SYNTHESIS OF TRIS- AND TETRAKIS(TROPOCORONAND)S HAVING SHORT LINKER CHAINS

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Abstract - The syntheses of tris- and tetrakis(tropocoronand)s, a new kind of macrocycles derived from three or four aminotropone imine moieties bridged by three or four short methylene linker chains are described. These tropocoronands were prepared by the reaction of bis(2-methoxytropone imine)salts with \(\alpha,\omega\)-alkanediamine using a template or with tropopodand derived from benzo[\(b\)]cyclohepta[\(e\)][1,4]-oxazine with \(N\)-acetyl-1,2-ethanediame by an intermolecular heterocycle exchange reaction.

Recently, we reported a very convenient, one pot synthesis of tetraazabis(tropocoronand)s (1)\(^2\) and tropopodands (2) by the reaction of cyclohepta[\(b\)][1,4]oxazine (3)\(^3\) with \(\alpha,\omega\)-alkanediamines (4) in high yields through an intermolecular heterocycle exchange reaction.\(^4\) This method, however, gave bicyclic pyrazino or diazepino compounds (5\(a,b\)),\(^5\) instead of the tropocoronand, when linker chains became short (n=2,3).\(^2\) While one of us (T.N) and his co-workers previously synthesized 1 (n=2-6) from reactive troponoids and \(\alpha,\omega\)-alkanediamines (4, R=H, n=2-6) via bis(2-aminotropone) (6, R=H, n=2-6) and then the bis-2-alkoxytropone imine derivatives (7, n=2-6) under a high dilution condition.\(^6\) Conversion of 6 (R=H, n=2) to the corresponding tropocoronand (1)(n=2) underwent in only 2% yield, but insted 2-phenyl-2-imidazol (8) was

Dedicated to Dr. Arnold Brossi on the occasion of his 70th birthday.
obtained as the major product in 51% yield.

We wish to report here the synthesis of tris- and tetrakis(tropocoronand)s having short linker chains and related compounds.

Results and Discussion

We first studied the reaction of \( \text{N,N'}\)-bis[2-methoxy-2,4,6-cycloheptatrienylium]-1,2-ethanedi-amine bisfluorosulfate (9a) with 1,2-ethanedi-amine (4a) to obtain bis(tropocoronand) (1, \( n=2 \)) or tetrakis(tropocoronand) (10a). Compound (9a) was prepared from 6a and methyl fluorosulfate in CH\(_2\)Cl\(_2\). However, treatment of 9a with 4a in the presence of Et\(_3\)N (1:1:1:2.5 ratio) in absolute methanol at 20 °C for 30 h afforded, after column chromatography, bicyclic compound (5a) (69% yield) as the main product besides a small amount of 10a (7%) and tris(tropocoronand) (11a, 13%).

Then, in an attempt to increase the yields of coronands, Na\(_2\)CO\(_3\) to a suspension of 9a and 4a in methanol, was added as a template, gradually depositing orange precipitates. The precipitates were collected and extracted
with chloroform and, after chromatography, much higher yields of tetrakis(tropocoronand) \((10a, \text{mp} > 300 ^\circ \text{C}, 32\%)\) and tris(tropocoronand) \((11a, \text{mp} 245-246 ^\circ \text{C}, 46\%)\) were obtained. Compound \((10a)\) showed uv absorption maxima at 262 (log \(\varepsilon\) 4.80), 345\(^b\) (4.51), 362 (4.61), 414 (4.46), 438 (4.33), and 465 nm (3.99) which resemble those of 1, and \(^1\)H nmr signals at \(\delta\) 3.67 (16H, s) due to methylene protons of symmetrical linker chains and at \(\delta\) 6.18 (t), 6.37 (d), and 6.79 (dd), (4:8: ratio) due to five adjacent protons on the four seven-membered rings. FAB-ms spectrum of \(10a\) gave the molecular ion peak at m/z 585 (MH\(^+\)). These spectral data established the structure of \(10a\). Compound \((11a)\) showed uv absorption maxima and nmr signals which resemble those of \(10a\). The mass spectrum [m/z 438 (M\(^+\))], however, revealed the structure of tris(tropocoronand) for \(11a\). Compound \((5a)\) was also isolated from the filtrate in 15% yield.

