J|A|C|S
COMMUNICATIONS

Water Exchange on Manganese(III) Porphyrins. Mechanistic Insights Relevant for Oxygen Evolving Complex and Superoxide Dismutation Catalysis

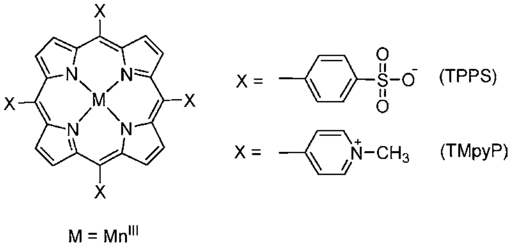
Dominik Lieb, Achim Zahl, Tatyana E. Shubina, and Ivana Ivanović-Burmazović*

Friedrich-Alexander-Universität Erlangen-Nürnberg, Department Chemie und Pharmazie,
Egerlandstr. 1, 91058 Erlangen, Germany

Received February 19, 2010; E-mail: ivana.ivanovic@chemie.uni-erlangen.de

Water exchange on metal cations is the essential process that determines their overall reactivity in aqueous media and tunes the redox activity of transition metal centers in particular.[1] Therefore, the water exchange behavior of a range of aqua-metal complexes has been investigated[2] and continues to be an active research area.[3] Interestingly, in the case of manganese there are only a few complexes that have been experimentally studied so far and all of them contain the Mn^{II} center.[4] Data for water exchange on Mn^{III} are desirable due to involvement of the Mn^{III} center in enzymatic[5] and nonenzymatic redox catalysis.[6] The kinetic parameters and mechanistic picture of the water exchange process on a Mn^{III} model system would especially provide valuable insights into the elementary reaction steps within the water splitting cycle of the Photosystem II (PSII) oxygen evolving complex (OEC) and superoxide dismutation (SOD) by manganese centers.

Chart 1. Manganese(III) Porphyrins Studied for Water Exchange



In this work the rate constants and the activation parameters for the water exchange process on Mn^{III} centers have been experimentally determined using ^{17}O NMR techniques. For the investigations Mn^{III} porphyrin complexes $[Mn^{III}(TPPS)S_2]^{n-}$ and $[Mn^{III}(TMpyP)S_2]^{n+}$ (Chart 1; S = H_2O and/or OH^-) have been selected due to their high solution stability in a wide pH range,[7] enabling the measurements of water exchange in the case of both diaqua and aqua-hydroxo complexes (Scheme 1). To obtain a better mechanistic understanding of these reactions we performed, for the first time, high-pressure NMR measurements on Mn^{III} systems,[8] where the solution stability of the selected complexes plays a crucial role as well. These complexes are also interesting since water-soluble Mn^{III} porphyrins are known as SOD mimics.

Scheme 1

$$[Mn^{III}(P)(H_2O)_2]^{z} + H_2O^* \xrightleftharpoons{k_{ex}} [Mn^{III}(P)(H_2O)(H_2O)^*]^{z} + H_2O \quad (1)$$

$$[Mn^{III}(P)(H_2O)OH]^{z-1} + H_2O^* \xrightleftharpoons{k_{ex}} [Mn^{III}(P)(H_2O^*)OH]^{z-1} + H_2O \quad (2)$$

The variable-temperature ^{17}O NMR line broadening measurements[8,9] resulted in the exchange rates (k_{ex}) and corresponding activation enthalpies ($\Delta H^{\ddagger}$) and activation entropies ($\Delta S^{\ddagger}$), as illustrated in Figure 1 for $[Mn^{III}(TMpyP)(H_2O)OH]^{4+}$ and summarized in Table 1. pH values were selected to facilitate the predominant existence of either diaqua (at pH 2) or aqua-hydroxo (at pH 10) forms of the studied complexes.[10] From the temperature dependence data appropriate temperatures were selected for the pressure dependence measurements.[8] In all cases, plots of $\ln(k_{ex})$ versus pressure (Figure 2) were linear within experimental error[8] and the volumes of activation were calculated directly from the slope ($= -\Delta V^{\ddagger}/RT$; Table 1). $\Delta V^{\ddagger}$ values are of especial significance because they can give a more precise indication of the intimate nature of the reaction mechanism, since $\Delta S^{\ddagger}$ values are in general intrinsically subjected to large errors due to the inherent extrapolation involved in their determination.[11]

