Geminal-Dialkyl-Effect-Controlled Site Selectivity of Fe(I)-Mediated C–H/C–C Bond Activation of Aliphatic Ketones

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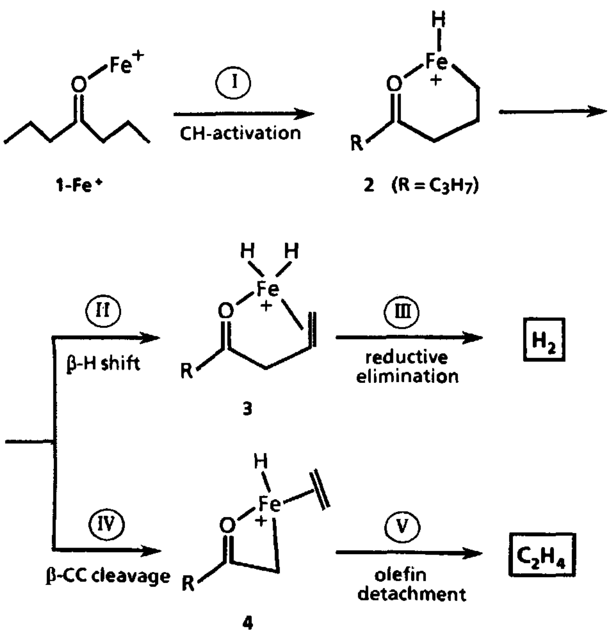
Depending on the internal energy content, due to the operation of a geminal dialkyl effect, the Fe^+-mediated dehydrogenation of α,α-dimethyl-substituted ketones preferably involves the more substituted alkyl chain.

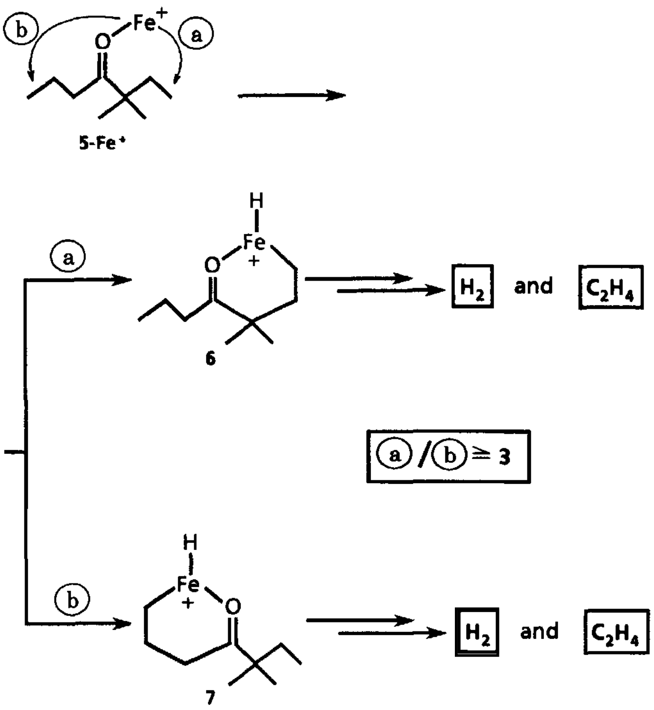
The rich gas-phase chemistry of transition-metal ions with aldehydes and ketones has recently been explored in several laboratories[1)]. Detailed studies[2)] revealed inter alia for Fe^+ complexes of many alkanones the operation of consecutive, remote C–H/C–C bond activation of different alkyl chains of the ketones, processes unprecedented in condensed-phase chemistry[3)]. In addition, from the investigation of isotopically labeled 4-heptanone/Fe^+ complexes (**1**-Fe^+), *intra*molecular isotope effects were determined. In this study[2)] it was demonstrated that the oxidatve addition of the (complexed) Fe^+ to a C–H bond (step I in Scheme 1) is not associated with a kinetic isotope effect. In contrast, for the generation of molecular hydrogen it is the reductive elimination (step III) that is subject to a sizable isotope effect (k_{H_2}/k_{HD} = 2.70). The β-hydrogen shift (II) is associated with a small isotope effect, k_H/k_D = 1.05. For ethylene loss from **1**-Fe^+, both the β-C–C cleavage (IV) and the olefin detachment (V) are subject to secondary isotope effects (k_H/k_D = 1.14 and $k_{C_2H_4}/k_{C_2H_2D_2}$ = 1.11, respectively).

Scheme 1



Since the formation of the cyclic intermediate **2** is mandatory for the generation of either H_2 and C_2H_4 from **1**-Fe^+, we wondered whether the geminal dialkyl effect[4)] (also known as Ingold-Thorpe effect[5)]) is operative in organometallic systems as well[6)]. To this end we compared the gas-phase chemistry[7)] of the Fe^+ complexes of 4-heptanone (**1**) with that of 3,3-dimethyl-4-heptanone (**5**) and its isotopomer **5a**.

