Biochemistry **1999**, *38*, 6056–6062; e) V. Cerovsky, J. Kockskämper, H. G. Glitsch, F. Bordusa, *ChemBioChem* **2000**, *2*, 126–129.

[5] a) R. Günther, F. Bordusa, *Chem. Eur. J.* **2000**, *6*, 463–467; b) R. Günther, A. Stein, F. Bordusa, *J. Org. Chem.* **2000**, *65*, 1672–1679.

[6] The enzymatic reactions were performed in a total volume of 0.5 mL containing 0.1M *N*-(2-hydroxyethyl)piperazine-*N'*-(2-ethanesulfonic acid) (Hepes), pH 8.0, 0.1M NaCl, 0.01M CaCl$_2$, 10% (*v*/*v*) dimethylformamide (DMF) at 25 °C. The amino acid and peptide esters were dissolved in 10% aqueous DMF while the carbohydrates were suspended in the appropriate buffer. Readjusting to pH 8.0 was achieved by adding NaOH. After mixing the reactants the reactions were initiated by addition of pre-incubated enzyme (1 mM DL-dithiothreitol, 2.5 mM CaCl$_2$ in water for 2 h). After defined time intervals the reactions were stopped by addition of trifluoroacetic acid (1% solution) and further analyzed as described in ref. [7]. To control for spontaneous reactions, parallel reactions without enzyme were analyzed in all cases. On the basis of these controls, non-enzymatic synthesis could be ruled out and the extent of spontaneous hydrolysis of the acyl donor esters was found to be less than 5%.

[7] The reactions were analyzed under optimized conditions by reversed-phase HPLC (LiChrospher, 5 μm, 125 × 3 mm; Merck). Detection was at 254 nm (monomeric carbohydrates) or 280 nm (moenomycin, Leu-enkephalin derivative). Mass spectra were recorded for separated and lyophilized probes by using MALDI-TOF (MALDI 5 V5.1.2, Kratos Kompakt) or ESI (Apex II/7 Tesla, Bruker-Daltonics) ionization. NMR spectroscopy (GEMINI 300, Varian) was used to verify the identity of the reactants and products (except moenomycin and its conjugates). Saponification experiments were performed by incubating the synthesis products in 50% aqueous methanol (pH 11) for 1 h and analysis by HPLC.

[8] For the synthesis of linear-type substrate mimetics see: N. Müller, F. Bordusa, *Anal. Biochem.* **2000**, *286*, 86–90, and references therein. The isomeric Z-Glu/Asp(OGp)-OH esters were prepared by condensation of Z-Glu/Asp-O*t*Bu and 4-[*N'*,*N''*-bis(Boc)-guanidino]phenol (ratio 1:2) using *N*-[(dimethylamino)-1*H*-1,2,3-triazolo[4,5b]pyridine-1-ylmethylene]-*N*-methylmethanaminium hexafluorophosphate *N*-oxide (HATU) as the coupling reagent, *N*-ethyldiisopropylamine as the general base, and DMF as the solvent at 0 °C. Treatment of the protected amino acid diester products with TFA resulted in the Boc/*t*Bu-cleavage leading to the final Z-Glu/Asp(OGp)-OH esters. The identity and purity of the esters were checked by analytical HPLC, NMR spectroscopy, and thermospray mass spectrometry. By using that optimized synthesis method, the isomeric esters were not formed.

[9] R. E. Rodriguez, F. D. Rodriguez, M. P. Sacristan, J. L. Torres, G. Valencia, J. M. G. Anton, *Neurosci. Lett.* **1989**, *101*, 89–94.

[10] a) U. Kempin, L. Hennig, D. Knoll, P. Welzel, D. Müller, A. Markus, J. van Heijenoort, *Tetrahedron* **1997**, *53*, 17669–17690; b) A. Anikin, A. Buchynskyy, U. Kempin, K. Stembera, P. Welzel, G. Lantzsch, *Angew. Chem.* **1999**, *111*, 3931–3935; *Angew. Chem. Int. Ed.* **1999**, *38*, 3703–3707.

[11] G. Lantzsch, H. Binder, H. Heerklotz, P. Welzel, G. Klose, *Langmuir* **1998**, *14*, 4095–4104.

[12] N. Wehofsky, S. W. Kirbach, M. Haensler, J.-D. Wissmann, F. Bordusa, *Org. Lett.* **2000**, *2*, 2027–2030.

