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Synthesis of [3^2]Bis([$2^4.3^1$]adamanzane), 1,4,8,11,15,18,22,25-Octaazapentacyclo-[20.6.2.$2^{4,25}$.$2^{8,15}$.$2^{11,18}$]hexatriacontane, and Crystal Structure of the Tetrachlorozincate Salt of the Tetraprotonated Octaamine

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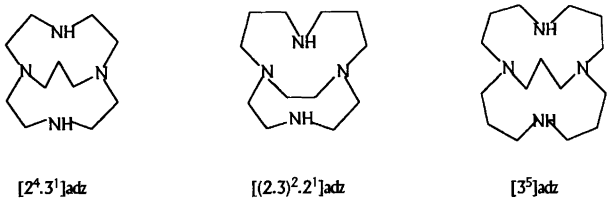
The reaction of [$2^4.3^1$]adamanzane, 1,4,7,10-tetraazabicyclo[5.5.3]pentadecane, with the bis(3-chloropropyl) derivative of [$2^4.3^1$]adamanzane, 4,10-bis(3-chloropropyl)-1,4,7,10-tetraazabicyclo[5.5.3]pentadecane, affords the dimeric octaamine [3^2]bis([$2^4.3^1$]adamanzane),1,4,8,11,15,18,22,25-octaazapentacyclo-[20.6.2.$2^{4,25}$.$2^{8,15}$.$2^{11,18}$]hexatriacontane. The tetraprotonated form having two inside and two outside bound hydrogen ions was isolated as a tetrachlorozincate salt, {[3^2]bis(i^+,i,i,o^+-H_2[$2^4.3^1$]adz)}$(ZnCl_4)_2 \cdot 1.5H_2O$ in high yield (62%), and its crystal structure was solved by X-ray diffraction at $T = 120$ K. The two halves of the cationic dimer are related by a centre of symmetry. The acidic hydrogen atom attached to N(1) is oriented away from the cavity, whereas the hydrogen atom attached to N(2) as well as the lone pairs at N(3) and N(4) point towards the inside of the cage. The acidic hydrogen atom at N(2) is hydrogen-bonded to N(4), the H(2)···N(4) distance being 1.74(3) Å.

From potentiometric measurements it is estimated that the tetraprotonated species has $pK_{a1} = 4.23(3)$ and $pK_{a2} = 5.43(12)$ (25 °C, 1 M NaCl), while the last two pK_a values are assumed to be greater than 14.

We recently presented syntheses of so-called bowl adamanzanes [$2^4.3^1$]adz, [$(2.3)^2.2^1$]adz and [3^5]adz (Fig. 1).[1–3] In coordination compounds with metal ions the rigid structure of these bowl-shaped ligands has a strong impact on the geometry around the central ion; depending upon the properties of the metal ion and the size of the tetraamine cavity complexes with octahedral, trigonal bipyramidal, square pyramidal and tetrahedral geometries have been obtained.[4–8] In octahedral complexes the adamanzanes constrain the configuration to *cis* as opposed to related macrocylic ligands, such as cyclen and cyclam, which form *cis* as well as *trans* complexes. One objective when synthesizing bowl adamanzanes has been their inherent ability to promote tetrahedral symmetry in coordination compounds, opening interesting avenues in context with metal ions which normally do not accomodate this geometry. This intent has recently been achieved in the synthesis of tetrahedral $Co([3^5]adz)^{2+}$, which is the first example of a cationic cobalt(II) aliphatic amine complex with tetrahedral symmetry.[8]



[$2^4.3^1$]adz [$(2.3)^2.2^1$]adz [3^5]adz

Fig. 1. Bowl adamanzanes.

The corresponding cage adamanzanes, tricyclic tetraamines, have also been reported.[3,9–11] The small cage [$2^4.3^2$]adz shown in Fig. 2 is made from the parent bowl amine [$2^4.3^1$]adz by reaction with the ditosylate of 1,3-propanediol.[9] The synthesis requires low concentrations of the reactants in order to minimize formation of polymeric by-products. During our attempts to optimize the yield we found that in more concentrated solutions

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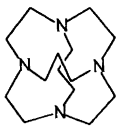


$[2^4.3^2]$adz

Fig. 2. Cage adamanzane, inside-coordinated proton not shown.

one by-product is a dimeric octaamine, i.e. two $[2^4.3^1]$adz entities bound together by two trimethylene bridges. However, the yield of this new octaamine was always low, and we never succeeded in isolating pure samples in a reasonable yield. In the present study this octaamine has been synthesized in a high yield also starting with $[2^4.3^1]$adz, but using a different strategy from that mentioned above.

