Crystal Structures of Salts of Mono- and Triprotonated [3⁶]Adamanzane, 1,5,9,13-Tetraazatricyclo[7.7.3.3⁵,¹³]docosane, and Equilibrium Studies of the Reactions between Mono-, Di- and Triprotonated Species, Respectively, Having None, One and Two Lone Pairs Pointing Outwards

Johan Springborg,[a],* Ulla Pretzmann,[a] Carl Erik Olsen[a] and Inger Søtofte[b]

[a]Chemistry Department, Royal Veterinary and Agricultural University, Thorvaldsensvej 40, DK-1871 Frederiksberg C, Denmark and Department of Chemistry, Technical University of Denmark, DTU 207, DK-2800 Lyngby, Denmark

Springborg, J., Pretzmann, U, Olsen, C. E. and Søtofte, I., 1998. Crystal Structures of Salts of Mono- and Triprotonated [3⁶]Adamanzane, 1,5,9,13-Tetraazatricyclo[7.7.3.3⁵,¹³]docosane, and Equilibrium Studies of the Reactions between Mono-, Di- and Triprotonated Species, Respectively, Having None, One and Two Lone Pairs Pointing Outwards. – Acta Chem. Scand. 52: 289–295. © Acta Chemica Scandinavica 1998.

The structures of bromide salt of the inside monoprotonated tricyclic amine 1,5,9,13-tetraazatricyclo[7.7.3.3⁵,¹³]docosane, i^+,i,i,i-[H[3⁶]adz]Br and of the tetrabromozincate bromide salt of its triprotonated form, i^+,i,o^+,o^+-[H₃[3⁶]adz][ZnBr₄]Br·H₂O have been determined by X-ray diffraction techniques.

In acidic solution i^+,i,i,i-H[3⁶]adz$^+$ reacts with one hydrogen ion and at the same time undergoes inversion at one nitrogen group to give the diprotonated species i^+,i,i,o^+-H₂[3⁶]adz^{2+} as shown by ¹H and ¹³C NMR spectroscopy and glass-electrode measurements. The thermodynamic data for the concentration equilibrium constant for the protonation/inversion reaction are $-\log K_{ia1} = 3.122(5)$ M, $\Delta H°(K_{ia1}) = 12.0(8)$ kJ mol^{-1}, $\Delta S°(K_{ia1}) = -20(3)$ J mol^{-1} K^{-1} (25 °C, $I = 1$ M (Na,H)Cl. The equilibration reaction between the mono- and dipotonated species is slow on the NMR timescale (25 °C). The lifetime of the diprotonated species has been studied by the temperature dependence of its ¹H NMR spectrum, which at room temperature corresponds to C_{3v} symmetry but at higher temperature exhibits coalescence corresponding to an approach toward a time-averaged T_d symmetry. The latter is interpreted as a fast exchange of the outside coordinated proton between the four sites in i^+,i,i,o^+-H₂[3⁶]adz^{2+}. The exchange reaction is acid catalyzed, and a pathway involving the triprotonated species i^+,i,o^+,o^+-H₃[3⁶]adz^{3+} is assumed to be the rate-determining step.

In acidic solution i^+,i,i,o^+-H₂[3⁶]adz^{2+} is very inert with respect to exchange of the inside coordinated proton ($k_{ex} < 3 \times 10^{-9}$ s^{-1}). The H[3⁶]adz$^+$ species is much more stable than its smaller analouge with respect to C–N cleavage. In 1–3 M HCl H[2⁴.3²]adz$^+$ is shown to undergo an acid catalyzed cleavage of one of the trimethylene bridges to give quantitatively the parent bowl adamanzane [2⁴.3¹]adz without further cleavage of N–C bonds. In contrast, the H[3⁶]adz$^+$ species withstands boiling for days in concentrated hydrochloric acid.

We recently presented[1,2] facile methods for the synthesis of the inside protonated forms of the small tricyclic tetraamines i^+,i,i,i-H[2⁴.3²]adz$^+$ and i^+,i,i,i-H[3⁶]adz$^+$, which both have all lone pairs pointing towards the centre of the cage (Fig. 1). Abbreviations and a nomenclature for assigning outwards and inwards oriented lone pair are given in Experimental. These are the first

examples of a macrotricyclic compounds containing only small chains ($n = 2$ or 3) with four donor atoms in an approximately tetrahedral arrangement. From the X-ray crystal structure of i^+,i,i,i-H[2⁴.3²]adz$^+$ it was shown that the proton in the center is hydrogen bonded to two nitrogen atoms with only weak interactions to the other two nitrogen atoms. From ¹H and ¹³C NMR studies it was shown that the i^+,i,i,i-H[2⁴.3²]adz$^+$ cation in solution has a time-averaged D_{2d} symmetry. The protonated
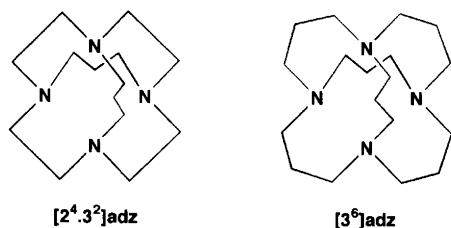
---

* To whom correspondence should be addressed.

