Dissertation zur Erlangung des Doktorgrades
der Fakultät für Chemie und Pharmazie
der Ludwig-Maximilians-Universität München

Development of Comprehensive Nucleofugality and Electrofugality Scales

Nicolas Streidl
aus
Augsburg

2010

Erklärung

Diese Dissertation wurde im Sinne von §13 Abs. 3 bzw. 4 der Promotionsordnung vom 29. Januar 1998 von Herrn Prof. Dr. Herbert Mayr betreut.

Ehrenwörtliche Versicherung

Diese Dissertation wurde selbständig und ohne unerlaubte Hilfe erarbeitet.

München, 05.08.2010

…………………………………
Nicolas Streidl

Dissertation eingereicht am	09.08.2010
1.Gutachter	Prof. Dr. Herbert Mayr
2.Gutachter	Prof. Dr. Hans Rudolf Pfaendler
Mündliche Prüfung am	23.09.2010

Danksagung

Mein herzlicher Dank gilt Herrn Prof. Dr. Herbert Mayr für seine herausragende und beispielhafte Betreuung während der Durchführung dieser Arbeit. Seine stete Hilfs- und Diskussionsbereitschaft hat maßgeblich zum Gelingen dieser Arbeit beigetragen.

Ich danke allen Mitgliedern des Prüfungsausschusses für ihre Teilnahmebereitschaft.

Ganz besonders möchte ich mich auch bei folgenden Personen bedanken, ohne die diese Arbeit nicht möglich gewesen wäre:

Dr. Armin Ofial, für zahlreiche Diskussionen und Unterstützung bei der Anfertigung meiner Publikationen. Danke Dr. O., jetzt kenne ich auch den Unterschied zwischen einem normalen und einem kursiven Punkt.

Unseren fleißigen „Heinzelfrauen“ Nathalie Hampel, Brigitte Janker und Hildegard Lipfert für die rasche Beschaffung aller notwendigen Dinge im täglichen Arbeitsalltag (Chemikalien, Gerätschaften, Str8ts, …)

Meinen aktuellen und ehemaligen Büro- und Laborkollegen Tanja Kanzian, Doro Richter, Johannes Ammer, Jan Keller, Jörg Lippstreu, Tobsi Nigst, Konstantin Troshin und Martin Westermaier für die stete Diskussionsbereitschaft und die praktische Unterstützung, vor allem aber für den Spaß, den wir auch außerhalb der Arbeit gemeinsam hatten. Ich hoffe, die entstanden Freundschaften werden das Ende dieser Arbeit lange überdauern!

Meinen weiteren Mitstreitern in der „Solvolyse“-Gruppe, Heike Schaller, Markus Horn und Christoph Nolte.

Allen anderen derzeitigen und ehemaligen Mitgliedern unseres Arbeitskreises, die für ein sehr angenehmes Arbeitsklima gesorgt haben und mir stets mit Rat und Tat zur Seite standen.

Meinen beiden Forschungspraktikantinnen Anna Antipova und Ramona Branzan für ihren großen Einsatz bei der Durchführung der experimentellen Arbeiten und die humorvolle Zusammenarbeit.

Für die zügige und kritische Durchsicht dieser Arbeit danke ich Johannes Ammer, Martin Breugst, Hans Laub, Tobsi Nigst und Roland Appel.

Matthias Scherr, für jahrelanges, stressfreies Zusammenleben im Wohnheim und in der WG mit vielen gelungene Schafkopf- und Fußballabenden, meist verbunden mit dem einen oder anderen isotonischen Hopfenkaltgetränk.

Meiner Freundin Ana für die moralische Unterstützung, dem Ausgleich neben der Chemie und vor allem dafür, dass sie immer für mich da war und ist.

Zuletzt möchte ich mich von ganzem Herzen bei meiner Familie bedanken, die mich nicht nur während meiner Ausbildung sondern Zeit meines Lebens immer unterstützt und mir Rückhalt gegeben hat. Ohne Euch hätte ich das nicht geschafft!

Publikationen

(1) **Suppression of Common Ion Return by Amines: A Methode to Measure Rates of Fast S_N1 Reactions**
Streidl, N.; Antipova, A.; Mayr, H. *J. Org. Chem* **2009**, *74*, 7328–7334.

(2) **Nucleophilicities and Nucleofugalities of Organic Carbonates**
Streidl, N.; Branzan, R.; Mayr, H. *Eur. J. Org. Chem.* **2010**, 4205–4210.

(3) **A Practical Guide for Estimating Rates of Heterolysis Reactions**
Streidl, N.; Denegri, B.; Kronja, O.; Mayr, H. *Acc. Chem. Res.* **2010**, accepted.

Konferenzbeiträge

(1) 06/2007 European Symposium on Organic Reactivity XI, Faro, Portugal, Posterpräsentation: "**Determination of Ionization Rates in Solvents of Low Nucleophilicity**"

(2) 02/2009 International Symposium on Modern Organic Chemistry, Monastir, Tunesien, Vortrag: "**How to Predict the Ionizing Power of Aprotic Solvents**"

Table of Contents

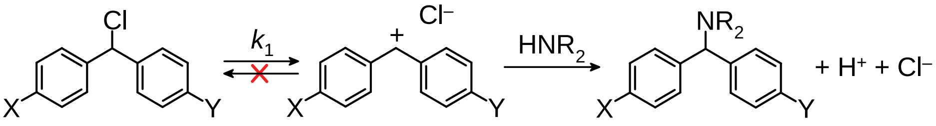
Chapter 0

Summary

0.1 Suppression of Common-Ion Return By Amines: A Method to Measure Rates of Fast S_N1 Reactions

Rate constants for solvolyses of benzhydryl chlorides (Scheme 0.1), which take place on the 10 millisecond to minute time scale, have been determined in aqueous acetone and acetonitrile by conductimetry, using conventional conductimeters as well as stopped-flow techniques. As shown in Figure 0.1 for the 4,4´-dimethoxybenzhydryl chloride, the solvolysis rates increase when increasing concentrations of secondary or tertiary amines are present until a limiting value is reached. Since there is no proportional increase of k_{obs} with increasing amine concentration, one can exclude the operation of S_N2 mechanisms and the asymptotic approach to a plateau indicates that $k_{obs} = k_1$ because common-ion return is suppressed. The amine effect, i.e., the acceleration of the solvolysis reactions due to suppression of common-ion return, increases with increasing stabilization of the generated carbenium ions.

Scheme 0.1: Suppression of Common Ion Return in the Presence of Amine Additives.



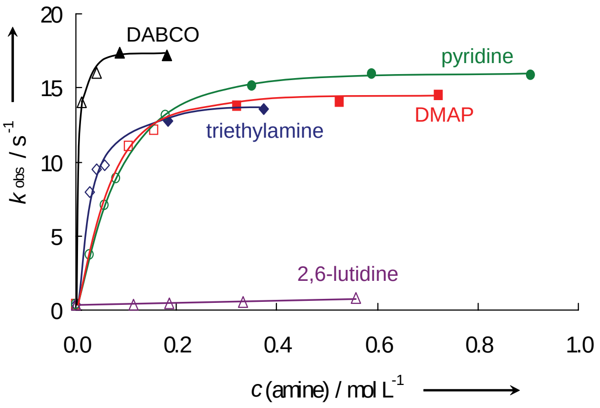


Figure 0.1: Observed rate constants of the solvolysis of 4,4´-dimethoxybenzhydryl chloride in 90% acetone (90A10W) in the presence of variable concentrations of amines.

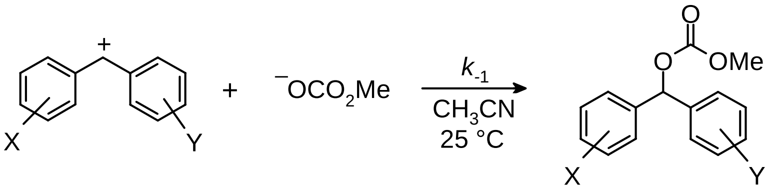
When various amines are used as trapping reagents, slight deviations in the measured rate constants are observed (Figure 0.1). These modest differences may be due to the fact that the amines intercept contact ion pairs as well as free ions in diffusionally limited reactions.

With the new data obtained by this method it was possible to close the gap between classical S_N1 reactions without common-ion return and S_N2C^+ reactions, where carbocations accumulate before they are trapped by the solvent or other nucleophiles.

0.2 Nucleophilicities and Nucleofugalities of Organic Carbonates

The kinetics of the reactions of the methyl carbonate ion with benzhydrylium ions in acetonitrile have been studied by UV/Vis spectrophotometry (Scheme 0.2).

Scheme 0.2: Reactions of the Methyl Carbonate Ion with Benzhydrylium Ions in Acetonitrile.



The resulting second-order rate constants log k_{-1} correlate linearly with the electrophilicity parameters E of the benzhydrylium ions (Figure 0.2) and the nucleophilicity parameters N_{25} = 16.03 and s_{25} = 0.64 for methyl carbonate in acetonitrile were derived by eq (0.1).

$$\log k = s(E + N) \tag{0.1}$$

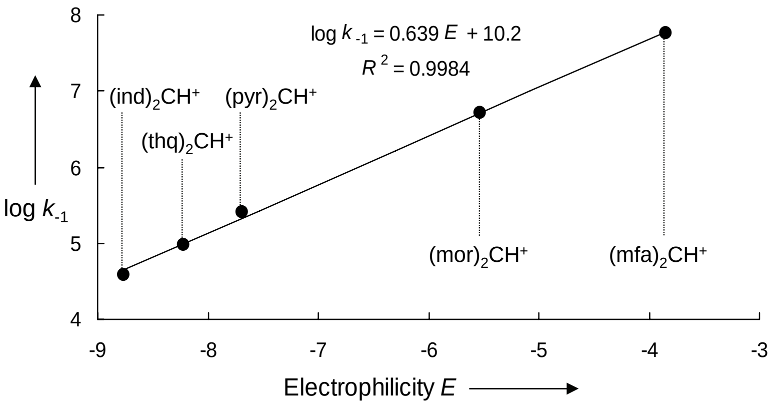
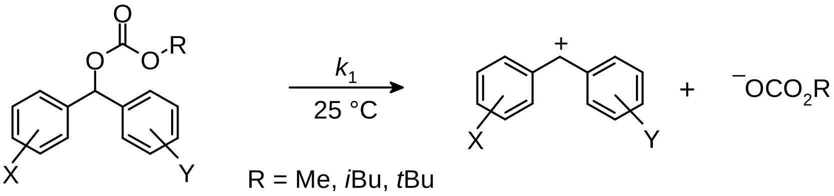


Figure 0.2: Plot of the second-order rate constants log k_{-1} (25 °C, acetonitrile) against the electrophilicity parameters E of the reference electrophiles for the reactions of $Bu_4N^+MeOCO_2^-$ with benzhydrylium ions.

The kinetics of the hydrolyses of ring-substituted benzhydryl alkyl carbonates were followed in different aqueous solvents by conductimetry (Scheme 0.3). Plots of the obtained first-order rate constants versus the electrofugality parameters E_f of benzhydrylium ions were linear as exemplified for benzhydryl *tert*-butyl carbonates (Figure 0.3).

Scheme 0.3: Hydrolysis Reactions of Benzhydryl Alkyl Carbonates in Aqueous Solvents.



The linear free-energy relationship (eq 0.2) was used to determine the nucleofugality parameters N_f and s_f of the $ROCO_2^-$ groups in different solvents, which are in a similar reactivity range as 4-nitrobenzoate and 3,5-dinitrobenzoate (Figure 0.4).

$$\log k_1 = s_f(N_f + E_f) \qquad (0.2)$$

While *tert*-butyl carbonates (*t*BocO-R) are highly labile under acidic conditions, they are considerably more stable in neutral media with respect to heterolytic cleavage of the O-R bond than other organic carbonates.

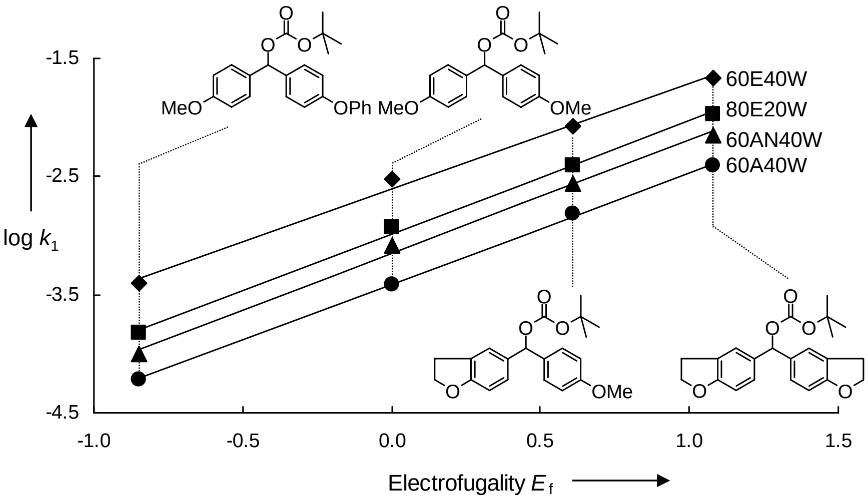


Figure 0.3: Plots of the first-order rate constants log k_1 of the solvolyses of substituted benzhydryl *tert*-butyl carbonates in different solvent mixtures against the electrofugality parameters E_f (mixtures of solvents are given (v/v); W = water, E = ethanol, AN = acetonitrile, A = acetone).

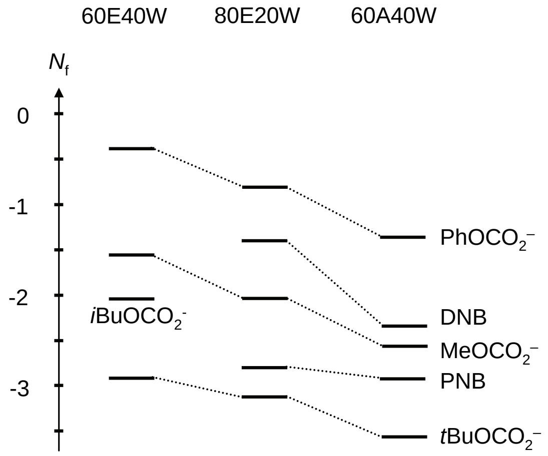


Figure 0.4: Comparison of the nucleofugalities of leaving groups in various solvents (DNB = 3,5-dinitrobenzoate, PNB = 4-nitrobenzoate).

0.3 Ionizing Power of Aprotic Solvents

Rate constants k_1 for the heterolysis (S_N1) reactions of a series of benzhydryl chlorides in aprotic solvents (DMSO, acetonitrile, carboxamides, etc.) have been determined conductimetrically by the "amine method" (see Chapter 2), i.e., by trapping of the intermediate carbocation by amines or triphenylphosphine and thus suppressing ion recombination.

Plots of the logarithmic first-order rate constants log k_1 versus the electrofugality parameters E_f of the reference benzhydrylium ions yielded linear correlations (exemplarily depicted in Figure 0.5 for DMSO, dichloromethane, and acetone), allowing to derive the nucleofugality parameters N_f and s_f for chloride in aprotic solvents according to the linear free-energy relationship (0.2).

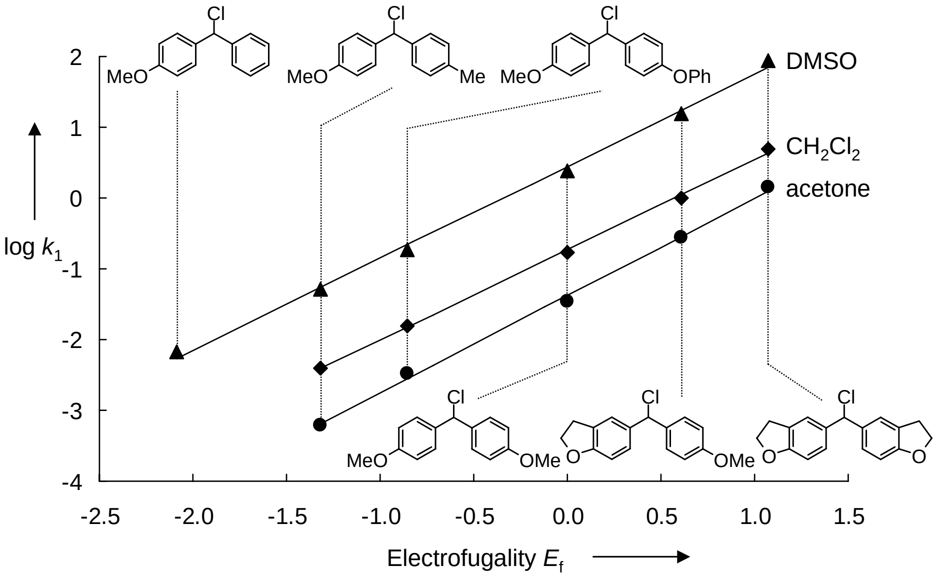


Figure 0.5: Plots of the first-order rate constants log k_1 of the heterolyses of benzhydryl chlorides in different aprotic solvents against the electrofugality parameters E_f.

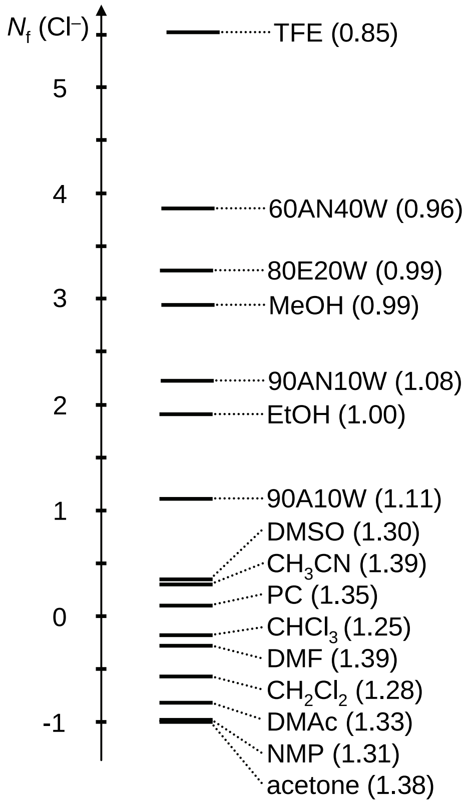


Figure 0.6: Comparison of the nucleofugality parameters N_f (s_f parameter in parentheses) of chloride in various protic and aprotic solvents.

DMSO, the aprotic solvent with the highest ionizing power in this series is about 1.5 orders of magnitudes less ionizing than ethanol. The leaving group ability of chloride differs more than 6.5 orders of magnitude between 2,2,2-trifluoroethanol (TFE) and acetone, the extremes of this scale (Figure 0.6).

These ionization rate constants were used to include aprotic solvents in the Y_{BnCl} scale (ionizing power of solvents) by Winstein and Grunwald. The aprotic solvents investigated in this study differ by 2.5 units in this scale. Though generally less ionizing than protic solvents, DMSO or acetonitrile are only one unit lower on the Y_{BnCl} scale than protic solvents like 2-propanol and 90% aqueous acetone (Figure 0.7).

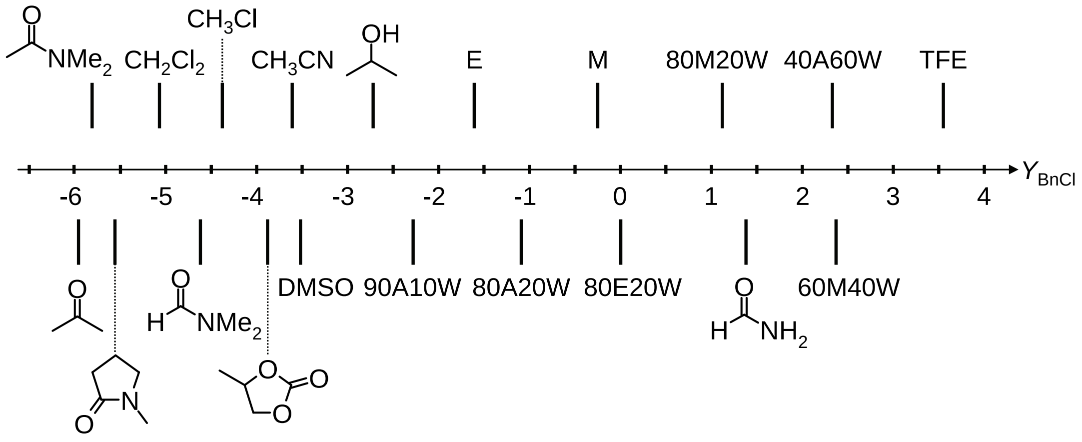


Figure 0.7: Y_{BnCl} scale for protic and aprotic solvents (mixtures of solvents are given (v/v); A = acetone, E = ethanol, M = methanol, TFE = 2,2,2-trifluoroethanol, W = water).

0.4 A Practical Guide for Estimating Rates of Heterolysis Reactions

A series of 39 benzhydrylium ions are proposed as reference electrofuges for the development of a comprehensive nucleofugality scale. Therefore, a total of 628 solvolysis rate constants for different benzhydryl derivatives (aryl$_2$CH–X) in various solvents were subjected to a least-squares minimization on the basis of eq (0.2). The good agreement between calculated and experimental rate constants is depicted in Figure 0.8 for a variety of nucleofuges.

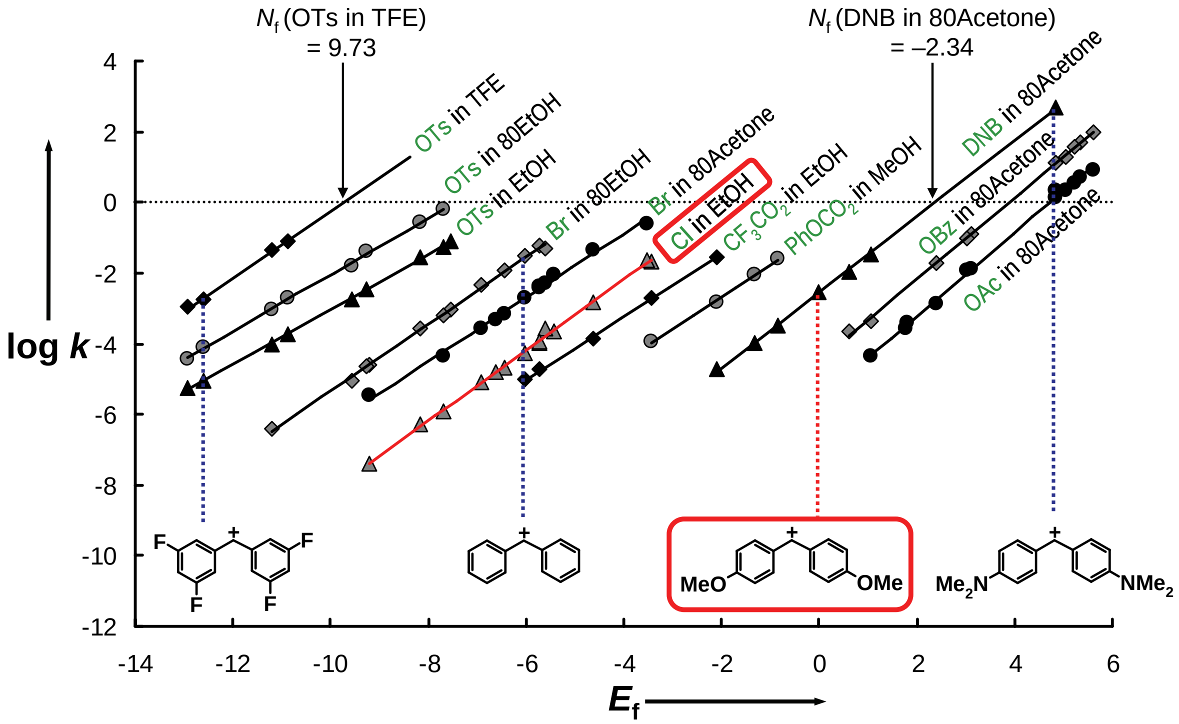


Figure 0.8: Plots of the solvolysis rate constants log *k* (at 25°C) for benzhydryl halides and various esters vs. the electrofugality parameters of benzhydrylium ions.

While it has long been known that good nucleophiles are not necessarily poor nucleofuges, it was now found that there is also no general inverse relationship between electrophilicity and electrofugality (Figure 0.9). Especially in the left part of Figure 0.9 where the amino-substituted benzhydrylium ions are located, the inverse relationship breaks down.

The set of 39 reference electrofuges can be used in combination with eq 0.2 to determine nucleofugalities of almost any leaving group/solvent combination, whereas the 110 reference nucleofuges can analogously be used to derive electrofugalities of other kind of carbocations as shown in Figure 0.10.

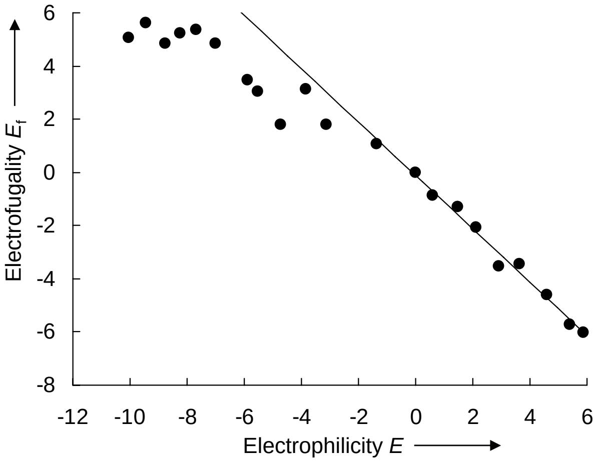


Figure 0.9: Correlation between electrophilicity and electrofugality.

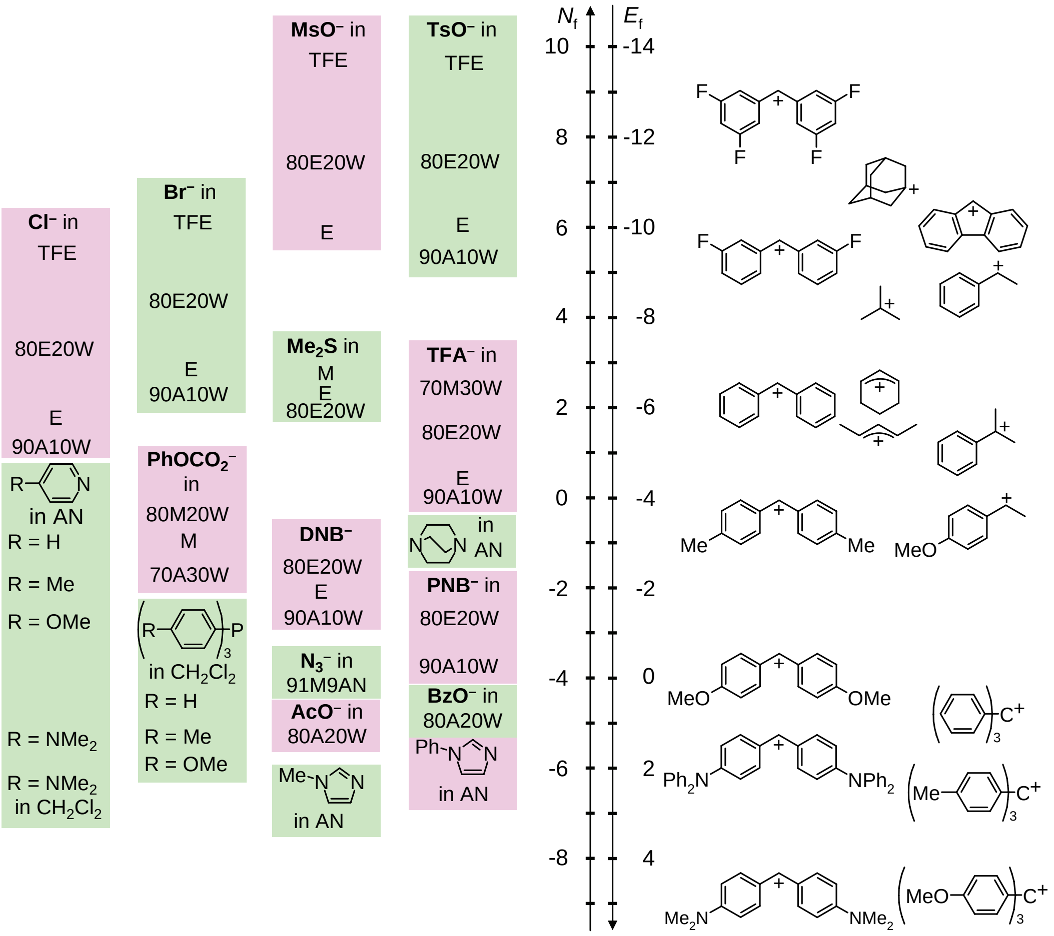


Figure 0.10: Nucleofugality and electrofugality scales: Combinations of electrofuges and nucleofuges at the same level cleave with a half-life of approximately one hour.

The simplicity of this approach is most attractive for the synthetic chemist, who is seeking orientation in a reactivity range of 25 orders of magnitude, which is provided by just considering the sum $E_f + N_f$ or by looking at graphs as shown in Figure 0.10 and Figure 0.11.

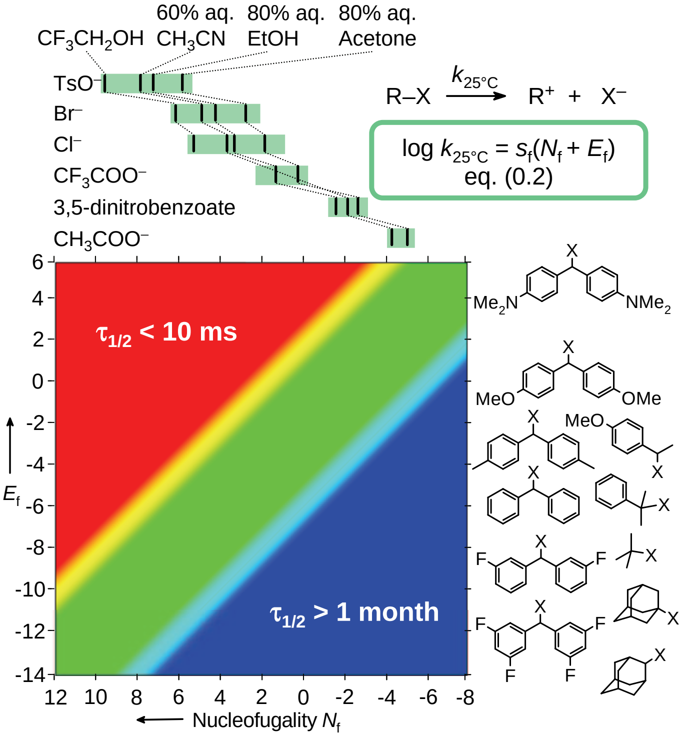


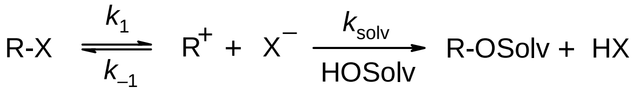
Figure 0.11: From high reactivity to inertness: A semiquantitative model for predicting S_N1 half-reaction times. Reactions on the green diagonal can be studied experimentally.

Chapter 1

Introduction and Objectives

One of the most important transformations in organic chemistry is the replacement of a leaving group attached to an aliphatic carbon atom by a nucleophile. In the late 1920s, Ingold differentiated between two mechanisms for these reactions:[1] In an S_N2 reaction, a new bond between the nucleophile and a carbon center is formed while simultaneously the bond to the leaving group is broken. In contrast, S_N1 reactions proceed via a stepwise mechanism, where in a first rate-determining step the substrate gets ionized yielding an anion (nucleofuge) and a carbenium ion (electrofuge). The electrofuge is then trapped by a solvent molecule, usually in a fast subsequent reaction (Scheme 1.1). If the reaction proceeds like this, the solvolysis rate constants (k_1) can be determined by simply following the formation of HX, either by conductimetric or titrimetric methods. Countless investigations on the rates of these kind of S_N1 reactions have been performed, and a linear free-energy relationship (eq 1.1) to quantitatively describe ionization processes was established by Winstein and Grunwald in 1948.[2]

Scheme 1.1. Simplified Solvolysis Scheme.



$$\text{R-X} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \text{R}^+ + \text{X}^- \xrightarrow[\text{HOSolv}]{k_\text{solv}} \text{R-OSolv} + \text{HX}$$

$$\log (k/k_0) = mY \tag{1.1}$$

k:	solvolysis rate constant in a certain solvent
k_0:	solvolysis rate constant in 80% aqueous ethanol
Y:	ionizing power of solvent ($Y = 0$ for 80% aqueous ethanol)
m:	characteristic parameter for substrate ($m = 1$ for *tert*-butyl chloride)

As already shown by Ingold in the 1940s,[3] not only trapping of the cation by the solvent but also recombination with the leaving group (common-ion return, k_{-1} in Scheme 1.1) can occur, when stabilized carbenium ions are generated in the ionization step. In such cases, the ionization step is not any longer rate-determining. Deviations from first-order kinetics are observed, as common-ion return becomes faster during the course of the reaction due to increasing concentration of X^{-}. As a consequence of the complicated rate laws in these reactions and the fact that common-ion return occurs primarily in very fast reactions, only few data of solvolyses leading to stabilized carbenium ions have been available in the literature.

In 2004, it was reported that S_N1 solvolyses with inverted rate profiles, i.e., a fast ionization step followed by a slow subsequent reaction with the solvent leading to accumulation of the carbocations (S_N2C^+ solvolyses[4]), can occur when derivatives of highly stabilized carbenium ions are investigated.[5] A few years later, a method was developed to determine the ionization rates of these reactions: Derivatives of amino-substituted benzhydryl systems were employed in solvolysis reactions, leading to colored benzhydrylium ions in the ionization step. As these colored carbenium ions have significant lifetimes or are even persistent under the reaction conditions, it was possible to directly observe the ionization step of the reactions by UV/Vis spectrophotometry.[6,7]

As the stabilities of the carbocations generated in ordinary S_N1 reactions and of those reacting by the S_N2C^+ mechanism differed dramatically, there were two separate data sets which were hardly linked with each other. It was the goal of this thesis to merge these two data sets by including them into our comprehensive nucleofugality and electrofugality scales based on eq (1.2),[5] which so far focused on classical S_N1 reactions.

$$\log k_1\ (25\ °\mathrm{C}) = s_\mathrm{f}(N_\mathrm{f} + E_\mathrm{f}) \qquad (1.2)$$

k_1: first-order (s^{-1}) rate constant

s_f, N_f: empirical, nucleofuge-specific parameters (leaving group and solvent)

E_f: empirical electrofugality parameter

In order to cover the whole spectrum of different solvolysis reactions by eq (1.2), it was necessary to close the gap between these two reaction types (classical S_N1 and S_N2C^+). For that purpose, a method to determine ionization rates of systems that proceed via carbocations of intermediate reactivity, i.e., systems that are heavily affected by common-ion return, had to be developed. In addition, this method should also be applicable to study heterolysis reactions in aprotic solvents that are usually used for S_N2 reactions, in order to make reliable predictions when concurrent S_N1 reactions are possible.

As the major parts of this thesis have already been published or submitted for publication, individual introductions will be given at the beginning of each chapter.

References

(1) Ingold, C. K.; Rothstein, E. *J. Chem. Soc.* **1928**, 1217–1221.

(2) Grunwald, E.; Winstein, S. *J. Am. Chem. Soc* **1948**, *70*, 846–854.

(3) Bateman, L. C.; Hughes, E. D.; Ingold, C. K. *J. Chem. Soc.* **1940**, 974–978.

(4) Gelles, E.; Hughes, E. D., Ingold, C. K. *J. Chem. Soc.* **1954**, 2918–2929.

(5) Denegri, B.; Minegishi, S.; Kronja, O.; Mayr, H. *Angew. Chem.* **2004**, *116*, 2353–2356; *Angew. Chem. Int. Ed.* **2004**, *43*, 2302–2305.

(6) Schaller, H. F.; Tishkov, A. A.; Feng, X.; Mayr, H. *J. Am. Chem. Soc.* **2008**, *130*, 3012–3022.

(7) Schaller, H. F.; Mayr, H. *Angew. Chem.* **2008**, *120*, 4022–4025; *Angew. Chem. Int. Ed.* **2008**, *47*, 3958–3961.

Chapter 2

Suppression of Common-Ion Return by Amines:

A Method to Measure Rates of Fast S_N1 Reactions

N. Streidl, A. Antipova, H. Mayr, *J. Org. Chem.* **2009**, *74*, 7328–7334.

2.1 Introduction

Rates of S_N1 reactions have been the major source of information on the stabilities of carbocations.[1] If the carbocation R^+ is a short-lived, high-energy intermediate, the transition state of the ionization process (k_1) can be approximated by the structure and energy of the carbocation. This hypothesis, previously based on Hammond's postulate,[2] has been examined by the determination of the rate constants of the reactions of the carbocations R^+ with the leaving groups X^- and the solvents HOSolv.[3-5] Many of these reactions have been found to be diffusionally limited and to proceed without activation energy. In these cases, the principle of microscopic reversibility requires that there is also no barrier for the forward reaction ($RX \rightarrow R^+ + X^-$), i. e., the activation free energy of the ionization step (k_1) equals the difference between the free energy of the ion pair (R^+X^-) and its precursor ($R{-}X$) (Figure 2.1, A).

Figure 2.1, D illustrates the other extreme, i. e., the heterolytic cleavage of a substrate which yields a persistent carbocation. In this case, the kinetics of the heterolysis reaction have been measured directly by monitoring the concentration of the colored carbocations.[6] In line with non-carbocation-like transition states, in such reactions the correlation between the rates of heterolysis and the "stabilities" of the carbocations (derived from the ionization equilibria) is rather poor. The same is true for S_N2C^+ reactions, where carbocations are formed as long-lived, directly observable intermediates, before they undergo subsequent reactions with the solvent (Figure 2.1, C).[7]

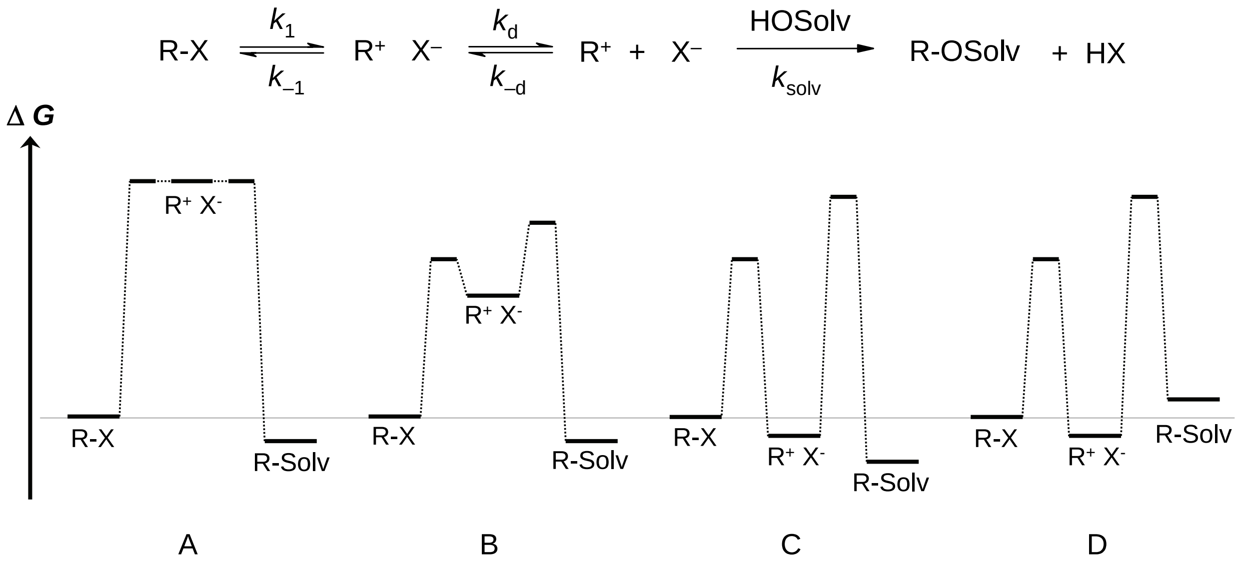


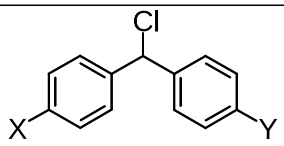
Figure 2.1: Qualitative free energy profiles for different types of solvolysis reactions.

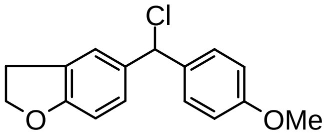
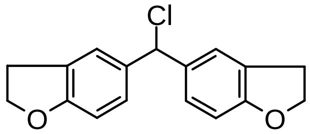
In the course of our efforts to develop a comprehensive scheme of heterolysis reactions ranging from classical S_N1 mechanisms on one end (Figure 2.1, A) over the S_N2C^+ mechanisms[7-9a] (Figure 2.1, C) to cases where persistent carbocations are generated which do not undergo subsequent reactions with the solvent (Figure 2.1, D),[6] we have now investigated S_N1 reactions, which proceed via carbocations of intermediate reactivity (Figure 2.1, B). These are typically fast reaction sequences, where the first step is reversible because the intermediate carbocation reacts faster with the leaving group than with the solvent. As the overall solvolysis rate constants of such reactions are retarded by the so-called common-ion return,[10,11] the rate of the ionization step (k_1) can only be measured directly when the recombination of the carbocation R^+ with the leaving group X^- is suppressed. In this work, we will demonstrate that this can efficiently be achieved by the addition of amines. Because under these conditions ionic products are generated from covalent substrates, the rates of the reactions can be followed by conductometry. When common ion return is suppressed in the common way by azide ions,[10a] the total number of ions remains constant during the reactions, and conductometry is not applicable. In this work we will demonstrate that conductometric studies of solvolysis reactions in the presence of amines are an efficient method to systematically study ionization rates of substrates which solvolyze in the millisecond to minute time scale for which only very few kinetic data are available in the literature.[1]

2.2 Results

Solvolyses of the benzhydryl chlorides **1a–j** (Table 2.1) in aqueous acetone or aqueous acetonitrile give rise to the formation of benzhydrols and equimolar amounts of HCl. By portionwise addition of a rapidly solvolyzing benzhydryl chloride (**1g**) and determination of the conductivity after completion of the solvolysis (a few seconds after each addition), the calibration curve of Figure 2.2 was obtained which showed that the conductivity is directly proportional to the amount of solvolyzed benzhydryl chloride.

Table 2.1: Benzhydryl Chlorides **1a–j** and Electrophilicity Parameters *E* of the Corresponding Benzhydrylium Ions **1a**$^+$–**j**$^+$.

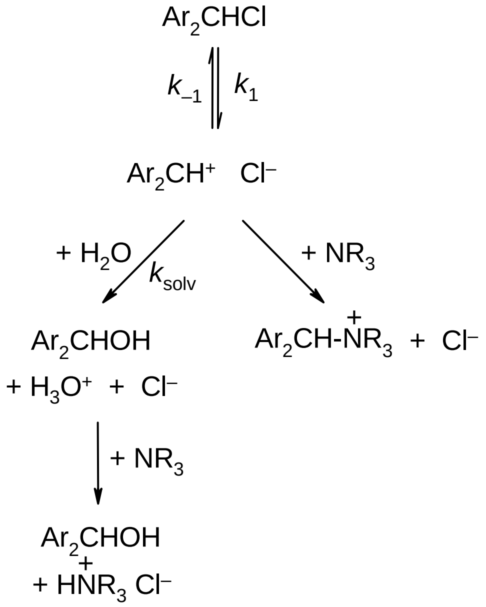


	X	Y	E^a
1a	Cl	Cl	6.02
1b	H	H	5.90
1c	Me	H	4.59
1d	Me	Me	3.63
1e	OMe	H	2.11
1f	OMe	Me	1.48
1g	OMe	OPh	0.61
1h	OMe	OMe	0.00
1i			–0.56^b
1j			–1.36

^{a} From ref 12. ^{b} Unpublished.

When the solvolyses were carried out in the presence of amines, benzhydrols and/or benzhydrylammonium salts are formed (Scheme 2.1). Calibration experiments as depicted in Figure 2.2 are reported in the Experimental Section which show that also under these conditions the concentration of the ions is directly proportional to the measured conductivity.

Scheme 2.1: Solvolyses of Benzhydryl Chlorides in the Presence of Tertiary Amines in Aqueous Solvents.



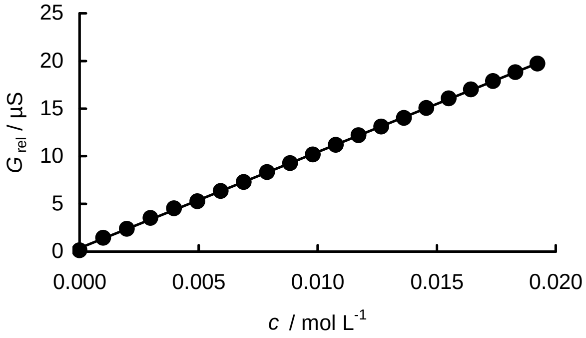


Figure 2.2: Plot of conductivity G_{rel} versus concentration of the solvolyzed substrate 4-methoxy-4´-phenoxybenzhydryl chloride **1g** without additives in 80% acetone (80A20W).

A typical example for the determination of the ionization rate constants is illustrated in Figure 2.3 for the solvolysis of 4,4´-dimethoxybenzhydryl chloride **1h** in 90% acetone (90A10W).

When **1h** (0.018 M) was dissolved in 90% acetone without any additives, 90% conversion was reached after 5 s, and the plot of conductivity versus time deviated noticeably from the mono-exponential function (eq 2.1), which is shown by the dashed line in Figure 2.3a.

$$G = G_{\max}[1 - \exp(-k_1 t)] + const. \qquad (2.1)$$

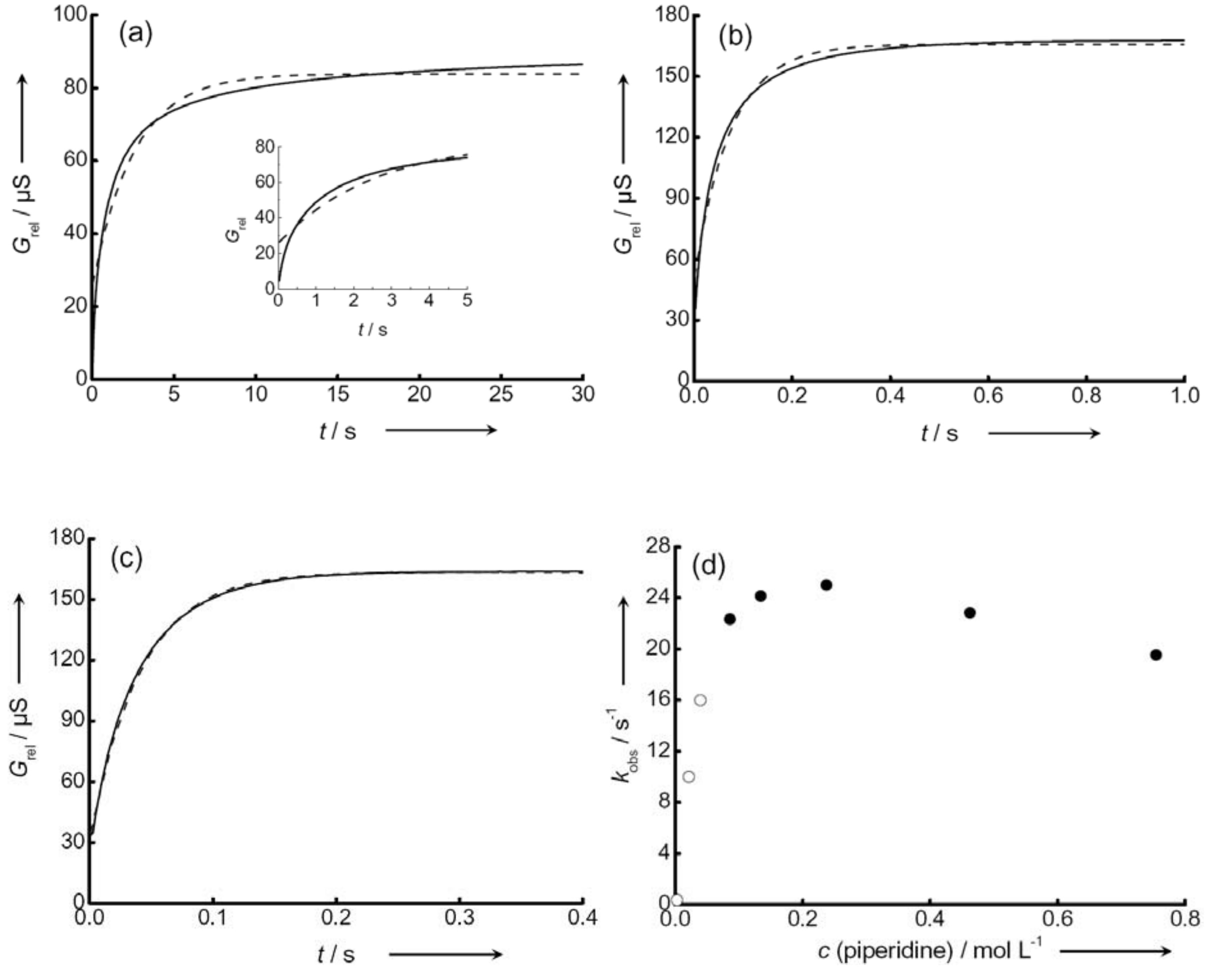


Figure 2.3: (a)-(c) Plots of conductivity versus time for the solvolysis of 4,4´-dimethoxybenzhydryl chloride **1h** (0.018 M) in 90% acetone (90A10W) at 25 °C in the presence of *c*(piperidine) = 0 mol L^{-1} (a); 0.04 mol L^{-1} (b); 0.24 mol L^{-1} (c); (d) plot of the observed rate constants k_{obs} versus *c*(piperidine) (open symbols represent kinetics that are not of first-order).

When the reaction was followed in a solution containing 0.04 M piperidine, 90% conversion was already achieved after 0.2 s, and the experimental line got closer to the dashed exponential function (Figure 2.3b). Accordance between the experimental graph and the exponential function was found when 0.24 M piperidine was present, and 90% of conversion was now achieved after 0.1 s (Figure 2.3c).

Because the rate laws to describe the kinetics in Figures 2.3a and 2.3b are rather complex (concentrations of Cl^- vary during the reactions) we did not attempt to describe these traces in detail. We rather extracted “first-order rate constants” k_{obs} from best fits of these graphs to the exponential function (eq 2.1). Though these values of k_{obs} are not well defined, they give useful information on the half-lives of the substrates under the given reaction conditions. When quoted in Tables, these concentration-dependent “rate constants” are displayed in italics, whereas in Figures they are represented by open symbols.

Figure 2.3d shows that the rate of the reaction increased significantly upon addition of small concentrations of piperidine, but decreased slightly as the piperidine concentration exceeds 0.24 M. Because ionization of the CCl bond requires solvation of the incipient chloride ion by hydrogen-bonding, one might explain the decrease of reactivity at high amine concentrations by a solvent effect: The water molecules which are needed for chloride solvation are not any longer fully available because they are already engaged in hydrogen bonding with the amine. An alternative explanation would be the change of the dielectric constant of the solvent when higher concentrations of amine are present.

A similar behavior was observed when the solvolysis of 4,4´-dimethoxybenzhydryl chloride **1h** was carried out in the presence of variable concentrations of triethylamine, 4-dimethylaminopyridine (DMAP), 1,4-diazabicyclo[2.2.2]octane (DABCO), and pyridine as depicted in Figure 2.4, where the slight reactivity decrease at higher amine concentrations, which is shown in the Experimental Section, has been cut off for the sake of clarity. Addition of the sterically shielded 2,6-lutidine (= 2,6-dimethylpyridine), which is a stronger Brønsted base than pyridine, does not affect the kinetics of the solvolysis reactions. This observation indicates that the amine effect is due to nucleophilic attack of the amine at the benzhydrylium system and not due to Brønsted base catalysis.

In accord with this interpretation, the solvolysis of 4,4´-dimethoxybenzhydryl chloride **1h** in 90% acetone (90A10W) in the presence of 0.25 M piperidine leads to the exclusive formation of the benzhydrylpiperidine **3** (Scheme 2.2).

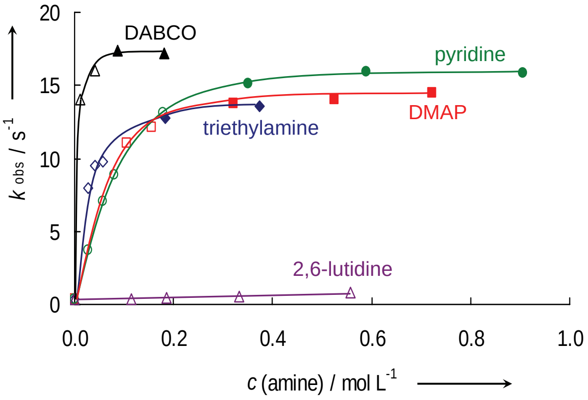
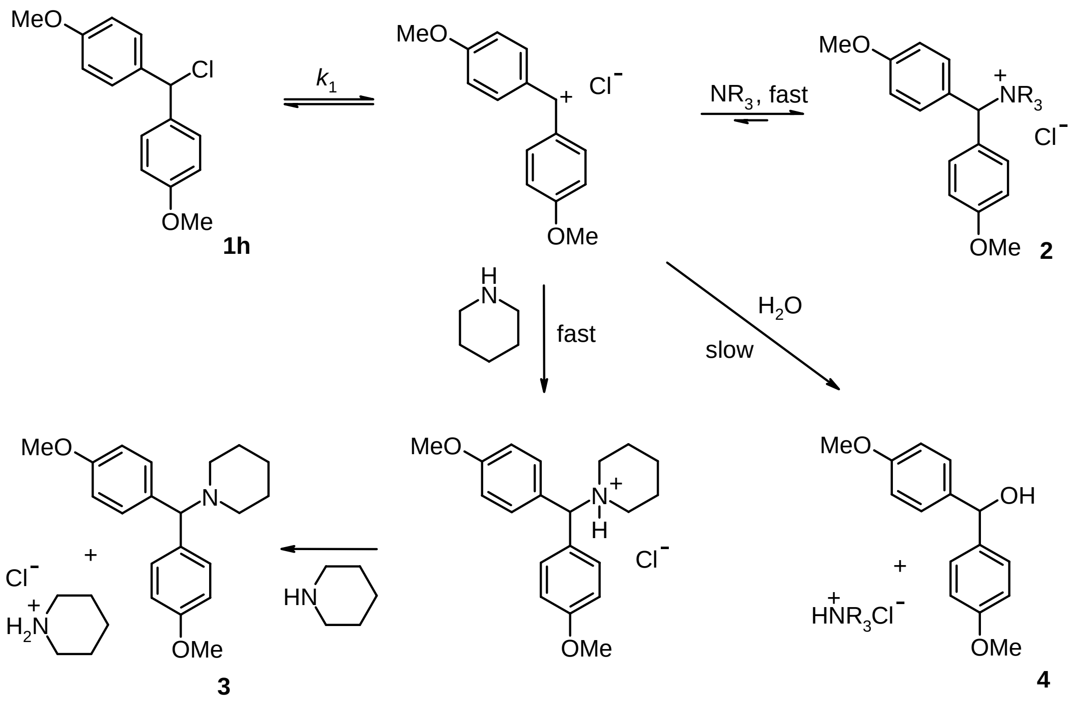


Figure 2.4: Observed rate constants of the solvolysis of 4,4´-dimethoxybenzhydryl chloride **1h** in 90% acetone (90A10W) in the presence of variable concentrations of amines (open symbols represent kinetics that are not of first-order).

Scheme 2.2: Heterolysis of 4,4´-Dimethoxybenzhydryl Chloride **1h** in Aqueous Solutions of Secondary and Tertiary Amines.



The benzhydrylammonium ions **2** obtained from **1h** and tertiary amines were not stable under the reaction conditions and hydrolyzed to give the corresponding benzhydrol **4**. However, because the ammonium chlorides **2** and $HNR_3^+Cl^-$ cannot be expected to have identical equivalent conductivities, the observation of mono-exponential rate laws at high amine concentrations indicates that the hydrolyses of the intermediate ammonium ions **2** occur after the complete consumption of **1h**.

The observation that the solvolysis rate constants k_{obs} reach plateaus when the amine concentrations exceed a certain value (Figures 2.3d and 2.4) excludes the operation of S_N2 mechanisms. It indicates that the acceleration of the gross reactions by amines is due to the suppression of common ion return, i.e., suppression of the reversibility of the first step of Scheme 2.2.

This interpretation is in line with the reactivities of 4-methoxybenzhydryl chloride (**1e**) studied under different conditions in 60% acetone (60A40W). The solvolysis of a 1 mM solution of **1e** follows first-order kinetics with a rate constant of 18.4 s^{-1} (at c(DMAP) = 0 mol L^{-1}) (Figure 2.5). Because of the low concentration of the substrate, recombination of the intermediate carbenium ion $\mathbf{1e}^+$ with Cl (c < 1 mM) does not efficiently compete with the trapping by water.

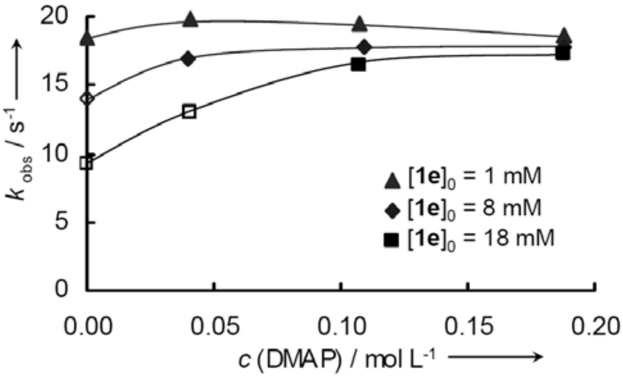


Figure 2.5: Solvolysis of 4-methoxybenzhydryl chloride (**1e**) in 60A40W at 25 °C at different substrate concentrations in the presence of DMAP (open symbols represent kinetics that are not of first-order, see text).

In an 8 mM solution of **1e**, the growing concentration of Cl^- during the reaction is responsible for the gradual retardation of the overall reaction as the common ion return increases during the reaction. The "best fit" to the exponential function yields a value of k_{obs} which is approximately 25% smaller than that of the 1 mM solution in the absence of an amine. The kinetics of the solvolysis reaction of an even more concentrated solution of **1e** ($[\mathbf{1e}]_0$ = 18 mM, [DMAP] = 0) showed a stronger deviation from the exponential function and a further significant decrease of k_{obs} due to increasing common ion return.

In line with the preceding mechanistic analysis, Figure 2.5 shows that higher amine concentrations are needed to suppress common ion return in the more concentrated substrate solutions. Remarkably, the first-order rate constants obtained at different substrate concentrations are almost identical (k_{obs}([**1e**])= 18.6 s^{-1} (1 mM), 17.7 s^{-1} (8 mM), 17.2 s^{-1} (18 mM)) in the presence of 0.19 M DMAP. As expected, the amine additives have a bigger effect on the observed rate constants of the concentrated solutions of **1e** than on the more dilute solutions.

According to Figure 2.6, the "best-fit rate constant" k_{obs} for the solvolysis of 4-methoxy-4′-methylbenzhydryl chloride **1f** (18 mM) in 90A10W in the absence of amine is reduced by a factor of 2.5 when common-ion return was enhanced by the addition of 18 mM $Bu_4N^+Cl^-$.This rate reduction can be compensated by adding amine; in the presence of high chloride ion concentrations, more DMAP is needed to suppress ion recombinations.

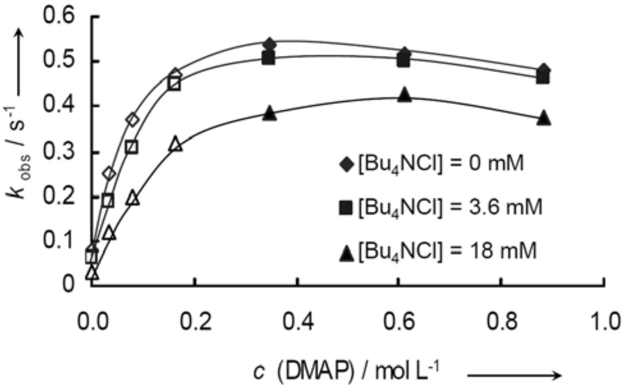


Figure 2.6: Solvolysis of 4-methoxy-4′-methylbenzhydryl chloride (**1f**) (0.018 M) in 90A10W at 25 °C in the presence of Bu_4NCl (open symbols represent kinetics that are not of first-order).

The situation described in Figures 2.3d and 2.4, i. e., increase of k_{obs} with increasing concentrations of nucleophilic amines until a plateau or shallow maximum is reached, has been observed for numerous solvolysis reactions in aqueous acetone and aqueous acetonitrile (see Experimental Section). Tables 2.2 and 2.3 list the maximum values of k_{obs} obtained with different amine additives. Because the maximum values of k_{obs} are reached at different amine concentrations, these rate constants do not refer to exactly the same reaction conditions because the nature of the solvent is slightly altered by the amines (up to 10 vol%). This is only a minute effect, however, compared with the large effects caused by the variation of the substituents in the substrates or variations of the water concentration in the solvents.

More severe are the uncertainties of some of the k_{obs} values in Tables 2.2 and 2.3, which have been obtained in the absence of amines. If they are printed in italics, they include a significant amount of common ion return and thus are specific for the selected concentration of the substrate (here: 0.018 M). As described above, these k_{obs} values reflect a "best fit" to the exponential function and thus give useful information about the gross reactivity at a certain substrate concentration, but are not real "constants".

This trapping method also works with other strong nucleophiles like PPh_3 as can be seen in entry 10 of Table 2.

Table 2.2. Maximum First-Order Rate Constants ($k_{\mathrm{obs,max}}$, $\mathrm{s^{-1}}$) for the Solvolysis Reactions of the Benzhydryl Chlorides **1c**–**j** (0.018 M) in the Presence of Amines in Aqueous Acetone at 25 °C.

	amine	1c	1d	1e	1f	1g	1h	1i	1j
	90% acetone/10% water, v/v (90A10W)								
1	without amine[a]	$\mathit{1.1 \times 10^{-4}}$[b]	$\mathit{1.4 \times 10^{-3}}$[c]	$\mathit{1.6 \times 10^{-2}}$	$\mathit{7.8 \times 10^{-2}}$	$\mathit{1.7 \times 10^{-1}}$	$\mathit{3.9 \times 10^{-1}}$	*2.2*	*6.2*
2	piperidine				6.30×10^{-1}	2.64	2.50×10^{1}	1.01×10^{2}	
3	NEt_3			4.43×10^{-2}	3.95×10^{-1}	1.68	1.36×10^{1}		2.89×10^{2}
4	DMAP	1.33×10^{-4}	1.89×10^{-3}	7.53×10^{-2}[d]	5.40×10^{-1}	2.09	1.45×10^{1}	1.04×10^{2}	4.00×10^{2}
5	DABCO			8.87×10^{-2}	5.81×10^{-1}	2.38	1.74×10^{1}		4.57×10^{2}
6	pyridine			7.89×10^{-2}	6.13×10^{-1}	2.29	1.59×10^{1}		
7	2,6-lutidine[a]						$\mathit{8.4 \times 10^{-1}}$		
8	2-chloro-pyridine[a]			$\mathit{1.9 \times 10^{-2}}$			$\mathit{5.4 \times 10^{-1}}$	*2.2*	
9	Proton Sponge[g]						1.21×10^{1}		
10	PPh_3						2.11×10^{1}		
	80% acetone/20% water, v/v (80A20W)								
11	without amine[a]	1.1×10^{-3}[e]	$\mathit{2.3 \times 10^{-2}}$[f]	$\mathit{3.3 \times 10^{-1}}$	*1.7*	*3.9*	$\mathit{1.5 \times 10^{1}}$		
12	piperidine			8.59×10^{-1}	5.56	1.58×10^{1}	1.57×10^{2}		
13	NEt_3						9.58×10^{1}		
14	DMAP	1.62×10^{-3}	2.80×10^{-2}	9.46×10^{-1}	5.77	1.73×10^{1}	1.37×10^{2}		
15	DABCO			8.25×10^{-1}	5.67	1.76×10^{1}	1.60×10^{2}		
16	pyridine			9.16×10^{-1}	6.06	1.75×10^{1}	1.56×10^{2}		
17	2-chloro-pyridine[a]			$\mathit{3.2 \times 10^{-1}}$					
	60% acetone/40% water, v/v (60A40W)								
18	without amine[a]			*9.2*	$\mathit{3.8 \times 10^{1}}$	$\mathit{6.3 \times 10^{1}}$			
19	DMAP			1.71×10^{1}	8.40×10^{1}	1.74×10^{2}			
20	DABCO			1.47×10^{1}					

[a] *Italics*: not first-order. [b] Solvolysis rate constants $k_1 = 1.11 \times 10^{-4}\ \mathrm{s^{-1}}$ (from ref 9b), $1.12 \times 10^{-4}\ \mathrm{s^{-1}}$ (from ref 13), and $1.15 \times 10^{-4}\ \mathrm{s^{-1}}$ (from ref 14). [c] Solvolysis rate constants $k_1 = 1.83 \times 10^{-3}\ \mathrm{s^{-1}}$ (from ref 9b) and $1.43 \times 10^{-3}\ \mathrm{s^{-1}}$ (from ref 13). [d] Measured at the stopped-flow conductometer; at the conventional conductometer $k_{\mathrm{obs,max}} = 7.23 \times 10^{-4}\ \mathrm{s^{-1}}$. [e] Solvolysis rate constants $k_1 = 1.76 \times 10^{-3}\ \mathrm{s^{-1}}$ (from ref 9b), $1.64 \times 10^{-3}\ \mathrm{s^{-1}}$ (from ref 15), and $1.60 \times 10^{-3}\ \mathrm{s^{-1}}$ (from ref 16). [f] Solvolysis rate constant $k_1 = 2.79 \times 10^{-2}\ \mathrm{s^{-1}}$ (from ref 9b). [g] N,N,N′,N′-Tetramethylnaphthalene-1,8-diamine.

Table 2.3. Maximum First-Order Rate Constants ($k_{obs,max}$, s^{-1}) for the Solvolyses of the Benzhydryl Chlorides **1a**-**h** (6.1×10^{-3} M) in the Presence of Amines in Aqueous Acetonitrile at 25 °C.

	amine	**1a**	**1b**	**1c**	**1d**	**1e**	**1g**	**1h**
				90% acetonitrile/10% water, v/v (90AN10W)				
1	without amine[a]		8.14×10^{-5}	2.50×10^{-3}	*4.2×10^{-2}*	*4.7×10^{-1}*	*6.0*	*1.8×10^{1}*
2	DABCO				4.42×10^{-2}	1.53	3.32×10^{1}	2.49×10^{2}
3	piperidine				4.36×10^{-2}	1.43	3.30×10^{1}	2.38×10^{2}
				80% acetonitrile/20% water, v/v (80AN20W)				
4	without amine[a]	1.09×10^{-4}	8.03×10^{-4}	2.28×10^{-2}	3.41×10^{-1}	*3.8*	*4.0×10^{1}*	
5	DABCO				3.45×10^{-1}	7.70	1.20×10^{2}	
6	piperidine					7.76	1.12×10^{2}	
				60% acetonitrile/40% water, v/v (60AN40W)				
7	without amine[a]	1.14×10^{-3}	8.29×10^{-3}	1.97×10^{-1}	*2.6*	*2.8×10^{1}*		
8	DABCO				2.76	4.08×10^{1}		
9	piperidine				2.63	3.56×10^{1}		

[a] *Italics*: $k_{obs,max}$ was obtained from the "best fit" and does not reflect the real first-order rate constants (see text).

2.3 Discussion

Qualitatively, the message from Tables 2.2 and 2.3 is clear: The effect of the amine additives increases as the solvolysis rate constants increase, i.e., as one moves from left to right in Tables 2.2 and 2.3. While the solvolyses of the methyl substituted benzhydryl chlorides **1c** and **1d** (0.018 M) in 90% acetone (90A10W) are only accelerated by a factor of 1.2 to 1.4 by added DMAP (cf. entries 1 and 4 in Table 2.2), the amine effect increases gradually when moving from left to right and reaches a factor of 65 for benzhydryl chloride **1j**, which ionizes 6.5 orders of magnitude faster than **1c** (compare entries 1 and 4 in Table 2.2).

The increasing importance of common-ion return with decreasing reactivity of the carbocations has previously been considered as a consequence of the reactivity-selectivity principle which claims that selectivity increases with decreasing reactivity. With the fall of the reactivity-selectivity principle[17] a more sophisticated explanation becomes necessary.

In previous work,[18] we have shown that eq 2.2 can be used to calculate the rate constants of the reactions of carbocations with a large variety of nucleophiles, including amines,[19] halide ions,[5b] and solvents.[5a]

$$\log k = s(E + N) \tag{2.2}$$

k: second-order (M^{-1} s^{-1}) or first-order (s^{-1}, for reactions with solvents) rate constants (20 °C)

s, N: empirical, nucleophile-specific parameters

E: empirical electrophilicity parameter

We will now employ eq 2.2 for rationalizing the effects reported in Tables 2.2 and 2.3. Figure 2.7 compares the pseudo-first order rate constants (calculated by eq 2.2) for the reactions of benzhydrylium ions with solvents, chloride ions (6.1×10^{-3} M),[20] and DABCO (0.1 M). The correlation line for the solvent was calculated by eq 2.2 from the published reactivity parameters $N = 5.02$ and $s = 0.89$ for 80% acetonitrile[5a] and the electrophilicity parameters E of the benzhydrylium ions **1a–j** (Table 2.1). Substitution of the published nucleophile-specific parameters $N = 13.30$ and $s = 0.60$ for the chloride ion in 80% acetonitrile[5b] (80AN20W) and the electrophilicity parameters E of the benzhydrylium ions **1a–j** (Table 1) into eq 2.2 yields the second-order rate constants, which are multiplied with the concentrations of Cl^- (6.1 mM)[20] to give the pseudo-first-order rate constants drawn in Figure 2.7. From the known nucleophilicity parameters N and s of secondary and tertiary amines in various solvents[19] one can derive that in 0.1 M solutions of amines in aqueous acetonitrile, most amines react faster than water and chloride as illustrated for the reaction of DABCO with benzhydrylium ions in Figure 2.7. Only highly reactive carbocations, where the diffusion limit is close, will react faster with water which is present in higher concentration.

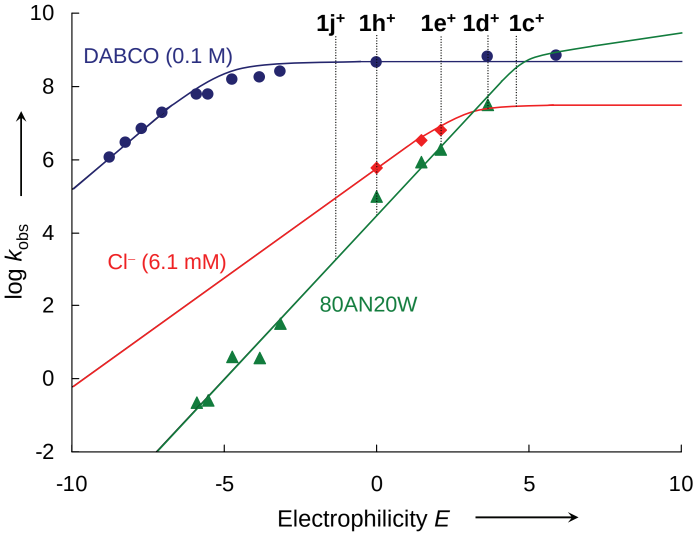


Figure 2.7: Rate constants (log k_{obs}) for the reactions of benzhydrylium ions with 80% acetonitrile, chloride ion (6.1 mM),[20] and DABCO (0.1 M) plotted against the electrophilicity E of the benzhydrylium ions.

We can now use the graph shown in Figure 2.7 to rationalize the observed rate effects. In agreement with the previously published small mass-law constants for the dimethyl substituted benzhydryl chloride **1d** ($\alpha = k_{-1}/k_{solv}$ = 74 M^{-1}) and monomethyl substituted benzhydryl chloride **1c** (α = 32 M^{-1}) in 80% acetone (80A20W),[16] ion recombination does not play an important role in the hydrolyses of these two compounds in aqueous acetonitrile when dilute solutions (i.e. small [Cl^-]) are considered (for **1d**$^+$ and **1c**$^+$, the green solvent graph is above the red Cl^- graph in Figure 2.7). As a result, the solvolysis rates of these compounds are almost unaffected by the addition of amines (Tables 2.2 and 2.3). When methoxy-substituted benzhydrylium ions with $E \leq 2.1$ are considered, the solvent graph drops below the chloride graph in Figure 2.7, suggesting that common-ion return becomes important in aqueous acetonitrile, in agreement with the deviation of the solvolysis kinetics from the first-order rate law. Because Figure 2.7 shows that in this range the amine graph is far above the graphs for the solvent and for Cl^-, one can explain why moderate amine concentrations are already sufficient to suppress the common-ion return und thus lead to an increase of the solvolysis rates. As discussed earlier,[5b] the different slopes of the chloride and solvent correlations account for the decreasing amount of ion-return as one moves from left to right in Figure 2.7. The decreasing magnitude of the amine effect as one moves from left to right in Figure 2.7 can be explained analogously.

The preceding discussion suggests that the rate acceleration by added amines is due to suppression of the common-ion return. One might, therefore, expect the same plateau for all reactive amines in Figure 2.4. This is not the case, and Tables 2.2 and 2.3 show that the maximal first-order rate constants for the various benzhydryl systems in the presence of different amines differ up to a factor of 2. Most notable, the relative heights of the plateaus do not reflect the relative amine nucleophilicities. Thus, pyridine leads generally to slightly higher limiting rates than DMAP despite of its lower nucleophilicity[19d] (see also Figure 2.4). These modest differences may be due to the fact that the amines intercept contact ion pairs as well as free ions. As the rates of these combinations of carbocations with amines are controlled by diffusion and not by activation, it is not surprising that the heights of the plateaus do not correlate with the previously reported order of nucleophilicities of amines.[19]

2.4 Conclusion

Nucleophilic secondary and tertiary amines have been found to suppress common ion return in the S_N1 reactions of rapidly ionizing benzhydryl chlorides without giving rise to S_N2 reactions. By employing amines as non-ionic trapping agents for carbocations instead of the commonly used azide ions it has become possible to follow the kinetics by conductometry and thus measure fast ionization processes on the millisecond time-scale, i.e., rates of formation of highly stabilized carbocations, for which only few kinetic data have so far been available. In this way, it has become possible to close the gap between S_N1 reactions without common-ion return and carbocation-like transition states (Figure 2.1, A) and S_N2C^+ reactions (Figure 2.1, C), where carbocations accumulate before they are trapped by the solvents or other nucleophiles.

2.5 References

(1) a) Streitwieser, A., Jr. *Solvolytic Displacement Reactions*; McGraw-Hill: New York, 1962. b) *Carbonium Ions*, Vol. 1–5; Olah, G. A., Schleyer, P. v. R., Eds.; Interscience: New York, 1968–1976. c) Vogel, P. *Carbocation Chemistry*; Elsevier: Amsterdam, 1985. d) *Advances in Carbocation Chemistry*, Vol. 1; Creary, X., Ed.; JAI Press: Greenwich, CT, 1989. e) *Advances in Carbocation Chemistry*, Vol. 2; Coxon, J. M., Ed.; JAI Press: Greenwich, CT, 1995. f) Katritzky, A. R. *Chem. Soc. Rev.* **1990**, *19*, 83–105. g) McClelland, R. A. In *Reactive Intermediate Chemistry*; Moss, R. A., Platz, M. S., Jones, M., Jr., Eds.; Wiley-Interscience: Hoboken, NJ, 2004; Chapter 1.

(2) Hammond, G. S. *J. Am. Chem. Soc.* **1955**, *77*, 334–338.

(3) a) Richard, J. P. In *Advances in Carbocation Chemistry*, Vol. 1; Creary, X., Ed.; JAI Press: Greenwich, CT, 1989; pp 121–169. b) Amyes, T. L.; Toteva, M. M.; Richard, J. P. In *Reactive Intermediate Chemistry*; Moss, R. A., Platz, M. S., Jones, M., Jr., Eds.; Wiley-Interscience: Hoboken, NJ, 2004; pp 41–69. c) Richard, J. P.; Amyes, T. L.; Toteva M. M.; Tsuji, Y. *Adv. Phys. Org. Chem.* **2004**, *39*, 1–26.

(4) a) McClelland, R. A. *Tetrahedron* **1996**, *52*, 6823–6858. b) Cozens, F. L.; Kanagasabapathy, V. M.; McClelland, R. A.; Steenken, S. *Can. J. Chem.* **1999**, *77*, 2069–2082. c) Pezacki, J. P.; Shukla, D.; Lusztyk, J.; Warkentin, J. *J. Am. Chem. Soc.*

1999, *121*, 6589–6598. d) Hallett-Tapley, G.; Cozens, F. L.; Schepp, N. P. *J. Phys. Org. Chem.* **2009**, *22*, 343–348.

(5) a) Minegishi, S.; Kobayashi, S.; Mayr, H. *J. Am. Chem. Soc.* **2004**, *126*, 5174–5181. b) Minegishi, S.; Loos, R.; Kobayashi, S.; Mayr, H. *J. Am. Chem. Soc.* **2005**, *127*, 2641–2649. c) Mayr, H.; Ofial, A. R. *Pure Appl. Chem.* **2009**, *81*, 667–683.

(6) Schaller, H. F.; Tishkov, A. A.; Feng, X.; Mayr, H. *J. Am. Chem. Soc.* **2008**, *130*, 3012–3022.

(7) Schaller, H. F.; Mayr, H. *Angew. Chem.* **2008**, *120*, 4022–4025; *Angew. Chem. Int. Ed.* **2008**, *47*, 3958–3961.

(8) a) Gelles, E.; Hughes, E. D.; Ingold, C. K. *J. Chem. Soc.* **1954**, 2918–2929. b) Ingold, C. K. *Structure and Mechanism in Organic Chemistry*, 2nd ed.; Cornell University Press: Ithaca, NY, 1969.

(9) a) Denegri, B.; Minegishi, S.; Kronja, O.; Mayr, H. *Angew. Chem.* **2004**, *116*, 2353–2356; *Angew. Chem. Int. Ed.* **2004**, *43*, 2302–2305. b) Denegri, B.; Streiter, A.; Jurić, S.; Ofial, A. R.; Kronja, O.; Mayr, H. *Chem. Eur. J.* **2006**, *12*, 1648–1656; *Chem. Eur. J.* **2006**, *12*, 5415.

(10) For reviews on common-ion rate depression, see: a) Raber, D. J.; Harris, J. M.; Schleyer, P. v. R. In *Ions and Ion Pairs in Organic Reactions*, Vol. 2; Szwarc, M., Ed.; Wiley: New York, 1974. b) Stang, P. J.; Rappoport, Z.; Hanack, M.; Subramanian, L. R. *Vinyl Cations*; Academic Press: New York, 1979; Chapter 6, pp 337–338. c) Rappoport, Z. In *Reactive Intermediates*; Abramovitch, R. A., Ed.; Plenum Press: New York, 1983; Vol. 3, pp 583–594. d) Kitamura, T.; Taniguchi, H.; Tsuno, Y. In *Dicoordinated Carbocations*; Rappoport, Z., Stang, P. J., Eds.; Wiley: Chichester, 1997; pp 321–376.

