

## Synthesis and X-ray Crystal Structure of Meso-5,5,7,12,12,14-hexamethyl-1,4,8,11-tetraazacyclotetradecane-1,8-di-(1-methylnaphthalene).

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Received: 19 December 2002; in revised form: 12 January 2003 / Accepted: 13 January 2003 /

Published: 28 February 2003

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**Abstract:** The pendant-arm macrocycle, meso-5,5,7,12,12,14-hexamethyl-1,4,8,11-tetraazacyclotetradecane-1,8-di-(1-methylnaphthalene) has been synthesized and its single crystal structure determined. The molecule crystallizes in a primitive monoclinic cell, with the space group  $P2_1/a$  (#14). The cell dimensions are  $a = 10.778(3)\text{\AA}$ ,  $b = 13.809(3)\text{\AA}$ ,  $c = 11.420(2)\text{\AA}$ ,  $\beta = 102.49(2)^\circ$ , volume =  $1659.5(6)\text{\AA}^3$ .

**Keywords:** Pendant-arm macrocycle, crystal structure, 1-methylnaphthalene

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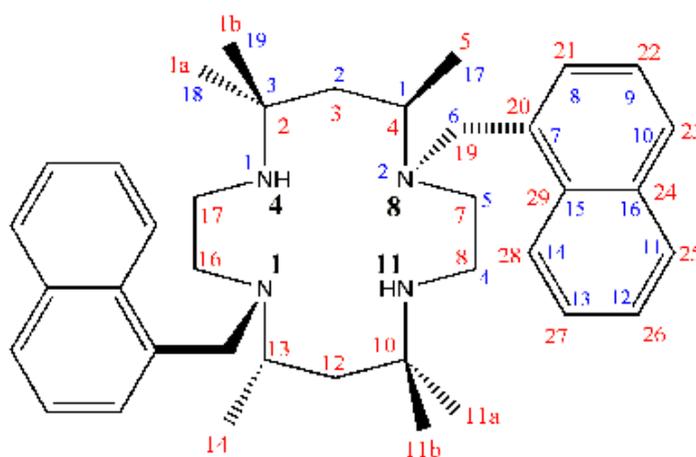
### Introduction

There is significant interest in the synthesis and properties of polyazamacrocycles bearing pendant-arms, particularly those having arms attached at the nitrogen atoms of the macrocycles. Most such functionalized macrocycles are often prepared by elaborate multi-step procedures, with synthesis of partially functionalized macrocycles being more difficult than fully-functionalized ones. Interest in these molecules and their transition metal complexes has focussed on applications to catalysis [1], ion-selectivity [2] and their use as radioimmunotherapy agents [3]. Recent reviews have examined

pendant-arm macrocycles as models for biological molecules [4] and the synthesis and reactivity of multinuclear macrocyclic complexes [5]. The synthesis and structure of polyazamacrocycles bearing pendant coordinating groups attached to the nitrogen donor atoms has been reviewed [6], as well as the synthesis and properties of transition metal complexes of tri- and tetraazamacrocycles [7].

We are currently interested in the effect of steric hindrance on the electron transfer properties of transition metal macrocycles. Our research involves the synthesis of pendant-arm polyazamacrocycles and their metal complexes, and the study of their redox kinetics [8]. This paper presents the synthesis and characterization of a tetraazamacrocycle derived from meso-5,5,7,12,12,14-hexamethyl-1,4,8,11-tetraazacyclotetradecane (“tetA”) bearing two pendant 1-methylnaphthalene groups, together with the X-ray crystal structure of the compound. The title pendant-arm macrocycle is shown in Figure 1. The red numbering in the figure refers to the NMR assignments (listed in the Experimental section below); the blue numbering corresponds to the atom labeling in the crystallographic data and the black numbering (1,4,8 and 11) correspond to the compound’s nomenclature.

**Figure 1.** Structural representation of the 1,8-di-(1-methylnaphthalene) derivative of tet A



The molecule is of particular interest for several reasons: as a tetraazamacrocycle it can coordinate to redox-active first-row transition metals; the pendant methylnaphthalenes provide steric bulk around the macrocycle, hindering close approach of redox agents and so should influence electron-transfer kinetics; and the methylnaphthalene groups introduce the possibility of interesting fluorescence behaviour of the macrocycle and its metal complexes.

