Fe(I)-Mediated Regio- and Stereoselective C–C/C–H Bond Activation of Internal Methylene Groups of α,ω-Diphenylalkanes

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For three α,ω-diphenylalkanes the mechanistic details of the Fe^+-mediated activation of C–H and C–C bonds in the gas phase have been elucidated by isotopic labelling experiments. The unimolecular reactions, i.e. dehydrogenation of the alkane chain, formation of ethylene from internal methylene groups, and generation of toluene, proceed largely with high selectivity. Particularly interesting are the results for the dehydrogenation of the Fe^+ complex **3**-Fe^+ of 1,8-diphenyloctane which involves to 93% the internal methylene groups C-4/C-5. In addition, the study of the stereoisotopomers **3c–d** provides evidence for the operation of isotopically sensitive branching ("metabolic switching") in the reaction, and the analysis of the data suggests that the selectivity of the reaction is, most likely, due to a sandwich-type structure.

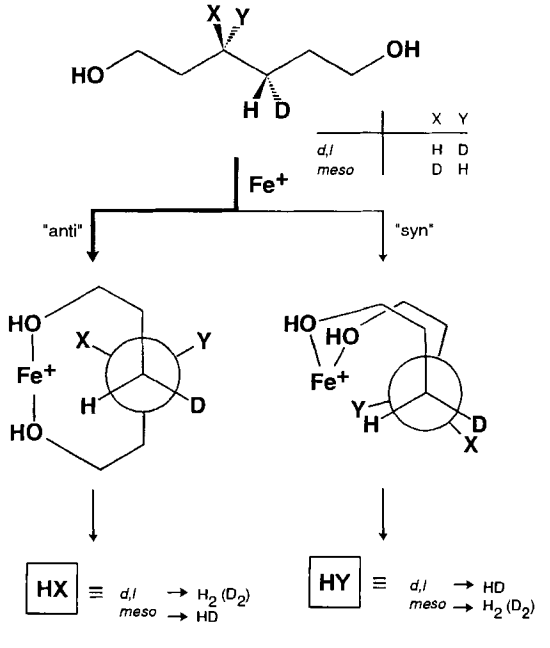
There is increasing evidence that multifunctional interactions govern the course of the intriguing gas-phase chemistry of "bare" transition-metal ions M^+ with organic molecules[1]. A few examples from our laboratory may suffice to illustrate this point:

(1) Cooperative effects of the two C=C bonds were invoked to explain the Fe^+-mediated, site-specific loss of C_2H_4 from the intact *internal* C-4/C-5 positions of 1,7-octadiene[2]. Similarly, the length of the spacer $[CH_2]_n$ determines to which extent a bare metal ion undergoes bidentate coordination to the C=C bond and the functional group X (X = Cl, Br, CN) in molecules $RCH{=}CH[CH_2]_nX$, and it is this interplay which determines the outcome and mechanisms of gas-phase C–H/C–C bond activations[3]. Also, chain-length effects were reported to dictate as to whether a retro-Fischer-Tropsch reaction takes place in the Fe^+ complexes of α,ω-dimethoxyalkanes[4], and the gas-phase behavior of α,ω-alkanedinitriles in their reactions with Fe^+ was found to be affected by the number of methylene units separating the two functional groups[5]. For example, in 1,8-dicyanooctane the Fe^+ is preferentially inserted in a C–H bond of the C-4/C-5-segment of the alkane chain, followed by a sequence of β-hydrogen transfer and reductive elimination of molecular hydrogen[5].

(2) A unique reactivity was recently observed[6] in the unimolecular chemistry of Fe^+ complexes of ω-silyl-substituted alkanenitriles. In contrast to the Fe^+ chemistry of the monofunctional carbon analogues[7], due to a metal-ion mediated cooperation of the $Si(CH_3)_3$ and the CN groups a double bond is regiospecifically formed next to the silyl group.