(11) For other recent work on ion-pair reactivities, see: a) Peters, K. S. *Acc. Chem Res.* **2007**, *40*, 1–7. b) Peters, K. S. *Chem. Rev.* **2007**, *107*, 859–873. c) Moss, R. A. *Acc. Chem. Res.* **1999**, *32*, 969–974. d) Moss, R. A. *J. Phys. Org. Chem.* **2009**, *22*, 265–273. e) Moss, R. A.; Fu, X.; Sauers, R. R. *J. Phys. Org. Chem.* **2007**, *20*, 1–10. f) Hao, W.; Parker, V. D. *J. Org. Chem.* **2008**, *73*, 48–55. g) Tsuji, Y; Richard, J. P. *Chem. Rec.* **2005**, *5*, 94–106. h) Huang, X.; Bennet, A. J. *Can. J. Chem.* **2004**, *82*, 1336–1340. i) Koo, I. S.; An, S. K.; Yang, K.; Lee, I.; Bentley, T. W. *J. Phys. Org. Chem.* **2002**, *15*, 758–764. j) Tsuji, Y.; Richard, J. P. *J. Am. Chem. Soc.* **2006**, *128*, 17139–17145. k) Jia, Z. S.; Ottosson, H.; Zeng, X.; Thibblin, A. *J. Org. Chem.* **2002**, *67*, 182–187. l) Tsuji, Y.; Mori, T.; Toteva, M. M.; Richard, J. P. *J. Phys. Org. Chem.* **2003**, *16*, 484–490.

(12) a) Mayr, H.; Bug, T.; Gotta, M. F.; Hering, N.; Irrgang, B.; Janker, B.; Kempf, B.; Loos, R.; Ofial, A. R.; Remennikov, G.; Schimmel, H. *J. Am. Chem. Soc.* **2001**, *123*, 9500–9512. b) Mayr, H.; Kempf, B.; Ofial, A: R. *Acc. Chem. Res.* **2003**, 36, 66-77.

(13) Berliner, E.; Malter, M. Q. *J. Org. Chem.* **1968**, *33*, 2595–2596.

(14) Verbit, L.; Berliner, E. *J. Am. Chem. Soc.* **1964**, *86*, 3307–3312.

(15) Liu, K.-T.; Lin, Y.-S.; Tsao, M.-L. *J. Phys. Org. Chem.* **1998**, *11*, 223–229.

(16) Bateman, L. C.; Church, M. G.; Hughes, E. D.; Ingold, C. K.; Taher, N. A. *J. Chem. Soc.* **1940**, 979–1011.

(17) Mayr, H.; Ofial, A. R. *Angew. Chem.* **2006**, *118*, 1876–1886; *Angew. Chem. Int. Ed.* **2006**, *45*, 1844–1854; and refs cited therein.

(18) a) Mayr, H.; Ofial, A. R. *Pure Appl. Chem.* **2005**, *77*, 1807–1821. b) Mayr, H.; Ofial, A. R. *J. Phys. Org. Chem.* **2008**, *21*, 584–595.

(19) a) Minegishi, S.; Mayr, H. *J. Am. Chem. Soc.* **2003**, *125*, 286–295. b) Phan, T. B.; Breugst, M.; Mayr, H. *Angew. Chem.* **2006**, *118*, 3954–3959; *Angew. Chem. Int. Ed.* **2006**, *45*, 3869–3874. c) Brotzel, F.; Chu, Y. C.; Mayr, H. *J. Org. Chem.* **2007**, *72*, 3679–3688. d) Brotzel, F.; Kempf, B.; Singer, T.; Zipse, H.; Mayr, H. *Chem. Eur. J.* **2007**, *13*, 336–345.

(20) This concentration corresponds to the final concentration of Cl^- at the end of the solvolysis reactions shown in Table 3, i.e. the maximum concentration of Cl^- during the measurement.

2.6 Experimental Section

2.6.1 General

Materials. Commercially available acetone and acetonitrile (content of H_2O < 50 ppm) was used without further purification for all experiments. Mixtures of solvents are given as (v/v) and the solvents are abbreviated: A = acetone, AN = acetonitrile, W = water. For example the solvent mixture 80A20W refers to a mixture of acetone and water in a ratio of 80/20 (v/v).

Benzhydryl chlorides **1a–j** were obtained from the reactions of benzhydrols with thionyl chloride in dichloromethane according to the procedure published before.[S1]

Kinetics. Solvolysis rates of the benzhydrylium chlorides were monitored by following the increase of the conductivity of the reaction mixtures (conductometer: Tacussel CD 810, Pt electrode: WTW LTA 1/NS). Typically, 10 to 80 mg of substrate was dissolved in 100 µL of acetone or acetonitrile, then injected into the solvent, and the conductance (*G*) was recorded at given time intervals.

For the study of solvolysis reactions with half lives of 10^{-2} s < $\tau_{1/2}$ < 10 s, a stopped-flow conductometer (Hi-Tech Scientific SF-61 DX2, platinum electrodes, cell volume: 21 µL, cell constant 4.24 cm^{-1}, minimum dead time 2.2 ms) was used in single-mixing mode. The benzhydryl chlorides were dissolved in pure acetone or acetonitrile and mixed right in front of the conductivity cell with aqueous acetone or acetonitrile to give solutions of the desired composition. The temperature of the solutions during all of the kinetic studies was kept constant (25.0 ± 0.1 °C) using a circulating bath thermostat.

Calibration. In order to prove that the conductivity increased proportionally with the concentration of the produced hydrochloric acid or pyridinium salts, we dissolved variable amounts of rapidly solvolyzing benzhydryl chlorides in acetone/water mixtures. On both conductometers used, plots of the conductivities obtained after some seconds versus the

---

[S1] Denegri, B.; Streiter, A.; Jurić, S.; Ofial, A. R.; Kronja, O.; Mayr, H. *Chem. Eur. J.* **2006**, *12*, 1648–1656; *Chem. Eur. J.* **2006**, *12*, 5415.

concentrations of the solvolyzed substrates were linear up to 0.02 M, i.e., in the concentration range used for the kinetic experiments (Figure S1 and S2).

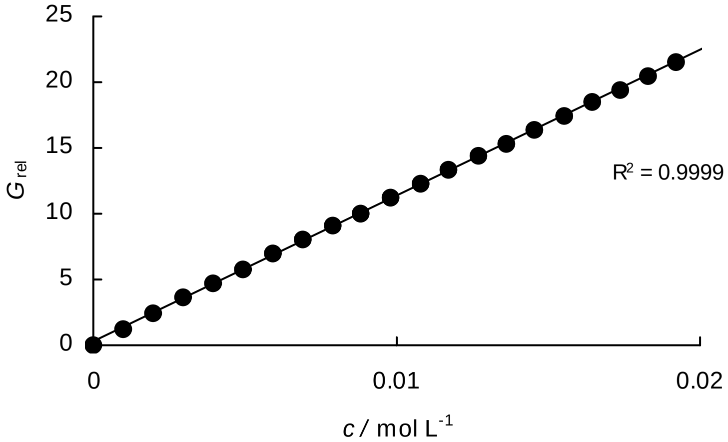


Figure S1: Plot of conductivity G_{rel} versus concentration of the solvolyzed substrate 4,4′-dimethoxybenzhydryl chloride **1h** with added DMAP (0.5 mol L^{-1}) in 80% aqueous acetone (80A20W) at the conventional conductometer.

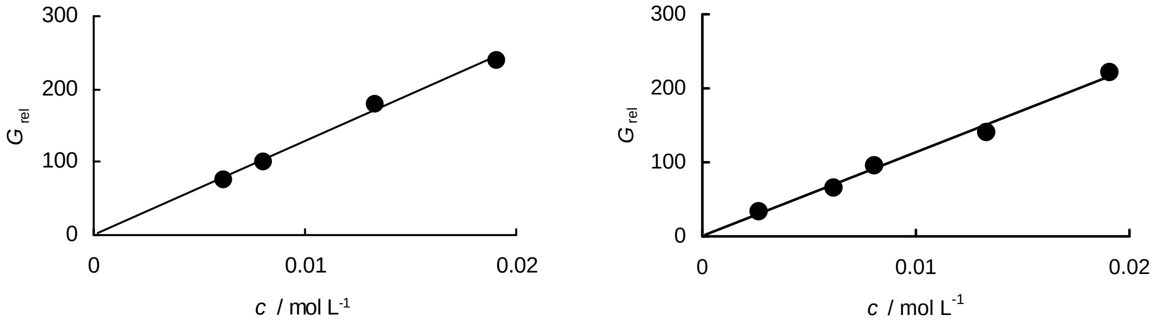


Figure S2: Plot of conductivity G_{rel} versus concentration of the solvolyzed substrate 4,4′-dimethoxybenzhydryl chloride **1h** without (left) and with added DMAP (0.5 mol L^{-1}, right) in 90% aqueous acetone (90A10W) from the stopped-flow conductometer.

The solvolysis of 4-methoxybenzhydryl chloride **1e** in 90% aqueous acetone (90A10W) could be studied at the conventional conductometer as well as the stopped-flow instrument. Figure S3 shows that the same results were obtained with both instruments, which confirms the consistency of the data obtained with both instruments.

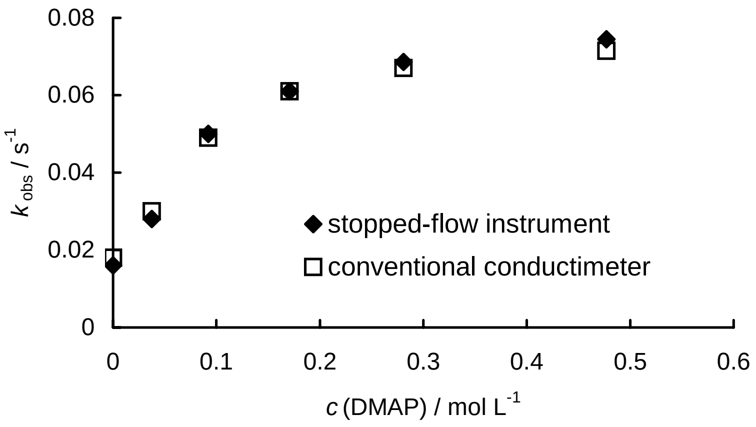


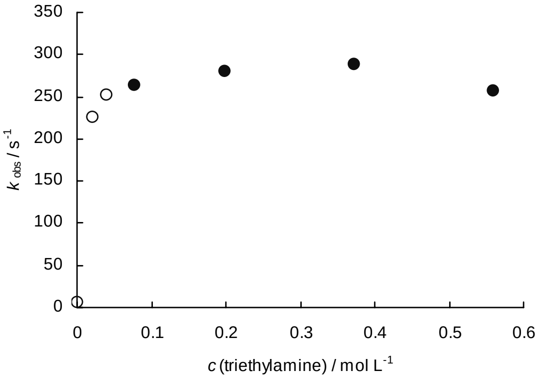
Figure S3: Solvolysis of 4-methoxybenzhydryl chloride **1e** (0.018 M) in 90A10W at 25 °C, studied both at the conventional conductometer and the stopped-flow instrument. (First-order rate constants observed for *c*(DMAP) > 0.2 M).

2.6.2 Solvolysis Reactions of Benzhydryl Chlorides in 90% Aqueous Acetone (90A10W)

Solvolysis reactions of bis-(2,3-dihydrobenzofuran-5-yl)-methyl chloride ***1j*** *in 90A10W*

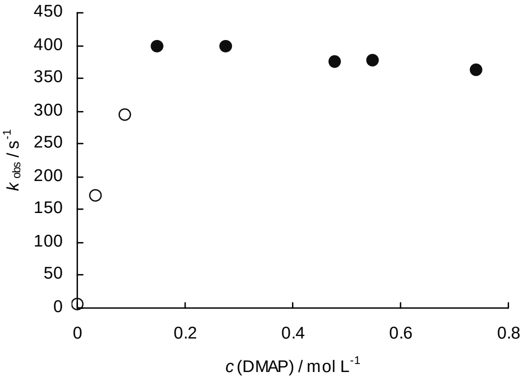
substrate concentration	**amine**	**solvent**	**method**
[**1j**] = 1.8×10^{-2} mol L^{-1}	triethylamine	90A10W	stopped-flow conductometry

No	c(triethylamine) / M	k_{obs} / s^{-1}	r^2
90AW400	0	6.2	0.9935
90AW411	0.021	2.1×10^2	0.9971
90AW412	0.039	2.4×10^2	0.9987
90AW413	0.077	2.60×10^2	0.9993
90AW415	0.198	2.81×10^2	0.9995
90AW416	0.372	$\mathbf{2.89 \times 10^2}$	0.9999
90AW417	0.559	2.58×10^2	0.9993



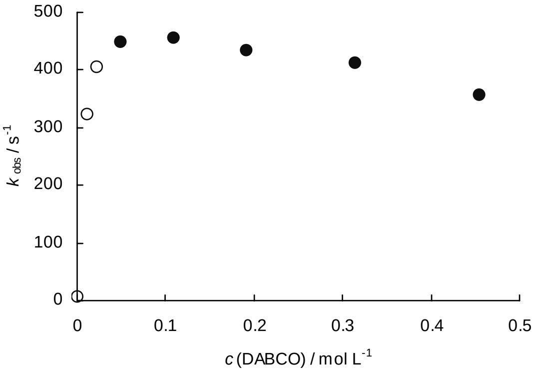
substrate concentration	**amine**	**solvent**	**method**
[**1j**] = 1.8×10^{-2} mol L^{-1}	DMAP	90A10W	stopped-flow conductometry

No	c(DMAP) / M	k_{obs} / s^{-1}	r^2
90AW400	0	6.2	0.9935
90AW401	0.033	1.7×10^2	0.9930
90AW402	0.088	2.95×10^2	0.9999
90AW403	0.147	3.99×10^2	0.9994
90AW404	0.276	$\mathbf{4.00 \times 10^2}$	0.9994
90AW405	0.478	3.75×10^2	0.9994
90AW406	0.549	3.77×10^2	0.9996
90AW407	0.741	3.63×10^2	0.9998



substrate concentration	**amine**	**solvent**	**method**
[**1j**] = 1.8×10^{-2} mol L^{-1}	DABCO	90A10W	stopped-flow conductometry

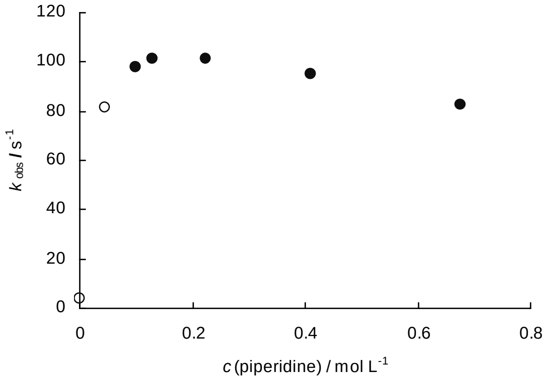
No	c(DABCO) / M	k_{obs} / s^{-1}	r^2
90AW400	0	6.2	0.9935
90AW231	0.011	3.2×10^2	0.9947
90AW232	0.021	4.1×10^2	0.9988
90AW233	0.049	4.50×10^2	0.9997
90AW234	0.108	**4.57×10^2**	0.9995
90AW235	0.190	4.35×10^2	0.9993
90AW236	0.313	4.12×10^2	0.9993
90AW237	0.455	3.57×10^2	0.9995



*Solvolysis reactions of (2,3-dihydrobenzofuran-5-yl)-(4´-methoxyphenyl)-methyl chloride **1i** in 90A10W*

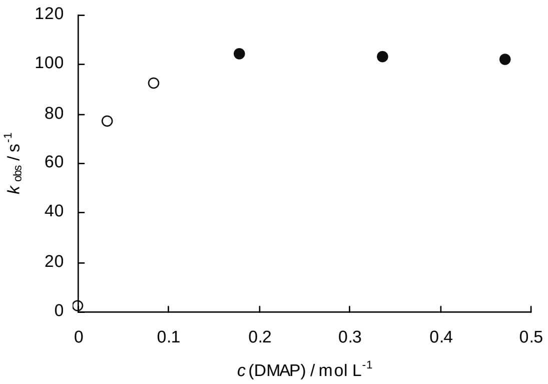
substrate concentration	**amine**	**solvent**	**method**
[**1i**] = 1.8×10^{-2} mol L^{-1}	piperidine	90A10W	stopped-flow conductometry

No	c(piperidine) / M	k_{obs} / s^{-1}	r^2
NSK17-0	0	2.2	0.9936
NSK48-1	0.045	8.2×10^1	0.9985
NSK48-2	0.098	9.79×10^1	0.9998
NSK48-3	0.130	1.01×10^2	0.9998
NSK48-4	0.224	**1.01×10^2**	0.9999
NSK48-5	0.410	9.49×10^1	0.9999
NSK48-6	0.675	8.24×10^1	0.9998



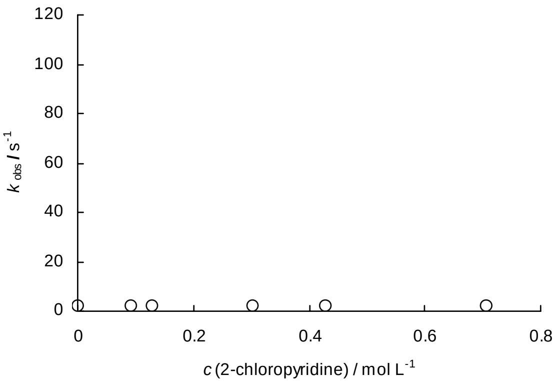
substrate concentration	**amine**	**solvent**	**method**
[**1i**] = 1.8×10^{-2} mol L^{-1}	DMAP	90A10W	stopped-flow conductometry

No	c(DMAP) / M	k_{obs} / s^{-1}	r^2
NSK17-0	0	2.2	0.9935
NSK17-1	0.033	7.7×10^1	0.9974
NSK17-2	0.083	9.2×10^1	0.9981
NSK17-3	0.179	**1.04×10^2**	0.9999
NSK17-4	0.336	1.03×10^2	0.9999
NSK17-5	0.472	1.02×10^2	0.9999



substrate concentration	**amine**	**solvent**	**method**
[**1i**] = 1.8×10^{-2} mol L^{-1}	2-chloropyridine	90A10W	stopped-flow conductometry

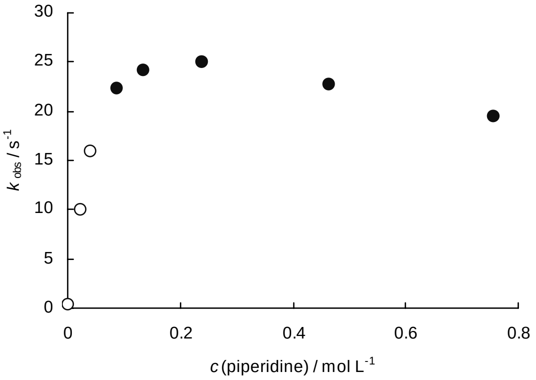
No	c(2-chloropyridine) / M	k_{obs} / s^{-1}	r^2
NSK17-0	0	**2.2**	0.9935
NSK49-2	0.093	2.2	0.9955
NSK49-3	0.128	2.2	0.9946
NSK49-4	0.301	2.2	0.9947
NSK49-5	0.428	2.2	0.9937
NSK49-6	0.706	2.2	0.9938



Solvolysis reactions of 4,4´-dimethoxybenzhydryl chloride ***1h*** *in 90A10W*

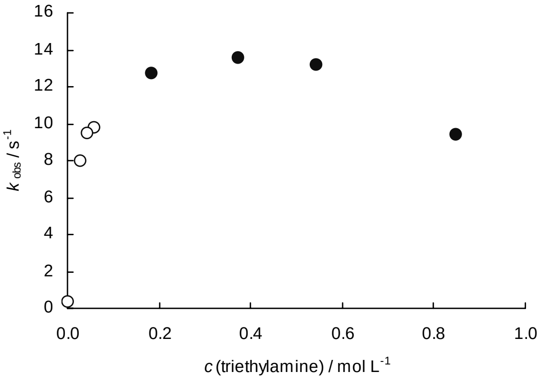
substrate concentration	**amine**	**solvent**	**method**
[**1h**] = 1.8×10^{-2} mol L^{-1}	piperidine	90A10W	stopped-flow conductometry

No	*c*(piperidine) / M	k_{obs} / s^{-1}	r^2
90A10W8	0	0.39	0.9624
90AW71	0.021	10	0.9743
90AW72	0.040	16	0.9891
90AW73	0.086	22.4	0.9972
90AW74	0.134	24.2	0.9981
90AW75	0.237	**25.0**	0.9989
90AW76	0.462	22.8	0.9991
90AW77	0.755	19.5	0.9992



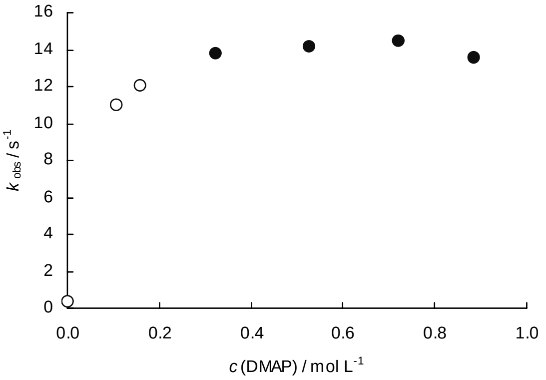
substrate concentration	**amine**	**solvent**	**method**
[**1h**] = 1.8×10^{-2} mol L^{-1}	triethylamine	90A10W	stopped-flow conductometry

No	*c*(triethylamine) / M	k_{obs} / s^{-1}	r^2
90A10W8	0	0.39	0.9624
90A10W1	0.027	8.0	0.9988
90A10W4	0.041	9.5	0.9968
90A10W2	0.057	9.8	0.9986
90A10W5	0.184	12.8	0.9993
90A10W6	0.373	**13.6**	0.9995
90A10W7	0.542	13.2	0.9994
90A10W9	0.846	9.43	0.9993



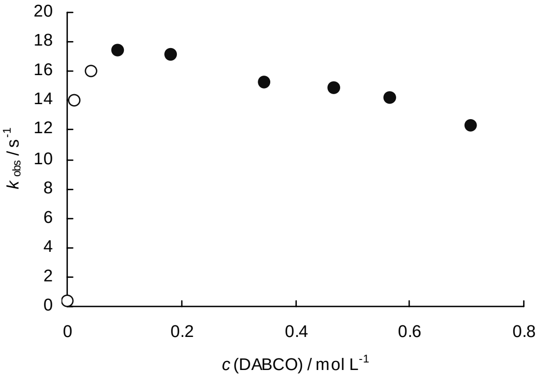
substrate concentration	**amine**	**solvent**	**method**
[**1h**] = 1.8×10^{-2} mol L^{-1}	DMAP	90A10W	stopped-flow conductometry

No	c(DMAP) / M	k_{obs} / s^{-1}	r^2
90A10W8	0	0.39	0.9624
90A10W12	0.105	11	0.9997
90A10W13	0.157	12	0.9997
90A10W14	0.322	13.8	0.9999
90A10W15	0.525	14.0	0.9999
90A10W16	0.722	**14.5**	0.9999
90A10W17	0.885	13.6	0.9999



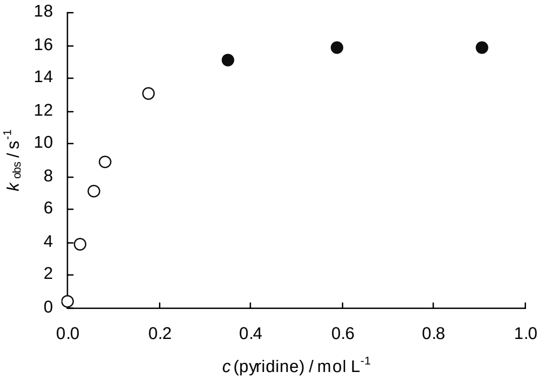
substrate concentration	**amine**	**solvent**	**method**
[**1h**] = 1.8×10^{-2} mol L^{-1}	DABCO	90A10W	stopped-flow conductometry

No	c(DABCO) / M	k_{obs} / s^{-1}	r^2
90A10W8	0	0.39	0.9624
90A10W26	0.012	14	0.9940
90A10W21	0.041	16	0.9985
90A10W22	0.088	**17.4**	0.9991
90A10W23	0.181	17.2	0.9998
90A10W24	0.346	15.3	0.9999
90A10W28	0.468	14.9	0.9996
90A10W25	0.566	14.2	0.9995
90A10W29	0.708	12.3	0.9995



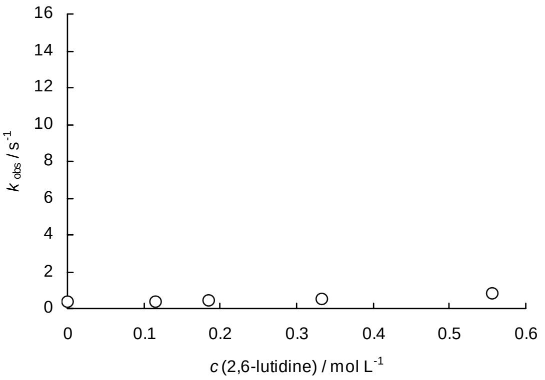
substrate concentration	**amine**	**solvent**	**method**
[**1h**] = 1.8×10^{-2} mol L^{-1}	pyridine	90A10W	stopped-flow conductometry

No	c(pyridine) / M	k_{obs} / s^{-1}	r^2
90A10W8	0	0.39	0.9624
90AW51	0.027	3.7	0.9932
90AW52	0.057	7.1	0.9955
90AW53	0.081	8.9	0.9966
90AW54	0.178	13	0.9985
90AW55	0.352	15.1	0.9995
90AW56	0.590	**15.9**	0.9996
90AW57	0.907	15.8	0.9997



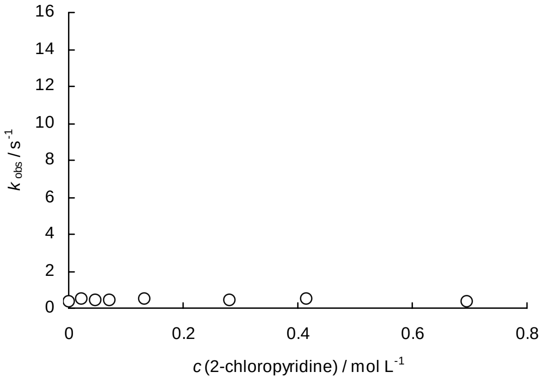
substrate concentration	**amine**	**solvent**	**method**
[**1h**] = 1.8×10^{-2} mol L^{-1}	2,6-lutidine	90A10W	stopped-flow conductometry

No	c(2,6-lutidine) / M	k_{obs} / s^{-1}	r^2
90A10W8	0	0.39	0.9624
90AW32	0.115	0.39	0.9879
90AW33	0.185	0.42	0.9799
90AW34	0.333	0.56	0.9721
90AW35	0.557	**0.84**	0.9575



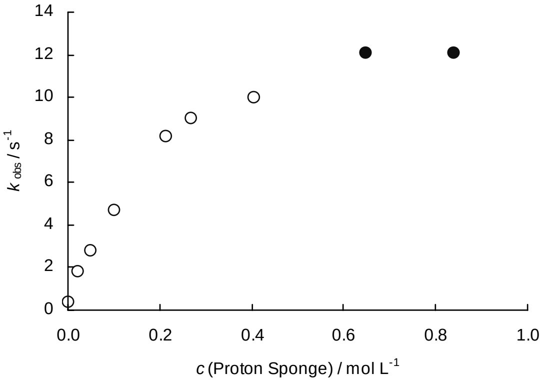
substrate concentration	**amine**	**solvent**	**method**
[**1h**] = 1.8×10^{-2} mol L^{-1}	2-chloropyridine	90A10W	stopped-flow conductometry

No	c(2-chloropyridine) / M	k_{obs} / s^{-1}	r^2
90A10W8	0	0.39	0.9624
90AW61	0.023	0.51	0.9583
90AW62	0.046	0.48	0.9660
90AW63	0.071	0.48	0.9606
90AW64	0.132	**0.54**	0.9650
90AW65	0.281	0.44	0.9441
90AW66	0.416	0.51	0.9276
90AW67	0.695	0.36	0.9600



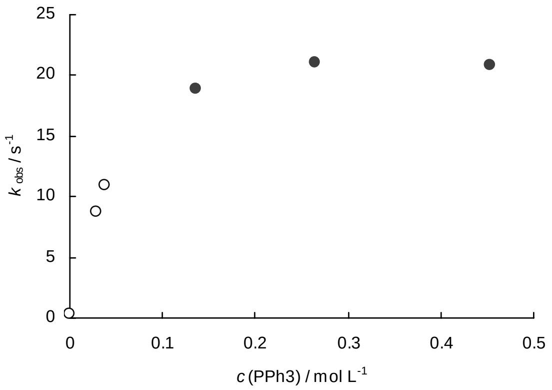
substrate concentration	**amine**	**solvent**	**method**
[**1h**] = 1.8×10^{-2} mol L^{-1}	Proton Sponge	90A10W	stopped-flow conductometry

No	c(Proton Sponge) / M	k_{obs} / s^{-1}	r^2
90A10W8	0	0.39	0.9624
90AW41	0.021	1.8	0.9876
90AW42	0.048	2.8	0.9921
90AW43	0.099	4.7	0.9950
90AW44	0.211	8.2	0.9970
90AW45	0.268	9.0	0.9987
90AW46	0.404	10	0.9988
90AW47	0.647	12.1	0.9986
90AW48	0.838	**12.1**	0.9989



substrate concentration	**nucleophile**	**solvent**	**method**
[**1h**] = 1.8×10^{-2} mol L^{-1}	PPh_3	90A10W	stopped-flow conductometry

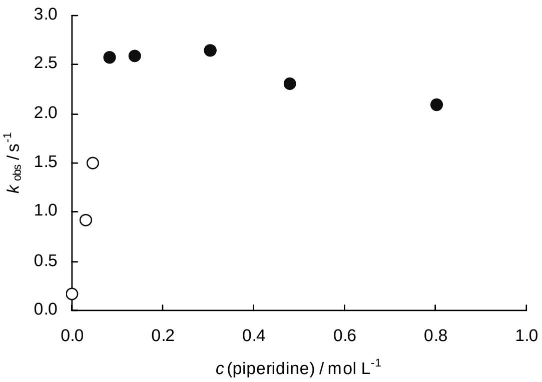
No	$c(PPh_3)$ / M	k_{obs} / s^{-1}	r^2
90A10W8	0	0.39	0.9624
90AW601	0.028	8.7	0.9941
90AW602	0.037	11	0.9964
90AW603	0.136	18.9	0.9996
90AW604	0.264	**21.1**	0.9999
90AW605	0.454	20.8	0.9999



*Solvolysis reactions of 4-methoxy-4´-phenoxybenzhydryl chloride **1g** in 90A10W*

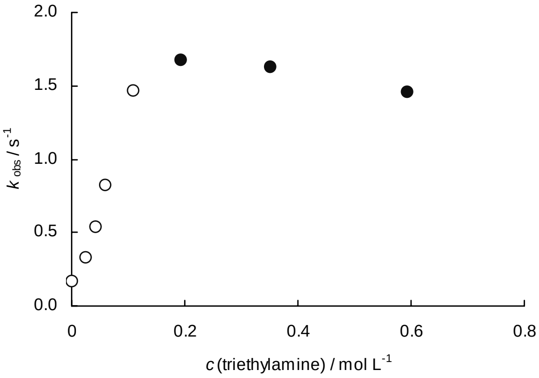
substrate concentration	**amine**	**solvent**	**method**
[**1g**] = 1.8×10^{-2} mol L^{-1}	piperidine	90A10W	stopped-flow conductometry

No	c(piperidine) / M	k_{obs} / s^{-1}	r^2
90AW100	0	0.17	0.9606
90AW138	0.032	0.98	0.9903
90AW132	0.047	1.5	0.9878
90AW133	0.084	2.57	0.9974
90AW134	0.138	2.59	0.9972
90AW135	0.306	**2.64**	0.9985
90AW136	0.479	2.31	0.9990
90AW137	0.804	2.10	0.9991



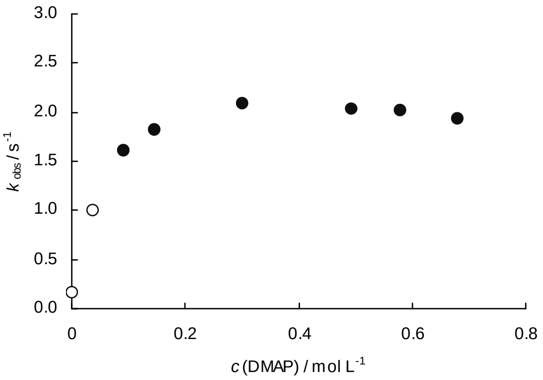
substrate concentration	**amine**	**solvent**	**method**
[**1g**] = 1.8×10^{-2} mol L^{-1}	triethylamine	90A10W	stopped-flow conductometry

No	*c*(triethylamine) / M	k_{obs} / s^{-1}	r^2
90AW100	0	0.17	0.9606
90AW111	0.024	0.33	0.9486
90AW112	0.043	0.54	0.9450
90AW113	0.060	0.82	0.9673
90AW114	0.109	1.5	0.9960
90AW115	0.193	**1.68**	0.9975
90AW116	0.351	1.63	0.9986
90AW117	0.593	1.46	0.9993



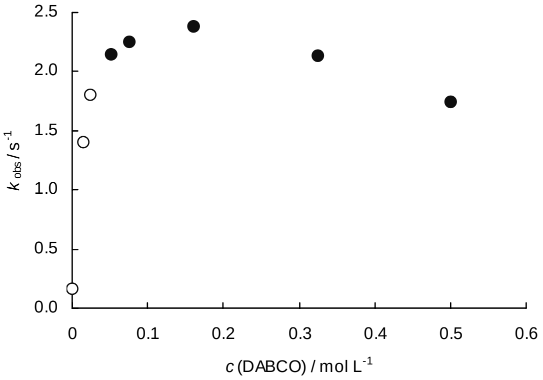
substrate concentration	**amine**	**solvent**	**method**
[**1g**] = 1.8×10^{-2} mol L^{-1}	DMAP	90A10W	stopped-flow conductometry

No	*c*(DMAP) / M	k_{obs} / s^{-1}	r^2
90AW100	0	0.17	0.9606
90AW101	0.036	1.0	0.9983
90AW102	0.090	1.61	0.9988
90AW103	0.146	1.83	0.9992
90AW104	0.300	**2.09**	0.9998
90AW105	0.493	2.04	0.9998
90AW106	0.579	2.02	0.9999
90AW107	0.679	1.94	0.9999



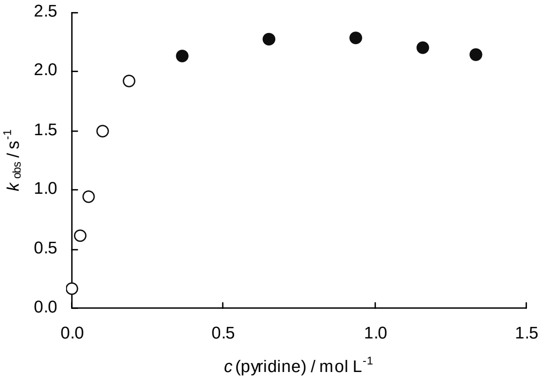
substrate concentration	**amine**	**solvent**	**method**
[**1g**] = 1.8×10^{-2} mol L^{-1}	DABCO	90A10W	stopped-flow conductometry

No	c(DABCO) / M	k_{obs} / s^{-1}	r^2
90AW100	0	0.17	0.9606
90AW111a	0.014	1.4	0.9958
90AW112a	0.024	1.8	0.9974
90AW113a	0.051	2.15	0.9988
90AW114a	0.075	2.25	0.9992
90AW115a	0.160	**2.38**	0.9997
90AW116a	0.325	2.13	0.9998
90AW117a	0.501	1.74	0.9991



substrate concentration	**amine**	**solvent**	**method**
[**1g**] = 1.8×10^{-2} mol L^{-1}	pyridine	90A10W	stopped-flow conductometry

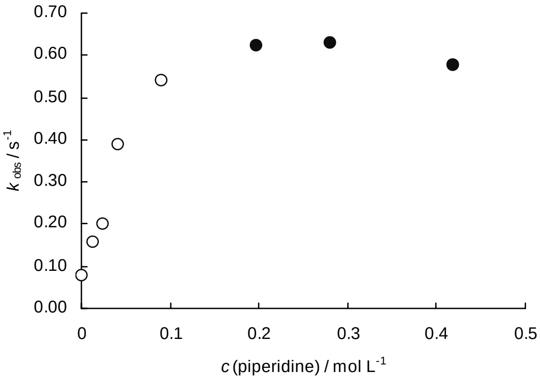
No	c(pyridine) / M	k_{obs} / s^{-1}	r^2
90AW100	0	0.17	0.9606
90AW121	0.027	0.61	0.9966
90AW122	0.054	0.94	0.9959
90AW123	0.102	1.5	0.9974
90AW124	0.187	1.9	0.9979
90AW125	0.367	2.13	0.9994
90AW126	0.651	2.28	0.9997
90AW127	0.936	**2.29**	0.9998
90AW128	1.156	2.21	0.9998
90AW129	1.333	2.15	0.9998



*Solvolysis reactions of 4-methoxy-4´-methylbenzhydryl chloride **1f** in 90A10W*

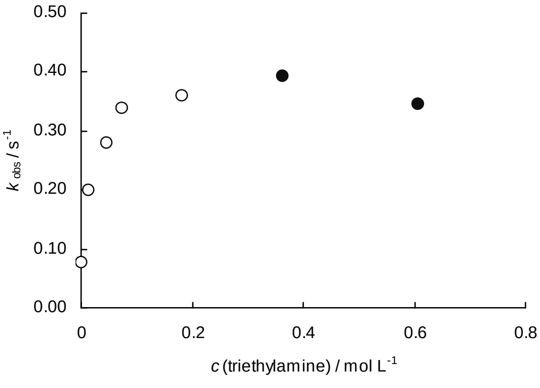
substrate concentration	**amine**	**solvent**	**method**
[**1f**] = 1.8×10^{-2} mol L^{-1}	piperidine	90A10W	stopped-flow conductometry

No	*c*(piperidine) / M	k_{obs} / s^{-1}	r^2
90AW180	0	7.8×10^{-2}	0.9944
90AW201	0.012	1.6×10^{-1}	0.9707
90AW202	0.023	2.0×10^{-1}	0.9735
90AW203	0.041	3.9×10^{-1}	0.9902
90AW204	0.090	5.4×10^{-1}	0.9953
90AW205	0.197	6.23×10^{-1}	0.9978
90AW206	0.279	**6.30×10^{-1}**	0.9989
90AW207	0.419	5.78×10^{-1}	0.9986



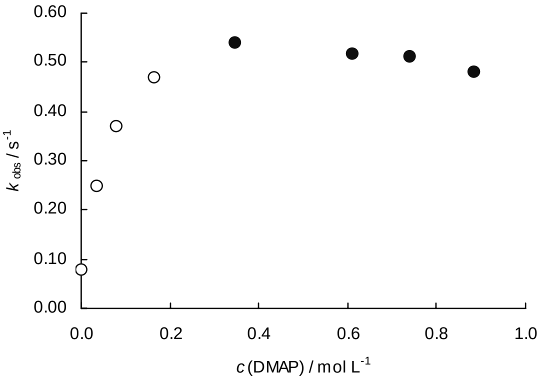
substrate concentration	**amine**	**solvent**	**method**
[**1f**] = 1.8×10^{-2} mol L^{-1}	triethylamine	90A10W	stopped-flow conductometry

No	*c*(triethylamine) / M	k_{obs} / s^{-1}	r^2
90AW180	0	7.8×10^{-2}	0.9944
90AW212	0.045	2.0×10^{-1}	0.9878
90AW213	0.073	2.8×10^{-1}	0.9933
90AW214	0.120	3.4×10^{-1}	0.9951
90AW215	0.181	3.6×10^{-1}	0.9960
90AW216	0.363	**3.95×10^{-1}**	0.9979
90AW217	0.606	3.47×10^{-1}	0.9987



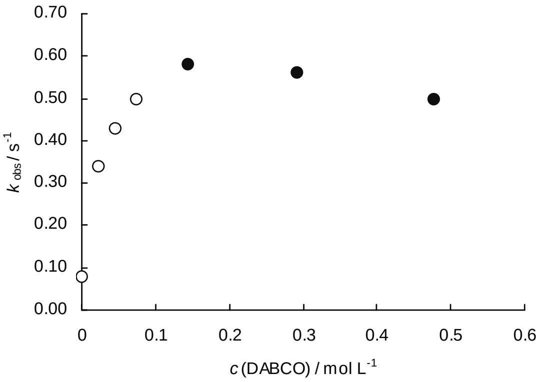
substrate concentration	**amine**	**solvent**	**method**
[**1f**] = 1.8×10^{-2} mol L^{-1}	DMAP	90A10W	stopped-flow conductometry

No	c(DMAP) / M	k_{obs} / s^{-1}	r^2
90AW180	0	7.8×10^{-2}	0.9944
90AW221	0.035	2.5×10^{-1}	0.9936
90AW222	0.079	3.7×10^{-1}	0.9953
90AW223	0.163	4.7×10^{-1}	0.9983
90AW224	0.347	$\mathbf{5.40 \times 10^{-1}}$	0.9990
90AW225	0.609	5.18×10^{-1}	0.9995
90AW226	0.739	5.13×10^{-1}	0.9995
90AW227	0.884	4.80×10^{-1}	0.9996



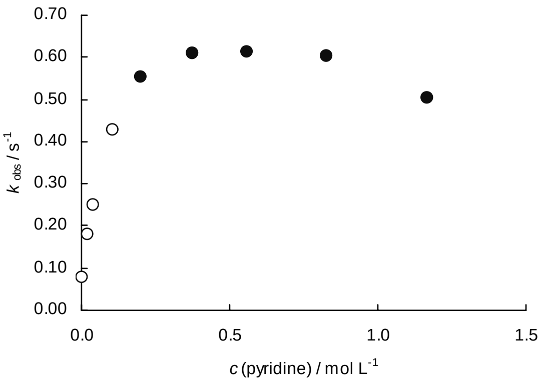
substrate concentration	**amine**	**solvent**	**method**
[**1f**] = 1.8×10^{-2} mol L^{-1}	DABCO	90A10W	stopped-flow conductometry

No	c(DABCO) / M	k_{obs} / s^{-1}	r^2
90AW180	0	7.8×10^{-2}	0.9944
90AW192	0.022	3.4×10^{-1}	0.9946
90AW193	0.046	4.3×10^{-1}	0.9950
90AW194	0.075	5.0×10^{-1}	0.9964
90AW195	0.144	$\mathbf{5.81 \times 10^{-1}}$	0.9985
90AW196	0.291	5.61×10^{-1}	0.9991
90AW197	0.477	4.97×10^{-1}	0.9994



substrate concentration	**amine**	**solvent**	**method**
[**1f**] = 1.8×10^{-2} mol L^{-1}	pyridine	90A10W	stopped-flow conductometry

Nr.	c(pyridine) / M	k_{obs} / s^{-1}	r^2
90AW180	0	7.8×10^{-2}	0.9944
90AW181	0.019	1.8×10^{-1}	0.9938
90AW182	0.040	2.5×10^{-1}	0.9917
90AW183	0.102	4.3×10^{-1}	0.9953
90AW184	0.200	5.54×10^{-1}	0.9980
90AW185	0.372	6.12×10^{-1}	0.9989
90AW186	0.555	**6.13×10^{-1}**	0.9991
90AW187	0.826	6.03×10^{-1}	0.9993
90AW188	1.166	5.05×10^{-1}	0.9993

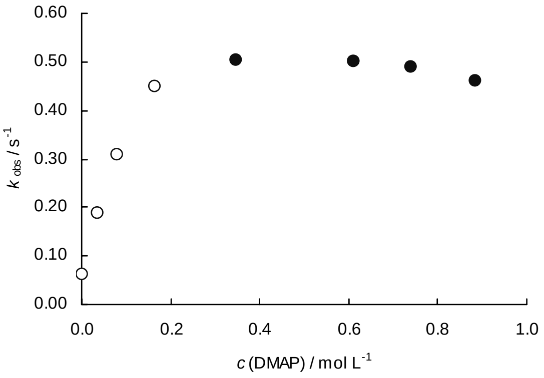


Solvolyses in the presence of Bu_4NCl:

substrate concentration	**amine**	**solvent**	**method**
[**1f**] = 1.8×10^{-2} mol L^{-1}	DMAP	90A10W	stopped-flow conductometry

additive: 3.6×10^{-3} mol L^{-1} Bu_4NCl (0.2 equiv.)

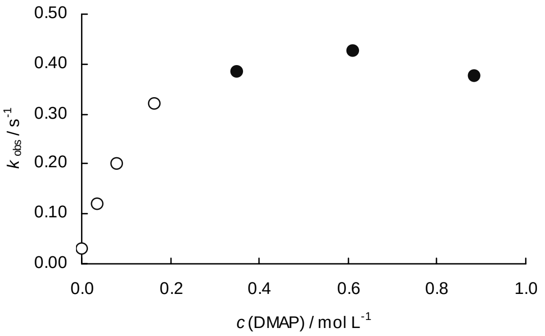
No	c(DMAP) / M	k_{obs} / s^{-1}	r^2
90AW220a	0	6.2×10^{-2}	0.9938
90AW221a	0.035	1.9×10^{-1}	0.9916
90AW222a	0.079	3.1×10^{-1}	0.9952
90AW223a	0.163	4.5×10^{-1}	0.9982
90AW224a	0.347	**5.06×10^{-1}**	0.9991
90AW225a	0.609	5.03×10^{-1}	0.9996
90AW226a	0.739	4.90×10^{-1}	0.9996
90AW227a	0.884	4.62×10^{-1}	0.9995



substrate concentration	**amine**	**solvent**	**method**
[**1f**] = 1.8×10^{-2} mol L^{-1}	DMAP	90A10W	stopped-flow conductometry

additive: 1.8×10^{-2} mol L^{-1} Bu_4NCl (1.0 equiv.)

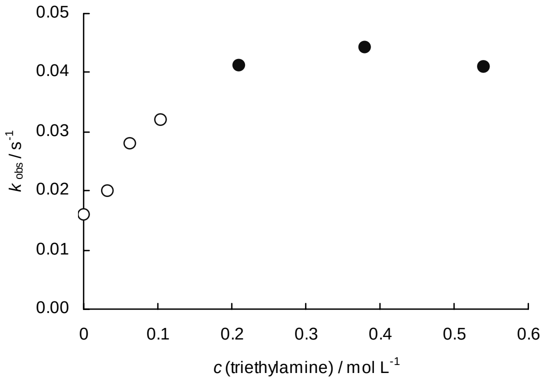
No	c(DMAP) / M	k_{obs} / s^{-1}	r^2
90AW220b	0	3.1×10^{-2}	0.9996
90AW221b	0.035	1.2×10^{-1}	0.9958
90AW222b	0.079	2.0×10^{-1}	0.9970
90AW223b	0.163	3.2×10^{-1}	0.9987
90AW224b	0.348	3.86×10^{-1}	0.9992
90AW225b	0.609	**4.27×10^{-1}**	0.9986
90AW227b	0.884	3.78×10^{-1}	0.9989



*Solvolysis reactions of 4-methoxybenzhydryl chloride **1e** in 90A10W*

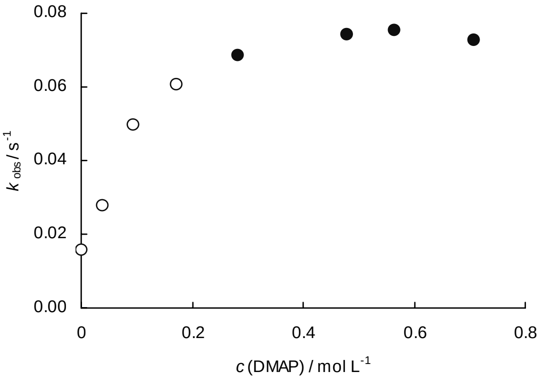
substrate concentration	**amine**	**solvent**	**method**
[**1e**] = 1.8×10^{-2} mol L^{-1}	triethylamine	90A10W	stopped-flow conductometry

No	c(triethylamine) / M	k_{obs} / s^{-1}	r^2
90AW150	0	1.6×10^{-2}	0.9954
90AW152	0.032	2.0×10^{-2}	0.9942
90AW153	0.061	2.8×10^{-2}	0.9933
90AW154	0.104	3.2×10^{-2}	0.9940
90AW155	0.210	4.12×10^{-2}	0.9970
90AW156	0.379	**4.43×10^{-2}**	0.9984
90AW157	0.540	4.11×10^{-2}	0.9988



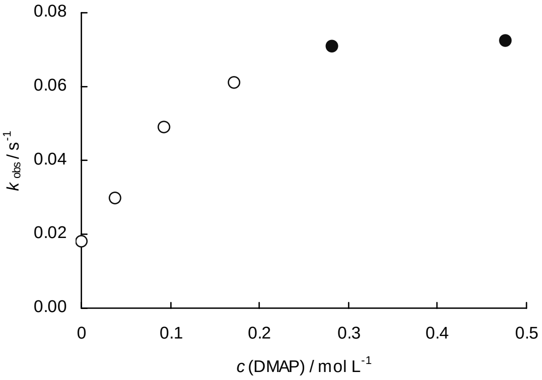
substrate concentration	**amine**	**solvent**	**method**
[**1e**] = 1.8×10^{-2} mol L^{-1}	DMAP	90A10W	stopped-flow conductometry

No	c(DMAP) / M	k_{obs} / s^{-1}	r^2
90AW150	0	1.6×10^{-2}	0.9954
90AW301	0.037	2.8×10^{-2}	0.9938
90AW302	0.092	5.0×10^{-2}	0.9989
90AW303	0.171	6.1×10^{-2}	0.9982
90AW304	0.281	6.86×10^{-2}	0.9990
90AW305	0.477	7.45×10^{-2}	0.9995
90AW306	0.563	$\mathbf{7.53 \times 10^{-2}}$	0.9994
90AW307	0.706	7.27×10^{-2}	0.9996



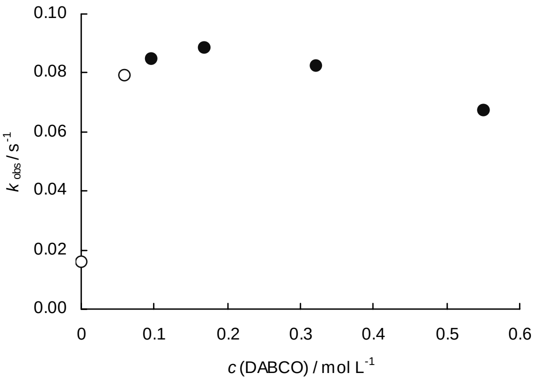
substrate concentration	**amine**	**solvent**	**method**
[**1e**] = 1.8×10^{-2} mol L^{-1}	DMAP	90A10W	conventional conductometry

No	c(DMAP) / M	k_{obs} / s^{-1}	r^2
200706-0	0	1.8×10^{-2}	0.9929
200706-1	0.037	3.0×10^{-2}	0.9542
200706-2	0.092	4.9×10^{-2}	0.9971
200706-3	0.171	6.1×10^{-2}	0.9960
200706-4	0.281	7.08×10^{-2}	0.9980
200706-5	0.477	$\mathbf{7.23 \times 10^{-2}}$	0.9988



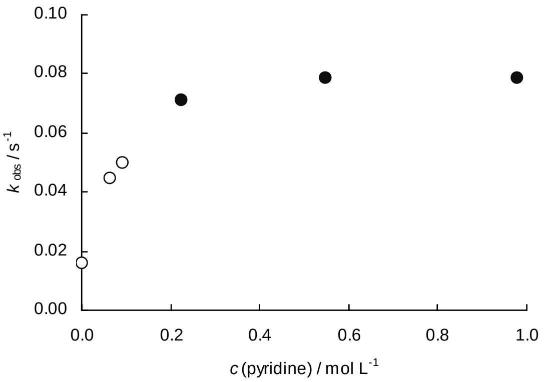
substrate concentration	**amine**	**solvent**	**method**
[**1e**] = 1.8×10^{-2} mol L^{-1}	DABCO	90A10W	stopped-flow conductometry

No	c(DABCO) / M	k_{obs} / s^{-1}	r^2
90AW150	0	1.6×10^{-2}	0.9954
90AW143	0.059	7.9×10^{-2}	0.9987
90AW144	0.095	8.51×10^{-2}	0.9990
90AW145	0.167	$\mathbf{8.87 \times 10^{-2}}$	0.9992
90AW146	0.321	8.24×10^{-2}	0.9997
90AW147	0.550	6.76×10^{-2}	0.9998



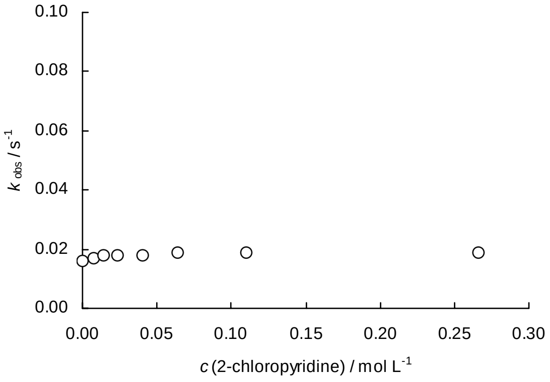
substrate concentration	**amine**	**solvent**	**method**
[**1e**] = 1.8×10^{-2} mol L^{-1}	pyridine	90A10W	stopped-flow conductometry

No	c(pyridine) / M	k_{obs} / s^{-1}	r^2
90AW150	0	1.6×10^{-2}	0.9954
90AW162	0.063	4.5×10^{-2}	0.9948
90AW163	0.091	5.0×10^{-2}	0.9948
90AW164	0.223	7.11×10^{-2}	0.9979
90AW165	0.547	7.87×10^{-2}	0.9986
90AW167	0.979	$\mathbf{7.89 \times 10^{-2}}$	0.9987



substrate concentration	**amine**	**solvent**	**method**
[**1e**] = 1.8×10^{-2} mol L^{-1}	2-chloropyridine	90A10W	stopped-flow conductometry

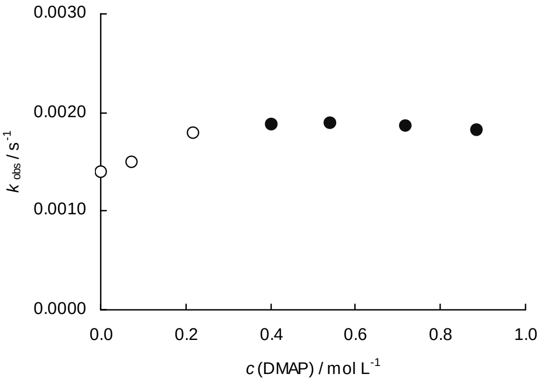
No	c(2-chloropyridine) / M	k_{obs} / s^{-1}	r^2
90AW150	0	1.6×10^{-2}	0.9954
90AW171	0.008	1.7×10^{-2}	0.9923
90AW172	0.014	1.8×10^{-2}	0.9954
90AW173	0.024	1.8×10^{-2}	0.9941
90AW174	0.041	1.8×10^{-2}	0.9932
90AW175	0.064	**1.9×10^{-2}**	0.9926
90AW176	0.110	1.9×10^{-2}	0.9928
90AW177	0.266	1.9×10^{-2}	0.9922



Solvolysis reactions of 4,4´-dimethylbenzhydryl chloride ***1d*** *in 90A10W*

substrate concentration	**amine**	**solvent**	**method**
[**1d**] = 1.8×10^{-2} mol L^{-1}	DMAP	90A10W	conventional conductometry

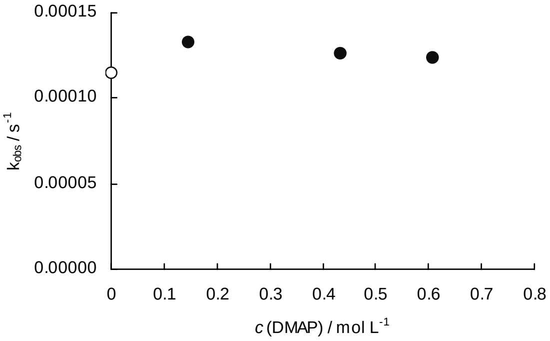
No	c(DMAP) / M	k_{obs} / s^{-1}	r^2
051206-0	0	1.4×10^{-3}	0.9952
051206-1	0.072	1.5×10^{-3}	0.9983
051206-2	0.218	1.8×10^{-3}	0.9978
051206-3	0.401	1.88×10^{-3}	0.9990
051206-4	0.541	**1.89×10^{-3}**	0.9995
051206-5	0.717	1.87×10^{-3}	0.9992
051206-6	0.886	1.83×10^{-3}	0.9992



Solvolysis reactions of 4-methylbenzhydryl chloride ***1c*** *in 90A10W*

substrate concentration	amine	solvent	method
[**1c**] = 1.8×10^{-2} mol L^{-1}	DMAP	90A10W	conventional conductometry

No	c(DMAP) / M	k_{obs} / s^{-1}	r^2
250107-0	0	1.1×10^{-4}	0.9975
121206-1	0.145	$\mathbf{1.33 \times 10^{-4}}$	0.9989
121206-2	0.432	1.26×10^{-4}	0.9994
121206-3	0.608	1.24×10^{-4}	0.9994

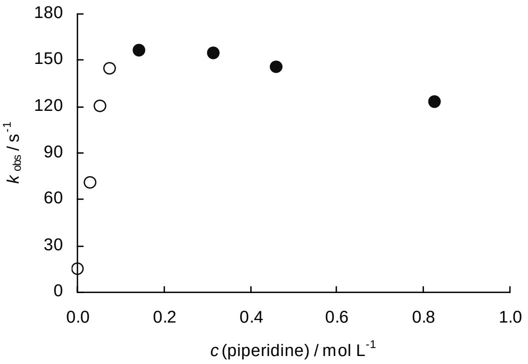


2.6.3 Solvolysis Reactions of Benzhydryl Chlorides in 80% Aqueous Acetone (80A20W)

Solvolysis reactions of 4,4´-dimethoxybenzhydryl chloride ***1h*** *in 80A20W*

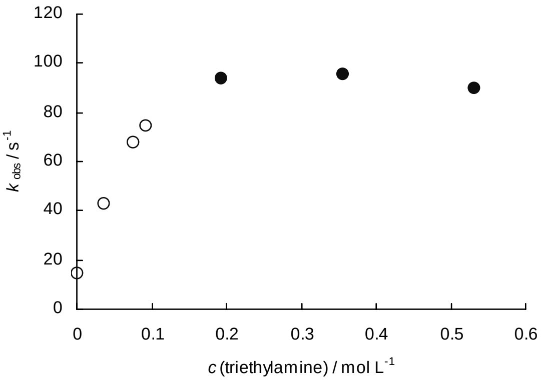
substrate concentration	amine	solvent	method
[**1h**] = 1.8×10^{-2} mol L^{-1}	piperidine	80A20W	stopped-flow conductometry

No	c(piperidine) / M	k_{obs} / s^{-1}	r^2
80AW00	0	1.5×10^{1}	0.9991
80AW131	0.030	7.1×10^{1}	0.9765
80AW132	0.053	1.2×10^{2}	0.9968
80AW133	0.074	1.4×10^{2}	0.9989
80AW134	0.144	$\mathbf{1.57 \times 10^{2}}$	0.9996
80AW135	0.313	1.55×10^{2}	0.9997
80AW136	0.460	1.46×10^{2}	0.9999
80AW137	0.826	1.23×10^{2}	0.9998



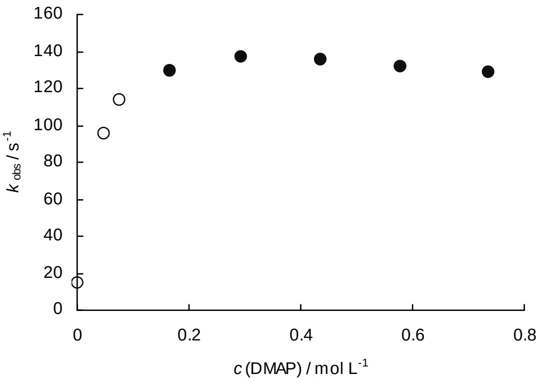
substrate concentration	**amine**	**solvent**	**method**
[**1h**] = 1.8×10^{-2} mol L^{-1}	triethylamine	80A20W	stopped-flow conductometry

No	*c*(triethylamine) / M	k_{obs} / s^{-1}	r^2
80AW00	0	1.5×10^1	0.9991
80AW12	0.035	4.3×10^1	0.9956
80AW13	0.075	6.8×10^1	0.9980
80AW14	0.092	7.5×10^1	0.9981
80AW15	0.193	9.38×10^1	0.9993
80AW16	0.355	$\mathbf{9.58 \times 10^1}$	0.9996
80AW17	0.531	9.00×10^1	0.9997



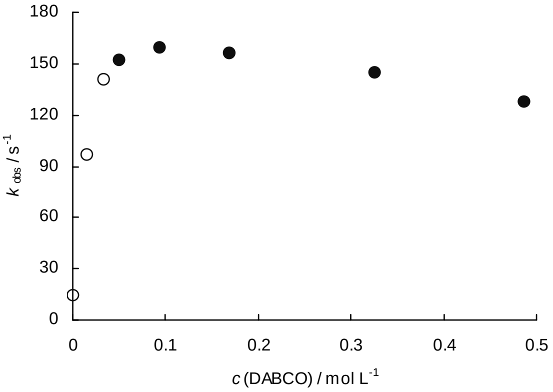
substrate concentration	**amine**	**solvent**	**method**
[**1h**] = 1.8×10^{-2} mol L^{-1}	DMAP	80A20W	stopped-flow conductometry

No	*c*(DMAP) / M	k_{obs} / s^{-1}	r^2
80AW00	0	1.5×10^1	0.9991
80AW01	0.049	9.6×10^1	0.9986
80AW02	0.075	1.1×10^2	0.9988
80AW03	0.164	1.30×10^2	0.9994
80AW04	0.292	$\mathbf{1.37 \times 10^2}$	0.9992
80AW05	0.434	1.36×10^2	0.9998
80AW06	0.577	1.32×10^2	0.9998
80AW07	0.736	1.29×10^2	0.9996



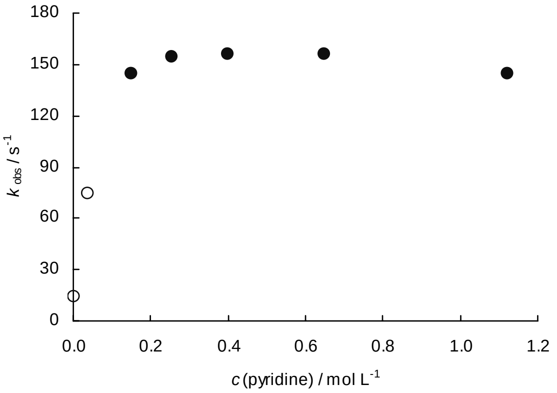
substrate concentration	**amine**	**solvent**	**method**
[**1h**] = 1.8×10^{-2} mol L^{-1}	DABCO	80A20W	stopped-flow conductometry

Nr.	*c*(DABCO) / M	k_{obs} / s^{-1}	r^2
80AW00	0	1.5×10^1	0.9991
80AW121	0.016	9.7×10^1	0.9893
80AW122	0.033	1.4×10^2	0.9991
80AW123	0.049	1.52×10^2	0.9995
80AW124	0.093	$\mathbf{1.60 \times 10^2}$	0.9997
80AW125	0.169	1.56×10^2	0.9998
80AW126	0.325	1.45×10^2	0.9999
80AW127	0.486	1.28×10^2	0.9999



substrate concentration	**amine**	**solvent**	**method**
[**1h**] = 1.8×10^{-2} mol L^{-1}	pyridine	80A20W	stopped-flow conductometry

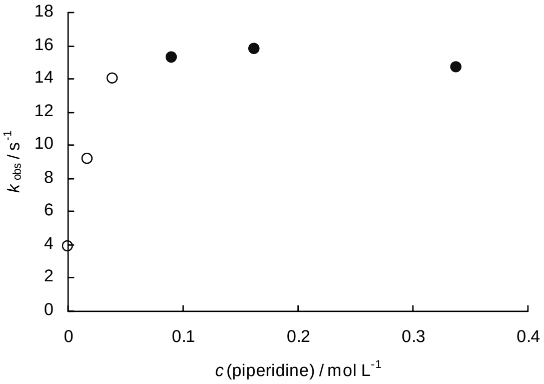
No	*c*(pyridine) / M	k_{obs} / s^{-1}	r^2
80AW00	0	1.5×10^1	0.9991
80AW141	0.036	7.5×10^1	0.9955
80AW143	0.148	1.45×10^2	0.9996
80AW144	0.255	1.55×10^2	0.9998
80AW145	0.398	$\mathbf{1.56 \times 10^2}$	0.9998
80AW146	0.645	1.56×10^2	0.9998
80AW147	1.120	1.45×10^2	0.9999



Solvolysis reactions of 4-methoxy-4´-phenoxybenzhydryl chloride ***1g*** *in 80A20W*

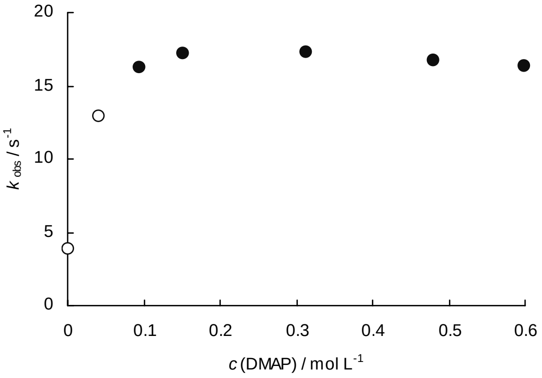
substrate concentration	**amine**	**solvent**	**method**
[**1g**] = 1.8×10^{-2} mol L^{-1}	piperidine	80A20W	stopped-flow conductometry

No	c(piperidine) / M	k_{obs} / s^{-1}	r^2
80AW210	0	3.9	0.9919
NSK58-1	0.017	9.2	0.9942
NSK58-2	0.038	1.4×10^1	0.9989
NSK58-3	0.090	1.53×10^1	0.9996
NSK58-4	0.162	**1.58×10^1**	0.9999
NSK58-5	0.337	1.47×10^1	0.9999



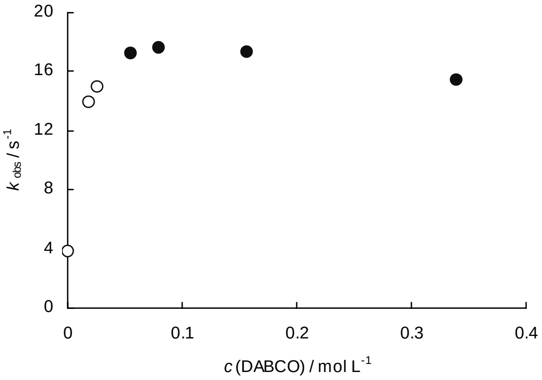
substrate concentration	**amine**	**solvent**	**method**
[**1g**] = 1.8×10^{-2} mol L^{-1}	DMAP	80A20W	stopped-flow conductometry

No	c(DMAP) / M	k_{obs} / s^{-1}	r^2
80AW210	0	3.9	0.9919
80AW221	0.040	1.3×10^1	0.9988
80AW222	0.094	1.63×10^1	0.9996
80AW223	0.151	1.72×10^1	0.9998
80AW224	0.312	**1.73×10^1**	0.9999
80AW225	0.479	1.68×10^1	0.9999
80AW226	0.598	1.64×10^1	0.9999



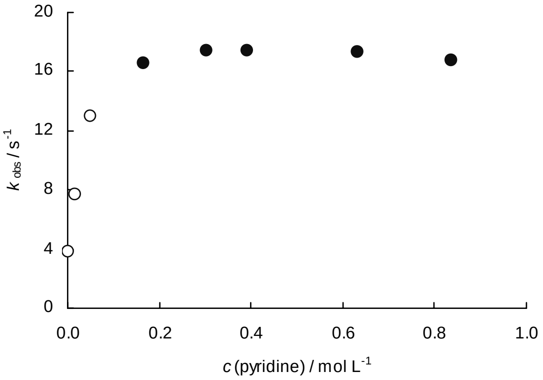
substrate concentration	**amine**	**solvent**	**method**
[**1g**] = 1.8×10^{-2} mol L^{-1}	DABCO	80A20W	stopped-flow conductometry

No	c(DABCO) / M	k_{obs} / s^{-1}	r^2
80AW210	0	3.9	0.9919
80AW211	0.018	1.4×10^1	0.9976
80AW212	0.025	1.5×10^1	0.9982
80AW213	0.055	1.73×10^1	0.9996
80AW214	0.079	**1.76×10^1**	0.9998
80AW215	0.156	1.74×10^1	0.9999
80AW216	0.339	1.55×10^1	0.9999



substrate concentration	**amine**	**solvent**	**method**
[**1g**] = 1.8×10^{-2} mol L^{-1}	pyridine	80A20W	stopped-flow conductometry

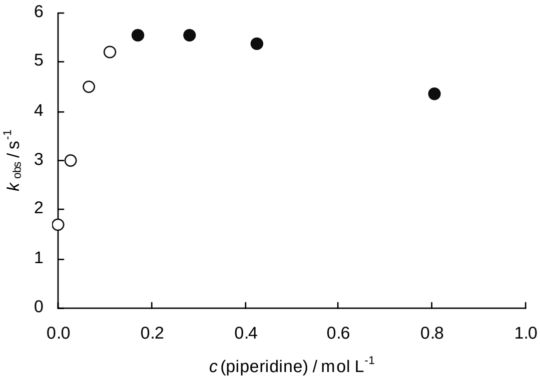
No	c(pyridine) / M	k_{obs} / s^{-1}	r^2
80AW210	0	3.9	0.9919
80AW251	0.017	7.7	0.9922
80AW252	0.047	1.3×10^1	0.9980
80AW253	0.165	1.66×10^1	0.9997
80AW254	0.301	**1.75×10^1**	0.9999
80AW255	0.391	1.75×10^1	0.9999
80AW256	0.631	1.74×10^1	0.9999
80AW257	0.836	1.68×10^1	0.9999



Solvolysis reactions of 4-methoxy-4´-methylbenzhydryl chloride ***1f*** *in 80A20W*

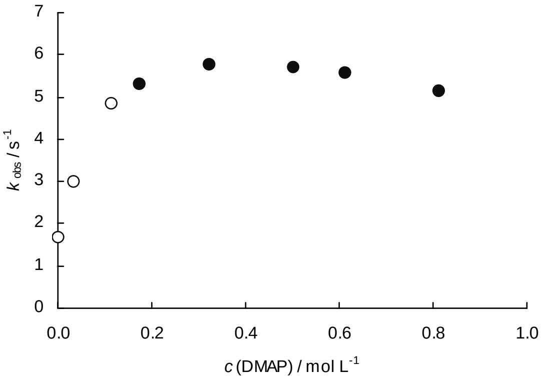
substrate concentration	**amine**	**solvent**	**method**
[**1f**] = 1.8×10^{-2} mol L^{-1}	piperidine	80A20W	stopped-flow conductometry

No	*c*(piperidine) / M	k_{obs} / s^{-1}	r^2
80AW300	0	1.7	0.9938
80AW431a	0.028	3.0	0.9871
80AW432a	0.064	4.5	0.9949
80AW433a	0.112	5.2	0.9974
80AW434a	0.169	5.55	0.9985
80AW435a	0.283	**5.56**	0.9988
80AW436a	0.425	5.37	0.9992
80AW437a	0.804	4.36	0.9995



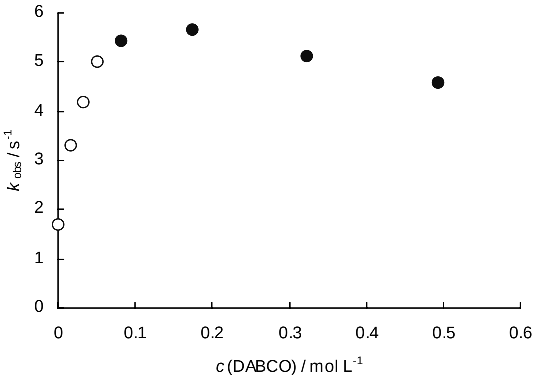
substrate concentration	**amine**	**solvent**	**method**
[**1f**] = 1.8×10^{-2} mol L^{-1}	DMAP	80A20W	stopped-flow conductometry

No	*c*(DMAP) / M	k_{obs} / s^{-1}	r^2
80AW300	0	1.7	0.9938
80AW301	0.032	3.0	0.9938
80AW302	0.112	4.9	0.9985
80AW303	0.174	5.32	0.9990
80AW304	0.322	**5.77**	0.9997
80AW305	0.501	5.70	0.9998
80AW306	0.612	5.57	0.9998
80AW307	0.812	5.15	0.9999



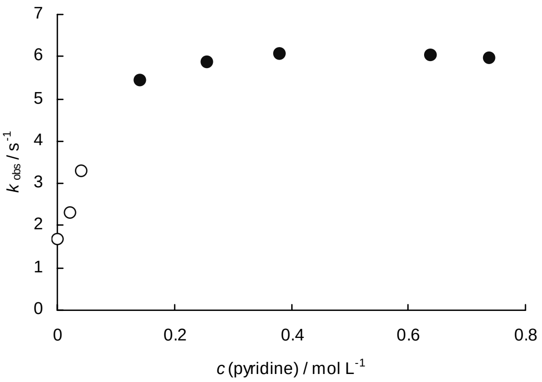
substrate concentration	**amine**	**solvent**	**method**
[**1f**] = 1.8 × 10^{-2} mol L^{-1}	DABCO	80A20W	stopped-flow conductometry

No	*c*(DABCO) / M	k_{obs} / s^{-1}	r^2
80AW300	0	1.7	0.9938
80AW311	0.017	3.3	0.9939
80AW312	0.033	4.2	0.9958
80AW313	0.050	5.0	0.9980
80AW314	0.081	5.42	0.9988
80AW315	0.173	**5.67**	0.9995
80AW316	0.322	5.11	0.9997
80AW317	0.493	4.58	0.9997



substrate concentration	**amine**	**solvent**	**method**
[**1f**] = 1.8 × 10^{-2} mol L^{-1}	pyridine	80A20W	stopped-flow conductometry

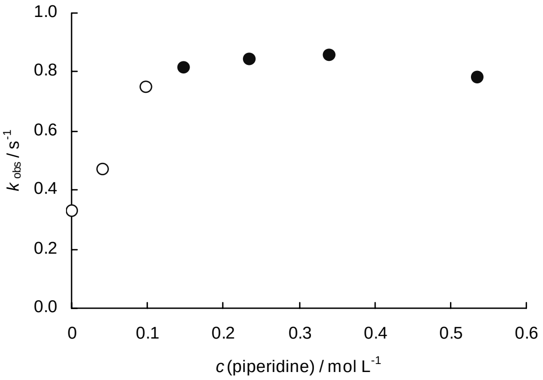
No	*c*(pyridine) / M	k_{obs} / s^{-1}	r^2
80AW300	0	1.7	0.9938
80AW321	0.022	2.3	0.9876
80AW322	0.041	3.3	0.9927
80AW323	0.141	5.45	0.9985
80AW324	0.255	5.87	0.9992
80AW325	0.380	**6.06**	0.9995
80AW326	0.638	6.04	0.9996
80AW327	0.739	5.99	0.9997



*Solvolysis reactions of 4-methoxybenzhydryl chloride **1e** in 80A20W*

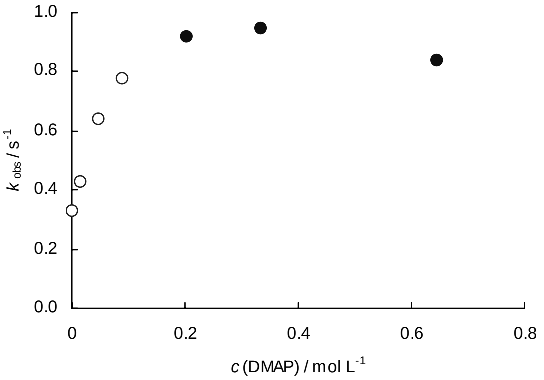
substrate concentration	**amine**	**solvent**	**method**
[**1e**] = 1.8×10^{-2} mol L^{-1}	piperidine	80A20W	stopped-flow conductometry

No	c(piperidine) / M	k_{obs} / s^{-1}	r^2
80AW100	0	3.3×10^{-1}	0.9950
80AW452	0.041	4.7×10^{-1}	0.9885
80AW453	0.097	7.5×10^{-1}	0.9959
80AW454	0.148	8.15×10^{-1}	0.9970
80AW455	0.235	8.42×10^{-1}	0.9979
80AW456	0.339	**8.59×10^{-1}**	0.9987
80AW457	0.535	7.84×10^{-1}	0.9990



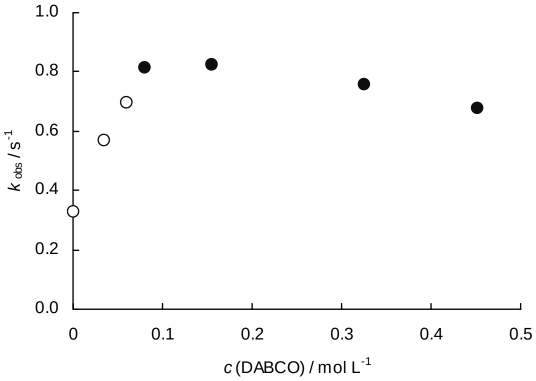
substrate concentration	**amine**	**solvent**	**method**
[**1e**] = 1.8×10^{-2} mol L^{-1}	DMAP	80A20W	stopped-flow conductometry

No	c(DMAP) / M	k_{obs} / s^{-1}	r^2
80AW100	0	3.3×10^{-1}	0.9950
80AW101	0.016	4.3×10^{-1}	0.9952
80AW102	0.047	6.4×10^{-1}	0.9972
80AW103	0.088	7.8×10^{-1}	0.9981
80AW104	0.202	9.19×10^{-1}	0.9993
80AW105	0.333	**9.46×10^{-1}**	0.9996
80AW107	0.644	8.41×10^{-1}	0.9998



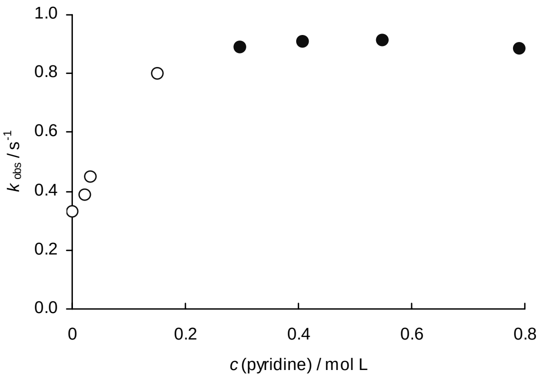
substrate concentration	**amine**	**solvent**	**method**
[**1e**] = 1.8×10^{-2} mol L^{-1}	DABCO	80A20W	stopped-flow conductometry

No	c(DABCO) / M	k_{obs} / s^{-1}	r^2
80AW100	0	3.3×10^{-1}	0.9950
80AW402	0.035	5.7×10^{-1}	0.9960
80AW403	0.059	7.0×10^{-1}	0.9980
80AW404	0.079	8.15×10^{-1}	0.9981
80AW405	0.155	$\mathbf{8.25 \times 10^{-1}}$	0.9983
80AW406	0.324	7.59×10^{-1}	0.9987
80AW407	0.451	6.77×10^{-1}	0.9989



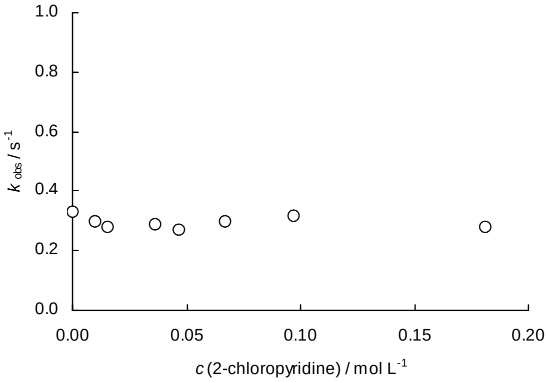
substrate concentration	**amine**	**solvent**	**method**
[**1e**] = 1.8×10^{-2} mol L^{-1}	pyridine	80A20W	stopped-flow conductometry