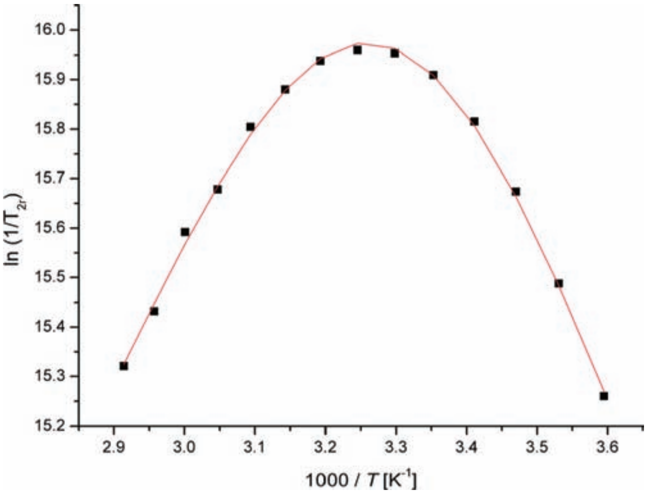


Figure 1. Temperature dependence of T_{2r} for water exchange on $[Mn^{III}(TMpyP)(H_2O)OH]^{4+}$ at pH 10. For complete experimental data see Figure S4.

The obtained water exchange rates (Table 1) are significantly faster than what would be expected for trivalent metal ions[12a,b] and are almost identical to the corresponding rate (k_{ex}) in the case of $[Mn(H_2O)_6]^{2+}$.[2] This high lability of the axially bound water can be explained by the *cis*-effect of porphyrin ligands and by the Jahn–Teller distortion in the d^4 high-spin electronic configuration of Mn^{III}. By way of comparison, the water exchange on the analogous Fe^{III} porphyrins is ca. 1 order of magnitude slower than that on Mn^{III} ($k_{ex} = (2.0 \pm 0.1) \times 10^6\ s^{-1}$ and $k_{ex} = (4.5 \pm 0.1) \times 10^5\ s^{-1}$ for $[Fe^{III}(TPPS)(H_2O)_2]^{3-}$ and $[Fe^{III}(TMpyP)(H_2O)_2]^{5+}$, respectively),[13] which is in agreement with the significantly longer metal–OH_2 bond found in $[Mn^{III}(TMpyP)(H_2O)_2]^{5+}$ (2.221 Å)[14] than in $[Fe^{III}(TMpyP)(H_2O)_2]^{5+}$ (2.086 Å)[15], respectively. Consequently, it seems that the Jahn–Teller effect is the predominant one and as such controls the exchange process and general substitution behavior of the Mn^{III} center.

10.1021/ja1014585

Table 1. Rate and Activation Parameters for Water Exchange on Manganese(III) Porphyrins (Errors are Standard Deviations)

	pH	k_{ex} [s^{-1}] (at 298 K)	$\Delta H^‡$ [kJ mol^{-1}]	$\Delta S^‡$ [J mol^{-1} K^{-1}]	$\Delta V^‡$ [cm^3 mol^{-1}]
$[Mn^{III}(TPPS)(H_2O)_2]^{3-}$	2	$(1.4 \pm 0.1) \pm 10^7$	32.7 ± 1.1	1.65 ± 3.9	2.9 ± 0.2 (at 308 K)
$[Mn^{III}(TPPS)(H_2O)OH]^{4-}$	10	$(2.5 \pm 0.7) \pm 10^7$	24.1 ± 2.0	-22.7 ± 9.9	5.7 ± 0.3 (at 308 K)
$[Mn^{III}(TMpyP)(H_2O)_2]^{5+}$	2	$(1.0 \pm 0.1) \pm 10^7$	40.7 ± 7.2	45.3 ± 5.0	2.2 ± 0.2 (at 283 K)
$[Mn^{III}(TMpyP)(H_2O)OH]^{4+}$	10	$(1.5 \pm 0.1) \pm 10^7$	33.9 ± 0.1	5.8 ± 2.0	0.5 ± 0.2 (at 283 K)