## Results and Discussion

Refluxing of tetA with 1-chloromethylnaphthalene in the presence of carbonate (to remove by-product HCl as NaCl, carbon dioxide and water) results in alkylation of the ring nitrogens *via* a nucleophilic substitution reaction, represented by:

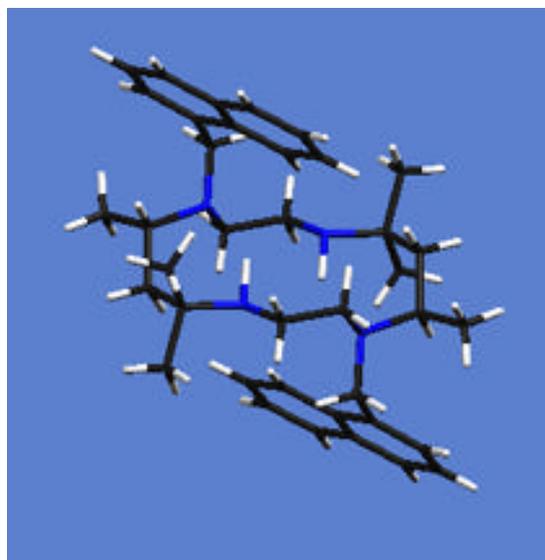


where R =  $-\text{CH}_2\text{C}_{10}\text{H}_7$ .

Generally, attempts to functionalize polyazamacrocycles by this method usually result in fully-substituted macrocycles. In the present system, the presence of the geminal dimethyl groups at the 5- and 12- positions of tet A introduce sufficient steric hindrance to limit substitution to the 1- and 8- positions only. While the synthetic procedure described in the Experimental section uses a 2:1 stoichiometric ratio of reactants, experiments using a stoichiometric excess ( $> 4.2:1$ ) of 1-chloromethylnaphthalene to tet A, with prolonged refluxing (2 weeks) still only produced the di-substituted product. The presence of unsubstituted N-H groups in the product was confirmed by the band at  $3259 \text{ cm}^{-1}$  in the infrared.

The title compound was found to be virtually insoluble in water, but very soluble in THF. Thus X-ray quality crystals were produced by allowing the THF to slowly evaporate from an 80% by volume solution of THF in water, containing the compound. The structure of the molecule, displayed using the Mercury 1.1 crystal structure visualization program (available as a free download from CCDC) is shown in Figure 2.

**Figure 2.** Mercury 1.1 display of meso-5,5,7,12,12,14-hexamethyl-1,4,8,11-tetraazacyclotetradecane-1,8-di-(1-methylnaphthalene)



The bond lengths and bond angles are listed in Tables 1 and 2.

**Table 1.** Bond lengths (Å)

atom	atom	Distance	Atom	atom	Distance
N1	C3	1.49(1)	N1	C4	1.46(1)
N2	C1	1.50(1)	N2	C5	1.47(1)
N2	C6	1.46(1)	C1	C2	1.51(1)
C1	C17	1.53(1)	C2	C3	1.52(1)
C3	C18	1.55(1)	C3	C19	1.54(1)
C4	C5	1.51(1)	C6	C7	1.52(1)
C7	C8	1.37(1)	C7	C15	1.41(1)
C8	C9	1.41(1)	C9	C10	1.35(1)
C10	C16	1.41(1)	C11	C12	1.34(1)
C11	C16	1.40(1)	C12	C13	1.40(1)
C13	C14	1.38(1)	C14	C15	1.42(1)
C15	C16	1.41(1)			

