Synthesis of new *N*-substituted imidazolyl and 1*H*-1,2,4-triazolyl derivatives of (η^6-arene)(η^5-cyclopentadienyl)iron(II) salts

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Abstract

A series of new imidazolyl and 1*H*-1,2,4-triazolyl derivatives of (η^6-arene)(η^5-cyclopentadienyl)iron(II) salts have been prepared by reaction of the corresponding chloroarene complexes with the sodium salts of the heterocycles. Good yields of *N*-substituted products were obtained in all cases under very mild conditions. In contrast to substitution by primary and secondary amines, both chlorines were displaced from [(η^5-1,2-dichlorobenzene)(η^5-Cp)Fe]PF$_6$], indicating electron withdrawal by the imidazolyl and triazolyl groups. Detailed ^{1}H and ^{13}C NMR analysis confirmed this point. NOE difference spectra were used for ^{13}C assignments, and evidence for conformational isomers in the 1,2-disubstituted complexes is presented.

Introduction

The ease with which halogen substituents are displaced by nucleophiles via S_NAr reactions in (haloarene) Fe$^+$Cp salts is well known and such reactions have been used to synthesise a wide range of new iron sandwich complexes [1,2].

Much of the earlier work concerned the use of heteroatomic nucleophiles. Recently reactions of a series enolate anions have been reported [3]. Little work has been done using nitrogen anions since the pioneering work of Nesmeyanov in this field [4]. The displacement of chloride by potassium phthalimide was used in the synthesis of amino derivatives of both arene [4] and Cp ring systems [5]. This useful reaction has not been exploited which is surprising in view of the possibility of arylation at both nitrogen (N) and carbon (C) centres of ambident nucleophiles such as pyrrolyl anions.

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$$\text{(equation 1 scheme)} \quad \xrightarrow{\text{(ArCl)CpFe}^+} \quad (1)$$
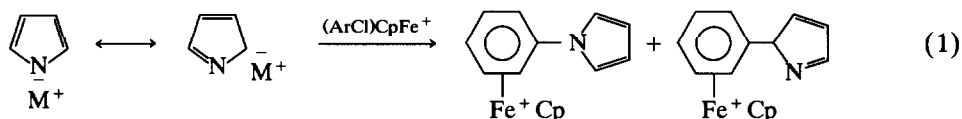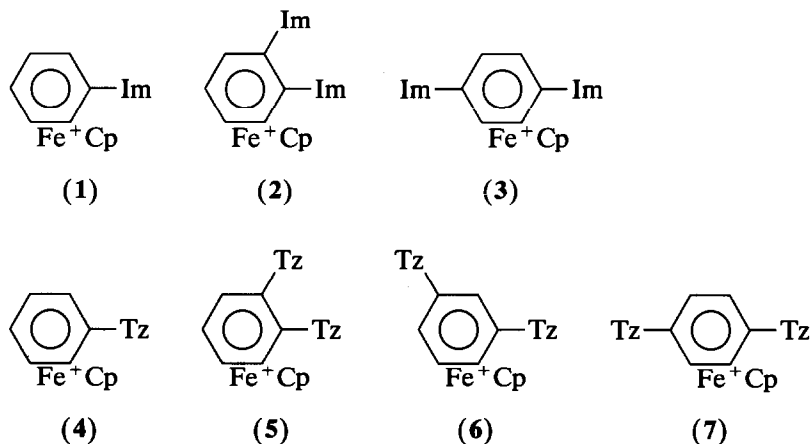
The product ratios (N/C) have been explained in terms of the principle of hard and soft acids and bases. Thus a "hard" electrophile will react at the "hard" nitrogen centre giving high N/C ratios. Softer electrophiles will increase the amount of attack at carbon. Such arguments have been used to rationalise the product ratios in the acylation of pyrrolyl ambident anions [6,7]. The potential of the above reactions for the synthesis of novel heterocyclic derivatives by decomplexation of the modified iron sandwich complexes has led the author to embark on a study of the synthesis of some of these heterocyclic derivatives. The work reported here concerns the preparation and characterisation of a number of imidazole and $1H$-1,2,4-triazole derivatives.