Fig. 1. Small tetraamine cages: [2⁴.3²]adamanzane (left) and [3⁶]adamanzane (right) reported by Springborg *et al.*[1,2]

amine is aprotic in the pH range 0–14, and it is extremely inert with respect to exchange of the inside bound proton. The rate constant for the dissociation of the proton in 1 M NaOD is less than 2×10^{-8} s^{-1} at 25 °C. The larger cage i$^+$,i,i,i-H[3⁶]adz$^+$ has a similar behaviour and its proton exchange is also very slow ($k_{ex} < 4 \times 10^{-8}$ s^{-1}). In contrast to the smaller cage, i$^+$,i,i,i-H[3⁶]adz$^+$ reacts with protons in acidic solutions as described in the present paper reporting the crystal structure of i$^+$,i,i,i-[H[3⁶]adz]Br and of a salt of the triprotonated species, i$^+$,i,o$^+$,o$^+$-[H₃[3⁶]adz][ZnBr₄]Br · H₂O, together with a thermodynamic study of the reactions between different protonated species.

Experimental

Abbreviations and nomenclature. A simplified nomenclature for this series of tricyclic tetraamines given recently[2,3] is illustrated in Fig. 1: [2⁴.3²]adz = [2⁴.3²]adamanzane = 1,4,8,11-tetraazatricyclo[6.6.2.2⁴,¹¹]octadecane. [3⁶]adz = [3⁶]adamanzane = 1,5,9,13 - tetraazatricyclo[7.7.3.3⁵,¹³]- docosane. Protonated forms may be written as for example H[2⁴.3²]adz$^+$ or H₂[3⁶]adz^{2+}. The orientation of the lone pairs at each nitrogen group is given by the prefixes i and o, respectively, to indicate lone pairs pointing inwards or outwards. In protonated forms i$^+$ and o$^+$, respectively, are used to designate inwards and outwards coordinated protons. The prefixes are mentioned in the order i$^+$, i, o$^+$ and o. As an example, the formulae i$^+$,i,o$^+$,o-H₂[3⁶]adz^{2+} means a diprotonated [3⁶]adamanzane with two lone pairs pointing inwards, two pointing outwards, one proton coordinated inside and one proton coordinated outside.

Materials. [H[3⁶]adz]Br and [H[2⁴.3²]adz]ClO₄ were prepared by published methods.[1,2] All other chemicals were of analytical grade.

Analyses. C, H, and N were made by the Microanalytical Laboratory at the H.C. Ørsted Institute, Copenhagen. Bromide analyses were made by potentiometric titration with silver nitrate.

NMR spectra. ¹H and ¹³C NMR spectra were measured at 5.87 T on a Bruker AC 250 NMR spectrometer equipped with a 5 mm probe. ¹H chemical shift values (δ) are reported in ppm and are referenced to internal

dioxane [δ(dioxane) = 3.75 ppm] for D₂O solutions. ¹³C chemical shift values (δ) are referenced to internal dioxane [δ(dioxane) = 67.40 ppm] for D₂O solutions. For CDCl₃ solutions chemical shift values (δ) are referenced to internal TMS [δ(TMS) = 0 ppm]. ¹³C DEPT NMR spectra were used to assign CH₂ carbon atoms.

Synthesis and crystal growing.

i$^+$,i,i,i-[H[3⁶]adz]Br. A solution of [H[3⁶]adz]Br (100 mg) in hot (80 °C) water (8 ml) was filtered and then left for some hours at room temperature. The crystals were filtered off and dried in the air. Yield 50 mg. Analytical data: Calculated for C₁₈H₃₇N₄Br: C, 55.5; H, 9.58; N, 14.39; Br, 20.52. Found: C, 54.5; H, 9.18; N, 14.06; Br, 20.58.

i$^+$,i,o$^+$,o$^+$-[H₃[3⁶]adz][ZnBr₄]Br · H₂O. A suspension of [H[3⁶]adz]Br (447 mg) in 1 M HBr (15 ml) was filtered, and thereby a small excess of the bromide salt was removed. A solution of 2 M Li₂ZnBr₄ (6 ml) was added slowly, and after some hours the white precipitate was filtered off, washed with ice-cold methanol and dried in the air. Yield 760 mg. The crude product (200 mg) was dissolved in 1 M HBr (20 ml) and the filtered solution was left in an open beaker. During 12–24 h evaporation had reduced the volume to 2 ml, and colorless crystals separated. The crystals were isolated by filtration, washed with ice-cold methanol and dried in the air. Yield 98 mg (41% based upon [H[3⁶]adz]Br). Analytical data: Calculated for C₁₈H₄₁N₄Br₅OZn: C, 27.2; H, 5.20; N, 7.05; Br, 50.3. Found: C, 26.0; H, 4.82; N, 6.64; Br, 49.1.

