111. Site-Selectivity in the Fe^+-Mediated C–H/C–C Bond Activation of Aldimines

Short Communication

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Dedicated to Prof. *Gerhard Spiteller* on the occasion of his 60th birthday

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It is demonstrated for the first time that the site-selectivity for the Fe^+-mediated C–H bond activation of aldimines $R^1N{=}CHR^2$ (R^1,R^2 = alkyl) involves the alkyl chain R^1 by a factor ≥ 12 in comparison to the alkenyl part R^2. This finding explains previous observations that dehydrogenation of intermediates formed by alkene loss from either R^1 or R^2 of $R^1N{=}CHR^2/Fe^+$ preferentially involves the alkyl part.

In a recent study [1], we demonstrated that the metastable ions of Fe^+ complexes of aldimines $R^1N{=}CHR^2$ exhibit a unique behavior in that the sequential loss of olefin/H_2 in the gas phase follows *two* distinct pathways: one corresponds to the remarkable pattern [2] of successive C–H/C–C bond activation [3] involving either alkyl chain R^1 and R^2 (*Scheme 1:* **1**-$Fe^+ \rightarrow$ **2** $\rightarrow$ **3**-$Fe^+ \rightarrow$ **4**). The seemingly less complicated path, proceeding directly from **2** to **5**, is of minor importance. Rather, **2** prefers to undergo reductive elimination (**2**$\rightarrow$**3**-Fe^+), followed by C–H bond activation of the *alkyl* chain of **3**. This mode of selective functionalization of two different segments of flexible molecules is without precedent in traditional organic and organometallic chemistry. A variant of consecutive elimination of olefin/H_2[1]) was encountered by the study of the Fe^+ complex of **6**. Based on labeling studies [1] [4], evidence was presented that the consecutive elimination of C_2H_4/H_2 from **6**-Fe^+ involves exclusively the C_6H_{13} part of the substrate; the olefin originates from the $\omega/(\omega - 1)$ positions. The formal Bu chain formed in the course of olefin detachment serves as a source for the generation of H_2 (*Scheme 1:* **6**-$Fe^+ \rightarrow$ **7** $\rightarrow$ **4**). Isomerization of **7** to generate – *via* **3**-Fe^+ – eventually **5**, followed by H_2 loss from the alkyl part was not observed.

This high site-selectivity for the reactions of the intermediates formed from **1** and **6** is, at first sight, at variance with the results from extensive studies in which the chain lengths of R^1 and R^2 in the two aldimines **I** and **II** were systematically varied [1] [4].

$R^1N{=}CHC_2H_5$ $\qquad$ $C_3H_7N{=}CHR^2$

I $R^1 = C_3H_7$–C_6H_{13} $\qquad$ **II** $R^2 = C_2H_5$–C_5H_{11}

[1]) Extensive MS/MS experiments together with studies of chain-length effects and employing labeled precursors demonstrate that the reverse sequence, *i.e.* loss of H_2 followed by elimination of C_nH_{2n} does not take place [4].

