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Capturing the Role of Explicit Solvent in the Dimerization of Ru^V(bda) Water Oxidation Catalysts

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Abstract: We present a ground breaking empirical valence bond study for a soluble transition metal complex. With this model we studied the full reaction of two Sun's catalyst monomers approaching and reacting in the Ru^V oxidation state. Analysis of the solvation shell in the reactant and along the reaction coordinate revealed that the oxo itself is hydrophobic, which adds a significant driving force to form the dimer. The effect of the solvent on the reaction between the prereactive dimer and the product was small. The solvent seem to lower the barrier for the isoquinoline (isoq) complex while it is increased for pyridines (py). Comparing the reaction in gas phase and solution we find that the proposed π -stacking interaction of the isoq ligands is entirely driven by the water medium.

Artificial photosynthesis is proposed as a renewable and sustainable solution to the future energy demands.^[1-2] In light-driven water splitting into its elements the energy of light is stored in the bonds of the products. The process is composed of two reactions: water oxidation ($2\text{H}_2\text{O} \rightarrow \text{O}_2 + 4\text{e}^- + 4\text{H}^+$) and proton reduction.^[3-6] Water oxidation requires strongly oxidizing conditions and involves four one-electron transfer reactions per oxygen molecule produced. Due to the harsh conditions and limited rates the water oxidation reaction is considered the bottleneck of the whole process.^[7] A wide array of catalysts have been synthesized to accelerate this reaction.^[8] Among these, a family of Ru(bda)L₂ catalysts (bda = 2,2'-bipyridine-6,6'-dicarboxylate, L = typically a nitrogen heterocycle such as py, Figure 1) stand out, with turnover frequencies of over 1000 per second.^[9]

The Ru(bda)L₂ complexes have been shown to follow second order kinetics with respect to the catalyst concentration, indicating that two catalysts are present in the rate determining step. Moreover a seven-coordinate Ru^{IV} dimer was isolated.^[9] Privalov and co-workers showed that the mechanism proceeds via interaction of two M-O units (I2M), and involves a radical coupling reaction between the oxygens of the Ru^V=O moieties (Scheme 1).^[10] Recently, we found that not only is the coupling possible, but that there is not an intrinsic barrier between the oxo fragments of the Ru^V=O moieties in this reaction.^[11] The origin of the activation energy relative to the pre-reactive dimer was shown to be due to inter- and intramolecular strain in the rest of the molecule, which is needed to get the oxo groups in close

the reaction, since kinetics show two monomers reacting in the rate limiting step, but could not specify how, due to lacking suitable computational methods. Herein, we show results from a study where the empirical valence bond (EVB) approach has been used for a synthetic metal complex with a catalytic metal center for the first time, which allowed us to study the reaction with fully explicitly solvated catalysts. This revealed unexpected solvation effects that explain why the dinuclear reaction is favored, a finding that is of substantial importance for the design of new catalysts operating by this mechanism.

Scheme 1. Proposed O-O bond formation mechanism.

Density functional theory (DFT) is highly accurate for describing catalytic metal complexes,^[12] but has limitations including small system size, limited simulation timescales, and restricted conformational sampling. Molecular mechanics (MM), on the other hand, can be used to compute large systems efficiently, with millions of atoms. However, in its standard form, MM is not suitable, or even applicable, for bond-breaking and bond-forming reactions. One solution to this problem is the EVB approach^[13] which uses fully classical descriptions of different key stationary points within a valence bond framework in order to describe chemical reactions.^[14] Since it is based on an MM description of the reactant and product states, EVB allows for a physically and quantitatively meaningful description of environmental effects.^[15] To date, EVB has mainly been applied to enzyme reactions^[16] and reactions of main-group elements in solution.^[17] Here we present the first study where EVB is applied to a reaction involving a catalytic transition metal center.

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contact. We concluded that solvation must play a large role in

Figure 1. Ru^V complexes included in this study.

