Supplementary Material (ESI) for Chemical Communications

Chemical Communications

Nanoscale Borromean links for real

Andrea J Peters, Kelly S Chichak, Stuart J Cantrill and J Fraser Stoddart*

California NanoSystems Institute and the Department of Chemistry and Biochemistry,
University of California, Los Angeles, 405 Hilgard Avenue, Los Angeles, CA 90095

Supporting Information

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* To whom correspondence should be addressed. E-mail: stoddart@chem.ucla.edu

EXPERIMENTAL SECTION

Materials and Methods

All solvents (EM Science) were dried prior to use according to literature procedures. Anhydrous EtOH (Gold Shield Chemical Co.) used as received. Deuterated solvents (Cambridge Isotope Laboratories) for NMR spectroscopic analyses were used as received. All reagents and starting materials were purchased from Aldrich and used without further purification. All ^{1}H NMR spectra were recorded on a Bruker Avance600 (600 and 150 MHz, respectively). All chemical shifts are reported in ppm relative to tetramethylsilane using the residual solvent peak as a reference standard. High resolution electrospray mass spectra (HR-ESI-MS) were obtained with MeOH or EtOH as the liquid carrier.

Syntheses

2: The zinc(II)-containing BR complex **1** (102.5 mg, 0.02 mmol) was dissolved in anhydrous EtOH under an Ar atmosphere at 22 °C. $NaBH_4$ (30 mg, 0.8 mmol) was added in one portion. The reaction mixture became cloudy immediately. It was stirred at 22 °C for 5 days. The reaction was then quenched by the addition of H_2O (5 mL) before the reaction mixture was treated with an excess of EDTA (350 mg) and heated under reflux for 30 min. Thereafter, the reaction mixture was allowed to cool down to room temperature and the solvents were evaporated off under reduced pressure. The crude product was suspended in H_2O (15 mL) and filtered. The white filter cake was washed with H_2O (10 x 5 mL) to remove excess of salts and then finally with Et_2O (3 x 5 mL). This procedure afforded 57 mg of the crude product as a white solid containing **2** and **3** in approximately a 1:3 molar ratio as determined from the integration of the resonances for H-g/g' in the ^{1}H NMR spectrum. Therefore, this observation suggests that approximately 40% of the BRs **1** followed a pathway in which all 12 imine bonds were reduced and the three rings stayed together to produce **2**, while the remaining 60% followed a pathway in which at least one of the rings was cleaved during the borohydride reduction, producing the two reduced macrocycles **3** and one linear fragment **4**. Further purification was not performed. Selected ^{1}H NMR data for **2** (600 MHz, CD_3SOCD_3): δ = 3.50 (s, 24H, H-c/d), 3.63 (s, 24H, H-c/d), 6.36 (dd, J = 5.4, 1.8 Hz, 12H, H-g), 6.59 (d, J = 8.4 Hz, 24H, H-e/f), 7.01 (d, J = 8.4 Hz, 24H, H-e/f), 7.21 (d, J = 7.4 Hz, 12H, H-b), 7.46 (d, J = 2.4 Hz, 12H, H-i), 7.62 (t, J = 7.2 Hz, 6H, H-a), and 7.89 (d, J = 5.4 Hz, 12H, H-h). The resonance for the N-H peak is not observed, presumably because it is broadened into the baseline on account of rapid exchange with H_2O present in the solvent. HR-ESI-MS of **2**: *m/z* (%) 1505.6834 (80) $[M+2H]^{2+}$, 1004.1120 (100) $[M+3H]^{3+}$, 753.3363 (36) $[M+4H]^{4+}$; calcd for $(C_{62}H_{54}N_{10}O_4)_3$: 3009.3147.

