^{13}C CP/MAS NMR studies of tetraazaannulenes: fast proton transfer in the solid state

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Full assignments of the high resolution ^{13}C CP/MAS solid state NMR spectra of a series of substituted dibenzotetraazaannulenes based on the parent macrocycle tetraazaannulene[†] (TAA) are reported. The expected number of resonances observed is compatible with the crystal structures in all cases, except that in the case of TAA only one resonance is observed in the region expected for C-8 and -15. This observation is interpreted as being a consequence of fast proton transfer in the solid-state coupled with rapid molecular rotation. Variable temperature studies of the maximum line broadening of the peaks indicates an activation energy of 8.4 kJ mol^{-1}. Methyl substituents on the ring lead to two peaks in the *C*=N/*C*–NH region; this is attributed to unequal populations of tautomers with no rotation of the molecule. The results are compared to literature ^{15}N data. Variable temperature data on the methyl substituted systems are also consistent with the reported ^{15}N data, confirming that the tautomers are unequally populated.

In macrocycles such as porphyrins fast intramolecular proton transfer takes place between the inner nitrogen atoms not only in solution but also in the solid state. The consequences of such motion on the X-ray crystallographic parameters and the solid state NMR spectra have been widely investigated.[1–4] For substituted porphyrins such as *meso*-tetratolylporphyrin, the X-ray structure[3] is consistent with the solid state NMR spectrum[4] in showing that the hydrogen atoms are completely disordered over the four nitrogen atoms. There are also cases, *e.g. meso*-tetraphenylporphyrin, where the X-ray structure shows that protons are localized on one particular pair of opposite nitrogen atoms and the NMR data show that the protons are moving rapidly between two unequally populated tautomers.

In porphyrin itself the NMR observations appear to be in conflict with the X-ray data. The ^{15}N NMR data show that there is concerted motion of the amine protons between two degenerate tautomers with a rate close to that observed in solution (*ca.* 10^4 Hz).[1] The X-ray crystal structure, however, shows that the protons are localized on only one pair of opposite N atoms, suggesting a greater population of one tautomer. To resolve this difficulty, it has been proposed recently that the proton transfer is coupled to a rotation of the molecule by 90° about the principal axis of symmetry (C_2). Consistent with this proposition deuterium labelling of the amine protons of porphyrin has been shown to slow the rate of molecular rotation in the solid state.[2] No significant slowing would have been observed if the rotation was not coupled to the proton transfer.

In this paper we describe ^{13}C CP/MAS spectra of a series of porphyrin analogues, the tetraazaannulenes (TAAs, Fig. 1), in order to investigate proton transfer amongst all four possible tautomers depicted. We shall demonstrate that for certain of the macrocycles the variable temperature data are in accordance with recently reported ^{15}N CP/MAS data.[5,6] In addition, we observe that the simplest molecule, TAA itself, appears to undergo a coupled proton transfer–molecular rotation, like that of porphyrin.

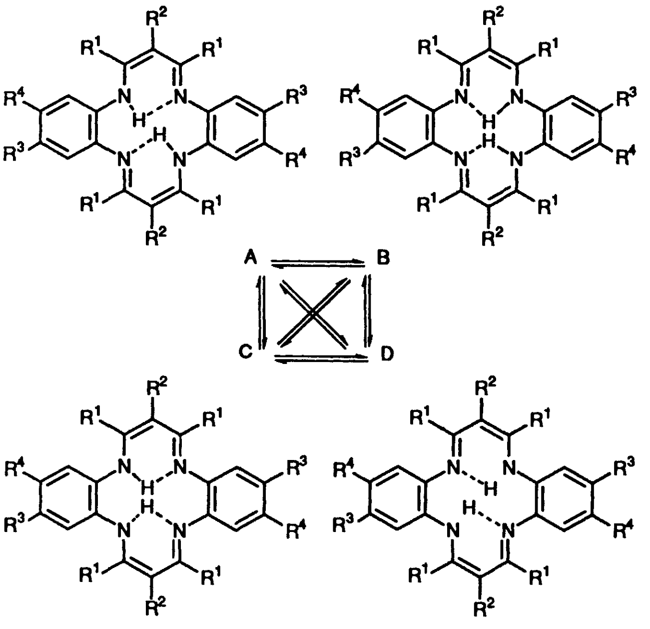

Fig. 1 Scheme for proton transfer in TAA and derivatives: TAA, $R^1 = R^2 = R^3 = R^4 = H$; DMTAA, $R^1 = R^3 = R^4 = H$, $R^2 = CH_3$; DXMTAA, $R^1 = H$, $R^2 = R^3 = R^4 = CH_3$; TMTAA, $R^1 = CH_3$, $R^2 = R^3 = R^4 = H$; PhTAA, $R^1 = R^3 = R^4 = H$, $R^2 = Ph$; PhCOTAA, $R^1 = R^3 = R^4 = H$, R^2 = 2-hydroxybenzoyl