Experimental

Abbreviations and nomenclature. The simplified nomenclature suggested for adamanzanes (bowls and cages) has been discussed recently[4,10,11] and is illustrated in Figs. 1 and 2 and below (adz = adamanzane):

Bowls:
$[2^4.3^1]$adz = 1,4,7,10-tetraazabicyclo[5.5.3]pentadecane
$[3^5]$adz = 1,5,9,13-tetraazabicyclo[7.7.3]nonadecane
$[(2.3)^2.2^1]$adz = 1,5,9,12-tetraazabicyclo[7.5.2]hexadecane

Cages:
$[2^4.3^2]$adz = 1,4,8,11-tetraazatricyclo[6.6.2.$2^{4,11}$]octadecane

The present octaamine has the IUPAC name 1,4,8,11,15,18,22,25-octaazapentacyclo[20.6.2.$2^{4,25}$.$2^{8,15}$.$2^{11,18}$]hexatriacontane. It consists of two $[2^4.3^1]$adz units linked together by two trimethylene bridges and based upon the adamanzane nomenclature it is given the name: $[3^2]$bis($[2^4.3^1]$adz), where the numbers in the first square bracket (3^2 is abbreviation for 3.3) refer to the number of carbon atoms in the two bridges that link the two (in this case identical) adamanzane units together. This nomenclature is easily extended to include less symmetrical octaamines as follows: Two $[2^4.3^1]$adz units linked by one trimethylene and one ethylene bridge are named [2.3]bis($[2^4.3^1]$adz). One $[2^4.3^1]$adz unit and one $[3^5]$adz unit linked together by two ethylene bridges are named $[2^2]$($[2^4.3^1]$adz)($[3^5]$adz).

Protonated forms and the orientation of the lone pairs and protons at each nitrogen group are named using the same rules[3,11] as defined for the cages: Suffixes *i* and *o*, respectively, indicate lone pairs pointing inwards or outwards with respect to the cavity of the dimer, and in protonated forms i^+ and o^+, respectively, are used to designate inwards and outwards oriented protons. As an example the tetraprotonated amine in the present study is named $[3^2]$bis(i^+,*i*,*i*,o^+-$H_2[2^4.3^1]$adz)$^{4+}$ showing that in each tetraamine-unit one proton is coordinated inside, one is coordinated outside and the remaining two lone pairs are oriented inwards.

Potentiometric titrations. The concentration of hydrogen ions was measured using Metrohm equipment and a Radiometer glass electrode combined with a calomel reference electrode (GK2401 B). The ionic strength was kept constant with NaCl (I = 1.00 M). The concentration acid dissociation constants were determined by dissolution of the tetraprotonated amine salt and titration with NaOH until a pH about 5.8 (corresponding to the addition of 1.6 mol NaOH per mol of amine). Below this pH the protolytic properties of the tetrachlorozincate anion can be ignored as shown by separate experiments titrating solutions of Li_2ZnCl_4 in 1 M NaCl. The concentration acid dissociation constants were calculated from the titration data by non-linear least-squares calculation using the program PROC NLIN (DUD method) from the SAS Institute INC, Cary, USA.

Materials. ($H_3[2^4.3^1]$adz)Br_3 was prepared as reported previously.[1] All other chemicals were of analytical grade. Solvents were dried using molecular sieves (0.3 nm) from Merck.

Analyses. Bromide and chloride analyses were made by potentiometric titrations with silver nitrate.

Mass spectra. Positive ion FABMS were obtained on a Jeol AX505W mass spectrometer using NBA as the matrix.

NMR spectra. ^{1}H and ^{13}C NMR spectra were measured on a Bruker Avance 400 NMR spectrometer (400 MHz). ^{1}H chemical shift values (δ) are reported in ppm and are referenced to internal dioxane [δ(dioxane) = 3.75 ppm] for D_2O solutions. ^{13}C chemical shift values (δ) are referenced to internal dioxane [δ(dioxane) = 67.40 ppm] for D_2O solutions. For $CDCl_3$ solutions chemical shift values (δ) are referenced to internal TMS [δ(TMS) = 0 ppm]. ^{13}C DEPT NMR spectra were used to assign CH_2 carbon atoms.

Syntheses. In all procedures care was taken to avoid contamination with moisture from the air, e.g. by using calcium chloride tubes in conections with reflux.

1. 4,10-{Bis(3-hydroxopropyl)-1,4,7,10-tetraazabicyclo[5.5.3]pentadecane} monohydrobromide. A mixture of ($H_3[2^4.3^1]$adz)Br_3 (5.00 g, 11 mmol), Na_2CO_3 (3.5 g, 33 mmol) and molecular sieves (2.7 g, 0.3 nm, Merck) in acetonitrile (54 ml) was refluxed for 18 h and then cooled. 3-Chloropropanol (2.08 g, 22 mmol) was added and the mixture was refluxed for 7 days. The filtered reaction mixture was evaporated to dryness using a rotary evaporator with an initial water bath temperature of 40 °C. When practically all the solvent had evaporated the temperature was raised to 80 °C for one additional hour. This gave 4.4 g of a white powder (98%

yield). Analytical data: Calculated for $C_{17}N_4H_{37}O_2Br$: Br, 19.52. Found: 19.46. ^{13}C NMR data in D_2O δ (ppm): 60.84 (CH_2–OH); 56.41, 54.77, 51.58 and 51.29 (CH_2–N); 29.49 and 20.82 (C–CH_2–C).