This is also demonstrated by the fact that the oppositely charged complexes of TPPS and TMpyP are equally labile, with the negligible faster exchange in the case of a negatively charged complex at a corresponding pH (Table 1). In the analogous Fe^{III} porphyrins, the negatively charged peripheral substituents of the porphyrin ring strongly influence the lability of the $Fe-OH_2$ bonds.[13] However, the already significantly elongated $Mn^{III}-OH_2$ bond does not appear to be effected by the charge of the peripheral substituents. This is also supported by our DFT calculations (OLYP/6-31G*)[8] which show only a slight difference in an average $Mn^{III}-OH_2$ bond found for a positively charged model porphyrin with protonated pyridine groups (2.446 Å) and for a simple model without any substituents on the porphyrin ring (2.437 Å). Although the water molecule *trans* to the coordinated hydroxide is expected to be much more labile, the aqua-hydroxo species of the studied Mn^{III} porphyrins have just slightly higher exchange rates than the corresponding diaqua species (Table 1). In the case when some other effects induce a prominent ground-state labilization, as the Jahn−Teller effect demonstrated by the significantly long $Mn^{III}-OH_2$ bond in our case (*vide supra*), the extent of *trans* labilization due to OH^- is usually negligible.[16] It seems that the *trans*-effect of the hydroxo group is minor in comparison to axial ligand labilization induced by the Jahn−Teller distortion on Mn^{III}.

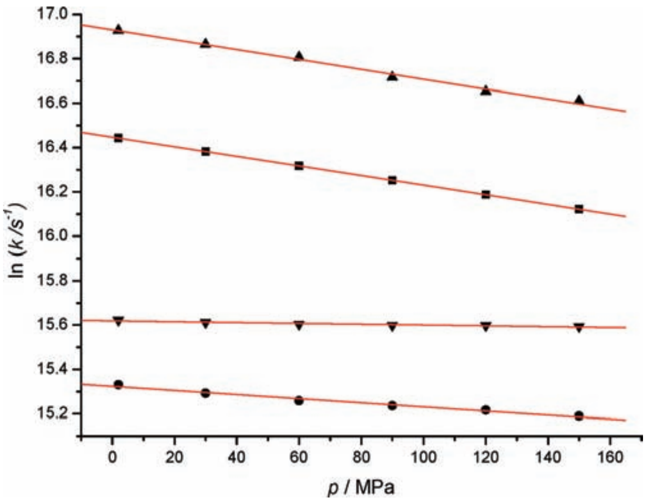


Figure 2. Pressure dependence of the water-exchange rate for (■) $[Mn(TPPS)(H_2O)_2]^{3-}$, (▲) $[Mn(TPPS)(H_2O)OH]^{4-}$ (308.2 K), (●) $[Mn(TMpyP)(H_2O)_2]^{5+}$, (▼) $[Mn(TMpyP)(H_2O)OH]^{4+}$ (283.2 K).

Since the effective charge on the metal center is more responsible for its lability than its formal +3 charge, we have calculated the effective charges for the diaqua and aqua-hydroxo species.[8] The significantly lower positive charge on the manganese center (ca. +1.5 for diaqua, almost independent of the used model/method; +1.4 for aqua-hydroxo)[8] contributes to its substitution lability as well.[17a]

Moderate to small values of $\Delta H^‡$ and $\Delta S^‡$ (Table 1) are an indication that an interchange water exchange mechanism is operative in all cases, independent of the complex charge and the nature of the axial ligand. The volume of activation offers clearer mechanistic insights, and its small positive values (Table 1) suggest that substitution of coordinated water follows a dissociative interchange (I_d) to a pure interchange (I) mechanism. The latter operates in the case of $[Mn^{III}(TMpyP)(H_2O)(OH)]^{4+}$ ($\Delta V^‡ = 0.5 \pm 0.2$ cm^3/mol), where, most probably, the already strongly elongated $Mn^{III}-OH_2$ bond in the ground state does not require a dissociative path for the exchange process. It should be mentioned that Cr^{II}, with the same $3d^4$ electron configuration, also undergoes very fast solvent exchange (1.2×10^8 s^{-1} for $Cr(CH_3OD)_6^{2+}$ at 298 K) with very similar activation parameters ($\Delta H^‡ = 29$ kJ mol^{-1} and $\Delta S^‡ = 17$ J mol^{-1} K^{-1}).[18] In general it follows that the substitution of coordinated water on the studied Mn^{III} porphyrins goes through a seven-coordinate transition state. By way of comparison, for the analogous Fe^{III} porphyrins, much larger $\Delta H^‡$ (ca. 70 kJ mol^{-1}) and more positive $\Delta S^‡$ (100 ± 10 J mol^{-1} K^{-1}) and $\Delta V^‡$ (ca. + 8 cm^3 mol^{-1}) values were obtained providing evidence for a dissociative water-exchange mechanism.[13]

