NH tautomerization of 2,7,18,23-tetramethyl-3,8,12,13,17,22-hexaethylsapphyrin

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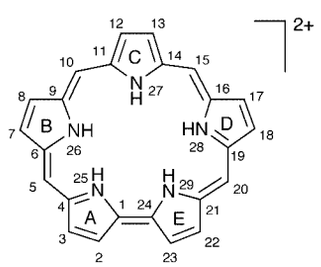
A planar, pyrrole-in macrocyclic geometry is favored for 2,7,18,23-tetramethyl-3,8,12,13,17,22-hexaethylsapphyrin ($SapH_3$) at all levels of protonation. This stands in marked contrast to 5,10,15,20-tetraphenylsapphyrin ($TPSH_3$) where two structures, planar and inverted are known. The ^{1}H NMR studies provide evidence consistent with the existence of tautomeric equilibria involving the neutral form of decaalkylsapphyrin and up to ten specific tautomeric species ({25-NH, 26-N, 27-NH, 28-N, 29-NH}, {25-NH, 26-NH, 27-N, 28-NH, 29-N}, {25-NH, 26-N, 27-NH, 28-NH, 29-N}, {25-N, 26-NH, 27-NH, 28-N, 29-NH}, {25-NH, 26-NH, 27-NH, 28-N, 29-N}, {25-N, 26-N, 27-NH, 28-NH, 29-NH}, {25-NH, 26-NH, 27-N, 28-N, 29-NH}, {25-NH, 26-N, 27-N, 28-NH, 29-NH}, {25-N, 26-NH, 27-NH, 28-NH, 29-N}, {25-N, 26-NH, 27-N, 28-NH, 29-NH}). Changes in the dynamics of these equilibria, rather than dimerization effects, are invoked to account for the splitting of ^{1}H NMR resonances observed at low temperature. ^{1}H NMR studies also reveal that decaalkylsapphyrin acts as a water and methanol binding receptor as evidenced by the upfield shift of water- or methanol-derived resonances. Under conditions of complexation, the water or methanol molecules are bound to the N_5 center of the sapphyrin molecule *via* a network of hydrogen bonds.

Introduction

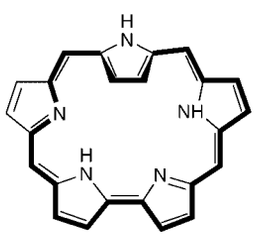
Sapphyrin is one of the simplest and best studied of all expanded porphyrins.[1,2] It is an aromatic pentapyrrolic system that possesses an overall 22 π-electron annulene-like framework (Scheme 1).



Scheme 1

As compared to porphyrins, sapphyrins are highly basic and act as proton scavengers. Because of this fact and the extra stability that protonation imparts, it has generally been the planar dicationic forms of sapphyrin that have been best characterized. The fact that the protonated derivatives of sapphyrin perform as efficient anion acceptors both in solution and in the solid state has undoubtedly contributed to this trend.[3–8] Indeed, it has been found that the protonated forms of sapphyrins bearing alkyl or substituted alkyl substituents in the β-pyrrolic positions (decaalkylsapphyrins) act as solution-phase carriers for nucleotides,[9] nucleotide analogues,[10] and amino acids.[11] However, in sharp contrast to the di- and even mono-cationic forms of these sapphyrins, for which numerous X-ray structures are available,[1,3–8] the corresponding neutral species remain relatively unexplored.

In the case of 5,10,15,20-tetraphenylsapphyrin ($TPSH_3$), the neutral form has been studied in detail and the existence of an inverted skeleton was explicitly proposed.[12] Furthermore, two fundamental structures, inverted and planar, have been detected in the case of the dications.[12–14] The interconversion between these forms involves a reversible "flip" of a single pyrrole unit (Scheme 2). This skeletal rearrangement is triggered by proton



Scheme 2

and/or anion addition and involves binding of anion(s) *via* a network of NH–anion hydrogen bonds.[12,14] Tautomeric interconversions are extremely fast even at 183 K and involve the rapid exchange of two internal imino protons between four structurally inequivalent internal nitrogens in two tautomers: {25-N, 26-NH, 27-NH, 28-N, 29-NH} and {25-NH, 26-N, 27-NH, 28-NH, 29-N}.[12]

5,10,15,20-Tetraphenyl-26,28-dioxasapphyrin, which presents an inverted skeleton at each level of protonation, contains only one exchangeable NH proton and the tautomeric equilibrium in this case involves interconversion between two degenerate asymmetric structures: {25-N, 26-O, 27-N, 28-O, 29-NH} and {25-NH, 26-O, 27-N, 28-O, 29-N}.[15,16]

The tautomeric equilibrium of 5,10,15,20-tetraphenyl-26,28-dithiasapphyrin has also been studied in detail.[15,17] These studies have provided support for the existence of a planar macrocyclic conformation and, separately, have served to reveal that facile tautomeric proton exchange takes place between N-25 and N-29.

