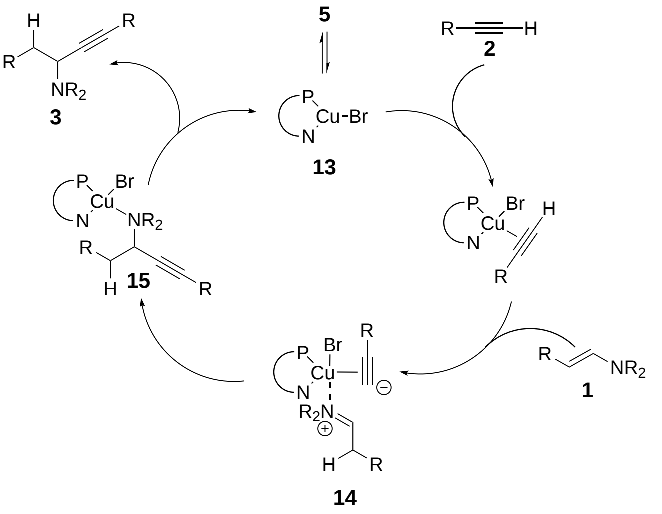

Scheme 5. Proposed mechanism.

high yields with up to 90% *ee*. The mild reaction conditions, the broad scope of the reaction, and the selective deprotection of the propargylamine products show the potential synthetic utility of this method. Further synthetic and mechanistic investigations of this new asymmetric reaction are currently underway.

Experimental Section

Typical procedures:

a) **3m**: CuBr (22 mg, 0.15 mmol, 5 mol%) was suspended in toluene (3 mL) in a 25-mL Schlenk tube under argon. A solution of **1d** (1.049 g, 3.60 mmol, 1.2 equiv), **2a** (0.306 g, 3.00 mmol, 1.0 equiv), and *n*-decane (0.300 g, 2.11 mmol) as internal standard in toluene (3 mL) was added at room temperature. The reaction mixture was stirred for 24 h at room temperature and then for 3 h at 60°C. Standard workup and purification by column chromatography (SiO_2, pentane/Et_2O 98:2) afforded the desired product as a white solid (1.115 g, 2.83 mmol, 94%).

b) (−)-**3a**: CuBr (3.6 mg, 0.025 mmol, 5 mol%) and (*R*)-(+)-Quinap (12.1 mg, 0.0275 mmol, 5.5 mol%) were suspended in toluene (2 mL) in a 10-mL Schlenk tube under argon. After 30 min, a solution of **1a** (0.173 g, 0.65 mmol, 1.3 equiv), **2a** (0.051 g, 0.50 mmol, 1.0 equiv) and *n*-decane (0.050 g, 0.35 mmol) as internal standard in toluene (2 mL) was added at room temperature. After stirring for 24 h, standard workup and purification by column chromatography (SiO_2, pentane/Et_2O 98:2) yielded **3a** as a colorless oil (0.144 g, 0.39 mmol, 78%).

Received: March 28, 2002 [Z19004]

---

[1] a) M. A. Huffman, N. Yasuda, A. E. DeCamp, E. J. J. Grabowski, *J. Org. Chem.* **1995**, *60*, 1590; b) M. Konishi, H. Ohkuma, T. Tsuno, T. Oki, G. D. VanDuyne, J. Clardy, *J. Am. Chem. Soc.* **1990**, *112*, 3715.

[2] a) J. R. Hauske, P. Dorff, S. Julin, G. Martinelli, J. Bussolari, *Tetrahedron Lett.* **1992**, *33*, 3715; b) M. Kolb, J. Barth, *Angew. Chem.* **1980**, *92*, 753; *Angew. Chem. Int. Ed. Engl.* **1980**, *19*, 725; c) H. Braun, F. P. Schmidtchen, A. Schneider, H. Simon, *Tetrahedron* **1991**, *47*, 3329; d) M. J. Burk, J. E. Feaster, *J. Am. Chem. Soc.* **1992**, *114*, 6266; e) D. Enders, J. Schankat, *Helv. Chim. Acta* **1995**, *78*, 970; f) J. Blanchet, M. Bonin, A. Chiaroni, L. Micouin, C. Riche, H.-P. Husson, *Tetrahedron Lett.* **1999**, *40*, 2935; g) C. Fischer, E. M. Carreira, *Org. Lett.* **2001**, *3*, 4319.

