Journal of Organometallic Chemistry, 350 (1988) C15–C19
Elsevier Sequoia S.A., Lausanne – Printed in The Netherlands

Preliminary communication

Lithium redox-responsive ferrocene bis-tertiary amide derivatives

Paul D. Beer, Harrison Sikanyika,

Department of Chemistry, The University of Birmingham, Birmingham B15 2TT (Great Britain)

Christopher Blackburn and Jerome F. McAleer

Medisense (U.K.), 38 Nuffield Way, Abingdon, Oxon OX14 1RL (Great Britain)

(Received May 16th, 1988)

Abstract

The addition of Li^+ to ferrocene bis-tertiary amide derivatives in acetonitrile results in a shift of the ferrocene oxidation wave to more positive potentials and the appearance of a new redox couple associated with a Li^+ complex.

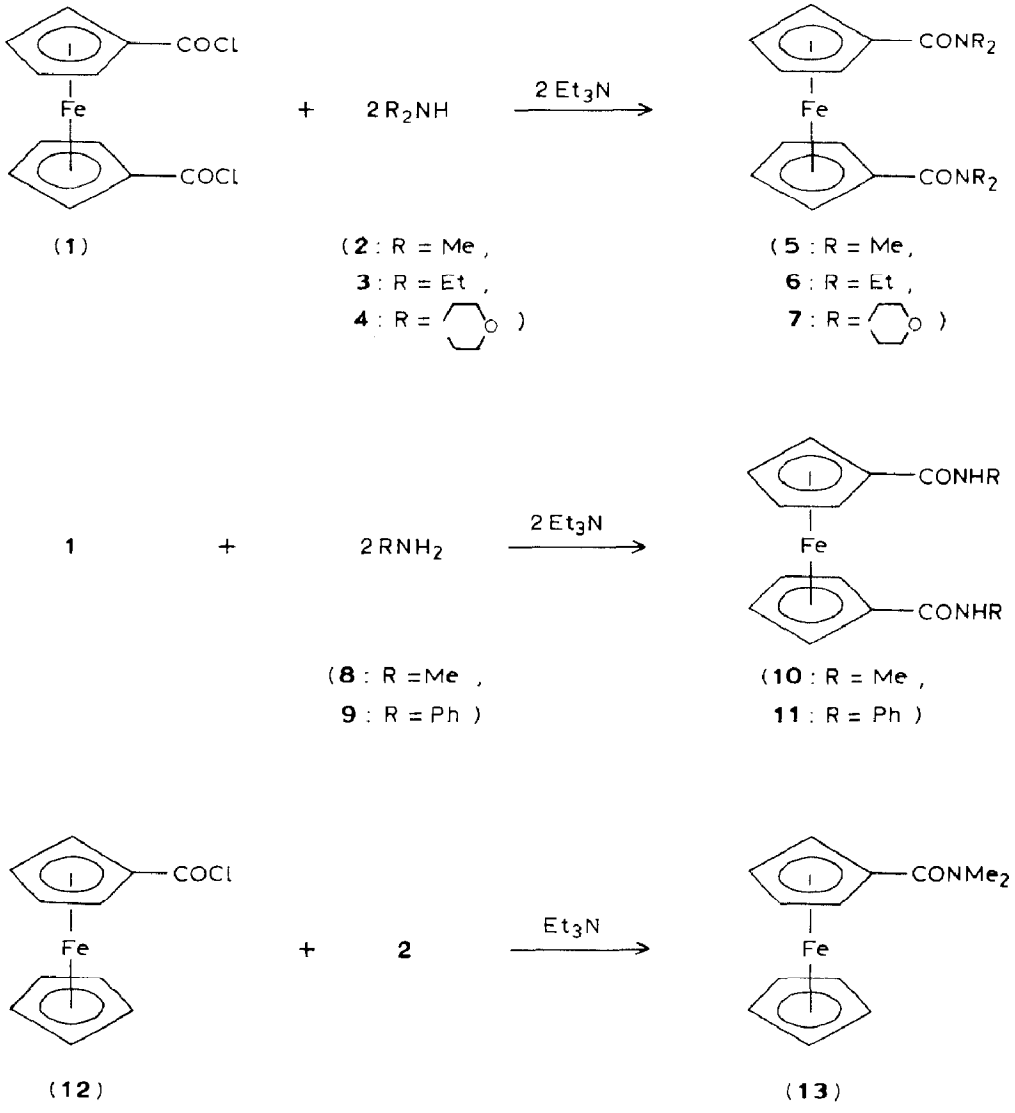
The design and synthesis of lithium ionophores for biological and analytical applications such as potentiometric assay of Li^+ in blood serum during therapy of manic depressive psychosis has been the subject of many recent publications [1–8]. Simon [5] has reported the preparation of a number of lipophilic 3,7-dioxaazela-amides and their use as ionophores in lithium ion selective liquid membrane electrodes. More recent work has shown that simple bis amides (without ethereal oxygen atoms in the side chain) can complex Li^+ with a selectivity of ca. 140 over Na^+ [7,8]. These reports prompted us to investigate the Li^+ binding properties of amides derived from ferrocene monocarboxylic and 1,1′-ferrocene dicarboxylic acids which might be expected to display shifts in redox potential upon complexation [9,10].