Investigation of Reactive Intermediates of Chemical Reactions in Solution by Electrospray Ionization Mass Spectrometry: Radical Chain Reactions[**]

Jens Griep-Raming, Sven Meyer, Torsten Bruhn, and Jürgen O. Metzger*

Dedicated to Professor Hans J. Schäfer
on the occasion of his 65th birthday

The reaction mechanism is the detailed, step-by-step description of a chemical reaction. Most chemical reactions take place through a complex sequence of steps via reactive intermediates. The most important reactive intermediates in organic chemical reactions in solution are carbocations, carbanions, carbenes, and radicals. Of course, chemists have been able to detect these intermediates indirectly by chemical and physical methods, and spectroscopic methods are available to study them directly and in detail.[1] For example, Olah investigated carbocations in "magic acid" solutions under nonreaction conditions.[2] Transient carbocations that contained an appropriate chromophore were studied by using UV spectroscopy.[3, 4] Radicals were explored by ESR spectroscopy and in appropriate cases by CIDNP (chemically induced dynamic nuclear polarization), and UV spectroscopy.[5, 6] However, it seems to be most remarkable that these methods (there may be some exceptions) are not generally suited to detect and to study these reactive intermediates directly in reaction solutions, for example, of a radical chain reaction. Furthermore, substrates, intermediates, and final products cannot be monitored by using these methods. Additional measurements have to be applied to do so. Clearly, it would be of great importance to have a simple method available to study a reaction by monitoring substrates and all intermediates and final products formed, and especially to detect and characterize simultaneously and directly the reactive intermediates. Such a method could give new and important insights in our understanding of reactions and their mechanisms. Furthermore, the method should be applicable to micro amounts of substrates and should allow a high throughput, thus contributing to a sustainable development.[7]

Recently, electrospray ionization mass spectrometry (ESIMS)[8] has been successfully applied to the investigation of some chemical reactions in solution. The investigations were mostly performed offline, for example, with the oxidation of tetrahydropterins to radical cations,[9] homogeneously catalyzed reactions such as the Suzuki reaction,[10] and the

---

[*] Prof. Dr. J. O. Metzger, Dipl.-Chem. S. Meyer, Dipl.-Chem. T. Bruhn
Fachbereich Chemie, Carl von Ossietzky Universität Oldenburg
Carl-von-Ossietzky-Strasse 9–11, 26111 Oldenburg (Germany)
Fax: (+49) 441-798-3329
E-mail: juergen.metzger@uni-oldenburg.de

Dr. J. Griep-Raming
Thermo Finnigan MAT GmbH
Barkhausenstrasse 2, 28197 Bremen (Germany)

[**] We thank the Deutsche Forschungsgemeinschaft for financial support of this work.

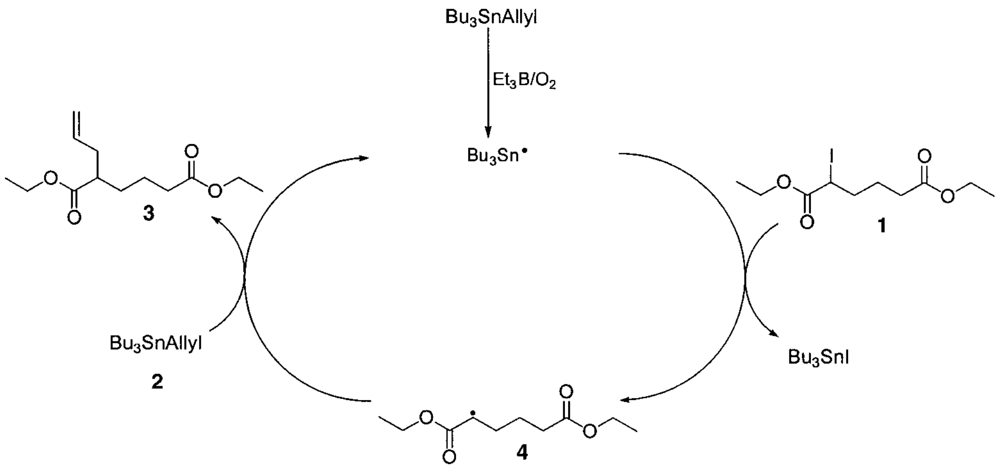
Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.

palladium-catalyzed oxidative self-coupling of aryl boronic acids.[11] Arakawa et al. used an online ESIMS system in which a flow-through photoreaction cell was attached to an electrospray interface. They detected intermediates of photochemical reactions of some transition-metal complexes that have a lifetime of a few minutes.[12] The oxidation of iron(II) bleomycin with iodosylbenzene was studied online and some intermediate species could be detected.[13] Chen and coworkers used ESIMS to generate and isolate the active species of homogeneously catalyzed reactions such as Ziegler–Natta polymerization[14] or olefin metathesis[15] and studied the reaction with the substrate in the gas phase. Feichtinger and Plattner used the same technique to investigate the formation and reactions of the active species of epoxidation catalysts, for example, oxomanganese–salen complexes.[16] We described the possibility of detecting stable radicals in solution by ESIMS[17] and we now report herein our results on the detection of transient radicals in radical chain reactions.