2. *{4,10-Bis(3-chloropropyl)-1,4,7,10-tetrazabicyclo[5.5.3]pentadecane} monohydrohalide.* A mixture of 4,10-{bis(3-hydroxopropyl)-1,4,7,10-tetraazabicyclo-[5.5.3]pentadecane} monohydrobromide (0.79 g, 1.93 mmol) and dichloromethane (5 ml) was cooled in ice and thionyl chloride (0.38 ml, 5.29 mmol) was added in small portions of 0.04 ml over a period of 10–15 min. The mixture was refluxed for 5 h, after which the dichloromethane was removed by evaporation. To the cold (room temperature) residue was added water (0.88 ml) in order to decompose the excess thionyl chloride. To the brownish mixture was then added an aqueous solution of sodium hydroxide (2.7 ml, 4 M) and the mixture was extracted with three 14-ml portions of chloroform. The combined organic extracts were dried with sodium sulfate, and then the solvent was removed by evaporation using a rotary evaporator. This gave 0.87 g of a brown oil of a mixed bromide–chloride salt of the monoprotonated amine. The yield is somewhat higher than the theoretical yield (0.83 g) indicating the presence of impurities. Analytical data: Calculated for $C_{17}N_4H_{34}Cl_2 \cdot HBr_{0.7}Cl_{0.3}$: Br(ionic) = 12.9; Cl(ionic) = 2.46. Found: Br(ionic) = 10.6; Cl(ionic) = 1.95. FABMS *m/z*: 365 ($M = C_{17}N_4H_{34}Cl_2$, most intense signal in the isotope cluster). ^{13}C NMR data in $CDCl_3$ δ (ppm): 57.52, 55.00, 51.61 and 50.87 (CH_2–N); 42.87 (CH_2–Cl); 29.14 and 20.99 (C–CH_2–C). The ^{13}C NMR spectrum did not show any significant presence of impurities. From the halide analysis an impurity content of 10–20% is estimated. However, the product was used without further purification in the following synthesis.

3. *{[3²]Bis(H_2[($2^4.3^1$)]adz)}($ZnCl_4$)$_2 \cdot 1.5H_2O$.* A mixture of crude 4,10-bis(3-chloropropyl)-1,4,7,10-tetraazabicyclo[5.5.3]pentadecane} monohydrohalide (2.28 g, corresponding to 4.21 mmol if the compound is 80% pure, see above), [H_3[$2^4.3^1$]adz]Br_3 (1.92, 4.21 mmol), Na_2CO_3 (2.7 g, 26 mmol) and molecular sieves (21 g, 0.3 nm, Merck) in acetonitrile (420 ml) was stirred at room temperature for 24 h and then refluxed for 7 days. The filtered solution was evaporated to dryness using a rotary evaporator with an initial water bath temperature of 40 °C. When practically all the solvent had evaporated the temperature was raised to 80 °C for one additional hour. This gave 2.41 g of a yellow powder which was dissolved in chloroform (54 ml). The organic phase was extracted three times with 4.5-ml portions of water. The combined aqueous extracts were evaporated to dryness using a rotary evaporator with an initial water bath temperature of 60 °C. When practically all the solvent had evaporated the temperature was raised to 80 °C for one additional hour giving 2.29 g of a yellow solid. This product was dissolved in 90–100 °C hot water (23 ml). Addition of 4 M Li_2ZnCl_4 (8 ml) to the hot solution followed by slow cooling to room temperature gave during some hours a yellow, crystalline precipitate. This was filtered off, washed with 96% ethanol and dried in the air. This product (2.92 g) was dissolved in water (73 ml) at room temperature and a white insoluble residue was removed by filtration. 1 M HCl (9 ml) was added to the filtrate and thereafter 4 M Li_2ZnCl_4 (20 ml) was added. A white precipitate formed almost immediately. After 1 h the precipitate was filtered off, washed with 96% ethanol and dried in the air. This gave 2.48 g (62%) of a pure salt. Analytical data. Calculated for $C_{28}H_{60}N_8Cl_8Zn_2 \cdot 1.5H_2O$: Cl, 29.8. Found: Cl, 29.8. ^1H NMR spectra are shown in Fig. 3 and ^{13}C NMR data are given in Table 1. FABMS *m/z*: 505 ($M = C_{28}H_{56}N_8$).

