Synthesis and Characterization of an Aza-cage, Basicity Behaviour and Crystal Structure of its Diprotonated Species

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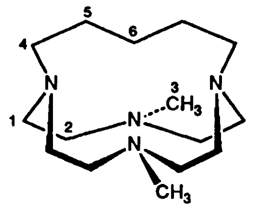
The synthesis and characterization of the macrobicycle 4,10-dimethyl-1,4,7,10-tetraazabicyclo[5.5.5]-heptadecane (**L**) is reported. The proton-transfer properties of **L** in aqueous solution have been investigated by potentiometry (25 °C, $I = 0.15$ mol dm^{-3}) and NMR spectroscopy (^{1}H and ^{13}C). **L** behaves as a fairly strong base in the first protonation step ($\log K_1 = 11.55$), and as a moderate base in the second step ($\log K_2 = 6.94$). ^{1}H and ^{13}C resonances have been assigned for both $[HL]^+$ and $[H_2L]^{2+}$ species. NMR experiments also indicate the stepwise protonation sites. Crystals of $[H_2L][ClO_4]_2$ are orthorhombic, space group $Pca2_1$, with $a = 13.130(1)$, $b = 16.185(4)$, $c = 20.320(6)$ Å, and $Z = 8$; final R value of 0.086 ($R_w = 0.079$) for 2383 unique observed reflections with $I > 3\sigma(I)$. Two independent $[H_2L]^{2+}$ cations are present in the unit cell; they differ from each other in the conformation of the hydrocarbon chain connecting the two unmethylated nitrogen atoms. In both cases the overall cage conformation is due to the presence of two internal hydrogen bonds, connecting the two bridgehead nitrogens and the two methylated nitrogens.

Continuing our systematic study on a series of aza-cages having remarkable ligational properties[1-11] we have synthesized the new cage 4,10-dimethyl-1,4,7,10-tetraazabicyclo[5.5.5]heptadecane, hereafter abbreviated as **L** (see Fig. 1). These are highly preorganized molecules, possessing a tridimensional cavity of fixed size. All are rather strong bases, at least in the first protonation step, few of these cages behave as 'fast proton sponges',[1,2,5,11] namely they are stronger bases than OH^- in aqueous solution and cannot be deprotonated. In trying to better understand these proton-transfer features we have synthesized cages without donor atoms in the bridging group connecting the two unmethylated nitrogen atoms.



L

Fig. 1 Structure of **L** with atom labelling used in NMR studies

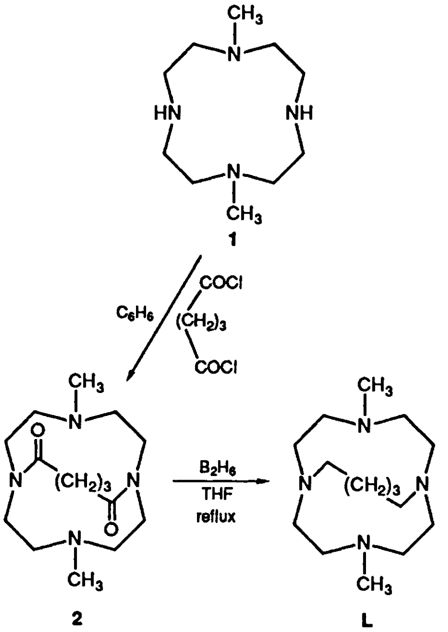


Fig. 2 Reaction pathway for the synthesis of the macrobicycle 4,10-dimethyl-1,4,7,10-tetraazabicyclo[5.5.5]heptadecane (**L**)

Experimental

Synthesis of **L**.—The reaction sequence to obtain **L** is reported in Fig. 2, and was adapted from similar procedures described in refs. 3, 7, 11 for related compounds. The starting macrocyclic compound 1,7-dimethyl-1,4,7,10-tetraazacyclododecane (**1**) was prepared as described in ref. 12.

Glutaric chloride. A sample of glutaric acid (12 g, 0.091 mol) was treated with thionyl chloride (216 g, 1.82 mol) at 50 °C for 20 h. The unreacted thionyl chloride was removed under reduced pressure, the residue was dissolved in dry benzene (50 cm^3) and the solvent was then evaporated. The last operation was repeated three times, and the resulting yellowish oil was used without further purification.

Bicyclic diamide (**2**). A 4.0 g (0.02 mol) sample of the *trans*-dimethylated tetraazamacrocycle (**1**) and 8 cm^3 of triethylamine in 500 cm^3 of dry benzene and 3.4 g (0.02 mol) of glutaric chloride in 500 cm^3 of dry benzene were added simultaneously to 1 dm^3 of dry benzene, under vigorous stirring, over a period of *ca.* 7 h at room temperature. After work up a white solid was obtained (3.7 g, 62.7%), m.p. 180–181 °C (Found: C, 60.8; H, 9.7; N, 18.7. Calc. for $C_{15}H_{28}N_4O_2$: C, 60.78; H, 9.52; N, 18.91%).

