

## Formation and Isolation of Huge Cyclic Oligomers: Polycondensation of 1,5-Bis(1-hydroxy-3,6,9-trioxanonyl)naphthalene and Terephthaloyl Chloride

Ingrid J. A. Mertens,<sup>a</sup> Leonardus W. Jenneskens,<sup>\*a</sup> Edward J. Vlietstra,<sup>a</sup> Anca C. van der Kerk-van Hoof,<sup>b</sup> Jan W. Zwikker,<sup>a</sup> Wilberth J. J. Smeets<sup>c</sup> and Anthony L. Spek<sup>c</sup>

<sup>a</sup> Debye Institute, Department of Physical Organic Chemistry, Utrecht University, Padualaan 8, 3584 CH Utrecht, The Netherlands

<sup>b</sup> Bijvoet Center for Biomolecular Research, Department of Mass Spectrometry, Utrecht University, PO Box 80083, 3508 TB Utrecht, The Netherlands

<sup>c</sup> Bijvoet Center for Biomolecular Research, Department of Crystal and Structural Chemistry, Utrecht University, Padualaan 8, 3584 CH Utrecht, The Netherlands

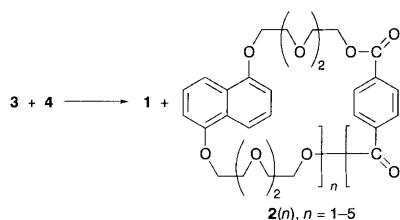
Polycondensation of 1,5-bis(1-hydroxy-3,6,9-trioxanonyl)naphthalene **3** and terephthaloyl chloride **4** gives giant macrocycles, *i.e.* crownphanes **2**(*n*) with 30*n* (*n* = 1–5) atom perimeters, in *ca.* 30% *m/m* overall yield; owing to self-complementarity by edge–face arene–arene interactions, a packing ratio of 71.8% is found for **2**(1).

Although cyclic oligomers are generated as side products under common polycondensation reaction conditions,<sup>1</sup> owing to their low overall yield (*ca.* 1–5% *m/m*) only a few representatives have hitherto been isolated and characterized.<sup>2</sup> Nevertheless, they are of interest to assess the differences and similarities between both cyclic and linear oligomers *vs.* the polymer.

Here we report novel results found during polycondensation of 1,5-bis(1-hydroxy-3,6,9-trioxanonyl)naphthalene **3** and terephthaloyl chloride **4**. Both in the melt (120 °C, 3 h<sup>1</sup>) and in solution ([**3**] = [**4**] = 0.33 and 0.033 mol l<sup>-1</sup>, respectively, solvent 1,2-dichloroethane and 4 equiv. of pyridine, 80 °C, 3 h<sup>1</sup>) a series of crownphanes **2**(*n*) (*n* = 1–5) is formed in considerable yield without the use of high dilution conditions (Scheme 1).<sup>4</sup> Initial evidence for their formation was obtained from TLC and GPC analysis<sup>†</sup> of the crude reaction mixtures. Precipitation of the high molecular weight fraction in methanol followed by chromatographic analysis (GPC/HPLC) of the viscous precipitate and the methanol fraction revealed that the low molecular weight compounds are soluble in methanol (four major products are discernible). Their overall yield with respect to polymer **1** increases in going from the melt to solution and is affected by the monomer concentration (melt: *ca.* 2% *m/m*; solution: [**3**] = [**4**] = 0.33 mol l<sup>-1</sup>, *ca.* 12% *m/m* and [**3**] = [**4**] = 0.033 mol l<sup>-1</sup> *ca.* 30% *m/m*). The four major, low molecular weight products identified in the methanol-soluble fraction and a fifth compound were isolated using a two-step preparative

