Carbocations

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“Carbocation Watching” in Solvolysis Reactions**

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Dedicated to Professor R. W. Hoffmann on the occasion of his 75th birthday

The mechanisms of S_N1 reactions were one of the most intensively studied topics in organic chemistry during the middle of the 20th century.[1] These reactions typically proceed with slow formation of the carbocations followed by fast subsequent reactions with the solvent (Scheme 1).

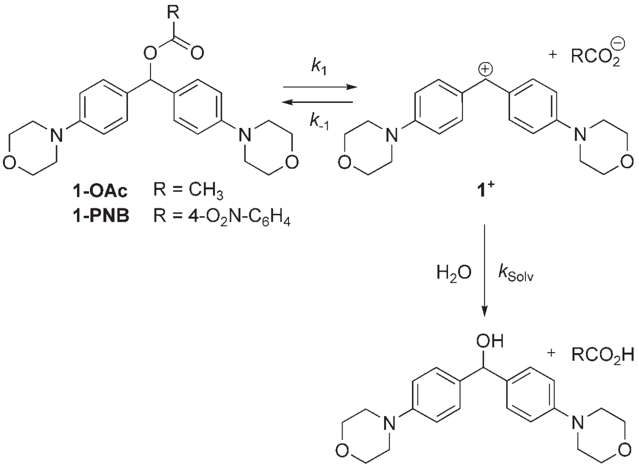
$$\mathrm{R{-}X} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{R}^{+} + \mathrm{X}^{-} \xrightarrow[\mathrm{HOSolv}]{k_{\mathrm{Solv}}} \mathrm{R{-}OSolv} + \mathrm{HX}$$

Scheme 1. A typical solvolysis reaction.

Detailed mechanistic studies by Winstein et al.[2] showed that intermediate carbocations can recombine with the leaving group at the ion-pair or free-ion stage before being trapped by the solvent. Since methods for studying fast reaction kinetics were not available at that time, most information on the relative rates of ionization, ion recombination, and reaction of the intermediate carbocation with the solvent was derived indirectly from measurement of the overall solvolysis rates.

Recently we have shown that the ionization rates of covalent benzhydryl esters can be observed photometrically if the resulting carbocations are highly stabilized and do not undergo subsequent reactions with the solvent.[3] We have also reported that the trifluoroethanolysis of chlorobis(*p*-methoxyphenyl)methane proceeds with instantaneous formation of the carbocation, and its subsequent combination with trifluoroethanol could be followed photometrically with a stopped-flow instrument.[4] Based on these results it was predicted that it should be possible to design systems where both the ionization and the following reaction can be measured. We have now realized such systems and report on the first solvolysis reactions in which the formation of carbocations and their subsequent disappearance in aqueous acetone and acetonitrile can be measured directly and fitted by the kinetic model depicted in Scheme 2.

When water was added to the colorless solution of 4,4′-bis(morpholino)benzhydryl acetate (**1-OAc**) in acetonitrile, the solution rapidly turned blue, then faded again within a couple of minutes. A video demonstrating such “carbocation watching” is provided in the Supporting Information (see also Experimental Section).



Scheme 2. Solvolysis reaction of 4,4′-bis(morpholino)benzhydryl carboxylates in aqueous acetone or acetonitrile.

Photometric monitoring of this process showed that the maximum of the carbocation concentration was reached after 7 s in 80 % aqueous acetonitrile. From the absorbance one could derive that at this point, the concentration of the carbocation corresponded to approximately 3 % of the initial substrate concentration. The fact that the blue color appears much faster than it disappears indicates that the small maximum concentration of the carbocation must result from the fast recombination of the carbocations with the acetate anions. Owing to the involvement of several rate and equilibrium constants (partial dissociation of acetic acid) we were not able to find a kinetic model that fits the resulting plot of the carbocation concentration versus time (see Figure S6 in the Supporting Information). However, the corresponding reaction in the presence of diisopropyl-methylamine ($(i\mathrm{Pr})_2\mathrm{NMe}$), which shows a similar absorbance–time correlation (Figure 1), could be fitted to the kinetic model shown in Scheme 1. The resulting rate constants and the Gepasi[5] fit of the carbocation concentration are shown in Figure 1.

When the solvolysis reaction of **1-OAc** was followed conductimetrically under the same conditions, a continuous increase of the ion concentration (see Figure S4 in the Supporting Information) was observed. We assumed a direct proportionality between conductivity and the concentration of $[(i\mathrm{Pr})_2\mathrm{NHMe}]^+\mathrm{OAc}^-$, and fitted this curve by Gepasi to obtain values of $k_{-1} = 1.09 \times 10^{-3}\ \mathrm{L\,mol^{-1}\,s^{-1}}$ and $k_{\mathrm{Solv}} = 2.01 \times$

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Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.