4,10-*Dimethyl*-1,4,7,10-*tetraazabicyclo*[5.5.5]*heptadecane* (**L**). A sample of BH_3·THF adduct [a solution of BH_3 (0.1 mol) in 100 cm^3 of THF] was added dropwise, under a nitrogen atmosphere, to a solution of **2** (2.31 g, 7.8 mmol) in dry THF (30 cm^3) cooled to ice temperature. After removal of the cooling

Table 1 Crystal data and intensity collection parameters for $[H_2L]\cdot[ClO_4]_2$

Formula	$C_{15}H_{34}N_4Cl_2O_8$
M	469.4
Space group	$Pca2_1$
a/Å	13.130(1)
b/Å	16.185(4)
c/Å	20.320(6)
U/Å^3	4318(2)
Z	8
D_c/g cm^{-3}	1.44
F(000)	2000
μ(Cu-Kα) cm^{-1}	31.78
T	Ambient
Scan rate/° min^{-1}	4
Scan mode	θ–2θ
Scan width/°	$0.8 + 0.14\mathrm{tg}\theta$
2θ range/°	5–130
No. of reflections collected	4192
Unique obs. reflections [$I > 3.0\sigma(I)$]	2383
Refined parameters	372
R^a	0.086
$R_w{}^b$	0.079

[a] $R = \Sigma||F_o| - |F_c||/\Sigma|F_o|$. [b] $R_w = [\Sigma w(|F_o| - |F_c|)^2/\Sigma wF_o{}^2]^{\frac{1}{2}}$.

bath the reaction mixture was allowed to warm to room temperature and was then refluxed for 3 h. The solution was cooled and the excess of diborane was cautiously destroyed with some drops of water. The solution was then evaporated to dryness, the white solid obtained was dissolved in HCl–H_2O–MeOH mixture (6:9:30) and refluxed for 4 h. The resulting solution was evaporated to dryness and then the residue was dissolved in 5 cm^3 of water, the solution was made alkaline by addition of a concentrated NaOH solution and extracted with chloroform (6 × 50 cm^3). The combined extracts were evaporated to dryness under reduced pressure affording a sticky oil. By sublimation the amine (**L**) was purified. Yield 0.92 g (44%) (Found: C, 67.0; H, 12.2; N, 20.7. Calc. for $C_{15}H_{32}N_4$: C, 67.11; H, 12.02; N, 20.87%).

Reagents.—NaCl (Merck Suprapur) was used as ionic medium. Standardized CO_2-free solutions of NaOH were prepared according to the procedure already described.[13]

Potentiometric Measurements.—The potentiometric titrations were carried out with a fully automatic apparatus, as described in ref. 14. Two titration curves (122 data points) were used to determine the protonation constants of **L**. The computer program SUPERQUAD[15] was used to process the potentiometric data and calculate the protonation and stability constants.

NMR Spectroscopy.—A 200 MHz Bruker Ac-200 instrument was used to record the ^{13}C spectra at an operating frequency of 50.32 MHz.

X-Ray Structure Analysis.—Analysis on a single crystal of $[H_2L][ClO_4]_2$ was carried out with an Enraf–Nonius CAD4 X-ray diffractometer; a summary of the crystallographic data is reported in Table 1. A colourless crystal of approximate dimensions 0.3 × 0.3 × 0.2 mm was mounted on the diffractometer and used for data collection at room temperature with graphite-monochromatized Cu-Kα radiation. Cell parameters were determined by least-squares refinement of diffractometer setting angles for 25 carefully centred reflections. The intensities of three standard reflections were monitored periodically during data collection. Intensity data were corrected for Lorentz and polarization effects, an absorption correction was applied once the structure was solved by using the Walker and Stuart method.[16] The structure was solved by direct methods of SIR 88[17] and subsequently refined by a full-matrix least squares technique. The function minimized was $\Sigma w(|F_o| - |F_c|)^2$, with $w = a/\sigma^2(F)$, where a is an adjustable parameter. The crystals of the compound belong to the orthorhombic family, space group $Pca2_1$. Two independent $[H_2L]^{2+}$ cations were present in the elemental cell. The hydrogen atoms were introduced in calculated positions, and their coordinates refined in agreement with those of the linked atoms, while their isotropic thermal parameters were maitained equal to those of the bound carbon atoms. Anisotropic thermal parameters were used for chlorine, oxygen and nitrogen atoms. The ΔF map carried out in the last refinement cycle did not allow us to localize the acidic hydrogen atoms of the $[H_2L]^{2+}$ cations. The final agreement factors were $R = 0.086$ and $R_w = 0.079$.