[3] R. Noyori, *Asymmetric Catalysis in Organic Synthesis*, Wiley, New York, **1994**.

[4] For a very efficient Zn-catalyzed enantioselective addition of alkynes to aldehydes, see: a) N. K. Anand, E. M. Carreira, *J. Am. Chem. Soc.* **2001**, *123*, 9687; b) E. El-Sayed, N. K. Anand, E. M. Carreira, *Org. Lett.* **2001**, *3*, 3017; c) D. E. Frantz, R. Faessler, C. S. Tomooka, E. M. Carreira, *Acc. Chem. Res.* **2000**, *33*, 373; d) D. E. Frantz, R. Faessler, E. M. Carreira, *J. Am. Chem. Soc.* **2000**, *122*, 1806.

[5] For a copper(I) chloride catalyzed reaction of alkynes with enamines, see: a) K. C. Brannock, R. D. Burpitt, J. G. Thweatt, *J. Org. Chem.* **1963**, *28*, 1462; see also: b) J. J. McNally, M. A. Youngman, S. L. Dax, *Tetrahedron Lett.* **1998**, *39*, 967; M. A. Youngman, S. L. Dax, *Tetrahedron Lett.* **1997**, *38*, 6347.

[6] K. Taguchi, F. H. Westheimer, *J. Org. Chem.* **1971**, *36*, 1570.

[7] P. Beeken, F. W. Fowler, *J. Org. Chem.* **1980**, *45*, 1336.

[8] a) J. M. Valk, G. A. Whitlock, T. P. Layzell, J. M. Brown, *Tetrahedron: Asymmetry* **1995**, *6*, 2593; b) E. Fernandez, K. Maeda, M. W. Hooper, J. M. Brown, *Chem. Eur. J.* **2000**, *6*, 1840.

[9] Crystal data for **5**: $M_r = 1287.82$, orthorhombic, space group $C2_{221}$, $a = 15.549(3)$, $b = 16.989(2)$, $c = 42.706(7)$ Å, $V = 11281(3)$ Å^3, $Z = 8$, $\rho_{calcd} = 1.516$ Mg m^{-3}, $Mo_{K\alpha}$ radiation ($\lambda = 0.71073$ Å), $\mu = 2.366$ mm^{-1}. Data were collected on a NONIUS MACH3 system at 295 K. The structure was solved by direct methods and refined on F_0^2 by full-matrix least-squares methods (SHELXS-86, SHELXL-93). All non-hydrogen atoms were refined anisotropically. $R1 = 0.0374$, $\omega R2 = 0.0834$ for all data with $I > 2\sigma(I)$. CCDC-182716 contains the supplementary crystallographic data (excluding structure factors) for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB21EZ, UK; fax: (+44)1223-336-033; or deposit@ccdc.cam.ac.uk).

[10] a) J. Qiong-Hua, L. De-Liang, W. Yu-Xian, X. Xin-Quan, *Acta Crystallogr.* **1998**, *C54*, 948; b) J. Zukerman-Schpector, E. E. Castellano, A. E. Mauro, M. R. Roveri, *Acta Crystallogr.* **1986**, *C42*, 302.

[11] a) S. Lemaire-Audoire, M. Savignac, J. P. Genêt, *Tetrahedron Lett.* **1995**, *36*, 1267; b) S. Lemaire-Audoire, M. Savignac, C. Dupuis, J. P. Genêt, *Bull. Soc. Chim. Fr.* **1995**, *132*, 1167.

[12] F. Garro-Helion, A. Mertouk, F. Guibé, *J. Org. Chem.* **1993**, *58*, 6109.

[13] All chiral propargylamines **3** showed the same sign of optical rotation.

[14] N. Jeong in *Transition Metals for Organic Synthesis*, *Vol. 1*, (Eds.: M. Beller, C. Bolm), Wiley-VCH, Weinheim, **1998**, 560.

[15] The stereochemistry of **11** was established by analysis of NOE data.