column chromatography procedure.<sup>†</sup> GPC and HPLC analysis of the isolated compounds showed that they possess different retention times [*t*<sub>R</sub>(GPC) and *t*<sub>R</sub>(HPLC)] and purity (HPLC) > 99% (*n* = 1–3) and > 95% (*n* = 4 and 5), respectively (Table 1). The *t*<sub>R</sub>(GPC) values indicate that the isolated compounds are structurally related; mass increments of *ca.* 550 amu are found with increasing *n*.<sup>†</sup> Concurrently, spectroscopy (<sup>1</sup>H, <sup>13</sup>C, two-dimensional CH-correlation NMR and FT-IR) unambiguously showed that they are composed of coupled monomers **3** and **4** in a 1 : 1 ratio. With the exception of the compound with *t*<sub>R</sub>(HPLC/GPC) = 5.31/11.13 for which an upfield shift of the terephthaloyl protons (Δδ = -0.40 ppm) is found, all <sup>1</sup>H and <sup>13</sup>C NMR spectra are identical. These results strongly suggest that the isolated compounds are the cyclic oligomers **2**(*n*) with different values of *n* (Scheme 1). This is corroborated by FAB-MS; in going from *n* = 1 to *n* = 5 [M + H]<sup>+</sup> and [M + H<sub>2</sub>O]<sup>+</sup> ions are found which differ by consecutive 554 amu increments (Table 1).<sup>†</sup> An excellent linear relationship is found between log(FAB-MS, [M + H]<sup>+</sup>) and *t*<sub>R</sub> (GPC; correlation coefficient *r*<sup>2</sup> = 0.996). In line with their macrocyclic character, only loss of (multiple) C<sub>2</sub>H<sub>4</sub>O (44 amu) fragments directly from the [M + H]<sup>+</sup> ion is found in the FAB-MS spectra.<sup>5</sup> Thermal analysis (DSC) showed that **2**(1,2) are crystalline compounds while **2**(3,4) only possess a glass transition temperature (Table 1). The redox properties of **2**(1–3) were assessed using cyclic voltammetry; an irreversible one-electron oxidation and one-electron reduction process was found for the naphthyl and terephthaloyl moieties, respectively (Table 1).<sup>†</sup> Since for **2**(1–3) the values of *E*<sub>pa</sub> and *E*<sub>pc</sub> are nearly similar, the redox-active moieties do not interact.

To our knowledge, **2**(3–5) belong to the largest cyclic oligomers which have hitherto been isolated.<sup>2,4,6</sup> The availability of the starting materials and the simple preparative column chromatography procedure allows the isolation of even **2**(5) on at least a 10–50 mg scale in one run. A rationalization for the high overall yield of cyclic oligomers is provided by <sup>1</sup>H NMR conformational analysis<sup>7</sup> of the 1-hydroxy-3,6,9-triox-



Scheme 1

Table 1 Salient properties of the cyclic oligomers **2**(*n*)<sup>†</sup>

<i>n</i>	Size	<i>t</i> <sub>R</sub> (GPC) <sup>a</sup> /min	<i>t</i> <sub>R</sub> (HPLC) <sup>b</sup> /min (% <i>m/m</i> )	Isolated yield <sup>c</sup> /% <i>m/m</i> [purity (%)]	FAB-MS ([M + H] <sup>+</sup> )	DSC <sup>d</sup> /°C	<i>E</i> <sub>pa</sub> , <i>E</i> <sub>pc</sub> <sup>e</sup> /V
1	30	11.13	5.31(21.9)	10.3 [>99]	555	116.7	1.07, -1.92
2	60	10.71	9.82(4.7)	3.2 [>99]	1109	125.0	1.05, -1.88
3	90	10.48	11.80(1.0)	1.2 [>99]	1663	0.5	1.03, -1.84
4	120	10.25	12.93(0.2)	1.2 [>95]	2217	0.0	—, —
5	150	10.09 <sup>f</sup>	14.53(—) <sup>f</sup>	0.13 [>95]	2771	—	—, —