All calculations, carried out on an IBM PS/2 computer model 80, were performed with the SHELX-76[18] set of programs which use the analytical approximation for the atomic scattering factors and anomalous dispersion corrections for all the atoms from the International Tables for Crystallography.[19] The molecular plots were produced by the ORTEP[20] program.

Tables of thermal parameters and atomic coordinates have been deposited at the Cambridge Crystallographic Data Centre.*

Calculations.—Molecular modelling and mechanics calculations were carried out with the use of PCMODEL[21] program, which uses the MM2 force field. Because of the lack of torsional parameters regarding the quaternary nitrogen (41 MM2 atom type) in the MM2 original force field, these have been set equal to those of the aminic nitrogen atom (8 MM2 atom type).

Results and Discussion

Protonation.—Under the employed experimental conditions **L** behaves at most as a diprotic base. In the first protonation step the macrobicycle **L** is a relatively strong base [log K_1 = 11.55(3)], and a moderate base [log K_2 = 6.94(3)] in the second protonation step (see Table 2). The third basicity constant is undetectable in aqueous solution, although the triprotonated salt is readily isolated as a solid. This basicity behaviour is rather similar to that found in many other cages of the series (see Table 2), what is unexpected is the dramatic decrease in the basicity strength of the first protonation step, compared with that of the related 'succinic' cage **L1**[11] (see Table 2). Indeed **L1**, which contains a four carbon atom chain connecting the two bridgehead nitrogens behaves as a 'proton sponge' with log K_1 > 14 (see Table 2); the addition of one carbon atom in the bridging group causes a reduction in the basicity strength of a few orders of magnitude. Instead the basicity behaviour of **L** resembles that found for the analogous cage **L4**[7] (see Table 2), having seven carbon atoms in the hydrocarbon chain. These results indicate that the proton-transfer properties are very sensitive to any molecular modification.[22] The marked decrease of the basicity strength for the second protonation step, typical of these molecules, has been ascribed to the positive charge repulsion experienced by two protons forced into close proximity by the rigid molecular frame. Very likely, because of the even more serious charge repulsion, the triprotonated species is not formed under the potentiometric experimental conditions.

NMR Studies.—The ^{13}C spectrum of the aminic cage **L** in $CDCl_3$ displays six signals at 59.6 (C-2), 54.7 (C-4), 54.3 (C-1),

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* For details of the deposition scheme see 'Instructions for Authors,' *J. Chem. Soc., Perkin Trans. 2*, 1993, issue 1.

Table 2 Basicity constants (logarithms) of cages in aqueous solution, at 25 °C, I = 0.5 mol dm^{-3}

Reaction	Cage[a] L	L1	L2	L3	L4	L5	L6	L7	L8	L9
$H^+ + L = HL^+$	11.55(3)[b]	>14	>14	>14	12.00	11.91	11.83	12.48	11.8	11.8
$HL^+ + H^+ = H_2L^{2+}$	6.94(3)[b]	7.8	8.41	11.21	7.86	8.78	9.53	9.05	10.0	8.3

[a] **L1** = 4,10-dimethyl-1,4,7,10-tetraazabicyclo[5.5.4]hexadecane, ref. 11; **L2** = 12,17-dimethyl-1,5,9,12,17-pentaazabicyclo[7.5.5]nonadecane, ref. 1; **L3** = 12,17-dimethyl-5-oxa-1,9,12,17-tetraazabicyclo[7.5.5]nonadecane, ref. 5; **L4** = 12,17-dimethyl-1,9,12,17-tetraazabicyclo[7.5.5]nonadecane, ref. 7; **L5** = 12,17-dimethyl-5-thia-1,9,12,17-tetraazabicyclo[7.5.5]nonadecane, ref. 3; **L6** = 5,12,17-trimethyl-1,5,9,12,17-pentazabicyclo[7.5.5]nonadecane, ref. 6; **L7** = 4,10-dimethyl-1,4,7,10,15-pentaazabicyclo[5.5.5]heptadecane, ref. 8; **L8** = 4,10,15-trimethyl-1,4,7,10,15-pentaazabicyclo[5.5.5]heptadecane, ref. 9; **L9** = 4-benzyl-10,15-dimethyl-1,4,7,10,15-pentaazabicyclo[5.5.5]heptadecane, ref. 10. [b] This work.

