136. Highly Selective Benzylic C–H Bond Activation of Toluene by 'Bare' FeO^+ in the Gas Phase

Short Communication

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The reaction of FeO^+ with toluene in the gas phase occurs at collision rate ($k_r = 1.36 \times 10^{-9}$ cm^3 molecule^{-1} s^{-1}), and labeling experiments demonstrate that the total products due to C–H bond activation involve to > 92% the benzylic position. In the 'hydride' abstraction process (formation of FeOH and $C_7H_7^+$), the H-atom originates exclusively from the benzylic position to generate a benzyl cation, and an intramolecular kinetic isotope effect $k_H/k_D = 1.75$ has been obtained. There is no evidence for the existence of isotopically sensitive branching ('metabolic switching') in the system studied.

Introduction. – C–H Bond activation of hydrocarbons by cationic iron-oxenoids is of fundamental interest in organic chemistry in general and in biochemistry in particular [1][2]. Recently, we reported the C–H bond activation of benzene [3] and methane [4] by 'bare' FeO^+ in the gas phase[3]. For the former system, in the course of the reaction an aromatic C–H bond is hydroxylated, and ultimately phenol is formed. An important aspect of hydroxylation of alkylarenes concerns the selectivity of aromatic *vs.* benzylic activation in alkylbenzenes. Here, we report the reactions of FeO^+ with toluene in the gas phase[4] and present evidence for almost exclusive benzylic C–H bond activation.

Experimental. – Most of the experiments were performed by using a *Spectrospin CMS 47 Fourier*-transform, 7.05-Tesla ion-cyclotron-resonance (FTICR) mass spectrometer, the experimental setup has been described in detail in [7]. In brief, Fe^+ ions were generated by laser desorption/laser ionization by focussing a beam of a Nd:YAG laser (*Spectron Systems*, 1064 nm) onto an Fe target. The ions are extracted from the external ion source and transferred to the analyzer cell by a system of electric potentials and lenses. The isolation of the $^{56}Fe^+$ isotope and all subsequent isolations of ions were performed by using FERETS [8]. FeO^+ was produced [9] by reacting it with pulsed-in N_2O and collisionally thermalized by an Ar buffer gas ($p = 2$–10×10^{-8} mbar). Toluene and its isotopomers were introduced *via* a leak valve ($p = 2$–5×10^{-9} mbar). Absolute rate constants of the reactions of FeO^+ with toluene and its isotopomers were determined by calibrating the reaction rates using rates of well-known ion/molecule processes. The error is estimated to ± 25%[5][6].

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[2] For a recent review, entitled 'Organometallic Chemistry in the Gas Phase', which includes more than 700 references and covers literature up to early 1991 pertinent to the topic of C–H bond activation, see [2].

[3] For other examples using FeO^+ as an efficient gas-phase oxidant, see [5].

[4] Work on the reactions of FeO^+ with higher alkylbenzenes is in progress and will be reported later [6].

[5] The pressures were corrected for the relative sensitivity of ion gauge for the various gases; for details, see [10].

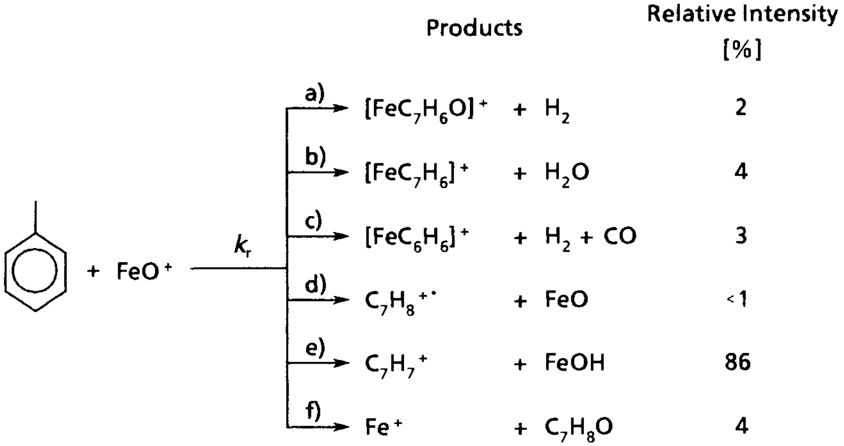
[6] For a recent example for the calibration of reaction rates, see [11].