3: The TFA salt (41.5 mg, 0.009 mmol) of the zinc(II)-containing BR complex **1** was dissolved in anhydrous EtOH (10 mL) under an Ar atmosphere at 22 °C. $NaBH_4$ (11.9 mg, 0.32 mmol) was added in one portion. The reaction mixture became cloudy immediately. It was stirred at 80 °C for 16 h. The reaction was then quenched by the addition of H_2O (5 mL). The reaction mixture was treated with an excess of EDTA (350 mg) and heated under reflux for 30 min. It was then allowed to cool down to room temperature before the solvents were evaporated off under reduced pressure. The crude product was suspended in H_2O (15 mL) and filtered. The white filter cake was washed with H_2O (10 x 5 mL) to remove excess of salts, followed by Et_2O (3 x 5 mL). This purification procedure afforded 21.1 mg of the crude product containing **3** and **4** as a white solid. Further purification was not performed. (Note: On a few occasions, a small amount of **2** was also present in the reaction mixture.) Selected ^{1}H NMR data for **3** (600 MHz, CD_3SOCD_3): δ = 3.75 (s, 8H, H-c'/d'), 3.81 (s, 8H, H- c'/d'), 6.87 (dd, J = 5.4, 3.0 Hz, 4H, H-g'), 7.04 (d, J = 8.4 Hz, 8H, H-e'/f'), 7.32 (d, J = 7.8 Hz, 4H, H-b'), 7.41 (d, J = 8.4 Hz, 8H, H-e'/f'), 7.64 (d, J = 2.4 Hz, 4H, H-i'), 7.74

(t, *J* = 7.8 Hz, 2H, H-a'), and 8.34 (d, *J* = 5.4 Hz, 4H, H-h'). A resonance for the N-H peak is not observed, presumably because it is broadened into the baseline as a result of rapid exchange with H_2O present in the solvent. HR-ESI-MS of **3**: *m/z* (%) 1003.4431 (100) [*M*+H]$^+$; calcd for ($C_{62}H_{54}N_{10}O_4$): 1003.4402. HR-ESI-MS of **4**: *m/z* (%) 1093.5147 (25) [*M*+H]$^+$; calcd for ($C_{66}H_{64}N_{10}O_6$): 1093.5083.

Characterisation

The partial ^{1}H-^{1}H COSY spectrum (Figure S1) shows the correlations between coupled protons in the reduced, demetallated BRs **2** (black) and in the reduced macrocycle **3** (red). For the BRs **2**, the resonance for the bipyridine protons H-g is coupled with both H-h and H-I, as indicated by the presence of cross peaks in the spectrum. Additionally, cross peaks are present between the resonances H-a and H-b on the pyridine ring as well as between the signals for H-e/f. The correlations present in the macrocycle **3** are similar. Cross peaks are present between the resonances for the bipyridine protons H-g', H-h', and H-i and the pyridine protons H-a' and H-b', as well as the resonances for H-e'/f'.