Paralleling what is true for the solid state analyses, ^{1}H NMR spectral studies of decaalkylsapphyrins have been largely

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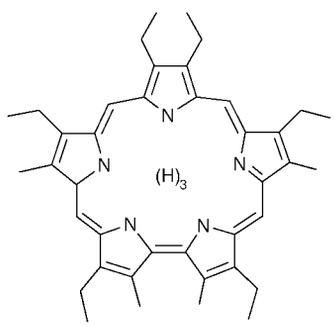
focused on the diprotonated forms.[4,5,7b] However, studies of the free-base form, are deemed essential if (1) the true nature of the neutral form is to be ascertained and (2) appropriate comparisons to the tetraarylsapphyrins are to be made. Also they are required if the NH tautomerization chemistry of sapphyrins is to be fully defined.

Typically, in Kekulé structural representations of neutral β-alkyl substituted sapphyrins, the NH protons are shown as being symmetrically located at the corners of an isosceles triangle, specifically the one defined by the 25-N, 27-N and 29-N pyrrolic nitrogens.[1,2] In principle, however, the three NH protons of β-alkyl substituted sapphyrins can be randomly distributed between the five pyrrole nitrogens so as to produce ten tautomers including four asymmetric degenerate pairs.[12,14,15] Whether any or all of these tautomeric forms is or is not an important constituent of the equilibrium mixture remains an open question. To address this issue we have carried out a detailed ^{1}H NMR spectral analysis of 2,7,18,23-tetramethyl-3,8,12,13,17,22-hexaethylsapphyrin ($SapH_3$) shown in Scheme 3 and now wish to report our findings.



Scheme 3

Results

The ^{1}H NMR spectrum of the neutral form of 2,7,18,23-tetramethyl-3,8,12,13,17,22-hexaethylsapphyrin in chloroform-*d* is shown in Fig. 1 (Trace A). The addition of TFA converts the neutral form into the well characterized dicationic species which reveals a diagnostic set of three NH 2 : 1 : 2 resonances, located at the characteristic upfield positions.[5,12] The formation of this latter dicationic species also causes the meso, α-CH_3 and α-CH_2 resonances to shift to lower field.

The neutral form of sapphyrin produces observable NH resonances but only under certain, well-defined conditions. For instance, at 293 K in chloroform-*d* saturated with aqueous KOH, the NH resonances are too broad to detect easily. On the other hand at 293 K neutralized sapphyrin samples, that are dried extensively before being subjected to ^{1}H NMR spectroscopic analysis, demonstrate a very broad (84–120 Hz) but detectable NH resonance in the −2 to −3.5 ppm chemical shift region with the exact values depending on the residual water concentration. Unfortunately, these drying procedures, while yielding the neutral form of decaalkylsapphyrin, also result in some decomposition as revealed by additional resonances labeled by asterisks in Fig. 1 and Fig. 2.

Under conditions where the samples are less rigorously dried, the integrated NH intensity, as compared to the corresponding *meso* resonance, was found to vary, showing unexpectedly high values (*i.e.*, in the integrated intensity range of 3 to 7 protons!). In the single ^{1}H NMR spectrum reported previously for a neutral decaalkylsapphyrin, similar, anomalously high NH signal intensities were noted but without comment.[3b] At low temperatures (*i.e.*, 203 K or below), the total intensity of NH resonance peak(s) is equal to 3 as expected for $SapH_3$. This is a finding that proved true for all experiments discussed in this report.

Based on the above observations, we propose that the "extra"

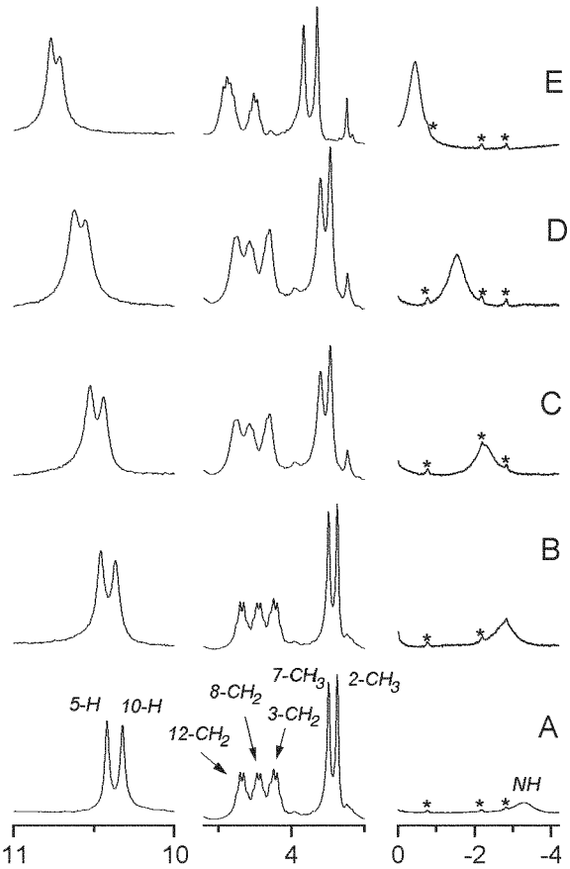


Fig. 1 ^{1}H NMR spectra (300 MHz) of $SapH_3$ in chloroform-*d* (2 mg/0.5 ml; 6.6 mM) at 293 K: (A) spectrum of $SapH_3$ alone; (B) spectrum after addition of 1 μl of chloroform-*d* saturated with water; (C) spectrum after addition of 2 μl of chloroform-*d* saturated with water; (D) spectrum after addition of 4 μl of chloroform-*d* saturated with water, (E) spectrum after addition of 14 μl of chloroform-*d* saturated with water. The specific resonance assignments, if given, follow the systematic numbering of the sapphyrin skeleton, * not identified decomposition products.

integrated NH signal intensity is due to the presence of adventitious water that would be present in solution at room temperature and moderate low temperatures but which would be absent at very low temperature due to precipitation (*i.e.*, freezing out). Support for this contention comes from titration studies wherein aliquots of chloroform-*d* saturated with water were added to an initial sample of dry $SapH_3$ in chloroform-*d* (Fig. 1).