For some comparative studies, experiments were performed by generating $[Fe,C_7,H_8,O]^+$ isomers in a chemical ionization source of a four-sector BEBE mass spectrometer [12] (B stands for magnetic and E for electric sector), by bombarding mixtures of either $Fe(CO)_5/N_2O$/toluene, $Fe(CO)_5$/benzyl alcohol, $Fe(CO)_5$/*o*-cresol, and $Fe(CO)_5$/anisol with electrons. Subsequently, the unimolecular decompositions of a B(1)/E(1)-mass-selected beam of corresponding $[Fe,C_7,H_8,O]^+$ ions were studied by using the MIKES technique [13].

The labeled toluenes were synthesized following well-known laboratory procedures and purified by preparative GC.

Results and Discussion. – The products of the reaction of FeO^+ with toluene are summarized in *Scheme 1*. The comparison of the overall rate constant ($k_{exp.} = 1.36 \times 10^{-9}$ cm^3 molecules^{-1} s^{-1}) with the collision rate constant as derived from the ADO theory [14] ($k_{ADO} = 1.31 \times 10^{-9}$ cm^3 molecule^{-1} s^{-1}) reveals that the reaction occurs with 100% efficiency. Thermoneutral charge transfer (CT) ($IP(C_7H_8) = 8.86$ eV; $IP(FeO) = 8.9 \pm 0.2$ eV) almost does not compete (< 1%) with the oxidation reactions[7]).

Scheme 1



k_r = $1.36 \cdot 10^{-9}$ cm^3 molecule^{-1} s^{-1}
k_{ADO} = $1.31 \cdot 10^{-9}$ cm^3 molecule^{-1} s^{-1}

The dominating reaction (86%) is loss of neutral FeOH generating $C_7H_7^+$ ions (*Reaction e*). This ion reacts subsequently with toluene *via* CH_2 transfer to form $C_8H_9^+$ (*Eqn. 1*).

$$C_7H_7^+ + C_7H_8 \rightarrow C_8H_9^+ + C_6H_6 \qquad (1)$$

Since in 1957 *Meyerson* and coworkers [17] proposed the tropylium structure for $C_7H_7^+$ ions derived from toluene, a number of publications dealing with this ion appeared in the literature[8]). In these studies, the $C_7H_7^+$ ions generated from toluene consisted of two

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[7]) A more recent value for the heat of formation of FeO^+ was taken from [15]. For all additional thermochemical data, see [16].

[8]) For a quite comprehensive coverage of the literature, see [18].

populations, the benzylium ion, responsible for the majority of these ions, and the energetically more stable tropylium ion. Initially, *Dunbar* and *Ausloos*, and others later reported [19] that benzylium ions – in contrast to the tropylium ion – are highly reactive and undergo consecutive ion/molecule reaction with toluene under formation of xylylene ions. For the $C_7H_7^+$ ions, produced from FeO^+ and toluene, a rate constant of $k_{exp.} = 3.0 \times 10^{-10}$ cm^3 molecule^{-1} s^{-1} was obtained for *Reaction 1*. This value is in reasonable agreement with the value of $k = 2.5 \times 10^{-10}$ cm^3 molecule^{-1} s^{-1} obtained by *Ausloos* [19f] for the reaction of benzylium ions with toluene. To check whether any tropylium ions are formed in the reaction of FeO^+ with toluene, the $C_7H_7^+$ ions were trapped with toluene for longer periods; however, no unreactive $C_7H_7^+$ ions, *i.e.* tropylium ions, were detected within experimental error (< 1%). Thus, we conclude that exclusively benzylium ions are formed in the C–H bond activation of toluene by FeO^+.