There are many synthetically important radical chain reactions in solution.[18] However, there is no method available to detect and to study directly the transient radicals in these reactions. Radicals are neutral species and neutral species can normally not be detected by ESIMS. However, it is well known that radical reactions can be mediated by Lewis acids if the substrate is a Lewis base that can chelate the metal atom of the Lewis acid in solution.[19] We have recently shown that dialkyl glutarates form complexes with Lewis acids such as $LiClO_4$, $MgBr_2$, and $Sc(OTf)_3$ in solution in diethyl ether.[20] We thought that these complexes, for example, of $Sc(OTf)_3$ should dissociate to form a chelate complex cation and a triflate anion, thus allowing the detection of the complexed ester by ESIMS.[21] This detection was possible: diethyl 2-iodoadipate (**1**; Scheme 1) was mixed with $Sc(OTf)_3$ (1.2 equiv) in diethyl ether and very intense ESI mass spectra were obtained which showed monomeric and dimeric complex ions of adipate **1** (Figure 1a).[22] The fact that in addition to monomeric also dimeric complex ions $[\mathbf{1}_2\cdot Sc_2(OTf)_5]^+$ are observed, which provides evidence for the respective dimeric complexes in solution, is already an important and new result, because up to now dimeric complexes in $Sc(OTf)_3$-mediated radical reactions have not been considered. In the presence of $Sc(OTf)_3$, adipate **1** reacts with allyltributyltin (**2**) in diethyl ether to give diethyl 2-allyladipate (**3**) via the radical intermediate **4** (Scheme 1).

For the investigation by ESIMS, this reaction was performed by mixing a solution of iodoester **1** and $Sc(OTf)_3$ in diethyl ether saturated with air and a solution of **2** and Et_3B under argon. The solutions were mixed by using an effective micromixer, which was coupled online to the ESI mass spectrometer.[23] The reaction times could be varied by the flow rate and/or the length of the transfer capillary between the mixer and the ion source.[24] Substrate **1** and product **3** could easily be detected and monitored by ESIMS. Most remarkably, a heterodimer complex ion of substrate and product $[\mathbf{1}\cdot\mathbf{3}\cdot Sc_2(OTf)_5]^+$ (*m/z* 1405) was detected. However, an intermediate radical complex ion $[\mathbf{4}\cdot Sc(OTf)_2]^+$ with an expected mass of *m/z* 544 could not be observed unambiguously because of chemical noise[25] in the mass spectrum (Figure 1b). That can easily be understood because the quasi-stationary concentration of the radical in the radical chain reaction is estimated to be approximately 10^{-7} M, four orders of magnitude lower than the concentration of the substrate **1** and of the product **3**. The signal of the intermediate radical ion is expected to disappear in the chemical noise. However, the intermediate radical **4** could be detected as a monomeric complex ion $[\mathbf{4}\cdot Sc(OTf)_2]^+$ by using the MS/MS technique[8] to filter out the signal of interest from baseline noise (Figure 1c).[26] From this observation, we deduced that **4** also should occur in the reaction solution as a heterodimer complex with substrate **1** and the respective ion should be detectable by MS/MS, which would thus provide additional, independent, and unambiguous evidence for the intermediate radical. The MS/MS spectrum of the heterodimer complex ion of substrate and radical $[\mathbf{1}\cdot\mathbf{4}\cdot Sc_2(OTf)_5]^+$ (*m/z* 1364) was indeed observed (Figure 1d). Two main and characteristic fragmentations of this ion are evident: dissociation by loss of the neutral radical complex $\mathbf{4}\cdot Sc(OTf)_3$ gives the substrate complex ion $[\mathbf{1}\cdot Sc(OTf)_2]^+$ (*m/z* 671) and, complementarily, loss of the neutral substrate complex $\mathbf{1}\cdot Sc(OTf)_3$ gives the radical complex ion $[\mathbf{4}\cdot Sc(OTf)_2]^+$ (*m/z* 544).

The tributyltin hydride or tris(trimethylsilyl)silane-mediated addition of alkyl iodides to alkenes is another syntheti-



Scheme 1. Triethylborane/oxygen-initiated radical chain reaction of **2** with **1** to give adipate **3** via radical **4**.

