COMMUNICATIONS

Water Exchange Controls the Complex-Formation Mechanism of Water-Soluble Iron(III) Porphyrins: Conclusive Evidence for Dissociative Water Exchange from a High-Pressure ^{17}O NMR Study[**]

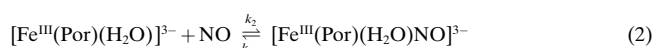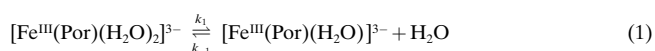Thorsten Schneppensieper, Achim Zahl, and Rudi van Eldik*

Transition metal porphyrins have received considerable attention from many groups, especially as a result of their catalytic activity in various oxidation processes.[1–3] Of fundamental interest is their high reactivity coupled to the ability to undergo fast ligand-substitution reactions and the redox cycling that forms an essential aspect of their solution-phase chemistry.[4–6] The investigated iron porphyrins are known to be model complexes for a number of enzymes and proteins. These heme proteins serve a wide-range of functions, and the nature of the axial ligand on the iron is thought to play a key role in controlling the properties of the heme proteins. Of particular interest are the oxidizing enzymes peroxidases, cytochrome P-450's, and catalases.[7, 8] In addition, various reports point to the important role of the metalloporphyrins such as cytochrome oxidase,[9] nitrile hydrase,[10] and catalase[11] as target molecules in mammalian biology. Mechanistic studies on and the substitution behavior of various metalloporphyrins have been reviewed.[12, 13]

In 1980 Hunt and co-workers[14] studied the water-exchange reactions of two water-soluble Fe^{III} porphyrins using ^{17}O NMR spectroscopic techniques. Both complexes, meso-tetrakis(N-methyl-4-pyridyl)porphine (H$_2$TMPyP) and meso-tetrakis(p-sulfonatophenyl)porphine (H$_2$TPPS), exhibited water-exchange reactions that are several orders of magnitude faster than aquated Fe^{III} ions in acidic medium.[15] These complexes were considered to be model compounds for aqueous porphyrin chemistry, since in aqueous solution the axial interaction of water with the metal is of fundamental importance in both ligand-substitution and redox processes. The fast water-exchange reactions were characterized by significantly positive activation entropies, but no mechanistic conclusions were drawn from this data.[14]

In the meantime, the application of high-pressure kinetic techniques has contributed significantly towards the elucidation of inorganic reaction mechanisms in general,[16] and that of solvent-exchange processes on transition metal centers in particular.[17] As far as we know, no studies have been performed on water-exchange reactions of water-soluble porphyrin complexes using high-pressure NMR spectroscopic techniques. Some mechanistic information on such reactions was obtained indirectly from the effect of pressure on ligand-substitution reactions of complexes of the type [M(TPPS)(H$_2$O)$_2$]$^{3-}$ and [M(TMPyP)(H$_2$O)$_2$]$^{5+}$, where M = Co^{III}, Rh^{III}, and Cr^{III}.[18–20] In these reactions the rapid substitution of water by thiourea and thiocyanate was characterized by significantly positive volumes of activation, from which a dissociative ligand-substitution mechanism was concluded. However, a clear distinction between a dissociative interchange (I$_d$) or a limiting dissociative (D) mechanism was not possible.

Quite recently, with the aid of laser flash-photolysis techniques, Ford and co-workers[21] studied the reversible binding of NO to [Fe^{III}(TPPS)(H$_2$O)$_2$]$^{3-}$ and [Fe^{III}(TMPS)(H$_2$O)$_2$]$^{3-}$, (H$_2$TMPS = meso-tetrakis(sulfonatomesityl)porphine). They suggested a dissociative mechansim on the basis of significantly positive volumes of activation found for both the "on" and "off" reactions. Their mechanistic interpretation of the data followed the concept of a dissociative (D) mechanism and consisted of reaction steps (1) and (2), Por = porphyrin.

$$[Fe^{III}(Por)(H_2O)_2]^{3-} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} [Fe^{III}(Por)(H_2O)]^{3-} + H_2O \qquad (1)$$

$$[Fe^{III}(Por)(H_2O)]^{3-} + NO \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} [Fe^{III}(Por)(H_2O)NO]^{3-} \qquad (2)$$

