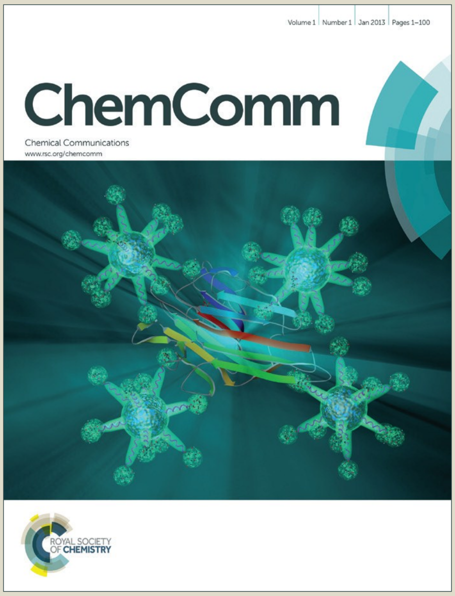
ChemComm

Accepted Manuscript



ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/chemcomm

Journal Name

COMMUNICATION

A theoretical study into a *trans*-dioxo Mn^V porphyrin complex that does not follow oxygen rebound mechanism in C-H bond activation reactions†

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

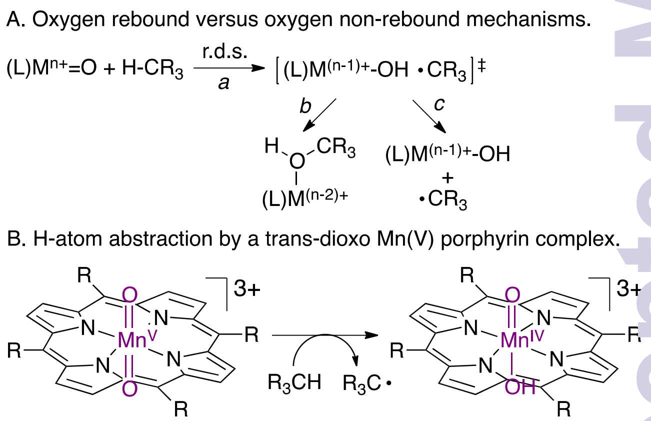
www.rsc.org/

Kyung-Bin Cho and Wonwoo Nam*

Previous experimental results revealed that the C-H bond activation reaction by a synthetic *trans*-dioxo Mn^V porphyrin complex, $[(TF_4TMAP)OMn^VO]^{3+}$, does not occur via the well-known oxygen rebound mechanism, which has been well demonstrated in $Fe^{IV}O$ porphyrin π-cation radical reactions. In the present study, theoretical calculations offer an explanation through the energetics involved in the C-H bond activation reaction, where a multi-spin state scenario cannot be excluded.

High-valent metal-oxo species are highly reactive intermediates capable of abstracting hydrogen atoms in C-H bond activation reactions by enzymes and their biomimetic compounds.[1–7] C-H bond activation mechanisms have been extensively investigated in cytochromes P450 enzymes and iron porphyrin models, especially using synthetic iron(IV)-oxo porphyrin π-cation radicals (Compound I), thereby proposing the so-called "oxygen rebound mechanism (ORM)" (Scheme 1A, pathway *b*).[8–11] Although the ORM has been widely accepted in alkane hydroxylation reactions by high-valent metal-oxo species over the several decades, the ORM has been challenged recently in the C-H bond activation of hydrocarbons by nonheme metal-oxo complexes.[12–17] In the latter reactions, the energy barrier for the oxygen rebound step between the metal-hydroxo species and the carbon radical is proposed to be higher than that for the escape of the carbon radical from the cage; recent experimental and computational results demonstrate that the C-H bond activation of hydrocarbons by nonheme metal-oxo species occurs via the oxygen non-rebound mechanism (ONRM) (Scheme 1A, pathway *c*).[12–17] However, the ORM versus ONRM has been discussed rarely in metalloporphyrin systems in a systematic way.

