
**Supramolecular Chemistry**
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# Self-complementary Tetracationic Cyclophanes Containing 4,4'-Bipyridinium and 2,5-Dimethoxy-1,4-xylyl Subunits

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**To cite this Article** Srinivasan, Kannupal and Rajakumar, Perumal(2005) 'Self-complementary Tetracationic Cyclophanes Containing 4,4'-Bipyridinium and 2,5-Dimethoxy-1,4-xylyl Subunits', Supramolecular Chemistry, 17: 3, 215 — 219
**To link to this Article: DOI:** 10.1080/10610270412331315190
**URL:** http://dx.doi.org/10.1080/10610270412331315190

*Supramolecular Chemistry*, April–May 2005 Vol. 17 (3), pp. 215–219



# Self-complementary Tetracationic Cyclophanes Containing 4,4′-Bipyridinium and 2,5-Dimethoxy-1,4-xylyl Subunits

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*Received (in Southampton, UK) 18 July 2004; Accepted 15 September 2004*

**4,4′-Bipyridinium-based tetracationic cyclophanes containing a 2,5-dimethoxy-1,4-xylyl unit were synthesized by using either *m*-terphenyl building blocks or incorporating a 4-hydroxy benzyl spacer between the complementary subunits. The cyclophanes show weak intramolecular charge-transfer (CT) bands in the visible region and one of the cyclophanes formed a green-coloured CT complex with ferrocene with an association constant ($K_a$) of 6.3 $M^{-1}$. The electrochemical parameters obtained for the cyclophanes indicate that all the redox processes are reversible.**

*Keywords*: Self-complementary cyclophanes; 4,4′-Bipyridine; 2,5-Dimethoxy-1,4-xylyl; *m*-Terphenyl; Redox potentials



## INTRODUCTION

Cyclophanes containing self-complementary (donor–acceptor) subunits are capable of exhibiting novel intramolecular charge-transfer (CT) and π–π stacking interactions [1–3]. 4,4′-Bipyridinium-based tetracationic cyclophanes are used extensively to construct a number mechanically interlocked compounds such as rotaxanes and catenanes [4]. Introduction of electron-rich spacers to bridge the bipyridinium units would result in cyclophanes of a self-complementary nature. Cyclophanes with hydroquinone- [5], TTF- [6,7] or phenothiazine-based [8] spacers are prominent examples of such self-complementary cyclophanes. The 2,5-dimethoxy-1,4-xylyl unit, despite its strong electron-donating ability, has not yet been incorporated into 4,4′-bipyridinium-based cyclophanes. These cyclophanes would not only show intriguing CT interactions but also function as both *exo* and *endo* receptors simultaneously [5]. We report here two approaches for the synthesis of self-complementary cyclophanes containing dimethoxyxylyl and bipyridinium subunits along with a focus on their complexation and electrochemical behaviour.

## RESULTS AND DISCUSSION

Synthesis of 4,4′-bipyridinium-based cationic cyclophanes is usually accomplished by the quarternization of 4,4′-bipyridine with corresponding dibromides in a two-step or a single-step procedure. Reaction of one equivalent of 1,4-bis(bromomethyl)-2,5-dimethoxy benzene (**1**) with five equivalents of 4,4′-bipyridine in refluxing $CH_3CN$ afforded the dicationic precyclophane **2** as an orange solid in 93% yield, after counterion exchange and recrystallization from acetone/$H_2O$ (Scheme 1).

By heating one equivalent of the precyclophane **2** with a slight excess of an appropriate dibromide under high dilution conditions, the corresponding tetracationic cyclophanes could be synthesized. Thus, the precyclophane **2** was heated under reflux with a slight excess of the dibromide **1** in $CH_3CN$. The resulting orange-coloured material was purified by column chromatography and repeated recrystallization. Even though the material was chromatographically homogeneous and $^1H$ and $^{13}C$ NMR spectra indicated its structure as **3**, careful analysis of its MALDI-TOF mass spectrum revealed that along with the (1 + 1) macrocycle **3**, other oligomers [(2 + 2) and (3 + 3) macrocycles] were present as inseparable components (Scheme 2).

