Self-complementary azolophanes

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By incorporating a *m*-terphenyl spacer, azolophanes containing imidazole, benzimidazole or benzotriazole and 2, 5-dimethoxy-1,4-xylyl subunits were synthesised by *N*-alkylation followed by quarternisation. The electrochemical parameters obtained for the azolophanes indicated that the redox processes are quasireversible.

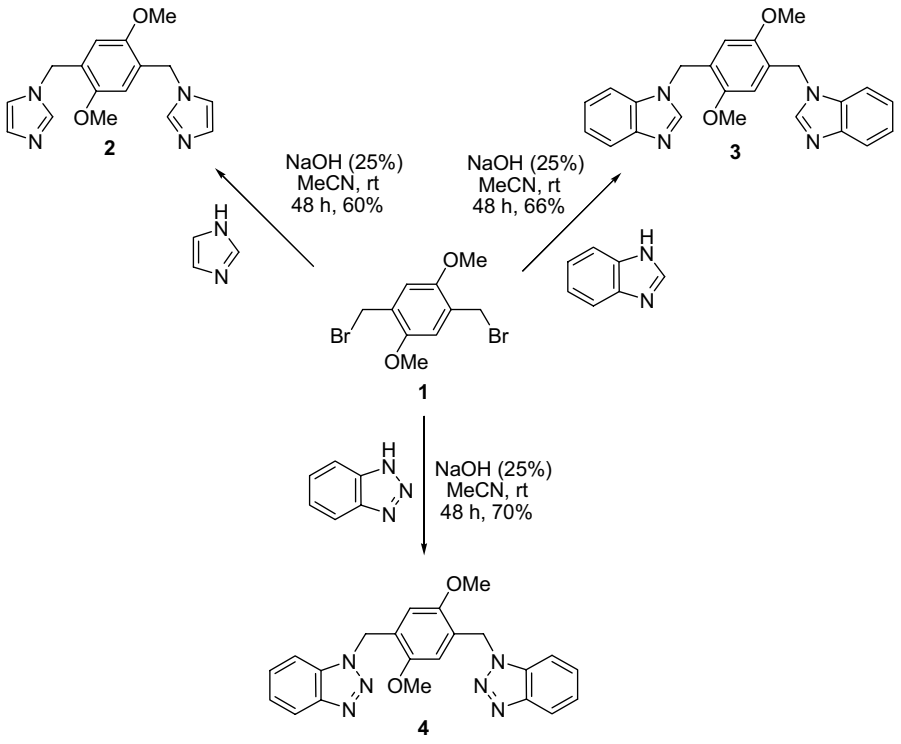
Keywords: self-complementary cyclophanes, azolophanes, 2,5-dimethoxy-1,4-xylyl, *m*-terphenyl, redox potentials

Interest in self-complementary (donor-acceptor) cyclophanes arises for three main reasons: (1) they are suitable candidates for studying non-covalent interactions[1-3] such as charge-transfer (CT) and π–π stacking; (2) they are capable of undergoing self-organisation to form two or three dimensional supramolecular array in the solid state,[2,4] which results in channel and tubular structures at the nanoscale level; and (3) they could function as both *exo* and *endo* receptors simultaneously.[4] Staab *et al.*[1,5-9] and others[2,4,10-13] have reported a variety of such self-complementary cyclophanes. Heterocyclic cyclophanes play a predominant role in host–guest chemistry and in particular, imidazole, benzimidazole and benzotriazole-based cyclophanes[14-17] (azolophanes) are considered as promising host molecules for inorganic ions as well as organic molecules. A number of azolophanes have been reported in the literature,[14-17] but their self-complementary version remains unexplored. We now report the synthesis of three self-complementary azolophanes and their electrochemical properties.

Results and discussion

The synthesis of azolophanes is usually accomplished by *N*-alkylation of an azole with a dibromide, followed by quarternisation of the resulting precyclophane with the same or a different dibromide. The same methodology was applied to synthesise the self-complementary azolophanes. Thus the treatment of 1 equivalent of 1,4-bis(bromomethyl)-2,5-dimethoxy benzene (**1**)[18] with 2.1 equivalents of imidazole, benzimidazole or benzotriazole in the presence of 25 % NaOH in acetonitrile at room temperature for 48 h afforded the precyclophanes **2–4** as white solids in 60, 66 and 70 % yields, respectively, after column chromatography (Scheme 1).