Compared to the iron(IV)-oxo porphyrin π-cation radical species, the chemistry of synthetic high-valent manganese(V)-oxo porphyrin species has been less clearly understood in oxidation reactions.[18] In the manganese porphyrin systems, *trans*-dioxo Mn^V porphyrin species (OMn^VO) has been proposed as a potential catalyst that has shown to be reactive in substrate oxidation reactions.[19,20] While the (OMn^VO) complex was fully characterized relatively recently,[19] earlier studies have postulated it coexisting with its protonated forms, ($HOMn^VO$) and (H_2OMn^VO), depending on the solution pHs.[21,22] The energetics of these species were also studied


A. Oxygen rebound versus oxygen non-rebound mechanisms.

$$(L)M^{n+}{=}O + H\text{-}CR_3 \xrightarrow[a]{\text{r.d.s.}} [(L)M^{(n-1)+}\text{-}OH \cdot CR_3]^{\ddagger}$$

B. H-atom abstraction by a trans-dioxo Mn(V) porphyrin complex.

Scheme 1 (A) ORM (*b*) versus ONRM (*c*) pathways after hydrogen atom abstraction by a metal-oxo species (*a*) occurs. (B) ONRM in the hydrocarbon C-H bond activation by a *trans*-dioxo Mn^V porphyrin species.

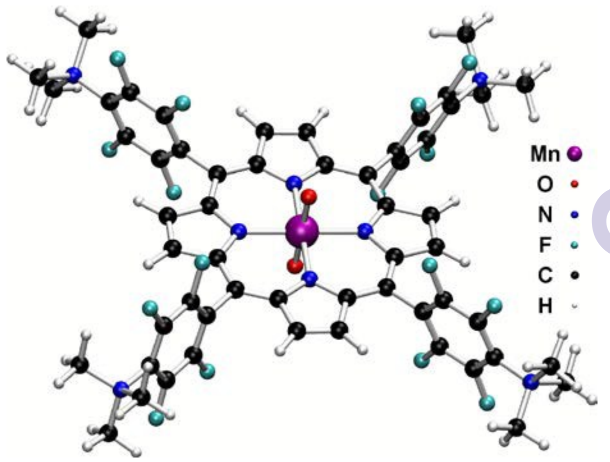


Fig. 1 The catalyst used in the current study, $[(TF_4TMAP)OMn^VO]^{3+}$ (**1**, TF_4TMAP = *meso*-tetrakis(2,3,5,6-tetrafluoro-*N*,*N*,*N*-trimethyl-4-aniliniumyl)porphyrinato dianion).

Department of Chemistry and Nano Science, Ewha Womans University, Seoul 03760, Korea. Fax: (+82)-2-3277-4114; E-mail: wwnam@ewha.ac.kr

† Electronic Supplementary Information (ESI) available: theoretical procedures and methods, energies, selected Mulliken spin density distributions and geometries. See DOI: 10.1039/x0xx00000x

theoretically,[23,24] and it was shown to involve spin state changes when it comes to simple oxygen transfer reactions to a free Br^{-} ion by ($H_2OMn^{V}O$).[23] Indeed, early experimental studies indicated that $Mn^{V}O$ porphyrin species may react through spin inversion, depending on ligands.[25] For our part, we have previously shown experimentally that the ($OMn^{V}O$) species can perform hydride transfer reactions.[26] This reaction, possibly being performed by the ($OMn^{V}OH$) species after protonation by solvent, was shown to do a proton-coupled electron transfer reaction, followed by an electron transfer.[26] Subsequent work also showed that a ($OMn^{V}O$) porphyrin complex, $[(TF_4TMAP)OMn^{V}O]^{3+}$ (**1**, Fig. 1), performed weak C-H bond activation reactions, but not strong C-H bond activations, as this may require protonation.[19] The Mn product formed in the weak C-H bond activation reactions was shown to be $[(TF_4TMAP)OMn^{IV}OH]^{3+}$ (Scheme 1B).[27] This indicates that the Mn complex was dissociated from the cage without recombining to the carbon radical (Scheme 1A, pathway *b* vs. *c*); it is consistent with a dissociation mechanism that we have shown recently for nonheme $Fe^{IV}O$, $Fe^{V}O$, $Mn^{IV}O$, $Cr^{IV}O$ and $Ru^{IV}O$ cases.[28,12–17] Herein, we attempt to describe this particular reaction in detail by theoretical means. Such calculations are not as trivial as it might seem, and we outline below some important aspects that has not been considered in other theoretical studies. We also gain some additional understanding of the structure and function of ($OMn^{V}O$) species that are not easily obtained by experimental methods.

