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Polyhedron 22 (2003) 763–768

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Anion binding at the core of branched ferrocene derivatives

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Received 8 August 2002; accepted 4 November 2002

Abstract

The anion binding ability of two ferrocenoyl amide derivatives with bulky branched substituents has been determined. NMR titration experiments indicated that in each case, the ability of these molecules to bind anions at the core through hydrogen bonding was poor as a consequence of the steric bulk of the substituents. Electrochemical experiments, however, indicated that anion binding could occur in the oxidised ferrocenium form as a consequence of electrostatic interactions. This binding was evidenced by the onset of EC mechanistic behaviour in the presence of halide anions. Square wave voltammetry was used to report on halide anion binding via a decrease in the peak current and a cathodic shift in the apparent redox potential of the receptors. The magnitude of this shift was dependent on the degree of dendritic functionalisation—indicating the ability of dendritic branching to act as a steric shield, hindering the penetration of guest anions. These results have implications for the design of sensors based on encapsulated binding sites.

Keywords: Anion; Dendrimer; Electrochemistry; Ferrocene; Receptor; Supramolecular

1. Introduction

There has recently been intense interest in the use of dendrimers as receptors in supramolecular chemistry [1]. In particular, a number of workers have focussed on the unique effects of encapsulating a selective binding site within a dendritic shell. Dendritically modified Fe(II) porphyrins have been investigated for their ability to bind guests such as O_2 through coordinative interactions and it has been shown that the branching can dramatically affect both the strength, selectivity and kinetics of gas binding [2]. By burying a hydrogen bonding 9,9′-spirobi[9*H*-fluorene] cleft within a dendritic shell, Smith and Diederich illustrated that the dendrimer could have an impact on the stereoselectivity of hydrogen bond mediated monosaccharide binding [3]. On the other hand, Diederich and co-workers have extensively developed dendrophanes [4], in which a cyclophane core is buried within flexible dendritic branching, and have shown that the branching has surprisingly little effect on the thermodynamics and kinetics of binding a polar guests such as steroids. Other receptors that have been encapsulated within dendritic shells include cyclotriveratrylene [5], β-cyclodextrin [6], functionalised binaphthyl derivatives [7] as well as a variety of other hydrogen bonding receptor units [8]. Perhaps surprisingly, given the intense recent interest in anion complexation [9], there has been relatively little development of dendritic anion receptors. There have been a number of reports in which anion receptor units placed at the periphery of a dendritic superstructure have demonstrated effective anion binding and sensing behaviour. Vögtle and co-workers utilised urea groups for oxyanion binding [10], whilst the groups of Moran and Astruc have both made use of metallocenes functionalised with hydrogen bonding groups to snare anionic guests [11]. Meanwhile, van Koten and co-workers have illustrated the ability of polycationic dendrimers to bind multiple anions within their interiors [12]. However, as yet, there have been no reports to the best of our knowledge, in which the properties of a single well-defined anion binding recognition unit at the core of a branched dendritic structure have been investigated.

Recently, we reported a series of dendrimers: **G0(Fc)**, **G1(Fc)** and **G2(Fc)**, the core of which comprised an encapsulated ferrocene unit [13]. Other groups have

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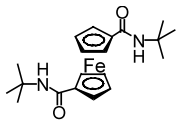
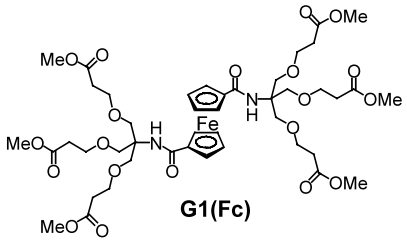
0277-5387/03/$ - see front matter
doi:10.1016/S0277-5387(02)01407-9