The binding of neutral substrates is rare but known in the area of expanded porphyrin chemistry.[1] In order to probe this phenomenon further in the case of $SapH_3$, a titration with methanol was performed (Fig. 2). In these titrations the presence of the methanol methyl group provided an independent spectroscopic probe that allowed the structure of the complex to be investigated. Specifically, this methyl resonance was identified at 2.37 ppm at a $SapH_3 : CH_3OH$ molar ratio of 2.7 : 1. As the titration proceeded further and the molar ration of $SapH_3$ to methanol increased this resonance moved gradually downfield (*i.e.*, in the direction of the signal for free methanol). Still, throughout the course of the titration the methyl signal remains upfield from that for free methanol, a fact that reflects plainly the contribution of the ring current shielding effect on the time-averaged chemical shift of the bound methanol substrate. Thus, the ^{1}H NMR data are consistent with this particular neutral substrate being held over the center of the sapphyrin macrocycle in the form of a hydrogen bonded complex. Such a conclusion appears valid even though the coordinated methanol remains in fast exchange with the bulk methanol in the solvent.

On a level that is very different from that associated with

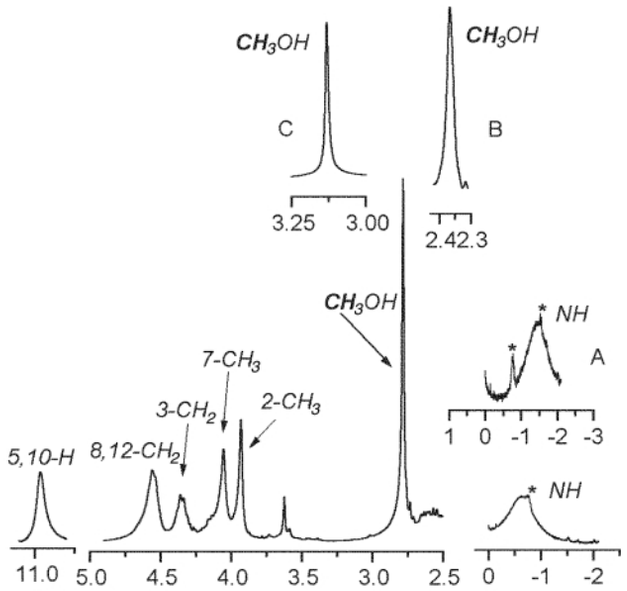
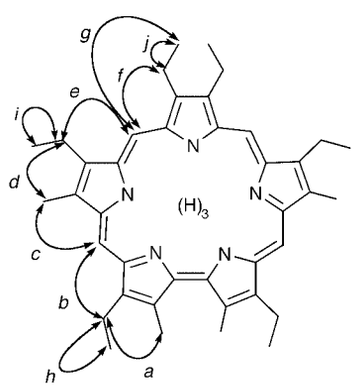


Fig. 2 ^{1}H NMR spectrum (300 MHz) of $SapH_3$ in chloroform-*d* (2 mg/0.5 ml; 6.6 mM) after addition of 0.075 µl of CH_3OH (293 K). Insets A and B present the selected regions after addition of 0.05 µl of CH_3OH. Inset C corresponds to the spectrum after the addition of 0.15 µl of CH_3OH. The peak marked with **CH$_3$OH** corresponds to that assigned to methanol, * not identified decomposition products.

characterizing a bound neutral substrate complex, a detailed analysis of the free-base $SapH_3$ required the unambiguous assignments of the sapphyrin resonances *per se*. These assignments were obtained by means of a 2D NOESY experiment. Here, as the starting point for making the requisite assignments, the unique 2-CH_3 located on the pyrrole A ring was used. These substituents give rise to signals that are sufficiently distant from any *meso* protons to allow for unambiguous assignments. Alternatively, the 10-CH *meso* proton, which is flanked solely by two methylene groups could be used as a convenient starting point. The connectivity pattern determined from these NOESY analyses is presented in Scheme 4 with specific assignments (δ)



Scheme 4

being as follows (Fig. 1, Trace A): 2-CH_3, 3.72; 7-CH_3, 3.78; 3-CH_2CH_3, 4.14; 8-CH_2CH_3, 4.26; 12-CH_2CH_3, 4.37; 3-CH_2CH_3, 1.79; 8-CH_2CH_3, 1.97; 12-CH_2CH_3, 1.99; 5-H, 10.49; 10-H, 10.39; NH, −3.4 ppm (293 K, $CDCl_3$).

