A novel redox-responsive pillar[6]arene-based inclusion complex with a ferrocenium guest

ARTICLE *in* CHEMICAL COMMUNICATIONS · APRIL 2013

Impact Factor: 6.83 · DOI: 10.1039/c3cc41903g · Source: PubMed

ChemComm

RSC Publishing

COMMUNICATION

View Article Online
View Journal | View Issue

Cite this: *Chem. Commun.*, 2013, **49**, 5085

Received 14th March 2013,
Accepted 15th April 2013

DOI: 10.1039/c3cc41903g

www.rsc.org/chemcomm

A novel redox-responsive pillar[6]arene-based inclusion complex with a ferrocenium guest†

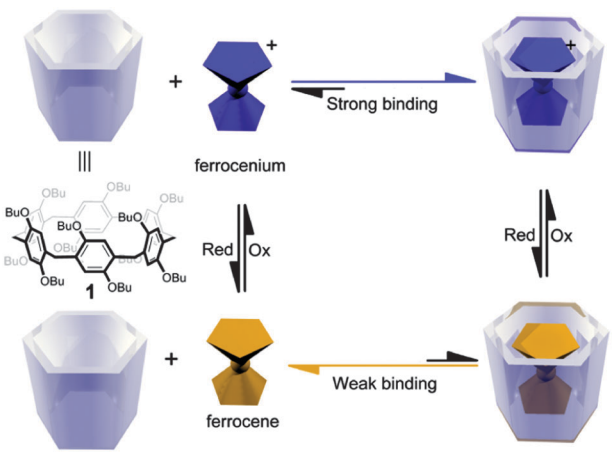
Wei Xia,[a] Xiao-Yu Hu,[a] Yong Chen,[b] Chen Lin*[a] and Leyong Wang*[a]

A novel and highly stable inclusion complex was formed between per-butylated pillar[6]arene and a ferrocenium cation, while the reduced form ferrocene only showed extremely weak binding affinity with per-butylated pillar[6]arene in organic solvents.

The application of redox chemistry as a powerful tool to control the host–guest complexation has attracted tremendous interest in the field of supramolecular chemistry and materials science.[1] The redox conversions of binding species, which often result in significant changes in charge and electron distribution, can obviously affect the binding affinity of host–guest complexation.[1a] Ferrocene (**Fc**), one of the most widely used redox species that can be oxidized into ferrocenium ($\mathbf{Fc}^+$) by chemicals or electrochemistry, has a unique structure and can bind with different kinds of macrocyclic hosts such as cyclodextrin,[2] cucurbituril,[3] and calixarene.[4] For example, much research has indicated that **Fc** could form strong inclusion complexes with cyclodextrin in the aqueous phase, while a significant loss of the binding affinity appeared after **Fc** was oxidized into $\mathbf{Fc}^+$.[1a] Recently, based on this electrochemical-controllable binding property, a lot of ferrocene-based redox-responsive supramolecular structures have been developed.[5]

Pillar[*n*]arenes (n = 5, 6), as a new class of supramolecular hosts,[6] have received considerable attention, and much compelling work has been achieved based on pillararenes, such as inclusion complexes,[7] supramolecular polymers,[8] and functional vesicles.[9] Although various kinds of guests for the formation of pillar[5]arene-based inclusion complexes have been reported,[10] suitable guests which could form stable inclusion complexes with pillar[6]arenes are still limited[8a,9d,11] and their binding constants are usually less than 1×10^4 M^{-1} except for the ultra-stable complexation between paraquat and a water-soluble pillar[6]arene reported by Huang *et al.*[9a] In addition, research on the development of novel guests which are able to form stimuli-responsive pillar[6]arene-based inclusion complexes has captured much more attention. For example, Huang and coworkers reported photo-responsive and pH-responsive pillar[6]arene host–guest systems.[9a,b,d] However, to the best of our knowledge, redox-controllable pillar[6]arene-based inclusion complexes have never been achieved, and particularly the one that possesses both structural stability and redox-response still remains a big challenge. Herein, we report a highly stable redox-responsive 1 : 1 inclusion complex of per-butylated pillar[6]arene (**1**) with $\mathbf{Fc}^+$ (Scheme 1) as well as its analogue cobaltocenium ($\mathbf{Cob}^+$) guest ion. Compared with the reduced form **Fc** that shows extremely weak binding affinity, its oxidized form, the $\mathbf{Fc}^+$ ion, shows much stronger binding ability with **1**, due to the efficient electron transfer from the electron-rich cavity of pillar[6]arene to $\mathbf{Fc}^+$. As a result, a stable redox-responsive pillar[6]arene-based inclusion complex could be achieved.