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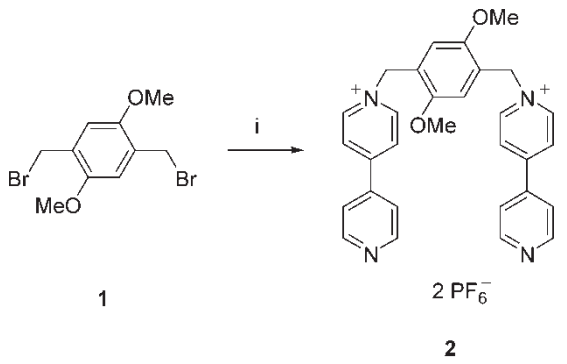
ISSN 1061-0278 print/ISSN 1029-0478 online © 2005 Taylor & Francis Group Ltd
DOI: 10.1080/10610270412331315190



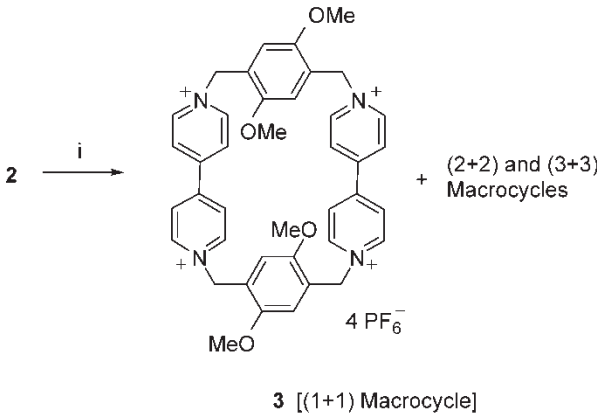

1 2

SCHEME 1 Reagents and conditions: (i) 4,4′-bipyridine (5 equiv.), $CH_3CN$, reflux, 12 h, then $NH_4PF_6$, $H_2O$, 93%.

Such oligomerization could be avoided by either using large and angular dibromides, such as *m*-terphenyl dibromides, or incorporating a spacer, such as a 4-hydroxy benzyl unit between the dimethoxyxylyl and bipyridinium subunits.

Incorporation of *m*-terphenyl building blocks into these kinds of cyclophanes would make the cyclophanes have non-collapsible rigid cavities with intra-annular functionality [9–13]. In addition, it would improve the yield of the cyclophanes without the use of any templates [13]. With these ideas in mind, the precyclophane **2** was heated under reflux with a slight excess of each of the *m*-terphenyl dibromides **4a–d** [14] in $CH_3CN$ under high dilution conditions to afford the tetracationic cyclophanes **5a–d** in 12–32% yields after column chromatography and counterion exchange (Scheme 3). The structures of the cyclophanes **5a–d** were confirmed by spectroscopic and analytical data.

In another approach, an extended dibromide **6** containing 4-hydroxybenzyl spacer was synthesized as reported earlier by our group [15]. As the dibromide is large enough, the target tetracationic cyclophane **7** could be obtained in a one-pot synthesis [13]. Thus, heating an equimolar mixture of the dibromide **6** and 4,4′-bipyridine in $CH_3CN$ under reflux and under high dilution conditions afforded the cyclophane **7** in 25% yield, after chromatography and counterion exchange (Scheme 4).




3 [(1+1) Macrocycle]

SCHEME 2 Reagents and conditions: (i) **1**, $CH_3CN$, reflux, 48 h, then $NH_4PF_6$, $H_2O$ (overall yield: 4%).

All the cyclophanes were orange in the solid state but when dissolved in $CH_3CN$, the solutions turned yellow. They showed weak intramolecular CT bands in the region 428–450 nm in $CH_3CN$ with extinction coefficients ($\varepsilon$) ranging from 40 to 128 $M^{-1}cm^{-1}$. When mixing an equimolar solution of **7** with ferrocene in $CH_3CN$, a green colour developed with a CT band centred around 610 nm with an association constant ($K_a$) of 6.3 $M^{-1}$ (determined by the Benesi-Hildebrand method [16]).

In cyclic voltammetry, all the cyclophanes exhibited two sets of redox waves corresponding to $[BIPY]^{4+}/[BIPY]^{2+}$ and $[BIPY]^{2+}/[BIPY]$ redox couples. The electrochemical parameters obtained for the cyclophanes are shown in Table I.