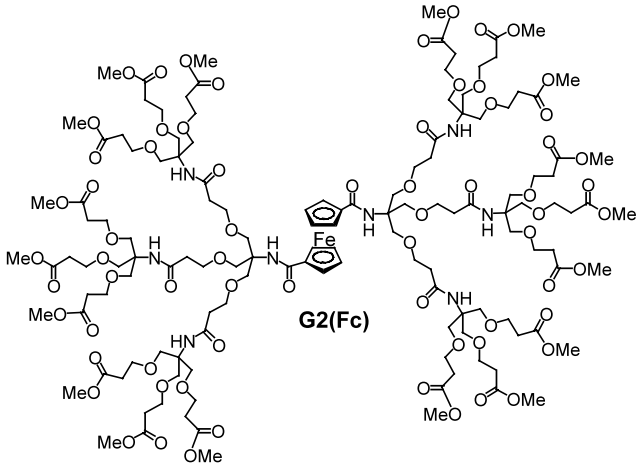
investigated the binding of such encapsulated ferrocene units within a cyclodextrin cavity [14]. However, we were intrigued by the potential of our amide-functionalised ferrocenes to act as encapsulated anion receptors and sensors. It is well-known, primarily through the work of Beer et al., that simple amide-functionalised ferrocene derivatives act as both anion receptors (through hydrogen bond formation) and electrochemical sensors (as a consequence of electrostatic interactions between the bound anion and the oxidised ferrocenium unit) [15]. This paper reports the effects of encapsulation on both the binding and sensing process, focussing in particular on the effect of steric bulk by comparing the anion binding properties of **G0(Fc)** and **G1(Fc)**.



G0(Fc)



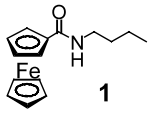
G1(Fc)



G2(Fc)

2. Results and discussion

Dendrimers **G0(Fc)** and **G1(Fc)** were synthesised using a convergent approach as reported previously [13]. For this study, **G2(Fc)** was not investigated, as it was felt that the increased number of amide groups within the branched shell itself would lead to a significant degree of non-specific binding within the branches, which would compete with the primary anion recognition process at the dendritic core. It is interesting to note that the respective yields reported previously for the synthesis of **G0(Fc)** and **G1(Fc)** were 74 and 51%, reflecting the increased steric hindrance of the coupling between dendritic branch and the ferrocene core. This is itself a dendritic effect on synthesis which is well-known for convergent coupling reactions in dendrimer chemistry [16], but it has significance when considering the anion binding potential of the ferrocenoyl dendrimers as it provides a direct measure of the inaccessibility of the encapsulated core. Compounds **G0(Fc)** and **G1(Fc)** were fully characterised by all standard techniques, as reported previously [13].



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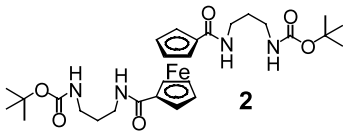

2

2.1. NMR titrations

Beer et al. have previously made extensive use of NMR titrations to monitor the anion binding capability of amide derivatised ferrocenes such as compounds **1** and **2** [15]. Evidence for anion binding is provided by shifts in the N–H peak(s) of the receptors on the addition of aliquots of an anion as its tetrabutylammonium (TBA) salt in chloroform. For example, on the addition of **1** equiv. of TBA chloride, the N–H peak of receptor 1 shifted by 0.1 ppm and that proximate to the ferrocene unit in receptor **2** by 0.3 ppm in $CDCl_3$ [15c]. Receptors **G0(Fc)** and **G1(Fc)** were therefore investigated in $CDCl_3$ using this NMR titration approach. Even on the addition of up to 12 equiv. of TBA chloride, however, the total shift in the N–H peak of **G0(Fc)** was only 0.018 ppm—a very small perturbation. Furthermore, smooth titration curves were not obtained with these sterically hindered receptors. This is perhaps not surprising given the level of error on such small NMR shifts. Similarly, TBA bromide and iodide, induced even smaller total shifts in the N–H peaks of this receptor (Fig. 1). This indicates that anions do not bind very effectively to the neutral receptor in chloroform solution—a result which can probably be attributed to the high steric bulk of the *t*-butyl group which is directly adjacent to the potential hydrogen bond donor N–H group, and will hinder access of the anionic guest. It was, however, notable that chloride did induce a larger perturbation than bromide, which in turn caused more perturbation than the iodide anion. This indicates that there is possibly some very weak interaction which is dependent on the charge density of the anion (highest for Cl^-).

