New *bis*Benzimidazole templates for threading through dibenzo-24-crown-8

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Experimental

General

All the reagents used were purchased from Aldrich or Lancaster and used as received without further purification. NMR spectra were recorded in the indicated solvents. Chemical shifts (δ) are reported in parts per million (ppm) relative to tetramethylsilane as internal standard. 1H NMR (400 MHz) and 13C NMR (100 MHz) spectra were recorded on a Bruker DPX400 spectrometer. The following abbreviations are used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet, br = broad. HR-ESI mass spectra were recorded on a Bruker MicrOTOF ESI-OF-MS. Infrared spectra were collected on a Perkin-Elmer Paragon 1000 FT-IR instrument. Melting points were recorded on Stuart SMP10 (Bibby) and are uncorrected. Elemental analysis were carried out by Warwick Analytical Services.

2.2 Synthesis


\[
\begin{align*}
\text{Phenylenediamine (10g, 0.1 mol) and succinic acid (5.98g, 0.50 mol) were added to 4M hydrochloric acid (100ml) in a 250 mL round bottomed flask, and the mixture was refluxed for 48 hours then gradually cooled to room temperature. The light green precipitate was filtered, washed with water then acetone and air dried. M.p >300°C. Yield (13.1g, 78 %) 1H NMR (400 MHz, DMSO): } & \delta = 7.85 (m, 4H, ArH), 7.65 (m, 4H, ArH) \\
& \text{and } 3.82 (s, 4H, CH}_2)
\end{align*}
\]
1, 2 Bis(benzimidazole-2-yl) ethane bis(perchlorate) (1a)

(CAUTION: perchlorates are toxic and harmful and potentially explosive. They should only be handled in small amounts taking appropriate precautions). 1,2 Bis-(benzimidazole-2-yl) ethane dihydrochloride (0.5g) was dissolved in formamide (5ml) with gentle warming and a few drops of concentrated hydrochloric acid were added to give a clear solution. The solution was allowed to cool to room temperature and perchloric acid (37%) (Caution: harmful, corrosive and powerful oxidising agent) was added drop wise with swirling till crystallisation started. The precipitate was filtered, washed with a small amount of water and air dried. The solid was then recrystallised by dissolving in acetonitrile and filtering then adding ethyl acetate till saturation. On standing colourless needles separated. M.p >300°C. \[^1^H\]NMR (400 MHz, CD\textsubscript{3}CN): δ= (NH not detected) 7.88 (m, 4H, ArH), 7.68 (m, 4H, ArH) and 3.82 (s, 4H, CH\textsubscript{2}), \[^{13}\text{C}\]NMR (100 MHz, CD\textsubscript{3}CN): δ= 150.3(2xArC), 130.4(4xArC), 126.7(4xArCH), 113.9(4xArCH) and 23.7(2xCH\textsubscript{2}).

\[^1^H\]NMR (400 MHz, CD\textsubscript{3}NO\textsubscript{2}): δ= (NH not detected) 7.78 (m, 4H, ArH), 7.55 (m, 4H, ArH) and 3.90 (s, 4H, CH\textsubscript{2}), \[^{13}\text{C}\]NMR (100 MHz, CD\textsubscript{3}NO\textsubscript{2}): δ= 150.2(2xArC), 130.5(4xArC), 126.7(4xArCH), 113.9(4xArCH) and 23.8(2xCH\textsubscript{2}).

IR (thin film): \(\nu = 3546, 3177, 1625, 1569, 1050\) and 751 cm\(^{-1}\).

Anal. Calculated for C\textsubscript{16}H\textsubscript{16}N\textsubscript{4}O\textsubscript{8}Cl\textsubscript{2}: C, 41.49; H, 3.48; N, 12.08; Cl, 15.31. Found: C, 41.45; H, 3.42; N, 11.93; Cl, 15.40.
1, 2 Bis(benzimidazole-2-yl) ethane bis(tetrafluoroborate) (1b)

The tetrafluoroborate salt was synthesised in a similar manner to the above except that a solution of tetrafluoroboric acid (48% solution in water) (Caution: harmful and corrosive) was added to the formamide solution of the chloride salt. The product was recrystallised from a concentrated solution of acetonitrile (charcoal) on the addition of ethyl acetate as colourless blocks. M.p. 275-278°C (decomp.) $^1$H NMR (400 MHz, CD$_3$CN): $\delta = 13.5$(brs, 4H, NH), 7.85 (m, 4H, ArH), 7.65  (m, 4H, ArH) and 3.80 (s, 4H, CH$_2$). $^{13}$C NMR (100 MHz, CD$_3$CN): $\delta = 150.4$(2xArC), 130.5(4xArC), 126.7(4xArCH), 113.9(4xArCH) and 23.7(2xCH$_2$).