Hydrolytic Activation of C–F Bonds in the Gas Phase by Intrinsically Unreactive Chromium Cations[**]

Ulf Mazurek, Detlef Schröder, and Helmut Schwarz[*]

To the best of our knowledge, hydrolytic activation of C–F bonds in the gas phase has hitherto been unknown.[1] Moreover, considering the facts that 1) thermalized chromium cations are generally unreactive in the gas phase,[2–6] 2) C–F bonds show a bond-dissociation energy of 105–110 kcal mol^{-1} [7, 8] thus being more stable than any other C–X bond, and 3) hexafluoroacetone is commercially available in the forms of sesqui- and trihydrates, which means it is

---

[*] Prof. Dr. H. Schwarz, Dipl.-Chem. U. Mazurek, Dr. D. Schröder
Institut für Chemie, Technische Universität Berlin
Straße des 17. Juni 135, 10623 Berlin (Germany)
Fax: (+49) 30-314-21102
E-mail: Helmut.Schwarz@www.chem.tu-berlin.de

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

stable against hydrolysis, one would not expect the contact of Cr^+ with hexafluoroacetone and water in the gas phase to cause any chemical reaction. Nonetheless, in the course of another study[6] we realized that chemical reactions are indeed observed, as summarized in Equations (1)–(4).

$$Cr^+ \xrightarrow[\substack{3.9\times10^{-11}\\(3.6\%)}]{+C_3F_6O} CrC_3F_6O^+ \tag{1}$$

$$CrC_3F_6O^+ \xrightarrow[\substack{8.8\times10^{-10}\\(37\%)}]{+H_2O,\,-HF} [CrC_3F_5O_2H^+] \xrightarrow[>100\,s^{-1}]{-HF} CrC_3F_4O_2^+ \xrightarrow[\substack{1.5\times10^{-9}\\(63\%)}]{+H_2O,\,-HF} CrC_3F_3O_3H^+ \tag{2}$$

$$\begin{tikzcd}
CrC_3F_3O_3H^+ \arrow[r, "+H_2O", "\substack{7.4\times10^{-11}\\(3.1\%)}"'] & CrC_3F_3O_4H_3^+ \arrow[r, "+H_2O", "\substack{4.6\times10^{-12}\\(0.20\%)}"'] \arrow[d, "\substack{\pm H_2O\\-HF}"', "\substack{1.6\times10^{-12}\\(0.07\%)}"] & CrC_3F_3O_5H_5^+ \arrow[r, "+H_2O", "\substack{2.2\times10^{-12}\\(0.09\%)}"'] & CrC_3F_3O_6H_7^+ & (3a) \\
 & CrC_3F_2O_4H_2^+ \arrow[r, "+H_2O", "\substack{9.8\times10^{-11}\\(3.9\%)}"'] & CrC_3F_2O_5H_4^+ \arrow[r, "+H_2O", "\substack{1.6\times10^{-12}\\(0.07\%)}"'] & CrC_3F_2O_6H_6^+ & (3b)
\end{tikzcd}$$

$$CrC_3F_2O_5H_4^+ \xrightarrow[-HF]{+C_3F_6O,\,+H_2O} CrC_6F_8O_7H_7^+,\ CrC_6F_6O_{10}H_{11}^+,\ CrC_6F_6O_9H_9^+,\ CrC_6F_8O_6H_5^+,\ \dots \tag{4}$$

Following its formation [Eq. (1)], the monoadduct $CrC_3F_6O^+$ undergoes F/OH exchange [Eq. (2)] and facile HF loss, thus forming $CrC_3F_4O_2^+$. The short-lived intermediate $CrC_3F_5O_2H^+$ cannot be observed directly. A second F/OH exchange transforms $CrC_3F_4O_2^+$ into $CrC_3F_3O_3H^+$, and subsequent complexation of water [Eq. (3)] yields $CrC_3F_3O_4H_3^+$. At this point, the reaction sequence bifurcates. While complexation of additional water molecules [Eq. (3a)] dominates the product spectrum, a smaller fraction of ions lose a fourth molecule of HF prior to further water addition [Eq. (3b)]. Figure 1 shows the temporal evolution of the ion concentrations from Cr^+ through $CrC_3F_2O_4H_2^+$.