(3) The study[8] of the Fe^+ complexes of α,ω-alkanediols has significantly added not only to the general understanding of the principles underlying the regio- and stereoselectivity of C–H bond activation, more importantly, these detailed investigations also provided for the first time evidence for the operation of isotopically sensitive branching ("metabolic switching") – a concept well-known to exist in enzymatic processes[9] – in transition-metal-mediated gas-phase processes. For example, rigorous labelling experiments demonstrated that the dehydrogenation of the 1,6-hexanediol/Fe^+ complex in the gas phase involves specifically the central C-3/C-4 positions, and the study of the stereospecifically labelled *d,l*- and *meso*-[3,4-D_2] isotopomers of this complex revealed that dehydrogenation proceeds via two competing pathways, i.e. the "*anti*" versus "*syn*" routes in Scheme 1. The extent to which these channels contribute to the product formation is – due to a kinetic isotope effect – controlled by the relative configuration at the labelled positions C-3/C-4. While for the *d,l* form, the "*anti*" route is favored in a ratio 49:1, this ratio drops to 4.3:1 for the *meso* form.

Scheme 1



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This result is an immediate manifestation of an isotopically sensitive branching: for the *meso* form any conceivable intermediate formed via the otherwise favoured "*anti*" route will invariably lead to the generation of HD. Thus, due to a kinetic isotope effect, the system "bypasses" this channel and explores to a larger extent the alternative path, which is disfavored by a factor of only 4.3. The opposite situation holds true for the *d,l*-labelled isotopomer. Here, the "*anti*" route has the option to undergo either loss of H_2 and D_2 (favoring the former by a factor of 5.53). Consequently, the need to an isotopically enforced switch to populate the "*syn*" path is much less pronounced, and this path is indeed by a factor of 49 less favored than the former.

The unexpected dehydrogenation results obtained for the Fe^+ complexes of $X[CH_2]_nX$ (X = OH, CN) on the one hand together with the well-known propensity of transition metals to form with arenes sandwich complexes led us to speculate whether the gas-phase chemistry of the Fe^+ complexes of α,ω-diphenylalkanes $Ph[CH_2]_nPh$ will reflect chain-length-dependent interactions of the bare Fe^+ with the two phenyl groups. If so, as a consequence of the reduced conformational flexibility, one would expect for sandwich-type Fe^+ complexes both regio- and stereoselective C–H bond activation of internal CH_2 groups. As we will see, this conjecture is exactly born out in the experiment[10], and in this article the results pertinent to this topic will be described.

Results and Discussion

In Table 1 the data for the major products formed in the unimolecular dissociation [metastable-ion (MI) mass spectra] of the $Ph[CH_2]_nPh/Fe^+$ complexes are given. Here, we will confine ourselves to a discussion of a few principal aspects of the systems with n = 4, 6, and 8. A full account of the mass-spectral findings, including the whole series n = 1–8, is given in ref.[10]. To obtain precise information on the part of the organic substrate which is activated by the metal ion, the isotopomers listed in Scheme 2 have been synthesized and the MI mass spectra of their Fe^+ complexes recorded. This data is given in Tables 2 and 3.

Table 1. Major products in the MI mass spectra of the Fe^+ complexes of $Ph[CH_2]_nPh$[a]

$Ph[CH_2]_nPh$	n	Δm of neutral products 2 (H_2)	28 (C_2H_4)	92 (C_7H_8)
1	4	65	13	21
2	6	58	–	22
3	8	93	–	–