To build on the above characterization work and to obtain some insight into the conformational and/or tautomeric exchange properties of $SapH_3$, several ^{1}H NMR temperature dependent spectroscopic studies were carried out. These studies were carried out in an attempt to vary, and perhaps slow down, the inherently fast rates of NH and water exchange. The results obtained served to reveal that the dynamics of these processes were only moderately dependent on the choice of solvent and on the method of sample preparation. On the other hand,

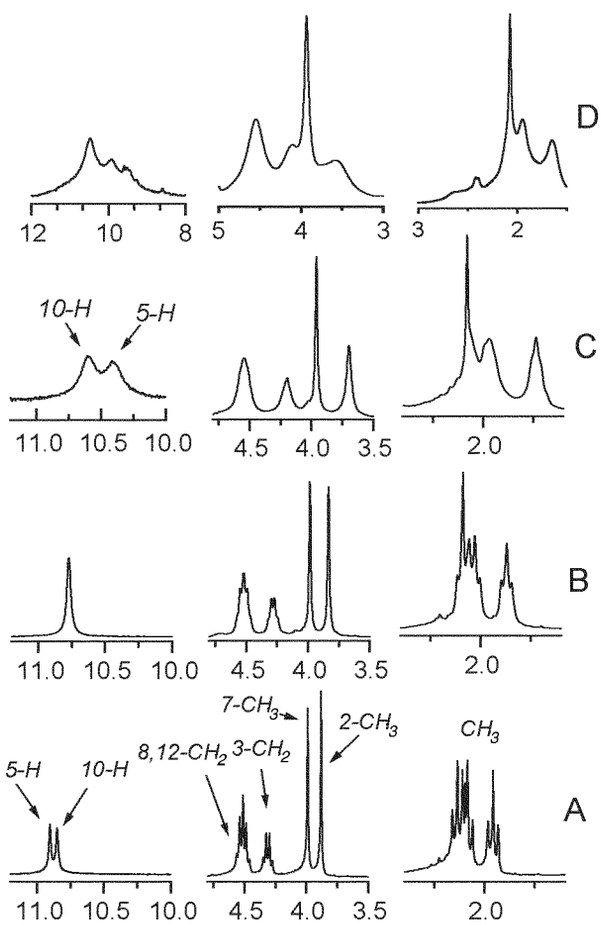


Fig. 3 ^{1}H NMR spectra of $SapH_3$ in dichloromethane-d_2 saturated with D_2O as function of temperature: (A) 293 K; (B) 243 K; (C) 203 K; (D) 193 K. Labeling as in Fig. 1.

systematic variable temperature studies of an $SapD_3$ sample (*i.e.*, neutral sapphyrin deuterated at the pyrrolic nitrogens), obtained by dissolving the sapphyrin in dichloromethane-d_2 saturated with D_2O, revealed significant changes in the sapphyrin-based signals, particularly for the 2-CH_3, 3-CH_2 and 5-CH resonances (Fig. 3). These latter signals were found to move upfield gradually as the temperature was decreased. The relative order of the 5-CH and 10-CH *meso* resonances changed upon lowering the temperatures (δ 5-CH > δ 10-CH above 243 K but δ 5-CH < δ 10-CH below this crossing point). The temperature dependence of the chemical shifts is considerably larger for signals ascribed to the bipyrrolic fragment of the sapphyrin molecule. In this case, the observed differences in chemical shift were accompanied by a considerable increase in the line widths of the relevant signals. The effect was most apparent in the case of the 5-CH *meso* resonances. In this instance, splitting was eventually observed as the temperature was lowered, with the relevant signals being spread out over the 9–12 ppm region at 179 K (Fig. 3, Trace D). The parallel experiments using $SapH_3$ gave concordant results, at least for the nonexchangeable protons. Interestingly, the NH protons resonated in the form of two broad features (not shown) at −4.8 ppm and −10.8 ppm at 179 K.

Based on the above analyses, we conclude that at the lower limit of achievable temperatures in dichloromethane-d_2 the ^{1}H NMR spectra demonstrate selective broadening which is ascribable to a reduction in the rate of exchange for the internal NH tautomeric migrations. On the other hand, further experimentation revealed that a specific combination of solvents, consisting of CF_2Br_2–CD_2Cl_2 50/50 v/v, gave spectra of reasonable quality, even at 158 K as shown in Fig. 4.