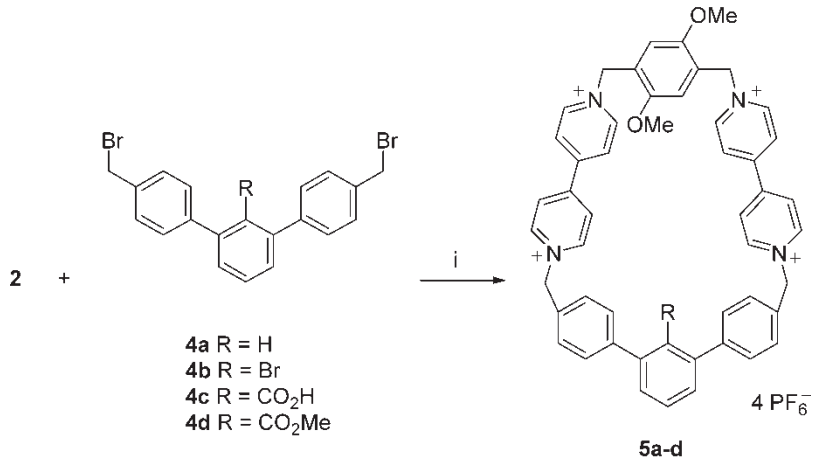
All the redox processes are reversible compared with ferrocene (for which we found the difference between anodic and cathodic peaks, $\Delta E_p = 74$ mV vs. Ag/AgCl, in DMSO at room temperature). The presence of either functional groups or non-identical spacers does not affect the reversibility. Because of the intramolecular CT interactions, the repulsion between the bipyridinium units is minimized in these cyclophanes. This kind of stabilization decreases the ability of the cyclophanes to accept electrons, resulting in high negative values of the redox potentials as compared to the Stoddart cyclophane [17].

Synthesis of other similar self-complementary cyclophanes and oxidation of these cyclophanes with ceric ammonium nitrate (CAN) are under investigation.

## EXPERIMENTAL

### General

Melting points were determined by using a Toshniwal melting point apparatus by the open capillary tube method and were uncorrected. Ultraviolet–visible spectra were recorded on a Shimadzu 260 spectrophotometer. IR spectra were recorded on a Shimadzu FTIR-8300 spectrophotometer. $^1H$ and $^{13}C$ NMR spectra were recorded on Jeol 500 MHz and Jeol 400 MHz spectrometers. FAB-MS spectra were recorded on a Jeol SX 102/DA-6000 mass spectrometer using a *m*-nitrobenzyl alcohol (NBA) matrix, MALDI-TOF MS spectra on a Voyager-DE PRO mass spectrometer using an α-cyano-4-hydroxycinnamic acid (CHCA) matrix, and EI-MS spectra on a Jeol DX-303 mass spectrometer. Elemental analyses were performed on a Perkin Elmer 240B instrument. Electrochemical studies were carried out on a CH Instruments electrochemical analyser.