Crystallographic data. The structures of the bromide salt of the inside monoprotonated tricyclic amine 1,5,9,13-tetraazatricyclo[7.7.3.3⁵,¹³]docosane, i$^+$,i,i,i-[H[3⁶]adz]-Br and of the tetrabromozincate bromide salt of its triprotonated form, i$^+$,i,o$^+$,o$^+$-[H₃[3⁶]adz][ZnBr₄]Br · H₂O have been determined by X-ray diffraction techniques at $T = 145$ K and $T = 120$ K, respectively. For [H[3⁶]adz]Br: $M_r = 389.42$, monoclinic, $C2$, $a = 15.232(8)$, $b = 8.786(5)$, $c = 15.220(10)$ Å, $\beta = 109.59(4)°$, $Z = 4$, $D_x = 1.35$ g cm^{-3}, Cu $K\alpha = 1.5418$ Å, $\mu = 29.6$ cm^{-1}, $F(000) = 832$, $R(F) = 0.0988$ for 1043 reflections with $I > 2\sigma(I)$ and $wR(F^2) = 0.3201$ for 1884 unique reflections. For [H₃[3⁶]adz][ZnBr₄]Br · H₂O: $M_r = 794.47$, triclinic, $P\bar{1}$, $a = 9.384(3)$, $b = 9.630(3)$, $c = 15.310(3)$ Å, $\alpha = 97.87(3)°$, $\beta = 91.23(3)°$, $\gamma = 97.77(3)°$, $Z = 2$, $D_x = 1.95$ g cm^{-3}, Mo $K\alpha = 0.71073$ Å, $\mu = 82.8$ cm^{-1}, $F(000) = 780$, $R(F) = 0.0962$ for 3605 reflections with $I > 2\sigma(I)$ and $wR(F^2) = 0.2821$ for 5919 unique reflections.

Results

Crystal structures. In the cation i$^+$,i,i,i-H[3⁶]adz$^+$ the lone pairs of the nitrogen atoms are all oriented towards the inside of the cavity (Fig. 2). The four nitrogen atoms
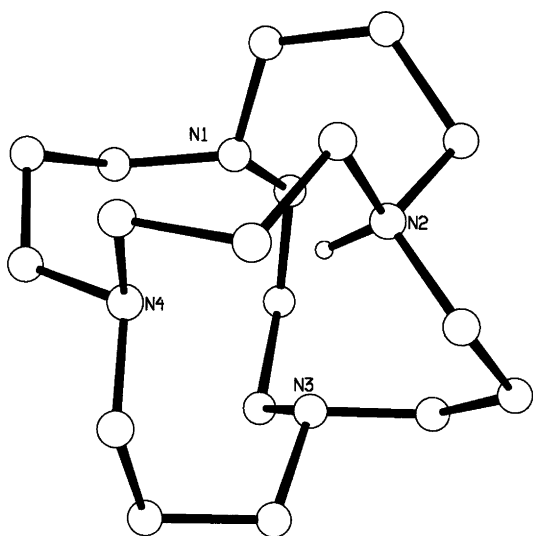
Fig. 2. View of the H[3⁶]adz⁺ cation.[4] The lone pairs of the four nitrogen atoms are all oriented towards the inside of the cavity. The hydrogen atom is at generated position.

form a slightly distorted tetrahedron about the centre (M) of the cavity with an average M–N distance of 2.4 Å. The N $\cdots$ N distances are in the range 3.02–3.23 Å, the longest distance being the N(1) $\cdots$ N(4) distance.

In the cation i⁺,i,o⁺,o⁺-H₃[3⁶]adz³⁺ the lone pairs of N(1) and N(3) are both oriented towards the inside of the cavity, whereas the other two lone pairs both are pointing away from the cavity (Fig. 3). The four nitrogen atoms form a slightly distorted tetrahedron about the centre (M) of the cavity with an average M–N distance of about 1.9 Å. The distances between the nitrogen atoms are in the range of 3.15–4.62 Å. The longest distance is between N(2) and N(4).
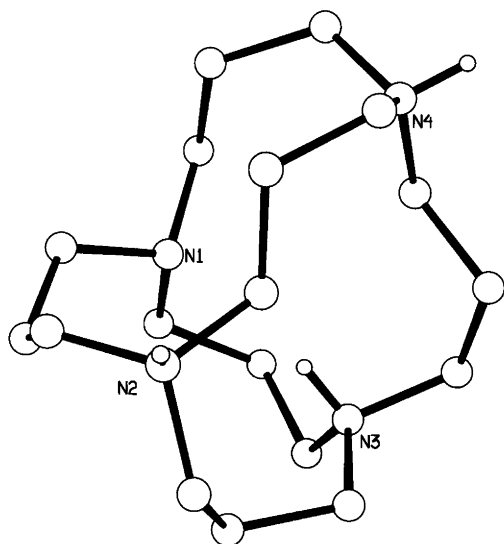

Fig. 3. View of the H₃[3⁶]adz³⁺ cation.[4] The lone pairs of N(1) and N(3) are both oriented towards the inside of the cavity, whereas the lone pairs of N(2) and N(4) are pointing away from the cavity. The hydrogen atoms are at generated positions.