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

The unimolecular dissociation of the Fe^+ complex **1**-Fe^+ of 1,4-diphenylbutane exhibits three major reaction channels, i.e. dehydrogenation, losses of ethylene and of C_7H_8 (on energetic grounds C_7H_8 most likely corresponds to toluene). The labelling experiments reveal that dehydrogenation involves the benzylic and homobenzylic positions. While this process can be described in terms of a 1,2 elimination (Scheme 3: **1** → **4** → **5**), neither a 1,1 elimination nor the combined activation of the internal methylene groups C-2/C-3 are operative. Toluene (C_7H_8) is also produced specifically, in that cleavage of the C-1/C-2 bond is followed by a β-hydrogen transfer; the reaction sequence is terminated by reductive elemination of C_7H_8 from the Fe^+ complex **7** (Scheme 3). As indicated by the data in Table 2, ethylene originates to 91% from the internal C-2/C-3 part of the C_4 chain of **1**, and it is likely that intermediate **6** serves as a branching point for the generation of C_2H_4 and C_7H_8. The labelling results further reveal that ethylene is formed to a minor extent (9%) from C-1/C-2, and the reaction may proceed via the sequence **1** → **9** → **10** (Scheme 3). We note that hydrogen-exchange processes are absent in all reactions described in Scheme 3. Thus, with regard to the generation of ethylene, the present system is another rare example for a metal-ion mediated *direct* C–C bond cleavage without prior C–H bond activation[12].

Table 2. Label distribution in the MI mass spectra of the Fe^+ complexes of the isotopomers of **1** and **2**[a]

	1a	**1b**	**2a**	**2b**	**2c**
H_2	–	–	17	5	94
HD	100	100	73	95	6
D_2	–	–	10	–	–
C_2H_4	–	95	–	–	–
$C_2H_2D_2$	9	5	–	–	–
C_2D_4	91	–	–	–	–
C_7H_8	–	–	–	88	–
C_7H_7D	100	–	100	12	–
$C_7H_6D_2$	–	100	–	–	100

[a] The intensities are for each group of neutrals normalized to Σ fragments = 100%.

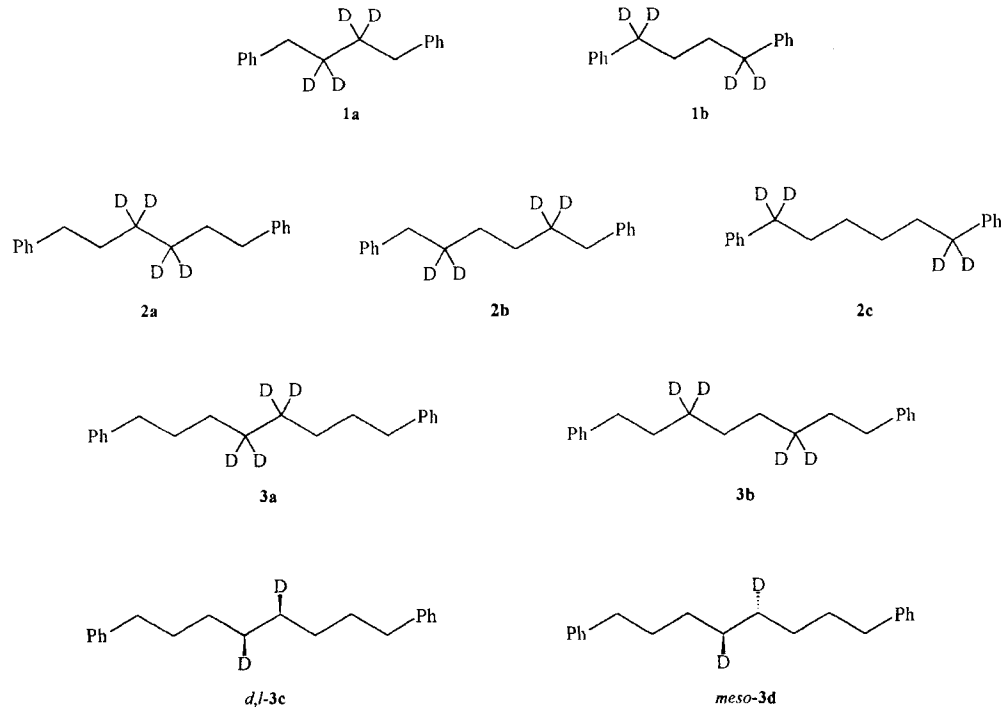
Table 3. Label distribution for the unimolecular dehydrogenation of the Fe^+ complexes of **3a–d**[a]

