

# Remote Functionalization of C-H and C-C Bonds by "Naked" Transition-Metal Ions (*Cosi Fan Tutte*)<sup>‡</sup>

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## Introduction

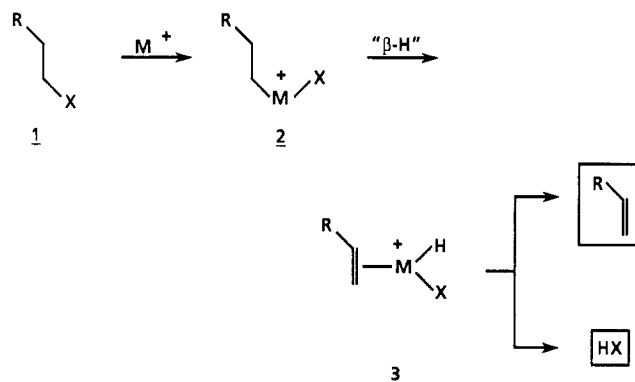
Gas-phase experiments with "naked" transition-metal ions offer a unique opportunity to probe, in the absence of any solvation, ion-pairing, and/or ligand effects, the intrinsic properties of reactive organometallic species and to evaluate the potential role these remarkable transients play in the initial steps of the activation of C-H and C-C bonds.<sup>1</sup> Not surprisingly, this topic is of fundamental interest in catalysis and has attracted considerable attention in the last decade.<sup>1,2</sup>

Many reactions of transition-metal ions M<sup>+</sup> with organic substrates can be described by a mechanism (Scheme I) suggested for the first time by Allison and Ridge.<sup>3</sup> Oxidative addition of the C-X bond (X = functional group) of the organic substrate 1 to M<sup>+</sup> generates 2, from which, via  $\beta$ -hydrogen transfer, the olefin-hydrido complex 3 is generated; depending on the binding energies, 3 then undergoes either ligand detachment (3  $\rightarrow$  RCH=CH<sub>2</sub>) or reductive elimination of HX.

The selective functionalization of *remote* C-H or C-C bonds, i.e., several carbon atoms away from the activating group X, represents a great challenge. While such processes are common to enzymes (for example, enzymatic conversion of stearic to oleic and/or microbiological hydroxylation of C-H bonds) which anchor a functional group and *geometrically* select a specific segment of the substrate, only a few cases in solution chemistry are reported<sup>4</sup> where a similar principle seems to be operative. Breslow<sup>4</sup> has coined the term *remote functionalization* for this method of coordination of a functional group followed by selective reactions at sites away from the (complexed) group X. We,<sup>1k,5</sup> and later others,<sup>6</sup> have recently demonstrated that remote functionalization can be achieved in the gas phase for quite a variety of *flexible* substrates including aliphatic nitriles,<sup>5</sup> isonitriles,<sup>7</sup> amines,<sup>3c,d</sup> alcohols,<sup>8</sup> ketones,<sup>9</sup> alkynes,<sup>11,10</sup> and allenes,<sup>11</sup> respectively. Specifically, we have shown that the C-H bond of a terminal methyl group of an alkyl chain can be oxidatively added to the "anchored" transition-metal ion M<sup>+</sup> (Scheme II). The

Helmut Schwarz, born in 1943 in Nickenich (West Germany), spent four years as a technician in chemical industry before he started to read chemistry (1966-1971) at the Technische Universität Berlin, TUB. After having obtained his Ph.D. with Ferdinand Bohlmann in 1972 and completed his "Habilitation" in 1974 (both at TUB), he was introduced to mass spectrometry by Josef Seibl (ETH Zürich), Klaus Blemann (MIT Cambridge), and Dudley H. Williams (Cambridge University). Since 1978 he has been associated with TUB as a Professor of Chemistry and has so far resisted all temptations to leave Berlin for good. Visiting appointments were held by him in a number of institutions, including Churchill College Cambridge (1978, 1981), Ecole Polytechnique Federale de Lausanne (1979, 1988), the Hebrew University of Jerusalem (1982, 1983), and the Israel Institute of Technology (Technion) in Haifa (1986). His current interests include, in addition to natural science, music (Mozart, Schubert) and (contemporary) art-no sports, please. To his great disappointment he has no vote in the election of the next principal conductor of the Berlin Philharmonic Orchestra.

Scheme I



insertion is followed by a  $\beta$ -hydrogen shift (5  $\rightarrow$  6) or  $\beta$ -cleavage of the C-C bond (5  $\rightarrow$  7) to generate inter-

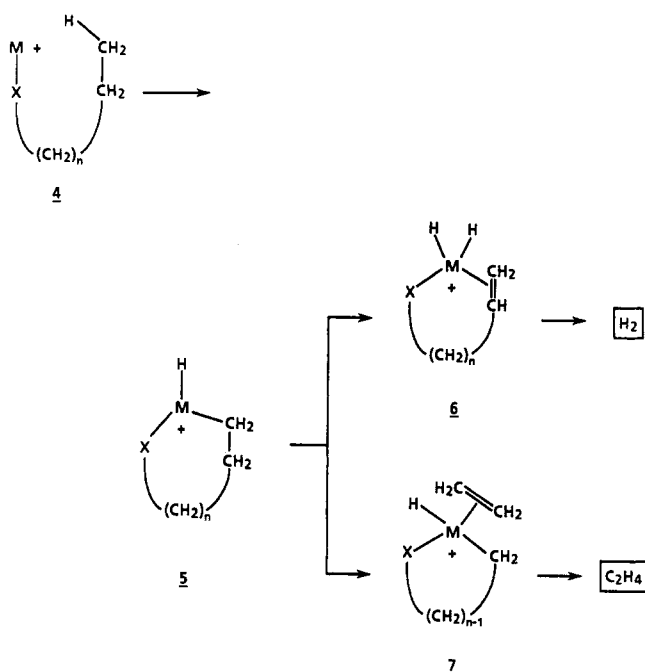
<sup>‡</sup> Dedicated to Professor Jack D. Dunitz, ETH Zürich.

