The present examples provide a rather general caveat: The literature is abundant with barriers and other properties of the reaction paths for many systems. This information is often important; however, in many cases it will not be sufficient to describe the chemical reaction. In fact, pure calculations of ξ and $\ddagger$ may be irrelevant. In any case, they should be complemented by evaluations of the reaction dynamics.

(5) On the other hand, reactions that do not follow ξ are also advantageous, since they explore different parts of the potential energy surface *V*, depending on educt excitation (compare parts a–c of Figure 1). In principle, this variability should allow us to determine all these regions of *V* by inversion techniques. For example, "transition state spectroscopy"[28] would not only yield information on potential barriers $\ddagger$ using thermal educts but also on the potential ridge using excited educts; likewise, very fast ground-state educts would yield information about the potential corner[15] and so on.

(6) The avoidance of the potential barrier $\ddagger$ by selective educt preparation implies (by time-reversed trajectories or wave packets) that collision complexes prepared close to $\ddagger$ yield specific energy release: They cannot decay into arbitrary but only into specific educt or product states. This conclusion corroborates a theorem of Ruf and Miller,[27] i.e. isomerization from $\ddagger$ along ξ will invariably end up along the molecular mode with lowest frequency (and of the same symmetry as ξ), typically a skeleton or backbone mode but hardly ever a localized R–H vibration.

The present conclusions are based on investigations of the simple collinear model reactions 2.1 and 2.2, which are at the disposal of available classical *and* quantum mechanical techniques. In the future, these studies should be extended to multidimensional systems, including atom plus diatom reactions with nonlinear barrier configurations and polyatomic reactions. Certainly it is a challenge to discover novel deviations from reaction paths in these systems. Most promising candidates include branching reactions where the branching region for classical trajectories or quantum wave packets is localized at a valley ridge inflection point before the bifurcation of $\xi^{3,29}$ and reactions of large molecules with high excitation of selective vibrational modes perpendicular to ξ.

Acknowledgment. We thank P. L. Gertitschke for helpful discussions of the FDBr tunneling path, documented in ref 15b, Professor K. Ruedenberg for suggesting that branching reactions may also deviate from the reaction path, and Professor W. H. Miller for sending us his preprint[28] prior to publication. B.H. also thanks the Studienstiftung des deutschen Volkes for a scholarship. Generous financial support by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie is gratefully acknowledged. The computations were carried out on the Siemens 7.860L Fujitsu computer of the Rechenzentrum der Universität Würzburg.

Registry No. F, 14762-94-8; HBr, 10035-10-6; D_2, 7782-39-0; muon, 12587-60-9.

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[28] (a) Arrowsmith, P.; Bartoszek, F. E.; Bly, S. H. P.; Carrington, T., Jr.; Carters, P. E.; Polanyi, J. C. *J. Chem. Phys.* **1980**, *73*, 5895. (b) Hering, P.; Brooks, P. R.; Curl, R. F., Jr.; Judson, R. S.; Lowe, R. S. *Phys. Rev. Lett.* **1980**, *44*, 687. (c) Jouvet, C.; Soep, B. *Chem. Phys. Lett.* **1983**, *96*, 426. (d) Maguire, T. C.; Brooks, P. R.; Curl, R. F.; Spence, J. H.; Ulvick, S. J. *J. Chem. Phys.* **1986**, *85*, 844.

[29] (a) Valtazanos, P.; Ruedenberg, K. *Theor. Chim. Acta* **1986**, *69*, 281. (b) Kraus, W. A.; DePristo, A. E. *Theor. Chim. Acta* **1986**, *69*, 309. (c) Basilevsky, M. V. *Theor. Chim. Acta* **1987**, *72*, 63. (d) Ruedenberg, K., private communication, 1987.