	3a	**3b**	**3c**	**3d**
H_2	8	97	63	34
HD	8	3	21	58
D_2	84	–	16	8

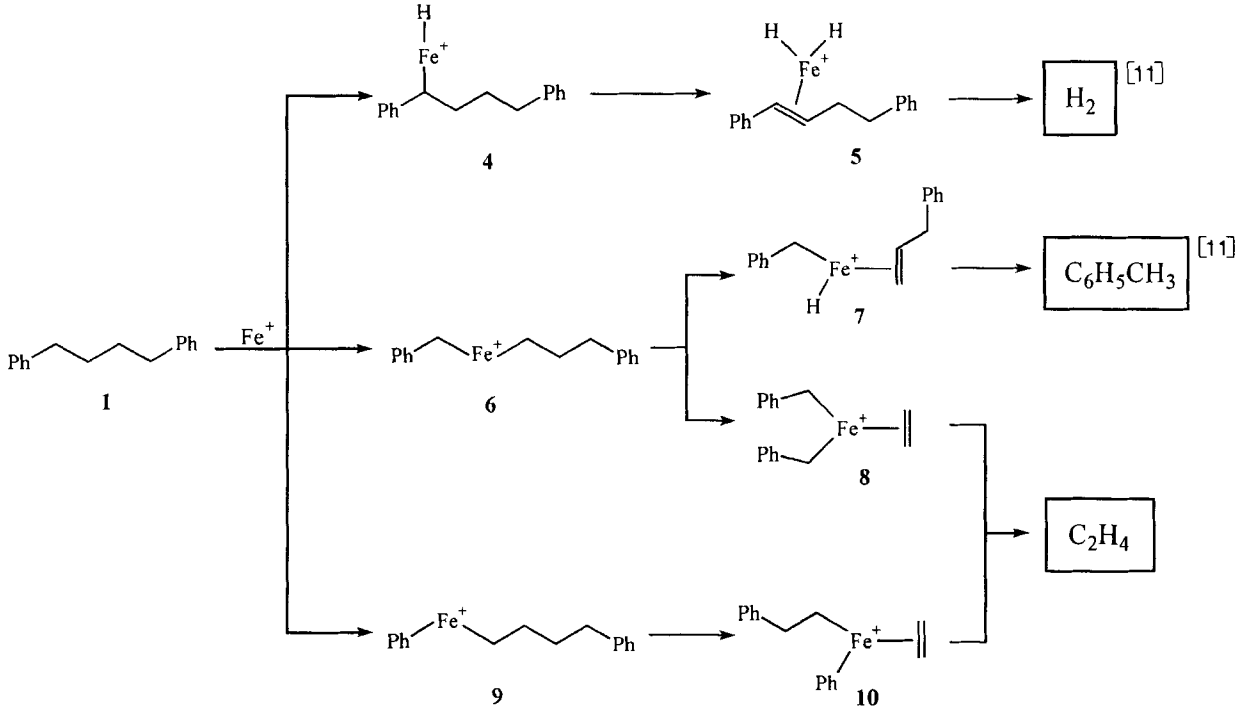
[a] Data are normalized to Σ $H_{2-x}D_x$ = 100%.