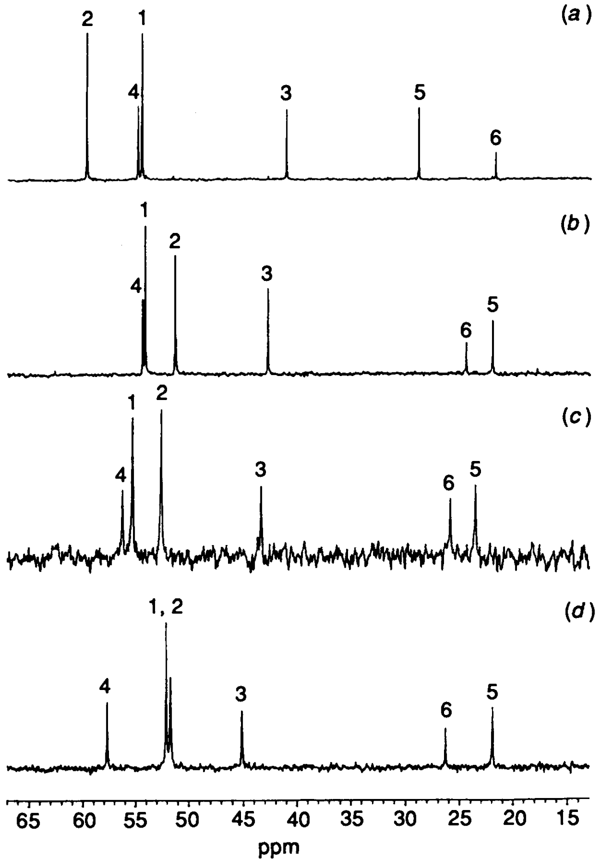

Fig. 3 ^{13}C NMR spectrum of **L** (*a*) and [HL][ClO$_4$] (*b*) in CDCl$_3$; [HL][ClO$_4$] (*c*) and [H$_2$L][ClO$_4$]$_2$ (*d*) in D$_2$O

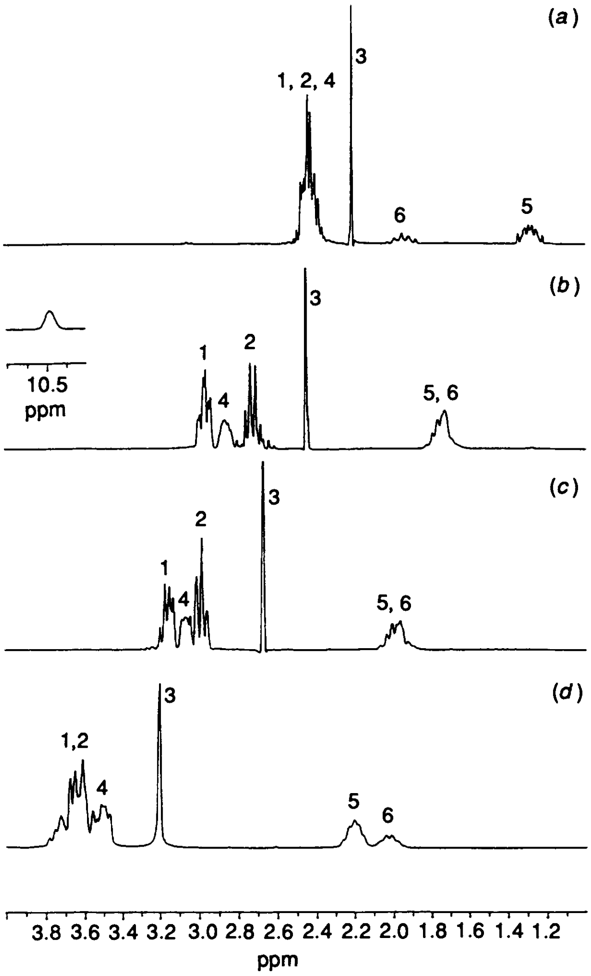

Fig. 4 ^1H NMR spectrum of **L** (*a*) and [HL][ClO$_4$] (*b*) in CDCl$_3$; with enlarged signal at 10.5 ppm; [HL][ClO$_4$] (*c*) and [H$_2$L][ClO$_4$]$_2$ (*d*) in water

41.0 (C-3), 28.8 (C-5) and 21.8 ppm (C-6) with relative intensities approximately 4:2:4:2:2:1 [see Fig. 3(*a*)]. These features indicate a C_{2v} time-averaged symmetry. The ^1H spectrum shows a complex signal pattern at 2.35–2.45 ppm, integrating for 20 protons, a singlet at 2.20 ppm (six protons), and two multiplets at 1.95 (two protons) and 1.28 ppm (four protons) [Fig. 4(*a*)]. From 2D ^1H–^1H homonuclear and ^1H–^{13}C heteronuclear correlations an assignment of the signals was made and it is reported in Figs. 3(*a*) and 4(*a*).

