X-Ray crystal structures of *trans*-6,13-dimethyl-6,13-diamino-1,4,8,11-tetraazacyclotetradecane.6HCl.2H_2O and its condensation product with pyridine-2-carboxaldehyde

Sneh L. Jain, Pravat Bhattacharyya, Sadie A. McLellan, David T. Richens, Philip Lightfoot, Alexandra M. Z. Slawin and J. Derek Woollins*

School of Chemistry, University of St Andrews, St Andrews, Fife KY16 9ST, Scotland

The X-ray crystal structures of *trans*-6,13-dimethyl-6,13-diamino-1,4,8,11-tetraazacyclotetradecane hexahydrochloride dihydrate (*trans*-diammac.6HCl.2H_2O) and the product **1** derived by condensation of *trans*-diammac with pyridine-2-carboxaldehyde, have been determined. For **1** intramolecular attack of macrocycle amine nitrogen atoms on the C=N bonds of the intermediate diimine gives a ring-closed tautomeric form, which comprises two imidazolidine rings fused to the macrocycle.

Keywords: macrocycle, diammac, X-ray crystallography, NMR

The chemistry of metal complexes containing macrocyclic ligands often differs dramatically from acyclic structural analogues due to their enhanced thermodynamic stability. Macrocyclic ligands that might otherwise be inaccessible by conventional synthetic routes can be assembled around a metal ion (templation). The free macrocycle can subsequently be obtained by reduction of, and decomplexation from, the metal centre.

6,13-dimethyl-6,13-diamino-1,4,8,11-tetraazacyclotetradecane (diammac, Fig. 1) possesses four endocyclic nitrogen atoms and two exocyclic amine substituents.[1-3] Diammac is synthesised in a multicomponent reaction involving copper(II) nitrate hydrate, 1,2-diaminoethane, formaldehyde and nitroethane in the presence of triethylamine. Both *trans*- and *cis*-isomers of diammac form hexacoordinate complexes with divalent and trivalent metal ions,[4-6] while pentadentate and tetradentate coordination modes are observed when one or both pendant amine groups are protonated.[1,7]

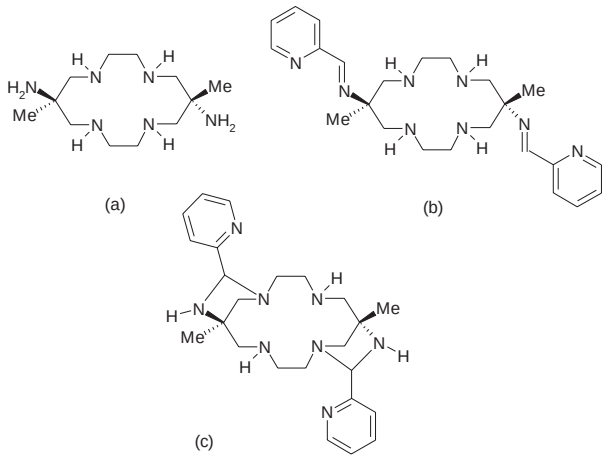


Fig. 1 (a) *Trans*-diammac, (b) the anticipated structure for **1**, (c) ring-closed form of product.

We report here the X-ray crystal structures of *trans*-diammac as its hexahydrochloride salt and the cyclised product **1** derived from its dehydrative condensation reaction with two equivalents of pyridine-2-carboxaldehyde.

Experimental

Materials

Trans-diammac was prepared by literature methods,[1,2] acetonitrile was dried and distilled from calcium hydride, all other reagents and solvents were used as supplied.