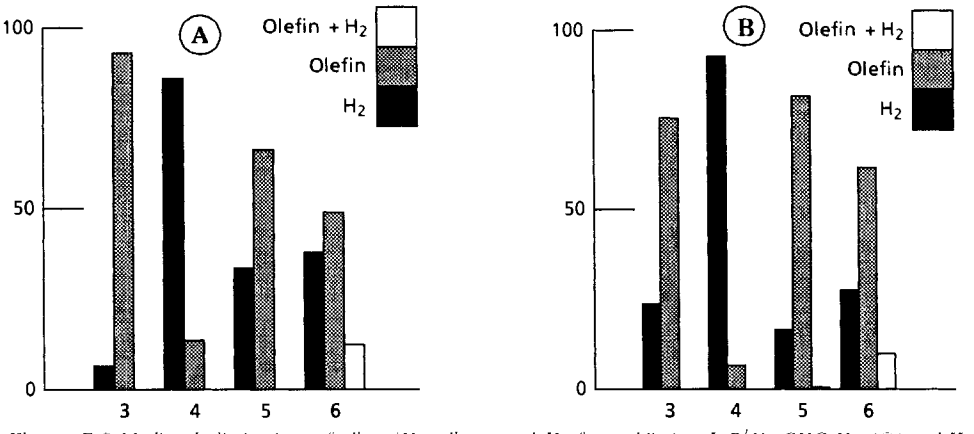
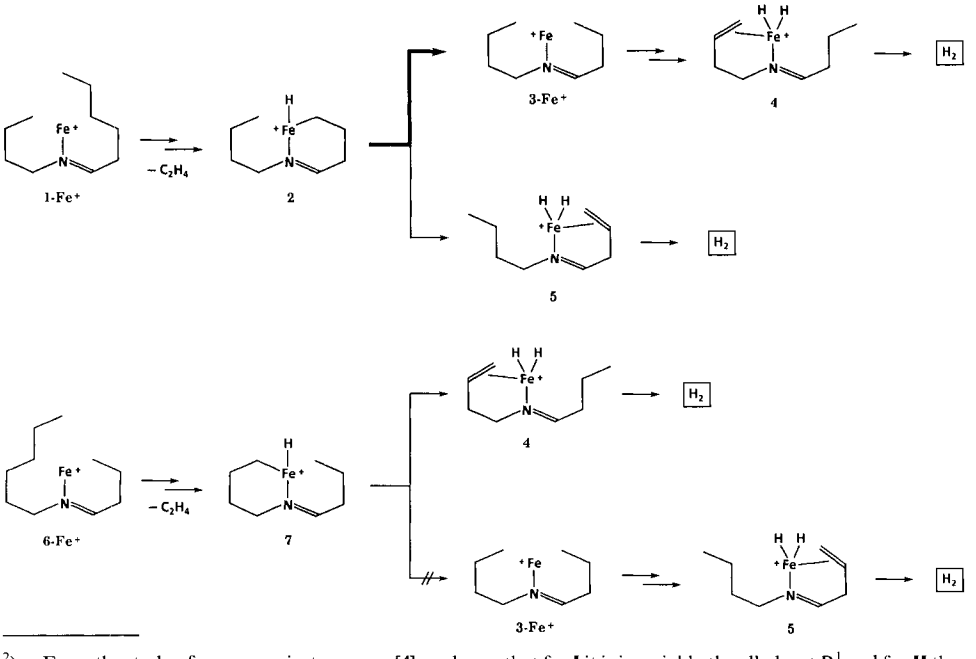


Figure. *Fe⁺-Mediated eliminations of alkene/H_2, alkene, and H_2 from aldimines* **I** *$R^1N{=}CHC_2H_5$,* (Ⓐ) *and* **II** *$C_3H_7N{=}CHR^2$* (Ⓑ), *as a function of chain length.* Note, that, for comparison purposes in **II**, the vinylic C-atom is included as part of the chain length.

According to the *Figure*[2]), one is tempted to conclude that C–H/C–C bond activation of both the alkyl (*Fig., A*) and alkenyl sites (*Fig., B*) occurs with the same ease; obviously, this interpretation is not in line with the findings described in *Scheme 1*.

Scheme 1



[2]) From the study of numerous isotopomers [4], we know that for **I** it is invariably the alkyl rest R^1 and for **II** the alkenyl site R^2 which is involved in the C–H/C–C bond activation. In addition, the preferred directionality for the insertion of the metal ion is such that six-membered metallacyclic intermediates are formed.

To resolve this discrepancy, we have studied[3]) the Fe^+-mediated dehydrogenation of substrate $C_4H_9N{=}CHC_3H_7$ (**3**) and its isotopomers $C_4H_9N{=}CH(CH_2)_2CD_3$ (**3a**) and $CD_3(CH_2)_3N{=}CHC_3H_7$ (**3b**). The results are given in the *Table*.