No	c(pyridine) / M	k_{obs} / s^{-1}	r^2
80AW100	0	3.3×10^{-1}	0.9950
80AW411	0.021	3.9×10^{-1}	0.9902
80AW412	0.032	4.5×10^{-1}	0.9912
80AW413	0.150	8.0×10^{-1}	0.9975
80AW414	0.297	8.90×10^{-1}	0.9986
80AW415	0.406	9.10×10^{-1}	0.9989
80AW416	0.547	$\mathbf{9.16 \times 10^{-1}}$	0.9993
80AW417	0.789	8.86×10^{-1}	0.9993



substrate concentration	**amine**	**solvent**	**method**
[**1e**] = 1.8 × 10^{-2} mol L^{-1}	2-chloropyridine	80A20W	stopped-flow conductometry

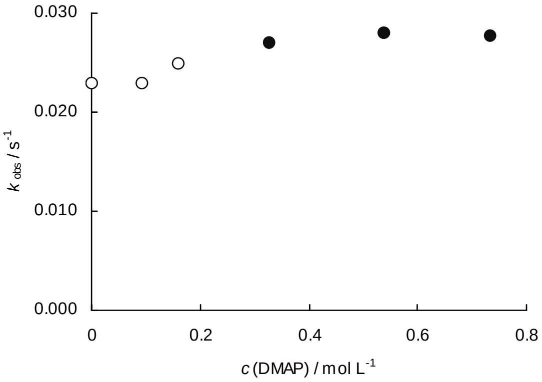
No	c(2-chloropyridine) / M	k_{obs} / s^{-1}	r^2
80AW100	0	3.3 × 10^{-1}	0.9950
80AW441	0.010	3.0 × 10^{-1}	0.9949
80AW442	0.015	2.8 × 10^{-1}	0.9927
80AW443	0.036	2.9 × 10^{-1}	0.9929
80AW444	0.047	2.7 × 10^{-1}	0.9940
80AW445	0.067	3.0 × 10^{-1}	0.9951
80AW446	0.097	**3.2 × 10^{-1}**	0.9957
80AW447	0.181	2.8 × 10^{-1}	0.9955



Solvolysis reactions of 4,4´-dimethylbenzhydryl chloride ***1d*** *in 80A20W*

substrate concentration	**amine**	**solvent**	**method**
[**1d**] = 1.8 × 10^{-2} mol L^{-1}	DMAP	80A20W	conventional conductometry

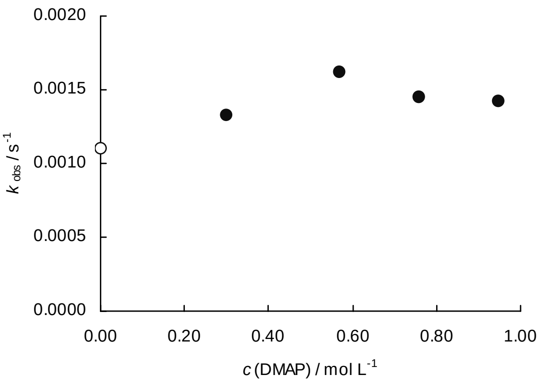
No	c(DMAP) / M	k_{obs} / s^{-1}	r^2
271106-1	0	2.3 × 10^{-2}	0.9982
301106-2	0.093	2.3 × 10^{-2}	0.9987
301106-3	0.159	2.5 × 10^{-2}	0.9989
301106-4	0.327	2.71 × 10^{-2}	0.9994
301106-5	0.537	**2.80 × 10^{-2}**	0.9993
301106-6	0.732	2.77 × 10^{-2}	0.9993



*Solvolysis reactions of 4-methylbenzhydryl chloride **1c** in 80A20W*

substrate concentration	**amine**	**solvent**	**method**
[**1c**] = 1.8×10^{-2} mol L^{-1}	DMAP	80A20W	conventional conductometry

No	c(DMAP) / M	k_{obs} / s^{-1}	r^2
071206-0	0	1.1×10^{-3}	0.9991
071206-2	0.300	1.33×10^{-3}	0.9976
071206-3	0.567	$\mathbf{1.62 \times 10^{-3}}$	0.9990
071206-4	0.758	1.45×10^{-3}	0.9993
071206-5	0.948	1.42×10^{-3}	0.9991

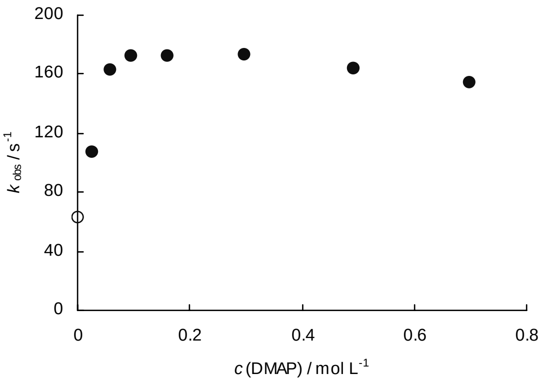


2.6.4 Solvolysis Reactions of Benzhydryl Chlorides in 60% Aqueous Acetone (60A40W)

*Solvolysis reactions of 4-methoxy-4´-phenoxybenzhydryl chloride **1g** in 60A40W*

substrate concentration	**amine**	**solvent**	**method**
[**1g**] = 1.8×10^{-2} mol L^{-1}	DMAP	60A40W	stopped-flow conductometry

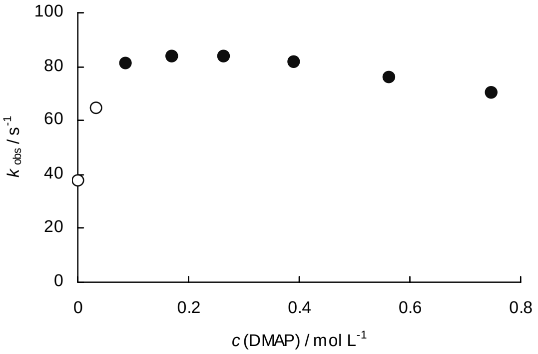
No	c(DMAP) / M	k_{obs} / s^{-1}	r^2
60AW300a	0	6.3×10^{1}	0.9994
60AW301a	0.026	1.08×10^{2}	0.9999
60AW302a	0.057	1.63×10^{2}	0.9999
60AW303a	0.094	1.73×10^{2}	0.9999
60AW304a	0.160	1.73×10^{2}	0.9999
60AW305a	0.298	$\mathbf{1.74 \times 10^{2}}$	0.9999
60AW306a	0.491	1.64×10^{2}	0.9999
60AW307a	0.697	1.55×10^{2}	0.9999



Solvolysis reactions of 4-methoxy-4´-methylbenzhydryl chloride ***1f*** *in 60A40W*

substrate concentration	**amine**	**solvent**	**method**
[**1f**] = 1.8×10^{-2} mol L^{-1}	DMAP	60A40W	stopped-flow conductometry

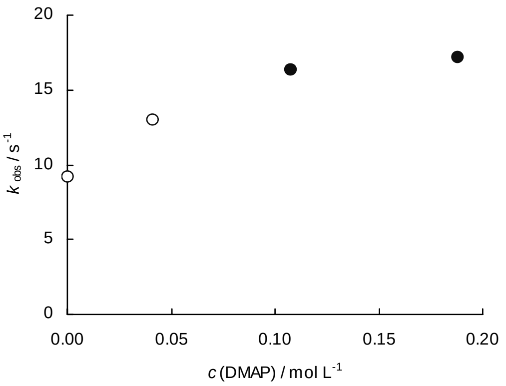
No	c(DMAP) / M	k_{obs} / s^{-1}	r^2
60AW200a	0	3.8×10^1	0.9994
60AW201a	0.033	6.5×10^1	0.9976
60AW202a	0.086	8.11×10^1	0.9993
60AW203a	0.169	8.38×10^1	0.9994
60AW204a	0.264	$\mathbf{8.40 \times 10^1}$	0.9998
60AW205a	0.389	8.20×10^1	0.9998
60AW206a	0.562	7.60×10^1	0.9996
60AW207a	0.746	7.03×10^1	0.9997



Solvolysis reactions of 4-methoxybenzhydryl chloride ***1e*** *in 60A40W*

substrate concentration	**amine**	**solvent**	**method**
[**1e**] = 1.8×10^{-2} mol L^{-1}	DMAP	60A40W	stopped-flow conductometry

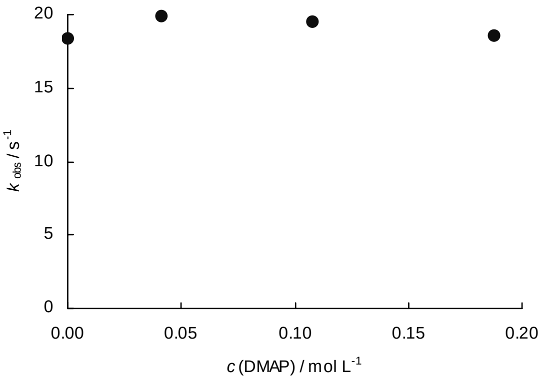
No	c(DMAP) / M	k_{obs} / s^{-1}	r^2
60AW100c	0	9.2	0.9997
60AW101c	0.041	1.3×10^1	0.9990
60AW102c	0.107	1.64×10^1	0.9997
60AW103c	0.188	$\mathbf{1.71 \times 10^1}$	0.9999



Variation of Substrate Concentration:

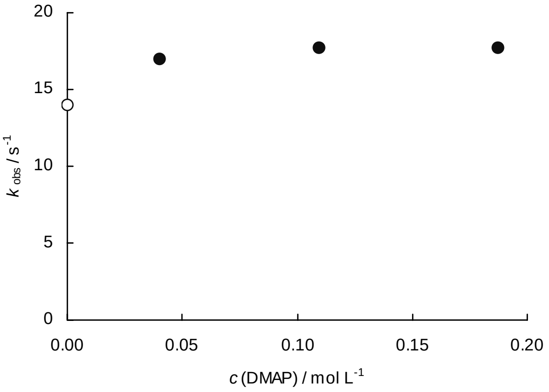
substrate concentration	**amine**	**solvent**	**method**
[**1e**] = 1.1×10^{-3} mol L^{-1}	DMAP	60A40W	stopped-flow conductometry

No	c(DMAP) / M	k_{obs} / s^{-1}	r^2
60AW100b	0	1.84×10^1	0.9999
60AW101b	0.041	**1.99×10^1**	0.9998
60AW102b	0.107	1.95×10^1	0.9999
60AW103b	0.188	1.86×10^1	0.9999



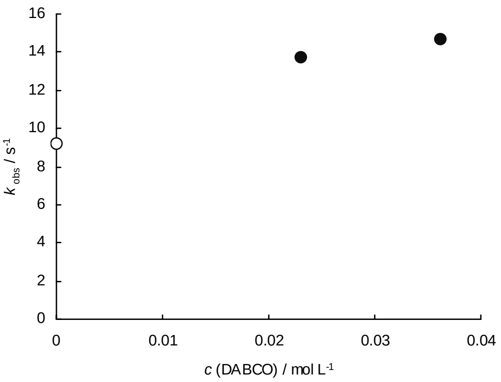
substrate concentration	**amine**	**solvent**	**method**
[**1e**] = 7.9×10^{-3} mol L^{-1}	DMAP	60A40W	stopped-flow conductometry

No	c(DMAP) / M	k_{obs} / s^{-1}	r^2
60AW100a	0	1.4×10^1	0.9987
60AW101a	0.040	1.70×10^1	0.9996
60AW102a	0.109	**1.77×10^1**	0.9999
60AW103a	0.188	1.77×10^1	0.9999



substrate concentration	**amine**	**solvent**	**method**
[**1e**] = 1.8×10^{-2} mol L^{-1}	DABCO	60A40W	stopped-flow conductometry

No	c(DABCO) / M	k_{obs} / s^{-1}	r^2
60AW100c	0	9.2	0.9997
60AW113c	0.023	1.37×10^1	0.9991
60AW112c	0.036	**1.47×10^1**	0.9994

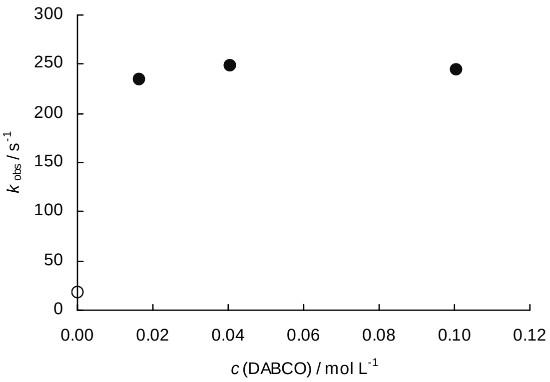


2.6.5 Solvolysis Reactions of Benzhydryl Chlorides in 90% Aqueous Acetonitrile (90AN10W)

*Solvolysis reactions of 4,4´-dimethoxybenzhydryl chloride **1h** in 90AN10W*

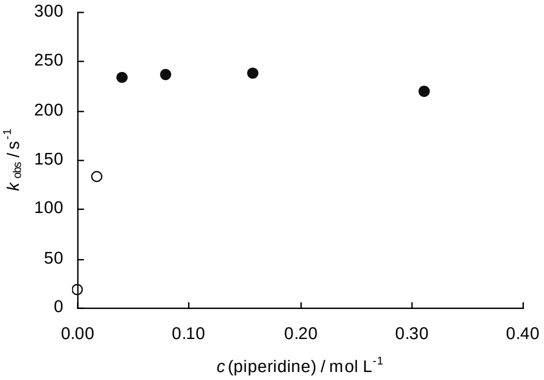
substrate concentration	**amine**	**solvent**	**method**
[**1h**] = 6.1×10^{-3} mol L^{-1}	DABCO	90AN10W	stopped-flow conductometry

No	c(DABCO) / M	k_{obs} / s^{-1}	r^2
NSK25-0	0	1.8×10^1	0.9916
NSK25-1	0.016	2.35×10^2	0.9996
NSK25-2	0.041	**2.49×10^2**	0.9999
NSK25-3	0.100	2.45×10^2	0.9999



substrate concentration	**amine**	**solvent**	**method**
[**1h**] = 6.1×10^{-3} mol L^{-1}	piperidine	90AN10W	stopped-flow conductometry

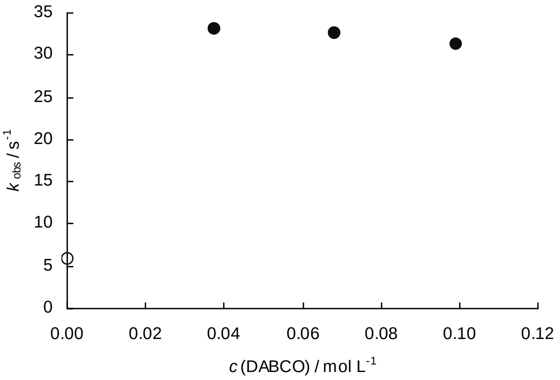
No	c(piperidine) / M	k_{obs} / s^{-1}	r^2
NSK25-0	0	1.8×10^1	0.9916
NSK59-1	0.017	1.3×10^2	0.9936
NSK59-2	0.041	2.33×10^2	0.9993
NSK59-3	0.079	2.37×10^2	0.9999
NSK59-4	0.158	$\mathbf{2.38 \times 10^2}$	0.9999
NSK59-5	0.311	2.19×10^2	0.9999



Solvolysis reactions of 4-methoxy-4´-phenoxybenzhydryl chloride ***1g*** *in 90AN10W*

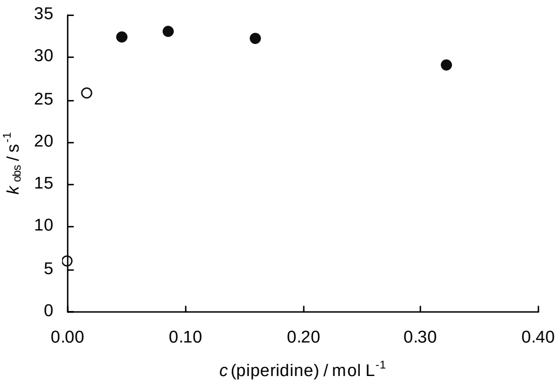
substrate concentration	**amine**	**solvent**	**method**
[**1g**] = 6.1×10^{-3} mol L^{-1}	DABCO	90AN10W	stopped-flow conductometry

No	c(DABCO) / M	k_{obs} / s^{-1}	r^2
NSK23-0	0	6.02	0.9912
NSK23-1	0.037	$\mathbf{3.32 \times 10^1}$	0.9998
NSK23-2	0.068	3.27×10^1	0.9998
NSK23-3	0.099	3.14×10^1	0.9999



substrate concentration	**amine**	**solvent**	**method**
[**1g**] = 6.1×10^{-3} mol L^{-1}	piperidine	90AN10W	stopped-flow conductometry

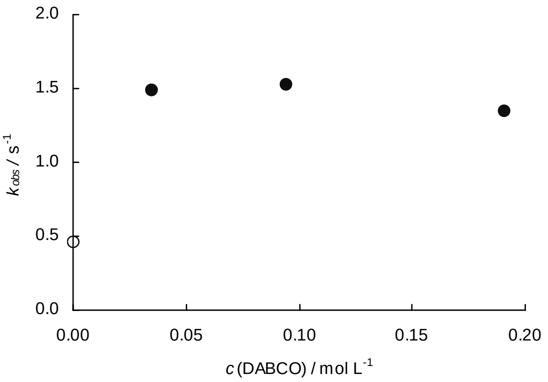
No	c(piperidine) / M	k_{obs} / s^{-1}	r^2
NSK23-0	0	6.02	0.9912
NSK56-1	0.017	2.6×10^1	0.9983
NSK56-2	0.047	3.23×10^1	0.9996
NSK56-3	0.085	**3.30×10^1**	0.9998
NSK56-4	0.160	3.22×10^1	0.9998
NSK56-5	0.322	2.90×10^1	0.9999



*Solvolysis reactions of 4-methoxybenzhydryl chloride **1e** in 90AN10W*

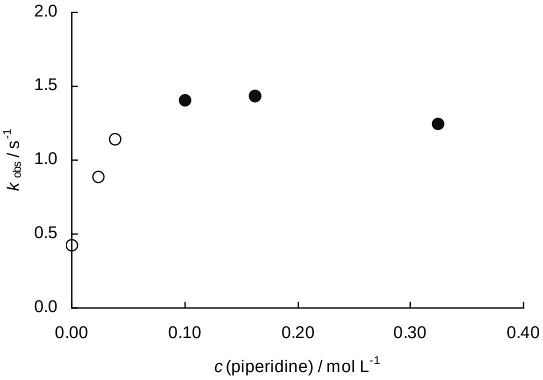
substrate concentration	**amine**	**solvent**	**method**
[**1e**] = 6.1×10^{-3} mol L^{-1}	DABCO	90AN10W	stopped-flow conductometry

No	c(DABCO) / M	k_{obs} / s^{-1}	r^2
NSK31-0	0	4.7×10^{-1}	0.9942
NSK31-1	0.035	1.49	0.9995
NSK31-2	0.094	**1.53**	0.9997
NSK31-3	0.191	1.35	0.9998



substrate concentration	**amine**	**solvent**	**method**
[**1e**] = 6.1×10^{-3} mol L^{-1}	piperidine	90AN10W	stopped-flow conductometry

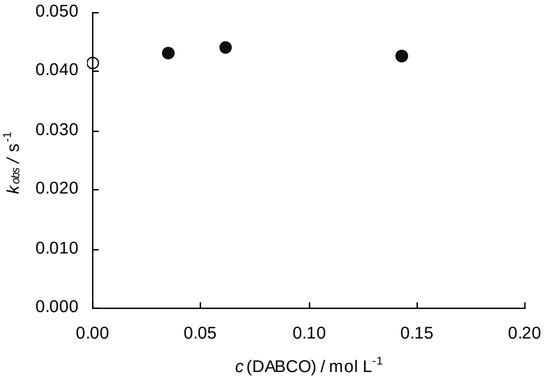
No	c(piperidine) / M	k_{obs} / s^{-1}	r^2
NSK31-0	0	4.7×10^{-1}	0.9942
NSK50-1	0.023	8.9×10^{-1}	0.9918
NSK50-2	0.038	1.1	0.9958
NSK50-3	0.100	1.41	0.9990
NSK50-4	0.162	**1.43**	0.9995
NSK50-5	0.325	1.25	0.9994



Solvolysis reactions of 4,4´-dimethylbenzhydryl chloride ***1d*** *in 90AN10W*

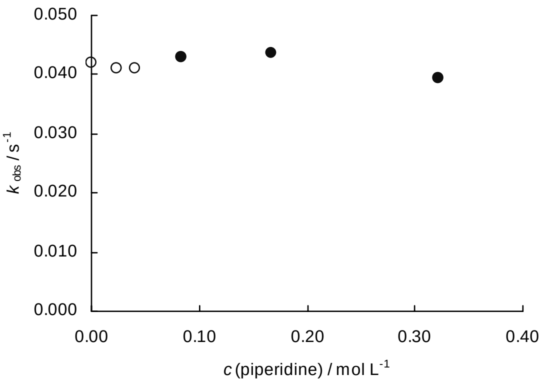
substrate concentration	**amine**	**solvent**	**method**
[**1d**] = 6.1×10^{-3} mol L^{-1}	DABCO	90AN10W	stopped-flow conductometry

No	c(DABCO) / M	k_{obs} / s^{-1}	r^2
NSK34-0	0	4.2×10^{-2}	0.9987
NSK34-1	0.035	4.32×10^{-2}	0.9995
NSK34-2	0.061	$\mathbf{4.42 \times 10^{-2}}$	0.9997
NSK34-3	0.143	4.28×10^{-2}	0.9998



substrate concentration	**amine**	**solvent**	**method**
[**1d**] = 6.1 × 10^{-3} mol L^{-1}	piperidine	90AN10W	stopped-flow conductometry

No	c(piperidine) / M	k_{obs} / s^{-1}	r^2
NSK34-0	0	4.2 × 10^{-2}	0.9987
NSK53-1	0.023	4.1 × 10^{-2}	0.9984
NSK53-2	0.040	4.1 × 10^{-2}	0.981
NSK53-3	0.083	4.27 × 10^{-2}	0.9986
NSK53-4	0.167	**4.36 × 10^{-2}**	0.9993
NSK53-5	0.322	3.94 × 10^{-2}	0.9996



Solvolysis reactions of 4-methylbenzhydryl chloride ***1c*** *in 90AN10W*

substrate concentration	**amine**	**solvent**	**method**
[**1c**] = 6.0 × 10^{-4} mol L^{-1}	---	90AN10W	conventional conductometry

No	k_{obs} / s^{-1}	r^2
NSK10-1	2.51 × 10^{-3}	0.9998
NSK10-1-1	2.44 × 10^{-3}	0.9998
NSK10-1-2	2.56 × 10^{-3}	0.9998

$k_1 = 2.50 \times 10^{-3}$ s^{-1}.

*Solvolysis reactions of benzhydryl chloride **1b** in 90AN10W*

substrate concentration	**amine**	**solvent**	**method**
[**1b**] = 6.0×10^{-4} mol L^{-1}	---	90AN10W	conventional conductometry

No	k_{obs} / s^{-1}	r^2
NSK12-1	8.11×10^{-5}	0.9999
NSK12-1-2	8.17×10^{-5}	0.9998

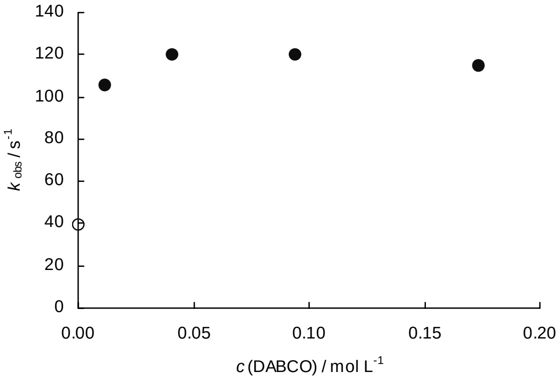
$k_1 = 8.14 \times 10^{-5}$ s^{-1}.

2.6.6 Solvolysis Reactions of Benzhydryl Chlorides in 80% Aqueous Acetonitrile (80AN20W)

*Solvolysis reactions of 4-methoxy-4´-phenoxybenzhydryl chloride **1g** in 80AN20W*

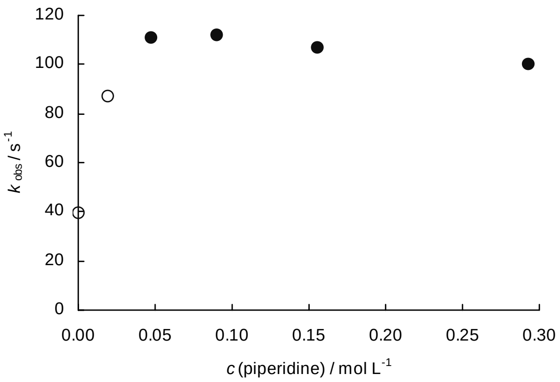
substrate concentration	**amine**	**solvent**	**method**
[**1g**] = 6.1×10^{-3} mol L^{-1}	DABCO	80AN20W	stopped-flow conductometry

No	c(DABCO) / M	k_{obs} / s^{-1}	r^2
NSK24-0	0	4.0×10^1	0.9962
NSK24-1	0.011	1.06×10^2	0.9994
NSK24-2	0.041	**1.20×10^2**	0.9999
NSK24-3	0.094	1.20×10^2	0.9999
NSK24-4	0.173	1.15×10^2	0.9999



substrate concentration	**amine**	**solvent**	**method**
[**1g**] = 6.1×10^{-3} mol L^{-1}	piperidine	80AN20W	stopped-flow conductometry

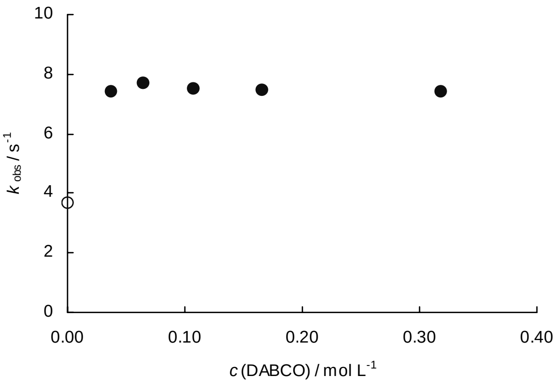
No	c(piperidine) / M	k_{obs} / s^{-1}	r^2
NSK24-0	0	4.0×10^1	0.9962
NSK57-1	0.019	8.7×10^1	0.9991
NSK57-2	0.047	1.11×10^2	0.9999
NSK57-3	0.090	$\mathbf{1.12 \times 10^2}$	0.9999
NSK57-4	0.156	1.07×10^2	0.9999
NSK57-5	0.293	1.00×10^2	0.9999



*Solvolysis reactions of 4-methoxybenzhydryl chloride **1e** in 80AN20W*

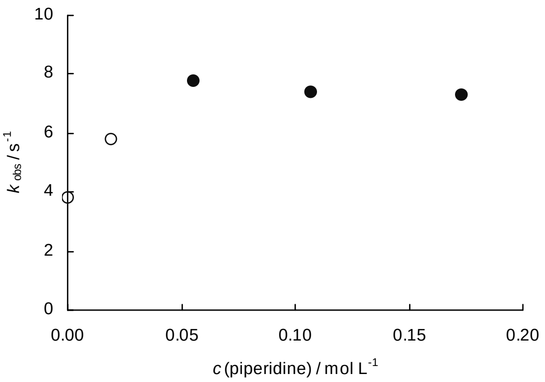
substrate concentration	**amine**	**solvent**	**method**
[**1e**] = 6.1×10^{-3} mol L^{-1}	DABCO	80AN20W	stopped-flow conductometry

No	c(DABCO) / M	k_{obs} / s^{-1}	r^2
NSK15-0	0	3.8	0.9961
NSK15-1	0.037	7.43	0.9995
NSK15-2	0.068	**7.70**	0.9998
NSK15-3	0.107	7.52	0.9998
NSK15-4	0.318	7.42	0.9999



substrate concentration	**amine**	**solvent**	**method**
[**1e**] = 6.1 × 10^{-3} mol L^{-1}	piperidine	80AN20W	stopped-flow conductometry

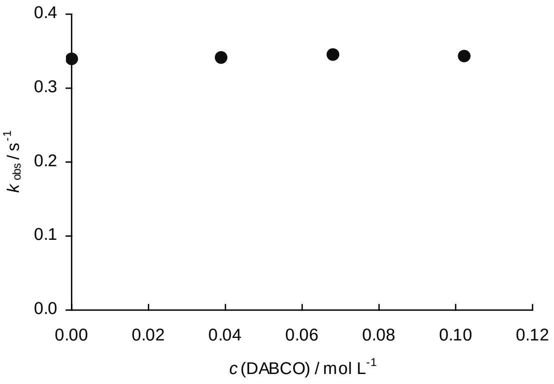
No	*c* (piperidine) / M	k_{obs} / s^{-1}	r^2
NSK15-0	0	3.8	0.9961
NSK51-1	0.019	5.8	0.9968
NSK51-2	0.056	**7.76**	0.9994
NSK51-3	0.107	7.41	0.9998
NSK51-4	0.173	7.33	0.9999



*Solvolysis reactions of 4,4´-dimethylbenzhydryl chloride **1d** in 80AN20W*

substrate concentration	**amine**	**solvent**	**method**
[**1d**] = 6.1 × 10^{-3} mol L^{-1}	DABCO	80AN20W	stopped-flow conductometry

No	*c*(DABCO) / M	k_{obs} / s^{-1}	r^2
NSK21-0	0	3.41 × 10^{-1}	0.9995
NSK21-1	0.039	3.41 × 10^{-1}	0.9996
NSK21-2	0.068	**3.45 × 10^{-1}**	0.9997
NSK21-3	0.102	3.28 × 10^{-1}	0.9997



*Solvolysis reactions of 4-methylbenzhydryl chloride **1c** in 80AN20W*

substrate concentration	**amine**	**solvent**	**method**
[**1c**] = 6.0×10^{-4} mol L^{-1}	---	80AN20W	conventional conductometry

No	k_{obs} / s^{-1}	r^2
NSK9-1	2.27×10^{-2}	0.9997
NSK9-1-2	2.28×10^{-2}	0.9997

$k_1 = 2.28 \times 10^{-2}$ s^{-1}.

*Solvolysis reactions of benzhydryl chloride **1b** in 80AN20W*

substrate concentration	**amine**	**solvent**	**method**
[**1b**] = 6.0×10^{-4} mol L^{-1}	---	80AN20W	conventional conductometry

No	k_{obs} / s^{-1}	r^2
NSK14-1	8.01×10^{-4}	0.9999
NSK14-1-4	8.04×10^{-4}	0.9998

$k_1 = 8.03 \times 10^{-4}$ s^{-1}.

*Solvolysis reactions of 4,4´-dichlorobenzhydryl chloride **1a** in 80AN20W*

substrate concentration	**amine**	**solvent**	**method**
[**1a**] = 6.0×10^{-4} mol L^{-1}	---	80AN20W	conventional conductometry

No	k_{obs} / s^{-1}	r^2
NSK26-1	1.12×10^{-4}	0.9999
NSK26-1-2	1.08×10^{-4}	0.9996
NSK-26-1-3	1.08×10^{-4}	0.9996

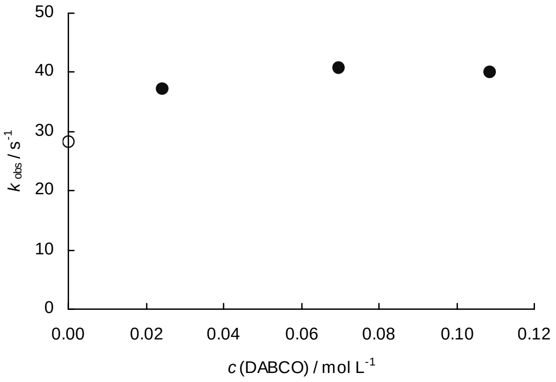
$k_1 = 1.09 \times 10^{-4}$ s^{-1}.

2.6.7 Solvolysis Reactions of Benzhydryl Chlorides in 60% Aqueous Acetonitrile (60AN40W)

*Solvolysis reactions of 4-methoxybenzhydryl chloride **1e** in 60AN40W*

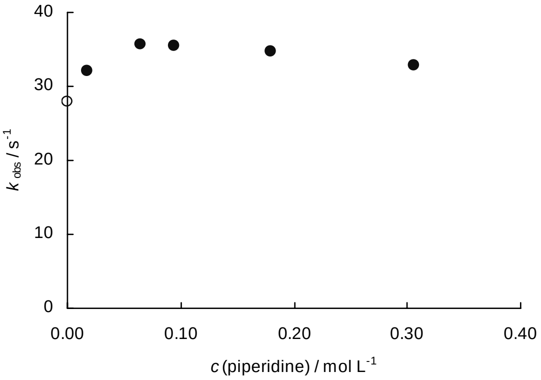
substrate concentration	**amine**	**solvent**	**method**
[**1e**] = 6.1×10^{-3} mol L^{-1}	DABCO	60AN40W	stopped-flow conductometry

No	c(DABCO) / M	k_{obs} / s^{-1}	r^2
NSK16-0	0	2.8×10^1	0.9995
NSK16-1	0.024	3.72×10^1	0.9997
NSK16-2	0.066	**4.08×10^1**	0.9998
NSK16-3	0.105	3.99×10^1	0.9998



substrate concentration	**amine**	**solvent**	**method**
[**1e**] = 6.1×10^{-3} mol L^{-1}	piperidine	60AN40W	stopped-flow conductometry

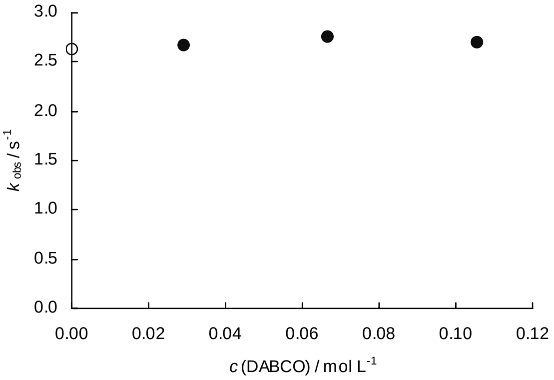
No	*c*(piperidine) / M	k_{obs} / s^{-1}	r^2
NSK16-0	0	2.8×10^1	0.9995
NSK52-3	0.017	3.21×10^1	0.9995
NSK52-2	0.064	**3.56×10^1**	0.9999
NSK52-1	0.094	3.54×10^1	0.9999
NSK52-4	0.179	3.47×10^1	0.9999
NSK52-5	0.305	3.28×10^1	0.9999



*Solvolysis reactions of 4,4´-dimethylbenzhydryl chloride **1d** in 60AN40W*

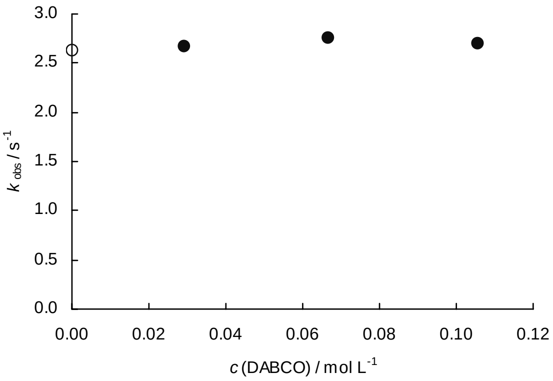
substrate concentration	**amine**	**solvent**	**method**
[**1d**] = 6.1×10^{-3} mol L^{-1}	DABCO	60AN40W	stopped-flow conductometry

No	*c*(DABCO) / M	k_{obs} / s^{-1}	r^2
NSK22-0	0	2.6	0.9981
NSK22-1	0.029	2.67	0.9985
NSK22-2	0.066	**2.76**	0.9994
NSK22-3	0.105	2.70	0.9996



substrate concentration	**amine**	**solvent**	**method**
[**1d**] = 6.1 × 10^{-3} mol L^{-1}	piperidine	60AN40W	stopped-flow conductometry

No	c(piperidine) / M	k_{obs} / s^{-1}	r^2
NSK22-0	0	2.6	0.9981
NSK55-1	0.026	**2.63**	0.9998
NSK55-2	0.051	2.58	0.9999
NSK55-3	0.081	2.46	0.9999
NSK55-4	0.175	2.26	0.9998



Solvolysis reactions of 4-methylbenzhydryl chloride ***1c*** *in 60AN40W*

substrate concentration	**amine**	**solvent**	**method**
[**1c**] = 6.0 × 10^{-4} mol L^{-1}	---	60AN40W	conventional conductometry

No	k_{obs} / s^{-1}	r^2
NSK11-1	1.88 × 10^{-1}	0.9995
NSK11-1-2	2.06 × 10^{-1}	0.9998

$k_1 = 1.97 \times 10^{-1}$ s^{-1}.

Solvolysis reactions of benzhydryl chloride ***1b*** *in 60AN40W*

substrate concentration	**amine**	**solvent**	**method**
[**1b**] = 6.0×10^{-4} mol L^{-1}	---	60AN40W	conventional conductometry

No	k_{obs} / s^{-1}	r^2
NSK13-1	8.22×10^{-3}	0.9998
NSK13-1-2	8.21×10^{-3}	0.9998
NSK-13-1-3	8.45×10^{-3}	0.9999

$k_1 = 8.29 \times 10^{-3}$ s^{-1}.

Solvolysis reactions of 4,4´-dichlorobenzhydryl chloride ***1a*** *in 60AN40W*

substrate concentration	**amine**	**solvent**	**method**
[**1a**] = 6.0×10^{-4} mol L^{-1}	---	60AN40W	conventional conductometry

No	k_{obs} / s^{-1}	r^2
NSK27-1	1.17×10^{-3}	0.9998
NSK27-1-2	1.14×10^{-3}	0.9998
NSK-27-1-3	1.11×10^{-3}	0.9997

$k_1 = 1.14 \times 10^{-3}$ s^{-1}.

Chapter 3

Nucleophilicities and Nucleofugalities of Organic Carbonates

N. Streidl, R. Branzan, H. Mayr, *Eur. J. Org. Chem.* **2010**, 4205–4210.

3.1 Introduction

Alkoxycarbonyl groups are widely used as protecting groups of alcohols and phenols, because they can easily be introduced and removed.[1] Under basic conditions organic carbonates, i.e., the diesters of carbonic acid, are typically more stable than the corresponding esters of carboxylic acids and they have found wide use in organic synthesis.[2,3] Recently, Denegri and Kronja have studied the nucleofugality (leaving group ability) of phenyl and methyl carbonate (k_1 in Scheme 3.1) in different solvents.[4] *tert*-Butyl carbonates (*t*BocO-R), the most prominent carbonates, were not included in this study. As these data are of particular interest for synthetically working chemists, we now report on the nucleofugality of the *t*BocO group. In order to characterize the electrofugalities of benzhydrylium ions which are better stabilized than the 4,4´-dimethoxybenzhydrylium ion, we have furthermore studied the nucleofugality of isobutyl carbonate and extended the work of Denegri and Kronja on the leaving group abilities of methyl carbonate; these data are needed for the construction of comprehensive nucleofugality and electrofugality scales.[5]

Scheme 3.1: Simplified Solvolysis Scheme.

$$\mathrm{R\text{-}OCO_2R'} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{R^+} + \mathrm{{}^-OCO_2R'} \xrightarrow[\mathrm{HOSolv}]{k_{\mathrm{solv}}} \mathrm{R\text{-}OSolv} + \mathrm{HOCO_2R'}$$

R = $\mathrm{Ar_2CH}$
R´ = Ph, Me, *i*Bu, *t*Bu

In previous work we compared the nucleophilic reactivities of halide[6] and carboxylate[7] ions toward benzhydrylium ions and demonstrated that the relative nucleophilicities are not the inverse of the relative nucleofugalities.[7] In order to extend this comparison to organic carbonates, we have now investigated the nucleophilic reactivity of the methyl carbonate ion by studying the rates of its reactions with benzhydrylium ions, which allows us to include the methyl carbonate ion in the comprehensive reactivity scales based on eq (3.1),[8]

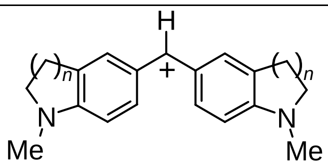
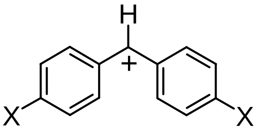
$$\log k = s(N + E) \tag{3.1}$$

where k is a second-order rate constant, E is an electrophilicity parameter, and N and s are nucleophile-specific parameters.

3.2 Results and Discussion

Determination of the Rates of the Combinations of Benzhydrylium Ions with the Methyl Carbonate Ion (k_{-1} in Scheme 3.2): The reactions of tetra-*n*-butylammonium methyl carbonate with the colored benzhydrylium ions gave colorless products in acetonitrile.

Table 3.1: Benzhydrylium Ions Ar_2CH^+ and Their Electrophilicity Parameters E.

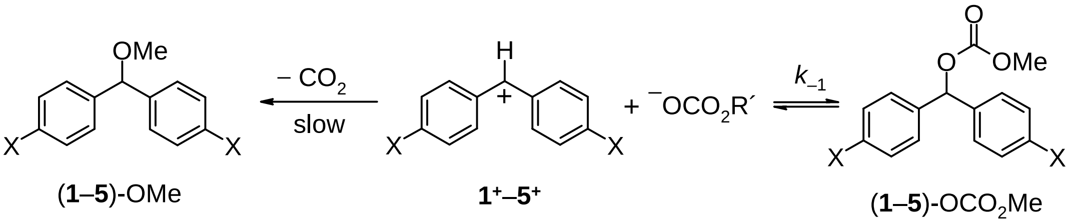
No	Ar_2CH^+		E^a
			
1$^+$	$(ind)_2CH^+$	$n = 1$	–8.76
2$^+$	$(thq)_2CH^+$	$n = 2$	–8.22
			
3$^+$	$(pyr)_2CH^+$	$X = N(CH_2)_4$	–7.69
4$^+$	$(mor)_2CH^+$	$X = N(CH_2CH_2)_2O$	–5.53
5$^+$	$(mfa)_2CH^+$	$X = N(CH_3)CH_2CF_3$	–3.85

[a] Electrophilicity parameter as defined by eq 3.1 (from ref. 8).

4-Methoxybenzhydryl methyl carbonate (**6**-OCO_2Me) was formed in quantitative yield and isolated as a stable compound. However, we were not able to isolate the corresponding products when using highly stabilized benzhydrylium ions (Table 3.1), as the products rapidly decarboxylate with formation of the corresponding benzhydryl methyl ethers (**1**–**5**)-OMe (Scheme 3.2). The mechanism of this decarboxylation reaction is not clear, because a solution of tetra-*n*-butylammonium methyl carbonate in acetonitrile did not decompose noticeably at

25 °C during the time of the kinetic investigations. Possibly ionization of (**1–5**)-OCO_2Me and recombination of the initially generated ion-pair does not exclusively regenerate the carbonates $Ar_2CH-OCO_2Me$; occasionally electrophilic attack at the methoxy oxygen of $H_3CO-CO_2^-$ yields a zwitterion which decomposes with formation of CO_2 and the observed benzhydryl methyl ethers.

Scheme 3.2: Combination Reaction of Benzhydrylium Ions with Methyl Carbonate and Subsequent Decarboxylation.



Most reactions were followed photometrically at the absorption maxima of Ar_2CH^+ by using a stopped-flow instrument. For studying reactions on the microsecond time-scale, the benzhydrylium ions were generated by laser pulse irradiation of benzhydryl tri-*n*-butylphosphonium tetrafluoroborates[9] in acetonitrile solution in the presence of tetra-*n*-butylammonium methyl carbonate. All reactions were performed under pseudo-first-order conditions (high excess of $n\text{-}Bu_4N^+MeOCO_2^-$) at 25 °C in acetonitrile. The first-order rate constants k_{obs} were obtained from the exponential decays of the absorbances of the electrophiles (Figure 3.1). Details are given in the Experimental Section.

As depicted in Figure 3.1 the absorbance of the electrophile does not fade completely during the monitored reaction time (0.1 s), indicating an equilibrium between covalent carbonates and ionic starting materials. However, when the reaction shown in Figure 3.1 was monitored for 2 seconds, complete disappearance of the absorbance of the benzhydrylium ion was observed, which is explained by the subsequent irreversible formation of the benzhydryl methyl ether (Scheme 3.2).

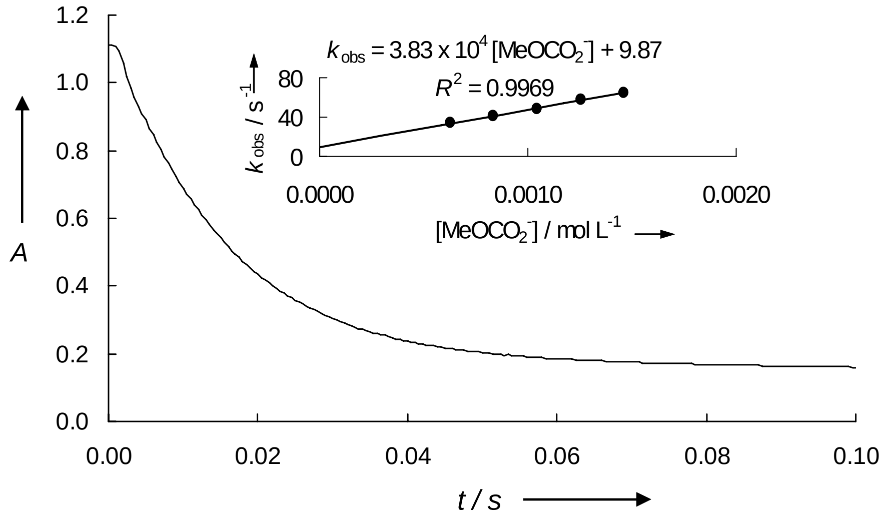


Figure 3.1: Exponential decay of the absorbance at 616 nm during the reaction of $(ind)_2CH^+$ (**1**$^+$) with $MeOCO_2^-$ in CH_3CN at 25 °C ($[(ind)_2CH^+] = 2.13\times 10^{-5}$ M; $[MeOCO_2^-] = 1.25 \times 10^{-3}$ M; $k_{obs} = 57.1$ s^{-1}). Insert: determination of the second-order rate constant k_{-1} (3.83×10^4 M^{-1} s^{-1}) as the slope of the correlation of the first-order rate constants k_{obs} versus $[MeOCO_2^-]$.

As illustrated in the insert of Figure 3.1, k_{obs} increases linearly with the concentration of $MeOCO_2^-$. The second-order rate constants k_{-1}, which are listed in Table 3.2, were obtained as the slopes of these plots [eq (3.2)].

$$k_{obs} = k_{-1}[MeOCO_2^-] \qquad (3.2)$$

Table 3.2: Second-order Rate Constants k_{-1} for the Reactions of Benzhydrylium Ions with $Bu_4N^+MeOCO_2^-$ in Acetonitrile at 25 °C.

No	Ar_2CH^+	E^a	k_{-1} / M^{-1} s^{-1}
1$^+$	$(ind)_2CH^+$	–8.76	3.83×10^4
2$^+$	$(thq)_2CH^+$	–8.22	9.69×10^4
3$^+$	$(pyr)_2CH^+$	–7.69	2.57×10^5
4$^+$	$(mor)_2CH^+$	–5.53	5.21×10^6
5$^+$	$(mfa)_2CH^+$	–3.85	5.77×10^7

[a] Electrophilicity parameter as defined by eq 3.1 (from ref. 8).

When the logarithms of the second-order rate constants k_{-1} are plotted against the previously reported electrophilicity parameters E of the benzhydrylium ions (Figure 3.2), a linear correlation is obtained, which yields the nucleophilicity parameter[10] N_{25} = 16.03 as the negative intercept on the abscissa (*E* axis) and the nucleophile-specific slope parameter[10] s_{25} = 0.64.

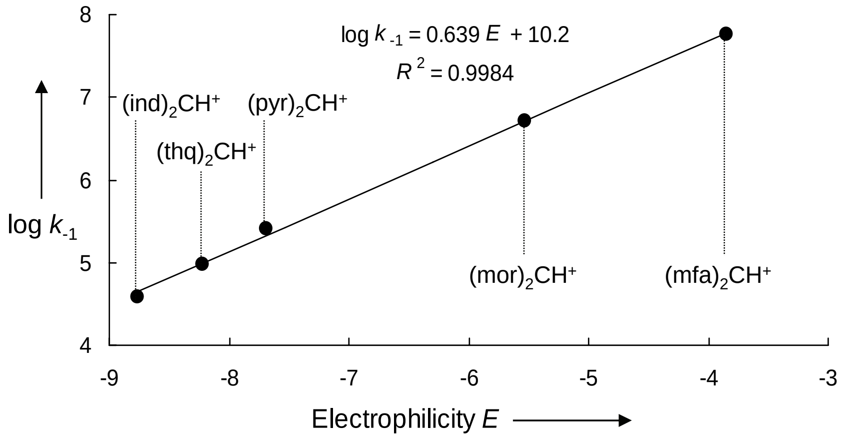


Figure 3.2: Plot of the second-order rate constants log k_{-1} (25 °C, acetonitrile) against the electrophilicity parameters E[8] of the reference electrophiles for the reactions of $Bu_4N^+MeOCO_2^-$ with benzhydrylium ions.

As depicted in Figure 3.3, the nucleophilicity parameter[10] N_{25} for methyl carbonate is in between those of benzoate and 4-nitrobenzoate (PNB).

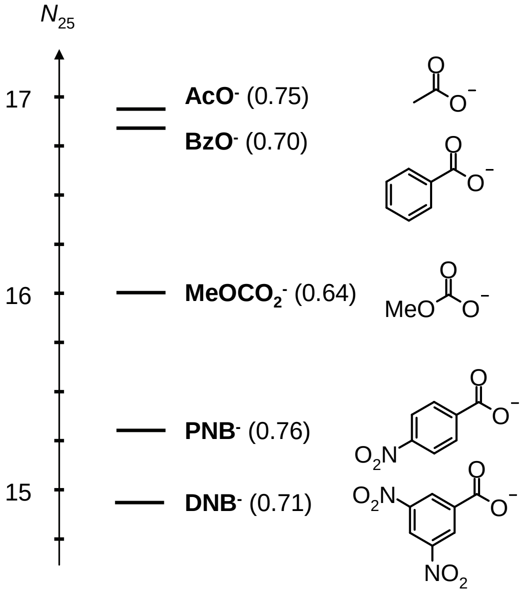


Figure 3.3: Comparison of the nucleophilicity parameters[7,10] N_{25} of common leaving groups in acetonitrile at 25 °C, s_{25} parameters in parentheses.

The nucleophilicity parameters *N* as defined by eq 3.1 reflect the relative reactivities of anions towards such electrophiles, which react with log k = 0. As the reactions of methyl carbonate and of carboxylates ($N \geq 15$) with such weak electrophiles ($E < -15$) are thermodynamically unfavorable and do not give rise to detectable equilibrium concentrations of covalent esters, it seems to be more appropriate to compare the relative nucleophilic reactivities of these anions towards stronger electrophiles. When $(thq)_2CH^+$ (**2**$^+$, $E = -8.22$) is used as reference electrophile, the nucleophilicity order in acetonitrile is:

$$AcO^- > BzO^- > PNB > MeOCO_2^- > DNB$$

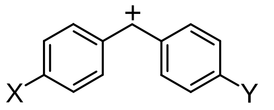
This sequence corresponds to the inverse order of the nucleofugalities of these compounds. However, nucleofugality is not generally the reverse of nucleophilicity, as exemplified by consideration of Cl^-, which is a far better nucleofuge than carboxylate ions but has a similar nucleophilicity as PNB.[6]

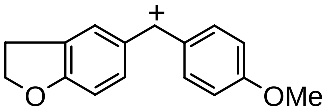
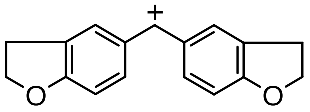
Determination of the Nucleofugalities of Organic Carbonates:

Synthesis of Precursors: The benzhydryl methyl carbonates **10-**OCO_2Me and **11-**OCO_2Me were prepared by combining the corresponding benzhydrols (see structures of benzhydryl moieties in Table 3.3) with methyl chloroformate in the presence of pyridine as previously described for (**6–9**)-OCO_2Me.[4] The same method has been used for the synthesis of the benzhydryl isobutyl carbonates (**6–11**)-OCO_2iBu from the corresponding benzhydrols and isobutyl chloroformate. The crude products were obtained as yellow oils which sometimes contained starting material (benzhydrol) and (particularly in case of the donor substituted benzhydryl systems **10**$^+$ and **11**$^+$) the aforementioned decarboxylation products (benzhydryl methyl or isobutyl ether). Attempts to purify the crude carbonates by crystallization or column chromatography resulted in decomposition. Therefore, the crude products have been used for the kinetic studies without further purification. As the side products are stable in aqueous organic solution and do not react with the benzhydryl carbonates, they do not interfere with the conductimetric measurements of the solvolysis reactions.

The benzhydryl *tert*-butyl carbonates (**8–11**)-OCO_2tBu were prepared by deprotonation of the corresponding benzhydrols with BuLi, followed by treatment with Boc_2O at –78 °C. Pure compounds were obtained by crystallization (in case of (**9–11**)-OCO_2tBu) or column chromatography (in case of **8-**OCO_2tBu).

Table 3.3. Electrofugality Parameters E_f of Benzhydrylium Ions.



	X	Y	E_f
6$^+$	OMe	H	–2.09[a]
7$^+$	OMe	Me	–1.32[a]
8$^+$	OMe	OPh	–0.86[a]
9$^+$	OMe	OMe	0.00
10$^+$			0.61[b]
11$^+$			1.07[b]

[a] These parameters revise previously published values from ref. 5. [b] Previously unpublished electrofugality parameters, based on this work and additional unpublished data.

Determination of Ionization Rates: The solvolysis rates of the benzhydryl carbonates were monitored by following the increase of the conductivity of the reaction mixtures. Because calibration experiments, i.e., portionwise addition of the rapidly solvolyzing benzhydryl methyl carbonate (**10**–OCO_2Me) into 50A50W and 60E40W and determination of the conductivity after completion of the solvolysis, showed a proportionality between conductivity (G) and the concentration of the substrates in the concentration range investigated (see Experimental Section), we were able to obtain first-order rate constants k_1 by fitting the time dependent conductivities G to the monoexponentional function (3.3).

$$G = G_{\max} [1 - \exp(-k_1 t)] + const. \tag{3.3}$$

Because all solvolyses studied in this work follow first-order rate laws, common ion return[11] (k_{-1} in Scheme 3.1) obviously does not occur. This is in line with previous work[7] where we have shown that acetate and benzoate ions, which are stronger nucleophiles than methyl carbonate ions, also do not show common ion return in solvolysis reactions under similar conditions. The conductimetrically measured rate constants listed in Table 3.4, therefore, correspond to the ionization rate constants k_1 defined in Scheme 3.1.

Table 3.4: Conductimetrically Measured Solvolysis Rate Constants (25 °C) of the Benzhydryl Alkyl Carbonates (**6–11**)-LG in Different Solvents.

solvent[a]	LG	electrofuge	k_1 / s^{-1}
50A50W	OCO$_2$Me	**10**	4.87×10^{-2}
		11	1.24×10^{-1}[b]
	OCO$_2$*i*Bu	**6**	1.09×10^{-4}
		7	4.81×10^{-4}
		8	1.20×10^{-3}
		9	7.16×10^{-3}
		10	2.13×10^{-2}
		11	5.97×10^{-2}
60A40W	OCO$_2$Me	**10**	1.91×10^{-2}
		11	4.66×10^{-2}[b]
	OCO$_2$*t*Bu	**8**	6.06×10^{-5}
		9	3.89×10^{-4}
		10	1.51×10^{-3}
		11	3.92×10^{-3}
70A30W	OCO$_2$Me	**10**	6.87×10^{-3}
		11	2.45×10^{-2}[b]
60E40W	OCO$_2$*i*Bu	**6**	2.31×10^{-4}
		7	1.00×10^{-3}
		8	2.24×10^{-3}
		9	1.66×10^{-2}
		10	5.40×10^{-2}
	OCO$_2$*t*Bu	**8**	3.94×10^{-4}
		9	3.05×10^{-3}
		10	8.54×10^{-3}
		11	2.15×10^{-2}
80E20W	OCO$_2$Me	**10**	4.72×10^{-2}
	OCO$_2$*t*Bu	**8**	1.50×10^{-4}
		9	1.15×10^{-3}
		10	3.96×10^{-3}
		11	1.07×10^{-2}
90E10W	OCO$_2$Me	**10**	2.33×10^{-2}
	OCO$_2$*i*Bu	**7**	1.81×10^{-4}
		8	5.80×10^{-4}
		9	4.53×10^{-3}
		10	1.45×10^{-2}
		11	4.14×10^{-2}
60AN40W	OCO$_2$*t*Bu	**8**	9.87×10^{-5}
		9	8.28×10^{-4}
		10	2.76×10^{-3}
		11	7.13×10^{-3}

[a] Mixtures of solvents are given as (v/v); solvents: A = acetone, AN = acetonitrile, E = ethanol, W = water.

[b] Stopped-flow kinetics.

Correlation Analyses: From the plots of log k_1 versus $\Sigma\sigma^+$, one derives Hammett reaction constants of $-2.9 < \rho < -2.4$ for the solvolysis reactions of benzhydryl carbonates in 60E40W (Figure 3.4). The magnitudes of the reaction constants ρ suggest transition states, which correspond to the carbocations.

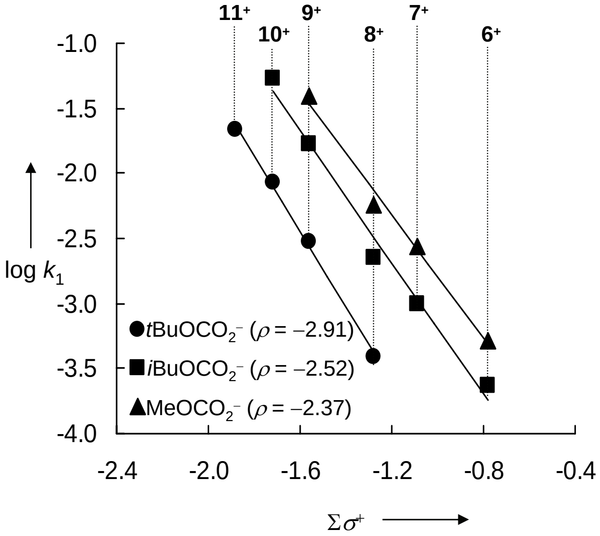


Figure 3.4: Plots of log k_1 of the solvolysis reactions of the benzhydryl alkyl carbonates in 60% aqueous ethanol (60E40W) vs Hammett´s substituent constants $\Sigma\sigma^+$ (k_1 for tBuOCO$_2^-$ and iBuOCO$_2^-$ from Table 4.4, k_1 for MeOCO$_2^-$ from ref. 4; σ^+ from ref. 12).

In previous work[5] we have demonstrated that eq (3.4) can be used for the calculation of the heterolysis rate constants k_1 of benzhydryl derivatives in various solvents.

$$\log k_1 \text{ (25 °C)} = s_f (N_f + E_f) \tag{3.4}$$

In eq (3.4) k_1 is a first-order rate constant (s^{-1}), s_f and N_f are nucleofuge-specific parameters (referring to combinations of leaving groups and solvents), and E_f is a carbocation-specific electrofugality parameter.

Plots of log k_1 (from this work and ref. 4) for the solvolysis reactions of various substituted benzhydryl carbonates versus the electrofugality parameters E_f of the benzhydrylium ions (see Table 3.3) are linear as exemplified in Figure 3.5 for the solvolyses of benzhydryl *tert*-butyl carbonates in different aqueous solvents. For analogous correlations of isobutyl and methyl carbonates see Experimental Section. From these correlations 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 correlations (Table 3.5). The nucleofugality parameters for methyl carbonate are in very good agreement with those published by Denegri and Kronja,[4] which were based on a smaller data set.

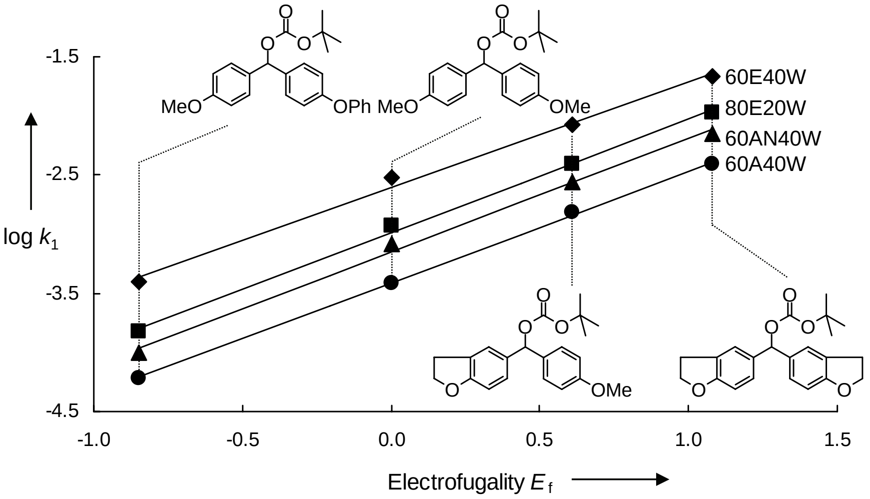


Figure 3.5: Plots of the first-order rate constants log k_1 of the solvolyses of substituted benzhydryl *tert*-butyl carbonates in different solvent mixtures against the electrofugality parameters E_f (mixtures of solvents are given (v/v); W = water, E = ethanol, AN = acetonitrile, A = acetone).

Table 3.5. Nucleofugality Parameters N_f and s_f of Organic Carbonates in Different Solvent Mixtures.

	N_f / s_f		
Solvent[a]	OCO_2Me	OCO_2*i*Bu	OCO_2*t*Bu
50A50W	–2.13 / 0.86[b]	–2.51 / 0.87	
60A40W	–2.56 / 0.88[b]		–3.62 / 0.94
70A30W	–2.83 / 0.94[b]		
60E40W	–1.59 / 0.89[b]	–2.04 / 0.89	–2.91 / 0.89
80E20W	–1.96 / 0.95[b]		–3.12 / 0.96
90E10W	–2.20 / 0.98[b]	–2.46 / 0.98	
60AN40W			–3.28 / 0.96

[a] Mixtures of solvents are given (v/v); W = water, E = ethanol, AN = acetonitrile, A = acetone. [b] These parameters differ slightly from previously published values which were based on a smaller data set for the correlation (ref. 4).

With these nucleofugality parameters it now becomes possible to directly compare the leaving group abilities of various carbonates with other commonly used leaving groups. As the slope parameters s_f of different leaving groups differ only slightly ($\Delta s_f \leq 0.08$), it appears justified to compare the nucleofugalities of these leaving groups on the basis of N_f (Figure 3.6).

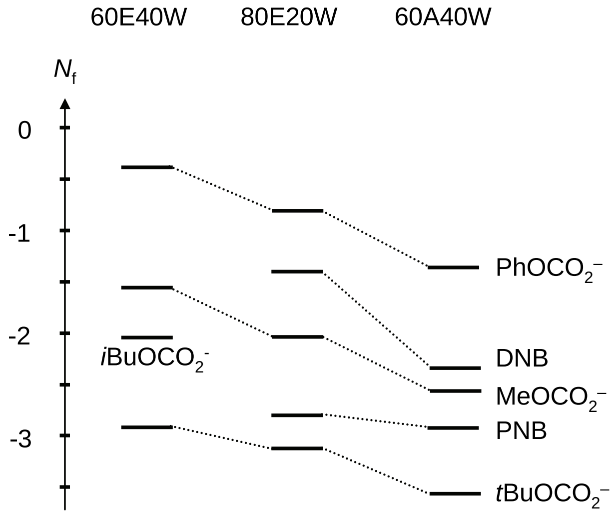


Figure 3.6: Comparison of the nucleofugalities of leaving groups in various solvents. (DNB = 3,5-dinitrobenzoate, PNB = 4-nitrobenzoate from ref. 5).

As depicted in Figure 3.6, phenyl carbonate which has previously been studied by Denegri and Kronja[4] is the most reactive carbonate investigated so far, ionizing about one order of magnitude faster than methyl carbonate. This difference in reactivity has been explained by the more efficient delocalization of the negative charge in phenyl carbonate.[4] Replacement of the methyl group by an isobutyl group reduces the reactivity by half an order of magnitude, and *tert*-butyl carbonate (*t*BocO) is the weakest nucleofuge of this series, approximately 10 times less reactive than isobutyl carbonate. Sterically hindered solvation of the *t*BocO$^-$ anion can be assumed to account for its low nucleofugality. In conclusion the carbonate reactivity can be altered by about 2.5 orders of magnitude by changing the substituent from phenyl (most reactive) to *tert*-butyl (least reactive), i.e., the half-life of 4-methoxybenzhydryl phenyl carbonate in 80 % aqueous ethanol at room temperature is about 4 min, whereas the half-life of the corresponding *tert*-butyl carbonate is about 19 h. Figure 3.6 furthermore shows that *t*BocO has a smaller leaving group ability than *p*-nitrobenzoate (PNB) or 3,5-dinitrobenzoate (DNB) in various solvents.[7]

3.3 Conclusions

The great synthetic value of the *t*Boc protecting group has generally been assigned to the ease of deprotection under acidic conditions. This work has demonstrated an additional advantage of the *t*Boc group. The *tert*-butoxycarbonyloxy group *t*$BuOCO_2^-$ is a considerably weaker nucleofuge than phenyl carbonate or other alkyl carbonates with the result that the *tert*-butyl carbonates *t*$BuOCO_2$-R are much less sensitive toward heterolytic cleavage of the O-R bond than other carbonates. The higher lability of *tert*-butyl carbonates under acidic conditions is thus combined with greater stability under neutral and basic conditions.

3.4 References

(1) a) Kocienski, P. J. *Protecting Groups*, 3rd ed., Thieme, Stuttgart, **2005**. b) Wuts, P. G. M.; Greene, T. W. *Greene´s Protective Groups in Organic Synthesis*, 4th ed., Wiley, Hoboken, NJ, **2007**.

(2) Shaikh, A.-A. G.; Sivaram, S. *Chem. Rev.* **1996**, *96*, 951–976.

(3) Parrish, J. P.; Salvatore, R. N.; Jung, K. W. *Tetrahedron* **2000**, *56*, 8207–8237.

(4) Denegri, B.; Kronja, O. *J. Org. Chem.* **2007**, *72*, 8427–8433.

(5) Denegri, B.; Streiter, A.; Juric, S.; Ofial, A. R.; Kronja, O.; Mayr, H. *Chem. Eur. J.* **2006**, *12*, 1648–1656; *Chem. Eur. J.* **2006**, *12*, 5415.

(6) Minegishi, S.; Loos, R.; Kobayashi, S.; Mayr H. *J. Am. Chem. Soc.* **2005**, *127*, 2641–2649.

(7) Schaller, H. F.; Tishkov, A. A.; Feng, X.; Mayr, H. *J. Am. Chem. Soc.* **2008**, *130*, 3012–3022.

(8) a) Mayr, H.; Bug, T.; Gotta, M. F.; Hering, N.; Irrgang, B.; Janker, B.; Kempf, B.; Loos, R.; Ofial, A. R.; Remennikov, G.; Schimmel, H. *J. Am. Chem. Soc.* **2001**, *123*, 9500–9512. b) Mayr, H.; Kempf, B.; Ofial, A. R. *Acc. Chem. Res.* **2003**, *36*, 66–77. c) Mayr, H.; Ofial, A. R. *Pure Appl. Chem.* **2005**, *77*, 1807–1821. d) Mayr, H.; Ofial, A. R. *J. Phys. Org. Chem.* **2008**, *21*, 584–595. e) For a comprehensive data base for nucleophilicity and electrophilicity parameters, see: www.cup.lmu.de/oc/mayr/.

(9) Ammer, J.; Mayr, H. *Macromolecules* **2010**, *43*, 1719–1723.

(10) The index 25 is added to the *N* and *s* parameters, as all rate constants k_{-1} in this work were measured at 25 °C for the sake of compatibility with ionization rate constants k_1 determined at 25 °C.

(11) For common ion rate depression see: a) Winstein, S.; Clippinger, E.; Fainberg, A. H.; Heck, R.; Robinson, G. C. *J. Am. Chem. Soc.* **1956**, *78*, 328–335. b) Raber, D. J.; Harris, J. M.; Schleyer, P. v. R. in: *Ions and Ion Pairs in Organic Reactions* (Ed.: Szwarc, M.), Wiley, New York, **1974**, vol. 2.

(12) a) Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165–195. b) Exner, O. *Correlation Analysis of Chemical Data*, Plenum Press, New York, **1988**.

3.5 Experimental Section

3.5.1 General

Commercially available acetone and acetonitrile (content of $H_2O < 50$ ppm) was used without further purification for all experiments. Dry ethanol was obtained by distillation of commercially available absolute ethanol from sodium/diethyl phtalate. Doubly distilled water (impendance 18.2 Ω) was prepared with a Milli-Q Plus machine from Millipore.

Mixtures of solvents are given as (v/v) and the solvents are abbreviated: A = acetone, AN = acetonitrile, E = ethanol W = water. For example the solvent mixture 80E20W refers to a mixture of ethanol and water in a ratio of 80/20 (v/v).

The benzhydrylium tetrafluoroborates were synthesized according to literature procedures.[S1] Tetra-*n*-butylammonium methyl carbonate was synthesized by bubbling CO_2 through a tetra-*n*-butylammonium methoxide solution in methanol.[S2] As the crude product still contained some methoxide, complete conversion of methoxide to methyl carbonate was achieved by treatment of a solution of the crude material in toluene with a stream of CO_2.

3.5.2 Solvolysis Reactions of Benzhydryl Alkyl Carbonates at 25 °C

Solvolysis rates of the benzhydrylium derivatives were monitored by following the increase of the conductivity of the reaction mixtures (conductometer: Tacussel CD 810, Pt electrode: WTW LTA 1/NS). Freshly prepared solvents (30 mL) were thermostated (±0.1 °C) at 25 °C for 5 min prior to adding the substrate. Typically 0.20 mL portions of a 0.09 M stock solution of the substrate in dichloromethane were injected into the solvent. Typically, each run was repeated at least once; the reported rate constants are the arithmetic means. In order to achieve

---

[S1] Mayr, H.; Bug, T.; Gotta, M. F.; Hering, N.; Irrgang, B.; Janker, B.; Kempf, B.; Loos, R.; Ofial, A. R.; Remennikov, G.; Schimmel, H. *J. Am. Chem. Soc.* **2001**, *123*, 9500–9512.

[S2] Berkessel, A.; Brandenburg, M. *Org. Lett.* **2006**, *8*, 4401–4404.

a complete ionization of the liberated weak acid, 2 to 40 equivalents of 1,8-bis(dimethylamino)naphthalene or piperidine was used as additive.

For the study of fast solvolysis reactions a stopped-flow conductometer (Hi-Tech Scientific SF-61 DX2, platinum electrodes, cell volume: 21 µL, cell constant 4.24 cm^{-1}, minimum dead time 2.2 ms) was used in single-mixing mode. The benzhydryl derivatives were dissolved in pure acetone or acetonitrile and mixed with aqueous acetone or acetonitrile.

After injection of the benzhydryl derivative into the solvolysing medium an increase of conductivity was observed, which was recorded at certain time intervals.

Calibration. Calibration experiments showed proportionality between final conductance and initial benzhydryl derivative concentration (Figure S1).

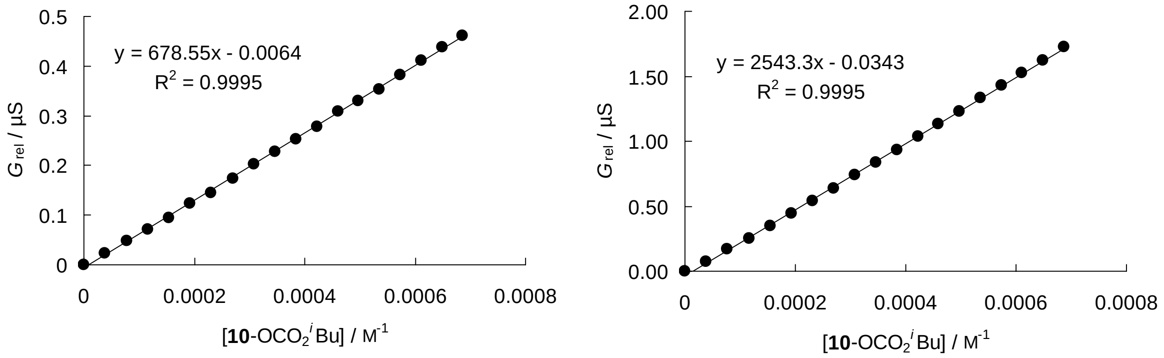


Figure S1: Initial concentration of **10**-OCO$_2$*i*Bu vs. conductance at t_∞ in 60E40W (left) and 50A50W (right). After the addition of a portion of **10**-OCO$_2$*i*Bu, the next conductivity value was taken when the conductivity remained constant for a least 100 s.

Table S1: Solvolysis Reactions of Benzhydryl Methyl Carbonates.

solvent	substrate	No	k_1 (individual) / s^{-1}	k_1 (average) / s^{-1}
50A50W	**10**-OCO_2Me	RBK37-4	4.88×10^{-2}	
		RBK37-5	4.86×10^{-2}	
				4.87×10^{-2}
	11-OCO_2Me	RBK28-1	1.24×10^{-1}	1.24×10^{-1}
60A40W	**10**-OCO_2Me	RBK38-1	1.89×10^{-2}	
		RBK38-2	1.91×10^{-2}	
		RBK38-3	1.92×10^{-2}	
				1.91×10^{-2}
	11-OCO_2Me	RBK26-1	4.66×10^{-2}	4.66×10^{-2}
70A30W	**10**-OCO_2Me	RBK39-1	6.90×10^{-3}	
		RBK39-2	6.87×10^{-3}	
		RBK39-3	6.85×10^{-3}	
				6.87×10^{-3}
	11-OCO_2Me	RBK25-1	2.45×10^{-2}	2.45×10^{-2}
80E20W	**10**-OCO_2Me	RBK36-3	4.75×10^{-2}	
		RBK36-4	4.69×10^{-2}	
				4.72×10^{-2}
90E10W	**10**-OCO_2Me	RBK35-2	2.31×10^{-2}	
		RBK35-4	2.35×10^{-2}	
				2.33×10^{-2}

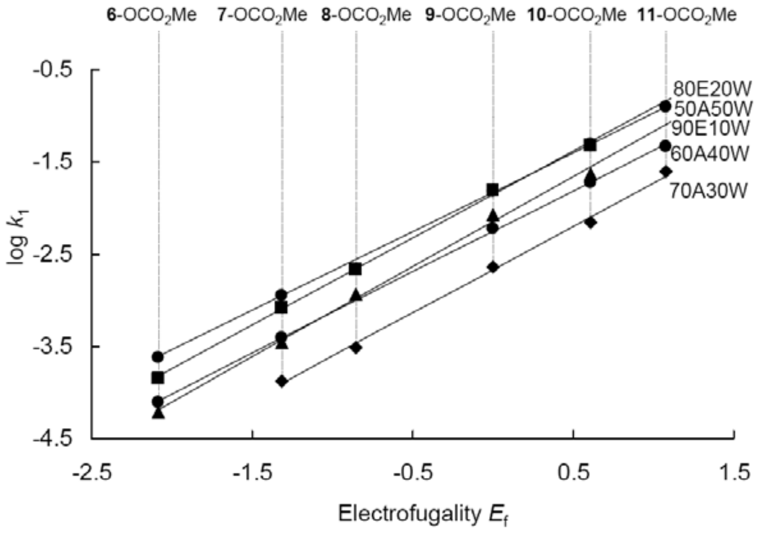


Figure S2: Plots of the first-order rate constants log k_1 (from this work and from ref. S3 of the solvolyses of substituted benzhydryl methyl carbonates in different solvent mixtures against the electrofugality parameters E_f (mixtures of solvents are given (v/v); W = water, E = ethanol, A = acetone).

[S3] Denegri, B.; Kronja, O. *J. Org. Chem.* **2007**, *72*, 8427–8433.

Table S2: Solvolysis Reactions of Benzhydryl Isobutyl Carbonates.

solvent	substrate	No	k_1 (individual) / s^{-1}	k_1 (average) / s^{-1}
50A50W	**6**-OCO$_2$*i*Bu	RBK41-1	1.10×10^{-4}	
		RBK41-2	1.07×10^{-4}	
				1.09×10^{-4}
	7-OCO$_2$*i*Bu	RBK08-1	4.66×10^{-4}	
		RBK08-3	4.81×10^{-4}	
		RBK08-4	4.95×10^{-4}	
				4.81×10^{-4}
	8-OCO$_2$*i*Bu	RBK22-1	1.20×10^{-3}	1.20×10^{-3}
	9-OCO$_2$*i*Bu	RBK07-2	7.06×10^{-3}	
		RBK07-4	7.25×10^{-3}	
				7.16×10^{-3}
	10-OCO$_2$*i*Bu	RBK32-2	2.13×10^{-2}	
		RBK32-4	2.13×10^{-2}	
				2.13×10^{-2}
	11-OCO$_2$*i*Bu	RBK21-1	6.05×10^{-2}	
		RBK21-2	5.89×10^{-2}	
				5.97×10^{-2}
60E40W	**6**-OCO$_2$*i*Bu	RBK24-4	2.31×10^{-4}	
		RBK24-5	2.31×10^{-4}	
				2.31×10^{-4}
	7-OCO$_2$*i*Bu	RBK04-1	1.01×10^{-3}	
		RBK04-2	9.98×10^{-4}	
				1.00×10^{-3}
	8-OCO$_2$*i*Bu	RBK18-1	2.32×10^{-3}	
		RBK18-2	2.16×10^{-3}	
				2.24×10^{-3}
	9-OCO$_2$*i*Bu	RBK34-11	1.70×10^{-2}	
		RBK34-3	1.60×10^{-2}	
		RBK34-12	1.67×10^{-2}	
				1.66×10^{-2}
	10-OCO$_2$*i*Bu	RBK31-2	5.41×10^{-2}	
		RBK31-6	5.44×10^{-2}	
		RBK31-8	5.36×10^{-2}	
				5.40×10^{-2}
90E10W	**7**-OCO$_2$*i*Bu	RBK09-3	1.79×10^{-4}	
		RBK09-4	1.82×10^{-4}	
				1.81×10^{-4}
	8-OCO$_2$*i*Bu	RBK19-3	5.75×10^{-4}	
		RBK19-4	5.87×10^{-4}	
		RBK19-5	5.77×10^{-4}	
				5.80×10^{-4}
	9-OCO$_2$*i*Bu	RBK10-2	4.53×10^{-3}	

Table S2: *Continued.*

solvent	substrate	No	k_1 (individual) / s^{-1}	k_1 (average) / s^{-1}
90E10W	**9**-OCO_2*i*Bu	RBK10-4	4.52×10^{-3}	
				4.53×10^{-3}
	10-OCO_2*i*Bu	RBK33-1	1.46×10^{-2}	
		RBK33-4	1.45×10^{-2}	
		RBK33-5	1.43×10^{-2}	
				1.45×10^{-2}
	11-OCO_2*i*Bu	RBK20-1	4.14×10^{-2}	
		RBK20-2	4.14×10^{-2}	
				4.14×10^{-2}

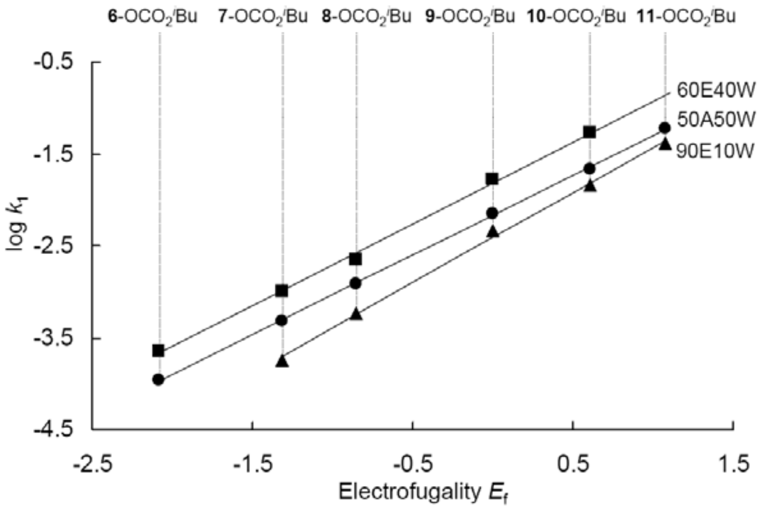


Figure S3: Plots of the first-order rate constants log k_1 of the solvolyses of substituted benzhydryl isobutyl carbonates in different solvent mixtures against the electrofugality parameters E_f (mixtures of solvents are given (v/v); W = water, E = ethanol, A = acetone).

