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Rates of axial ligand rotation in diamagnetic d^6 Co(III) and Fe(II) porphyrinates

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Abstract

In order to investigate the rates of rotation of pyridine and imidazole ligands in diamagnetic low-spin d^6 Co(III) and Fe(II) porphyrinate systems, we have synthesized tetramesitylporphyrinate (TMP) complexes of each of these metals with pyridine and imidazole ligands and investigated them as a function of temperature by ^{1}H NMR spectroscopy. We have already reported that for TMPFe(III) and -Co(III) complexes with hindered imidazoles the TMP *o*-CH_3 resonances can be used to measure the rates of rotation (N.V Shokhirev, T.Kh. Shokhireva, J.R. Polam, C.T. Watson, K. Raffii, U. Simonis and F.A. Walker, *J. Phys. Chem. A, 101* (1997) 2778). For the bis-1,2-dimethylimidazole complex, [TMPCo(1,2-Me_2Im)$_2$]BF_4, at ambient temperatures ligand rotation is slow but measureable on the NMP time scale, and four *o*-CH_3 resonances are observed, as we have already reported. In contrast, as shown in the present work, for the bis-4-dimethylaminopyridine complex, [TMPCo(4-NMe_2Py)$_2$]BF_4, ligand rotation is extremely rapid at ambient temperatures. At temperatures below −50°C at 300 MHz the *o*-CH_3 resonance broadens and the rates of rotation can be estimated using the modified Bloch equations simplified for the fast exchange regime. The activation parameters $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ have been determined, and the extrapolated rate constant at 25°C, $k_{ex} \geq 1.1 \times 10^6\ s^{-1}$. These results contradict previous reports (J. Huet and A. Gaudemer, *Org. Magn. Reson., 15* (1981) 347; I. Cassidei, H. Bang, J.O. Edwards and R. G. Lawler, *J. Phys. Chem., 95* (1991) 7186) that pyridine ligands bound to Co(III) porphyrinates do not rotate at room temperature in homogeneous solution. For unhindered imidazole complexes, such as [TMPCo(NMeIm)$_2$]$^+BF_4^-$, no broadening of the *o*-CH_3 resonance is observed, even at −90°C, and thus the rate of axial ligand rotation is too fast to measure, even at that low temperature (or the difference in chemical shift of the two resonances expected if ligand rotation is slow is very small). For the corresponding Fe(II) porphyrinate complexes, the rates of pyridine and unhindered imidazole rotation are too fast to measure, even at −90°C. The 2-methylimidazole complex undergoes chemical reactions that prevent detailed study of this system by NMR spectroscopy, but the 1,2-dimethylimidazole complex is stable and of similar structure (ruffled porphyrinate ring, axial ligands in perpendicular planes) to the Co(III) and Fe(III) analogs, with the rate constant for ligand rotation, $k_{ex} \sim 1\ s^{-1}$, at −90°C. Assuming a similar activation enthalpy to those of the Co(III) and Fe(III) systems, the rate of rotation of axial ligands in [TMPFe(1,2-Me_2Im)$_2$] at 25°C is estimated to be about $2 \times 10^4\ s^{-1}$. © 1997 Elsevier Science S.A.

Keywords: Kinetics; Cobalt complexes; Iron complexes; Diamagnetic complexes; Porphyrinate complexes

1. Introduction

Heme proteins have extremely well-defined metal binding sites that include not only the four nitrogens of the porphyrinate ring, but also the axial ligand(s) provided to the metal by the protein. These axial ligands may be provided by the side chains of histidine, methionine, cysteine, tyrosine, or the N-terminal amino group of the polypeptide. Not only are the ligands provided by the amino acid side chains that are covalently attached to the protein backbone, but they are held in very exact orientations by protein structural constraints, including steric crowding, and, particularly in the case of histidine ligands, hydrogen bonding of the NH group of the imidazole ring to amide carbonyl groups of the protein backbone [1,2]. With respect to steric crowding, the $-SCH_3$ group of coordinated methionines in a wide variety of cytochrome *c* has been shown to exhibit one or the other of the two possible chiralities, and NMR spectroscopy provides a sensitive tool for determining which chirality is exhibited by a given cytochrome *c* [3]. Thus, in both the cases of histidine- and methionine-ligated heme proteins just mentioned, as with all other axial ligands provided by proteins, there is no pos-

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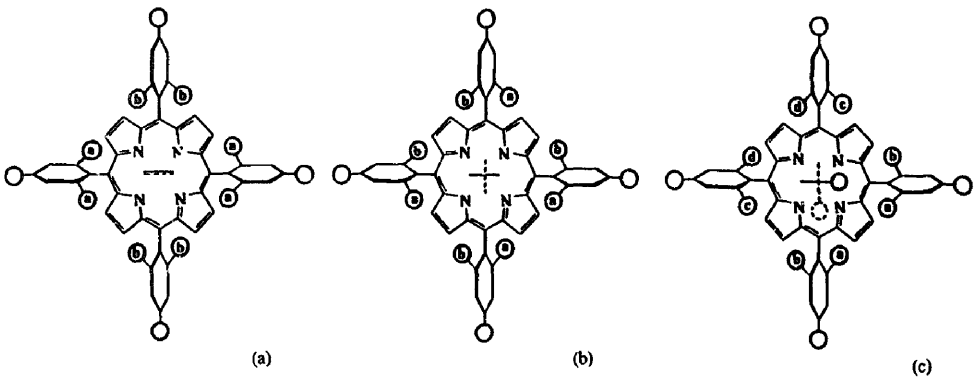

Fig. 1. Diagrams of the possible orientations of symmetrical pyridine ligands on Co(III) and Fe(II) tetramesitylporphyrinates, showing that there are two types of mesityl o-CH_3 groups for either perpendicular (a) or parallel (b) orientation of the ligands, that must lie over the *meso* positions of the porphyrin ring. (c) The four types of mesityl o-CH_3 groups created by perpendicular orientation of unsymmetrical ligands.

sibility of rotation of the axial ligands about the metal–ligand bond.