While the addition of water to $CrC_3F_3O_4H_3^+$ to yield $CrC_3F_3O_5H_5^+$ and eventually $CrC_3F_3O_6H_7^+$ dominates the reaction system, $CrC_3F_2O_5H_4^+$ formed from $CrC_3F_2O_4H_2^+$ constitutes a second bifurcation point of the reaction sequence. To a lesser extent, $CrC_3F_2O_5H_4^+$ continues to complex water molecules [Eq. (3b)]; to a larger extent, however, partially hydrolyzed Cr^+-hexafluoroacetone diadducts, predominantly $CrC_6F_8O_7H_7^+$ and $CrC_6F_6O_{10}H_{11}^+$, are formed [Eq. (4)]. These diadducts are susceptible to further F/OH exchange.[9] Additional F/OH exchange reactions that transform the cations $CrC_3F_3O_3H^+$, $CrC_3F_3O_4H_3^+$, and $CrC_3F_3O_5H_5^+$ shown in Equation (3a) in a "diagonal-mode" fashion into their congeners $CrC_3F_2O_4H_2^+$, $CrC_3F_2O_5H_4^+$, and $CrC_3F_2O_6H_6^+$, respectively, [Eq. (3b)] could not be proven beyond doubt. Figure 2 shows the temporal evolution of the ion concentrations starting from $CrC_3F_3O_3H^+$. Three aspects of the complex reaction sequence shall be addressed in more detail.

a) The first three of the hydrolysis reactions are more efficient than any following transformation by at least one order of magnitude. Furthermore, the very first C–F bond activation constitutes the rate-limiting hydrolysis reaction, thus indicating remarkable synergistic effect: the more C–F bonds that are transformed into C–O bonds, the more facile the next C–F bond cleavage (up to $n=3$).

b) The structures of the observed cations may be governed either by pure complexation of the chromium cation or by insertion of the metal ion into one of the bonds of the ligand. Deliberate decomposition of $CrC_3F_3O_3H^+$, however, implies that no metal insertion into a C–C or C–F bond has taken place during the first three C–F bond cleavage steps.[10] Furthermore, $CrC_3F_3O_4H_3^+$ was found to lose only water in an analogous experiment, thus supporting the previous results. We conclude that the C–F bond activation reported herein does not proceed through the "harpoon" mechanism

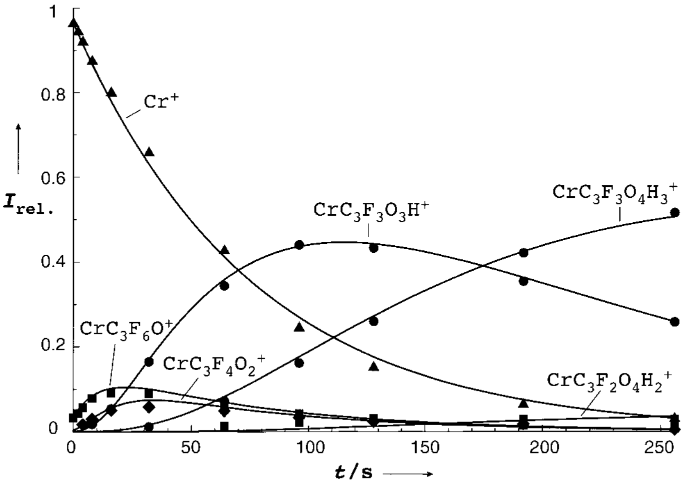

Figure 1. Complexation of thermalized chromium cations at a hexafluoroacetone pressure of 1.0×10^{-7} mbar and initial reactions with background water. For clarity, some data points close to the abscissa as well as side products were omitted.

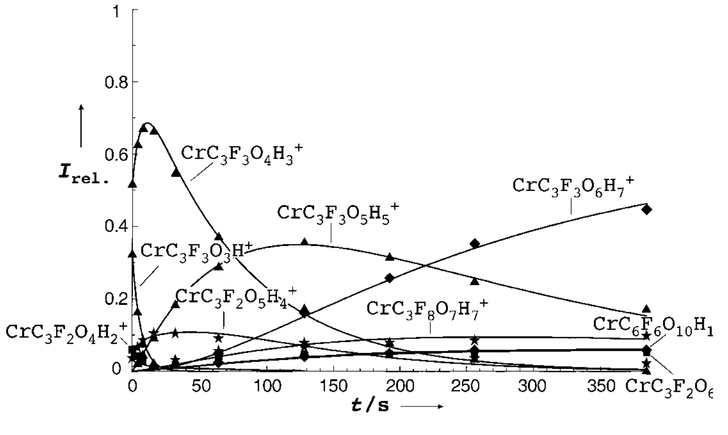

Figure 2. Hydrolysis of $CrC_3F_6O^+$ at a water pressure of 5.0×10^{-8} mbar. As a result of the fast rate of the first hydrolysis steps, the reactions could only be followed by starting with $CrC_3F_3O_3H^+$. For clarity, some data points close to the abscissa as well as side products were omitted. Of the partially hydrolyzed diadducts, only their major representatives $CrC_6F_8O_7H_7^+$ and $CrC_6F_6O_{10}H_{11}^+$ are shown.