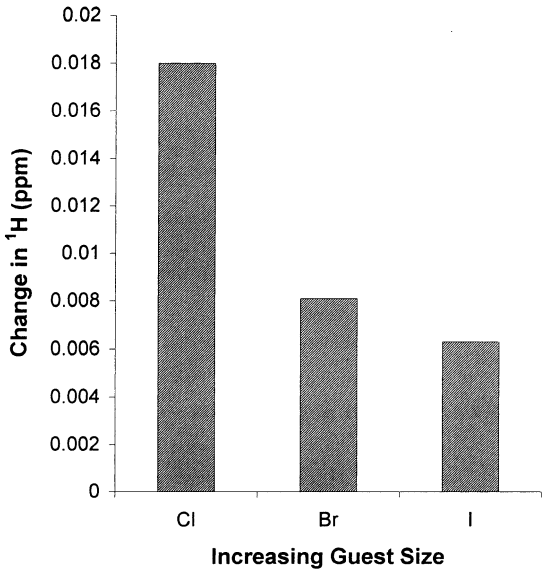

Fig. 1. NMR shifts of the N–H peak of **G0(Fc)** induced by the addition of 12 equiv. of TBA halide salts (*solvent:* $CDCl_3$).

For **G1(Fc)**, the anion induced NMR shifts were even smaller, and once again, smooth binding curves were not obtained. This is consistent with a sterically hindered binding site which can only bind anionic guests very weakly, leading to small perturbations in the NMR spectrum.

These sterically hindered neutral ferrocene derivatives are therefore much less effective anion binding hosts than those previously reported by Beer et al. [15]. Nonetheless, we decided to investigate whether 'switching on' a cationic charge on the ferrocene unit via electrochemical oxidation would give rise to enhanced anion binding.

2.2. Electrochemical investigations

It is well-known that when oxidised, ferrocene derivatives bind anions more effectively than when neutral as a consequence of electrostatic interactions between the ferrocenium group and the bound anion [15]. This gives rise to a shift in the redox potential. The enhancement in anion binding strength on the introduction of the positive charge (K_{ox}/K_{red}) can be directly related to the redox shift induced by addition of anions.

We therefore investigated the electrochemistry of **G0(Fc)** and **G1(Fc)** dissolved in acetonitrile, in the presence of TBA chloride, bromide and iodide. The addition of TBA chloride led to the flattening of the reduction wave (Fig. 2), typical of an EC mechanistic response (as described previously) [15b,15c]. This clearly indicates the fact that the chloride anion interacts with the oxidised ferrocenium compound. The presence of the chloride anion had a small effect on the position of E_{ox}, which shifted cathodically < 20 mV (cathodic shifts