The interaction between **Fc** and **1** was initially investigated using ^{1}H NMR titration experiments (see ESI,† Fig. S5–S7). Titration spectra suggest a fast chemical exchange process on the NMR time



Scheme 1 Cartoon representation of the formation of a highly stable redox-responsive inclusion complex.

[a] *Key Laboratory of Mesoscopic Chemistry of MOE, Center for Multimolecular Chemistry, School of Chemistry and Chemical Engineering, Nanjing University, Nanjing 210093, China. E-mail: linchen@nju.edu.cn, lywang@nju.edu.cn; Fax: +86 025 83597090; Tel: +86 025 83592529*

[b] *Department of Chemistry, State Key Laboratory of Elemento-Organic Chemistry, Nankai University, Tianjin 300071, China*

† Electronic supplementary information (ESI) available: Synthesis and characterization data; determination of the association constants; fluorescence spectra; cyclic voltammograms and theoretical study. See DOI: 10.1039/c3cc41903g

scale, and the chemical shift of phenyl protons on **1** shows only moderate downfield shifts ($\Delta\delta$ = 0.30 ppm) upon the addition of 60.0 equiv. of **Fc**. Based on the 1 : 1 binding stoichiometry of pillar[6]arene **1** with **Fc**, the binding constant of **1** with **Fc** was determined to be (18 ± 0.5) M^{-1} ($CDCl_3$–CD_3CN = 5/1, v/v), which, in contrast to the highly stable complexes of **Fc** with β-cyclodextrin and cucurbit[7]uril in the aqueous phase,[2a,3a] respectively, is much weaker without the contribution of the hydrophobic effect.

Considering the electron-rich cavity of pillararenes, it is reasonable that pillar[6]arene may form a more stable complex with cationic $\mathbf{Fc}^+$ similar to other reported positive charged guests.[9d,11] Consequently, $\mathbf{Fc}^+$ was expected to be a suitable guest to bind pillar[6]arene **1** more strongly, while **Fc** has exhibited extremely weak binding affinity. With respect to the paramagnetic $\mathbf{Fc}^+$, it is difficult to study its host–guest complexation using NMR techniques. In this case, the diamagnetic $\mathbf{Cob}^+$ ion, which has been demonstrated to have a similar binding ability to $\mathbf{Fc}^+$ in the research of cyclodextrin,[12] was chosen as an analogue of $\mathbf{Fc}^+$. Therefore, the complexation of cobaltocenium hexafluorophosphate ($\mathbf{Cob}^+\mathbf{PF_6}^-$) and **1** was investigated using ^{1}H NMR titration experiments. Different from the fast chemical exchange of **Fc** with **1**, the host–guest complexation of $\mathbf{Cob}^+$ with **1** exhibited slow chemical exchange on the NMR time scale (Fig. 1), indicating their strong binding ability. As shown in Fig. 1, the intensity of phenyl protons (H_A) of **1** exhibited obvious decrease upon addition of $\mathbf{Cob}^+\mathbf{PF_6}^-$. Meanwhile, two new signals (H_A' and H_C', δ = 7.10 and 3.66 ppm, respectively) with increasing intensity were observed due to the possibly newly formed inclusion complex, and they did not change anymore after the addition of 1.0 equiv. $\mathbf{Cob}^+\mathbf{PF_6}^-$. In addition, the cyclopentadienyl protons (H_C) from the free $\mathbf{Cob}^+$ were not observed until more than 1.0 equiv. $\mathbf{Cob}^+$ was added. The significant upfield shifts of phenyl protons of **1** ($\Delta\delta$ = 0.39 ppm, H_A to H_A') and the cyclopentadienyl protons of $\mathbf{Cob}^+$ ($\Delta\delta$ = −2.12 ppm, H_C to H_C') were due to the shielding effect of the electron-rich cavities of pillar[6]arene for $\mathbf{Cob}^+$. Furthermore, control experiments showed that the replacement of **1** by its building subunit 1,4-dibutoxybenzene could not induce any chemical shift (see ESI,† Fig. S24). All these results strongly suggested the formation of a highly stable 1 : 1 inclusion complex of pillar[6]arene **1** and $\mathbf{Cob}^+$, and their binding constant was further determined to be (3.7 ± 1.0) × 10^4 M^{-1} ($CDCl_3$–DMSO-d_6 = 5/1, v/v, see ESI†). Moreover, further evidence of a 1 : 1 host–guest complex was obtained using HRMS (see ESI,† Fig. S23). Based on the similar properties of $\mathbf{Cob}^+$ to those of $\mathbf{Fc}^+$, we supposed that in our case $\mathbf{Fc}^+$ could also form a highly stable 1 : 1 inclusion complex with pillar[6]arene **1** in organic solvents, which is not only opposite from β-cyclodextrin, which prefers to bind the reduced form **Fc** strongly in aqueous solution,[2a] but also distinct from cucurbit[7]uril, which has strong binding ability with both **Fc** and $\mathbf{Fc}^+$.[3a,13]