In contrast to the proteins, it has long been assumed that in model hemes in which axial ligands are not covalently attached to the porphyrinate ligand, axial ligand rotation is generally rapid at ambient temperatures. NMR investigations of low-spin Fe(III) model hemes have confirmed that even in the case of the hindered ligands 2-methylimidazole [4–8], 2-ethyl- and 2-isopropylimidazole [6], 1,2-dimethylimidazole [4,6] and benzimidazole [6], ligand rotation is fast at room temperature. In comparison, for two $[TMPCo(L)_2]^+$-BF_4^- complexes (L = 2-MeImH, 1,2-Me_2Im) the rotation of axial ligands is slow, but measurable, at room temperature [7]. However, two previous reports concerning seemingly less sterically hindered bis-(pyridine) complexes of Co(III) porphyrinates found that axial ligand rotation (of pyridine ligands) was extremely slow or non-existent at ambient temperatures [9,10]. These reports are in strong contradiction to the findings for six-coordinate low-spin Fe(III) porphyrinates, for which the barriers to rotation of pyridine ligands have been estimated from molecular mechanics calculations to be ≤ 8 kJ mol^{-1} [11], and the calculated rate constants for rotation of 2-methylimidazole ligands in $[TMPFe(2\text{-}MeImH)_2]^+ClO_4^-$ and related complexes are extremely large at ambient temperatures [7]; only at temperatures lower than -10°C are the four *ortho*-methyl and four pyrrole proton signals resolved at 300 MHz [4,7]. For the $[TMPCo(2\text{-}MeImH)_2]^+BF_4^-$ analog, the four *ortho*-methyl resonances are resolved at ambient temperatures [7,12], and the rate of ligand rotation is a factor of 10^3 slower than for Fe(III), yet measurable [7]. We were therefore interested that broadening of the o-CH_3 resonance of $[TMPCo(4\text{-}NMe_2Py)_2]^+$-$BF_4^-$ is observed at temperatures lower than -50°C at 300 MHz [13]. This broadening suggested that a chemical exchange process was creating multiple magnetic environments for the o-CH_3 groups of the porphyrinate ligand at these temperatures. It should be recognized that pyridine ligands prefer to bind to metalloporphyrinates with their ligand planes lying over the *meso* positions of the porphyrinate ring in perpendicular planes for low-spin d^5 Fe(III) [14], but in parallel planes for low-spin d^6 Fe(II) [15] [1], and most [14] but not all [16] low-spin d^6 Co(III) porphyrinates. Under such conditions, two magnetic environments are created by the slowed rotation of symmetrical, planar axial ligands in either parallel or perpendicular planes, as shown in Fig. 1(a) and (b), while four magnetic environments are created by slow rotation of unsymmetrical planar axial ligands in perpendicular planes, Fig. 1(c). Detailed NMR investigations of TMPCo(III) complexes with pyridine and imidazole axial ligands reported herein have shown that, as in the case of low-spin Fe(III), axial ligand rotation is extremely rapid at ambient temperatures for non-hindered pyridine and imidazole ligands, although for ligands for which rates can be measured for both Co(III) and Fe(III), the rates of rotation are slower in the former than in the latter complexes. We also attempted to extend these investigations to the other d^6 metal of interest in biological systems, Fe(II), but found that pyridine ligand rotation is too fast to measure, even at -90°C, although the rate of rotation of 1,2-dimethylimidazole could be measured at this temperature. We have attempted to rationalize how earlier reports, based on T_1 data of the ^{13}C atoms of the coordinated pyridine ligands [9,10], could have arrived at the conclusion that axial ligands of Co(III) porphyrinates do not rotate at ambient temperatures.

2. Experimental

Reagent grade chemicals were purchased from Aldrich and solvents from Fisher. Deuterated solvents were purchased

[1] We have suspected for some time, and the present work shows conclusively, that hindered imidazole complexes of iron(II) porphyrinates, such as those of 2-MeImH and 1,2-Me_2Im are exceptions, and have their axial ligands in perpendicular planes.

from Cambridge Isotopes. Tetramesitylporphyrin was purchased from Midcentury. Chromatographic grade silica gel (60–200 mesh) was purchased from Davison Chemical. Syntheses of axial ligand complexes were performed under argon using standard Schlenk and inert atmosphere techniques. All solvents were of reagent grade quality and were dried, distilled and degassed before use. All NMR solvents were dried and degassed by repeated freeze–pump–thaw before use; spectra were obtained in d_8-toluene and d_2-dichloromethane.

Cobalt(II) was inserted into tetramesitylporphyrin using the method of Simonis et al. [17]. 500 mg (0.634 mmol) of $TMPH_2$ were dissolved in 100 ml $CHCl_3$ and 256 mg (1.0 mmol) of cobalt(II) acetate in 30 ml 1:1 $CHCl_3/CH_3OH$ were added and the reaction mixture was allowed to reflux for 8 h. Metal insertion was monitored by TLC. After rotoevaporating the solvent to dryness, 15 ml $CHCl_3$ and 15 ml water were added and the excess Co(II) acetate was removed by repeated washings of the organic layer with water. The product was evaporated to dryness. Yield of TMPCo(II): 440 mg (88%). ^{1}H NMR ($CDCl_3$, ppm): 15.2 (bs, 8H, pyrrole-H); 9.2 (s, 8H, m-H); 4.0 (s, 12H, p-CH_3); 3.5 (bs, 24H, o-CH_3).