<sup>a</sup> *t*<sub>R</sub> [**2**(*n*), GPC] in the soluble fraction after precipitation of **1** from [**3**] = [**4**] = 0.033 mol l<sup>-1</sup>. <sup>b</sup> *t*<sub>R</sub> [**2**(*n*), HPLC] in the soluble fraction after precipitation of **1**; % *m/m* of **2**(*n*) in parentheses from [**3**] = [**4**] = 0.033 mol l<sup>-1</sup>. <sup>c</sup> Preparative column chromatography; purity (HPLC) in square brackets. <sup>d</sup> DSC (second heating run); melt transition *T*<sub>m</sub> for **2**(1,2) and a glass transition *T*<sub>g</sub> for **2**(3,4). For **2**(5) neither a melt transition nor glass transition could be observed. <sup>e</sup> *E*<sub>pa</sub> and *E*<sub>pc</sub> from naphthyl and terephthaloyl moiety, respectively. <sup>f</sup> Not discernible in the soluble fraction obtained after precipitation; *t*<sub>R</sub> [**2**(5), GPC/HPLC] determined after preparative chromatography.

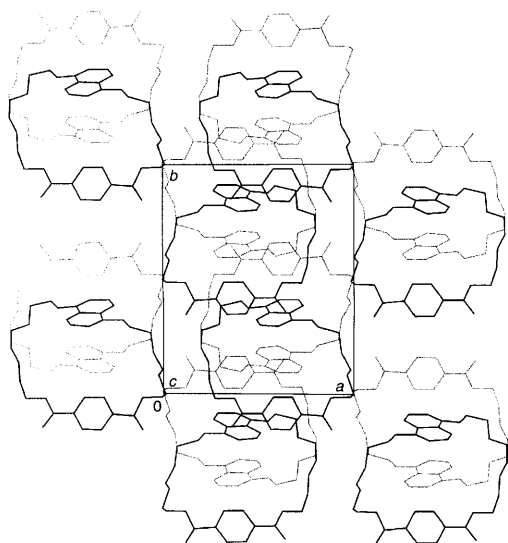
anonyl side chains of **3** at 25 °C (solvent; [<sup>2</sup>H<sub>2</sub>]dichloromethane or 1,1,2,2-[<sup>2</sup>H<sub>2</sub>]tetrachloroethane) and 80 °C (solvent 1,1,2,2-[<sup>2</sup>H<sub>2</sub>]tetrachloroethane). At both temperatures the consecutive O-CH<sub>2</sub>-CH<sub>2</sub>-O units are present in their *gauche* conformer  $x_g$  [**3**; 25 °C,  $x_g$  0.94, 0.92 and 0.90; 80 °C,  $x_g$  0.92, 0.88 and 0.85, respectively] leading to favourable pre-orientation for intramolecular ring-closure.

The cyclic nature of compounds **2**(*n*) was further ascertained by a single-crystal X-ray structure determination of **2**(1).<sup>‡</sup> Despite its 30-atom perimeter it possesses a very high packing ratio (71.8%). An examination of its solid-state packing motif indicates that minimalization of dipole-dipole and, in particular, weak non-covalent arene-arene interactions play an important role. Inversion symmetry-related terephthaloyl units of molecules **2**(1) pack face-to-face (distance 3.425 Å and interplanar angle 0.0°).<sup>‡</sup> Furthermore, as shown in Table 2, the distances between the centres of gravity (CG) of the six-membered rings of the naphthyl [CG(1) and CG(2)] and terephthaloyl [CG(3)] units of symmetry related molecules **2**(1) [ $d(\text{CG}-\text{CG})$  4.792–5.483 Å] and their interplanar dihedral angles [*ca.* 45 and 88°] are in line with those expected for attractive edge-face arene-arene interactions.<sup>8</sup> As a consequence, the cavity of a molecule **2**(1) is occupied by both a terephthaloyl and a naphthyl unit of two symmetry-related molecules **2**(1), giving a solid-state packing motif of infinite sheets of interpenetrating molecules in the *bc* plane at  $a = 1/2$

**Table 2** Edge-face arene-arene interactions between the aromatic moieties in the solid-state packing motif of **2**(1)