Under the selected experimental conditions, $k_{on} = k_1 k_2 [NO]/k_{-1}$ and $k_{off} = k_{-2}$. The effect of pressure on k_{on} resulted in positive activation volumes, $+13 \pm 1$ and $+8.3 \pm 1.5$ cm^{3}mol^{-1}, for por = TMPS and TPPS, respectively, underlining the overall dissociative nature of the binding reaction. The complexity of the rate expression for k_{on}, however, did not allow a more detailed interpretation since $\Delta V^{\ddagger}(k_{on}) = \Delta V^{\ddagger}(k_1) + \Delta V^{\ddagger}(k_2) - \Delta V^{\ddagger}(k_{-1})$. The authors argued, as in the cases mentioned above,[18–20] that $\Delta V^{\ddagger}(k_2) - \Delta V^{\ddagger}(k_{-1})$ is expected to be small as a result of the rapid binding of NO and H$_2$O, respectively, such that $\Delta V^{\ddagger}(k_{on})$ mainly presents $\Delta V^{\ddagger}(k_1)$.

We have now studied the water-exchange reactions of [Fe^{III}(TPPS)(H$_2$O)$_2$]$^{3-}$ (**1**), [Fe^{III}(TMPyP)(H$_2$O)$_2$]$^{5+}$ (**2**), and [Fe^{III}(TMPS)(H$_2$O)$_2$]$^{3-}$ (**3**), that is, reaction (1), in more detail using high-pressure ^{17}O NMR spectroscopic techniques.
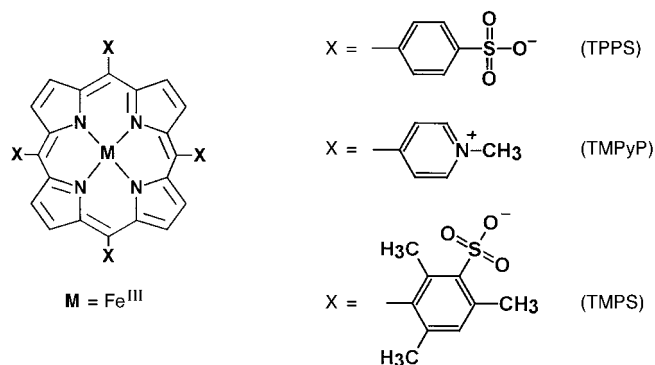
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The selected porphines TPPS, TMPyP, and TMPS vary in steric hindrance and charge, and thus allow the influence of these factors on the water-exchange process to be studied. The results clearly support the operation of a dissociative mechanism in all cases and enable a more detailed interpretation of the activation volumes reported for the complex-formation reactions mentioned above.

Temperature dependence: An analysis of the data for the three investigated porphyrins (see Figures 2–4 in the Supporting Information) gave the activation parameters summarized in Table 1. The fastest exchange rates are observed for the negatively charged $[Fe^{III}(TMPS)(H_2O)_2]^{3-}$ and $[Fe^{III}(TPPS)(H_2O)_2]^{3-}$ complexes, with $k_{ex} = (2.1 \pm 0.1) \times 10^7$ s^{-1} and $k_{ex} = (2.0 \pm 0.1) \times 10^6$ s^{-1} at 298 K, respectively. The decrease in rate constant for the TPPS complex is associated with an increase in ΔH^+ from 61 ± 1 kJ mol^{-1} to 67 ± 2 kJ mol^{-1}. The positive charged porphyrin $[Fe^{III}(TMPyP)(H_2O)_2]^{5+}$ is less labile with $k_{ex} = (4.5 \pm 0.1) \times 10^5$ s^{-1} at 298 K, for which ΔH^+ increases further to 71 ± 2 kJ mol^{-1}. For all the investigated porphyrins almost an identical entropy of activation, 100 ± 10 J K^{-1} mol^{-1}, was found. This large positive value suggests that a dissociative water-exchange mechanism is operative in all cases.

By way of comparison, Hunt and co-workers[14] found significantly lower, but almost equal values for the activation enthalpy for the oppositely charged complexes of TPPS and TMPyP. In addition, they found k_{ex} to be 20 times larger for the TPPS than for the TMPyP complex. These differences were ascribed to an entropic effect since their values for the activation entropy differed significantly. The data of Hunt and co-workers[14] were calculated under the assumption that only one water molecule is coordinated to the metal center in both systems. However, according to data published later, two water molecules are bound to the TMPS[22] and TPPS, as well as to the TMPyP[23] complexes in an octahedral coordination geometry. This assumption could have led to deviations in the reported rate and activation parameters, since the number of coordinated water molecules affects the data calculation. In addition, as a 400 MHz NMR spectrometer was employed in our study more accurate data can be expected.