In our initial attempts, we tried to quarternise each of the precyclophanes **2–4** with 1 equivalent of the same dibromide **1** in acetonitrile under high dilution conditions. Unfortunately, the resulting products were a mixture of inseparable oligomeric and polymeric compounds, as shown by TLC and ^{1}H NMR spectroscopy. Such oligomerisation/polymerisation results from the repulsion between the electron-rich methoxy groups of the reactants during cyclisation. This could be avoided by using a large and angular dibromide[13] such as *m*-terphenyl dibromide **5**[19]. The use of *m*-terphenyl spacer may also improve the yield of the cyclophanes without the use of any templates.[20] With this in mind, each of the precyclophanes **2–4** was heated with 1 equivalent of *m*-terphenyl dibromide **5**, in acetonitrile at reflux under high dilution conditions for 5 days to afford the self-complementary azolophanes **6–8** as white solids in 23, 39 and 31 %, respectively, after purification (Scheme 2).



Scheme 1

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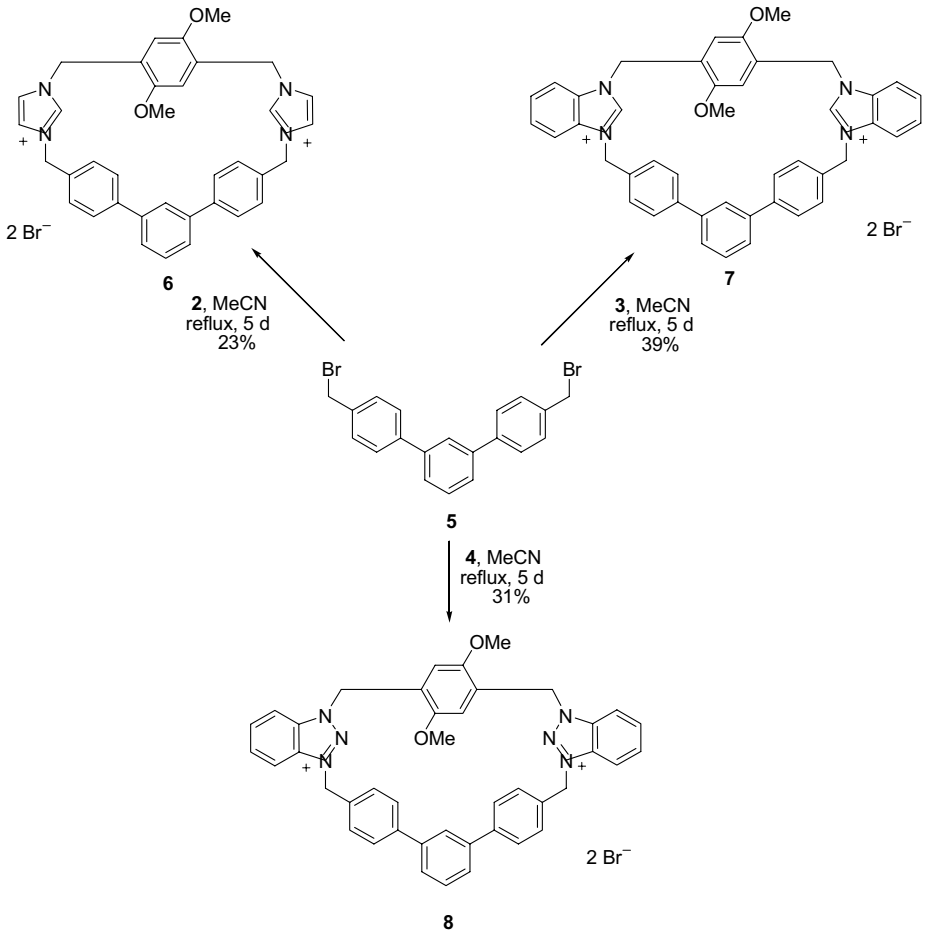

Scheme 2

The self-complementary azolophanes **6–8** are cationic in nature and, therefore, could be reduced electrochemically.[14] The redox potentials obtained for the cyclophanes **6–8** in DMSO at 25 °C are shown in the Table 1. The cyclic voltammogram of cyclophane **6** is shown in Fig. 1.