2.1. Synthesis of $[TMPCoL_2]BF_4$

The methods of Balch et al. [18] and Sugimoto et al. [17] were used. A 100 mg sample of TMPCo(II) (0.118 mmol) was dissolved in a mixture of 30 ml methanol and 20 ml $CHCl_3$. To each of three such solutions NH_4BF_4 (50 mg, 0.477 mmol) and one of the desired axial ligands, either 1,2-dimethylimidazole (32 mg), 4-dimethylaminopyridine (43 mg, 0.35 mmol) or *N*-methylimidazole (30 μl, 0.35 mmol), were added and the solution refluxed overnight with exposure to air. The samples were checked for completeness of reaction by TLC, and upon completion the solvent was evaporated and the sample redissolved in dichloromethane and filtered. The filtrate was chromatographed on silica gel using ethyl acetate as the eluting solvent. The first two fractions, which were shown by ^{1}H NMR spectroscopy to be TMPCo(III) having no and one nitrogenous axial ligand [19], were discarded and the main, third fraction was collected and evaporated to dryness. Yields: $[TMPCo(N\text{-MeIm})_2]BF_4$, 105 mg, 77%, others very similar. ^{1}H NMR (CD_2Cl_2, ppm): $[TMPCo(N\text{-MeIm})_2]BF_4$: 8.83 (s, 8H, pyrrole-H); 7.25 (s, 8H, m-H); 4.63 (t, 2H, ligand 5-H); 2.57 (s, 12H, p-CH_3); 2.02 (s, 6H, ligand N–CH_3); 1.56 (s, 24H, o-CH_3); 0.99 (bs, 2H, ligand 2-H); 0.57 (t, 2H, ligand 4-H); very similar to that reported previously for the TPP analog [20]. $[TMPCo(4\text{-}NMe_2Py)_2]BF_4$: 8.85 (s, 8H, pyrrole-H); 7.31 (s, 8H, m-H); 4.13 (d, 4H, ligand 3,5-H); 2.61 (s, 12H, p-CH_3); 2.07 (s, 12H, $N(CH_3)_2$); 1.54 (s, 24H, o-CH_3); 0.57 (d, 4H, ligand 2,6-H); similar to those reported previously for TPP/substituted pyridine analogs in $CDCl_3$ [19]. $[TMPCo(1,2\text{-}Me_2Im)_2]BF_4$ (0°C): 8.83 (s, 2H, pyrrole-H); 8.81 (s, 2H, pyrrole-H); 8.76 (s, 2H, pyrrole-H); 8.74 (s, 2H, pyrrole-H); 7.46 (s, 4H, m-H); 6.91 (s, 2H, m-H); 6.85 (s, 2H, m-H); 4.54 (d, 2H, ligand 5-H); 2.84 (s, 6H, o-CH_3); 2.82 (s, 6H, o-CH_3); 2.52 (s, 6H, p-CH_3); 2.50 (s, 6H, p-CH_3); 1.91 (s, 6H, ligand N-CH_3); 0.10 (s, 6H, o-CH_3); −0.08 (d, 2H, ligand 4-H); −0.15 (s, 12H, o-CH_3); −2.05 (s, 6H, ligand 2-CH_3); the ^{1}H NMR shifts for the latter complex are very similar to those reported recently for $[TMPCo(1,2\text{-}Me_2Im)_2]Cl$ in $CDCl_3$ [12].

2.2. Synthesis of TMPFeCl

100 mg (0.12 mmol) of $TMPH_2$ were dissolved in a minimum amount of dichloromethane. Approximately 130 mg (1 mmol) of ferrous chloride (anhydrous, Alfa) were dissolved in a minimum amount of a 3:1 dichloromethane/methanol solution and added to the $TMPH_2$ solution. The mixture was refluxed under nitrogen until iron insertion was complete. The progress of the reaction was monitored by TLC and by UV–Vis spectroscopy. The solvent was removed by rotary evaporation and dichloromethane was added to dissolve the iron porphyrin, which was then washed four times with water in a separatory funnel in order to remove excess $FeCl_2$ and its oxidation products. The dichloromethane layer was then chromatographed on silica gel, eluting first with dichloromethane to remove traces of $TMPH_2$ and then with 9:1 dichloromethane:methanol. Fractions were monitored by UV–Vis spectroscopy. The iron-containing fractions were combined, evaporated to dryness and redissolved in dichloromethane. Gaseous HCl was then passed through the iron porphyrin solution for 1 min and excess HCl removed by bubbling with nitrogen gas. The solvent was then evaporated. Yield: 98 mg TMPFeCl (88%).

2.3. Synthesis of $[TMPFe(L)_2]$

10 mg (0.0115 mmol) of TMPFeCl and 40 mg (1 mmol) of sodium borohydride were transferred to a Schlenk flask and 10 ml dry THF were added and the solution stirred for 2 h. The color of the reaction mixture turned from brownish to brick red. To each of three such solutions one of the ligands was added in excess: 4-dimethylaminopyridine, 6.9 mg (0.057 mmol); 4-cyanopyridine, 6 mg (0.057 mmol); 1,2-dimethylimidazole, 10 mg (0.104 mmol) was added and the solution stirred for 15 min; the reaction appeared to be instantaneous. The solvent was removed under reduced pressure. The NMR solvent, (d_8-toluene, 1 ml) was added and the solution was filtered into a septum-screw-cap NMR tube in a glove box. All samples were stable under argon atmosphere at room temperature over the course of weeks. Optical spectra (nm) (log ε), CH_2Cl_2: 423 (5.01), 530 (4.10), 561 (3.99) (4-NMe_2Py complex); 421 (5.09), 527 (4.16), 558 (4.03) (4-CNPy complex), in agreement with literature values [15]. Mössbauer spectra of the bis-4-CNPy and -4-NMe_2Py complexes and the three-dimensional X-ray structure of the former are reported elsewhere [15]. The Mössbauer spectrum of the bis-1,2-Me_2Im complex has been reported