The condensation of 1,1′-bis-chlorocarbonylferrocene (**1**) and chlorocarbonylferrocene (**12**) with a variety of amines gave excellent yields of the corresponding ferrocene amide products [11*] (Scheme 1). All of the compounds gave satisfactory elemental analysis, ^1H and ^{13}C NMR spectra, and molecular masses by mass spectrometry.

^{13}C NMR spectroscopy was used initially to investigate the complexation of **5–7**, **10**, **11** and **13** with lithium. The stepwise addition of $LiBF_4$ to an acetonitrile

* Reference number with asterisk indicates a note in the list of references.

0022-328X/88/$03.50



Scheme 1

solution of **5** led to considerable shifts of the carbonyl carbon signal of up to 2 ppm. The stoichiometry of **5** to lithium calculated from the resulting $\Delta\delta$ (ppm) vs. [$LiBF_4$] titration curves was found to be 2/1. This result suggests Li^+ is forming a four coordinate complex with two molecules of **5** binding to the metal through the four carbonyl oxygen donor atoms. This type of coordination chemistry is commonly found for lithium [2,8,12,13]. Analogous observations were noted with bis amides **6** and **7**. However, no NMR evidence for lithium complexation with the secondary bis amides (**10** and **11**) or mono tertiary amide (**13**) was found. These results suggest that 1,1′-bis-tertiary amide ferrocene compounds can only bind the lithium cationic guest.

Positive ion FAB mass spectrometry of **5** with $LiNO_3$ in a water/glycerol matrix gave gas phase ions at m/z 551 and 279 indicating the formation of both 2/1 and 1/1 complexes of **5** with Li^+ under these conditions.

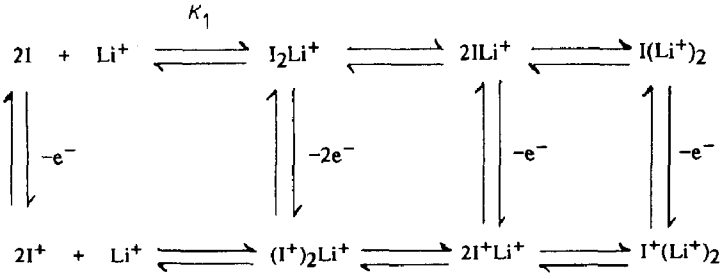
Table 1

Electrochemical data, peak potentials (volts) [a]

Compound	No. $LiBF_4$		4 equiv. $LiBF_4$		
			free ligand		new couple
	E_{pa}	E_{pc}	E_{pa}	E_{pc}	E_{pa}
5	1.08	1.00	1.14	1.07	1.44
6	1.02	0.94	1.07	0.99	1.41
7	1.01	0.91	1.05	0.97	1.33
10	1.08	1.01	1.13	1.06	–
11	1.18	1.10	1.18	1.11	–
13	0.96	0.88	0.95	0.88	–
14	0.97	0.88	1.02	0.92	–

[a] Obtained from cyclic voltammetry studies in dry MeCN solvent containing 0.1 *M* $Bu^n_4N^+$ BF_4^- as supporting electrolyte. Solutions 5×10^{-3} molar in **5** to **7**, **13** and **14** and 1.5×10^{-3} molar in **10** and **11** were prepared under nitrogen and treated with the calculated quantity of 1.0 *M* $LiBF_4$ in MeCN. After allowing to equilibrate for 2 h, solutions were transferred to the electrochemical cell using dry syringes. Measurements were made at $21\pm1°C$ at 50 mV s^{-1} scan rate using a glassy carbon working electrode and Ag, AgCl[Me_4N^+ Cl^- (sat.)] reference electrode.