Crystals for X-ray diffraction studies were obtained as follows. A solution of the tetrachlorozincate salt (60 mg) in hot water (2 ml) was cooled slowly to room temperature and then left in the open in a small test tube. Over a period of 4 days at room temperature some of the solvent evaporated and colourless crystals formed. The crystals were filtered off and washed with 96% ethanol.

X-Ray techniques. Crystal data for the compound are listed in Table 2. The crystal of the compound was cooled to 120 K using a Cryostream nitrogen gas cooler system.[12] The data were collected on a Siemens SMART Platform diffractometer with a CCD area sensitive detector. The intensities were corrected for Lorenz, polarization and absorption effects. The structures were solved by direct methods and refined by the full-matrix least-squares technique. The non-hydrogen atoms were refined anisotropically. The hydrogen atoms could all be located from electron-density difference maps and were refined isotropically. The hydrogen atoms of the water molecule were refined with fixed O–H bond lengths at 0.9 Å. The

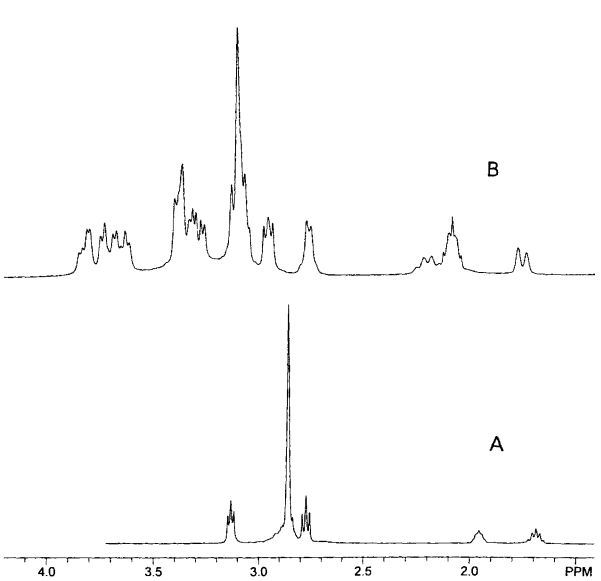


Fig. 3. ^1H NMR spectra of (A) [3²]bis(i^+,*i*, *i*,o^+-H_2[$2^4.3^1$]adz)$^{4+}$ (0.02 M tetrachlorozincate salt in D_2O) and (B) [3²]bis(i^+,*i*,*i*,*i*-H[$2^4.3^1$]adz)$^{2+}$ (0.02 M tetrachlorozincate salt in 1 M NaOD).

Table 1. ^{13}C NMR chemical shift data at 25 °C.

Species	δ (ppm) CH_2–N							δ (ppm) C–CH_2–C	
LH_4^{4+},[a]	59.83	58.92	57.99	57.17	55.68	53.60	50.00	24.85	18.48
LH_2^{2+},[b]	58.21	55.11	54.42	51.01				21.65	21.45

[a] LH_4^{4+} = [3²]bis(i^+,*i*,*i*,*o*$^+$-H_2[2⁴.3¹]adz)$^{4+}$, 0.02 M tetrachlorozincate salt in D_2O. [b] LH_2^{2+} = [3²]bis(i^+,*i*,*i*,*i*-H[2⁴.3¹]adz)$^{2+}$, 0.02 M tetrachlorozincate salt in 1 M NaOD. As discussed in the text complete deprotonation of the amine in this solvent cannot be excluded, but it is highly unlikely.

Table 2. Crystal and experimental data.

Formula	$C_{28}H_{63}Cl_8N_8O_{1.50}Zn_2$
Formula weight	950.20
Crystal system	Monoclinic
Space group	$P2_1/c$
Unit-cell dimensions:	
a/Å	11.434(2)
b/Å	9.617(2)
c/Å	18.981(4)
β/°	100.00(3)
Unit-cell volume, *V*/Å^3	2055.6(7)
Formula units per unit cell, *Z*	2
F(000)	990
Calculated density, D_x/g cm^{-3}	1.535
Radiation	Mo Kα
Wavelength, λ/Å	0.71073
Linear absorption coefficient/mm^{-1}	1.723
Temperature, *T*/K	120(2)
Crystal description	Colourless
Crystal size/mm	0.06 × 0.11 × 0.20
Intensity data collection:	
Siemens SMART CCD diffractometer	
ω-Rotation with narrow frames	
θ-Range/°	1.81–29.63
Range of *h*	−15–15
Range of *k*	−12–12
Range of *l*	−26–14
No. of measured reflections	13727
Total no. of unique reflections	5244
No. of independent reflections, [$I>2\sigma(I)$]	3906
R (int)	0.0385
Corrections	Lorenz, polarization and absorption
Transmission factors	1.0000–0.8550
Structure refinement:	
Minimization of	$\Sigma w(\|F_o\|^2-\|F_c\|^2)^2$
Anisotropic thermal parameters	All non-hydrogen atoms
Isotropic thermal parameters	Hydrogen atoms
No. of refined parameters	344
Weighting scheme	$[\sigma^2(F^2_o)+(0.0223P)^2+1.8305P]^{-1}$, $P=(F_o^2+2F_c^2)/3$
$R=\Sigma\|\|F_o\|-\|F_c\|\|/\Sigma\|F_o\|$	0.0376 (obs. data)
$wR2=[\Sigma w\|F^2_o-F^2_c\|^2/\Sigma wF_o^4]^{1/2}$	0.0813 (all data)
$S=[\Sigma w(\|F_o\|^2-\|F_c\|^2)^2/(N_{obs}-N_{var})]^{1/2}$	1.076
Final $(\Delta/\sigma)_{max}$	0.093
Final $\Delta\rho_{min}$ and $\Delta\rho_{max}$/e Å^{-3}	−0.554 and 0.593