**Table 2.** Bond Angles(°)

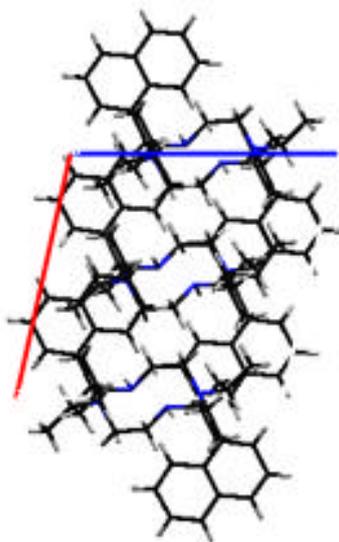
atom	atom	atom	Angle	atom	atom	atom	angle
C3	N1	C4	115.1(7)	C1	N2	C5	111.3(7)
C1	N2	C6	112.6(7)	C5	N2	C6	110.8(7)
N2	C1	C2	112.4(8)	N2	C1	C17	114.3(8)
C2	C1	C17	111.5(9)	C1	C2	C3	120.3(9)
N1	C3	C2	107.8(8)	N1	C3	C18	113.1(8)
N1	C3	C19	108.4(8)	C2	C3	C18	109.7(8)
C2	C3	C19	108.7(9)	C18	C3	C19	109.0(9)
N1	C4	C5	113.2(8)	N2	C5	C4	114.8(8)
N2	C6	C7	112.9(8)	C6	C7	C8	120.1(9)
C6	C7	C15	121.1(9)	C8	C7	C15	119(1)
C7	C8	C9	122(1)	C8	C9	C10	120(1)
C9	C10	C16	121(1)	C12	C11	C16	120(1)
C11	C12	C13	122(1)	C12	C13	C14	120(1)
C13	C14	C15	119.9(9)	C7	C15	C14	121.9(9)
C7	C15	C16	120(1)	C14	C15	C16	118.1(9)
C10	C16	C11	121(1)	C10	C16	C15	119(1)
C11	C16	C15	121(1)				

The C-C, C-N, C-H bond lengths are in the normal range, as are the bond angles. The macrocycle maintains a conformation with the 1-methylnaphthalene arms *trans* to one another and to the adjacent

methyl groups at the 5- and 14- positions of the macrocycle. This is the sterically least hindered conformation. The molecule has a centre of inversion, and there is hydrogen-bonding between N(1)-H and N(2), which serves to lend some rigidity to the macrocyclic ring. The naphthalene groups within each molecule are co-planar and are folded over the face of the macrocycle, effectively blocking access to the macrocycle's cavity. It may be seen from the packing diagram (Figure 3) that there is long-range stacking of the naphthalene rings along the b axis of the unit cell.

Interestingly, we found little or no interaction between the macrocycle and nickel(II) ions in aqueous THF solutions when we attempted to prepare the nickel(II) complex of the ligand. While we were initially surprised by this observation, the crystal structure suggests that the macrocycle presents a very hydrophobic periphery, with access to the central cavity blocked by the pendant 1-methyl-naphthalene moieties.

**Figure 3.** Packing diagram, viewing along the b axis of the unit cell



Current studies in our laboratory on this compound indicate that the macrocycle does form a complex with copper(II) ions, where the macrocyclic ligand is deformed, resulting in exposure of the cavity. This work will be reported later.

## Experimental

### General

NMR Spectra were obtained using a Bruker Avance 300MHz spectrometer, using deuterated chloroform ( $\text{CDCl}_3$ ) as solvent. FTIR Spectra were obtained as KBr pellets, using a Bruker Equinox 55 spectrometer.

X-Ray quality crystals of the title complex were obtained by slow effusion of THF from an aqueous THF solution of the macrocycle. A colourless plate crystal (0.06 x 0.20 x 0.24 mm) was mounted on a glass fibre. The X-ray structure determination was performed on a Rigaku AFC5R diffractometer, using graphite monochromated MoK $\gamma$  radiation ( $\lambda = 0.71073 \text{ \AA}$ ) and a rotating anode generator. The structure was solved by direct methods [9] and expanded using Fourier techniques [10]. All calculations were performed using the teXsan [11] crystallographic software package of Molecular Structure Corporation. Atomic coordinates and equivalent anisotropic displacement parameters, together with torsion angles have been deposited with CCDC as supplementary information [12]. The crystallographic parameters are given in Table 3.

