

## Calix[4]naphthalenes: Cyclic Tetramers of 1-Naphthol and Formaldehyde

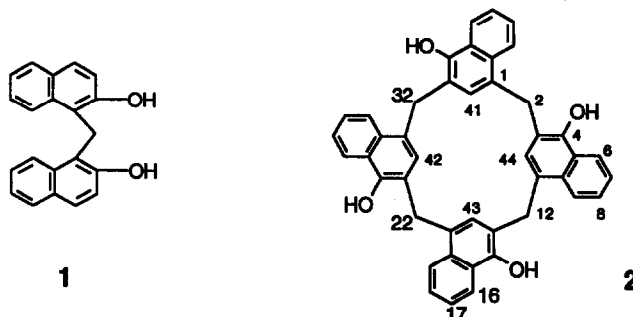
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**Abstract:** Three isomeric cyclic tetramers that are analogous to the calix[4]arenes and the calix[4]resorcinarenes are produced from the base-catalysed condensation of 1-naphthol and formaldehyde in refluxing dimethylformamide.

The complexity of the reaction of 1-naphthol with formaldehyde is well-known<sup>1,2,3</sup> and it has been assumed that cross-linked polymers are formed. By way of contrast, the reaction of 2-naphthol with formaldehyde under either base<sup>4</sup> or acid<sup>5</sup> catalysis readily affords a single product, *bis*-(2-hydroxy-1-naphthyl)-methane (1). We herein report our discovery that the base-catalyzed condensation of 1-naphthol with formaldehyde yields three isomeric cyclic tetramers. These are the first members of the class of naphthol-formaldehyde oligomers to be reported and we propose they be named "calix[4]naphthalenes" by analogy with the well-known calix[n]arenes and calix[n]resorcinarenes.<sup>6,7</sup>

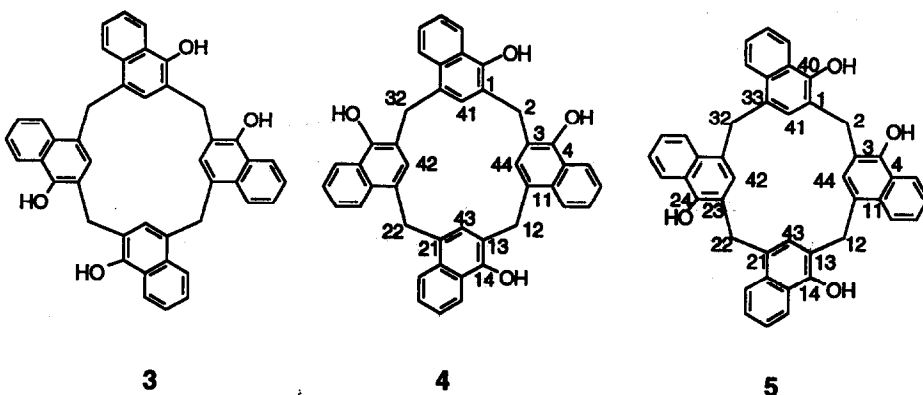
Fractional crystallization of the crude product mixture obtained from the reaction<sup>8</sup> in DMF of 1-naphthol, formaldehyde and potassium carbonate affords three products whose mass spectra indicate them to be isomeric tetramers, each having a molecular ion peak at  $m/e = 624$ . The four cyclic tetrameric isomers that are possible are depicted as 2-5. The first product that can be isolated from the reaction mixture crystallizes from acetone to yield a compound whose <sup>13</sup>C NMR spectrum shows twelve signals. By symmetry considerations 2 has



$C_4$  symmetry and thus should exhibit only eleven <sup>13</sup>C NMR signals. APT-<sup>13</sup>C NMR however reveals that the two highest-field signals at  $\delta$  31.9 and 30.7 are respectively due to a methylene and a methyl carbon. The latter signal can be shown to be due to acetone, but whether or not it is present as a true inclusion complex is uncertain at this

stage since it cannot be removed from the product by overnight heating under vacuum. The carbonyl carbon signal of acetone is normally of much lower intensity than the methyl signal and is not evident in the  $^{13}\text{C}$  NMR spectra of our product. The  $^{13}\text{C}$  NMR (see Table 1),  $^1\text{H}$  NMR, HETCOR, NOED spectra, and MS data are all consistent for structure 2. In the  $^1\text{H}$  NMR spectrum the methylene protons appear as a singlet at  $\delta$  4.29 at ambient temperature, indicating conformational flexibility.<sup>9</sup>