If FeO^+ is reacted with $C_6H_5CD_3$ (*Table 1*), no significant change of the overall branching ratios is observed, pointing to the operation of a minor *intermolecular* kinetic isotope effect [20]. Similar to the unlabeled toluene, the dominating reaction is due to the loss of FeOD, and all the labeled $C_7H_5D_2^+$ ions undergo subsequent reaction with $C_6H_5CD_3$ to form $C_8H_5D_4^+$ exclusively.

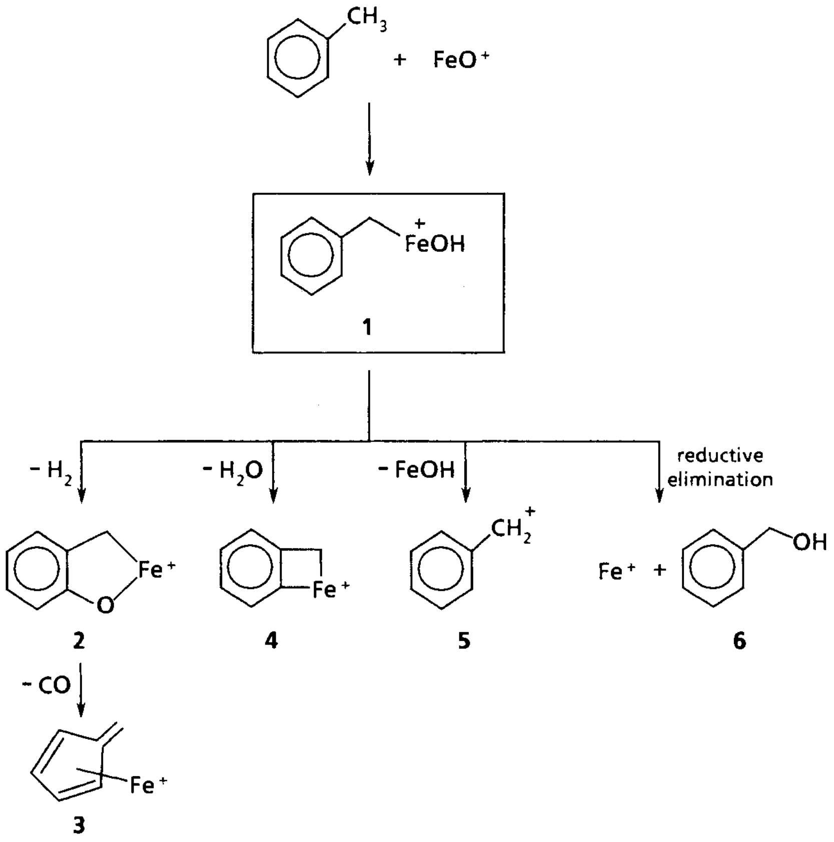
Table 1. *Neutral Products Formed in the Reaction of FeO^+ with Toluene and Its Isotopomers*

Precursor	H_2	HD	H_2O	HDO	CO/H_2	CO/HD	FeOH	FeOD	CT	Fe^+
$C_6H_5CH_3$	2		4		3		86		< 1	4
$C_6H_5CHD_2$	1	1	2	1	1	1	41	48	< 1	1
$C_6H_5CD_3$		2		3		3		85	< 1	6

An *intramolecular* kinetic isotope effect of $k_H/k_D = 1.75 \pm 0.05$ is operative in the benzylic C–H bond activation as derived from the reaction of FeO^+ with $C_6H_5CHD_2$ (*Table 1*). In comparison with kinetic isotope effects for benzylic hydroxylation by iron-oxenoids in the condensed phase, this value is rather small. Further, no evidence points to the operation of isotopically sensitive branching ('metabolic switching') [21] in the course of the reaction. Such a phenomenon has been observed in the Cyctochrome-P-450-mediated hydroxylation of alkylbenzenes, where, due to the presence of isotopes in the benzylic position, the hydroxylation reaction is to some extent shifted from this site to different sites of the molecule [21b, c, e, f]. We ascribe the small value for the kinetic isotope effect (KIE) to the high exothermicity of the hydrogen-abstraction reaction ($\Delta H_R = -24$ kcal mol^{-1}). However, it should be noted that similarly low KIE have been observed in the condensed phase, if charge transfer from a cationic iron oxenoid to the arene is rate-determining [22].