Results and discussion

The (chloroarene) iron Cp hexafluorophosphates were prepared by conventional methods. Reactions of these complexes with sodium imidazolate (NaIm) were initially performed in refluxing acetone but it quickly became clear that no heating was necessary and that the reactions proceeded smoothly at room temperature. The solvent of choice was acetonitrile and reaction times were usually 1–2 h. Corresponding reactions with sodium 1,2,4-triazolate required longer times for completion ($\sim$ 24 h). All the derivatives were obtained in good yields and gave satisfactory elemental analyses. It was noted that all the heterocyclic complexes showed some sensitivity to light and were stored in dark plastic containers.

The following complexes have been synthesised and characterised as their hexafluorophosphate salts (Im = imidazol-1-yl, Tz = $1H$-1,2,4-triazol-1-yl).

$$\text{(structures 1, 2, 3 with Fe}^+\text{Cp)}$$

(1)   (2)   (3)

$$\text{(structures 4, 5, 6, 7 with Fe}^+\text{Cp)}$$

(4)   (5)   (6)   (7)

Attempts to prepare the monoimidazolyl derivative from $[(\eta^6\text{-}1,2\text{-}C_6H_4Cl_2)Fe^+Cp][PF_6]$ always resulted in mixtures containing the bis substitution product.

$$\text{(structure) } \text{Cl} + \text{NaIm} \longrightarrow \text{(structures with Im)} \quad (2)$$
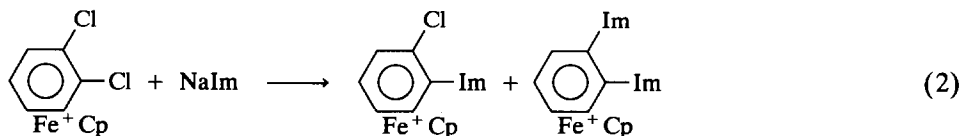
Displacement by simple primary amines usually results in only one chlorine being displaced, possibly due to deprotonation of the nitrogen substituent. This strongly discourages a second nucleophilic attack by increasing the electron density on the arene ring via a strong + M effect [8]. The above result suggests that the imidazole nitrogen lone pair is delocalised around the imidazole ring rather than the complexed arene ring. This point will be further elaborated in the discussion of the NMR spectra.

NMR analysis

The data for the imidazole complexes are presented in Table 1 . The numbering system adopted is illustrated for the monoimidazolyl derivative (**1**).
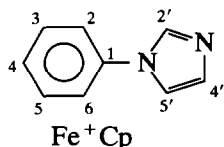
Both ¹H and ¹³C NMR data are consistent with products obtained by attack by nitrogen rather than carbon. In the ¹H NMR spectra, signals due to H2′, H4′ and H5′ are always observed with integral ratios to both arene and Cp signals commensurate with nitrogen substituted products.

NOE difference spectra were used to confirm the ¹H assignments. For **1**, irradiation at the H2,6 frequency caused the loss of the signals at 7.22 (assigned to H4′) and 5.27 ppm (Cp). Similarly, irradiation at the H2′ frequency resulted in the loss of all signals except the doublet at 7.07 ppm (H2,6). This is good evidence that the arene and imidazole rings are coplanar in solution since the NOE effect results from a short range through-space interaction. In the case of 1-phenylimidazole itself, irradiation at the H2, H2′ and H5′ frequencies caused all other signals to collapse which indicates free rotation about the interannular C–N bond. It follows, therefore, that the NOE enhancements observed for the complexed species **1** are due to restricted rotation about the interannular bond which is caused by the steric hindrance of the Cp ring.