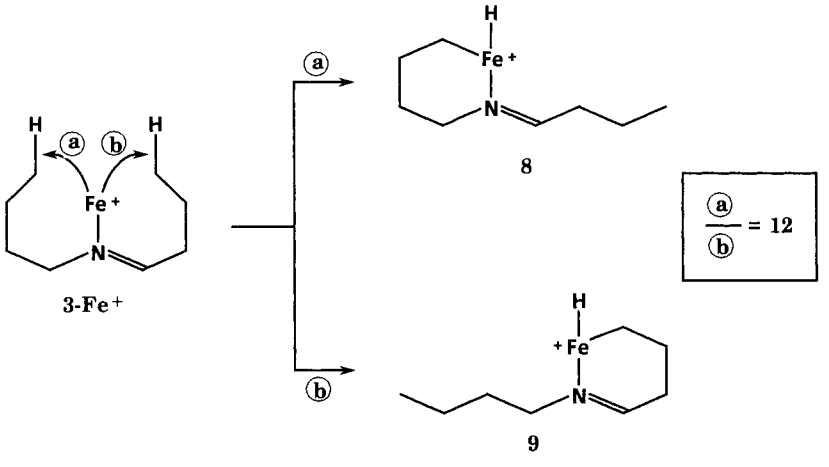
Table. *Isotopomer Distribution for the Losses of H_2 and HD from the Fe^+ Complexes of* **3**, **3a**, *and* **3b**[a])

Precursor		H_2	HD
$C_4H_9N{=}CHC_3H_7$	**3**	100	–
$C_4H_9N{=}CH(CH_2)_2CD_3$	**3a**	96	4
$CD_3(CH_2)_3N{=}CHC_3H_7$	**3b**	14	86

[a]) Data are expressed in $\Sigma H_2/HD = 100\%$.

From this data, by using a procedure similar to the one described by *Gelb et al.* [7] for the calculation of site selectivities and isotope effects in enzymatic functionalization of C–H bonds, we arrive at the following conclusions[4]). *i*) The overall kinetic isotope effect k_{H_2}/k_{HD} for the reductive elimination of H_2 corresponds to 1.97. *ii*) The site-selectivity Q, defined as the ratio for the contribution of the alkyl *vs.* alkenyl part of **3** (*Scheme 2*), is

Scheme 2



[3]) The experimental set-up has been described repeatedly in earlier papers. Briefly, Fe^+ ions are generated by 100-eV electron-impact ionization of $[Fe(CO)_5]$. The ions were then reacted with the organic substrates in the ion source of our modified ZAB mass spectrometer, which is of *BEBE* configuration (*B* stands for magnetic and *E* for electric sector). The resulting complexes are accelerated to 8-keV kinetic energy and mass-selected by using $B(1)E(1)$; the unimolecular reactions (MI spectra) occurring in the field-free region between $E(1)$ and $B(2)$ were recorded by scanning $B(2)$. Signal-averaging techniques were used to increase the signal-to-noise-ratio. All compounds studied were synthesized and purified by standard laboratory procedures and characterized by spectroscopic techniques. In line with previous studies [5], we assume an (*E*)-configuration for the C=N bond of the aldimines. For a detailed description of the machine, see [6].

[4]) As the set of equations is underdetermined, in the present case one has to assume that the kinetic isotope effect for the activation of the $\omega/(\omega - 1)$ bonds of the left (alkyl) and right site (alkenyl) of **3** is identical. This assumption is not unreasonable.

determined to $Q = 12$; *i.e.* 92% of H_2 originates from the alkyl chain and only 8% from the CH_3CH_2 group of the alkenyl part.

The latter finding is in excellent agreement with the data summarized in *Scheme 1;* it clearly demonstrates that activation of C–H bonds of the alkyl chain is favored (**3**-$Fe^+ \rightarrow$ **8**). As to the discrepancy noted above, we do not think this to be real on the following grounds: the alkenyl part of aldimines is activated only, when no equivalent sites exist on the alkyl chain and *vice versa*. This, for example, applies, if R^1 is too short for forming strain-free metallacycles. If, however, the two chains permit the formation of, preferentially [4], six-membered metallacyclic intermediates, it is always the alkyl chain which is involved in the oxidative addition to the (complexed) metal ion. We assume that electronic effects are not likely to be involved, as the properties of the terminal C–H bonds to be activated are, to a first approximation, comparable for the alkyl and alkenyl chain. Rather, we think that the site-selectivity observed is due to two structural features which enforce each other: due to different hybridization of the C(α)-atoms of the alkyl and alkenyl chains, the C(β)/C(α)/N angle of the former is smaller than that of the latter (109° *vs.* 120°). In addition, the N=C–C unit is stiffer than the analogous N–C–C moiety towards deformation; consequently, the folding-back of the two chains, which is a necessary condition for the intramolecular insertion, is easier to achieve for the alkyl than the alkenyl chain.

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