[3] G. Jung, A. G. Beck-Sickinger, *Angew. Chem.* **1992**, *104*, 375–391; *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 367–383.

[4] For a recent review on solid-phase oligosaccharide synthesis see: P. H. Seeberger, W.-C. Haase, *Chem. Rev.* **2000**, *100*, 4349–4393. a) For a first investigation of solid-phase oligosaccharide synthesis with an automated synthesizer see: O. J. Plante, E. R. Palmacci, P. H. Seeberger, *Science* **2001**, *291*, 1523–1527; b) E. R. Palmacci, O. J. Plante, P. H. Seeberger, *Eur. J. Org. Chem.* **2002**, 595–606.

[5] a) T. Zhu, G.-J. Boons, *Chem. Eur. J.* **2001**, *7*, 2382–2389; b) T. Zhu, G.-J. Boons, *J. Am. Chem. Soc.* **2000**, *122*, 10222–10223; c) K. C. Nicolaou, N. Watanabe, J. Li, J. Pastor, N. Winssinger, *Angew. Chem.* **1998**, *110*, 1636–1638; *Angew. Chem. Int. Ed.* **1998**, *37*, 1559–1561; d) K. C. Nicolaou, N. Winssinger, J. Pastor, F. DeRoose, *J. Am. Chem. Soc.* **1997**, *119*, 449–452.

[6] R. Liang, L. Yan, J. Loebach, M. Ge, Y. Uozumi, K. Sekanina, N. Horan, J. Gildersleeve, A. Smith, K. Biswas, D. E. Kahne, *Science* **1996**, *274*, 1520–1522.

[7] Y. Ito, T. Ogawa, *J. Am. Chem. Soc.* **1997**, *119*, 5562–5566.

[8] S. J. Danishefsky, K. F. McClure, J. T. Randolph, R. B. Ruggeri, *Science* **1993**, *260*, 1307–1309.

[9] a) M. C. Hewitt, P. H. Seeberger, *J. Org. Chem.* **2001**, *66*, 4233–4243; b) R. B. Andrade, O. J. Plante, L. G. Melean, P. H. Seeberger, *Org. Lett.* **1999**, 1811–1814.

[10] R. Rodebaugh, S. Joahi, B. Fraser-Reid, M. H. Geysen, *J. Org. Chem.* **1997**, *62*, 5660–5663.

[11] O. Seitz, C. -H, Wong, *J. Am. Chem. Soc.* **1997**, *119*, 8766–8776.

[12] a) M. Grathwohl, R. R. Schmidt, *Synthesis* **2001**, 2263–2272; b) X. Wu, M. Grathwohl, R. R. Schmidt, *Org. Lett.* **2001**, *3*, 747–750; c) F. Roussel, L. Knerr, R. R. Schmidt, *Eur. J. Org. Chem.* **2001**, 2066–2073; d) L. Knerr, R. R. Schmidt, *Eur. J. Org. Chem.* **2000**, 2803–2808; e) L. Knerr, R. R. Schmidt, *Synlett* **1999**, 1802–1804; f) J. Rademann, A. Geyer, R. R. Schmidt, *Angew. Chem.* **1998**, *110*, 1309–1313; *Angew. Chem. Int. Ed.* **1998**, *37*, 1241–1245; g) J. Rademann, R. R. Schmidt, *J. Org. Chem.* **1997**, *62*, 3650–3653; h) A. Heckel, E. Mross, K.-J. Jung, J. Rademann, R. R. Schmidt, *Synlett* **1998**, 171–173.

[13] a) R. R. Schmidt, *Angew. Chem.* **1986**, *98*, 213–236; *Angew. Chem. Int. Ed. Engl.* **1986**, *25*, 212–235; b) R. R. Schmidt, W. Kinzy, *Adv. Carbohydr. Chem. Biochem.* **1994**, *50*, 21–123.

[14] F. Roussel, L. Knerr, M. Grathwohl, R. R. Schmidt, *Org. Lett.* **2000**, *2*, 3043–3046.

[15] F. Roussel, M. Takhi, R. R. Schmidt, *J. Org. Chem.* **2001**, *66*, 8540–8548.

[16] For recent examples of N-glycan synthesis in solution see: M. V. Chiesa, R. R. Schmidt, *Eur. J. Org. Chem.* **2000**, 3541–3554 and references [5–15] therein.

[17] S. P. Douglas, D. M. Whitfield, J. J. Krepinsky, *J. Am. Chem. Soc.* **1995**, *117*, 2116–2117.

[18] For leading references on β-mannopyranoside synthesis see: R. Weingart, R. R. Schmidt, *Tetrahedron Lett.* **2000**, *41*, 8753–8758.

