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By How Much is Protonated Benzene Stabilized by Coordination of Iron Tricarbonyl?

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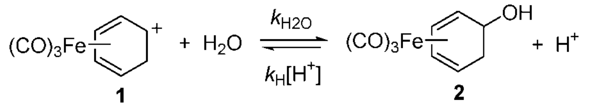
Among reactive intermediates the benzenonium ion (cyclohexadienyl cation) is a familiar example of instability and reactivity. Its lifetime in aqueous solution is <100 ps, and in one molar acid less than one molecule per mole of benzene is protonated.[1] The discovery more than 50 years ago that the same ion coordinated to an iron tricarbonyl group (**1**) can be recrystallized from water[2] is a striking example of the effect of metal complexation upon carbocation stability. Perhaps equally striking is that reaction of the metal complex with hydroxide ion leads not to deprotonation but to nucleophilic reaction at the formal charge center to yield the coordinated benzene hydrate (2,4-cyclohexadienol) **2**.[2,3]

Conversion of **1** to its hydrate in aqueous sodium bicarbonate[3] implies that the equilibrium constant K_R relating the two species (Scheme 1) should be measurable at mildly acidic pH. We have found that monitoring the dependence of an absorbance change at 250 nm upon pH in cacodylic and acetic acid buffers furnishes a titration curve consistent with $pK_R = 4.74$ (Figure 1).

Scheme 1



$$K_R = \frac{[2][H^+]}{[1]} = \frac{k_{H2O}}{k_H[H^+]}$$

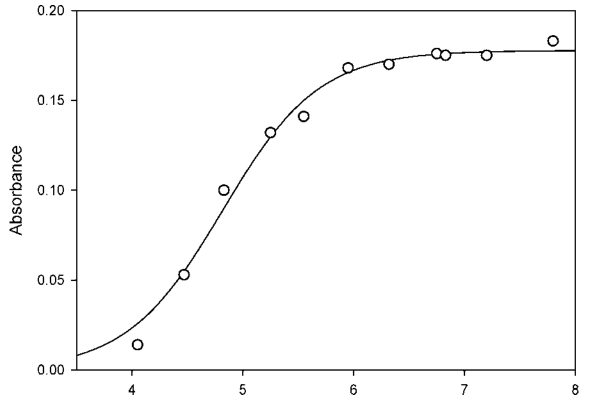


Figure 1. Change in absorbance at 250 nm upon quenching $Fe(CO)_3$ coordinated cyclohexadienyl cation in aqueous buffers against pH.

The change in absorbance in Figure 1 is associated with a kinetic relaxation which can be measured in the range pH 3−8 using a spectrophotometer equipped with a rapid mixing accessory. A plot of first-order rate constants against pH is shown in Figure 2. It is consistent with the occurrence of pH-independent and hydrogen-ion-dependent processes with rate constants $k_{H_2O} = 0.18$ s^{-1} and $k_H = 7.2 \times 10^3$ M^{-1} s^{-1}, respectively. Combining these constants yields $K_R = k_{H_2O}/k_H = 3.3 \times 10^{-5}$ and $pK_R = 4.60$ in good agreement with the spectrophotometric titration.

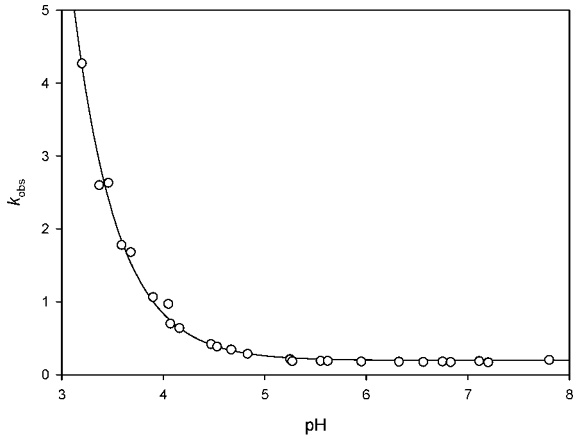


Figure 2. Plot of first-order rate constants against pH for the hydrolysis of $Fe(CO)_3$ coordinated cyclohexadienyl cation.