(1) Selected references: (a) Müller, J. *Angew. Chem., Int. Ed. Engl.* 1972, 11, 653. (b) Müller, J. *The Organic Chemistry of Iron*; Academic Press: New York, 1978; Vol. 1, 145. (c) Beauchamp, J. L.; Stevens, A. E.; Corderman, R. R. *Pure Appl. Chem.* 1979, 51, 976. (d) Gregor, I. K.; Guilhaus, M. *Mass Spectrom. Rev.* 1984, 3, 39. (e) Freiser, B. S. *Talanta* 1985, 32, 697. (f) Allison, J. *Prog. Inorg. Chem.* 1986, 34, 627. (g) Armentrout, P. B. In *Structure/Reactivity and Thermochemistry of Ions*; Ausloos, P., Lias, S. G., Eds.; D. Reidel: Dordrecht, 1987; No. 193, p 97. (h) Ridge, D. P. *Ibid.* 1987; No. 193, p 165. (i) Squires, R. R. *Chem. Rev.* 1987, 87, 623. (j) Armentrout, P. B. In *Gas Phase Inorganic Chemistry*; Russell, D. H., Ed.; Plenum: New York, in press. (k) Czekay, G.; Drewello, T.; Eller, K.; Lebrilla, C. B.; Prüsse, T.; Schulze, C.; Steinrück, N.; Sülzle, D.; Weiske, T.; Schwarz, H. In *Organometallics in Organic Synthesis*; Werner, H., Erker, G., Eds.; Springer Verlag: Heidelberg, in press. (l) More than 100 references on the reactions of bare transition-metal ions with organic substrates, together with a detailed discussion of the reactions of gaseous octyne isomers with Fe<sup>+</sup>, may be found in Schulze et al.: Schulze, C.; Schwarz, H.; Peake, D. A.; Gross, M. L. *J. Am. Chem. Soc.* 1987, 109, 2368. (m) Beauchamp, J. L. In *High Energy Processes in Organometallic Chemistry*; Suslick, K. E., Ed.; ACS Symposium Series 333; American Chemical Society: Washington, DC, 1987. (n) Buckner, S. W.; Freiser, B. S. *Polyhedron* 1988, 7, 1583. (o) Allison, J.; Mavridis, A.; Harrison, J. F. *Polyhedron* 1988, 7, 1559.

(2) Selected reviews: (a) Parshall, G. W. *Catalysis* 1977, 1, 335. (b) Haggin, J. *Chem. Eng. News* 1982, 60, 13. (c) Muetterties, E. L. *J. Chem. Soc. Rev.* 1983, 11, 283. (d) Shilov, A. E. *Activation of Saturated Hydrocarbons by Transition Metal Complexes*; D. Reidel: Dordrecht, 1984. (e) Bergman, R. G. *Science* 1984, 223, 902. (f) Crabtree, R. H. *Chem. Rev.* 1985, 85, 245. (g) Silvestre, J.; Hoffmann, R. *Helv. Chim. Acta* 1985, 68, 1461. (h) Green, M. L.; O'Hare, D. *Pure Appl. Chem.* 1985, 57, 1897. (i) Baudry, D.; Ephritikine, M.; Felkin, H.; Filleben-Khan, T.; Gault, Y.; Holmes-Smith, R.; Yngues, L.; Zakrezewski, J. In *Organic Synthesis*; Streith, J., Prinzbach, H., Schill, G., Eds.; Blackwell Scientific Publications: Oxford, 1985; p 25. (j) Halpern, J. *Inorg. Chim. Acta* 1985, 100, 41. (k) Rothwell, I. P. *Polyhedron* 1985, 4, 77. (l) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, CA, 1987. (m) de Meijere, A., tom Dieck, H., Eds.; *Organometallics in Organic Synthesis: Aspects of a Modern Interdisciplinary Field*; Springer-Verlag: Heidelberg, 1988. (n) Jones, W. D.; Feher, F. J. *Acc. Chem. Res.* 1989, 22, 91.

(3) (a) Allison, J.; Ridge, D. P. *J. Am. Chem. Soc.* 1979, 101, 4998. (b) Babinec, S. J.; Allison, J. *Ibid.* 1984, 106, 7718. (c) For a revision and modification of this otherwise quite general mechanism, in the reactions of primary amines and alcohols with Fe<sup>+</sup> and Co<sup>+</sup>, see: Karrass, S.; Eller, K.; Schulze, C.; Schwarz, H. *Angew. Chem., Int. Ed. Engl.* 1989, 28, 607. (d) Karrass, S. *Diploma Thesis*, Technical University Berlin, 1988. (e) Karrass, S.; Prüsse, T.; Eller, K.; Schwarz, H. *J. Am. Chem. Soc.*, submitted.

Scheme II



mediates from which eventually reductive elimination of  $H_2$  or ligand detachment occurs. This behavior contrasts sharply with that depicted in Scheme I, and it demonstrates that *selective C-H activation can indeed be achieved at positions remote from the functional group X*.

In the present Account the discussion will be confined to recent results from our laboratory. While most of the data will be concerned with the chemistry of aliphatic nitriles, the reactions of alkynes with bare transition-metal ions will be briefly mentioned. Particular attention will be paid to the following problems: (i) Which step constitutes the rate-determining step (RDS) in the generation of  $H_2$  and  $C_2H_4$  from 4? (ii) Does the (complexed) metal ion  $M^+$  specifically insert in C-H bonds, which is the favored if not exclusive mode in solution organometallic chemistry,<sup>2</sup> or can a C-C bond also be added oxidatively to  $M^+$ ? In this context, the pertinent problem of  $\beta$ -methyl migration to a metal ion center will be discussed. (iii) To what

extent is the trajectory of approach<sup>12</sup> for the oxidative addition of a C-H bond governed by the nature of  $M^+$ , and what role does the chain length play in the formation of metallacycles 5? (iv) Preliminary data will be reported on reactions in which the metal ion is allowed to form bidentate complexes.