The small positive volumes of activation are also consistent with the strong ground-state labilization induced by the Jahn−Teller effect. In the case of such strong labilization, the lower activation barrier (Table 1) will induce an “early” (reactant-like) transition state along the reaction coordinate of the volume profile, characterized by the small absolute magnitude of the volume of activation.[16]

The $[Mn^{III}(TMpyP)(H_2O)_2]^{5+}$ complex possesses SOD activity with an apparent catalytic rate constant of approximately $k_{cat} = 1 \times 10^7$ M^{-1} s^{-1} (at 21 °C).[6b] The herein observed corresponding second-order exchange rate constant ($k_{ex}/[H_2O] = 1.36 \times 10^5$ M^{-1} s^{-1} at 21 °C, obtained from our temperature dependence data; see Table S4) is much lower than k_{cat}. In terms of a possible inner-sphere catalytic pathway, it means that water release cannot be a rate-determining step and that incoming superoxide plays a role in the overall substitution process. This is in accordance with an interchange character of the water substitution on the studied Mn^{III} porphyrins, similar to what we found previously for seven-coordinate pentaazamacrocyclic Mn^{II} SOD mimics.[4a]

In addition to experimental[12] and theoretical[17] studies on the OEC, investigations of ligand exchange in model complexes can help to reveal the nature of the water-derived substrates and their binding sites within the OEC.[19] Thus, our results also offer valuable information for further interpretation of the water substrate binding measurements in photosystem II that show different exchange rates with bulk ^{18}O-water of the two substrate water molecules.[12a−d,17a] The magnitude of the herein determined exchange rates on Mn^{III} supports, in general, the postulation that the fast-exchanging water is bound to a Mn ion, whereas the slowly exchanging water is associated with Ca^{II}.[12a−d,17a] However, there is a considerable discrepancy between the rates of 10^7 s^{-1} (Table 1) and those for PSII (ca. 10^2 s^{-1} for the fast exchanging site).[12a−d] A difference could be expected because the Mn_4Ca cluster of OEC does not contain a porphyrin but a carboxylate amino acid (besides one histidine), oxo and hydroxo ligands.[12e] However, those ligands would not decrease the lability of Mn^{III} for at least 5 orders of magnitude, rather the opposite. In the case of the corresponding Fe^{III} complexes it is known that those with carboxylate ligands (both six- and seven-coordinate EDTA type complexes)[20a] exhibit approximately 1 order of magnitude faster water exchange than the porphyrin complexes.[13] Carboxylate groups induce similar labilization in the case of Mn^{II} when compared to $[Mn(H_2O)_6]^{2+}$ and pentaazamacrocyclic complexes.[4] At the same time oxo ligands enhance the reactivity of the bound waters as well. Bridging μ_3-O in the oxo-centered carboxylate-bridged metal(III) trimers of Ru, Rh, and Cr and the terminal oxo group in $VO(OH_2)_5^{2+}$ accelerate the terminal water exchange for several orders of magnitude.[20b] The labilization effect of the oxo ligand is stronger than that of the terminal and bridging hydroxo groups in the Rh^{III} case,[16] whereas in the more labile Cr^{III} systems the O^{2-}, terminal, and bridging OH^- groups are all comparable in terms of their effect on the rate of bound water exchange.[20c] Thus, the difference between the ligand systems in the studied complexes and the OEC cannot be the reason for the significantly slower exchange rates observed in the latter case. One might speculate that the water is either not bound along the Jahn−Teller axis or is bound as a (hydr)oxo or to Mn^{IV}.[21] The latter option seems interesting, since it is known that Cr^{III} (isoelectronic to Mn^{IV}) and its oligomers can be converted from quite inert to relatively labile ions by increasing the OH^-/Cr^{III} ratio independent of the terminal or bridging nature of OH^- groups.[20c] For example, rates of $\sim 10^2\ s^{-1}$ were postulated, for both water exchange and intramolecular OH-bridge formation, for ions with a OH^-/Cr^{III} ratio of 3.[20c] Since Mn^{IV} is expected to be less labile than Cr^{III}, similar H_2O and OH^- exchange rates might be achieved with more than three O^{2-}, OH^- or $-COO^-$ groups per Mn center as spectator ligands. Although hydroxo groups coordinated to Mn^{III} were not found to exchange with the bulk solvent because they are substitution inert on the time scale of our experiments, they will certainly exchange significantly faster than on Mn^{IV}. However, it is difficult to speculate how many O^{2-}, OH^-, or $-COO^-$ groups per Mn center would be able to tune the OH^- exchange rate on Mn^{III} to be $\sim 10^2\ s^{-1}$. Regarding the oxo form of substrate water binding, it is known that both μ_3-O and μ_2-O bridges in $Mn^{III}Mn_3^{IV}$-oxo cubane and di-μ-oxo $Mn_2^{III/IV\ (IV/IV)}$ dimers, respectively, exhibit a quite slow exchange (ca. $10^{-5}\ s^{-1}$ for μ_3-O and $10^{-7}-10^{-3}\ s^{-1}$ for μ_2-O) and they were not considered as appropriate binding modes for the fast isotope exchange in the OEC.[19] The presence of terminally bound water and labile Mn^{III} accelerates μ_2-oxo exchange up to $\sim 10^{-3}\ s^{-1}$, but the presence of negative carboxylate or phosphate groups seems to be ineffective.[19] Despite all these effects, the protein environment with a specific hydrogen bond network, regional polarizability, steric situation, and substrate diffusion might significantly modulate the mechanism of water binding. A well structured hydrogen bond network with an aqua-ligated Ca moiety nearby the Mn center could decrease the exchange rate by partial deprotonation of the substrate molecule. It is also known from the μ-O exchange in ribonucleotide reductase that the protein environment can decrease the rate of ligand exchange 10^4 times compared to inorganic model complexes.[19b]