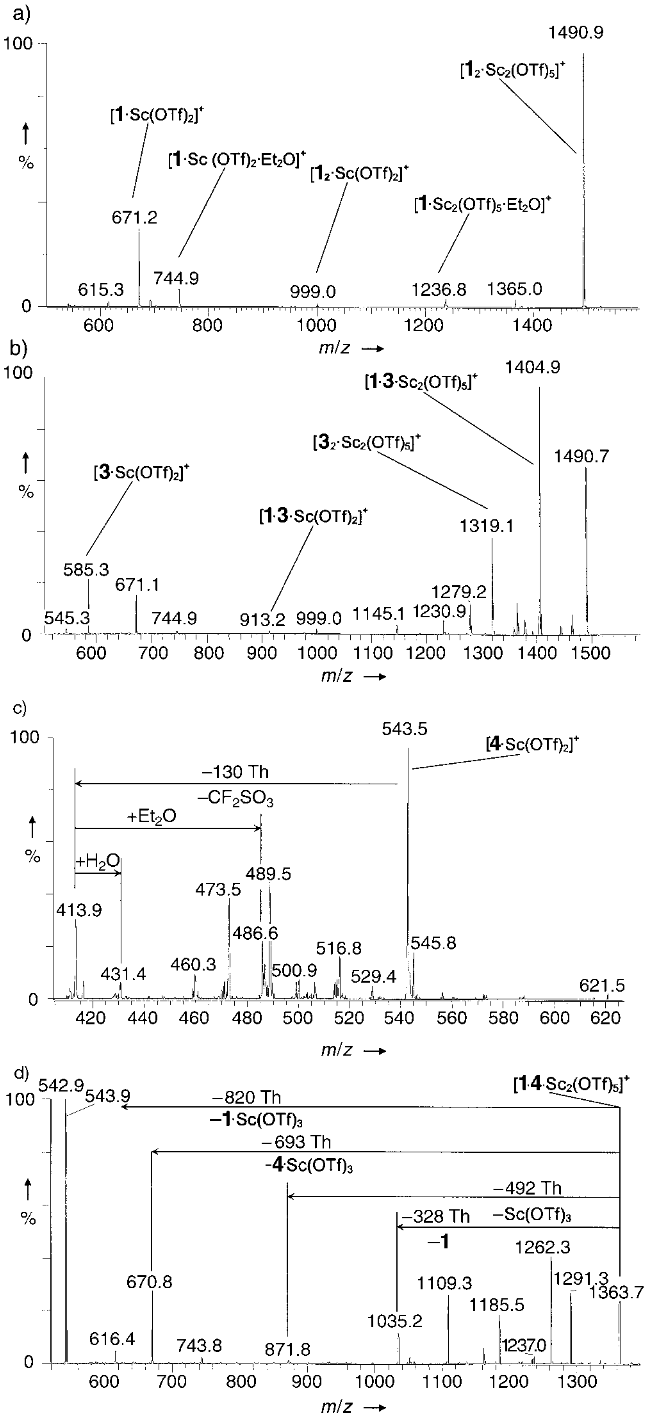
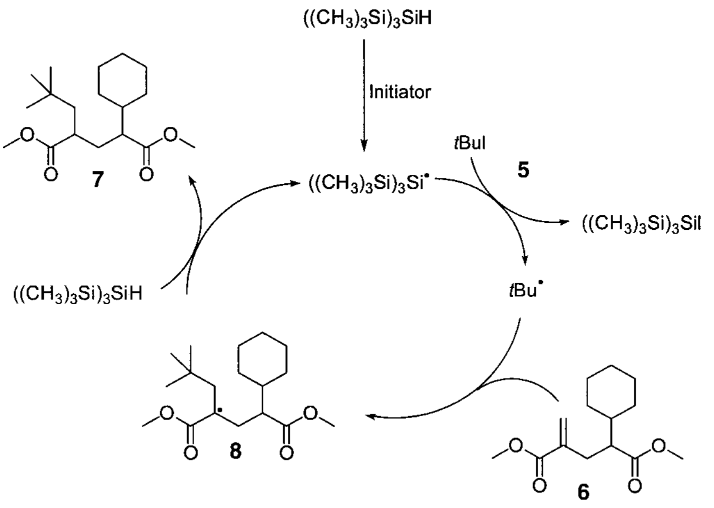


Figure 1. a) Positive-mode ESI mass spectrum of a solution of **1** in the presence of Sc(OTf)$_3$ in diethyl ether. Monomeric [**1** · Sc(OTf)$_2$]$^+$ (*m/z* 671) and dimeric [**1**$_2$ · Sc$_2$(OTf)$_5$]$^+$ (*m/z* 1491) complex ions are observed. b) Positive-mode ESI mass spectrum of the reaction solution of **1** and **2** in the presence of Sc(OTf)$_3$ in diethyl ether; new signals (compare with Figure 1 a) are observed and assigned to the product **3**: [**3** · Sc(OTf)$_2$]$^+$ (*m/z* 585), [**3**$_2$ · Sc$_2$(OTf)$_5$]$^+$ (*m/z* 1319), and the heterodimer complex ion [**1** · **3** · Sc$_2$(OTf)$_5$]$^+$ (*m/z* 1405). c) The MS/MS spectrum of the radical complex ion [**4** · Sc(OTf)$_2$]$^+$ (*m/z* 544) of the same reaction solution shows the characteristic fragmentation of CF$_2$SO$_3$ (−130 Th (Thomson)) to give fragment ion *m/z* 414 accompanied by adduct ions with H$_2$O (*m/z* 432) and diethyl ether (*m/z* 488), which are formed by ion–molecule reactions in the ion trap.[27] d) The MS/MS spectrum of the substrate–radical complex ion [**1** · **4** · Sc$_2$(OTf)$_5$]$^+$ (*m/z* 1364) of the same reaction solution shows fragmentation to give the substrate complex ion [**1** · Sc(OTf)$_2$]$^+$ (*m/z* 671) and the radical complex ion [**4** · Sc(OTf)$_2$]$^+$ (*m/z* 544).