On the basis of our data, steric hindrance on the porphyrin increases k_{ex} by a factor of 10, as expected for the effect of steric decompression on a dissociative activation process, whereas the positively charged TMPyP complex has an exchange rate that is approximately 50 times lower than that of the TMPS complex. That k_{ex} for the negatively charged complexes is significantly higher than for the TMPyP system,

suggests that the crucial factor for the exchange rate, besides the steric decompression, is the negatively charged peripheral substituents that increase the electron density on the metal center and labilize the axial metal–ligand (water) bonds.

Pressure dependence: From the temperature-dependence data, appropriate temperatures were selected for the pressure-dependence measurements. Plots of $\ln(1/T_{2r})$ versus pressure for all three $[Fe^{III}(Por)(H_2O)_2]$ complexes are shown in Figure 1. In all cases, the plots are linear within the experimental error limits and the volume of activation could be calculated directly from the slope ($= -\Delta V^+/RT$). Very similar values are obtained for complexes **1** and **2**, $\Delta V^+ = +7.9 \pm 0.2$ and $+7.4 \pm 0.4$ cm^3 mol^{-1}, respectively, compared to the significantly higher value of $+11.9 \pm 0.3$ cm^3 mol^{-1} for the sterically demanding complex **3** (see Table 1).
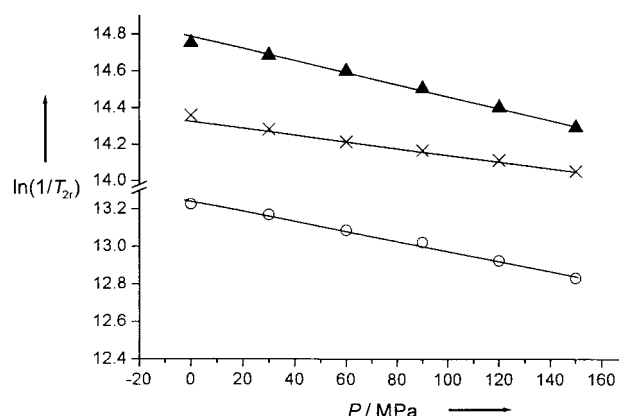

Figure 1. Pressure dependence of T_{2r} for water exchange on $[Fe^{III}(TPPS)(H_2O)_2]^{3-}$ (○, 288 K), $[Fe^{III}(TMPYP)(H_2O)_2]^{5+}$ (×, 318 K), and $[Fe^{III}(TMPS)(H_2O)_2]^{3-}$ (▲, 279 K). For experimental conditions see Figures 2–4 in the Supporting Information.

It follows that the opposite charges on complexes **1** and **2** do not affect the substitution mechanism of coordinated water, and the reported ΔV^+ data support the operation of a dissociative interchange (I_d) mechanism.[16, 17] The introduction of steric hindrance through the bulky mesityl groups on complex **3** enhances the water-exchange rate, and the more positive ΔV^+ value suggests that substitution of coordinated water follows a limiting dissociative (D) mechanism. In fact, the reported value of $+11.9 \pm 0.3$ cm^3 mol^{-1} in the latter case is very close to the limiting value of $+13$ cm^3 mol^{-1} predicted for water exchange on an octahedral metal complex following a limiting dissociative mechanism.[17, 24, 25] This means that the

Table 1. Rate and activation parameters for water-exchange reactions of iron(III) porphyrin complexes. The errors shown are standard deviations given by the computer program.

	k_{ex}^{298} [s^{-1}]	ΔH^+ [kJ mol^{-1}]	ΔS^+ [J K^{-1} mol^{-1}]	ΔV^+ [cm^3 mol^{-1}]	k_{ex}[a] [s^{-1}]	Ref.
$[Fe(TPPS)(H_2O)_2]^{3-}$ **1**	$(2.0 \pm 0.1) \times 10^6$	67 ± 2	99 ± 10	$+7.9 \pm 0.2$[b]	$7.5 \times 10^5 / 8.5 \times 10^5$	this work
	$(1.4 \pm 0.01) \times 10^7$	57.3 ± 0.4	84.5 ± 1.3	–	–	[14]
$[Fe(TMPyP)(H_2O)_2]^{5+}$ **2**	$(4.5 \pm 0.1) \times 10^5$	71 ± 2	100 ± 6	$+7.4 \pm 0.4$[c]	$2.1 \times 10^6 / 2.7 \times 10^6$	this work
	$(7.8 \pm 0.1) \times 10^5$	57.7 ± 0.4	61.5 ± 1.3	–	–	[14]
$[Fe(TMPS)(H_2O)_2]^{3-}$ **3**	$(2.1 \pm 0.1) \times 10^7$	61 ± 1	100 ± 5	$+11.9 \pm 0.3$[d]	$3.8 \times 10^6 / 3.9 \times 10^6$	this work