The second compound that can be isolated crystallizes from ethyl acetate. Its  $^{13}\text{C}$  NMR spectrum reveals only twenty one clearly resolved signals but its APT- $^{13}\text{C}$  spectrum shows that a pair of quaternary carbon signals and a pair of aromatic methine signals overlap. In addition, the height of one of the aliphatic methylene carbon signals is double that of each of the other two, confirming the presence of twenty three carbon signals which is predicted for 4.  $^1\text{H}$  NMR, HETCOR, NOED spectra and MS data are also consistent for structure 4 which has  $C_2$  symmetry. In its  $^1\text{H}$  NMR spectrum the methylene protons appear as three singlets at  $\delta$  4.08, 4.29 and 4.40 having relative intensities of 1:2:1. This isomer is thus also conformationally flexible.



The third isomer, which is the most difficult to isolate, crystallizes from diethyl ether. Its  $^{13}\text{C}$  NMR spectrum shows only forty two clearly resolved signals, with some obvious overlapping in a group of methine aromatic carbon signals which are centred around  $\delta$  124.5. In the  $^1\text{H}$  NMR spectra the methylene protons appear as signals of equal intensities at  $\delta$  4.09, 4.21, 4.32 and 4.45.  $^1\text{H}$  NMR, HETCOR, NOED spectra and MS data are also consistent for structure 5 which does not possess any symmetry. This isomer is also conformationally flexible at ambient temperatures. The  $^1\text{H}$  NMR spectra of the crude reaction product reveal that 2, 4, and 5 are the major components of the mixture, with no evidence at present for any significant amount of 3. A ratio of 1.0:2.2:3.0 for 2:4:5 can be estimated from the integration of the intra-annular aromatic protons at C41-C44 that are observed in the  $^1\text{H}$  NMR spectra of the crude reaction product.

**Table 1.** Selected  $^{13}\text{C}$  NMR Chemical Shifts for compounds **2**, **4** and **5** in  $\text{DMSO-}d_6$  ( $\delta_{\text{ppm}}$ ) at 75 MHz. Assignments based upon  $^{13}\text{C}$ -APT; HETCOR and NOED spectra. Signals denoted \* were not unambiguously assigned.

<b>2</b>		<b>4</b>		<b>5</b>	
carbon	$\delta_{\text{C}}$	carbon	$\delta_{\text{C}}$	carbon	$\delta_{\text{C}}$
2,12,22&32	31.9	12&32	31.6	32	30.0
		22	33.6	12	31.6
		2	36.7	22	31.7
				2	33.2
3,13,23&33	119.9	1&3	120.3	1;3	120.2*;120.4*
		13&31	120.9	13;23	120.6*;120.9*
41,42,43&44	128.6	41&44	128.5	41	128.2
		42&43	129.4	43	128.7
				42	129.1
				44	129.4
1,11,21&31	131.5	21&23	131.2	11;21	131.1*;131.3*
		11&33	131.4	31;33	131.4*;131.5*
4,14,24&34	147.9	14&30	147.3	4;14	147.6*;147.7*
		4&40	147.8	24;40	147.9*;148.0*

**Acknowledgements.** We thank Dr. D. J. Burnell for his ongoing interest and advice; Dr. C. R. Jablonski and Ms. N. Brunet for the NMR spectra; and Dr. B. Gregory and Ms. M. Baggs for the mass spectra. Memorial University and N.S.E.R.C. are acknowledged for the financial support of one of us (Z.L.).