$^1$H NMR (400 MHz, CD$_3$NO$_2$): $\delta = $(NH not detected) 7.75 (m, 4H, ArH), 7.55 (m, 4H, ArH) and 3.88 (s, 4H, CH$_2$). $^{13}$C NMR (100 MHz, CD$_3$NO$_2$): $\delta = 150.1$(2xArC), 130.4(4xArC), 126.8(4xArCH), 113.9(4xArCH) and 23.9(2xCH$_2$).

IR (thin film): $\nu = 3599, 2964, 1627, 1573, 1058, 1004$ and 759 cm$^{-1}$.

HR-LSIMS-MS: m/z [1b$\cdot$BF$_4$]$^+$ calc.: 351.1399, found: 351.1404.

1, 2 Bis(benzimidazole-2-yl) ethane bis(trifluoromethanesulphonate) (1c)

1, 2 Bis-(benzimidazole-2-yl) ethane dihydrochloride was dissolved in trifluoromethanesulphonic acid with careful heating. (CAUTION: trifluoromethane sulphonic acid is corrosive and harmful). A small amount of deionised water was added to the solution which on cooling gave a light blue precipitate. The product was recrystallised from a concentrated solution of acetonitrile (charcoal) on the addition of ethyl acetate as colourless blocks. M.p. 296-298°C. $^1$H NMR (400 MHz, CD$_3$CN): $\delta =$
12.70 (brs, 4H, NH), 7.85 (m, 4H, ArH), 7.65 (m, 4H, ArH) and 3.80 (s, 4H, CH$_2$). $^{13}$C NMR (100 MHz, CD$_3$CN): $\delta$ = 149.9(2xArC), 130.3(4xArC), 126.9(4xArCH), 113.9(4xArCH) and 23.7(2xCH$_2$).

$^1$H NMR (400 MHz, CD$_3$NO$_2$): $\delta$ = (NH not detected) 7.80 (m, 4H, ArH), 7.50 (m, 4H, ArH) and 3.90 (s, 4H, CH$_2$). $^{13}$C NMR (100 MHz, CD$_3$NO$_2$): $\delta$ = 150.2(2xArC), 130.5(4xArC), 126.6(4xArCH), 113.8(4xArCH) and 24.0(2xCH$_2$).

IR (thin film): $\nu$ = 3540, 2951, 1628, 1574, 1022, 754 and 620 cm$^{-1}$.

Anal. Calculated for C$_{18}$H$_{16}$N$_4$O$_6$F$_6$S$_2$(H$_2$O)$_2$: C, 36.12; H, 3.37; N, 9.36; S, 10.72. Found: C, 36.02; H, 3.32; N, 9.16.

1, 2 Bis(benzimidazole-2-yl)ethane bis(hexafluorophosphate) (1d)

(CAUTION: hexafluorophosphoric acid is corrosive and harmful. It and its salts should only be handled in small amounts taking appropriate precautions). The hexafluorophosphate salt was synthesised in a similar manner to the above except that on cooling a solution of hexafluorophosphoric acid (50% solution in water, 1ml) (Caution: harmful and corrosive) was added to the formamide solution of the chloride salt to give a clear solution. Distilled water was then added dropwise till crystallisation occurred. The crystals were filtered off and air dried. M.p. (softens 180°C) 250-254°C (*decomp.). $^1$H NMR (400 MHz, CD$_3$CN): $\delta$ = (NH not detected) 7.85 (m, 4H, ArH), 7.65 (m, 4H, ArH) and 3.80 (s, 4H, CH$_2$).

$^{13}$C NMR (100 MHz, CD$_3$CN): $\delta$ = 150.2(2xArC), 130.4(4xArC), 126.8(4xArCH), 113.8(4xArCH) and 23.6(2xCH$_2$).

$^1$H NMR (400 MHz, CD$_3$NO$_2$): $\delta$ = (NH not detected) 7.80 (m, 4H, ArH), 7.55 (m, 4H, ArH) and 3.90 (s, 4H, CH$_2$). $^{13}$C NMR (100 MHz, CD$_3$CN): $\delta$ = 149.9(2xArC), 130.3(4xArC), 126.9(4xArCH), 113.9(4xArCH) and 23.7(2xCH$_2$).

IR (thin film): $\nu$ = 3585, 2960, 1633, 1577, 817 and 755 cm$^{-1}$.