The ^{13}C and ^1H spectra of [HL][ClO$_4$] in CDCl$_3$ are reported in Figs. 3(*b*) and 4(*b*) respectively. The ^1H spectrum displays a broad signal at 10.5 ppm integrating for one proton, assigned to the ammonium proton. By using ^1H–^1H homonuclear and ^1H–^{13}C heteronuclear correlations and homonuclear decoupling experiments, the ^1H and ^{13}C signals have been fully assigned. A tentative hypothesis on the nitrogen atoms involved in the first protonation can be made. In a homonuclear decoupling experiment the resonances of the hydrogens of C-5 and C-6 have been selectively irradiated [see Fig. 5(*b*)]. The signal at 2.8 ppm, due to the hydrogens of C-4, turns into a doublet under this condition. By adding D$_2$O or MeOD to the chloroform solution of [HL][ClO$_4$], the signal at 10.5 ppm disappears and, by decoupling again the hydrogen atoms of C-4 from those of C-5 and C-6, the signal at 2.8 ppm gives rise to a singlet [see Fig. 5(*c*)]. In these conditions the multiplet at 2.95–2.88 ppm gives rise to a triplet. This experiment indicates a coupling between the N-H hydrogen and the protons of C-4, with J = 2.4 Hz. When the resonances of the hydrogens of C-2 are selectively irradiated, the signals at 2.95–2.88 ppm give rise to a doublet [Fig. 5(*d*)]. Again, adding MeOD or D$_2$O to this solution and decoupling the hydrogen atoms of C-1 from those of C-2, the signal at 2.9 ppm turns into a singlet [Fig. 5(*e*)]. The same experiment carried out decoupling the hydrogens of C-2 from those of C-1, shows no coupling between the hydrogens of C-2 and the acidic hydrogen.

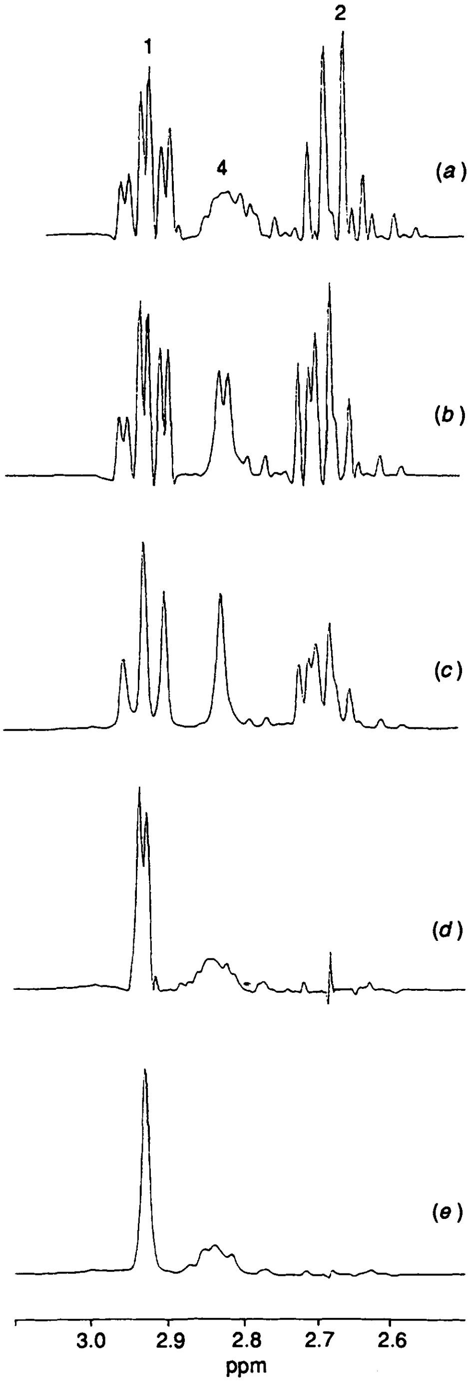

Fig. 5 ^1H NMR spectrum of $[HL][ClO_4]$ in $CDCl_3$ in the 3.1–2.5 ppm range (*a*), with selective irradiation of the hydrogens' resonances of C-5 and C-6 (*b*), with selective irradiation of the hydrogens' resonances of C-5 and C-6 in presence of D_2O (*c*), with selective irradiation of the hydrogens' resonances of C-2 (*d*), and with selective irradiation of the hydrogens' resonances of C-2 in the presence of D_2O (*e*)

Table 3 Selected bond distances/Å and angles/° of $[H_2L][ClO_4]_2$, with estimated standard deviations in parentheses