The experimental setup for the study of organometallic species in the gas phase has been described in the original papers.<sup>11,5,7,10,11</sup> Briefly, a VG Instruments ZAB-HF-3F triple-sector mass spectrometer is employed, which is of BEB configuration (B stands for magnetic and E for electric sector). In a typical experiment, transition-metal ions  $M^+$  are generated either by electron-impact ionization of a suitable organometallic precursor, for example  $Fe(CO)_5$ , or by bombarding a salt target, as for example  $FeSO_4$ , with fast atoms. The so-formed metal ions  $M^+$ , which may well bear some ligands L, are allowed to react in the ion source with gaseous organic substrates RX to generate complexes of the general "structure"<sup>13</sup>  $RX/M^+$ . These complexes, having 8-keV translational energy, are then mass selected with B(1)E, and their products due to either spontaneous or collision-induced dissociations are recorded by scanning B(2). Tandem mass spectrometry (MSMS)<sup>14</sup> is also employed to further characterize the organometallic species.

### The Reactions of Aliphatic RCN/ $M^+$ Complexes

Based on chain length effect studies and the investigation of labeled precursors, a mechanism has been suggested that is in keeping with the high selectivity observed for the  $Fe^+$ -mediated losses of  $H_2$  and  $C_2H_4$  from aliphatic, unbranched nitriles RCN.<sup>5a</sup> For  $C_4$ - $C_7$  nitriles, hallmarks are the complete absence of any scrambling processes and the specific generation of  $H_2$  and  $C_2H_4$  from the  $\omega$  and  $(\omega - 1)$  positions of the alkyl chain. The study of intramolecular kinetic isotope effects<sup>5c</sup> demonstrates that the oxidative addition of the C-H bond to the complexed metal ion (Scheme II,  $X = CN$ ;  $4 \rightarrow 5$ ) is not rate-determining. For the generation of  $C_2H_{4-x}D_x$ , it is the ligand detachment that is subject to a kinetic isotope effect ( $k_H/k_D = 1.25$  per deuterium atom). For the  $Fe^+$ -mediated generation of a hydrogen molecule from 4, isotope effects were observed for both the  $\beta$ -hydrogen transfer  $5 \rightarrow 6$  ( $k_H/k_D = 1.59$ ) and the reductive elimination of hydrogen ( $k_{H_2}/k_{HD} = 1.70$  and  $k_{HD}/k_{D_2} = 1.44$ ).

The unprecedented behavior of the RCN/ $Fe^+$  complexes contrasts with that of other unsaturated systems, such as alkenes<sup>15</sup> where allylic activations of C-H and

(4) For reviews on this concept, see: (a) Breslow, R. *Chem. Soc. Rev.* 1972, 1, 553. (b) Breslow, R. *Acc. Chem. Res.* 1980, 13, 170. (c) Breslow, R.; Adams, A.; Guv, T.; Hunger, J. *Lect. Heterocycl. Chem.* 1987, 9, 43. (d) For an industrial application of this concept, see: Kerb, U.; Stahnke, M.; Schulze, P.-E.; Wiechert, R. *Angew. Chem., Int. Ed. Engl.* 1981, 20, 88.

(5) (a) Lebrilla, C. B.; Schulze, C.; Schwarz, H. *J. Am. Chem. Soc.* 1987, 109, 98. (b) Drewello, T.; Eckart, K.; Lebrilla, C. B.; Schwarz, H. *Int. J. Mass Spectrom. Ion Processes* 1987, 76, R1. (c) Lebrilla, C. B.; Drewello, T.; Schwarz, H. *Ibid.* 1987, 79, 287. (d) Lebrilla, C. B.; Drewello, T.; Schwarz, H. *J. Am. Chem. Soc.* 1987, 109, 5639. (e) Prüsse, T.; Lebrilla, C. B.; Drewello, T.; Schwarz, H. *Ibid.* 1988, 110, 5986. (f) Prüsse, T.; Drewello, T.; Lebrilla, C. B.; Schwarz, H. *Ibid.* 1989, 111, 2857. (g) Czekay, G.; Drewello, T.; Schwarz, H. *Ibid.*, in press. (h) Czekay, G.; Drewello, T.; Eller, K.; Zummack, W.; Schwarz, H. *Organometallics*, in press.

(6) Strepnowski, R. M.; Allison, J. *Organometallics* 1988, 7, 2097. (7) (a) Eller, K.; Lebrilla, C. B.; Drewello, T.; Schwarz, H. *J. Am. Chem. Soc.* 1988, 110, 3068. (b) Eller, K.; Schwarz, H. *Chem. Ber.*, in press.

(8) Prüsse, T.; Schwarz, H. *Organometallics*, submitted.

(9) Schröder, D.; Schwarz, H., in preparation.

(10) (a) Schulze, C.; Schwarz, H. *Chimia* 1987, 41, 29. (b) Schulze, C.; Schwarz, H. *J. Am. Chem. Soc.* 1988, 110, 67. (c) Schulze, C.; Weiske, T.; Schwarz, H. *Organometallics* 1988, 7, 898.