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7. In principle, four naphthalene rings can be linked to one another at several different positions by methylene bridges. This could result in the formation of structural isomers whose "lower rim" is either of the same size, as in the case of the examples reported herein (16-membered carbocycle), or are of different sizes (12-28-membered carbocycle). Based on the naming and numbering system used for the calix[n]arenes<sup>6</sup>, compounds 2, 4 and 5 could be named as 4,14,24,34-tetrahydroxycalix[4]-naphthalene; 4,14,30,40-tetrahydroxycalix[4]naphthalene and 4,14,24,40-tetrahydroxycalix[4]naphthalene, respectively.
8. **Preparation of 2, 4 and 5.** To a solution of 1.44 g of purified 1-naphthol in 10 ml of DMF were added 0.70 ml of formalin solution (37%) and 1.0 ml of aqueous 10% potassium carbonate. The mixture was refluxed under nitrogen for 30 h and then cooled to 5 °C overnight. The precipitate was filtered, washed with deionized water until the washings were neutral to pH paper, and dried under vacuum overnight. Crystallization from acetone gave 0.15 g (9.6%) of 2 as a colourless powder, mp >300 °C (with decomposition). <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>): δ 4.29 (s, H-2,H-12,H-22,H-32), 6.62 (s, H-41,H-42,H-43,H-44), 7.53 (m, H-7,H-8,H-17,H-18,H-27,H-28,H-37,H-38), 8.02 (m, H-9,H-19,H-29,H-39), 8.19 (m, H-6,H-16,H-26,H-36); <sup>13</sup>C (DMSO-*d*<sub>6</sub>) for selected assignments see Table I: δ 30.7 (acetone), 31.9, 119.9, 122.6, 123.8, 124.5, 125.2, 125.8, 128.0, 128.6, 131.5, 147.9; IR (KBr): 3404 cm<sup>-1</sup>; MS *m/z*: 624 (M<sup>+</sup>, 52%). The mother liquor from the first filtration was poured onto a mixture of 5 g of ice and 10 ml of 5% aqueous HCl with stirring. The precipitate was filtered, washed with water until the washings were neutral to pH paper, and dried under vacuum. Crystallization from ethyl acetate gave 0.25 g (16%) of 4 as a colourless powder, mp >300 °C (with decomposition). <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>): δ 4.08 (s, H-22), 4.29 (s, H-12,H-32), 4.40 (s, H-2), 6.72 (s, H-41,H-44), 6.83 (s, H-42,H-43), 7.40 (m, H-7,H-8,H-16,H-18,H-26,H-27,H-36,H-37), 7.78 (d, H-9,H-35), 8.08 (m, H-19,H-25), 8.18 (m, H-16,H-28), 8.31 (d, H-6,H-38); <sup>13</sup>C (DMSO-*d*<sub>6</sub>) for selected assignments see Table I: δ 31.6, 33.6, 36.7, 120.3, 120.9, 122.2, 122.8, 123.7, 123.9, 124.6, 124.8, 125.3, 125.4, 125.9, 127.6, 127.7, 128.5, 128.7, 128.4, 131.2, 131.4, 147.3, 147.8 IR (KBr): 3404 cm<sup>-1</sup>; MS *m/z*: 624 (M<sup>+</sup>, 18%). The mother liquor from the ethyl acetate crystallization was evaporated to dryness. The residue was crystallized from diethyl ether to give 79 mg (5.0%) of 5 as a light yellow powder, mp >250 °C (with decomposition). <sup>1</sup>H NMR (MSO-*d*<sub>6</sub>): δ 4.09 (s, H-2), 4.21 (s, H-22), 4.32 (s, H-12), 4.45 (s, H-32), 6.64 (s, H-44), 6.66(s, H-41), 6.70 (s, H-42), 6.80 (s, H-43), 7.40 (m, H-7,H-8,H-17,H-18,H-27,H-28,H-36,H-37), 7.79 (d, H-35), 7.97 (d, H-19), 7.98 (d, H-29), 8.08 (d, H-9), 8.18-8.22 (m, H-6,H-16,H-26,H-38); <sup>13</sup>C (DMSO-*d*<sub>6</sub>) for selected assignments see Table I: δ 30.0, 31.6, 31.7, 33.2, 120.2, 120.4, 120.6, 120.9, 122.3, 122.4, 122.5, 122.8, 123.5, 123.6, 123.8, 124.0, 124.3, 124.4, 124.5(X3), 125.1, 125.2, 125.4, 125.5, 125.6, 125.7, 125.8, 127.5, 127.7, 127.9, 128.1, 128.2, 128.7, 129.1, 129.4, 131.1, 131.3, 131.4, 131.5, 147.6, 147.7, 147.9, 148.0; IR (KBr): 3404 cm<sup>-1</sup>; MS *m/z*: 624 (M<sup>+</sup>, 39%).
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(Received in USA 21 September 1992; accepted 22 February 1993)