An Efficient Synthesis of the First Electroactive Phosphorus-containing Bisferrocene Macrocycles

Béatrice Delavaux-Nicot,* Yannick Guari, Bénédicte Douziech and René Mathieu*

Laboratoire de Chimie de Coordination du CNRS, UPR 8241 lié par conventions à l'Université Paul Sabatier et à l'Institut National Polytechnique de Toulouse, 205, route de Narbonne, 31077 Toulouse Cedex, France

Condensation reactions of the phosphodihydrazide $XP(Ph)(NMeNH_2)_2$ (X = O **1a**, S **1b**) with ferrocene-1,1′-dicarboxaldehyde **2** afford in good yield the first examples of phosphorus ferrocenyl macrocycles $Fe[C_5H_4CH{=}NNMeP(X)PhNMeN{=}CHC_5H_4]_2Fe$ (X = O **3a**, S **3b**) and **3b** can be converted to the new compounds $Fe[C_5H_4CH_2NHNMeP(S)PhNMeNHCH_2C_5H_4]_2Fe$ **5** and $[Fe\{C_5H_4CH{=}NNMeP(S)(Me)PhNMeN{=}CHC_5H_4\}_2Fe][CF_3SO_3]_2$ **6** by reaction with, respectively, LAH and CF_3SO_3Me; **5** represents a novel prototype of an anion receptor which electrochemically recognises the $H_2PO_4^-$, HSO_4^- and Cl^- anions.

The design of receptors containing ferrocenyl groups for electrochemical recognition is a recurrent theme in contemporary chemistry.[1] Studies concerning phosphorus-containing macrocycles are now well documented and offer a range of synthetic methods.[2] Despite the development of these two areas, to the best of our knowledge, no examples of macrocycles incorporating ferrocenyl and phosphorus groups have been reported and only rare examples of phosphorus-containing macrocycles with bound ferrocenyl groups have been described.[3]

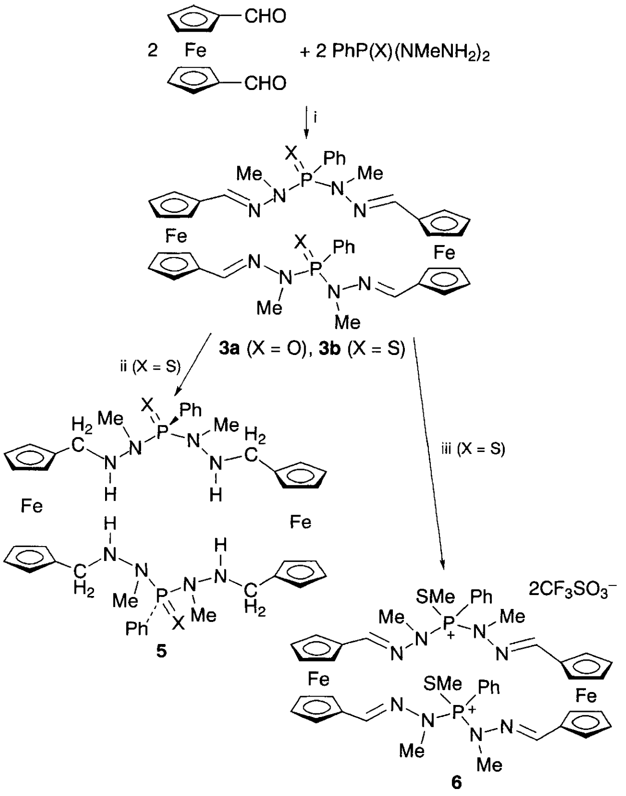
Previously, we have demonstrated that it was possible to selectively synthesize a new class of acyclic phosphorus-containing ferrocenyl ligands of general formula $XP(NMeN{=}CHFc)_nPh_{3-n}$ (n = 2, 3; X = O, S).[4] This was achieved by the condensation reaction of phosphohydrazides $XP(NMeNH_2)_nPh_{3-n}$ (n = 2, 3; X = O, S) with ferrocene carbaldehyde. Thus, we decided to exploit this synthetic approach and reactions of $XP(Ph)(NMeNH_2)_2$ (X = O, S) with ferrocene-1,1′-dicarboxaldehyde were investigated. Herein, we report the first examples of macrocycles incorporating two 1,1′-disubstituted ferrocenes and two phosphorus groups which were obtained by the method described. Isolation of new derivatives of this series (Scheme 1) and electrochemical studies of these compounds are also reported.