To calibrate the calculations, we have compared the different spin states of **1**. We first used the B3LYP functional (B3LYP/Def2-TZVPP//LACVP, see methods section in ESI) as previous experiences with it in heme systems are very good.[11] Using a truncated model (for calibration purposes only) with H atoms replacing the four *meso* substituents, the calculations yielded the S = 0 (singlet) spin state as the ground state, 7.7 and 10.6 kcal/mol lower than the S = 1 (triplet) and S = 2 (quintet) states, respectively. Description of the valence orbitals have been discussed in the literature for *trans*-dioxo metal porphyrin species,[29] which can be applied to the OMnO case as well. The singlet state was found to be a closed shell species with the δ orbital as HOMO (Fig. 2). The two Mn-O distances were found to be symmetrical at 1.65 Å each.

The lowest triplet state has a (π_{xz}^{2}, π_{yz}^{2}, δ^{α}, $\pi^{*}_{xz}{}^{\alpha}$, $\pi^{*}_{yz}{}^{0}$) configuration. However, the one electron occupancy of the π^{*}_{xz} orbital breaks the symmetry of the electron distribution, and one Mn-O bond length is now clearly longer than the other (1.72 vs. 1.95 Å). This results in uneven orbital mixing between the *p* orbitals of the two oxygens and the *d* orbitals of the metal, departing from the simplistic and symmetric view in Fig. 2. Many more electron configuration possibilities are now created, and several higher energy configurations are readily obtained by calculations as well (ESI, Table S1). Thus, we found it imperative to perform a detailed analysis of the obtained wave function whenever the triplet state was involved in every stage of the calculations, to ensure that the electron configuration is the lowest energy one.

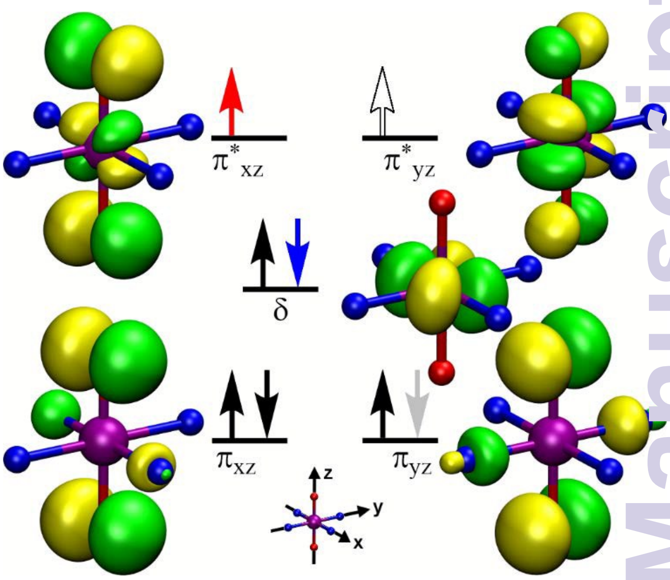


Fig. 2 Five valence orbitals of *trans*-dioxo metal species that are of interest in the current study. The black+grey+blue arrow combination represent the electron configuration for the singlet *trans*-dioxo $OMn^{V}O$ species. The black+grey+red combination represent the energetically lowest triplet state, and the black+red+white combination the lowest quintet state. Other higher energy configurations are quite easily obtained computationally, requiring careful analysis of the output. In many configurations, the both Mn-O bond lengths are not the same, causing less symmetrical orbital hybridisation.

The quintet state features a (π_{xz}^{2}, π_{yz}^{α}, δ^{α}, $\pi^{*}_{xz}{}^{\alpha}$, $\pi^{*}_{yz}{}^{\alpha}$) configuration. Notably, the lack of a singly occupied porphyrin ligand a_{2u} orbital even in this configuration shows that this orbital is unlikely to play a role in the *trans*-dioxo Mn chemistry, unlike for instance in Compound I in P450. Also here, an alternative high energy configuration was found that was discarded after analysis (ESI, Table S1).