The Coordination of Bare Fe^+ to Aliphatic Isonitriles Differs from that of Fe^+ and Nitriles[†]

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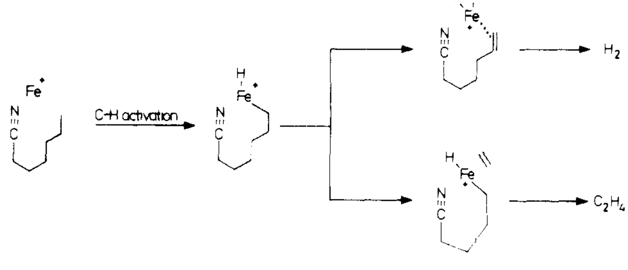
Contribution from the Institut für Organische Chemie der Technischen Universität Berlin, Strasse des 17. Juni 135, D-1000 Berlin 12, Federal Republic of Germany. *Received August 24, 1987*

Abstract: Circumstantial evidence is presented which suggests that both *side-on* and *end-on* complexes are formed in the reactions of aliphatic, unbranched isonitriles RNC (R = C_2H_5–n-C_6H_{13}) with Fe^+ in the gas phase. Depending on the chain length of the alkyl groups, two distinct processes are observed for either complexes upon collisional activation. One corresponds to oxidative addition of CH/CC bonds in the vicinity of the functional group to eventually cleave the R–NC bond (R = alkyl). This reaction, which is not observed for isomeric RCN/Fe^+ complexes, dominates for R = C_2H_5–C_4H_9 and is caused by a *side-on* complexation of the RNC triple bond. For isonitriles with R = C_5H_{11} and C_6H_{13}, this process is still operative; the major reaction, however, corresponds to H_2 loss which is shown to involve functionalization of remote CH bonds, as has been demonstrated earlier for RCN/M^+ complexes (M = Fe, Co, Ni). The experimental data further suggest that the binding energy of *side-on* complexes is larger for RNC/Fe^+ than for RCN/Fe^+. Metal ion induced isomerization of the type RNC → RCN does not seem to occur in the gas phase.

The comparison of the behavior between nitriles (RCN) and isonitriles (RNC) and their role in synthetis[1a] is of fundamental interest in both organic and organometallic chemistry.[1] While the two types of molecules behave similarly in many respects, they differ in others as, for example, in the direction of the dipole moment and, as will be shown in this communication, in their reaction with bare transition metal ions in the gas phase. Recent work has provided evidence that metal ions M^+ (M = Fe,[2-4] Co,[3,4] and Ni[4]) coordinate in the gas phase through the lone-pair electrons of the nitrogen atom of the nitrile resulting in an *end-on* complexation.[5] By using mass spectrometric techniques this type of complexation is reflected in highly site-specific, collision-induced[6] dissociation processes of these complexes which show that

Scheme I



[†] Dedicated to Professor U. Schöllkopf, Göttingen, on the occasion of his 60th birthday.

0002-7863/88/1510-3068$01.50/0

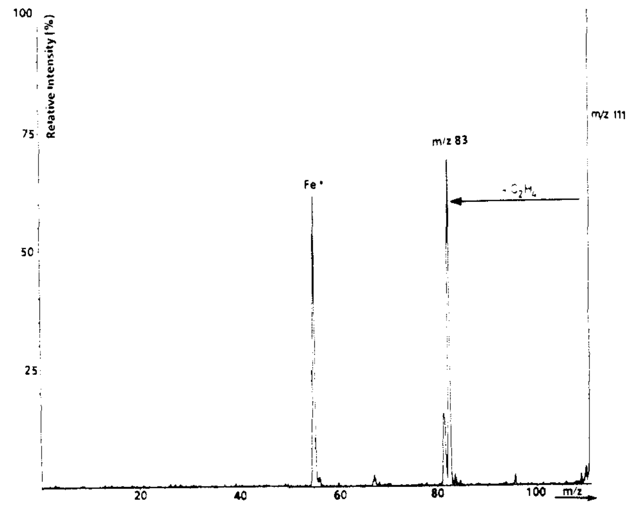


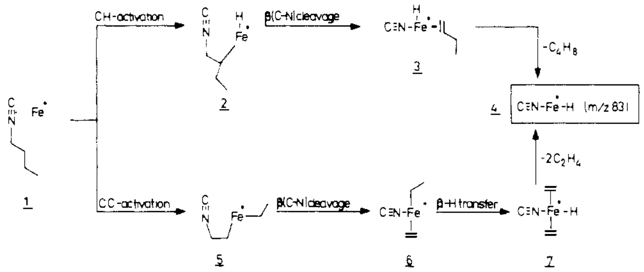
Figure 1. Collision-induced dissociation of CH_3CH_2NC/Fe^+.