[19] For a highly selective β-mannopyranoside synthesis see: A. A.-H. Abdel-Rahman, S. Jonke, E. S. H. El Ashry, R. R. Schmidt, *Angew. Chem.* **2002**, *114*, 3100–3103; *Angew. Chem. Int. Ed.* **2002**, *41*, 2710–2716.

[20] M. Grathwohl, Diplomarbeit, University of Konstanz, **1997**.

[21] T. Bieg, W. Szeja, *J. Carbohydr. Chem.* **1985**, *4*, 441–446.

[22] L. Liang, T.-H. Chan, *Tetrahedron Lett.* **1998**, *39*, 355–358.

[23] R. R. Schmidt, X. Wu, unpublished results.

[24] O. Kanie, S. C. Crawley, M. M. Palcic, O. Hindsgaul, *Carbohydr. Res.* **1993**, *243*, 139–164.

First Direct Observation of the Two Distinct Steps in an S_N1 Reaction[**]

Herbert Mayr* and Shinya Minegishi

The differentiation of bimolecular (S_N2) and unimolecular nucleophilic substitutions (S_N1) by Ingold and co-workers marks the beginning of the mechanistic period of organic chemistry.[1] Since then, countless investigations on the rates and products of S_N1 reactions have been performed. A considerable part of our knowledge of the relationships between structure and reactivity of carbocations (R^+), the intermediates of these reactions, has been derived from solvolysis studies[2–5] [Eq. (1)].

$$R{-}Cl \xrightleftharpoons{\text{slow}} R^+ + Cl^- \xrightarrow[\text{fast}]{\text{SolvOH}} R{-}OSolv + HCl \qquad (1)$$

The discovery by Olah and co-workers that many types of carbocations exist as long-lived species in superacidic solutions, media of low nucleophilicity, allowed the direct observation of carbocations by spectroscopic methods.[6,7]

In recent years, much information on the rates of the reactions of carbocations with nucleophiles,[8,9] including solvents (SolvOH) of S_N1 reactions,[10,11] became available. In agreement with earlier conclusions from solvolysis studies,[12,13] the rates of decay of laser-flash photolytically generated carbocations in 2,2,2-trifluoroethanol (TFE) revealed this alcohol as a weakly nucleophilic solvent.[10] Accordingly, we have now found a first-order rate constant of $12.7 \pm 0.4\ \mathrm{s^{-1}}$ for the decay of bis(4-methoxyphenyl)carbenium tetrafluoroborate (**1**-BF_4) in TFE/acetonitrile (91:9 (v/v)) at 20 °C, corresponding to a half-life of 55 ms (Table 1, entry 1). This rate constant is only slightly reduced in the presence of tetra-*n*-butylammonium chloride (*n*Bu_4NCl) (Table 1, entry 2) and remains almost constant as the TFE/CH_3CN ratio is reduced from 91:9 to 20:80 (Table 1, entries 3–5). Entries 6 and 7 in Table 1 indicate that the presence of 0.5 M $NaClO_4$ or $LiClO_4$ does not affect the rate of the reaction of $\mathbf{1}^+$ with TFE.[14]

The ethanolysis rate constant of chlorobis(4-methoxyphenyl)methane (**1**-Cl), that is the rate of the S_N1 reaction in ethanol, has previously been determined as $k = 57\ \mathrm{s^{-1}}$ at 25 °C, a million times higher than the ethanolysis rate constant of the parent chlorodiphenylmethane ($5.34 \times 10^{-5}\ \mathrm{s^{-1}}$).[15] Since chlorodiphenylmethane, on the other hand, was reported to undergo solvolysis in TFE/water (97:3 (w/w)) with $k = 1.05\ \mathrm{s^{-1}}$,[16] we extrapolated an S_N1 reactivity of **1**-Cl in TFE/water (97:3 (w/w)) of $57\ \mathrm{s^{-1}} \times (1.05/5.34 \times 10^{-5}) = 1.1 \times 10^6\ \mathrm{s^{-1}}$.

The ionization of **1**-Cl in TFE was thus expected to be 10^5 times faster than the reaction of $\mathbf{1}^+$ with this solvent. Since

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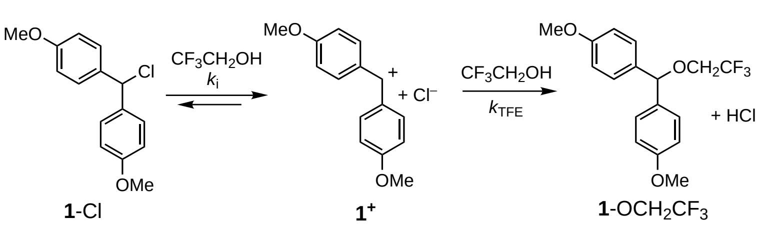
Table 1. Kinetics of the reaction of **1**-BF_4 in TFE/CH_3CN solutions at 20°C.