In a synthesis of \(10a\) and \(11a\) from the reaction of \(9a\) with \(4a\), a template effect was found by the addition of some metals as shown in Table 1.

The same reaction of \(9b\) with \(4a\) in the presence of \(\text{Na}_2\text{CO}_3\) afforded the corresponding tetrakis- and tris(tropocoronand)s \((10b, 11b)\) along with \(5c\). The reaction of \(9c\) and \(4b\) with \(\text{Na}_2\text{CO}_3\) in methanol gave tetrakis(tropocoronand) \((13, 16\%)\), bis-(tropocoronand) \((1, \text{n}=3, 55\%)\), and \(5b\) (25\%).

Table. 1. Template Effect of Some Alkaline Metals on Synthesis of Tris and Tetrakis(tropocoronand)s \((10a\) and \(11a)\) by the Reaction of \(9a\) and \(4a\).

<table>
<thead>
<tr>
<th>Neutralization reagents</th>
<th>Yields (%) of products</th>
</tr>
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<tbody>
<tr>
<td>Metal source</td>
<td>amine</td>
</tr>
<tr>
<td>(\text{Na}_2\text{CO}_3)</td>
<td>Et(_3) N</td>
</tr>
<tr>
<td>(\text{Na}_2\text{CO}_3)</td>
<td>---</td>
</tr>
<tr>
<td>(\text{K}_2\text{CO}_3)</td>
<td>Et(_3) N</td>
</tr>
<tr>
<td>(\text{Li}_2\text{CO}_3)</td>
<td>Et(_3) N</td>
</tr>
<tr>
<td>---</td>
<td>Et(_3) N</td>
</tr>
</tbody>
</table>

Next we studied the reaction of \(9a\) with podand \((2, \text{n}=2)\) to obtain tris(coronand) \((11a)\). Compound \((2)\) was prepared by hydrolysis of the diacetyl derivative \((13)\) which was available by treatment of \(3\) with \(N\)-acetyl-1,2-ethanediamine \((4c)\) (1:4) in absolute ethanol at 80 °C for 30 h under an inert atmosphere.\(^7\) Compound \((13)\) (yellow needles, mp 170-171 °C) showed uv absorption maxima similar to the previously known
tropopodands\textsuperscript{2} and the structure was determined on the basis of nmr, ir, and mass spectra (see Experimental section). Upon heating in ethanol containing H\textsubscript{2}SO\textsubscript{4} and H\textsubscript{2}O, compound (13) gave sulfate (14) (yellow needles, mp 220-223 °C). Composition formula of 14 was determined by the elemental analysis, closely agreeable with \((C\textsubscript{11}H\textsubscript{18})\textsubscript{2} \cdot 5H\textsubscript{2}SO\textsubscript{4} \cdot H\textsubscript{2}O\). Compound (2) \((n=2)\) was quantitatively obtained from 14 upon neutralization. The reaction of 9\textsubscript{a} with 14 in methanol at 20 °C for 30 h was conducted likewise. The precipitates which formed were collected, extracted with chloroform, and recrystallized from chloroform-methanol to give 11\textsubscript{a} in 67% yield. Compound (5\textsubscript{a}) was also obtained from the filtrate after chromatography.

![Chemical structures](image)

The heterocycle exchange reaction of 3 with 2 \((n=2, 1:1.2 \text{ ratio})\) gave 5\textsubscript{a} (83%) and a small amount of 11\textsubscript{a}\textsuperscript{1} (4%) instead of bis(coronand) (1) \((n=2)\). Although we attempted the synthesis of bis(aminotroponeimine) derivative (15\textsubscript{a}) from the reaction of 9\textsubscript{a} and 4\textsubscript{a} (1: excess), only 5\textsubscript{a} was isolated.

