses described above.

A quantitative rationalization for this observation is given in Figure 9, where the first-order rate constants of the reactions of
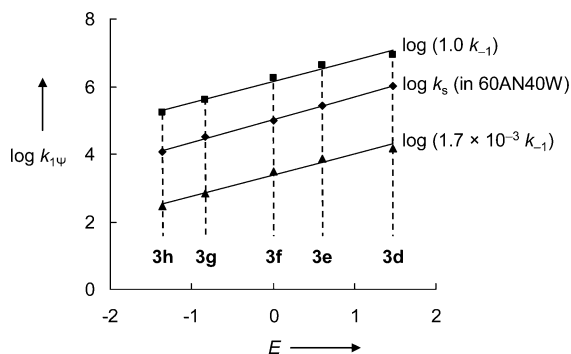

Figure 9. Plot of log $k_{1\psi}$ for the reactions of benzhydrylium ions with aqueous acetonitrile 60AN40W (k_s) and with fluoride in 60AN40W ($k_{1\psi} = [F^-]k_{-1}$) at fluoride concentrations of 1.0 M (upper graph) and at 1.7 mM (lower graph) versus their electrophilicity parameters E.

various benzhydrylium ions with water in 60% aqueous acetonitrile are compared with the corresponding pseudo-first-order rate constants with fluoride (i.e., $k_{-1}[F^-]$) at different concentrations of fluoride. At substrate concentrations which are typical for solvolysis experiments (1.7 mM), the reaction with F^- is approximately 10^2 times slower than the reaction with the solvent. Only when high concentrations of fluoride are employed, the reaction with F^- is faster than the reaction with water as demonstrated for the solvolysis of bis(p-tolyl)-methyl chloride $[(4\text{-}MeC_6H_4)_2CHCl]$ in a 0.54 M solution of $nBu_4N^+ F^-$ in 60AN40W (Figure 4).

CONCLUSION

The rate constants for the forward and backward reactions of benzhydryl fluoride ionization can be combined to construct quantitative energy profiles for the solvolysis reactions (Figure 10), which differ significantly from those previously derived for benzhydryl chlorides and bromides.

While S_N1 solvolyses of benzhydryl chlorides and bromides, which are commonly investigated at room temperature (i.e., 0.1 s $< \tau_{1/2} < 1$ d), have carbocation-like transition states (i.e., barrier-free combinations of R$^+$ with Cl$^-$ or Br$^-$), solvolysis reactions of benzhydryl fluorides, which proceed with similar rates, typically do not have carbocation-like transition states. As shown in Figure 10, the solvolysis of **2b**, for which a solvolysis half-life of approximately 63 h can be calculated, still yields a carbocation that does not undergo barrier-free recombination with the fluoride ion in aqueous acetonitrile. For the more rapidly ionizing substrates **2f** ($\tau_{1/2} = 88$ s) and **2h** ($\tau_{1/2}^{\text{calcd}} = 8$ s) the energy well for the resulting carbocations is much deeper, and one can extrapolate that similar situations should be encountered for other alkyl halides with comparable ionization rates. One
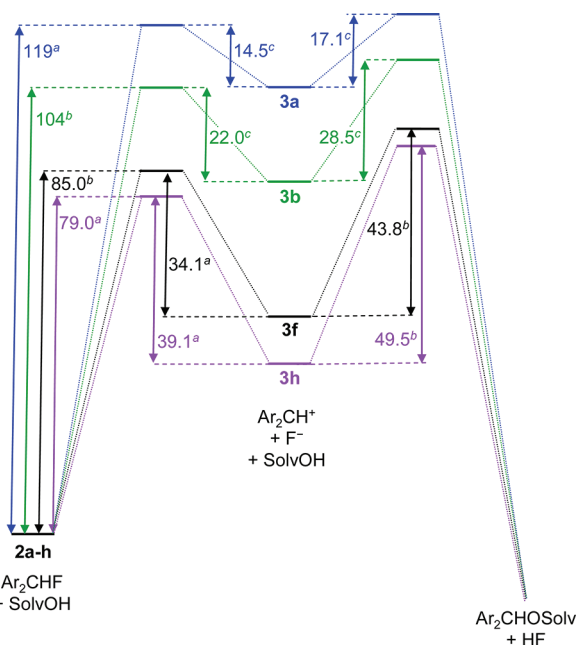