Entry	TFE/CH_3CN[a]	Additive	k_{TFE} [s^{-1}][b]
1	91:9		12.7[c]
2	91:9	nBu$_4$NCl (0.01 M)	10.3
3	80:20		13.5
4	60:40		13.1
5	20:80		10.0
6	20:80	$NaClO_4$ (0.5 M)	10.0
7	20:80	$LiClO_4$ (0.5 M)	10.4

[a] Solvent ratio in (v/v). [b] Reactions were monitored at $\lambda = 500$ nm. [c] Four independent experiments gave a standard deviation for k_{TFE} of ± 0.4.

intermediates, which are produced faster than they are consumed, enrich during a reaction sequence, we were prompted by these considerations to search for the intermediate bis(4-methoxyphenyl)carbenium ion $\mathbf{1}^+$ during the trifluoroethanolysis of **1**-Cl [Eq. (2)].



(2)

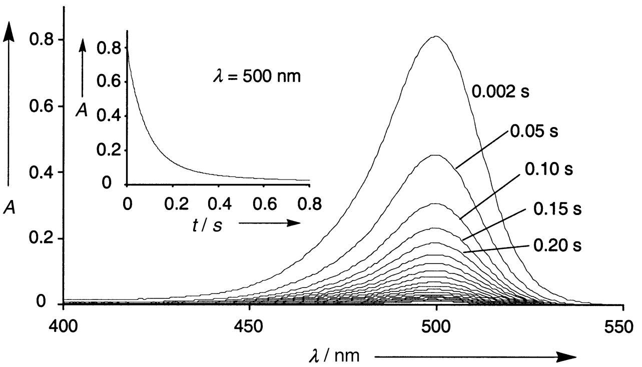


Figure 1. Decay of the absorbance of the carbenium ion $\mathbf{1}^+$ generated from **1**-Cl in TFE/CH_3CN (91:9 (v/v)) at 20°C.

Table 2. Kinetics of the solvolysis of **1**-Cl in TFE/CH_3CN solutions at 20°C.

Entry	[**1**-Cl]$_0$ [M]	TFE/CH_3CN[a]	Additive	A_{max}[b]	k_i [s^{-1}]	k_{TFE} [s^{-1}]
1	8.51×10^{-6}	91:9		0.81	fast	11.4
2	8.51×10^{-6}	91:9	nBu$_4$NCl (5×10^{-4} M)	0.83	fast	11.1
3	8.51×10^{-6}	91:9	nBu$_4$NCl (1×10^{-3} M)	0.81	fast	11.0
4	8.51×10^{-6}	91:9	nBu$_4$NCl (5×10^{-3} M)	0.68	fast	10.6
5	8.51×10^{-6}	91:9	nBu$_4$NCl (1×10^{-2} M)	0.54[c]	fast	10.6
6	7.44×10^{-6}	80:20		0.67	fast	14.1
7	7.44×10^{-6}	70:30		0.61	fast	14.8
8	7.44×10^{-6}	60:40		0.55	fast	13.2
9	7.44×10^{-6}	50:50		0.50	fast	12.4
10	7.44×10^{-6}	40:60		0.37	fast	(6.47)[d]
11	7.44×10^{-6}	30:70		0.20	–[e]	(3.80)[d]
12	1.10×10^{-5}	30:70	$LiClO_4$ (1.0 M)	0.64	7×10^2	12.7
13	7.44×10^{-6}	20:80		0.10	–[e]	(2.66)[d]
14	7.44×10^{-6}	20:80	$NaClO_4$ (1.0 M)	0.26	3×10^2	10.1
15	1.10×10^{-5}	20:80	$LiClO_4$ (1.0 M)	0.52	5×10^2	10.4

[a] Solvent ratio in (v/v). [b] Maximum absorbance at $\lambda = 500$ nm during the course of the reaction. [c] Maximum absorbance at $\lambda = 499$ nm during the course of the reaction. [d] The rate constant (k_{TFE}) has to be considered as an approximation. The initial carbocation absorbance was small and did not show an exponential decay because of incomplete ionization. [e] The rate constant of ionization (k_i) was not determined because of a too small increase of absorbance in the cation formation step.