In the Fe^+ complex of 1,6-diphenylhexane (**2**), toluene is generated in a manner closely analogous to that of the lower homologue **1**-Fe^+. Most interesting is the observation that dehydrogenation no longer favors activation of the methylene groups C-1/C-2. If one corrects for symmetry factors and ignores for the sake of simplicity kinetic isotope effects associated with the β-hydrogen transfer and the reductive elimination of molecular hydrogen, the contribution of C-1/C-2 to the total dehydrogenation path does not exceed 10%. As indicated by the labelling data in Table 2, the interaction of the metal ion with the aliphatic C–H bonds is shifted to the more internal part of the hexane chain, and a comparison of **2a–c** suggests that the positions C-2/C-3 contribute to ca. 85%; the fact that from the central C-3/C-4 methylene groups of **2** only 5% of molecular hydrogen originates, indicates that this region is not easily accessible for the metal ion. With regard to exchange processes,

Scheme 2



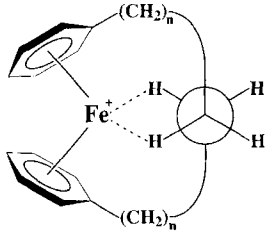
Scheme 3



the data for **2b–c** demonstrate that hydrogen scrambling is not involved in the Fe^+-mediated C–H bond activation of 1,6-diphenylhexane.

An entirely new scenario in the gas-phase chemistry of α,ω-diphenylalkane-Fe^+ complexes is encountered for 1,8-diphenyloctane (**3**). The unimolecular dissociation of **3**-Fe^+ is dominated by the dehydrogenation of the complex (93%), with very minor processes due to loss of 2 H_2 (1%), C_7H_9 (2%), C_9H_{12} (3%), and $C_{10}H_{14}$ (1%). The analysis of the isotopomers **3a–d** (Table 3) demonstrates that the centre of action involves the chemically inert, central part of the methylene chain, i.e. C-4/C-5; after correcting for symmetry factors, one can estimate that >92% of the total hydrogen originates from C-4/C-5. This observation clearly evidences the operation of a chelate effect such that the Fe^+ does not randomly attack various C–H bonds of the methylene

chain. Rather, the metal ion most likely first forms a sandwich complex with the two arene rings[13], thus preventing most of the alkane C–H bonds to interact with the metal ion. Crude model considerations indicate, however, that at least two conformations (**11** and **12**) are conceivable in which the central C-4/C-5 methylene groups are brought in the vicinity (<2.2 Å) of the metal ion thus permitting the oxidative insertion of Fe^+ in these aliphatic C–H bonds. This idea gains further support by the analysis of the *d,l* and *meso* stereoisomers **3c–d**. As has been outlined earlier in great detail for the Fe^+ complexes of 1,6- and 1,8-alkanediols[8], the effects observed for the Fe^+ complexes of **3c–d** can also be explained in terms of Scheme 1, and if we apply a similar analysis to the 1,8-diphenyloctane system, the data in Table 3 allow an estimate for the contribution of the "*anti*" versus "*syn*" paths to the dehydrogenation of **3**-Fe^+[14]. For the *d,l* form **3c** the "*anti*" route (proceeding via a conformer similar to **11**) is favored by a factor of ca. 3.8. Due to the operation of a kinetic isotope effect, for the *meso* form **3d** the branching ratio "*anti*" versus "*syn*" is reduced to 1.4. Molecular modeling work is in progress aimed at substantiating our experimental findings.



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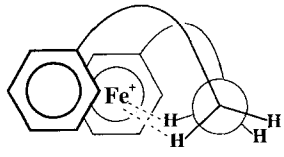

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The results reported here demonstrate that cooperative effects of functional groups are by no means confined to "classical" substituents, e.g. OH, CN, or $Si(Me)_3$; rather – provided the chain length, separating the phenyl rings, permits the formation of energetically accessible conformations – a "bare" metal ion may be complexed to generate, in the gas phase, sandwich-like structures. These π complexes in turn determine in which region of the otherwise flexible alkyl chain the metal ion is oxidatively inserted.