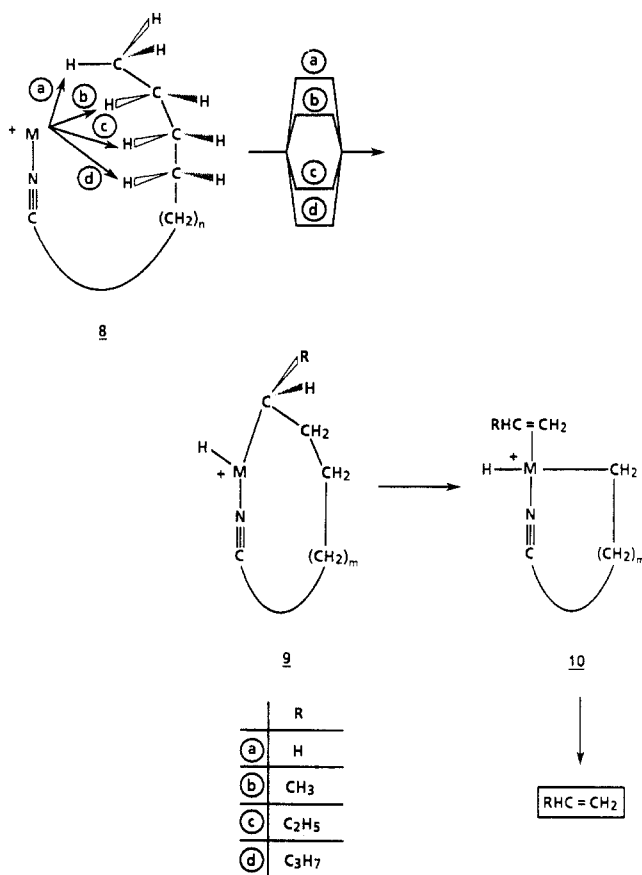
(11) Steinrück, N.; Schwarz, H. *Organometallics* 1989, 8, 759.

(12) For this concept, see: (a) Dunitz, J. D. *X-Ray Analysis and the Structure of Organic Molecules*; Cornell University Press: Ithaca, NY, 1979. (b) Bürgi, H. B.; Dunitz, J. D. *Acc. Chem. Res.* 1983, 16, 153.

(13) As proposed by Müller,<sup>1a</sup> "suggested structures are hypothetical in most cases studied in mass spectrometry. They are based on plausibility arguments using as much direct and indirect evidence available for experiments and model considerations. Nevertheless, their heuristic merits are undeniable in chemistry as long as speculations remain within acceptable limits." Similarly, the neutrals formed from the organic metal complexes are in most cases not structurally characterized but inferred indirectly from the mass differences between the mass-selected precursor and observed daughter ions. Fortunately, on energetic grounds there cannot exist any possible doubt as to the actual structure of many neutrals (for example,  $\Delta m = 2$  corresponds to  $H_2$ ,  $\Delta m = 16$  to  $CH_4$ ,  $\Delta m = 28$  to  $C_2H_4$ , etc.).

(14) (a) McLafferty, F. W., Ed. *Tandem Mass Spectrometry*; Wiley Interscience: New York, 1983. (b) Busch, K. L.; Glish, G. L.; McLuckey, S. A. *Mass Spectrometry/Mass Spectrometry: Techniques and Applications of Tandem Mass Spectrometry*; VCH Publishers: New York, 1988.

Scheme III

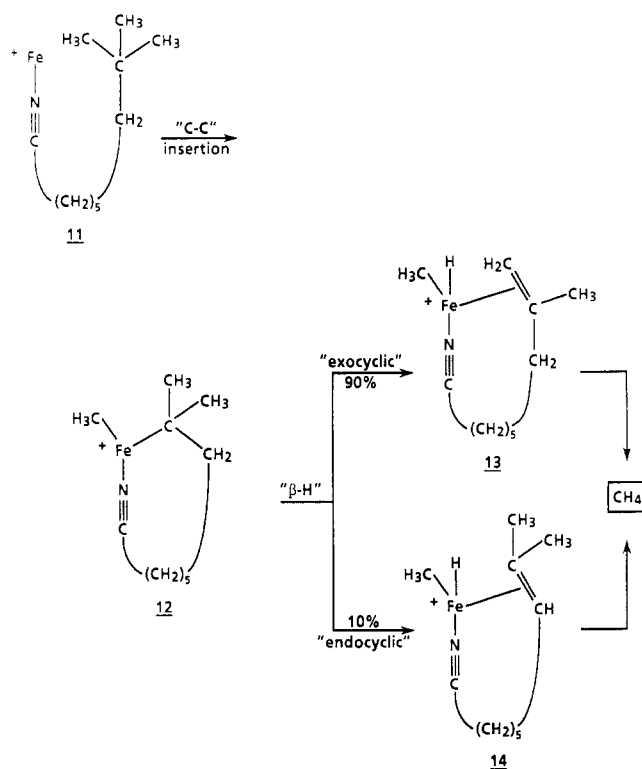


C-C bonds are reported to be the major reactions. The unique gas-phase chemistry of RCN/Fe<sup>+</sup> (and also other metal ions, see below) is due to the initial interaction of the CN group with M<sup>+</sup>. For all transition-metal ions studied, except for Cu<sup>+</sup>,<sup>16</sup> the preferred coordination leads to an "end-on" complex 8 (Scheme III) characterized by a "linear" or near-linear —CH<sub>2</sub>—C≡N—M<sup>+</sup> entity. This linear arrangement constrains the remainder of the molecule in such a manner that M<sup>+</sup> reactivates C-H bonds while trying to minimize the strain. For nitriles containing four to seven carbon atoms, this deformation results in the exclusive activation of the terminal methyl group (Scheme III, path a). However, as the carbon chain is lengthened,<sup>5d</sup> activation of the internal C-H bonds starts to dominate. This is evidenced by the following experimental findings: (i) Hydrogen is no longer exclusively provided by the ω and (ω - 1) positions; it also originates from internal C-H bonds. (ii) The fact that internal C-H bonds are oxidatively added (Scheme III, 8 → 9; trajectories b, c, and d) has the consequence that, in addition to C<sub>2</sub>H<sub>4</sub>, higher alkenes RCH=CH<sub>2</sub> are eliminated. Highly interesting and not yet fully understood is the finding that the trajectory of interaction for the step 8 → 9 differs for Fe<sup>+</sup> versus Co<sup>+</sup> and Ni<sup>+</sup>.<sup>5c,d</sup> For Fe<sup>+</sup>, insertion in an internal bond commences at position C(8), while for M = Co, Ni reaction at C(7) is favored. While it is trivial to state that the trajectory of