Table S3: Solvolysis Reactions of Benzhydryl *tert*-Butyl Carbonates.

solvent	substrate	No	k_1 (individual) / s^{-1}	k_1 (average) / s^{-1}
60E40W	**8**-OCO$_2$*t*Bu	NSK155-1	3.83×10^{-4}	
		NSK155-2	4.01×10^{-4}	
		NSK155-3	3.99×10^{-4}	
				3.94×10^{-4}
	9-OCO$_2$*t*Bu	NSK154-1	3.18×10^{-3}	
		NSK154-4	2.89×10^{-3}	
		NSK154-5	3.08×10^{-3}	
				3.05×10^{-3}
	10-OCO$_2$*t*Bu	NSK151-2	8.55×10^{-3}	
		NSK151-4	8.51×10^{-3}	
		NSK151-5	8.55×10^{-3}	
				8.54×10^{-3}
	11-OCO$_2$*t*Bu	NSK150-6	2.10×10^{-2}	
		NSK150-7	2.20×10^{-2}	
		NSK150-8	2.16×10^{-2}	
				2.15×10^{-2}
80E20W	**8**-OCO$_2$*t*Bu	NSK152-1	1.47×10^{-4}	
		NSK152-2	1.52×10^{-4}	
				1.50×10^{-4}
	9-OCO$_2$*t*Bu	NSK140-1	1.13×10^{-3}	
		NSK140-2	1.17×10^{-3}	
				1.15×10^{-3}
	10-OCO$_2$*t*Bu	NSK144-1	3.97×10^{-3}	
		NSK144-2	3.91×10^{-3}	
		NSK144-3	3.99×10^{-3}	
				3.96×10^{-3}
	11-OCO$_2$*t*Bu	NSK142-1	1.10×10^{-2}	
		NSK142-2	1.07×10^{-2}	
		NSK142-3	1.03×10^{-2}	
				1.07×10^{-2}
60A40W	**8**-OCO$_2$*t*Bu	NSK156-1	5.90×10^{-5}	
		NSK156-2	6.22×10^{-5}	
				6.06×10^{-5}
	9-OCO$_2$*t*Bu	NSK141-1	3.84×10^{-3}	
		NSK141-2	3.94×10^{-3}	
				3.89×10^{-4}
	10-OCO$_2$*t*Bu	NSK145-1	1.57×10^{-3}	
		NSK145-3	1.47×10^{-3}	
		NSK145-4	1.50×10^{-3}	
				1.51×10^{-3}
	11-OCO$_2$*t*Bu	NSK143-2	3.93×10^{-3}	
		NSK143-3	3.91×10^{-3}	
				3.92×10^{-3}
60AN40W	**8**-OCO$_2$*t*Bu	NSK153-2	9.80×10^{-5}	

Table S3: *Continued.*

solvent	substrate	No	k_1 (individual) / s^{-1}	k_1 (average) / s^{-1}
60AN40W	**8**-OCO_2tBu	NSK153-3	9.93×10^{-5}	
				9.87×10^{-5}
	9-OCO_2tBu	NSK146-1	8.20×10^{-4}	
		NSK146-2	8.39×10^{-4}	
		NSK146-3	8.25×10^{-4}	
				8.28×10^{-4}
	10-OCO_2tBu	NSK148-1	2.75×10^{-3}	
		NSK148-2	2.78×10^{-3}	
		NSK148-	2.76×10^{-3}	
				2.76×10^{-3}
	11-OCO_2tBu	NSK147-1	7.15×10^{-3}	
		NSK147-2	7.20×10^{-3}	
		NSK147-3	7.05×10^{-3}	
				7.13×10^{-3}

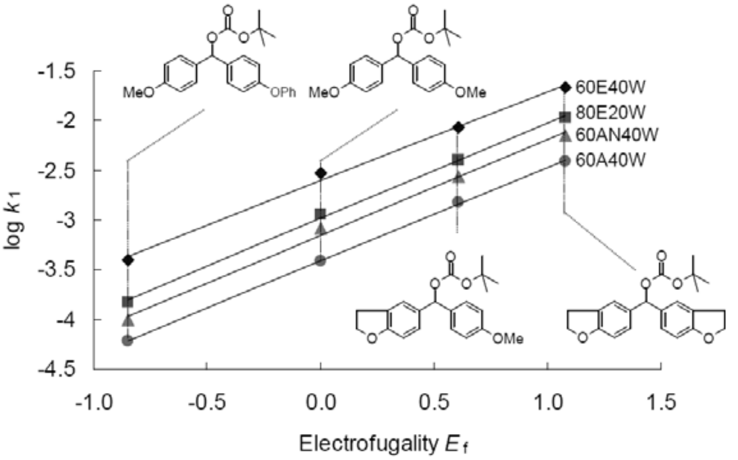


Figure S4: Plots of the first-order rate constants log k_1 of the solvolyses of substituted benzhydryl *tert*-butyl carbonates in different solvent mixtures against the electrofugality parameters E_f (mixtures of solvents are given (v/v); W = water, E = ethanol, A = acetone, AN = acetonitrile).

3.5.3 Kinetics of the Reactions of Benzhydrylium Ions with Tetra-*n*-butylammonium Methyl Carbonate (TBAMC)

The kinetics of the reactions of the benzhydrylium ions with tetra-*n*-butylammonium methyl carbonate (TBAMC) were followed by UV-Vis spectroscopy in acetonitrile at 25 °C. All experiments were performed under pseudo-first-order conditions (excess of $MeOCO_2^-$).

For most reactions a stopped-flow spectrophotometer system (Applied Photophysics SX.18MV-R) was used. The kinetic runs were initiated by mixing equal volumes of acetonitrile solutions of the tetra-*n*-butylammonium methyl carbonate (TBAMC) and the benzhydrylium tetrafluoroborates. The temperature was kept constant at 25 °C in all experiments by using a circulating water bath.

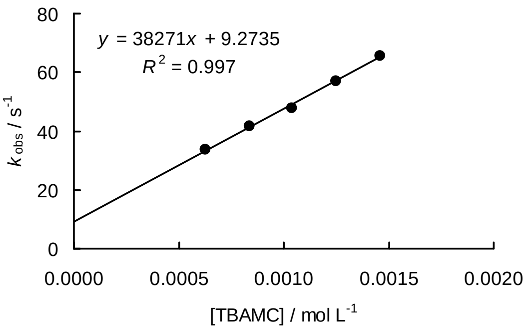
For determining the rates of the reactions of Ar_2CH^+ with $MeOCO_2^-$ with reaction times below 10 ms, benzhydrylium ions were generated by laser-flash photolysis of solutions of benzhydryl tri-*n*-butylphosphonium tetrafluoroborates (P-salt) in acetonitrile at 25 °C. A solution of known concentration of the precursor in acetonitrile was mixed with a known concentration of tetra-*n*-butylammonium methyl carbonate (TBAMC) and the resulting colorless solution was then irradiated with a 6.5-ns laser pulse (Innolas SpitLight 600 Nd:YAG laser, fourth harmonic at λ = 266 nm: power/pulse of 40-60 mJ) to generate the benzhydrylium ions Ar_2CH^+.

From the exponential decays of the absorbances at λ_{max} of the electrophiles **1^+-5^+**, the first-order rate constants k_{obs} (s^{-1}) were obtained.

Rate Constants for the Reactions of Tetra-*n*-butylammonium Methyl Carbonate (TBAMC) with $(ind)_2CH^+$ (**1**$^+$) in CH_3CN (Stopped-flow, 25 °C, λ = 616 nm)

No	[**1**$^+$]$_0$ / M	[TBAMC]$_0$ / M	[TBAMC]$_0$ / [**1**$^+$]$_0$	k_{obs} /s^{-1}
133_01	2.13×10^{-5}	6.26×10^{-4}	29	3.36×10^{1}
133_02	2.13×10^{-5}	8.35×10^{-4}	39	4.16×10^{1}
133_03	2.13×10^{-5}	1.04×10^{-3}	49	4.78×10^{1}
133_04	2.13×10^{-5}	1.25×10^{-3}	59	5.71×10^{1}
133_05	2.13×10^{-5}	1.46×10^{-3}	69	6.57×10^{1}

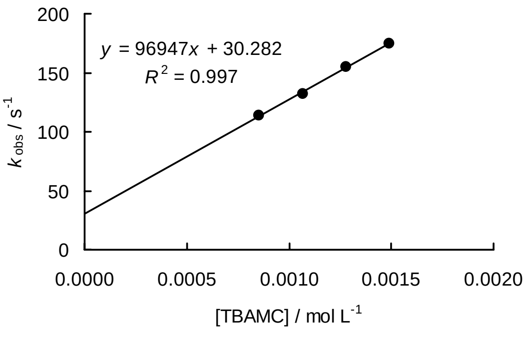
$k_2 = 3.83 \times 10^{4}$ M^{-1} s^{-1}



Rate Constants for the Reactions of Tetra-*n*-butylammonium Methyl Carbonate (TBAMC) with $(thq)_2CH^+$ (**2**$^+$) in CH_3CN (Stopped-flow, 25 °C, λ = 619 nm)

No	[**2**$^+$]$_0$ / M	[TBAMC]$_0$ / M	[TBAMC]$_0$ / [**2**$^+$]$_0$	k_{obs} /s^{-1}
131_03	2.04×10^{-5}	8.52×10^{-4}	42	1.14×10^{2}
131_04	2.04×10^{-5}	1.07×10^{-3}	52	1.32×10^{2}
131_05	2.04×10^{-5}	1.28×10^{-3}	63	1.55×10^{2}
131_06	2.04×10^{-5}	1.49×10^{-3}	73	1.75×10^{2}

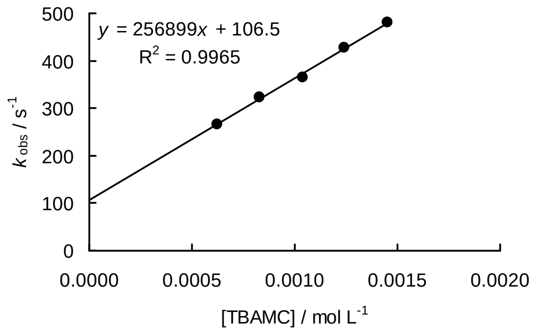
$k_2 = 9.69 \times 10^{4}$ M^{-1} s^{-1}



Rate Constants for the Reactions of Tetra-*n*-butylammonium Methyl Carbonate (TBAMC) with (pyr)$_2$CH$^+$ (**3**$^+$) in CH$_3$CN (Stopped-flow, 25 °C, λ = 611 nm)

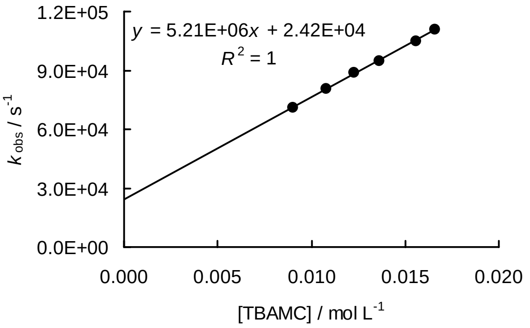
No	[**3**$^+$]$_0$ / M	[TBAMC]$_0$ / M	[TBAMC]$_0$ / [**3**$^+$]$_0$	k_{obs} /s^{-1}
129_01	2.04×10^{-5}	6.21×10^{-4}	30	2.67×10^{2}
129_02	2.04×10^{-5}	8.28×10^{-4}	41	3.23×10^{2}
129_03	2.04×10^{-5}	1.04×10^{-3}	51	3.65×10^{2}
129_04	2.04×10^{-5}	1.24×10^{-3}	61	4.27×10^{2}
129_05	2.04×10^{-5}	1.45×10^{-3}	71	4.81×10^{2}

$k_2 = 2.57 \times 10^5$ M^{-1} s^{-1}



Rate Constants for the Reactions of Tetra-*n*-butylammonium Methyl Carbonate (TBAMC) with (mor)$_2$CH$^+$ (**4**$^+$) (precursor: (mor)$_2$CH–P(n-butyl)$_3{}^+$BF$_4{}^-$, P-salt) in CH$_3$CN (laser-flash photoylsis, 25 °C, λ = 611 nm)

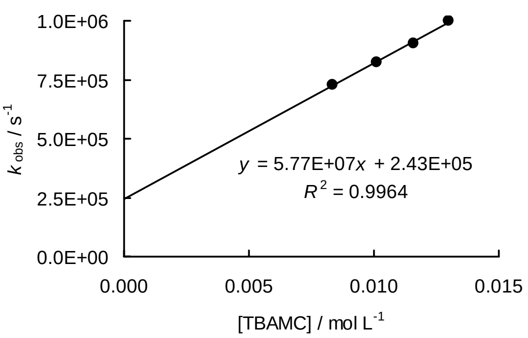
[P-salt]$_0$ / M	[TBAMC]$_0$ / M	k_{obs} /s^{-1}
1.34×10^{-5}	9.01×10^{-3}	7.10×10^{4}
1.34×10^{-5}	1.08×10^{-2}	8.04×10^{4}
1.34×10^{-5}	1.23×10^{-2}	8.88×10^{4}
1.34×10^{-5}	1.36×10^{-2}	9.46×10^{4}
1.34×10^{-5}	1.56×10^{-2}	1.05×10^{5}
1.34×10^{-5}	1.66×10^{-2}	1.11×10^{5}



$k_2 = 5.21 \times 10^6$ M^{-1} s^{-1}

Rate Constants for the Reactions of Tetra-*n*-butylammonium Methyl Carbonate (TBAMC) with $(mfa)_2CH^+$ (**5**$^+$) (precursor: $(mfa)_2CH–P(n\text{-butyl})_3{}^+BF_4{}^–$, P-salt) in CH_3CN (laser-flash photoylsis, 25 °C, λ = 586 nm)

$[\text{P-salt}]_0$ / M	$[\text{TBAMC}]_0$ / M	k_{obs} /s^{-1}
2.44×10^{-5}	8.35×10^{-3}	7.28×10^{5}
2.44×10^{-5}	1.01×10^{-2}	8.26×10^{5}
2.44×10^{-5}	1.16×10^{-2}	9.03×10^{5}
2.44×10^{-5}	1.30×10^{-2}	1.00×10^{6}



$k_2 = 5.77 \times 10^{7}$ M^{-1} s^{-1}

3.5.4 Preparation of the Benzhydryl Alkyl Carbonates

^{13}C – NMR Shifts of Benzhydryl Alkyl Carbonates

	benzhydryl substituents		benzhydryl			
substrate	Me and/or MeO	furanyl	benzhydryl center	C_{arom}	C_{arom} (quaternary)	carbonate
6-OCO$_2$*i*Bu	55.2	–	80.3	113.9, 126.7, 127.9, 128.5, 128.6	132.0, 140.0, 159.4	18.9, 27.8, 74.2, 154.8
7-OCO$_2$*i*Bu	21.1, 55.2	–	80.2	113.8, 126.7, 128.5, 129.1	132.1, 137.1, 137.6, 159.3	18.9, 27.7, 74.1, 154.8
8-OCO$_2$*i*Bu	55.3	–	79.9	113.9, 118.5, 119.1, 123.4, 128.4 (2x), 129.7	131.9, 134.7, 156.8, 157.1, 159.4	18.9, 27.8, 74.2, 154.8
8-OCO$_2$*t*Bu	55.2	–	79.1	113.9, 118.5, 119.0, 123.4, 128.4 (2x), 129.7	132.2, 135.1, 156.9 (2x), 159.3	27.8, 82.4, 152.9
9-OCO$_2$*i*Bu	55.2	–	80.1	113.8, 128.3	132.1, 159.3	18.9, 27.8, 74.1, 154.8
9-OCO$_2$*t*Bu	55.2	–	79.3	113.8, 128.3	132.5, 159.2	27.8, 82.2, 153.0
10-OCO$_2$Me	55.1	29.5, 71.3	80.5	108.9, 113.7, 123.8, 127.2, 128.1	127.5, 131.9, 132.1, 159.2, 159.9	54.7, 155.1
10-OCO$_2$*i*Bu	55.2	29.5, 71.3	80.3	109.0, 113.8, 123.8, 127.2, 128.1	127.3, 132.1, 132.3, 159.2, 159.9	18.8, 27.7, 74.0, 154.7
10-OCO$_2$*t*Bu	55.2	29.6, 71.3	79.5	109.0, 113.8, 123.8, 127.2, 128.1	127.3, 132.4, 132.7, 159.1, 159.8	27.8, 82.2, 153.0
11-OCO$_2$Me	–	29.6, 71.4	80.9	109.0, 123.7, 127.1	127.3, 132.1, 159.9	54.8, 155.2
11-OCO$_2$*i*Bu	–	29.6, 71.4	80.7	109.0, 123.7, 127.1	127.3, 132.3, 159.9	18.9, 27.8, 74.1, 154.8
11-OCO$_2$*t*Bu	–	29.6, 71.3	79.8	109.0, 123.7, 126.9	127.2, 132.6, 159.7	27.8, 82.2, 153.0

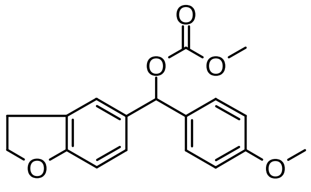
^{13}C – NMR shifts are given in ppm.

Synthesis of Benzhydryl Methyl and Isobutyl Carbonates

General procedure for the preparation of benzhydryl methyl and isobutyl carbonates:

In a flame dried, nitrogen-flushed three-necked round-bottom flask, equipped with a reflux condenser and a dropping funnel, the substituted benzhydrol (1 eq) and pyridine (6 eq) were dissolved in dry toluene or benzene. A solution of methyl chloroformate or isobutyl chloroformate (3 eq) in dry toluene or benzene was added dropwise to the well-stirred solution at ambient temperature. After 45 min the solid pyridinium chloride was removed by filtration, while the excess of pyridine was removed by 0.04 M aqueous HCl. The organic layer was washed twice with water. After drying over anhydrous $MgSO_4$ the solvent was evaporated in vacuo and impurities were distilled off at 60 °C at 5×10^{-3} mbar. Additional purification (column chromatography, methods for crystallization) resulted with the decomposition of the carbonates. According to the NMR spectra, the crude product did not contain noticeable impurities besides sometimes benzhydrol (starting material) and benzhydryl methyl or isobutyl ether (decarboxylation products), which do not interfere in the kinetic studies.

2,3-Dihydro-5-benzofuranyl-(4-methoxyphenyl)methyl methyl carbonate (**10**-OCO_2Me) was obtained from 2,3-dihydro-5-benzofuranyl-(4-methoxyphenyl)methanol (0.26 g, 1.0 mmol) and pyridine (0.48 mL, 5.9 mmol) in benzene (15 mL) and methyl chloroformate (0.23 mL, 3.0 mmol) in benzene (10 mL) as a pale yellow oil (0.11 g, 37 %), which was contaminated with starting material [2,3-dihydro-5-benzofuranyl-(4-methoxyphenyl)methanol] and decarboxylation product [2,3-dihydro-5-benzofuranyl-(4-methoxyphenyl)methyl ether]. Additional purification resulted in decomposition of the product.

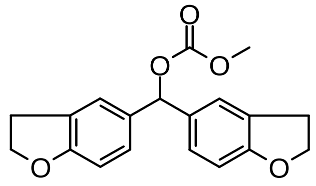

10-OCO_2Me

^{1}H NMR (600 MHz, $CDCl_3$): δ = 3.17 (t, $^3J_{HH}$ = 8.8 Hz, 2 H, CH_2), 3.79 (s, 3 H, OCO_2CH_3), 3.80 (s, 3 H, OCH_3), 4.55 (t, $^3J_{HH}$ = 8.8 Hz, 2 H, CH_2), 6.65 (s, 1 H, Ar_2CH), 6.74–6.77 (m, 1 H, ArH), 6.88–6.91 (m, 2 H, ArH), 7.09–7.14 (m, 1 H, ArH), 7.20–7.21 (m, 1 H, ArH), 7.30–7.32 (m, 2 H, ArH).

^{13}C NMR (150 MHz, CDCl$_3$): δ = 29.5 (t, CH$_2$), 54.7 (q, CH$_3$), 55.1 (q, CH$_3$), 71.3 (t, CH$_2$), 80.5 (d, CH), 108.9 (d), 113.7 (d), 123.8 (d), 127.2 (d), 127.5 (s), 128.1 (d), 131.9 (s), 132.1 (s), 155.1 (s), 159.2 (s), 159.9 (s).

HR-MS (EI, 70eV): calcd. for $C_{18}H_{18}O_5$: 314.1154, found 314.1163.

Bis(2,3-Dihydro-5-benzofuranyl)methyl methyl carbonate (**11**–OCO$_2$Me) was obtained from bis(2,3-dihydro-5-benzofuranyl)methanol (0.27 g, 1.0 mmol) and pyridine (0.48 mL, 5.9 mmol) in benzene (15 mL) and methyl chloroformate (0.23 mL, 3.0 mmol) in benzene (10 mL) as a pale yellow oil (0.59 g, 59 %), which was contaminated with starting material [bis(2,3-dihydro-5-benzofuranyl)methanol]. Additional purification resulted in decomposition of the product.

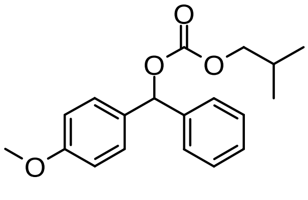


11–OCO$_2$Me

^{1}H NMR (600 MHz, CDCl$_3$): δ = 3.17 (t, $^3J_{HH}$ = 8.8 Hz, 4 H, CH$_2$), 3.78 (s, 3 H, OCO$_2$CH$_3$), 4.56 (t, $^3J_{HH}$ = 8.8 Hz, 4 H, CH$_2$), 6.59 (s, 1 H, Ar$_2$CH), 6.73–6.74 (m, 2 H, ArH), 7.10–7.12 (m, 2 H, ArH), 7.18–7.20 (m, 2 H, ArH).

^{13}C NMR (150 MHz, CDCl$_3$): δ = 29.6 (t, CH$_2$), 54.8 (q, CH$_3$), 71.4 (t, CH$_2$), 80.9 (d, CH), 109.0 (d), 123.7 (d), 127.1 (d), 127.3 (s), 132.1 (s), 155.2 (s), 159.9 (s).

4-Methoxybenzhydryl isobutyl carbonate (**6**-OCO$_2$*i*Bu) was obtained from 4-methoxybenzhydrol (0.21 g, 1.0 mmol) and pyridine (0.48 mL, 5.9 mmol) in toluene (15 mL) and isobutyl chloroformate (0.39 mL, 3.0 mmol) in toluene (10 mL) as a pale yellow oil (0.24 g, 76 %).



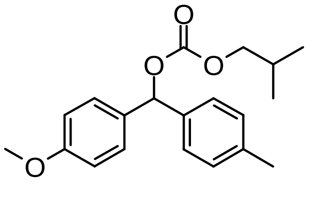
6-OCO$_2$*i*Bu

^{1}H NMR (300 MHz, CDCl$_3$): δ = 0.94 (d, $^3J_{HH}$ = 6.7 Hz, 6 H, CH(C$\underline{H}_3$)$_2$), 1.90–2.04 (m, 1 H, CH$_2$C$\underline{H}$), 3.79 (s, 3 H, OCH$_3$), 3.92 (d, $^3J_{HH}$ = 6.7 Hz, 2 H, CH$_2$), 6.67 (s, 1 H, Ar$_2$CH), 6.85–6.88 (m, 2 H, ArH), 7.25–7.39 (m, 7 H, ArH).

^{13}C NMR (75.5 MHz, CDCl$_3$): δ = 18.9 (q, CH$_3$), 27.8 (d, CH), 55.2 (q, OCH$_3$), 74.2 (t, CH$_2$), 80.3 (d, Ar$_2$CH), 113.9 (d), 126.7 (d), 127.9 (d), 128.5 (d), 128.6 (d), 132.0 (s), 140.0 (s), 154.8 (s), 159.4 (s).

HR-MS (EI, 70eV): calcd. for $C_{19}H_{22}O_4$: 314.1518, found 314.1506.

4-Methoxy-4´-methylbenzhydryl isobutyl carbonate (**7**-OCO$_2$*i*Bu) was obtained from 4-methoxy-4´-methylbenzhydrol (0.23 g, 1.0 mmol) and pyridine (0.48 mL, 5.9 mmol) in toluene (15 mL) and isobutyl chloroformate (0.39 mL, 3.0 mmol) in toluene (10 mL) as a pale yellow oil (0.29 g, 88 %).

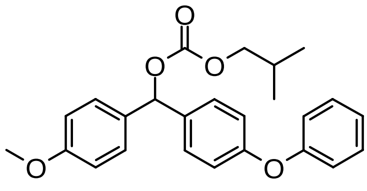


7-OCO$_2$*i*Bu

^{1}H NMR (300 MHz, CDCl$_3$): δ = 0.95 (d, $^3J_{HH}$ = 6.7 Hz, 6 H, CH(C$\underline{H}_3$)$_2$), 1.92–2.07 (m, 1 H, CH$_2$C$\underline{H}$), 2.35 (s, 3 H, CH$_3$) 3.79 (s, 3 H, OCH$_3$), 3.94 (d, $^3J_{HH}$ = 6.7 Hz, 2 H, CH$_2$), 6.66 (s, 1 H, Ar$_2$CH), 6.86–6.89 (m, 2 H, ArH), 7.15–7.18 (m, 2 H, ArH), 7.29–7.33 (m, 4 H, ArH).

^{13}C NMR (75.5 MHz, CDCl$_3$): δ = 18.9 (q, CH($\underline{C}$H$_3$)$_2$), 21.1 (q, CH$_3$), 27.7 (d, CH), 55.2 (q, OCH$_3$), 74.1 (t, CH$_2$), 80.2 (d, Ar$_2$CH), 113.8 (d), 126.7 (d), 128.5 (d), 129.1 (d), 132.1 (s), 137.1 (s), 137.6 (s), 154.8 (s), 159.3 (s).

4-Methoxy-4´-phenoxybenzhydryl isobutyl carbonate (**8**-OCO$_2$*i*Bu) was obtained from 4-methoxy-4´-phenoxybenzhydrol (0.31 g, 1.0 mmol) and pyridine (0.48 mL, 5.9 mmol) in toluene (15 mL) and isobutyl chloroformate (0.39 mL, 3.0 mmol) in toluene (10 mL) as a pale yellow oil (0.22 g, 54 %), which was contaminated with decarboxylation product 4-methoxy-4´-phenoxybenzhydryl isobutyl ether. Additional purification resulted in decomposition of the product.

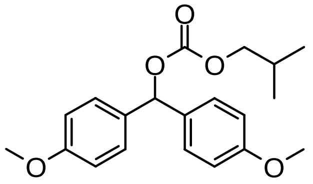


8-OCO$_2$*i*Bu

^{1}H NMR (600 MHz, CDCl$_3$) δ = 0.95 (d, $^3J_{HH}$ = 6.7 Hz, 6 H, CH(C$\underline{H}_3$)$_2$), 1.94–2.01 (m, 1 H, CH$_2$C$\underline{H}$), 3.80 (s, 3 H, OCH$_3$), 3.94 (d, $^3J_{HH}$ = 6.7 Hz, 2 H, CH$_2$), 6.66 (s, 1 H, Ar$_2$CH), 6.87–6.90 (m, 2 H, ArH), 6.95–7.01 (m, 4H, ArH), 7.10–7.12 (m, 1 H, ArH), 7.26–7.35 (m, 6 H, ArH).

^{13}C NMR (150 MHz, CDCl$_3$): δ = 18.9 (q, CH($\underline{C}$H$_3$)$_2$), 27.8 (d, CH), 55.3 (q, OCH$_3$), 74.2 (t, CH$_2$), 79.9 (d,Ar$_2$CH), 113.9 (d), 118.5 (d), 119.1 (d), 123.4 (d), 128.4 (2×d), 129.7 (d), 131.9 (s), 134.7 (s), 154.8 (s), 156.8 (s), 157.1 (s), 159.4 (s).

4,4´-Dimethoxybenzhydryl isobutyl carbonate (**9**-OCO$_2$*i*Bu) was obtained from 4,4´-dimethoxybenzhydrol (0.24 g, 1.0 mmol) and pyridine (0.48 mL, 5.9 mmol) in toluene (15 mL) and isobutyl chloroformate (0.39 mL, 3.0 mmol) in toluene (10 mL) as a pale yellow oil (0.31 g, 90 %).



9-OCO$_2$*i*Bu

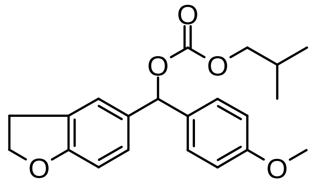
^{1}H NMR (600 MHz, CDCl$_3$): δ = 0.94 (d, $^3J_{HH}$ = 6.7 Hz, 6 H, CH(C$\underline{H}_3$)$_2$), 1.93–2.00 (m, 1 H, CH$_2$C$\underline{H}$), 3.79 (s, 6 H, 2 × OCH$_3$), 3.92 (d, $^3J_{HH}$ = 6.7 Hz, 2 H, CH$_2$), 6.63 (s, 1 H, Ar$_2$CH), 6.86–6.88 (m, 4 H, ArH), 7.26–7.29 (m, 4 H, ArH).

^{13}C NMR (150 MHz, CDCl$_3$): δ = 18.9 (q, CH$_3$), 27.8 (d, CH), 55.2 (q, OCH$_3$), 74.1 (t, CH$_2$), 80.1 (d, Ar$_2$CH), 113.8 (d), 128.3 (d), 132.1 (s), 154.8 (s), 159.3 (s).

HR-MS (EI, 70eV): calcd. for $C_{20}H_{24}O_5$: 344.1624, found 344.1616.

2,3-Dihydro-5-benzofuranyl-(4-methoxyphenyl)methyl isobutyl carbonate (**10**-OCO$_2$*i*Bu) was obtained from 2,3-dihydro-5-benzofuranyl-(4-methoxyphenyl)methanol (0.26 g, 1.0 mmol) and pyridine (0.48 mL, 5.9 mmol) in benzene (15 mL) and isobutyl chloroformate

(0.39 mL, 3.0 mmol) in benzene (10 mL) as a pale yellow oil (0.13 g, 37 %), which was contaminated with decarboxylation product (2,3-dihydro-5-benzofuranyl-(4-methoxyphenyl)isobutyl ether). Additional purification resulted in decomposition of the product.

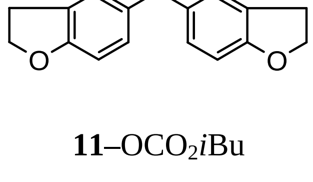


10-OCO_2*i*Bu

^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.95 (d, $^3J_{HH}$ = 6.7 Hz, 6 H, $CH(C\underline{H}_3)_2$), 1.95–2.01 (m, 1 H, $CH_2C\underline{H}$), 3.17 (t, $^3J_{HH}$ = 8.7 Hz, 2 H, CH_2), 3.79 (s, 3 H, OCH_3), 3.94 (d, $^3J_{HH}$ = 6.7 Hz, 2 H, CH_2), 4.55 (t, $^3J_{HH}$ = 8.7 Hz, 2 H, CH_2), 6.63 (s, 1 H, Ar_2CH), 6.73–6.76 (m, 1 H, ArH), 6.87–6.90 (m, 2 H, ArH), 7.07–7.13 (m, 1 H, ArH), 7.17–7.20 (m, 1 H, ArH), 7.27–7.33 (m, 2 H, ArH).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 18.8 (q, $CH(\underline{C}H_3)_2$), 27.7 (d, CH), 29.5 (t, CH_2), 55.2 (q, CH_3), 71.3 (t, CH_2), 74.0 (t, CH_2), 80.3 (d, CH), 109.0 (d), 113.8 (d), 123.8 (d), 127.2 (d), 127.3 (s), 128.1 (d), 132.1 (s), 132.3 (s), 154.7 (s), 159.2 (s), 159.9 (s).

Bis(2,3-Dihydro-5-benzofuranyl)methyl isobutyl carbonate (**11**–OCO_2*i*Bu) was obtained from bis(2,3-dihydro-5-benzofuranyl)methanol (0.27 g, 1.0 mmol) and pyridine (0.48 mL, 5.9 mmol) in benzene (15 mL) and isobutyl chloroformate (0.39 mL, 3.0 mmol) in benzene (10 mL) as a pale yellow oil (0.35 g, 95 %), which was contaminated with starting material [bis(2,3-dihydro-5-benzofuranyl)methyl isobutyl ether]. Additional purification resulted in decomposition of the product.



11–OCO_2*i*Bu

^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.94 (d, $^3J_{HH}$ = 6.7 Hz, 6 H, $CH(C\underline{H}_3)_2$), 1.93–2.00 (m, 1 H, $CH_2C\underline{H}$), 3.18 (t, $^3J_{HH}$ = 8.6 Hz, 4 H, CH_2), 3.92 (d, $^3J_{HH}$ = 6.7 Hz, 2 H, CH_2), 4.56 (t, $^3J_{HH}$ = 8.6 Hz, 4 H, CH_2), 6.59 (s, 1 H, Ar_2CH), 6.71–6.75 (m, 2 H, ArH), 7.05–7.13 (m, 2 H, ArH), 7.15–7.20 (m, 2 H, ArH).

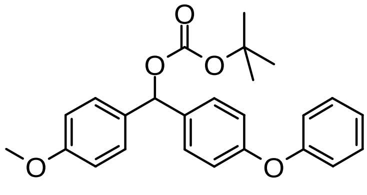
^{13}C NMR (150 MHz, CDCl$_3$): δ = 18.9 (q, CH($\underline{C}$H$_3$)$_2$), 27.8 (d, CH), 29.6 (t, CH$_2$), 71.4 (t, CH$_2$), 74.1 (t, CH$_2$), 80.7 (d, CH), 109.0 (d), 123.7 (d), 127.1 (d), 127.3 (s), 132.3 (s), 154.8 (s), 159.9 (s).

Synthesis of benzhydryl tert-butyl carbonates

General procedure for the preparation of benzhydryl *tert*-butyl carbonates:

In a flame dried, nitrogen-flushed round-bottom flask the substituted benzhydrol (1 eq) was dissolved in dry THF at –78 °C. BuLi (15 % solution in hexane, 1.1 eq) was added dropwise and the solution was stirred for 5 min. The lithium diarylmethoxide solution was then added dropwise to a solution of Boc$_2$O (1.25 eq) in THF at –78 °C. After complete addition the solution was allowed to warm up to room temperature overnight. The solution was washed twice with water and then dried over anhydrous MgSO$_4$. After evaporation of the solvent in vacuo the residue was either purified by crystallization or column chromatography.

4-Methoxy-4´-phenoxybenzhydryl *tert*-butyl carbonate (**8-**OCO$_2t$Bu) was obtained from 4-methoxy-4´-phenoxybenzhydrol (1.23 g, 4.01 mmol) and BuLi (4.4 mmol) in THF (20 mL) and Boc$_2$O (1.1 g, 5.0 mmol) in THF (20 mL). After column chromatography (n-pentane/diethylether 7:3, R$_f$ = 0.67) of the crude product 0.46 g (1.1 mmol, 27 %) **8-**OCO$_2t$Bu were isolated a colorless oil.

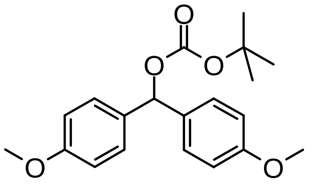


8-OCO$_2t$Bu

^{1}H NMR (600 MHz, CDCl$_3$): δ = 1.48 (s, 9 H, (CH$_3$)$_3$), 3.80 (s, 3 H, OCH$_3$), 6.62 (s, 1 H, Ar$_2$CH), 6.87–6.90 (m, 2 H, ArH), 6.95–7.02 (m, 4 H, ArH), 7.09–7.12 (m, 1 H, ArH), 7.29–7.35 (m, 6 H, ArH).

^{13}C NMR (150 MHz, CDCl$_3$): δ = 27.8 (q, ($\underline{C}$H$_3$)$_3$), 55.2 (q, OCH$_3$), 79.1 (d, Ar$_2$CH), 82.4 (s), 113.9 (d), 118.5 (d), 119.0 (d), 123.4 (d), 128.4 (2×d), 129.7 (d), 132.2 (s), 135.1 (s), 152.9 (s), 156.9 (2×s), 159.3 (s).

4,4´-Dimethoxybenzhydryl *tert*-butyl carbonate (**9**-OCO_2*t*Bu) was obtained from 4,4´-dimethoxybenzhydrol (0.98 g, 4.0 mmol) and BuLi (4.4 mmol) in THF (20 mL) and Boc_2O (1.1 g, 5.0 mmol) in THF (20 mL). After recrystallization (n-pentane/diethylether 1:1) at –60 °C 0.89 g (2.6 mmol, 65 %) **9**-OCO_2*t*Bu were isolated as colorless crystals (mp: 84.5 – 85.5 °C).

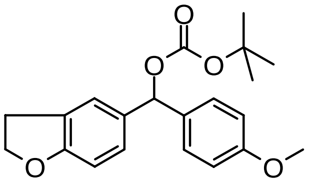


9-OCO_2*t*Bu

^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.47 (s, 9 H, $(CH_3)_3$), 3.80 (s, 6 H, OCH_3), 6.59 (s, 1 H, Ar_2CH), 6.84–6.89 (m, 4 H, ArH), 7.25–7.30 (m, 4 H, ArH).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 27.8 (q, CH_3), 55.2 (q, OCH_3), 79.3 (d, Ar_2CH), 82.2 (s), 113.8 (d), 128.3 (d), 132.5 (s), 153.0 (s), 159.2 (s).

2,3-Dihydro-5-benzofuranyl-(4-methoxyphenyl)methyl *tert*-butyl carbonate (**10**-OCO_2*t*Bu) was obtained from 2,3-dihydro-5-benzofuranyl-(4-methoxyphenyl)methanol (1.03 g, 4.02 mmol) and BuLi (4.4 mmol) in THF (20 mL) and Boc_2O (1.1 g, 5.0 mmol) in THF (20 mL). After recrystallization (n-pentane/diethylether 1:1) at –60 °C 0.75 g (2.1 mmol, 52 %) **10**-OCO_2*t*Bu were isolated as colorless crystals.

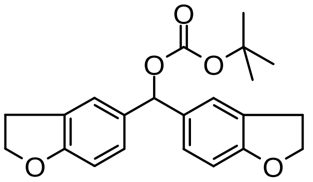


10-OCO_2*t*Bu

^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.47 (s, 9 H, $(CH_3)_3$), 3.16 (t, $^3J_{HH}$ = 8.7 Hz, 2 H, CH_2), 3.79 (s, 3 H, OCH_3), 4.55 (t, $^3J_{HH}$ = 8.7 Hz, 2 H, CH_2), 6.56 (s, 1 H, Ar_2CH), 6.72–6.74 (m, 1 H, ArH), 6.85–6.88 (m, 2 H, ArH), 7.09–7.11 (m, 1 H, ArH), 7.15–7.17 (m, 1 H, ArH), 7.26–7.29 (m, 2 H, ArH).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 27.8 (q, CH_3), 29.6 (t, CH_2), 55.2 (q, OCH_3), 71.3 (t, CH_2), 79.5 (d, CH), 82.2 (s), 109.0 (d), 113.8 (d), 123.8 (d), 127.2 (d), 127.3 (s), 128.1 (d), 132.4 (s), 132.7 (s), 153.0 (s), 159.1 (s), 159.8 (s).

Bis(2,3-Dihydro-5-benzofuranyl)methyl *tert*-butyl carbonate (**11**-OCO_2*t*Bu) was obtained from Bis(2,3-dihydro-5-benzofuranyl)methanol (1.07 g, 3.99 mmol) and BuLi (4.4 mmol) in THF (20 mL) and Boc_2O (1.1 g, 5.0 mmol) in THF (20 mL). After recrystallization (n-pentane/diethylether 1:1) at –60 °C 0.66 g (1.8 mmol, 45 %) **11-**OCO_2*t*Bu were isolated as colorless crystals (mp: 135 – 136 °C).



11-OCO_2*t*Bu

^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.47 (s, 9 H, $(CH_3)_3$), 3.17 (t, $^3J_{HH}$ = 8.7 Hz, 4 H, CH_2), 4.55 (t, $^3J_{HH}$ = 8.7 Hz, 4 H, CH_2), 6.54 (s, 1 H, Ar_2CH), 6.72–6.74 (m, 2 H, ArH), 7.09–7.12 (m, 2 H, ArH), 7.16–7.18 (m, 2 H, ArH).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 27.8 (q, CH_3), 29.6 (t, CH_2), 71.3 (t, CH_2), 79.8 (d, CH), 82.2 (s), 109.0 (d), 123.7 (d), 126.9 (d), 127.2 (s), 132.6 (s), 153.0 (s), 159.7 (s).

Chapter 4

Ionizing Power of Aprotic Solvents

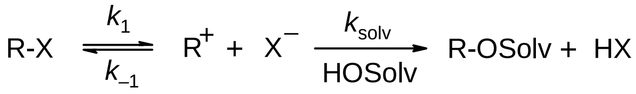
4.1 Introduction

In 1948 Winstein and Grunwald reported that rates of the S_N1 solvolyses of neutral RX substrates in different solvents (Scheme 4.1) can be described by the linear free-energy relationship (equation 4.1).[1]

$$\log (k/k_0) = mY \tag{4.1}$$

In equation (4.1), the solvent ionizing power *Y* (*Y* = 0 for 80% aqueous ethanol) is defined as the ratio of solvolysis rates of *tert*-butyl chloride ($m = 1$) in a given solvent (k) and in 80% aqueous ethanol (k_0) at 25 °C.

Scheme 4.1: Simplified Solvolysis Scheme.



$$\text{R-X} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \text{R}^+ + \text{X}^- \xrightarrow[\text{HOSolv}]{k_{\text{solv}}} \text{R-OSolv} + \text{HX}$$

Initially assumed to be applicable to all types of S_N1 solvolyses, it was soon realized that deviations from eq 4.1 were due to variable solvation of the developing carbocations, particulary of alkyl and aryl groups.[2-9] As a consequence, numerous *Y* scales of solvent ionizing power have later been introduced for a more reliable prediction of the solvolysis rate constants for structurally related compounds.[3a,10-14] However, most of these scales were restricted to protic solvents like alcohols, water, or their mixtures with aprotic solvents, i.e., solvents which are able to trap the intermediate carbocation irreversibly, so that the course of the reactions can be followed by monitoring the formation of the acid HX. Only few aprotic solvents have so far been investigated.[13] S_N1 reactivities of *tert*-butyl halides and adamantyl derivatives have been studied in moderately basic solvents, like dimethylformamide and acetamide, which become alkylated by highly reactive carbenium ions.[15] The ionization rates of adamantyl arenesulfonates have been investigated in acetonitrile solutions by titrimetric determination of the consumption of added azide ions; under these conditions the intermediate adamantyl cations are either trapped directly by azide ions or are intercepted by the solvent to give *N*-adamantyl-nitrilium ions which undergo 1,3-dipolar cycloadditions with the azide ions.[16]

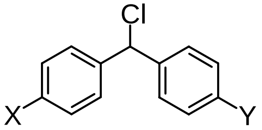
Another method which was used to determine heterolysis rate constants in aprotic solvents is the so-called “verdazyl method” introduced by Dvorko,[17] in which triphenylverdazyl radicals react with the solvent-separated ion-pair. The reaction rates are usually monitored spectrophotometrically following the decrease of the absorbance of the radical. We now report about a more direct and general method to determine the ionizing power of aprotic solvents.

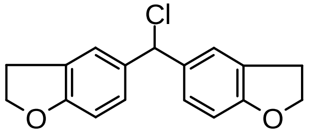
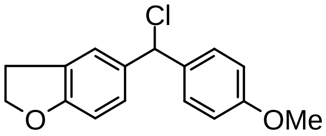
Recently, we have shown that amines and phosphines can suppress common ion return in S_N1 solvolysis reactions of benzhydryl chlorides in protic solvents (acetone/water and acetonitrile/water mixtures) without reacting by the S_N2 mechanism.[18] By trapping the intermediate carbocations quantitatively and formation of benzhydrylammonium ions, we were able to determine ionization rate constants conductimetrically using conventional and stopped-flow techniques. This methodology has now been employed to determine the ionization rates of the benzhydryl chlorides **1a–f** (Table 4.1) in aprotic solvents. These rate constants will be used to include these solvents into previously established scales of solvent ionizing power *Y* and to calculate nucleofugality parameters N_f and s_f of chloride ions in aprotic solvents according to the linear free-energy relationship eq (4.2).[19,20]

$$\log k\ (25\ °\text{C}) = s_f(N_f + E_f) \qquad (4.2)$$

In equation (4.2), the heterolysis rate constant k (s^{-1}) is expressed as a function of the solvent-independent electrofuge-specific parameter E_f and the nucleofuge-specific parameters s_f and N_f, which refer to combinations of leaving groups and solvents.

Table 4.1: Benzhydryl Chlorides **1a–f** and Electrofugality Parameters E_f[20] of the Corresponding Benzhydrylium Ions **$1a^+$–f^+**.

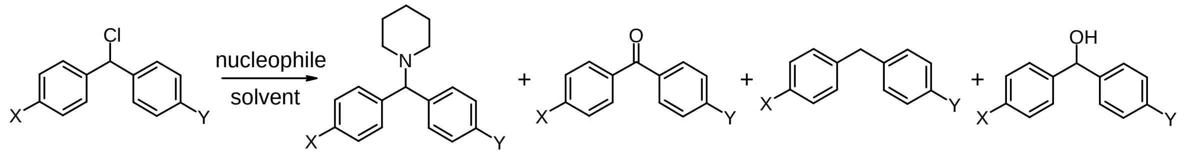


	X	Y	E_f
1a			1.07
1b			0.61
1c	OMe	OMe	0.00
1d	OMe	OPh	–0.86
1e	OMe	Me	–1.32
1f	OMe	H	–2.09

4.2 Results

Product Analysis. In the absence of additives, solutions of the benzhydryl chlorides **1a-f** were stable in all solvents in this study (CH_3CN, DMSO, dimethylacetamide, dimethylformamide, *N*-methyl-2-pyrrolidinone, propylene carbonate, $CHCl_3$, CH_2Cl_2 and acetone). When piperidine or triphenylphosphine was added, the formation of **2-5** was observed by NMR or GC-MS after aqueous workup (Table 4.2).

Table 4.2: Products of the Reactions of **1** with Piperidine or PPh_3 in Different Solvents at 20 °C.



1 **2** **3** **4** **5**

solvent[a]	**substrate**	**nucleophile**	**crude products (by GC-MS)**[b]	**yields of isolated products**[c]
CH_3CN	**1c**	piperidine	100% **2c**	80% **2c**
	1f	piperidine	100% **2f**	85% **2f**
DMSO	**1c**	piperidine	97% **2c**, 3% **3c**	72% **2c**
	1f	piperidine	68% **2f**, 32% **3f**	58% **2f**, 28% **3f**
DMAc	**1c**	piperidine	76% **2c**, 9% **3c**, 15% **4c**	60% **2c**
DMF	**1c**	piperidine	100% **2c**	80% **2c**
acetone	**1c**	piperidine	100% **2c**	84% **2c**
$CHCl_3$	**1c**	PPh_3	100% **5c**	100% **5c**

[a] Solvent abbreviations: DMSO = dimethyl sulfoxide, DMAc = dimethylacetamide, DMF = dimethylformamide. [b] After aqueous workup. [c] After recrystallization or column chromatography.

Kinetics. As previously shown for reactions of other benzhydryl halides in protic solvents and DMSO,[18,21] it is possible to follow the reaction course by conductivity measurements, as ionic products are formed from covalent starting material and the observed conductivity is directly proportional to the concentration of the products. Therefore, we were able to obtain rate constants k_{obs} by fitting the time dependent conductivities G to the monoexponential function (4.3).

$$G = G_{\text{max}}\,[1 - \exp(-k_{\text{obs}}t)] + \textit{const.} \tag{4.3}$$

A typical example for such experiments is illustrated in Figure 4.1 for the reaction of 2,3-dihydro-5-benzofuranyl-(4-methoxyphenyl)-methyl chloride (**1b**) with variable concentrations of piperidine in acetonitrile.

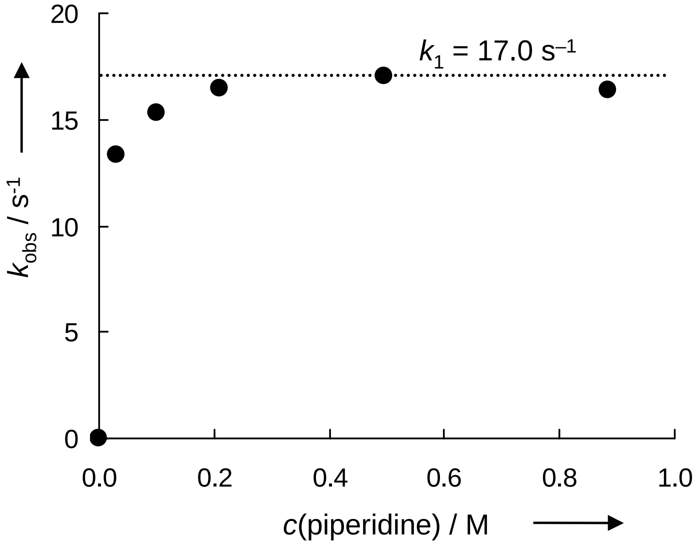
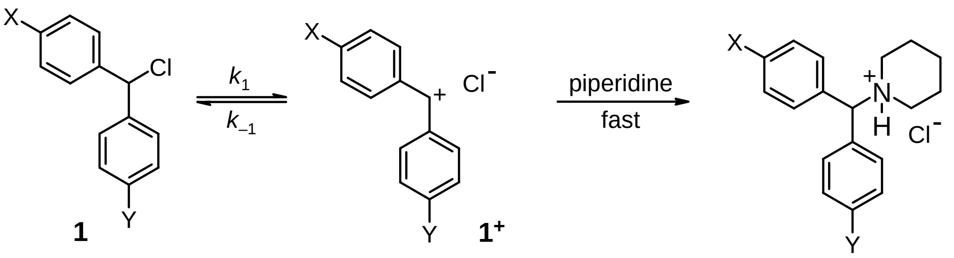


Figure 4.1: Plot of the observed rate constants k_{obs} versus c(piperidine) for the reaction of 2,3-dihydro-5-benzofuranyl-(4-methoxyphenyl)-methyl chloride (**1b**) with piperidine in acetonitrile.

As mentioned above, in the absence of piperidine, **1b** is stable in pure acetonitrile, and there is no observable change of conductivity. In the presence of a low concentration of piperidine [c(piperidine) = 0.03 M] a time dependent change in conductivity can be observed, which after fitting to eq (4.3) yields a rate constant of $k_{obs} = 13.3\ s^{-1}$. As depicted in Figure 4.1 the observed rate constants increase further with increasing piperidine concentrations. A maximum rate constant of $k_{obs,max} = 17.0\ s^{-1}$ is finally observed at c(piperidine) = 0.50 M, whereas at higher piperidine concentrations the rate constants decrease slightly.

The observation that the rate constants k_{obs} increase with increasing piperidine concentrations until a plateau is reached at a certain concentration of piperidine indicates the operation of an S_N1 mechanism (Scheme 4.2): After the initial reversible ionization of the substrate **1** to give the ion-pair **1**$^+$**Cl**$^-$, the benzhydrylium ion **1**$^+$ is irreversibly trapped by piperidine, and the ion recombination is suppressed (k_{-1} in Scheme 4.2). The operation of an S_N2 mechanism can be excluded, because in this case k_{obs} would increase linearly with the piperidine concentration.

Scheme 4.2: Heterolyses of Benzhydryl Chlorides in the Presence of Piperidine.



The situation described in Figure 4.1, i.e., increase of k_{obs} with increasing piperidine concentration until a plateau is reached, has been observed for numerous reactions of benzhydryl chlorides **1a–f** with piperidine in different aprotic solvents (see Experimental Section). When pyridine was used for trapping the intermediate carbocations, a somewhat lower plateau was observed (for **1c** in acetonitrile $k_{max,piperidine}/k_{max,pyridine} = 1.6$, Figure 4.2).

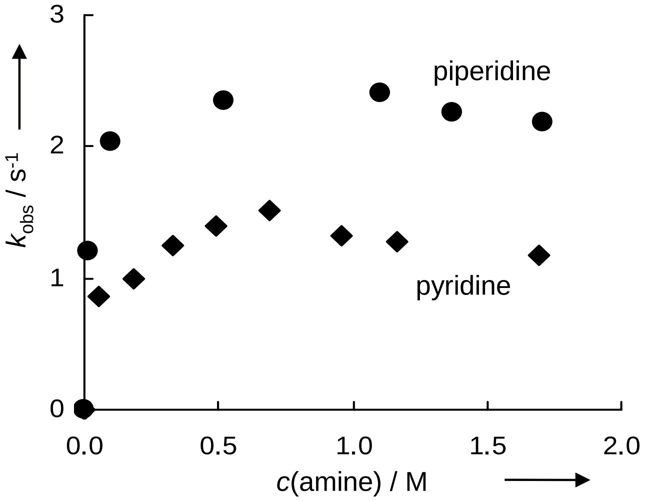


Figure 4.2: Plot of the observed rate constants k_{obs} versus *c*(amine) for the reactions of dimethoxybenzhydryl chloride (**1c**) with piperidine and pyridine in pure acetonitrile.

Plateaus of similar, but not identical heights, had also been observed when different amines or triphenylphosphine were used to trap benzhydrylium ions, which were reversibly generated from benzhydryl chlorides in aqueous acetone or acetonitrile.[18] The small differences of the plateaus obtained with different nucleophiles can again be explained by the fact that the diffusion-limited trapping reactions will partially occur at the ion-pair stage.

The dependence of the heights of these plateaus on the nature of the trapping nucleophiles is negligible compared to the influence of the solvent and the substituents X and Y on the magnitude of k_{max}. Therefore, k_{max} values obtained with different trapping reagents are jointly listed as k_1 in Table 4.3. Whereas piperidine was the preferred nucleophile for trapping, it reacts with dichloromethane, chloroform,[22] and propylene carbonate, and therefore cannot be employed in these solvents. For that reason piperidine was replaced by PPh_3 in CH_2Cl_2 and $CHCl_3$, and by pyridine in propylene carbonate, where PPh_3 is poorly soluble.

Table 4.3: Conductimetrically Measured Rate Constants (k_1, 25 °C) of the Reactions of Benzhydryl Chlorides **1a–f** with Different Trapping Reagents.

solvent[a]	substrate	electrofugality E_f	k_1 / s^{-1}
CH_3CN[b]	**1a**	1.07	9.51×10^{1}
	1b	0.61	1.70×10^{1}
	1c	0.00	2.40
	1d	–0.86	1.47×10^{-1}
	1e	–1.32	3.77×10^{-2}
	1f	–2.09	3.60×10^{-3}
DMSO[b]	**1a**	1.07	8.85×10^{1}
	1b	0.61	1.57×10^{1}
	1c	0.00	2.46
	1d	–0.86	1.89×10^{-1}
	1e	–1.32	5.03×10^{-2}
	1f	–2.09	6.78×10^{-3}
DMAc[b]	**1a**	1.07	2.35
	1b	0.61	4.81×10^{-1}
	1c	0.00	7.86×10^{-2}
	1d	–0.86	6.66×10^{-3}
	1e	–1.32	1.37×10^{-3}
DMF[b]	**1a**	1.07	1.44×10^{1}
	1b	0.61	2.55
	1c	0.00	3.69×10^{-1}
	1d	–0.86	2.73×10^{-2}
	1e	–1.32	6.02×10^{-3}
NMP[b]	**1a**	1.07	1.45
	1b	0.61	2.94×10^{-1}
	1c	0.00	5.32×10^{-2}
	1d	–0.86	4.16×10^{-3}
	1e	–1.32	1.04×10^{-3}
PC[c]	**1a**	1.07	4.63×10^{1}
	1b	0.61	8.47
	1c	0.00	1.22
	1d	–0.86	1.05×10^{-1}
	1e	–1.32	2.47×10^{-2}
$CHCl_3$[d]	**1a**	1.07	1.54×10^{1}
	1b	0.61	3.17
	1c	0.00	4.98×10^{-1}
	1d	–0.86	5.82×10^{-2}

Table 4.3: *Continued.*

solvent[a]	substrate	electrofugality E_f	k_1 / s^{-1}
CH_2Cl_2[d]	**1a**	1.07	4.84
	1b	0.61	1.02
	1c	0.00	1.72×10^{-1}
	1d	–0.86	1.54×10^{-2}
	1e	–1.32	4.00×10^{-3}
acetone[b]	**1a**	1.07	1.40
	1b	0.61	2.71×10^{-1}
	1c	0.00	3.49×10^{-2}
	1d	–0.86	3.31×10^{-3}
	1e	–1.32	6.12×10^{-4}

[a] Solvent abbreviations: DMSO = dimethyl sulfoxide, DMAc = dimethylacetamide, DMF = dimethylformamide, NMP = *N*-methyl-2-pyrrolidone, PC = propylene carbonate. [b] Piperidine as trapping reagent. [c] Pyridine as trapping reagent. [d] Triphenylphosphine as trapping reagent.

Figure 4.3 shows that the heterolysis rate constants in aprotic solvents of α,α-dimethylbenzyl (cumyl) chloride, which were determined by Dvorko´s verdazyl technique,[17] correlate linearly (slope of 1.11) with those of dimethoxybenzhydryl chloride (**1c**) which were determined by the “amine method” in this work.

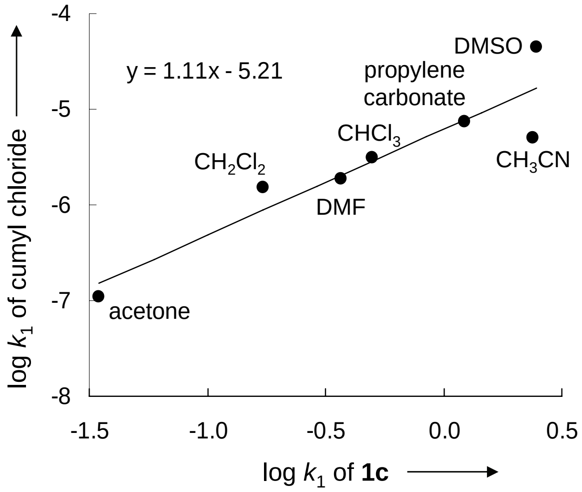
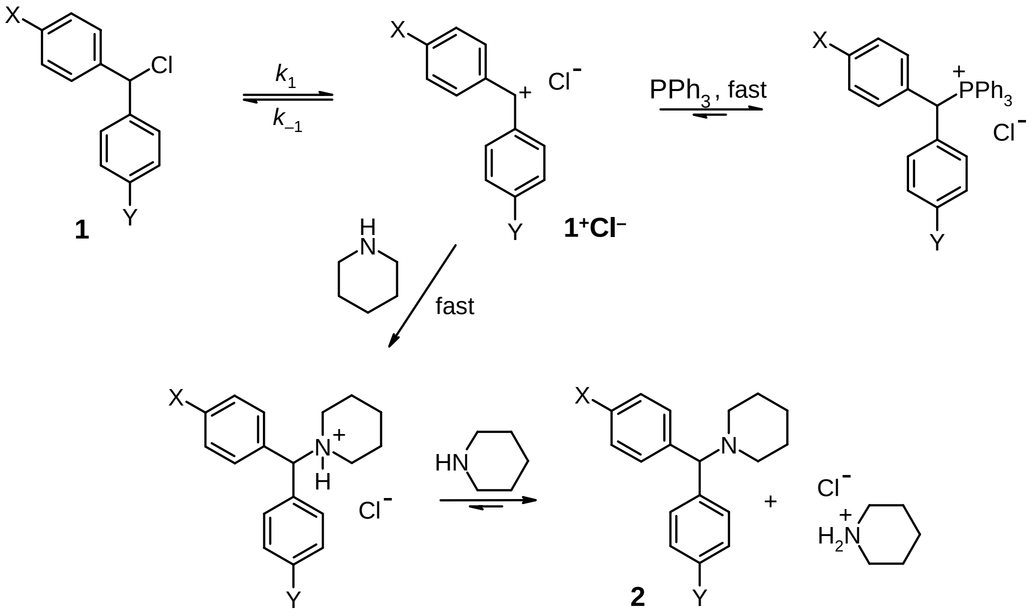


Figure 4.3: Correlation of the heterolysis rate constants log k_1 of cumyl chloride (by verdazyl method[17]) with those of dimethoxybenzhydryl chloride (**1c**) in various aprotic solvents.

4.3 Discussion

Reaction Mechanism. The reactions of the benzhydryl chlorides **1a–f** with piperidine or triphenylphosphine in acetonitrile, dimethylformamide, acetone, $CHCl_3$, or CH_2Cl_2 give rise to the formation of 1-benzhydryl-piperidines **2** or benzhydryl phosphonium salts (Scheme 4.3). As pointed out before, the non-linearity of the plots of k_{obs} versus the concentration of the trapping reagents and the existence of plateaus in these plots (Figures 4.1, 4.2 and Experimental Section) suggest that the reactions proceed via the S_N1 mechanism: After ionization of **1**, the intermediate carbocation is trapped by either piperidine or triphenylphosphine.

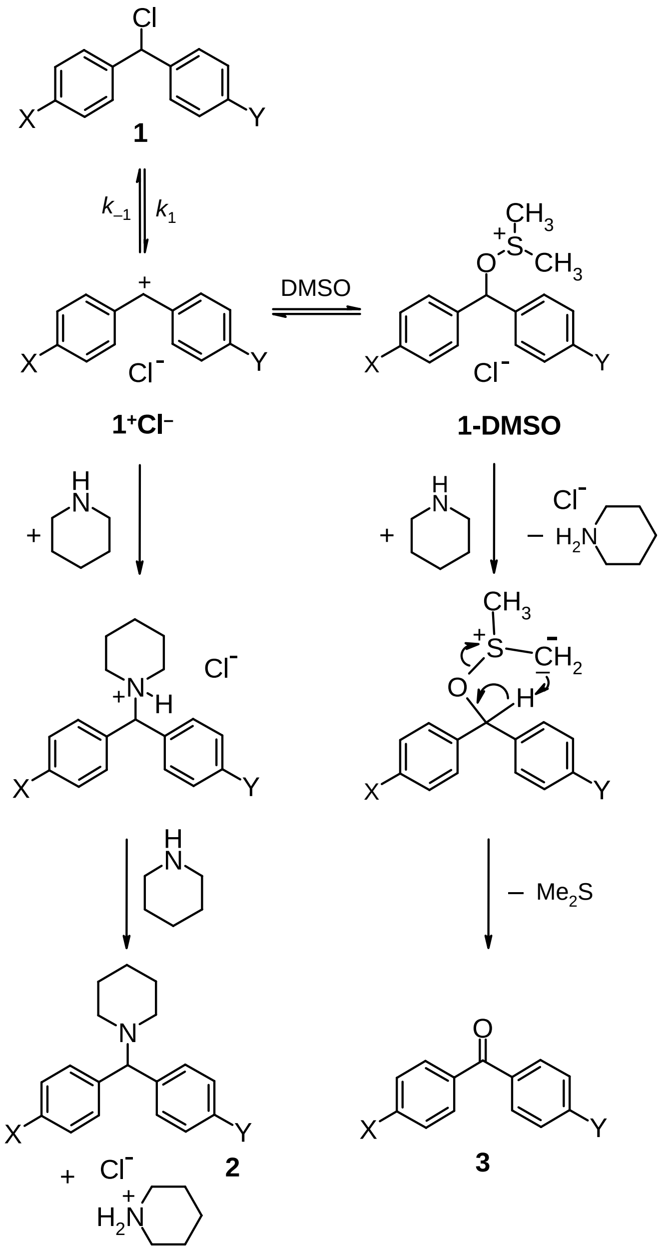
Scheme 4.3: Heterolyses of Benzhydryl Chlorides in the Presence of Piperidine or Triphenylphosphine.



In the absence of nucleophiles, the benzhydryl chlorides **1a-f** are stable in all solvents listed in Table 4.3 indicating that the covalent benzhydryl chlorides **1** are favored in the ionization equilibria. In the presence of low concentrations of the trapping reagents, ion recombination is accompanied by trapping of **1^+Cl^-** with triphenylphosphine or piperidine to yield benzhydrylphosphonium salts or 1-benzhydryl-piperidines **2**, respectively. When the concentration of the trapping reagent is increased, the observed rate constants increase due to the fact that ion recombination (k_{-1}) is more and more suppressed. At a certain concentration, a maximum rate constant $k_{obs,max}$ is observed indicating that ion recombination is completely suppressed and that ionization of **1** to the ion pair **1^+Cl^-** is rate-determining. Thus, the observed rate constants $k_{\mathrm{obs,max}}$ correspond to the ionization rate constants k_1 defined in Scheme 4.1. The slight decrease of reactivity at high concentrations of amines can be explained by a change of solvent polarity.

The situation is different in DMSO solution, because DMSO is a stronger O-nucleophile than water and ordinary alcohols.[21] When **1** is dissolved in pure DMSO, a reversible ionization leads to **1^+Cl^-**, which is reversibly attacked by DMSO to form **1-DMSO** (Scheme 4.4). As conductivity does not change, one can conclude that in these equilibria the covalent benzhydryl chlorides **1** are the dominating species. In contrast, the corresponding benzhydryl bromides have been observed to react with DMSO also in the absence of amine.[21]

Scheme 4.4: Heterolyses of Benzhydryl Chlorides in DMSO in the Presence of Piperidine.



When piperidine is present, two reaction pathways are possible: The left path in Scheme 4.4 is identical to that shown in Scheme 4.3, where the intermediate carbocation is trapped by piperidine to form 1-benzhydryl-piperidines **2**. Alternatively (right path in Scheme 4.4) an oxysulfonium ion **1-DMSO** is formed, which yields a sulfur ylide by deprotonation at a methyl group. Eventually, proton shift and cleavage of the O–S bond yields the benzophenones **3** (Kornblum oxidation).[23]

Why does one obtain a much higher percentage of benzophenone with **1f** than with **1c** in DMSO/piperidine (Table 4.2)? As previously shown,[24] eq 4.4 can be used to calculate the rate constants of the reactions of carbocations with a large variety of nucleophiles, including amines,[25] halide ions,[26] and solvents.[27]

$$\log k = s(E + N) \tag{4.4}$$

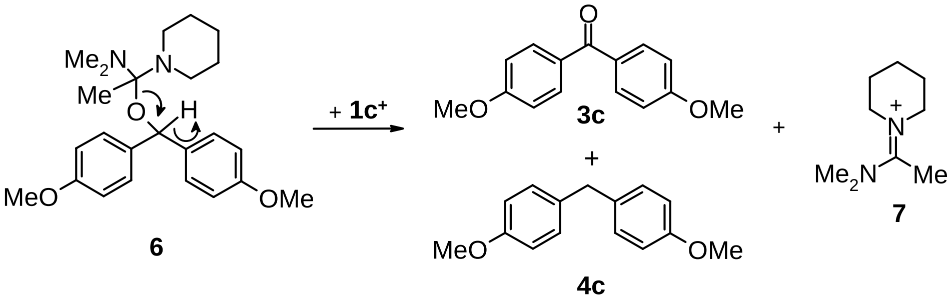
In eq (4.4) k is a second-order ($\mathrm{M}^{-1}\mathrm{s}^{-1}$) or first-order ($\mathrm{s}^{-1}$, for reactions with solvents) rate constant, s and N are empirical, nucleophile-specific parameters, and E is the empirical electrophilicity parameter.

From the electrophilicity parameters for the benzhydrylium ions[24] **1c**$^+$ (E = 0.00) and **1f**$^+$ (E = 2.11) and the nucleophile-specific parameters for piperidine (N = 17.19, s = 0.71)[28] one calculates $k > 5 \times 10^9$ $\mathrm{M}^{-1}\mathrm{s}^{-1}$ for the reactions of both benzhydrylium ions with piperidine, i.e., trapping of **1c**$^+$ and **1f**$^+$ is diffusion limited. Assuming a second-order rate constant of $k_2 = 5 \times 10^9$ $\mathrm{M}^{-1}\mathrm{s}^{-1}$ for the diffusion limited reaction of a carbocation with a neutral nucleophile, multiplication with c(piperidine) = 0.5 M yields pseudo-first-order rate constants of $k_{\mathrm{obs}} = 2.5 \times 10^9$ s^{-1} for the reactions of **1c**$^+$ and **1f**$^+$ with piperidine. This value is significantly larger than the first-order rate constant calculated by eq (4.4) for the reaction of DMSO (N_1 = 11.3, s = 0.74)[21] with **1c**$^+$ ($k_1 = 2.30 \times 10^8$ s^{-1}). Thus, the main product of the reaction is the 1-benzhydryl-piperidine **2c**, and only traces (GC-MS: 3%) of the benzophenone **3c** can be detected.

From the reactivity parameters for DMSO (N_1 = 11.3, s = 0.74) and **1f**$^+$ (E = 2.11)[24] one calculates a first-order rate constant of 8×10^9 s^{-1}, which is in the same order of magnitude as the pseudo-first-order rate constant for the diffusionally limited reaction of **1f**$^+$ with piperidine (c = 0.5 M). The formation of comparable quantities of **2f** and **3f** can thus be explained.

When **1c** was dissolved in dimethylacetamide (DMAc) or *N*-methyl-2-pyrrolidone (NMP) in the presence of piperidine, dimethoxybenzophenone (**3c**) and bis(4-methoxyphenyl)methane (**4c**) are formed as minor products besides **2c** as major product (GC-MS: ≥ 75% yield). Presently, we do not definitely know how **3c** and **4c** are formed under these conditions. A conceivable mechanism may be the attack of the solvent and piperidine at the dimethoxybenzhydrylium ion (**1c**$^+$) with formation of **6**. Hydride abstraction from **6** by another dimethoxybenzhydrylium ion (**1c**$^+$) may then lead to formation of **3c**, **4c**, and the amidinium ion **7** (Scheme 4.5).

Scheme 4.5: Possible Hydride Transfer during the Heterolysis Reaction of **1c** in Dimethylacetamide in the Presence of Piperidine.



Hammett Correlation. From the plots of log k_1 (i.e., $k_{\mathrm{obs,max}}$) versus $\Sigma\sigma^+$, one derives Hammett reaction constants of $\rho \approx -4$ for the heterolysis reactions of benzhydryl chlorides **1a–f** in various aprotic solvents, as exemplified for acetonitrile, dimethylformamide (DMF) and dimethylacetamide (DMAc) in Figure 4.4 (for Hammett correlations of the other solvents in this study see Experimental Section).

The excellent linear correlations and the magnitude of the reaction constants ρ suggest transition states, where the positive charge of the carbocations is fully developed. The Hammett plot thus supports the conclusion from the kinetic data, that $k_{\mathrm{obs,max}}$ corresponds to the ionization step of an S_N1 reaction and not an S_N2-type attack of the amine at the benzhydryl chlorides. It is in line with previous findings for the reactions of benzhydryl bromides with amines in DMSO, where only the first-order rate constants k_1 (S_N1 reaction) but not the second-order rate constants k_2 (S_N2 reaction) correlated with Hammett´s substituent constants.[21]

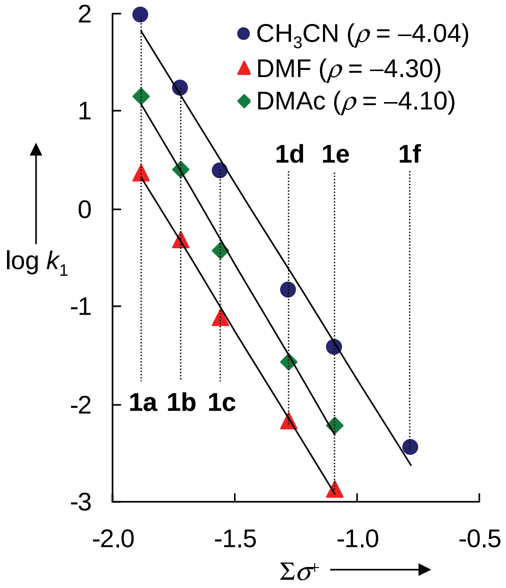


Figure 4.4: Plots of log k_1 (= $k_{obs,max}$) of the heterolysis reactions of the benzhydryl chlorides **1a–1f** in different solvents versus Hammett´s substituent constants $\Sigma\sigma^+$ (σ^+ from ref. 29).

Nucleofugality of Chloride in Different Solvents. In previous work,[19,20] we have demonstrated that eq 4.2 can be used for the calculation of the heterolysis rate constants k_1 of benzhydryl derivatives in various solvents. Plots of log k_1 (i.e., the maximum observed first-order rate constants $k_{obs,max}$) versus the electrofugality parameters E_f of the benzhydrylium ions (see Table 4.1) are linear as exemplified in Figure 4.5 for the heterolyses of the benzhydryl chlorides **1a–f** in DMSO, CH_2Cl_2, and acetone. For analogous correlations in acetonitrile, dimethylacetamide (DMAc), dimethylformamide (DMF), *N*-methyl-2-pyrrolidone (NMP), propylene carbonate (PC), and $CHCl_3$ see Experimental Section. From these correlations one can extract the nucleofugality parameters N_f of chloride in these solvents as the negative intercepts on the abscissa (E_f axis) and the s_f parameters as the slopes (Table 4.4).

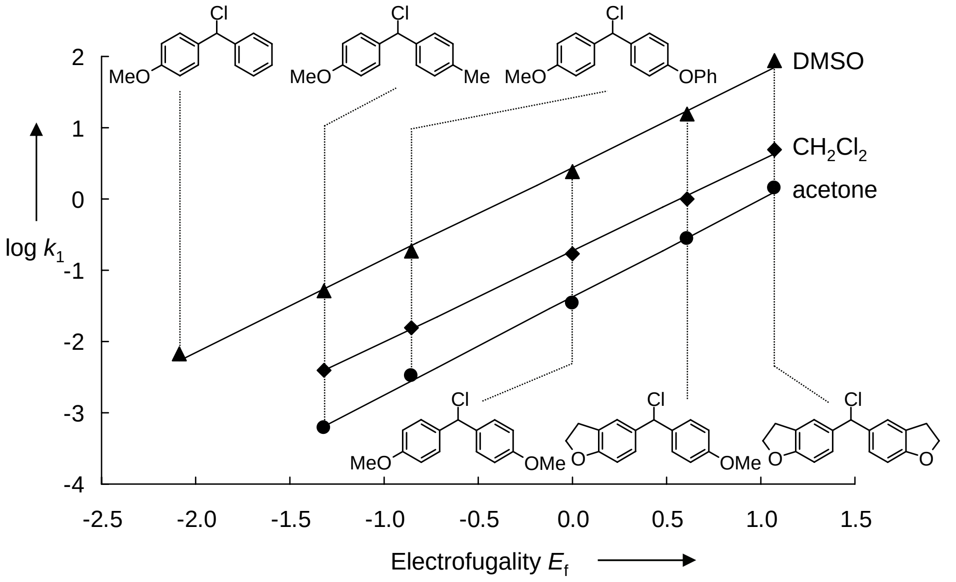


Figure 4.5: Plots of the first-order rate constant log k_1 ($k_{\mathrm{obs,max}}$ at the plateaus) of the heterolyses of benzhydryl chlorides **1a–f** in different solvents in the presence of trapping reagents against the electrofugality parameters E_f.

Table 4.4: Nucleofugality Parameters N_f and s_f of Chloride in Different Solvents.

Solvent	N_f	s_f
DMSO	0.35	1.30
CH_3CN	0.30	1.39
propylene carbonate (PC)	0.10	1.35
$CHCl_3$	–0.18	1.25
dimethylformamide (DMF)	–0.28	1.39
CH_2Cl_2	–0.57	1.28
dimethylformamide (DMAc)	–0.82	1.33
N-methyl-2-pyrrolidone (NMP)	–0.98	1.31
acetone	–1.00	1.38

As shown in Table 4.4, the s_f parameters of chloride in the aprotic solvents are substantially higher ($1.25 \le s_\mathrm{f} \le 1.39$) than the s_f parameters of chloride in protic solvents (usually $0.85 \le s_\mathrm{f} \le 1.11$).[20] How can these differences be explained? Substitution of the nucleophilicity parameters N and s of chloride in acetonitrile ($N = 17.20$, $s = 0.60$)[26] and the electrophilicity parameters E of the benzhydrylium ions $\mathbf{1a}^+$–$\mathbf{f}^+$ ($-1.36 < E < 2.11$)[24] into eq 4.4 yields the second-order rate constants $k > 3 \times 10^9$ M^{-1} s^{-1} for the reactions of these benzhydrylium ions with Cl^-, showing that all these reactions are diffusionally limited or at least very close to diffusion limit in acetonitrile and therefore proceed without activation energy. As the other solvents used in this study are of similar or lower polarity than acetonitrile, the combinations of the carbocations with Cl^- will also proceed without barrier in these solvents. The principle of microscopic reversibility now requires that there is also no barrier for the backward reaction (**1** → $\mathbf{1}^+$ + Cl^-), i.e., the activation free energies of the ionization (heterolysis) step (k_1) equal the differences between the free energies of the ions $\mathbf{1}^+$ + Cl^- and their precursors **1**. The smaller s_f parameters in more polar solvents, therefore, reflect the fact the differences in Gibbs free-energies between covalent precursors **1** and ion-pairs $\mathbf{1^+Cl^-}$ are somewhat attenuated in alcohols and water.

With the newly determined nucleofugality parameters N_f and s_f from Table 4.4 it now becomes possible to directly compare the leaving group ability of chloride in protic and aprotic solvents (Figure 4.6).

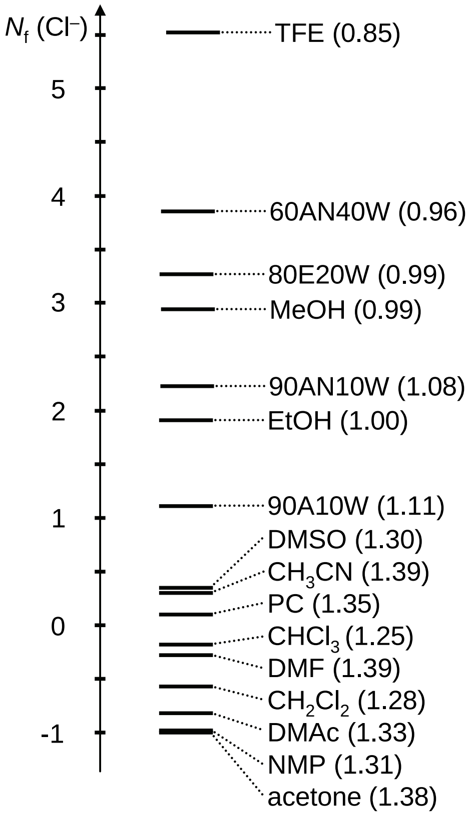


Figure 4.6: Comparison of the nucleofugality parameters N_f (s_f parameter in parentheses) of chloride in various protic and aprotic solvents (data from this work and ref. 20). Mixtures of solvents are given (v/v); A = acetone, AN = acetonitrile, E = ethanol, TFE = 2,2,2-trifluoroethanol, W = water.