Below pH 8 hydrolysis of **1** is reversible and insensitive to ionic strength between $I = 0$ and 0.2 M. In the range pH 8−11 a further change in absorbance occurs, and in borate, carbonate, or amine buffers, the reaction is no longer reversible, possibly because of nucleophilic reactions of the buffer bases with the cation. Above pH 11 the cation reacts with a hydroxide ion, and the rate constant $k_{OH} = 10^5$ M^{-1} s^{-1} at 0 °C has been reported by Kane-Maguire.[3]

Examination of NMR spectra in D_2O and in D_2O containing 0.1 M sodium cacodylate confirms that the changes in UV spectra below pH 8 correspond with NMR spectra reported by Birch[2] for the $Fe(CO)_3$ cyclohexadienyl cation tetrafluoroborate salt and the isolated hydrate (**2**), respectively. Kinetic and spectrophotometric measurements in D_2O give equilibrium and kinetic solvent isotope effects $K_R^{H_2O}/K_R^{D_2O} = 3.0$ and $k_{D_2O}/k_{H_2O} = 2.1$ which are of the magnitude expected of hydrolysis of a carbocation.[4]

Spectrophotometric measurements in methanol containing 5% aqueous HCl give a further titration curve corresponding to $pK_R = 1.0$ for the methanolysis reaction shown in eq 1, in which the coordinated cation is denoted R^+. Again the spectrophotometric changes track changes in NMR spectra.

The difference in pK_R values between water and methanol ($\Delta pK_R = 3.8$) is characteristic of a reaction at a carbocation center and derives from two factors, the 100-fold greater "carbon" than proton basicity of MeO^- than HO^{-5} and the greater (proton) basicity of MeOH than water.[6]

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$$\mathrm{R^+ + 2MeOH} \overset{K_{\mathrm{RMeOH}}}{\rightleftharpoons} \mathrm{ROMe + MeOH_2^+} \qquad (1)$$

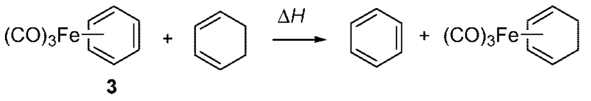
In water, the value of $\mathrm{p}K_\mathrm{R} = 4.7$ for **1** may be compared with $\mathrm{p}K_\mathrm{R} = -2.3$ for the uncoordinated cyclohexadienyl cation (eq 2).[1]

$$\mathrm{C_6H_7^+ + H_2O} \overset{\mathrm{p}K_{\mathrm{R}=-2.3}}{\rightleftharpoons} \mathrm{C_6H_7OH + H^+} \qquad (2)$$

The positive difference in $\mathrm{p}K_\mathrm{R}$ values, $\Delta\mathrm{p}K_\mathrm{R} = 7.0$, indicates a greater stabilization of the cyclohexadienyl cation by $\mathrm{Fe(CO)_3}$ than of cyclohexadiene.

That the coordinated cation undergoes nucleophilic attack rather than deprotonation is diagnostic of a carbocation reacting to form a nonaromatic double bond.[1,7] A natural inference is that the structure of $\mathrm{Fe(CO)_3}$-coordinated benzene **3**, which is the product of deprotonation, contains two coordinated double bonds and one double bond which is olefinic in character. Although benzene iron tricarbonyl is not known, iron derivatives of methyl naphthalenes[8] and anthracene[9] have been reported.

The olefinic character of the uncoordinated double bond of benzene iron tricarbonyl (**3**) is corroborated by DFT calculations which give $\Delta H = -35.3$ kcal mol^{-1} as the difference in heats of hydrogenation of a double bond of coordinated and uncoordinated benzene based on the isodesmic reaction of eq 3 and B3LYP calculations at levels /SDD, /LanL2DZ and /6-311+ G(3df,3pd)//B3LYP/SDD,[10] which agreed within ±0.4 kcal mol^{-1}.

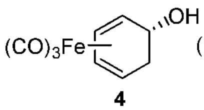


(3)

If we combine the calculated ΔH with an experimental heat of hydrogenation of benzene to cylcohexadiene of 5.5 kcal mol^{-1} the implied heat of hydrogenation of the coordinated benzene is -29.8 kcal mol^{-1}. This is much closer to -28.7 kcal mol^{-1} for cyclohexene than 5.5 kcal mol^{-1} for a π-bond of benzene.