For **4**, irradiation at the frequency of the signal assigned to H3′ (8.27 ppm) causes all signals to disappear. Thus H3′ is correctly assigned. Irradiation at H2,6 removes the H3′ and Cp signals but leaves the H3, H4 and H5′ signals unchanged. Irradiation at the provisionally assigned H5′ peak results in the disappearance of all signals except the doublet at 7.23 ppm (H2,6). This confirms the assignments of H3′ and H5′ and the coplanarity of the arene and triazole rings. Similar experiments with **5** gave no NOE difference signals which is the expected result for orthogonal triazole ring substituents. The lack of NOE difference signals when Cp is irradiated is evidence of rapid rotation of the latter ring in the complex. Comparison of the ¹H NMR data for 1-methylimidazole [9] (H2, H4, H5 appear at 7.47, 7.08 and 6.88 ppm, respectively) shows that all the imidazolyl protons are deshielded in **1** presumably due to the effect of the positive charge on iron. H5′ however lies upfield from H2′ indicating that lone pair delocalisation around the imidazole ring is still significant. These conclusions are confirmed by the similarity in the ¹³C shifts of the imidazole ring carbons in **1** and those in 1-phenylimidazole [10] in which C2′, C4′, C5′ appear at 135.8, 130.1 and 118.4 ppm respectively. The

Table 1

^{1}H and ^{13}C NMR data for imidazole (Im) derivatives of [arene]CpFe$^+$ salts in solvent acetone-d_6

^{1}H data ^{a}

Arene	H2	H3	H4	H5	H6	H2'	H4'	H5'	Cp
C$_6$H$_5$Im	7.07d (6.6)	6.72t (6.4)	6.54t (6.4)	6.72t (6.6)	7.07d (6.6)	8.40brs	7.22brs	7.95brs	5.27s
1,2-C$_6$H$_4$Im$_2$	–	7.08brs	7.08brs	7.08brs	7.08brs	7.80brs	6.86brs	7.30brs	5.60, 5.59s
1,4-C$_6$H$_4$Im$_2$	7.31s	7.31s	–	7.31s	7.31s	8.44brs	7.20brs	7.98brs	5.27s

^{13}C data ^{b}

Arene	C1	C2	C3	C4	C5	C6	C2'	C4'	C5'	Cp
C$_6$H$_5$Im	107.50q	80.56	88.09	87.70	88.09	80.56	136.97	132.02	118.57	78.69
1,2-C$_6$H$_4$Im$_2$	102.99q	102.99q	85.61	88.24	88.24	85.61	138.53	131.20	121.05	80.40
1,4-C$_6$H$_4$Im$_2$	106.73q	80.35	80.35	106.73q	80.35	80.35	137.18	132.15	118.73	79.27

^{a} Chemical shifts in ppm relative to TMS. Multiplicity: s, singlet; brs, broad singlet; d, doublet; t, triplet. Coupling constants in Hz in parentheses. ^{b} Chemical shifts in ppm relative to TMS, q = quaternary carbon.

Table 2

¹H and ¹³C NMR data for 1H-1,2,4-triazole (Tz) derivatives of [arene]CpFe⁺ salts in solvent acetone-d_6

¹H data ᵃ

Arene	H2	H3	H4	H5	H6	H3'	H5'	Cp
C₆H₅Tz	7.23 (6.3)	6.70m	6.54t (5.1)	6.7m	7.23d (6.3)	8.27s	9.23s	5.20s
1,2-C₆H₄(Tz)₂	–	7.20m	6.90m	6.90m	7.20m	8.16s 8.13s ᵇ	8.60s 8.57s ᵇ	5.52s 5.50s ᵇ
1,3-C₆H₄(Tz)₂	8.16 (1.6)	–	7.45dx2 (6.5, 1.6)	7.09t (6.5)	7.45dx2 (6.5, 1.6)	8.41s	9.47s	5.33s
1,4-C₆H₄(Tz)₂	7.59s	7.59s	–	7.59s	7.59s	8.35s	9.36s	5.32s