Figure 10. Free energy profiles (kJ mol^{-1}) for the solyolyses of differently substituted benzhydryl fluorides in 80AN20W at 25 °C (20 °C for the reactions of **3a**−**h** with nucleophiles). [a]Calculated by using eq 1. [b]Direct measurement. [c]Calculated by using eq 3.

can, therefore, conclude that only alkyl fluorides that give much less stabilized carbocations, i.e., substrates RF that require heating to solvolyze within reasonable time periods, will ionize via carbocation-like transition states.

■ EXPERIMENTAL SECTION

Materials. *Silver Carbonate.* Prepared according to a literature procedure by combining diluted aqueous solutions of silver nitrate with potassium bicarbonate.[60]

Ando's Fluorination Agent. Prepared according to the literature procedure by Ando.[46] Silver carbonate (10 g, 36 mmol) was mixed with calcium fluoride (40 g, 0.51 mol) and ground thoroughly. The mixture was transferred to a Teflon round-bottom flask equipped with a Teflon stirring bar, before water (40 mL) was added. Then conc HF (3.0 mL, 73 mmol) was slowly added to the stirred suspension, using a plastic syringe equipped with a Teflon tube. The suspension was stirred for 30 min, followed by evaporation of the water and drying for several hours in the vacuum (1.3×10^{-3} mbar at 40−50 °C). The fluorination agent (49 g, 98%) was obtained as a slightly yellowish free-flowing granular powder (Ando reported a colorless powder). The reagent can be stored in an opaque flask under air and can be used for at least 1 month, but we recommend storage in a glovebox under argon. The concentration of active fluorination agent (AgF) was 1.5 mmol/g in the resulting material.

Benzhydryl Bromides. Used previously but some were only partially characterized.[61−66] For their synthesis, the corresponding benzhydrols were refluxed with acetyl bromide (10 equiv) for 15 min, followed by evaporation under vacuum. The remaining residue was crystallized from CH_2Cl_2/n-pentane (ca. 1/10). In some cases good results were also obtained with only 5 equiv of acetyl bromide. In general, better results were achieved with the high excess of acetyl bromide, which often yielded crystalline material after evaporation of the acetyl bromide and acetic anhydride.

4,4′-Dimethylbenzhydryl Bromide (1b). Obtained from 4,4′-dimethylbenzhydrol (3.99 g, 18.8 mmol) and acetyl bromide (23.1 g, 188 mmol): 4.15 g (80%), colorless crystals; mp 48.0−48.6 °C. ^{1}H NMR spectra agreed with literature data.[62] ^{1}H NMR (300 MHz, CDCl$_3$): δ 2.35 (s, 6 H), 6.28 (s, 1 H), 7.13−7.16 (m, 4 H), 7.34−7.37 (m, 4 H). ^{13}C NMR (75.5 MHz, CDCl$_3$): δ 21.2, 55.9, 128.5,

129.3, 138.0, 138.5. MS (+EI): m/z (%) = 195.2 (100) [M$^+$ − Br]. Anal. Calcd for $C_{15}H_{15}Br$ (275.2): C, 65.47; H, 5.49. Found: C, 65.70; H, 5.55.

4-Methoxybenzhydryl Bromide (1c). Obtained from 4-methoxybenzhydrol (2.25 g, 10.5 mmol) and acetyl bromide (12.9 g, 105 mmol): 2.17 g (74%), colorless crystals; mp 49.5−50.9 °C. ^{1}H NMR spectra agreed with literature data.[66] ^{1}H NMR (300 MHz, CDCl$_3$): δ 3.79 (s, 3 H), 6.30 (s, 1 H), 6.84−6.87 (m, 2 H), 7.25−7.38 (m, 5 H), 7.45−7.48 (m, 2 H). ^{13}C NMR (75.5 MHz, CDCl$_3$): δ 55.5, 55.8, 114.1, 128.1, 128.5, 128.6, 129.9, 133.5, 141.4, 159.5. MS (+EI): m/z (%) = 197.2 (100) [M$^+$ − Br].