The electrochemical properties of **5**–**7**, **10**, **11** and **13** were investigated by cyclic voltammetry in anhydrous acetonitrile containing $Bu^n_4N^+BF_4^-$ as supporting electrolyte. Each compound exhibited one reversible wave associated with the ferrocene–ferrocenium redox couple (Table 1). Addition of $LiBF_4$ to a solution of **5** led to a progressive shift of the redox wave towards more positive potentials. This shift was visible after the addition of 0.5 equiv. of $LiBF_4$ (Fig. 1a and 1b). Solutions treated with larger amounts of $LiBF_4$ (≥ 2 equiv.) showed an additional effect. Thus, following an equilibration period, a new redox couple at some 300 mV more positive potentials than the initial wave was observed (Fig. 1c). The height of the new wave increased further at the expense of the initial wave for solutions containing 4 equiv. of $LiBF_4$ (Fig. 1d). Somewhat surprisingly, in the presence of ≥ 6 equiv. $LiBF_4$ the height of the new wave diminished compared with that observed at the 4 equiv. level. Analogous effects were observed with **6** and **7** (Table 1), but no new waves and no significant shifts in the waves due to the free amides were observed with **10**, **11** and **13**, supporting the NMR evidence that Li^+ does not complex with these ligands.



Scheme 2. Redox and complexation equilibria for a ferrocene 1,1′-bis-tertiary amide ligand, I. $K_j = \vec{k}_j/\overleftarrow{k}_j$.

A possible explanation for these electrochemical results is shown in Scheme 2, where I refers to a ferrocene bis amide ionophore (i.e. **5**, **6** or **7**). Since the shift in potential of the wave due to I is observed at low Li^+ concentration levels (compara-

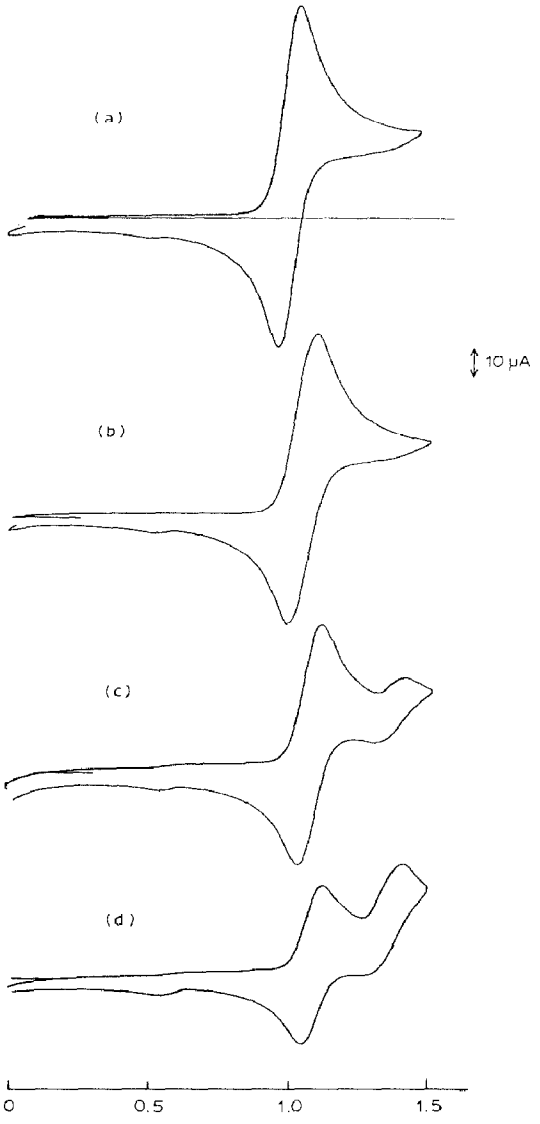
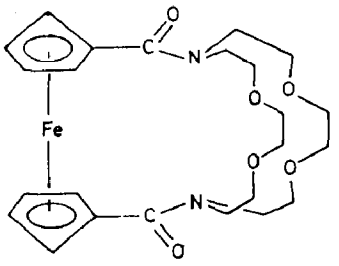