[a] For comparison with the value of k_{ex} from the temperature-dependence data at normal pressure, the value of k_{ex} from the pressure-dependence data was extrapolated to normal pressure at the temperature at which ΔV^+ was determined. [b] Measured at 288 K. [c] Measured at 318 K. [d] Measured at 279 K.

degree of bond cleavage in the transition state is significantly higher for complex **3** than in **1** and **2**.

Returning to the motivation for this work, our results on the water-exchange mechanism of the porphyrins studied are in excellent agreement with the mechanistic interpretation offered by Ford and co-workers[21] for the complex-formation reactions of **1** and **3** with NO. Their reported activation volumes of $+8.3 \pm 1.5$ and $+13 \pm 1$ cm^{3}mol^{-1} for these reactions, respectively, are almost identical to those reported for the water-exchange reactions in the present study. Their conclusion that the observed $\Delta V^{\pm}$ for the "on" reaction with NO mainly represents $\Delta V^{\pm}(k_1)$ for reaction (1), is perfectly correct as shown by the data reported here. Thus the formation of **1** and **3** is not only controlled by the rate but also by the mechanism of the water-exchange process. Depending on the structural and electronic situation this process tends to occur according to an I$_d$ or D mechanism, the complex-formation reactions with nucleophiles such as NO follow the same mechanism.

The water-exchange rate and associated activation enthalpy of iron(III) porphyrins are significantly affected by the charge on the porphine and to a lesser degree by steric compression. The mechanism of the process, however, is controlled by steric factors and varies between a dissociative interchange and a limiting dissociative mechanism. Thus the lability of the axial-bound solvent molecules in these systems plays a key role in the mechanism and substitution behavior of porphyrin- and heme-based systems. High-pressure NMR spectroscopic techniques present a powerful tool to add to the mechanistic understanding of such processes, which could lead to a more profound understanding of the reactions and processes in biologically relevant macrocyclic systems such as metmyoglobin and cytochrome P-450.

Experimental Section

Na$_3$[Fe^{III}(TPPS)(H$_2$O)$_2$] (Na$_3$-**1**) was synthesized as described elsewhere.[26] [Fe^{III}(TMPyP)(H$_2$O)(OH)](pts)$_4$ (**2**-pts$_4$), where pts = *p*-toluenesulfonate, and Na$_3$[Fe^{III}(TMPS)(H$_2$O)$_2$] (Na$_3$-**3**) were purchased from Frontier Scientific Ltd. Fine Chemicals Utah, USA, and used without further purification. Ca. 20% enriched ^{17}O-labeled water (D-Chem Ltd. Tel Aviv, Israel) was used for the ^{17}O NMR water-exchange measurements. NaClO$_4$ (Aldrich) was used to adjust the ionic strength to 0.5 M, and HClO$_4$ (**1** and **3**) and tosylic acid (**2**) were used to adjust the pH of the solution. No salt was added in the case of **2** to avoid precipitation. The porphyrin samples were prepared by combining weighted amounts of salt, perchloric or tosylic acid, and water. The resulting solution was transferred to the NMR tube. The pH was determined on identical samples prepared in ordinary water. The water exchange measurements were performed at pH 3 (for **1** and **3**) and pH 1.1 (for **2**), where only the monomeric aqua forms of the porphyrins are present in solution. The complex concentrations were 3.4×10^{-2} M (**1**), 2.0×10^{-2} M (**2**), and 3.0×10^{-2} M (**3**).