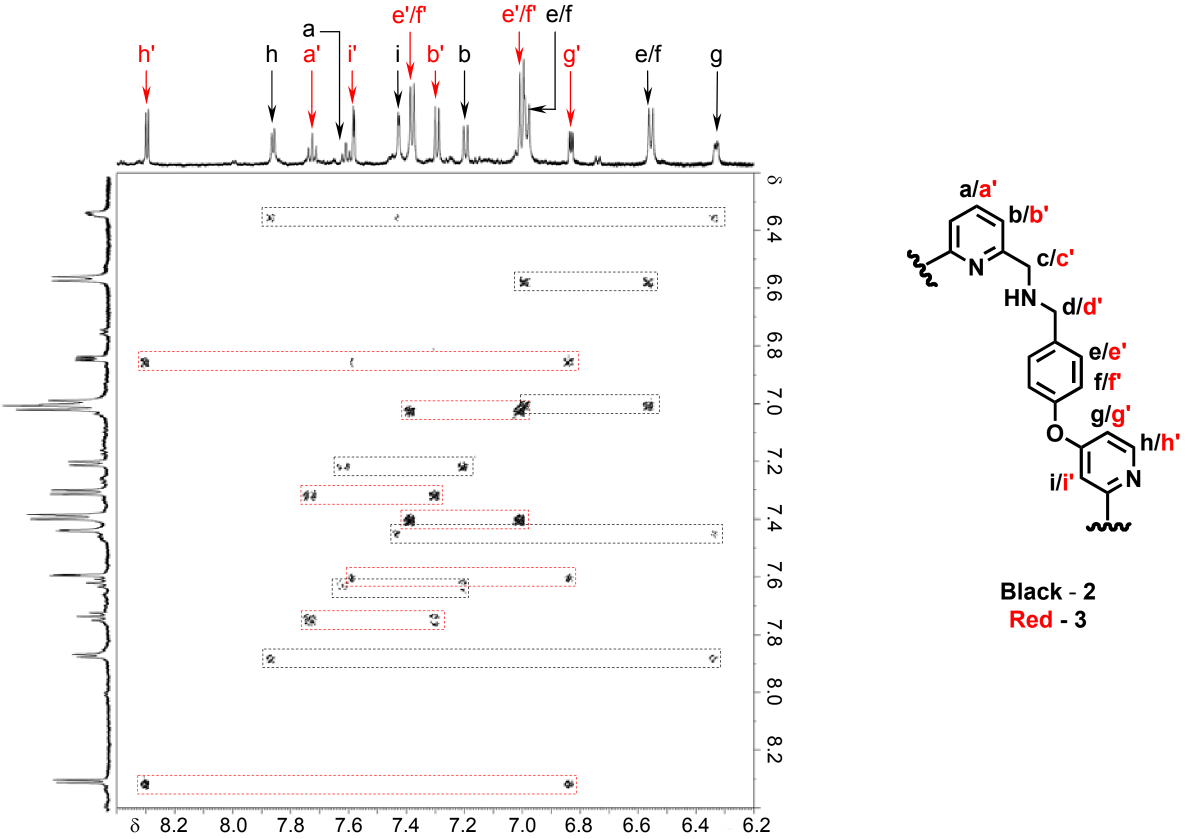

Fig. S1 Partial ^{1}H-^{1}H COSY spectrum (600 MHz; CD_3SOCD_3) of a mixture of the demetallated, reduced BRs **2** (black) and single macrocycle **3** (red) along with the partial structure and proton assignments of one ring.

In common with the ^{1}H NMR spectrum of the reaction mixture, which was shown to contain both the demetallated BRs **2** and the macrocycle **3** (Conditions **A**), the HR-ESI-MS of this solution also shows the presence of both these species. The triply charged ion [*M*+3H]$^{3+}$ for **2** and the singly charge ion [*M*+H]$^+$ for **3** appear in the same region of the ESI-MS with a calculated [*M*+3H]$^{3+}$ for **2** = 1004.1122 and [*M*+H]$^+$ of **3** = 1003.4402 (Figure S2c). Since **2** is triply charged, the isotopic

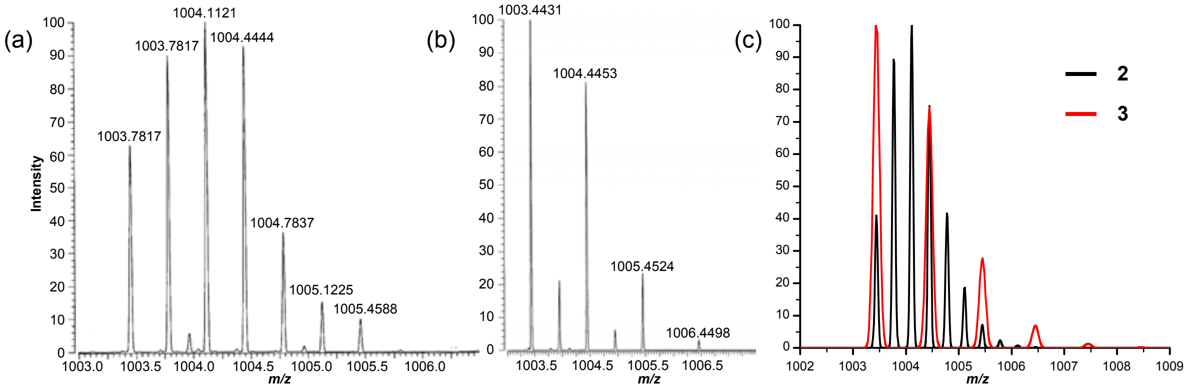

Fig. S2 Partial HR-ESI MS of (a) the [*M*+3H]$^{3+}$ region of the demetallated BR **2**, (b) the [*M*+H]$^{+}$ region of the macrocycle **3** and (c) the calculated isotopic distribution (iMass) for **2**, [*M*+3H]$^{3+}$, (—) and **3,** [*M*+H]$^{+}$, (—).

distribution will show three mass peaks for every one mass unit, whereas **3** is only singly charged and therefore will have one peak for every mass unit in the isotopic distribution. Figure S2a shows the expanded region for the [*M*+3H]$^{3+}$ peak of **2** and Table S1 lists the calculated and experimental intensities of the isotope peaks in this region for both **2** and **3**. The experimental intensities of the peaks at *m/z* = 1003.44 and 1004.44 for **2** [*M*+3H]$^{3+}$ are greatly elevated relative to the calculated values. This increase in intensity arises from overlap of these peaks with those for **3**[*M*+H]$^{+}$ which is present in the reaction mixture. The experimental intensities of the other peaks (*m/z* = 1003.77, 1004.11, 1004.77 and 1005.12) for **2** [*M*+3H]$^{3+}$ correlate with the calculated intensities since there is no overlap with peaks from the macrocycle **3** at these mass units (Figure S2b). This observation provides additional evidence for the presence of both **2** and **3** in the reaction mixture (Conditions **A**).