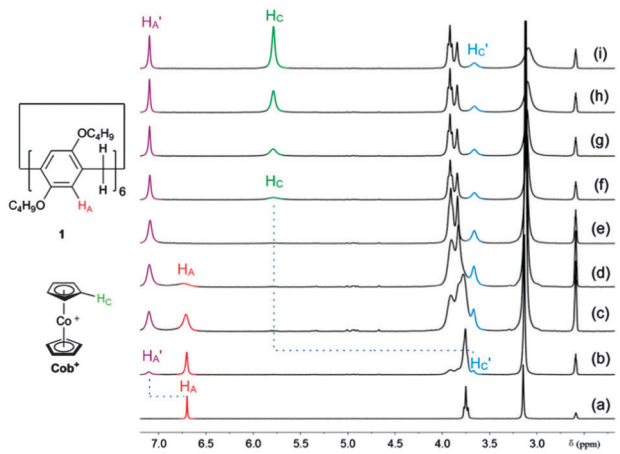


Fig. 1 Partial ^{1}H NMR spectra (300 MHz, 298 K, $CDCl_3$–DMSO-d_6 = 5/1, v/v) of **1** (2.0 mM) in the presence of increasing concentrations of $\mathbf{Cob}^+\mathbf{PF_6}^-$ (mM): (a) 0.00, (b) 0.40, (c) 1.0, (d) 1.4, (e) 2.0, (f) 3.0, (g) 4.0, (h) 6.0, (i) 8.0. H_A and H_C come from free host and free guest, respectively. H_A' and H_C' come from the corresponding complexing host and guest, respectively. The above mixed solvent system was employed to avoid overlapping of the signals. An additional NMR titration study in $CDCl_3$–CD_3CN (5/1, v/v) is also available in the ESI.†

In order to provide further evidence for the assumption that $\mathbf{Fc}^+$ could have similar binding affinity to $\mathbf{Cob}^+$ in our case, fluorescent titration experiments were carried out using a mono-carbazole-functionalized pillar[6]arene (**3**), in which a fluorescent carbazole group was introduced into the pillar[6]arene backbone (see ESI,† Schemes S1 and S2). Fluorescent titration experiments were performed by measuring the emission of the carbazole group on **3** with increasing amounts of $\mathbf{Fc}^+\mathbf{PF_6}^-$ or $\mathbf{Cob}^+\mathbf{PF_6}^-$, and the binding constants of **3** with $\mathbf{Fc}^+$ and $\mathbf{Cob}^+$ were determined to be (2.0 ± 0.1) × 10^4 M^{-1} and (3.1 ± 0.1) × 10^4 M^{-1} ($CHCl_3$–CH_3CN = 5/1, v/v), respectively (see ESI,† Fig. S12–S15), which confirmed that both $\mathbf{Fc}^+$ and $\mathbf{Cob}^+$ bind pillar[6]arene strongly to form a stable inclusion complex.

A 2D NOESY experiment further confirmed that $\mathbf{Cob}^+$ was included in the cavity of **1** (see ESI,† Fig. S16). What is more, an optimized structure of $[\mathbf{Cob}\subset\mathbf{1}]^+$ was obtained using the density functional theory (DFT) calculation (see ESI,† Fig. S25). The optimized geometry indicated that $\mathbf{Cob}^+$ was located in the center of the electron-rich cavity of pillar[6]arene. Furthermore, a comparative study of per-butylated pillar[5]arene (**PBP[5]**) with **Fc** or $\mathbf{Cob}^+\mathbf{PF_6}^-$ was carried out using ^{1}H NMR titration experiments (see ESI,† Fig. S26 and S27), which indicated that both **Fc** and $\mathbf{Cob}^+\mathbf{PF_6}^-$ exhibited no complexation with **PBP[5]**.