4-Methoxy-4′-methylbenzhydryl Bromide (1d). Obtained from 4-methoxy-4′-methylbenzhydrol (2.33 g, 10.2 mmol) and acetyl bromide (13.0 g, 102 mmol): 2.03 g (69%), colorless crystals; mp 39.1−40.2 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ 2.35 (s, 3 H), 3.81 (s, 3 H), 6.30 (s, 1 H), 6.85−6.88 (m, 2 H), 7.14−7.16 (m, 2 H), 7.35−7.40 (m, 4 H). ^{13}C NMR (75.5 MHz, CDCl$_3$): δ 21.2, 55.5, 56.0, 114.0, 128.4, 129.3, 129.8, 133.7, 138.0, 138.5, 159.4. MS (+EI): m/z (%) = 211.2 (100) [M$^+$ − Br].

4-Methoxy-4′-phenoxybenzhydryl Bromide (1e). Obtained from 4-methoxy-4′-phenoxybenzhydrol (1.98 g, 6.46 mmol) and acetyl bromide (7.95 g, 64.7 mmol): 2.03 g (67%), slightly pink crystals; mp 61.3−62.0 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ 3.81 (s, 3 H), 6.32 (s, 1 H), 6.86−7.11 (m, 7 H), 7.33−7.44 (m, 6 H). ^{13}C NMR (75.5 MHz, CDCl$_3$): δ 55.47, 55.52, 114.0, 118.4, 119.4, 123.8, 129.8, 129.9, 130.0, 133.5, 136.1, 156.8, 157.3, 159.5 MS (+EI): m/z (%) = 289.3 (100) [M$^+$ − Br].

4,4′-Dimethoxybenzhydryl Bromide (1f). Obtained from 4,4′-dimethoxybenzhydrol (1.31 g, 5.36 mmol) and acetyl bromide (6.61 g, 53.8 mmol): 1.27 g (77%), slightly pink crystals; mp 72.8−73.9 °C. ^{1}H NMR spectra agreed with literature data.[65] ^{1}H NMR (400 MHz, CDCl$_3$): δ 3.80 (s, 6 H), 6.32 (s, 1 H), 6.85−6.87 (m, 4 H), 7.37−7.39 (m, 4 H). ^{13}C NMR (100 MHz, CDCl$_3$): δ 55.5, 56.1, 113.9, 129.8, 133.7, 159.3. MS (+EI): m/z (%) = 227.2 (100) [M$^+$ − Br]. Anal. Calcd for $C_{15}H_{15}BrO_2$ (307.2): C, 58.65; H, 4. 92. Found: C, 58.67; H, 4.90.

4,4′-Dimethylbenzhydryl Fluoride (2b). In a carefully dried Schlenk flask, the fluorination agent (4.85 g, containing 7.28 mmol AgF) was suspended in acetonitrile (12 mL). A solution of 1b (1.00 g, 3.63 mmol) in acetonitrile (5 mL) was added dropwise at 0 °C. After stirring for 30 min, the solution was filtered, and the solvent was removed under reduced pressure at room temperature. The crude product was distilled in the vacuum (bp 160 °C/5.0 × 10^{-3} mbar) to give 2b as a colorless oil: 0.61 g (78%). ^{1}H NMR (400 MHz, CD$_3$CN): δ 2.33 (s, 6 H), 6.47 (d, $^2J_{HF}$ = 47.0 Hz, 1 H), 7.19−7.26 (m, 8 H). ^{13}C NMR (100.6 MHz, CD$_3$CN): δ 21.2, 95.2 (d, $^1J_{CF}$ = 170.0 Hz), 127.2 (d, $^3J_{CF}$ = 6.0 Hz), 130.1, 138.5 (d, $^2J_{CF}$ = 22.1 Hz), 139.3 (d, $^5J_{CF}$ = 2.0 Hz). ^{19}F NMR (376 MHz, CD$_3$CN): δ −166.2 (d, $^2J_{FH}$ = 47 Hz). MS (+ EI): m/z (%) = 214.3 (42) [M$^+$], 199.2 (100) [$C_{14}H_{12}F^+$]. Anal. Calcd for $C_{15}H_{15}F$ (214.3): C, 84.08; H, 7.06. Found: C, 84.27; H, 6.78.