A similar reaction of 9\textsubscript{a} with 4\textsubscript{c}, however afforded diacetyl derivative (15\textsubscript{b}) in a high yield. Therefore, podand (2) \((n=2)\) and the initially formed intermediate (a) or (15\textsubscript{a}) in the reaction of 9\textsubscript{a} with 4\textsubscript{a} are presumed to readily cyclize at the terminal amino group to give pyrazino derivative (5\textsubscript{a}) by extruding ethanediamine group as shown in the formulas below. The formation of bis(tropocoronand) (1, \(n=2\)) and 2-phenylimidazol (8) shown in the previous report\textsuperscript{6} was not observed in all of the present experiments.
EXPERIMENTAL

The melting points were determined with a Yanagimoto MP-35 melting-point apparatus and were uncorrected. The IR and UV spectra were measured in CDCl₃ with a JEOL JNM-GX270 (100 or 270 MHz for ¹H and 67.8 MHz for ¹³C) spectrometer using TMS as an internal standard. The assignments of all signals were made by employing a first-order analysis with the aid of a decoupling technique. The mass spectra were taken on a JEOL JMS-DX300 mass spectrometer at 70 eV. The TLC analyses and column chromatography were carried out with Merck Kieselgel60F-254 plates and Wako gel C-200 using methanol-NaCl aq (1:1) as an eluent.

N,N'-Bis(2-methoxy-2,4,6-cycloheptatrienylidene)-1,2-ethanediammonium bis(fluorosulfate) (9a): A solution of 6a (1.00 g, 3.73 mmol) and methyl fluorosulfate (1.70 g, 14.9 mmol) in CH₂Cl₂ (10 ml) was stirred for 24 h at room temperature. The precipitates were collected, washed with cold CH₂Cl₂ and dried in vacuo to give, upon recrystallization from methanol, 9a (1.68 g, 91%) as pale yellow scales; mp 209 °C; UV λ max (MeOH) 248 (log ε 4.52), 338 (4.05), 372 nm (4.20); ¹H NMR (270 MHz, CD₃OD) δ 4.13 (4H, s, CH₂x2), 4.26 (6H, s, OCH₃x2), 7.65 (2H, t, J=9 Hz, H-5,5'), 7.80 (2H, d, J=11 Hz, H-7,7'), 7.90 (2H, dd, J=11 and 9 Hz, H-6,6'), 7.93 (2H, d, J=11 Hz, H-3,3'), 8.11 (2H, dd, J=11 and 9 Hz, H-4,4').

Anal. Calcd for C₁₈H₂₂N₂O₈F₂S₂: C, 43.54; H, 4.47; N, 5.68. Found: C, 43.83; H, 4.75; N, 5.37.

N,N'-Bis(S-isopropyl-1-oxo-2,4,6-cycloheptatrien-2-yl)-1,2-ethanediamine (6c): A solution of 5-isopropyl-2-methoxympone (500 mg, 2.81 mmol) and 4a (85 mg, 1.41 mmol) in ethanol (2 ml) was heated at 80 °C for 4 h and then the solution was set aside at room temperature, depositing crystals after several hours. The precipitates were filtered off, giving 6c (430 mg, 87% yield) as yellow leaflets after recrystallization from ethanol; mp 219-222 °C; UV λ max (CHCｌ₃) 245 (log ε 3.77), 343 (3.55), 389 (3.27), 410 nm (3.42); IR (KBr) ν 3260, 2950, 1605, 1580, 1550, 1500, 1440, 1385, 1255, 1015, 845, 725, 635 cm⁻¹; ¹H NMR (270 MHz, CDCl₃) δ 1.22 (12H, d, J=7 Hz, CH₃x4), 2.80 (2H, septet, J=7 Hz, CH₂x2), 3.09 (2H, septet, J=7 Hz, CH₂x2), 4.15 (4H, s, CH₂x2), 6.51 (2H, d, J=10.7 Hz, H-3,3'), 7.11 (2H, dd, J=10.7 and 2 Hz, H-4,4'), 7.22 (2H, dd, J=12.2 and 2 Hz, H-6,6'), and 7.24 (2H, br, NH₂2); ¹³C NMR (67.8 MHz, CDCl₃) δ 23.9, 37.2, 41.2, 109.1, 129.7, 133.3, 137.3, 143.6, 153.8, 176.2. Anal. Calcd. for C₂₂H₂₈N₂O₂: C, 43.54; H, 4.47; N, 5.37. Found: C, 43.83; H, 4.75; N, 5.37.