$\mathbf{Fc}^+$ is usually quite unstable in polar organic solvents and gradually decomposes in the presence of oxygen.[14] During our research, we found that $\mathbf{Fc}^+\mathbf{PF_6}^-$ decomposed very quickly in $CHCl_3$–CH_3CN (5/1, v/v) solution when it was exposed to air, whereas, with an excess amount of **1**, the stability of $\mathbf{Fc}^+$ could be dramatically improved, which offers the potential for much wider applications of $\mathbf{Fc}^+$ in organic solvents. Fig. 2 shows the obvious difference in the

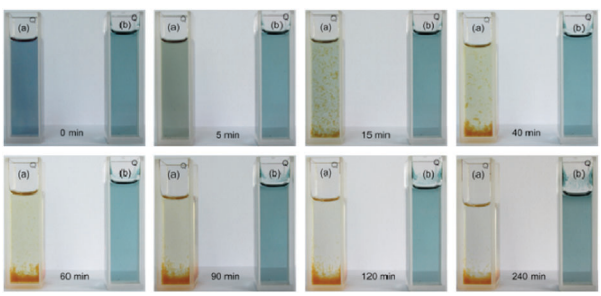


Fig. 2 Stability test of $\mathbf{Fc}^+$ in the absence (a) and presence (b) of **1** in $CHCl_3$–CH_3CN (5/1, v/v) exposed to air. An excess amount of **1** (6.0 equiv.) was used in this test (the volume of the solution gradually decreased due to evaporation).

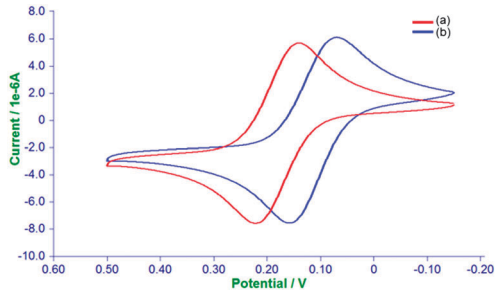


Fig. 3 Cyclic voltammograms of **Fc** (0.5 mM) in mixed solutions ($CHCl_3$–CH_3CN = 5/1, v/v, containing 0.1 M $TBAClO_4$) in the absence (a) and the presence (b) of **1**. Scan rate = 50 mV s^{-1}. An excess amount of **1** (16.0 mM) was used in this test.

stability of Fc^+ solution exposed to air in the absence and presence of **1**. The blue-colored solution of pure $Fc^+PF_6^-$ turned colorless and a yellow precipitate was formed within less than 30 min. However, the $Fc^+PF_6^-$ solution in the presence of **1** remained unchanged for hours (for a quantitative study, see ESI,† Fig. S19). This obvious improvement of stability is probably attributed to the formation of a stable inclusion complex between Fc^+ and **1**, which might prevent Fc^+ from the attack of dissolved oxygen in solution.

More importantly, the resulting inclusion complex between Fc^+ and **1** was then studied using cyclic voltammetry experiments where the conversion of **Fc**/Fc^+ in the absence and the presence of **1** was performed using electrochemistry, respectively (Fig. 3 and Fig. S17, ESI†). Both of the cyclic voltammograms were quasi-reversible with nearly equal i_{pa} and i_{pc}, in which the potential difference ΔE_p was around 0.080 V. The cathodic shift of $E^{0\prime}$ suggested that the oxidized form Fc^+ has stronger binding ability with **1** than that of **Fc**[3a,15] and the inclusion complex formed between **1** and Fc^+ exhibited a redox-response.

In summary, we have demonstrated that per-butylated pillar[6]arene **1** could form a novel 1 : 1 stable inclusion complex with Fc^+ as well as Cob^+, while the reduced counterpart **Fc** showed extremely weak binding affinity. The binding properties of Fc^+/**Fc** with pillar[6]arene were quite different from those of Fc^+/**Fc** with cyclodextrin and cucurbituril derivatives that have been reported. Furthermore, pillar[6]arene **1** that binds Fc^+ strongly can dramatically improve the stability of Fc^+ in organic solvents due to the formation of the stable inclusion complex. More importantly, cyclic voltammetry studies indicated that the resulting inclusion complex of Fc^+ with **1** exhibited a good redox-response. Its application in supramolecular chemistry and materials science is now underway in our lab.

We gratefully thank the financial support from the National Basic Research Program of China (2013CB922101), National Natural Science Foundation of China (21202083, 20932004) and Natural Science Foundation of Jiangsu (BK2011551).