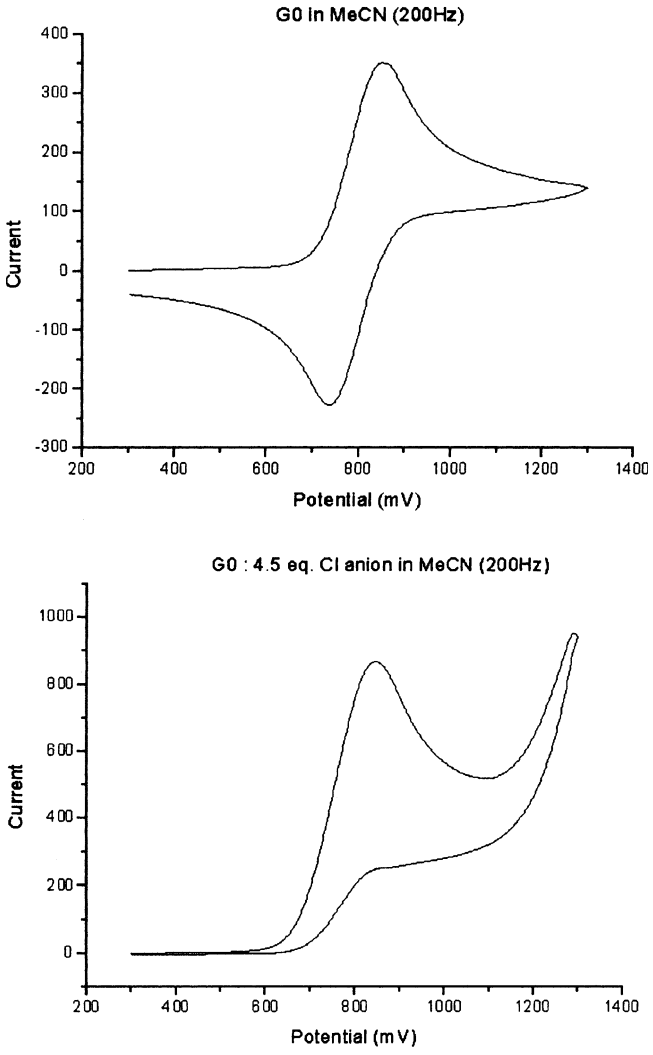

Fig. 2. Cyclic voltammograms of receptor **G0** in CH_3CN without and with the presence of 4.5 equiv. of TBA chloride (scan rate 200 mV s^{-1}).

are often seen in ferrocene-anion binding because the oxidation process becomes easier in the presence of the negatively charged ion as a consequence of electrostatic stabilisation). Compound **G1(Fc)** showed a similar EC mechanistic response to TBA chloride, but the potential of E_{ox} was completely unaffected by the halide anion (although the oxidation wave was significantly broadened). This EC response indicates there is again an interaction between ferrocenium and chloride. It should be noted that unfunctionalised ferrocene displays no electrochemical response to the presence of halide anions [15b]. This indicates the importance of the ligand groups appended to the ferrocene unit in helping to bind the anion and generate the electrochemical response rather than simple ion pairing interactions alone being responsible. Furthermore, all these studies were performed in the presence of 100 equiv. of BF_4^- (from base electrolyte), indicating a degree of anion selectivity.

Square wave voltammetry (SWV) provides a good way of probing the electrochemistry of the ferrocene core further in the presence of TBA chloride. It is established that SWV is an effective means of probing EC mechanistic processes [17]. It is known that an EC mechanism has the effect of lowering the peak current and shifting the apparent potential for reversible and quasi-reversible redox couples. The peak current decreases because the chemical process consumes the electrochemically produced species so that it is unavailable for re-reduction during the experiment. Consequently, a substantial fraction of the reverse current is unrealised and does not contribute to the net current. The lack of a reverse wave means that for an oxidation process, the EC mechanism should cause the potential to shift to less positive values.

We therefore measured the square wave voltammograms of **G0(Fc)** and **G1(Fc)** in the presence of TBA chloride. As expected for the onset of an EC mechanistic process the peak potential shifted cathodically (Fig. 3). However, it was particularly noteworthy that the addition of 4.5 equiv. of chloride caused a larger shift in potential for **G0(Fc)** than for **G1(Fc)**. This indicates that the chloride anion has a greater effect on the electrochemistry of the non-encapsulated ferrocene unit, indicating that the accessibility of the ferrocene group plays a key role in controlling its interaction with an anionic guest.