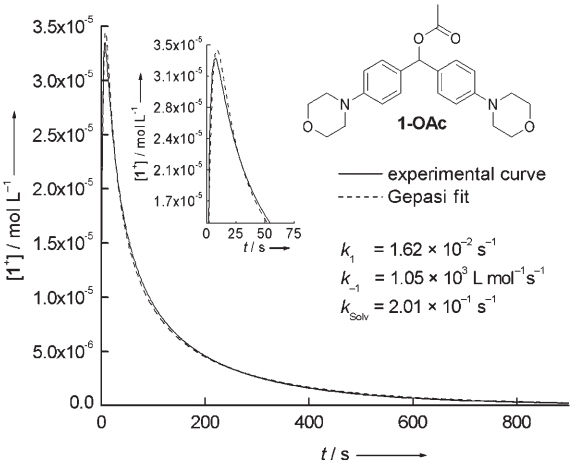


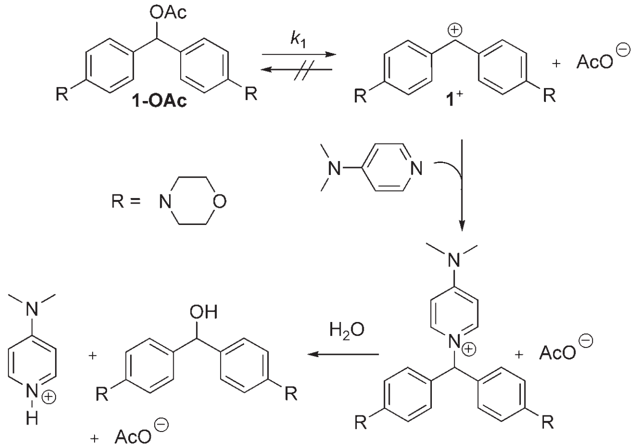
Figure 1. Formation and consumption of the blue $\mathbf{1}^+$ ion (monitored photometrically at 612 nm) during the solvolysis of **1-OAc** (1.09 mmol L^{-1}) in 80% aqueous acetonitrile in the presence of (iPr)$_2$NMe (5.24 mmol L^{-1}) at 25 °C.

10^{-1} s^{-1}, which are almost identical to those derived photometrically. In contrast, the value for the ionization constant ($k_1 = 2.13\times10^{-2}$ s^{-1}) is 25% larger than that derived from the absorbance of the intermediate carbocation (see Figure 1).[6] The value of k_{Solv} derived from Figure 1 and the conductimetrical curve is similar to that previously reported for the hydrolysis of $\mathbf{1}^+BF_4^-$ in 80% aqueous acetonitrile (0.251 s^{-1} at 20 °C).[7]

The high degree of reversibility of the ionization step (mass law effect, common-ion rate depression) implies that the increase of conductivity does not follow an exponential function (see Figure S3 in the Supporting Information). However, when the solvolysis of **1-OAc** (0.62 mmol L^{-1}) was performed in the presence of 4-(dimethylamino)pyridine (DMAP, 5.02 mmol L^{-1}) or quinuclidine (5.24 mmol L^{-1}), the solution did not turn blue, and a monoexponential increase of conductivity was observed (see Figures S1 and S2 in the Supporting Information) owing to quantitative trapping of the intermediate carbocations by these amines (Scheme 3).[8]

The resulting first-order rate constants, $k_1 = 2.04\times10^{-2}$ s^{-1} (in the presence of DMAP) and 2.01×10^{-2} s^{-1} (in the presence of quinuclidine), were the same (within the experimental error) as those derived from experiments in which the intermediate carbocations were visible (Figure 1 and Figure S4 in the Supporting Information).

In the presence of extra tetrabutylammonium acetate, the ionization equilibrium lies far to the side of the covalent benzhydryl acetates; therefore, we were not able to study the solvolysis of **1-OAc** photometrically at constant acetate anion concentrations. However, the ionization equilibria of the corresponding p-nitrobenzoates lie more towards the side of the ions, and it was possible to study their solvolyses at almost constant concentrations of p-nitrobenzoate anions (PNB$^-$). Figure 2 shows that the maximum concentration of the intermediate carbocation, which is reached after 0.7 to 1.0 s, decreases with increasing concentrations of nBu$_4$N$^+$PNB$^-$. The maxima of the curves correspond to stationary points, where Equations (1) or (2) hold.



Scheme 3. Trapping of the intermediate benzhydrylium ions by DMAP.