Fig. 1. Cyclic voltammetry in acetonitrile solution of (a) compound **5** (3 mmol), (b) **5**+0.5 equiv. Li^+, (c) **5**+2 equiv. Li^+, (d) **5**+4 equiv. Li^+. Sweep rate 50 mV s^{-1} scanning from 0 to +1.5 V.

ble to those added in the NMR titration experiments) we attribute this effect to the formation of a labile 2/1 complex I_2Li^+. Electrochemical oxidation of this species is followed by rapid decomplexation to give the free ligand I^+, and therefore no new redox couple associated with I_2Li^+ is detected. Larger amounts of $LiBF_4$ would be expected to displace the equilibria in favour of the 1/1 complex ILi^+ and the new redox couple is attributed to this species. This implies that complex I^+Li^+ is either stable or undergoes slow decomplexation on the voltammetric timescale, and indeed, the reverse wave, corresponding to the reduction I^+Li^+ is also observed. Since even larger amounts ($\geqslant 6$ equiv.) of $LiBF_4$ did not lead to complete conversion to ILi^+, the presence of a third species is likely. This could be a complex $I(Li^+)_2$ [13] indistinguishable from I electrochemically because of either a similar redox potential and/or rapid decomplexation of $I^+(Li^+)_2$.

We envisage the shift in redox potential resulting from the complexation $I \rightarrow ILi^+$ as arising from the electrostatic effect of Li^+ held (cooperatively by the two amide carbonyls) close to the Fe redox centre. It is noteworthy that the ferrocene cryptand (**14**), which has a *trans* orientation of the two carbonyl groups both in solution [14] and in the solid state [15], does not exhibit a new redox couple in the presence of $LiBF_4$.

With Na^+ and K^+ guest cations no detectable changes in the respective cyclic voltammograms or NMR spectra of any of the ferrocene amide derivatives were found.



(**14**)

Acknowledgements. We thank the British Council for financial support to (H.S.) and Medisense, Research Corporation Trust, and L and D Blond for additional financial support. We also thank the SERC for use of the high field NMR service at the University of Warwick.

References

1 K. Kimura, S. Kitazawa and T. Shono, Chem. Lett., (1984) 639.
2 E. Metzger, D. Ammann, U. Schefer, E. Pretsch and W. Simon, Chimia, 38 (1984) 440.
3 K. Kimura, H. Yano, S. Kitazawa and T. Shono, J. Chem. Soc. Perkin Trans. II, (1986) 1945.
4 B.P. Czech, D.A. Babb and R.A. Bartsch, J. Org. Chem., 49 (1984) 4805.
5 E. Metzger, R. Aeschimann, M. Egli, G. Suter, R. Dohner, D. Ammann, M. Dobler and W. Simon, Helv. Chim. Acta, 69 (1986) 1821.
6 A. Shanzer, D. Samuel and R. Korenstein, J. Am. Chem. Soc., 105 (1983) 3815.
7 V.P.Y. Gadzekpo, J.M. Hungerford, A.M. Kadry, Y.A. Ibrahim, R.Y. Xie and G.D. Christian. Anal. Chem., 58 (1986) 1948.
8 E. Metzger, D. Amman, R. Asper and W. Simon, Anal. Chem., 58 (1986) 132.
9 T. Saji and I. Kinoshita. J. Chem. Soc. Chem. Commun., (1986) 716.
10 M.P. Andrews, C. Blackburn, J.F. McAleer and V.D. Patel, J. Chem. Soc. Chem. Commun., (1987) 1122.
11 Compounds **5**, **6**, **7** have been reported previously, P.D. Beer, P.J. Hammond, C. Dudman, I.P. Danks, C.D. Hall, J.P. Knychala and M.C. Grossel, J. Organomet. Chem., 306 (1986) 367.
12 A. Zeevi and R. Margalit, J. Membrane Biol., 86 (1985) 61.
13 U. Olsher, G.A. Elgavish and J. Jagur-Grodzinski, J. Am. Chem. Soc., 102 (1980) 3338.
14 P.J. Hammond, A.P. Bell and C.D. Hall, J. Chem. Soc. Perkin I, (1983) 707.
15 P.D. Beer, C.D. Bush and T.A. Hamor, J. Organomet. Chem., 339 (1988) 133.