population factor for the water molecule is 0.75. Programs used for data collection, data reduction and absorption were SMART, SAINT and SADABS.[13,14] The program SHELXTL 95[15] was used to solve the structure and for molecular graphics. PLATON[16] was used for molecular geometry calculations. The atomic coordinates are listed in Table 3. Further crystallographic details may be obtained from one of the authors (I.S.) on request.

Results

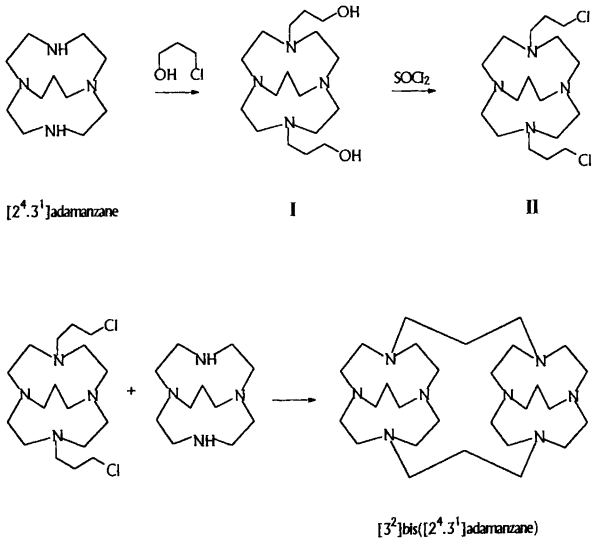
Syntheses. The macropentacyclic octaamine has been made from the bowl adamanzane [H_3[2⁴.3¹]adz]Br_3 as shown in Scheme 1. The *N*,*N*′-bis(3-hydroxopropyl) derivative **I** was obtained in high yield (98%). Despite the synthesis taking place under very basic conditions the product was isolated as a monoprotonated bromide salt. This indicates that **I** in Scheme 1 is a very strong base, which is unsurprising considering that the parent monoprotonated bowl H[2⁴.3¹]adz$^+$ has pK_a > 15. Likewise, the *N*,*N*′-bis(3-chloropropyl) derivative **II** is assumed to be a very strong base and was isolated as a monoprotonated amine as a mixed chloride and bromide salt. This product is not pure, but was used in the final reaction without further purification. The reaction between [2⁴.3¹]adz and **II** was performed using stoichiometric amounts giving after several purification procedures the tetraprotonated octaamine as a pure tetrachlorozincate salt (yield 62%). The structure was established by elemental analysis and FABMS (see Experimental), ^1H and ^{13}C NMR data, acid–base properties (see below) and an X-ray diffraction study as described in the following.

*Crystal structure of {[3²]bis(*i$^+$,i,i,o$^+$-H_2[(2⁴.3¹)]-*adz)}(*$ZnCl_4)_2 \cdot 1.5H_2O$*.* Selected bond lengths and bond angles are listed in Table 4. The labelling of the atoms is shown in Fig. 4. The compound consists of [3²]bis(i^+,*i*,*i*,*o*$^+$-H_2[2⁴.3¹]adz)$^{4+}$ and $ZnCl_4^{2-}$ ions and water molecules. The two halves of the cationic dimer are related by a centre of symmetry. The acidic hydrogen atom attached to N(1) is oriented away from the cavity, whereas the hydrogen atom attached to N(2) and the lone pairs at N(3) and N(4) are all pointing towards the inside of the cage. The acidic hydrogen atom at N(2) is hydrogen bonded to N(4), the H(2)···N(4) distance being 1.74(3) Å. The N(2)···N(4) distance is 2.620(3) Å, which is close to those of 2.567(4) and 2.636(7) Å found in H_3[2⁴.3¹]adz^{3+} and i^+,*i*,*i*,*i*-H[2⁴.3²]adz$^+$, respectively.[1,9] The N(1)···N(3) distance is 4.554(3) Å, which is shorter than 5.194(7) Å found in H_3[2⁴.3¹]adz^{3+} and longer than 3.081(7) Å found in H[2⁴.3²]adz$^+$. In H_3[2⁴.3¹]adz^{3+} the acidic hydrogen

Table 3. Fractional atomic coordinates and isotropic displacement parameters (in Å).