As to the minor products in *Scheme 1*, we can conclude the following from the labeling experiments: the loss of molecular hydrogen involves one H-atom from the Me group and one from the Ph ring, most probably originating from the *ortho*-position. Similarly, H_2O being formed contains both a Me and a ring H-atom. The loss of H_2/CO can be assigned to a consecutive loss of H_2 and CO. Following this conjecture, these reactions may lead to the formation of the metallacycles **2** (dehydrogenation), **4** (H_2O loss) and **3** (combined dehydrogenation/decarbonylation). The formation of similar metallacycles in the reactions of 'bare' metal cations with substituted arenes have been

Scheme 2



reported previously [23]. We note that the insertion structure **1** (*Scheme 2*) may well serve as a central intermediate en route to all reaction products reported in *Scheme 1*.

We have performed an additional experiment aimed at further testing our assertion that ring hydroxylation does not occur in the reaction FeO^+ with toluene. To this end, we have studied the unimolecular fragmentations of mass-selected $[Fe,C_7,H_8,O]^+$ ions as being derived from toluene/FeO^+ (System *I*), benzyl alcohol/Fe^+ (*II*), *o*-cresol/Fe^+ (*III*), and anisol/Fe^+ (*IV*). Although unimolecular fragmentations often obey quite different energetics, and the time window differs from that of ion/molecule reactions, a comparison of both is often revealing and may allow further conclusions with respect to reaction mechanisms and intermediates[9]. Indeed, as shown in *Table 2*, the results of systems *I* and *II* are very similar, and the minor differences in intensities can be accounted for in terms of internal energy contents of both ions formed *via* different routes. However, system *III*, which can be viewed as a model for a formal ring-oxidation product, is substantially

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[9] For a detailed comparison of ion/molecule reactions (as studied by ICR) and unimolecular reactions (as probed by the MIKES technique), see [24].

Table 2. *Neutral Molecules Formed in the Unimolecular Decomposition of* $[Fe,C_7,H_8,O]^+$ *Ions as Generated from Different Precursors and* $Fe(CO)_5$ *under Chemical Ionization* (see text)

Precursor (System)	H_2	H_2O	CH_2O	FeOH
$C_6H_5CH_3/N_2O/Fe(CO)_5$ (*I*)	11	35		54
$C_6H_5CH_2OH/Fe(CO)_5$ (*II*)	7	33		60
$o\text{-}C_6H_4(CH_3)OH/Fe(CO)_5$ (*III*)	2	97		1
$C_6H_5OCH_3/Fe(CO)_5$ (*IV*)	23	< 1	76	

different, *i.e.* the losses of dihydrogen as well as FeOH are almost absent. The anisol complex/Fe^+ (*IV*) is given for comparison: the predominant formaldehyde loss, which is absent for the other ions, indicates that no insertion of the FeO^+ unit in the aryl–CH_3 bond is involved in the oxygenation of toluene. Thus, only the minor H_2O loss channel in the reaction of FeO^+ with toluene (*Schemes 1* and *2*) can be due to ring-hydroxylation processes.

In summary, we conclude that toluene is rapidly oxidized by 'bare' FeO^+ in the gas phase; at least 92% of the total products formed under ICR conditions can be accounted for by benzylic C–H bond activation. This is a remarkable finding in view of the fact that C–H bond activation of alkylbenzenes by means of traditional organometallic complexes in most cases involves activation of an aryl rather than an aliphatic C–H bond [1] [2][10]).

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[10]) For further examples and a detailed discussion of mechanistic aspects, see [25].

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