As mentioned before, the s_f parameters of chloride in aprotic solvents are exceptionally high. Thus, for a precise comparison with other nucleofuges with smaller s_f parameters, s_f should not be neglected. However, the N_f parameters in Figure 4.6 show the qualitative trend of the leaving group ability (S_N1 reactivity) of chloride in aprotic and protic solvents. The nucleofugalities of chloride in the aprotic solvents studied in this work range from $-1 < N_f < 0.5$. DMSO, the aprotic solvent with the highest ionizing power of this series, is about 1.5 orders of magnitude less ionizing than ethanol. The leaving group ability of chloride decreases by more than 6.5 orders of magnitude from TFE (2,2,2-trifluoroethanol) to acetone, the extremes of this scale. Thus, while the half-life of methoxybenzhydryl chloride (**1f**) in acetone in presence of a trapping agent is about 3.5 h, it is shorter than 1 ms in TFE.

Determination of Y Values for Aprotic Solvents. In the Winstein-Grunwald[1] relationship (eq 4.1) the solvent ionizing power is expressed by the empirical parameter Y. As most readers will be familiar with the Y scale,[1–14] the information given by the N_f scale in Figure 4.6 shall now be converted into Winstein-Grunwald Y values.

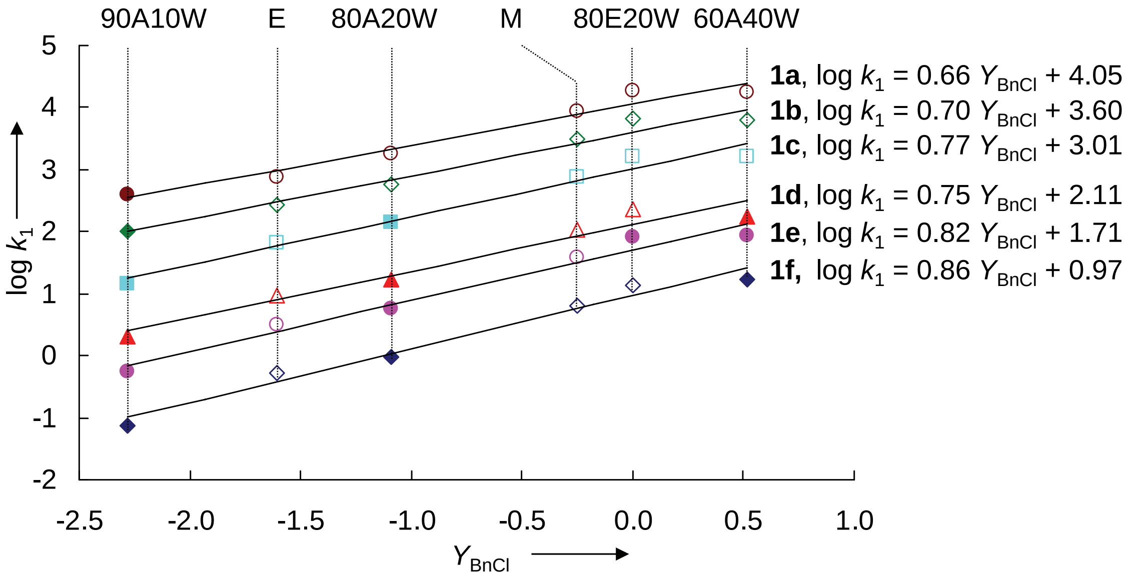


Figure 4.7: Plot of the first-order rate constants log k_1 for the solvolyses of **1a–f** in different solvents (full symbols determined by conductivity measurements from ref. 20, open sympols calculated by eq 4.2) against the solvent ionizing power Y_{BnCl} (mixtures of solvents are given (v/v); A = acetone, E = ethanol, M = methanol, W = water).

In line with previous reports,[30] the heterolysis rates (log k_1) of the benzhydryl chlorides **1a–f** correlate well with Y values (solvent ionizing power) derived from secondary benzyl derivatives like the Y_{BnCl} scale (Figure 4.7).[10] As the stopped-flow conductivity technique is only applicable to solvent mixtures where a solution of the substrate in an inert aprotic solvent is mixed with the protic solvent, it was not possible to determine k_1 experimentally for all heterolysis reactions of **1a–f** plotted in Figure 4.7. The great reliability of eq (4.2) for predicting benzhydryl solvolysis rate constants (see Figure 4.5) allowed us, however, to supplement missing experimental rate constants in Figure 4.7 by calculated values (N_{f}, s_{f}, and E_{f} from ref. 20) which are identified by open symbols.

Substitution of the heterolysis rate constants k_1 of benzhydryl chlorides **1a–f** in aprotic solvents (Table 4.3) into the correlation equations in Figure 4.7 yields Y_{BnCl} values for these solvents, which are listed in Table 4.5. As the correlations of the solvolysis rate constants of benzhydryl chlorides **1a–f** in protic solvents with other Y scales, like Y_{OTs}, are of lower quality, we have not attempted to determine Y_{OTs} for aprotic solvents from the rate constants in Table 4.3. However, previously published Y_{OTs} values for CH_3CN, DMF and DMAc (–3.21, –4.14, and –4.99, respectively)[13] are approximately 0.5 units less negative than the Y_{BnCl} values determined in this work (Table 4.5).

Table 4.5: Calculated Solvent Ionizing Power Y_{BnCl} for Aprotic Solvents.

Solvent[a]	**1f**	**1e**	**1d**	**1c**	**1b**	**1a**	average Y_{BnCl}[b]
DMSO	–3.65	–3.67	–3.78	–3.40	–3.43	–3.19	–3.52 (±0.22)
CH_3CN	–3.97	–3.82	–3.92	–3.42	–3.39	–3.14	–3.61 (±0.34)
PC		–4.05	–4.12	–3.80	–3.82	–3.61	–3.88 (±0.21)
$CHCl_3$			–4.46	–4.30	–4.43	–4.34	–4.38 (±0.07)
DMF		–4.79	–4.89	–4.47	–4.56	–4.38	–4.62 (±0.22)
CH_2Cl_2		–5.01	–5.23	–4.90	–5.13	–5.10	–5.07 (±0.13)
DMAc		–5.58	–5.72	–5.34	–5.60	–5.57	–5.56 (±0.14)
NMP		–5.72	–5.99	–5.56	–5.90	–5.89	–5.81 (±0.17)
acetone		–6.00	–6.12	–5.80	–5.95	–5.91	–5.96 (±0.12)

[a] Solvent abbreviations: DMSO = dimethyl sulfoxide, DMAc = dimethylacetamide, DMF = dimethylformamide, NMP = *N*-methyl-2-pyrrolidone, PC = propylene carbonate. [b] Standard deviations in parentheses.

The Y_{BnCl} values derived from the solvolysis rate constants of different benzhydryl chlorides are in fair agreement. However, it is obvious that the Y values calculated for DMSO, CH_3CN

and propylene carbonate increase continuosly when going from less to more stabilized carbocations. For reasons, which are presently not known, these three solvents differentiate more between highly and less stabilized benzhydrylium ions than the more polar protic solvents and the less polar aprotic solvents.

The different aprotic solvents in this study differ almost 2.5 units in their ionizing power Y_{BnCl}, ranging from the least ionizing solvent acetone (Y_{BnCl} = –5.96) to best ionizing solvent DMSO (Y_{BnCl} = –3.52). Though aprotic solvents generally have a smaller ionizing power than protic solvents, Figure 4.8 shows that protic solvents like isopropanol and 90% aqueous acetone are only one unit higher on the Y_{BnCl} scale than DMSO and acetonitrile.

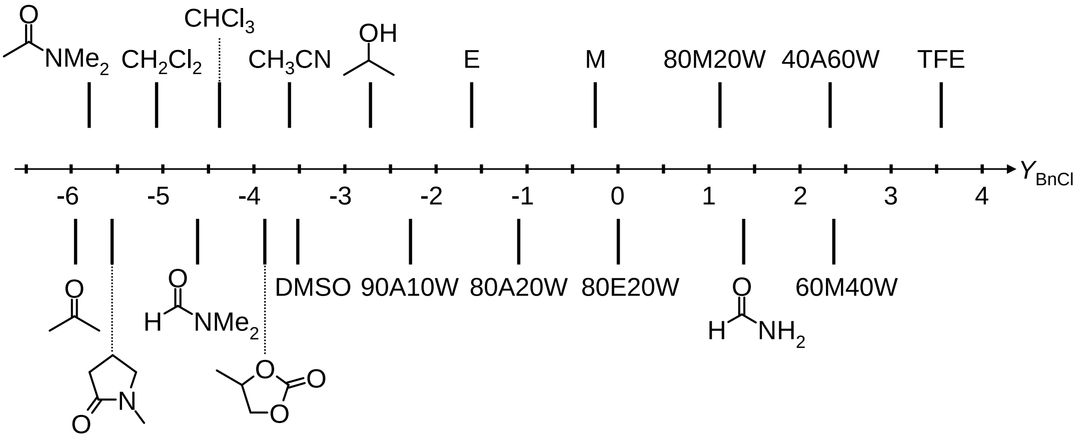


Figure 4.8: Y_{BnCl} scale for protic and aprotic solvents (this work and from ref. 10; mixtures of solvents are given (v/v); A = acetone, E = ethanol, M = methanol, TFE = 2,2,2-trifluoroethanol, W = water).

Comparison with Other Solvent Polarity Scales. It is well recognized that there is no universal solvent polarity scale, and, even worse, the term “polarity” itself is “rather ill-defined” as stated by the IUPAC.[31] Figure 4.9 compares the suitability of different solvent polarity parameters for predicting the S_N1 rates of a typical benzhydryl chloride (e.g. **1c**).

Among the well-known solvent polarity scales, the worst correlation is found with the dielectric constants ε (Figure 4.9, top left). Thus, methanol and *N*-methyl-2-pyrrolidone (NMP) have almost the same dielectric constant (ε = 32.7 and 32.2, respectively) but **1c** is ionized about 4 orders of magnitude faster in methanol than in NMP.

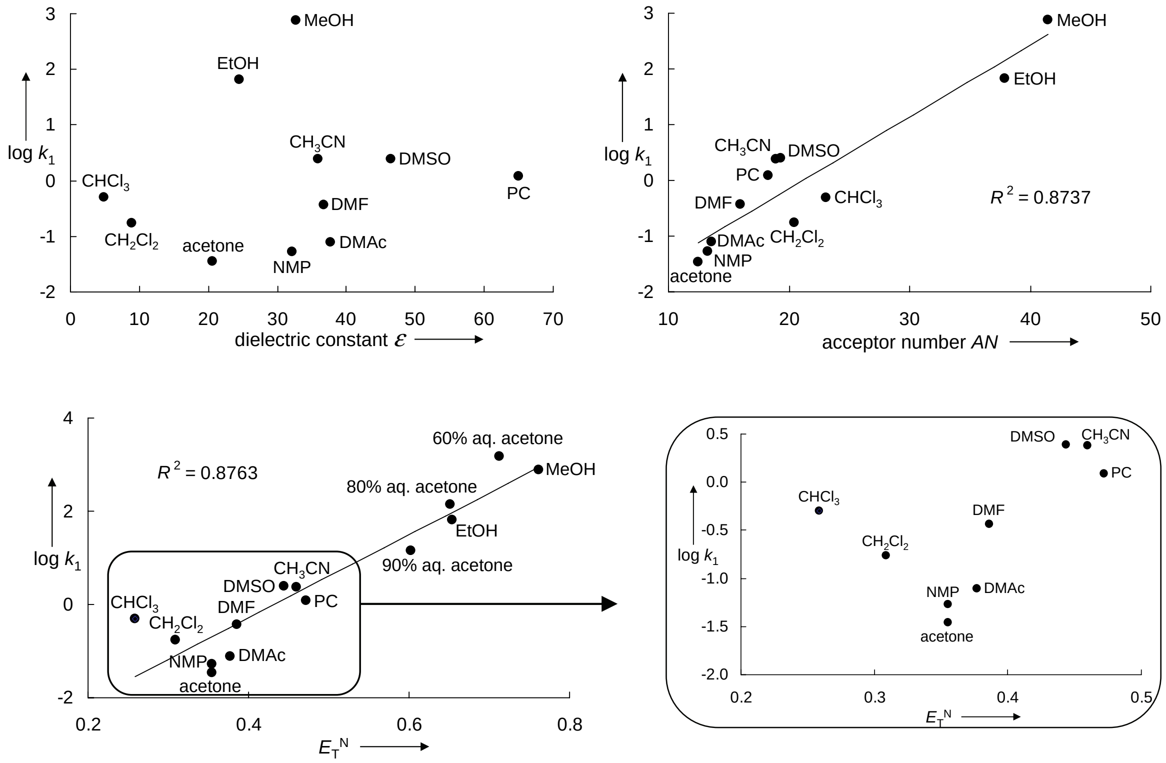


Figure 4.9. Plots of the first-order rate constants log k_1 for the solvolyses of **1c** in different solvents against the dielectric constant ε (top left), acceptor number *AN* (top right) and E_T^N (bottom left and zoom on aprotic solvents bottom right). (constants from ref. 32, additional E_T^N values for acetone/water mixtures from ref. 33).

Figure 9 top right and bottom left show better correlations ($R^2 \approx 0.87$) between the ionization rates of **1c** with acceptor numbers *AN* by Gutmann and coworkers,[34] and the empirical solvent parameters E_T^N by Dimroth and Reichardt,[35] respectively. However, when only the E_T^N values of aprotic solvents are considered (Figure 4.9, bottom right), the correlation breaks down (R^2 = 0.32). An analogous zoom for the correlation with acceptor numbers of aprotic solvents, which is shown in the Experimental Section reveals that the deviations from the regression lines with *AN* and E_T^N are not even systematic, e.g., chloroform has a lower ionizing ability than predicted by its acceptor number *AN*, but a higher ionizing power than predicted by E_T^N. As none of the common solvent polarity parameters is suitable for predicting the ionizing power of aprotic solvents, the method introduced in this work is recommended for a systematic investigation of ionization rates in aprotic solvents.

4.4 Conclusion

It has been shown that the “amine method” to prevent ion recombination in heterolysis reactions can be applied to determine ionization rates of substrates in aprotic solvents. By this means nucleofugality parameters N_f and s_f of chloride in aprotic solvents were derived. The introduction of typical S_N2 solvents into Winstein´s Y_{BnCl} scale should be helpful for chemists in choosing the right solvent for stereospecific S_N2 reactions, as now the probability of concurrent S_N1 reactions with loss of stereochemical information in the product can be predicted more accurately than by help of physical or empirical parameters describing solvent polarity, which correlate only moderately (and even worse when just aprotic solvents are considered) with the ionizing power of solvents. Ongoing research in our group is now focusing on the change of mechanism from S_N1 to S_N2 in the reactions of these substrates and other benzhydryl derivatives with amines and other strong nucleophiles as shown in the reactions of benzhydryl bromides with amines in DMSO.

4.5 References

(1) Grunwald, E.; Winstein, S. *J. Am. Chem. Soc* **1948**, *70*, 846–854.

(2) Kevill, D. N.; D´Souza, M. J. *J. Chem. Res. Synop.* **1993**, 174–175.

(3) (a) Fainberg, A. H.; Winstein, S. *J. Am. Chem. Soc.* **1956**, *78*, 2770–2777. (b) Fainberg, A. H.; Winstein, S. *J. Am. Chem. Soc.* **1957**, *79*, 1597–1602. (c) Fainberg, A. H.; Winstein, S. *J. Am. Chem. Soc.* **1957**, *79*, 1602–1608. (d) Fainberg, A. H.; Winstein, S.; *J. Am. Chem. Soc.* **1957**, *79*, 1608–1612.

(4) Winstein, S.; Fainberg, A. H.; Grunwald, E. *J. Am. Chem. Soc.* **1957**, *79*, 4146–4155.

(5) Bunton, C. A.; Mhala, M. M.; Moffatt, J. R. *J. Org. Chem.* **1984**, *49*, 3639–3641.

(6) Liu, K.-T.; Sheu, H.-C. *J. Org. Chem.* **1991**, *56*, 3021–3025.

(7) Bentley, T. W.; Koo, I. S.; Norman, S. J. *J. Org. Chem.* **1991**, *56*, 1604–1609.

(8) Bentley, T. W.; Dau-Schmidt, J.-P.; Llewellyn, G.; Mayr, H. *J. Org. Chem.* **1992**, *57*, 2387–2392.

(9) Richard, J. P.; Toteva, M. M.; Amyes, T. L. *Org. Lett.* **2001**, *3*, 2225–2228.

(10) (a) Liu, K.-T.; Sheu, H.-C.; Chen, V.; Ciu, P.-F.; Hu, C. R. *Tetrahedron Lett.* **1990**, *31*, 3611–3614. (b) Liu, K.-T.; Chang, L.-H.; Yu, D.-G.; Chen, P.-S.; Fan, J.-T. *J. Phys. Org. Chem.* **1997**, *10*, 879–884.

(11) Liu, K.-T.; Chin, C.-P.; Lin, Y.-S.; Tsao, M.-L. *J. Chem. Res. Synop.* **1997**, 18–19.

(12) Liu, K.-T.; Lin, Y.-S.; Tsao, M.-L.; *J. Phys. Org. Chem.* **1998**, *11*, 223–229.

(13) Bentley, T. W.; Llewellyn, G. *Prog. Phys. Org. Chem.* **1990**, *17*, 121–159.

(14) Kevill, D. N. In *Advances in Quantitative Structure-Property Relationships*, Vol. 1 (Ed.: Charton, M.), JAI Press, Greenwich, CT, **1996**, pp. 81–115.

(15) (a) Saito, S.; Doihara, K.; Moriwake, T.; Okamoto, K. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 1565–1566. (b) Ross, S. D.; Labes, M. M. *J. Am. Chem. Soc.* **1957**, *79*, 4155–4159.

(16) Kevill, D. N.; Kim, C.-B. *J. Org. Chem.* **1974**, *39*, 3085–3089.

(17) (a) Dvorko, G. F.; Ponomareva, E. A.; Ponomarev, M. E. *J. Phys. Org. Chem.* **2004**, *17*, 825–836. (b) Dvorko, G. F., Ponomareva, E. A., Ponomareva, N. E.; Zaliznyi, V. V.; Koshchii, I. V. *Russ. J. Gen. Chem.* **2007**, *77*, 1535–1558.

(18) Streidl, N.; Antipova, A.; Mayr, H. *J. Org. Chem.* **2009**, *74*, 7328–7334.

(19) Denegri, B.; Streiter, A.; Juric, S.; Ofial, A. R.; Kronja, O.; Mayr, H. *Chem. Eur. J.* **2006**, *12*, 1648–1656; *Chem. Eur. J.* **2006**, *12*, 5415.

(20) Streidl, N.; Denegri, B.; Kronja, O.; Mayr, H. *Acc. Chem. Res.* **2010**, *accepted.*

(21) Phan, T. B.; Nolte, C.; Kobayashi, S.; Ofial, A. R.; Mayr, H. *J. Am. Chem. Soc.* **2009**, *131*, 11392–11401.

(22) Nevstad, G. O.; Songstad, J. *Acta Chem. Scand. B* **1984**, *38*, 469–477.

(23) (a) Kornblum, N.; Jones, W. J.; Anderson, G. J. *J. Am. Chem. Soc.* **1959**, *81*, 4113–4114. (b) Kornblum, N.; Powers, J. W.; Anderson, G. J.; Jones, W. J.; Larson, H. O.; Levand, O.; Weaver, W. M. *J. Am. Chem. Soc.* **1957**, *79*, 6562–6562. (c) Dave, P.; Byun, H.-S.; Engel, R. *Synth. Commun.* **1986**, *16*, 1343–1346.

(24) (a) Mayr, H.; Bug, T.; Gotta, M. F.; Hering, N.; Irrgang, B.; Janker, B.; Kempf, B.; Loos, R.; Ofial, A. R.; Remennikov, G.; Schimmel, H. *J. Am. Chem. Soc.* **2001**, *123*, 9500–9512. (b) Mayr, H.; Kempf, B.; Ofial, A. R. *Acc. Chem. Res.* **2003**, *36*, 66–77. (c) Mayr, H.; Ofial, A. R. *Pure Appl. Chem.* **2005**, *77*, 1807–1821. (d) Mayr, H.; Ofial, A. R. *J. Phys. Org. Chem.* **2008**, *21*, 584–595. (e) For a comprehensive data base for nucleophilicity and electrophilicity parameters, see: www.cup.lmu.de/oc/mayr/.

(25) (a) Minegishi, S.; Mayr, H. *J. Am. Chem. Soc.* **2003**, *125*, 286–295. (b) Phan, T. B.; Breugst, M.; Mayr, H. *Angew. Chem.* **2006**, *118*, 3954–3959; *Angew. Chem. Int. Ed.* **2006**, *45*, 3869–3874. (c) Brotzel, F.; Chu, Y. C.; Mayr, H. *J. Org. Chem.* **2007**, *72*,

3679–3688. (d) Brotzel, F.; Kempf, B.; Singer, T.; Zipse, H.; Mayr, H. *Chem. Eur. J.* **2007**, *13*, 336–345.

(26) Minegishi, S.; Loos, R.; Kobayashi, S.; Mayr, H. *J. Am. Chem. Soc.* **2005**, *127*, 2641–2649.

(27) Minegishi, S.; Kobayashi, S.; Mayr, H. *J. Am. Chem. Soc.* **2004**, *126*, 5174–5181.

(28) Minegishi, S.; Mayr, H. *J. Am. Chem. Soc.* **2003**, *125*, 286–295.

(29) (a) Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165–195. (b) Exner, O. *Correlation Analysis of Chemical Data*, Plenum Press, New York, **1988**.

(30) Denegri, B.; Ofial, A. R.; Juric, S.; Streiter, A.; Kronja, O.; Mayr, H. *Chem. Eur. J.* **2006**, *12*, 1657–1666.

(31) *IUPAC. Compendium of Chemical Terminology*, 2nd ed. (the "Gold Book"). Compiled by A. D. McNaught and A. Wilkinson. Blackwell Scientific Publications, Oxford **1997**.

(32) Reichardt, C. *Solvents and Solvent Effects in Organic Chemistry*; Wiley: Weinheim, **2003**.

(33) Skwierczynski, R. D.; Connors, K. A. *J. Chem. Soc., Perkin Trans. 2* **1994**, 467–472.

(34) Mayer, U.; Gutmann, V.; Gerger, W. *Monatsh. Chem.* **1975**, *106*, 1235–1257.

(35) (a) Dimroth, K.; Reichardt, C.; Siepmann, T.; Bohlmann, F. *Liebigs Ann. Chem.* **1963**, *661*, 1–37. (b) Reichardt, C. *Chem. Rev.* **1994**, *94*, 2319–2358.

4.6 Experimental Section

4.6.1 General

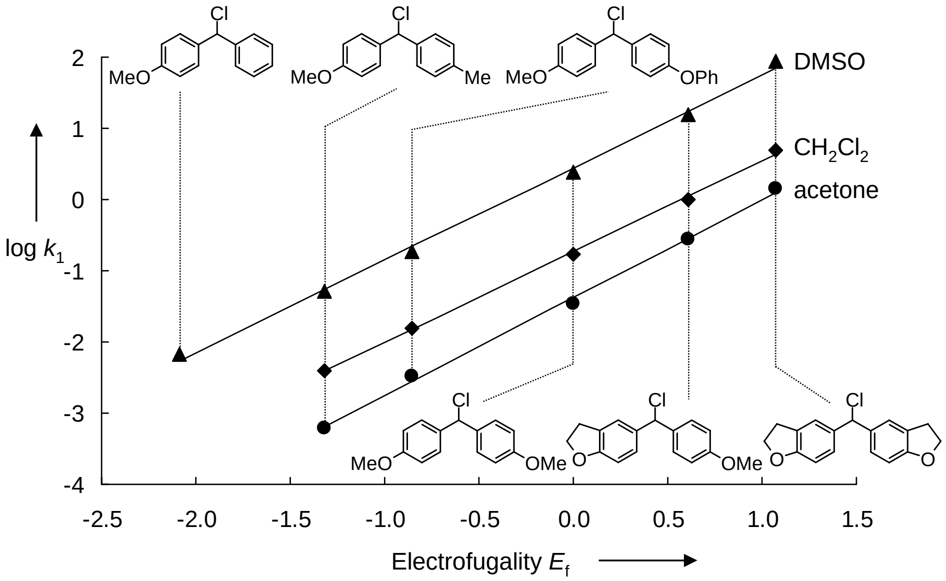
Materials. Commercially available solvents (content of $H_2O < 50$ ppm) were used without further purification for all experiments. Benzhydryl chlorides **1a–f** were obtained from the reactions of benzhydrols with thionyl chloride in dichloromethane according to the procedure published before.[S1]

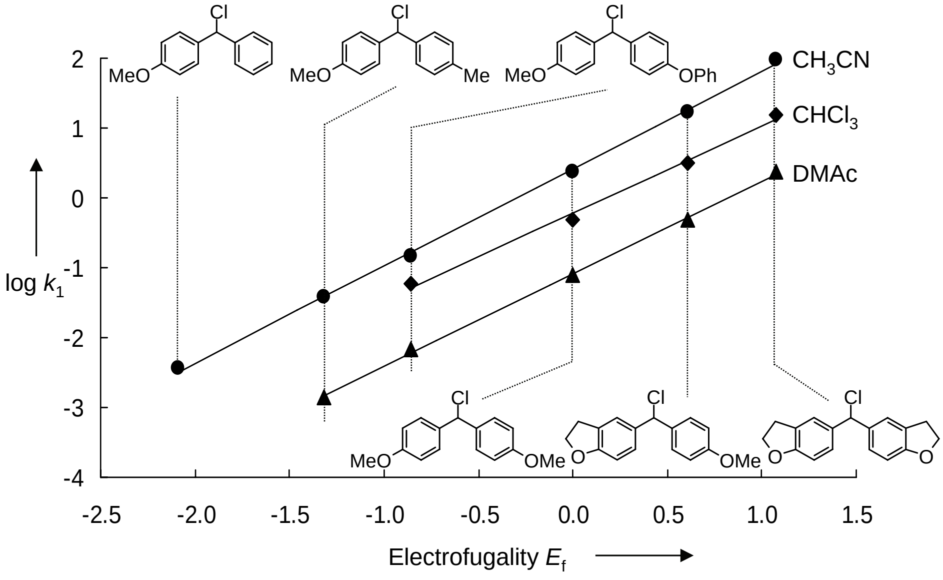
Kinetics. Heterolysis rates of the benzhydrylium chlorides were monitored by following the increase of the conductivity of the reaction mixtures (conductometer: Tacussel CD 810, Pt electrode: WTW LTA 1/NS). A defined amount of trapping reagent (piperidine, pyridine or triphenylphosphine) was dissolved in the solvent (30 mL) which was then thermostated (± 0.1 °C) at 25.0 °C for 5 min. Typically, 10 to 80 mg of substrate was dissolved in 100 µL of the corresponding solvent, then injected into the solvent, and the conductance (G) was recorded at given time intervals.

For the study of solvolysis reactions with half lives of 10^{-2} s $< \tau_{1/2} <$ 10 s, a stopped-flow conductometer (Hi-Tech Scientific SF-61 DX2, platinum electrodes, cell volume: 21 µL, cell constant 4.24 cm^{-1}, minimum dead time 2.2 ms) was used in single-mixing mode. The benzhydryl chlorides were dissolved in pure solvents and mixed with the same solvent containing the trapping reagent within the conductivity cell.

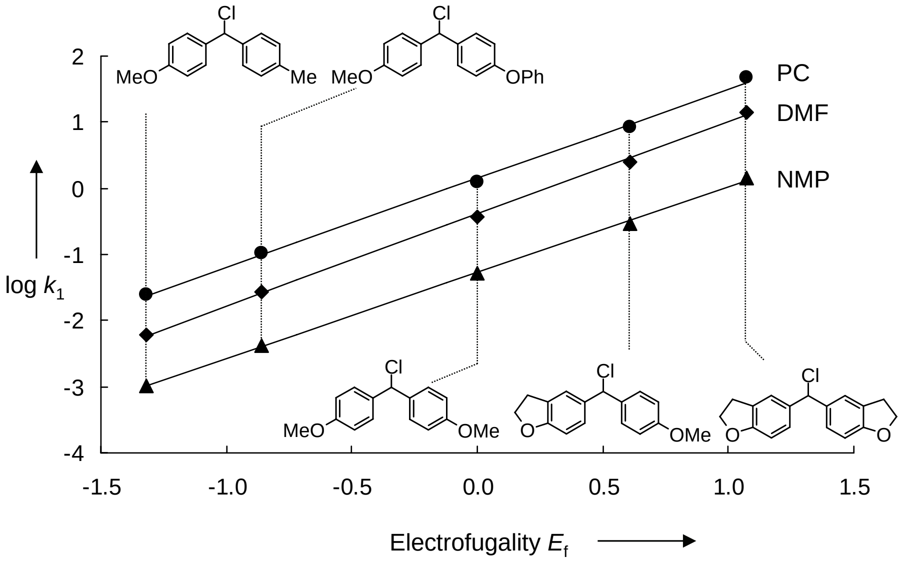
[S1] Denegri, B.; Streiter, A.; Jurić, S.; Ofial, A. R.; Kronja, O.; Mayr, H. *Chem. Eur. J.* **2006**, *12*, 1648–1656; *Chem. Eur. J.* **2006**, *12*, 5415.

4.6.2 Determination of Nucleofugality Parameters N_f and s_f of Chloride in Aprotic Solvents



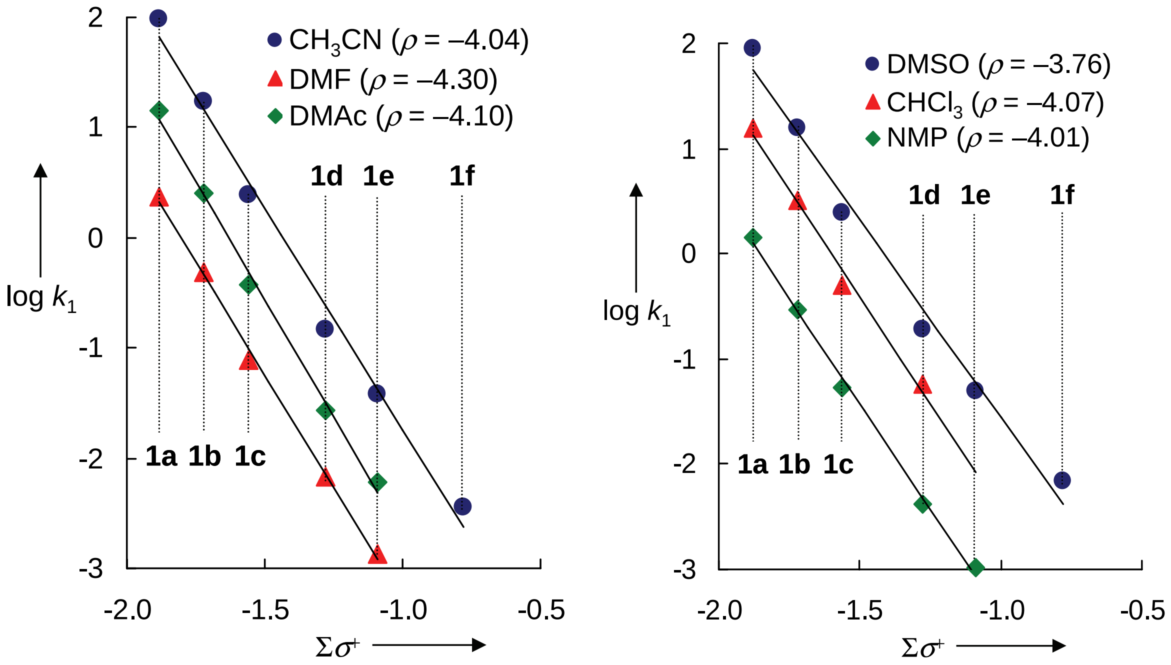


DMAc = dimethylacetamide

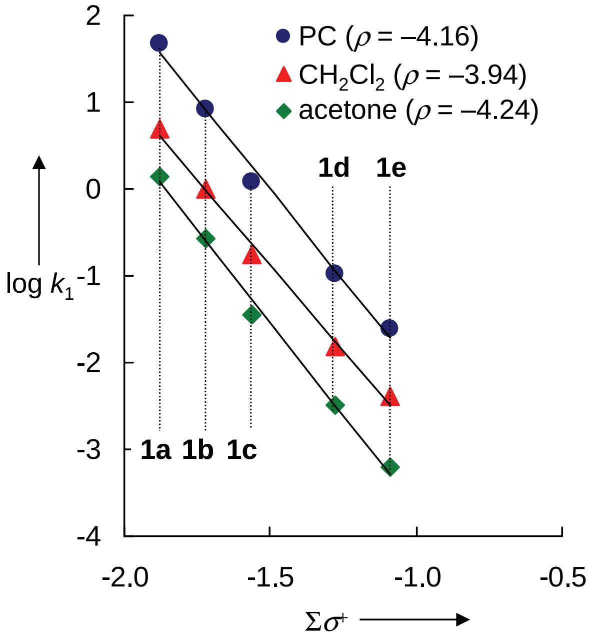


PC = propylene carbonate, DMF = dimethylformamide, NMP = *N*-methyl-2-pyrrolidinone

4.6.3 Hammett Correlations for the Heterolyses of Benzhydryl Chlorides in Aprotic Solvents

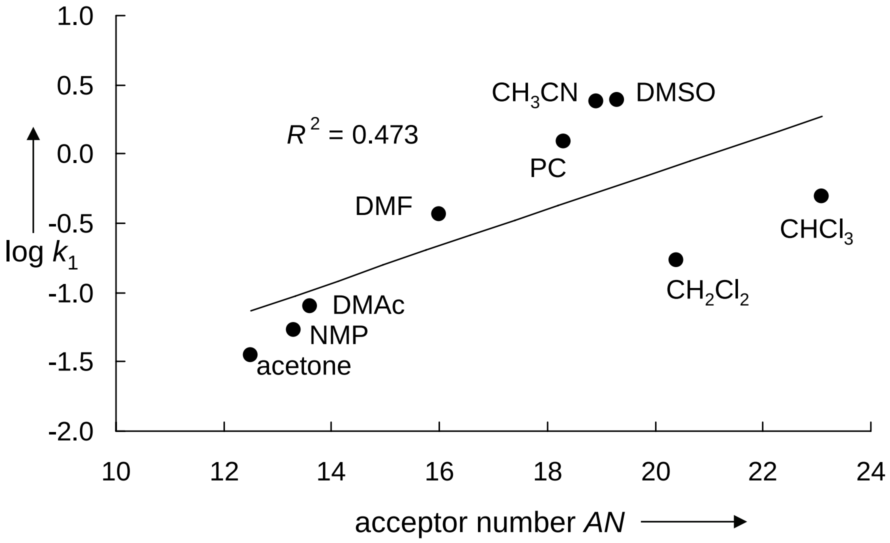


DMF = dimethylformamide, DMAc = dimethylacetamide, NMP = *N*-methyl-2-pyrrolidinone



PC = propylene carbonate

4.6.4 Plot of k_1 of the Solvolyses of 1c versus Acceptor Number *AN* of Aprotic Solvents



4.6.5 Product Studies

General Procedure. 0.40 mmol of benzhydryl chloride and 2.13 g (25.0 mmol) piperidine or 6.56 g (25.0 mmol) triphenylphosphine were dissolved in 50 mL of the corresponding solvent and stirred for at least 5 half-lives. After the reaction was finished, 50 mL of water was added and the mixture was extracted with diethyl ether (2×) and dichloromethane (2×). Then the organic layer was washed twice with water and once with brine. The solvent was dried ($MgSO_4$) and evaporated under reduced pressure, and the crude residue was either recrystallized or purified by column chromatography. The products were identified by NMR and/or GCMS and the analytical data were in agreement with those previously published in the literature: 1-(4,4′-dimethoxybenzhydryl)-piperidine[S2] **2c**, 4,4′-dimethoxybenzophenone[S3] **3c**, bis(4-methoxyphenyl)methane[S4], 4,4′-dimethoxybenzhydrol[S5], 1-(4-methoxybenzhydryl)-piperidine[S6] **2f**, 4-methoxybenzophenone[S7] **3f**.

DMSO:

1c with piperidine: GC-MS of crude product: 97% **2c** and 3% **3c**, after recrystallization from ethanol 72 % isolated yield of **2c**.

1f with piperidine: GC-MS of crude product: 68% **2f** and 32% **3f**, after column chromatography (diethyl ether/pentane) 58% isolated yield of **2f** and 28% isolated yield of **3f**.

CH_3CN:

1c with piperidine: GC-MS of crude product: 100% **2c**, after recrystallization from ethanol 80% isolated yield of **2c**.

[S2] Tomashenko, O.; Sokolov, V.; Tomashevskiy, A.; Buchholz, H. A.; Welz-Biermann, U.; Chaplinski, V.; de Meijere, A. *Eur. J. Org. Chem.* **2008**, 5107–5111.

[S3] Babu, S. A.; Yasuda, M.; Baba, A. *Org. Lett.* **2007**, *9*, 405–408.

[S4] Hofmann, M.; Hampel, N.; Kanzian, T.; Mayr, H. *Angew. Chem.* **2004**, *116*, 5518–5521; *Angew. Chem. Int. Ed.* **2004**, *43*, 5402–5405.

[S5] Denegri, B.; Kronja, O. *J. Org. Chem.* **2007**, *72*, 8427–8433.

[S6] Le Gall, E.; Haurena, C.; Sengmany, S.; Martens, T.; Troupel, M. *J. Org. Chem.* **2009**, *74*, 7970–7973.

[S7] Xing, D.; Guan, B.; Cai, G.; Fang, Z.; Yang, L.; Shi, Z. *Org. Lett.* **2006**, *8*, 693–696.

1f with piperidine: GC-MS of crude product: 100% **2f**, after column chromatography (diethyl ether/pentane) 85% isolated yield of **2f**.

dimethylformamide DMF:

1c with piperidine: GC-MS of crude product: 100% **2c**, after recrystallization from ethanol 80% isolated yield of **2c**.

acetone:

1c with piperidine: GC-MS of crude product: 100% **2c**, after recrystallization from ethanol 84% isolated yield of **2c**.

dimethylacetamide DMAc:

1c with piperidine: GC-MS of crude product: 76% **2c**, 9% **3c**, 15% bis(4-methoxyphenyl)methane; after column chromatography (dichloromethane/pentane) 60% isolated yield of **2c**.

$CHCl_3$:

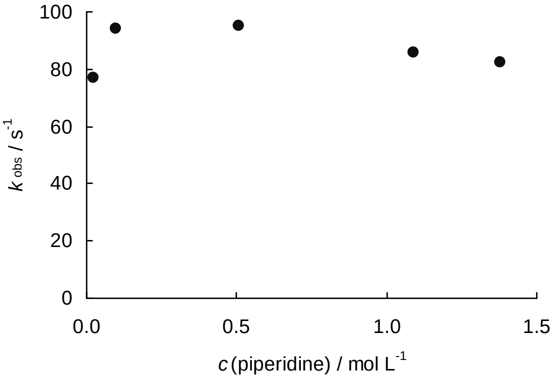
1c with piperidine: after aqueous workup and recrystallization from *i*-hexane 95% isolated yield of 4,4´-dimethoxybenzhydrol.

4.6.6 Solvolysis Reactions of Benzhydryl Chlorides in Aprotic Solvents at 25 °C

Solvolysis Reactions of Benzhydryl Chlorides in Acetonitrile

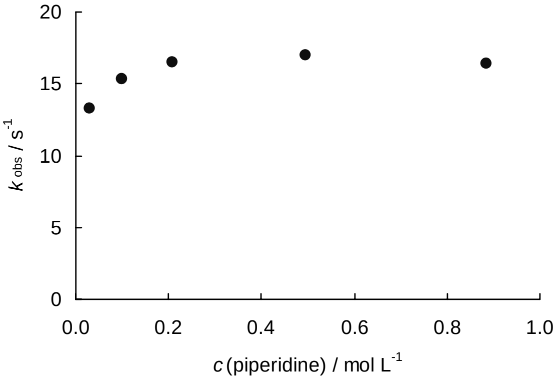
substrate concentration	**amine**	**solvent**	**method**
[**1a**] = 6.1×10^{-3} mol L^{-1}	piperidine	acetonitrile	stopped-flow conductometry

No	*c*(piperidine) / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK8-1	0.022	7.69×10^1	0.9979
NSK8-2	0.097	9.40×10^1	0.9984
NSK8-3	0.509	$\mathbf{9.51 \times 10^1}$	0.9992
NSK8-4	1.09	8.56×10^1	0.9979
NSK8-5	1.38	8.22×10^1	0.9993



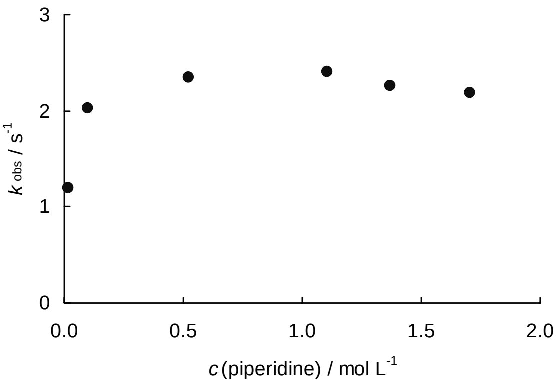
substrate concentration	**amine**	**solvent**	**method**
[**1b**] = 6.1×10^{-3} mol L^{-1}	piperidine	acetonitrile	stopped-flow conductometry

No	*c*(piperidine) / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK20-1	0.030	1.33×10^1	0.9986
NSK20-2	0.100	1.53×10^1	0.9990
NSK20-3	0.209	1.65×10^1	0.9989
NSK20-4	0.495	$\mathbf{1.70 \times 10^1}$	0.9990
NSK20-5	0.884	1.64×10^1	0.9990



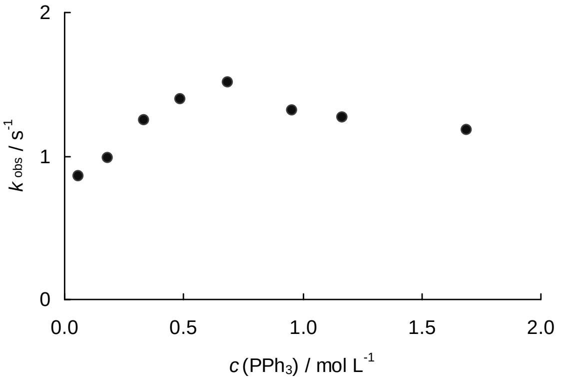
substrate concentration	**amine**	**solvent**	**method**
[**1c**] = 6.1×10^{-3} mol L^{-1}	piperidine	acetonitrile	stopped-flow conductometry

No	c(piperidine) / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK1-1	0.015	1.20	0.9963
NSK1-2	0.101	2.03	0.9986
NSK1-3	0.521	2.34	0.9989
NSK1-4	1.10	**2.40**	0.9985
NSK1-6	1.37	2.26	0.9995
NSK1-5	1.71	2.19	0.9984



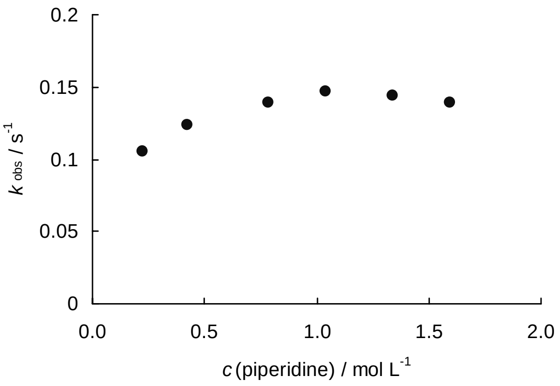
substrate concentration	**trapping reagent**	**solvent**	**method**
[**1c**] = 6.1×10^{-3} mol L^{-1}	pyridine	acetonitrile	stopped-flow conductometry

No	c(pyridine) / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK200-7	0.060	8.58×10^{-1}	0.9991
NSK200-8	0.180	9.89×10^{-1}	0.9994
NSK200-2	0.332	1.25	0.9997
NSK200-3	0.487	1.40	0.9998
NSK200-4	0.687	**1.51**	0.9999
NSK200-9	0.955	1.32	0.9999
NSK200-5	1.167	1.27	0.9999
NSK200-6	1.692	1.18	0.9996



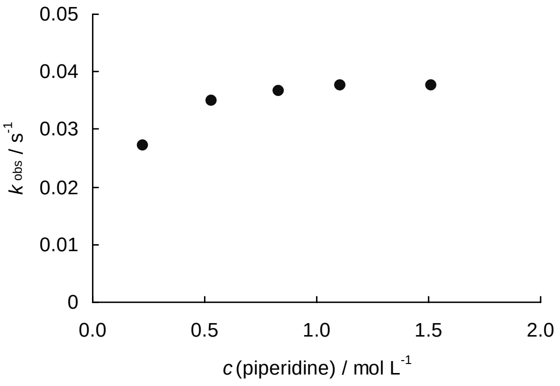
substrate concentration	**amine**	**solvent**	**method**
[**1d**] = 6.0×10^{-4} mol L^{-1}	piperidine	acetonitrile	conventional conductometry

No	c(piperidine) / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK6-1	0.225	1.05×10^{-1}	0.9968
NSK6-2	0.426	1.24×10^{-1}	0.9988
NSK6-3	0.786	1.38×10^{-1}	0.9990
NSK6-4	1.04	**1.47×10^{-1}**	0.9985
NSK6-6	1.34	1.44×10^{-1}	0.9984
NSK6-5	1.59	1.39×10^{-1}	0.9989



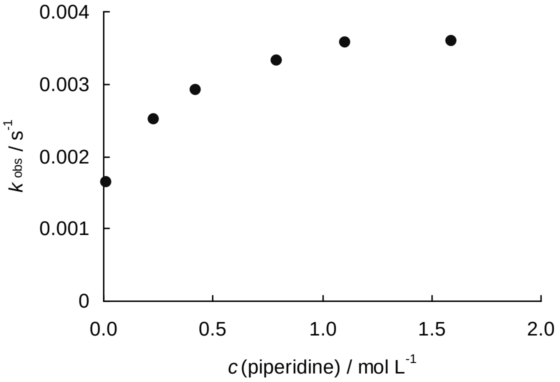
substrate concentration	**amine**	**solvent**	**method**
[**1e**] = 6.1×10^{-3} mol L^{-1}	piperidine	acetonitrile	stopped-flow conductometry

No	c(piperidine) / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK42-1	0.226	2.73×10^{-2}	0.9993
NSK42-2	0.531	3.50×10^{-2}	0.9990
NSK42-3	0.828	3.67×10^{-2}	0.9991
NSK42-4	1.10	**3.77×10^{-2}**	0.9987
NSK42-5	1.51	3.77×10^{-2}	0.9988



substrate concentration	**amine**	**solvent**	**method**
[**1f**] = 6.0×10^{-4} mol L^{-1}	piperidine	acetonitrile	conventional conductometry

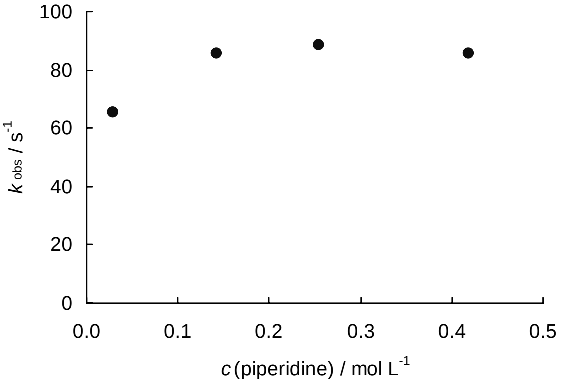
No	c(piperidine) / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK4-1	0.013	1.64×10^{-3}	0.9975
NSK4-2	0.233	2.51×10^{-3}	0.9988
NSK4-3	0.423	2.91×10^{-3}	0.9985
NSK4-4	0.794	3.32×10^{-3}	0.9981
NSK4-5	1.11	3.58×10^{-3}	0.9991
NSK4-6	1.59	**3.60×10^{-3}**	0.9991



Solvolysis Reactions of Benzhydryl Chlorides in DMSO

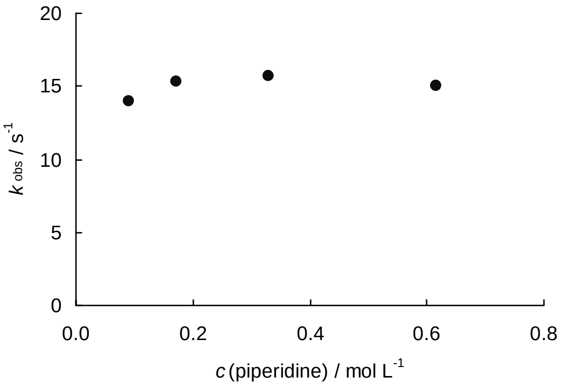
substrate concentration	**amine**	**solvent**	**method**
[**1a**] = 6.1×10^{-3} mol L^{-1}	piperidine	DMSO	stopped-flow conductometry

No	c(piperidine) / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK43-1	0.014	6.53×10^{1}	0.9999
NSK43-2	0.067	8.57×10^{1}	0.9999
NSK43-3	0.119	**8.85×10^{1}**	0.9999
NSK43-4	0.419	8.57×10^{1}	0.9999



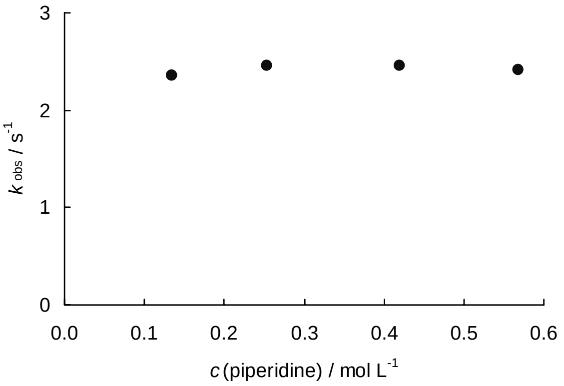
substrate concentration	**amine**	**solvent**	**method**
[**1b**] = 6.1×10^{-3} mol L^{-1}	piperidine	DMSO	stopped-flow conductometry

No	*c*(piperidine) / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK45-1	0.043	1.40×10^{1}	0.9994
NSK45-2	0.080	1.53×10^{1}	0.9995
NSK45-3	0.154	$\mathbf{1.57 \times 10^{1}}$	0.9993
NSK45-4	0.289	1.50×10^{1}	0.9987



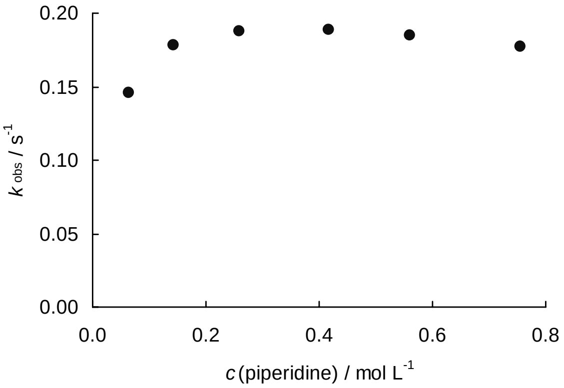
substrate concentration	**amine**	**solvent**	**method**
[**1c**] = 6.1×10^{-3} mol L^{-1}	piperidine	DMSO	stopped-flow conductometry

No	*c*(piperidine) / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK39-2	0.135	2.35	0.9999
NSK39-3	0.254	2.45	0.9999
NSK39-4	0.421	**2.46**	0.9998
NSK39-5	0.568	2.41	0.9999



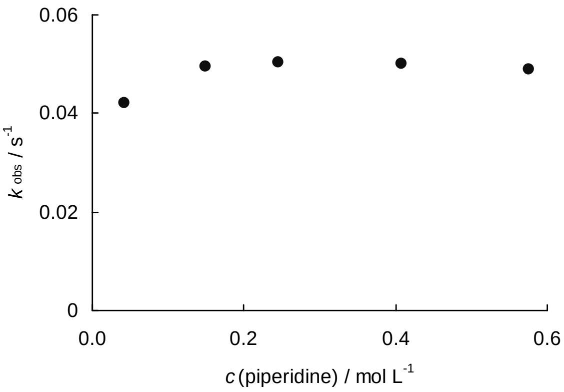
substrate concentration	**amine**	**solvent**	**method**
[**1d**] = 6.1×10^{-3} mol L^{-1}	piperidine	DMSO	stopped-flow conductometry

No	c(piperidine) / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK40-1	0.064	1.46×10^{-1}	0.9998
NSK40-2	0.143	1.78×10^{-1}	0.9996
NSK40-3	0.158	1.88×10^{-1}	0.9998
NSK40-4	0.416	$\mathbf{1.89 \times 10^{-1}}$	0.9998
NSK40-5	0.559	1.85×10^{-1}	0.9999
NSK40-6	0.756	1.77×10^{-1}	0.9999



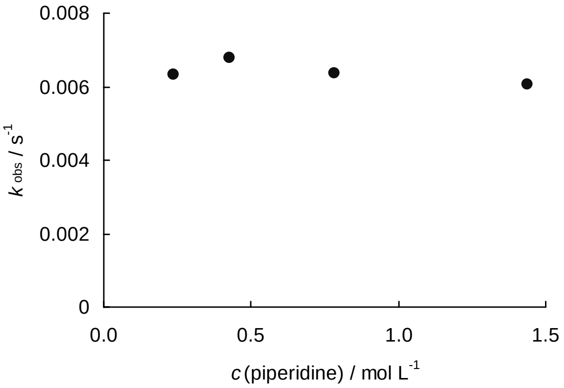
substrate concentration	**amine**	**solvent**	**method**
[**1e**] = 6.1×10^{-3} mol L^{-1}	piperidine	DMSO	stopped-flow conductometry

No	c(piperidine) / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK41-1	0.043	4.22×10^{-2}	0.9998
NSK41-2	0.149	4.94×10^{-2}	0.9996
NSK41-3	0.246	$\mathbf{5.03 \times 10^{-2}}$	0.9998
NSK41-4	0.408	5.00×10^{-2}	0.9998
NSK41-5	0.577	4.90×10^{-2}	0.9999



substrate concentration	**amine**	**solvent**	**method**
[**1f**] = 6.0×10^{-4} mol L^{-1}	piperidine	DMSO	conventional conductometry

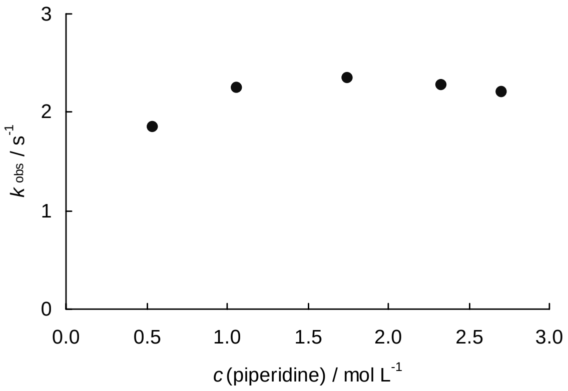
No	c(piperidine) / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK35-2	0.237	6.31×10^{-3}	0.9990
NSK35-3	0.428	**6.78×10^{-3}**	0.9986
NSK35-4	0.784	6.37×10^{-3}	0.9982
NSK35-5	1.437	6.06×10^{-3}	0.9975



Solvolysis Reactions of Benzhydryl Chlorides in Dimethylacetamide (DMAA)

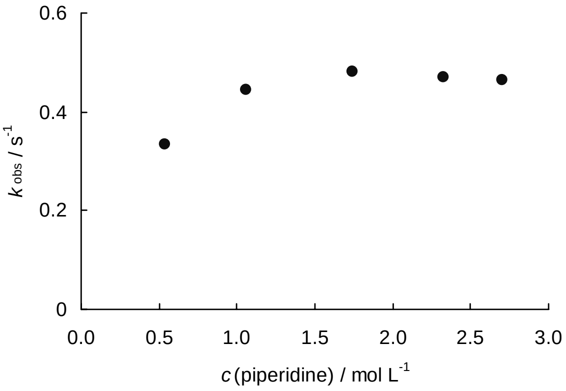
substrate concentration	**amine**	**solvent**	**method**
[**1a**] = 6.1×10^{-3} mol L^{-1}	piperidine	DMAc	stopped-flow conductometry

No	c(piperidine) / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK75-1	0.536	1.85	0.9992
NSK75-2	1.063	2.25	0.9994
NSK75-3	1.744	**2.35**	0.9996
NSK75-4	2.327	2.28	0.9997
NSK75-5	2.701	2.21	0.9997



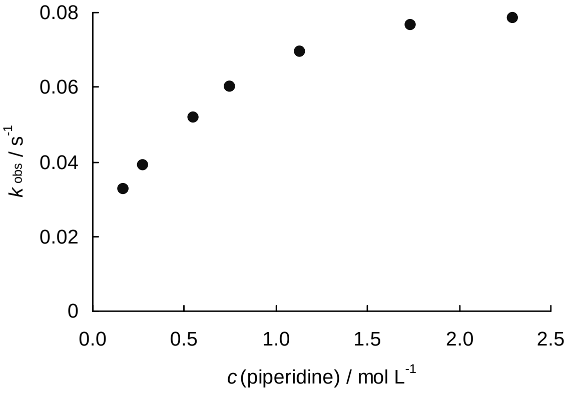
substrate concentration	**amine**	**solvent**	**method**
[**1b**] = 6.1×10^{-3} mol L^{-1}	piperidine	DMAc	stopped-flow conductometry

No	c(piperidine) / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK74-1	0.536	3.33×10^{-1}	0.9990
NSK74-2	1.063	4.44×10^{-1}	0.9994
NSK74-3	1.744	**4.81×10^{-1}**	0.9995
NSK74-4	2.327	4.71×10^{-1}	0.9995
NSK74-5	2.701	4.65×10^{-1}	0.9996



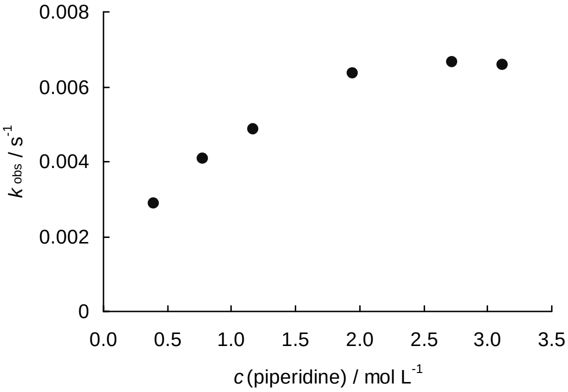
substrate concentration	**amine**	**solvent**	**method**
[**1c**] = 6.1×10^{-3} mol L^{-1}	piperidine	DMAc	stopped-flow conductometry

No	c(piperidine) / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK73-1	0.169	3.28×10^{-2}	0.9990
NSK73-2	0.273	3.90×10^{-2}	0.9990
NSK73-3	0.549	5.20×10^{-2}	0.9992
NSK73-4	0.749	6.01×10^{-2}	0.9991
NSK73-5	1.130	6.95×10^{-2}	0.9992
NSK73-6	1.734	7.67×10^{-2}	0.9993
NSK73-7	2.293	**7.86×10^{-2}**	0.9995



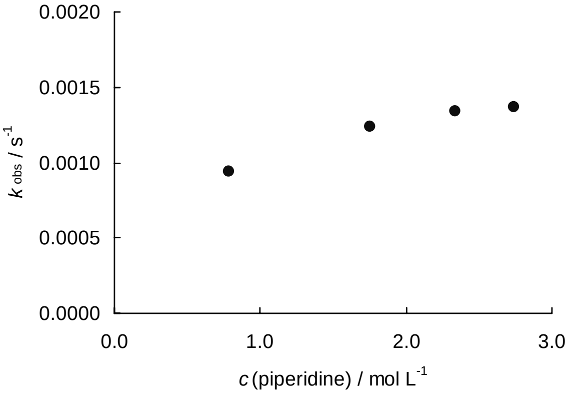
substrate concentration	**amine**	**solvent**	**method**
[**1d**] = 6.0×10^{-4} mol L^{-1}	piperidine	DMAc	conventional conductometry

No	*c*(piperidine) / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK80-1	0.388	2.87×10^{-3}	0.9985
NSK80-2	0.782	4.06×10^{-3}	0.9993
NSK80-15	1.170	4.86×10^{-3}	0.9996
NSK80-11	1.947	6.36×10^{-3}	0.9994
NSK80-13	2.725	**6.66×10^{-3}**	0.9994
NSK80-14	3.114	6.57×10^{-3}	0.9994



substrate concentration	**amine**	**solvent**	**method**
[**1e**] = 6.0×10^{-4} mol L^{-1}	piperidine	DMAc	conventional conductometry

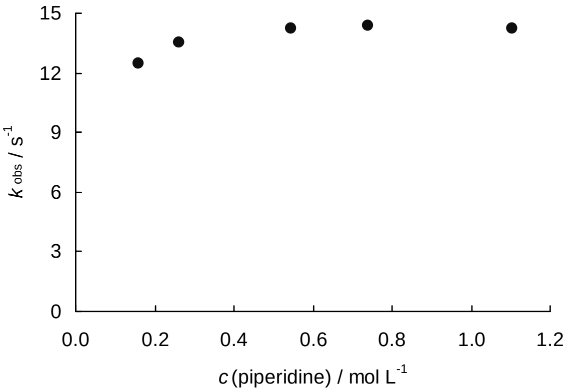
No	*c*(piperidine) / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK86-1	0.786	9.44×10^{-4}	0.9993
NSK86-2	1.751	1.24×10^{-3}	0.9993
NSK86-3	2.335	1.34×10^{-3}	0.9992
NSK86-4	2.745	**1.37×10^{-3}**	0.9992



Solvolysis Reactions of Benzhydryl Chlorides in Dimethylformamide (DMF)

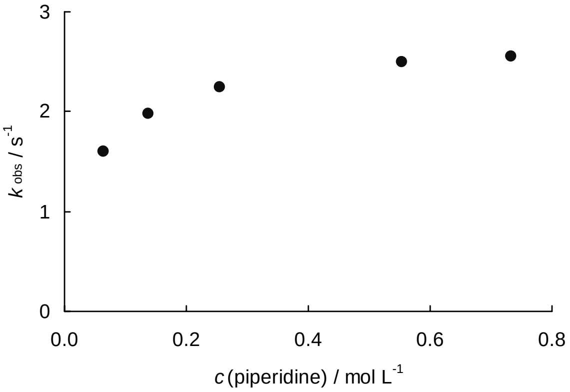
substrate concentration	**amine**	**solvent**	**method**
[**1a**] = 6.1×10^{-3} mol L^{-1}	piperidine	DMF	stopped-flow conductometry

No	c(piperidine) / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK63-1	0.158	1.25×10^1	0.9997
NSK63-2	0.262	1.35×10^1	0.9997
NSK63-3	0.547	1.42×10^1	0.9998
NSK63-4	0.739	$\mathbf{1.44 \times 10^1}$	0.9998
NSK63-5	1.106	1.42×10^1	0.9998



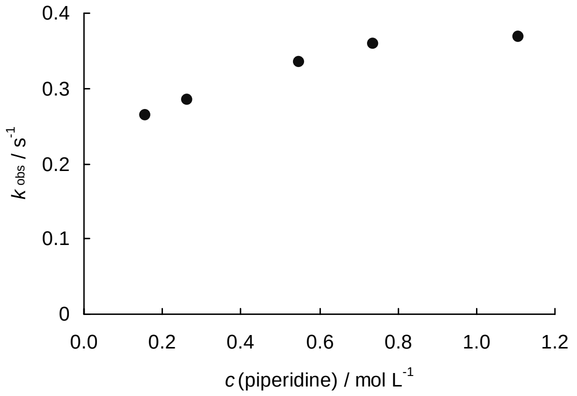
substrate concentration	**amine**	**solvent**	**method**
[**1b**] = 6.1×10^{-3} mol L^{-1}	piperidine	DMF	stopped-flow conductometry

No	c(piperidine) / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK62-1	0.064	1.60	0.9995
NSK62-2	0.139	1.97	0.9995
NSK62-3	0.254	2.24	0.9995
NSK62-4	0.553	2.50	0.9995
NSK62-5	0.732	**2.55**	0.9995



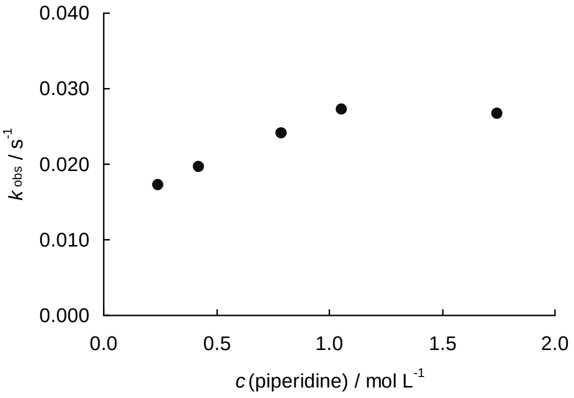
substrate concentration	**amine**	**solvent**	**method**
[**1c**] = 6.1×10^{-3} mol L^{-1}	piperidine	DMF	stopped-flow conductometry

No	c(piperidine) / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK64-1	0.158	2.64×10^{-1}	0.9984
NSK64-2	0.262	2.84×10^{-1}	0.9987
NSK64-3	0.547	3.35×10^{-1}	0.9986
NSK64-4	0.739	3.59×10^{-1}	0.9985
NSK64-5	1.106	**3.69×10^{-1}**	0.9990



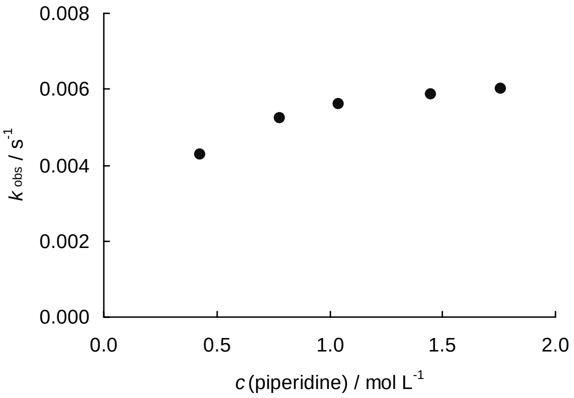
substrate concentration	**amine**	**solvent**	**method**
[**1d**] = 6.0×10^{-4} mol L^{-1}	piperidine	DMF	conventional conductometry

No	c(piperidine) / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK66-1	0.240	1.72×10^{-2}	0.9988
NSK66-2	0.420	1.97×10^{-2}	0.9987
NSK66-3	0.786	2.41×10^{-2}	0.9989
NSK66-4	1.057	**2.73×10^{-2}**	0.9984
NSK66-6	1.745	2.67×10^{-2}	0.9983



substrate concentration	**amine**	**solvent**	**method**
[**1e**] = 6.0×10^{-4} mol L^{-1}	piperidine	DMF	conventional conductometry

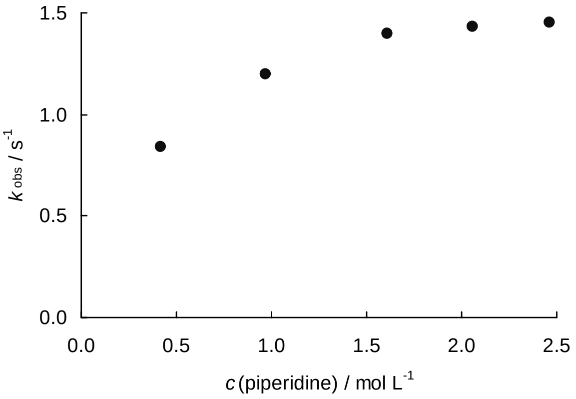
No	c(piperidine) / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK68-2	0.427	4.28×10^{-3}	0.9996
NSK68-3	0.779	5.23×10^{-3}	0.9995
NSK68-4	1.038	5.59×10^{-3}	0.9994
NSK68-5	1.447	5.87×10^{-3}	0.9992
NSK66-6	1.757	**6.02×10^{-3}**	0.9991



Solvolysis Reactions of Benzhydryl Chlorides in N-Methyl-2-pyrrolidone (NMP)

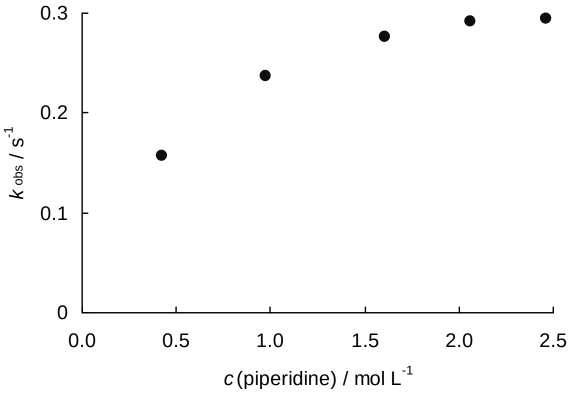
substrate concentration	**amine**	**solvent**	**method**
[**1a**] = 6.1×10^{-3} mol L^{-1}	piperidine	NMP	stopped-flow conductometry

No	c(piperidine) / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK77-1	0.423	8.41×10^{-1}	0.9992
NSK77-2	0.974	1.20	0.9994
NSK77-3	1.610	1.40	0.9994
NSK77-4	2.061	1.43	0.9996
NSK77-5	2.466	**1.45**	0.9996



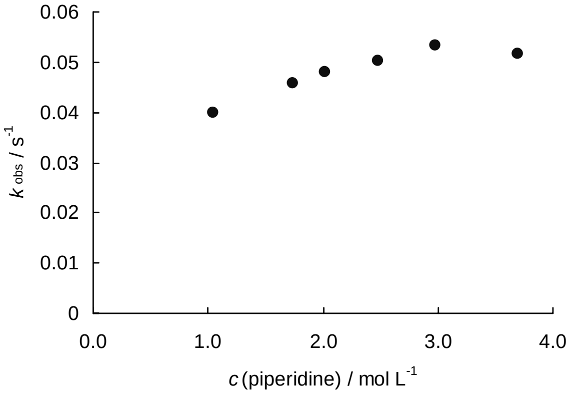
substrate concentration	**amine**	**solvent**	**method**
[**1b**] = 6.1×10^{-3} mol L^{-1}	piperidine	NMP	stopped-flow conductometry

No	c(piperidine) / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK76-1	0.423	1.57×10^{-1}	0.9992
NSK76-2	0.974	2.37×10^{-1}	0.9994
NSK76-3	1.610	2.76×10^{-1}	0.9995
NSK76-4	2.061	2.92×10^{-1}	0.9995
NSK76-5	2.466	**2.94×10^{-1}**	0.9996



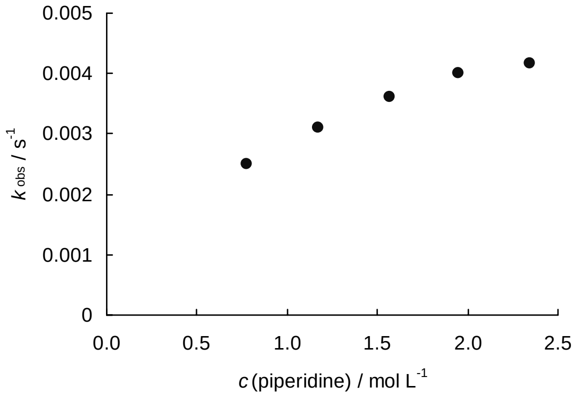
substrate concentration	**amine**	**solvent**	**method**
[**1c**] = 6.1×10^{-3} mol L^{-1}	piperidine	NMP	stopped-flow conductometry

No	c(piperidine) / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK79-1	1.048	3.98×10^{-2}	0.9994
NSK79-2	1.736	4.59×10^{-2}	0.9997
NSK79-3	2.018	4.79×10^{-2}	0.9997
NSK79-4	2.477	5.02×10^{-2}	0.9999
NSK79-5	2.977	**5.32×10^{-2}**	0.9999
NSK79-6	3.692	5.17×10^{-2}	0.9999



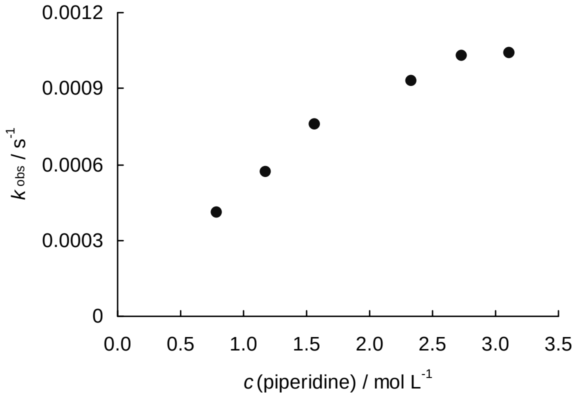
substrate concentration	**amine**	**solvent**	**method**
[**1d**] = 6.0×10^{-4} mol L^{-1}	piperidine	NMP	conventional conductometry

No	c(piperidine) / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK85-1	0.778	2.51×10^{-3}	0.9980
NSK85-2	1.175	3.10×10^{-3}	0.9993
NSK85-3	1.569	3.60×10^{-3}	0.9990
NSK85-4	1.949	4.00×10^{-3}	0.9988
NSK85-5	2.346	$\mathbf{4.16 \times 10^{-3}}$	0.9982



substrate concentration	**amine**	**solvent**	**method**
[**1e**] = 6.0×10^{-4} mol L^{-1}	piperidine	NMP	conventional conductometry

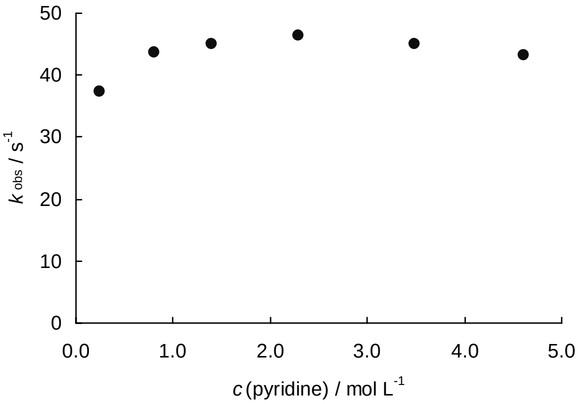
No	c(piperidine) / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK83-1	0.787	4.08×10^{-4}	0.9974
NSK83-2	1.174	5.71×10^{-4}	0.9990
NSK83-9	1.562	7.78×10^{-4}	0.9988
NSK83-5	2.339	9.28×10^{-4}	0.9960
NSK83-6	2.730	1.03×10^{-3}	0.9985
NSK83-7	3.115	$\mathbf{1.04 \times 10^{-3}}$	0.9983



Solvolysis Reactions of Benzhydryl Chlorides in Propylene Carbonate (PC)

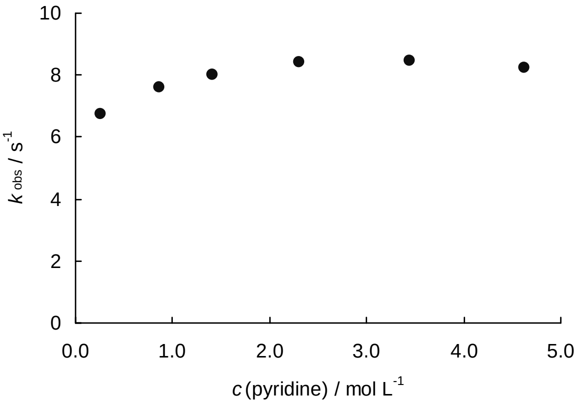
substrate concentration	**amine**	**solvent**	**method**
[**1a**] = 6.1×10^{-3} mol L^{-1}	pyridine	PC	stopped-flow conductometry

No	*c*(pyridine) / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK113-1	0.251	3.73×10^1	0.9995
NSK113-2	0.805	4.36×10^1	0.9997
NSK113-3	1.404	4.50×10^1	0.9997
NSK113-4	2.287	$\mathbf{4.63 \times 10^1}$	0.9998
NSK113-5	3.480	4.51×10^1	0.9998
NSK113-6	4.604	4.32×10^1	0.9998



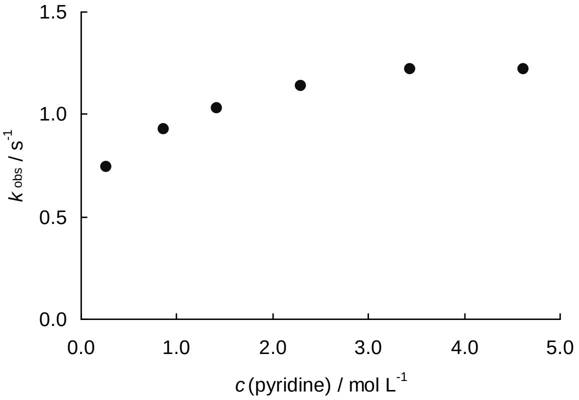
substrate concentration	**amine**	**solvent**	**method**
[**1b**] = 6.1×10^{-3} mol L^{-1}	pyridine	PC	stopped-flow conductometry

No	*c*(pyridine) / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK111-1	0.264	6.74	0.9999
NSK111-2	0.862	7.61	0.9999
NSK111-3	1.411	8.00	0.9999
NSK111-4	2.299	8.41	0.9999
NSK111-5	3.441	**8.47**	0.9999
NSK111-6	4.620	8.23	0.9999



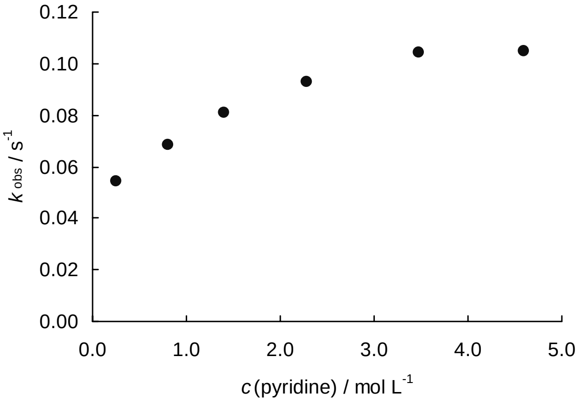
substrate concentration	**amine**	**solvent**	**method**
[**1c**] = 6.1×10^{-3} mol L^{-1}	pyridine	PC	stopped-flow conductometry

No	*c*(pyridine) / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK110-1	0.264	7.46×10^{-1}	0.9999
NSK110-2	0.862	9.28×10^{-1}	0.9999
NSK110-3	1.411	1.03	0.9999
NSK110-4	2.299	1.14	0.9999
NSK110-5	3.441	**1.22**	0.9999
NSK110-6	4.620	1.22	0.9999



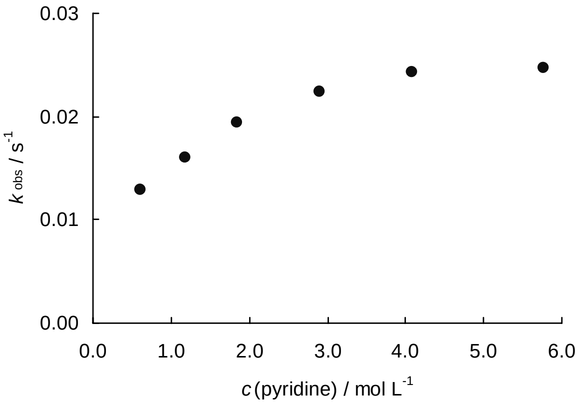
substrate concentration	**amine**	**solvent**	**method**
[**1d**] = 6.1×10^{-3} mol L^{-1}	pyridine	PC	stopped-flow conductometry

No	*c*(pyridine) / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK112-1	0.251	5.41×10^{-2}	0.9999
NSK112-2	0.805	6.85×10^{-2}	0.9999
NSK112-3	1.404	8.08×10^{-2}	0.9999
NSK112-4	2.287	9.30×10^{-2}	0.9999
NSK112-5	3.480	1.04×10^{-1}	0.9999
NSK112-6	4.604	$\mathbf{1.05 \times 10^{-1}}$	0.9999