In summary of the above discussion, $Mn^{III}-H_2O$ can emerge as the substrate binding mode for the fast exchanging site in PSII only if a prominent deceleration (ca. 10^5 times) by a protein environment is enabled. Labilization by coordination of O^{2-}, OH^-, or $-COO^-$ can facilitate operation of the $Mn^{IV}-(H)OH$ binding mode, but a protein deceleration effect would not be desirable, whereas for the $Mn^{III}-OH$ case most probably both effects would be required. A μ-O binding side is very unlikely for the fast exchanging substrate.

In conclusion, we have experimentally demonstrated by a high-pressure ^{17}O NMR study that water exchange on Mn^{III} porphyrins is a fast process of an I_d to I mechanism, strongly influenced by a Jahn−Teller effect and as such almost independent of a porphyrin charge and a *trans* ligand. The obtained results are valuable for revealing the kinetic and mechanistic aspects of SOD and water oxidation catalysis by the Mn centers.

Acknowledgment. The authors gratefully acknowledge financial support from DFG through SFB 583 “Redox-active metal complexes” (D.L., A.Z., T.E.S., and I.I.-B.) and a grant from LRZ HLRBII (T.E.S.).

Supporting Information Available: Full experimental details, treatment of data, and theoretical calculations. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) Ivanovic-Burmazovic, I.; van Eldik, R. *Dalton Trans.* **2008**, *39*, 5259–5275.
(2) (a) Merbach, A. E.; Nicolle, G. M.; Helm, L. *Adv. Inorg. Chem.* **2005**, *57*, 327–379. (b) Richens, D. T. *Chem. Rev.* **2005**, *105*, 1961–2002.
(3) Ohlin, C. A.; Villa, M. E.; Rustad, J. R.; Casey, W. H. *Nat. Mater.* **2010**, *9*, 11–19.
(4) (a) Dees, A.; Zahl, A.; Puchta, R.; van Eikema Hommes, N. J. R.; Heinemann, F. W.; Ivanović-Burmazović, I. *Inorg. Chem.* **2007**, *46*, 2459–2470. (b) Balogh, E.; He, Z.; Hsieh, W.; Liu, S.; Toth, E. *Inorg. Chem.* **2007**, *46*, 238–250. (c) Maigut, J.; Meier, R.; Zahl, A.; van Eldik, R. *J. Am. Chem. Soc.* **2008**, *130*, 14556–14569. (d) Drahoš, B.; Kotek, J.; Hermann, P.; Lukeš, I.; Tóth, E. *Inorg. Chem.* **2010**, *49*, 3224–3238.
(5) (a) Whittaker, M. M.; Barynin, V. V.; Antonyuk, S. V.; Whittaker, J. W. *Biochemistry* **1999**, *38*, 9126–9136. (b) Jackson, T. A.; Karapetian, A.; Miller, A.-F.; Brunold, T. *Biochemistry* **2005**, *44*, 1504–1520. (c) Messinger, J. *Biochim. Biophys. Acta* **2000**, *1459*, 481–488.
(6) (a) Limburg, J.; Vrettos, J. S.; Liable-Sands, L. M.; Rheingold, A. L.; Crabtree, R. H.; Brudvig, G. W. *Science* **1999**, *283*, 1524–1527. (b) Riley, D. P. *Chem. Rev.* **1999**, *99*, 2573–2587. (c) Liao, S.; List, B. *Angew. Chem., Int. Ed.* **2010**, *49*, 628–631.