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Experimental

The experimental setup has been described in earlier papers[2–8]. Briefly, a 1:5–10 mixture of $Fe(CO)_5$ and the organic substrate is bombarded with 100-eV electrons in the chemical ionization source (repeller voltage ca. 0 V) of a modified ZAB mass spectrometer of *BEBE* geometry (*B* stands for magnetic and *E* for electric sector)[15]. Although the actual mechanism by which the complexes are formed is yet unknown, the pressure in the ion source is high enough to permit collisional cooling thus increasing the lifetime of the complexes FeL^+ (L = α,ω-diphenylalkane) such that time-delayed decomposition reactions after ca. 1 μs take place (metastable-ion dissociations). Organometallic complexes corresponding to FeL^+ having 8-keV kinetic energy are mass-selected and focussed with *B*(1)*E*(1) at a resolution $m/\Delta m$ sufficient to separate isobaric multiplets (typically $m/\Delta m$ = 3000–4000, 10% valley definition). Unimolecular reactions occurring in the field-free region between *E*(1) and *B*(2) were recorded by scanning *B*(2). Spectra were recorded on-line, and 10–20 spectra were accumulated by using signal-averaging techniques employing the AMD Intectra data system. It should be kept in mind that the neutrals formed from the organometallic complexes are not structurally characterized but inferred indirectly from the mass differences between mass-selected precursor and observed daughter ions. On energetic grounds there cannot possibly exist any doubt that the mass differences Δm = 2, 28, and 92 can safely be assigned to molecular hydrogen, ethylene and toluene, respectively. In addition, further support for this assignment is provided by the study of labelled isotopomers. – All compounds were synthesized by standard laboratory procedures, purified by gas-chromatographic means and fully characterized by NMR and MS. A schematic description for the synthesis of the stereoisotopomers **3c**, **d** of 1,8-diphenyloctane is given in Scheme 4.

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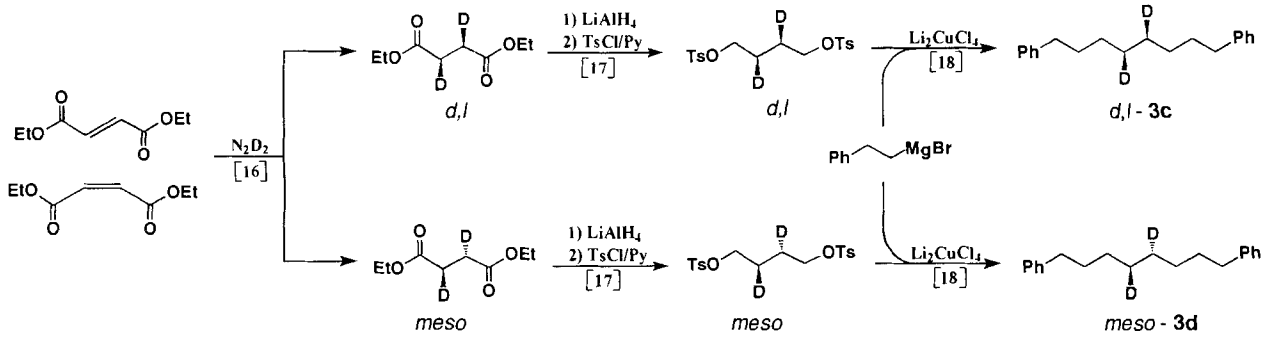
Scheme 4



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[10] N. Raabe, Diplomarbeit, Technische Universität Berlin, **1993**.

[11] Dehydrogenation of **3** can also commence with oxidative insertion of Fe^+ in the homobenzylic C–H bond followed by β-hydrogen transfer from C-1. Similarly, for the formation of **7** the sequence of C–C/C–H bond activation events can be reversed. A clear-cut distinction is not yet possible. Also, we have not determined the stereochemistry of the C=C bond of the intermediate **5**.

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[13] The gas-phase chemistry of Fe^+ complexes of 1-phenylalkanes does *not* exhibit the remarkable site-selectivity observed for **3**-Fe^+: O. Blum, P. O'Bannon, H. Schwarz, manuscript in preparation.

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