¹³C data ᵃ

Arene	C1	C2	C3	C4	C5	C6	C3'	C5'	Cp
C₆H₅Tz	106.69q	80.47	88.06	88.20	88.06	80.47	154.25	144.51	78.89
1,2-C₆H₄(Tz)₂	102.83q	102.83q	86.15	88.63	88.63	86.15	153.61	147.00	81.46
1,3-C₆H₄(Tz)₂	106.37q	72.44	106.37q	79.72	87.13	79.72	154.56	145.14	80.72
1,4-C₆H₄(Tz)₂	106.31q	80.74	80.74	106.31q	80.74	80.74	154.45	144.87	79.39

ᵃ See legend of Table 1. ᵇ Disappear on further recrystallisation.

C5' shifts are almost identical. For a comparable series of structures, ^{13}C shifts correlate well with electron densities on the carbon atoms concerned. Thus there appears to be little change in the mesomeric effect (which would place electron density at C5') on complexation by the Fe^+Cp moiety. This is further reinforced by the shift of the *para* (C4) carbon for **1**. Relative to the parent benzene complex ($\delta_C = 88.88$ ppm), C4 has a substituent chemical shift (SCS) of -1.18 ppm (*cf*. SCS = -1.2 ppm for phenylimidazole [10]) and is much less shielded than the *para* carbon of the dimethylaminobenzene complex [11] (SCS = -7.7 ppm).

One interesting feature of the ^{1}H NMR spectrum of **2** is the appearance of two Cp signals. Steric hindrance will restrict rotation about the C–N bond. This should result in a large dihedral angle between the imidazolyl and arene rings. Due to the asymmetric disposition of the N atoms, three conformational isomers should therefore exist: one with both N3 atoms above the arene plane, another with both N3 atoms below the arene plane and finally the one-up, one-down conformation. It is tempting to ascribe the observed Cp signals to this phenomenon.

Significant differences in both proton and carbon shifts occur for **2**, compared with **1** and **3** whose shifts are very similar. For **2** the large dihedral angle between the imidazole and benzene rings eliminates any $+M$ effect from the N1 lone pair causing the ^{1}H shifts in particular to approach those of imidazole itself (H2 = 7.73, H4, H5 = 7.14 ppm).

The NMR data for the triazole derivatives appear in Table 2. The ^{1}H NMR spectra of these complexes shows that they are all 1H-1,2,4 rather than 4H-1,3,4-triazoles. This indicates that electron density in the triazole anion is greatest at N1 (N2) and is probably a reflection of the electronegativity of the two contigous N atoms. As for the imidazoles, there is no evidence of any carbon bound species. Both ^{1}H and ^{13}C data are very similar, except of course for the data for the heterocyclic rings. ^{1}H data for the 1,2-disubstituted complex **5** indicates the presence of conformational isomers. A doubling of both Cp and H3', H5' signals occurs. This multiplicity is removed by further crystallisation. The ^{13}C spectra, however, show no evidence of this phenomenon. The 1H-1,2,4-triazolyl substituent has an even lower mesomeric interaction with the arene ring than the imidazolyl group as seen from the low SCS value of -0.68 ppm. As with **2**, **5** also shows somewhat anomalous ^{1}H and ^{13}C shifts due to the different disposition of the substituent groups.

Experimental

The chlorobenzene, 1,2-dichlorobenzene, 1,3-dichlorobenzene and 1,4-dichlorobenzene sandwich complexes were prepared by literature methods [12]. 1-Phenylimidazole and the sodium salts of imidazole and 1,2,4-triazole were purchased from Aldrich Chemical Company Ltd. and used without further purification.

Preparation of imidazole derivatives

(a) *(η^6-N-phenylimidazole)(η^5-cyclopentadienyl)iron(II) hexafluorophosphate.* (η^6-chlorobenzene)(η^5-cyclopentadienyl)iron(II) hexafluorophosphate (1.9 g, 5 mmol) was dissolved in dry acetone (15 ml) and sodium imidazolate (0.6 g, 6.7 mmol) added to give a green solution. The whole was brought to reflux whereupon the solution rapidly became light-brown in colour. The mixture was

refluxed for 1 h, cooled and filtered. The filtrate was diluted with ether until crystallisation occurred which was completed by cooling to 0°C. The resulting light brown crystalline precipitate was filtered and air dried to give 0.82 g (40%) of the desired product.