postulated for both lanthanoid cations[11, 12] and Ca^+.[13] If the ligand $C_3F_3O_3H$ is assumed to possess the structure of trifluoropyruvic acid, one may conclude that 1) the keto group of hexafluoroacetone remains unchanged, 2) one of the trifluoromethyl groups is completely hydrolyzed and eventually turned into a carboxylic acid group, and 3) both the newly formed carboxylic acid group and the other (unchanged) trifluoromethyl group chelate the chromium cation, whereas the keto group does not interact for steric reasons. c) Both HF losses from $CrC_3F_5O_2H^+$ [Eq. (2)] and $CrC_3F_3O_4H_3^+$ [Eq. (3)] may proceed through two alternative pathways: intramolecularly formed HF may readily dissociate from the complex in a unimolecular reaction as a result of its weak coordination or the HF loss may be assisted by an additional water molecule coordinating to the complex[6, 14, 15] in a bimolecular reaction. In an FT-ICR mass spectrometer, unimolecular dissociations originate from metastable parent ions, which cannot be detected in general. A bimolecular reaction, however, cannot proceed with unlimited rate. Consequently, we postulate that the unobserved cation $CrC_3F_5O_2H^+$ loses HF in an unimolecular reaction. A bimolecular reaction would have to occur with a reaction efficiency of 5500 % (!) of the collision rate to account for the observed ion intensities' temporal evolution. In contrast, the observed cation $CrC_3F_3O_4H_3^+$ loses HF in a bimolecular reaction. The rate constants reported in Equations (2) and (3) were calculated accordingly.

To summarize, we were able to activate the strong C–F bond by interaction with an intrinsically unreactive cation. This activation was sufficient to facilitate hydrolysis of the C–F bond. Most remarkably, considering the relatively inefficient Cr^+–hexafluoroacetone adduct formation, the even lower reactivity of Cr^+ towards water[6] is essential for the reactions reported herein. If the association of water and Cr^+ was more efficient, the chromium cations would be consumed by this reaction and would no longer be available for activating hexafluoroacetone. A systematic study of structurally related compounds (e.g., trifluoroacetone) will be necessary to reveal whether the hitherto single observation of a cation-assisted hydrolytic C–F bond activation can be transformed into a general concept.[33]

Experimental Section

Chemicals: Methane (Linde, 99.95 %) and metallic chromium (Balzers, > 99.9 %) were used as purchased. Tap water was used without further purification. The water was added into a half-micro test tube directly connected to the gas-inlet system of the mass spectrometer and degassed by two freeze-pump-thaw cycles. Hexafluoroacetone was liberated from its sesquihydrate (Merck-Schuchardt, > 97 %) by reaction and additional dehydration with phosphorus pentoxide (P_4O_{10}) by adopting established procedures.[16–19]

Mass spectrometer: All experiments were performed on a Bruker Spectrospin CMS-47X FT-ICR mass spectrometer whose setup and operation have been described previously[20, 21] as well as pressure measurement in the reaction cell[22] and both generation and study of chromium cations.[4–6] The background pressure in the reaction cell was 2.0×10^{-9} mbar. Reaction conditions: 1) adduct formation [Eq. (1)]: methane-thermalized cations $^{52}Cr^+$, C_3F_6O pressure 1.0×10^{-7} mbar, maximum reaction time 256 s; 2) hydrolysis reactions [Eq. (2)]: $CrC_3F_6O^+$ was generated by pulsing-in C_3F_6O to $^{52}Cr^+$ and subsequent isolation, effective water pressure 3.0×10^{-9} mbar, maximum reaction time 12 s; 3) complexation by water [Eq. (3)]: $CrC_3F_6O^+$ generated by pulsing-in and isolation as before, water pressure 5.0×10^{-8} mbar, maximum reaction time 384 s; 4) connectivity of $CrC_3F_3O_3H^+$: the ion was generated by pulsing-in C_3F_6O to Cr^+ and subsequent reaction with background water; the ion of interest was isolated and subjected to a CID experiment[23] in the presence of 7.0×10^{-8} mbar of argon.