Atom	*x*	*y*	*z*	U_{eq}[a]
N(1)	0.0790(2)	0.5277(2)	0.16542(11)	0.0143(4)
C(1)	0.0495(2)	0.3849(3)	0.13455(14)	0.0184(5)
C(2)	0.1141(2)	0.2657(3)	0.17745(14)	0.0173(5)
N(2)	0.2126(2)	0.2104(2)	0.14326(11)	0.0135(4)
C(3)	0.1677(2)	0.1238(3)	0.07854(13)	0.0162(5)
C(4)	0.2459(2)	0.1423(3)	0.02179(14)	0.0171(5)
N(3)	0.2654(2)	0.2912(2)	0.00897(11)	0.0152(4)
C(5)	0.3892(2)	0.3379(3)	0.03105(15)	0.0212(6)
C(6)	0.3956(3)	0.4645(3)	0.07943(14)	0.0211(6)
N(4)	0.3505(2)	0.4285(2)	0.14581(11)	0.0164(4)
C(7)	0.3034(2)	0.5515(3)	0.17909(15)	0.0198(6)
C(8)	0.1822(2)	0.6008(3)	0.14143(14)	0.0186(5)
C(9)	0.3079(3)	0.1415(3)	0.19579(14)	0.0204(5)
C(10)	0.3811(3)	0.2507(3)	0.24240(14)	0.0220(6)
C(11)	0.4403(2)	0.3539(3)	0.19850(15)	0.0215(6)
C(12)	0.2141(2)	0.3371(3)	−0.06363(14)	0.0197(5)
C(13)	−0.0793(2)	0.6482(3)	0.07454(13)	0.0208(6)
C(14)	−0.0313(2)	0.6184(3)	0.15348(13)	0.0185(6)
Zn(1)	0.76569(3)	0.14936(3)	0.12538(2)	0.01803(8)
Cl(2)	0.90537(5)	−0.01935(6)	0.16954(3)	0.01648(13)
Cl(3)	0.81670(7)	0.22823(7)	0.02258(3)	0.0260(2)
Cl(4)	0.78529(7)	0.32143(7)	0.20857(4)	0.0268(2)
Cl(5)	0.58826(6)	0.04430(8)	0.11468(4)	0.0321(2)
Ow[b]	0.4020(4)	0.8132(5)	0.1049(2)	0.0753(15)

[a] $U_{eq} = \frac{1}{3}\Sigma_i\Sigma_j U_{ij} a_i^* a_j^* a_i \cdot a_j$. [b] The population factor for Ow is 0.75.



Scheme 1. Synthesis of bis-adamanzane. All the macrocyclic amines are strong bases and have one or several protons coordinated even under strong basic condition. The protons have been omited for clarity.

atoms at N(1) and N(3) are oriented away from the center of the cavity as is the case for H(1) at N(1) in the present structure, whereas in $H[2^4.3^2]adz^+$ the acidic hydrogen atom is inside the cage. In the $H_2[2^4.3^1]adz^{2+}$ part of the cation in the present structure the 12-membered cyclen ring has approximate *m* symmetry with respect to the plane perpendicular to the plane of the ring through N(1) and N(3). This was also found in $H_3[2^4.3^1]adz^{3+}$ and $H[2^4.3^2]adz^+$. The C–N bond

Table 4. Selected bond lengths (in Å) and bond angles (in °).