Effect of Solvent on Formation and Structure of the Prereactive Dimer – Hydrophobic Oxygen Atoms

In our recent report^[11] we observed no correlation between the activation energy and the experimental reaction rate for the [Ru^{VO}(bda)L₂]⁺ complexes, with or without implicit solvation. Herein, EVB-MD with full explicit solvation was developed and used to better understand the details of the solvent effects (see Supporting Information for details). Analysis of the trajectories of the Ru^V monomers revealed some intriguing results. The radial distribution functions of the monomer between the Ru=O oxygen (O⁷) and water oxygen and hydrogen, show that the first solvation shell contains 2.7 waters. More interestingly the shell structure is more distinct between O⁷-O than O⁷-H, and the O⁷-O distance is close to that of O⁷-H. This result indicates that water does not form hydrogen bonds with the oxo. Detailed analysis of the hydrogen bonding (H-bonding) between the all the oxygen atoms further strengthened this observation (Table 1). O¹ has on average 0.66 hydrogen bonds to water, O² 0.17 hydrogen bonds, while O⁷ had close to none - 0.02 hydrogen bonds. These results indicate that the oxo species, which was designed to react with water, is actually *hydrophobic* (see also extended DFT calculations that provide further evidence of this hydrophobicity in the Supporting Information).

The hydrophobic oxo is initially quite counterintuitive but it could be key to the high reactivity of the complex. Since the reaction relies on the formation of the prereactive dimer, with the oxos pointing towards each other, there must be a driving force for this formation or the complex can only react *via* the less efficient WNA pathway. When the prereactive dimer and the product complex are formed, the number of hydrogen bonds of O¹ stays intact (monomer 0.66, prereactive dimer 0.64, product 0.63), but O² changes from 0.17 to 0.09 to 0.01 in the monomer, prereactive dimer and product complexes, respectively. For O⁷, the H-bonding stays at a low and virtually nonexistent value along the reaction coordinate. Since the Ru^{IV}-OH species is known to interact with water from the crystal structure we also parametrized a model to study the solvation on this species. Here the situation is qualitatively different. The number of hydrogen bonds to the oxygen atoms are 0.47 to O¹, 0.23 to O² and 0.16 to O⁷. There is also significant interaction between the hydroxide proton and water. We deduce that the hydrophilic channel seen in the Ru^{IV}-OH crystal does not exist for the Ru^V=O species, where water is instead excluded from the reacting region.

Table 1. The average H-bond number formed between complex 1 and 4 with H₂O.

H-bond	O ¹	O ²	O ⁷
1-monomer	0.66	0.17	0.02
1-prereactive	0.64	0.09	0.02
1-dimer	0.63	0.01	0.00
4-monomer	0.63	0.16	0.04
4-prereactive	0.70	0.12	0.02
4-dimer	0.51	0.00	0.00
Ru ^{IV} -OH	0.47	0.23	0.16

EVB Model and Effects of Solvation on O-O Bond Formation

In Table 2, the calculated energetics of the four catalysts are listed (Figure 2 shows the reaction coordinate of py and isoq). For the py derivatives, we observe a solvent-induced increase in the calculated activation free energy compared to the gas-phase. For the more hydrophobic 4, the solvent has the opposite effect. For comparison, we have also provided in Table 2 data from our previous calculations in explicit solvent using the PBF solvent model,^[11] showing that the EVB and DFT calculations give $\Delta\Delta G^*$ within 4 kcal/mol of each other, depending on the complex, as well as following the same qualitative trend in $\Delta\Delta G^*$.

Figure 2. The energy profile of complexes 1 and 4.

Table 2. Activation free energy for forward ($\Delta\Delta G$) and reverse ($\Delta\Delta G^*$) reaction of complexes 1-4. All values are in kcal/mol.

Complex	$\Delta\Delta G^{[a]}$ gas	$\Delta\Delta G^{*[a]}$ gas	$\Delta\Delta G^{[b]}$ water	$\Delta\Delta G^{*[b]}$ water
1	3.3	23.5	4.8 (6.3)	24.1 (22.2)
2	1.1	22.8	2.7 (3.6)	22.2 (21.9)
3	4.0	21.0	4.7 (5.5)	21.4 (19.9)
4	7.9	24.8	7.1 (6.4)	28.9 (24.6)

[a] All values calculated with DFT in the gas phase. [b] All values are calculated with EVB in an explicit TIP3P water environment. DFT results with the PBF solvation model^[11] are provided in parenthesis for comparison.

Figure 3. The structure of the complex **4** transition state in the (top) gas phase and (bottom) solvent phase. These structures highlight key π -stacking interactions (distances in Å) formed in the solvent but not in the gas-phase.