Basically, these low temperature spectra served to reveal a

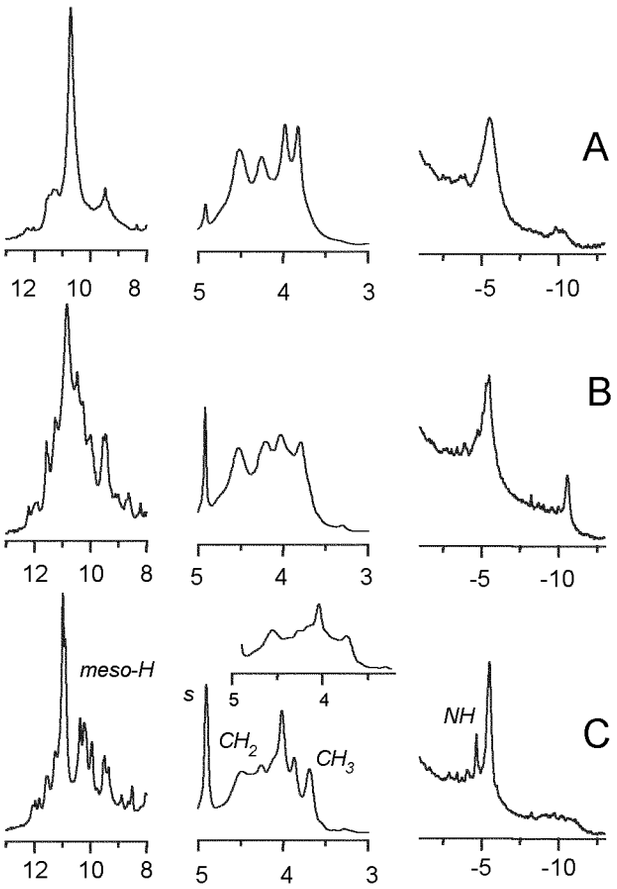


Fig. 4 ^{1}H NMR spectra of $SapH_3$ in CF_2Br_2–CD_2Cl_2 50/50 as function of temperature: (A) 203 K; (B) 183 K; (C) 158.3 K (inset at 173 K).

rather complex pattern consisting of several broad overlapped lines in each of the analytically useful regions, including the NH one. At this temperature, the *meso* and 2-CH_3 resonances are clearly split with respect to how they appear at 203 K. In fact, the *meso* signals become split in such a way that roughly equal parts of the intensity are found upfield and downfield with respect to the position observed at 203 K. Unfortunately, the complexity of these very low temperature signals precluded a detailed assignment. Nonetheless they do serve to establish unambiguously that $SapH_3$ consists not of a single species but is rather a mixture of symmetric and unsymmetric tautomers.

Discussion

The ^{1}H NMR data presented above, including that associated with temperature dependent studies and the various methanol and TFA addition analyses, are consistent with 2,7,18,23-tetramethyl-3,8,12,13,17,22-hexaethylsapphyrin (decaalkylated sapphyrin; $SapH_3$) adopting a planar structure in solution. These same data provide a starting point for making a comparison with 5,10,15,20-tetraphenylsapphyrin ($TPSH_3$).

The original ^{1}H NMR studies of $TPSH_3$ revealed a number of spectral features that served as useful indicators of the structure.[12–15] The extraordinary upfield position of the 12,13-H pyrrole proton, in conjunction with the very large downfield position of the 27-H resonance, were deemed consistent with an inverted geometry. In the context of the present study, these shift limits are therefore used as the defining "fingerprint" of an inverted sapphyrin structure.

In the case of $TPSH_5^{2+}$ the roughly planar geometry establishes what are essentially normal porphyrin-like shifts for the crucial 27-NH and 12,13-H pyrrole resonances. A hypothetical inverted structure of decaalkylsapphyrin should therefore result in the 27-NH resonance being observed in the downfield region, as determined previously for $TPSH_3$.[12] Accordingly, such a hypothetical structure would be expected to display a set of 12,13-ethyl resonances that are distinctly upfield shifted with respect to the 3,22- and 8,17-ones. On the other hand, a typical porphyrinic pattern would be predicted if $SapH_3$ adopts a planar, pyrrole-in geometry.

As it transpires (*cf.* Results section), the alkyl and NH resonances of 2,7,18,23-tetramethyl-3,8,12,13,17,22-hexaethylsapphyrin in any state of protonation are found at chemical shift values that are characteristic of a planar, pyrrole-in structure. Thus a conformational geometry is inferred for this decaalkylsapphyrin that stands in marked contrast to that deduced for tetraphenylsapphyrin.[12,14] It is our opinion, that in the case of $SapH_3$ and its protonated derivatives $SapH_4^+$ and $SapH_5^{2+}$ the steric hindrance of the 12,13-ethyl groups provides an impediment that precludes inversion of the C-pyrrole ring. In the case of the corresponding $TPSH_3$ system, the bulky *meso* phenyl groups provide an essential steric feature that serves to stabilize the inverted structure.[12–18]

A number of other distinct features were observed in the ^{1}H NMR spectrum of the decaalkylsapphyrin $SapH_3$. These include factors such as line broadening and peak splitting that also relate to the various putative dynamic processes that might involve the sapphyrin molecule directly. In this context the following dynamic processes have been considered: (a) binding of water by the sapphyrin NH-rich core, (b) NH tautomeric equilibria, (c) dimerization (aggregation).

It has been found recently that polypyrrolic macrocycles may act as receptors for neutral substrates.[19] So far, however, sapphyrin has not been explored in this context. On the other hand, it is known that two water molecules are involved in hydrogen bonding within the macrocyclic core of the tris-hydrochloride salt of rosarin, a nonaromatic, hexapyrrolic expanded porphyrin.[20] Likewise, the binding of water molecules by 2,6-pyridinium crown ethers and macrocyclic pyridine oligomers has been established.[21,22] While not strictly analogous, these previous findings led us to postulate that sapphyrin could be acting as a water-binding receptor. We thus considered equilibria (1) and (2), wherein the water molecule (molecules) would

$$SapH_3 + H_2O \rightleftharpoons SapH_3(H_2O) \quad (1)$$

$$SapH_3(H_2O) + H_2O \rightleftharpoons SapH_3(H_2O)_2 \quad (2)$$

be bound to the center of the molecule *via* a network of hydrogen bonds. The fast exchange of the NH and coordinated H_2O protons produces a single resonance at 293 K. This signal is shifted upfield compared to that for H_2O in chloroform-*d*. This is a reflection of the strong aromatic ring current effect of the sapphyrin moiety and the influence it has on the bound H_2O proton resonances. In accord with this hypothesis the position and intensity of the combined H_2O resonance was found to depend on the presence (and concentration) of water in the system.