Notes and references

1 (*a*) A. E. Kaifer, *Acc. Chem. Res.*, 1998, **32**, 62–71; (*b*) J. H. R. Tucker and S. R. Collinson, *Chem. Soc. Rev.*, 2002, **31**, 147–156.
2 (*a*) R. Isnin, C. Salam and A. E. Kaifer, *J. Org. Chem.*, 1991, **56**, 35–41; (*b*) A. Harada and S. Takahashi, *J. Chem. Soc., Chem. Commun.*, 1984, 645–646; (*c*) T. Matsue, D. H. Evans, T. Osa and N. Kobayashi, *J. Am. Chem. Soc.*, 1985, **107**, 3411–3417; (*d*) Y. Liu, R.-Q. Zhong, H.-Y. Zhang and H.-B. Song, *Chem. Commun.*, 2005, 2211–2213.
3 (*a*) W. S. Jeon, K. Moon, S. H. Park, H. Chun, Y. H. Ko, J. Y. Lee, E. S. Lee, S. Samal, N. Selvapalam, M. V. Rekharsky, V. Sindelar, D. Sobransingh, Y. Inoue, A. E. Kaifer and K. Kim, *J. Am. Chem. Soc.*, 2005, **127**, 12984–12989; (*b*) M. V. Rekharsky, T. Mori, C. Yang, Y. H. Ko, N. Selvapalam, H. Kim, D. Sobransingh, A. E. Kaifer, S. Liu, L. Isaacs, W. Chen, S. Moghaddam, M. K. Gilson, K. Kim and Y. Inoue, *Proc. Natl. Acad. Sci. U. S. A.*, 2007, **104**, 20737–20742.
4 L. Zhang, A. Macias, T. Lu, J. I. Gordon, G. W. Gokel and A. E. Kaifer, *J. Chem. Soc., Chem. Commun.*, 1993, 1017–1019.
5 (*a*) M. Nakahata, Y. Takashima, H. Yamaguchi and A. Harada, *Nat. Commun.*, 2011, **2**, 511; (*b*) Q. Yan, J. Yuan, Z. Cai, Y. Xin, Y. Kang and Y. Yin, *J. Am. Chem. Soc.*, 2010, **132**, 9268–9270; (*c*) Y. Ahn, Y. Jang, N. Selvapalam, G. Yun and K. Kim, *Angew. Chem., Int. Ed.*, 2013, **52**, 3140–3144.
6 (*a*) P. J. Cragg and K. Sharma, *Chem. Soc. Rev.*, 2012, **41**, 597–607; (*b*) M. Xue, Y. Yang, X. Chi, Z. Zhang and F. Huang, *Acc. Chem. Res.*, 2012, **45**, 1294–1308; (*c*) T. Ogoshi, S. Kanai, S. Fujinami, T.-a. Yamagishi and Y. Nakamoto, *J. Am. Chem. Soc.*, 2008, **130**, 5022–5023; (*d*) C. Han, F. Ma, Z. Zhang, B. Xia, Y. Yu and F. Huang, *Org. Lett.*, 2010, **12**, 4360–4363.
7 (*a*) T. Ogoshi, Y. Nishida, T.-a. Yamagishi and Y. Nakamoto, *Macromolecules*, 2010, **43**, 3145–3147; (*b*) Z. Zhang, C. Han, G. Yu and F. Huang, *Chem. Sci.*, 2012, **3**, 3026–3031; (*c*) Q. P. Duan, W. Xia, X. Y. Hu, M. F. Ni, J. L. Jiang, C. Lin, Y. Pan and L. Y. Wang, *Chem. Commun.*, 2012, **48**, 8532–8534; (*d*) X.-Y. Hu, P. Y. Zhang, X. Wu, W. Xia, T. X. Xiao, J. L. Jiang, C. Lin and L. Y. Wang, *Polym. Chem.*, 2012, **3**, 3060–3063; (*e*) X.-Y. Hu, X. Wu, Q. Duan, T. Xiao, C. Lin and L. Wang, *Org. Lett.*, 2012, **14**, 4826–4829; (*f*) T. Ogoshi, T. Aoki, R. Shiga, R. Iizuka, S. Ueda, K. Demachi, D. Yamafuji, H. Kayama and T.-a. Yamagishi, *J. Am. Chem. Soc.*, 2012, **134**, 20322–20325; (*g*) C. Li, L. Zhao, J. Li, X. Ding, S. Chen, Q. Zhang, Y. Yu and X. Jia, *Chem. Commun.*, 2010, **46**, 9016–9018; (*h*) T. Ogoshi, D. Yamafuji, T. Aoki and T.-a. Yamagishi, *Chem. Commun.*, 2012, **48**, 6842–6844; (*i*) N. L. Strutt, R. S. Forgan, J. M. Spruell, Y. Y. Botros and J. F. Stoddart, *J. Am. Chem. Soc.*, 2011, **133**, 5668–5671.