Edge-face <sup>a,b</sup>	$d(\text{CG}-\text{CG})/\text{Å}$	Interplanar dihedral angle/ <sup>o</sup>
CG(1)-CG(3) [(1 - <i>x</i> , 1/2 + <i>y</i> , 3/2 - <i>z</i> )]	5.482	88.5
CG(1)-CG(3) [(1 - <i>x</i> , - <i>y</i> , 1 - <i>z</i> )]	5.068	47.6
CG(1)-CG(3) [ <i>x</i> , 1/2 - <i>y</i> , 1/2 + <i>z</i> ]	4.792	88.5
CG(2)-CG(1) [ <i>x</i> , 1/2 - <i>y</i> , <i>z</i> - 1/2]	5.319	43.5
CG(2)-CG(3) [(1 - <i>x</i> , - <i>y</i> , 1 - <i>z</i> )]	5.906	45.7
CG(2)-CG(3) [ <i>x</i> , 1/2 - <i>y</i> , 1/2 + <i>z</i> ]	5.536	89.6

<sup>a</sup> Centres of gravity of the six-membered rings of the naphthyl [CG(1) and CG(2)] and terephthaloyl [CG(3)] units of **2**(1), respectively: CG(1) [0.5849(1), 0.32398(8), 0.7565(1)], CG(2) [0.6391(1), 0.38030(8), 0.6035(1)] and CG(3) [0.6245(1), -0.08327(8), 0.4450(1)]. Symmetry operations are depicted in square brackets.<sup>‡</sup> <sup>b</sup> Edge-face interactions between naphthyl-naphthyl and terephthaloyl-naphthyl moieties of symmetry-related molecules **2**(1).



**Fig. 1** Packing motif of **2**(1); projection in *ab* plane. Some molecules **2**(1) are highlighted and hydrogen atoms are omitted for clarity.

separated by oligo(ethyleneglycol) chain packing layers at  $a = 0$  and  $a = 1$ , *i.e.* **2**(1) is self-complementary and possesses both host and guest behaviour (Fig. 1). The packing motif is complemented by weak intra- and inter-molecular C-H...O interactions.<sup>9‡</sup>

Financial support (A. L. S. and W. J. J. S.) from SON/NWO is gratefully acknowledged.

Received, 9th May 1995; Com. 5/02906F

## Footnotes

<sup>‡</sup> GPC: Shodex mixed bed column, eluent THF, UV (254 nm) and RI detection, polystyrene standards [**1**; melt:  $M_w$  27 000,  $M_w/M_n$  2.28, and solution:  $M_w$  13 500,  $M_w/M_n$  1.80 (**3**) = [**4**] = 0.33 mol l<sup>-1</sup>) and  $M_w$  3500,  $M_w/M_n$  1.14 (**3**) = [**4**] = 0.033 mol l<sup>-1</sup>]. HPLC: reversed-phase C<sub>18</sub> column (3 μm), gradient elution acetonitrile-water (1 : 1 to 1 : 0), UV (254 nm) detection. TLC: silica; eluent acetone-*n*-hexane 1 : 1 v/v. Preparative column chromatography (column volume 550 ml, silica; eluent acetone-*n*-hexane 1 : 1 v/v): **2**(1) and **2**(2) were isolated directly from the methanol soluble fraction, while **2**(3-5) were initially isolated as a mixture and further purified in a second preparative column chromatography run (column volume 60 ml, silica; eluent acetone-*n*-hexane 1 : 1 v/v). CV: acetonitrile-0.1 mol l<sup>-1</sup> NBu<sub>4</sub>PF<sub>6</sub>, scan rate 100 mV s<sup>-1</sup>; *E* vs. SCE. DSC: Mettler DSC 12E, heating/cooling rate 5 °C min<sup>-1</sup>. FAB-MS: JEOL JMS SX/SX 102A four-sector mass spectrometer operated at 8 kV (resolution 3100 amu) with a JEOL MS-FAB 10D FAB gun operated with a 10 mA emission current (matrix *m*-nitrobenzyl alcohol).