Experimental

TAA and DMTAA were made by heating either tetramethoxypropane or 2-methyl-3-ethoxyacrolein with 1,2-diaminobenzene.[7] TMTAA was prepared as its Ni complex by template synthesis and subsequently demetallated to give the free macrocycle. All were purified by recrystallization from *N,N*-dimethylformamide (DMF).

The NMR spectra were collected using standard pulse sequences, as follows.[8] ^{13}C CP/MAS NMR spectra were measured at 125.758 MHz on a Bruker MSL 500 spectrometer at 296 K. High power ^1H decoupling and magic angle spinning were employed; the magic angle was set from time to time using KBr. Ground samples were packed into rotors (ZrO_2, 4 mm o.d.) and used at a spinning speed of 5–9 kHz. At least two spinning speeds were used for the ambient-temperature spectra

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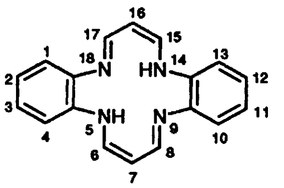
[†] *Abbreviations:* TAA = 5,14-dihydrodibenzo[*b,i*][1,4,8,11]tetraazacyclotetradecene; DMTAA = 7,16-dimethyl-TAA; TMTAA = 6,8,15,17-tetramethyl-TAA; DMXTAA = 2,3,7,11,12,16-hexamethyl-TAA;PhTAA = 7,16-diphenyl-TAA;PhCOTAA = 7,16-di(2-hydroxybenzoyl)-TAA.

Table 1 ^{13}C Chemical shifts of TAA compounds (± 0.1 ppm)



	C-16	C-15, C-8	C-9a, -13a[a]	C-10, -13	C-11, -12
TAA	97.5	145.0	137.2, 138.0	113.1, 114.1, 115.0[b]	122.3, 124.2
DMTAA[c]	103.4[a]	140.0, 153.0	136.8, 137.7	113.2, 116.6	122.5, 124.7
DMXTAA[c]	104.9[a]	140.3, 152.3	134.9	113.5, 116.9	131.0,[a] 135.0[c]
TMTAA[c,d]	99.8	154.2, 157.5, 161.1, 161.7	135.9, 138.0, 139.9, 141.4	122.1	125.4
TMTAA[c,e]	98.5	159.5	139.0	123.4	123.6

[a] Quaternary (demonstrated by NQS). [b] There are more than two peaks here, perhaps because this compound has a different crystal structure with $Z = 4$ and the molecule not lying on a centre of symmetry. [c] The number and positions of the methyl resonances were as expected. [d] Molecule does not lie on a centre of symmetry; there may be twice the number of resonances. [e] Solution ($CDCl_3$).