N,N'-Bis(5-isopropyl-1-oxo-2,4,6-cycloheptatrien-2-yl)-1,2-ethanediamine (6c): A solution of 5-isopropyl-2-methoxympone (500 mg, 2.81 mmol) and 4a (85 mg, 1.41 mmol) in ethanol (2 ml) was heated at 80 °C for 4 h and then the solution was set aside at room temperature, depositing crystals after several hours. The precipitates were filtered off, giving 6c (430 mg, 87% yield) as yellow leaflets after recrystallization from ethanol; mp 219-222 °C; UV λ max (CHCｌ₃) 245 (log ε 3.77), 343 (3.55), 389 (3.27), 410 nm (3.42); IR (KBr) ν 3260, 2950, 1605, 1580, 1550, 1500, 1440, 1385, 1255, 1015, 845, 725, 635 cm⁻¹; ¹H NMR (270 MHz, CDCl₃) δ 1.22 (12H, d, J=7 Hz, CH₃x4), 2.80 (2H, septet, J=7 Hz, CH₂x2), 3.09 (2H, septet, J=7 Hz, CH₂x2), 4.15 (4H, s, CH₂x2), 6.51 (2H, d, J=10.7 Hz, H-3,3'), 7.11 (2H, dd, J=10.7 and 2 Hz, H-4,4'), 7.22 (2H, dd, J=12.2 and 2 Hz, H-6,6'), and 7.24 (2H, br, NH₂2); ¹³C NMR (67.8 MHz, CDCl₃) δ 23.9, 37.2, 41.2, 109.1, 129.7, 133.3, 137.3, 143.6, 153.8, 176.2. Anal. Calcd. for C₂₂H₂₈N₂O₂: C, 43.54; H, 4.47; N, 5.37. Found: m/z 352.2170 N,N'-Bis(5-isopropyl-2-methoxy-2,4,6-cycloheptatrienylidene)-1,2-ethanediammonium bis(fluorosulfate) (9b): A solution of 6c (500 mg, 1.42 mmol) in CH₂Cl₂ (10 ml) was treated as above with methyl fluorosulfate (630 mg, 5.52 mmol) to give 9b (758 mg, 92%): Pale yellow scales (from MeOH); mp 125-128 °C; UV λ max (MeOH) 248 (log ε 4.61), 335 (4.12), 374 nm (4.28); ¹H NMR (270 MHz, CDCl₃) δ 1.32 (12H, d, J=7 Hz, CH₃x4), 3.09 (2H, septet, J=7 Hz, CH₂x2), 4.15 (4H, s, CH₂x2),
4.25 (6H, s, OCH₃x2), 7.74 (2H, d, J=11 Hz, H-7,7'), 7.83 (2H, dd, J=11 and 2 Hz, H-6,6'), 7.99 (2H, d, J=12 Hz, H-3,3''), 8.13 (2H, dd, J=12 and 2 Hz, H-4,4''); ¹³C nmr (67.8 MHz, CD₃OD) δ 23.7 (CH₃), 38.7, 42.6 (CH₂), 58.6 (OCH₃), 122.5, 124.7, 138.2, 146.3, 156.8, 158.3, 159.3. Anal. Calcd for C₂₄H₃₄N₂O₈F₂S₂: C, 49.64; H, 5.90; N, 4.82. Found: C, 49.39; H, 5.82; N, 4.61.

N,N'-Bis(2-methoxy-2,4,6-cycloheptatrienyldene)-1,3-propanediammonium bis(fluorosulfate) (9c): Treatment of 6b₆a (900 mg, 3.19 mmol) with methyl fluorosulfate (1.45 g, 12.7 mmol) in CH₂Cl₂ (20 ml) similarly gave 9c (1.49 g, 92%): Pale yellow crystals (from MeOH); mp 205-207°C; uv λ max (MeOH) 246 (log ε 4.66), 333 (4.16), 364 nm (4.29); ¹H nmr (270 MHz, CD₃OD) S 2.26 (2H, quintet, CH₂), 3.87 (4H, t, J=7 Hz, CH₂x2), 4.27 (6H, s, CH₃x2), 7.58 (2H, t, J=9 Hz, H-5,5'), 7.73 (2H, d, J=10 Hz, H-7,7'), 7.86 (2H, ddd, J=10, 9 and 1 Hz, H-6,6'), 7.88 (2H, d, J=11.5 Hz, H-3,3'), 8.01 (2H, ddd, J=11.5, 9, and 1 Hz, H-4,4'); ¹³C nmr (67.8 MHz, CD₃OD) δ 26.8 (CH₂), 42.4 (N-CH₂), 58.8 (OCH₃), 121.6, 124.5, 134.1, 140.6, 146.0, 159.3, 160.8. Anal. Calcd for C₁₉H₂₄N₂O₈F₂S₂: C, 44.70; H, 4.73; N, 5.49. Found: C, 44.64; H, 5.03; N, 5.41.