[21,24]. Optical spectrum (tetrahydrofuran, 1 M 1,2-Me_2Im): 431, 534, 564 nm. NMR (d_8-toluene, ppm): [TMPFe(1,2-$Me_2Im)_2$] (−90°C): 8.62 (s, 8H, pyrrole-H); 7.29, 7.25, 6.95 (2H, 2H, 4H, m-H resonances nearly obscured by solvent in 1D spectrum, but observed in 2D spectrum); 4.02 (s, 2H, ligand 5-H); 3.13, 3.10 (2s, 12H, o-CH_3); 2.53, 2.49 (2s, 12H, p-CH_3); 0.86 (s, 6H, o-CH_3); 0.48 (s, 6H, o-CH_3); 0.38 (s, 2H, ligand 4-H); −1.34 (s, 6H, ligand 2-CH_3), all very similar to those of the Co(III) analog reported above. [TMPFe(4-$NMe_2Py)_2$] (−40°C): 8.65 (s, 8H, pyrrole-H); 7.15 (s, 8H, m-H); 4.15 (d, 4H, ligand 3,5-H); 2.55 (d, 4H, ligand 2,6-H); 2.42 (s, 12H p-CH_3); 2.05 (s, 24H, o-CH_3); separate free (2.45 ppm) and coordinated N–CH_3 resonances are not observed due to chemical exchange. [TMPFe(4-$CNPy)_2$] (−40°C): 8.60 (s, 8H, pyrrole-H); 7.04 (s, 8H, m-H); 3.90 (d, 4H, ligand 3,5-H); 2.45 (s, 12H, p-CH_3); 2.22 (d, 4H, ligand 2,6-H); 1.70 (s, 24H, o-CH_3).

One- and tw ,mensional proton NMR spectra were recorded on a Varian Unity 300 NMR spectrometer operating at 299.995 MHz. All spectra of TMPCo(III) complexes were recorded in CD_2Cl_2 and spectra of TMPFe(II) complexes were recorded in toluene-d_8, in each case over the temperature range of −90 to +30°C. The spectra were referenced to residual solvent protons. One-dimensional spectra were collected using the standard one-pulse experiment with a spectral bandwidth of 5 kHz, a block size of 16K data points, a 30° pulse, and 32–64 transients. Phase sensitive NOESY/EXSY spectra were acquired over a bandwidth of 4 kHz using the standard (90°–t_1–90°-τ_m–90°–t_2) pulse sequence with 512 t_2 data points and 128 t_1 increments. Recycle delays ranged from 2.5 to 3 s. The mixing times were 700 ms (Co(III), +21°C) and 500 ms (Fe(II), −90°C). Usually, 32 transients were obtained for each t_1 increment. Data were processed with a Gaussian apodization function in both dimensions and zero-filled to give final matrices of 1024 t_1 × 1024 t_2 data points prior to Fourier transformation. Diagonal and cross-peak intensity data were analyzed as described previously [7].

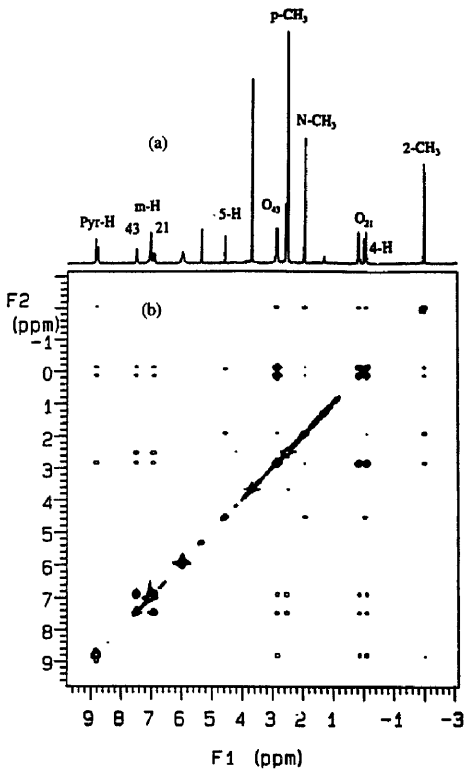

Fig. 2. (a) 1D ^{1}H NMR spectra of [TMPCo(1,2-$Me_2Im)_2$]BF_4 in CD_2Cl_2 at +21°C, showing the four separate o-CH_3 resonances observed for this complex, which are in slow exchange on the NMR time scale; (b) 2D phase-sensitive NOESY/EXSY spectrum, recorded at the same temperature with a mixing time of 700 ms, showing chemical exchange (multiple contours) and NOE (single circles) cross peaks. The rate of ligand rotation calculated from this spectrum is 4.5 s^{-1} [7]. The peaks at 2.5, 3.7, 6.0 and 7.0 ppm are due to excess 1,2-Me_2Im in the solution, and the peak at 5.3 ppm is due to $CDHCl_2$.

3. Results and discussion

In Fig. 2 is shown an example of the proton NMR spectra of the bis-(1,2-dimethylimidazole) complex of TMPCo(III), [TMPCo(1,2-$Me_2Im)_2$]$^+BF_4^-$, at 21°C, where it can be seen that, as reported previously [12,13], four different *ortho*-methyl resonances are observed for the mesityl groups of the TMP ligand; thus, axial ligand rotation is slow on the NMR time scale for this complex at room temperature. The intensities of the EXSY cross peaks have been analyzed to obtain the rates of ligand rotation for this complex, as has been reported elsewhere [7]. For the NOESY/EXSY spectrum shown in Fig. 2(b) the calculated rate constant is 4.5 s^{-1}.

In contrast to the ^{1}H NMR spectra of the hindered imidazole complexes, in Fig. 3 is shown an example of the 1D proton NMR spectra of a bis-(pyridine) complex of TMPCo(III), [TMPCo(4-$NMe_2Py)_2$]$^+BF_4^-$. As can be seen, at temperatures below −50°C the o-CH_3 resonance of the mesityl groups broadens significantly while the other resonances remain essentially unchanged in width. The excess linewidth of the o-CH_3 resonance can be explained by the existence of a kinetic process that begins to freeze out different magnetic environments for the o-CH_3 resonances of individual mesityl rings below −50°C. Because of the symmetry of the 4-dimethylaminopyridine ligand, only two different magnetic environments are possible, independent of whether the axial ligands are in parallel or perpendicular planes, as shown in the schematic diagrams of Fig. 1(a) and (b). This is different from the case of the 2-methyl- and 1,2-dimethylimidazole ligands whose slow rates of ligand rotation for the TMPCo(III) complexes have already been reported [7], in that these unsymmetrical ligands, arranged in perpendicular