Determination of the equilibrium constant for the protonation of i⁺,i,i,i-[H[3⁶]adz]⁺ *to give* i⁺,i,i,o⁺-H₂[3⁶]adz²⁺. Using ¹H and ¹³C NMR spectroscopy we recently[2] found that the cation H[3⁶]adz⁺ in solution has all nitrogen lone-pairs pointing towards the centre of the cage, i⁺,i,i,i-H[3⁶]adz⁺. This is in agreement with the present crystal structure determination of the bromide salt as described above. In the same study[2] it was estimated on basis of semi-quantitative experiments that the cage does not react with acid at pH>2, which however is not true. As discussed below the cage does react with acid at about pH 3, as shown in eqn. (1) (the assignment of the i,i,i,o structure of the diprotonated species is discussed later):

$$i^+,i,i,o^+-H_2[3^6]adz^{2+} \underset{}{\overset{K_{ia1}}{\rightleftharpoons}} i^+,i,i,i-H[3^6]adz^+ + H^+$$

(1)
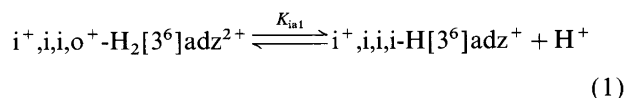
The reaction with acid is fast and reversible: [H[3⁶]adz]Br dissolves instantaneously in 1 M HBr and is much more soluble in this solvent than in water owing to the formation of the diprotonated species; when the acidic solution is neutralized with concentrated sodium hydroxide a white precipitate of [H[3⁶]adz]Br forms within seconds. This shows that the timescale for the equilibration reaction is less than seconds. Potentiometric glass-electrode titrations showed that the monoprotonated amine, H[3⁶]adz⁺, reacts with one H⁺ ion. The results for titrations at three different temperatures are given in Table 1.

¹H and ¹³C NMR experiments confirmed these results. The ¹³C NMR spectra of solutions of [H[3⁶]adz]Br at different [H⁺] are shown in Fig. 4. As the hydrogen ion concentration increases, the two ¹³C NMR signals for the H[3⁶]adz⁺ cation gradually decrease and a new pattern of five resonance lines appear. The ¹³C NMR spectra of the most acidic solutions (0.1 and 1.0 M H⁺) were identical with five resonance lines (see also below) and correspond to the diprotonated species (Fig 4). The ¹H NMR spectra show a similar change. These results together with the potentiometric data show that H₂[3⁶]adz²⁺ does not react with another proton for pH⩾0 and therefore pK_{ia2}<0 (K_{ia2} defined analogously to K_{ia1}).

The ¹H NMR spectrum in 3 M DCl at 25 °C is identical

Table 1. Thermodynamic data for the 'acid dissociation constant' of i⁺,i,i,o⁺-H₂[3⁶]adz²⁺ in 1 M NaCl [eqn. (1)].

$T/°C$	pK_{ia1}(obs)[a]	pK_{ia1}(calc)[b]
15.0	3.202	3.195(8)
–	3.178	–
25.0	3.129	3.122(5)
—	3.127	—
40.0	3.019	3.022(8)

[a]Determined by glass-electrode titrations. [b]Calculated from $\Delta H°(K_{ia1})$ = 12.0(8) kJ mol⁻¹ and $\Delta S°(K_{ia1})$ = −20(3) J mol⁻¹ K⁻¹.
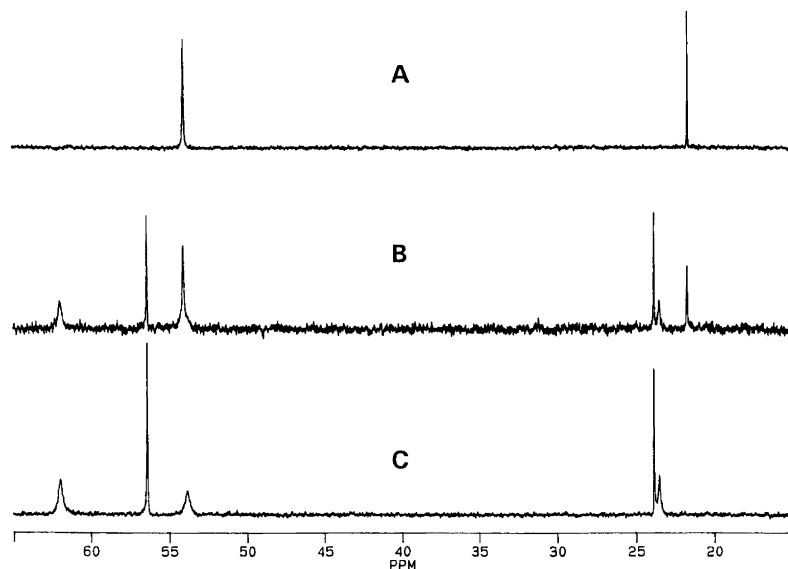
Fig. 4. ^{13}C NMR spectra of [H[3^6]adz]Br. (A) 0.026 M bromide salt in 0.01 M NaOD (pure H[3^6]adz$^+$); (B) 0.015 M bromide salt in 0.006 M DCl, 0.994 M NaCl (mixture); (C) 0.026 M bromide salt in 1 M DCl (pure H$_2$[3^6]adz^{2+}). $T = 298$ K.