**Reaction of 9a with 4a.**

(a): A suspension of 9a (200 mg, 0.40 mmol), 4a (27 mg, 0.45 mmol), and Et₃N (200 mg, 1.98 mmol) in methanol (5 ml) was stirred for 30 h at room temperature. The reaction mixture was concentrated in vacuo and the residue was extracted with chloroform. After concentration the desidue was passed through a silica gel column using methanol-NaCl aq (1:1) as eluent to give 5a (81 mg, 69% yield), 10a (8 mg, 7%) and 11a (15 mg, 13%).

(b) The reaction in the presence of sodium carbonate: To a suspension of 9a (200 mg, 0.40 mmol) and Na₂CO₃ (200 mg, 1.89 mmol) in methanol (10 ml) were added 4a (27 mg, 0.45 mmol) and Et₃N (50 mg, 0.50 mmol), and the mixture was stirred for 30 h at room temperature. Precipitates were collected, and extracted with chloroform. The extracts were combined with the filtrate and concentrated in vacuo. The residue was dissolved in chloroform and chromatographed as described above to give 5a (18 mg, 15%), 10a (38 mg, 32%) and 11a (54 mg, 46%). The reactions of 9a, 4a (mole ratio 1:1), Et₃N and K₂CO₃ or Li₂CO₃ similarly gave 5a, 10a and 11a, and the yields are given in Table 1.

7,8,16,17,25,26,34,35-Octahydro-6H,15H,24H,33H-tetracyclohepta[b,h,n,l][1,4,7,10,13,-16,19,22]octaazacyclotetracosine (10a): Yellow needles (from CHCl₃); mp > 300 °C; uv λ max (CHCl₃) 262 (log ε 4.80), 345 (4.51), 362 (4.61), 414 (4.46), 438 (4.33), 465 nm (3.99); ir (KBr) ν 3210, 2900, 2845, 2825, 1605, 1588, 1548, 1535, 1530, 1510, 1493, 1470, 1450, 1425, 1414, 1380, 1350,
1270, 1205, 1115, 1005, 970, 928, 820, 745, 705, 620 cm⁻¹; 1H nmr (270 MHz, CDCl₃) δ 3.67 (16H, s, CH₂x8), 6.18 (4H, t, J=9 Hz, H-5x4), 6.37 (8H, d, J=11 Hz, H-3,7 x4), 6.79 (8H, dd, J=11 and 9 Hz, H-4,6x4); FAB-ms m/z 585 (MH⁺). Anal. Calcd for C₃₆H₄₀N₈: C, 73.94; H, 6.89; N, 19.16. Found: C, 73.65; H, 6.62; N, 18.89.

7,8,16,17,25,26-Hexahydro-6H,15H,24H-tricyclohepta[b,h,n][1,4,7,10,13,16]hexaaaazacyclooctadecine (11a): Yellow needles (from CHCl₃-MeOH); mp 245-246 °C; uv λ max (CHC₃) 264 (log ε 4.86), 345sh (4.58), 362 (4.70), 411 (4.55), 436 (4.37), 465 nm (3.90); ir (KBr) ν 3250, 2850, 1585, 1505, 1460, 1260, 1120, 880, 740, 700, 620 cm⁻¹; 1H nmr (270 MHz, CDCl₃) δ 3.66 (12H, s, CH₂x6), 6.17 (3H, t, J=9.5 Hz, H-5x3), 6.35 (6H, d, J=11.5 Hz, H-3,7 x3), 6.80 (6H, dd, J=11.5 and 9.5 Hz, H-4,6x3); 1³C nmr (67.8 MHz, CDCl₃) δ 46.1 (CH₂), 110.4 (C-3,7), 117.8 (C-5), 133.4 (C-4,6), 153.7 (C-1,2); ms (70 eV) m/z 438 (M⁺, 39%), 409 (7), 305 (12), 279 (22), 159 (56), 147 (87), 131 (100). Anal. Calcd for C₂₇H₃₀N₈: C, 73.94; H, 6.88; N, 19.16. Found: C, 73.57; H, 6.72; N, 19.15.