Table I. Collision-Induced Dissociations of RNC/Fe^+ Complexes

	RNC, R =				
ionic fragments[a]	C_2H_5	n-C_3H_7	n-C_4H_9	n-C_5H_{11}	n-C_6H_{13}
Fe^+	42	23	14	7	3
m/z 83 $(Fe/HCN)^+$	48	72	61	15	9
$[RNC/Fe - H_2]^+$			15	73	83
other ionic fragments	<10	<5	<10	<5	<5

[a] Intensities are expressed in % Σ fragments = 100%.

Scheme II



a CH bond of the (terminal) methyl group is oxidatively added to the complexed metal ion as depicted in Scheme I for M = Fe. The CH activation is then completed by reductive elimination of either H_2 or C_2H_4 from the ω and $(\omega - 1)$ positions of the alkyl chain. CH bonds in the vicinity of the functional group are not activated. If the alkyl chain length is too short (less than C_4) to allow oxidative addition of the terminal CH bond, the only reaction observed corresponds to ligand detachment, i.e., formation of RCN and bare M^+.

In this report we describe the reactions of RNC/Fe^+ complexes (R = C_2H_5–n-C_6H_{13}), which are distinct from those of the analogous RCN/Fe^+ system. In addition to terminal CH activation for isonitriles with longer alkyl chains, CH and CC bonds in the vicinity of the isonitrile group are involved in the gas-phase chemistry, and the results indicate that *side-on* coordinated species may serve as the reactive intermediates.[7]

Experimental Section

Fe^+ was generated in a FAB[8] source of a Vacuum Generators (VG) ZAB-HF-3F triple sector mass spectrometer of BEB configuration (B stands for magnetic and E for electric sector)[9] by bombarding $FeSO_4$, dissolved in water, with 8-keV xenon atoms, using a procedure originally developed by Campana et al.[10] The sputtered Fe^+ (or species of complex, unknown composition) was then reacted with isonitriles, RNC (pressure ca. 10^{-3} torr);[11] the resulting complex (RNC/Fe^+) was accelerated to 8-keV kinetic energy, mass selected by using BE, and collided in a collision cell with He (pressure ca. 10^{-5} torr) to induce fragmentation.[6] Spectra were recorded by scanning the second magnet and accumulated by using the VG 11/250 data system. Organometallic complexes RCN/M^+ (M = Fe, Co, Ni) formed via FAB have been shown[4,12] to produce results practically identical with those for complexes formed through ion/molecule reactions of neutral organic substrates with, for example, $Fe(CO)_x^+$ (x = 1, 2), generated via electron impact ionization of $Fe(CO)_5$. In the present case we observe that the collisional activation spectra of RNC/Fe^+ are practically indistinguishable for both modes of complex generation. The isonitriles were either commercially available (butyl isonitrile) or were synthesized using established procedures.[13] D-Labeled isotopomers were obtained by standard laboratory methods; they were purified by gas chromatography and fully characterized by NMR spectroscopy and mass spectrometry.

Results and Discussion

The difference in the collision-induced reactivity between complexes of Fe^+ with RCN and RNC can already be observed with ethyl isocyanide (R = C_2H_5) (Figure 1). Collision-induced fragmentation of the CH_3CH_2NC/Fe^+ complex yields products which corresponds to the loss of C_2H_4 to generate m/z 83, elimination of $C_2H_5^{\bullet}$ to form m/z 82, and a ligand detachment reaction to produce Fe^+. The corresponding nitrile complex, CH_3CH_2CN/Fe^+, does not produce fragment ions other than the loss of the ligand upon collisional activation.[2-4] Furthermore, the loss of H_2 which always accompanies loss of C_2H_4 in the RCN/Fe^+ system (Scheme I) is, interestingly, absent at least for CH_3CH_2NC/Fe^+.

