¹H N.M.R. Kinetic Studies of Hydrogen–Deuterium Exchange of Ferrocene and some Monosubstituted Derivatives

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Nmr spectroscopy has been used to determine the rates of exchange in the various positions of ferrocene and some monosubstituted ferrocenes (–Br, –COOH, –CN). The activation parameters have also been measured. A quantitative estimate of the interannular transmission effect has been made, which is suggested to be operating through a primarily inductive mechanism. It is suggested that the exchange involves the preliminary formation of a π-complex between the electrophile and the cyclopentadienyl rings.

Introduction

In a previous work we examined the additivity of the substituents on the half-wave potential for a large number of substituted ferrocene derivatives [1]. Now we examine the influence of similar substituents on the reactivity of the cyclopentadienyl rings by the investigation of the hydrogen-deuterium exchange under acidic conditions. Since ferrocene and its derivatives are easily oxidized under strong acidic conditions to the unreactive paramagnetic ferroci-

TABLE I. First-Order Rate Constants for H–D Exchange of Monosubstituted Ferrocenes in the Unsubstituted Ring.

Substituent	$10^7 k, s^{-1}$ (100 °C)	$10^7 k, s^{-1}$ (120 °C)	$10^7 k, s^{-1}$ (140 °C)	E_a kcal/mol
H	1.4	6.5	25.6	22 ± 1
Br	0.05	0.25	1.1	23 ± 1
COOH	0.02	0.1	0.5	23 ± 1
CN	–	0.03	0.1	24 ± 1

TABLE II. First-Order Rate Constants for H–D Exchange of Monosubstituted Ferrocenes in the Substited Ring.

Substituent	$10^7 k, s^{-1}$ (100 °C)		$10^7 k, s^{-1}$ (140 °C)	
	2.5	3.4	2.5	3.4
H	1.4	1.4	25.6	25.6
Br	a	a	0.37	0.25
COOH	a	a	0.1	0.15
CN	a	a	a	a

[a]Exchange negligible in the used conditions.

TABLE III Correlations between the Relative Rates of Exchange and Some Selected Parameters

Parameter[b]	Slope of Regression Line[a]	Correlation Coefficient
σ_m	−4 267 (−4 460)	0 9884
σ_p	−3 663 (−3 524)	0 9658
$(\sigma_m + 2\sigma_p)/3$	−3 898 (−3 919)	0 9999
$\Delta E_{1/4}$	−6 881 (−6 937)	0 9953

[a]Values in parenthesis are referred to the same correlations for the solvolysis of methylferrocenylcarbinyl acetates   [b]The parameter values are those according to the literature H H Jaffè, *Chem Rev*, *53*, 191 (1953), D H McDaniel and H C Brown, *J Org Chem*, *23*, 420 (1958)

TABLE IV ^{1}H NMR Parameters of Substituted Ferrocenes in Tetradeuterioacetic Acid (δ, 90 MHz)

Compound	Cp Ring	2 5 Protons[a]	3 4 Protons[a]
Ferrocene	4 15	4 15	4 15
Bromoferrocene	4 21	4 38	4 12
Carboxyferrocene	4 27	4 83	4 50
Acetylferrocene	4 25	4 87	4 62
Cyanoferrocene	4 36	4 74	4 48

[a]Position of the centered triplet

nium ion, so far all the reported kinetic investigations involve a complex process of purification through the reduction of the ferrocinium cation to ferrocene, the isolation of ferrocene itself in the solid state and the determination of the deuterium content [2–5]

Results and Discussion

We report the direct determination of rate constants by recording the ^{1}H nmr spectra in tetradeuterioacetic acid, which also allows to distinguish and determine the exchange at 2,5 and 3,4 positions of the substituted ring or in the unsubstituted ring, thus giving the rate at a particular position of the ferrocene system Previously, only overall rate constants have been determined [2–4]

The rate constants for the H–D exchange of a group of substituted ferrocenes are collected in Tables I and II, the reactivity changes are in agreement with the well-known polar effects of the substituents, although they are quantitatively different for the two cyclopentadienyl (Cp) rings

The data of Table I show that the rate constants for the exchange of the unsubstituted ring are sharply different for the four substrates, thus indicating that the effect of a substituent is efficiently transmitted from one ring to another Taking as reference the rate constant of cyanoferrocene, the spread in reactivity of the unsubstituted ring is as follows CN COOH Br H = 1 5 12 260

Similar evidence for the interannular transmission through the iron atom is reached from the ratio of the rate constants $k_{subst}/k_{unsubst}$, which gives values of nearly 25% and 20% for the bromo and carboxy substituents, respectively These values appear to be in good accordance with those obtained by Butter and Beachell on the basis of the correlation of σ constants with proton shielding values [6]