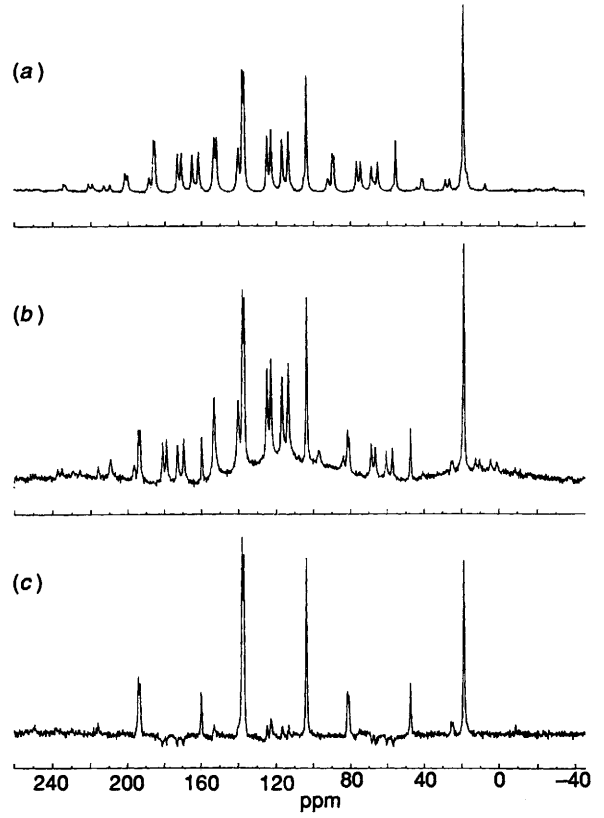


Fig. 2 ^{13}C CP/MAS NMR spectra (296 K) of DMTAA at various spinning speeds: (*a*) 6; (*b*) 7; (*c*) 7 kHz with NQS

of each sample in order to identify spinning side-bands. Contact times for cross-polarization were typically 1 ms and recycle delays of 5–15 s, sufficient to ensure almost total ^1H relaxation were employed. Chemical shifts are referenced relative to the CH_2 in adamantane at 38.56 ppm.

Results

The free macrocycles have well resolved CP/MAS spectra [Fig. 2(*a*)] but with a large number of spinning side-bands due to the high field and the large chemical shift anisotropy expected for a rigid planar aromatic molecule. The spinning side-bands are readily identified by spinning the sample at a different frequency [Fig. 2(*b*)]. The crystal structures of the free macrocycles DMTAA and its derivative DMXTAA, show that these macrocycles are sited on special positions and inversion centres and thus only nine unique ring carbon and benzene carbon environments are expected.[9] This is confirmed by the solid state NMR spectra. The nine observed ^{13}C resonances may be readily assigned on the basis of the non-quaternary suppressed (NQS) spectrum [Fig. 2(*c*)] and the expected shift ranges (Table 1). The most significant observation is that two resonances are observed for the methine carbons C-15 (C–NH) and C-8 (C=N) of the C_2N_2 unit. A similar assignment is arrived at for the structurally related compound DMXTAA.

The assignments (Table 1) are consistent along the series and the number of carbon environments is generally consistent with the reported crystal structures.[9–11] However, for TAA itself only one peak at 145.0 ppm is observed for the carbon nucleus adjacent to the nitrogen atoms. This is despite the fact that the crystal structure[10] does not demand a centre of inversion for TAA and so in principle there ought to be a slight splitting of each peak, since the two halves of the molecules are no longer related by symmetry. Peak splitting is indeed observed, but only for the C-10, -13 set of resonances. The crystal structure parameters reveal only slight differences in the geometry of each half of the molecule and thus the splittings of all the peaks may not be resolved.

This single resonance for C-15 (C–NH) and C-8 (C=N) in TAA, has a chemical shift midway between the separated chemical shifts for C-15 and -8 in DMTAA. We assign this to a carbon adjacent to a nitrogen atom which on average is bonded to a proton for 50% of the time. On cooling (Fig. 3), this peak is observed to broaden significantly. We interpret this behaviour to be a consequence of the fast proton transfer process interfering with the proton dipolar decoupling, which has a frequency of *ca.* 60 kHz.[12] In accord with theory,[12] a plot of the linewidth *vs.* T^{-1} is linear, yielding an activation energy for the proton transfer process of 8.4 kJ mol^{-1} (2.0 kcal mol^{-1}). Unfortunately, we cannot reach a sufficiently low temperature for the resonance to begin to sharpen again; hence, we cannot obtain the full rate expression.

We have also investigated the temperature dependence of the ^{13}C NMR spectra of the other molecules in the CN region. For DMTAA, we observe two peaks in the C=N and C–NH region at 288 K at 140.0 and 153.0 ppm which move apart on cooling, the one at 140.0 ppm apparently moving more rapidly to higher field.‡

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‡ Variable temperature spectra of DMTAA and TMTAA have been deposited under the Supplementary Publications Scheme. For details see, 'Instructions for Authors (1995)', *J. Chem. Soc., Perkin Trans. 2*, 1995, issue 1 [Supp. Pub. No. 57068 (3 pp)].