* Correspondence. E-mail: jdw3@st-and.ac.uk

Synthesis of **1**: Under dinitrogen, a solution of pyridine-2-carboxaldehyde (0.268 g, 2.15 mmol) in acetonitrile (150 cm^3) was added dropwise to *trans*-diammac (0.324 g, 1.25 mmol) in acetonitrile (150 cm^3). The solution was stirred at room temperature overnight, turning cloudy yellow in appearance. On cooling the solution to 5 °C overnight **1** precipitated as a colourless solid, which was collected by filtration, washed with cold acetonitrile and dried. Yield 0.299 g (55 %). Storage of the filtrate at –20 °C gave clear plates suitable for X-ray crystallography. δ_H (300 MHz, $CDCl_3$): 8.57 (d, 2H, J = 5, C_5H_4N), 7.74 (d, 2H, J = 8, C_5H_4N), 7.68 (dt, 2H, J = 2 and 7, C_5H_4N), 7.25 (m, 2H, C_5H_4N), 4.28 (s, 2H, CH), 3.45 (d, 2H, J = 9, NH), 2.74-2.43 (m, 12H, CH_2), 2.16 (d, 2H, J = 10, CH_2), 1.78 (dt, 2H, J = 4 and 12 Hz, CH_2), 1.18 (s, 6H, CH_3). δ_C (75.6 MHz, $CDCl_3$): 27.40 (CH_3), 48.1, 49.6, 59.5, 59.9, 66.5 (CH_2), 85.3 (CH), 122.9, 123.7, 136.6, 149.3, 159.3 (aromatics). Selected IR data (KBr, cm^{-1}): 3306s (ν_{NH}). EI MS: *m/z* 436 M^+, 330 [M^+ - $pyCH_2N$].

X-ray crystallography

X-Ray diffraction studies were performed at 293 K using a Bruker SMART-CCD diffractometer with graphite-monochromated Mo-Kα radiation (λ = 0.71073 Å). All data were corrected for Lorentz polarisation and long-term intensity fluctuations. The structures were solved by direct methods. Non-hydrogen atoms were refined with anisotropic displacement parameters, hydrogen atoms bound to carbon were idealised and fixed (C–H 0.95 Å), amine protons were located using ΔF maps and allowed to refine subject to a distance constraint, water-bound protons were fixed (O-H 0.98 Å). Structural refinements were by the full-matrix least-squares method on F^2 using SHELXTL-PC[8] for **1** and teXsan[9] for *trans*-diammac.6HCl.2H_2O.

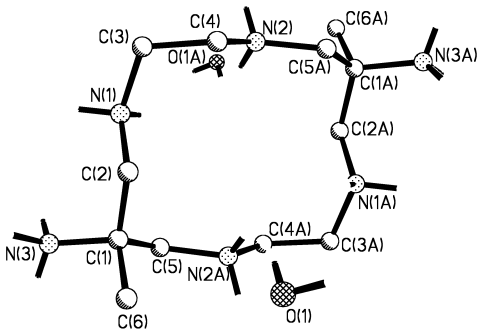
Trans-diammac.6HCl.2H_2O: $C_{12}H_{40}N_6Cl_6O_2$, M = 513.20, orthorhombic, *Pbca*(#61), a = 11.578(5), b = 19.538(8), c = 10.468(8) Å, U = 2367(2) $Å^3$, Z = 4, D_c = 1.439 Mg m^{-3}, μ = 0.745 mm^{-1}, F(000) = 1088, crystal size 0.35 x 0.30 x 0.05 mm. Of 2029 data collected, 1158 were unique, which refined to R(F) = 0.031, wR = 0.030 [$I > 2\sigma(I)$].

1: $C_{24}H_{36}N_8$, M = 436.62, monoclinic, $P2(1)/c$, a = 7.2164(15), b = 14.096(3), c = 12.193(3) Å, β =103.752(4)°, U = 1204.8(4) $Å^3$, Z = 2, D_c = 1.204 Mg m^{-3}, μ = 0.076 mm^{-1}, F(000) = 472, crystal size 0.12 × 0.11 × 0.03 mm. Of 6701 data collected, 1692 were unique (R_{int} = 0.1260), which refined to $R1$ = 0.0823, $wR2$ = 0.1877 [$I > 2\sigma(I)$].