The phosphodihydrazides $XP(Ph)NMeNH_2)_2$[5] (X = O **1a**, S **1b**) react smoothly with $(C_5H_4CHO)_2Fe$[6] **2** at 60 °C in THF to give a deep red solution of the major compound $Fe[C_5H_4CH{=}NNMeP(X)PhNMeN{=}CHC_5H_4]_2Fe$ (X = O **3a**, S **3b**) isolated in 85 and 62% yield, respectively.† Desorption chemical ionisation mass spectrometry of **3a** and **3b** (NH_3 carrier gas) shows $M + H^+$ molecular peaks at expected values of 841 and 873 for a [2 + 2] cyclocondensation reaction. The IR spectra of these compounds exhibit weak ν(C=N) vibrations at 1592 and 1590 cm^{-1}. In the ^1H NMR spectrum the CH=N resonance is obscured because of the phenyl protons in the same region (δ 7.05–7.55 in $CDCl_3$), but in the ^{13}C NMR spectra, resonances observed at δ 131.8 (J_{CH} 161 Hz) for **3a** and 131.6 (J_{CH} 161 Hz) for **3b** are characteristic of those due to imino groups. The downfield shifts of the macrocycles in the $^{31}P\{^1H\}$ spectra (δ +7.7 for **3a** and +8.4 for **3b**) are comparable to those observed for the acyclic ferrocenyl derivatives $XP(NMeN{=}CHFc)_2Ph$ (X = O **4a**, S **4b**).[4a,c]

However, NMR data showing complex signals especially for the NMe groups in the ^1H NMR spectra suggest the existence of conformers in solution. To verify this, low temperature NMR experiments have been carried out. For example, in the case of **3a**, at 193 K a broadening of the signals is observed in the ^1H NMR spectra while the apparent $^{31}P\{^1H\}$ triplet becomes a multiplet. The most important changes are observed in the $^{13}C\{^1H\}$ spectra: complex signals appear for the NMe, CH=N and phenyl groups whereas the C_{ipso} signal is unchanged and the (C_5H_4) resonances evolve to three complex signals centred at δ 70.5, 67.7, and 78.2. Moreover, upon warming to 358 K a sample of **3a** in $[^2H_5]$pyridine, the apparent triplet observed in the $^{31}P\{^1H\}$ spectra at 298 K becomes a singlet at the same shift (δ 22.5). This phenomenon is reversible. These low and high temperature NMR results ascertain the existence of conformers in solution which are probably induced by restricted rotation along the (C_5H_4) CH=NNP linkage.[7]

Two other macrocycles have been synthesized from **3b** either by reduction of the imine function or by alkylation of the P–S bond. This last experiment was done in the hope of producing hydrosoluble cationic macrocycles.

The imino groups in complex **3b** can be reduced with LAH in refluxing THF. After hydrolysis, compound **5** is the only product observed by NMR in solution. The IR spectrum shows a (N–H) stretch at 3379 cm^{-1}. ^1H NMR spectra of the isolated product are consistent with the reduction of the imino groups: a CH_2 signal (AB quartet) centred at δ 3.40 (J_{HH} 12 Hz) and a broad singlet attributed to the NH function at δ 2.99 are observed.[8] This compound exhibits a unique signal in the ^{13}C NMR for the C_{ipso} of the substituted rings at δ 83.8 and a set of only four signals (δ 68.2, 68.4, 69.0, 69.5) for the (C_5H_4) groups consistent with a structure of higher symmetry than **3b** and **3a**.



Scheme 1 *Reagents and conditions*: i, THF, 60 °C; ii, LAH (20 equiv.), THF, reflux; iii, CF_3SO_3Me (3 equiv.), CH_2Cl_2, room temp.

Treatment of **3b** with 3 equiv. of CF_3SO_3Me in dichloromethane gives compound **6** which has been isolated in 86% yield. This compound has low solubility in common organic solvents and is insoluble in water. Characterization has been achieved by NMR in CD_3CN: a doublet at δ 2.52 (J_{PH} 15.9 Hz) (^1H NMR), and a singlet at δ 13.9 (^{13}C NMR) are resonances assignable to the thiomethyl bonded to phosphorus.[9] Furthermore, the IR spectrum shows the presence of the $CF_3SO_3^-$ group.[10]

The electrochemical behaviour of the new compounds **3a**, **3b**, **5**, **6** has been investigated (Table 1). Cyclic voltammograms of each species presents a quasi-reversible oxidation wave corresponding to a two electrons process and, interestingly, compound **3b** can be quantitatively recovered after a full cycle of oxidation and reduction by electrolysis.