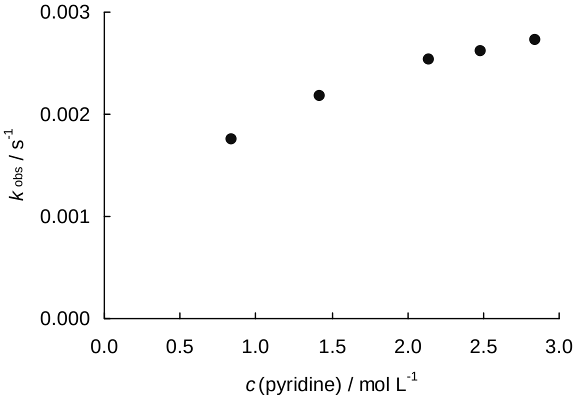
substrate concentration	**amine**	**solvent**	**method**
[**1e**] = 6.1×10^{-3} mol L^{-1}	pyridine	PC	stopped-flow conductometry

No	c(pyridine) / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK114-1	0.611	1.29×10^{-2}	0.9999
NSK114-2	1.184	1.60×10^{-2}	0.9999
NSK114-3	1.841	1.94×10^{-2}	0.9999
NSK114-4	2.901	2.24×10^{-2}	0.9999
NSK114-5	4.082	2.43×10^{-2}	0.9999
NSK114-6	5.763	**2.47×10^{-2}**	0.9999



substrate concentration	**amine**	**solvent**	**method**
[**1f**] = 6.0×10^{-4} mol L^{-1}	pyridine	PC	conventional conductometry

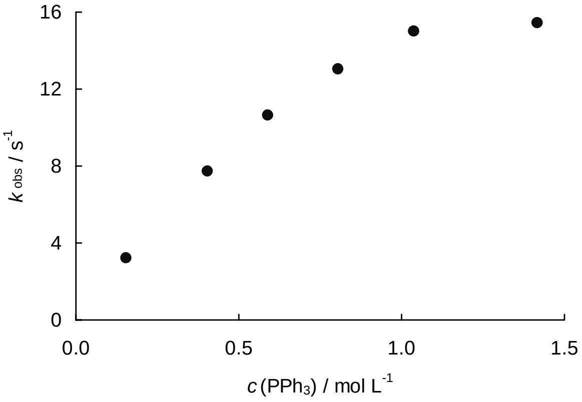
No	c(pyridine) / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK115-1	0.841	1.75×10^{-3}	0.9987
NSK115-2	1.422	2.18×10^{-3}	0.9991
NSK115-3	2.142	2.54×10^{-3}	0.9998
NSK115-4	2.481	2.62×10^{-3}	0.9998
NSK115-5	2.844	**2.73×10^{-3}**	0.9999



Solvolysis Reactions of Benzhydryl Chlorides in $CHCl_3$

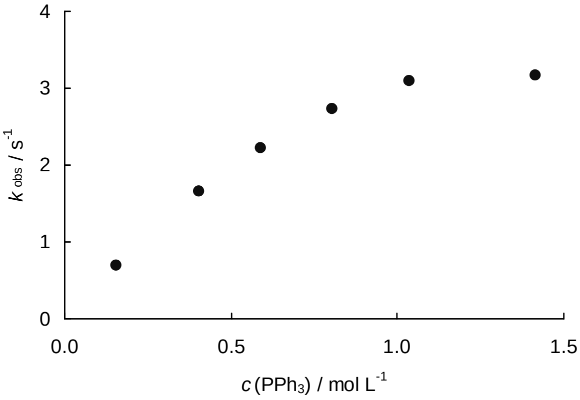
substrate concentration	**nucleophile**	**solvent**	**method**
[**1a**] = 6.1×10^{-3} mol L^{-1}	PPh_3	$CHCl_3$	stopped-flow conductometry

No	$c(PPh_3)$ / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK93-1	0.154	3.21	0.9999
NSK93-2	0.406	7.73	0.9999
NSK93-3	0.591	1.06×10^1	0.9999
NSK93-4	0.805	1.30×10^1	0.9999
NSK93-5	1.038	1.49×10^1	0.9999
NSK93-6	1.417	$\mathbf{1.54 \times 10^1}$	0.9995



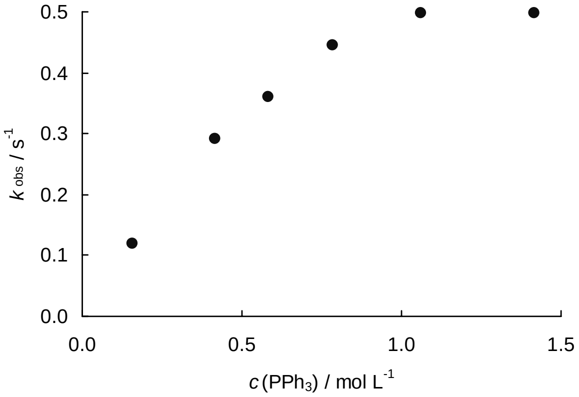
substrate concentration	**nucleophile**	**solvent**	**method**
[**1b**] = 6.1×10^{-3} mol L^{-1}	PPh_3	$CHCl_3$	stopped-flow conductometry

No	$c(PPh_3)$ / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK94-1	0.154	7.01×10^{-1}	0.9999
NSK94-2	0.406	1.66	0.9999
NSK94-3	0.591	2.22	0.9999
NSK94-4	0.805	2.73	0.9999
NSK94-5	1.038	3.10	0.9999
NSK94-6	1.417	**3.17**	0.9998



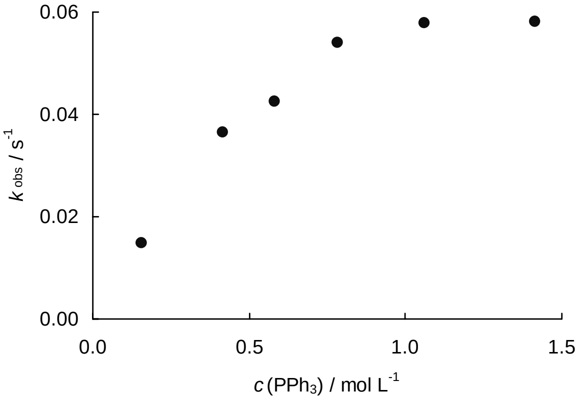
substrate concentration	**nucleophile**	**solvent**	**method**
[**1c**] = 6.1×10^{-3} mol L^{-1}	PPh_3	$CHCl_3$	stopped-flow conductometry

No	$c(PPh_3)$ / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK95-1	0.159	1.20×10^{-1}	0.9999
NSK95-2	0.415	2.91×10^{-1}	0.9999
NSK95-3	0.583	3.60×10^{-1}	0.9999
NSK95-4	0.784	4.45×10^{-1}	0.9998
NSK95-5	1.006	$\mathbf{4.98 \times 10^{-1}}$	0.9996
NSK95-6	1.416	4.98×10^{-1}	0.9994



substrate concentration	**nucleophile**	**solvent**	**method**
[**1d**] = 6.1×10^{-3} mol L^{-1}	PPh_3	$CHCl_3$	stopped-flow conductometry

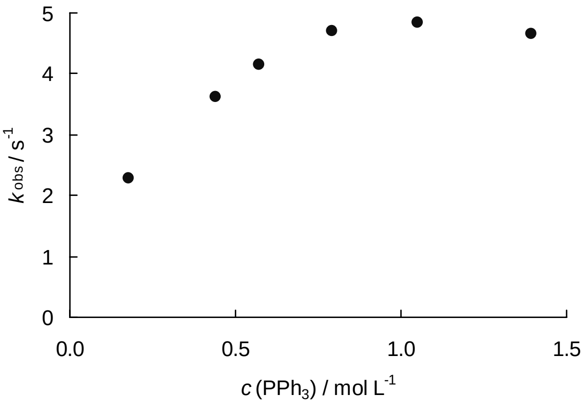
No	$c(PPh_3)$ / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK96-1	0.159	1.48×10^{-2}	0.9991
NSK96-2	0.415	3.65×10^{-2}	0.9999
NSK96-3	0.583	4.25×10^{-2}	0.9999
NSK96-4	0.784	5.40×10^{-2}	0.9999
NSK96-5	1.006	5.79×10^{-2}	0.9998
NSK96-6	1.416	$\mathbf{5.82 \times 10^{-2}}$	0.9998



Solvolysis Reactions of Benzhydryl Chlorides in CH_2Cl_2

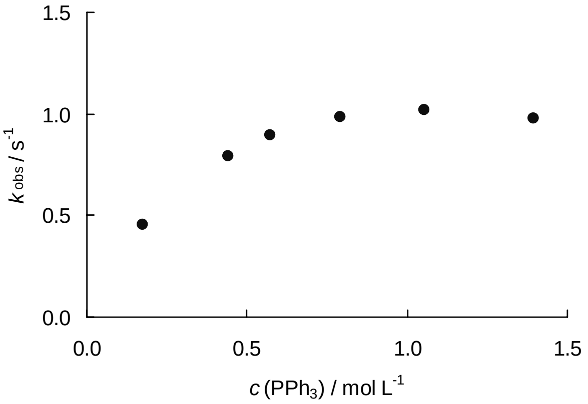
substrate concentration	**nucleophile**	**solvent**	**method**
[**1a**] = 6.1×10^{-3} mol L^{-1}	PPh_3	CH_2Cl_2	stopped-flow conductometry

No	$c(PPh_3)$ / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK91-1	0.177	2.28	0.9982
NSK91-2	0.442	3.61	0.9995
NSK91-3	0.573	4.14	0.9992
NSK91-4	0.793	4.71	0.9990
NSK91-5	1.052	**4.84**	0.9994
NSK91-6	1.393	4.66	0.9996



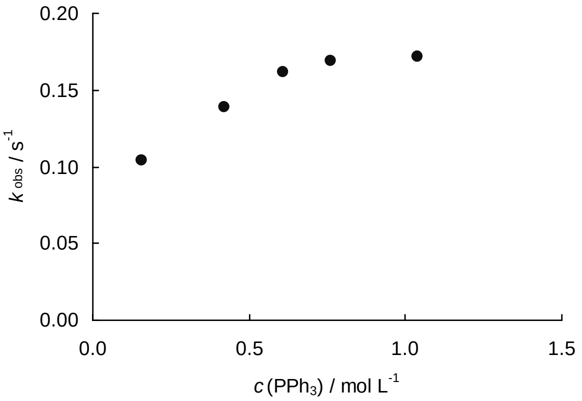
substrate concentration	**nucleophile**	**solvent**	**method**
[**1b**] = 6.1×10^{-3} mol L^{-1}	PPh_3	CH_2Cl_2	stopped-flow conductometry

No	$c(PPh_3)$ / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK90-1	0.177	4.51×10^{-1}	0.9986
NSK90-2	0.442	7.93×10^{-1}	0.9992
NSK90-3	0.573	8.96×10^{-1}	0.9993
NSK90-4	0.793	9.82×10^{-1}	0.9993
NSK90-5	1.052	**1.02**	0.9994
NSK90-6	1.393	9.75×10^{-1}	0.9996



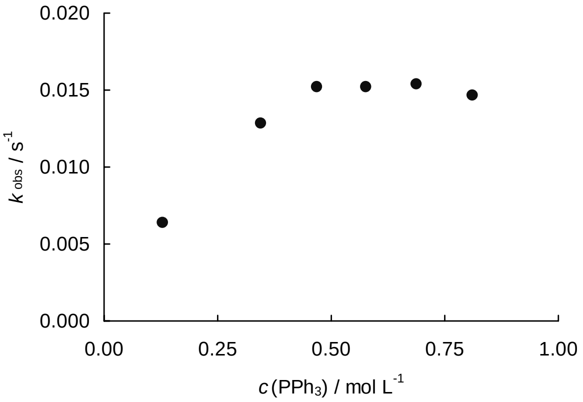
substrate concentration	**nucleophile**	**solvent**	**method**
[**1c**] = 6.1×10^{-3} mol L^{-1}	PPh_3	CH_2Cl_2	stopped-flow conductometry

No	$c(PPh_3)$ / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK89-1	0.156	1.04×10^{-1}	0.9991
NSK89-2	0.420	1.39×10^{-1}	0.9995
NSK89-3	0.607	1.62×10^{-1}	0.9995
NSK89-4	0.759	1.69×10^{-1}	0.9992
NSK89-5	1.04	**1.72×10^{-1}**	0.9996



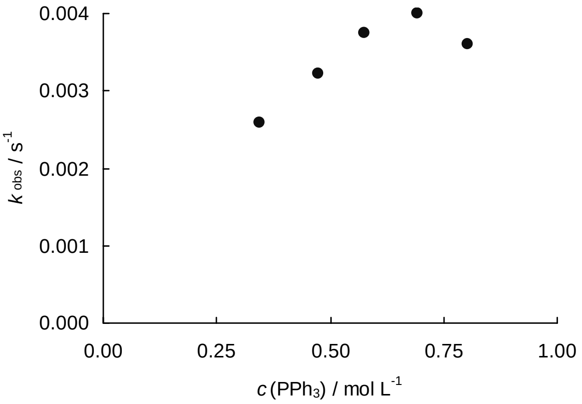
substrate concentration	**nucleophile**	**solvent**	**method**
[**1d**] = 6.0×10^{-4} mol L^{-1}	PPh_3	CH_2Cl_2	conventional conductometry

No	$c(PPh_3)$ / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK88-6	0.115	6.41×10^{-3}	0.9993
NSK88-1	0.345	1.28×10^{-2}	0.9973
NSK88-2	0.470	1.52×10^{-2}	0.9965
NSK88-3	0.577	1.52×10^{-2}	0.9952
NSK88-4	0.689	**1.54×10^{-2}**	0.9992
NSK88-5	0.812	1.46×10^{-2}	0.9990



substrate concentration	**nucleophile**	**solvent**	**method**
[**1e**] = 6.0×10^{-4} mol L^{-1}	PPh_3	CH_2Cl_2	conventional conductometry

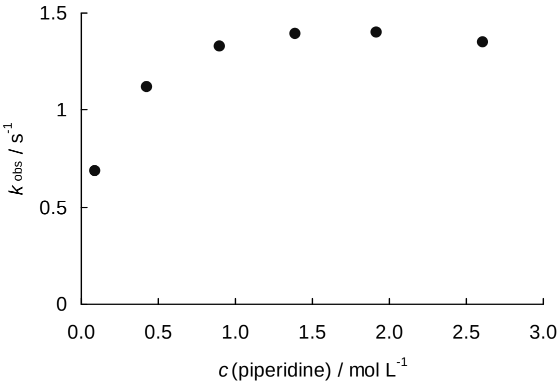
No	c(PPh_3) / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK87-3	0.345	2.59×10^{-3}	0.9989
NSK87-4	0.473	3.23×10^{-3}	0.9983
NSK87-5	0.576	3.75×10^{-3}	0.9938
NSK87-6	0.692	$\mathbf{4.00 \times 10^{-3}}$	0.9968
NSK87-7	0.802	3.60×10^{-3}	0.9980



Solvolysis Reactions of Benzhydryl Chlorides in Acetone

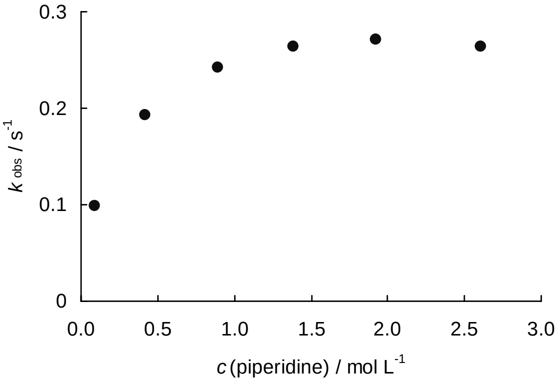
substrate concentration	**nucleophile**	**solvent**	**method**
[**1a**] = 6.1×10^{-3} mol L^{-1}	piperidine	acetone	stopped-flow conductometry

No	c(piperidine) / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK98-1	0.090	6.85×10^{-1}	0.9996
NSK98-2	0.413	1.12	0.9997
NSK98-3	0.897	1.33	0.9999
NSK98-4	1.390	1.39	0.9999
NSK98-5	1.922	**1.40**	0.9999
NSK98-6	2.605	1.35	0.9999



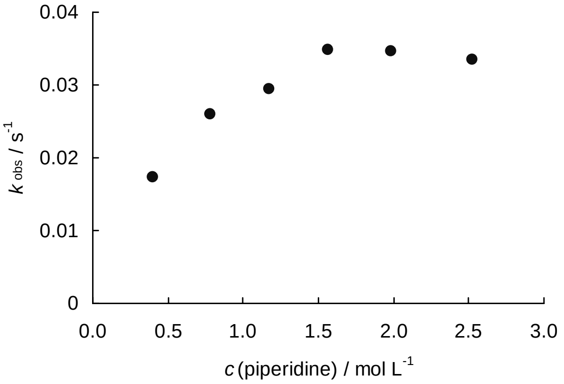
substrate concentration	**nucleophile**	**solvent**	**method**
[**1b**] = 6.1×10^{-3} mol L^{-1}	piperidine	acetone	stopped-flow conductometry

No	c(piperidine) / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK99-1	0.090	9.88×10^{-2}	0.9996
NSK99-2	0.413	1.93×10^{-1}	0.9999
NSK99-3	0.897	2.42×10^{-1}	0.9999
NSK99-4	1.390	2.64×10^{-1}	0.9999
NSK99-5	1.922	**2.71×10^{-1}**	0.9999
NSK99-6	2.605	2.64×10^{-1}	0.9999



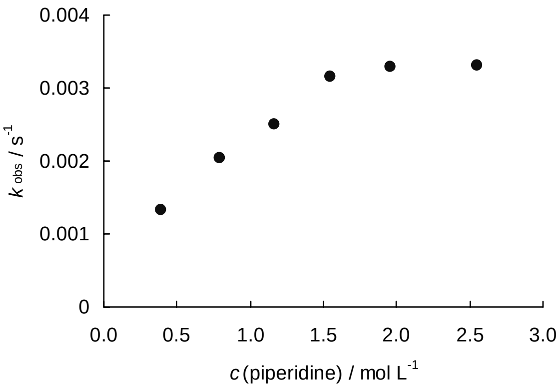
substrate concentration	**nucleophile**	**solvent**	**method**
[**1c**] = 6.1×10^{-3} mol L^{-1}	piperidine	acetone	conventional conductometry

No	c(piperidine) / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK100-1	0.404	1.74×10^{-2}	0.9961
NSK100-2	0.781	2.59×10^{-2}	0.9977
NSK100-3	1.176	2.94×10^{-2}	0.9986
NSK100-4	1.569	**3.49×10^{-2}**	0.9978
NSK100-5	1.983	3.46×10^{-2}	0.9970
NSK100-6	2.527	3.35×10^{-2}	0.9976



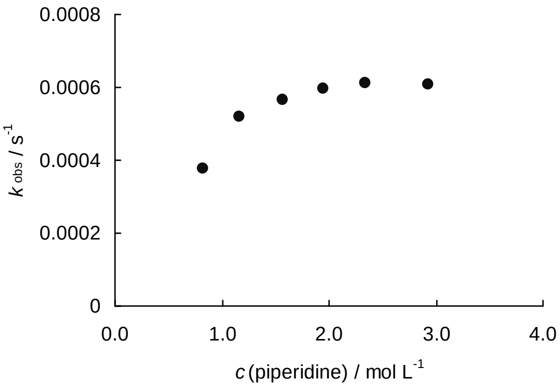
substrate concentration	**nucleophile**	**solvent**	**method**
[**1d**] = 6.1×10^{-3} mol L^{-1}	piperidine	acetone	conventional conductometry

No	*c*(piperidine) / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK101-1	0.388	1.32×10^{-3}	0.9988
NSK101-2	0.792	2.03×10^{-3}	0.9990
NSK101-3	1.170	2.50×10^{-3}	0.9990
NSK101-4	1.551	3.15×10^{-3}	0.9992
NSK101-5	1.954	3.29×10^{-3}	0.9991
NSK101-6	2.556	**3.31×10^{-3}**	0.9986



substrate concentration	**nucleophile**	**solvent**	**method**
[**1e**] = 6.1×10^{-3} mol L^{-1}	piperidine	acetone	conventional conductometry

No	*c*(piperidine) / mol L^{-1}	k_{obs} / s^{-1}	r^2
NSK102-1	0.828	3.76×10^{-4}	0.9993
NSK102-2	1.169	5.18×10^{-4}	0.9993
NSK102-3	1.565	5.66×10^{-4}	0.9991
NSK102-4	1.943	5.96×10^{-4}	0.9991
NSK102-5	2.337	**6.12×10^{-4}**	0.9992
NSK102-6	2.922	6.08×10^{-4}	0.9982



Chapter 5

A Practical Guide for Estimating Rates of Heterolysis Reactions

Streidl, N.; Denegri, B.; Kronja, O.; Mayr, H. *Acc. Chem. Res.* **2010**, accepted.

5.1 Introduction

A universally valid ranking of leaving group abilities does not exist. The same reasons that prevent the construction of general nucleophilicity and electrophilicity scales[1] also inhibit the construction of general nucleofugality and electrofugality scales. While it is well recognized that *absolute* ionization rates of substrates R–X are strongly affected by the nature of the solvent,[2,3] it has to be noted that also *relative* leaving group abilities of groups X^- (k_1, Scheme 5.1) are solvent-dependent.[4–6] Furthermore, ground-state effects, i.e., electronic as well as steric interactions between leaving groups and other substituents at the reaction center are variable (e. g. anomeric effect,[7–13] back strain[14–16]) and account for the dependence of the relative leaving group abilities of X^- on the nature of the electrofuges R^+. For these reasons, relative leaving group abilities have to be defined with respect to a certain solvent and a certain electrofuge.

Scheme 5.1: Simplified Solvolysis Scheme.

$$\text{R-X} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \text{R}^+ + \text{X}^- \xrightarrow[\text{HOSolv}]{k_{\text{solv}}} \text{R-OSolv} + \text{HX}$$

Even if it is acknowledged that neither general nucleofugality nor general electrofugality scales can exist, the question arises whether there is a way of estimating the order of magnitude of the ionization rate of a certain substrate R–X in a certain solvent.

The classical way of predicting the influence of solvents on solvolysis rate constants is the Winstein-Grunwald equation (5.1),[2] where k is the rate constant under consideration, k_0 is the rate constant in 80% aqueous ethanol, Y is the solvent ionizing power (defined as log k of *tert*-

butyl chloride), and *m* is a substrate-specific term, describing the sensitivity of the solvolysis rate constant on variation of the solvent ($m = 1$ for *tert*-butyl chloride).

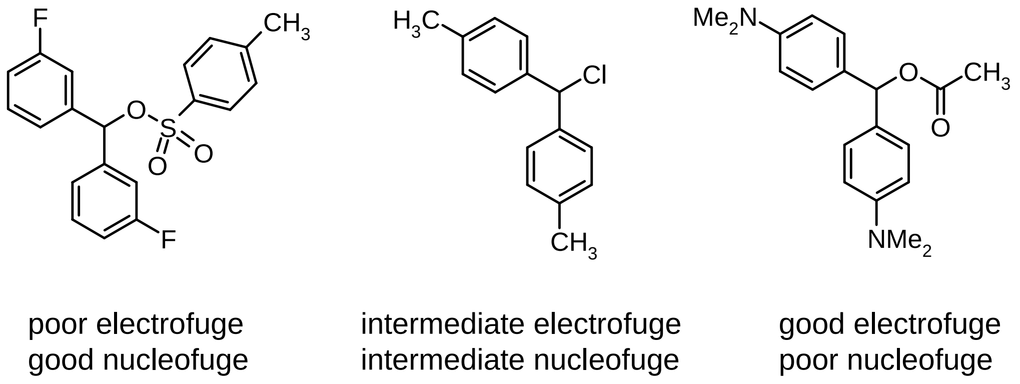
$$\log (k/k_0) = mY \tag{5.1}$$

Numerous alternative *Y*-scales have later been reported[5,17] to give better correlations with other types of substrates than the original *Y*-scale, which was based on the solvolysis rates of *tert*-butyl chloride. Without judging the merit of these correlations, it is obvious that they focus on relative rate constants and not on absolute ionization rates, which are needed in daily laboratory practice.

A couple of years ago, we have suggested to solve this problem by developing comprehensive nucleofugality and electrofugality scales,[18] using an approach similar to that which gave access to the most comprehensive nucleophilicity and electrophilicity scales presently available.[1,19] By defining differently substituted benzhydrylium ions as reference electrofuges, it was possible to keep the steric environment of the reaction center constant while varying the stabilization of the resulting benzhydrylium ions by many orders of magnitude.

As illustrated in Scheme 5.2, one can employ acceptor-substituted benzhydrylium ions as reference electrofuges for differentiating the nucleofugalities of good leaving groups, methyl- and methoxy-substituted benzhydrylium ions for comparing leaving groups of intermediate reactivity, and amino-substituted benzhydrylium ions for characterizing poor leaving groups.

Scheme 5.2: Substrates with Adjusted Electrofugal and Nucleofugal Properties.



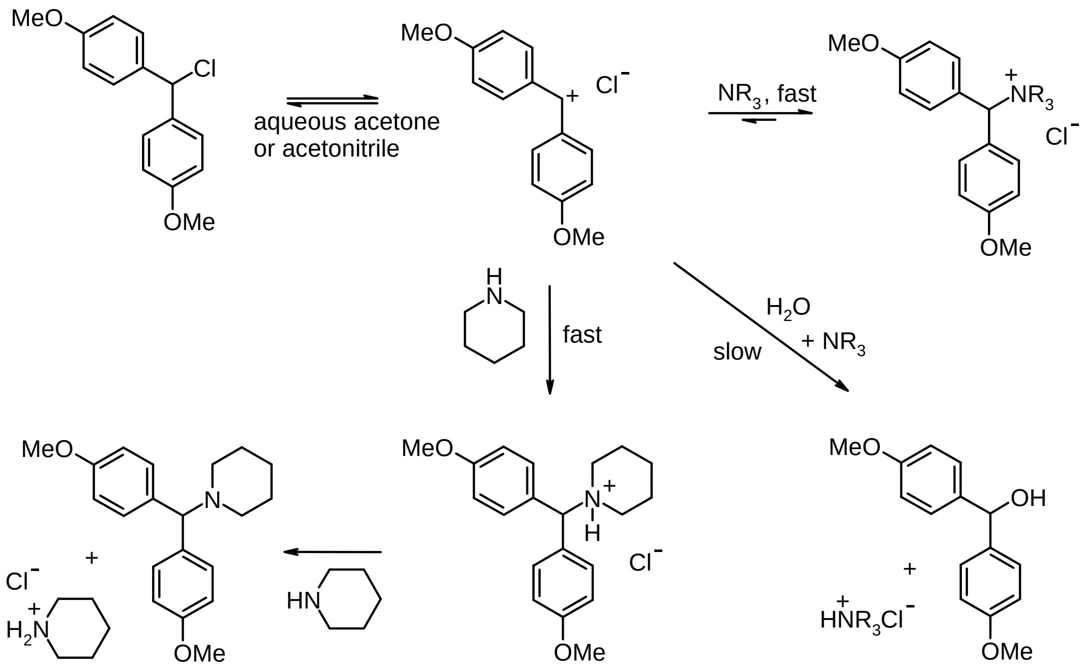
5.2 Determination of Ionization Rate Constants

Most rate constants reported in the literature are in the experimentally most easily accessible range between 10^{-2} and 10^{-5} s^{-1} (half-lives 1 min to 1 day). Since in conventional S_N1 reactions, a slow ionization step is followed by the fast trapping of the carbocation by the solvent, k_1 has usually been derived from the rate of formation of the acid HX,[20] which can be determined conductimetrically or titrimetrically as described in the literature.[21] Though this procedure disregards potential cation-anion combinations at the ion-pair stage, as demonstrated by Winstein and Goering with a variety of methods (e.g. racemization of optically active substrates or isotopomerization),[21–23] first-order rate constants referring to the rates of formation of HX are generally considered to be a good approximation for the ionization rate constants k_1 and are collected in Table S1 (Experimental Section).

Problems arise, however, when solvolyses of substrates are investigated which give rise to the formation of highly stabilized carbocations. As already noted by Ingold,[24] deviations from first-order kinetics are observed in such cases, because now also diffusionally equilibrated carbocations R^+ are not quantitatively trapped by the solvent but can recombine with the leaving group X^- (external ion return). Since the concentration of X^- increases during the course of the reaction, the degree of reversibility increases with the degree of conversion and causes the deviation from first-order kinetics.[24,25]

While external ion return has commonly been suppressed by N_3^- additives,[21] we have recently reported that suppression of external ion return can also be achieved by adding nucleophilic amines, which quantitatively trap the intermediate carbenium ions without turning on the S_N2 mechanism (Scheme 5.3).[26a] This procedure offers the great advantage over the azide method that now the rates of the reactions can be monitored conductimetrically, because ionic products are formed from covalent precursors. By using stopped-flow techniques it is thus possible to easily determine ionization rate constants on the millisecond time scale, which provides access to a barely investigated field of carbocation chemistry.[27] Another great advantage of this method is that it is also applicable for the determination of ionization rates in aprotic solvents that are not capable of trapping the intermediate carbocation.[26b]

Scheme 5.3: Heterolysis of 4,4′-Dimethoxybenzhydryl Chloride in Aqueous Solutions of Secondary and Tertiary Amines.



As shown in Figure 5.1, the conductimetrically measured rate constants for the solvolyses of 4,4′-dimethoxybenzhydryl chloride in 90% aqueous acetone, which were determined in a stopped-flow instrument by mixing a solution of the benzhydryl chloride in acetone with a solution of the amines in aqueous acetone, increase significantly with increasing concentrations of DABCO, pyridine, DMAP, or triethylamine. From the levelling of k_{obs} at 13.6–17.4 s^{-1}, corresponding to half-lives of 40–51 ms, we have excluded the occurrence of S_N2 reactions. A slightly higher limiting rate constant was observed when piperidine was added to trap the intermediate carbenium ions ($k_{\text{obs}} = 25.0\ s^{-1}$). 2,6-Lutidine, a stronger base than pyridine, does not increase the conductimetric rate constant, indicating that the amines do not act as Brønsted bases. We, therefore, concluded that nucleophilic amines suppress common-ion return by trapping the intermediate carbenium ions and formation of benzhydryl ammonium ions as depicted in Scheme 5.3.

The similar, but not identical heights of the plateaus observed with different amines indicate that the collapse of ion-pairs, in contrast to external ion return, cannot be completely suppressed by the amines. It should be noted that the plateau for pyridine is somewhat higher than that of the 10^3 times stronger nucleophile DMAP.[26] As the reactions of the 4,4′-dimethoxybenzhydryl cation with these amines are diffusion-limited,[1,26] the relative nucleophilicities of the amines are not relevant for the rate of trapping the carbocations.

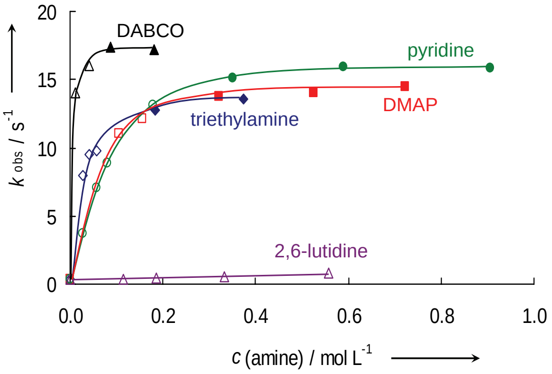
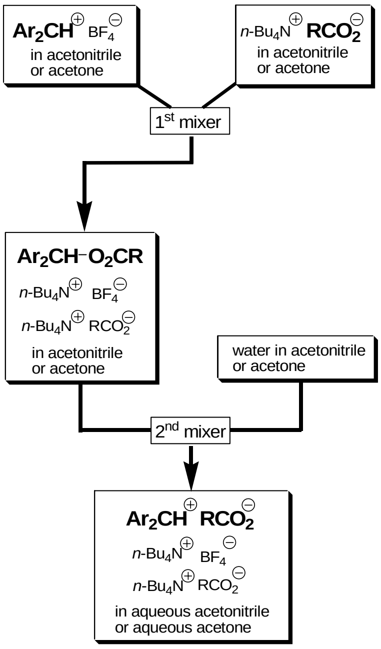


Figure 5.1: Observed rate constants of the solvolysis of 4,4′-dimethoxybenzhydryl chloride (0.018 M^{-1}) in 90% aqueous acetone (90A10W) in the presence of variable concentrations of amines (open symbols represent kinetics that are not of first-order).

A further experimental technique has been developed for studying the ionization rates of benzhydrylium carboxylates $Ar_2CH–O_2CR$, which are derived from highly stabilized benzhydrylium ions. Due to the low stability of these esters, they cannot be isolated in substance, and the double-mixing-technique illustrated in Scheme 5.4 was employed to determine their ionization rates.[28]

Scheme 5.4: Generation and Subsequent Ionization of Benzhydryl Carboxylates in a Double-Mixing Stopped Flow Spectrometer.



In the first mixer of a stopped-flow instrument, a solution of $Ar_2CH^+BF_4^-$ in acetonitrile or acetone was combined with a solution of 1 to 100 equivalents of $n$$Bu_4N^+RCO_2^-$ in the same solvent. The colorless solution thus obtained was then combined with an equal volume of aqueous acetonitrile or acetone in a second mixer. In the resulting aqueous acetone or acetonitrile solution, the covalent ester $Ar_2CH–O_2CR$ ionizes and gives rise to the formation of the colored benzhydrylium ion, which is monitored photometrically. As described in the original article,[28] salt effects on the rates of ionization are negligible in the concentration ranges investigated in line with the observations by Hojo.[29] This method allows the determination of ionization rates in solvent mixtures, but not in pure solvents.

Ionization rate constants, which have either been determined by us or have been collected from the literature are listed in Table S1 of the Experimental Section.

5.3 Correlation Analysis

The most comprehensive nucleophilicity scale presently available is based on equation (5.2), where electrophiles are characterized by one parameter (E) and nucleophiles are characterized by two (N and s).[1,19,30]

$$\log k\ (20\ °\mathrm{C}) = s(N + E) \qquad (5.2)$$

It has been demonstrated, that the nucleophile-specific, solvent dependent parameters N and s, which are generally derived from the rates of the reactions of the nucleophiles under consideration with benzhydrylium ions of variable electrophilicity can be employed to predict rate constants for the reactions of a variety of carbenium ions and Michael acceptors with π-, n- and σ-nucleophiles.[1,19,30]

A couple of years ago, eq (5.3) which is not only formally analogous to eq (5.2), has been suggested to correlate ionization rate constants of substrates with widely variable structure.[18] In analogy to eq (5.2), eq (5.3) characterizes electrofuges by one parameter (E_f) and nucleofuges by two (N_f, s_f). As solvent variation affects the leaving group abilities of different groups X^- quite differently, the nucleofuge-specific parameters N_f and s_f are generally defined for combinations of leaving groups and solvents, e.g. for Cl^- in EtOH or for $CH_3CO_2^-$ in 60%

aqueous acetonitrile. As most solvolysis rate constants have been measured at 25 °C, the reference temperature for eq (5.3) differs from that for eq (5.2).

$$\log k\ (25\ °\mathrm{C}) = s_\mathrm{f}(N_\mathrm{f} + E_\mathrm{f}) \tag{5.3}$$

A set of 39 benzhydrylium ions **E1-E39** have been selected as reference electrofuges (Table 5.1), and combinations of common leaving groups, for example *p*-tosylate (OTs), bromide, chloride, trifluoroacetate, 3,5-dinitrobenzoate (DNB), 4-nitrobenzoate (PNB), benzoate (OBz), and acetate (OAc) with commonly used solvents were defined as reference nucleofuges (**N1-N101** in protic solvents, **N102-N110** in aprotic solvents, Table 5.2). Solvolysis rate constants of substrates composed of the electrofuges **E1-E39** and the nucleofuges **N1-N110** are listed in Table S1 (Experimental Section).

Table 5.1: Reference Electrofuges.

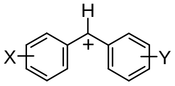
	Electrofuges 		Nucleofuges used for the characterization	Electro-fugality E_f
No.	X =	Y =		
E1	3,5-Cl_2	3,5-Cl_2	**N1, N3, N4, N12**	–12.93
E2	3,5-F_2	3,5-F_2	**N1, N2, N3, N4, N5, N8**	–12.60
E3	3,5-Cl_2	3-Cl	**N1, N3, N4, N6, N12, N14, N19**	–11.20
E4	3,5-F_2	3-F	**N1, N2, N3, N4, N5, N6, N8, N9, N10, N11, N12**	–10.88
E5	3-Cl	3-Cl	**N3, N4, N6, N7, N12, N14, N19**	–9.55
E6	3-F	3-F	**N2, N3, N4, N5, N6, N7, N8, N9, N10, N11, N12, N14, N16, N19**	–9.26
E7	4-NO_2	H	**N13, N14, N17, N20, N21, N22, N26**	–9.20
E8	3-Cl	4-Cl	**N3, N4, N6, N7, N12, N14, N15, N19, N20, N21, N22**	–8.15
E9	3-Cl	H	**N3, N4, N12, N13, N14, N17, N19, N20, N21, N22, N26, N27, N29, N30, N31, N34**	–7.69
E10	3-F	H	**N2, N4, N5, N6, N7, N9, N10, N11, N13, N14, N16, N19, N23**	–7.53
E11	4-Cl	4-Cl	**N12, N14, N15, N17, N19, N20, N21, N22, N23, N24, N27**	–6.91
E12	4-Br	H	**N17, N20, N22, N27**	–6.62
E13	4-Cl	H	**N14, N15, N17, N18, N20, N21, N22, N27, N29, N30, N31, N32, N34, N35, N36, N37, N39, N40, N41**	–6.44
E14	H	H	**N7, N12, N13, N14, N15, N16, N17, N18, N19, N20, N21, N22, N23, N24, N25, N26, N27, N28, N29, N30, N31, N32, N33, N34, N35, N36, N37, N38, N39, N40, N41, N43, N44, N45, N46, N47, N48, N49, N50, N51, N52, N53, N69, N81**	–6.03
E15	3-Me	H	**N17, N20, N21, N22, N27**	–5.73

Table 5.1: *Continued.*

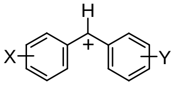
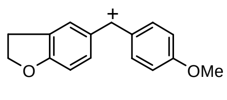
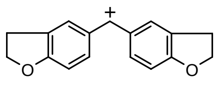
	Electrofuges 		Nucleofuges used for the characterization	Electro-fugality E_f
No.	X =	Y =		
E16	4-F	H	**N13, N14, N15, N17, N18, N20, N21, N22, N27, N28, N29, N30, N31, N32, N33, N34, N35, N36, N37, N38, N39, N40, N41, N42, N43, N44, N45, N46, N47, N48, N49, N50, N51, N52, N53**	–5.72
E17	4-OPh	4-NO_2	**N13, N14, N15, N17, N19, N20, N21, N22, N26, N27**	–5.60
E18	3,5-Me_2	H	**N17, N20, N21, N22, N27**	–5.43
E19	4-Me	H	**N15, N16, N17, N18, N20, N21, N22, N23, N24, N25, N26, N27, N28, N30, N31, N32, N33, N34, N35, N36, N37, N38, N39, N40, N41, N42, N43, N44, N45, N46, N47, N48, N49, N50, N51, N52, N53, N54, N55, N56, N58, N59**	–4.63
E20	4-OPh	H	**N17, N18, N22, N27**	–3.52
E21	4-Me	4-Me	**N18, N22, N23, N24, N25, N27, N28, N36, N37, N38, N41, N42, N45, N47, N48, N49, N51, N52, N53, N54, N55, N56, N57, N58, N59, N60, N61, N62, N63, N64, N81**	–3.44
E22	4-OMe	H	**N23, N24, N25, N26, N27, N28, N49, N54, N55, N56, N57, N58, N59, N60, N61, N62, N63, N64, N65, N66, N69, N71, N72, N73, N74, N75, N76, N77, N78, N79, N81, N87, N89, N102, N103**	–2.09
E23	4-OMe	4-Me	**N26, N27, N28, N55, N56, N57, N58, N59, N60, N61, N62, N63, N64, N65, N66, N69, N70, N71, N72, N73, N74, N75, N76, N77, N78, N79, N80, N81, N87, N88, N89, N102, N103, N104, N106, N107, N108, N109, N110**	–1.32
E24	4-OMe	4-OPh	**N24, N25, N26, N27, N28, N57, N60, N61, N64, N65, N66, N69, N70, N71, N72, N73, N74, N75, N76, N77, N80, N81, N87, N88, N89, N90, N91, N92, N93, N102, N103, N104, N105, N106, N107, N108, N109, N110**	–0.86
E25	4-OMe	4-OMe	**N25, N27, N28, N65, N66, N67, N69, N70, N71, N72, N73, N74, N75, N76, N77, N78, N79, N80, N81, N82, N83, N84, N87, N88, N89, N90, N91, N92, N93, N99, N102, N103, N104, N105, N106, N107, N108, N109, N110**	0.00
E26			**N28, N67, N68, N69, N70, N76, N77, N78, N79, N80, N82, N83, N84, N85, N86, N87, N88, N89, N90, N91, N92, N93, N94, N96, N98, N100, N102, N103, N104, N105, N106, N107, N108, N109, N110**	0.61
E27			**N28, N67, N68, N69, N70, N78, N79, N80, N82, N83, N84, N85, N86, N88, N89, N90, N91, N92, N93, N94, N96, N98, N99, N100, N101, N102, N103, N104, N105, N106, N107, N108, N109, N110**	1.07
E28	4-$N(Ph)_2$	4-$N(Ph)_2$	**N95, N97, N98, N99, N101**	1.78
E29	4-$N(CH_2CF_3)(Ph)$	4-$N(CH_2CF_3)(Ph)$	**N98, N99, N100, N101**	1.79

Table 5.1: *Continued.*

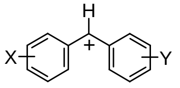
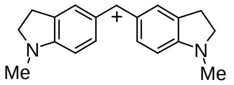
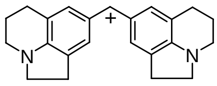
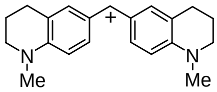
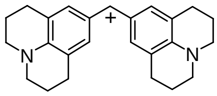
No.	Electrofuges  X =	Y =	Nucleofuges used for the characterization	Electro-fugality E_f
E30	4-$N(CH_3)_2$	H	**N94, N95, N96, N98, N99, N100, N101**	2.38
E31	4-$N(CH_2CH_2)_2O$	4-$N(CH_2CH_2)_2O$	**N84, N94, N95, N96, N97, N98, N99, N100, N101**	3.03
E32	4-$N(CH_2CF_3)(CH_3)$	4-$N(CH_2CF_3)(CH_3)$	**N94, N95, N96, N97, N98, N99, N100, N101**	3.13
E33	4-N(Ph)(CH_3)	4-N(Ph)(CH_3)	**N84, N85**	3.46
E34			**N85, N86, N94, N95, N96, N97, N98, N99, N100, N101**	4.83
E35	4-$N(CH_3)_2$	4-$N(CH_3)_2$	**N69, N70, N84, N85, N86, N94, N95, N96, N97, N98, N99, N100, N101**	4.84
E36			**N85, N86, N94, N95, N96, N97, N98, N99, N100, N101**	5.05
E37			**N86, N94, N95, N96, N97, N98, N99, N100, N101**	5.22
E38	4-$N(CH_2)_4$	4-$N(CH_2)_4$	**N70, N84, N85, N86, N94, N95, N96, N97, N98, N99, N100, N101**	5.35
E39			**N85, N86, N94, N95, N96, N97, N98, N99, N100, N101**	5.61

Table 5.2: Reference Nucleofuges.

Entry	Leaving group[a]	Solvent[b]	Electrofuges used for the characterization	N_f	s_f
N1	OTs	TFE	**E1, E2, E3, E4**	9.73	0.94
N2		M	**E2, E4, E6, E10**	7.33	0.82
N3		80E20W	**E1, E2, E3, E4, E5, E6, E8, E9**	7.45	0.80
N4		E	**E1, E2, E3, E4, E5, E6, E8, E9, E10**	6.09	0.78
N5		60AN40W	**E2, E4, E6, E10**	7.97	0.82
N6		80A20W	**E3, E4, E5, E6, E8, E10**	6.00	0.83
N7		90A10W	**E5, E6, E8, E10, E14**	5.38	0.89
N8	OMs	80E20W	**E2, E4, E6**	7.49	0.84
N9		E	**E4, E6, E10**	5.82	0.80
N10		60AN40W	**E4, E6, E10**	7.70	0.83
N11		80A20W	**E4, E6, E10**	5.85	0.84
N12	Br	TFE	**E1, E3, E4, E5, E6, E8, E9, E11, E14**	6.19	0.95
N13		M	**E7, E9, E10, E14, E16, E17**	4.23	0.99
N14		80E20W	**E3, E5, E6, E7, E8, E9, E10, E11, E13, E14, E17, E16**	4.36	0.95
N15		E	**E8, E11, E13, E14, E16, E17, E19**	2.93	0.93
N16		60AN40W	**E6, E10, E14, E19**	5.23	0.99
N17		80A20W	**E7, E9, E11, E12, E13, E14, E15, E16, E17, E18, E19, E20**	3.01	0.90
N18		90A10W	**E13, E14, E16, E19, E20, E21**	2.29	1.01
N19	Cl	TFE	**E3, E5, E6, E8, E9, E10, E11, E14, E17**	5.54	0.85
N20		M	**E7, E8, E9, E11, E12, E13, E14, E15, E16, E17, E18, E19**	2.91	0.99
N21		80E20W	**E7, E8, E9, E11, E13, E14, E15, E16, E17, E18, E19**	3.24	0.99

Table 5.2: *Continued.*

Entry	Leaving group[a]	Solvent[b]	Electrofuges used for the characterization	N_f	s_f
N22		E	**E7, E8, E9, E11, E12, E13, E14, E15, E16, E17, E18, E19, E20, E21**	1.82	1.00
N23		60AN40W	**E10, E11, E14, E19, E21, E22**	3.84	0.96
N24		80AN20W	**E11, E14, E19, E21, E22, E24**	2.96	1.00
N25		90AN10W	**E14, E19, E21, E22, E24, E25**	2.23	1.08
N26		60A40W	**E7, E9, E14, E17, E19, E22, E23, E24**	3.30	0.97
N27		80A20W	**E9, E11, E12, E13, E14, E15, E16, E17, E18, E19, E20, E21, E22, E23, E24, E25**	2.03	1.05
N28		90A10W	**E14, E16, E19, E21, E22, E23, E24, E25, E26, E27**	1.14	1.11
N29	HFB	60M40W	**E9, E13, E14, E16**	3.06	0.84
N30		70M30W	**E9, E13, E14, E16, E19**	2.71	0.84
N31		80M20W	**E9, E13, E14, E16, E19**	2.33	0.84
N32		90M10W	**E13, E14, E16, E19**	2.09	0.89
N33		M	**E14, E16, E19**	1.52	0.90
N34		60E40W	**E9, E13, E14, E16, E19**	2.30	0.86
N35		70E30W	**E13, E14, E16, E19**	1.99	0.86
N36		80E20W	**E13, E14, E16, E19, E21**	1.80	0.88
N37		90E10W	**E13, E14, E16, E19, E21**	1.37	0.88
N38		E	**E14, E16, E19, E21**	0.77	0.93
N39		50A50W	**E13, E14, E16, E19**	2.31	0.87
N40		60A40W	**E13, E14, E16, E19**	1.86	0.88
N41		70A30W	**E13, E14, E16, E19, E21**	1.52	0.91
N42		80A20W	**E16, E19, E21**	1.01	0.91
N43	TFA	70M30W	**E14, E16, E19**	2.47	0.81
N44		80M20W	**E14, E16, E19**	2.13	0.83
N45		90M10W	**E14, E16, E19, E21**	1.75	0.84
N46		60E40W	**E14, E16, E19**	2.11	0.82
N47		70E30W	**E14, E16, E19, E21**	1.83	0.84
N48		80E20W	**E14, E16, E19, E21**	1.42	0.82
N49		E	**E14, E16, E19, E21, E22**	0.34	0.89
N50		50A50W	**E14, E16, E19**	2.03	0.81
N51		60A40W	**E14, E16, E19, E21**	1.66	0.86
N52		70A30W	**E14, E16, E19, E21**	1.23	0.88
N53		80A20W	**E14, E16, E19, E21**	0.65	0.88
N54		90A10W	**E19, E21, E22**	0.21	0.97
N55	$PhOCO_2$	80M20W	**E19, E21, E22, E23**	–0.33	0.81
N56		90M10W	**E19, E21, E22, E23**	–0.61	0.85
N57		M	**E21, E22, E23, E24**	–0.95	0.90
N58		60E40W	**E19, E21, E22, E23**	–0.40	0.81
N59		70E30W	**E19, E21, E22, E23**	–0.57	0.85
N60		80E20W	**E21, E22, E23, E24**	–0.74	0.90
N61		90E10W	**E21, E22, E23, E24**	–0.91	0.96
N62		50A50W	**E21, E22, E23**	–1.06	0.77
N63		60A40W	**E21, E22, E23**	–1.39	0.83
N64		70A30W	**E21, E22, E23, E24**	–1.73	0.88
N65	DNB	80E20W	**E22, E23, E24, E25**	–1.43	0.98
N66		E	**E22, E23, E24, E25**	–2.05	1.09
N67		60AN40W	**E25, E26, E27**	–2.06	0.97
N68		60A40W	**E22**[c]**, E23**[c]**, E24**[c]**, E25**[c]**, E26, E27**	–2.20	0.90
N69		80A20W	**E14, E22, E23, E24, E25, E26, E27, E35**	–2.34	1.10
N70		90A10W	**E23, E24, E25, E26, E27, E35, E38**	–2.68	1.13
N71	$MeOCO_2$	80M20W	**E22, E23, E24, E25**	–1.43	0.94
N72		90M10W	**E22, E23, E24, E25**	–1.66	0.97
N73		M	**E22, E23, E24, E25**	–2.00	1.01
N74		60E40W	**E22, E23, E24, E25**	–1.59	0.89
N75		70E30W	**E22, E23, E24, E25**	–1.74	0.93

Table 5.2: *Continued.*

Entry	Leaving group[a]	Solvent[b]	Electrofuges used for the characterization	N_f	s_f
N76		80E20W	**E22, E23, E24, E25, E26**	–1.96	0.95
N77		90E10W	**E22, E23, E24, E25, E26**	–2.20	0.98
N78		50A50W	**E22, E23, E25, E26, E27**	–2.13	0.86
N79		60A40W	**E22, E23, E25, E26, E27**	–2.56	0.88
N80		70A30W	**E23, E24, E25, E26, E27**	–2.83	0.94
N81	PNB	80E20W	**E14, E21, E22, E23, E24, E25**	–2.78	0.95
N82		60AN40W	**E25, E26, E27**	–3.30	0.91
N83		80AN20W	**E25, E26, E27**	–3.41	0.98
N84		60A40W	**E25, E26, E27, E31, E33, E35, E38**	–2.79	1.11
N85		80A20W	**E26, E27, E33, E34, E35, E36, E38, E39**	–3.40	1.16
N86		90A10W	**E26, E27, E34, E35, E36, E37, E38, E39**	–3.70	1.17
N87	^{i}BuOCO$_2$	60E40W	**E22, E23, E24, E25, E26**	–2.04	0.89
N88		90E10W	**E23, E24, E25, E26, E27**	–2.46	0.98
N89		50A50W	**E22, E23, E24, E25, E26, E27**	–2.51	0.87
N90	^{t}BuOCO$_2$	60E40W	**E24, E25, E26, E27**	–2.91	0.89
N91		80E20W	**E24, E25, E26, E27**	–3.12	0.96
N92		60AN40W	**E24, E25, E26, E27**	–3.28	0.96
N93		60A40W	**E24, E25, E26, E27**	–3.62	0.94
N94	BzO	60AN40W	**E26, E27, E30, E31, E32, E34, E35, E36, E37, E38, E39**	–3.92	1.02
N95		80AN20W	**E28, E30, E31, E32, E34, E35, E36, E37, E38, E39**	–4.19	1.12
N96		60A40W	**E26, E27, E30, E31, E32, E34, E35, E36, E37, E38, E39**	–3.89	1.15
N97		80A20W	**E28, E31, E32, E34, E35, E36, E37, E38, E39**	–4.46	1.17
N98	AcO	60AN40W	**E26, E27, E28, E29, E30, E31, E32, E34, E35, E36, E37, E38, E39**	–4.18	1.08
N99		80AN20W	**E25, E27, E28, E29, E30, E31, E32, E34, E35, E36, E37, E38, E39**	–4.52	1.11
N100		60A40W	**E26, E27, E29, E30, E31, E32, E34, E35, E36, E37, E38, E39**	–4.05	1.17
N101		80A20W	**E27, E28, E29, E30, E31, E32, E34, E35, E36, E37, E38, E39**	–4.73	1.18
N102	Cl	DMSO	**E22, E23, E24, E25, E26, E27**	0.35	1.30
N103		CH_3CN	**E22, E23, E24, E25, E26, E27**	0.30	1.39
N104		PC	**E23, E24, E25, E26, E27**	0.10	1.35
N105		$CHCl_3$	**E24, E25, E26, E27**	–0.18	1.25
N106		DMF	**E23, E24, E25, E26, E27**	–0.28	1.39
N107		CH_2Cl_2	**E23, E24, E25, E26, E27**	–0.57	1.28
N108		DMAc	**E23, E24, E25, E26, E27**	–0.82	1.33
N109		NMP	**E23, E24, E25, E26, E27**	–0.98	1.31
N110		acetone	**E23, E24, E25, E26, E27**	–1.00	1.38

[a] HFB = heptafluorobutyrate, TFA = trifluoroacetate, DNB = 3,5-dinitrobenzoate, PNB = 4-nitrobenzoate. [b] Mixtures of solvents are given as (v/v); A = acetone, AN = acetonitrile, E = ethanol, M = methanol, TFE = 2,2,2-trifluoroethanol, W = water, PC = propylene carbonate, DMF = dimethylformamide, DMAc = dimethylacetamide, NMP = *N*-methyl-2-pyrrolidinone. [c] Rate constants have not been available when the least-square minimization of the whole data set was performed.

The electrofugality of the 4,4′-dimethoxybenzhydrylium ion **E25** was defined as zero, E_f(**E25**) = 0.0, and the slope for Cl^- in EtOH was set to one, s_f(**N22**) = 1.0. With these fixations, the first-order rate constants listed in Table S1 (Experimental Section) were subjected to a least-squares fit according to eq (5.3), and $\Sigma\Delta^2$ as defined in eq (5.4) was minimized to yield the optimized parameters E_f (Table 5.1) as well as N_f and s_f (Table 5.2).[31]

Slight deviations of these parameters from previously published values are due to the extended data basis for the new parameters.

$$\Sigma\Delta^2 = \Sigma(\log k_{\mathrm{solv}} - \log k_{\mathrm{calc}})^2 = \Sigma(\log k_{\mathrm{solv}} - s_{\mathrm{f}}(N_{\mathrm{f}} + E_{\mathrm{f}}))^2 \qquad (5.4)$$

The good fit of these correlations is illustrated by Figure 5.2, and the small deviations between calculated and experimental rate constants (average factor of 1.1) are listed in Table S1 (Experimental Section).

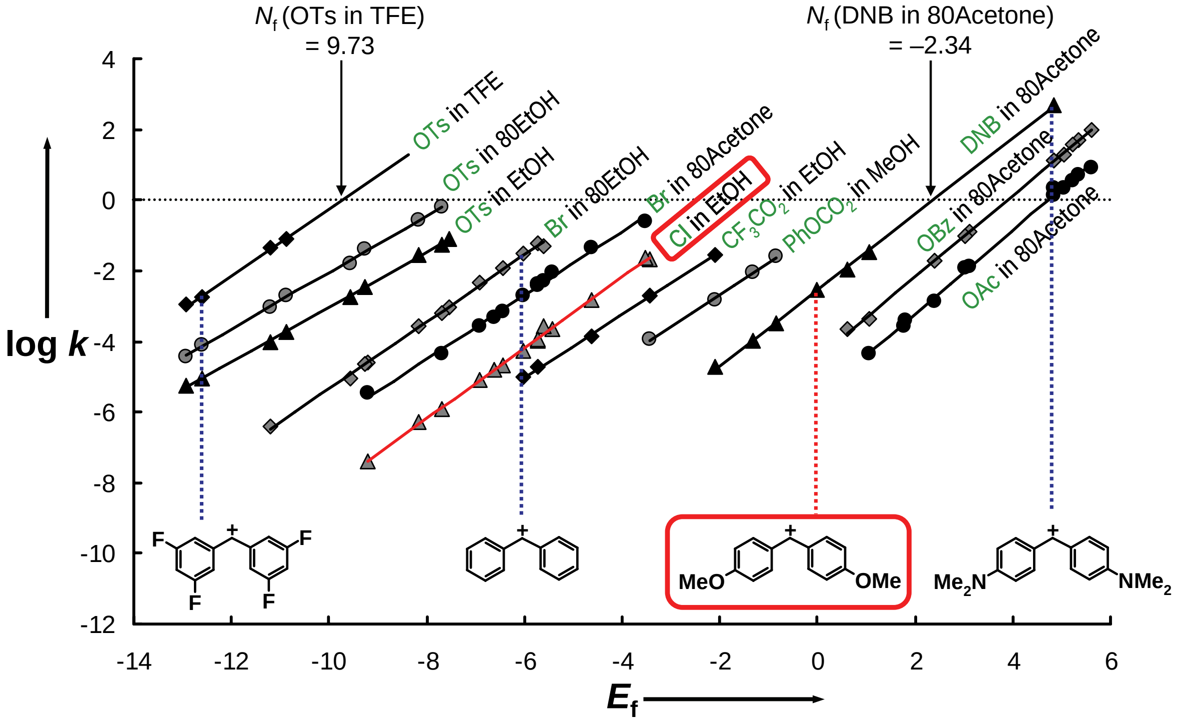


Figure 5.2: Plots of solvolysis rate constants log *k* (at 25 °C) for benzhydryl halides and various esters vs. the electrofugality parameters of benzhydrylium ions (Determination of N_{f} as the negative intercepts on the abscissa and s_{f} as the slopes of the correlations). – 80EtOH and 80Acetone correspond to 80E20W and 80A20W, TFE = 2,2,2-trifluoroethanol.

In cases where different solvolysis rate constants were reported for the same substrate under the same conditions, and we were unable to unequivocally select one or the other, we generally used that rate constant for the final correlation which agreed best with the value calculated by eq (5.3).

Like eq (5.2), eq (5.3) is an untypical format of a linear free energy relationship. As both, N_f and s_f, are nucleofuge-specific parameters, eq (5.3) is equivalent to eq (5.5) where E_f and s_f are the same as in eq (5.2) and $N_f' = s_f N_f$.

$$\log k\ (25\ °\mathrm{C}) = N_f' + s_f E_f \qquad (5.5)$$

What is the difference between eqs (5.3) and (5.5)? None, if one is going to calculate ionization rate constants log *k* from either N_f, s_f and E_f (eq 5.3) or from N_f', s_f and E_f (eq 5.5)! It is trivial that a straight line can alternatively be expressed by the intercept on the y-axis (N_f' in eq 5.5) or on the x-axis (N_f in eq 5.3). As the authors are aware of the difficulties, which some readers have with the unconventional form of eq (5.3),[32] ref. 33 explains in detail why it is more practical to use eq (5.3) instead of eq (5.5).

5.4 Electrofugalities of Benzhydrylium Ions

Figure 5.3 shows a linear correlation between the electrofugality parameters and $\Sigma\sigma^+$. In line with previous investigations of Tsuno and Fujio,[34] highly unsymmetrically substituted systems deviate positively from the correlation line, because in these cases the aryl ring with the weaker electron donor is twisted out of the plane and allows the aryl ring with the better electron donor to get into full conjugation with the carbenium center.

As σ^+ values for annelated nitrogen rings have not been derived from cumyl solvolyses but were calculated indirectly from the electrophilicities of the benzhydrylium ions **E28-E39**,[19] these substituents are not included in the Hammett-correlation of Figure 5.3. Instead, the effect of these strong donor groups will directly be analyzed by the correlation between electrofugality and electrophilicity (Figure 5.4).

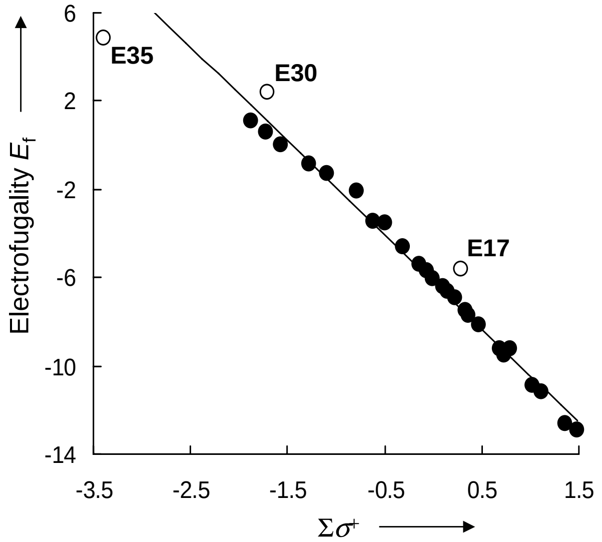


Figure 5.3: Correlation of the electrofugality parameters E_f of benzhydrylium ions (**E1-E27**, Table 5.1) with Hammett σ constants (from ref.[35,36]). $E_f = -4.26\Sigma\sigma^+ - 6.19$, $n = 27$, r^2=0.9916; the deviating points (o) are not included in the correlation.

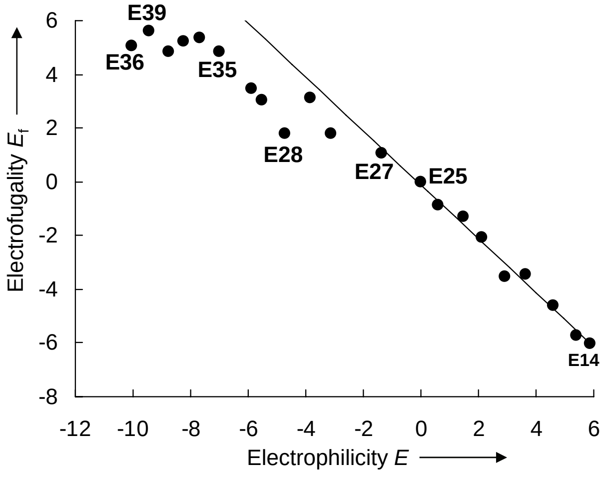


Figure 5.4: Correlation between electrophilicity (from ref.[19]) and electrofugality.

One can recognize a linear correlation between E_f and E in the right part of Figure 5.4, which refers to methyl and alkoxy-substituted benzhydrylium ions ($-2 < E < 6$). In this range, ionization rates (as expressed by E_f) decrease linearly with increasing electrophilic reactivity (E). The linear correlation breaks down for amino-substituted benzhydrylium ions ($E < -2$). The bis(dihydrofuranyl)-substituted benzhydrylium ion **E27**, for example, reacts 10^3 times faster with nucleophiles than the bis(diphenylamino)-substituted analogue **E28**, but the rates of their formation by ionization of the corresponding carboxylates differ by only a factor of 5. Furthermore, benzhydrylium ions **E35** and **E36**, which differ by almost three orders of magnitude in electrophilicity, are generated with almost identical rates (comparable electrofugality).

An alternative illustration of the breakdown of the correlation between E_f and E is presented in Figure 5.5 which compares two series of directly measured rate constants. One can clearly see that the rates of the reactions of the benzhydrylium ions **E34-E39** with 4-methylimidazole[37] (the same is true for reactions with any other nucleophile) do not give any information about the relative rates of ionization of the corresponding benzhydryl acetates.

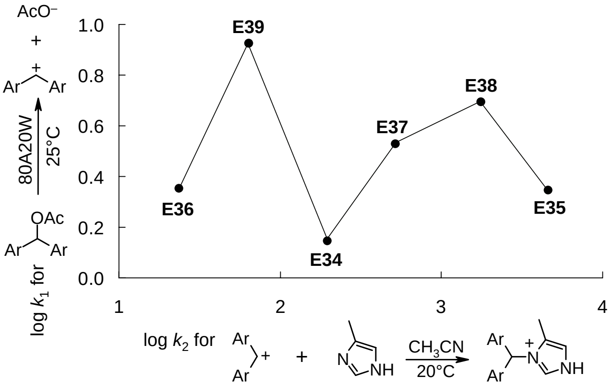


Figure 5.5: Plot of the first-order rate constants log k_1 for the solvolysis reactions of benzhydryl acetates in 80 % aqueous acetone versus the second-order rate constants log k_2 of the combination reactions of benzhydrylium ions with 4-methylimidazole (from ref. 37).

Why are electrofugalities not always inversely correlated with electrophilicities? Figure 5.6 shows that the Gibbs energy diagrams for the hydrolyses of methyl- and dimethylamino-substituted benzhydryl derivatives, which proceed with similar rates, differ significantly. Whereas the transition state of the ionization of 4,4-dimethylbenzhydryl chloride (**E21-Cl**) is carbocation-like, the transition state of the ionization of the bis(dimethylaminophenyl)methyl acetate (**E35-OAc**) is not carbocation-like. In order to compare ionization processes of similar rates, the change from less to more stabilized carbocations has to be accompanied by a change from good to weak leaving groups.

From the diffusion-controlled reactions of methyl substituted benzhydrylium ions with Cl^- and Br^-, we had concluded that the combinations of these ions occur without barrier.[38] According to the principle of microscopic reversibility, there can also not be a barrier for the reverse reaction (ionization process), and the transition states for the ionization of the methyl-substituted benzhydryl chlorides correspond to the Gibbs energies of the resulting carbocations (Figure 5.6, left). Since in these cases the ionization rate constants reflect the stabilities of the carbocations, electrofugalities are inversely correlated with the corresponding electrophilicities.

As highly stabilized carbocations are not generated through carbocation-like transition states (Figure 5.6, right), the Gibbs activation energies $\Delta G^{\#}$ of the corresponding ionization processes are not solely controlled by the stabilization of the carbocations but also by the intrinsic barriers, the relative magnitudes of which can hardly be predicted. As a result, electrofugalities are not any longer the reverse of the electrophilicities, as discussed in detail in ref. 28. An analogous situation has recently been observed in correlations between the electrofugalities and electrophilicities of tritylium ions.[39]

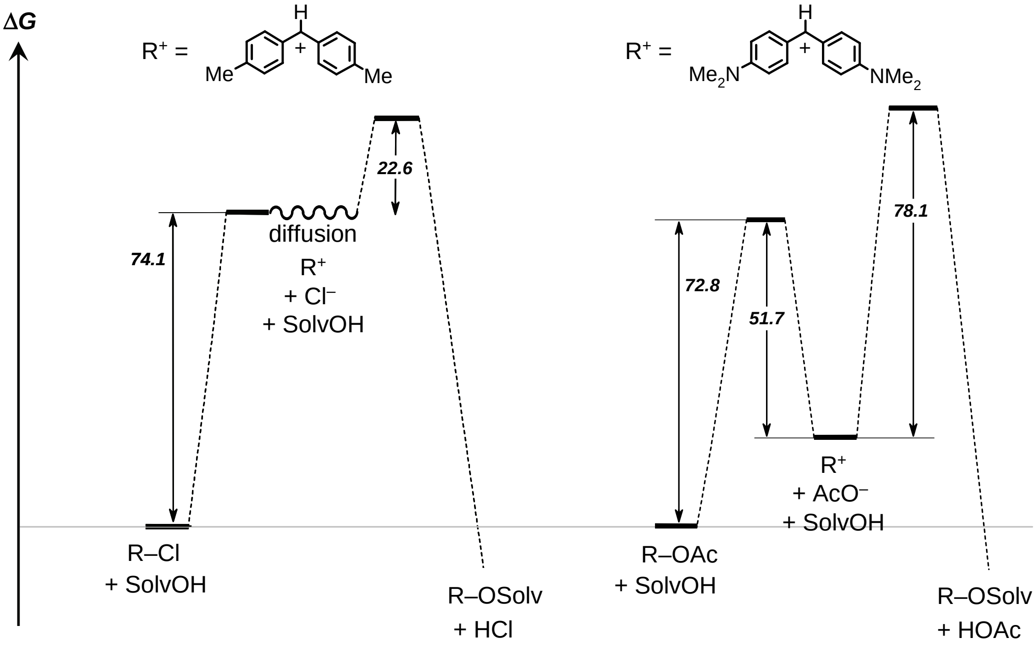


Figure 5.6: Gibbs energy profiles for the solvolyses of $(4\text{-}CH_3C_6H_4)_2CHCl$ (**E21-Cl**) in 80% aqueous ethanol and $(4\text{-}Me_2NC_6H_4)_2CHOAc$ (**E35-OAc**) in 90% aqueous acetone (at 25°C, ΔG in kJ mol^{-1}).[38] – In both solvolysis reactions, the ionization step is rate-determining, because the recombination of R^+ with the leaving group X^- is slower than the subsequent irreversible reaction with the solvent due to the low concentration of X^-.

The benzhydrylium ions listed in Table 5.1, which cover a reactivity range of 18 orders of magnitude, can now be used as reference electrofuges to characterize nucleofuges in a reactivity range of more than 25 orders of magnitude, because common kinetic methods allow one to measure ionization rate constants from 10^{-6} to 10^{2} s^{-1}. When selecting suitable reference electrofuges, it should be noted, however, that **one or several of the chlorine-substituted benzhydryl compounds E1**, **E3**, **E5**, **E8**, **and E9 caused severe skin irritations**. Though the solvolysis rate constants of these compounds have been used for the least-squares minimization to derive the reactivity parameters in Tables 5.1 and 5.2, we advise not to work with these compounds, and replace them by the corresponding fluoro-derivatives **E2**, **E4**, **E6**, and **E10**, which have similar reactivities, but so far did not show any harmful effects.[40]

5.5 Nucleofugalities of the Reference Nucleofuges

The nucleofugality parameters N_f and s_f of the reference nucleofuges **N1-N110** which have been used to derive the E_f values of the reference electrofuges **E1-E39** are summarized in Table 5.2. Figure 5.7 illustrates an increase of nucleofugality by 11 units in N_f from acetate to tosylate in 80% aqueous acetone. As s_f is generally close to 1, this difference corresponds to an increase of reactivity by a factor of 10^{11}, or relative half-lives ranging from 1 second to 3000 years.

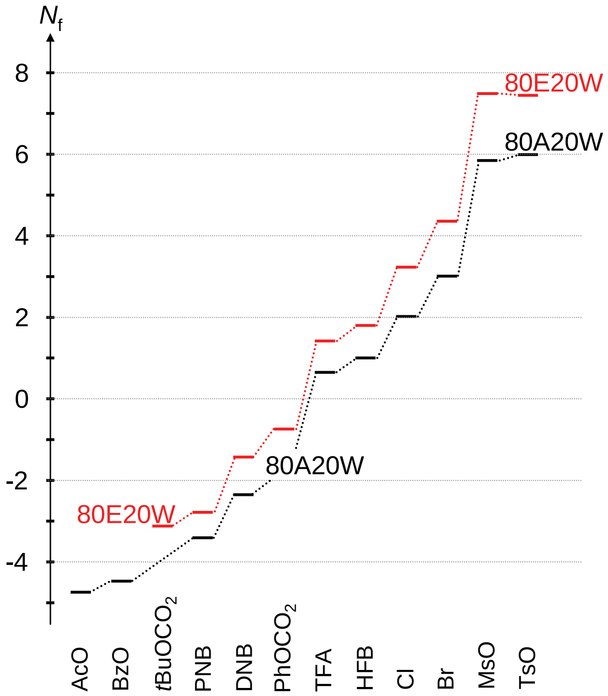


Figure 5.7: Nucleofugality scale.

Though the small differences in s_f are difficult to explain, at least one trend appears to be general: Whenever a certain leaving group is investigated in a series of solvents where only the ratio organic component/water is changed, s_f decreases slightly with increasing amount of water as exemplified in Figure 5.8 for phenyl carbonate in different ethanol/water mixtures.[20,41]

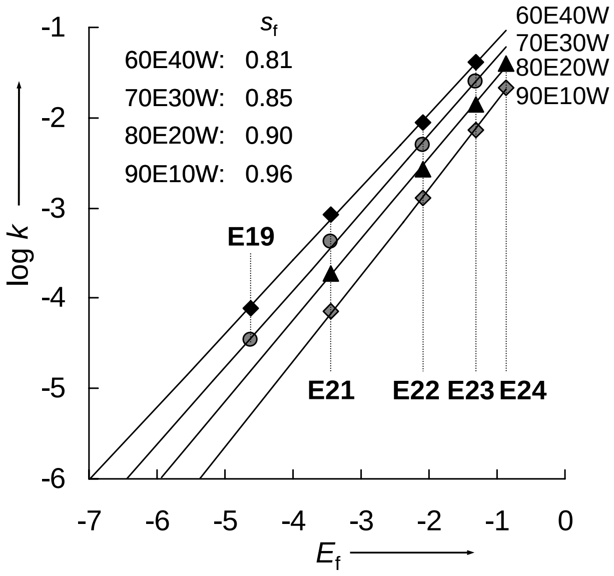


Figure 5.8. Plots of the observed first-order rate constants k (at 25°C) for the solvolyses of benzhydryl phenyl carbonates[20] in aqueous ethanol (solvents given as v/v) against the electrofugality parameters E_f of the benzhydrylium ions.

As this trend is also observed for solvolyses of benzhydryl chlorides in aqueous acetonitrile and aqueous acetone, i.e., substrates where the recombination of leaving groups with carbocations is diffusion-controlled, the change of s_f cannot be due to a change of the ionic character of the transition state. The absence of a barrier between substrates and ions implies that the ionic character is fully developed in the transition states, and the smaller s_f values in the water-rich solvent mixtures indicate that the differences in carbocation stabilization which are observed in the less polar, water-poor solutions are slightly attenuated in the more polar, water-rich solutions. From the small differences of s_f one can derive that differential solvation of the carbocations, i.e., the differences of the solvation energies of differently stabilized benzhydrylium ions are rather small.

Presently, we do not yet know the rate constants for the combinations of benzhydrylium ions with tosylate or trifluoroacetate anions under the conditions of the solvolysis reactions. We, therefore, cannot confirm the assumption that the smaller values of s_f in these reaction series are due to transition states in which the carbocationic character is not yet fully developed.

5.6 Characterization of Further Nucleofuges

The availability of electrophilicity parameters for a series of electrofuges of widely differing reactivity (Table 5.1) now allows us to characterize nucleofugalities of almost any leaving group.

If a series of rate constants are available, which refer to benzhydrylium ions of significantly different electrofugality, one can plot the first-order rate constants log k_1 for these solvolysis reactions against the electrofugality parameters E_f from Table 5.1. As shown for three examples in Figure 5.9, the nucleofugality parameters N_f are then obtained as the negative intercepts on the abscissa (E_f axis) and the s_f parameters correspond to the slopes of these correlations. In this way, the parameters listed in Table 5.3 have been calculated from the solvolysis rate constants listed in Table S2 of the Experimental Section.

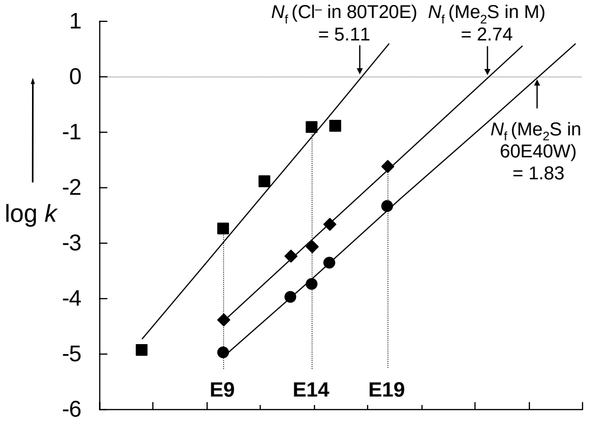


Figure 5.9: Plots of the first-order rate constants k (at 25°C) of the solvolyses of benzhydryl chlorides (in 80T20E) and benzhydryl dimethyl sulfonium ions (in M and 60E40W) against the electrofugality parameters E_f to yield the nucleofugality parameters N_f and s_f (mixtures of solvents are given (v/v); E = ethanol, M = methanol, T = 2,2,2-trifluoroethanol, W = water).

Table 5.3: Nucleofugality Parameters of Further Nucleofuges.

Leaving group	Solvent[a]	Electrofuges used for the characterization	N_f	s_f
OMs	TFE	**E2, E4**	9.84	1.00
Br	80M20W	**E7, E9, E17**	5.34	1.00
	90M10W	**E7, E9, E14, E16, E17**	4.83	0.99
	70E30W	**E7, E9, E14, E16, E17**	4.83	0.96
	90E10W	**E7, E14, E17**	3.73	0.93
	50A50W	**E7, E9, E11**	5.11	0.93
	60A40W	**E7, E9, E14, E16, E17**	4.67	0.97
	70A30W	**E7, E9, E14, E16, E17**	3.96	0.95
	60T40E	**E7, E9, E14, E16, E17**	5.14	1.08
	80T20E	**E7, E9, E14, E17**	5.86	1.15
Cl	80M20W	**E7, E9, E17, E19**	4.12	1.00
	90M10W	**E7, E9, E14, E17, E19**	3.56	0.99
	60E40W	**E9, E14, E17**	4.09	0.97
	70E30W	**E7, E9, E11, E14, E17**	3.63	0.96
	90E10W	**E7, E13, E14, E15, E17, E18, E19**	2.62	0.98
	50A50W	**E7, E9, E14, E17, E19**	4.26	1.03
	70A30W	**E7, E9, E14, E17, E19**	2.72	1.00
	40T60E	**E11, E14, E17, E19**	3.45	1.04
	60T40E	**E7, E9, E11, E14, E17, E19**	4.44	1.16
	80T20E	**E7, E9, E11, E14, E17**	5.11	1.15
	2-propanol	**E9, E11, E12, E13, E14, E15, E16, E18, E19, E21, E22**	0.41	0.93
Me_2S	M	**E9, E13, E14, E16, E19**	2.74	0.89
	80M20W	**E9, E13, E14, E16, E19**	2.40	0.89
	60M40W	**E9, E13, E14, E16, E19**	2.06	0.85
	E	**E9, E13, E14, E16, E19**	2.40	0.87
	80E20W	**E9, E13, E14, E16, E19**	1.96	0.86
	60E40W	**E9, E13, E14, E16, E19**	1.83	0.86
AcO	80M20W	**E23, E24, E25**	–3.92	0.91
	60M40W	**E23, E24, E25**	–3.59	0.87
DNB	90E10W	**E22, E23, E24, E25**	–1.54	1.06
	70A30W	**E22, E23, E24, E25**	–2.28	0.98

[a] Mixtures of solvents are given as (v/v); A = acetone, AN = acetonitrile, E = ethanol, M = methanol, TFE or T = 2,2,2-trifluoroethanol, W = water.

If only one or few ionization rate constants referring to benzhydrylium ions with similar E_f values are available, one can assume $s_f = 1.00$ and get an estimate for N_f by substituting these values into eq 5.3. This method can also be used for the determination of N_f if the heterolysis rate constants k_1 have not been measured directly but were calculated from the second-order rate constants k_2 of the reverse reactions (combination of nucleophile and electrophile) and the corresponding equilibrium constants K by using equation (5.6).

$$k_1 = k_2/K \qquad (5.6)$$

As all but one of the N_f parameters in Table 5.4 refer to systems where at least two, mostly three or more heterolysis rate constants have been used as the experimental basis, Table S3 (Experimental Section) again compares calculated and experimental rate constants. Generally, the agreement is satisfactory (average factor 1.5), and significant deviations (factor 3 and 6) are only found for two phosphines.

Table 5.4: Nucleofugality Parameters of Further Nucleofuges (Determined at 20 °C Unless Noted Otherwise).