From the data of the Table II it appears that the effect of the substituents on the substituted ring is clearly more pronounced as proved also by the necessity to rise the temperature to 140 °C in order to record the exchange The reactivity of the 3,4 positions is slightly lower with respect to that of the 2,5 ones for the carboxy derivative, while the contrary holds for bromoferrocene This trend is probably due to a complex combination of inductive and resonance effects of the substituents which cannot be easily evaluated It must be noted, however, that similar results were obtained for the H–D exchange in the various positions of phenylferrocene [5]

Table III lists the results of the least-squares analyses on the plots of the relative exchange rates *versus* $\Delta E_{1/4}$, Hammett's σ_m and σ_p constants, and an arbitrary calculated constant $(\sigma_m + 2\sigma_p)/3$ introduced by Hill [7]

The Hammett plots, although limited to few substrates, show a good correlation with σ_m and σ_p values and in particular with $(\sigma_m + 2\sigma_p)/3$, this latter kind of linear correlation would suggest that the ring–metal bonds must transmit electronic effects by a mechanism that is primarily inductive in nature

[7], These correlations are in good agreement with the linear free energy correlation of heteroannular substituent effects in the ferrocene chemistry, including the ionization constants of substituted ferrocenoid acids [8–11], the infrared carbonyl stretching frequencies of ferrocenoic acids and esters [12], and the proton shielding values [6]. Particularly relevant is the correspondence between the correlations reported in this work and those found in the solvolysis of methylferrocenylcarbinyl acetates [7] (Table III).

Good correlations are obtained also (Table III) with respect to the quarter-wave potentials, which may indicate that the transmission of the electronic effects of the substituents is performed by a mechanism which affects also the electron density on the iron.

In this respect the mechanistic path of the H–D exchange needs further discussion. It is well known that two mechanisms were suggested for the electrophilic substitution in ferrocene derivatives. The former [13] considers the formation of the metal-protonated species as intermediate, the alternative mechanism [14] includes the addition of a proton to the Cp ring with the formation of a σ-complex.

Although the data of this work cannot conclusively elucidate the exchange mechanism, it must be pointed out that on the basis of the results described in a recent paper [15] metal protonation must be excluded in acetic acid owing to its mild acidic properties and probably also for steric reasons. Consequently our results favor a mechanism involving the rapid formation of a π-complex between the acid and the π-cloud of a Cp ring, followed by the formation of an undetected σ-complex, which decomposes into the substitution product.

Experimental

Materials

Tetradeuterioacetic acid (Merck) was used without further purification. Anhydrous sodium sulphite (Merck Analytical Reagent) was dried in oven and used without any further purification.

Ferrocene derivatives were prepared according to the literature: Ferrocene [16], Bromoferrocene [17], Cyanoferrocene [18], Ferrocenoic acid [19].

Technique

Due to the easy oxidation of ferrocene and the sensitivity of the pmr technique to the presence of paramagnetic ions, the solvent for the exchange work had to be carefully chosen. The oxidation was slow in glacial acetic acid purged with argon, but unfortunately it was still too rapid for an appropriate use as solvent.

We discovered that a small amount (0.01 g) of anhydrous sodium sulphite was sufficient to prevent oxidation in acetic acid. This is probably due to the rapid reduction of the oxidized species, the reduction process being far more rapid than the oxidation.

With this technique we produced very clean ^{1}H nmr spectra of ferrocenes, even after considerable times at elevated temperatures.

A solution of ferrocene (0.04–0.05 M) was prepared in glacial tetradeuterioacetic acid (1ml) containing sodium sulphite (0.01 g), tetramethylammonium bromide (0.0015 g) and TMS (0.004 g). The solution was divided into two and sealed in two nmr tubes, previously dried at 150 °C and flushed with oxygen-free nitrogen. Therefore all the spectra were recorded on a Bruker HX-90 spectrometer operating at 90 MHz. The ^{1}H nmr data of the used substrates are collected in Table IV.

The extent of the reaction was measured by integration of the appropriate peak in the pmr spectrum and comparison with reference peak (tetramethylammonium bromide of TMS). In each case, a minimum of ten, and usually fifteen, integrals were measured. Comparison of the two signals (proton and reference) at time t gives a ratio R_t which is proportional to the number of protons remaining at the exchanging position. Thus R_t must follow the first-order rate law: $\ln R_t/R_o = kt$ where R_o is the ratio of the signals at time t = 0 and k is the first-order rate constant. k values may be obtained from the slopes of the plots of log R_t versus t.

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