(15) (a) Armentrout, P. B.; Halle, L. F.; Beauchamp, J. L. *J. Am. Chem. Soc.* 1981, 103, 6624. (b) Larsen, B. S.; Ridge, D. P. *Ibid.* 1984, 106, 1912. (c) Peake, D. A.; Gross, M. L. *Anal. Chem.* 1985, 57, 115.

(16) For RCN/Cu<sup>+</sup> the chemistry is such that a "side-on" complex is initially generated; as a consequence, C-H and C-C bonds in the vicinity of the functional group are activated: Lebrilla, C. B.; Drewello, T.; Schwarz, H. *Organometallics* 1987, 6, 2450.

Scheme IV



interaction is governed by the ring size, it should be kept in mind that the size of the ring itself is a reflection of the back-bonding ability of the metal ion, since this controls the distortion of the —CH<sub>2</sub>—C≡N—M<sup>+</sup> moiety from linearity.

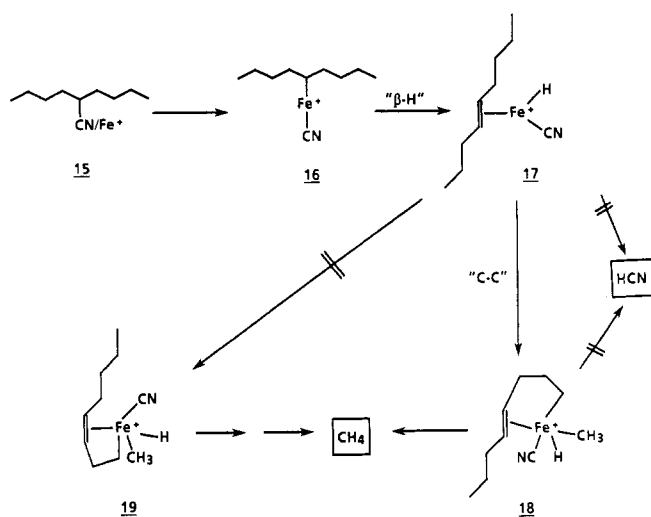
Unequivocal evidence for the direct oxidative addition of *remote* C-C bonds was provided by the study of *tert*-butyl substituted nitriles.<sup>5e</sup> For example, Fe<sup>+</sup>-mediated demethanation of 8,8-dimethylnonane-nitrile 11 follows the sequence depicted in Scheme IV, commencing with insertion of Fe<sup>+</sup> into a terminal H<sub>3</sub>C—C bond, followed by β-hydrogen transfer from either an "exocyclic" (ca. 90%) or an "endocyclic" (ca. 10%) C-H bond (Scheme IV).<sup>17</sup> There was no experimental support for the operation of the long-sought-after β-methyl migration<sup>18</sup> in the system studied.

A most unexpected mode of Fe<sup>+</sup>-induced demethanation was recently unraveled to exist for α-*branched* aliphatic nitriles of the general structure R<sup>1</sup>R<sup>2</sup>CHCN (R<sup>1,2</sup> = alkyl).<sup>5h</sup> For example, from the complex 15 in addition to H<sub>2</sub> and C<sub>2</sub>H<sub>4</sub>, methane is generated. While H<sub>2</sub> and C<sub>2</sub>H<sub>4</sub> are formed according to Scheme II (M = Fe; X = CN), methane is generated in an unprecedented reaction mechanism which consists of the following steps: (i) insertion of Fe<sup>+</sup> in the C-CN bond, (ii) β-hydrogen transfer to the metal center, (iii) oxidative addition of a remote H<sub>3</sub>C—C bond, and (iv) re-

(17) For the metal ion mediated alkane formation, in most cases reported it is not possible to distinguish between the two reaction sequences, i.e., (i) insertion of M<sup>+</sup> in a C-C bond followed by β-hydrogen transfer or (ii) oxidative addition of a C-H bond followed by β-alkyl migration to the metal center. Both variants generate the same intermediate from which eventually reductive elimination of RH occurs.

(18) While β-alkyl migrations are reported to exist in a few organometallic systems in solution (for example, see: Watson, P. L.; Roe, D. C. *J. Am. Chem. Soc.* 1982, 104, 6471), they are extremely rare in the gas phase. [(a) Houriet, R.; Halle, L. F.; Beauchamp, J. L. *Organometallics* 1983, 2, 1818. (b) Reference 5h, if they exist at all: (c) Reference 3c. (d) Eller, K.; Drewello, T.; Zummack, W.; Allspach, T.; Annen, U.; Regitz, M.; Schwarz, H. *J. Am. Chem. Soc.*, in press.