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(1) For typical examples, see: (a) Schöllkopf, U. *Pure Appl. Chem.* **1979**, *51*, 1347. (b) Patai, S. Ed. *The Chemistry of Functional Groups*: Wiley Interscience: New York, 1970; 853–884. (c) Meier, M.; Müller, B.; Rüchardt, C. *J. Org. Chem.* **1987**, *52*, 648. (d) Friend, C. M.; Stein, J.; Muetterties, E. L. *J. Am. Chem. Soc.* **1981**, *103*, 767.

(2) Lebrilla, C. B.; Schulze, C.; Schwarz, H. *J. Am. Chem. Soc.* **1987**, *109*, 98.

(3) Lebrilla, C. B.; Drewello, T.; Schwarz, H. *J. Am. Chem. Soc.* **1987**, *109*, 5639.

(4) Lebrilla, C. B.; Drewello, T.; Schwarz, H. *Int. J. Mass Spectrom. Ion. Processes* **1987**, *79*, 287.

(5) There exist a few experimental studies which deal with the coordination of nitriles to metals. For references, see: (a) Andrews, M. A.; Knobler, C. B.; Kaesz, H. D. *J. Am. Chem. Soc.* **1979**, *101*, 7260. (b) Wexler, R. M.; Muetterties, E. L. *J. Phys. Chem.* **1984**, *88*, 4037. (c) Jacobson, D. B.; Freiser, B. S. *J. Am. Chem. Soc.* **1984**, *106*, 4623. (d) Fewer yet are theoretical calculations dealing with this subject. One such investigation which, however, deals only with the HCN ligand and which is based on concepts of qualitative MO theory may be found in: Howell, J. A. S.; Saillard, J. Y.; LeBenze, A.; Jaouen, G. *J. Chem. Soc., Dalton Trans.* **1982**, 2533.

(6) For leading references, see: Levsen, K.; Schwarz, H. *Mass Spectrom. Rev.* **1983**, *2*, 77.

(7) Very recently it was demonstrated that the collision-induced reactions of RCN/Cu^+ complexes may also be explained in terms of *side-on* coordinated intermediates: Lebrilla, C. B.; Drewello, T.; Schwarz, H. *Organometallics* **1987**, *6*, 2450.

(8) FAB stands for fast atom bombardment. For leading references, see: Barber, M.; Bordoli, R. S.; Elliott, G. J.; Sedgwick, R. D.; Tyler, A. N. *Anal. Chem.* **1982**, *54*, 6451.

(9) For a description of the machine, see: (a) Weiske, T. Ph.D. Thesis, Technical University Berlin, D. 83, 1985. (b) Terlouw, J. K.; Weiske, T.; Schwarz, H.; Holmes, J. L. *Org. Mass Spectrom.* **1986**, *21*, 665. (c) Schulze, C.; Schwarz, H.; Paeke, D. A.; Gross, M. L. *J. Am. Chem. Soc.* **1987**, *109*, 2368.

(10) (a) Freas, R. B.; Ross, M. M.; Campana, J. E. *J. Am. Chem. Soc.* **1985**, *107*, 6195. (b) Freas, R. B.; Campana, J. E. *Ibid.* **1985**, *107*, 6202.

(11) It should be mentioned that the detailed mechanism by which the RNC/Fe^+ complexes are formed is open to speculation. The pressure in the ion source is, however, high enough to collisionally stabilize the complex by multiple collisions.

(12) (a) Drewello, T.; Eckart, K.; Lebrilla, C. B.; Schwarz, H. *Int. J. Mass Spectrom. Ion Processes* **1987**, 76, R1. (b) Schulze, C.; Schwarz, H. *J. Am. Chem. Soc.* **1987**, *10*, 67.

(13) (a) Weber, W. P.; Gokel, G. W..; Ugi, I. K. *Angew. Chem.* **1972**, *84*, 587. (b) Weber, W. P.; Gokel, G. W. *Tetrahedron Lett.* **1972**, 1637.