The singlet state as the ground state has been verified experimentally[27] and is also in agreement with two other computational studies.[23,24] However, these studies put the singlet-triplet state energy difference significantly higher than 7.7 kcal/mol as in the current case. One study put the spin state energy difference to 21.3 kcal/mol using the PW91PW91 functional (within the Car-Parrinello scheme),[23] while the other calculated this difference to be at 25.5 kcal/mol using the BLYP functional.[24] Thus, to verify this large functional dependence, we performed single-point calculations with different functionals on the B3LYP obtained geometry (X/Def2-TZVPP//B3LYP/LACVP, where X is the functional tested). The calculations verified that all of the tested functionals yield significantly higher energy difference than B3LYP (ESI, Table S2). This may have consequences for the two-spin state reactivity as discussed later (*vide infra*). For now, we present in this study energy values from B3LYP/Def2-TZVPP//LACVP calculations, as detailed in ESI, Methods section.

We then investigated the C-H bond activation reaction of xanthene by **1** (including the *meso* substituents). The starting singlet ground state (i.e., reference point 1, **RP1**, Fig. 3) leads to a transition state 17.0 kcal/mol higher than **RP1**. The resulting ($OMn^{IV}OH$) intermediate together with the substrate radical rests at 15.4 kcal/mol below **RP1**. In comparison, the triplet state starts the reaction at 9.5 kcal/mol above **RP1**, but the transition state is lower than the singlet state, at 13.4

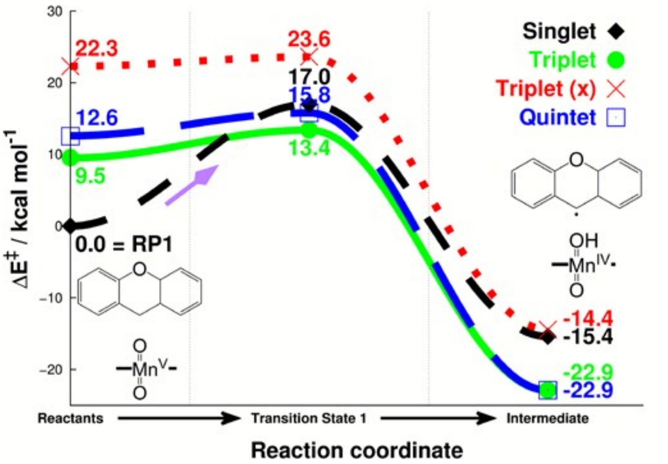


Fig. 3 Energy profile of the C-H activation reaction of xanthene by **1** in different spin states. The singlet state (◆, black, short dashed line) is the ground state at the beginning of the reaction, but has the third highest energy barrier of the spin states studied here, surpassing even that of the quintet state (☐, blue, long dashed line) at TS1. The lowest energy barrier is found by one of the triplet states (●, green, solid line), while an alternative triplet spin configuration (✕, red, dotted line, "(x)") is consistently higher in energy.

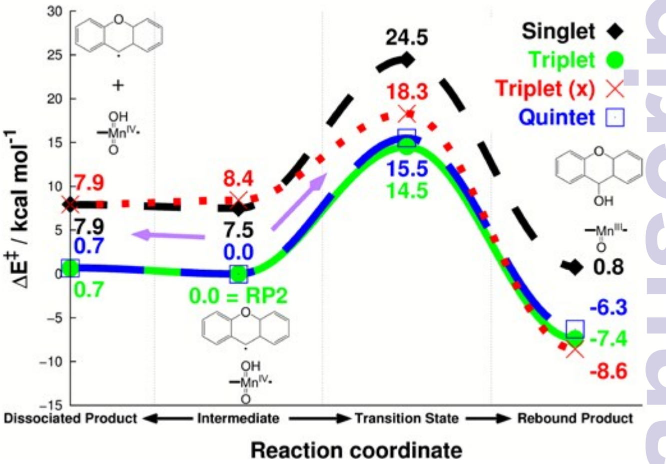


Fig. 4 Starting from the Intermediate stage, substrate dissociation (going left) require much less energy than performing the rebound reaction (going right) when reacting $[(TF_4TMAP)OMn^{V}OH]^{3+}$ with xanthene radical, in all the spin states. A dissociation reaction is therefore suggested, with ensuing secondary reactions that leads to less than 50% hydroxylated products as proposed earlier.[28,12–17]