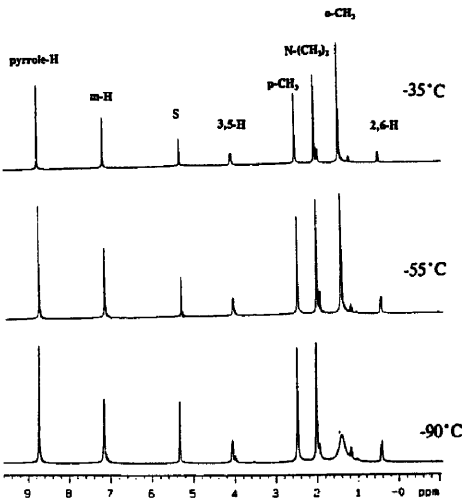

Fig. 3. 1D ^{1}H NMR spectra of $[TMPCo(4\text{-}NMe_2Py)_2]BF_4$ in CD_2Cl_2 at various temperatures, showing the assignment of the spectrum and the broadening of the o-CH_3 resonance with decreasing temperature. Small signals near 1.2, 2.0 and 4.0 ppm are due to the presence of traces of ethyl acetate in the sample.

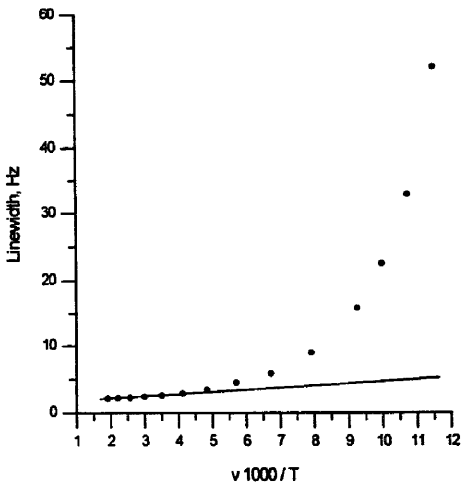

Fig. 4. Temperature dependence of the linewidths of the o-CH_3 resonance of $[TMPCo(4\text{-}NMe_2Py)_2]BF_4$ showing the extreme broadening of the o-CH_3 resonance. The difference between the straight line extrapolation and the observed linewidth of the o-CH_3 resonance is attributed to a chemical exchange process involving the rotation of axial ligands.

planes, create four different magnetic environments for the o-CH_3 groups (Fig. 1(c)).

For chemical exchange that is fast on the NMR time scale, with equal abundance of the two exchanging species, the modified Bloch equations can be simplified to the expression

$$k_{ex} = \pi(\Delta\nu)^2/2(W^* - W_o) \quad (1)$$

where $\Delta\nu$ is the chemical shift difference (in Hz) of the two no-exchange lines, W^* is the width at half-height of the observed, exchange-broadened line, and W_o is the width at half-height of each of the lines in the absence of exchange [22]. Since W_o (and presumably W^*) is proportional to the rotational correlation time of the molecule, τ_c, which is in turn proportional to η/T, we have plotted the linewidth of the o-CH_3 resonance of $[TMPCo(4\text{-}NMe_2Py)_2]BF_4$ as a function of η/T, as shown in Fig. 4. The nearly flat, high temperature part of this plot represents the dependence of the linewidth of the extremely fast-exchange lines on η/T. Extrapolation of this line into the regime where chemical exchange becomes measurable on the NMR time scale allows us to determine the difference in linewidth, $W^* - W_o$, that is a result of chemical exchange. However, since we cannot cool the sample to a low enough temperature to bring the system to the slow or no-exchange regime, we cannot measure the difference in chemical shift of the two no-exchange o-CH_3 resonances. We have assumed that the minimum difference in chemical shift, in Hz, $\Delta\nu$, must be at least as large as the maximum linewidth at half height observed, or 52 Hz (-90°C), although this value of $\Delta\nu$ would mean that the lineshape at this temperature should be distinctly non-Lorentzian, which is not the case (Fig. 3). Nevertheless, we have used the value of 52 Hz for $\Delta\nu$ in our calculations as the minimum possible value; for larger values of $\Delta\nu$ the calculated rate constants would simply be scaled by the constant quantity $(\Delta\nu)^2/2704$. Thus, our assumption that $\Delta\nu = 52$ Hz will not affect the calculated ΔH^*, though it will affect the calculated ΔS^* and k_{ex}.

With the assumption that $\Delta\nu = 52$ Hz, we have calculated k_{ex} at temperatures ranging from 188 to 228 K and constructed an Eyring plot, shown in Fig. 5. The activation enthalpy and entropy obtained from this plot are $\Delta H^* = 26.2$ kJ mol^{-1} and $\Delta S^* = -60.4$ J mol^{-1} K^{-1}; these values predict that the minimum rate of rotation of 4-NMe_2Py ligands about the Co–N bonds of $[TMPCo(4\text{-}NMe_2Py)_2]^+BF_4^-$ at 25°C is 1.1×10^6 s^{-1}. Assumption of a larger value of $\Delta\nu$, for example 100 Hz, would lead to a less negative value of ΔS^* (-30.5 J mol^{-1} K^{-1}) and a larger rate constant (4.1×10^6 s^{-1}). Thus, we conclude that 4-dimethylaminopyridine ligands are rotating at least a million times per second at room temperature! This rate is at least 2×10^5 faster than that of the 1,2-dimethylimidazole ligands of $[TMPCo(1,2\text{-}Me_2Im)_2]BF_4$ reported previously ($k_{ex}(298) = 5.1$ s^{-1}).