Leaving group	Solvent[a]	Electrofuges for characterization	N_f	s_f[b]
$\underline{\mathrm{S}}\mathrm{CN}$	AN	**E28, E31, E32**	(1.89)	1.00
$\mathrm{SC}\underline{\mathrm{N}}$	AN	**E31, E33**	(–3.09)	1.00
$(4\text{-MeOC}_6\text{H}_4)_3\text{P}$	CH_2Cl_2	**E34, E36, E37, E39**	(–5.91)	1.00
$(4\text{-MeC}_6\text{H}_4)_3\text{P}$	CH_2Cl_2	**E36, E37, E39**	(–5.20)	1.00
Ph_3P	CH_2Cl_2	**E34, E35, E36, E37, E38, E39**	(–4.44)	1.00
$(4\text{-ClC}_6\text{H}_4)_3\text{P}$	CH_2Cl_2	**E28, E33, E37**	(–2.93)	1.00
azide	45M55AN	**E34, E36, E37, E39**	(–3.81)	1.00
	91M9AN	**E34, E36, E37, E39**	(–3.85)	1.00
	91E9AN	**E34, E36, E37, E39**	(–4.38)	1.00
nitrite	AN	**E34, E36, E39**	(–3.76)	1.00
DMAP	CH_2Cl_2	**E34, E36, E37, E39**	(–5.32)	1.00
	AN	**E34, E36, E39**	(–6.29)	1.00
4-(1-pyrrolidinyl)pyridine	CH_2Cl_2	**E36, E39**	(–5.33)	1.00
4-methoxypyridine	CH_2Cl_2	**E31, E33, E35, E38**	(–2.80)	1.00
4-methylpyridine	CH_2Cl_2	**E29, E31, E33, E35**	(–1.91)	1.00
pyridine	CH_2Cl_2	**E29, E31, E33**	(–0.99)	1.00
DABCO	AN	**E34, E37, E38**	(–1.00)	1.00
$\underline{\mathrm{S}}\mathrm{O_2Ph}$[c]	50AN50W	**E34, E36, E37, E39**	(–4.69)	1.00
	60AN40W	**E34, E36, E39**	(–4.87)	1.00
$\mathrm{S}\underline{\mathrm{O}}\mathrm{_2Ph}$	DMSO	**E25**	(–3.10)	1.00
1-methylimidazole	AN	**E34, E36, E37**	(–6.29)	1.00
1-phenylimidazole	AN	**E35, E37, E38**	(–5.59)	1.00
1-methylbenzimidazole	AN	**E34, E35, E37, E38**	(–6.01)	1.00
isoquinoline	AN	**E31, E33, E35**	(–3.04)	1.00

[a] Mixtures of solvents are given as (v/v); AN = acetonitrile, E = ethanol, M = methanol, TFE or T = 2,2,2-trifluoroethanol, W = water. [b] s_f fixed to 1.00. [c] at 25 °C.

5.7 Conclusions

The correlation equation (5.3), where electrofuges (carbocations) are characterized by one (E_f) and nucleofuges (combinations of leaving groups and solvents) are characterized by two parameters (N_f and s_f) predicts the ionization rates of benzhydryl derivatives with high precision. The 39 benzhydrylium ions in Table 5.1, which cover a reactivity range of 18 orders of magnitude, and the 110 combinations of common leaving groups and solvents in Table 5.2, which cover a reactivity range of 15 orders of magnitude, can be used as references to derive the reactivity parameters N_f, s_f and E_f of other nucleofuges and electrofuges, respectively. Though the correlations are of lower quality when other types of carbocations are considered, analysis of a smaller set of data has shown that eq (5.3) also works well for other types of aryl substituted carbenium ions.[42] Substitution of solvolysis rate constants for *tert*-butyl chlorides and bromides and of 1-adamantyl chloride, bromide, tosylate, trifluoroacetate and dimethylsulfonium ion and the corresponding N_f and s_f parameters from Table 5.2 into eq (5.3) led to electrofugalities E_f for the tertiary carbenium ions which varied by two units.[42] As a consequence, k_{exp}/k_{calc} ranges from 0.1 to 10, which we consider tolerable for qualitative predictions by a 3-parameter equation covering a reactivity range of more than 25 orders of magnitude. A practical guide to estimate solvolyis half-lives is given in Table 5.5.

Table 5.5: Solvolysis Half-lives for Benzhydryl Derivatives.

$\tau_{1/2}$	k_1 / s^{-1}	$s_f(N_f+E_f)$
1 min	1.2×10^{-2}	–2.0
1 hour	1.9×10^{-4}	–3.7
1 day	8.0×10^{-6}	–5.1
1 month	2.6×10^{-7}	–6.6

A severe failure of eq (5.3) can be expected for alkoxy- and amino-substituted carbenium ions, however, because in these cases geminal interactions between the alkoxy- or the amino group with the leaving group will modify the ground-state energies.

In Figure 5.10, the resulting reactivity parameters for electrofuges and nucleofuges are arranged in opposite ordering, and systems with $N_f + E_f = -4$ are set at the same level. As s_f typically ranges from 0.8 to 1.1, eq (5.3) yields heterolysis half-lives from 0.3 to 5 h for combinations of electrofuges and nucleofuges at the same horizontal level; such combinations can easily be studied kinetically. More important, however, is another aspect of Figure 5.10: When the electrofuges are located several units above the nucleofuge in Figure 5.10, one can be confident that the heterolysis of such a combination will not occur at room temperature. If, however, a nucleofuge is located several units above an electrofuge, a substrate consisting of these two fragments will experience a very fast heterolytic cleavage, and it will be difficult or impossible to handle such a compound in the corresponding solvent.

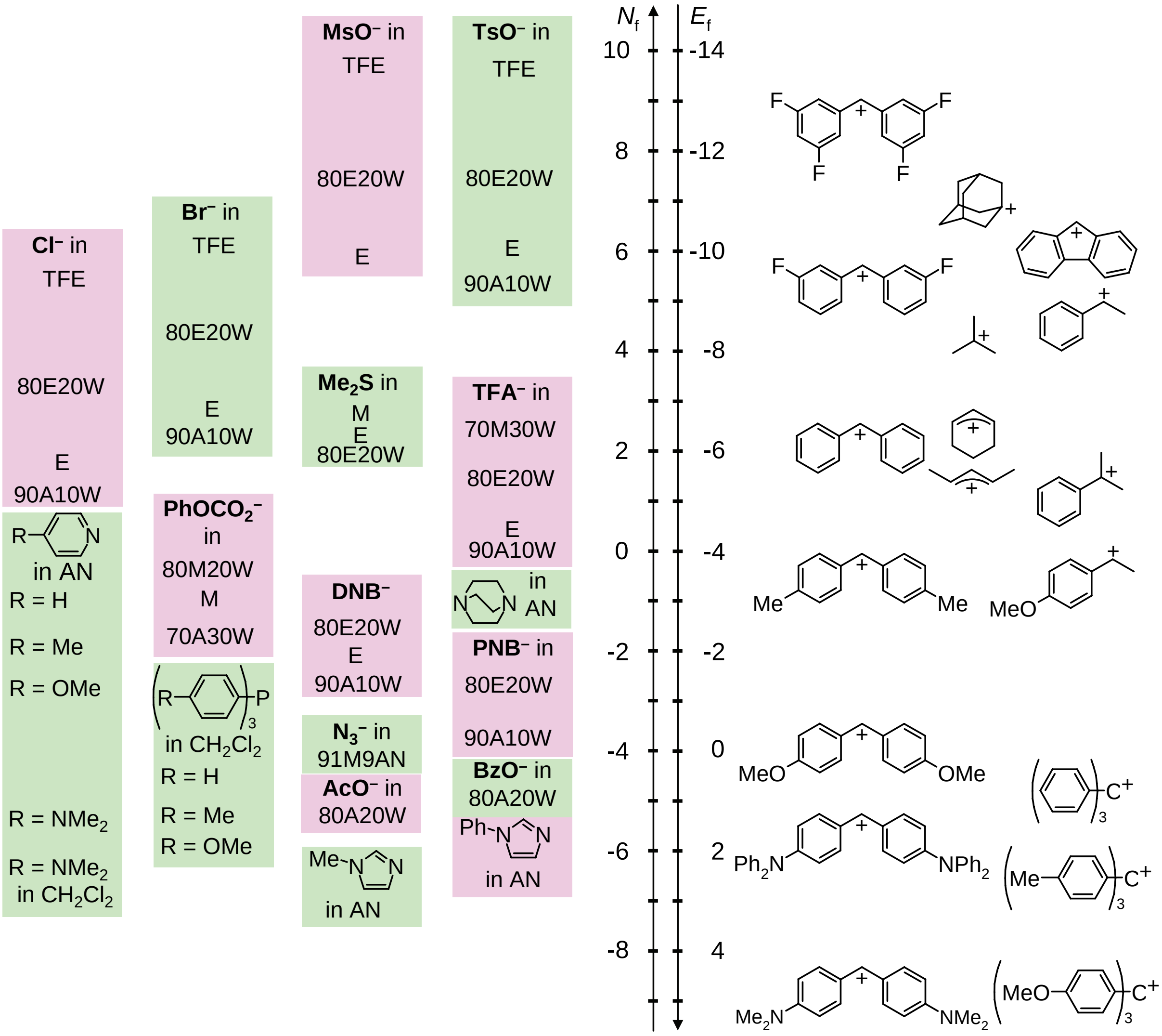


Figure 5.10: A semiquantitative model for heterolysis reactions: Combinations of electrofuges and nucleofuges at the same level cleave with a half-life of approximately one hour.

The reactivity parameters of the reference electrofuges in Table 5.1 and the reference nucleofuges in Table 5.2 can now be used to determine nucleofugalities N_f/s_f of almost any leaving group solvent-pair and electrofugalities of almost any carbocation in order to develop a semiquantitative basis of heterolytic processes.

5.8 References

(1) Mayr, H.; Ofial, A. R. *J. Phys. Org. Chem.* **2008**, *21*, 584–595.

(2) Grunwald, E.; Winstein, S. *J. Am. Chem. Soc* **1948**, *70*, 846–854.

(3) Fainberg, A. H.; Winstein, S. *J. Am. Chem. Soc.* **1956**, *78*, 2770–2777.

(4) Winstein, S.; Fainberg, A. H.; Grunwald, E. *J. Am. Chem. Soc.* **1957**, *79*, 4146–4155.

(5) Bentley, T. W.; Llewellyn, G. *Prog. Phys. Org. Chem.* **1990**, *17*, 121–159.

(6) Kevill D. N. In *Advances in Quantitative Structure-Property Relationships*, Vol. 1; Charton, M., Ed.; JAI Press: Greenwich, CT, 1996; pp. 81–115.

(7) Schleyer, P. v. R.; Jemmis, E. D.; Spitznagel, G. W. *J. Am. Chem. Soc.* **1985**, *107*, 6393–6394.

(8) Verevkin, S. P. *J. Chem. Thermodyn.* **2000**, *32*, 207–215.

(9) Cioslowski, J.; Varnali, T. *J. Phys. Chem.* **1996**, *100*, 18725–18730.

(10) Rakus, K.; Verevkin, S. P.; Peng, W.-H.; Beckhaus, H.-D.; Rüchardt, C. *Liebigs Ann.* **1995**, 2059–2067.

(11) Richard, J. P.; Amyes, T. L.; Rice, D. J. *J. Am. Chem. Soc.* **1993**, *115*, 2523–2524.

(12) Apeloig, Y.; Biton, R.; Abu-Freih, A. *J. Am. Chem. Soc.* **1993**, *115*, 2522–2523.

(13) Kirmse, W.; Goer, B. *J. Am. Chem. Soc.* **1990**, *112*, 4556–4557.

(14) Brown, H. C.; Fletcher, R. S. *J. Am. Chem. Soc.* **1949**, *71*, 1845–1854.

(15) See ref. [20a] in: Fry, J. L.; Lancelot, C. J.; Lam, L. K. M.; Harris, J. M.; Bingham, R. C.; Raber, D. J.; Hall, R. E.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1970**, *92*, 2538–2540.

(16) Brown, H. C. *The Nonclassical Ion Problem*; Plenum Press: New York, 1977.

(17) Liu, K.-T.; Lin, Y.-S.; Tsao, M.-L. *J. Phys. Org. Chem.* **1998**, *11*, 223–229 and references cited therein.

(18) Denegri, B.; Streiter, A.; Juric, S.; Ofial, A. R.; Kronja, O.; Mayr, H. *Chem. Eur. J.* **2006**, *12*, 1648–1656; *Chem. Eur. J.* **2006**, *12*, 5415.

(19) Mayr, H.; Bug, T.; Gotta, M. F.; Hering, N.; Irrgang, B.; Janker, B.; Kempf, B.; Loos, R.; Ofial, A. R.; Remennikov, G.; Schimmel, H. *J. Am. Chem. Soc.* **2001**, *123*, 9500–9512.

(20) When X^- is the conjugate base of a weak acid, a proton sponge [e.g. 1,8-bis(dimethylamino)-naphthalene] was commonly added to enforce complete dissociation of HX: Denegri, B.; Kronja, O. *J. Org. Chem.* **2007**, *72*, 8427–8433.

(21) Raber, D. J.; Harris, J. M.; Schleyer, P. v. R. In *Ions and Ion Pairs in Organic Reactions*, Vol. 2; Szwarc, M., Ed.; Wiley: New York, 1974.

(22) Goering, H. L.; Hoermer, G. S.; Linsay, E. C. *J. Am. Chem. Soc.* **1971**, *93*, 1230–1234 and references cited therein.

(23) Diaz, A. F.; Lazdins, I.; Winstein, S. *J. Am. Chem. Soc.* **1968**, *90*, 1904–1905.

(24) Bateman, L. C.; Church, M. G.; Hughes, E. D.; Ingold, C. K.; Taher, N. A. *J. Chem. Soc.* **1940**, 979–1011.

(25) Stang, P. J.; Rappoport, Z.; Hanack, M.; Subramanian, L. R. *Vinyl Cations*; Academic Press: New York, 1979; Chapter 6, pp 337–338.

(26) (a) Streidl, N.; Antipova, A.; Mayr, H. *J. Org. Chem.* **2009**, *74*, 7328–7334. (b) Streidl, N. Chapter 4, Dissertation Ludwig-Maximilians-Universität München, 2010.

(27) For the determination of fast ionization processes in equilibrating systems see: Kessler, H.; Feigel, M. *Acc. Chem. Res.* **1982**, *15*, 2–8.

(28) Schaller, H. F.; Tishkov, A. A.; Feng, X.; Mayr, H. *J. Am. Chem. Soc.* **2008**, *130*, 3012–3022.

(29) Manege, L. C.; Ueda, T.; Hojo, M.; Fujio, M. *J. Chem. Soc., Perkin Trans. 2* **1998**, 1961–1966.

(30) Mayr, H.; Kempf, B.; Ofial, A. R. *Acc. Chem. Res.* **2003**, *36*, 66–77.

(31) The minimization was done by using the program "*What´sBest!* 7.0 Professional" by Lindo Systems.

(32) Bentley, T. W. *Chem. Eur. J.* **2006**, *12*. 6514–6520.

(33) As N_f' = log k for $E_f = 0$ (eq 5.5), N_f' corresponds to log k_0 in a typical linear free-energy relationship. N_f' thus reflects the measured or extrapolated rate constant for the solvolysis of (p-MeOC$_6$H$_4$)$_2$CHX in the corresponding solvent. However, ionization rate constants between $10^5 - 10^{10}$ s^{-1} (half-lives of ns to μs) which are extrapolated for the ionizations of (p-MeOC$_6$H$_4$)$_2$CHOTs in different solvents are without practical relevance. As tosyl-leaving groups are commonly used for the formation of carbocations with low stabilities ($E_f = -8$ to -14) these N_f' values do not give a good estimate for the leaving group abilities of tosylates in practice without consideration of s_f. The quantities N_f in eq (5.3), on the other hand, correspond to the intercepts of the correlation lines on the abscissa and thus reflect the relative nucleofugalities of leaving groups with respect to variable electrofuges, which ionize with rate constants of 1 s^{-1}. Despite the less straightforward definition of N_f by eq (5.3), the numerical values of N_f have a direct practical meaning. Since the intercepts with the abscissa are within or close to the experimentally accessible range, they always reflect relative leaving group abilities of X$^-$ as they are observed in reality. As the absolute value of the sum ($N_f + E_f$) is always a

small number for substrates which undergo S_N1 reactions under typical reaction conditions, one can neglect s_f in qualitative discussions and estimate ionization half-lives by just adding two numbers, $E_f + N_f$, as specified in the main text.

(34) Tsuno, Y.; Fujio, M. *Adv. Phys. Org. Chem.* **1999**, *32*, 267–385.

(35) Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165–195.

(36) Exner, O. *Correlation Analysis of Chemical Data*; Plenum Press: New York, 1988.

(37). Baidya, M.; Brotzel, F.; Mayr, H. *Org. Biomol. Chem.* **2010**, *8*, 1929–1935.

(38) Mayr, H.; Ofial, A. R. *Pure Appl. Chem.* **2009**, *81*, 667–683.

(39) Horn, M.; Mayr, H. *Chem. Eur. J.* **2010**, EarlyView.

(40) Nolte, C.; Mayr, H. *Eur. J. Org. Chem.* **2010**, 1435–1439.

(41) Denegri, B.; Kronja, O. *J. Phys. Org. Chem.* **2009**, *22*, 495–503.

(42) Denegri, B.; Ofial, A. R.; Juric, S.; Streiter, A.; Kronja, O.; Mayr, H. *Chem. Eur. J.* **2006**, *12*, 1657–1666.

5.9 Experimental Section

Tables S1-S3 in this Experimental Section list the rate constants used for the correlations, whereas the short cuts for the references of the data can be found in Table S4.

Table S1: Solvolysis Rate Constants at 25°C.

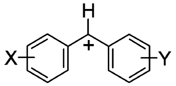
Nucleofuges					Electrofuges								
No	Leaving group	Solvent	N_f	s_f	No			E_f	k_{exp} / s^{-1}	k_{calc} / s^{-1a}	k_{exp} / k_{calc}	used in correl.	ref. short cuts
N1	OTs	TFE	9.73	0.94	E4	3,5-F$_2$	3-F	-10.88	7.99E-02	8.24E-02	0.97	☑	[Nol10]
					E3	3,5-Cl$_2$	3-Cl	-11.20	4.36E-02	4.10E-02	1.06	☑	[Den06]
					E2	3,5-F$_2$	3,5-F$_2$	-12.60	1.73E-03	1.97E-03	0.88	☑	[Nol10u]
					E1	3,5-Cl$_2$	3,5-Cl$_2$	-12.93	1.07E-03	9.69E-04	1.10	☑	[Den06]
N2		M	7.33	0.82	E10	3-F	H	-7.53	8.33E-01	6.86E-01	1.21	☑	[Nol10]
					E6	3-F	3-F	-9.26	2.07E-02	2.66E-02	0.78	☑	[Nol10]
					E4	3,5-F$_2$	3-F	-10.88	1.13E-03	1.23E-03	0.92	☑	[Nol10]
					E2	3,5-F$_2$	3,5-F$_2$	-12.60	5.51E-05	4.79E-05	1.15	☑	[Nol10]
N3		80E20W	7.45	0.80	E9	3-Cl	H	-7.69	6.54E-01	6.38E-01	1.03	☑	[Den06]
					E8	3-Cl	4-Cl	-8.15	2.72E-01	2.71E-01	1.00	☑	[Den06]
					E6	3-F	3-F	-9.26	4.07E-02	3.53E-02	1.15	☑	[Nol10]
					E5	3-Cl	3-Cl	-9.55	1.59E-02	2.04E-02	0.78	☑	[Den06]
					E4	3,5-F$_2$	3-F	-10.88	1.94E-03	1.74E-03	1.11	☑	[Nol10]
					E3	3,5-Cl$_2$	3-Cl	-11.20	9.13E-04	9.64E-04	0.95	☑	[Den06]
					E2	3,5-F$_2$	3,5-F$_2$	-12.60	8.15E-05	7.28E-05	1.12	☑	[Nol10]
					E1	3,5-Cl$_2$	3,5-Cl$_2$	-12.93	3.64E-05	3.98E-05	0.91	☑	[Den06]
N4		E	6.09	0.78	E10	3-F	H	-7.53	8.22E-02	7.59E-02	1.08	☑	[Nol10]
					E9	3-Cl	H	-7.69	5.57E-02	5.74E-02	0.97	☑	[Den06]
					E8	3-Cl	4-Cl	-8.15	2.83E-02	2.51E-02	1.13	☑	[Den06]
					E6	3-F	3-F	-9.26	3.35E-03	3.51E-03	0.95	☑	[Nol10]
					E5	3-Cl	3-Cl	-9.55	1.83E-03	2.07E-03	0.88	☑	[Den06]
					E4	3,5-F$_2$	3-F	-10.88	1.89E-04	1.93E-04	0.98	☑	[Nol10]
					E3	3,5-Cl$_2$	3-Cl	-11.20	9.65E-05	1.09E-04	0.89	☑	[Den06]
					E2	3,5-F$_2$	3,5-F$_2$	-12.60	8.90E-06	8.97E-06	0.99	☑	[Nol10]
					E1	3,5-Cl$_2$	3,5-Cl$_2$	-12.93	5.81E-06	5.01E-06	1.16	☑	[Den06]
N5		60AN40W	7.97	0.82	E10	3-F	H	-7.53	2.14E+00	2.30E+00	0.93	☑	[Nol10]
					E6	3-F	3-F	-9.26	9.53E-02	8.80E-02	1.08	☑	[Nol10]
					E4	3,5-F$_2$	3-F	-10.88	4.26E-03	4.02E-03	1.06	☑	[Nol10]
					E2	3,5-F$_2$	3,5-F$_2$	-12.60	1.45E-04	1.55E-04	0.94	☑	[Nol10]

Table S1: *Continued*.

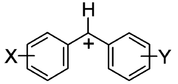
Nucleofuges					Electrofuges								
No	Leaving group	Solvent	N_f	s_f	No			E_f	k_{exp} / s^{-1}	k_{calc} / s^{-1a}	k_{exp} / k_{calc}	used in correl.	ref. short cuts
N6		80A20W	6.00	0.83	E10	3-F	H	-7.53	5.59E-02	5.35E-02	1.04	☑	[Nol10]
					E8	3-Cl	4-Cl	-8.15	1.41E-02	1.64E-02	0.86	☑	[Den06]
					E6	3-F	3-F	-9.26	2.42E-03	2.02E-03	1.20	☑	[Nol10]
					E5	3-Cl	3-Cl	-9.55	1.07E-03	1.15E-03	0.93	☑	[Den06]
					E4	3,5-F_2	3-F	-10.88	1.10E-04	9.08E-05	1.21	☑	[Nol10]
					E3	3,5-Cl_2	3-Cl	-11.20	4.05E-05	4.93E-05	0.82	☑	[Den06]
N7		90A10W	5.38	0.89	E14	H	H	-6.03	3.01E-01	2.65E-01	1.14	☑	[Den06]
					E10	3-F	H	-7.53	1.16E-02	1.22E-02	0.95	☑	[Nol10]
					E8	3-Cl	4-Cl	-8.15	2.60E-03	3.44E-03	0.76	☑	[Den06]
					E6	3-F	3-F	-9.26	4.24E-04	3.60E-04	1.18	☑	[Nol10]
					E5	3-Cl	3-Cl	-9.55	2.05E-04	1.96E-04	1.05	☑	[Den06]
N8	OMs	80E20W	7.49	0.84	E6	3-F	3-F	-9.26	3.37E-02	3.29E-02	1.02	☑	[Nol10]
					E4	3,5-F_2	3-F	-10.88	1.35E-03	1.42E-03	0.95	☑	[Nol10]
					E2	3,5-F_2	3,5-F_2	-12.60	5.27E-05	5.14E-05	1.03	☑	[Nol10]
N9		E	5.82	0.80	E10	3-F	H	-7.53	4.34E-02	4.24E-02	1.02	☑	[Nol10]
					E6	3-F	3-F	-9.26	1.70E-03	1.78E-03	0.96	☑	[Nol10]
					E4	3,5-F_2	3-F	-10.88	9.12E-05	8.90E-05	1.02	☑	[Nol10]
N10		60AN40W	7.70	0.83	E10	3-F	H	-7.53	4.82E-02	5.09E-02	0.95	☑	[Nol10]
					E6	3-F	3-F	-9.26	2.52E-03	2.26E-03	1.12	☑	[Nol10]
					E4	3,5-F_2	3-F	-10.88	8.04E-05	8.47E-05	0.95	☑	[Nol10]
N11		80A20W	5.85	0.84	E10	3-F	H	-7.53	3.87E-02	3.86E-02	1.00	☑	[Nol10]
					E6	3-F	3-F	-9.26	1.37E-03	1.38E-03	0.99	☑	[Nol10]
					E4	3,5-F_2	3-F	-10.88	5.92E-05	5.90E-05	1.00	☑	[Nol10]
N12	Br	TFE	6.19	0.95	E14	H	H	-6.03	1.10E+00	1.42E+00	0.77	☑	[Den06]
					E11	4-Cl	4-Cl	-6.91	1.52E-01	2.09E-01	0.73	☑	[Den06]
					E9	3-Cl	H	-7.69	6.62E-02	3.77E-02	1.76	☑	[Den06]
									8.57E-02	3.77E-02	2.27		[Liu95]
					E8	3-Cl	4-Cl	-8.15	1.40E-02	1.37E-02	1.02	☑	[Den06]
					E6	3-F	3-F	-9.26	1.49E-03	1.22E-03	1.22	☑	[Nol10]

Table S1: *Continued.*

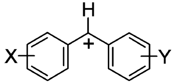
Nucleofuges					Electrofuges								
No	Leaving group	Solvent	N_f	s_f	No			E_f	k_{exp} / s^{-1}	k_{calc} / s^{-1a}	k_{exp} / k_{calc}	used in correl.	ref. short cuts
					E5	3-Cl	3-Cl	-9.55	6.70E-04	6.39E-04	1.05	☑	[Den06]
					E4	3,5-F_2	3-F	-10.88	2.54E-05	3.47E-05	0.77	☑	[Nol10]
					E3	3,5-Cl_2	3-Cl	-11.20	1.99E-05	1.72E-05	1.16	☑	[Den06]
					E1	3,5-Cl_2	3,5-Cl_2	-12.93	3.41E-07	3.94E-07	0.87	☑	[Den06]
N13		M	4.23	0.99	E17	4-OPh	4-NO_2	-5.60	4.74E-02	4.49E-02	1.06	☑	[Liu02]
					E16	4-F	H	-5.72	2.92E-02	3.43E-02	0.85	☑	[Liu95]
					E14	H	H	-6.03	1.76E-02	1.68E-02	1.05	☑	[Liu95]
									1.58E-02	1.68E-02	0.94		[Dvo89]
					E10	3-F	H	-7.53	5.75E-04	5.49E-04	1.05	☑	[Nol10]
					E9	3-Cl	H	-7.69	4.22E-04	3.85E-04	1.10	☑	[Liu97]
					E7	4-NO_2	H	-9.20	1.14E-05	1.23E-05	0.93	☑	[Liu98]
N14		80E20W	4.36	0.95	E17	4-OPh	4-NO_2	-5.60	4.72E-02	6.76E-02	0.70	☑	[Liu02]
					E16	4-F	H	-5.72	5.88E-02	5.22E-02	1.13	☑	[Liu95]
									6.05E-02	5.22E-02	1.16		[Den06]
					E14	H	H	-6.03	3.04E-02	2.62E-02	1.16	☑	[Liu95]
									3.44E-02	2.62E-02	1.61		[Den06]
					E13	4-Cl	H	-6.44	1.21E-02	1.08E-02	1.12	☑	[Liu95]
					E11	4-Cl	4-Cl	-6.91	4.81E-03	3.88E-03	1.24	☑	[Den06]
					E10	3-F	H	-7.53	9.47E-04	9.88E-04	0.96	☑	[Nol10]
					E9	3-Cl	H	-7.69	6.48E-04	7.03E-04	0.92	☑	[Liu95]
					E8	3-Cl	4-Cl	-8.15	2.59E-04	2.56E-04	1.01	☑	[Den06]
					E7	4-NO_2	H	-9.20	2.63E-05	2.59E-05	1.02	☑	[Liu95]
					E6	3-F	3-F	-9.26	2.30E-05	2.31E-05	1.00	☑	[Nol10]
					E5	3-Cl	3-Cl	-9.55	8.99E-06	1.21E-05	0.74	☑	[Den06]
					E3	3,5-Cl_2	3-Cl	-11.20	3.84E-07	3.28E-07	1.17	☑	[Den06]
N15		E	2.93	0.93	E19	4-Me	H	-4.63	2.95E-02	2.68E-02	1.10	☑	[Den06]
					E17	4-OPh	4-NO_2	-5.60	3.55E-03	3.39E-03	1.05	☑	[Liu02]
					E16	4-F	H	-5.72	2.38E-03	2.64E-03	0.90	☑	[Den06]
					E14	H	H	-6.03	1.34E-03	1.35E-03	0.99	☑	[Den06]
									1.24E-03	1.35E-03	0.92		[Win57]
									1.23E-03	1.35E-03	0.91		[Dvo89]
									1.20E-03	1.35E-03	0.89		[Liu97]

Table S1: *Continued.*

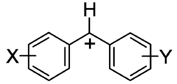
Nucleofuges					Electrofuges								
No	Leaving group	Solvent	N_f	s_f	No			E_f	k_{exp} / s^{-1}	k_{calc} / s^{-1a}	k_{exp} / k_{calc}	used in correl.	ref. short cuts
					E13	4-Cl	H	-6.44	5.00E-04	5.65E-04	0.88	☑	[Den06]
					E11	4-Cl	4-Cl	-6.91	2.10E-04	2.08E-04	1.01	☑	[Den06]
					E8	3-Cl	4-Cl	-8.15	1.58E-05	1.46E-05	1.08	☑	[Den06]
N16		60AN40W	5.23	0.99	E19	4-Me	H	-4.63	4.57E+00	3.99E+00	1.15	☑	[Nol10]
					E14	H	H	-6.03	1.44E-01	1.62E-01	0.89	☑	[Nol10]
					E10	3-F	H	-7.53	4.59E-03	5.28E-03	0.87	☑	[Nol10]
					E6	3-F	3-F	-9.26	1.18E-04	1.04E-04	1.13	☑	[Nol10]
N17		80A20W	3.01	0.90	E20	4-OPh	H	-3.52	2.59E-01	3.47E-01	0.75	☑	[Min72]
					E19	4-Me	H	-4.63	4.54E-02	3.50E-02	1.30	☑	[Den06]
					E18	3,5-Me$_2$	H	-5.43	8.99E-03	6.62E-03	1.36	☑	[Min73]
					E17	4-OPh	4-NO$_2$	-5.60	5.19E-03	4.67E-03	1.11	☑	[Liu02]
					E16	4-F	H	-5.72	3.71E-03	3.66E-03	1.01	☑	[Den06]
					E15	3-Me	H	-5.73	4.08E-03	3.54E-03	1.15	☑	[Min72]
					E14	H	H	-6.03	1.91E-03	1.90E-03	1.01	☑	[Liu97]
									2.03E-03	1.90E-03	1.07		[Den06]
									2.00E-03	1.90E-03	1.05		[Min72]
									1.53E-03	1.90E-03	0.81		[Ing52]
					E13	4-Cl	H	-6.44	6.81E-04	8.17E-04	0.83	☑	[Den06]
									6.74E-04	8.17E-04	0.82		[Min72]
					E12	4-Br	H	-6.62	4.60E-04	5.63E-04	0.82	☑	[Min72]
					E11	4-Cl	4-Cl	-6.91	2.72E-04	3.09E-04	0.88	☑	[Den06]
					E9	3-Cl	H	-7.69	4.42E-05	6.09E-05	0.73	☑	[Min72]
					E7	4-NO$_2$	H	-9.20	3.33E-06	2.64E-06	1.26	☑	[Kee64]
N18		90A10W	2.29	1.01	E21	4-Me	4-Me	-3.44	6.24E-02	7.04E-02	0.89	☑	[Den06]
					E20	4-OPh	H	-3.52	6.86E-02	5.79E-02	1.18	☑	[Den06]
					E19	4-Me	H	-4.63	4.08E-03	4.47E-03	0.91	☑	[Den06]
									6.28E-04	4.47E-03	0.14		[Kee62]
					E16	4-F	H	-5.72	3.60E-04	3.58E-04	1.01	☑	[Den06]
					E14	H	H	-6.03	1.87E-04	1.73E-04	1.08	☑	[Den06]
									1.88E-04	1.73E-04	1.09		[Liu97]
									1.8 E-04	1.73E-04	1.04		[Swa53]

Table S1: *Continued*.

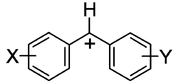
Nucleofuges					Electrofuges								
No	Leaving group	Solvent	N_f	s_f	No			E_f	k_{exp} / s^{-1}	k_{calc} / s^{-1a}	k_{exp} / k_{calc}	used in correl.	ref. short cuts
									1.64E-04	1.73E-04	0.95		[Kee62]
					E13	4-Cl	H	-6.44	6.45E-05	6.72E-05	0.96	☑	[Den06]
N19	Cl	TFE	5.54	0.85	E17	4-OPh	4-NO_2	-5.60	6.34E-01	8.93E-01	0.71	☑	[Liu02]
					E14	H	H	-6.03	6.17E-01	3.81E-01	1.62	☑	[Den06]
					E11	4-Cl	4-Cl	-6.91	6.40E-02	6.82E-02	0.94	☑	[Den06]
					E10	3-F	H	-7.53	2.10E-02	1.99E-02	1.06	☑	[Nol10]
					E9	3-Cl	H	-7.69	1.47E-02	1.47E-02	1.00	☑	[Liu98]
									1.52E-02	1.47E-02	1.03		[Den06]
					E8	3-Cl	4-Cl	-8.15	4.85E-03	5.90E-03	0.82	☑	[Den06]
					E6	3-F	3-F	-9.26	3.87E-04	6.76E-04	0.57	☑	[Nol10]
					E5	3-Cl	3-Cl	-9.55	7.20E-04	3.78E-04	1.90	☑	[Den06]
					E3	3,5-Cl_2	3-Cl	-11.20	1.39E-05	1.47E-05	0.95	☑	[Den06]
N20		M	2.91	0.99	E19	4-Me	H	-4.63	1.98E-02	2.02E-02	0.98	☑	[Liu98]
									1.94E-02	2.02E-02	0.96		[Nis67a]
					E18	3,5-Me_2	H	-5.43	3.87E-03	3.27E-03	1.18	☑	[Nis67b]
					E17	4-OPh	4-NO_2	-5.60	2.18E-03	2.23E-03	0.98	☑	[Liu02]
					E16	4-F	H	-5.72	1.38E-03	1.71E-03	0.81	☑	[Nis67a]
					E15	3-Me	H	-5.73	1.74E-03	1.65E-03	1.05	☑	[Nis67a]
					E14	H	H	-6.03	8.33E-04	8.35E-04	1.00	☑	[Win57]
									1.02E-03	8.35E-04	1.22		[Gri71]
									8.28E-04	8.35E-04	0.99		[Nis67a]
									8.15E-04	8.35E-04	0.98		[Alt52]
									8.10E-04	8.35E-04	0.97		[Liu98]
					E13	4-Cl	H	-6.44	2.97E-04	3.32E-04	0.89	☑	[Nis67a]
									3.80E-04	3.32E-04	1.14		[Alt52]
					E12	4-Br	H	-6.62	2.39E-04	2.20E-04	1.09	☑	[Nis67a]
					E11	4-Cl	4-Cl	-6.91	1.15E-04	1.14E-04	1.01	☑	[Nis67b]
									1.05E-04	1.14E-04	0.92		[Alt52]
					E9	3-Cl	H	-7.69	1.93E-05	1.94E-05	0.99	☑	[Liu98]
									2.03E-05	1.94E-05	1.05		[Nis67a]
									2.12E-05	1.94E-05	1.09		[Alt52]
					E8	3-Cl	4-Cl	-8.15	8.21E-06	6.76E-06	1.21	☑	[Nis67c]
					E7	4-NO_2	H	-9.20	5.50E-07	6.25E-07	0.88	☑	[Alt52]

Table S1: *Continued*.

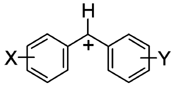
Nucleofuges					Electrofuges								
No	Leaving group	Solvent	N_f	s_f	No			E_f	k_{exp} / s^{-1}	k_{calc} / s^{-1a}	k_{exp} / k_{calc}	used in correl.	ref. short cuts
N21		80E20W	3.24	0.99	E19	4-Me	H	-4.63	4.20E-02	4.29E-02	0.98	☑	[Liu98]
									4.64E-02	4.29E-02	1.08		[Den06]
					E18	3,5-Me$_2$	H	-5.43	5.84E-03	6.94E-03	0.84	☑	[Sch60]
					E17	4-OPh	4-NO$_2$	-5.60	4.26E-03	4.74E-03	0.90	☑	[Liu02]
					E16	4-F	H	-5.72	3.67E-03	3.63E-03	1.01	☑	[Den06]
					E15	3-Me	H	-5.73	3.40E-03	3.50E-03	0.97	☑	[Sch60]
					E14	H	H	-6.03	1.72E-03	1.77E-03	0.97	☑	[War27]
									2.04E-03	1.77E-03	1.15		[Den06]
									2.08E-03	1.77E-03	1.18		[Har81]
									1.95E-03	1.77E-03	1.10		[Liu98]
									1.94E-03	1.77E-03	1.10		[Sch60]
					E13	4-Cl	H	-6.44	7.29E-04	7.05E-04	1.03	☑	[Den06]
									7.35E-04	7.05E-04	1.04		[Har81]
					E11	4-Cl	4-Cl	-6.91	2.86E-04	2.43E-04	1.18	☑	[Den06]
									2.89E-04	2.43E-04	1.19		[Har81]
					E9	3-Cl	H	-7.69	3.56E-05	4.13E-05	0.86	☑	[Liu98]
					E8	3-Cl	4-Cl	-8.15	1.53E-05	1.44E-05	1.06	☑	[Den06]
					E7	4-NO$_2$	H	-9.20	1.30E-06	1.33E-06	0.98	☑	[Liu98]
N22		E	1.82	1.00	E21	4-Me	4-Me	-3.44	2.17E-02	2.39E-02	0.91	☑	[Den06]
									2.02E-02	2.39E-02	0.85		[Sch88]
									1.83E-02	2.39E-02	0.77		[Nor28c]
									1.70E-02	2.39E-02	0.71		[Nis67b]
					E20	4-OPh	H	-3.52	2.22E-02	1.97E-02	1.13	☑	[Sch88]
									1.41E-02	1.97E-02	0.82		[Nor28c]
					E19	4-Me	H	-4.63	1.54E-03	1.55E-03	0.99	☑	[Den06]
									1.27E-03	1.55E-03	0.82		[Liu98]
									1.24E-03	1.55E-03	0.80		[Ing40a]
									1.23E-03	1.55E-03	0.79		[Nis67a]
									1.23E-03	1.55E-03	0.79		[Bad58]
									7.22E-04	1.55E-03	0.47		[Nor28b]
					E18	3,5-Me$_2$	H	-5.43	2.25E-04	2.43E-04	0.93	☑	[Nis67b]

Table S1: *Continued.*

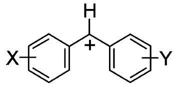
Nucleofuges					Electrofuges								
No	Leaving group	Solvent	N_f	s_f	No			E_f	k_{exp} / s^{-1}	k_{calc} / s^{-1a}	k_{exp}/ k_{calc}	used in correl.	ref. short cuts
									2.09E-04	2.43E-04	0.86		[Bad58]
					E17	4-OPh	4-NO_2	-5.60	2.67E-04	1.65E-04	1.62	☑	[Liu02]
					E16	4-F	H	-5.72	1.07E-04	1.26E-04	0.85	☑	[Den06]
									9.30E-05	1.26E-04	0.74		[Nis67a]
					E15	3-Me	H	-5.73	1.12E-04	1.22E-04	0.92	☑	[Nis67a]
									1.37E-04	1.22E-04	1.12		[Pac58]
									9.23E-04	1.22E-04	0.76		[Nor28c]
					E14	H	H	-6.03	5.75E-05	6.10E-05	0.94	☑	[War27]
									5.72E-05	6.10E-05	0.94		[Ham37]
									5.54E-05	6.10E-05	0.91		[Den06]
									5.42E-05	6.10E-05	0.89		[Liu98]
									5.41E-05	6.10E-05	0.89		[Win57]
									5.39E-05	6.10E-05	0.88		[Pac58]
									5.37E-05	6.10E-05	0.88		[Bad58]
									5.34E-05	6.10E-05	0.88		[Nis67a]
									5.30E-05	6.10E-05	0.87		[Ing40a]
									4.85E-05	6.10E-05	0.80		[Nor28a]
									4.43E-05	6.10E-05	0.73		[Nor28b]
					E13	4-Cl	H	-6.44	2.06E-05	2.39E-05	0.86	☑	[Nis67a]
									1.78E-05	2.39E-05	0.74		[Nor28b]
					E12	4-Br	H	-6.62	1.61E-05	1.58E-05	1.02	☑	[Nis67a]
									1.47E-05	1.58E-05	0.91		[Nor28c]
					E11	4-Cl	4-Cl	-6.91	8.07E-06	8.10E-06	1.00	☑	[Nis67b]
									6.7 E-06	8.10E-06	0.83		[Nor28b]
					E9	3-Cl	H	-7.69	1.25E-06	1.34E-06	0.93	☑	[Nis67a]
									1.21E-06	1.34E-06	0.90		[Pac58]
									9.88E-07	1.34E-06	0.74		[Nor28c]
					E8	3-Cl	4-Cl	-8.15	5.03E-07	4.60E-07	1.09	☑	[Nis67c]
					E7	4-NO_2	H	-9.20	4.24E-08	4.10E-08	1.03	☑	[Nis67a]

Table S1: *Continued.*

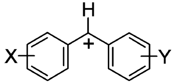
Nucleofuges					Electrofuges								
No	Leaving group	Solvent	N_f	s_f	No			E_f	k_{exp} / s^{-1}	k_{calc} / s^{-1a}	k_{exp} / k_{calc}	used in correl.	ref. short cuts
N23		60AN40W	3.84	0.96	E22	4-OMe	H	-2.09	4.08E+01	4.77E+01	0.86	☑	[Str09]
					E21	4-Me	4-Me	-3.44	2.76E+00	2.44E+00	1.13	☑	[Str09]
					E19	4-Me	H	-4.63	1.97E-01	1.77E-01	1.11	☑	[Str09]
					E14	H	H	-6.03	8.29E-03	8.01E-03	1.03	☑	[Str09]
					E11	4-Cl	4-Cl	-6.91	1.14E-03	1.16E-03	0.98	☑	[Str09]
					E10	3-F	H	-7.53	2.67E-04	2.92E-04	0.91	☑	[Nol10]
N24		80AN20W	2.96	1.00	E24	4-OMe	4-OPh	-0.86	1.20E+02	1.28E+02	0.94	☑	[Str09]
					E22	4-OMe	H	-2.09	7.70E+00	7.47E+00	1.03	☑	[Str09]
					E21	4-Me	4-Me	-3.44	3.45E-01	3.33E-01	1.04	☑	[Str09]
					E19	4-Me	H	-4.63	2.28E-02	2.14E-02	1.07	☑	[Str09]
					E14	H	H	-6.03	8.03E-04	8.40E-04	0.96	☑	[Str09]
					E11	4-Cl	4-Cl	-6.91	1.09E-04	1.11E-04	0.98	☑	[Str09]
N25		90AN10W	2.23	1.08	E25	4-OMe	4-OMe	0.00	2.49E+02	2.61E+02	0.95	☑	[Str09]
					E24	4-OMe	4-OPh	-0.86	3.32E+01	3.08E+01	1.08	☑	[Str09]
					E22	4-OMe	H	-2.09	1.53E+00	1.44E+00	1.06	☑	[Str09]
					E21	4-Me	4-Me	-3.44	4.42E-02	4.97E-02	0.89	☑	[Str09]
					E19	4-Me	H	-4.63	2.50E-03	2.56E-03	0.98	☑	[Str09]
					E14	H	H	-6.03	8.14E-05	7.72E-05	1.05	☑	[Str09]
N26		60A40W	3.30	0.97	E24	4-OMe	4-OPh	-0.86	1.74E+02	2.26E+02	0.77	☑	[Str09]
					E23	4-OMe	4-Me	-1.32	8.40E+01	8.13E+01	1.03	☑	[Str09]
					E22	4-OMe	H	-2.09	1.71E+01	1.47E+01	1.16	☑	[Str09]
					E19	4-Me	H	-4.63	6.16E-02	5.23E-02	1.18	☑	[Liu98]
					E17	4-OPh	4-NO_2	-5.60	5.77E-03	6.04E-03	0.96	☑	[Liu02]
					E14	H	H	-6.03	2.76E-03	2.31E-03	1.19	☑	[Liu98]
					E9	3-Cl	H	-7.69	4.80E-05	5.79E-05	0.83	☑	[Liu98]
					E7	4-NO_2	H	-9.20	1.95E-06	2.01E-06	0.97	☑	[Liu98]
N27		80A20W	2.03	1.05	E25	4-OMe	4-OMe	0.00	1.37E+02	1.33E+02	1.03	☑	[Str09]
					E24	4-OMe	4-OPh	-0.86	1.73E+01	1.67E+01	1.04	☑	[Str09]
					E23	4-OMe	4-Me	-1.32	5.77E+00	5.51E+00	1.05	☑	[Str09]
					E22	4-OMe	H	-2.09	9.46E-01	8.59E-01	1.10	☑	[Str09]
					E21	4-Me	4-Me	-3.44	2.80E-02	3.31E-02	0.85	☑	[Str09]

Table S1: *Continued*.

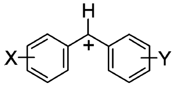
Nucleofuges					Electrofuges								
No	Leaving group	Solvent	N_f	s_f	No			E_f	k_{exp} / s^{-1}	k_{calc} / s^{-1a}	k_{exp} / k_{calc}	used in correl.	ref. short cuts
									2.79E-02	3.31E-02	0.84		[Den06]
					E20	4-OPh	H	-3.52	2.64E-02	2.70E-02	0.98	☑	[Den06]
					E19	4-Me	H	-4.63	1.76E-03	1.88E-03	0.96	☑	[Den06]
									1.64E-03	1.88E-03	0.87		[Liu98]
									1.62E-03	1.88E-03	0.86		[Str09]
									1.60E-03	1.88E-03	0.85		[Ing40b], [Arn50]
									1.57E-03	1.88E-03	0.84		[Sch60], [Har73]
									1.56E-03	1.88E-03	0.83		[Ing40a]
					E18	3,5-Me_2	H	-5.43	2.25E-04	2.70E-04	0.83	☑	[Sch60]
					E17	4-OPh	4-NO_2	-5.60	2.05E-04	1.80E-04	1.14	☑	[Liu02]
					E16	4-F	H	-5.72	1.34E-04	1.35E-04	0.99	☑	[Den06]
					E15	3-Me	H	-5.73	1.22E-04	1.30E-04	0.94	☑	[Sch60]
					E14	H	H	-6.03	6.07E-05	6.33E-05	0.96	☑	[Ber68]
									7.37E-05	6.33E-05	1.16		[Str64]
									7.30E-05	6.33E-05	1.15		[Min72]
									7.28E-05	6.33E-05	1.15		[Ing40a]
									7.27E-05	6.33E-05	1.15		[Kee64]
									7.24E-05	6.33E-05	1.14		[Ing40b], [Ber58]
									7.23E-05	6.33E-05	1.14		[Arn50]
									7.17E-05	6.33E-05	1.13		[Liu98]
									7.00E-05	6.33E-05	1.11		[Ing52]
									6.82E-05	6.33E-05	1.08		[Den06]
									6.74E-05	6.33E-05	1.06		[Koh63]
					E13	4-Cl	H	-6.44	2.31E-05	2.37E-05	0.97	☑	[Sch71]
									1.93E-05	2.37E-05	0.81		[Ber68]
					E12	4-Br	H	-6.62	1.66E-05	1.53E-05	1.08	☑	[Ber68]
					E11	4-Cl	4-Cl	-6.91	8.40E-06	7.63E-06	1.10	☑	[Ber68]
									1.45E-05	7.63E-06	1.90		[Har73]
					E9	3-Cl	H	-7.69	1.20E-06	1.15E-06	1.04	☑	[Liu98]

Table S1: *Continued*.

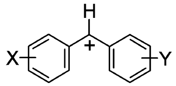
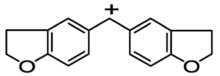
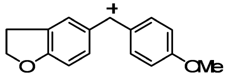
Nucleofuges					Electrofuges								
No	Leaving group	Solvent	N_f	s_f	No			E_f	k_{exp} / s^{-1}	k_{calc} / s^{-1a}	k_{exp} / k_{calc}	used in correl.	ref. short cuts
N28		90A10W	1.14	1.11	E27			1.07	4.00E+02	2.82E+02	1.42	☑	[Str09]
					E26			0.61	1.04E+02	8.60E+01	1.21	☑	[Str09]
					E25	4-OMe	4-OMe	0.00	1.45E+01	1.83E+01	0.79	☑	[Str09]
					E24	4-OMe	4-OPh	-0.86	2.09E+00	2.05E+00	1.02	☑	[Str09]
					E23	4-OMe	4-Me	-1.32	5.40E-01	6.32E-01	0.85	☑	[Str09]
					E22	4-OMe	H	-2.09	7.53E-02	8.88E-02	0.85	☑	[Str09]
					E21	4-Me	4-Me	-3.44	1.89E-03	2.84E-03	0.67	☑	[Str09]
									1.83E-03	2.84E-03	0.64		[Den06]
					E19	4-Me	H	-4.63	1.33E-04	1.37E-04	0.97	☑	[Str09]
									1.15E-04	1.37E-04	0.84		[Ber64]
									1.12E-04	1.37E-04	0.82		[Ber68]
									1.11E-04	1.37E-04	0.81		[Den06]
									9.47E-05	1.37E-04	0.69		[Liu98]
									9.46E-05	1.37E-04	0.69		[Ing40b]
					E16	4-F	H	-5.72	9.78E-06	8.49E-06	1.15	☑	[Den06]
					E14	H	H	-6.03	4.40E-06	3.80E-06	1.16	☑	[Liu98]
									5.54E-06	3.80E-06	1.46		[Ber64]
									5.07E-06	3.80E-06	1.33		[Ber68]
									4.60E-06	3.80E-06	1.21		[Ing40b]
N29	HFB	60M40W	3.06	0.84	E16	4-F	H	-5.72	5.78E-03	5.94E-03	0.97	☑	[Den09]
					E14	H	H	-6.03	3.16E-03	3.23E-03	0.98	☑	[Den09]
					E13	4-Cl	H	-6.44	1.58E-03	1.47E-03	1.07	☑	[Den09]
					E9	3-Cl	H	-7.69	1.28E-04	1.31E-04	0.98	☑	[Den09]
N30		70M30W	2.71	0.84	E19	4-Me	H	-4.63	2.72E-02	2.53E-02	1.08	☑	[Den09]
					E16	4-F	H	-5.72	2.95E-03	3.12E-03	0.95	☑	[Den09]
					E14	H	H	-6.03	1.58E-03	1.70E-03	0.93	☑	[Den09]
					E13	4-Cl	H	-6.44	7.83E-04	7.77E-04	1.01	☑	[Den09]
					E9	3-Cl	H	-7.69	7.36E-05	7.01E-05	1.05	☑	[Den09]

Table S1: *Continued.*

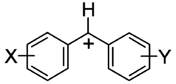
Nucleofuges					Electrofuges								
No	Leaving group	Solvent	N_f	s_f	No			E_f	k_{exp} / s^{-1}	k_{calc} / s^{-1a}	k_{exp} / k_{calc}	used in correl.	ref. short cuts
N31		80M20W	2.33	0.84	E19	4-Me	H	-4.63	1.36E-02	1.20E-02	1.13	☑	[Den09]
					E16	4-F	H	-5.72	1.37E-03	1.48E-03	0.93	☑	[Den09]
					E14	H	H	-6.03	7.10E-04	8.05E-04	0.88	☑	[Den09]
					E13	4-Cl	H	-6.44	3.63E-04	3.67E-04	0.99	☑	[Den09]
					E9	3-Cl	H	-7.69	3.61E-05	3.29E-05	1.1	☑	[Den09]
N32		90M10W	2.09	0.89	E19	4-Me	H	-4.63	5.91E-03	5.61E-03	1.05	☑	[Den09]
					E16	4-F	H	-5.72	5.40E-04	6.03E-04	0.9	☑	[Den09]
					E14	H	H	-6.03	3.05E-04	3.16E-04	0.97	☑	[Den09]
					E13	4-Cl	H	-6.44	1.51E-04	1.37E-04	1.1	☑	[Den09]
N33		M	1.52	0.9	E19	4-Me	H	-4.63	1.62E-03	1.62E-03	1	☑	[Den09]
					E16	4-F	H	-5.72	1.70E-04	1.70E-04	1	☑	[Den09]
					E14	H	H	-6.03	8.88E-05	8.87E-05	1	☑	[Den09]
N34		60E40W	2.3	0.86	E19	4-Me	H	-4.63	9.55E-03	9.89E-03	0.97	☑	[Den09]
					E16	4-F	H	-5.72	1.22E-03	1.14E-03	1.07	☑	[Den09]
					E14	H	H	-6.03	5.64E-04	6.08E-04	0.93	☑	[Den09]
					E13	4-Cl	H	-6.44	2.92E-04	2.71E-04	1.08	☑	[Den09]
					E9	3-Cl	H	-7.69	2.18E-05	2.26E-05	0.96	☑	[Den09]
N35		70E30W	1.99	0.86	E19	4-Me	H	-4.63	5.56E-03	5.51E-03	1.01	☑	[Den09]
					E16	4-F	H	-5.72	6.65E-04	6.42E-04	1.04	☑	[Den09]
					E14	H	H	-6.03	3.11E-04	3.44E-04	0.9	☑	[Den09]
					E13	4-Cl	H	-6.44	1.63E-04	1.54E-04	1.06	☑	[Den09]
N36		80E20W	1.8	0.88	E21	4-Me	4-Me	-3.44	3.77E-02	3.64E-02	1.04	☑	[Den09]
					E19	4-Me	H	-4.63	3.13E-03	3.27E-03	0.96	☑	[Den09]
					E16	4-F	H	-5.72	3.69E-04	3.59E-04	1.03	☑	[Den09]
					E14	H	H	-6.03	1.70E-04	1.89E-04	0.9	☑	[Den09]
					E13	4-Cl	H	-6.44	9.06E-05	8.29E-05	1.09	☑	[Den09]
N37		90E10W	1.37	0.88	E21	4-Me	4-Me	-3.44	1.60E-02	1.50E-02	1.07	☑	[Den09]
					E19	4-Me	H	-4.63	1.25E-03	1.34E-03	0.93	☑	[Den09]
					E16	4-F	H	-5.72	1.46E-04	1.47E-04	0.99	☑	[Den09]

Table S1: *Continued*.

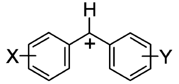
Nucleofuges					Electrofuges								
No	Leaving group	Solvent	N_f	s_f	No			E_f	k_{exp} / s^{-1}	k_{calc} / s^{-1a}	k_{exp} / k_{calc}	used in correl.	ref. short cuts
					E14	H	H	-6.03	6.80E-05	7.74E-05	0.88	☑	[Den09]
					E13	4-Cl	H	-6.44	3.92E-05	3.39E-05	1.16	☑	[Den09]
N38		E	0.77	0.93	E21	4-Me	4-Me	-3.44	3.33E-03	3.43E-03	0.97	☑	[Den09]
					E19	4-Me	H	-4.63	2.78E-04	2.72E-04	1.02	☑	[Den09]
					E16	4-F	H	-5.72	3.04E-05	2.67E-05	1.14	☑	[Den09]
					E14	H	H	-6.03	1.20E-05	1.36E-05	0.88	☑	[Den09]
N39		50A50W	2.31	0.87	E19	4-Me	H	-4.63	9.42E-03	9.65E-03	0.98	☑	[Den09]
					E16	4-F	H	-5.72	1.18E-03	1.09E-03	1.08	☑	[Den09]
					E14	H	H	-6.03	5.64E-04	5.82E-04	0.97	☑	[Den09]
					E13	4-Cl	H	-6.44	2.52E-04	2.58E-04	0.98	☑	[Den09]
N40		60A40W	1.86	0.88	E19	4-Me	H	-4.63	3.62E-03	3.63E-03	1.00	☑	[Den09]
					E16	4-F	H	-5.72	4.07E-04	3.97E-04	1.03	☑	[Den09]
					E14	H	H	-6.03	2.02E-04	2.09E-04	0.97	☑	[Den09]
					E13	4-Cl	H	-6.44	9.24E-05	9.14E-05	1.01	☑	[Den09]
N41		70A30W	1.52	0.91	E21	4-Me	4-Me	-3.44	1.81E-02	1.82E-02	0.99	☑	[Den09]
					E19	4-Me	H	-4.63	1.53E-03	1.51E-03	1.01	☑	[Den09]
					E16	4-F	H	-5.72	1.60E-04	1.55E-04	1.03	☑	[Den09]
					E14	H	H	-6.03	7.64E-05	8.01E-05	0.95	☑	[Den09]
					E13	4-Cl	H	-6.44	3.46E-05	3.42E-05	1.01	☑	[Den09]
N42		80A20W	1.01	0.91	E21	4-Me	4-Me	-3.44	6.26E-03	6.13E-03	1.02	☑	[Den09]
					E19	4-Me	H	-4.63	4.86E-04	5.07E-04	0.96	☑	[Den09]
					E16	4-F	H	-5.72	5.30E-05	5.18E-05	1.02	☑	[Den09]
N43	TFA	70M30W	2.47	0.81	E19	4-Me	H	-4.63	1.79E-02	1.79E-02	1.00	☑	[Den09]
					E16	4-F	H	-5.72	2.37E-03	2.35E-03	1.01	☑	[Den09]
					E14	H	H	-6.03	1.29E-03	1.30E-03	0.99	☑	[Den09]
N44		80M20W	2.13	0.83	E19	4-Me	H	-4.63	8.56E-03	8.57E-03	1.00	☑	[Den09]
					E16	4-F	H	-5.72	1.08E-03	1.08E-03	1.00	☑	[Den09]
					E14	H	H	-6.03	5.89E-04	5.90E-04	1.00	☑	[Den09]

Table S1: *Continued*.

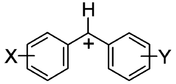
Nucleofuges					Electrofuges								
No	Leaving group	Solvent	N_f	s_f	No			E_f	k_{exp} / s^{-1}	k_{calc} / s^{-1a}	k_{exp} / k_{calc}	used in correl.	ref. short cuts
N45		90M10W	1.75	0.84	E21	4-Me	4-Me	-3.44	3.89E-02	3.80E-02	1.02	☑	[Den09]
					E19	4-Me	H	-4.63	3.65E-03	3.81E-03	0.96	☑	[Den09]
					E16	4-F	H	-5.72	4.65E-04	4.63E-04	1.00	☑	[Den09]
					E14	H	H	-6.03	2.56E-04	2.52E-04	1.02	☑	[Den09]
N46		60E40W	2.11	0.82	E19	4-Me	H	-4.63	8.45E-03	8.56E-03	0.99	☑	[Den09]
					E16	4-F	H	-5.72	1.16E-03	1.09E-03	1.06	☑	[Den09]
					E14	H	H	-6.03	5.77E-04	6.03E-04	0.96	☑	[Den09]
N47		70E30W	1.83	0.84	E21	4-Me	4-Me	-3.44	4.49E-02	4.48E-02	1.00	☑	[Den09]
					E19	4-Me	H	-4.63	4.43E-03	4.51E-03	0.98	☑	[Den09]
					E16	4-F	H	-5.72	5.83E-04	5.51E-04	1.06	☑	[Den09]
					E14	H	H	-6.03	2.88E-04	3.00E-04	0.96	☑	[Den09]
N48		80E20W	1.42	0.82	E21	4-Me	4-Me	-3.44	2.30E-02	2.21E-02	1.04	☑	[Den06]
									2.52E-02	2.21E-02	1.14		[Den09]
					E19	4-Me	H	-4.63	2.26E-03	2.32E-03	0.97	☑	[Den09]
									2.10E-03	2.32E-03	0.91		[Den06]
					E16	4-F	H	-5.72	3.07E-04	2.95E-04	1.04	☑	[Den09]
									3.27E-04	2.95E-04	1.11		[Den06]
					E14	H	H	-6.03	1.55E-04	1.62E-04	0.96	☑	[Den06]
									1.49E-04	1.62E-04	0.92		[Den09]
N49		E	0.34	0.98	E22	4-OMe	H	-2.09	2.86E-02	2.82E-02	1.01	☑	[Den06]
					E21	4-Me	4-Me	-3.44	1.89E-03	1.81E-03	1.04	☑	[Den06]
					E19	4-Me	H	-4.63	1.40E-04	1.60E-04	0.88	☑	[Den06]
					E16	4-F	H	-5.72	1.84E-05	1.74E-05	1.06	☑	[Den06]
					E14	H	H	-6.03	9.37E-06	9.17E-06	1.02	☑	[Den06]
N50		50A50W	2.03	0.81	E19	4-Me	H	-4.63	7.60E-03	7.63E-03	1.00	☑	[Den09]
					E16	4-F	H	-5.72	1.01E-03	9.90E-04	1.02	☑	[Den09]
					E14	H	H	-6.03	5.40E-04	5.48E-04	0.99	☑	[Den09]
N51		60A40W	1.66	0.86	E21	4-Me	4-Me	-3.44	3.04E-02	3.00E-02	1.01	☑	[Den09]
					E19	4-Me	H	-4.63	2.78E-03	2.85E-03	0.98	☑	[Den09]

Table S1: *Continued.*

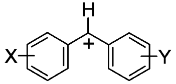
Nucleofuges					Electrofuges								
No	Leaving group	Solvent	N_f	s_f	No			E_f	k_{exp} / s^{-1}	k_{calc} / s^{-1a}	k_{exp} / k_{calc}	used in correl.	ref. short cuts
					E16	4-F	H	-5.72	3.34E-04	3.31E-04	1.01	☑	[Den09]
					E14	H	H	-6.03	1.78E-04	1.77E-04	1.01	☑	[Den09]
N52		70A30W	1.23	0.88	E21	4-Me	4-Me	-3.44	1.16E-02	1.16E-02	1.00	☑	[Den09]
					E19	4-Me	H	-4.63	1.04E-03	1.05E-03	0.99	☑	[Den09]
					E16	4-F	H	-5.72	1.17E-04	1.17E-04	1.00	☑	[Den09]
					E14	H	H	-6.03	6.18E-05	6.17E-05	1.00	☑	[Den09]
N53		80A20W	0.65	0.88	E21	4-Me	4-Me	-3.44	3.77E-03	3.53E-03	1.07	☑	[Den06]
					E19	4-Me	H	-4.63	2.85E-04	3.16E-04	0.90	☑	[Den06]
					E16	4-F	H	-5.72	3.24E-05	3.47E-05	0.93	☑	[Den06]
					E14	H	H	-6.03	2.04E-05	1.83E-05	1.11	☑	[Min72]
N54		90A10W	0.21	0.97	E22	4-OMe	H	-2.09	1.44E-02	1.50E-02	0.96	☑	[Den06]
					E21	4-Me	4-Me	-3.44	7.97E-04	7.35E-04	1.08	☑	[Den06]
					E19	4-Me	H	-4.63	4.95E-05	5.17E-05	0.96	☑	[Den06]
N55	$PhOCO_2$	80M20W	-0.33	0.81	E23	4-OMe	4-Me	-1.32	5.03E-02	4.65E-02	1.08	☑	[Den07]
					E22	4-OMe	H	-2.09	9.36E-03	1.11E-02	0.84	☑	[Den07]
					E21	4-Me	4-Me	-3.44	1.03E-03	8.97E-04	1.15	☑	[Den07]
					E19	4-Me	H	-4.63	9.31E-05	9.78E-05	0.95	☑	[Den07]
N56		90M10W	-0.61	0.85	E23	4-OMe	4-Me	-1.32	2.40E-02	2.29E-02	1.05	☑	[Den07]
					E22	4-OMe	H	-2.09	4.48E-03	5.05E-03	0.89	☑	[Den07]
					E21	4-Me	4-Me	-3.44	4.06E-04	3.58E-04	1.13	☑	[Den07]
					E19	4-Me	H	-4.63	3.30E-05	3.48E-05	0.95	☑	[Den07]
N57		M	-0.95	0.90	E24	4-OMe	4-OPh	-0.86	2.58E-02	2.34E-02	1.10	☑	[Den07]
					E23	4-OMe	4-Me	-1.32	8.87E-03	8.97E-03	0.99	☑	[Den07]
					E22	4-OMe	H	-2.09	1.53E-03	1.81E-03	0.85	☑	[Den07]
					E21	4-Me	4-Me	-3.44	1.19E-04	1.10E-04	1.08	☑	[Den07]
N58		60E40W	-0.40	0.81	E23	4-OMe	4-Me	-1.32	4.09E-02	4.00E-02	1.02	☑	[Den07]
					E22	4-OMe	H	-2.09	8.76E-03	9.50E-03	0.92	☑	[Den07]
					E21	4-Me	4-Me	-3.44	8.55E-04	7.64E-04	1.12	☑	[Den07]

Table S1: *Continued.*

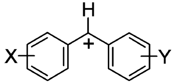
Nucleofuges					Electrofuges								
No	Leaving group	Solvent	N_f	s_f	No			E_f	k_{exp} / s^{-1}	k_{calc} / s^{-1a}	k_{exp} / k_{calc}	used in correl.	ref. short cuts
					E19	4-Me	H	-4.63	7.85E-05	8.28E-05	0.95	☑	[Den07]
N59		70E30W	-0.57	0.85	E23	4-OMe	4-Me	-1.32	2.47E-02	2.43E-02	1.02	☑	[Den07]
					E22	4-OMe	H	-2.09	5.00E-03	5.35E-03	0.93	☑	[Den07]
					E21	4-Me	4-Me	-3.44	4.17E-04	3.77E-04	1.11	☑	[Den07]
					E19	4-Me	H	-4.63	3.47E-05	3.64E-05	0.95	☑	[Den07]
N60		80E20W	-0.74	0.90	E24	4-OMe	4-OPh	-0.86	3.93E-02	3.73E-02	1.05	☑	[Den07]
					E23	4-OMe	4-Me	-1.32	1.42E-02	1.44E-02	0.99	☑	[Den07]
					E22	4-OMe	H	-2.09	2.71E-03	2.94E-03	0.92	☑	[Den07]
					E21	4-Me	4-Me	-3.44	1.89E-04	1.81E-04	1.04	☑	[Den07]
N61		90E10W	-0.91	0.96	E24	4-OMe	4-OPh	-0.86	2.18E-02	2.05E-02	1.06	☑	[Den07]
					E23	4-OMe	4-Me	-1.32	7.17E-03	7.41E-03	0.97	☑	[Den07]
					E22	4-OMe	H	-2.09	1.27E-03	1.36E-03	0.93	☑	[Den07]
					E21	4-Me	4-Me	-3.44	7.22E-05	6.95E-05	1.04	☑	[Den07]
N62		50A50W	-1.06	0.77	E23	4-OMe	4-Me	-1.32	1.56E-02	1.50E-02	1.04	☑	[Den07]
					E22	4-OMe	H	-2.09	3.61E-03	3.85E-03	0.94	☑	[Den07]
					E21	4-Me	4-Me	-3.44	3.64E-04	3.56E-04	1.02	☑	[Den07]
N63		60A40W	-1.39	0.83	E23	4-OMe	4-Me	-1.32	5.85E-03	5.81E-03	1.01	☑	[Den07]
					E22	4-OMe	H	-2.09	1.33E-03	1.35E-03	0.99	☑	[Den07]
					E21	4-Me	4-Me	-3.44	1.04E-04	1.04E-04	1.00	☑	[Den07]
N64		70A30W	-1.73	0.88	E24	4-OMe	4-OPh	-0.86	5.09E-03	5.47E-03	0.93	☑	[Den07]
					E23	4-OMe	4-Me	-1.32	2.32E-03	2.16E-03	1.07	☑	[Den07]
					E22	4-OMe	H	-2.09	4.69E-04	4.57E-04	1.03	☑	[Den07]
					E21	4-Me	4-Me	-3.44	2.94E-05	3.01E-05	0.98	☑	[Den07]
N65	DNB	80E20W	-1.43	0.98	E25	4-OMe	4-OMe	0.00	3.93E-02	3.91E-02	1.01	☑	[Den06]
					E24	4-OMe	4-OPh	-0.86	5.59E-03	5.63E-03	0.99	☑	[Den06]
					E23	4-OMe	4-Me	-1.32	1.98E-03	1.99E-03	0.99	☑	[Den06]
					E22	4-OMe	H	-2.09	3.50E-04	3.48E-04	1.01	☑	[Den06]

Table S1: *Continued.*

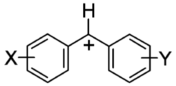
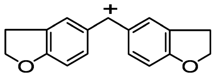
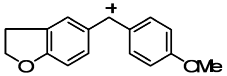
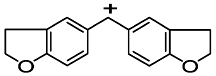
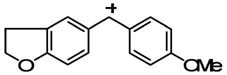
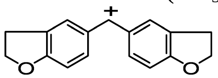
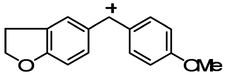
Nucleofuges					Electrofuges								
No	Leaving group	Solvent	N_f	s_f	No			E_f	k_{exp} / s^{-1}	k_{calc} / s^{-1a}	k_{exp} / k_{calc}	used in correl.	ref. short cuts
N66		E	-2.05	1.09	E25	4-OMe	4-OMe	0.00	5.79E-03	5.86E-03	0.99	☑	[Den06]
					E24	4-OMe	4-OPh	-0.86	7.52E-04	6.80E-04	1.11	☑	[Den06]
					E23	4-OMe	4-Me	-1.32	1.88E-04	2.14E-04	0.88	☑	[Den06]
					E22	4-OMe	H	-2.09	3.22E-05	3.09E-05	1.04	☑	[Den06]
N67		60AN40W	-2.06	0.97	E27			1.07	1.11E-01	1.11E-01	1.00	☑	[SchPhD]
					E26			0.61	3.96E-02	3.95E-02	1.00	☑	[SchPhD]
					E25	4-OMe	4-OMe	0.00	1.02E-02	1.02E-02	1.00	☑	[SchPhD]
N68		60A40W	-2.20	0.90	E27			1.07	9.03E-02	9.52E-02	0.95	☑	[SchPhD]
					E26			0.61	3.68E-02	3.67E-02	1.00	☑	[SchPhD]
					E25	4-OMe	4-OMe	0.00	1.20E-02[b]	1.03E-02	1.16		[Den09b]
					E24	4-OMe	4-OPh	-0.86	1.52E-03[b]	1.73E-03	0.88		[Den09b]
					E23	4-OMe	4-Me	-1.32	6.74E-04[b]	6.67E-04	1.01		[Den09b]
					E22	4-OMe	H	-2.09	1.38E-04[b]	1.35E-04	1.02		[Den09b]
N69		80A20W	-2.34	1.10	E35	4-N(CH$_3$)$_2$	4-N(CH$_3$)$_2$	4.84	4.80E+02	5.59E+02	0.86	☑	[Sch08a]
					E27			1.07	3.47E-02	4.01E-02	0.87	☑	[SchPhD]
					E26			0.61	1.12E-02	1.23E-02	0.91	☑	[SchPhD]
					E25	4-OMe	4-OMe	0.00	2.99E-03	2.64E-03	1.13	☑	[Den06]
					E24	4-OMe	4-OPh	-0.86	3.34E-04	3.00E-04	1.11	☑	[Den06]
					E23	4-OMe	4-Me	-1.32	1.08E-04	9.33E-05	1.16	☑	[Den06]
					E22	4-OMe	H	-2.09	1.85E-05	1.33E-05	1.39	☑	[Den06]
					E14	H	H	-6.03	4.39E-10	6.04E-10	0.73	☑	[Min72]

Table S1: *Continued*.

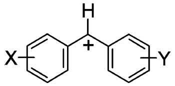
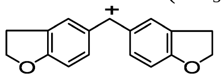
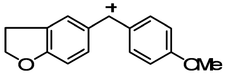
Nucleofuges					Electrofuges								
No	Leaving group	Solvent	N_f	s_f	No			E_f	k_{exp} / s^{-1}	k_{calc} / s^{-1a}	k_{exp} / k_{calc}	used in correl.	ref. short cuts
N70		90A10W	-2.68	1.13	E38	4-N(CH$_2$)$_4$	4-N(CH$_2$)$_4$	5.35	1.06E+03	1.04E+03	1.02	☑	[Sch08a]
					E35	4-N(CH$_3$)$_2$	4-N(CH$_3$)$_2$	4.84	2.53E+02	2.71E+02	0.93	☑	[Sch08a]
					E27			1.07	1.61E-02	1.54E-02	1.05	☑	[SchPhD]
					E26			0.61	5.11E-03	4.60E-03	1.11	☑	[SchPhD]
					E25	4-OMe	4-OMe	0.00	9.42E-04	9.50E-04	0.99	☑	[Den06]
					E24	4-OMe	4-OPh	-0.86	1.01E-04	1.03E-04	0.98	☑	[Den06]
					E23	4-OMe	4-Me	-1.32	2.87E-05	3.10E-05	0.93	☑	[Den06]
N71	MeOCO$_2$	80M20W	-1.43	0.94	E25	4-OMe	4-OMe	0.00	4.36E-02	4.43E-02	0.98	☑	[Den07]
					E24	4-OMe	4-OPh	-0.86	6.60E-03	6.88E-03	0.96	☑	[Den07]
					E23	4-OMe	4-Me	-1.32	2.82E-03	2.52E-03	1.12	☑	[Den07]
					E22	4-OMe	H	-2.09	4.49E-04	4.74E-04	0.95	☑	[Den07]
N72		90M10W	-1.66	0.97	E25	4-OMe	4-OMe	0.00	2.36E-02	2.42E-02	0.98	☑	[Den07]
					E24	4-OMe	4-OPh	-0.86	3.56E-03	3.54E-03	1.01	☑	[Den07]
					E23	4-OMe	4-Me	-1.32	1.34E-03	1.26E-03	1.06	☑	[Den07]
					E22	4-OMe	H	-2.09	2.16E-04	2.25E-04	0.96	☑	[Den07]
N73		M	-2.00	1.01	E25	4-OMe	4-OMe	0.00	9.31E-03	9.57E-03	0.97	☑	[Den07]
					E24	4-OMe	4-OPh	-0.86	1.35E-03	1.30E-03	1.04	☑	[Den07]
					E23	4-OMe	4-Me	-1.32	4.56E-04	4.47E-04	1.02	☑	[Den07]
					E22	4-OMe	H	-2.09	7.28E-05	7.48E-05	0.97	☑	[Den07]
N74		60E40W	-1.59	0.89	E25	4-OMe	4-OMe	0.00	3.97E-02	3.80E-02	1.04	☑	[Den07]
					E24	4-OMe	4-OPh	-0.86	5.76E-03	6.54E-03	0.88	☑	[Den07]
					E23	4-OMe	4-Me	-1.32	2.76E-03	2.54E-03	1.09	☑	[Den07]
					E22	4-OMe	H	-2.09	5.22E-04	5.23E-04	1.00	☑	[Den07]
N75		70E30W	-1.74	0.93	E25	4-OMe	4-OMe	0.00	2.55E-02	2.45E-02	1.04	☑	[Den07]
					E24	4-OMe	4-OPh	-0.86	3.58E-03	3.93E-03	0.91	☑	[Den07]
					E23	4-OMe	4-Me	-1.32	1.53E-03	1.47E-03	1.04	☑	[Den07]
					E22	4-OMe	H	-2.09	2.88E-04	2.84E-04	1.01	☑	[Den07]

Table S1: *Continued.*

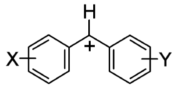
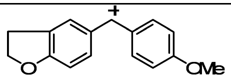
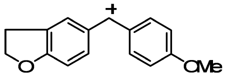
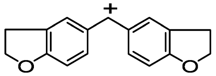
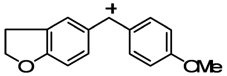
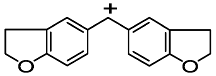
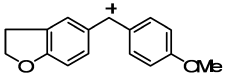
Nucleofuges					Electrofuges								
No	Leaving group	Solvent	N_f	s_f	No			E_f	k_{exp} / s^{-1}	k_{calc} / s^{-1a}	k_{exp} / k_{calc}	used in correl.	ref. short cuts
N76		80E20W	-1.96	0.95	E26			0.61	4.73E-02	5.25E-02	0.90	☑	[Str10]
					E25	4-OMe	4-OMe	0.00	1.57E-02	1.40E-02	1.12	☑	[Den07]
					E24	4-OMe	4-OPh	-0.86	2.16E-03	2.15E-03	1.00	☑	[Den07]
					E23	4-OMe	4-Me	-1.32	8.20E-04	7.88E-04	1.04	☑	[Den07]
					E22	4-OMe	H	-2.09	1.39E-04	1.47E-04	0.95	☑	[Den07]
N77		90E10W	-2.20	0.98	E26			0.61	2.33E-02	2.76E-02	0.84	☑	[Str10]
					E25	4-OMe	4-OMe	0.00	8.46E-03	7.06E-03	1.20	☑	[Den07]
					E24	4-OMe	4-OPh	-0.86	1.14E-03	1.03E-03	1.11	☑	[Den07]
					E23	4-OMe	4-Me	-1.32	3.44E-04	3.65E-04	0.94	☑	[Den07]
					E22	4-OMe	H	-2.09	6.13E-05	6.47E-05	0.95	☑	[Den07]
N78		50A50W	-2.13	0.86	E27			1.07	1.24E-01	1.24E-01	1.00	☑	[Str10]
					E26			0.61	4.87E-02	4.93E-02	0.99	☑	[Str10]
					E25	4-OMe	4-OMe	0.00	1.50E-02	1.49E-02	1.01	☑	[Den07]
					E23	4-OMe	4-Me	-1.32	1.12E-03	1.10E-03	1.02	☑	[Den07]
					E22	4-OMe	H	-2.09	2.39E-04	2.42E-04	0.99	☑	[Den07]
N79		60A40W	-2.56	0.88	E27			1.07	4.66E-02	4.91E-02	0.95	☑	[Str10]
					E26			0.61	1.90E-02	1.91E-02	0.99	☑	[Str10]
					E25	4-OMe	4-OMe	0.00	6.02E-03	5.56E-03	1.08	☑	[Den07]
					E23	4-OMe	4-Me	-1.32	3.87E-04	3.83E-04	1.01	☑	[Den07]
					E22	4-OMe	H	-2.09	7.78E-05	8.05E-05	0.97	☑	[Den07]

Table S1: *Continued*.