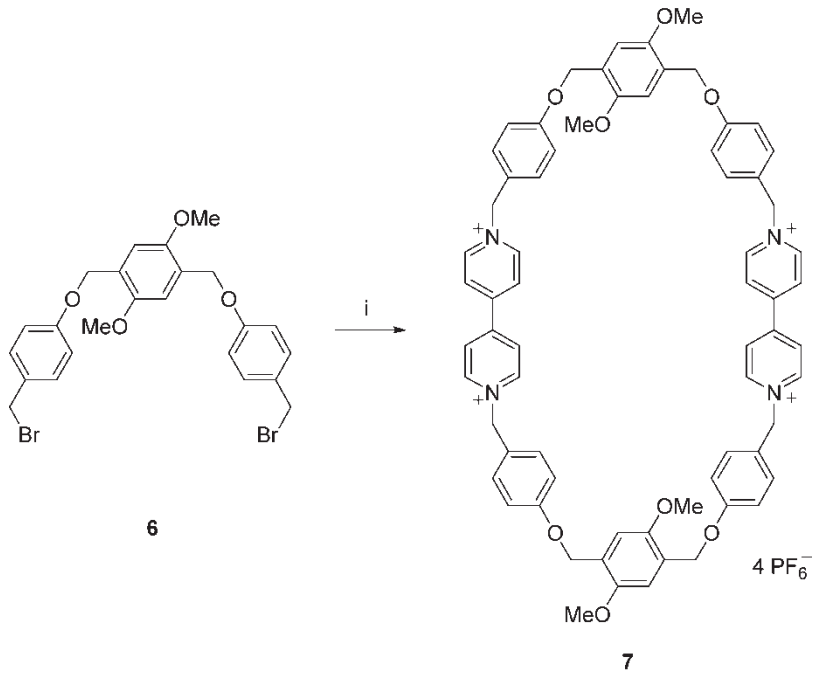

SCHEME 3 Reagents and conditions: (i) $CH_3CN$, reflux, 48 h, then $NH_4PF_6$, $H_2O$; afforded **5a** (12%), **5b** (28%), **5c** (16%) and **5d** (32%).

### Synthesis of the Dicationic Precyclophane 2

A solution of 1,4-bis(bromomethyl)-2,5-dimethoxybenzene (**1**) (0.81 g, 2.50 mmol) in dry $CH_3CN$ (25 mL) was added dropwise with stirring to a solution of 4,4′-bipyridine (1.95 g, 12.5 mmol) in refluxing dry $CH_3CN$ (20 mL) for 6 h under nitrogen. The reaction mixture was heated under reflux for a further 24 h and then cooled to room temperature. The precipitated solid was filtered and washed thoroughly with ether (20 mL). The solid was then dissolved in $H_2O$ (20 mL), solid $NH_4PF_6$ (1.00 g) was added and the mixture stirred for 30 min. The precipitate was filtered, washed thoroughly with $H_2O$ and then recrystallized from acetone/$H_2O$ (7:3) to give the dicationic precyclophane **2** as an orange solid. Yield 93%; mp $>$ 240°C (dec.); $^1$H NMR (500 MHz, DMSO-$d_6$) $\delta$ 3.83 (s, 6H), 5.79 (s, 4H), 7.49 (s, 2H), 7.98–7.99 (m, 4H), 8.55 (d, $J = 6.9$ Hz, 4H), 8.85–8.86 (m, 4H), 9.22 (d, $J = 6.9$ Hz, 4H); $^{13}$C NMR (125 MHz, DMSO-$d_6$) $\delta$ 56.8, 59.8, 115.9, 122.5, 124.3, 125.9, 141.4, 146.1, 151.5, 152.1, 153.3; $m/z$ (FAB-MS) 621 $[M - PF_6]^+$; Anal. Calcd for $C_{30}H_{28}F_{12}N_4O_2P_2$(%): C, 47.01; H, 3.68; N, 7.31. Found: C, 47.18; H, 3.59; N, 7.32.

### General Procedure for the Synthesis of Tetracationic Cyclophanes

The dicationic precyclophane **2** (0.35 mmol) was heated under reflux with a slight excess of the corresponding dibromide (0.40 mmol) in $CH_3CN$




SCHEME 4 Reagents and conditions: (i) 4,4′-bipyridine, $CH_3CN$, reflux, 48 h, then $NH_4PF_6$, $H_2O$, 25%.

TABLE I The electrochemical parameters obtained for the cyclophanes in DMSO at 25°C

| Cyclophane | $E^1_{1/2}$(mV) | $\Delta E^1_p$(mV) | $E^2_{1/2}$(mV) | $\Delta E^2_p$(mV) |
|---|---|---|---|---|
| **5a** | −365 | 82 | −747 | 86 |
| **5b** | −345 | 78 | −720 | 76 |
| **5c** | −362 | 84 | −844 | 73 |
| **5d** | −339 | 81 | −731 | 82 |
| **7** | −380 | 87 | −694 | 70 |

$E^1_{1/2}$ and $E^2_{1/2}$ are the averages of the cathodic and anodic peak potentials of the first and second redox processes, respectively. $\Delta E^1_p$ and $\Delta E^2_p$ are the differences between the cathodic and anodic peak potentials of the first and second redox processes, respectively.