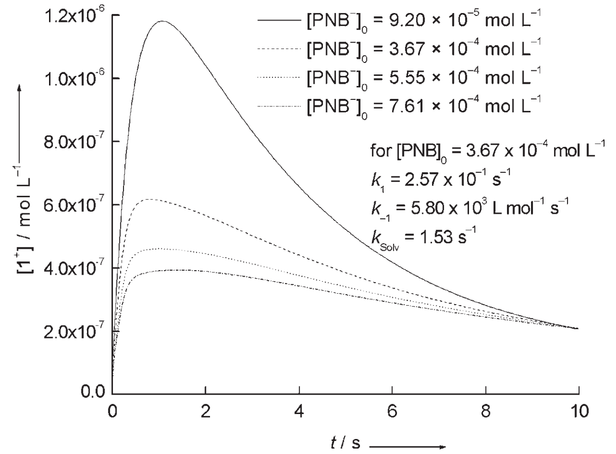


Figure 2. Formation and consumption of the blue $\mathbf{1}^+$ ion (monitored photometrically at 612 nm) during the solvolysis of **1-PNB** (1.04×10^{-5} mol L^{-1}) in 80% aqueous acetone in the presence of different amounts of nBu$_4$N$^+$PNB$^-$ at 25 °C.

$$\frac{d[\mathbf{1}^+]}{dt} = k_1[\mathbf{1\text{-}PNB}] - k_{-1}[\mathbf{1}^+][\mathbf{PNB}^-] - k_{Solv}[\mathbf{1}^+] = 0 \qquad (1)$$

$$\frac{[\mathbf{1}^+]}{[\mathbf{1\text{-}PNB}]} = \frac{k_1}{k_{-1}[\mathbf{PNB}^-] + k_{Solv}} \qquad (2)$$

In accordance with Equation (2), the maxima of the concentrations of the carbocations decrease as the concentrations of the carboxylate anions increase. At a concentration of 9.20×10^{-5} mol L^{-1} of nBu$_4$N$^+$PNB$^-$, the observed carbocation absorbance corresponds to a concentration of $\mathbf{1}^+$ that is approximately 12% of the initial concentration of **1-PNB**. Figure 2 shows that the curves corresponding to higher carbocation concentrations decline faster, resulting in a crossing of the plots at 10 s. This observation reflects the common-ion effect: At high carboxylate anion concentrations, the overall hydrolysis reactions proceed more slowly, and small equilibrium concentrations of carbocations are preserved for an extended period of time.

The individual curves in Figure 2, except that for the lowest concentration of $n\mathrm{Bu}_4\mathrm{N}^+\mathrm{PNB}^-$, can be fitted satisfactorily by the kinetic model of Scheme 1. From all curves in Figure 2 Gepasi arrives at the same value of $k_\mathrm{Solv} = (1.49 \pm 0.4)\,\mathrm{s}^{-1}$, which is 1.5 times larger than that reported for the hydrolysis of 4,4′-bis(morpholino)benzhydrylium tetrafluoroborate in the same solvent at 20 °C.[7] The other rate constants depend slightly on the ionic strengths of the solutions (see the Supporting Information). Thus the ion-combination constant k_{-1} decreases from $(5800 \pm 50)\,\mathrm{M}^{-1}\mathrm{s}^{-1}$ at $[\mathrm{PNB}^-]_0 = 0.37\,\mathrm{mmol\,L}^{-1}$ to $(2980 \pm 50)\,\mathrm{M}^{-1}\mathrm{s}^{-1}$ at $[\mathrm{PNB}^-]_0 = 0.76\,\mathrm{mmol\,L}^{-1}$. The unexpected finding that the ionization rate constant k_1 is also calculated to decrease from $0.257\,\mathrm{s}^{-1}$ (for $[\mathrm{PNB}^-]_0 = 0.37\,\mathrm{mmol\,L}^{-1}$) to $0.161\,\mathrm{s}^{-1}$ (for $[\mathrm{PNB}^-]_0 = 0.76\,\mathrm{mmol\,L}^{-1}$) may be explained by the fact that ion pairing, which is more important in the more concentrated salt solutions, is not considered in our kinetic model, which generally assumes $[\mathrm{PNB}^-]_0 = [n\mathrm{Bu}_4\mathrm{N}^+\mathrm{PNB}^-]_0$.

When the solvolyses of **1-PNB** were studied in 60% aqueous acetone at variable *p*-nitrobenzoate anion concentrations, similar absorbance–time correlations were observed, but the concentration maxima of the intermediate carbocations were higher (corresponding to 27–32% ionization) and less affected by the carboxylate anion concentration (Figure 3). As expected, the ionization equilibria lie more towards the side of the ions in the more polar solvent.