Analysis of results: Reaction sequences were derived from the temporal evolution of ion intensities and complementary double-resonance experiments.[24] Reaction kinetics were analyzed by using a computer program that determines rate constants and distribution ratios based on the experimentally observed temporal evolution of ion intensities, and a flexible kinetic model.[25] Unless otherwise noted, the reaction rate constants are reported as effective bimolecular rate constants in units of $cm^3 molecules^{-1} s^{-1}$ whereas reaction efficiencies ϕ in parenthesis are given as fractions of the measured bimolecular rate constants and the gas-kinetic collision rates[28] according to the capture theory.[26, 27] The absolute error of the experimentally determined rate constants is in the range of ± 30 %,[22] whereas the relative rates are more precise (± 10 %).[22] The rate constant of the formation of the monoadduct formation [Eq. (1)] is thought to be more imprecise (± 40 %) as a result of the rough estimation of the polarizability of hexafluoroacetone. The effective water pressure is only one and a half times the background pressure, thus the same wider error margin is assessed for the reactions shown in Equation (2).

Received: March 6, 2001 [Z 18838]

---

[1] On April 9, 2002, a SciFinder search for the keywords "*C–F bond activation gas phase*" by using the search menu "*Explore by Research Topic*" returned seven references. Of these, only four (refs. [11–13, 29]) refer to C–F bond activation at all; none of the returned references relates to hydrolysis.

[2] S. W. Buckner, J. R. Gord, B. S. Freiser, *J. Am. Chem. Soc.* **1988**, *110*, 6606–6612.

[3] J. B. Schilling, J. L. Beauchamp, *Organometallics* **1988**, *7*, 194–199.

[4] U. Mazurek, D. Schröder, H. Schwarz, *Collect. Czech. Chem. Commun.* **1998**, *63*, 1498–1512.

[5] U. Mazurek, H. Schwarz, *Inorg. Chem.* **2000**, *39*, 5586–5590.

[6] U. Mazurek, D. Schröder, H. Schwarz, *Eur. J. Inorg. Chem.* **2002**, in press.

[7] K. P. C. Vollhardt, N. E. Schore, *Organische Chemie*, 3rd ed., Wiley-VCH, Weinheim, **2000**, p. 88.

[8] M. B. Smith, J. March, *March's Advanced Organic Chemistry*, 5th ed., Wiley, New York, **2001**, p. 911.

[9] The complexation of $CrC_3F_2O_5H_4^+$ with another molecule of hexafluoroacetone or its hydrate(s) as summarized in Equation (4) is supposed to originate from hexafluoroacetone hydrate formation. It is plausible that this hydrate formation, in turn, originates from pulsing hexafluoroacetone into the reaction cell. Supposedly, the hydrates stick to the walls of the reaction cell more efficiently than hexafluoroacetone itself does.

[10] $CrC_3F_3O_3H^+$ was subjected to a CID experiment[23] in the presence of argon (7.0×10^{-8} mbar). The fragment ions observed were mostly Cr^+, as well as CrF^+, CrF_2^+, and their hydrolysis products[6]. Chromium-free cations and cationic organochromium complexes were not detected. Our interpretation refers to the chelate structure of $CrC_3F_3O_3H^+$ discussed in more detail in the text. Upon decomposition, kinetically excited $CrC_3F_3O_3H^+$ cations may lose Cr^+ when colliding with argon. However, upon collision with background water, one or more of the chelation-weakened C–F bonds might be broken, thus causing the formation of CrF^+ or CrF_2^+, or $CrOH^+$ or $Cr(OH)_2^+$, respectively, and HF, besides the corresponding neutral organic fragment.

[11] C. Heinemann, N. Goldberg, I. C. Tornieporth-Oetting, T. M. Klapötke, H. Schwarz, *Angew. Chem.* **1995**, *107*, 225–229; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 213–217.