When the chain length of the isonitrile is increased (Table I), one observes that the C_2H_4 loss is not really the consistent product formed from all RNC/Fe^+ complexes, as is the case with RCN/Fe^+; rather it is the production of *m/z* 83, an $[Fe/HCN]^+$ ion.[14] The presence of this species clearly indicates that the interaction of the "complexed" Fe^+ does not involve remote CH/CC bonds of the alkyl chain but rather prefers cleavage of the R–NC single bond, and for R = C_2H_5, *n*-C_3H_7, and *n*-C_4H_9 this process gives rise to the base peak in the spectrum. This cleavage is geometrically impossible with an *end-on* coordinated RNC/Fe^+ complex; such an intermediate would be expected to behave similarly to the well-studied RCN/Fe^+ system (Scheme I). Which alternatives are chemically feasible? It is tempting to explain the cleavage of the R–NC bond by Fe^+ in the same way as has been done in the gas-phase chemistry of alkali metal ions and ketones, i.e., "dissociative attachment"[15] whereby the metal ion associates with a functional group and causes the organic substrate to rearrange and/or cleave. To investigate this possibility the corresponding RNC/Na^+ complexes were produced and subjected to the same conditions as the analogous RNC/Fe^+ species. However, the major reaction for all RNC/Na^+ complexes corresponds to ligand detachment. Signals due to the formation of $(Na/CN)^+$ or $(Na/HCN)_+$ were practically absent. Thus, it is implied that dissociative attachment can be ruled out as a major mechanism for Fe^+-induced cleavage of the R–NC bond. The second alternative ascribes the formation of the *m/z* 83 ion to the intermediate generation of a *side-on* bonded RNC/Fe^+ complex, as has been done[7] for the RCN/Cu^+ system. In fact, the collisional activation spectrum of the latter also contains abundant signals due to cleavage of the R–CN bond and the generation of $(Cu, H, C, N)^+$ species of unknown structure.

A simple mechanism may be invoked to account for the formation of *m/z* 83. This involves *side-on* coordination of the isonitrile group followed by CH activation of the β hydrogens and terminated by reductive elimination of an olefin to generate *m/z* 83 (Scheme II: **1** → **2** → **3** → **4**). This suggestion was tested by generating the complexes of Fe^+ with the labeled nitriles **1a** ($CH_3(CH_2)_2CD_2NC$), **1b** ($CH_3CH_2CD_2CH_2NC$), and **1c** ($CD_3(CH_2)_3NC$), respectively. If only the sequence **1** → **2** → **3** → **4** were operative, one should observe a quantitative shift from the *m/z* 83 to the *m/z* 84 fragment ion for **1b**–Fe^+, and *no* shifts for **1a**–Fe^+ and **1c**–Fe^+. This is not the case. The hydrogen transferred from the alkyl chain of **1b** to the $(Fe/CN)^+$ fragment originates to roughly 30% from the β-methylene group; 70% is provided by other CH bonds. Similarly, in the spectrum of **1c**–Fe^+ *m/z* 83 and 84 are formed in a ratio of ca. 7:1, and the α-methylene group also participates in the hydrogen transfer reactions (*m/z* 83 versus *m/z* 84 ca. 6:1). These findings suggest that other mechanisms are operative, perhaps similar to the one proposed[16] for the reaction of metal ions (like Ni^+) with *n*-alkanes, i.e., CC insertion precedes activation of CH bonds (for example, Scheme II: **1** → **5** → **6** → **7**).