A further equilibrium constant, $\mathrm{p}K_{\mathrm{H_2O}}$, for the addition of water to coordinated benzene **3** to give the hydrate **2** may be estimated by supposing that ΔH for the reaction of eq 3 is unaffected by replacing a methylene hydrogen by OH in the coordinated and uncoordinated cyclohexadienes. Then, if entropic and solvation contributions cancel, the difference in values of $\mathrm{p}K_{\mathrm{H_2O}}$ for benzene and coordinated benzene at 25 °C is given by $\Delta H/1.364 = 25.9$. From $\mathrm{p}K_{\mathrm{H_2O}} = 22.2$ previously estimated for benzene,[11] we obtain $\mathrm{p}K_{\mathrm{H_2O}} = -3.7$ for the iron tricarbonyl compound, the negative sign of which is again indicative of the olefinic character of the uncoordinated double bond.[11] From the relationship $\mathrm{p}K_\mathrm{a} = \mathrm{p}K_\mathrm{R} - \mathrm{p}K_{\mathrm{H_2O}}$[12] we also obtain $\mathrm{p}K_\mathrm{a} = 8.4$ for **1**, which is significantly larger than $\mathrm{p}K_\mathrm{R} = 4.7$, in sharp contrast to the uncoordinated cation, for which $\mathrm{p}K_\mathrm{R} = -2.3$ and $\mathrm{p}K_\mathrm{a} = -24.6$. The difference in $\mathrm{p}K_\mathrm{a}$ values, $\Delta\mathrm{p}K_\mathrm{a} = 33$, corresponds to $\Delta G° = 45$ kcal mol^{-1} and better reflects the dramatic difference in behavior of the two ions than the difference in $\mathrm{p}K_\mathrm{R}$ values ($\Delta\mathrm{p}K_\mathrm{R} = 7$).

The above measurements and calculation apply to the *exo* isomer of the $\mathrm{Fe(CO)_3}$ coordinated 2-hydroxycylohexadiene, **5**. Following Birch, the *endo* isomer **6** may be prepared from the $\mathrm{Fe(CO)_3}$ complex of the keto tautomer of phenol by reduction with $\mathrm{NaBH_4}$.[2] Measurement of a rate constant $k_\mathrm{H} = 2.0 \times 10^{-3}$ M^{-1} s^{-1} for acid-catalyzed conversion of this isomer to the coordinated cyclohexadienyl cation demonstrates that the *endo* reactant is 10^7-fold less reactive than its *exo* isomer.



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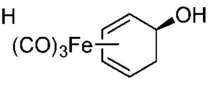
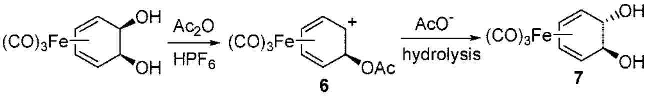


5

The low reactivity of **5** might suggest that it is stabilized by a favorable bonding interaction between the metal center and *endo* hydroxyl group. However, Lewis and Johnson have shown that in mildly acidic methanol *O*-methyl derivatives of **4** and **5** are slowly interconverted to an equilibrium ratio [*endo*]/[*exo*] = 2.[13] If a similar ratio applies to **4** and **5**, the slower rate for the *endo* isomer implies a larger kinetic barrier to reaction. This must be the result of a stereoelectronic effect similar to that favoring inversion over retention of stereochemistry in $\mathrm{S_N2}$ substitution.

In conclusion we note that the stereoselectivity of the reaction of the coordinated cyclohexadienyl cation with water and the effect of $\mathrm{Fe(CO)_3}$ coordination on the basicity of benzene may offer insights into the mechanism of action of iron-containing dioxygenase enzymes.[14] The stereoselectivity also has implications for synthetic applications of $\mathrm{Fe(CO)_3}$-coordinated dienyl cations,[15] including conversion of *cis*-benzene-dihydrodiols to their *trans* isomers by the pathway shown in Scheme 2, in which the *trans* coordinated diol **7** is the kinetic product of *exo* nucleophilic trapping of a coordinated carbocation intermediate **6**. [16]

Scheme 2



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Supporting Information Available: Energies and geometries of calculated structures in eq 3 and complete ref 10. This material is available free of charge via the Internet at http://pubs.acs.org.

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