It is interesting to note that the difference in redox shifts of **G0(Fc)** and **G1(Fc)** induced by Cl^- directly parallels the difference in reaction yields for their synthesis (74 and 51%, respectively). This indicates that a similar explanation underlies both of these effects. As described above, this can probably be ascribed to the relative steric accessibility of the ferrocene core—both decreasing the ability of chloride anions to bind and decreasing the ability of the dendritic focal point to react with the encapsulated ferrocene.

In addition to the effect on peak potential, the addition of chloride anions also decreased the peak current observed by SWV (Fig. 4). As explained above, this is a consequence of the chemical process consuming the electrochemically produced species [17]. The peak current of **G0(Fc)** was more perturbed than that of **G1(Fc)** by chloride anions, again indicating its greater accessibility to the guest.

Previously [13], we have argued for this series of dendrimers that the dendritic shell shields the core from the polar solvent/electrolyte, generating a dendritic effect on the redox potentials. The fact that the cathodic shift and effect on peak current induced by chloride anions is smaller for **G1(Fc)** than for **G0(Fc)** is in agreement with our argument that the accessibility of the core to ionic species decreases with increasing functionalisation—affecting the observed redox potential. The increased difficulty of localising charge inside dendritic structures has also been indicated by our recent studies of cation binding dendritic crown ethers [18].

The interaction of **G0(Fc)** and **G1(Fc)** with bromide anions was then investigated electrochemically. This study is complicated by the bromide oxidation process, which occurs at potentials just higher than the oxidation of the ferrocene unit. It was not possible to follow anion binding via cyclic voltammetry because the ferrocene redox process became a shoulder on the oxidation wave corresponding to Br^-. SWV, however, provided a useful means for probing the apparent potential of the

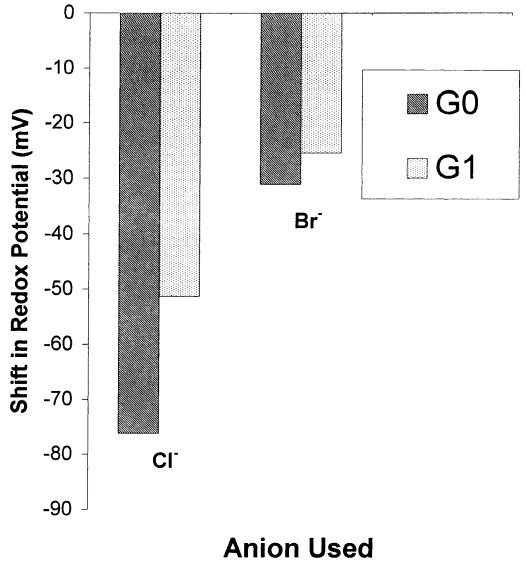

Fig. 3. Shift in redox potential of **G0(Fc)** and **G1(Fc)** induced by the addition of 4.5 equiv. of TBA chloride or bromide (*solvent:* CH_3CN).

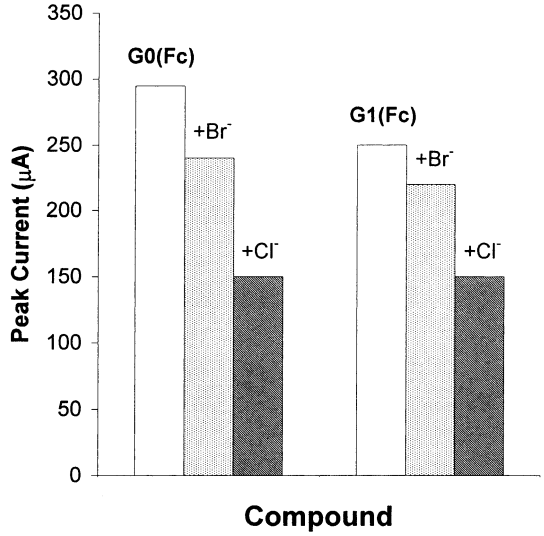

Fig. 4. Peak current (μA) observed using SWV for **G0(Fc)** and **G1(Fc)** (2 mM) without and with the presence of 4.5 equiv. of TBA halide salts (*solvent:* CH_3CN).

redox couple, as a clear peak maximum could be observed. Once again, there was a cathodic shift in the potential, but this was smaller than that induced by chloride anions (Fig. 3). This indicates a weaker interaction between bromide anions and the oxidised ferrocenium unit. Furthermore, the peak current decreased—although not as significantly as on the addition of chloride anions (Fig. 4). Again, **G0(Fc)** was more perturbed by the addition of an anionic guest than **G1(Fc)**—indicating the role played by the dendritic branches in screening the redox active binding site.