Reaction of 9b with 4a: A suspension of 9b (200 mg, 0.34 mmol), 4a (23 mg, 0.38 mmol), Et₃N (50 mg, 0.50 mmol) and Na₂CO₃ (200 mg, 1.89 mmol) in methanol (10 ml) was similarly treated as above to give 5c (23 mg, 18%), 10b (41 mg, 32%) and 11b (56 mg, 43%).

7,8,16,17,25,26,34,35-Octahydro-6H,15H,24H,33H-3,12,21,30-tetraisopropyltetracyclohepta[b,h,n][1,4,7,10,13,16,19,22]octaazacyclotetracosine (10b): Yellow needles (from CHCl₃); mp > 300 °C; uv λ max (CHC₃) 264 (log ε 5.31), 345sh (5.05), 365 (5.12), 417 (4.95), 435 nm (4.86); ir (KBr) ν 3220, 2950, 2850, 1580, 1505, 1440, 1390, 1290, 1260, 1120, 815 cm⁻¹; 1H nmr (500 MHz, CDCl₃) δ 1.17 (24H, d, J=7 Hz, CH₃x8), 2.63 (4H, septet, J=7 Hz, CHx4), 3.64 (16H, s, CH₂x8), 6.36 (8H, d, J=11.5 Hz, H-4,6x4), 6.70 (8H, d, J=11.5 Hz, H-3,7x4); FAB-ms m/z 753 (MH⁺). Anal. Calcd for C₄₈H₆₄N₈: C, 76.56; H, 8.57; N, 14.88. Found: C, 76.28; H, 8.63; N, 14.61.

7,8,16,17,25,26-Hexahydro-6H,15H,24H-3,12,21-triisopropyltetracyclohepta[b,h,n][1,4,7,10,13,16]hexaaazacyclooctadecine (11b): Yellow needles (from CHCl₃-MeOH); mp 235-236 °C; uv λ max (CHCl₃) 265 (log ε 4.64), 345sh (4.41), 364 (4.51), 414 (4.32), 432 nmsh (4.21); ir (KBr) ν 3220, 2950, 2800, 1580, 1445, 1390, 1300, 1260, 815 cm⁻¹; 1H nmr (500 MHz, CDCl₃) δ 1.17 (24H, d, J=7 Hz, CH₃x8), 2.63 (3H, septet, J=7 Hz, CHx3), 3.62 (12H, s, CH₂x6), 6.32 (6H, d, J=11.5 Hz, H-4,6x3), 6.70 (6H, d, J=11.5 Hz, H-3,7x3); 1³C nmr (67.8 MHz, CDCl₃) δ 24 (CH₃), 36.5 (CH), 46 (CH₂), 110 (C-3,7), 131.5 (C-4,6), 137 (C-5), 152 (C-1,2); ms (70 eV) m/z 564 (M⁺, 28%), 549 (13), 535 (9), 375 (1), 363
1H-2,3-Dihydro-7-isopropylcyclohepta[bl,4]pyrazine (5c): Yellow oil; uv λ max (MeOH) 252 (log ε 4.49), 368 (3.84), 428 nm (3.81); 1H nmr (100 MHz, CDCl3) δ 1.12 (6H, d, J=7 Hz, CH3x2), 2.56 (1H, septet, J=7 Hz, -CH-x2), 3.48 (4H, s, CH2x2), and 6.58 (4H, s, H-5,6,8,9). Found: m/z 188.1337. Calcd for C12H16N2 M. 188.1313.

Reaction of 9c with 4b: Compound (9c) (200 mg, 0.39 mmol) similarly was treated with 4b (32 mg, 0.43 mmol) in the presence of Et3N (50 mg, 0.50 mmol) and Na2CO3 (200 mg, 1.89 mmol) in methanol (10 ml) gave 12 (25 mg, 16%), 1 (n=3) (101 mg, 65%) and 5c (17 mg, 11%).