**Table 3.** Crystallographic parameters

Empirical Formula	C <sub>38</sub> H <sub>52</sub> N <sub>4</sub>
Formula Weight	564.86
Crystal Color, Habit	colourless, plate
Crystal Dimensions	0.06 x 0.20 x 0.24 mm
Crystal System	monoclinic
Lattice Type	Primitive
Space Group	P2 <sub>1</sub> /a (#14)
Lattice Parameters	a = 10.778(3) Å b = 13.809(3) Å c = 11.420(2) Å $\beta = 102.49(2)^\circ$
Volume	1659.5(6) Å <sup>3</sup>
No. of Reflections Used for Unit Cell Determination (2 $\theta$ range)	25 ( 20.4 - 26.0°)
Omega Scan Peak Width at Half-height	0.25°
Z value	2
D <sub>calc</sub>	1.130 g/cm <sup>3</sup>
F <sub>000</sub>	616.00
$\mu(\text{MoK}\gamma)$	0.66 cm <sup>-1</sup>
Function Minimized	$S w ( F_o  -  F_c )^2$
Least Squares Weights	$1/s^2(F_o) = 4F_o^2/s^2(F_o^2)$
p-factor	0.0142
Anomalous Dispersion	All non-hydrogen atoms
No. Observations (I > 3.00s(I))	588
No. Variables	101
Reflection/Parameter Ratio	5.82
Residuals: R; R <sub>w</sub>	0.059 ; 0.056
Goodness of Fit Indicator	2.31

Max Shift/Error in Final Cycle	0.00
Maximum peak in Final Diff. Map	0.16 e <sup>-</sup> /Å <sup>3</sup>
Minimum peak in Final Diff. Map	-0.18 e <sup>-</sup> /Å <sup>3</sup>

### Syntheses

1-Chloromethylnaphthalene (Aldrich) was used as received. Tet A was synthesized as the dihydrate according to the literature [13] and was recrystallized from water prior to use. Its purity was checked by MP (143-145°C; Lit.146-148°C [14]) and <sup>1</sup>H-NMR (ppm): 1.06 and 1.05 (2 s, 12 H, 1), 1.38 (m, 4 H, 3), 2.80 (m, 2 H, 4), 0.98 (d, J = 6.0 Hz, 6 H, 5), 3.2 (br s, 4H, 6), 2.80 (m, 2 H, 7) and 2.26 (d of t, J = 2.2 Hz and 11 Hz, 2 H, 7), 2.80 (m, 2 H, 5 and 8) and 2.52 (d of t, J = 2.6 Hz and 12 Hz, 5 and 8); <sup>13</sup>C-NMR (ppm): 24.4 (1a), 29.1 (1b), 53.3 (2), 52.0 (3), 51.4 (4), 21.6 (5), 48.3 (7) and 42.4 (8); the IR spectrum (KBr) showed peaks at 3403 (N-H), 1177 (C-C-N), 1156 (C-N), 754 (N-H), and 511 cm<sup>-1</sup> (C-N-C).

### *Meso-5,5,7,12,12,14-hexamethyl-1,4,8,11-tetraazacyclotetradecane-1,8-di-(1-methylnaphthalene)*

To a stirred solution of 1-chloromethylnaphthalene (8.66g, 0.0490 mol) in THF (20 mL) was added tetA.2H<sub>2</sub>O (7.75g, 0.0242 mol) in methanol (100 mL) and a solution containing Na<sub>2</sub>CO<sub>3</sub> (5.20g, 0.0490 mol) in water (40 mL). The reaction mixture was refluxed for 24 hours. The solution was cooled to room temperature and the white solid that had precipitated during the reaction was filtered, washed with cold water and air-dried. The solid was recrystallized from THF and water (yield 6.75 g (81.4 %)). M.P. 257 - 260 °C; <sup>1</sup>H-NMR (ppm): 0.90 (s, 6H, 1a), 0.03 (s, 6H, 1b), 2.38 (m, 2H, 3) and 0.95 ppm (d, J = 3.0 Hz, 2H, 3), 2.93 (m, 2H, 4), 1.00 (d, J = 6.0 Hz, 6H, 5), 3.23 and 1.75 (2 br s, 2H, 6 and 15), 3.45 (d of t, J = 3.0 Hz and 12 Hz, 2H, 7) and 2.39 (m, 2H, 7), 2.93 (m, 2H, 8) and 2.39 (m, 2H, 8), 4.61 (d, J = 12 Hz, 2H, 19) and 3.37 (d, J = 12 Hz, 2H, 19), 7.81 (m, 1H, 21), 7.81 (m, 1H, 22), 9.27 (d, J = 8.4 Hz, 1H, 23), 7.42 (m, 1H, 25), 7.54 (m, 1H, 26), 7.54 (m, 1H, 27) and 7.42 (m, 1H, 28); <sup>13</sup>C-APT NMR (ppm): 29.0 (1a), 22.0 (1b), 52.9 (2), 46.8 (3), 49.6 (4), 11.6 (5), 45.9 (7), 39.3 (8), 51.8 (19), 135.8 (20), 128.1 (21 and 22), 127.2 (23), 134.1 (24), 128.6 (25), 125.7 (26), 125.8 (27), 125.0 (28) and 133.5 (29); the IR spectrum (KBr) showed peaks at 3259 (N-H), 1597 and 1510 (aromatic ring stretch), 1198 (C-C-N), 779 to 807 (C-H out of plane deformation), 477 and 649 cm<sup>-1</sup> (in plane ring deformation).

