$E^{\circ\prime} = -1.8$ V vs SCE,[14] the electron-transfer proceeds readily:

$$C_5H_5FeC_6(CH_3)_6 + O_2 \rightarrow C_5H_5FeC_6(CH_3)_6^+ + O_2^{-}\cdot$$

It has recently been shown[15] that electron transfer occurs in media of low dielectric constant between two radicals of greatly different electronegativities, yielding ion pairs.

Although $O_2^{-}\cdot$ is a weak base on the grounds that the pK_a of $HO_2\cdot$ is 4.88, a solution of $O_2^{-}\cdot$ behaves as if it is strongly basic and can promote proton transfer from acids with an approximate pK_a value of 23 as has been emphasized recently.[16]

As further evidence, KO_2 reacts with **3b** in Me_2SO or with equimolar 18-crown-6 in THF to give **2** in 30 min at room temperature.[17] Also note that the mass spectrum of **1** shows an important peak at $[M - 1]^+$, 282.106, consistent with an easy deprotonation of the cation **2**.

A reaction between cobaltocene and O_2 has been reported to produce an oxygen bridge between two η^4-C_5H_5 groups,[18a] but this and other radical-type reactions of cobaltocene[18b] can be understood on the basis of their low redox potential (−1.2 V/SCE)[19] and the important ligand character of its e_{1g}^* HOMO.[20] The interaction of η^5-C_5H_4RFe–η^6-arene with $^3O_2$ is probably not relevant to this latter reaction. An endoperoxide can be involved if $^1O_2$ is the interacting species or alternatively an Fe^I–O_2 bond (or Fe^{II}–$O_2^{-}\cdot$, depending on one's point of view) as an intermediate would imply a partial decoordination of the arene ligand. We plan to investigate this mechanism in more detail since the peculiar reactions of dioxygen described here usefully mimic the reactivity of $O_2^{-}\cdot$ vs. $^1O_2$ in biologically significant systems.

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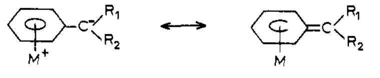
(4) Full characterization of **1** will be published separately.

(5) ^1H NMR (δ, C_6D_6): C_5H_5, 3.48 (s, 5), CH_2; 3.60 (s, 2); CH_3, 2.07 (s, 9) 1.76 (s, 6). ^{13}C NMR (δ, ppm, C_6D_6): C_5H_5, 75.64; CH_3, 16.31 16.9; cyclohexadienyl, 145.0, 90.1, 83.5, and 57.05 $J({=}CH_2) = 156, 5$ Hz.

(6) Treichel et al. have recorded the crystal structure of η^6-fluorenyl Fe–η^5-C_5H_5,[6a,b] showing that it is a zwitterion (A) in which no carbon atom is decoordinated from the η^6-benzene ligand. However all reported complexes with deprotonated arenes give NMR shifts showing that neither of the two following mesomeric structures (A and B) is present in a pure form.[6]



(A) (B)

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(11) The following spectral data were obtained for 4. ^1H NMR (δ Me_2SO-d_6): C_5H_5, 4.70–4.90; CH_3, 2.60; CH_2, 2.50. ^{13}C NMR (δ, ppm, D_2O): C_5H_5, 80.7; C_6 ring, 101.1; CH_3, 19.3; CH_2, 80.2; CO_2^-, 163.0. IR: $\nu_{CO_2^-}$ 1610 cm^{-1} (Nujol). Spectra data for **5** follow. ^1H NMR (δ, Me_2SO-d_6): C_5H_5, 4.52–4.86; CH_3, 2.45; CH_2, 2.37. ^{13}C NMR (δ, ppm, CD_2Cl_2): C_5H_5, 83; C, 99.6–101.3; CH_3, 21.6–22.6; CH_2, 83.4; CS_2, 148.61. IR: $\nu_{CS_2^-}$ 1170 cm^{-1} (Nujol). Satisfactory elemental analysis were obtained for **4** and **5** (C, H, S, Fe).

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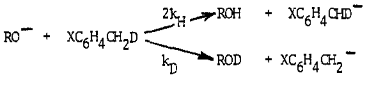
Intramolecular Kinetic Isotope Effect in Gas-Phase Proton-Transfer Reactions

Sir:

In spite of the potential usefulness of kinetic isotopic effects (KIE) toward the detailed understanding of energy surfaces of ion-molecule reactions and the dynamics of these processes, there has been little activity in this area. An early study of the intramolecular KIE in the reaction of rare gas ions with HD revealed that at near-thermal energies an inverse isotope effect is observed ($k_H/k_D < 1$).[1] This fact has been interpreted as arising from the unimolecular decomposition of a long-lived intermediate XHD^+. At higher ion translational energies, where $k_H/k_D > 1$, a direct reaction model provides satisfactory agreement with experiment.[2]

In the present communication, we report preliminary results on intramolecular kinetic isotope effects of a series of gas-phase proton-transfer reactions, where variation of R and X provides a convenient way of varying the exothermicity of the reaction.