N(1)–C(1)	1.50(2)	N(1)–C(8)	1.51(2)
N(1)–C(11)	1.49(2)	C(1)–C(2)	1.49(2)
C(2)–N(2)	1.48(2)	N(2)–C(3)	1.42(2)
N(2)–C(9)	1.47(2)	C(3)–C(4)	1.50(2)
C(4)–N(3)	1.52(2)	N(3)–C(5)	1.48(2)
N(3)–C(15)	1.48(2)	C(5)–C(6)	1.48(2)
C(6)–N(4)	1.45(2)	N(4)–C(7)	1.46(2)
N(4)–C(10)	1.49(2)	C(7)–C(8)	1.51(2)
C(11)–C(12)	1.49(2)	C(12)–C(13)	1.47(2)
C(13)–C(14)	1.46(2)	C(14–C(15)	1.55(2)
N(5)–C(16)	1.55(2)	N(5)–C(23)	1.49(2)
N(5)–C(26)	1.46(2)	C(16)–C(17)	1.52(2)
C(17)–N(6)	1.49(2)	N(6)–C(18)	1.50(2)
N(6)–C(24)	1.44(2)	C(18)–C(19)	1.45(2)
C(19)–N(7)	1.45(2)	N(7)–C(20)	1.40(2)
N(7)–C(30)	1.55(2)	C(20)–C(21)	1.47(2)
C(21)–N(8)	1.48(2)	N(8)–C(22)	1.48(2)
N(8)–C(25)	1.50(2)	C(22)–C(23)	1.44(2)
C(26)–C(27)	1.53(2)	C(27)–C(28)	1.52(2)
C(28)–C(29)	1.48(2)	C(29)–C(30)	1.56(2)
C(8)–N(1)–C(11)	113(1)	C(1)–N(1)–C(11)	107(1)
C(1)–N(1)–C(8)	113(1)	N(1)–C(1)–C(2)	113(1)
C(1)–C(2)–N(2)	112(1)	C(2)–N(2)–C(9)	107(1)
C(2)–N(2)–C(3)	114(1)	C(3)–N(2)–C(9)	112(1)
N(2)–C(3)–C(4)	110(1)	C(3)–C(4)–N(3)	109(1)
C(4)–N(3)–C(15)	109(1)	C(4)–N(3)–C(5)	109(1)
C(5)–N(3)–C(15)	109(1)	N(3)–C(5)–C(6)	114(1)
C(5)–C(6)–N(4)	115(1)	C(6)–N(4)–C(10)	113(1)
C(6)–N(4)–C(7)	113(1)	C(7)–N(4)–C(10)	111(1)
N(4)–C(7)–C(8)	110(1)	N(1)–C(8)–C(7)	108(1)
N(1)–C(11)–C(12)	116(1)	C(11)–C(12)–C(13)	114(1)
C(12)–C(13)–C(14)	117(1)	C(13)–C(14)–C(15)	116(1)
N(3)–C(15)–C(14)	111(1)	C(23)–N(5)–C(26)	103(1)
C(16)–N(5)–C(26)	112(1)	C(16)–N(5)–C(23)	114(1)
N(5)–C(16)–C(17)	112(1)	C(16)–C(17)–N(6)	114(1)
C(17)–N(6)–C(24)	111(1)	C(17)–N(6)–C(18)	109(1)
C(18)–N(6)–C(24)	113(1)	N(6)–C(18)–C(19)	112(1)
C(18–C(19)–N(7)	111(1)	C(19)–N(7)–C(30)	111(1)
C(19)–N(7)–C(20)	119(1)	C(20)–N(7)–C(30)	104(1)
N(7)–C(20)–C(21)	117(1)	C(20)–C(21)–N(8)	113(1)
C(21)–N(8)–C(25)	108(1)	C(21)–N(8)–C(22)	115(1)
C(22)–N(8)–C(25)	110(1)	N(8)–C(22)–C(23)	108(1)
N(5)–C(23)–C(22)	113(1)	N(5)–C(26)–C(27)	111(1)
C(26)–C(27)–C(28)	119(2)	C(27)–C(28)–C(29)	117(1)
C(28)–C(29)–C(30)	115(1)	N(7)–C(30)–C(29)	115(1)