4,4′-Dimethoxybenzhydryl Fluoride (2f). In a carefully dried Schlenk flask, the fluorination agent (3.91 g, containing 5.86 mmol AgF) was suspended in acetonitrile (5 mL). A solution of 1f (1.5 g, 4.88 mmol) in acetonitrile (10 mL) was added dropwise at 0 °C. After stirring for 30 min, the solution was filtered, and the solvent was removed under reduced pressure at room temperature. The crude product was crystallized from CH$_2$Cl$_2$/n-pentane to give 2f as slightly pink crystals: 0.60 g (50%); mp 72.8−73.9 °C. To avoid decomposition, 2f was stored under argon at −35 °C. ^{1}H NMR (400 MHz, CD$_3$CN): δ 3.78 (s, 6 H), 6.45 (d, $^2J_{HF}$ = 48.0 Hz, 1 H), 6.92−6.95 (m, 4 H), 7.26−7.30 (m, 4 H). ^{13}C NMR (100 MHz, CD$_3$CN): δ 55.9, 94.9 (d, $^1J_{CF}$ = 169.0 Hz), 114.8, 128.9 (d, $^3J_{CF}$ = 6.0 Hz), 133.5 (d, $^2J_{CF}$ = 23.0 Hz), 160.7 (d, $^5J_{CF}$ = 2.0 Hz). MS (+ EI): m/z (%) = 246.1 (0.1) [M$^+$], 228.1 (38) [$C_{15}H_{16}O_2^+$], 227.1 (100) [M$^+$−F]. HRMS (+EI) Calcd. for $C_{15}H_{15}FO_2$: 246.1056; Found: 246.1045.

Further benzhydryl fluorides were prepared in solution and directly used for the solvolytic investigations without prior isolation (see below).

Kinetics of Solvolysis Reactions. *Preparation of Stock Solutions of the Benzhydryl Fluorides 2c−e for Kinetic Measurements.* In a carefully dried Schlenk flask, the fluorinating agent (1.00 g containing 1.5 mmol AgF) was suspended in MeCN (3 mL). A solution of the corresponding benzhydryl bromide (1.0 mmol) in MeCN (2 mL) was added to the stirred suspension at 0 °C. After 30 min, the solution was filtered (^{1}H NMR spectroscopic analysis in CD$_3$CN showed quantitative conversion of 1c−e as well as formation of 2c−e indicated by the characteristic doublet for CHF). The clear solutions were used directly for solvolytic measurements and could be used for approximately 2 days.

Calibration. Calibration experiments were performed by stepwise addition of 50 μL portions of a 0.2 M solution of 2e in acetonitrile to 30 mL of 80E20W (80% ethanol, 20% water) containing 0.08 M piperidine. After the addition of a portion of 2e the conductance after at least 200 s (for 2e in 80E20W: $\tau_{1/2}$ = 49 s) was recorded before the next portion of 2e was added. Plots of the conductance against the initial concentration of added benzhydryl fluoride 2e were linear (Figure S1 in Supporting Information), demonstrating that solvolytic rate constants can be determined reliably by time-dependent conductance measurements.