to that of the diprotonated species measured at $I = 1$ M. In 6 M DCl the dominant part of the ^1H spectrum corresponds to that of the diprotonated species, i$^+$,i,i,o$^+$-H$_2$[3^6]adz^{2+}, but additional peaks indicate the presence of a new species, probably the triprotonated species i$^+$,i,o$^+$,o$^+$-H$_3$[3^6]adz^{3+} (Fig. 5).

Determination of the structure of i$^+$,i,i,o$^+$-H$_2$[3^6]adz^{2+} from NMR measurements. The second protonation could in principle occur either inside or outside the cage. Inside protonation, however, is in conflict with the observed inertness of the inside coordinated proton of the cage in DCl solutions (see below). The protonation therefore must occur outside, and at least one of the four bridge-head nitrogen atoms has to undergo inversion giving an outwards pointing lone pair. The most reasonable explanation is that only one nitrogen atom inverts and then reacts with a hydrogen ion, giving a diprotonated

species with the structure as shown in Fig. 6. The NMR data confirm this proposal. The ^{13}C NMR spectrum of the diprotonated species has three C–N signals (53.81, 56.38 and 61.94 ppm) and two C–C–C signals (23.51 and 23.84 ppm), and this unambiguously shows that the cation has a time-averaged C_{3v} symmetry, in agreement with the proposed structure, allthough the resonance lines were not assigned.
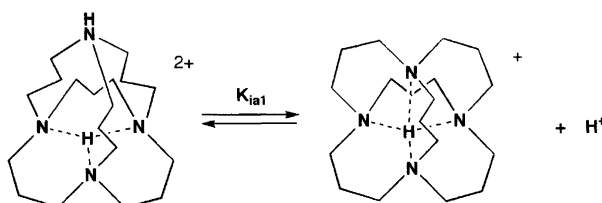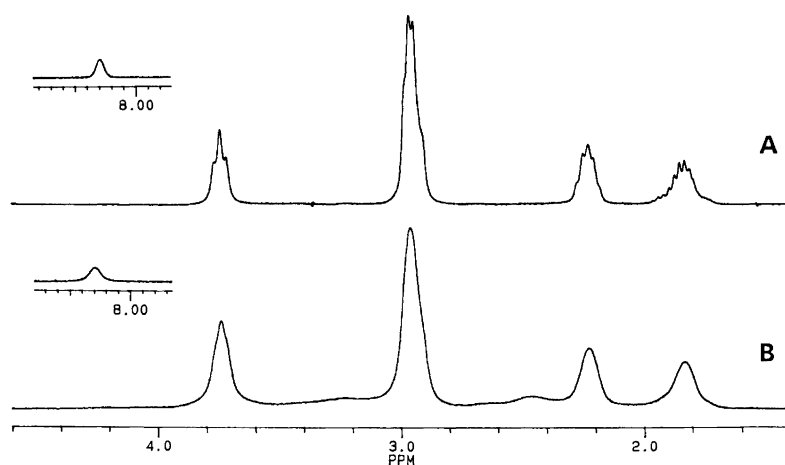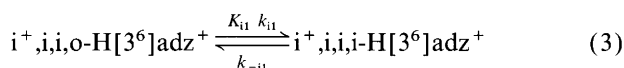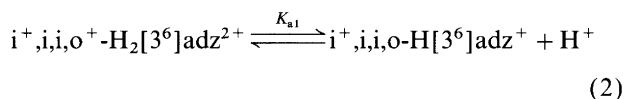

Fig. 6. i$^+$,i,i,o$^+$-H$_2$[3^6]adz^{2+} is a strong acid.

Fig. 5. ^1H NMR spectra of [H[3^6]adz]Br in 1 M DCl (A) and 6 M DCl (B). $T = 298$ K.