Table S1 Calculated and experimental intensities (%) of the *m/z* peaks in the HR-ESI-MS of **2** [*M*+3H]$^{3+}$ and **3** [*M*+H]$^{+}$.

	2 [*M*+3H]$^{3+}$		**3** [*M*+H]$^{+}$	
Calcd *M*$^{+}$	Calcd %	Exp %	Calcd %	Exp %
1003.44	41	63	100	100
1003.77	89	88	0	0
1004.11	100	100	0	0
1004.44	75	93	75	82
1004.77	37	41	0	0
1005.12	15	18	0	0
1005.45	7	10	28	22

The HR-ESI-MS of a TFA treated methanolic solution containing the macrocycle **3** and the linear fragment **4** is shown in Figure S3. The spectrum shows a peak at *m/z* = 1003.4099 corresponding to the mass of the macrocycle **3** along with a peak at *m/z* = 1065.4847 which correlates with the mass of the linear fragment which we suggest is the dimethyl acetal shown in Figure S3 (blue structure). This result indicates that, in the acidic methanolic solution, the ethoxy groups of **4** were exchanged for methoxy groups producing the dimethyl acetal derivative from the former diethyl acetal **4**. This data provides further evidence for the proposed structure **4** for the linear fragment produced in the borohydride reduction.

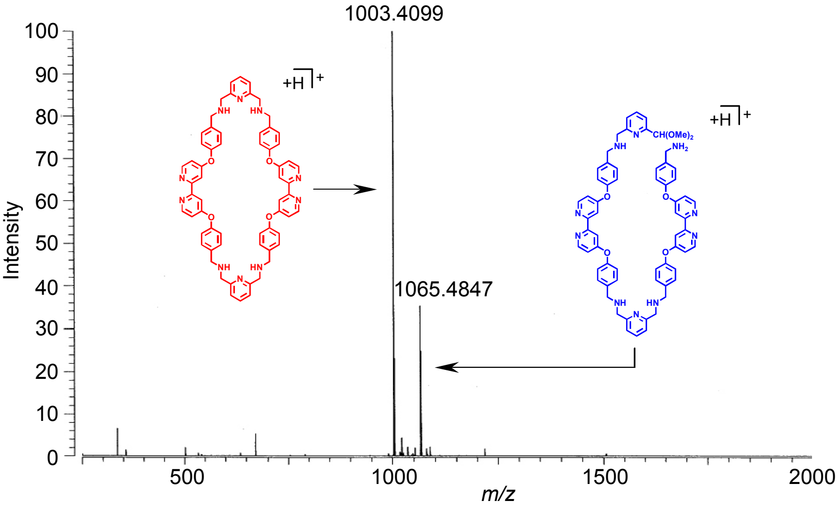

Fig. S3 HR-ESI-MS of a methanolic solution plus TFA containing the macrocycle **3** and a derivative of the linear fragment **4** in which the diethyl acetal was converted to a dimethyl acetal (blue structure).

Although the BR compound **1** contains an inner cavity with a volume of 250 Å^3 that is lined with 12 oxygen atoms, due to the rigidity of the BR system, which is a result, in part, of the 30 metal-ligand bonds present in the structure, we have been unsuccessful in attempting to access this cavity and bind a guest molecule, once the rings have been formed. Since it is expected that the reduced and demetallated BR structure **2** is more flexible than **1**, we attempted to study its ability to bind a guest species, such as sodium inside the cavity. Figure S4a shows the partial ^{1}H NMR spectrum of a reaction mixture containing **2** and **3** (labeled black and red, respectively) in CD_3CN. There is also evidence in this spectrum for another highly symmetrical product (labeled green). Upon the addition of an excess of $NaBF_4$ to this mixture, the ^{1}H NMR spectrum, taken immediately thereafter (Figure S4b), shows the disappearance of the resonances for **2** and an increase in the other highly symmetrical product labeled in green. We attribute this other product to be a Na-adduct of the reduced, demetallated BRs **2**, presumably with the Na$^+$ ion occupying the electron-rich inner cavity of the BRs.