Attempts were made to investigate the binding of TBA iodide electrochemically, but the redox process corresponding to iodide oxidation overlaps with the ferrocene redox wave, and therefore anion binding could not be monitored in any meaningful way.

For **G0(Fc)** and **G1(Fc)**, the attachment of dendritic branching hinders the ability to sense halide anions. In other words, a negative dendritic effect is observed. The dendroclefts reported previously by Smith and Diederich also suffered from a decreased response at higher dendritic generation [3]. In order to design systems in the future that will exhibit enhanced sensing properties at the core of a dendrimer, it will be important to have binding sites which are well-defined and remain open at higher generations so that guest binding itself is not inhibited. Furthermore, the coupling mechanism between the guest species and the sensor unit should preferably be enhanced within the dendritic environment (this could be achieved for example through dendritic control of micropolarity).

3. Conclusions

This paper builds upon our recent publication by considering further the effects of encapsulation on a redox-active ferrocene moiety [13]. Sterically hindered ferrocenoyl amides such as **G0(Fc)** and **G1(Fc)** are poor halide anion receptors when uncharged. However, on oxidation, electrostatic interactions between the ferrocenium ion and halide anions are switched on, giving rise to an EC mechanistic response. SWV was used to provide a sensory response to the anion binding process. It was illustrated that more charge dense anions have a greater effect on the potential ($Cl^- > Br^-$), and furthermore, that **G0(Fc)** was more electrochemically perturbed by the presence of anionic guests than **G1(Fc)**, presumably because of the greater ability of anions to penetrate to the binding site of the smaller molecule. These results have implications for the design of sensors based on encapsulated binding sites.

4. Experimental

4.1. General methods

All ^1H and ^{13}C NMR experiments were carried out either on a JEOL-E270 (270 MHz) or a Bruker AMX 500 (500 MHz) instrument, according to requirements and referenced to residual solvent. The electrochemical studies were carried out on an EG & G Princeton Applied Research potentiostat/galvanostat model 273 with a standard three electrode configuration, consisting of glassy carbon working electrode, platinum counter electrode and an Ag/AgCl reference electrode. Compounds **G0(Fc)** and **G1(Fc)** were synthesised according to our previously published methods [13].

4.2. NMR titrations

Solutions (in $CDCl_3$) were made in which the receptor (2 mM) was mixed with increasing amounts of TBA halide salt (concentrations up to 25 mM) and the ^1H NMR spectrum of the receptor was monitored, in particular the chemical shift of the N–H protons.

4.3. Electrochemical titrations

Each compound (2 mM) was studied in CH_3CN with a supporting electrolyte of TBA tetrafluoroborate (0.1 M) using cyclic voltammetry with scan rates of 50–500 mV s^{-1}. TBA halide anion was added up to a concentration of approximately 10 mM. Each mixture was also investigated using SWV at a range of different frequencies.

Acknowledgements

We gratefully acknowledge financial support from EPSRC and Cytec Engineered Materials in the form of a CASE award (to D.L.S.).