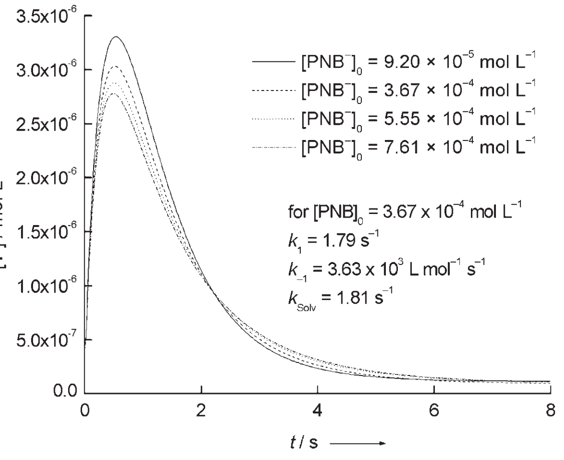


Figure 3. Formation and consumption of the blue $\mathbf{1}^+$ ion (monitored photometrically at 612 nm) during the solvolysis of **1-PNB** ($1.04 \times 10^{-5}\,\mathrm{mol\,L}^{-1}$) in 60% aqueous acetone in the presence of different amounts of $n\mathrm{Bu}_4\mathrm{N}^+\mathrm{PNB}^-$ at 25 °C.

The same values for k_1 and k_Solv are derived from the different curves, and k_{-1} is calculated to decrease by 27% when $[\mathrm{PNB}^-]$ increases from $0.37\,\mathrm{mmol\,L}^{-1}$ to $0.76\,\mathrm{mmol\,L}^{-1}$ (see the Supporting Information). In line with expectation, the variation of ion strength is less important in the more polar solvent.

Comparison of the rate constants in 80% aqueous acetone (Figure 2) and 60% aqueous acetone (Figure 3) shows that the doubling of the water concentration increases the ionization constant k_1 by a factor of 7 while k_{-1} and k_Solv remain almost constant. In accordance with this finding we had previously reported that the nucleophilicities of 80% and 90% aqueous acetone (k_Solv) are almost identical.[9]

"Carbocation watching" was also possible during the solvolysis of the benzhydrylium *p*-nitrobenzoate **2-PNB** in 80% and 60% aqueous acetone. Since replacement of the morpholino groups by the *N*-methylanilino groups accelerates ionization (k_1) more than it affects ion recombination (k_{-1}) (cf. Figures 2–4), larger equilibrium concentrations of benzhydrylium ions are produced when **2-PNB** is solvolyzed under the same conditions as **1-PNB**. As a consequence of the higher concentration of the intermediate carbocations, the agreement of the individual rate constants k_1, k_{-1}, and k_Solv obtained at different carboxylate anion concentrations is much better than in the case of **1** (see the Supporting Information).

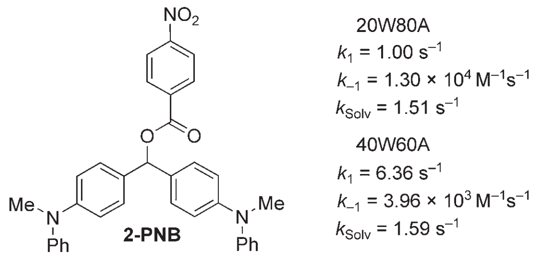


Figure 4. Rate constants for the solvolysis of the **2-PNB** ($9.48 \times 10^{-4}\,\mathrm{mol\,L}^{-1}$) in 80% and 60% aqueous acetone in the presence of $3.67 \times 10^{-4}\,\mathrm{mol\,L}^{-1}$ $n\mathrm{Bu}_4\mathrm{N}^+\mathrm{PNB}^-$.

$\mathrm{S_N2C^+}$ reactions, postulated more than 50 years ago by Ingold et al.,[10] have thus been established as the missing link between conventional $\mathrm{S_N1}$ reactions, where carbocations appear as short-lived intermediates, and the domain of stable carbocations, where subsequent reactions of carbocations do not occur.[11,3] Our philicity[12] and fugality[13] scales can be employed to identify the range where the change of mechanism occurs.

Experimental Section

Demonstration experiment: A colorless solution was obtained by dissolving 4,4′-bis(morpholino)benzhydryl acetate (**1-OAc**, ≈10 mg) in acetone (8 mL) at room temperature. When 8 mL of water was added, the solution turned blue (4,4′-bis(morpholino)benzhydrylium ion $\mathbf{1}^+$) and subsequently faded within about 80 s (formation of the colorless benzhydrol). A video of this experiment is provided in the Supporting Information.

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