cally important radical reaction.[28, 29] The addition of *tert*-butyl iodide (**5**) to dimethyl 2-cyclohexyl-4-methyleneglutarate (**6**) mediated by (Me$_3$Si)$_3$SiH gives the addition product **7** in good yields (Scheme 2).[20] We studied this reaction by ESIMS and could easily monitor substrate **6** and product **7** (Figure 2 a). We could also detect the intermediate adduct radical **8** by MS/MS as complex ion [**8** · Sc(OTf)$_2$]$^+$ and independently as heterodimer [**6** · **8** · Sc$_2$(OTf)$_5$]$^+$ (Figure 2 b,c).[30]



Scheme 2. Tris(trimethylsilyl)silane-mediated addition of *tert*-butyl iodide (**5**) to glutarate **6** to give stereoselectively **7** via adduct radical **8**.[20]

The detection of the heterodimer radical complex ions in Sc(OTf)$_3$-mediated radical reactions provides information that can not be obtained by other techniques and may be important for the stereochemical outcome, for example, of the hydrogen transfer to radical **8**.[20] This information can only be obtained by ESIMS because this technique allows all ionic species in solution to be detected and characterized by their MS/MS spectrum.

In conclusion, we have shown for the first time that transient radicals in radical chain reactions can be detected unambiguously by ESIMS. Furthermore, substrates and products can easily be monitored. New insights have been obtained in the mechanism of Sc(OTf)$_3$-mediated radical chain reactions. The method seems to be generally applicable to the investigation of reactions in solution and to the detection of intermediates, and most importantly, of reactive intermediates. For example, we have been studying the dissociation of carbon–heteroatom bonds as the rate-determining step of S$_N$1 and E1 reactions. All significant effects described in textbooks of organic chemistry could easily be demonstrated by direct measurement of the carbocations and the respective anions formed in the dissociation equilibrium. The method can be applied to all reactions in solution, as long as the species of interest are ionic species or can be ionized.[17]

Received: February 13, 2002 [Z18704]