### Acknowledgements

We are grateful to the Natural Sciences and Engineering Research Council (NSERC) of Canada for financial support, and the University of Prince Edward Island for a Senate Committee on Research Grant (SCRUG). Funding for the NMR and FTIR spectrometers was provided by the Canadian Foundation for Innovation (CFI), the Atlantic Canada Opportunities Agency (ACOA) and a generous

donation from the Levesque Foundation. We are indebted to Dr. S. Cameron, Dalhousie University for the crystal structure determination.

## References

1. Collin, J.-P.; Sauvage, J.-P. *J. Chem. Soc. Chem. Commun.*, **1987**, 1075.
2. Kimura, E.; Koike, T.; Takahashi, M. *J. Chem. Soc. Chem. Commun.*, **1985**, 385.
3. Cox, J.P.L.; Jankowski, K.J.; Katakya, R.; Parker, D.; Beeley, N.R.A.; Boyce, B.A.; Eaton, M.A.W.; Miller, K.; Millian, A.T.; Harrison, A.; Walker, C. *J. Chem. Soc. Chem. Commun.*, **1989**, 797; Morphy, J.R.; Parker, D.; Katakya, R.; Harrison, A.; Eaton, M.A.W.; Millian, A.; Phipps, A.; Walker, C. *J. Chem. Soc. Chem. Commun.*, **1989**, 792.
4. Costamagna, J.; Ferraudi, G.; Matsuhiro, B.; Campos-Vallette, M.; Canales, J.; Villagrán, M.; Vargas, J.; Aguirre, M.J. *Coord. Chem. Rev.*, **2000**, 196, 125.
5. McAuley, A.; Subramanian, S. *Coord. Chem. Rev.*, **2000**, 200-202, 75.
6. Wainwright, K.P. *Coord. Chem. Rev.*, **1997**, 166, 35.
7. Haines, R.I. *Rev. Inorg. Chem.*, **2001**, 21, 165.
8. Haines, R.I.; Baldwin, R. *Transition Met. Chem.*, **2002**, 27, 284; Bissessur, R.; Haines, R.I.; Hutchings, D.R.; Bruening, R. *Chem. Commun.*, **2001**, 1598; Haines, R.I.; Hutchings, D.R.; McCormack, T.M. *J. Inorg. Biochem.*, **2001**, 85, 1; Haines, R.I.; Hutchings, D.R.; Lucas, R.J.; Miller, D. *Can. J. Chem.*, **2001**, 79, 54.
9. SIR92: Altomare, A.; Cascarano, M.; Giacovazzo, C.; Guagliardi, A. *J. Appl. Cryst.*, **1994**, 26, 343.
10. DIRDIF94: Beurskens, P.T.; Admiraal, G.; Beurskens, G.; Bosman, W.P.; de Gelder, R.; Israel, R.; and Smits, J.M.M. The DIRDIF-94 program system, Technical Report of the Crystallography Laboratory, University of Nijmegen, The Netherlands, **1994**.
11. teXsan for Windows version 1.05: Crystal Structure Analysis Package, Molecular Structure Corporation, **1997-8**.
12. CCDC 199958 contains the supplementary crystallographic data for this paper. These data can be obtained, free of charge, via [www.ccdc.cam.ac.uk/conts/retrieving.html](http://www.ccdc.cam.ac.uk/conts/retrieving.html) (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; email: deposit@ccdc.cam.ac.uk).
13. Douglas, B.E. in *Inorganic Syntheses*, Vol.18, John Wiley and Sons: New York, **1978**; p10-13.
14. Curtis, N.F.; *J. Chem. Soc.*, **1964**, 2644.

*Sample Availability:* Samples of meso-5,5,7,12,12,14-hexamethyl-1,4,8,11-tetraazacyclotetradecane-1,8-di-(1-methylnaphthalene) are available from MDPI