All the three cyclophanes exhibited a set of quasireversible redox peaks. The quasireversibility may be explained as follows. The radicals formed during the reduction cannot undergo intramolecular recombination due to rigid non-collapsible aromatic spacers. Hence they undergo either intermolecular irreversible recombination or reversal to the original state during oxidation. The $E_{1/2}$ of value of benzotriazolophane **8** showed a small shift towards less-positive value as compared to the corresponding values of azolophanes **6** and **7** due to the presence of two more nitrogen atoms.

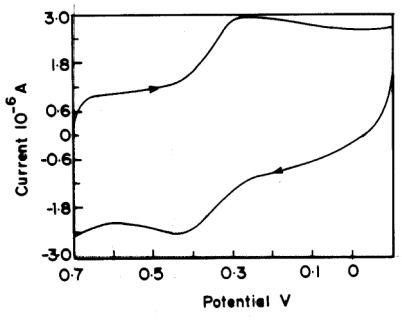

Fig. 1 Cyclic voltammogram of the cyclophane **6** in DMSO at 25 °C.

Table 1 Redox potentials of azolophanes **6–8** in DMSO at 25 °C

Cyclophane[a]	E_{pc} (mV)	E_{pa} (mV)	$E_{1/2}$ (mV)	ΔEp (mV)
6	257	444	351	187
7	264	440	352	176
8	244	448	346	204

[a]E_{pc} and E_{pa} are the cathodic and anodic peak potentials respectively. $E_{1/2}$ is the average of the cathodic and anodic peak potentials. ΔEp is the difference between the cathodic and anodic peak potentials.

Experimental

General

Melting points were determined by using a Toshniwal melting point apparatus with an open capillary tube and were uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on JEOL 500 MHz, JEOL 400 MHz, Bruker 400 MHz and Bruker ARX 200 MHz spectrometers. The FAB–MS spectra were recorded on a JEOL SX 102/DA-6000 mass spectrometer using a *m*-nitrobenzyl alcohol (NBA) matrix and EI-MS spectra on JEOL DX-303 mass spectrometer. Elemental analyses were performed on a Perkin–Elmer 240B elemental analyser. Electrochemical studies were carried out on a CH Instruments electrochemical analyser.

General procedure for the preparation of precyclophanes

NaOH solution (25 %, 7.5 ml) was added to a solution of imidazole/benzimidazole/benzotriazole (21 mmol) in CH_3CN (50 ml), and stirred for 10 min. The dibromide (10 mmol) in acetonitrile (20 ml) was added at once and stirred at room temperature for 48 h. The reaction mixture was evaporated *in vacuo* and the residue obtained was extracted with CH_2Cl_2 (3 × 100 ml), washed with water (2 × 100 ml); brine (150 ml) and dried. The solvent was removed under vacuum and the residue was chromatographed (neutral alumina) using hexane/$CHCl_3$ (1: 3) as eluent.

Precyclophane **2**: White solid; Yield 60 %; m.p. 186 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.70 (s, 6H), 5.06 (s, 4H), 6.47 (s, 2H), 6.90 (s, 2H), 7.03 (s, 2H), 7.52 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 45.8, 56.0, 111.6, 119.4, 125.6, 129.5, 137.7, 151.0; EI-MS: *m/z* (%) 298 (M^+, 68), 231 (43), 147 (40), 136 (36), 107 (100); Anal. Calcd for $C_{16}H_{18}N_4O_2$: C, 64.4, H, 6.1, N, 18.8; Found: C, 64.8, H, 6.05, N, 18.6 %.

Precyclophane **3**: White solid; Yield 66 %; m.p. 194 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.63 (s, 6H), 5.25 (s, 4H), 6.52 (s, 2H), 7.22–7.34 (m, 6H), 7.77–7.82 (m, 2H), 7.93 (s, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 43.8, 55.9, 109.9, 111.7, 120.3, 122.1, 122.9, 124.5, 133.9, 143.5, 143.8, 151.0; EI-MS: *m/z* (%) 398 (M^+, 30), 317 (23), 281 (60), 185 (15), 165 (26), 118 (59), 91 (100); Anal. Calcd for $C_{24}H_{22}N_4O_2$: C, 72.3, H, 5.6, N, 14.1; Found: C, 72.4, H, 5.5, N, 14.4 %.