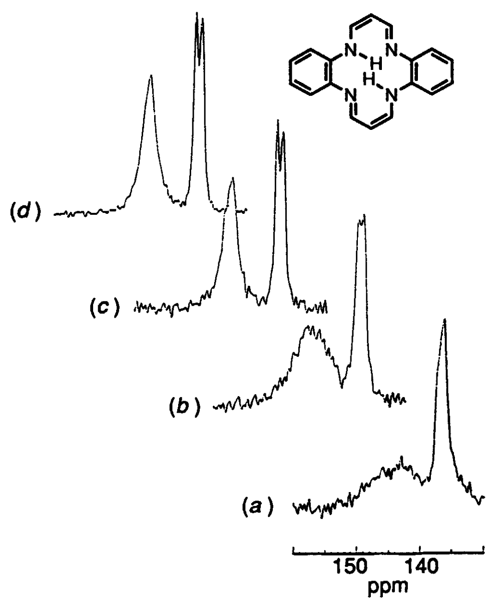

Fig. 3 Variable temperature ^{13}C CP/MAS spectra of TAA (CN region)

At room temperature TMTAA has an averaged set of C=N and C–NH (C-15, -8) resonances which appear as a cluster of four peaks between 161.7 and 154.1 ppm at room temperature. The range of chemical shifts (154.2–161.7) seems to span the averaged chemical shift, 159.5, observed for C-15, -8 in solution (Table 1). We deduce that the solid state spectrum shows incomplete averaging of the two environments. Similarly, the C-9a, -13a resonances appear as a group of four resonances. The crystal structure again has one molecule in the asymmetric unit and no centre of symmetry. A possible explanation for this splitting is discussed below. We note that the benzene carbons, C-10–13 are all similar in chemical shift, in contrast to those of the planar macrocycles which divide into two groups (C-13, -10 and C-12, -11); this reflects the lower interaction between the benzene rings and the C_3N_2 group in TMTAA. These splittings cannot be due to ^{14}N coupling, which is expected to be negligible at this field strength. On cooling,‡ the 154.1 ppm peak shifts upfield. The 161.7 ppm doublet collapses to a singlet.

TMTAA is sufficiently soluble that we were able to lithiate the nitrogen atoms with butyllithium in tetrahydrofuran and to quench the dilithiated material with D_2O to generate [$^2H_3$]TMTAA. The enrichment was judged to be > 90% on the basis of the decrease in the NH stretch at 3413 cm^{-1} and the increase in the ND stretch at 2385 cm^{-1}. The ^{13}C NMR spectral changes match those of the undeuteriated macrocycle very closely, confirming that the changes in C-15, -8 separation are due to purely thermodynamic changes in the population of the various tautomers. Similarly, it should be noted that no line-broadening was observed in the ^{15}N spectrum of TMTAA.[5]

Discussion

It is convenient to consider the substituted macrocycles first. The presence of two peaks in the C=N and C–NH region for DMTAA is consistent with ^{15}N data, which suggests that two unequally populated tautomers are present at room temperature.[6] The degeneracy of the two tautomers is lifted by a rhombic distortion of the N_4 plane induced by crystal packing effects. The distortion is clearly seen from crystallographic data, such as the sides, diagonals and bond angles of the quadrangle defined by the four N atoms (Table 2). Indeed, the crystal structure shows that the NH bonds are localized upon one particular opposite pair of nitrogen atoms. From the temperature dependence of the ^{15}N NMR spectra it was shown that one of the tautomers is favoured over the other by a reaction enthalpy of 3.8 ± 0.4 kJ mol^{-1} and neglible entropy. The increased separation of the CN peaks as the temperature was lowered is consistent with a greater localization of the protons onto one particular pair (presumably opposite pair) of nitrogen atoms. Limbach *et al.* enriched the macrocycles DMTAA[6] and TMTAA[5] with ^{15}N in order to carry out a ^{15}N NMR study of the tautomerism. For DMTAA at low temperature two ^{15}N resonances 'm' and 'n' are observed in the sp^3 (high field) and sp^2 (low field) regions respectively. As the temperature is raised the separation between the lines decreases but reaches a limiting value rather than completely vanishing (coalescing) at room temperature. The limiting separation is characteristic of two unequally populated tautomers (say, A and D, Fig. 1). If the other tautomers B and C were involved then four lines would have been observed in the low temperature spectrum. The implication is that concerted double proton transfer between A and D occurs in DMTAA.