Results and discussion

Trans-diammac was crystallised from hydrochloric acid. The bond lengths and angles of *trans*-diammac.6HCl.2H_2O (Fig. 2) are congruent with data for the tetrahydroperchlorate hexahydrate salt.[3] The *trans* configuration of the pendant amine groups attached to the macrocycle is confirmed, all of the nitrogen atoms are protonated. The molecule is centrosymmetric through the centroid of the ring, for simplicity diametrically opposite atoms within the structure have been given equivalent atomic labels. The macrocycle nitrogen atoms are involved in two hydrogen-bonding interactions with chloride anions (Table 1). The H…Cl distances for the amine protons H(12)–H(15) of N(1) and N(2) lie between 2.01(4)–2.11(4) Å, with the longest hydrogen-bond distances being associated with the protons H(16)–H(18) at N(3). Each water molecule is engaged in hydrogen-bonding interactions with two chloride anions and one exocyclic amine

a)



b)

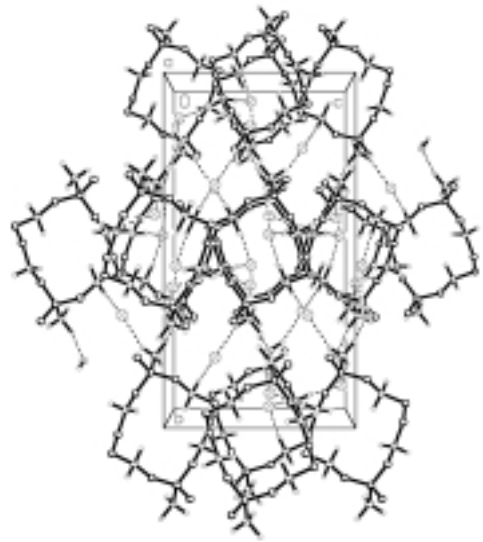


Fig. 2 (a) Molecular structure of *trans*-diammac.6HCl.2H_2O (C-H atoms omitted for clarity). (b) packing diagram looking down the *a* axis illustrating the N-H…Cl H bonding network. Selected bond lengths (Å) and angles (o) (esd's in parentheses). N(1)-C(2) 1.494(4), N(2)-C(4) 1.502(4), N(3)-C(1) 1.508(5), C(1)C(5) 1.535(5), C(3)-C(4) 1.517(5), N(1)-C(3) 1.519(5), N(2)-C(5) 1.499(4), C(1)-C(2) 1.531(5), C(1)-C(6) 1.530(1), N(3)-C(1)-C(6) 107.2(3), C(2)-C(1)-C(6) 106.9(3), N(1)-C(2)-C(1) 116.6(3), N(2)-C(4)-C(3) 113.8(3), C(4)-N(2)-C(5) 113.2(3), C(2)-N(1)-C(3) 113.5(3), N(3)-C(1)-C(2) 109.0(3), N(3)-C(1)-C(5) 105.6(3), C(2)-C(1)-C(5) 115.1(3), C(5)-C(1)-C(6) 112.8(3), N(1)-C(3)-C(4) 115.4(3), N(2)-C(5)-C(1) 113.0(3).

Table 1 Hydrogen-bonding distances (Å) and angles (º) for *trans*-diammac.6HCl.2H_2O (esd's in parentheses). The hydrogen-bond donor atoms are denoted as *D* and the acceptors as *A*

	D–H	H…A	D…A	D–H…A
O(1)–H(19)…Cl(1)	0.84(5)	2.46(5)	3.198(4)	147(5)
O(1)–H(20)…Cl(2)	0.86(5)	2.27(5)	3.110(4)	166(5)
N(1)–H(12)…Cl(1)	1.10(4)	2.01(4)	3.096(3)	169(3)
N(1)–H(13)…Cl(3)	1.00(3)	2.01(4)	3.003(3)	168(3)
N(2)–H(14)…Cl(1)	0.99(4)	2.11(4)	3.081(4)	165(3)
N(2)–H(15)…Cl(2)	0.96(4)	2.10(4)	3.058(4)	171(3)
N(3)–H(16)…Cl(2)	0.98(5)	2.19(5)	3.115(4)	157(4)
N(3)–H(17)…Cl(3)	0.88(3)	2.33(3)	3.158(4)	156(3)
N(3)–H(18)…O(1)	1.05(5)	1.73(5)	2.756(5)	162(4)