We then attempted to measure the rate of *N*-methylimidazole rotation in $[TMPCo(N\text{-}MeIm)_2]^+BF_4^-$ by the same fast-exchange dynamic NMR techniques, but found that the degree of broadening of the o-CH_3 resonance was much less (≤ 1 Hz more than predicted by a plot of linewidth versus η/T similar to that shown in Fig. 4). If these small broadenings truly indicate a slowed rate of ligand rotation, then, again assuming $\Delta\nu = 52$ Hz, we estimate that $\Delta H^* \sim 3.6$ kJ mol^{-1}, $\Delta S^* \sim -94$ J mol^{-1} K^{-1} and $k_{ex}(298) \sim 2 \times 10^7$ s^{-1}. Alternatively, if $\Delta\nu$ is smaller in this case, as might be

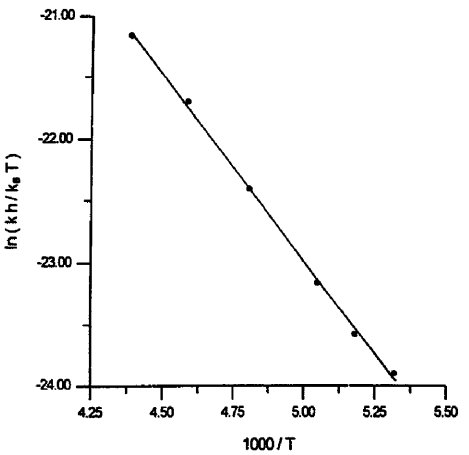

Fig. 5. Eyring plot of the kinetic data obtained for rotation of the 4-dimethylaminopyridine ligands of $[TMPCo(4\text{-}NMe_2Py)_2]^+$ in CD_2Cl_2. Calculated values of ΔH^* and ΔS^* are 26.2 kJ mol^{-1} and -60.4 J mol^{-1} K^{-1}; the extrapolated rate constant at 25°C is 1.1×10^5 s^{-1}. (These values of ΔS^* and $k_{ex}(298)$ are based upon the assumption that $\Delta\nu = 52$ Hz, as discussed in the text.)

expected because of the smaller steric repulsion between the non-hindered imidazole and the *o*-CH_3 groups of TMP, the ΔS^* would be even more negative and $k_{ex}(298)$ would be smaller. In either case, the unreasonably large negative values of ΔS^*, in light of both the value obtained above for axial ligand rotation in $[TMPCo(4\text{-}NMe_2Py)_2]^+BF_4^-$ and those reported for the more sterically-hindered 2-MeImH (-62 J mol^{-1} K^{-1}) and 1,2-Me_2Im (-81 J mol^{-1} K^{-1}) axial ligand complexes of TMPCo(III) suggest that these data are not representative of the ligand rotation of *N*-methylimidazole, but rather that the ≤ 1 Hz broadening of the *o*-CH_3 resonance at temperatures below -70°C represents a slight change in the η/T dependence of the resonance; in support of this, the N–Me resonance of the coordinated ligand shows the same linewidth dependence. Thus, we conclude that at the lowest temperature studied (-85°C), the rate of *N*-methylimidazole rotation is too fast to measure by dynamic NMR techniques in the fast exchange regime or that there is essentially no difference in chemical shift of the two *o*-CH_3 resonances and thus ligand rotation cannot be detected by ^{1}H NMR methods.

Having obtained some information concerning the rate of ligand rotation on diamagnetic $[TMPCoL_2]^+$ complexes, we then attempted to measure the rates of rotation of 4-dimethylamino- and 4-cyanopyridine and imidazole ligands on diamagnetic $[TMPFeL_2]$, in this case in toluene-d_8. We found no broadening of the *o*-CH_3 resonance, even at -90°C, for either of these complexes, indicating that pyridine ligand rotation is extremely fast on low-spin Fe(II) porphyrinates. Because of the extreme sensitivity of Fe(II) porphyrinates to traces of O_2, NMR samples were prepared in an argon-filled glove box using de-gassed toluene-d_8, and septum-screw-cap NMR tubes; these procedures were found to be adequate for our previous ^{57}Fe NMR studies, both those involving indirect [23] and direct [24] detection for complexes having pyridine or *N*-methylimidazole ligands. However, when we attempted to prepare the bis-(2-methylimidazole) complex by the same methods we found that it oxidized within the course of 1 h. Repeated attempts to prevent this oxidation by more rigorous de-gassing procedures were not successful, and we thus concluded that the complex autoxidizes in the presence of excess 2-MeImH. Though we were not able to detect hydrogen gas being evolved in this autoxidation process, the fact that our previous methods [23,24] were successful in producing a stable bis-(1,2-dimethylimidazole) complex in the presence of excess ligand is consistent with the hypothesis that H_2 is the other product of this autoxidation.

We therefore turned our attention to investigation of the $[TMPFe(1,2\text{-}Me_2Im)_2]$ complex by ^{1}H NMR spectroscopy at very low temperatures. It should be noted that although bis complexes of hindered imidazoles are not formed by TPPFe(II), they are stable for so-called 'hindered' ferrous porphyrinates, including TMPFe(II), $(2,6\text{-}Cl_2)_4$TPPFe(II) and $(2,6\text{-}Br_2)_4$TPPFe(II) in the presence of a 15 mM or greater excess of 2-methylimidazole in DMF solution at room temperature [25]. However, in the presence of a 80 mM excess of 1,2-Me_2Im, a concentration tolerable for NMR studies of the ~20 mM complex, the bis-ligand complex is in rapid exchange with trace amounts of the high-spin mono-ligand complex, and thus very low temperature studies are required. (It is not unreasonable that the 1,2-Me_2Im complex is less stable than the 2-MeImH complex (in the absence of autoreduction of the latter) because of the slightly greater steric hindrance provided by the 1,2-dimethyl substitution.) At -70°C, three *o*-CH_3 resonances of the TMP ligand (one of intensity double that of each of those of the other two), with chemical shifts similar to those of the same groups in $[TMPCo(1,2\text{-}Me_2Im)_2]^+BF_4^-$ (Fig. 2(a)), became resolved, and at -80 and -90°C all four *o*-CH_3 and both *p*-CH_3 resonances were resolved, as shown in Fig. 6(a). The spectrum resulting from a phase-sensitive NOESY/EXSY experiment at -90°C is shown in Fig. 6(b), where both chemical exchange and NOE cross peaks are observed. Unlike the Co(III) NOESY/EXSY spectrum of Fig. 2, where NOE cross peaks are of opposite phase while chemical exchange cross peaks are the same phase as the diagonal peaks, all cross peaks are of the same phase as the diagonal, indicating that the NOEs are negative [26], as expected for the considerably higher viscosity of the solution at -90°C.