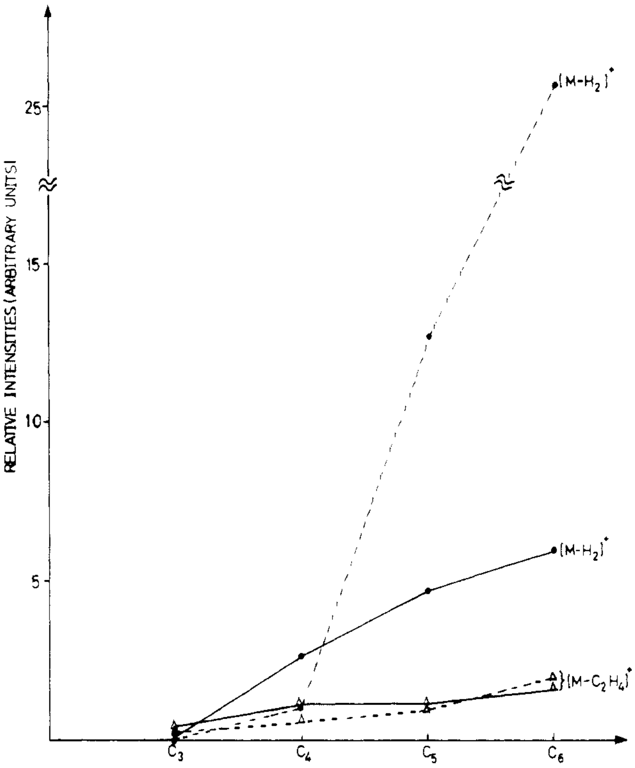

Figure 2. Relative intensities (in arbitrary units) for collision-induced losses of H_2 (●) and C_2H_4 (△) from RCN/Fe^+ (—) and RNC/Fe^+ (---) as a function of the chain length (carbon numbers given do not include the CN carbon atom).

As stated in ref. 14, proposed structures are fictitious; thus it could well be that the CN ligand of species **3**, **4**, **6**, and **7** contains a (NC–Fe) rather than a (CN–Fe) bond. Similarly, there are additional pathways conceivable for the rearrangement **5** → **7**. Note, however, that at some stages the reactions must be reversible in order to account for the labeling data of **1a** and **1c**.

An interesting feature of the spectra reported in Table I is the appearance of H_2 loss as the alkyl chain is lengthened. The reaction is absent for the ethyl and propyl isonitriles; it begins with R = C_4H_9 and corresponds to the most prominent reaction for $C_6H_{13}NC$. The chain length dependence of H_2 production is consistent with the idea that terminal positions are involved in this reaction, perhaps analogous to Scheme I for the RCN/Fe^+ system. This suggestion is supported by the study of the Fe^+ complexes with **1a**, **1b**, and **1c**. From **1a**–Fe^+ and **1b**–Fe^+ exclusively H_2 is eliminated, while **1c**–Fe^+ (which contains a CD_3CH_2 unit at the terminus of the alkyl chain) generates predominantly HD. Terminal CH activation, however, is the hallmark of an *end-on* complexed system! Thus, it appears that for isonitriles (in contrast to nitriles) *both* types of coordination of Fe^+ are present. Upon collisional activation, the *side-on* complex dominates the chemistry of RNC/Fe^+ species containing *shorter alkyl groups*; from the *end-on* complex, if formed at all, upon collisional activation only ligand detachment may occur. On the other hand, for RNC/Fe^+ complexes with longer alkyl chains it is the *end-on* intermediate which upon collision leads to the most prominent reaction products (i.e., H_2 loss). This dichotomy of a functional group is, to the best of our knowledge, unprecedented in the reactivity of organometallic complexes in the gas phase.

Finally, it may be appropriate to speculate on the very distinct behavior of short-chain RCN/Fe^+ versus RNC/Fe^+ systems. The former undergo exclusively ligand detachment while the latter, in addition to this reaction, give rise to the formation of *m/z* 83. The genesis of this ion has been explained (Scheme II) in form of a *side-on* complexed isonitrile. It is quite possible that *side-on* complexation, to some extent, also occurs for the RCN/Fe^+ system. If the binding energy for this complex is too small,

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[14] For *m/z* 83, which has the elemental composition (Fe, H, C, N), there exist several structural possibilities as, for example, $HCN-Fe^+$, $HNC-Fe^+$, $H-Fe^+-NC$, $H-Fe^+-CN$, etc. Without detailed spectroscopic studies and state-of-the-art high-level ab initio MO calculations, *none* of the proposed structures are proven. In fact, in nearly all cases studied in mass spectrometry (including the present one), the suggested structures are hypothetical as they are based on plausible considerations using as much direct and indirect "evidence" as available from experiments and model considerations. Nevertheless, the heuristic merits of such structural assignments are undeniable in chemistry. For the generation of $M(CNH)^+$ species (M = Ag, Cu) in secondary ion mass spectrometry of isocyanide complexes of Ag^+ and Cu^+, see: (a) Detter, L. D.; Pachuta, S. J.; Cooks, R. G.; Walton, R. A. *Talanta* **1986**, *33*, 917. (b) Dettler, L. D.; Cooks, R. G.; Walton, R. A. *Inorg. Chim. Acta* **1986**, *115*, 55.