Scheme 2



The interpretation of the data given in Table 1 is straightforward. Comparison of the data for the Fe^+-mediated dehydrogenation of **1a** (which is subject to an overall kinetic isotope effect k_{H_2}/k_{HD} = 2.70) with **5a** clearly reveals that the ratio for losses of H_2/HD from **5a**, which equals 9.38, is atypical if it were only to reflect the operation of kinetic isotope effects. In fact, in no single case of the

Table 1. Labeling distribution for the Fe^+-mediated formation of hydrogen, methane, and ethylene from 4-heptanone (**1**) and 3,3-dimethyl-4-heptanone (**5**) isotopomers[a,b]

Precursor		Δm							
		Hydrogen		Methane	Ethylene and ethylene/hydrogen				
		2	3	16	28	29	30	31	32
$C_3H_7C(O)C_3H_7$	(**1**)	80			20				
$CD_3[CH_2]_2C(O)C_3H_7$	(**1a**)	62.8	23.3		7.3		6.6		
$C_3H_7C(O)C(CH_3)_2C_2H_5$	(**5**)	80		1	17		2		
$CD_3[CH_2]_2C(O)C(CH_3)_2C_2H_5$	(**5a**)	75	8	1	11	<0.5	3	<1	1

[a] Intensities are given in Σneutrals = 100%. — [b] Data for **1** and **1a** are given for comparison; for the data of the complete set of isotopomers, see ref.[2].

transition-metal-ion-mediated dehydrogenation of numerous organic substrates studied, we ever observed $k_{H_2}/k_{HD} > 4$. Thus, we interpret the increased loss of H_2 from **5a** as a consequence of the existence of the geminal dialkyl effect. If we conservatively assume $k_{H_2}/k_{HD} \approx 3$ for **5a** (in analogy to **1a**), it follows that activation of the substituted propyl chain is favoured by a factor >3 (Scheme 2). The analysis of the data for ethylene loss arrives at a similar conclusion.

Further support for this interpretation is provided by studying the complexes of **5** (and **5a**) with $Fe(CO)^+$. This mass-selected complex first expels CO, and the resulting complex **5**-Fe^+ has an energy content lowered by the $(OC)-Fe^+$ binding energy; this has two implications: (i) In line with previous studies[1], the $Fe(ketone)^+$ complex is not capable to bring about C—C bond activation. (ii) The only process observed corresponds to dehydrogenation, and starting from **5a** H_2 and HD are generated in a 28:1 ratio. Again, if we assume an isotope effect $k_{H_2}/k_{HD} > 3$, we are left with a preference of activation of the more substituted alkyl chain (path a, Scheme 2) by a factor of 9. Obviously, the geminal dialkyl groups exert a pronounced effect on the ease by which metallacyclic intermediates are generated in the course of organometallic processes in the gas phase involving bare transition-metal ions.

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CAS Registry Numbers

$C_3H_7C(O)C_3H_7$: 123-19-3 / $C_3H_7C(O)C(CH_3)_2C_2H_5$: 55131-17-4 / Fe^+: 14067-02-8 / D_2: 7782-39-0

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[1] For extensive references, see: D. Schröder, K. Eller, T. Prüsse, H. Schwarz, *Organometallics*, in press.

[2] D. Schröder, H. Schwarz, *J. Am. Chem. Soc.* **112** (1990) 5947.

[3] For reviews on the concept of *remote functionalization*, both in solution[3a–c] and in the gas phase[3d–f], see: [3a] R. Breslow, *Chem. Soc. Rev.* **1** (1972) 553. — [3b] R. Breslow, *Acc. Chem. Res.* **13** (1980) 170. — [3c] R. Breslow, A. Adams, T. Guo, J. Hunger, *Lect. Heterocycl. Chem.* **9** (1987) 43. — [3d] H. Schwarz, *Acc. Chem. Res.* **22** (1989) 282. — [3e] K. Eller, H. Schwarz, *Chimia* **43** (1989) 371. — [3f] K. Eller, S. Karraß, H. Schwarz, *Ber. Bunsenges. Phys. Chem.* **94** (1990) 1201. — [3g] K. Eller, H. Schwarz, *Chem. Rev.*, in press.

[4] [4a] N. L. Allinger, V. Zalkov, *J. Org. Chem.* **25** (1960) 701. — [4b] E. L. Eliel, *Stereochemie der Kohlenwasserstoffverbindungen*, p. 242, Verlag Chemie, Weinheim 1966.

[5] [5a] R. M. Beesley, C. K. Ingold, J. F. Thorpe, *J. Chem. Soc.* **107** (1915) 1080. — [5b] C. K. Ingold, *J. Chem. Soc.* **119** (1921) 305.

[6] For a gas-phase analogue of the Ingold-Thorpe effect in the proton-catalyzed cyclization of *N*-benzoyl α-amino acid derivatives, see: G. Höfle, G. Höhne, J. Respondek, H. Schwarz, *Org. Mass Spectrom.* **12** (1977) 477.

[7] The experimental set-up has been described repeatedly in earlier papers[1,2]. A modified four-sector mass spectrometer with a $B(1)E(1)B(2)E(2)$ configuration was used for the measurements (for a description of the machine, see: R. Srinivas, D. Sülzle, T. Weiske, H. Schwarz, *Int. J. Mass Spectrom. Ion Processes*, in press). In a typical experiment, $Fe(CO)_5$ and the ketone of interest were introduced simultaneously by the gas inlet system into the chemical ionization source (repeller voltage 0 V) and bombarded with an electron beam of 100 eV. Organometallic ions corresponding to $Fe(ketone)^+$ having 8 keV kinetic energy are mass-selected at a resolution of 3000—5000 (10% valley definition) by using $B(1)E(2)$; B stands for magnetic and E for electrostatic sector. Unimolecular reactions occurring in the 3rd field-free region were recorded by scanning $B(2)$. The spectra due to metastable-ion dissociations were on-line processed with the AMD-Intectra data system, and 5—20 scans were averaged to improve the signal-to-noise ratio. The reproducibility of the data is better than ±1%. — All compounds were synthesized by standard laboratory procedures, purified by chromatographic means, and fully characterized by NMR and MS. For details, see: [7a] M. B. Stringer, J. H. Bowie, J. L. Holmes, *J. Am. Chem. Soc.* **108** (1986) 3888. — [7b] G. J. Currie, M. B. Stringer, J. H. Bowie, J. L. Holmes, *Austr. J. Chem.* **40** (1987) 1365.

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