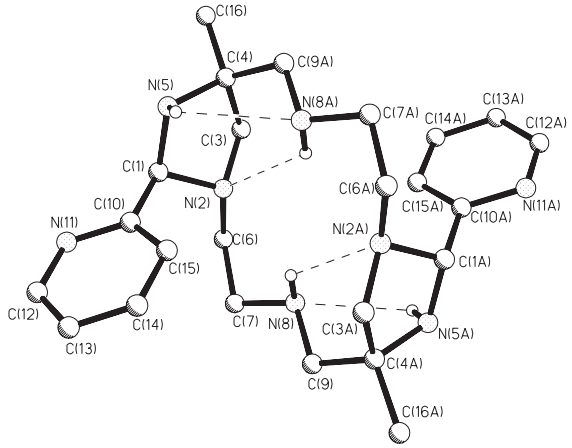


Fig. 3 Molecular structure of **1** (C–H bonds omitted for clarity). Selected bond lengths (Å) and angles (º) (esd's in parentheses). C(1)–N(5) 1.471(7), C(6)–C(7) 1.508(7), C(1)–C(10) 1.483(7), C(7)–N(8) 1.456(6), C(1)–N(2) 1.489(6), N(8)–C(9) 1.454(7), N(2)–C(3) 1.441(6), C(9)–C(4A) 1.516(8), N(2)–C(6) 1.454(7), C(10)–N(11) 1.352(7), C(3)–C(4) 1.520(8), C(10)–C(15) 1.354(7), C(4)–N(5) 1.496(7), N(11)–C(12) 1.339(7), C(4)–C(9A) 1.516(8), C(12)–C(13) 1.342(8), C(4)–C(16) 1.531(7), C(13)–C(14) 1.362(9), C(6)–C(7) 1.508(7), N(5)–C(1)–C(10) 111.9(5), N(5)–C(1)–N(2) 103.6(4), C(10)–C(1)–N(2) 114.1(4), C(3)–N(2)–C(6) 114.2(5), C(3)–N(2)–C(1) 101.0(4), C(6)–N(2)–C(1) 115.5(4), N(2)–C(3)–C(4) 104.6(5), N(5)–C(4)–C(9A) 111.0(5), N(5)–C(4)–C(3) 102.4(4), C(9A)–C(4)–C(3) 112.4(5), N(5)–C(4)–C(16) 110.1(5), C(9A)–C(4)–C(16) 109.2(5), C(3)–C(4)–C(16) 111.7(5), C(1)–N(5)–C(4) 107.3(5), N(2)–C(6)–C(7) 113.7(5), N(8)–C(7)–C(6) 107.9(4), C(9)–N(8)–C(7) 115.1(4), N(8)–C(9)–C(4A) 113.3(4).