[15] Burnier, R. C.; Byrd, G. D.; Freiser, B. S. *Anal. Chem.* **1980**, *52*, 1641.

[16] (a) Halle, L. F.; Houriet, R.; Kappes, M. M.; Staley, R. H.; Beauchamp, J. L. *J. Am. Chem. Soc.* **1982**, *104*, 6293. (b) Jacobson, D. B.; Freiser, B. S. *Ibid.* **1983**, *105*, 736. (c) Houriet, R.; Halle, L. F.; Beauchamp, J. L. *Organometallics* **1983**, *2*, 1818. (d) Jacobson, D. B.; Freiser, B. S. *J. Am. Chem. Soc.* **1983**, *105*, 5197. (e) Hanratty, M. A.; Beauchamp, J. L.; Illies, A. J.; Bowers, M. T. *Ibid.* **1985**, *107*, 1788. (f) Hettich, R. L.; Jackson, T. C.; Stanko, E. M.; Freiser, B. S. *Ibid.* **1986**, *108*, 5086. (g) Tolbert, M. A.; Mandich, M. L.; Halle, L. F.; Beauchamp, J. L. *Ibid.* **1986**, *108*, 5675. (h) Hanratty, M. A.; Beauchamp, J. L.; Illies, A. J.; Koppen, P. v.; Bowers, M. T. *Ibid.* **1987**, *110*, 1.

collisional activation will result in ligand detachment rathter than oxidative addition of a CH or CC bond to the π-complexed Fe^+. If this hypothesis holds true, the observation of the m/z 83 ion from the RNC/Fe^+ system would then imply that the binding energy of a *side-on* complexed isonitrile to Fe^+ is larger than that of a nitrile function. Obviously, this tempting suggestion represents a challenge for theoretical chemistry.

A referee has raised the question whether the reactivity of RNC with Fe^+ may be due to an isomerization of the type RNC → RCN, a reaction which has been known for more than a century[17] and which indeed occurs under a variety of conditions.[18] In the present case this possibility can be ruled out on the following ground. The reactivity of $C_nH_{2n+1}CN/Fe^+$ complexes for alkyl nitriles with $3 \leq n \leq 6$ is such that *both* H_2 and C_2H_4 loss occurs upon collisional activation, presumably in competition from a common intermediate.[2,3] This is also borne out by the data shown in Figure 2. In contrast, the RNC/Fe^+ system behaves distinctly different in that with increasing chain length the loss of C_2H_4 does not any longer correspond to the elimination of H_2. It is the latter reaction which dominates the chemistry of the RNC/Fe^+ system while for the isomeric RCN/Fe^+ complexes elimination of both H_2 and C_2H_4 occurs.

Acknowledgment. Financial support of our work by the Deutsche Forschungsgemeinschaft, Fonds der Chemischen Industrie, Stiftung Volkswagenwerk, and Technische Universität Berlin, is gratefully acknowledged.

Registry No. C_2H_5CN, 624-79-3; n-C_3H_7CN, 627-36-1; n-C_4H_9CN, 2769-64-4; n-$C_5H_{11}CN$, 18971-59-0; n-$C_6H_{13}CN$, 15586-23-9; Fe^+, 14067-02-8.

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(17) Weith, W. *Ber. Dtsch. Chem. Ges.* **1873**, *6*, 210.

(18) Selected examples for isomerizations RNC → RCN in solution are described in ref 1c and for isomerization at metal surfaces in ref 1d; for gas-phase reactions, see: Fletcher, F. J.; Rabinovitch, B. S.; Watkins, K. W.; Locker, D. J. *J. Phys. Chem.* **1966**, *70*, 2823.