<sup>‡</sup> Crystal data for **2**(1): C<sub>30</sub>H<sub>34</sub>O<sub>10</sub>,  $M = 554.59$ , colourless plate-shaped crystal (0.05 × 0.30 × 0.62 mm), monoclinic,  $P2_1/c$ ,  $a = 13.8318(11)$ ,  $b = 16.0285(9)$ ,  $c = 12.5574(11)$  Å,  $\beta = 107.56(1)^\circ$ ,  $V = 2654.3(4)$  Å<sup>3</sup>,  $Z = 4$ ,  $D_c = 1.388$  Mg m<sup>-3</sup>,  $F(000) = 1176$ ,  $\mu(\text{Mo-K}\alpha) = 1.0$  cm<sup>-1</sup>, 7889 reflections ( $1.27 < \theta < 24.18^\circ$ ,  $\omega$ - $2\theta$  scan;  $T = 150$  K) were measured on an Enraf-Nonius CAD4T diffractometer (rotating anode, graphite-monochromated Mo-K $\alpha$  radiation,  $\lambda = 0.71073$  Å). Data were corrected for Lorentz polarization effects and for a linear decay (1%) of the intensity control reflections, and merged into a dataset of 3928 unique reflections ( $R_i = 0.0540$ ). The structure was solved by direct methods (SHELXS-86) and difference Fourier techniques. One of the oxygen atoms [O(25)] within the ring is disordered [0.151(9) : 0.849(9)] over two positions. Hydrogen atoms were introduced at calculated positions and refined riding on their carrier atoms. All non-H atoms (except the minor disordered O atom) were refined on  $F^2$  (SHELXL-93) using all 3928 unique reflections, with anisotropic thermal parameters. Convergence was reached at  $R_1 = 0.0548$  for 2198 reflections with  $I > 2.0\sigma(I)$  and 367 parameters;  $wR_2 = 0.1189$ ,  $S = 0.95$  for all 3928 reflections,  $w = 1/[\sigma^2(F) + (0.0473P)^2]$ . A final difference Fourier map shows no residual density outside -0.35, 0.39 e Å<sup>-3</sup>. Bond lengths, valence and dihedral angles are in line with expectation. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Information for Authors, Issue No. 1.

## References

- 1 Cf. M. Ballauf, *Makromol. Chem., Rapid Commun.*, 1986, **7**, 407.
- 2 W. Memeger, Jr., J. Lazar, D. Ovenall, A. J. Arduengo, III and R. A. Leach, *Macromol. Symp.*, 1994, **77**, 105; D. J. Brunelle, H. O. Krabbenhoff and D. K. Bonauto, *Macromol. Symp.*, 1994, **77**, 117; B. R. Wood, J. A. Semleyn and P. Hodge, *Polymer*, 1994, **35**, 1542; M. Rothe and M. Zieger, *Tetrahedron Lett.*, 1994, **35**, 9011 and references cited therein.
- 3 S. Inokuma, S. Sakai and J. Nishimura, *Top. Curr. Chem.*, 1994, **172**, 87 and references cited therein.
- 4 High dilution conditions; F. Vögtle, S. Meier and R. Hoss, *Angew. Chem., Int. Ed. Engl.*, 1992, **31**, 1619 and references cited therein.
- 5 D. A. Jaeger and R. R. Whitney, *J. Org. Chem.*, 1975, **40**, 92.
- 6 Cf. C. Bazzicalupi, A. Bencini, V. Fusi, M. Micheloni, P. Paoletti and B. Valtancoli, *J. Org. Chem.*, 1994, **59**, 7508 and references cited therein.
- 7 E. Riande, M. Jimeno, R. Salvador, J. de Abajo and J. Guzman, *J. Phys. Chem.*, 1990, **94**, 7435 and references cited therein.
- 8 W. L. Jorgensen and D. L. Severance, *J. Am. Chem. Soc.*, 1990, **112**, 4768; C. A. Hunter and J. K. M. Sanders, *J. Am. Chem. Soc.*, 1990, **112**, 5525 and references cited therein.
- 9 G. A. Jeffrey, H. Maluszynska and J. Mitra, *Int. J. Biol. Macromol.*, 1985, **7**, 336.