Analysis: Found: C, 41.5; H, 3.27; N, 6.65. $C_{14}H_{13}F_6FeN_2P$ calc.: C, 41.0; H, 3.17; N, 6.83%.

(b) $(\eta^6\text{-}1,2\text{-}bis\text{-}N\text{-}imidazolylbenzene)(\eta^5\text{-}cyclopentadienyl)iron(II)$ hexafluorophosphate. $(\eta^6\text{-}1,2\text{-}dichlorobenzene)(\eta^5\text{-}cyclopentadienyl)iron(II)$ hexafluorophosphate (1.64 g, 4.0 mmol) and sodium imidazolate (0.72 g, 8.0 mmol) were stirred in dry acetonitrile (20 ml) for 3 h at 20°C. The mixture was filtered and evaporated to give 1.40 g crude product (74%) which was recrystallised from MeCN/Et$_2$O.

Analysis: Found: C, 42.9; H, 3.4; N, 11.2. $C_{17}H_{15}F_6FeN_4P$ calc.: C, 42.9; H, 3.2; N, 11.8%.

The 1,4-bis-N-imidazolyl benzene complex was obtained in 70% yield using the above procedure.

Preparation of 1H-1,2,4-triazole derivatives

These derivatives generally require longer reaction times as exemplified below.

$(\eta^6\text{-}N\text{-}phenyl\text{-}1H\text{-}1,2,4\text{-}triazole)(\eta^5\text{-}cyclopentadienyl)iron(II)$ hexafluorophosphate. $(\eta^6\text{-}chlorobenzene)(\eta^5\text{-}cyclopentadienyl)iron(II)$ hexafluorophosphate (1.5 g, 4 mmol) was stirred overnight with sodium 1,2,4-triazolate (0.80 g, 8.8 mmol) in dry MeCN. The mixture was filtered and worked up as before to give a 90% yield of crude product which was recrystallised from MeCN/Et$_2$O.

Analysis: Found: C, 37.5; H, 2.9; N, 10.1. $C_{13}H_{12}F_6FeN_3P$ calc.: C, 38.0; H, 2.9; N, 10.2%.

The bis-1,2-(1H-1',2',4'-triazolyl)benzene complex was prepared in 85% yield by an identical procedure. Analysis: Found: C, 37.7; H, 2.6; N, 17.5. $C_{15}H_{13}F_6FeN_6P$ calc.: C, 37.7; H, 2.7; N, 17.6%.

The bis-1,3-analogue was also prepared as above in 47% yield. Analysis: Found: C, 37.5; H, 3.0; N, 16.8. $C_{15}H_{13}F_6FeN_6P$ calc.: C, 37.7; H, 2.7; N, 17.6%.

Likewise, the bis-1,4-derivative was obtained in 80% yield. Analysis: Found: C, 37.6; H, 2.7; N, 17.6. $C_{15}H_{13}F_6FeN_6P$ calc.: C, 37.7; H, 2.7; N, 17.6%.

NMR and analytical data

^{1}H and ^{13}C NMR were run on a JEOL EX 270 spectrometer. ^{1}H shift assignments were made initially by reference to the work of Jacquier *et al.* [13] for both imidazole and triazole complexes and confirmed by NOE difference spectroscopy. ^{13}C shift assignments were made in accordance with the previous spectral analyses [14–16]. The ^{13}C shifts of the arene carbons of **1** were assigned by reference to the uncomplexed arene [17]. Assignments for the remaining complexes was made using the SCS values obtained from **1** and **3**. Microanalyses were performed by the Analytical Department of the University of Manchester.

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