6,7,8,9,16,17,18,26,27,28,29,36,37,38,39-Hexadecahyrotetracyclohepta[b,i,p,r][1,4,-8,11,15,18,22,25]octaazacyclooctacosine (12): Yellow needles (from CHCl3-MeOH); mp > 300 °C; uv λ max (CHCl3) 261 (log ε 4.90), 346sh (4.60), 360 (4.68), 415 (4.55), 441sh (4.38), 465 nm (3.87); ir (KBr) ν 3200, 2900, 2820, 1585, 1505, 1450, 1380, 1270, 1120, 740, 700, 620 cm−1; 1H nmr (270 MHz, CDC13) δ 2.25 (8H, quintet, J=7 Hz, CH2x4), 3.44 (16H, t, J=7.3 Hz, CH2x8), 6.14 (4H, t, J=9 Hz, H-5x4), 6.31 (8H, d, J=11 Hz, H-3,7 x4), 6.77 (8H, dd, J=11 and 9 Hz, H-4,6x4); 13C nmr (67.8 MHz, CDCl3) δ 30.1 (CHz), 44.5 (CHz), 110.4 (C-3,7), 117.7 (C-5), 133.4 (C-4,6), 153.7 (C-1,2); FAB-ms m/z 641 (MH+). Anal. Calcd for C40H48Ns: C, 74.97; H, 7.55; N, 17.49. Found: C, 74.65; H, 7.63; N, 17.28.

N-Acetyl-N'-(2-[2-acetamidoethyl]amino)-2,4,6-cycloheptatrienylidene]-1,2-ethanediamine (13): A mixture of 33 (500 mg, 2.56 mmol) and N-acetyl-1,2-ethanediamine (4e) (1.04 g, 10.2 mmol) in absolute ethanol (6 ml) was heated at 80 °C for 30 h under an argon atmosphere. After concentration in vacuo, the residue dissolved in chloroform was washed with 10% aqueous NaOH and water. The organic layer was concentrated and then passed through a silica gel column using benzene-methanol (20:1) as an eluent to give 13 (660 mg, 90%); Yellow needles (from CHCl3); mp 170-171 °C ; uv λ max (MeOH) 260 (log ε 4.31), 327sh (3.73), 347 (3.98), 357 (4.02), 396sh (3.81), 415 (3.90), 436sh (3.76), 463 nm (3.29); ir (KBr) ν 3450, 3300, 3290, 2850, 1640, 1590, 1560, 1540, 1510, 1490, 1450, 1395, 1370, 1265, 1140, 1030, 960, 740, 700 cm−1; 1H nmr (270 MHz, CDCl3) δ 2.06 (6H, s, CH3x2), 3.36 (4H, m, CH2x2), 3.68 (4H, m, CH2x2), 6.18 (1H, t, J=10 Hz, H-5), 6.22 (2H, d, J=10 Hz, H-3,7), 6.76 (2H, t, J=10 Hz, H-4,6), 7.15 (2H, br, NH); ms (70 eV) m/z 290 (M+, 7%), 218 (64), 204 (26), 159 (15), 133 (100), 86 (86). Found: m/z 290.1766. Calcd for C15H22N4O2: M, 290.1742.
Hydrolysis of 13. A solution of 13 (400 mg, 1.38 mmol), H2O (0.5 ml) and H2SO4 (0.5 ml) in ethanol (10 ml) was heated at 80 °C for 20 h. After having been set aside overnight at room temperature, the pale yellow needles which formed was collected and washed with cold methanol to give sulfate (14) (362 mg, 56%). The filtrate was neutralized with 10% NaOH, extracted with chloroform. The extracts were concentrated in vacuo. The residue was dissolved in chloroform and passed through a silica-gel column using methanol-NaCl aq (1:1) as an eluent to give 5a (23 mg, 11%) and unreacted 13 (107 mg, 27%). Sulfate (14) was neutralized to give, upon extraction with chloroform, 2 (n=2) quantitatively.