HR-LSIMS-MS: m/z [1d⋅PF$_6$]$^+$ calc.: 409.1011, found: 409.1019
Pseudorotaxanes with dibenzo-24-crown-8 in d₃-acetonitrile

Letters used to specify hydrogen positions in ¹H NMR of pseudorotaxanes.

Perchlorate thread with crown 1a⊂dibenzo-24-crown-8(ClO₄)₂. ¹H NMR (400 MHz, CD₃CN): δ= 12.50 (brs, 4H, NH), 7.50 (brs, 2H, ArH thread a), 7.45 (brs, 2H, ArH thread b), 6.72 (brs, 2H, ArH crown d), 6.59 (brs, 2H, ArH crown e), 4.08 (brs, 4H, CH₂ thread c), 4.02 (brs, 8H, CH₂ crown f) and 3.93 (brs, 16H, CH₂ crown g and h). HR-ESI-MS: m/z [1a⊂DB24C8·ClO₄]⁺ calc.: 811.2946, found: 811.2945.

Tetrafluoroborate thread with crown 1b⊂dibenzo-24-crown-8(BF₄)₂. ¹H NMR (400 MHz, CD₃CN): δ= 12.40 (brs, 4H, NH), 7.51 (brs, 4H, ArH thread a), 7.45 (brs, 4H, ArH thread b), 6.72 (brs, 4H, ArH crown d), 6.60 (brs, 4H, ArH crown e), 4.08 (brs, 4H, CH₂ thread c), 4.03 (brs, 8H, CH₂ crown f) and 3.93 (brs, 16H, CH₂ crown g and h). HR-ESI-MS: m/z [1b⊂DB24C8·BF₄]⁺ calc.: 799.3496, found: 799.3510.

Trifluoromethanesulphonate thread with crown 1c⊂dibenzo-24-crown-8(CF₃SO₃)₂. ¹H NMR (400 MHz, CD₃CN): δ= 12.60 (brs, 4H, NH), 7.50 (brs, 4H, ArH thread a), 7.43 (brs, 4H, ArH thread b), 6.70 (brs, 4H, ArH crown d), 6.57 (brs, 4H, ArH crown e), 4.08 (brs, 4H, CH₂ thread c), 4.00 (brs, 8H, CH₂ crown f), 3.98 (brs, 8H, CH₂ crown h) and 3.93 (brs, 8H, CH₂ crown g), HR-ESI-MS: m/z [1c⊂DB24C8·CF₃SO₃]⁺ calc.: 861.2987, found: 861.2991.

Hexafluorophosphate thread with crown 1d⊂dibenzo-24-crown-8(PF₆)₂. ¹H NMR (400 MHz, CD₃CN): δ= 12.50 (brs, 4H, NH), 7.50 (brs, 4H, ArH thread a), 7.45 (brs, 4H, ArH thread b), 6.72 (brs, 4H, ArH crown d), 6.59 (brs, 4H, ArH crown e), 4.08 (brs, 4H, CH₂ thread c), 4.02 (brs, 8H, CH₂ crown f), 3.98 (brs, 8H, CH₂ crown h) and 3.93 (brs, 8H, CH₂ crown g), HR-ESI-MS: m/z [1d⊂DB24C8·PF₆]⁺ calc.: 861.2987, found: 861.2991.
thread c), 4.02 (brs, 8H, CH\textsubscript{2} crown f) and 3.93 (brs, 16H, CH\textsubscript{2} crown g and h). HR-ESI-MS: m/z [\textbf{1dCD24C8PF6}]\textsuperscript{+} calc.: 857.3108, found: 857.3104.

**NMR spectra** \textsuperscript{1}H NMR (400 MHz) and \textsuperscript{13}C NMR (100 MHz) spectra were recorded on a Bruker DPX400 spectrometer at 25\degree C.

Thread \textbf{1a} \textsuperscript{1}H and \textsuperscript{13}C NMR
Thread 1b $^1$H and $^{13}$C NMR
Thread 1c $^1$H and $^{13}$C NMR
Thread 1d \(^1\)H and \(^{13}\)C NMR
**Binding constant measurements**

The solutions for binding constant measurement were made by dilutions using volumetric glassware and pipettes and recorded at 25° C. A typical experiment is detailed below. **1a** (ClO$_4$)$_2$ (46.3mg) and dibenzo-24-crown-8 (44.8mg) were dissolved in CD$_3$CN (10ml). 1ml of this solution was then taken and diluted to 5ml with CD$_3$CN to give a solution with a thread and crown concentration of 2mM each respectively.