Kinetics. The following solvents were commercially available and used as received: acetone (99.8%), acetonitrile (extra dry, water content <50 ppm), methanol (99.8%). Commercially available absolute ethanol was freshly distilled from sodium/diethyl phthalate. Doubly distilled water (impendance 18.2 Ω) was obtained from a water purification system. Solvolysis rate constants of benzhydryl derivatives (Table 2 and Table S2 in the Supporting Information) were monitored by conventional conductometry. Freshly prepared solvents (30 mL, with amine additive in case of benzhydryl fluorides 2) were thermostatted (±0.1 °C) at the given temperature for 5 min prior to adding the substrate. Typically 0.25 mL of a 0.2 M stock solution of the benzhydryl derivative in acetonitrile was injected into the solvent upon which an increase of conductance was observed. This increase was recorded at certain time intervals resulting in about 3000 data points for each measurement. The first-order rate constants k_1 (s^{-1}) were obtained by least-squares fitting of the conductance data to a single-exponential equation $G_t = G_\infty(1 - e^{-k_1t}) + C$. Each rate constant was typically averaged from at least three kinetic runs. Only in two cases (2f in 90A10W and 2b in 80E20W) measurements were performed only once as these reactions were very slow. All solvolyses reported in Table 2 and Table S2 in the Supporting Information were performed at 25 °C.

Nucleophilic Reactivity of Fluoride in Different Solvents. *Solvents and Fluoride Sources.* KF of p.a. grade, CsF (99.9%) and tetrabutylammonium fluoride trihydrate (98%) were used as fluoride sources for the kinetic experiments. Acetonitrile (extra dry, water content <50 ppm) and methanol (99.8%) were used without further purification for laser-flash experiments. Commercially available absolute ethanol was freshly distilled from sodium/diethyl phthalate. Doubly distilled water (Impedance 18.2 Ω) was prepared with a water purification system.

Laser-Flash Photolysis. The measurements were performed in an air-conditioned laboratory at 20 ± 1 °C. The benzhydryl cations 3b−j were generated by irradiating solutions ($A_{266\ nm} \approx 0.1$−1.0) of the precursor salts 4b−j with a 7 ns laser pulse (7 ns pulse width, 266 nm, 40−60 mJ/pulse). The benzhydryl cations 3b−h were generated from the triphenylphosphonium salts 4b−h. For the photogeneration of 3i,j, stock solutions of the tributylphosphonium salts 4i,j in acetonitrile were prepared by mixing the appropriate amounts of benzhydrylium tetrafluoroborates 3i,j and tributylphosphine. The system was equipped with a fluorescence flow cell and a synchronized diaphragm liquid pump that allowed complete replacing of the sample volume between subsequent laser pulses. Kinetics were measured by following the UV−vis absorbance decay of the benzhydryl cations at their absorbance maxima. Averaged data obtained from ≥48 individual runs were used for further evaluations. First-order rate constants (k_{obs}) were calculated by least-squares fitting of the absorbance data to a single exponential function $A_t = A_0\ e^{-k_{obs}t} + C$. The second-order rate

constants (k_{-1}) were obtained using the slopes of the linear plots of k_{obs} against the fluoride ion concentration. First-order rate constants (k_s) were obtained from independent measurements with laser-photolytically generated benzhydrylium ions in the absence of fluoride ions.

Stopped-Flow Method. The kinetics of the reactions of F$^-$ with **3k,l** were determined by using the stopped-flow method and isolated benzhydrylium tetrafluoroborates as described previously.[35] The decay of their absorbance was monitored by UV–vis spectroscopy at the absorption maxima of **3k,l**. Pseudo-first-order rate constants k_{obs} were obtained from at least six runs at each fluoride concentration. The absorbance-time curves were fitted to the single exponential function $A_t = A_0\, e^{-k_{obs}t} + C$ to yield the rate constants k_{obs} (s^{-1}). The second-order rate constants k_{-1} (M^{-1} s^{-1}) for the reactions of **3** with fluoride ions were obtained from the slopes of linear plots of k_{obs} versus the fluoride concentrations.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Details for the kinetic procedures, product studies, and copies of NMR spectra of **1b–f**, **2b**, and **2f**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes
The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

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