Scheme V



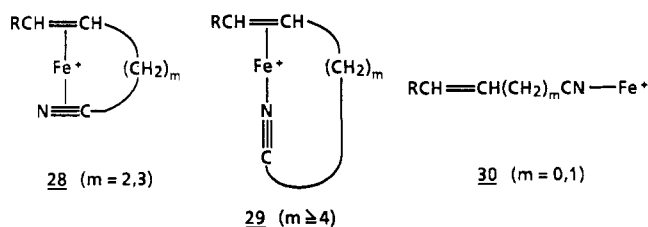
ductive elimination of  $\text{CH}_4$  (Scheme V). For the  $\beta$ -hydrogen transfer, we observe a primary isotope effect ( $k_{\text{H}}/k_{\text{D}} = 1.22$ ), and for the reductive elimination of  $\text{CH}_{4-x}\text{D}_x$ , a secondary isotope effect ( $k_{\text{H}}/k_{\text{D}} = 1.1$  per deuterium). Noteworthy are the observations that none of the intermediates, generated en route from 15 to the products 18 and  $\text{CH}_4$ , undergo reductive elimination of  $\text{HCN}$ . It is also interesting to note that oxidative addition of a  $\text{H}_3\text{C}-\text{C}$  bond from the propyl chain of intermediate 17 cannot compete with the reaction  $17 \rightarrow 18$ . This discrimination very likely reflects a kinetic preference for the formation of the "metallacycle" 18 versus 19.

The study of  $\text{Fe}^+$  complexes of  $\alpha$ -branched nitriles provided also for the first time compelling evidence that an "anchored" transition-metal ion is capable of *activating in succession different sites of a flexible molecule*.<sup>5h</sup> For example, losses of both  $\text{C}_2\text{H}_6$  and  $\text{C}_3\text{H}_8$  from the complex 20 actually correspond to the consecutive eliminations of  $\text{RCH}=\text{CH}_2$  ( $\text{R} = \text{H}, \text{CH}_3$ ) and  $\text{H}_2$ . Labeling data further reveals that *both* alkyl chains are involved in the overall reaction. The mechanism, depicted in Scheme VI for the loss of " $\text{C}_3\text{H}_8$ ", is in keeping with all experimental findings.<sup>19</sup>

The interplay of two functional groups having different binding energies to  $\text{M}^+$  and the effect of the methylene chain separating the two groups was studied recently<sup>5f</sup> with particular emphasis on the question of  $\text{Fe}^+$ -mediated, *directed* allylic C-C bond cleavages (Scheme VII,  $\text{X} = \text{CN}$ ). A cooperative interaction is realized only for systems with  $m > 2$ , and it involves, without exception, the "exocyclic" allylic C-C bond (Scheme VII, path a). Activation of "endocyclic" bonds (path b) is not observed. The actual nature of bidentate complexation of  $\text{M}^+$  and in particular the question of "side-on" versus "end-on" complexation of the CN group, is also dependent upon the chain length  $(\text{CH}_2)_m$ . For  $m = 2$  or 3 the data suggest that the "productive" interaction involves a binding situation as indicated in 28, while for a larger separation ( $m \geq 4$ ) of the two functional groups, the chemistry is best described by 29. Most interestingly, if the "metallacycle" formed

would be too small ( $m = 0, 1$ ),  $\text{Fe}^+$  does not "feel" the presence of the double bond. Complexation occurs in an "end-on" fashion at the CN group (30), and the so-formed complex exhibits a chemistry that is very similar to that of saturated, unbranched alkyl nitriles. Obviously, the chain length separating the CN group and the CC double bond causes a "switching" coordination behavior.

While the dichotomy of the nitrile group to form "side-on" or "end-on" complexes with  $\text{Fe}^+$  (28 versus 29) is due to the generation of bidentate complexes, for aliphatic, saturated isonitriles RNC data were reported that point to both kinds of complexation modes even in the absence of further functional groups.<sup>7</sup> The "side-on" complexes of  $\text{RNC}/\text{Fe}^+$  cause activation in the vicinity of the functional group (as was also observed for  $\text{RCN}/\text{Cu}^+$  complexes<sup>16</sup>); the "end-on" complexation of  $\text{RNC}$  with  $\text{Fe}^+$  results in functionalization of remote C-H bonds (loss of  $\text{H}_2$ ) in analogy to the reactions of  $\text{RCN}$  with  $\text{M}^+ = \text{Fe}^+, \text{Co}^+, \text{Ni}^+$ .



### Complexes of Transition-Metal Ions with Alkynes

For unsaturated hydrocarbons, like olefins, the gas-phase reactions commence with complexation of the respective  $\pi$ -bond by the metal ions, followed by oxidative addition of the allylic C-C bond to  $\text{M}^+$ . The rearrangement is completed by  $\beta$ -hydrogen transfer to produce, starting from alkenes, bis(olefin) complexes 32 and/or 33 (Scheme VIII) as originally proposed by Beauchamp et al.<sup>15a</sup> and later confirmed by Ridge, Gross, and their co-workers,<sup>15b,c</sup> The specificity of the overall reaction is such that, via detachment of the less strongly bound olefin, an unambiguous location of the double bond can be achieved. However, as indicated in Scheme V, allylic activation must not necessarily be the dominant mode of C-C bond activation. The functionalization of a *remote* C-C bond can well occur ( $17 \rightarrow 18$ ).

Similarly, it was recently observed that propargylic insertion processes, the study of which was pioneered by Gross et al.<sup>20</sup> and later refined in a joint "Nebraska-Berlin" study,<sup>11</sup> are not the only mode by which  $\text{Fe}^+$  reacts with alkynes.<sup>11,10a,21</sup> Moreover, other transition-metal ions like  $\text{Cr}^+$  and  $\text{Mn}^+$  exhibit highly unusual reactions with gaseous alkynes.<sup>10b,c</sup> A few selected examples will be discussed in the following.