Immediately after mixing the colorless solution of **1**-Cl in CH_3CN with the tenfold volume of TFE (dried by distillation over $CaSO_4$) in a stopped-flow apparatus, the well-known UV/Vis spectrum of the cation $\mathbf{1}^+$ with an absorption maximum at $\lambda = 500$ nm was observable (Figure 1). This spectrum is identical to that obtained for $\mathbf{1}^+$ in pure CH_3CN ($\lambda_{max} = 500$ nm).[17]

From the molar absorption coefficient ($\lg\varepsilon = 5.10$),[17] one can derive that immediately after mixing, the concentration of $\mathbf{1}^+$ equals 80% of that of the initial concentration of **1**-Cl ($c_0 = 8.5\times10^{-6}$ M). This band disappeared with a first-order rate constant of 11.4 s^{-1} (Figure 1), that is, a similar rate as previously observed (Table 1) for the reaction of **1**-BF_4 with TFE under the same conditions.

Only small changes of the rate of the first-order decay were observable when the TFE/CH_3CN ratio was reduced from 91:9 to 50:50 (Table 2, entries 1 and 6–9). Addition of tetra-n-butylammonium chloride caused a slight decrease of the rate of the carbocation decay (Table 2, entries 1–5). In the presence of 10^{-2} M nBu$_4$NCl, a hypsochromic shift of $\Delta\lambda = 1$ nm and a decrease of the intensity of the absorption band by 35% was observed. In all cases, the maximum of the carbocation absorption (A_{max}) was detected immediately after mixing, in accord with the high ionization rate constant of **1**-Cl estimated above.

Attempts to slow down the ionization reaction to measurable rates by employing TFE/CH_3CN mixtures with a smaller solvent ionizing power than pure TFE[12] were not successful. While the maximal absorbance was still observed immediately after mixing, even in TFE/CH_3CN in the ratio 30:70 (v/v) (Table 2, entry 11), the absorption coefficients were considerably smaller than in solutions with a high TFE/CH_3CN ratio, indicating that under these conditions the ionization equilibrium (first step in Equation (2)) was shifted towards the covalent diarylchloromethane **1**-Cl. Because of incomplete ionization, the carbocation consumption did not show an exponential decay in the cases with small initial absorbance, and the rate constants of entries 10, 11, and 13 in Table 2 have to be considered as approximations.

Formation as well as decay of the carbocation $\mathbf{1}^+$ was observable, however, in a TFE/CH_3CN mixture (20:80 (v/v)) which contained 1.0 M of $LiClO_4$[14] (Figure 2).

At the maximum of the carbocation concentration, that is, 7 ms after mixing, 40% of the initial **1**-Cl was observable as

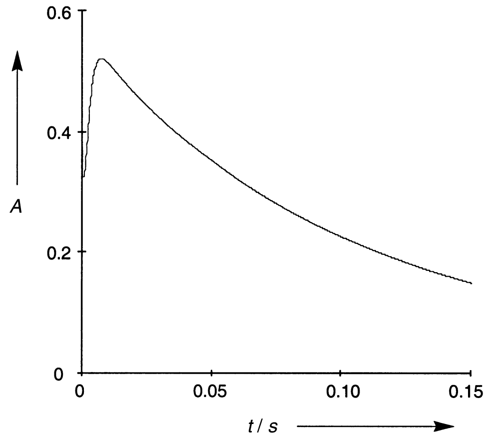


Figure 2. Generation and decay of 1^+ observed after dissolving **1**-Cl in TFE/CH_3CN (20:80 (v/v)) containing 1.0 M of $LiClO_4$.

the diarylmethyl cation 1^+. The carbocation, which was formed with a rate constant (k_i) of $5\times10^2\,s^{-1}$ was consumed with a rate constant (k_{TFE}) of 10.4 s^{-1} under these conditions (Table 2, entry 15). Analogously, formation and consumption of 1^+ was observable in other TFE/CH_3CN mixtures containing alkali metal perchlorates[14] (Table 2, entries 12 and 14).

The direct observation of the carbocationic intermediate demonstrated in this experiment is certainly not a singular case. Increasing stabilization of the carbocation and decreasing solvent nucleophilicity transform the generally accepted energy profiles of S_N1 reactions with carbocations as short-lived intermediates (Figure 3, upper graph) into energy profiles which imply the buildup of significant concentrations of the intermediate carbocations (Figure 3, lower graph).

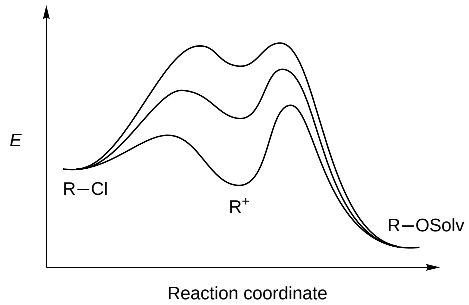


Figure 3. Schematic energy profiles for solvolytic displacement reactions in TFE. Upper graph: Slow ionization (conventional S_N1). Lower graph: Rate-determining carbocation–nucleophile combination with directly observable intermediate. Ion-pairing and proton transfer steps are neglected.