As the temperature is lowered, excess water begins to freeze out from the dichloromethane-d_2 sapphyrin solution and the equilibrium begins to shift towards the nonhydrated form for which the integrated intensity of the NH signal is smaller than for the corresponding hydrated forms. The characteristic upfield changes of the signals ascribed to 2-CH_3, 3-CH_2 and 5-CH groups that accompany this proposed process are consistent with the suggested mechanism. In this context we note that protonation of the sapphyrin core is expected to produce shifts in these signals towards lower field in analogy to what was observed when $SapH_3$ was titrated with TFA. Thus, to the extent that loss of one or more bound H_2O molecules can be considered as reducing the average degree of sapphyrin NH protonation, the shift to higher field that accompanies the reduction in temperature is reasonable and expected.

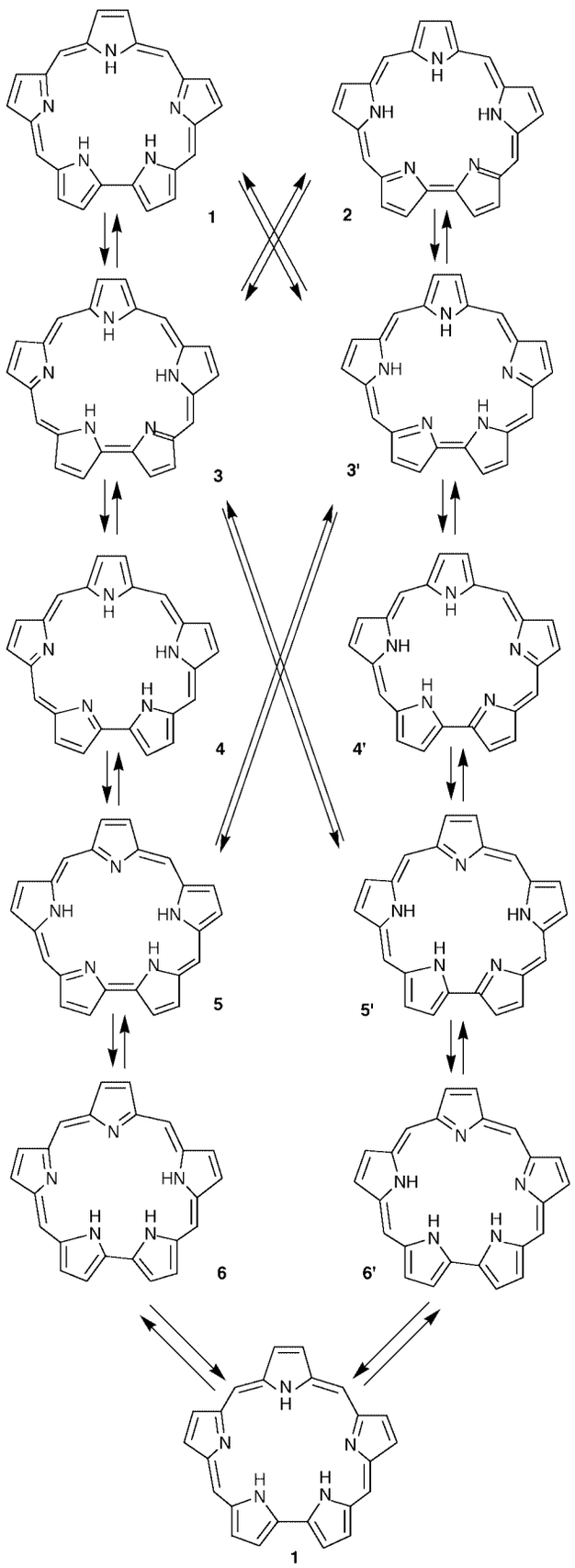
While not analyzed in detail, the changes that would accompany a titration with methanol are expected to be similar. Here, the binding equilibria can be described by eqn. (3).

$$SapH_3 + nCH_3OH \rightleftharpoons SapH_3(CH_3OH)_n \qquad (3)$$

With the neutral substrate molecular recognition properties of $SapH_3$ established to a satisfactory level, it becomes appropriate to begin trying to characterize this species in greater detail. In the case of pure, nonhydrated free-base $SapH_3$, a number of conceivable tautomeric forms are possible. These are shown in Scheme 5. This Scheme includes all degenerate pairs, *e.g.* (**3**, **3′**), (**4**, **4′**), (**5**, **5′**) and (**6**, **6′**), which will give identical ^{1}H NMR spectra. Therefore, the number of potentially discernible ^{1}H NMR patterns is actually only six. In any event, in the construction of Scheme 5 it is assumed, in analogy to what is true for porphyrins and diheterosapphyrins, that the tautomerization process involves a single NH proton transfer between two adjacent pyrrole nitrogens. Tautomers **1** and **2** are symmetric with respect to the mirror symmetry plane passing through 27-N and the middle of the C^1–C^{24} bond. The "effective" higher symmetry can be generated by a single proton exchange involving only one degenerate pair, namely, **5**–**5′**. A stepwise process serves to produce the same effect in the case **3**, **3′**, **4**, **4′** and **6**, **6′** pairs.