[12] H. H. Cornehl, G. Hornung, H. Schwarz, *J. Am. Chem. Soc.* **1996**, *118*, 9960–9965.

[13] J. N. Harvey, D. Schröder, W. Koch, D. Danovich, S. Shaik, H. Schwarz, *Chem. Phys. Lett.* **1997**, *278*, 391–397.

[14] D. K. Bohme, *Int. J. Mass Spectrom. Ion Processes* **1992**, *115*, 95–110.

[15] A. J. Chalk, L. Radom, *J. Am. Chem. Soc.* **1997**, *119*, 7573–7578.

[16] A. L. Henne, J. W. Shepard, E. J. Young, *J. Am. Chem. Soc.* **1950**, *72*, 3577–3579.
[17] R. N. Haszeldine, *J. Chem. Soc.* **1953**, 3565–3573.
[18] R. N. Haszeldine, *J. Chem. Soc.* **1954**, 1273–1279.
[19] A. T. Morse, P. B. Ayscough, L. C. Leitch, *Can. J. Chem.* **1955**, *33*, 453–457.
[20] K. Eller, H. Schwarz, *Int. J. Mass Spectrom. Ion Processes* **1989**, *93*, 243–257.
[21] K. Eller, W. Zummack, H. Schwarz, *J. Am. Chem. Soc.* **1990**, *112*, 621–627.
[22] D. Schröder, H. Schwarz, D. E. Clemmer, Y. Chen, P. B. Armentrout, V. I. Baranov, D. K. Böhme, *Int. J. Mass Spectrom. Ion Processes* **1997**, *161*, 175–191.
[23] R. B. Cody, S. C. Burnier, B. S. Freiser, *Anal. Chem.* **1982**, *54*, 96–101.
[24] M. B. Comisarow, V. Grassi, G. Parisod, *Chem. Phys. Lett.* **1978**, *57*, 413–416.
[25] U. Mazurek, H. Schwarz, *ICR Kinetics*, v. 3.0.1, TU Berlin, Berlin, **1998**, available upon request.
[26] T. Su, W. J. Chesnavich, *J. Chem. Phys.* **1982**, *76*, 5183–5185.
[27] T. Su, *J. Chem. Phys.* **1988**, *89*, 5355.
[28] Parameters: water: dipole moment 1.854 D,[30] polarizability 1.45×10^{-24} cm^3,[30] relative ion gauge sensitivity 0.97;[31] hexafluoroacetone: dipole moment 0.395 D,[32] polarizability 7.5×10^{-24} cm^3 (estimation based on the data for acetone and fluorinated methanes CH$_n$F$_{4-n}$[30]), relative ion gauge sensitivity 2.59.[31]
[29] J. N. Harvey, D. Schröder, W. Koch, D. Danovich, S. Shaik, H. Schwarz, *Chem. Phys. Lett.* **1997**, *273*, 164–170.
[30] *CRC Handbook of Chemistry and Physics*, 79th ed. (Ed.: D. R. Lide), CRC Press, Boca Raton, FL, **1998**.
[31] J. E. Bartmess, R. M. Georgiadis, *Vacuum* **1983**, *33*, 149–153.
[32] J. U. Grabow, N. Heineking, W. Stahl, *Z. Naturforsch. A* **1991**, *46*, 229–232.
[33] **Note added in proof** (June 3, 2002): Since the submission of this paper several publications have appeared on C–F bond activation; see for example: K. Uneyama, H. Amii, *J. Fluorine Chem.* **2002**, *114*, 127–131; K. Guennou de Cadenet, R. Rumin, F. Y. Pétillon, D. S. Yufit, K. W. Muir, *Eur. J. Inorg. Chem.* **2002**, 639–657; D. Zhang, C. Liu, S. Bi, *J. Phys. Chem. A* **2002**, *106*, 4153–4157.

Anti-Markovnikov Hydroamination of Terminal Alkynes**

Annegret Tillack, Ivette Garcia Castro,
Christian G. Hartung, and Matthias Beller*

Dedicated to Professor Dr. Lutz F. Tietze
on the occasion of his 60th birthday

Imines are of significant importance as intermediates for the synthesis of various amines and carbonyl compounds. In general, the synthesis of imines includes amination of a suitable aldehyde or ketone. A more atom-efficient route is the direct hydroamination of alkynes.[1] This method has the additional advantage that no water is produced as a by-product. Hence, various domino reactions (e.g. direct nucleophilic addition of organometallic reagents) are possible, which do not work in the presence of water.