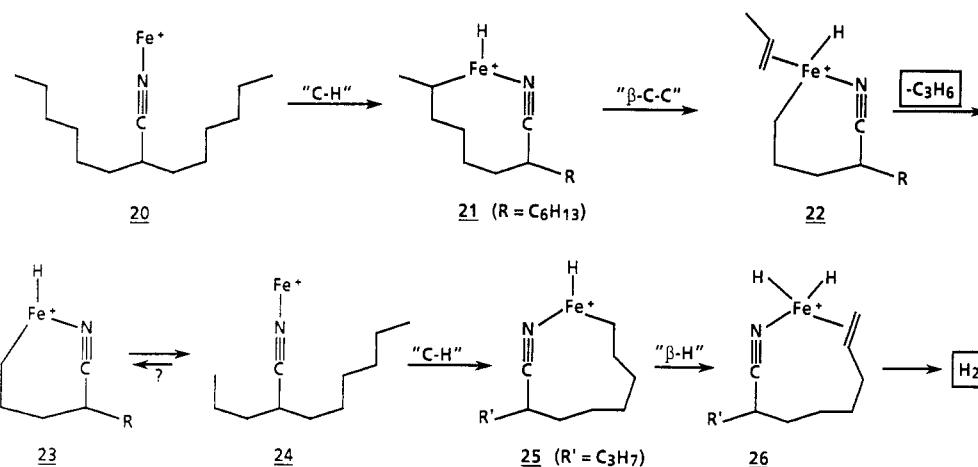
For the  $\text{Fe}^+$ -induced regiospecific dehydrogenation of 2-octyne, all experimental data are in keeping with the mechanism shown in Scheme IX, which represents another example of remote functionalization of a C-H bond. Interestingly, the traditional reaction sequence, i.e., oxidative addition of the (complexed)  $\text{Fe}^+$  to a propargylic C-C bond, followed by  $\beta$ -hydrogen transfer and subsequent dehydrogenation of an intermediate

(19) Very recently we provided evidence that an analogous principle is also operative in the  $\text{Fe}^+$ -mediated "alkane" formation from ketones. (a) Reference 9. (b) Czekay, G.; Eller, K.; Schröder, D.; Schwarz, H. *Angew. Chem., Int. Ed. Engl.*, in press.

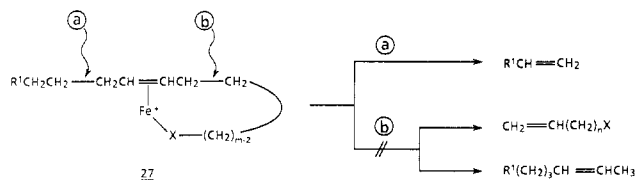
(20) Peake, D. A.; Gross, M. L. *Organometallics* 1986, 5, 1236.

(21) Schulze, C.; Weiske, T.; Schwarz, H. *Chimia* 1986, 40, 362.

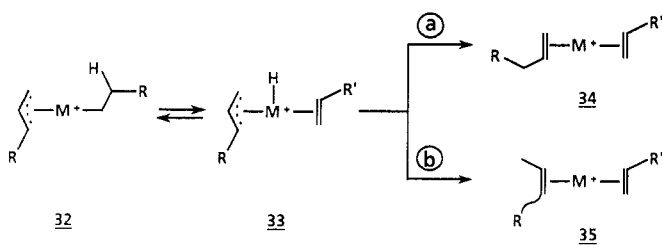
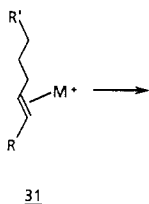
Scheme VI



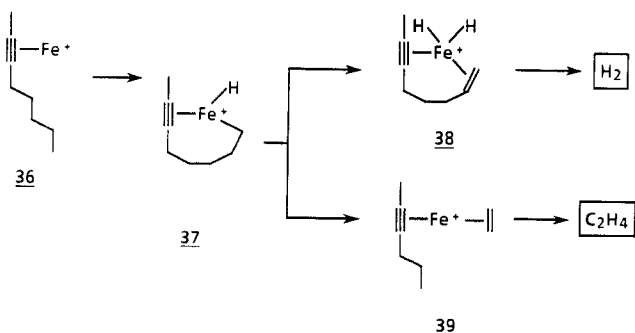
Scheme VII



Scheme VIII



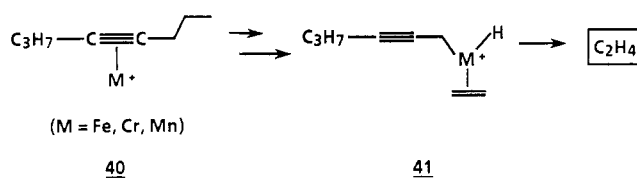
Scheme IX



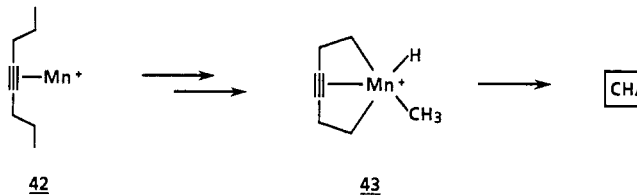
butene ligand cannot account for the observed specificity. The key intermediate is the "metallacycle" 37, which also allows description of the regiospecific loss of  $C_2H_4$  involving C(7)/C(8).<sup>10a</sup>

Similarly, unexpected observations were made for the  $Fe^+$ -induced loss of  $C_2H_4$  from 4-octyne.<sup>21</sup> While the insertion reactions are not associated with kinetic isotope effects, a ratio of  $k_H/k_D = 1.10$  per deuterium was observed for the detachment of  $C_2H_{4-x}D_x$ . Hydrogen-

Scheme X



Scheme XI



exchange processes do not precede the elimination of ethylene. A mechanism is suggested in Scheme X.