All of the expected chemical exchange cross peaks are observed for $[TMPFe(1,2\text{-}Me_2Im)_2]$, and, as in the case of the corresponding Co(III) complex of Fig. 2, the two closely-spaced *o*-CH_3 resonances near 3 ppm are not well resolved in the 2D experiment due to low digital resolution. The expected NOE peaks observed include those between the *o*-CH_3 and *m*-H resonances, all of the latter of which are obscured in the 1D spectrum by the intense solvent resonances, but are resolved in the 2D spectrum of Fig. 6(b); the

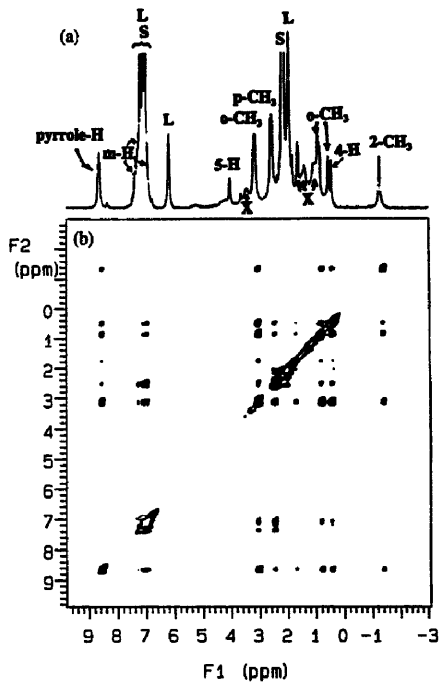

Fig. 6. Phase-sensitive ^{1}H NOESY/EXSY spectrum of [TMPFe(1,2-$Me_2Im)_2$] in toluene-d_8, recorded at −90°C with a mixing time of 500 ms, showing both chemical exchange and NOE cross peaks. In addition to the major peaks of the complex, intense resonances due to solvent (S), free ligand (L) and several unknown impurities (X) are marked; none of these show cross peaks in the 2D spectrum. The rate constant for axial ligand rotation estimated from the o-CH_3 cross peak intensities by the methods described previously [7] is 1 s^{-1}.

NOEs between these m-H and the two p-CH_3 resonances near 2.5 ppm are also resolved. There are also NOEs between the ligand 2-CH_3 (−1.34 ppm) and each of the o-CH_3 resonances that result from a combination of an NOE between the 2-CH_3 and one of the o-CH_3 groups (o-CH_3(3), as we have shown conclusively elsewhere for the Co(III) analog [27]), plus chemical exchange between o-CH_3s. NOEs are also observed between the (broad) pyrrole-H resonance (actually six pyrrole-H resonances (two singlets and an AB quartet) are expected but not resolved) and each of the o-CH_3 resonances, as well as the ligand 2-CH_3. All of these are also present in the NOESY/EXSY spectrum of [TMPCo(1,2-$Me_2Im)_2$]BF_4 complex (Fig. 2), most with remarkably similar chemical shifts, suggesting that the structures of the two complexes are very similar, and, by comparison to the Fe(III) analogs [4,7,28], insuring that the Fe(II) complex indeed has its bulky 1,2-Me_2Im ligands in perpendicular planes. The two pairs of o-CH_3 resonances (0.48, 0.86 ppm and 3.10, 3.13 ppm) are almost equally displaced from the position of the o-CH_3 resonance of [TMPFe(4-$NMe_2Py)_2$] (2.05 ppm), suggesting that, as for the Co(III) analog where it was possible to suppress chemical exchange enough to see the NOE between o-CH_3(3) and the 2-CH_3 ligand resonance [27], the two downfield resonances are from those of methyl groups that are forced outside the porphyrin ring current, and are thus in the same plane as the bulky 1,2-Me_2Im ligand, while the two resonances at 0.48 and 0.86 ppm are from methyl groups that are inside the porphyrin ring current, and are thus in the plane perpendicular to the bulky ligand; the types of o-CH_3 groups on one side of the porphyrinate ring are repeated on the other side.

Two sets of unexpected NOE cross peaks are also observed: one between the pyrrole-H and the m-H, and another set between the o-CH_3 resonances near 3 ppm (and weaker cross peaks between the other two o-CH_3 resonances) and the p-CH_3 resonances near 2.5 ppm. The former set may result from overlapping ridges of the strong solvent peaks with the pyrrole-H ridges, and the latter may result from NOEs transferred through the m-H resonances in combination with chemical exchange among m-H. A number of small, broad impurity peaks are also observed in the 1D spectrum of this highly air-sensitive complex (marked as X), but none of them exhibit cross peaks either with each other or with resonances of the complex.

Based upon the intensities of the observed chemical exchange cross peaks, a rate constant of 1 s^{-1} is estimated from the spectrum of Fig. 6 using the methods described in Ref. [7]. From a similar NOESY/EXSY spectrum at −80°C a rate constant of ~1 s^{-1} was also estimated (spectrum not shown). Based upon these two estimates, if we assume that the ΔH^* of rotation is similar to those measured for rotation of 2-MeImH and 1,2-Me_2Im on TMPFe(III) and TMPCo(III) (44–51 kJ mol^{-1}), then the extrapolated rate constant for rotation of 1,2-Me_2Im in [TMPFe(1,2-$Me_2Im)_2$] is $k_{ex}(298) \sim 2\times10^4$ s^{-1}. This number is a ficticious one, however, because ligand dissociation and exchange are extremely rapid at room temperature.