The hydrogens of the ethylenic chain and the N-H proton present a AX_2YZ spin system. ($\delta_A = 10.5, \delta_X = 2.92, \delta_Y = 2.71, \delta_Z = 2.66$, $J_{AX} = 1.90$ Hz, $J_{XY} = J_{XZ} = 5.46$ Hz, $J_{YZ} = -13.79$ Hz.) From this analysis of the ^1H spectrum of $[HL][ClO_4]$ in $CDCl_3$, it can be concluded that the first protonation of L takes place essentially on the bridgehead nitrogen atoms. This is confirmed by comparing the free amine [Fig. 4(*a*)] and the monoprotonated species [Fig. 4(*b*)] ^1H spectra. While in the free amine the signals of the hydrogens of C-1, C-2 and C-4 have very similar chemical shifts, in the $[HL][ClO_4]$ species the resonances of the hydrogens of C-1 and C-4 (placed in the α-position with respect to the bridgehead nitrogens) bear a remarkable downfield shift. Instead, the signal of the hydrogens of the methyl groups does not shift appreciably. With respect to the free amine, the ^{13}C spectrum of the monoprotonated species shows an upfield shift of the signal of C-2 and C-5, in agreement with the β-shift reported for the protonation of polyamines.[23] Beside that, the C_{2v} time-averaged symmetry, showed by the $[HL][ClO_4]$ spectra, suggests that the proton is rapidly exchanged between the bridgehead nitrogens. On adding H_2O or MeOH to the solution, the signal at 10.5 (N–H proton) does not disappear, indicating instead a slow exchange with mobile protons of the solvent, on the NMR time scale. The ^{13}C spectrum of $[HL][ClO_4]$ in D_2O displays similar features to that in $CDCl_3$, as shown in Fig. 3(*c*). The most significant differences in the ^1H spectrum are the disappearance of the ^1H resonance at 10.5 ppm and the change of the spin system formed by the hydrogens of C-1 and C-2. A different conformation of the ethylenic chains of the molecule could explain this difference of spin system in D_2O and $CDCl_3$.

With respect to $[HL][ClO_4]$ in D_2O, in the ^1H NMR spectrum of $[H_2L][ClO_4]_2$ in D_2O [Fig. 4(*d*)] the signal of the methyl group shifts remarkably downfield; furthermore in the ^{13}C NMR spectrum the resonance of C-1 (in the β-position to bridgehead nitrogens), bears an upfield shift of *ca.* 3 ppm [see Fig. 3(*d*)]. These spectral features suggest that the second

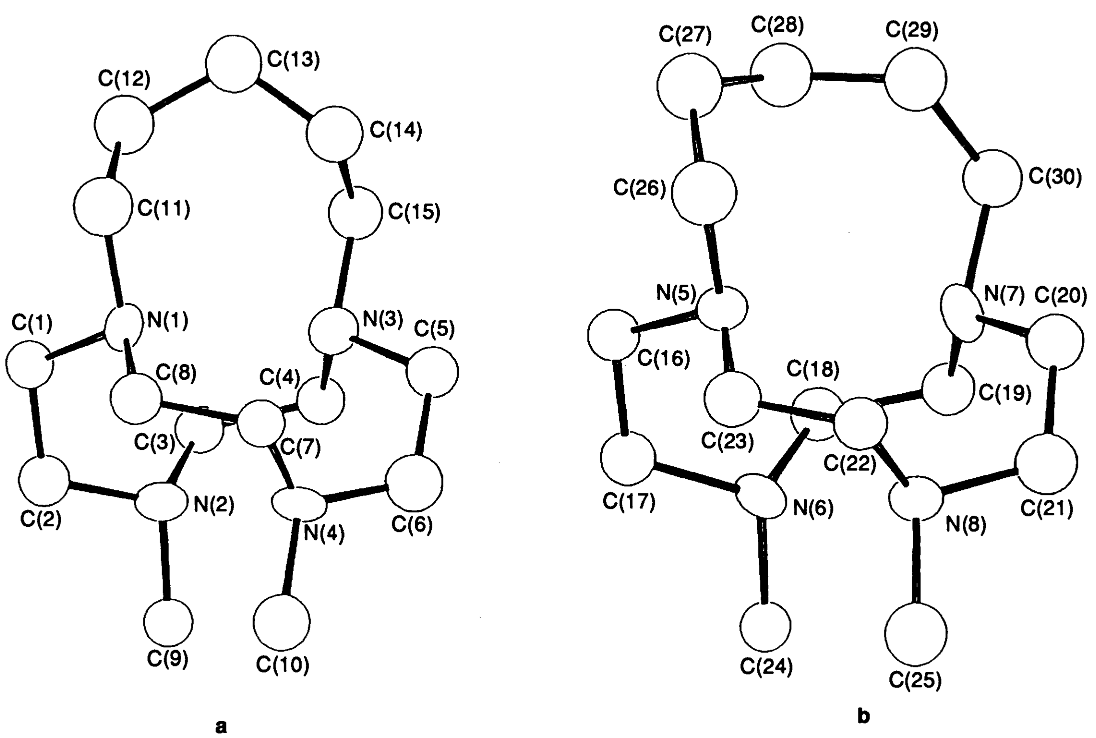

Fig. 6 ORTEP drawing of the $[H_2L]^{2+}$ cations **a** and **b**

Table 4 Energy terms (kcal mol^{-1}) for molecular mechanics calculation

Molecule	Isomer	STR	BND	SB	TOR	VDW	QQ	Total
a	BB	4.26	14.08	0.19	21.11	10.40	53.30	103.34
a	MM	4.22	13.87	0.41	21.79	13.05	50.06	103.41
a	BM1	4.71	10.75	−0.13	21.11	8.28	42.85	87.57
a	BM2	4.79	11.55	−0.12	21.38	8.12	42.96	89.68
b	BB	4.29	14.26	0.16	21.10	10.39	51.60	101.91
b	MM	4.05	15.26	0.43	21.40	13.15	50.15	104.45
b	BM1	4.57	11.37	−0.06	21.52	8.86	43.36	89.63
b	BM2	4.71	12.50	−0.12	21.22	8.11	43.98	90.41

protonation involves the nitrogen atoms bearing methyl groups.