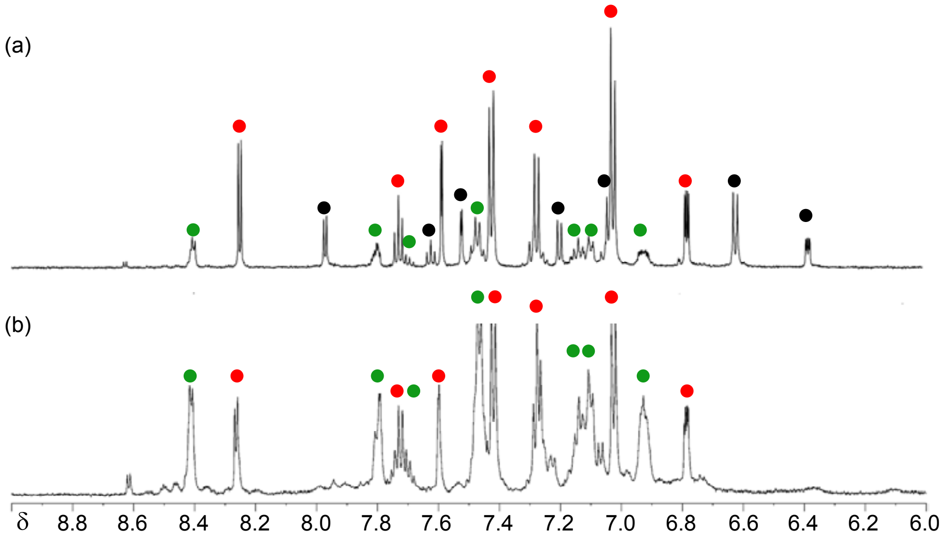

Fig. S4 Partial ^{1}H NMR (600 MHz; CD_3CN) of (a) a reaction mixture containing **2** (•) and **3** (•) along with another product (•) and (b) the reaction mixture after the addition of an excess of $NaBF_4$.

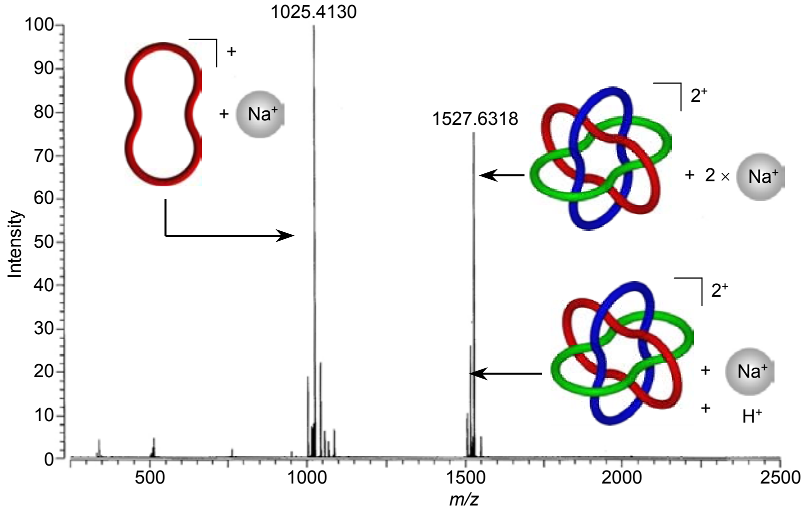

Fig. S5 HR-ESI-MS of a MeCN solution containing the reduced and demetallated BRs **2** and the single macrocycle **3** after the addition of an excess of NaBH$_4$.

The HR-ESI-MS of the MeCN solution containing the reduced, demetallated BRs **2** and the single macrocycle **3** after the addition of an excess of NaBH$_4$ is shown in Figure S5. The mass spectrum suggests evidence for the presence of Na$^+$ ion adducts of the reduced BRs **2** as well as a sodium adduct of a single macrocycle **3**. This rationalisation arises from the fact that there are two doubly charged ions m/z = 1527.6318 and m/z = 1516.6643 which correlate with the Na-adducts of the BR **2**, namely [M+2Na]$^{2+}$ and [M+Na+H]$^{2+}$, respectively. Additionally, there is the presence of a singly charged ion m/z = 1025.4130 which correlates with a Na$^+$ ion adduct of the macrocycle **3**, [M+Na]$^+$. Although this experimental data does not provide unambiguous evidence for the binding of the Na$^+$ guest species inside the cavity of the BRs, we suggest that it is likely that the Na$^+$ ions would occupy the electron-rich inner core of the BR macrocycles.