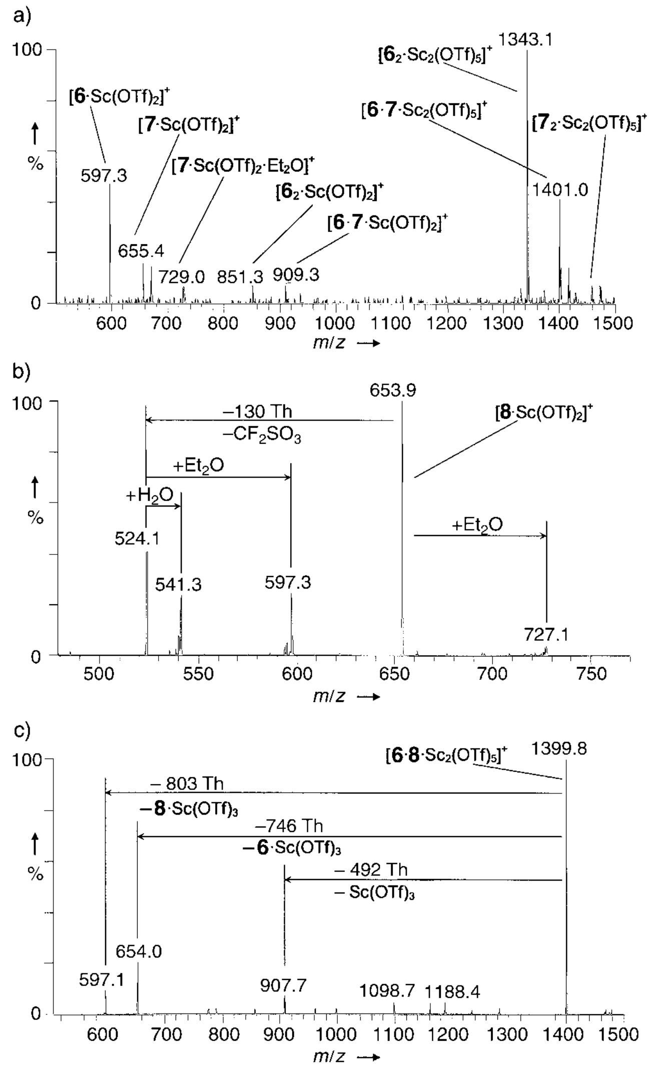


Figure 2. a) Positive-mode ESI mass spectrum of the tris(trimethylsilyl)silane-mediated addition of *tert*-butyl iodide to **6** in the presence of Sc(OTf)$_3$ in diethyl ether to give the addition product **7** (see Supporting Information). Monomeric and dimeric complex ions of substrate **6** (*m*/*z* 597, 851, 1343), product **7** (*m*/*z* 655, 729, 1457), and heterodimer complex ions of **6** and **7** (*m*/*z* 909, 1401) are observed. A signal of the intermediate radical complex ion (*m*/*z* 654) is not evident. b) The MS/MS of the ion at *m*/*z* 654 shows the fragmentation of the radical complex ion [**8** · Sc(OTf)$_2$]$^+$. The loss of CF$_2$SO$_3$ (− 130 Th) and the attachment of H$_2$O and diethyl ether to the complex ions is characteristic.[31] c) The MS/MS spectrum of the ion at *m*/*z* 1400 shows the loss of **8** · Sc(OTf)$_3$ (803 Th) to give [**6** · Sc(OTf)$_2$]$^+$ (*m*/*z* 597) (see Figure 2a), and loss of **6** · Sc(OTf)$_3$ (746 Th) to give [**8** · Sc(OTf)$_2$]$^+$ (*m*/*z* 654) (see Figure 2b).

[1] M. B. Smith, J. March, *March's Advanced Organic Chemistry*, 5th ed., Wiley, New York, **2001**, pp. 218–273.

[2] G. A. Olah, *Angew. Chem.* **1995**, *107*, 1519–1532; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1393–1405.

[3] *Carbonium Ions, Vol. 1* (Eds.: G. A. Olah, P. von R. Schleyer), Interscience Publishers, New York, **1968**; "Carbokationen, Carbokationen-Radikale": D. Lenoir, H.-U. Siehl, *Methoden der Organischen Chemie* (*Houben-Weyl*), *4th ed. 1952–*, *Vol. E19c*, pp. 35–43.

[4] H. Mayr, *Angew. Chem.* **1990**, *102*, 1415–1428; *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 1371–1384.

[5] J. K. Kochi, *Free Radicals*, Wiley, New York, **1973**.

[6] J. Fossey, D. Lefort, J. Sorba, *Free Radicals in Organic Chemistry*, Wiley, New York, **1995**, pp. 5–18.

[7] M. Eissen, J. O. Metzger, E. Schmidt, U. Schneidewind, *Angew. Chem.* **2002**, *114*, 402–425; *Angew. Chem. Int. Ed.* **2002**, *41*, 414–436.

[8] *Electrospray Ionization Mass Spectrometry—Fundamentals, Instrumentation and Applications* (Ed.: R. B. Cole), Wiley, New York, **1997**.

[9] a) A. Schäfer, B. Fischer, H. Paul, R. Bosshard, M. Hesse, M. Viscontini, *Helv. Chim. Acta* **1992**, *75*, 1955–1964; b) A. Schäfer, H. Paul, B. Fischer, M. Hesse, M. Viscontini, *Helv. Chim. Acta* **1995**, *78*, 1763–1776.

[10] A. Aliprantis, J. Canary, *J. Am. Chem. Soc.* **1994**, *116*, 6985–6986.

[11] M. A. Aramendía, F. Lafont, M. Moreno-Manas, R. Pleixats, A. Roglans, *J. Org. Chem.* **1999**, *64*, 3592–3594.

[12] a) R. Arakawa, S. Tachiyashiki, T. Matsuo, *Anal. Chem.* **1995**, *67*, 4133–4138; b) R. Arakawa, F. Matsuda, G.-e. Matsubayashi, T. Matsuo, *J. Am. Soc. Mass Spectrom.* **1997**, *8*, 713–717, and references therein.

[13] J. W. Sam, X.-J. Tang, R. S. Magliozzo, J. Peisach, *J. Am. Chem. Soc.* **1995**, *117*, 1012–1018.

[14] D. Feichtinger, D. A. Plattner, P. Chen, *J. Am. Chem. Soc.* **1998**, *120*, 7125–7126.

[15] a) C. Adlhart, C. Hinderling, H. Baumann, P. Chen, *J. Am. Chem. Soc.* **2000**, *122*, 8204–8214; b) C. Adlhart, P. Hofmann, P. Chen, *Helv. Chim. Acta* **2000**, *83*, 3306–3311; c) M. Volland, C. Kiener, P. Chen, P. Hofmann, *Chem. Eur. J.* **2001**, *7*, 4621–4632.

[16] D. Feichtinger, D. Plattner, *Chem. Eur. J.* **2001**, *7*, 591–599.

[17] a) J. O. Metzger, J. Griep-Raming, *Eur. J. Mass Spectrom.* **1999**, *5*, 157–163; b) J. Griep-Raming, J. O. Metzger, *Anal. Chem.* **2000**, *72*, 5665–5668.

[18] *Radicals in Organic Synthesis* (Eds. P. Renaud, M. P. Sibi), Wiley-VCH, Weinheim, **2001**.

[19] P. Renaud, M. Gerster, *Angew. Chem.* **1998**, *110*, 2704–2722; *Angew. Chem. Int. Ed.* **1998**, *19*, 2562–2722.