The occurrence of such scenarios can easily be predicted from available ionization and combination rate constants as demonstrated herein. Since ionization and nucleophile addition must be uncoupled when the intermediate is observable, the investigation of such reaction cascades may open a new era in the study of solvolytic displacement reactions. As salt and solvent effects on the two steps of the reaction can now be studied separately, many ambiguities in the earlier interpretations of the mechanisms of solvolytic displacement reactions can be resolved.

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[1] a) C. K. Ingold, E. Rothstein, *J. Chem. Soc.* **1928**, 1217 – 1221; b) C. K. Ingold, *Structure and Mechanism in Organic Chemistry*, 2nd ed., Cornell University, New York, **1969**.
[2] *Carbonium Ions, Vol. 1–5* (Eds.: G. A. Olah, P. von R. Schleyer), Interscience, New York, **1968–1976**.
[3] P. Vogel, *Carbocation Chemistry*, Elsevier, Amsterdam, **1985**.
[4] a) X. Creary, *Advances in Carbocation Chemistry, Vol. 1*, JAI, Greenwich, CT, **1989**; b) J. M. Coxon, *Advances in Carbocation Chemistry, Vol. 2*, JAI, Greenwich, CT, **1995**.
[5] a) "Carbocations": R. A. Cox in *Organic Reaction Mechanisms* (Eds.: A. C. Knipe, W. E. Watts), Wiley, Chichester, **1985–2001**; b) A. Streitwieser, Jr., *Solvolytic Displacement Reactions*, McGraw-Hill, New York, **1962**.
[6] G. A. Olah, W. S. Tolgyesi, S. J. Kuhn, M. E. Moffatt, I. J. Bastien, E. B. Baker, *J. Am. Chem. Soc.* **1963**, *85*, 1328 – 1334.
[7] G. A. Olah, *Angew. Chem.* **1995**, *107*, 1519 – 1532; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1393 – 1405.
[8] H. Mayr, M. Patz, *Angew. Chem.* **1994**, *106*, 990 – 1010; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 938 – 957.
[9] H. Mayr, T. Bug, M. F. Gotta, N. Hering, B. Irrgang, B. Janker, B. Kempf, R. Loos, A. R. Ofial, G. Remennikov, H. Schimmel, *J. Am. Chem. Soc.* **2001**, *123*, 9500 – 9512.
[10] R. A. McClelland, *Tetrahedron* **1996**, *52*, 6823 – 6858.
[11] J. P. Richard, T. L. Amyes, M. M. Toteva, *Acc. Chem. Res.* **2001**, *34*, 981 – 988.
[12] T. W. Bentley, G. Llewellyn, *Prog. Phys. Org. Chem.* **1990**, *17*, 121 – 158.
[13] D. N. Kevill in *Advances in Quantitative Structure-Property Relationships, Vol. 1* (Ed.: M. Charton), JAI, Greenwich, CT, **1996**, pp. 81 – 115.
[14] For salt effects in solvolysis reactions, see: D. J. Raber, J. M. Harris, P. von R. Schleyer in *Ions and Ion Pairs in Organic Reactions, Vol. 2* (Ed.: M. Szwarc), Wiley, New York, **1974**, pp. 247 – 374.
[15] C. Schade, H. Mayr, *Tetrahedron* **1988**, *44*, 5761 – 5770.
[16] C. A. Bunton, M. M. Mhala, J. R. Moffatt, *J. Org. Chem.* **1984**, *49*, 3639 – 3641.
[17] J. Bartl, S. Steenken, H. Mayr, R. A. McClelland, *J. Am. Chem. Soc.* **1990**, *112*, 6918 – 6928.

A Europium-Ion-Based Luminescent Sensing Probe for Hydrogen Peroxide**

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Molecular probes and molecular sensors for hydrogen peroxide (H_2O_2) are important in the environmental and bioanalytical sciences for a number of reasons. H_2O_2 is present in small but significant concentrations in the atmosphere[1] and the marine environment.[2] It is widely used in industry for bleaching, cleaning, and disinfection,[3] and released to the environment in large quantities.[4] H_2O_2 is one of the products of the activity of almost all oxidases,[5] and this enables a quantitative assay of a) the activity of the respective enzyme, b) numerous substrates including glucose,[6] and c) a so-called

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