Compound **5** also presents a minor oxidation wave at 0.58 V *vs.* SCE at slow scan rate owing to the oxidation of the amino groups[8] and preliminary studies for anion recognition shows that the addition of successive stoichoimetric amounts of Cl^- (up to 4 equiv.) to a CH_2Cl_2 solution of **5** lead to the increase of this wave without noticeable change for the first wave. Further addition of Cl^- has no effect. These results suggest the compound **5** is electrochemically sensitive to the presence of Cl^- ions, probably through hydrogen bonding interactions between the NH group and the Cl^- ion.[11]

In light of recent results in selective electrochemical recognition of anions by metallocene acyclic or macrocyclic ligands containing NH groups,[12] these first observations about Cl^- recognition prompted us to extend the study to other various anions like dihydrogen phosphate or hydrogen sulfate anions. The preliminary results of this study are gathered in Table 2. Significant cathodic perturbations of the ferrocenyl oxidation current peak potentials are observed in the two cases and the largest magnitude of cathodic shift is observed with the $H_2PO_4^-$ anion. It is noteworthy that the shapes of the oxidation wave change from a reversible redox process to an EC mechanism specially for the $H_2PO_4^-$ anion and this phenomenon increases with the anion concentration. Moreover, as the concentration of the anion increases from 2 equiv. to 12 equiv. we observe a shift of E_{pa} to 320 mV which is certainly the result of a competitive partial protonation of the amino groups.[13]

When an equimolar mixture of $H_2PO_4^-$, HSO_4^- and Cl^- anions (2 equiv.) are added to a dichloromethane electrochemical solution of **5** the anodic current peak potential shifts cathodically to 288 mV (ΔE = 202 mV), which is approximately the same value as that induced by the $H_2PO_4^-$ anion alone. This is in favour of a selective electrochemical recognition of $H_2PO_4^-$ but the sensitivity of E_{pa} to the anion concentration prevents us from performing conclusive simple competition experiments with a high excess of the HSO_4^- anion.

In the absence of crystals of **5** suitable for X-ray structure determination, molecular mechanic calculations have been done using the program Cache™ (release 3.5). Results of these calculations show that the most stable conformation fits with a situation (schematized Scheme 1) in which the P=S groups are directed outside the cavity defined by the four NH groups. The estimated size of this cavity is 5 Å which is compatible with the size of the $H_2PO_4^-$ and HSO_4^- anions.

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Table 1 Electrochemical data for the isolated macrocycles[a]

Compound	$E_{1/2}$/V	P^b/mV	n	E_{pa}/V	ΔE_p/mV	$R/_p$
3a	0.48	64	—[c]	0.53	51	1.1
3b	0.48	80	2	0.53	90	1.0
5	0.44	69	2	0.49	44	0.9
6	0.66	84	2	0.72	71	0.8

[a] Experimental conditions: Pt electrode in 0.1 mol dm^{-3} solution of $NBu^n_4PF_6$ in CH_2Cl_2 except **6** in MeCN, complex concentration *ca.* 10^{-3} mol dm^{-3}. [b] P = slope of the linear regression of $E = f(\log |i/id - i|)$. [c] Slow adsorption on electrode prevents full electron count by electrolysis.

Table 2 Electrochemical data for **5**[a]

	Ferrocenyl redox couple/mV
E_{pa}(free)	490
E_{pc}(free)	446
$\Delta E(H_2PO_4^-)^b$	230
$\Delta E(HSO_4^-)^b$	80
$\Delta E(Cl^-)^{b,c}$	<5

[a] Experimental conditions: Pt electrode in 0.1 mol dm^{-3} solution of $NBu^n_4PF_6$ in CH_2Cl_2, complex concentration *ca.* 10^{-3} mol dm^{-3}. [b] Cathodic shifts of the anodic current peak potential of the Fc/Fc⁺ couple produced by presence of anions (*ca.* 2.5 equiv.) added as their tetrabutylammonium salts. [c] See text.