[20] a) A. Hayen, R. Koch, J. O. Metzger, *Angew. Chem.* **2000**, *112*, 2898–2900; *Angew. Chem. Int. Ed.* **2000**, *39*, 2758–2761; b) A. Hayen, R. Koch, W. Saak, D. Haase, J. O. Metzger, *J. Am. Chem. Soc.* **2000**, *122*, 12458–12468.

[21] It has been shown that nonpolar organic compounds such as alkenes can be ionized in ESIMS by adding transition-metal salts, for example, AgNO$_3$ to form π complexes: E. Bayer, P. Gfrörer, C. Rentel, *Angew. Chem.* **1999**, *111*, 1046–1049; *Angew. Chem. Int. Ed.* **1999**, *38*, 992–995.

[22] The experiments were carried out on an LCQ mass spectrometer (Thermo Finnigan, San José, CA, USA). The standard ESI source of the LCQ was used with a stainless-steel metal capillary (110 μm i.d., 240 μm o.d., 120.5 mm length, Metal Needle Kit, Thermo Finnigan). Notably, we cannot draw a direct conclusion from the signal intensities to the relative concentration of the respective species in solution because of the characteristics of the ion trap. Some experiments have been performed on a FT-ICR mass spectrometer Apex II (Bruker Daltonics) and gave the exact masses of the monomeric and dimeric complex ions of substrates and of the products. We thank Dr. J. R. Wesener (Bayer AG) for the possibility of performing these measurements.

[23] Adipate **1** (20 μmol, 1×10^{-3} M) and scandium triflate (24 μmol, 1.2 equiv) were dissolved in diethyl ether (20 mL). The solution was cooled to 0 °C and saturated with air by using a glass syringe. A solution of triethyl borane (50 μmol, 2.5 equiv) and allyltributyltin (100 μmol, 5 equiv) was prepared in diethyl ether (20 mL) under argon. The solutions were mixed using a dual syringe pump feeding in a micromixer with a low dead volume that was coupled directly to the ESI source.

[24] The volume of the spray capillary (120.5 mm length, 110 μm i.d.) is about 1.14 μL. The flow rate can be varied from 2.5 to 100 μL min^{-1}. Thus, the direct connection of the mixer with the spray capillary allows reaction times from 0.7 to 28 s. Longer reaction times are easily possible by using a fused-silica transfer capillary of variable length between the mixer and the spray capillary. Mass spectra were measured at reaction times of approximately 1 s up to some minutes.

[25] Of course, there is a peak at *m*/*z* 544, which falls in the intensity range of chemical noise.

[26] To detect transient radical cation [**4** · Sc(OTf)$_2$]$^+$ by MS/MS, the parent ion (*m*/*z* 544) was collected for up to 2000 ms in the ion trap (isolation width 1.5 *m*/*z*) and then fragmented by collision (CID) with a background gas (in this case, helium). The MS/MS spectrum given in Figure 1c) was obtained. The analogous MS/MS experiment was

performed to detect heterodimer radical cation $[\mathbf{1}\cdot\mathbf{4}\cdot Sc_2(OTf)_5]^+$ at *m*/*z* 1364 (Figure 1 d). Control experiments of substrate **1** and product **3** in the presence of $Sc(OTf)_3$ showed no signals that could be assigned to the proposed radical intermediate in the case of the heterodimer radical complex ion. In the case of the monomer radical complex ion, the substrate **1** showed signals that can be assigned to this ion, possibly by homolytic cleavage of the C–I bond in the heated capillary. However, the intensity of these signals is only about one tenth of that in the case of the reaction.

[27] The water and diethyl ether adduct complex ions ($[M\cdot Sc(OTf)_2\cdot H_2O]^+$, $[M\cdot Sc(OTf)_2\cdot Et_2O]^+$) indicate two special features: a rising front peak flank and a negative mass shift. Both phenomena are observed only with quadrupole ion trap analyzers and with particularly unstable (easily fragmentable) ions.

[28] W. B. Motherwell, D. Crich, *Free Radical Chain Reactions in Organic Synthesis*, Academic Press, London, **1992**, pp. 179–212.

[29] C. Chatgilialoglu in *Radicals in Organic Synthesis* (Eds. P. Renaud, M. P. Sibi), Wiley-VCH, Weinheim, **2001**, pp. 28–49.

[30] Glutarate **6** (20 µmol, $1\cdot 10^{-3}$ M), scandium triflate (24 µmol, 1.2 equiv), and *tert*-butyl iodide (80 µmol, 4 equiv) were dissolved in diethyl ether (20 mL). The solution was cooled to 0 °C and saturated with air by using a glass syringe. A solution of triethyl borane (50 µmol, 2.5 equiv) and tris(trimethylsilyl)silane (80 µmol, 4 equiv) was prepared in diethyl ether (20 mL) under argon. The reaction and measurement were performed as described in refs. [23] and [26]. The MS/MS spectrum of *m*/*z* 654 ($[\mathbf{8}\cdot Sc(OTf)_2]^+$, Figure 2 b) and of *m*/*z* 1400 ($[\mathbf{6}\cdot\mathbf{8}\cdot Sc_2(OTf)_5]^+$, Figure 2 c) were obtained. Control measurements of substrate **6** and product **7** in the presence of $Sc(OTf)_3$ showed no signals that can be assigned to the monomeric and heterodimeric radical complex ions.