(250 ml) for 48 h. The reaction mixture was cooled to room temperature and the solvent was reduced to one-fifth of its volume under reduced pressure. The precipitated solid was collected, dried and purified by column chromatography over $SiO_2$ using $CH_3OH/H_2O$/satd. aq. $NH_4Cl$ (6:3:1) as eluent. The cyclophane-containing fractions were combined and the solvent was evaporated under vacuum. The residue was dissolved/suspended in $H_2O$ (50 mL), solid $NH_4PF_4$ (0.25 g) was added, and the precipitate was filtered, washed thoroughly with $H_2O$ and dried to give the pure tetracationic cyclophane as an orange solid.



### *Tetracationic Cyclophane 5a*

From **2** (268 mg) and **4a** (166 mg), **5a** was obtained. Yield 12%; mp > 236°C (dec.); $^1$H NMR (500 MHz, DMSO-$d_6$) $\delta$ 3.90 (s, 6H), 5.88 (s, 4H), 6.03 (s, 4H), 7.55–7.74 (m, 14H), 8.65 (d, $J$ = 6.9 Hz, 4H), 8.75 (d, $J$ = 6.9 Hz, 4H), 9.47 (d, $J$ = 6.9 Hz, 4H), 9.55 (d, $J$ = 6.9 Hz, 4H); $^{13}$C NMR (125 MHz, DMSO-$d_6$) $\delta$ 57.2, 59.6, 63.7, 116.0, 124.6, 126.2, 127.3, 127.4, 128.3, 128.6, 129.5, 130.3, 134.6, 140.8, 141.9, 146.2, 146.5, 149.3, 149.4, 152.0; $m/z$ (FAB-MS) 1022 $[M-2PF_6]^+$; Anal. Calcd for $C_{50}H_{44}F_{24}N_4O_2P_4$(%): C, 45.75; H, 3.38; N, 4.27. Found: C, 45.57; H, 3.42; N, 4.33.

### *Tetracationic Cyclophane 5b*

From **2** (268 mg) and **4b** (198 mg), **5b** was obtained. Yield 28%; mp > 242°C (dec.); $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 3.88 (s, 6H), 5.90 (s, 4H), 6.10 (s, 4H), 7.48–7.70 (m, 13H), 8.63 (d, $J$ = 6.9 Hz, 4H), 8.88 (d, $J$ = 6.9 Hz, 4H), 9.42 (d, $J$ = 6.9 Hz, 4H), 9.58 (d, $J$ = 6.9 Hz, 4H); $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 57.0, 59.6, 62.9, 116.6, 124.2, 126.3, 127.8, 128.6, 128.8, 129.5, 130.1, 134.8, 141.0, 142.2, 146.3, 146.4, 147.9, 149.6, 149.8, 152.8; $m/z$ (FAB-MS) 1246 $[M-PF_6]^+$; Anal. Calcd for $C_{50}H_{43}BrF_{24}N_4O_2P_4$(%): C, 43.15; H, 3.11; N, 4.03. Found: C, 43.45; H, 3.16; N, 3.88.

### *Tetracationic Cyclophane 5c*

From **2** (268 mg) and **4c** (184 mg), **5c** was obtained. Yield 16%; mp > 270°C (dec.); IR (cm$^{-1}$) 3400 (O—H), 1712 (C═O); $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 3.88 (s, 6H), 5.78 (s, 4H), 5.98 (s, 4H), 7.36–7.62 (m, 13H), 8.45 (d, $J$ = 6.8 Hz, 4H), 8.58 (d, $J$ = 6.8 Hz, 4H), 9.38 (d, $J$ = 6.8 Hz, 4H), 9.50 (d, $J$ = 6.8 Hz, 4H); $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 56.9, 60.1, 63.3, 116.2, 124.6, 126.3, 127.5, 127.8, 128.3, 128.6, 129.4, 130.0, 135.0, 139.9, 142.0, 146.0, 146.3, 149.6, 149.8, 153.0, 171.8; $m/z$ (FAB-MS) 1211 $[M-PF_6]^+$; Anal. Calcd for $C_{51}H_{44}F_{24}N_4O_4P_4$(%): C, 45.15; H, 3.27; N, 4.13. Found: C, 45.45; H, 3.22; N, 4.01.