Precyclophane **4**: White solid; Yield 70 %; m.p. 199 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.71 (s, 6H), 5.79 (s, 4H), 6.71 (s, 2H), 7.28–7.51 (m, 6H), 8.00–8.04 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 46.0, 56.0, 109.9, 112.3, 119.7, 123.8, 124.2, 127.2, 132.9, 145.9, 150.8; EI-MS: *m/z* (%) 400 (M^+, 100), 370 (8), 341 (11), 282 (19), 252 (6), 222 (19), 180(11), 134 (16); Anal. Calcd for $C_{22}H_{20}N_6O_2$: C, 66.0, H, 5.0, N, 21.0; Found: C,65.7, H, 5.1, N, 21.2 %.

General procedure for the synthesis of cyclophanes

m-Terphenyl dibromide **5** (1 mmol) was added to the solution of the corresponding precyclophane (1 mmol) in dry acetonitrile (300 ml), and heated under reflux for 5 days. After completion of the reaction, the cyclophane was obtained by the filtration of the reaction mixture. The cyclophane was thoroughly washed with acetonitrile and dried *in vacuo*.

Cyclophane **6**: White solid; Yield 23 %; m.p. > 260 °C (dec.); ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.77 (s, 6H), 5.36 (s, 4H), 5.51 (s, 4H), 7.27–7.36 (m, 2H), 7.54–7.66 (m, 10 H), 7.79–7.84 (m, 6H), 9.52 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 48.0, 51.4, 55.9, 114.2, 122.9, 123.6, 126.1, 127.4, 128.2, 128.8, 128.9, 129.6, 134.3, 136.4, 140.3, 141.9, 150.9; FAB-MS: *m/z* 634 (M^+–Br), 554 (M^+–2Br); Anal. Calcd for $C_{36}H_{34}Br_2N_4O_2$: C, 60.5, H, 4.8, N, 7.8; Found: C,60.3, H, 4.75, N, 8.0 %.

Cyclophane **7**: White solid; Yield 39 %; m.p. > 270 °C (dec.); ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.87 (s, 6H), 5.71 (s, 4H), 5.91 (s, 4H), 7.57–7.68 (m, 12H), 7.75–7.82 (m, 4H), 7.89 (s, 1H), 8.01 (m, 2H), 8.11 (m, 2H), 10.28 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 46.3, 49.2, 56.2, 113.9, 114.9, 122.7, 125.1, 126.1, 126.5, 126.7, 127.4, 128.8, 129.6, 130.5, 130.9, 133.4, 140.0, 140.2, 143.1, 151.4; FAB-MS: *m/z* 734 (M^+–Br), 654 (M^+–2Br); Anal. Calcd for $C_{44}H_{38}Br_2N_4O_2$: C, 64.9, H, 4.7, N, 6.9; Found: C,64.95, H, 4.7, N, 7.1 %.

Cyclophane **8**: White solid; Yield 31 %; m.p. > 220 °C (dec.); ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.55 (s, 6H), 6.11 (s, 4H), 6.26 (s, 4H), 7.34–7.68 (m, 14H), 7.90 (bs, 4H), 8.04–8.25 (m, 4H); FAB-MS: *m/z* 736 (M^+–Br), 656 (M^+–2Br); Anal. Calcd for $C_{42}H_{36}Br_2N_6O_2$: C, 61.8, H, 4.4, N, 10.3; Found: C,62.1, H, 4.5, N, 10.35 %.

Electrochemical measurements

Electrochemical experiments were carried out in nitrogen-purged DMSO solutions at room temperature. The solutions for electrochemistry were held at a concentration in the range of 10^{-3} M of the electroactive species. Tetrabutylammonium perchlorate (0.1 M) was included as a 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 a counter electrode. The potential range was cycled from 0.8 to –0.3 V at a scan rate of 100 mV/s.

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