In the ^{1}H NMR spectrum, multiplets situated around 1.85, 2.25, 2.85 and 3.75 ppm, respectively, integrate for 6, 6, 18 and 6 protons. The multiplet at 3.75 ppm is tentatively assigned to the three identical CH_2 groups bound to the nitrogen atom having an outwards oriented proton, and the multiplet at 2.85 ppm to the remaining three and six, respectively, identical CH_2 groups bound to the nitrogen atoms having inwards oriented lone pairs. The multiplets at 2.25 ppm and 1.85 ppm belong to the two different C–CH_2–C groups. The spectrum has a broad resonance line at 8.15 ppm, which is assigned to the inside coordinated proton. Finally, it is noted that the proposed structure for the diprotonated species is in agreement with the crystallographic results for the triprotonated species (see above).

The reaction in eqn. (1) can be described as two consecutive reactions [eqns. (2) and (3)]. The suggestion that the acid–base and inversion reactions occur as a concerted process can not be excluded, but is ignored in the following.

$$\mathrm{i^+,i,i,o^+}\text{-}H_2[3^6]\mathrm{adz}^{2+} \xrightleftharpoons{K_{a1}} \mathrm{i^+,i,i,o}\text{-}H[3^6]\mathrm{adz}^+ + H^+$$

(2)

$$\mathrm{i^+,i,i,o}\text{-}H[3^6]\mathrm{adz}^+ \xrightleftharpoons[k_{-i1}]{K_{i1}\, k_{i1}} \mathrm{i^+,i,i,i}\text{-}H[3^6]\mathrm{adz}^+$$

(3)

The diprotonated bicyclic tetraamine $H_2[3^5]\mathrm{adz}^{2+}$ has $pK_a = 9.65$, and it seems likely that the outwards oriented proton in $\mathrm{i^+,i,i,o^+}$-$H_2[3^6]\mathrm{adz}^{2+}$ has a similar acidity. Thus, assuming that $pK_{a1} = 10$ and using the relation $K_{ia1} = K_{a1}K_{i1} = 8 \times 10^{-4}\,M^{-1}$ it is estimated that $K_{i1} = 10^7$.

^1H *NMR studies of the life-time of the* i^+,i,i,o^+-*$H_2[3^6]adz^{2+}$ species.* The observation that the ^{1}H and ^{13}C NMR spectra of the diprotonated species correspond to a time-averaged C_{3v} symmetry shows that the equilibration [eqn. (1)] is slow relative to the ^{13}C NMR timescale. The outwards oriented proton $\mathrm{i^+,i,i,o^+}$-$H_2[3^6]\mathrm{adz}^{2+}$ therefore exchanges slow between the four different sites (Fig. 7).

The lifetime of $\mathrm{i^+,i,i,o^+}$-$H_2[3^6]\mathrm{adz}^{2+}$ was roughly estimated from measurements of the temperature dependence of the NMR spectra of acidic solutions, in which this species is present quantitatively and other species, such as the mono- or triprotonated forms, only are present in negligible concentrations. The ^{13}C NMR spectra show a significant line-broadening with increasing temperature causing absence of detectable signals at the highest temperature used (363 K). Similarly, the ^{1}H NMR spectra exhibit increasing coalescence with increasing temperature. In the case of a fast exchange the four multiplets would merge into a triplet and a pentet. This was not obtained, but a beginning coalescence is observed at 363 K as shown in Figs. 8 and 9. From the degree of coalescence it is concluded that the exchange rates at 363 K vary as follows: $k_{ex}(0.1\,M\,H^+) < k_{ex}\,(1.0\,M\,H^+)$
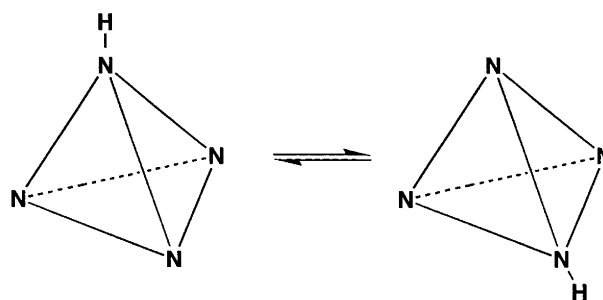
$\mathrm{i^+,i,i,o^+}$-$H_2[3^6]\mathrm{adz}^{2+}$

Fig. 7. Simplified structure for two of the four possible sites for outside coordinated hydrogen ion in $\mathrm{i^+,i,i,o^+}$-$H_2[3^6]$adamanzane (inside coordinated hydrogen ion omitted).