N(1)–C(1)	1.508(3)	C(5)–C(6)	1.519(4)
N(1)–C(8)	1.510(3)	C(6)–N(4)	1.483(3)
N(1)–C(14)	1.517(3)	N(4)–C(7)	1.485(3)
C(1)–C(2)	1.522(4)	N(4)–C(11)	1.487(3)
C(2)–N(2)	1.492(3)	C(7)–C(8)	1.520(4)
N(2)–C(9)	1.498(3)	C(9)–C(10)	1.526(4)
N(2)–C(3)	1.499(3)	C(10)–C(11)	1.528(4)
C(3)–C(4)	1.525(4)	C(12)–C(13)^i	1.525(4)
C(4)–N(3)	1.476(3)	C(13)–C(12)^i	1.525(4)
N(3)–C(12)	1.469(3)	C(13)–C(14)	1.531(3)
N(3)–C(5)	1.474(3)		
C(1)–N(1)–C(8)	116.1(2)	C(5)–N(3)–C(4)	114.5(2)
C(1)–N(1)–C(14)	110.0(2)	N(3)–C(5)–C(6)	111.1(2)
C(8)–N(1)–C(14)	111.1(2)	N(4)–C(6)–C(5)	109.8(2)
N(1)–C(1)–C(2)	115.1(2)	C(6)–N(4)–C(7)	112.4(2)
N(2)–C(2)–C(1)	111.6(2)	C(6)–N(4)–C(11)	112.5(2)
C(2)–N(2)–C(9)	112.7(2)	C(7)–N(4)–C(11)	110.9(2)
C(2)–N(2)–C(3)	112.2(2)	N(4)–C(7)–C(8)	114.6(2)
C(9)–N(2)–C(3)	113.9(2)	N(1)–C(8)–C(7)	114.2(2)
N(2)–C(3)–C(4)	110.8(2)	N(2)–C(9)–C(10)	110.1(2)
N(3)–C(4)–C(3)	110.7(2)	C(9)–C(10)–C(11)	112.4(2)
C(12)–N(3)–C(5)	112.5(2)	N(4)–C(11)–C(10)	111.2(2)
C(12)–N(3)–C(4)	113.5(2)	N(3)–C(12)–C(13)^i	112.6(2)
		C(12)^i–C(13)–C(14)	109.4(2)
		N(1)–C(14)–C(13)	113.7(2)

Symmetry code: ^{i}: $-x, -y+1, -z$.

lengths in the ring average 1.491(5) Å, which is close to the value of 1.495(6) Å found in $H_3[2^4.3^1]adz^{3+}$, but longer than the value of 1.463(7) Å found in $H[2^4.3^2]adz^+$. The C–C bond lengths average 1.522(1) Å, which is in agreement with 1.523(6) Å

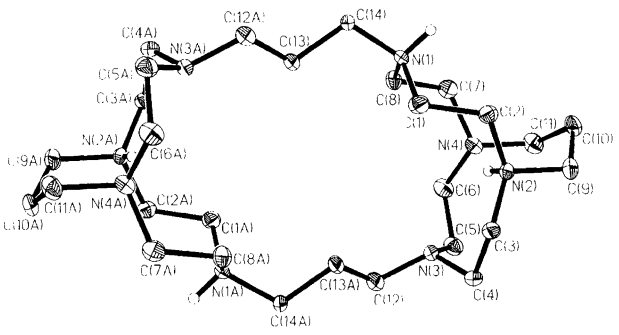


Fig. 4. View of the $[3^2]$bis(i^+,*i*,*i*,o^+-$H_2[2^4.3^1]$adz)$^{4+}$ cation. Thermal ellipsoids are drawn at the 50% probability level. With exception of H(1) attached to N(1) and H(2) attached to N(2), the hydrogen atoms have been omitted for clarity.

found in $H[2^4.3^2]adz^+$ and 1.514(4) Å found in $H_3[2^4.3^1]adz^{3+}$. The three N–C bonds at N(1) seem somewhat longer and those at N(3) slightly shorter than the other N–C bonds.

The two 10-membered rings in the $H_2[2^4.3^2]adz^{2+}$ part of the cation have approximately *m* symmetry with respect to the plane perpendicular to the plane of the ring through N(1), C(10) and N(3), C(10), respectively. In the cation $H_3[2^4.3^1]adz^{3+}$ N(1), N(3) and the middle carbon atom in the $(CH_2)_3$ bridge are positioned on a mirror plane.

The shortest distance across the centre of symmetry in the cation $\{[3^2]bis(o^+,i^+,i,i\text{-}H_2[2^4.3^1]\ adz\}^{4+}$ is C(13)···C(13)^i [i = $-x$, $1-y$, $-z$] of 4.605(6) Å.The N···N^i distances are in the range 6.249(4)–9.020(5) Å. The space between the two $\{H_2[2^4.3^1]adz\}^{2+}$ halves of the cation is rather large, allowing for the possibility of making a complex ion with two metal ions coordinated to four nitrogen atoms each. The conformation of the cyclen ring may change to make the two distances N(1)···N(3) and N(2)···N(4) more alike, as found in $\{Cu([2^4.3^1]\ adz)Br\}^+$ and in $[\{Cu([2^4.3^1]adz)\}_3(\mu_3\text{-}CO_3)]^{4+}$ the distance here being 3.9 and 3.2 Å, respectively.[4,5]

In the $ZnCl_4^{2-}$ anion the bond lengths and angles are in agreement with values found in similar compounds. The crystal packing is influenced by hydrogen bonds, the N(1)–H(1)···Cl(2) ($1-x$, $\frac{1}{2}+y$, $\frac{1}{2}-z$) distance being 3.139(2) Å [D···A] and the Ow–H(1)···Cl(5) (x, $1+y$, z) and the Ow–H(2)···Cl(3) ($1-x$, $1-y$, $-z$) being 3.061(4) and 3.189(4) Å, respectively.