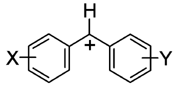
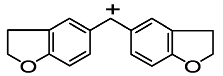
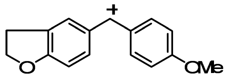
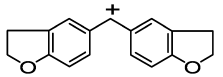
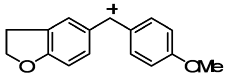
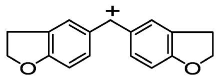
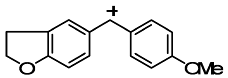
Nucleofuges					Electrofuges								
No	Leaving group	Solvent	N_f	s_f	No			E_f	k_{exp} / s^{-1}	k_{calc} / s^{-1a}	k_{exp} / k_{calc}	used in correl.	ref. short cuts
N80		70A30W	-2.83	0.94	E27			1.07	2.46E-02	2.21E-02	1.11	☑	[Str10]
					E26			0.61	6.87E-03	8.03E-03	0.86	☑	[Str10]
					E25	4-OMe	4-OMe	0.00	2.29E-03	2.15E-03	1.07	☑	[Den07]
					E24	4-OMe	4-OPh	-0.86	3.04E-04	3.34E-04	0.91	☑	[Den07]
					E23	4-OMe	4-Me	-1.32	1.33E-04	1.23E-04	1.08	☑	[Den07]
N81	PNB	80E20W	-2.78	0.95	E25	4-OMe	4-OMe	0.00	2.65E-03	2.27E-03	1.17	☑	[Den06]
					E24	4-OMe	4-OPh	-0.86	3.35E-04	3.49E-04	0.96	☑	[Den06]
					E23	4-OMe	4-Me	-1.32	1.11E-04	1.27E-04	0.87	☑	[Den06]
					E22	4-OMe	H	-2.09	2.38E-05	2.36E-05	1.01	☑	[Den06]
					E21	4-Me	4-Me	-3.44	1.19E-06	1.24E-06	0.96	☑	[Mcl82]
					E14	H	H	-6.03	4.50E-09	4.26E-09	1.06	☑	[Ben91]
N82		60AN40W	-3.30	0.91	E27			1.07	9.95E-03	9.58E-03	1.04	☑	[SchPhD]
					E26			0.61	3.39E-03	3.62E-03	0.94	☑	[SchPhD]
					E25	4-OMe	4-OMe	0.00	1.05E-03	1.02E-03	1.03	☑	[SchPhD]
N83		80AN20W	-3.41	0.98	E27			1.07	4.50E-03	5.09E-03	0.88	☑	[SchPhD]
					E26			0.61	2.21E-03	1.78E-03	1.24	☑	[SchPhD]
					E25	4-OMe	4-OMe	0.00	4.11E-04	4.52E-04	0.91	☑	[SchPhD]
N84		60A40W	-2.79	1.11	E38	4-$N(CH_2)_4$	4-$N(CH_2)_4$	5.35	7.02E+02	6.86E+02	1.02	☑	[Sch08a]
					E35	4-$N(CH_3)_2$	4-$N(CH_3)_2$	4.84	1.76E+02	1.84E+02	0.96	☑	[Sch08a]
					E33	4-$N(Ph)(CH_3)$	4-$N(Ph)(CH_3)$	3.46	6.36E+00	5.45E+00	1.17	☑	[Sch08b]
					E31	4-$N(CH_2CH_2)_2O$	4-$N(CH_2CH_2)_2O$	3.03	1.80E+00	1.85E+00	0.97	☑	[Sch08b]

Table S1: *Continued*.

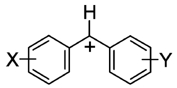
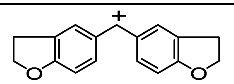
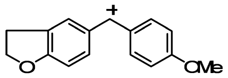
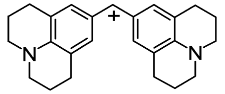
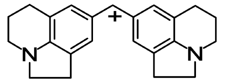
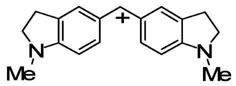
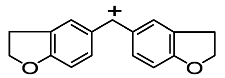
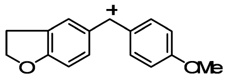
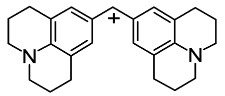
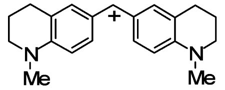
Nucleofuges					Electrofuges								
No	Leaving group	Solvent	N_f	s_f	No	 X	Y	E_f	k_{exp} / s^{-1}	k_{calc} / s^{-1a}	k_{exp}/ k_{calc}	used in correl.	ref. short cuts
					E27			1.07	9.36E-03	1.26E-02	0.74	☑	[SchPhD]
					E26			0.61	3.57E-03	3.85E-03	0.93	☑	[SchPhD]
					E25	4-OMe	4-OMe	0.00	1.07E-03	8.19E-04	1.31	☑	[SchPhD]
		80A20W	-3.40	1.16	E39			5.61	3.53E+02	3.61E+02	0.98	☑	[Sch08a]
					E38	4-N(CH$_2$)$_4$	4-N(CH$_2$)$_4$	5.35	1.56E+02	1.81E+02	0.86	☑	[Sch08a]
					E36			5.05	1.03E+02	7.99E+01	1.29	☑	[Sch08a]
					E35	4-N(CH$_3$)$_2$	4-N(CH$_3$)$_2$	4.84	3.82E+01	4.58E+01	0.83	☑	[Sch08a]
					E34			4.83	5.58E+01	4.53E+01	1.23	☑	[Sch08a]
					E33	4-N(Ph)(CH$_3$)	4-N(Ph)(CH$_3$)	3.46	1.00E+00	1.16E+00	0.86	☑	[Sch08b]
					E27			1.07	1.99E-03	2.05E-03	0.97	☑	[SchPhD]
					E26			0.61	6.32E-04	5.93E-04	1.07	☑	[SchPhD]
		90A10W	-3.70	1.17	E39			5.61	1.63E+02	1.75E+02	0.93	☑	[Sch08a]
					E38	4-N(CH$_2$)$_4$	4-N(CH$_2$)$_4$	5.35	6.59E+01	8.67E+01	0.76	☑	[Sch08a]
					E37			5.22	5.59E+01	5.97E+01	0.94	☑	[Sch08a]

Table S1: *Continued*.

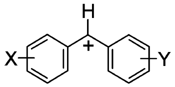
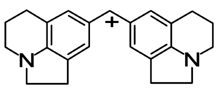
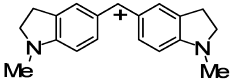
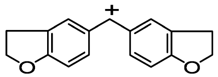
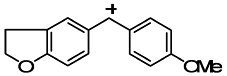
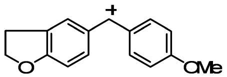
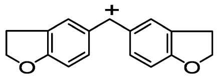
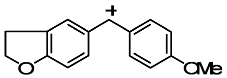
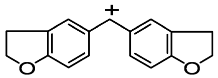
Nucleofuges					Electrofuges									
No	Leaving group	Solvent	N_f	s_f	No	X		Y	E_f	k_{exp} / s^{-1}	k_{calc} / s^{-1a}	k_{exp} / k_{calc}	used in correl.	ref. short cuts
					E36				5.05	5.22E+01	3.79E+01	1.38	☑	[Sch08a]
					E35	4-N(CH$_3$)$_2$		4-N(CH$_3$)$_2$	4.84	2.06E+01	2.15E+01	0.96	☑	[Sch08a]
					E34				4.83	2.59E+01	2.13E+01	1.22	☑	[Sch08a]
					E27				1.07	6.40E-04	8.38E-04	0.76	☑	[SchPhD]
					E26				0.61	2.92E-04	2.38E-04	1.23	☑	[SchPhD]
N87	*i*BuOCO$_2$	60E40W	-2.04	0.89	E26				0.61	5.40E-02	5.31E-02	1.02	☑	[Str10]
					E25	4-OMe		4-OMe	0.00	1.66E-02	1.53E-02	1.08	☑	[Str10]
					E24	4-OMe		4-OPh	-0.86	2.24E-03	2.64E-03	0.85	☑	[Str10]
					E23	4-OMe		4-Me	-1.32	1.00E-03	1.02E-03	0.98	☑	[Str10]
					E22	4-OMe		H	-2.09	2.31E-04	2.12E-04	1.09	☑	[Str10]
N88		90E10W	-2.46	0.98	E27				1.07	4.14E-02	4.36E-02	0.95	☑	[Str10]
					E26				0.61	1.45E-02	1.53E-02	0.95	☑	[Str10]
					E25	4-OMe		4-OMe	0.00	4.53E-03	3.87E-03	1.17	☑	[Str10]
					E24	4-OMe		4-OPh	-0.86	5.80E-04	5.60E-04	1.04	☑	[Str10]
					E23	4-OMe		4-Me	-1.32	1.81E-04	1.98E-04	0.91	☑	[Str10]
N89		50A50W	-2.51	0.87	E27				1.07	5.97E-02	5.75E-02	1.04	☑	[Str10]

Table S1: *Continued*.

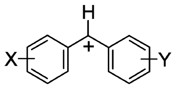
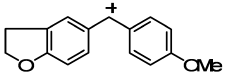
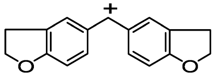
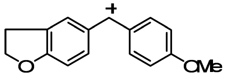
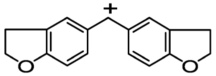
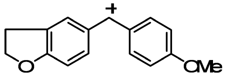
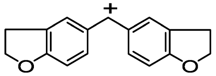
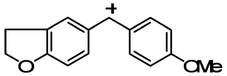
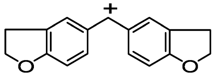
Nucleofuges					Electrofuges									
No	Leaving group	Solvent	N_f	s_f	No				E_f	k_{exp} / s^{-1}	k_{calc} / s^{-1a}	k_{exp}/ k_{calc}	used in correl.	ref. short cuts
					E26				0.61	2.13E-02	2.28E-02	0.93	☑	[Str10]
					E25	4-OMe		4-OMe	0.00	7.16E-03	6.79E-03	1.05	☑	[Str10]
					E24	4-OMe		4-OPh	-0.86	1.20E-03	1.23E-03	0.98	☑	[Str10]
					E23	4-OMe		4-Me	-1.32	4.80E-04	4.92E-04	0.98	☑	[Str10]
					E22	4-OMe		H	-2.09	1.09E-04	1.06E-04	1.03	☑	[Str10]
N90	*t*BuOCO$_2$	60E40W	-2.91	0.89	E27				1.07	2.15E-02	2.28E-02	0.94	☑	[Str10]
					E26				0.61	8.54E-03	8.76E-03	0.97	☑	[Str10]
					E25	4-OMe		4-OMe	0.00	3.00E-03	2.51E-03	1.20	☑	[Str10]
					E24	4-OMe		4-OPh	-0.86	3.94E-04	4.32E-04	0.91	☑	[Str10]
N91		80E20W	-3.12	0.96	E27				1.07	1.07E-02	1.11E-02	0.96	☑	[Str10]
					E26				0.61	3.96E-03	3.98E-03	0.99	☑	[Str10]
					E25	4-OMe		4-OMe	0.00	1.15E-03	1.04E-03	1.11	☑	[Str10]
					E24	4-OMe		4-OPh	-0.86	1.50E-04	1.58E-04	0.95	☑	[Str10]
N92		60AN40W	-3.28	0.96	E27				1.07	7.13E-03	7.66E-03	0.93	☑	[Str10]
					E26				0.61	2.76E-03	2.74E-03	1.01	☑	[Str10]
					E25	4-OMe		4-OMe	0.00	8.28E-04	7.14E-04	1.16	☑	[Str10]
					E24	4-OMe		4-OPh	-0.86	9.87E-05	1.07E-04	0.92	☑	[Str10]
N93		60A40W	-3.62	0.94	E27				1.07	3.92E-03	4.01E-03	0.98	☑	[Str10]

Table S1: *Continued.*

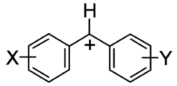
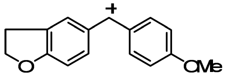
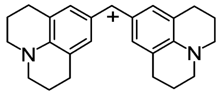
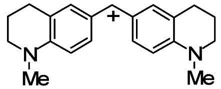
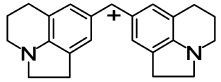
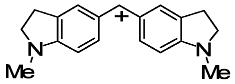
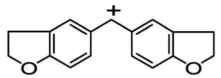
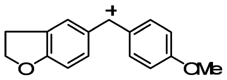
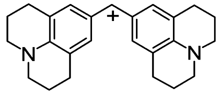
Nucleofuges					Electrofuges								
No	Leaving group	Solvent	N_f	s_f	No			E_f	k_{exp} / s^{-1}	k_{calc} / s^{-1a}	k_{exp} / k_{calc}	used in correl.	ref. short cuts
					E26			0.61	1.51E-03	1.46E-03	1.03	☑	[Str10]
					E25	4-OMe	4-OMe	0.00	3.89E-04	3.91E-04	0.99	☑	[Str10]
					E24	4-OMe	4-OPh	-0.86	6.06E-05	6.09E-05	1.00	☑	[Str10]
N94	BzO	60AN40W	-3.92	1.02	E39			5.61	6.79E+01	5.35E+01	1.27	☑	[Sch08a]
					E38	4-N(CH$_2$)$_4$	4-N(CH$_2$)$_4$	5.35	3.60E+01	2.91E+01	1.24	☑	[Sch08a]
					E37			5.22	2.45E+01	2.10E+01	1.17	☑	[Sch08a]
					E36			5.05	1.19E+01	1.41E+01	0.84	☑	[Sch08a]
					E35	4-N(CH$_3$)$_2$	4-N(CH$_3$)$_2$	4.84	7.62E+00	8.61E+00	0.89	☑	[Sch08a]
					E34			4.83	5.16E+00	8.53E+00	0.60	☑	[Sch08a]
					E32	4-N(CH$_2$CF$_3$)(CH$_3$)	4-N(CH$_2$CF$_3$)(CH$_3$)	3.13	1.91E-01	1.53E-01	1.25	☑	[SchPhD]
					E31	4-N(CH$_2$CH$_2$)$_2$O	4-N(CH$_2$CH$_2$)$_2$O	3.03	1.32E-01	1.23E-01	1.07	☑	[SchPhD]
					E30	4-N(CH$_3$)$_2$	H	2.38	2.56E-02	2.67E-02	0.96	☑	[SchPhD]
					E27			1.07	7.98E-04	1.22E-03	0.65	☑	[SchPhD]
					E26			0.61	5.81E-04	4.07E-04	1.43	☑	[SchPhD]
N95		80AN20W	-4.19	1.12	E39			5.61	4.49E+01	3.92E+01	1.15	☑	[Sch08a]
					E38	4-N(CH$_2$)$_4$	4-N(CH$_2$)$_4$	5.35	2.11E+01	2.01E+01	1.05	☑	[Sch08a]

Table S1: *Continued*.

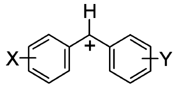
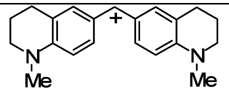
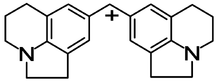
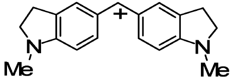
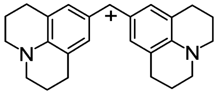
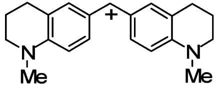
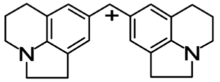
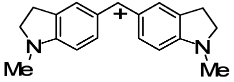
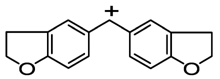
Nucleofuges					Electrofuges								
No	Leaving group	Solvent	N_f	s_f	No			E_f	k_{exp} / s^{-1}	k_{calc} / s^{-1a}	k_{exp} / k_{calc}	used in correl.	ref. short cuts
					E37			5.22	1.47E+01	1.41E+01	1.04	☑	[Sch08a]
					E36			5.05	9.58E+00	9.11E+00	1.05	☑	[Sch08a]
					E35	4-N(CH$_3$)$_2$	4-N(CH$_3$)$_2$	4.84	4.28E+00	5.31E+00	0.81	☑	[Sch08a]
					E34			4.83	5.16E+00	5.26E+00	0.98	☑	[Sch08a]
					E32	4-N(CH$_2$CF$_3$)(CH$_3$)	4-N(CH$_2$CF$_3$)(CH$_3$)	3.13	6.06E-02	6.46E-02	0.94	☑	[SchPhD]
					E31	4-N(CH$_2$CH$_2$)$_2$O	4-N(CH$_2$CH$_2$)$_2$O	3.03	4.96E-02	5.08E-02	0.98	☑	[SchPhD]
					E30	4-N(CH$_3$)$_2$	H	2.38	7.26E-03	9.59E-03	0.76	☑	[SchPhD]
					E28	4-N(Ph)$_2$	4-N(Ph)$_2$	1.78	2.79E-03	2.02E-03	1.38	☑	[SchPhD]
N96		60A40W	-3.89	1.15	E39			5.61	9.50E+01	9.72E+01	0.98	☑	[Sch08a]
					E38	4-N(CH$_2$)$_4$	4-N(CH$_2$)$_4$	5.35	5.05E+01	4.88E+01	1.03	☑	[Sch08a]
					E37			5.22	3.63E+01	3.38E+01	1.07	☑	[Sch08a]
					E36			5.05	1.93E+01	2.16E+01	0.89	☑	[Sch08a]
					E35	4-N(CH$_3$)$_2$	4-N(CH$_3$)$_2$	4.84	1.27E+01	1.24E+01	1.02	☑	[Sch08a]
					E34			4.83	1.38E+01	1.23E+01	1.12	☑	[Sch08a]
					E32	4-N(CH$_2$CF$_3$)(CH$_3$)	4-N(CH$_2$CF$_3$)(CH$_3$)	3.13	1.28E-01	1.32E-01	0.97	☑	[SchPhD]
					E31	4-N(CH$_2$CH$_2$)$_2$O	4-N(CH$_2$CH$_2$)$_2$O	3.03	9.40E-02	1.03E-01	0.91	☑	[SchPhD]
					E30	4-N(CH$_3$)$_2$	H	2.38	1.84E-02	1.85E-02	0.99	☑	[SchPhD]
					E27			1.07	4.17E-04	5.72E-04	0.73	☑	[SchPhD]

Table S1: *Continued*.

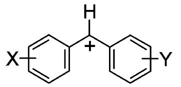
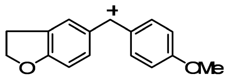
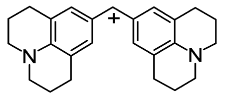
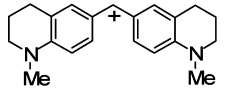
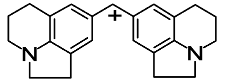
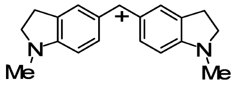
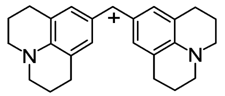
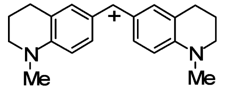
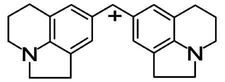
Nucleofuges					Electrofuges								
No	Leaving group	Solvent	N_f	s_f	No			E_f	k_{exp} / s^{-1}	k_{calc} / s^{-1a}	k_{exp} / k_{calc}	used in correl.	ref. short cuts
					E26			0.61	2.33E-04	1.66E-04	1.40	☑	[SchPhD]
N97		80A20W	-4.46	1.17	E39			5.61	1.97E+01	2.22E+01	0.89	☑	[Sch08a]
					E38	4-N(CH$_2$)$_4$	4-N(CH$_2$)$_4$	5.35	9.83E+00	1.10E+01	0.89	☑	[Sch08a]
					E37			5.22	7.14E+00	7.59E+00	0.94	☑	[Sch08a]
					E36			5.05	4.97E+00	4.82E+00	1.03	☑	[Sch08a]
					E35	4-N(CH$_3$)$_2$	4-N(CH$_3$)$_2$	4.84	3.49E+00	2.74E+00	1.27	☑	[Sch08a]
					E34			4.83	2.89E+00	2.71E+00	1.07	☑	[Sch08a]
					E32	4-N(CH$_2$CF$_3$)(CH$_3$)	4-N(CH$_2$CF$_3$)(CH$_3$)	3.13	2.35E-02	2.71E-02	0.87	☑	[SchPhD]
					E31	4-N(CH$_2$CH$_2$)$_2$O	4-N(CH$_2$CH$_2$)$_2$O	3.03	2.52E-02	2.11E-02	1.19	☑	[SchPhD]
					E28	4-N(Ph)$_2$	4-N(Ph)$_2$	1.78	6.64E-04	7.20E-04	0.92	☑	[SchPhD]
N98	AcO	60AN40W	-4.18	1.08	E39			5.61	3.99E+01	3.53E+01	1.13	☑	[Sch08a]
					E38	4-N(CH$_2$)$_4$	4-N(CH$_2$)$_4$	5.35	2.20E+01	1.85E+01	1.19	☑	[Sch08a]
					E37			5.22	1.34E+01	1.31E+01	1.02	☑	[Sch08a]
					E36			5.05	6.90E+00	8.60E+00	0.80	☑	[Sch08a]
					E35	4-N(CH$_3$)$_2$	4-N(CH$_3$)$_2$	4.84	4.54E+00	5.10E+00	0.89	☑	[Sch08a]

Table S1: *Continued*.

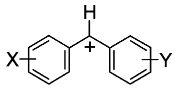
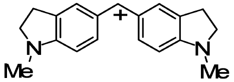
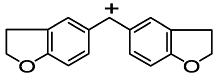
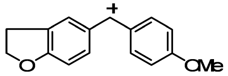
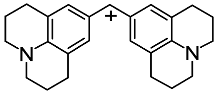
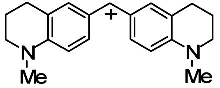
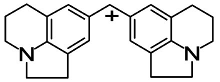
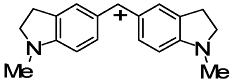
Nucleofuges					Electrofuges								
No	Leaving group	Solvent	N_f	s_f	No			E_f	k_{exp} / s^{-1}	k_{calc} / s^{-1a}	k_{exp} / k_{calc}	used in correl.	ref. short cuts
N99		80AN20W	-4.52	1.11	E34			4.83	4.52E+00	5.05E+00	0.90	☑	[Sch08a]
					E32	4-N(CH_2CF_3)(CH_3)	4-N(CH_2CF_3)(CH_3)	3.13	8.73E-02	7.15E-02	1.22	☑	[SchPhD]
					E31	4-N(CH_2CH_2)$_2$O	4-N(CH_2CH_2)$_2$O	3.03	5.53E-02	5.66E-02	0.98	☑	[SchPhD]
					E30	4-N(CH_3)$_2$	H	2.38	1.30E-02	1.13E-02	1.15	☑	[SchPhD]
					E29	4-N(CH_2CF_3)(Ph)	4-N(CH_2CF_3)(Ph)	1.79	2.37E-03	2.59E-03	0.92	☑	[SchPhD]
					E28	4-N(Ph)$_2$	4-N(Ph)$_2$	1.78	2.10E-03	2.49E-03	0.84	☑	[SchPhD]
					E27			1.07	4.43E-04	4.29E-04	1.03	☑	[SchPhD]
					E26			0.61	1.40E-04	1.34E-04	1.04	☑	[SchPhD]
					E39			5.61	1.97E+01	1.64E+01	1.20	☑	[Sch08a]
					E38	4-N(CH_2)$_4$	4-N(CH_2)$_4$	5.35	8.57E+00	8.45E+00	1.01	☑	[Sch08a]
					E37			5.22	5.87E+00	5.93E+00	0.99	☑	[Sch08a]
					E36			5.05	3.63E+00	3.85E+00	0.94	☑	[Sch08a]
					E35	4-N(CH_3)$_2$	4-N(CH_3)$_2$	4.84	1.77E+00	2.25E+00	0.79	☑	[Sch08a]
					E34			4.83	2.23E+00	2.22E+00	1.00	☑	[Sch08a]
					E32	4-N(CH_2CF_3)(CH_3)	4-N(CH_2CF_3)(CH_3)	3.13	2.60E-02	2.79E-02	0.93	☑	[SchPhD]
					E31	4-N(CH_2CH_2)$_2$O	4-N(CH_2CH_2)$_2$O	3.03	2.03E-02	2.19E-02	0.93	☑	[Sch08b]
					E30	4-N(CH_3)$_2$	H	2.38	5.55E-03	4.17E-03	1.33	☑	[SchPhD]
					E29	4-N(CH_2CF_3)(Ph)	4-N(CH_2CF_3)(Ph)	1.79	1.04E-03	9.17E-04	1.13	☑	[SchPhD]
					E28	4-N(Ph)$_2$	4-N(Ph)$_2$	1.78	9.55E-04	8.82E-04	1.08	☑	[SchPhD]

Table S1: *Continued*.

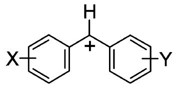
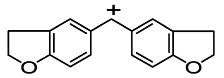
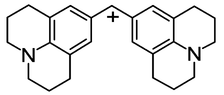
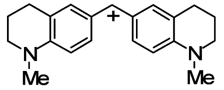
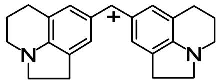
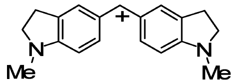
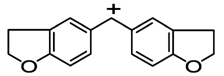
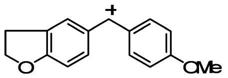
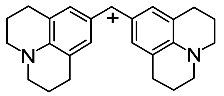
Nucleofuges					Electrofuges								
No	Leaving group	Solvent	N_f	s_f	No	 X	Y	E_f	k_{exp} / s^{-1}	k_{calc} / s^{-1a}	k_{exp} / k_{calc}	used in correl.	ref. short cuts
					E27			1.07	1.19E-04	1.45E-04	0.82	☑	[SchPhD]
					E25	4-OMe	4-OMe	0.00	8.83E-06	9.22E-06	0.96	☑	[SchPhD]
N100		60A40W	-4.05	1.17	E39			5.61	6.15E+01	6.74E+01	0.91	☑	[Sch08a]
					E38	4-N(CH$_2$)$_4$	4-N(CH$_2$)$_4$	5.35	3.59E+01	3.35E+01	1.07	☑	[Sch08a]
					E37			5.22	2.49E+01	2.31E+01	1.08	☑	[Sch08a]
					E36			5.05	1.36E+01	1.47E+01	0.93	☑	[Sch08a]
					E35	4-N(CH$_3$)$_2$	4-N(CH$_3$)$_2$	4.84	9.30E+00	8.34E+00	1.12	☑	[Sch08a]
					E34			4.83	9.41E+00	8.25E+00	1.14	☑	[Sch08a]
					E32	4-N(CH$_2$CF$_3$)(CH$_3$)	4-N(CH$_2$CF$_3$)(CH$_3$)	3.13	7.25E-02	8.31E-02	0.87	☑	[SchPhD]
					E31	4-N(CH$_2$CH$_2$)$_2$O	4-N(CH$_2$CH$_2$)$_2$O	3.03	5.00E-02	6.46E-02	0.77	☑	[SchPhD]
					E30	4-N(CH$_3$)$_2$	H	2.38	1.32E-02	1.13E-02	1.17	☑	[SchPhD]
					E29	4-N(CH$_2$CF$_3$)(Ph)	4-N(CH$_2$CF$_3$)(Ph)	1.79	1.86E-03	2.31E-03	0.81	☑	[SchPhD]
					E27			1.07	3.66E-04	3.32E-04	1.10	☑	[SchPhD]
					E26			0.61	1.09E-04	9.48E-05	1.15	☑	[SchPhD]
N101		80A20W	-4.73	1.18	E39			5.61	8.37E+00	1.11E+01	0.75	☑	[Sch08a]
					E38	4-N(CH$_2$)$_4$	4-N(CH$_2$)$_4$	5.35	4.95E+00	5.47E+00	0.90	☑	[Sch08a]

Table S1: *Continued*.

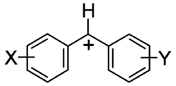
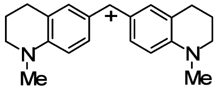
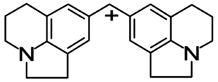
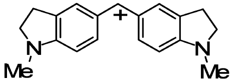
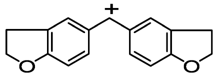
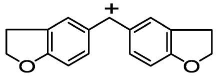
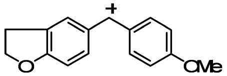
Nucleofuges					Electrofuges								
No	Leaving group	Solvent	N_f	s_f	No			E_f	k_{exp} / s^{-1}	k_{calc} / s^{-1a}	k_{exp} / k_{calc}	used in correl.	ref. short cuts
					E37			5.22	3.36E+00	3.76E+00	0.89	☑	[Sch08a]
					E36			5.05	2.24E+00	2.37E+00	0.95	☑	[Sch08a]
					E35	4-N(CH_3)$_2$	4-N(CH_3)$_2$	4.84	2.22E+00	1.34E+00	1.66	☑	[Sch08a]
					E34			4.83	1.40E+00	1.33E+00	1.05	☑	[Sch08a]
					E32	4-N(CH_2CF_3)(CH_3)	4-N(CH_2CF_3)(CH_3)	3.13	1.34E-02	1.27E-02	1.06	☑	[SchPhD]
					E31	4-N(CH_2CH_2)$_2$O	4-N(CH_2CH_2)$_2$O	3.03	1.25E-02	9.81E-03	1.27	☑	[SchPhD]
					E30	4-N(CH_3)$_2$	H	2.38	1.32E-03	1.68E-03	0.79	☑	[SchPhD]
					E29	4-N(CH_2CF_3)(Ph)	4-N(CH_2CF_3)(Ph)	1.79	4.01E-04	3.37E-04	1.19	☑	[SchPhD]
					E28	4-N(Ph)$_2$	4-N(Ph)$_2$	1.78	2.80E-04	3.24E-04	0.86	☑	[SchPhD]
					E27			1.07	4.31E-05	4.74E-05	0.91	☑	[SchPhD]
N102	Cl	DMSO	0.35	1.30	E27			1.07	8.85E+01	6.94E+01	1.28	☑	[Str10a]
					E26			0.61	1.57E+01	1.73E+01	0.91	☑	[Str10a]
					E25	4-OMe	4-OMe	0.00	2.46E+00	2.81E+00	0.88	☑	[Str10a]
					E24	4-OMe	4-OPh	-0.86	1.89E-01	2.17E-01	0.87	☑	[Str10a]
					E23	4-OMe	4-Me	-1.32	5.03E-02	5.48E-02	0.92	☑	[Str10a]
					E22	4-OMe	H	-2.09	6.78E-03	5.50E-03	1.23	☑	[Str10a]

Table S1: *Continued.*

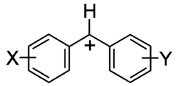
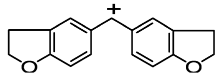
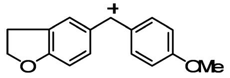
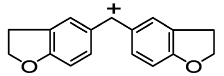
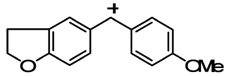
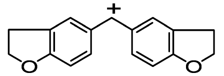
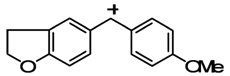
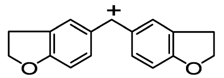
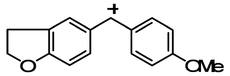
Nucleofuges					Electrofuges								
No	Leaving group	Solvent	N_f	s_f	No			E_f	k_{exp} / s^{-1}	k_{calc} / s^{-1a}	k_{exp} / k_{calc}	used in correl.	ref. short cuts
N103		CH_3CN	0.30	1.39	E27			1.07	9.51E+01	8.11E+01	1.17	☑	[Str10a]
					E26			0.61	1.70E+01	1.82E+01	0.93	☑	[Str10a]
					E25	4-OMe	4-OMe	0.00	2.40E+00	2.60E+00	0.92	☑	[Str10a]
					E24	4-OMe	4-OPh	-0.86	1.47E-01	1.66E-01	0.89	☑	[Str10a]
					E23	4-OMe	4-Me	-1.32	3.77E-02	3.79E-02	0.99	☑	[Str10a]
					E22	4-OMe	H	-2.09	3.60E-03	3.21E-03	1.12	☑	[Str10a]
N104		PC	0.10	1.35	E27			1.07	4.63E+01	3.97E+01	1.17	☑	[Str10a]
					E26			0.61	8.47E+00	9.36E+00	0.90	☑	[Str10a]
					E25	4-OMe	4-OMe	0.00	1.22E+00	1.42E+00	0.86	☑	[Str10a]
					E24	4-OMe	4-OPh	-0.86	1.05E-01	9.92E-02	1.06	☑	[Str10a]
					E23	4-OMe	4-Me	-1.32	2.47E-02	2.37E-02	1.04	☑	[Str10a]
N105		$CHCl_3$	-0.18	1.25	E27			1.07	1.54E+01	1.32E+01	1.17	☑	[Str10a]
					E26			0.61	3.17E+00	3.46E+00	0.92	☑	[Str10a]
					E25	4-OMe	4-OMe	0.00	4.98E-01	6.03E-01	0.83	☑	[Str10a]
					E24	4-OMe	4-OPh	-0.86	5.82E-02	5.12E-02	1.14	☑	[Str10a]
N106		DMF	-0.28	1.39	E27			1.07	1.44E+01	1.27E+01	1.13	☑	[Str10a]
					E26			0.61	2.55E+00	2.84E+00	0.90	☑	[Str10a]
					E25	4-OMe	4-OMe	0.00	3.69E-01	4.05E-01	0.91	☑	[Str10a]
					E24	4-OMe	4-OPh	-0.86	2.75E-02	2.60E-02	1.06	☑	[Str10a]
					E23	4-OMe	4-Me	-1.32	6.02E-03	5.92E-03	1.02	☑	[Str10a]

Table S1: *Continued.*

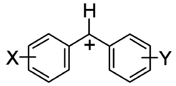
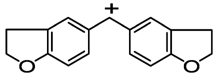
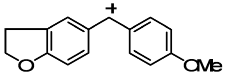
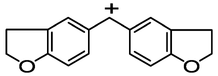
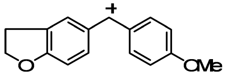
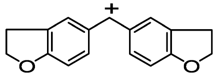
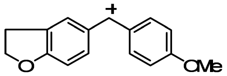
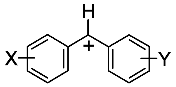
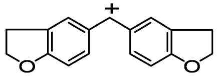
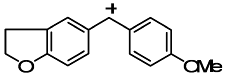
Nucleofuges					Electrofuges								
No	Leaving group	Solvent	N_f	s_f	No	X	 Y	E_f	k_{exp} / s^{-1}	k_{calc} / s^{-1a}	k_{exp} / k_{calc}	used in correl.	ref. short cuts
N107		CH_2Cl_2	-0.57	1.28	E27			1.07	4.86E+00	4.36E+00	1.11	☑	[Str10a]
					E26			0.61	1.02E+00	1.11E+00	0.92	☑	[Str10a]
					E25	4-OMe	4-OMe	0.00	1.72E-01	1.86E-01	0.92	☑	[Str10a]
					E24	4-OMe	4-OPh	-0.86	1.54E-02	1.50E-02	1.03	☑	[Str10a]
					E23	4-OMe	4-Me	-1.32	4.00E-03	3.87E-03	1.03	☑	[Str10a]
N108		DMAc	-0.82	1.33	E27			1.07	2.35E+00	2.19E+00	1.07	☑	[Str10a]
					E26			0.61	4.81E-01	5.26E-01	0.91	☑	[Str10a]
					E25	4-OMe	4-OMe	0.00	7.86E-02	8.19E-02	0.96	☑	[Str10a]
					E24	4-OMe	4-OPh	-0.86	6.66E-03	5.94E-03	1.12	☑	[Str10a]
					E23	4-OMe	4-Me	-1.32	1.37E-03	1.45E-03	0.94	☑	[Str10a]
N109		NMP	-0.98	1.31	E27			1.07	1.45E+00	1.33E+00	1.09	☑	[Str10a]
					E26			0.61	2.94E-01	3.29E-01	0.89	☑	[Str10a]
					E25	4-OMe	4-OMe	0.00	5.32E-02	5.33E-02	1.00	☑	[Str10a]
					E24	4-OMe	4-OPh	-0.86	4.16E-03	4.09E-03	1.02	☑	[Str10a]
					E23	4-OMe	4-Me	-1.32	1.04E-03	1.03E-03	1.01	☑	[Str10a]

Table S1: *Continued*.

Nucleofuges					Electrofuges								
No	Leaving group	Solvent	N_f	s_f	No			E_f	k_{exp} / s^{-1}	k_{calc} / s^{-1a}	k_{exp} / k_{calc}	used in correl.	ref. short cuts
N110		acetone	-1.00	1.38	E27			1.07	1.40E+00	1.25E+00	1.12	☑	[Str10a]
					E26			0.61	2.71E-01	2.87E-01	0.94	☑	[Str10a]
					E25	4-OMe	4-OMe	0.00	3.49E-02	4.19E-02	0.83	☑	[Str10a]
					E24	4-OMe	4-OPh	-0.86	3.31E-03	2.77E-03	1.19	☑	[Str10a]
					E23	4-OMe	4-Me	-1.32	6.12E-04	6.44E-04	0.95	☑	[Str10a]

---

[a] calculated by log $k = s_f (N_f + E_f)$, small deviations are due to calculations with more significant digits of N_f, s_f and E_f. [b] Rate constants have not been available when the least-squares minimization of the whole data set was performed.

Table S2: Solvolysis Rate Constants at 25°C.

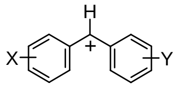
	Nucleofuges			Electrofuges							
Leaving group	Solvent	N_f	s_f	No			E_f	k_{exp} / s^{-1}	k_{calc} / s^{-1a}	k_{exp} / k_{calc}	ref. short cuts
OMs	TFE	-9.84	1.00	E4	3,5-F_2	3-F	-10.88	9.21E-02	9.21E-02	1.00	[Nol10]
				E2	3,5-F_2	3,5-F_2	-12.60	1.78E-03	1.78E-03	1.00	[Nol10]
Br	80M20W	5.34	1.00	E17	4-OPh	4-NO_2	-5.60	5.41E-01	5.57E-01	0.97	[Liu02]
				E9	3-Cl	H	-7.69	4.98E-03	4.64E-03	1.07	[Liu95]
				E7	4-NO_2	H	-9.20	1.40E-04	1.46E-04	0.96	[Liu95]
	90M10W	4.83	0.99	E17	4-OPh	4-NO_2	-5.60	1.69E-01	1.72E-01	0.98	[Liu02]
				E16	4-F	H	-5.72	1.18E-01	1.31E-01	0.90	[Liu95]
				E14	H	H	-6.03	7.15E-02	6.47E-02	1.11	[Liu95]
				E9	3-Cl	H	-7.69	1.59E-03	1.47E-03	1.08	[Liu95]
				E7	4-NO_2	H	-9.20	4.49E-05	4.73E-05	0.95	[Liu95]
	70E30W	4.83	0.96	E17	4-OPh	4-NO_2	-5.60	1.46E-01	1.80E-01	0.81	[Liu02]
				E16	4-F	H	-5.72	1.39E-01	1.38E-01	1.01	[Liu95]
				E14	H	H	-6.03	9.27E-02	6.96E-02	1.33	[Liu95]
				E9	3-Cl	H	-7.69	1.58E-03	1.76E-03	0.90	[Liu95]
				E7	4-NO_2	H	-9.20	6.39E-05	6.21E-05	1.03	[Liu95]
	90E10W	3.73	0.93	E17	4-OPh	4-NO_2	-5.60	1.52E-02	1.82E-02	0.84	[Liu02]
				E14	H	H	-6.03	8.86E-03	7.23E-03	1.23	[Liu97]
				E7	4-NO_2	H	-9.20	7.80E-06	7.99E-06	0.98	[Liu97]
	50A50W	5.11	0.93	E11	4-Cl	4-Cl	-6.91	2.12E-02	2.14E-02	0.99	[Den06]
				E9	3-Cl	H	-7.69	4.13E-03	4.07E-03	1.02	[Liu95]
				E7	4-NO_2	H	-9.20	1.62E-04	1.63E-04	0.99	[Liu95]
	60A40W	4.67	0.97	E17	4-OPh	4-NO_2	-5.60	1.12E-01	1.25E-01	0.90	[Liu02]
				E16	4-F	H	-5.72	1.05E-01	9.56E-02	1.10	[Liu98]
				E14	H	H	-6.03	5.45E-02	4.77E-02	1.14	[Liu98]
				E9	3-Cl	H	-7.69	9.21E-04	1.16E-03	0.79	[Liu98]
				E7	4-NO_2	H	-9.20	4.42E-05	3.94E-05	1.12	[Liu98]
	70A30W	3.96	0.95	E17	4-OPh	4-NO_2	-5.60	2.72E-02	2.74E-02	0.99	[Liu02]
				E16	4-F	H	-5.72	2.09E-02	2.11E-02	0.99	[Liu95]
				E14	H	H	-6.03	1.20E-02	1.07E-02	1.12	[Swa53]
				E9	3-Cl	H	-7.69	2.30E-04	2.82E-04	0.81	[Liu95]
				E7	4-NO_2	H	-9.20	1.15E-05	1.03E-05	1.11	[Liu95]
	60T40E	5.14	1.08	E17	4-OPh	4-NO_2	-5.60	2.15E-01	3.21E-01	0.67	[Liu02]
				E16	4-F	H	-5.72	2.44E-01	2.38E-01	1.03	[Liu95]
				E14	H	H	-6.03	1.43E-01	1.10E-01	1.30	[Liu95]
				E9	3-Cl	H	-7.69	2.47E-03	1.75E-03	1.41	[Liu95]
				E7	4-NO_2	H	-9.20	3.23E-05	4.07E-05	0.79	[Liu95]
	80T20E	5.86	1.15	E17	4-OPh	4-NO_2	-5.60	1.07E+0 0	1.97E+0 0	0.54	[Liu02]
				E14	H	H	-6.03	9.75E-01	6.30E-01	1.55	[Liu95]
				E9	3-Cl	H	-7.69	1.33E-02	7.78E-03	1.71	[Liu95]
				E7	4-NO_2	H	-9.20	9.92E-05	1.43E-04	0.70	[Liu95]
Cl	80M20W	4.12	1.00	E19	4-Me	H	-4.63	3.26E-01	3.10E-01	1.05	[Liu98]
				E17	4-OPh	4-NO_2	-5.60	2.95E-02	3.33E-02	0.88	[Liu02]
				E9	3-Cl	H	-7.69	3.14E-04	2.73E-04	1.15	[Liu98]
				E7	4-NO_2	H	-9.20	7.91E-06	8.47E-06	0.93	[Liu98]
	90M10W	3.56	0.99	E19	4-Me	H	-4.63	9.16E-02	8.81E-02	1.04	[Liu98]
				E17	4-OPh	4-NO_2	-5.60	8.56E-03	9.66E-03	0.89	[Liu02]
				E14	H	H	-6.03	3.74E-03	3.63E-03	1.03	[Win57]
				E9	3-Cl	H	-7.69	9.16E-05	8.26E-05	1.11	[Liu98]
				E7	4-NO_2	H	-9.20	2.51E-06	2.65E-06	0.95	[Liu98]

Table S2: *Continued.*

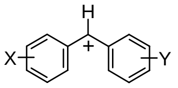
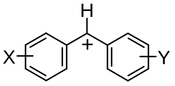
Nucleofuges				Electrofuges							
Leaving group	Solvent	N_f	s_f	No			E_f	k_{exp} / s^{-1}	k_{calc} / s^{-1a}	k_{exp} / k_{calc}	ref. short cuts
	60E40W	4.09	0.97	E17	4-OPh	4-NO_2	-5.60	2.89E-02	3.40E-02	0.85	[Liu02]
				E14	H	H	-6.03	1.59E-02	1.30E-02	1.23	[Liu98]
				E9	3-Cl	H	-7.69	3.02E-04	3.15E-04	0.96	[Liu98]
	70E30W	3.63	0.96	E17	4-OPh	4-NO_2	-5.60	1.04E-02	1.26E-02	0.83	[Liu02]
				E14	H	H	-6.03	6.03E-03	4.84E-03	1.25	[Liu98]
				E11	4-Cl	4-Cl	-6.91	8.30E-04	6.86E-04	1.21	[Har81]
				E9	3-Cl	H	-7.69	9.02E-05	1.21E-04	0.74	[Liu98]
				E7	4-NO_2	H	-9.20	4.59E-06	4.25E-06	1.08	[Liu98]
	90E10W	2.62	0.98	E19	4-Me	H	-4.63	1.06E-02	1.07E-02	0.99	[Liu98]
				E18	3,5-Me_2	H	-5.43	1.63E-03	1.76E-03	0.92	[Sch60]
				E17	4-OPh	4-NO_2	-5.60	1.20E-03	1.20E-03	1.00	[Liu02]
				E15	3-Me	H	-5.73	8.81E-04	8.96E-04	0.98	[Sch60]
				E14	H	H	-6.03	4.93E-04	4.55E-04	1.08	[War27]
				E13	4-Cl	H	-6.44	1.91E-04	1.80E-04	1.06	[Har81]
				E7	4-NO_2	H	-9.20	3.43E-07	3.53E-07	0.97	[Liu98]
	50A50W	4.26	1.03	E19	4-Me	H	-4.63	6.65E-01	4.13E-01	1.61	[Liu98]
				E17	4-OPh	4-NO_2	-5.60	2.49E-02	4.16E-02	0.60	[Liu02]
				E14	H	H	-6.03	1.38E-02	1.50E-02	0.92	[Liu98]
				E9	3-Cl	H	-7.69	2.83E-04	2.95E-04	0.96	[Liu98]
				E7	4-NO_2	H	-9.20	9.71E-06	8.26E-06	1.18	[Liu98]
	70A30W	2.72	1.00	E19	4-Me	H	-4.63	1.21E-02	1.21E-02	1.00	[Liu98]
				E17	4-OPh	4-NO_2	-5.60	1.29E-03	1.29E-03	1.00	[Liu02]
				E14	H	H	-6.03	5.10E-04	4.77E-04	1.07	[Liu98]
				E9	3-Cl	H	-7.69	8.94E-06	1.03E-05	0.87	[Liu98]
				E7	4-NO_2	H	-9.20	3.39E-07	3.15E-07	1.08	[Liu98]
	40T60E	3.45	1.04	E19	4-Me	H	-4.63	7.03E-02	5.94E-02	1.18	[Liu98]
				E17	4-OPh	4-NO_2	-5.60	4.37E-03	5.86E-03	0.75	[Liu02]
				E14	H	H	-6.03	2.10E-03	2.10E-03	1.00	[Liu98]
				E11	4-Cl	4-Cl	-6.91	2.90E-04	2.56E-04	1.13	[Rap83]
	60T40E	4.44	1.16	E19	4-Me	H	-4.63	7.57E-01	6.00E-01	1.26	[Liu98]
				E17	4-OPh	4-NO_2	-5.60	2.49E-02	4.54E-02	0.55	[Liu02]
				E14	H	H	-6.03	1.47E-02	1.45E-02	1.02	[Liu98]
				E11	4-Cl	4-Cl	-6.91	1.76E-03	1.39E-03	1.26	[Rap83]
				E9	3-Cl	H	-7.69	2.47E-04	1.75E-04	1.41	[Liu98]
				E7	4-NO_2	H	-9.20	2.52E-06	3.15E-06	0.80	[Liu98]
	80T20E	5.11	1.15	E17	4-OPh	4-NO_2	-5.60	1.25E-01	2.71E-01	0.46	[Liu02]
				E14	H	H	-6.03	1.19E-01	8.65E-02	1.38	[Liu98]
				E11	4-Cl	4-Cl	-6.91	1.29E-02	8.37E-03	1.54	[Rap83]
				E9	3-Cl	H	-7.69	1.77E-03	1.06E-03	1.68	[Liu98]
				E7	4-NO_2	H	-9.20	1.17E-05	1.92E-05	0.61	[Liu98]
	2-propanol	0.41	0.93	E22	4-OMe	H	-2.09	2.70E-02	2.78E-02	0.97	[Nis67a]
				E21	4-Me	4-Me	-3.44	1.56E-03	1.55E-03	1.01	[Nis67b]
				E19	4-Me	H	-4.63	1.23E-04	1.22E-04	1.01	[Nis67a]
				E18	3,5-Me_2	H	-5.43	2.14E-05	2.20E-05	0.97	[Nis67b]
				E16	4-F	H	-5.72	1.16E-05	1.18E-05	0.98	[Nis67a]
				E15	3-Me	H	-5.73	1.14E-05	1.16E-05	0.98	[Nis67a]
				E14	H	H	-6.03	6.06E-06	6.10E-06	0.99	[Nis67a]
				E13	4-Cl	H	-6.44	2.49E-06	2.54E-06	0.98	[Nis67a]
				E12	4-Br	H	-6.62	2.04E-06	1.73E-06	1.18	[Nis67a]
				E11	4-Cl	4-Cl	-6.91	1.06E-06	9.30E-07	1.14	[Nis67b]
				E9	3-Cl	H	-7.69	1.45E-07	1.75E-07	0.83	[Nis67a]

Table S2: *Continued.*

Nucleofuges				Electrofuges							
Leaving group	Solvent	N_f	s_f	No			E_f	k_{exp} / s^{-1}	k_{calc} / s^{-1a}	k_{exp} / k_{calc}	ref. short cuts
Me_2S	M	2.74	0.89	E19	4-Me	H	-4.63	2.40E-02	2.07E-02	1.16	[Jur10]
				E16	4-F	H	-5.72	2.14E-03	2.22E-03	0.96	[Jur10]
				E14	H	H	-6.03	8.43E-04	1.17E-03	0.72	[Jur10]
				E13	4-Cl	H	-6.44	5.83E-04	5.07E-04	1.15	[Jur10]
				E9	3-Cl	H	-7.69	4.23E-05	3.90E-05	1.08	[Jur10]
	80M20W	2.40	0.89	E19	4-Me	H	-4.63	1.10E-02	1.04E-02	1.05	[Jur10]
				E16	4-F	H	-5.72	1.24E-03	1.12E-03	1.10	[Jur10]
				E14	H	H	-6.03	4.40E-04	5.97E-04	0.74	[Jur10]
				E13	4-Cl	H	-6.44	2.92E-04	2.58E-04	1.13	[Jur10]
				E9	3-Cl	H	-7.69	2.07E-05	2.01E-05	1.03	[Jur10]
	60M40M	2.06	0.85	E19	4-Me	H	-4.63	6.37E-03	6.42E-03	0.99	[Jur10]
				E16	4-F	H	-5.72	8.43E-04	7.53E-04	1.12	[Jur10]
				E14	H	H	-6.03	3.18E-04	4.09E-04	0.78	[Jur10]
				E13	4-Cl	H	-6.44	2.18E-04	1.83E-04	1.19	[Jur10]
				E9	3-Cl	H	-7.69	1.52E-05	1.56E-05	0.97	[Jur10]
	E	2.40	0.87	E19	4-Me	H	-4.63	1.28E-02	1.17E-02	1.09	[Jur10]
				E16	4-F	H	-5.72	1.52E-03	1.33E-03	1.14	[Jur10]
				E14	H	H	-6.03	4.85E-04	7.16E-04	0.68	[Jur10]
				E13	4-Cl	H	-6.44	3.46E-04	3.16E-04	1.10	[Jur10]
				E9	3-Cl	H	-7.69	2.81E-05	2.60E-05	1.08	[Jur10]
	80E20W	1.96	0.86	E19	4-Me	H	-4.63	5.59E-03	4.93E-03	1.13	[Jur10]
				E16	4-F	H	-5.72	5.52E-04	5.66E-04	0.98	[Jur10]
				E14	H	H	-6.03	2.55E-04	3.06E-04	0.83	[Jur10]
				E13	4-Cl	H	-6.44	1.32E-04	1.35E-04	0.97	[Jur10]
				E9	3-Cl	H	-7.69	1.26E-05	1.13E-05	1.11	[Jur10]
	60E40W	1.83	0.86	E19	4-Me	H	-4.63	4.60E-03	3.88E-03	1.19	[Jur10]
				E16	4-F	H	-5.72	4.36E-04	4.46E-04	0.98	[Jur10]
				E14	H	H	-6.03	1.82E-04	2.41E-04	0.75	[Jur10]
				E13	4-Cl	H	-6.44	1.06E-04	1.07E-04	0.99	[Jur10]
				E9	3-Cl	H	-7.69	1.03E-05	8.94E-06	1.15	[Jur10]
AcO	80M20W	–3.92	0.91	E25	4-OMe	4-OMe	0.00	2.73E-04	2.68E-04	1.02	[Den10]
				E24	4-OMe	4-OPh	-0.86	4.19E-05	4.41E-05	0.95	[Den10]
				E23	4-OMe	4-Me	-1.32	1.74E-05	1.68E-05	1.03	[Den10]
	60M40W	–3.59	0.87	E25	4-OMe	4-OMe	0.00	7.64E-04	7.42E-04	1.03	[Den10]
				E24	4-OMe	4-OPh	-0.86	1.21E-04	1.32E-04	0.92	[Den10]
				E23	4-OMe	4-Me	-1.32	5.53E-05	5.23E-05	1.06	[Den10]
DNB	90E10W	–1.54	1.06	E25	4-OMe	4-OMe	0.00	2.39E-02	2.38E-02	1.00	[Den9b]
				E24	4-OMe	4-OPh	-0.86	3.11E-03	2.95E-03	1.05	[Den9b]
				E23	4-OMe	4-Me	-1.32	8.83E-04	9.66E-04	0.91	[Den9b]
				E22	4-OMe	H	-2.09	1.54E-04	1.49E-04	1.04	[Den9b]
	70A30W	-2.28	0.98	E25	4-OMe	4-OMe	0.00	6.35E-03	5.78E-03	1.10	[Den9b]
				E24	4-OMe	4-OPh	-0.86	7.25E-04	8.29E-04	0.87	[Den9b]
				E23	4-OMe	4-Me	-1.32	2.82E-04	2.94E-04	0.96	[Den9b]
				E22	4-OMe	H	-2.09	5.60E-05	5.16E-05	1.08	[Den9b]

[a] calculated by $\log k = s_f (N_f+E_f)$, small deviations are due to calculations with more significant digits of N_f, s_f and E_f.

Table S3: Heterolysis Rate Constants at 20°C (Unless Noted Otherwise).

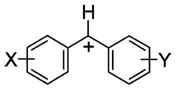
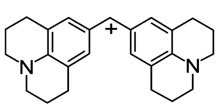
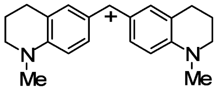
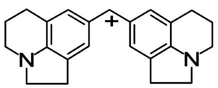
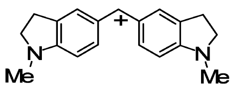
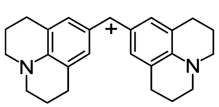
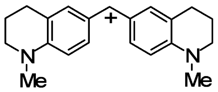
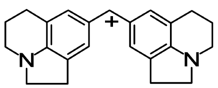
Nucleofuges				Electrofuges							
Leaving group	Solvent	N_f	s_f	No			E_f	k_{exp} / s^{-1}	k_{calc} / s^{-1c}	k_{exp} / k_{calc}	ref. short cuts
$\underline{\text{S}}$CN	AN	(1.89)	1.00	E32	4-N(CH_2CF_3)(CH_3)	4-N(CH_2CF_3)(CH_3)	3.13	7.08E+04^{a}	1.05E+05	0.67	[Loo03]
				E31	4-N(CH_2CH_2)$_2$O	4-N(CH_2CH_2)$_2$O	3.03	6.50E+04^{a}	8.34E+04	0.78	[Loo03]
				E28	4-N(Ph)$_2$	4-N(Ph)$_2$	1.78	8.93E+03^{a}	4.69E+03	1.90	[Loo03]
SC$\underline{\text{N}}$	AN	(-3.09)	1.00	E33	4-N(Ph)(CH_3)	4-N(Ph)(CH_3)	3.46	1.84E+00^{a}	2.37E+00	0.78	[Loo03]
				E31	4-N(CH_2CH_2)$_2$O	4-N(CH_2CH_2)$_2$O	3.03	1.13E+00^{a}	8.79E-01	1.28	[Loo03]
(4-MeOC_6H_4)$_3$P	CH_2Cl_2	(-5.91)	1.00	E39			5.61	5.71E-01^{a}	5.00E-01	1.14	[Kem05]
				E37			5.22	1.00E-01^{a}	2.04E-01	0.49	[Kem05]
				E36			5.05	2.83E-01^{a}	1.38E-01	2.05	[Kem05]
				E34			4.83	7.21E-02^{b}	8.30E-02	0.87	[Kem05]
(4-MeC_6H_4)$_3$P	CH_2Cl_2	(-5.20)	1.00	E39			5.61	2.97E+00^{a}	2.59E+00	1.15	[Kem05]
				E37			5.22	3.35E-01^{a}	1.06E+00	0.32	[Kem05]
				E36			5.05	1.96E+00^{a}	7.13E-01	2.75	[Kem05]

Table S3: *Continued.*

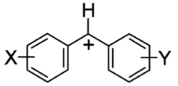
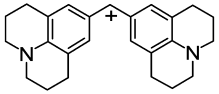
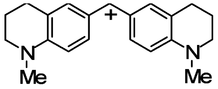
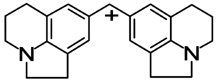
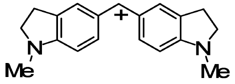
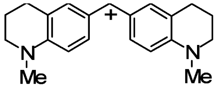
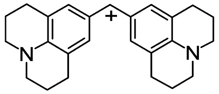
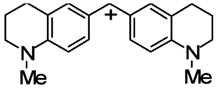
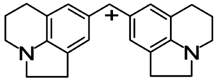
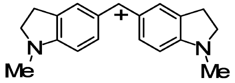
Nucleofuges				Electrofuges							
Leaving group	Solvent	N_f	s_f	No			E_f	k_{exp} / s^{-1}	k_{calc} / s^{-1c}	k_{exp} / k_{calc}	ref. short cuts
Ph_3P	CH_2Cl_2	(-4.44)	1.00	E39			5.61	4.60E+01[a]	1.47E+01	3.14	[Kem05]
				E38	4-N(CH_2)$_4$	4-N(CH_2)$_4$	5.35	2.28E+00[a]	8.06E+00	0.28	[Kem05], [BaiPhD]
				E37			5.22	4.13E+00[b]	5.97E+00	0.69	[Kem05]
				E36			5.05	2.54E+01[a]	4.04E+00	6.29	[Kem05]
				E35	4-N(CH_3)$_2$	4-N(CH_3)$_2$	4.84	4.55E-01[a]	2.49E+00	0.18	[Kem05]
				E34			4.83	3.45E+00[b]	2.43E+00	1.42	[Kem05], [BaiPhD]
(4-ClC_6H_4)$_3$P	CH_2Cl_2	(-2.93)	1.00	E37			5.22	1.17E+02[a]	1.93E+02	0.61	[Kem05]
				E33	4-N(Ph)(CH_3)	4-N(Ph)(CH_3)	3.46	2.45E+00[a]	3.35E+00	0.73	[Kem05]
				E28	4-N(Ph)$_2$	4-N(Ph)$_2$	1.78	1.58E-01[a]	7.00E-02	2.26	[Kem05]
azide	45M55AN	(-3.81)	1.00	E39			5.61	9.00E+01	6.29E+01	1.43	[Pha06]
				E37			5.22	1.74E+01	2.56E+01	0.68	[Pha06]
				E36			5.05	2.36E+01	1.73E+01	1.36	[Pha06]
				E34			4.83	7.88E+00	1.04E+01	0.76	[Pha06]

Table S3: *Continued.*

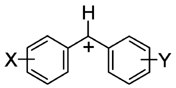
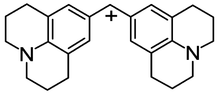
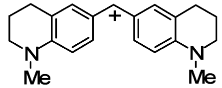
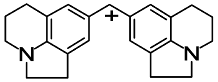
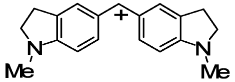
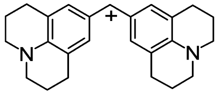
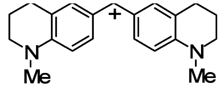
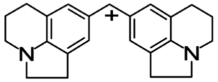
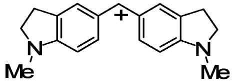
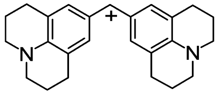
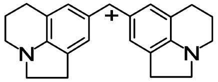
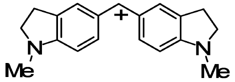
Nucleofuges				Electrofuges						
Leaving group	Solvent	N_f	s_f	No		E_f	k_exp / s^{-1}	k_calc / s^{-1c}	k_exp / k_calc	ref. short cuts
1.00	91M9AN	(-3.85)	1.00	E39		5.61	7.52E+01	5.70E+01	1.32	[Pha06]
				E37		5.22	2.08E+01	2.32E+01	0.90	[Pha06]
				E36		5.05	1.96E+01	1.57E+01	1.25	[Pha06]
				E34		4.83	6.40E+00	9.46E+00	0.68	[Pha06]
1.00	91E9AN	(-4.38)	1.00	E39		5.61	2.42E+01	1.71E+01	1.42	[Pha06]
				E37		5.22	4.50E+00	6.97E+00	0.65	[Pha06]
				E36		5.05	7.99E+00	4.71E+00	1.70	[Pha06]
				E34		4.83	1.83E+00	2.84E+00	0.64	[Pha06]
1.00	AN	(-3.76)	1.00	E39		5.61	7.21E+01^a	7.04E+01	1.02	[Tis05]
				E36		5.05	2.72E+01^a	1.94E+01	1.40	[Tis05]
				E34		4.83	8.14E+00^a	1.17E+01	0.70	[Tis05]

Table S3: *Continued.*

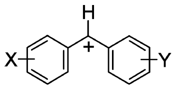
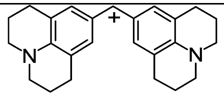
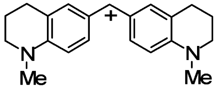
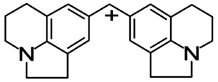
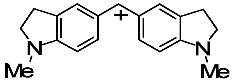
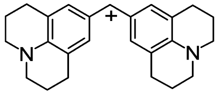
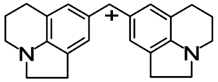
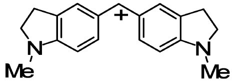
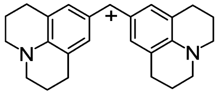
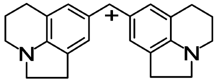
Nucleofuges				Electrofuges							
Leaving group	Solvent	N_f	s_f	No			E_f	k_{exp} / s^{-1}	k_{calc} / s^{-1c}	k_{exp} / k_{calc}	ref. short cuts
DMAP	CH_2Cl_2	(-5.32)	1.00	E39			5.61	1.68E+00[a]	1.94E+00	0.87	[Bro07]
				E37			5.22	4.80E-01[a]	7.91E-01	0.61	[Bro07]
				E36			5.05	1.13E+00[a]	5.35E-01	2.11	[Bro07]
				E34			4.83	2.90E-01[a]	3.22E-01	0.90	[Bro07]
	AN	(-6.29)	1.00	E39			5.61	2.04E-01[a]	2.07E-01	0.99	[Bai07]
				E36			5.05	8.65E-02[a]	5.70E-02	1.52	[Bai07]
				E34			4.83	2.30E-02[a]	3.44E-02	0.67	[Bai07]
4-(1-pyrrolidinyl)-pyridine	CH_2Cl_2	(-5.33)	1.00	E39			5.61	1.58E+00[b]	1.89E+00	0.83	[BaiPhD] [Bro07]
				E36			5.05	6.25E-01[b]	5.21E-01	1.20	[BaiPhD] [Bro07]
4-methoxypyridine	CH_2Cl_2	(-2.80)	1.00	E38	4-$N(CH_2)_4$	4-$N(CH_2)_4$	5.35	2.18E+02[b]	3.57E+02	0.61	[BaiPhD]
				E35	4-$N(CH_3)_2$	4-$N(CH_3)_2$	4.84	7.36E+01[b]	1.10E+02	0.67	[BaiPhD]
				E33	4-N(Ph)(CH_3)	4-N(Ph)(CH_3)	3.46	9.44E+00[b]	4.60E+00	2.05	[BaiPhD]
				E31	4-$N(CH_2CH_2)_2O$	4-$N(CH_2CH_2)_2O$	3.03	2.04E+00[b]	1.71E+00	1.19	[BaiPhD]

Table S3: *Continued.*

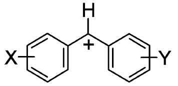
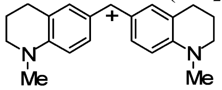
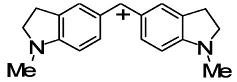
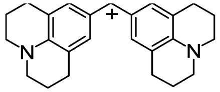
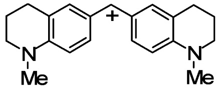
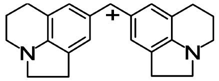
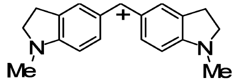
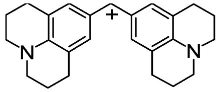
Nucleofuges				Electrofuges							
Leaving group	Solvent	N_f	s_f	No			E_f	k_{exp} / s^{-1}	k_{calc} / s^{-1c}	k_{exp} / k_{calc}	ref. short cuts
4-methylpyridine	CH_2Cl_2	(-1.91)	1.00	E35	4-$N(CH_3)_2$	4-$N(CH_3)_2$	4.84	3.44E+02[b]	8.44E+02	0.41	[BaiPhD] [Bro07]
				E33	4-$N(Ph)(CH_3)$	4-$N(Ph)(CH_3)$	3.46	4.64E+01[b]	3.52E+01	1.32	[BaiPhD] [Bro07]
				E31	4-$N(CH_2CH_2)_2O$	4-$N(CH_2CH_2)_2O$	3.03	1.04E+01[b]	1.31E+01	0.79	[BaiPhD] [Bro07]
				E29	4-$N(CH_2CF_3)_2$	4-$N(CH_2CF_3)_2$	1.79	1.76E+00[a]	7.52E-01	2.34	[Bro07]
pyridine	CH_2Cl_2	(-0.99)	1.00	E33	4-$N(Ph)(CH_3)$	4-$N(Ph)(CH_3)$	3.46	2.59E+02[b]	2.92E+02	0.89	[BaiPhD] [Bro07]
				E31	4-$N(CH_2CH_2)_2O$	4-$N(CH_2CH_2)_2O$	3.03	5.63E+01[b]	1.08E+02	0.52	[BaiPhD] [Bro07]
				E29	4-$N(CH_2CF_3)_2$	4-$N(CH_2CF_3)_2$	1.79	1.35E+01[a]	6.24E+00	2.17	[Bro07]
DABCO	AN	(-1.00)	1.00	E38	4-$N(CH_2)_4$	4-$N(CH_2)_4$	5.35	1.42E+04[a]	2.25E+04	0.63	[Bai07]
				E37			5.22	1.79E+04[a]	1.67E+04	1.07	[Bai07]
				E34			4.83	1.00E+04[a]	6.79E+03	1.47	[Bai07]
SO₂Ph[d]	50AN50W	(-4.69)	1.00	E39			5.61	1.09E+01	8.40E+00	1.30	[Bai10a]
				E37			5.22	2.97E+00	3.42E+00	0.87	[Bai10a]
				E36			5.05	2.51E+00	2.31E+00	1.09	[Bai10a]
				E34			4.83	1.14E+00	1.39E+00	0.82	[Bai10a]
	60AN40W	(-4.87)	1.00	E39			5.61	6.02E+00	5.53E+00	1.09	[Bai10a]

Table S3: *Continued.*

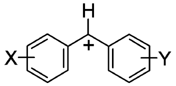
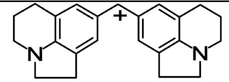
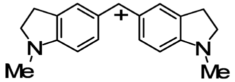
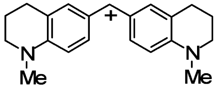
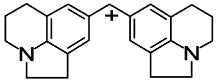
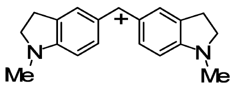
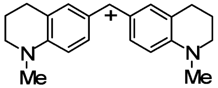
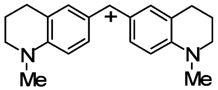
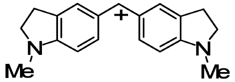
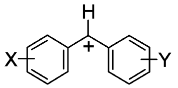
Nucleofuges				Electrofuges							
Leaving group	Solvent	N_f	s_f	No			E_f	k_{exp} / s^{-1}	k_{calc} / s^{-1c}	k_{exp} / k_{calc}	ref. short cuts
				E36			5.05	1.67E+00	1.52E+00	1.10	[Bai10a]
				E34			4.83	7.70E-01	9.18E-01	0.84	[Bai10a]
S<u>O</u>$_2$Ph	DMSO	(-3.10)	1.00	E25	4-OMe	4-OMe	0.00	8.09E-04	8.09E-04	1.00	[Bai10a]
1-methylimidazole	AN	(-6.29)	1.00	E37			5.22	5.00E-02[a]	8.51E-02	0.59	[Bai10b]
				E36			5.05	1.00E-01[a]	5.76E-02	1.74	[Bai10b]
				E34			4.83	3.40E-02[a]	3.47E-02	0.98	[Bai10b]
1-phenylimidazole	AN	(-5.59)	1.00	E38	4-N(CH$_2$)$_4$	4-N(CH$_2$)$_4$	5.35	5.60E-01[a]	5.76E-01	0.97	[Bai10b]
				E37			5.22	5.20E-01[a]	4.27E-01	1.22	[Bai10b]
				E35	4-N(CH$_3$)$_2$	4-N(CH$_3$)$_2$	4.84	1.50E-01[a]	1.78E-01	0.84	[Bai10b]
1-methylbenzimidazole	AN	(-6.01)	1.00	E38	4-N(CH$_2$)$_4$	4-N(CH$_2$)$_4$	5.35	1.60E-01[a]	2.20E-01	0.73	[Bai10b]
				E37			5.22	2.30E-01[a]	1.63E-01	1.41	[Bai10b]
				E35	4-N(CH$_3$)$_2$	4-N(CH$_3$)$_2$	4.84	4.00E-02[a]	6.80E-02	0.59	[Bai10b]
				E34			4.83	1.10E-01[a]	6.64E-02	1.66	[Bai10b]

Table S3: *Continued.*

Nucleofuges				Electrofuges							
Leaving group	Solvent	N_f	s_f	No			E_f	k_{exp} / s^{-1}	k_{calc} / s^{-1c}	k_{exp} / k_{calc}	ref. short cuts
isoquinoline	AN	(-3.04)	1.00	E35	4-N(CH$_3$)$_2$	4-N(CH$_3$)$_2$	4.84	4.07E+01^a	6.37E+01	0.64	[BaiPhD]
				E33	4-N(Ph)(CH$_3$)	4-N(Ph)(CH$_3$)	3.46	3.66E+00^a	2.66E+00	1.38	[BaiPhD]
				E31	4-N(CH$_2$CH$_2$)$_2$O	4-N(CH$_2$CH$_2$)$_2$O	3.03	1.12E+00^a	9.86E-01	1.14	[BaiPhD]

[a] calculated from experimental equilibrium constant K and second-order rate constant k_2 by $k=k_2/K$. [b] calculated from experimental equilibrium constant K and calculated (from N and s parameters) second-order rate constant k_2 by $k=k_2/K$. [c] calculated by $\log k = s_f (N_f+E_f)$, small deviations are due to calculations with more significant digits of N_f, s_f and E_f. [d] at 25°C

Table S4: Reference Short Cuts.

ref. short cut	reference
[Alt52]	S. Altscher, R. Baltzly, S. W. Blackman, *J. Am. Chem. Soc.* **1952**, *74*, 3649–3652.
[Arn50]	R. T. Arnold, K. Murai, R. M. Dodson, *J. Am. Chem. Soc.* **1950**, 72, 4193–4195.
[Bad58]	G. Baddeley, S. Varma, M. Gordon, *J. Chem. Soc.* **1958**, 3171–3174.
[Bai07]	M. Baidya, S. Kobayashi, F. Brotzel, U. Schmidhammer, E. Riedle, H. Mayr, *Angew. Chem.* **2007**, *119*, 6288–6292; *Angew. Chem. Int. Ed.* **2007**, *46*, 6176–6179.
[Bai10a]	M. Baidya, S. Kobayashi, H. Mayr, *J. Am. Chem. Soc.* **2010**, *132*, 4796–4805.
[Bai10b]	M. Baidya, F. Brotzel, H. Mayr, *Org. Biomol. Chem.* **2010**, *8*, 1929–1935.
[BaiPhD]	M. Baidya, Dissertation, Ludwig-Maximilians-Universität München, 2009.
[Ben91]	T. W. Bentley, M. Christl, S. J. Norman, *J. Org. Chem.* **1991**, *56*, 6238–6240.
[Ber58]	E. Berliner, M. M. Chen, *J. Am. Chem. Soc.* **1958**, *80*, 343–347.
[Ber64]	L. Verbit, E. Berliner, *J. Am. Chem. Soc.* **1964**, *86*, 3307–3312.
[Ber68]	E. Berliner, M. Q. Malter, *J. Org. Chem.* **1968**, *33*, 2595–2596.
[Bro07]	F. Brotzel, B. Kempf, T. Singer, H. Zipse, H. Mayr, *Chem. Eur. J.* **2007**, *13*, 336–345.
[Den10]	B. Denegri, O.Kronja, *Croat. Chem. Acta* **2010**, *83*, 223–226.
[Den06]	B. Denegri, A. Streiter, S. Juric, A. R. Ofial, O. Kronja, H. Mayr, *Chem. Eur. J.* **2006**, *12*, 1648–1656; *Chem. Eur. J.* **2006**, *12*, 5415.
[Den07]	B. Denegri, O. Kronja, *J. Org. Chem.* **2007**, *72*, 8427–8433.
[Den09]	B. Denegri, O. Kronja, *J. Org. Chem.* **2009**, *74*, 5927–5933.
[Den09b]	B. Denegri, O. Kronja, *J. Phys. Org. Chem.* **2009**, *22*, 495–503.
[Dvo89]	G. F. Dvorko, N. Yu. Evtushenko, *J. Gen. Chem. USSR* **1989**, *59*, 1216–1220; *Zh. Obshch. Khim.* **1989**, *59*, 1371–1376.
[Gri71]	G. W. Gribble, M. S. Smith, *J. Org. Chem.* **1971**, *36*, 2724–2727.
[Ham37]	N. T. Farinacci, L. P. Hammett, *J. Am. Chem. Soc.* **1937**, *59*, 2542–2546.
[Har73]	J. M. Harris, A. Becker, D. C. Clark, J. F. Fagan, S. L. Kennan, *Tetrahedron Lett.* **1973**, 3813–3816.
[Har81]	S. G. Shafer, J. M. Harris, *J. Org. Chem.* **1981**, *46*, 2164–2169.
[Ing40a]	E. D. Hughes, C. K. Ingold, N. A. Taher, *J. Chem. Soc.* **1940**, 949–956.
[Ing40b]	L. C. Bateman, M. G. Church, E. D. Hughes, C. K. Ingold, N. A. Taher, *J. Chem. Soc.* **1940**, 979–1011.
[Ing52]	O.T. Benfey, E. D. Hughes, C. K. Ingold, *J. Chem. Soc.* **1952**, 2488–2493.
[Jur10]	S. Juric, B. Denegri, O. Kronja, *J. Org. Chem.* **2010**, ASAP.
[Kee62]	A. Singh, L. J. Andrews, R. M. Keefer, *J. Am. Chem. Soc.* **1962**, *84*, 1179–1185.
[Kee64]	E. A. Jeffery, R. K. Bansal, L. J. Andrews, R. M. Keefer, *J. Org. Chem.* **1964**, *29*, 3365–3370.
[Kem05]	B. Kempf, H. Mayr, *Chem. Eur. J.* **2005**, *11*, 917–927.
[Koh63]	G. R. Cowie, H. J. M. Fitchies, G. Kohnstam, *J. Chem. Soc.* **1963**, 1585–1593.
[Liu95]	K.-T. Liu, C.-P. Chin, Y.-S. Lin, M.-L. Tsao, *Tetrahedron Lett.* **1995**, *36*, 6919–6922.
[Liu97]	K.-T. Liu, C.-P. Chin, Y.-S. Lin, M.-L. Tsao, *J. Chem. Res. (S)* **1997**, 18–19.
[Liu98]	K.-T. Liu, Y.-S. Lin, M.-L. Tsao, *J. Phys. Org. Chem.* **1998**, *11*, 223–229.

Table S4: *Continued.*

ref. short cut	reference
[Liu02]	K.-T. Liu, C.-S. Chuang, B.-Y. Jin, *J. Phys. Org. Chem.* **2002**, *15*, 21–28.
[Loo03]	R. Loos, S. Kobayashi, H. Mayr, *J. Am. Chem. Soc.* **2003**, *125*, 14126–14132.
[Mcl82]	D. J. McLennan, P. L. Martin, *J. Chem. Soc. Perkin Trans. 2* **1982**, 1091–1097.
[Min72]	J. Mindl, P. Pivoňka, M. Večeřa, *Collect. Czech. Chem. Commun.* **1972**, *37*, 3496–3505.
[Min73]	J. Mindl, M. Večeřa, *Collect. Czech. Chem. Commun.* **1973**, *38*, 3496–3505.
[Nis67a]	S. Nishida, *J. Org. Chem.* **1967**, *32*, 2692–2695.
[Nis67b]	S. Nishida, *J. Org. Chem.* **1967**, *32*, 2695–2697.
[Nis67c]	S. Nishida, *J. Org. Chem.* **1967**, *32*, 2697–2701.
[Nol10]	C. Nolte, H. Mayr, *Eur. J. Org. Chem.* **2010**, 1435–1439.
[Nol10u]	C. Nolte, H. Mayr, **2010**, unpublished.
[Nor28a]	J. F. Norris, A. A. Morton, *J. Am. Chem. Soc.* **1928**, *50*, 1795–1803.
[Nor28b]	J. F. Norris, C. Banta, *J. Am. Chem. Soc.* **1928**, *50*, 1804–1808.
[Nor28c]	J. F. Norris, J. T. Blake, *J. Am. Chem. Soc.* **1928**, *50*, 1808–1812.
[Pac58]	J. Packer, J. Vaughan, A. F. Wilson, *J. Org. Chem.* **1958**, *23*, 1215–1216.
[Pha06]	T. B. Phan, H. Mayr, *J. Phys. Org. Chem.* **2006**, *19*, 706–713.
[Rap83]	Z. Rappoport, H. Ben-Yacov, J. Kaspi, *J. Org. Chem.* **1978**, *43*, 3678–3684.
[Sch60]	W. M. Schubert, R. G. Minton, *J. Am. Chem. Soc.* **1960**, *82*, 6188–6193.
[Sch88]	a) C. Schade, H. Mayr, *Tetrahedron* **1988**, *44*, 5761–5770; b) C. Schade, *Dissertation*, Med. Universität zu Lübeck, 1988.
[Sch8a]	H. F. Schaller, A. A. Tishkov, X. Feng, H. Mayr, *J. Am. Chem. Soc.* **2008**, *130*, 3012–3022.
[Sch8b]	H. F. Schaller, H. Mayr, *Angew. Chem.* **2008**, *120*, 4022–4025; *Angew. Chem. Int. Ed.* **2008**, *47*, 3958–3961.
[SchPhD]	H. Schaller, Dissertation, Ludwig-Maximilians-Universität München, 2008.
[Str10]	N. Streidl, R. Branzan, H. Mayr, *Eur. J. Org. Chem.* **2010**, 4205–4210.
[Str10a]	N. Streidl, Chapter 4, Dissertation Ludwig-Maximilians-Universität München, 2010.
[Str64]	A. Streitwieser, Jr., H. S. Klein, *J. Am. Chem. Soc.* **1964**, *86*, 5170–5173.
[Str09]	N. Streidl, A. Antipova, H. Mayr, *J. Org. Chem.* **2009**, *74*, 7328–7334.
[Tis05]	A. A. Tishkov, U. Schmidhammer, S. Roth, E. Riedle, H. Mayr, *Angew. Chem.* **2005**, *117*, 4699–4703; *Angew. Chem. Int. Ed.* **2005**, *44*, 4623–4626.
[Swa53]	C. G. Swain, C. B. Scott, K. H. Lohmann, *J. Am. Chem. Soc.* **1953**, *75*, 136–140.
[War27]	A. M. Ward, *J. Chem. Soc.* **1927**, 2285–2295.
[Win57]	S. Winstein, A. H. Fainberg, E. Grunwald, *J. Am. Chem. Soc.* **1957**, *79*, 4146–4155.

LEBENSLAUF

Persönliche Daten

Nicolas Streidl

geboren am 16.02.1980

ledig, Staatsangehörigkeit: deutsch

Geburtsort Augsburg

Schulen

1986-1990	Grundschule Gablingen
1990-1999	Paul-Klee-Gymnasium Gersthofen
Jun 1999	Abitur

Grundwehrdienst

Jul 1999 – Apr 2000	Grundwehrdienst in Holzdorf und Kaufbeuren

Studium und Promotion

Okt 2000 - Mai 2005	Chemiestudium an der Ludwig-Maximilians-Universität München, Wahlfach Patentrecht
Jun 2005- Dez 2005	Diplomarbeit im Arbeitskreis Prof. H. Mayr, LMU, Titel: „Chemoselektivität der Reaktionen von Benzhydrylestern mit Nucleophilen“
Jan 2006-heute	Promotion im Arbeitskreis Prof. H. Mayr, LMU Wissenschaftliche Betreuung von Studenten im Praktikum

München, 09.08.2010