When comparing **1** and **4** a striking difference was found in the π -stacking tendency. In the gas phase, neither appears to adopt π -stacked geometries. Instead, the hydrogen atoms of the py and isoq ligands interact with the electronegative carboxylate oxygen atoms. In aqueous solution, **4** clearly twists to give a π -stacked configuration (Figure 3). The distance between the center of mass of the isoq at the transition state is 5.42 Å in the gas phase, and only 4.1 Å in solution. The angle α between two normal vectors perpendicular to the planes of two rings reduces to 16° from 42°, and the angle β between a normal vector perpendicular to one ring and a vector connecting the two centres of mass reduced to 10° from 12°. Hence, the solvent seems to drive the formation of the π -stacked configuration.^[18]

As the reaction proceeds, the π -stacking increases, as indicated by the distance decreasing from 6.26 Å to 3.96 Å. For **1** the situation is different. In the reactant dimer, the ligands remain in their non-stacked configuration also in water. This is true throughout the reaction and the distance between the py ligands is 6.35 Å in the reactant and 5.58 Å in the product, the angle α is ~50° and the angle β is 19° in two states.

In summary, we have created the first EVB model for solution phase transition metal complexes with catalytic metal centers. The EVB force fields allowed for a full study of the impact of the solvent on the reaction. By simulating the monomer, prereactive dimer, product, and the full path for the O-O bond formation, we found interesting effects of the solvent. The most striking was the interaction between the Ru bound oxo and water. H-bonding was more or less absent and the arrangement of the water molecules indicated a hydrophobic interaction. This effect explains why the two Ru^V=O monomers form the prereactive dimer, with the geometry where the two oxos are pointing towards each other. Once the prereactive dimer is formed the O-O bond is readily formed. The effect of the solvent on intrinsic O-O forming step was small. The H-bonding pattern indicated that already at the prereactive dimer, the H-bonding between O² and water is absent, while the O¹ retains H-bonding with water throughout the reaction. A striking effect of the solvent was observed for **4**, where no π -stacking was observed in the gas phase, but in aqueous solution the complex adopts a geometry with clear π -stacking. This indicates that the π -stacking interaction is entirely solvent-driven. This effect is not observed for **1**, where the π -system is smaller. We believe that the results of this study have found one the key properties for water oxidation catalysts that operate via O-O radical coupling - the *hydrophobic oxo*. This property facilitates the formation of the prereactive dimer. Once the dimer is formed the reaction proceeds with a minimal barrier, in line with our recent DFT based results. The effect of water on the O-O step was minimal, and the supramolecular properties are likely the key to highly active catalysts.

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Keywords: water oxidation • diradical coupling reaction • empirical valence bond • hydrophobic oxo • solvation effect

- [1] E. Amouyal, *Sol. Energy Mater. Sol. Cells* **1995**, 38, 249-276.
- [2] M. D. Kärkäs, O. Verho, E. V. Johnston, B. Åkermark *Chem. Rev.* **2014**, 114, 11863-12001.
- [3] T. J. Meyer, *Nature* **2008**, 451, 778-779.
- [4] P. E. M. Siegbahn, *Inorg. Chem.* **2008**, 47, 1779-1786.
- [5] R. Eisenberg, H. Gray, *Inorg. Chem.* **2008**, 47, 1697-1699.
- [6] L. Sun, L. Hammarström, B. Åkermark, S. Styring, *Chem. Soc. Rev.* **2001**, 30, 36-49.
- [7] V. Balzani, A. Gredi, M. Venturi, *ChemSusChem* **2008**, 1, 26-58.