In conclusion, NMR experiments as a function of pH allow the localization of the protonation sites in solution. To corroborate these results and in order to obtain structural information a crystal structure determination has been carried out. Although di- and tri-protonated salts have been isolated, only crystals of the diprotonated salt were suitable for X-ray analysis.

Crystal Structure of $[H_2L][ClO_4]_2$.—The crystal structure of the compound consists of discrete $[H_2L]^{2+}$ cations and $[ClO_4]^-$ anions. Fig. 6 shows an ORTEP drawing of the two independent $[H_2L]^{2+}$ cations with their atom labelling. Bond lengths and angles are reported in Table 3. The overall conformations of the two independent cations are similar with the most significant difference on the conformation of the five carbon atom chain. The corresponding torsion angles are: N(1)–C(11)–C(12)–C(13), −101(2)°; C(11)–C(12)–C(13)–C(14), 56(2)°; C(12)–C(13)–C(14)–C(15), 59(2)°; C(13)–C(14)–C(15)–N(3), 107(2)° for **a** (see Fig. 6) and N(5)–C(26)–C(27)–C(28), −47(2)°; C(26)–C(27)–C(28)–C(29), 51(2)°; C(27)–C(28)–C(29)–C(30), 126(2)°; C(28)–C(29)–C(30)–N(7), −69(2)° for **b** (see Fig. 6). In both cations each nitrogen atom is in the *endo* configuration. Although the acidic hydrogens have not been located in the Fourier difference map, their position can be easily inferred considering the relative disposition of the bridgehead and methylated nitrogens in both the two independent cations. In fact the tetrahedral position of the bridgehead nitrogen atoms, which are facing each other, as well as those of the methylated nitrogen atoms, together with the short distances between N(1)–N(3) [2.86(1) Å] and between N(2)–N(4) [2.81(2) Å] for **a** and N(5)–N(7) [2.96(2) Å] and N(6)–N(8) [2.84(1) Å] for **b** strongly suggest the presence of linear hydrogen bonds. It is therefore reasonable to locate the two acidic hydrogens between N(1)–N(3), N(2)–N(4) in molecule **a** and N(5)–N(7), N(6)–N(8) in molecule **b**. In conclusion, the conformation shown is the result of the presence of these two hydrogen bonds, connecting pairs of opposite nitrogen atoms.

Molecular Mechanics.—Molecular mechanics calculations have been carried out on both molecules **a** and **b**. The energies of the diprotonated species were obtained by energy minimizations using as starting geometries those obtained from the X-ray analysis, localizing the two protons on each nitrogen pair in turn. For each molecule there are four different ways to arrange the two hydrogen atoms: (i) hydrogen atoms located on the two bridgehead nitrogen atoms, indicated as **BB** in Table 4; (ii) hydrogen atoms located on the two methylated nitrogens, isomers as **MM** in Table 4; (iii) hydrogen atoms located on adjacent nitrogen atoms. In case (iii) there are two different isomers depending upon the different conformation of the two ethylenic chains joining the methylated and bridgehead nitrogen atoms (see Fig. 6). These conformational isomers have been indicated in Table 4 as BM1 and BM2 respectively. In all cases the possibility of hydrogen bond formation was taken into consideration. Details on the energy terms are reported in Table 4. As expected for charged, small and rigid molecules the most important energetic term is the electrostatic one (QQ); the difference in the total energy content of each isomer mainly reflects the different values for the QQ and van der Waals (VDW) terms (see Table 4). Calculations show that the lowest energy is achieved when the two protons are bound to adjacent nitrogen atoms, allowing the formation of two strong hydrogen bonds as already suggested by the geometrical features of both cations $[H_2L]^{2+}$. In particular the BM1 isomer for both molecules **a** and **b** has been found to have the lowest energy content. On the other hand in the BM2 isomer the two protons are localized on the further apart nitrogen pair.

These results are in good agreement with those found in NMR solution studies, where the two adjacent nitrogens have been indeed found to be involved in the diprotonated species, as well as with the geometrical features displayed by the cations in the solid state.

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