In analysing the spectra, Limbach *et al.* assume that the chemical shifts of the N and NH resonances are the same in each tautomer and that, *e.g.*, the chemical shift of the sp^3 N is proportional to the probability that the N atom is protonated in the different tautomers. For DMTAA the ratio of the line separation at temperature T, $\Delta_T = \delta_m - \delta_n$, to that at low temperature, $\Delta_o = \delta_m{}^o - \delta_n{}^o$, is related to the equilibrium constant K_{AD} for the exchange between the tautomers A and D.[6]

$$A \rightleftharpoons D; \quad K_{AD} = [D]/[A]$$

$$\Delta_T/\Delta_o = (1 - K_{AD})/(1 + K_{AD})$$

From the ^{15}N data $\Delta_T/\Delta_o = 0.6$ and hence $K_{AD} = 0.25$. The reason for the unequal population is probably related to the rhombic distortion in DMTAA (Table 2) which favours protonation of the N atoms on the long diagonal.

Now this Δ_T/Δ_o value (0.6) should be applicable to the ^{13}C NMR data for the carbons (C-15 and -8) most affected by the protonation of the N atom. Thus, our observed $\Delta_T{}^{mn} = \delta(\text{C-15}) - \delta(\text{C-8}) = 13$ ppm, at room temperature for DMTAA should be increased by a factor of $(0.6)^{-1}$ at low temperature to 22 ppm. At the lowest temperature we were able to reach for this system (205 K), the separation was observed to be 17 ppm.

Apparently, no exchange broadening is observed, but might be expected at temperatures lower than we employed, where for example the chemical shift difference at 200 K (1600 Hz) would be comparable to the rate of proton transfer as measured by ^{15}N NMR (< 2 kHz at T < 200 K). The lack of exchange broadening precludes the extraction of kinetic data on the proton transfer rate.

The observation of four C=N/C–NH resonances for TMTAA is consistent with the ^{15}N spectra at room temperature, in which four N resonances were seen. These are assigned to the four different tautomers of Fig. 1, which are unequally populated due to a rhombic distortion. The crystal structure[11] shows that the H atoms are spread over N atoms around the ring as follows: 0.75, 0.25, 0.75, 0.25. The ^{15}N peaks behaved as two sets of resonances on cooling, evidence for two different proton transfer rates in each half of the molecule.[5] Decoupling of the proton motion in each half of the molecule is not unexpected since it is non-planar (saddle-shaped) due to steric interactions. For TMTAA, the proton transfer is not concerted. Thus, four ^{15}N resonances are observed, (mnpq), consisting of two sp^2 (nq) and two sp^3 (mp) resonances showing that all tautomeric states A–D (Fig. 1) are populated. Here, the two sets of resonances have different temperature dependences; thus for mn, $\Delta_T{}^{mn}/\Delta_0{}^{mn} = 0.6$ while for pq, $\Delta_T{}^{pq}/\Delta_0{}^{pq} = 0.325$ at 288 K.

Table 2 Comparison of X-ray crystallographic data of TAA molecules

	Bond lengths/Å						Bond angles/°			
Name	N-1–N-2	N-2–N-3	N-3–N-4	N-4–N-1	N-1–N-3	N-2–N-4	N-1–N-2–N-3	N-2–N-3–N-4	Torsion angle	Ref.
TAA[a]	2.788	2.674	2.795	2.670	3.791	3.936	87.881	92.029	1.355	10
DMTAA	2.753	2.675	2.753	2.675	3.766	3.910	88.0	92.00	0.00	9
DMXTAA	2.742	2.693	2.742	2.693	3.799	3.888	89.0	91.0	0.00	9
TMTAA[b]	2.713	2.676	2.700	2.685	3.749	3.868	88.172	91.54	1.354	11
PhTAA	2.725	2.679	2.739	2.682	3.801	3.853	89.391	90.66	−1.644	13
PhCOTAA[c]	2.733	2.694	2.733	2.694	3.841	3.834	90.108	89.89	0.00	14

[a] Although the authors (ref. 10) suggest the protons are delocalized, the CN bond lengths indicate localized protons. [b] 75% 25% delocalized protons in X-ray. [c] Fully delocalized protons.