In Table 1 are summarized the activation parameters ΔH^*, ΔS^*, ΔG^*_{298} and the rate constants for axial ligand rotation at 25°C for the three metallotetramesitylporphyrinate systems studied herein and those reported previously [7]. As can be seen, axial ligand rotation at room temperature is very rapid on low-spin d^6 Fe(II) and Co(III), as well as low-spin d^5 Fe(III). Of the three, rotation is slowest on Co(III) porphyrinates, though still exceptionally rapid for pyridine and non-hindered imidazole ligands; Fe(III) rates appear to be somewhat slower than those of Fe(II). For a given metalloporphyrinate, rates appear to increase in the order (hindered imidazole) < (pyridine) < (unhindered imidazole), in line with expectations based on the steric demands of hindered ligands as compared to six- and five-membered ring heterocycles.

Two research groups have previously concluded, on the basis of ^{13}C T_1 data, that axial pyridine ligands bound to tetraphenylporphyrinatocobalt(III) do not rotate at all at ambient temperatures [9,10]. The present results, which are based upon conventional dynamic ^{1}H NMR line broadening

Table 1
Activation enthalpies, entropies, room temperature free energies and rate constants for d^6 Co(III) and Fe(II) tetramesitylporphyrinate ligand rotation, and comparison to those of d^5 Fe(III) porphyrinates

Complex	Solvent	$\Delta H^{\ddagger}$ (kJ mol^{-1})	$\Delta S^{\ddagger}$ (J mol^{-1} K^{-1})	$\Delta G^{\ddagger}_{298}$ (kJ mol^{-1})	$k_{ex}(298)$ (s^{-1})	Reference
d^6 Fe(II)						
[TMPFe(4-NMe$_2$Py)$_2$]	toluene-d_8	–[a]	–[a]	–[a]	very fast[a]	this work
[TMPFe(4-CNPy)$_2$]		–[a]	–[a]	–[a]	very fast[a]	this work
[TMPFe(1,2-Me$_2$Im)$_2$]		46 (assumed)	2 (estimated)	48.6 (est.)	$\sim 2\times10^4$	this work
d^6 Co(III)						
[TMPCo(NMeIm)$_2$]$^+$	dichloromethane-d_2	–[a]	–[a]	–[a]	very fast[a]	this work
[TMPCo(4-NMe$_2$Py)$_2$]$^+$		26.2	≥ -60.4	≥ 38.6	$\geq 1.1\times10^6$	this work
[TMPCo(2-MeImH)$_2$]$^+$		48.1	−61.5	66.5	14.4	[7]
[TMPCo(1,2-Me$_2$Im)$_2$]$^+$		43.9	−84.1	69.0	5.1	[7]
d^5 Fe(III)						
[TMPFe(2-MeImH)$_2$]$^+$	dichloromethane-d_2	51.0	2.6	50.2	9.7×10^3	[7]
		54.0	15.5	49.4	1.4×10^4	[4]
[TMPFe(1,2-Me$_2$Im)$_2$]$^+$		52.7	21.8	46.0	5.4×10^4	[4]
[(2,6-Cl$_2$)$_4$TPPFe(2-MeImH)$_2$]$^+$		46.4	3.8	45.2	7.2×10^4	[7]
[(2,6-Br$_2$)$_4$TPPFe(2-MeImH)$_2$]$^+$		49.0	15.1	44.4	10.1×10^4	[7]

[a] Too rapid to be measured by NMR techniques.

data in the fast exchange regime [22], show that the rate of rotation of axial pyridine ligands is exceptionally rapid on the NMR timescale (of either ^{1}H or ^{13}C) at ambient temperatures, and that the rate of pyridine ligand rotation can only be placed on the fast exchange limit of measurement by ^{1}H NMR techniques at temperatures below −50°C. The question immediately arises as to how and why the ^{13}C T_1 data could have been so misleading to the previous workers [9,10]. While we do not have a final, complete answer to this puzzling question, we wish to point out that these tetramesitylporphyrinate, bis-(axial ligand) metal(III) complexes have rotational correlation times, τ_c, that place them very close to the T_1 minimum for ^{1}H at 200 (or 300) MHz at ambient temperatures [29], and not far from the T_1 minimum for ^{13}C. Furthermore, the phase of NOESY cross peaks changes from negative at 21°C (Fig. 2) to positive at −90°C (Fig. 6), indicating that upon change in viscosity the τ_c values of these complexes change enough to move them from the positive NOE regime expected for small molecules to the negative NOE regime expected for large molecules [26]. The rotational correlation time that we have measured for [TMPFe(2-MeImH)$_2$]$^+$ClO$_4^-$ in CD_2Cl_2 at −82°C from proton NOE buildup curves (3.3 ns) [29] is more than a factor of 25 longer than that estimated for [TPPCo(Py)$_2$]$^+$BF$_4^-$ in CD_2Cl_2 from ^{13}C T_1s at room temperature [9]. When the difference in η/T at the temperatures of the two measurements is accounted for, our τ_c is still a factor of 5.7 longer than that reported previously [9] (though for a slightly larger porphyrinate complex), and the previous value is unreasonably short for an ion pair whose diameter is of the order of 17.5 Å or so. In addition, solvation of Co(III) porphyrinate complexes having the BF$_4^-$ anion may be stronger than for the same Fe(III) porphyrinates having the ClO$_4^-$ anion, thus creating a larger effective size of the rotating complex [7]. Thus, at the 50 MHz ^{13}C frequency used previously it is likely that the [TPPCo(Py)$_2$]$^+$BF$_4^-$ complex is extremely close to the T_1 minimum, and it is thus likely that very minor effects that are difficult to pinpoint could cause the ^{13}C T_1s of *o*- and *m*-C resonances of axial pyridine ligands to be very similar to that of the *p*-C resonance, thus leading to the incorrect conclusion that the axial ligands were not rotating. In any case, the present dynamic ^{1}H NMR results are incontrovertible: pyridine (and non-hindered imidazole) ligand rotation on Co(III) tetraphenylporphyrinates is exceptionally rapid at ambient temperatures, and, based upon an estimate of the rate of rotation of 1,2-dimethylimidazole on [TMPFe(1,2-Me$_2$Im)$_2$] at −90°C, the rates of ligand rotation on Fe(II) porphyrinates are approximately four orders of magnitude faster than those on Co(III) porphyrinates.

Acknowledgements

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