(1)

$$RO^- + XC_6H_4CH_2D \xrightarrow{2k_H} ROH + XC_6H_4CHD^- \qquad RO^- + XC_6H_4CH_2D \xrightarrow{k_D} ROD + XC_6H_4CH_2^- \quad (1)$$

Previous measurements by ICR of the absolute rate constant for the methoxide–toluene reaction show that it is an order of magnitude smaller than a typical ion–molecule collision rate constant.[3] On the other hand, excitation function measurements for this same reaction suggest that there is no activation energy for the process.[4] These gas-phase reactions are also very useful for comparison with primary KIE observed in slow proton transfer reactions in solution, typical of carbon acids. The solution processes apparently exhibit a maximum effect when $\Delta pK \sim 0$,[5,6] an observation which has been rationalized

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Table I. Isotope Effect, k_H/k_D, for Reaction 1[a,b]

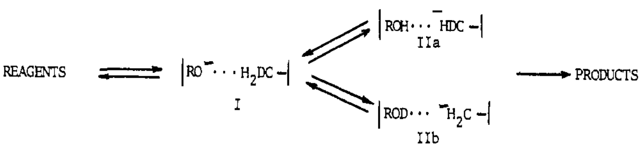
	CH_3O^-	$C_2H_5O^-$	$(CH_3)_2CHO^-$	$(CH_3)_3CCO^-$	$(CH_3)_3CCH_2O^-$
p-$CH_3C_6H_4CH_2D$	0.83 (1.7)[c]				
$C_6H_5CH_2D$	0.84 (−0.2)				
$C_6H_5CHDCH_3$	0.88 (−0.9)	0.81 (2.3)[c]			
m-$FC_6H_4CH_2D$	1.49 (−6.5)	0.97 (−3.5)	0.81 (−1.3)	0.66 (−0.5)	0.69 (1)
p-$ClC_6H_4CH_2D$	1.59 (−7)	1.31 (−4)	0.94 (−2)	0.77 (−1)	0.76 (0.3)
m-$ClC_6H_4CH_2D$	1.56 (−8.5)	1.28 (−5.5)	1.15 (−3.5)	0.71 (−2.5)	0.74 (−1)

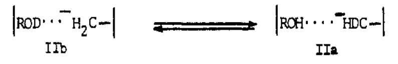
[a] Typical root-mean-square deviation for the measurements is better than ±0.07. [b] The exothermicities ($\Delta H°$) of the reactions are given in parentheses in kcal mol^{-1}. The first three lines are accurate values based on the acidity scale of Bartmess, J. E.; McIver, R. T., Jr., private communication. The other values are estimates based on the assumption that the substituent effect in toluenes is similar to that observed in the gas-phase acidity of phenols. [c] These reactions were studied at neutral pressures above 10^{-5} Torr.

within the framework of transition-state (TS) theory in terms of the symmetry or extent of proton transfer in the TS.

Our measurements of k_H/k_D by ICR[7] are shown in Table I along with the thermochemistry for the reactions. The results show a definite trend for k_H/k_D starting as a normal isotope effect for appreciably exothermic reactions (>3 kcal mol^{-1}) and proceeding smoothly toward an inverse isotope effect as the reaction approaches thermoneutrality or becomes endothermic.

Our observations can be rationalized in terms of the likely potential energy surface for these reactions. Brauman[8] has recently proposed a dynamic model to account for the slowness of several reactions involving carbon acids in the gas phase. For our systems, the reaction can be represented as going through a double minima potential with a central energy barrier. The intermediate complexes (I and II) are expected to be weakly bound species with stabilities in the range of 10 kcal mol^{-1}. For very exothermic processes, the potential energy diagram will be asymmetric, and the intramolecular KIE might be expected to be determined by the relative frequency factors for abstracting a proton or a deuteron in complex I. Thus, it is interesting to notice that for these reactions the experimental k_H/k_D values are in the vicinity of $(m_D/m_H)^{1/2}$. As the reaction becomes less exothermic, and the potential energy surface more symmetric, the behavior in the second intermediate complex will become important. Thus, we propose that the branching ratio for these systems will be influenced by the equilibrium partition between IIa and IIb. Estimates of the equilibrium isotope effect for the separated systems calculated from approximate vibrational frequencies yield values ranging from 0.52 to 0.71.[9] These values are, interestingly enough, close to the limiting values observed for the *inverse* isotope effect in near-thermoneutral or endothermic reactions. That appreciable scrambling can take place in complexes like IIa and IIb of endothermic reactions has been recently shown by DePuy[10] for systems similar to those studied in the present work.





We believe that the present results open up a wide range of applications of isotope effects in mechanistic studies of ion-molecule reactions.

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Preparation of Vinblastine, Vincristine, and Leurosidine, Antitumor Alkaloids from *Catharanthus* spp. (Apocynaceae)

Sir:

Antitumor alkaloids of the vinblastine group have been the subject of numerous chemical, biological, pharmacological, and clinical studies for the past 20 years. Efforts to achieve the synthesis of this type of compound culminated in 1974 when we discovered a new method for coupling the two obvious precursors of the vinblastine-type alkaloids, i.e., catharanthine (**1**) and vindoline (**2**)[1a,b] leading to $\Delta^{15'(20')}$-20′-deoxyvinblastine (**3**, anhydrovinblastine). We also disclosed a strategy to be used to synthesize compounds of this class, for example, vinblastine (**4**), vincristine (**5**), leurosidine (**6**), and leurosine (**7**). Several other research teams subsequently investigated this method of coupling.

Two theoretical approaches can be considered for the preparation of these bisindole alkaloids from **1** as starting material.

In the first method which has been used to prepare the bisindole alkaloids **4**, **5**,[2] and **7**,[3,4] carbon atoms C_{15} and/or C_{20} of **1** are functionalized *before* using the coupling reaction. Such an approach is not very efficient, and side reactions often occur

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