Footnote

† *Selected data* for **3a**. ^1H NMR ($CDCl_3$, 250 MHz) δ 2.94 (m, 12H, Me), 4.11 (br s), 4.36 (m, 16H, C_5H_4), 7.13, 7.51, 7.95 (each m, 14H, C_6H_5 and CH=N); $^{31}P\{^1H\}$ NMR ($CDCl_3$, 81.0 MHz) δ 23.3 (apparent t); ^{13}C NMR ($CDCl_3$, 62.8 MHz) δ 30.8 (q, J_{CH} 139 Hz, Me), 67.3 (m, J_{CH} 173 Hz), 68.3 (m, J_{CH} 176 Hz), 69.9 (m, J_{CH} 176 Hz), 70.2 (m, J_{CH} 182 Hz), 82.2 (br s, C_5H_4), 127.6 (dm, J_{CP} 14, J_{CH} 161 Hz), 129.8 (d, J_{CP} 168 Hz), 133.3 (dd, J_{CP} 9, J_{CH} 166 Hz), 136.1 (dd, J_{CP} 14, J_{CH} 161 Hz, C_6H_5), 131.8 (dm, J_{CH} 161 Hz, CH=N); *m/z* (DCI) M + 1⁺ = 841.

3b: ^1H NMR ($CDCl_3$, 200 MHz) δ 3.00 (m, 12H, Me), 4.06, 4.25, 4.32, 4.37 (each br s, 16 H, C_5H_4), 7.06 (br s), 7.17 (br s), 7.50 (br s), 8.16 (m, 14H, C_6H_5, CH=N); $^{31}P\{^1H\}$ NMR ($CDCl_3$, 81.0 MHz) δ 77.8 (s); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 50.32 MHz) δ 31.2 (d, $^2J_{CP}$ 8.4 Hz, Me), 67.1, 67.6, 68.3, 69.0, 70.1, 82.1, 82.2 (each s, C_5H_4), 127.3 (d, J_{CP} 14 Hz), 131.8 (d, $^1J_{CP}$ 136 Hz), 133.6 (d, J_{CP} 10 Hz), 137.1 (d, J_{CP} 14 Hz, C_6H_5), 131.6 (br s, CH=N); *m/z* (CDI) M + 1⁺ = 873.

5: ^1H NMR ($CDCl_3$, 200 MHz) δ 2.77 (d, J_{PH} 11.5 Hz, 12H, Me), 2.99 (br s, 4H, NH), 3.40 (AB multiplet, J_{HH} 12 Hz, 2H, CH_2), 3.89 (m, 16H, C_5H_4), 7.43, 8.03 (each m, 10H, C_6H_5); $^{31}P\{^1H\}$ NMR ($CDCl_3$, 81.0 MHz) δ 81.9 (s); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 35.4 (qd, J_{CP} 7, J_{CH} 137 Hz, Me), 47.5 (td, J_{CP} 7, J_{CH} 137 Hz, CH_2), 68.2 (m, J_{CH} 176 Hz), 68.4 (m, J_{CH} 176 Hz), 69.0 (m, J_{CH} 174 Hz), 69.5 (m, J_{CH} 176 Hz), 83.8 (br s, C_5H_4), 127.4 (dm, J_{CP} 13, J_{CH} 161 Hz), 131.1 (dd, J_{CP} 3, J_{CH} 161 Hz), 132.2 (d, J_{CP} 131 Hz), 132.6 (dm, J_{CP} 10, J_{CH} 165 Hz, C_6H_5); *m/z* (DCI) M + 1⁺ = 881.

6: ^1H NMR (CD_3CN, 200 MHz) δ 2.52 (d, J_{PH} 15.9 Hz, 6H, CH_3S), 3.30 (d, J_{PH} 10.0 Hz, 12H, MeN), 4.44, 4.62 (each br s, 12H, C_5H_4), 7.9 (m, 4H, CH=N and C_6H_5); $^{31}P\{^1H\}$ NMR (CD_3CN, 81.0 MHz) δ 78.0 (s); $^{13}C\{^1H\}$ NMR (CD_3CN, 50.3 MHz) δ 13.9 (s, CH_3S), 33.5 (d, J_{CP} 6 Hz, CH_3N) 69.7, 69.8, 73.2, 80.47, (each s, C_5H_4), 131.0 (d, J_{CP} 14 Hz), 134.7 (d, J_{CP} 12 Hz), 136.9 (d, J_{CP} 4 Hz), 146.4 (d, J_{CP} 16 Hz, H=N and C_6H_5); IR (KBr) ν/cm^{-1}: 1602 (C=N), 1262, 1030, 638 ($CF_3SO_3^-$).

All new compounds gave satisfactory elemental analyses.

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