References

[1] (a) F. Zeng, S.C. Zimmerman, Chem. Rev. 97 (1997) 1681;
(b) V.V. Narayanan, G.R. Newkome, Top. Curr. Chem. 197 (1998) 19;
(c) D.K. Smith, F. Diederich, Top. Curr. Chem. 210 (2000) 183;
(d) S.C. Zimmerman, L.J. Lawless, Top. Curr. Chem. 217 (2001) 95.
[2] (a) J.P. Collman, L. Fu, A. Zingg, F. Diederich, Chem. Commun. (1997) 193;
(b) P. Weyermann, F. Diederich, J. Chem. Soc., Perkin Trans. 1 (2000) 4231;
(c) A. Zingg, B. Felber, V. Gramlich, L. Fu, J.P. Collman, F. Diederich, Helv. Chim. Acta 85 (2002) 333;
(d) D.-L. Jiang, T. Aida, Chem. Commun. (1996) 1523.

[3] (a) D.K. Smith, F. Diederich, Chem. Commun. (1998) 2501;
(b) D.K. Smith, A. Zingg, F. Diederich, Helv. Chim. Acta 82 (1999) 1225.
[4] (a) S. Mattei, P. Seiler, F. Diederich, V. Gramlich, Helv. Chim. Acta 78 (1995) 1904;
(b) P. Wallimann, P. Seiler, F. Diederich, Helv. Chim. Acta 79 (1996) 779;
(c) P. Wallimann, S. Mattei, P. Seiler, F. Diederich, Helv. Chim. Acta 80 (1997) 2368;
(d) S. Mattei, P. Wallimann, B. Kenda, W. Amrein, F. Diederich, Helv. Chim. Acta 80 (1997) 2391;
(e) T. Habicher, F. Diederich, V. Gramlich, Helv. Chim. Acta 82 (1999) 1066;
(f) B. Kenda, F. Diederich, Angew. Chem., Int. Ed. 37 (1998) 3154.
[5] (a) J.-F. Nierengarten, L. Oswald, J.-F. Eckert, J.-F. Nicoud, N. Armaroli, Tetrahedron Lett. 40 (1999) 5681;
(b) M. Numata, A. Ikeda, C. Fukuhara, S. Shinkai, Tetrahedron Lett. 40 (1999) 6945;
(c) J.-F. Eckert, D. Byrne, J.-F. Nicoud, L. Oswald, J.-F. Nierengarten, M. Numata, A. Ikeda, S. Shinkai, N. Armaroli, New J. Chem. 24 (2000) 749.
[6] (a) G.R. Newkome, L.A. Godínez, C.N. Moorefield, Chem. Commun. (1998) 1821;
(b) J. Suh, S.S. Hah, S.H. Lee, Bioorg. Chem. 25 (1997) 63;
(c) F. Ortega-Caballero, J.J. Giménez-Martínez, L. García-Fuentes, E. Ortiz-Salmerón, F. Santoyo-González, A. Vargas-Berenguel, J. Org. Chem. 66 (2001) 7786;
(d) A. Vargas-Berenguel, F. Ortega-Caballero, F. Santoyo-González, J.J. García-Lopez, J.J. Giménez-Martínez, L. García-Fuentes, E. Ortiz-Salmerón, Chem. Eur. J. 8 (2002) 812.
[7] (a) A. Bähr, B. Felber, K. Schneider, F. Diederich, Helv. Chim. Acta 83 (2000) 1346;
(b) L.Z. Gong, Q.S. Hu, L. Pu, J. Org. Chem. 66 (2001) 2358;
(c) V.J. Pugh, Q.S. Hu, X.B. Zuo, F.D. Lewis, L. Pu, J. Org. Chem. 66 (2001) 6136.
[8] (a) G.R. Newkome, B.D. Woosley, E. He, C.N. Moorefield, R. Güther, G.R. Baker, G.H. Escamilla, J. Merrill, H. Luftmann, Chem. Commun. (1996) 2737;