- [8] a) S. W. Gersten, G. J. Samuels, T. J. Meyer, *J. Am. Chem. Soc.* **1982**, *104*, 4029-4230; b) C. Sens, I. Romero, M. Rodríguez, A. Llobet, T. Parella, J. Benet-Buchholz, *J. Am. Chem. Soc.* **2004**, *126*, 7798-7799; c) R. Zong, R. P. Thummel, *J. Am. Chem. Soc.* **2005**, *127*, 12802-12803; d) J. J. Concepcion, J. W. Jurss, J. L. Templeton, T. J. Meyer, *J. Am. Chem. Soc.* **2008**, *130*, 16462-16463; e) S. Masaoka, K. Sakai, *Chem. Lett.* **2009**, *38*, 182-183; f) N. Kaveevivitchai, R. Zoug, H.-W. Tseng, R. Chitta, R. P. Thummel, *Inorg. Chem.* **2012**, *51*, 2930-2939; g) N. D. McDaniel, F. J. Coughlin, L. L. Tinker, S. J. Bernhard, *J. Am. Chem. Soc.* **2008**, *130*, 210-217; h) J. F. Hull, D. Balcells, J. D. Blakemore, C. D. Incarvit, O. Eisenstein, G. W. Brudvig, R. H. Crabtree, *J. Am. Chem. Soc.* **2010**, *132*, 16017-16029; i) E. A. Karlsson, B. L. Lee, T. Åkermark, E. V. Johnston, M. D. Kärkäs, J. Sun, Ö. Hansson, J. E. Bäckvall, B. Åkermark, *Angew. Chem., Int. Ed.* **2011**, *50*, 11715-11718; j) W. Ellis, M. D. McDaniel, S. Bernhard, T. J. Collins, *J. Am. Chem. Soc.* **2010**, *132*, 10990-10991; k) S. M. Banett, K. I. Goldberg, J. M. Mayer, *Nat. Chem.* **2012**, *4*, 498-502; l) D. J. Wasylenko, C. Ganesamoorthy, J. Borau-Garcia, C. P. Berlinguette, *Chem. Commun.* **2011**, *47*, 4249-4251.
- [9] a) L. Duan, L. Wang, A. K. Inge, A. Fischer, X. Zou, L. Sun, *Inorg. Chem.* **2013**, *52*, 7844-7852. (b) L. Duan, F. Bozoglian, S. Mandal, B. Stewart, T. Privalov, A. Llobet, L. Sun, *Nature Chem.* **2012**, *4*, 418-423. (c) L. Duan, C. M. Araujo, M. S. G. Ahlquist, L. Sun, *PNAS* **2012**, *109*, 15584-15588. (d) L. Wang, L. Duan, Y. Wang, M. S. G. Ahlquist, L. Sun, *Chem. Commun.* **2014**, *50*, 12947-12950.
- [10] J. Nyhlén, L. Duan, B. Åkermark, L. Sun, T. Privalov, *Angew. Chem. Int. Ed.* **2010**, *49*, 1773-1777
- [11] T. Fan, S. Zhan, M. S. G. Ahlquist, *ACS Catal.* **2016**, *6*, 8308-8312.
- [12] J. A. Pople, *Angew. Chem. Int. Ed.* **1999**, *38*, 1894-1902.
- [13] A. Warshel, *Computer Modelling of Chemical Reactions in Enzymes and Solutions*, Wiley-Interscience, USA, 1997.
- [14] A. Shurki, E. Derat, A. Barrozo, S. C. L. Kamerlin, *Chem. Soc. Rev.* **2015**, *44*, 1037-1052.
- [15] S. C. L. Kamerlin and A. Warshel, *WIREs Comput. Mol. Sci.* **2011**, *1*, 30-45.
- [16] a) M. Roca, B. Messer, D. Hilvert, A. Warshel, *PNAS* **2008**, *105*, 13877-13882. b) M. H. M. Olsson, A. Warshel, *J. Am. Chem. Soc.* **2004**, *126*, 15167-15179. c) A. Kohen, R. Cannio, S. Bartolucci, J. P. Klinman, *Nature* **1999**, *399*, 496-499.
- [17] a) Y. Zhao, D. G. Trular, *Theor. Chem. Acc.* **2006**, *120*, 215-241. b) M. Kazemi, J. Åqvist, *Nat. Commun.* **2015**, *6*, 7293-7299. c) A. Tahat, *J. Comput. Chem.* **2016**, *37*, 1935-1946. d) T. Mabuchi, A. Fukushima, T. Tokumasu, *J. Chem. Phys.* **2015**, *143*, 014501.
- [18] Y. An, J. W. G. Bloom, S. E. Wheeler, *J. Phys. Chem. B* **2015**, *119*, 14441-14450.

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A cat in water. An empirical valence bond study of the $\text{Ru}(\text{bda})\text{L}_2$ water oxidation catalysts with full explicit solvation reveals the hydrophobic nature of the key $\text{Ru}^{\text{V}}=\text{O}$ intermediate.

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