N-[2-(2-Aminoethyl)amino-2,4,6-cycloheptatrienylidene]-1,2-ethanediamine (2, n=2): Yellow crystals; mp 110-112 °C; uv \( \lambda_{\max} \) (CHCl3) 240\text{sh}, 262, 348, 360, 418, 423, 465 nm\text{sh}; ir (KBr) v 3380, 3180, 2940, 2870, 1590, 1570, 1530, 1505, 1465, 1455, 1425, 1387, 1332, 1265, 1210, 1132, 980, 880, 815, 735, 703 cm\(^{-1}\); \( ^1\)H nmr (270 MHz, CDCl3) \( \delta \) 1.76 (4H, br, \text{NH}_2\text{x2}), 3.06 (4H, t, J=6 Hz, \text{CH}_2\text{x2}), 3.38 (4H, t, J=6 Hz, \text{CH}_2\text{x2}), 6.18 (1H, t, J=9.5 Hz, H-5), 6.33 (2H, d, J=11 Hz, H-3,7), 6.77 (2H, dd, J=11 and 9.5 Hz, H-4,6); \( ^{13}\)C nmr (67.8 MHz, CDCl3) \( \delta \) 42.13 (t, \text{CH}_2), 49.30 (t, \text{CH}_2), 110.57 (d, C-3,7), 118.21 (d, C-5), 133.13 (d, C-4,5), 153.48 (s, C-1,2); ms (70 eV) m/z 206 (M\(^+\), 10%), 176 (99), 145 (56), 133 (100). Found: m/z 206.1535. Calcd for C\(_{11}\)H\(_{17}\)N\(_4\): M, 206.1531.


Reaction of 9a with 14: Treatment of 9a (200 mg, 0.40 mmol) with 14 (206 mg, 0.22 mmol), Et\(_3\)N (50 mg, 0.50 mmol) and Na\(_2\)CO\(_3\) (200 mg, 1.98 mmol) in methanol (10 ml) in a manner similar to that described above for 9a with 4a gave 11a (117 mg, 67%) and 5a (21 mg, 9%).

Reaction of 3 with 2 (n=2): A solution of 3 (200 mg, 1.02 mmol) and 2 (n=2) (250 mg, 1.21 mmol) in absolute ethanol (2 ml) was heated at 70 °C for 30 h under an argon atmosphere. After concentration in vacuo, the residue dissolved in chloroform was washed with 10% aqueous NaOH and water, concentrated and then passed through a silica gel column using methanol-NaCl aq (1:1) solution as an eluent to give 11a (16 mg, 4%) and 5a (123 mg, 83%).

N,N'-Bis[2-(2-acetamidoethyl)amino-2,4,6-cycloheptatrienylidene]-1,2-ethanediamine (15b): A suspension of 9a (200 mg, 0.403 mmol), 4c (150 mg, 1.47 mmol), and Na\(_2\)CO\(_3\) (100 mg, 1.47 mmol) in methanol (10 ml) was treated as above to give, upon recrystallization from chloroform, 15b as yellow needles (153 mg, 87%); mp 176-180 °C; uv \( \lambda_{\max} \) (MeOH) 260 (log \( \varepsilon \) 4.53), 349 (4.21), 357 (4.23), 414 nm (4.16); ir (KBr) v 3450, 3290, 2920, 2850, 1640, 1590, 1540, 1510, 1460, 1430, 1385, 1370, 1270, 1205,
1085, 880, 860, 740, 700, 605 cm\(^{-1}\); \(^1\)H nmr (270 MHz, CDCl\(_3\)) \(\delta\) 1.95 (6H, s, CH\(_2\)x2), 2.18 (2H, t, J=6.7 Hz, NHAcx2), 3.48 (8H, m, CH\(_2\)x4), 3.62 (4H, m, CH\(_2\)x2), 6.10 (2H, s, NHx2), 6.22 (2H, t, J=10.5 Hz, H-5), 6.27 (2H, d, J=10 Hz, H-7 or 3), 6.33 (2H, d, J=11 Hz, H-3 or 7), 6.83 (4H, m, J=10.5 Hz, H-4,6); FAB-ms m/z 437 (MH\(^+\)). Anal. Calcd for C\(_{24}\)H\(_{32}\)N\(_6\)O\(_2\): C, 66.03; H, 7.39; N, 19.25. Found: C, 66.23; H, 7.64; N, 18.96.

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REFERENCES
7. We used a small sealed tube under an argon atmosphere to avoid oxygen on refluxing. A stopped bottle can also be used more conveniently.
8. For convenience, numbering of the seven-memberd ring of 10, 11, and 12 on the nmr assignments are shown in the formulas.

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