(b) S.C. Zimmerman, Y. Wang, P. Bharathi, J.S. Moore, J. Am. Chem. Soc. 120 (1998) 2172;
(c) Y. Wang, F. Zeng, S.C. Zimmerman, Tetrahedron Lett. 38 (1997) 5459;
(d) D.K. Smith, Chem. Commun. (1999) 1685;
(e) G.M. Dykes, L.J. Brierley, D.K. Smith, P.T. McGrail, G.J. Seeley, Chem. Eur. J. 7 (2001) 4730.
[9] (a) A. Bianchi, K. Bowman-James, E. Garcia-España (Eds.), Supramolecular Chemistry of Anions, Wiley–VCH, New York, 1997;
(b) P.D. Beer, P.A. Gale, Angew. Chem., Int. Ed. 40 (2001) 486;
(c) P.A. Gale, Coord. Chem. Rev. 213 (2001) 79;
(d) P.A. Gale, Coord. Chem. Rev. 199 (2000) 181.
[10] H. Stephan, H. Spies, B. Johannsen, L. Klein, F. Vögtle, Chem. Commun. (1999) 1875.
[11] (a) C. Valério, J.-L. Fillaut, J. Ruiz, J. Guittard, J.-C. Blais, D. Astruc, J. Am. Chem. Soc. 119 (1997) 2588;
(b) C. Valério, E. Alonso, J. Ruiz, J.-C. Blais, D. Astruc, Angew. Chem., Int. Ed. 38 (1999) 1747;
(c) C.M. Casado, I. Cuadrado, B. Alonso, M. Moran, J. Losada, J. Electroanal. Chem. 463 (1999) 87.
[12] A.W. Kleij, R. van de Coevering, R.J.M.K. Gebbink, A.M. Noordman, A.L. Spek, G. van Koten, Chem. Eur. J. 7 (2001) 181.
[13] D.L. Stone, D.K. Smith, P.T. McGrail, J. Am. Chem. Soc. 124 (2002) 856.
[14] (a) C.M. Cardona, T.D. McCarley, A.E. Kaifer, J. Org. Chem. 65 (2000) 1857;
(b) P.R. Ashton, V. Balzani, M. Clemente-Leon, B. Colonna, A. Credi, N. Jayaraman, F.M. Raymo, J.F. Stoddart, M. Venturi, Chem. Eur. J. 8 (2002) 673.
[15] (a) P.D. Beer, Z. Chen, A.J. Goulden, A.R. Graydon, S.E. Stokes, T. Wear, J. Chem. Soc., Chem. Commun. (1993) 1834;
(b) Z. Chen, A.R. Graydon, P.D. Beer, J. Chem. Soc., Faraday Trans. 92 (1996) 97;
(c) P.D. Beer, A.R. Graydon, A.O.M. Johnson, D.K. Smith, Inorg. Chem. 36 (1997) 2112;
(d) M. Shere, J.L. Sessler, A. Gebauer, V. Lynch, Chem. Commun. (1998) 85;
(e) P.A. Gale, M.B. Hursthouse, M.E. Light, J.L. Sessler, C.N. Warriner, R.S. Zimmerman, Tetrahedron Lett. 42 (2001) 6759;
(f) O. Reynes, F. Maillard, J.-C. Moutet, G. Royal, E. Saint-Aman, G. Stanciu, J.-P. Dutasta, I. Gosse, J.-C. Mulatier, J. Organomet. Chem. 637–639 (2001) 356;
(g) B. Tomapatanaget, T. Tuntulani, Tetrahedron Lett. 42 (2001) 8105.
[16] S.M. Grayson, J.M.J. Fréchet, Chem. Rev. 101 (2001) 3819.
[17] (a) J.J. O'Dea, J. Osteryoung, R.A. Osteryoung, Anal. Chem. 53 (1981) 695;
(b) A.B. Miles, R.G. Compton, J. Phys. Chem. B 104 (2000) 5331;
(c) V. Mirceski, J. Electroanal. Chem. 508 (2001) 138.
[18] G.M. Dykes, D.K. Smith, G.J. Seeley, Angew. Chem., Int. Ed. 41 (2002) 3254.