for $I = 1.0$ M and $k_{ex}(0.1\,M\,H^+) \ll k_{ex}$ (3.0 M H^+) for $I = 3.0$ M. Furthermore k_{ex} in 3 M DCl is larger than k_{ex} in 1 M DCl. These results show unambigously that the exchange reaction is acid catalyzed. From the peak separations of the centres of the two multiplets of the C–CH_2–C groups it is estimated[5] roughly that $k_{ex} < 10\,s^{-1}$ at 298 K for all acid concentrations studied and that $k_{ex} = 10^2 - 5 \times 10^2\,s^{-1}$ at 263 K for [H^+] = 0.1 and 1.0 M ($I = 1.0$ M) and [H^+] = 3 M ($I = 3.0$ M). It seems reasonable to assume that inversion takes place only at non-protonated lone-pairs, and the possible pathways are shown in Scheme 1. The exchange between the four different diprotonated species, may take place via unprotonated species, in which case the exchange should decrease with increasing concentration of hydrogen ions. In the case of an exhange via the monoprotonated $\mathrm{i^+,i,i,o}$ species the rate should not be affected by the hydrogen ion concentration. Both pathways therefore do not contribute significantly to the observed exchange rate. Finally, an exchange via the triprotonated species, which is present in very low concentration at the experimental conditions, predicts an increase in rate by increasing acid concentration in agreement with the experiments.

The existence of a triprotonated species is indicated by the measurements in 6 M DCl discussed above and unambiguously shown by the isolation of the salt $\mathrm{i^+,i,o^+,o^+}$-[$H_3[3^6]$adz][ZnBr$_4$]Br·H_2O and its characterization by a single-crystal X-ray diffraction analysis as discussed above.

Inertness of the inside coordinated proton in i^+,i,i,o^+-*$H_2[3^6]adz^{2+}$.* The intensity of the ^{1}H signal for the amine proton does not decrease with time even for the most acidic solutions studied (12 months, 25 °C, 1 M DCl). The inertness of the inside coordinated proton is thus unaffected by the subsequent inversion and protonation reactions, and the rate constant, k_{ex}, for exchange of the inside coordinated proton in $\mathrm{i^+,i,i,o^+}$-$H_2[3^6]\mathrm{adz}^{2+}$ is less than $3 \times 10^{-9}\,s^{-1}$ (1 M DCl, 25 °C). The inertness of $\mathrm{i^+,i,i,o^+}$-$H_2[3^6]\mathrm{adz}^{2+}$ with respect to

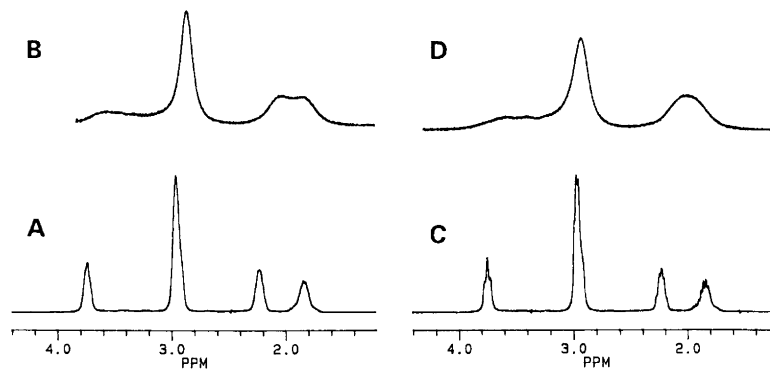*Fig. 8.* ^{1}H NMR spectra of [H[3^6]adz]Br in 0.1 M DCl, 0.9 M NaCl at 298 K (A) and 363 K (B) and in 1 M DCl at 298 K (C) and 363 K (D).