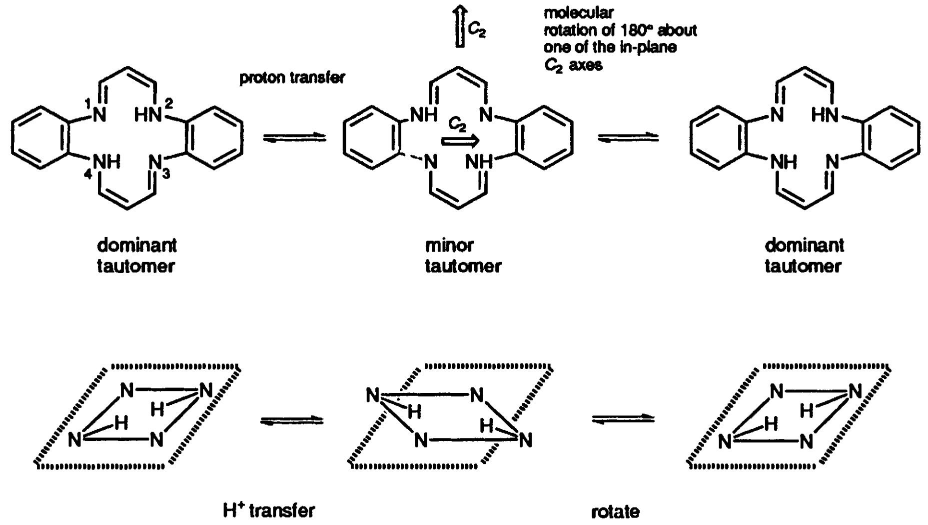

Fig. 4 Mechanism of proton transfer in TAA

From this ^{15}N data we would predict a change in the ^{13}C spectrum at low temperature. From the outer peaks of the imine/enamine group (161.7 and 154.2 ppm), we observe Δ_T^{mn} = 915 Hz and from the inner resonances (161.1 and 157.5) Δ_T^{pq} = 400 Hz leading to predictions of the low-temperature separations being Δ_0^{mn} = 1525 Hz and Δ_0^{pq} = 1415 Hz. Thus the peaks become almost equally separated at low temperature, which is consistent with the ^{15}N spectra. At the lowest temperature reachable for this system, we observed a peak separation of the two outer peaks of 10 ppm (1260 Hz).

Finally, we turn to the simplest of the molecules investigated, TAA. The derived activation energy for TAA indicates a very fast proton transfer at room temperature. The crystal structure of this compound shows an even greater rhombic distortion (Table 2) of the central four nitrogens than that of DMTAA and so we might expect NMR evidence of two unequally populated tautomers. Yet the ^{13}C spectrum shows just one line in the CN region, indicating that the tautomers are equally populated. As far as we can tell, the only phenomenon that would account for both the NMR and the crystallographic data is the coupling of the proton transfer to a molecular rotation which brings the NH groups into their original orientation in the crystal. Because of the symmetry of the molecule (C_{2h}) the rotation would have to be 180° about either of the two C_2 axes in the molecular plane (Fig. 4). We propose that this coupled motion is encouraged by the extreme nature of the distortion and twisting of the N_4 atoms from a square arrangement and the consequent favouring of one particular tautomer by the crystal packing forces. This is illustrated schematically in the lower half of Fig. 4. It is perhaps surprising that an out of plane rotation is so facile; however, the crystal packing appears to allow for such a rotation. An in-plane rotation, by 90° about the C_4 axis, has been proposed for D_{2h} porphyrins.[2]

This analysis of the data allows us to predict the ^{13}C NMR behaviour of two other TAA molecules which have had their crystal structures reported (Table 2). The four N atoms of PhCOTAA form almost a perfect rectangle, which is nearly square. More importantly, the H atoms are disordered over all four N atoms. We thus predict that the tautomers of this molecule are equally populated and that there is only one ^{13}C line in the CN region. The structure of PhTAA shows localized H atoms and a distorted N arrangement close to that of DMXTAA. Its solid state NMR behaviour should therefore be similar.

Conclusions

High resolution ^{13}C CP/MAS spectra of the DMTAA and TMTAA macrocycles are consistent with ^{15}N data concerning fast proton transfer, *i.e.* there are unequally populated tautomers whose energy difference is probably related to a lattice-induced rhombohedral distortion of the lattice.[5,6] We also appear to reproduce in the ^{13}C spectra evidence for participation of all four tautomers for TMTAA but only two tautomers for DMTAA. Our data concerning the simplest macrocycle, TAA, for which there is no corresponding ^{15}N spectra, suggest equal population of tautomers. If this observation is to be squared with the X-ray data then a coupled proton transfer–molecular rotation similar to that proposed for the porphyrin system may well be involved. The rate of proton transfer (*ca.* 60 kHz) leads to maximum line broadening with an activation barrier of 8.4 kJ mol^{-1}.

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