8 (*a*) T. Ogoshi, H. Kayama, D. Yamafuji, T. Aoki and T.-a. Yamagishi, *Chem. Sci.*, 2012, **3**, 3221–3226; (*b*) N. L. Strutt, H. Zhang, M. A. Giesener, J. Lei and J. F. Stoddart, *Chem. Commun.*, 2012, **48**, 1647–1649; (*c*) Y. F. Guan, M. F. Ni, X.-Y. Hu, T. X. Xiao, S. H. Xiong, C. Lin and L. Y. Wang, *Chem. Commun.*, 2012, **48**, 8529–8531; (*d*) Z. Zhang, Y. Luo, J. Chen, S. Dong, Y. Yu, Z. Ma and F. Huang, *Angew. Chem., Int. Ed.*, 2011, **50**, 1397–1401.
9 (*a*) G. Yu, X. Zhou, Z. Zhang, C. Han, Z. Mao, C. Gao and F. Huang, *J. Am. Chem. Soc.*, 2012, **134**, 19489–19497; (*b*) G. Yu, M. Xue, Z. Zhang, J. Li, C. Han and F. Huang, *J. Am. Chem. Soc.*, 2012, **134**, 13248–13251; (*c*) Y. Yao, M. Xue, J. Chen, M. Zhang and F. Huang, *J. Am. Chem. Soc.*, 2012, **134**, 15712–15715; (*d*) G. Yu, C. Han, Z. Zhang, J. Chen, X. Yan, B. Zheng, S. Liu and F. Huang, *J. Am. Chem. Soc.*, 2012, **134**, 8711–8717.
10 (*a*) X. Shu, J. Fan, J. Li, X. Wang, W. Chen, X. Jia and C. Li, *Org. Biomol. Chem.*, 2012, **10**, 3393–3397; (*b*) C. Li, K. Han, J. Li, H. Zhang, J. Ma, X. Shu, Z. Chen, L. Weng and X. Jia, *Org. Lett.*, 2012, **14**, 42–45; (*c*) Y. Ma, X. Ji, F. Xiang, X. Chi, C. Han, J. He, Z. Abliz, W. Chen and F. Huang, *Chem. Commun.*, 2011, **47**, 12340–12342; (*d*) C. Han, G. Yu, B. Zheng and F. Huang, *Org. Lett.*, 2012, **14**, 1712–1715; (*e*) T. Ogoshi, M. Hashizume, T.-a. Yamagishi and Y. Nakamoto, *Chem. Commun.*, 2010, **46**, 3708–3710.
11 (*a*) C. Li, X. Shu, J. Li, J. Fan, Z. Chen, L. Weng and X. Jia, *Org. Lett.*, 2012, **14**, 4126–4129; (*b*) Y. Ma, X. Chi, X. Yan, J. Liu, Y. Yao, W. Chen, F. Huang and J.-L. Hou, *Org. Lett.*, 2012, **14**, 1532–1535; (*c*) T. Ogoshi, K. Kida and T. Yamagishi, *J. Am. Chem. Soc.*, 2012, **134**, 20146–20150.
12 (*a*) A. U. Moozyckine, J. L. Bookham, M. E. Deary and D. M. Davies, *J. Chem. Soc., Perkin Trans. 2*, 2001, 1858–1862; (*b*) Y. Wang, S. Mendoza and A. E. Kaifer, *Inorg. Chem.*, 1998, **37**, 317–320.
13 W. Ong and A. E. Kaifer, *Organometallics*, 2003, **22**, 4181–4183.
14 (*a*) G. Zotti, G. Schiavon, S. Zecchin and D. Favretto, *J. Electroanal. Chem.*, 1998, **456**, 217–221; (*b*) J. P. Hurvois and C. Moinet, *J. Organomet. Chem.*, 2005, **690**, 1829–1839.
15 S. Mendoza, E. Castaño, Y. Meas, L. A. Godínez and A. E. Kaifer, *Electroanalysis*, 2004, **16**, 1469–1477.