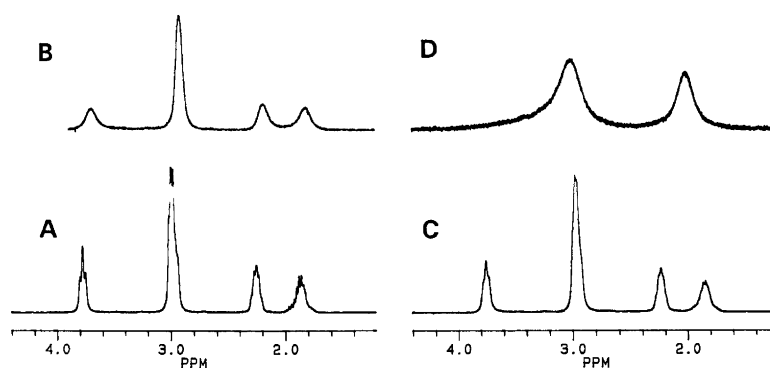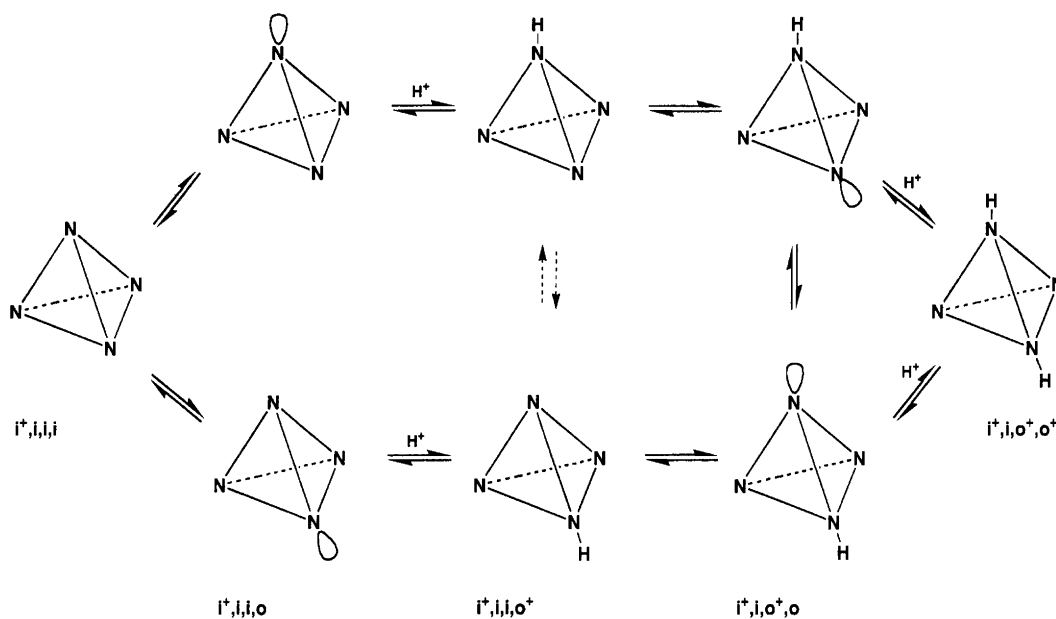*Fig. 9.* ^{1}H NMR spectra of [H[3^6]adz]Br in 0.1 M DCl, 3.0 M NaCl at 298 K (A) and 363 K (B) and in 3 M DCl at 298 K (C) and 363 K (D).

Scheme 1. This simplified scheme shows how the outside coordinated proton in i$^+$,i,i,o$^+$-H$_2$[3^6]adz^{2+} may exchange position between the four different sites by three different routes: (A) via the monoprotonated species; (B) via the diprotonated species having two lone pairs pointing outwards, i$^+$,i,o,o$^+$ isomer; (C) via the triprotonated i$^+$,i,o$^+$,o$^+$ species. Only the last pathway explains the observed increase in exchange rate by increasing concentration of hydrogen ions.

exchange of the inside coordinated proton is easily understood considering that the proton is totally encapsulated in a very rigid, yet relatively strainless, cage. Any movement in the direction of dissociation of the proton will at some point go through a very strained transition state. This extreme inertness places the $H_2[3^6]adz^{2+}$ cation together with the its monoprotonated form and the smaller, monoprotonated cage $H[2^4.3^2]adz^+$ as some of the most inert protonated amines reported in the literature.[1,2]

Stability of $i^+,i,i,i-H[2^4.3^2]adz^+$ and $i^+,i,i,i-H[3^6]adz^+$ in strong acid. The $H[3^6]adz^+$ species and its protonated forms are very inert with respect to C–N cleavage Thus, it was shown that boiling of a solution of $H[3^6]adz^+$ in 12 M HCl for 1 week does not give any detectable (^{13}C NMR) formation of C–N cleavage products. In this respect it behaves very differently from its smaller analouge $H[2^4.3^2]adz^+$. This latter amine is aprotic in the pH region 0–14 and it is stable in basic solutions for months at room temperature. Solutions in, for instance, 0.1 M HCl are likewise stable for at least some days as previously reported.[1] However, in the present study we found that in more acidic solutions the small cage undergoes an acid catalyzed cleavage of one of the trimethylene bridges to give quantitatively (as measured by ^{13}C NMR) the parent bowl adamanzane $[2^4.3^1]adz$ without further cleavage of N–C bonds as shown in
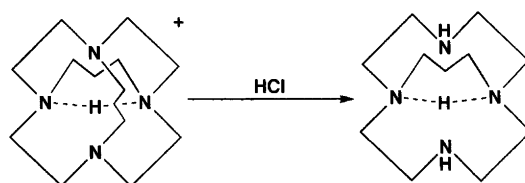
Scheme 2. Reaction of $H[2^4.3^2]adz^+$ in 1 M HCl.

Scheme 2. At present we have not identified the product originating from the trimethylene bridge.

References

1. Springborg, J., Olsen, C. E. and Søtofte, I. *Acta Chem. Scand.* 49 (1995). 555.
2. Springborg, J., Pretzmann, U. and Olsen, C. E. *Acta Chem. Scand.* 50 (1996) 294.
3. Springborg, J. and Søtofte, I. *Acta Chem. Scand.* 51 (1997). 357.
4. Motherwell, W. D. S. and Clegg, W. *PLUTO. Program for Plotting Molecular and Crystal Structures.* University of Cambridge, Cambridge 1978.
5. Macomber, R. S. *NMR Spectroscopy.* Hartcourt Brace Javanovich, New York 1988.