(7) For the investigations we have also probed different Mn^{III}−salen complexes and $[(terpy)(H_2O)Mn^{III}(\mu\text{-}O)_2Mn^{IV}(terpy)(H_2O)]^{3+}$; however, they were not stable towards pH, temperature, and pressure variations.
(8) For experimental details and complete data, see Supporting Information.
(9) To support line broadening measurements, the temperature dependence of the reduced chemical-shift difference was also studied.
(10) Ruhlmann, L.; Nakamura, A.; Vos, J. G.; Fuhrhop, J.-H. *Inorg. Chem.* **1998**, *37*, 6052–6059.
(11) van Eldik, R.; Merbach, A. E. *Comments Inorg. Chem.* **1992**, *12*, 341.
(12) (a) Hillier, W.; Wydrzynski, T. *Coord. Chem. Rev.* **2008**, *252*, 306–317. (b) Hendry, G.; Wydrzynski, T. *Biochemistry* **2003**, *42*, 6209–6217. (c) Hillier, W.; Hendry, G.; Burnap, R. L.; Wydrzynski, J. *Biol. Chem.* **2001**, *50*, 46917–46924. (d) Singh, S.; Debus, R. J.; Wydrzynski, T.; Hillier, W. *Philos. Trans. R. Soc. London, Ser. B* **2008**, *363*, 1229–1235. (e) Loll, B.; Kern, J.; Saenger, W.; Biesiadka, J. *Nature* **2005**, *438*, 1040–1044.
(13) Schneppensieper, T.; Zahl, A.; van Eldik, R. *Angew. Chem., Int. Ed.* **2001**, *40* (9), 1678–1680.
(14) Prince, S.; Koerber, F. *Acta Crystallogr.* **1993**, *C49*, 1158–1160.
(15) Korber, F. C. F.; Smith, J. R. L.; Prince, S.; Rizkallah, P.; Reynoldsa, C. D.; Shawcross, D. R. J. *Chem. Soc., Dalton Trans.* **1991**, *12*, 3291–3294.
(16) Drljaca, A.; Zahl, A.; van Eldik, R. *Inorg. Chem.* **1998**, *37*, 3948–3953.
(17) (a) Sproviero, E. M.; Shinopoulos, K.; Gascón, J. A.; McEvoy, J. P.; Brudvig, G. W.; Batista, V. S. *Philos. Trans. R. Soc. London, Ser. B* **2008**, *363*, 1149–1156. (b) Sproviero, E. M.; Gascón, J. A.; McEvoy, J. P.; Brudvig, G. W.; Batista, V. S. *J. Am. Chem. Soc.* **2008**, *130*, 3428–3442. (c) Siegbahn, P. E. M. *Acc. Chem. Res.* **2009**, *42*, 1871–1880. (d) Siegbahn, P. E. M. *J. Am. Chem. Soc.* **2009**, *131*, 18238–18239.
(18) Chong-de, L.; Jordan, R. B. *Inorg. Chem.* **1987**, *26*, 3855–3857.
(19) (a) Tagore, R.; Chen, H.; Crabtree, R. H.; Brudvig, G. W. *J. Am. Chem. Soc.* **2006**, *128*, 9457–9465. (b) Tagore, R.; Crabtree, R. H.; Brudvig, G. W. *Inorg. Chem.* **2007**, *46*, 2193–2203. (c) Ohlin, C. A.; Brimblecombe, R.; Spicca, L.; Casey, W. H. *Dalton Trans.* **2009**, *27*, 5278–5280.
(20) (a) Helm, L.; Mehrbach, A. E. *Chem. Rev.* **2005**, *105*, 1929–1959. (b) Houston, J. R.; Yu, P.; Casey, W. H. *Inorg. Chem.* **2005**, *44*, 5176–5182. (c) Crimp, S. J.; Spicca, L.; Krouse, H. R.; Swaddle, T. W. *Inorg. Chem.* **1994**, *33*, 465–470.
(21) Thanks to the reviewer these explanations are considered.

JA1014585