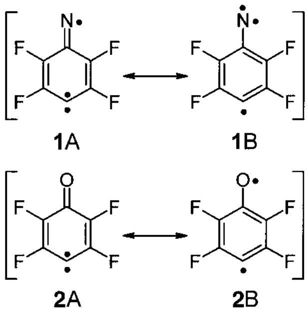
[31] The shape of the peak at *m*/*z* 597 provides unambiguous evidence for the addition of diethyl ether to the complex ion with *m*/*z* 524; see also ref. [27].

2,3,5,6-Tetrafluorophenylnitren-4-yl: A Quartet-Ground-State Nitrene Radical[**]

Hans Henning Wenk and Wolfram Sander[*]

Dedicated to Professor Walter Siebert
on the occasion of his 65th birthday

The interaction of unpaired electrons coupled by conjugated π-systems has been studied intensively during the last decade.[1–3] Also, a few heterospin systems combining different spin-carrying units within one molecule have been described. As these studies were aimed at the development of molecular magnets,[4] stable organic radicals were utilized, which were coupled to photochemically generated nitrene[5, 6] or carbene[7–9] units through *m*- or *p*-phenylene linkers. Systems containing highly reactive radicals (e.g. the phenyl radical) in addition to a nitrene or carbene have not been investigated so far. A molecule of this type is 2,3,5,6-tetrafluorophenylnitren-4-yl (**1**), which is formally generated by substituting a nitrogen atom for an oxygen atom in tetrafluorooxocyclohexadienylidene (**2**).



For compound **2**, a triplet ground state has been determined experimentally by using ESR[10] and IR spectroscopy[11], as well as theoretically based on quantum-chemical calculations. The electronic structure of **2** can be described by the resonance structures **2 A** (carbene) and **2 B** (phenyl/phenoxyl diradical). For the nitrene radical **1**, which bears an additional unpaired electron, DFT calculations predict a quartet ground state 2.7 kcal mol^{-1} below the lowest doublet state (UB3LYP/6-311G(d,p) + ZPE). The electronic structure of **1** is also qualitatively represented by two resonance structures: structure **1 A** corresponds to a combination of a carbene with an iminyl radical, structure **1 B** to that of a nitrene and a phenyl radical. Two electrons are localized in the σ plane, one at the nitrogen atom (iminyl radical), the other at the C4 atom of the phenyl ring (phenyl radical). The third unpaired electron is delocalized over the π system and exhibits high spin densities at the nitrogen atom as well as at the C4 atom. Thus, **1** can be represented by the electronic structure of a delocalized carbene (**1 A**) and a delocalized nitrene (**1 B**), which share a common π electron. Both carbenes and nitrenes have similar structures: open-shell systems with triplet ground states, and thus the parallel alignment of the spins of all three electrons is energetically most favorable; this leads to a quartet ground state.

Photolysis of aryl azides in cryogenic matrices is a well-established method for the generation of triplet aryl nitrenes.[12–14] Short-wavelength irradiation of aryl iodides has recently been applied to generate various fluorinated phenyl radicals and didehydrobenzenes, which were studied by matrix-isolation spectroscopy.[15, 16] Therefore, 4-iodo-2,3,5,6-tetrafluoroazidobenzene (**7**; see Scheme 2) was used as a precursor for **1**. The perfluorinated system was chosen because, in contrast to the unsubstituted phenylnitrene (**3**),[12, 17] for 2,6-difluorinated phenylnitrene derivatives the irreversible ring expansion to the corresponding didehydroazepine (**4**; Scheme 1) was not observed under the conditions of matrix isolation.[13, 14, 18] Instead, 2,6-difluorophenylnitrene and pentafluorophenylnitrene (**5**) react reversibly to the azirine derivatives (**6**) upon irradiation with light of wavelength 444 nm.[14]

The IR spectrum of **7**, matrix isolated in solid argon at 3 K, exhibits the characteristic ν(NN) vibration of the azido group at 2131 cm^{-1} (Figure 1 a). The absorptions of **7** disappear upon

---

[*] Prof. Dr. W. Sander, Dipl.-Chem. H. H. Wenk
Lehrstuhl für Organische Chemie II
Ruhr-Universität Bochum
44780 Bochum (Germany)
Fax: (+49) 234-321-4353
E-mail: wolfram.sander@ruhr-uni-bochum.de

[**] This work was financially supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. We thank Professor W. T. Borden for the discussion of the high-spin system.