[1] A. P. Hong, D. W. Bahnemann, M. R. Hoffmann, *J. Phys. Chem.* **1987**, *91*, 6245.
[2] B. Meunier, *Chem. Rev.* **1992**, *92*, 1411.
[3] G. Behra, L. Sigg, *Nature* **1990**, *344*, 419.
[4] V. Lepentsiotis, R. van Eldik, *J. Chem. Soc. Dalton Trans.* **1998**, 999.
[5] V. Lepentsiotis, R. van Eldik, F. F. Prinsloo, J. J. Pienaar, *J. Chem. Soc. Dalton Trans.* **1999**, 2759.
[6] J. Lee, J. A. Hunt, J. T. Groves, *J. Am. Chem. Soc.* **1998**, *120*, 7493.
[7] H. B. Dunford, *Adv. Inorg. Chem.* **1982**, *4*, 41.
[8] Y. Watanabe, J. T. Groves, *The Enzymes*, Vol. 20, Academic Press, San Diego, CA, **1992**, p. 405.
[9] M. W. J. Cleeter, J. M. Cooper, V. M. Darley-Usmar, S. Moncada, A. H. V. Scapira, *FEBS Lett.* **1994**, *345*, 50.
[10] T. Noguchi, J. Honda, T. Nagamune, H. Sasabe, Y. Inoue, I. Endo, *FEBS Lett.* **1995**, *358*, 9.
[11] G. C. Brown, *Eur. J. Biochem.* **1995**, *232*, 188.
[12] D. K. Lavallee, *Coord. Chem. Rev.* **1985**, *61*, 55.
[13] M. Hoshino, L. Laverman, P. C. Ford, *Coord. Chem. Rev.* **1999**, *187*, 75.
[14] I. J. Ostrich, G. Liu, H. W. Dodgen, J. P. Hunt, *Inorg. Chem.* **1980**, *19*, 619.
[15] T. W. Swaddle, A. E. Merbach, *Inorg. Chem.* **1981**, *20*, 4212.
[16] a) A. Drljaca, C. D. Hubbard, R. van Eldik, T. Asano, M. V. Basilevsky, W. J. le Noble, *Chem. Rev.* **1988**, *98*, 2167; b) R. van Eldik, C. Dücker-Benfer, F. Thaler, *Adv. Inorg. Chem.* **2000**, *49*, 1.
[17] L. Helm, A. E. Merbach, *Coord. Chem. Rev.* **1999**, *187*, 151.
[18] S. Funahashi, M. Inamo, K. Ishihara, M. Tanaka, *Inorg. Chem.* **1982**, *21*, 447.
[19] J. G. Leipoldt, R. van Eldik, H. Kelm, *Inorg. Chem.* **1983**, *22*, 4146.
[20] G. J. Lamprecht, J. G. Leipoldt, T. W. Swaddle, *Inorg. Chim. Acta* **1987**, *129*, 21.
[21] L. E. Laverman, M. Hoshino, P. C. Ford, *J. Am. Chem. Soc.* **1997**, *119*, 12663.
[22] S.-H. Cheng, Y.-S. Chen, Y. O. Su, *J. Chin. Chem. Soc.* **1991**, *38*, 15.
[23] M. Ivanca, A. G. Lappin, W. R. Scheidt, *Inorg. Chem.* **1991**, *30*, 711.
[24] F. P. Rotzinger, *J. Am. Chem. Soc.* **1997**, *119*, 5230.
[25] M. Hartmann, T. Clark, R. van Eldik, *J. Phys. Chem. A* **1999**, *103*, 9899.
[26] E. B. Fleischer, J. M. Palmer, T. S. Srivastava, A. Chatterjee, *J. Am. Chem. Soc.* **1971**, *93*, 3162.

Controlling the Lability of Square-Planar Pt^{II} Complexes through Electronic Communication between π-Acceptor Ligands**

Deogratius Jaganyi, Andreas Hofmann, and Rudi van Eldik*

Dedicated to Professor Ernst-G. Jäger on the occasion of his 65th birthday

Studies on the substitution mechanism of low-spin d^8 square-planar complexes for many years centered around the σ *trans* influence or *trans* effect.[1] For Pt^{II} complexes this has involved detailed systematic studies of different *trans* groups[2] using a range of different nucleophiles.[3] Mechanistic studies established that ligand-substitution reactions of Pt^{II} complexes mainly occur by an associative process involving a trigonal-bipyramidal intermediate. In recent years, volumes of activation ($\Delta V^{\pm}$) obtained from high-pressure kinetic measurements, have been used in distinguishing mechanistic pathways of substitution reactions; negative values indicating

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