In terms of experiment, the various alkyl signals on pyrrole rings B and D and also on rings A and E are seen to be equivalent. This observation, in conjunction with a single quartet seen for the 12,13-CH_2 protons at 293 K, can be readily rationalized by assuming that $SapH_3$, like $TPSH_3$ and many other porphyrins, undergoes NH tautomerizm at a rate that is rapid on the ^{1}H NMR timescale. Such a fast exchange process yields, among other things, a time-averaged symmetrical distribution for the NH protons.[12,23–29]

From the present ^{1}H NMR analyses, it becomes possible to evaluate qualitatively the relative stabilities of the particular tautomeric forms of $SapH_3$. In the case of porphyrin and its various tetrapyrrolic isomers, it has been found that a *trans* arrangement of the NH protons is generally favored relative to a *cis*-like one.[23–27] A similar conclusion holds in the case of the neutral form of tetraphenylsapphyrin.[12,14] In the case of the latter system, which is perhaps the one most germane to the present study, the 27-NH proton does not contribute to the tautomeric equilibria. Two other protons are located in *trans*-like positions on the diagonally opposed pairs 25-N, 28-N or 26-N,29-N of the trapezoid-like core defined by the four inward-pointing nitrogens. The planar structure of decaalkylated sapphyrins requires that at least one set of NH protons adopts an intrinsic *cis*-like orientation. In spite of this, it is still reasonable to consider that the actual number of *cis* NH pairs will determine the relative stability of tautomeric forms in question. Such reasoning would lead to the expectation that tautomers **1**, **3** and **5** should be favored relative to **2**, **4** and **6**. On the other hand, it has been suggested that the tautomeric preference of porphyrins is mainly due to an electrostatic effect, *i.e.* hydrogen bonding and imino nitrogen lone pair–lone pair repulsions.[29] Both these latter effects are strongly dependent on the relative location of the interacting nitrogens. Accordingly, the actual stability of a given NH tautomer will also depend, at least in a precise way, on the type of *cis*-interaction(s) present in the structure. To the extent such an hypothesis is valid, it would lead to the prediction that a *cis* NH arrangement that involves 27-N and adjacent 26-N and 28-N nitrogens is less destabilizing than other possible *cis* NH–NH pairs as a result of the larger nitrogen–nitrogen, and consequently greater NH–NH separation, that it would allow. An amalgamation of these considerations leads to the following ordering: 25-NH,29-NH destabilization > 25-NH,28-NH destabilization > 26-NH,27-NH destabilization. In other words these considerations lead to the prediction that tautomers **3**, **1** and **5** should be more stable than tautomer **2** and that tautomers **4** and **6** should be particularly unstable.



Scheme 5

To obtain further insights into the relative energies of tautomers **1**–**6**, structure optimizations were carried out using density function theory.[18] Final estimates of the total electronic

energies were performed at the B3LYP level with the 6-31G** basis set using the B3LYP/6-31G fully optimized structures. Such analyses gave rise to predictions of planar and delocalized structures with bond lengths and angles that are similar to those deduced from X-ray diffraction analyses of sapphyrin dications.[3,5,7] Further, these calculations led to the following predictions of relative energy with respect to the tautomer **3**: **1,** 1.434; **2**, 6.434; **3**, 0.0; **4**, 16.123; **5**, 4.118; **6**, 12.285 kcal mol^{-1}.[18] These results are thus consistent with the qualitative predictions discussed above.

Given the above considerations, it becomes possible to imagine a ^{1}H NMR spectrum that is exceedingly complex. In the worst case scenario, *i.e.*, assuming the slow exchange of NH protons, the ^{1}H NMR spectrum of $SapH_3$ will consist of a mole-fraction weighted superposition of the ^{1}H NMR patterns of each tautomer. Considering the fact that six out of the ten tautomeric forms are distinguishable by ^{1}H NMR spectroscopy (at least in principle), one can expect up to twenty resonances in the *meso* region (*ca.* 10 ppm) and up to 16 NH resonances in the upfield spectral region (−2 to −11 ppm). In those cases where the rates of NH exchange are of an intermediate nature (*i.e.*, some are fast and some are slow on the ^{1}H NMR timescale) an intermediate number of lines would be expected with these lines being subject to possible broadening. In the case of the fast NH exchange (*i.e.*, rapid interconversion between conceivable tautomers) the system will display a simplified spectrum that is reflective of what is an "effective" C_{2v} symmetry and will do so in spite of the inherently complex nature of the system.

A detailed analysis of the ^{1}H NMR spectral data collected at the low temperature limit (*i.e.*, 158 K) supports the contention that the neutral form of sapphyrin should be treated as a collection of somewhat independent tautomeric species. However, even at this limit some of these tautomeric species remain in exchange, as reflected by the severe broadening of the relevant resonances. Consequently, we are not in a position to assign a particular set of resonances in a given spectral region to a specific set of localized NH protons (*i.e.*, to a given molecular structure). However, the upfield and downfield spread of the *meso* resonances seen at 158 K, as compared to what is seen at 293 K, is consistent with the proposed model. Specifically, the downfield *meso*-CH resonances are assigned to the CH groups flanked by the protonated pyrroles, whereas those at higher field are ascribed to those surrounded by unprotonated pyrrolidine type moieties.