### *Tetracationic Cyclophane 5d*

From **2** (268 mg) and **4d** (190 mg), **5d** was obtained. Yield 32%; mp > 222°C (dec.); IR (cm$^{-1}$) 1726 (C═O); $^1$H NMR (500 MHz, DMSO-$d_6$) $\delta$ 3.27 (s, 3H), 3.85 (s, 6H), 5.76 (s, 4H), 5.92 (s, 4H), 7.39–7.66 (m, 13H), 8.51 (d, $J$ = 6.9 Hz, 4H), 8.66 (d, $J$ = 6.9 Hz, 4H), 9.36 (d, $J$ = 6.9 Hz, 4H), 9.42 (d, $J$ = 6.9 Hz, 4H); $^{13}$C NMR (125 MHz, DMSO-$d_6$) $\delta$ 52.5, 56.8, 59.8, 63.4, 115.8, 124.1, 126.0, 127.5, 127.8, 128.2, 128.6, 128.8, 129.6, 134.0, 140.1, 141.8, 146.3, 146.4, 149.0, 149.3, 151.8, 169.4; $m/z$ (FAB-MS) 1225 $[M-PF_6]^+$; Anal. Calcd for $C_{52}H_{46}F_{24}N_4O_4P_4$(%): C, 45.56; H, 3.38; N, 4.09. Found: C, 45.78; H, 3.30; N, 4.28.

### *Tetracationic Cyclophane 7*

A mixture of dibromide **6** (386 mg, 0.72 mmol) and 4,4′-bipyridine (112 mg, 0.72 mmol) was refluxed for 48 h in dry $CH_3CN$ (150 mL). The reaction mixture was then cooled to room temperature and the solvent was reduced to one-fifth of its volume under vacuum. The residue obtained was purified as outlined in the general procedure for the synthesis of tetracationic cyclophanes to give **7** as an orange solid. Yield 25%; mp 238°C (dec.); $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 3.73 (s, 12H), 4.68 (s, 8H), 5.80 (s, 8H), 7.02 (d, $J$ = 8.3 Hz, 8H), 7.19 (s, 4H), 7.38 (d, $J$ = 8.3 Hz, 8H), 8.60 (d, $J$ = 5.9 Hz, 8H), 9.31 (d, $J$ = 5.9 Hz, 8H); $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 56.1, 60.2, 68.4, 111.8, 114.4, 122.6, 126.8, 129.7, 133.9, 145.8, 149.3, 151.7 (two peaks); $m/z$ (FAB-MS) 1354 $[M-2PF_6]^+$; Anal. Calcd for $C_{68}H_{64}F_{24}N_4O_8P_4$(%): C, 49.65; H, 3.92; N, 3.41. Found: C, 49.48; H, 3.76; N, 3.54.

### Determination of Association Constant ($K_a$) by UV–Vis Spectroscopy (Benesi–Hildebrand Method)

An aliquot (3.5 mL) of a standard stock solution of cyclophane **7** (0.0052 M) in $CH_3CN$ was placed in a quartz cuvette. A known amount of ferrocene was added by incremental amounts (0.016, 0.032, 0.049, 0.067 and 0.086 M) and changes in the absorbance ($A$) at 610 nm were recorded. A plot of [concentration of **7**]/$A$ vs 1/[concentration of ferrocene] was linear.

From the slope and intercept of the plot, the values of $\varepsilon$ ($\varepsilon = \text{intercept}^{-1}$) and $K_a$ ($K_a = \text{intercept} \times \text{slope}^{-1}$) were evaluated as $526\,M^{-1}\,cm^{-1}$ and $6.3\,M^{-1}$ respectively. The plot was linear suggesting that the predominant species in solution was a 1:1 complex.

### Electrochemical Measurements

Electrochemical experiments were carried out in nitrogen-purged DMSO solutions at room temperature. The solutions for electrochemistry were held at a concentration of about $10^{-3}$ M of the electroactive species. $TBAPF_6$ (0.1 M) was included as supporting electrolyte. A glassy carbon electrode was used as the working electrode; its surface was routinely polished with a 0.05-μm alumina-water slurry on a felt surface prior to use. All potentials were recorded against a saturated Ag/AgCl electrode and a platinum wire was used as counter electrode. The potential range was cycled from 0 to $-1.2$ V at a scan rate of $50\,mV\,s^{-1}$ for all samples.

### *Acknowledgements*

K.S. thanks CSIR, India, for financial support. The authors thank SAIF, Madras, for NMR spectra and MALDI-TOF MS, and RSIC, Lucknow, for FAB-MS.

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