Acid dissociation constants. The bis-adamanzane dimer has four acidic protons: two coordinated inside and two outside the pentacyclic cage. Following our previous studies of protonated forms of bowl and cage adamanzanes it seems reasonable to assume that the two NH groups oriented outwards are more acidic than the two NH groups oriented inwards. Potentiometric glass electrode measurements showed that the tetraprotonated compound $[3^2]bis(H_2[2^4.3^1]adz)^{4+}$ has $pK_{a1}=4.23(3)$ and $pK_{a2}=5.43(12)$, and the two constants therefore refer to the two outward-oriented protons. In the present study we have no experimental evidence as to the acidity of the two inside-cooordinated protons. However, considering that $H[2^4.3^1]adz^+$ has $pK_a > 15$, along with the very weak acidities of the protonated forms of its derivatives **I** and **II**, it seems reasonable to assume that the inside diprotonated octaamine is a very weak acid as well. Therefore, in the following it will be assumed that pK_{a3} and pK_{a4} are both greater than 14.

NMR spectra. The ^1H NMR spectra of the di- and tetraprotonated species are shown in Fig. 3. The spectra of $\{[3^2]bis(H_2[2^4.3^1]adz)\}(ZnCl_4)_2$ in D_2O and 10^{-3} M DCl are identical in agreement with $pK_{a1}=4.23$ of the tetraprotonated species. In more acidic solutions the ^1H NMR spectrum changes suggesting further protonation, the details of which have not been studied. In no case were ^1H NMR signals for the inside coordinated protons observed.

The ^{13}C NMR spectrum of the tetraprotonated species $[3^2]bis(i^+,i,i,o^+\text{-}H_2[2^4.3^1]adz)^{4+}$ has seven resonance lines in the region 50–60 ppm corresponding to CH_2–N carbon atoms and two resonance lines in the region 18–25 ppm corresponding to C–CH_2–C carbon atoms (Table 1). If all the protons bound to the four nitrogen atoms were exchanging slowly on the ^{13}C NMR timescale the expected number of CH_2–N carbon signals would be at least 12. The observed higher symmetry is most likely explained by a fast exchange of either inside or outside coordinated protons (a fast exchange of all NH protons would result in a higher symmetry than that observed, corresponding to only four CH_2–N carbon signals, see below). A fast shuttling of the inside coordinated proton between the two identical bridgehead nitrogen atoms [N(2) and N(4)] in each of the two tetramine units of the dimer requires only a neglible movement of the proton and is likely to occur at high frequency, as suggested previously[10] for the $H[3^6]adz^+$ cation. The outside-coordinated proton may also change position; this, however, requires simultaneous inversion of the lone pairs of several nitrogen atoms and is likely to take place at a much slower rate. It is therefore suggested that in the tetraprotonated species on the ^{13}C NMR timescale the two inside-coordinated protons are bound equally to both bridgehead nitrogen atoms while the outside-coordinated protons are bound to one specific nitrogen atom. This is in agreement with the observed number of seven CH_2–N resonance lines and two C–CH_2–C resonance lines.

The ^{13}C NMR spectrum of the diprotonated species $[3^2]bis(H[2^4.3^1]adz)^{2+}$ (obtained from measurements of $\{[3^2]bis(H_2[2^4.3^1]adz)\}(ZnCl_4)_2$ in 1 M NaOD) exhibit four sharp signals for CH_2–N and two signals for C–CH_2–C (Table 1). The presence of four CH_2–N signals corresponds to the assumption made above of a fast shuttling in each of the two tetraamine cavities of the inside coordinated proton between the two bridgehead nitrogen atoms [N(2) and N(4)].

Concluding remarks. The present octaamine is related to the bowl adamanzanes (Fig. 1) and expected to have several features in common with these. Coordination of Cu^{II}, Co^{II}, Co^{III}, Ni^{II} and Zn^{II} with bowl adamanzanes has been reported,[4–8] and a common characteristic feature is their inertness with respect to hydrolysis of the amine ligand. As an example the dissociation of $Cu([2^3.3^1]adz)Cl^+$ in hydrochloric acid into tetrachlorocuprate(II) anion and protonated amine is 5×10^5 times slower than the corresponding reaction of $Cu(cyclen)^{2+}$.

The closed, cage-like structures of the bis-adamanzanes such as in the present $[3^2]bis([2^4.3^1]adz)$ are expected to affect the properties of their coordination compounds. One obvious possibility is an even more pronounced inertness in relation to hydrolysis. The conformation of $[3^2]bis([2^4.3^1]adz)$ having all eight lone pairs pointing inside the cavity has a size and geometry suitable for coordination of one metal ion in each of the two tetra-amine units. The distance between the 'centres' of the two units of the cavity is about 4 Å, allowing for bridging of two encapsulated metal ions by small ligands such as chloride or oxide. These aspects are now being pursued.

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