The ratio of bound to unbound was obtained from the $^1$H NMR spectra from the integration of the thread and crown aromatics and averaging over two experiments.

**Experimental binding constants**

For a discussion of the factors contributing to the experimentally measured binding constants for pseudorotaxane systems in solvents of low dielectric constant, see (a) Jones, J. W.; Gibson, H. W. *J. Am. Chem. Soc.* 2003, 125, 70017004. (b) Huang, F.; Jones, J. W.; Slebodnik, C.; Gibson, H. W. *J. Am. Chem. Soc.* 2003, 125, 14458-14464. The binding constants reported here should be considered as approximate as they do not take into account the extent of ion pair dissociation of the dicationic thread and its counter ions as an intrinsic part of the thread / crown binding event. $K_a$ was calculated from the formula below.

$$K_a = \frac{[\text{pseudorotaxane}]}{[\text{thread}]_{\text{unbound}} \times [\text{crown}]_{\text{unbound}}}$$

$[\text{thread}]_{\text{unbound}}$ and $[\text{crown}]_{\text{unbound}}$ are the original concentrations of thread and crown set up in the experiment minus the concentration of thread or crown bound up in the rotaxane. These values are calculated from the ratio of bound and unbound thread and crown obtained from the integrals of the $^1$H NMR experiment. The units of $K_a$ are expressed in M$^{-1}$.

<table>
<thead>
<tr>
<th>thread</th>
<th>acetonitrile</th>
<th>nitromethane</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1a</strong> (ClO$_4$)</td>
<td>5.0 x10$^2$</td>
<td>18.4 x10$^2$</td>
</tr>
<tr>
<td><strong>1b</strong> (BF$_4$)</td>
<td>4.7 x10$^2$</td>
<td>14.3 x10$^2$</td>
</tr>
<tr>
<td><strong>1c</strong> (TFSA$^-$)</td>
<td>3.3 x10$^2$</td>
<td>4.7 x10$^2$</td>
</tr>
<tr>
<td><strong>1d</strong> (PF$_6$)</td>
<td>6.7 x10$^2$</td>
<td>30.5 x10$^2$</td>
</tr>
</tbody>
</table>
$^1$Hnmr spectra of pseudorotaxanes at 2mM concentration of thread and crown in acetonitrile at 25°C.
$^1$Hnmr spectra of pseudorotaxanes at 2mM concentration of thread and crown in nitromethane at 25°C.
ESI accurate mass recorded on a Bruker MicrOTOF.

ESI mass spec of $1a\subset$dibenzo-24-crown-8 in acetonitrile.

ESI mass spec of $1b\subset$dibenzo-24-crown-8 in acetonitrile.
ESI mass spec of 1c\(\subset\)dibenzo-24-crown-8 in acetonitrile.

\[ C_{41}H_{48}F_3N_4O_{11}S^+ \]
Exact Mass calc.: 861.2987

ESI mass spec of 1d\(\subset\)dibenzo-24-crown-8 in acetonitrile.

\[ C_{40}H_{48}N_4O_6(PF_6)^+ \]
Exact Mass calc.: 857.3108
Job Plot

Job plot of 1a and dibenzo-24-crown-8 by the continuous variation method keeping the sum of [1a][dibenzo-24-crown-8] equal to 4mM. The maximum at 0.522 verifies the 1:1 stoichiometry of the pseudorotaxane complex. For practical details see Hirose, K. J. Inclusion Phenom. Macro. Chem. 2001, 39, 193-209.

X-ray experimental

Crystals were coated in an inert oil prior to transfer to a cold nitrogen gas stream at 180K on a Bruker-AXS SMART three circle area detector diffractometer system equipped with Mo Kα radiation (λ = 0.71073 Å). Data were collected with narrow (0.3 ° in ω) frame exposures. Intensities were corrected semi-empirically for absorption, based on symmetry-equivalent and repeated reflections (SADABS). Structures were solved by direct methods (SHELXL) with additional light atoms found by Fourier methods. Hydrogen atoms were constrained with a riding model except the NH hydrogens which were located in a fourier map; U(H) was set at 1.2 (1.5 for methyl and NH hydrogens) times Ueq for the parent atom. Programs used were Bruker AXS SMART (control),
SAINT (integration) and SHELXTL for structure solution and refinement. The Open Source software Jmol was used for molecular graphics. We thank Oxford Diffraction for recording the reflection data for $1b\subset$dibenzo-24-crown-8. Crystals suitable for X-ray analysis were either grown from a saturated solution of acetonitrile or from nitromethane by the slow infusion of diethyl ether.


ii) Jmol open source molecular viewer.