The homogeneously catalyzed intermolecular hydroamination of alkynes is known to proceed in the presence of Hg and Tl salts,[2] alkali metals (Cs),[3] Ti,[4] Zr,[5] Nd,[6] U, and Th[7] complexes. In addition, complexes of late-transition metals (such as Ru, Pd,[8] and Rh[9]) have been used as catalysts for this transformation. Clearly, catalysts based on cheap and easily available titanium and zirconium complexes offer significant advantages compared to those based on toxic metals (Hg, Tl) or more expensive (U, Th, Ru, Pd, and Rh) complexes.

Recently, important progress in the intermolecular hydroamination of alkynes with titanium complexes was made by Johnson and Bergman[10] and by Doye and co-workers.[4] While the former group developed the modified titanium complex [Cp(ArNH)(py)Ti=NAr] (Cp = cyclopentadienyl, py = pyridyl) and used it for the reaction of 2,6-dimethylaniline and diphenylacetylene, the latter group described an efficient and general method for the hydroamination of various internal alkynes using dimethyltitanocene as a catalyst. Bytschkov and Doye showed that the turnover frequency of this catalyst can be enhanced by using microwaves.[4c] Kinetic measurements by Bergman[10] and Doye[11] also established a general mechanism of the dimethyltitanocene-catalyzed intermolecular hydroamination of alkynes. Surprisingly little attention was paid to the hydroamination of terminal alkynes using titanium catalysts,[12] although the regioselective, sequential amination and hydroxylation of compounds that are unsaturated at the terminal position is one of the most challenging goals for industrial catalysis. Herein we report the first example of a titanocene-catalyzed anti-Markovnikov hydroamination of terminal aliphatic alkynes.

Some time ago we started a program on catalytic amination reactions of olefins and alkynes.[13, 9] Inspired by the work of Doye and Bergman, we also recently looked for easily available and stable titanocene complexes. Here, titanocene alkyne complexes of the type [$\mathrm{Cp_2Ti(\eta^2\text{-}Me_3SiC{\equiv}CR)}$] (Rosenthal's catalyst)[14] appeared to be suited as amination catalysts.[15] These complexes ([$\mathrm{Cp_2Ti(\eta^2\text{-}Me_3SiC{\equiv}CSiMe_3)}$] **1**[14a] and [$\mathrm{Cp_2Ti(\eta^2\text{-}Me_3SiC{\equiv}CPh)}$] **2**[14b]) are easily synthesized by reaction of titanocene dichloride with the corresponding silylated alkyne.

Compared to previously used titanocene precatalysts, the titanacyclopropene complexes **1** and **2** are safe and stable under argon at room temperature for many months in German version. Indeed, hydroamination of internal alkynes (diphenylacetylene, 1-phenylpropyne) with aniline or *tert*-butylamine proceeds in excellent yields in the presence of **1** (81–98 % yield after hydrolysis with HCl, Table 1). As shown in Table 2, different terminal aliphatic alkynes react with *tert*-butylamine with extremely high regioselectivity (> 98 %), in high yields (84–98%), and within a short time (2–24 h), by using 0.5–2.5 mol % of catalyst **1**, to give the imines **4a**–**e** and **5**. Although the reactions proceed smoothly with 0.5 mol % of catalyst, we used 2.5 mol % in general because of the shorter reaction time.

Pleasingly, only the anti-Markovnikov products were obtained, which is explained by the selective formation of the

---

[*] Prof. Dr. M. Beller, Dr. A. Tillack, Dr. I. Garcia Castro,
Dr. C. G. Hartung
Institut für Organische Katalyseforschung (IfOK)
Universität Rostock e.V.
Buchbinderstrasse 5–6, 18055 Rostock (Germany)
Fax: (+49) 381-466-9324
E-mail: matthias.beller@ifok.uni-rostock.de

[**] We acknowledge financial support of this project from the Deutsche Forschungsgemeinschaft (DFG) and the state of Mecklenburg-West Pommerania. C. Mewes, Dr. C. Fischer, H. Baudisch, and S. Buchholz are thanked for their excellent technical support.

1433-7851/02/4114-2541 $ 20.00+.50/0