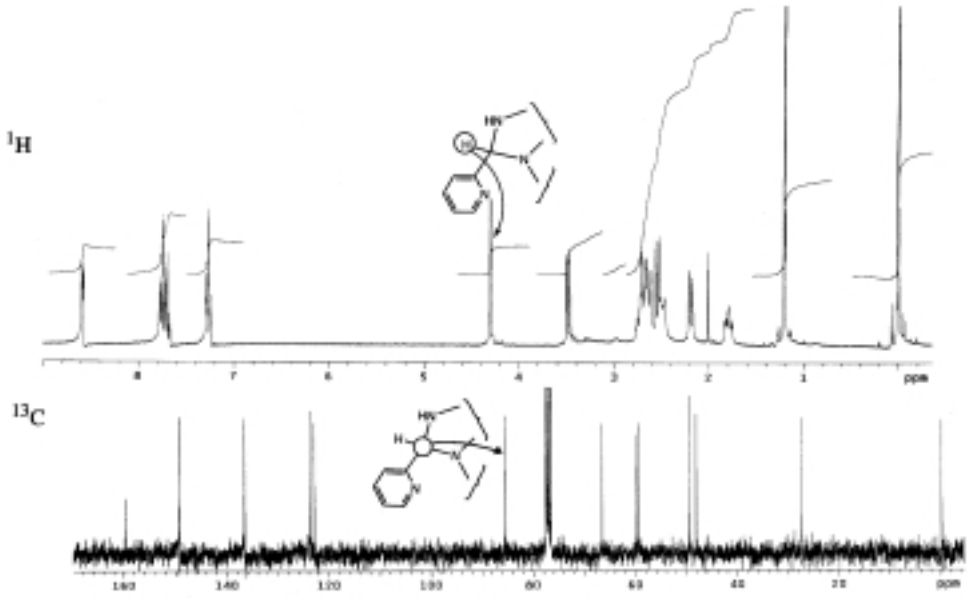


Fig. 4 ^{1}H and ^{13}C{^{1}H} NMR spectra of **1** ($CDCl_3$).

group, the H…Cl distances are in the range 2.27(5)–2.46(5) Å and H(18)…O(1) is 1.73(5) Å. In contrast, in *trans*-diammac. $4HClO_4.6H_2O$ the hydrogen-bond distances between amine hydrogens and oxygen atoms of water molecules [H…O 1.61–2.14 Å] are rather shorter than to the perchlorate anions [H…O 2.19–2.68 Å].

Comba has synthesised 6,13-bis(2-pyridinyl)-1,4,8,11-tetraazacyclotetradecane, in which the pendant amine groups of diammac are replaced by 2-pyridyl rings.[10] In order to prepare a similar molecule with a potentially higher denticity, *trans*-diammac was reacted with two equivalents of pyridine-2-carboxaldehyde in anhydrous acetonitrile. We anticipated a dehydrative condensation reaction leading to a pyridylimine-substituted macrocycle *trans*-6,13-bis (2-pyridylmethyleneimino)-6,13-dimethyl-1,4,8,11-tetraazacyclotetradecane **1** (Fig. 1)**,** which retained the original *trans*-stereochemistry of the precursor.

X-ray crystallography showed that in the solid state **1** exists in the imidazolidine tautomeric form (Fig. 3), with retention of the *trans*-arrangement of methyl groups. The imidazolidine rings fused at either side of the 14 membered macrocycle in **1** are formed by attack of N(2) and N(2A) on the carbon atoms of the imine bonds; Bernhardt reported similar ring closure when *trans*-diammac reacts with sterically undemanding aldehydes,[11] although bulkier aldehydes do not suffer this fate.[12,13] Molecule **1** has a centre of symmetry at the centroid of the macrocycle. The amine groups participate in hydrogen-bonding interactions with each other [N(5)–H(5N)…N(8) 2.44(5), N(8)–H(8N)...N(2A) 2.36(4) Å] but the pyridyl nitrogen atoms are uninvolved in either intra- or intermolecular interactions. The macrocycle C-N lengths in **1** show minor shortening (*ca*. 0.04 Å) relative to *trans*-diammac.$6HCl.2H_2O$.

A signal in the $^{13}C\{^1H\}$ spectrum for **1** at δ 85.3 is assigned to the C(1) atom, the methine proton at this centre gives a singlet at δ 4.28 in the ^1H NMR (Fig. 4). The absence of imine environments in either spectrum confirms that the intramolecular cyclisation of **1** is retained in solution. The hydrogen-bonding observed in the solid state may help to stabilise the imidazolidine form.

Supplementary material

Atomic coordinates, thermal parameters and bond lengths and angles have been deposited at the Cambridge Crystallographic Data Centre (CCDC). www.ccdc.cam.ac.uk Any request to CCDC for this material should quote the full literature citation and the reference number: 227080 & 227081.

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