Models for Strong Interactions in Proteins and Enzymes. 1. Enhanced Acidities of Principal Biological Hydrogen Donors

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Abstract: The acid dissociation energies of several key biological hydrogen donors are found to fall into a narrow range, ΔH°_{acid} = 352–355 kcal/mol. The strong acidities of these donor groups enhance the hydrogen bond strengths involved in the protein α-helix, imidazole enzyme centers and DNA. Specifically, the peptide link is modeled by the dipeptide analogue CH_3CO-Ala-OCH_3. Its acidity is strengthened, i.e., ΔH°_{acid} is decreased by 8 kcal/mol compared with other amides, due to electrostatic stabilization by the second carbonyl in the peptide $-CON^-CH(CH_3)CO-$ grouping. The acidity of imidazole is also strengthened by 8 kcal/mol compared with that of the parent molecule, pyrrole, primarily due to resonance stabilization of the ion. Hydrogen donor NH_2 groups of adenine and cytosine are modeled by 4-aminopyrimidine, and the acidity of this amine group is strengthened by ring aza substitution. An intrinsic acidity optimized for hydrogen bonding strength therefore emerges as a common property of the diverse hydrogen donors in the protein α-helix, enzymes and DNA. This property may therefore be in part responsible for the natural selection of these molecules as principal biological hydrogen donors.

Hydrogen bonding plays a central role in the structures and energetics of biopolymers. For example, the α-helix structure of proteins involves hydrogen bonds where the amide NH function serves as a hydrogen donor. Hydrogen bonds in DNA and the interactions of imidazole in enzymes also involve NH·O and NH·N interactions. Zeeger-Huyskens demonstrated that a correlation exists between the strength of hydrogen bonds and the proton affinities of the components (in this case, the proton affinity of N^-, i.e., the acidity of NH).[1] The intrinsic NH acidities of biomolecules are therefore relevant to NH·O and NH·N hydrogen bonds that determine the α-helix structure of proteins and base pairing in DNA.

While the above interactions involve neutral molecules, hydrogen bonds involving ions are also relevant to biological systems. Intermediates in enzyme reactions go through ionic transition states. These transition states are stabilized by hydrogen bonding to polar groups in the environment.[2] The strengths of these ionic hydrogen bonds are in turn related to the acidity difference $\Delta\Delta H^\circ_{acid}$ of the components.[3-9] These interactions take place in protein interiors from which the solvent is partially or fully excluded and therefore can be modeled by gas-phase ionic complexes.

This and the following paper[3] will present gas-phase studies relevant to hydrogen bonding of biomolecules. The first paper will deal with intrinsic acidities, which are related to the hydrogen donor strengths in both neutral and ionic hydrogen bonds. The second paper will deal with the strength of ionic interactions of

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(1) Zeeger-Huyskens, T. *J. Mol. Struct.* **1986**, *135*, 93 (*THEOCHEM* **1986**, *28*, 93). Hydrogen bond strengths are shown to be inversely correlated to the difference in the proton affinities of the components. For cationic complexes $AH^+ \cdot B$, the relevant parameters are the relative PAs of the neutral, deprotonated species A and B. For neutral complexes AH·B, the relevant parameters are similarly the proton affinities of the deprotonated components, i.e., PA(B) and PA(A^-), where the latter is equal to ΔH°_{acid}(AH). For neutral hydrogen bonds, the correlation between PA(A^-) – PA(B) and ΔH°_D shows a slope of about 0.1.

(2) Warshel, A. *Acc. Chem. Res.* **1981**, *14*, 284.

(3) Meot-Ner (Mautner), M. *J. Am. Chem. Soc.*, following paper in this issue.

(4) Meot-Ner (Mautner), M. *J. Am. Chem. Soc.* **1984**, *106*, 1257.

(5) Larson, J. W.; McMahon, T. B. *J. Am. Chem. Soc.* **1983**, *101*, 2944.

(6) Meot-Ner (Mautner), M.; Sieck, L. W. *J. Phys. Chem.* **1985**, *89*, 5222.

(7) Yamdagni, R.; Kebarle, P. *J. Am. Chem. Soc.* **1971**, *93*, 7139.

(8) Caldwell, G.; Rozeboom, M. D.; Kiplinger, J. P.; Bartmess, J. E. *J. Am. Chem. Soc.* **1984**, *106*, 4660.

(9) Meot-Ner (Mautner), M.; Sieck, L. W. *J. Am. Chem. Soc.* **1984**, *106*, 4660.