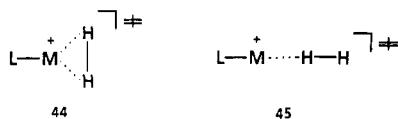
The behavior of  $Cr^+$  is quite unique in that, on the other hand, it has in common with  $Fe^+$  the high site specificity of the  $C_2H_4$  loss from 4-octyne (no hydrogen scrambling); however, in contrast to  $Fe^+$ , the formation of 41 is associated with a kinetic isotope effect  $k_H/k_D = 1.30$ , while no isotope effect is operative for the loss of ethylene (note that the reverse holds true for  $Fe^+$ ). Obviously, for the  $Cr^+$  system the oxidative addition of the terminal C-H bond to  $Cr^+$  constitutes the rate-determining step.<sup>10c</sup> The  $Mn(4\text{-octyne})^+$  complex (40,  $M = Mn$ ) also undergoes loss of  $C_2H_4$ .<sup>10c,22</sup> While a major part of the reaction can be described in terms of Scheme X, labeling data prove that, in addition, partial exchange of the hydrogens of C(2)/C(3)—but not C(1)—occurs, and the experimental results were explained by the operation of reversible  $\alpha$ -hydrogen rearrangements.<sup>10c</sup>

The  $Cr^+$  and  $Mn^+$  complexes exhibit, in addition to  $C_2H_4$  loss from 4-octyne, two more processes (elimination of  $H_2$  and  $CH_4$ , respectively), which are quite remarkable and indicative for the decisive role of the metal ion in the activation of C-H/C-C bonds.<sup>10b,c</sup>  $Mn^+$  induces an unprecedented 1,6-elimination (!) of  $CH_4$  across the CC triple bond of 4-octyne to generate an as yet unknown manganese metallacycloalkyne 43 (Scheme XI). This mechanism is not operative for the  $Cr(4\text{-octyne})^+$  system, from which  $CH_4$  is generated via

a rather conventional 1,2-elimination mode.

A distinct behavior of  $Mn^+$  and  $Cr^+$  is also observed for the metal ion induced dehydrogenation of 4-octyne. According to extensive labeling experiments,<sup>10c</sup>  $Mn^+$  activates to 83% the C(1)/C(2) positions and to 17% C(2)/C(3), and the hydrogen molecule is reductively eliminated in a formal 1,2-fashion. However, for the  $Cr^+$  complex of 4-octyne, 78% of  $H_2$  loss originates from C(2)/C(3) and only 22% from C(1)/C(2). In spite of these distinct behaviors, the two metal ions have in common the fact that the reductive elimination of hydrogen is rate-determining. The insertion of the (complexed) metal ion into the C-H bond is not associated with a discernible isotope effect. This finding is very reminiscent of the reactions described above for the  $RCN/Fe^+$  system.

With regard to the  $Cr^+$ - and  $Mn^+$ -induced  $H_2$  loss from 4-octyne, the kinetic isotope effects clearly prove that the reductive elimination proceeds via a transition state that is best described as a "side-on"  $H_2$ -coordinated metal ion (44,  $L = C_8H_{12}$ ) and not an "end-on" complex (45).<sup>10c,23</sup> This result is in excellent agreement with a theoretical analysis for  $H_2$  addition to metal complexes;<sup>24</sup> according to the Saillard-Hoffmann analysis,<sup>24</sup> using extended Hückel molecular orbital theory, the perpendicular (i.e., "end-on") approach of  $H_2$  to, for example, a  $C_{4v}$  square pyramidal metal fragment is purely repulsive. In contrast, the parallel approach which eventually generates a "side-on" bond complex is the favored mode of interaction.



### Concluding Remarks

This account has attempted to demonstrate that selective activation of remote C-H and C-C bonds of simple, flexible organic molecules  $RX$  can be easily achieved by "anchoring" a bare transition-metal ion to the functional group. The few systems that surfaced in the last two years already indicate that these reac-

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tions seem to be without precedent in organometallic chemistry performed under more conventional conditions. Moreover, they provide for the first time compelling evidence for Breslow's concept of "remote functionalization" in organometallic systems.

Future work will inter alia focus on questions like the following:

(i) What is the gas-phase chemistry of polyfunctional molecules with "naked" transition-metal ions? Can one expect cooperative effects such that supramolecular structures will be induced by the transition-metal ions?

(ii) With regard to the more traditional chemistry of charged  $ML_n^+$  complexes, it will be interesting to probe whether successive ligation of  $M^+$  will affect the reactions described in this Account. In this context the question of whether stereochemical effects are operative deserves special attention.

(iii) The observation that the reactivity of bare  $M^+$  with gaseous substrates is strongly metal ion dependent suggests the study of heteronuclear complexes  $(M'M)^+$ . It would be no surprise to observe a chemistry being distinctly different from that of either  $M^+$  and  $M'^+$ .<sup>25</sup>

(iv) Lastly, state-selective studies of the electronic states of the metal ions will most certainly add to the understanding of the chemistry of naked  $M^+$  with organic substrates.

No doubt, in spite of the already impressive number of papers published in this rapidly developing area within the last decade, the understanding of the details of the elementary steps is still in its infancy.

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(25) In fact, extensive studies by Freiser et al. already indicate the rich chemistry of homo- and heteronuclear complexes  $(M'M)^+$ : (a) reference 1e,n. (b) Hettich, R. L.; Freiser, B. S. *J. Am. Chem. Soc.* 1987, 109, 3537. (c) Buckner, S. W.; Gord, J. R.; Freiser, B. S. *J. Chem. Phys.* 1988, 88, 3678.

## Catalytic Antibodies

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With the advent of hybridoma technology<sup>1</sup> it has become possible to generate homogeneous, high-affinity

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antibodies that selectively recognize a large number of structurally diverse ligands. Antibodies have been generated against biopolymers such as nucleic acids, peptides, and polysaccharides; natural products such as steroids and prostaglandins; and small synthetic

(1) Kohler, G.; Milstein, C. *Nature* 1975, 256, 495. (b) Seiler, F., et al. *Angew. Chem., Int. Ed. Engl.* 1985, 24, 139. Goding, J. W. *Antibodies: Principles and Practice*; Academic Press: New York, 1986.