For the predicative H_2O binding and NH tautomerization studies, alluded to above, to be useful we felt it was also necessary to address the question of whether $SapH_3$ undergoes appreciable dimerization in solution. Previously it was demonstrated that the diprotonated decaalkylsapphyrins $SapH_5^{2+}$ can dimerize (oligomerize) under appropriate experimental conditions.[4,5,30]

Two different limiting modes of dimerization, namely π–π stacking and solvent-mediated aggregation, were invoked in the case of the dicationic decaalkylsapphyrins. In principle these could operate in the case of the neutral form as well. Thus, π–π interactions, giving rise to the species of the general formula $(SapH_3)_n$ were considered as were various types of hydrogen bonding networks involving, for instance, the residual water molecules (*i.e.*, $\{SapH_3 \cdots (H_2O)_n \cdots SapH_3\}$). To make the analysis of these various putative aggregates more tractable, several idealized scenarios were considered as plausible models for the presumed constituent (or product) dimers, namely: (a) total overlap of the two sapphyrin π-systems, (b) one pyrrole subunit stacked over another pyrrole subunit, (c) two pyrrole subunits stacked over two other pyrrolic subunits.

Within the confines of these assumptions, it was expected that lowering the temperature would lead to an increase in the extent of dimerization. Such an increase should, in turn, serve to shift the observed sapphyrin resonances towards higher field. Thus, the fact that resonances ascribed to the *meso* protons were seen to shift to both higher and lower field as the temperature was lowered is considered inconsistent with mere dimer formation. Rather, it is far better accounted for in terms of the changes in tautomeric equilibria and dynamics alluded to above. Still, while the dominant species in solution were considered to be monomeric under the experimental conditions of the present study, subtle features, including the observation of multiple resonances and the exact chemical shifts of a given signal could reflect the presence of small concentrations of dimers or other higher order aggregates.

Conclusion

The present solution phase studies serve to establish that for free-base decaalkylated sapphyrins a planar, pyrrole-in macrocyclic geometry is favored at any protonation level. This stands in marked contrast to what is true for tetraphenylsapphyrin where two structures, namely normal planar and inverted, are observed. The present ^{1}H NMR studies provided some evidence for the existence of a complex tautomeric equilibria wherein up to ten tautomeric forms ({25-NH, 26-N, 27-NH, 28-N, 29-NH} **1**, {25-N, 26-NH, 27-NH, 28-NH, 29-N} **2**, {25-NH, 26-N, 27-NH, 28-NH, 29-N} **3**, {25-N, 26-NH, 27-NH, 28-N, 29-NH} **3′**, {25-N, 26-N, 27-NH, 28-NH, 29-NH} **4**, {25-NH, 26-NH, 27-NH, 28-N, 29-N} **4′**, {25-N, 26-NH, 27-N, 28-NH, 29-NH} **5**, {25-NH, 26-NH, 27-N, 28-NH, 29-N} **5′**, {25-NH, 26-NH, 27-N, 28-N, 29-NH} **6**, {25-NH, 26-N, 27-N, 28-NH, 29-NH} **6′**) could in principle be involved. On the basis of detailed analyses, it is considered that changes in the dynamics of these equilibria, rather than dimerization or other aggregation effects, are responsible for the changes in the ^{1}H NMR spectral features observed as the analysis temperature was varied.

Experimental

Solvents and reagents

Chloroform-*d*, and dichloromethane-d_2 (Aldrich) were dried by passing over a column of activated basic alumina. TFA (Aldrich) was used as received.

Preparation of compounds

Decaalkylsapphyrin was synthesized as previously described.[3b]

NMR sample preparation

Two procedures were used to prepare ^{1}H NMR samples of the neutral form. In the first procedure a biphasic dichloromethane–aqueous KOH saturated system was generated and used directly in the ^{1}H NMR studies. In the second procedure a similar biphasic mixture was generated, the organic layer first being separated from the aqueous phase, evaporated and dried thoroughly under vacuum before being redissolved in purified deuterated solvents. Usually NMR samples were prepared in a dry-box. To avoid contamination from traces of DCl/HCl which are often found in chlorinated solvents, the ^{1}H NMR samples were prepared directly before measurements using freshly deacidified solvents and *thoroughly neutralized* sapphyrin.

Titration studies

In the ^{1}H NMR titration experiments, appropriate solutions containing the putative substrate (*i.e.*, TFA in chloroform-*d*, chloroform-*d* saturated with water, and methanol dissolved in chloroform-*d*) were made up and gradually added by syringe to the sample solution with the progress of the reaction being followed by ^{1}H NMR spectroscopy. Usually, the starting concentration of the sapphyrin sample was 6 mM.

Instrumentation

^{1}H NMR spectra were measured on a Bruker 300 AMX spectrometer operating in the quadrature detection mode. The residual ^{1}H NMR resonances of the deuterated solvents were used as secondary references.

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