kcal/mol. Hence, a spin state change before the transition state would allow the reaction to utilize a 3.6 kcal/mol lower barrier than a spin-conserved singlet pathway. Moreover, at the intermediate state, the triplet is clearly more favourable at -22.9 kcal/mol relative to **RP1**. Hence, while we do not know the spin-orbit coupling matrix for the system, which is required to predict how facile the spin state change occurs, there are incentives for the reaction to spin-flip at any point of the reaction before the intermediate formation. Indeed, our minimum energy crossing point (MECP) search resulted in structures both before (at 10.8 kcal/mol) and near the transition state (16.3 kcal/mol), see ESI Table S4, where spin crossing could occur. As a comparison, we also used one of the high energy triplets ("x") to perform the reaction. This resulted in a consistently higher energy than the other triplet state, showing that care must be taken in choosing the right triplet for calculations. The quintet state exhibits a low transition state barrier as well (15.8 kcal/mol), thus being a contender to mediating the reaction, if an initial double spin flip can occur.

Going beyond the initial C-H activation reaction, the competition between a P450-type ORM versus a dissociative ONRM was investigated by comparing the rebound barrier versus the dissociation energy of the substrate radical (Fig. 4). Setting the reference point as the triplet intermediate structure (**RP2**), the ORM features a barrier of 24.5, 14.5 and 15.5 kcal/mol relative to **RP2** for the singlet, triplet and quintet, respectively. Such high barriers would have most likely rendered this step as rate-limiting, which is not supported by KIE measurements.[27] The dissociated state, where the substrate radical is considered to have dissociated out of the cage, is in contrast 7.9, 0.7 and 0.7 kcal/mol above **RP2** for the singlet, triplet and quintet states, respectively. Hence, the calculations clearly favour ONRM in this reaction, which is consistent with the experimental results.[27] It is also in agreement with the postulation that ORM is slow with strong donor axial ligands (i.e. =O, *vide infra*).[18]

We are now ready to discuss the question of functional versus multi-spin state reactions. As stated before, use of alternative functionals yield very high triplet energies at the reactant state (ESI, Table S1). On one hand, these higher energies according to the other functionals would make the singlet to triplet excitation impossible, and the reaction would occur on the singlet surface. The high-spin bias of B3LYP is well known, which seems to be manifested here, and this could be one of the uncommon cases where B3LYP fails spectacularly. On the other hand, B3LYP has worked well for heme systems in the past,[11] and the fact that the triplet state is lower in energy at the intermediate state (verified by experiment[27] as well as with the tested functionals, ESI Table S3) means that the system probably changes its spin state somewhere along the reaction pathway anyway. In a theoretical study, it was indeed found with B3LYP that a spin state change should occur in related corrolazine-$Mn^{V}O$ species as long as the correct triplet electron configuration is calculated.[30,31] This two-spin state reactivity with two electron displacements are akin to what has been proposed in a number of papers regarding metal-oxo reactions, and indeed shown recently in a combined experimental and theoretical work in $Fe^{IV}O$ systems.[32] As experiments cannot confirm exactly how much higher in energy the triplet is at the reactant state, we regard this issue somewhat unresolved until *ab initio* calculations are performed on this system. Hence, we merely observe that if B3LYP is reliable, a spin crossing before the TS should be a substantial possibility. Nevertheless, this issue does not alter the conclusion that the ONRM occurs in the present study. Moreover, the results also support that **1** is not completely inactive but it is within possibility that it can do weak C-H activation reactions without an initial protonation, in line with experiments done at pH 10.5.[27] The obtained reaction energy barriers, 17.0, 13.4 and 15.8 kcal/mol for the singlet, triplet and quintet spin states, respectively, all lie within conceivable error margins to the experimentally obtained value of 13.2 kcal/mol (derived from the k_2 value of $5.7 \cdot 10^2$ M^{-1} s^{-1} at 15 °C through the Eyring equation),[27] with incidentally the triplet value being closest to the experiments.

It was postulated that with less strong axial ligand, the rebound activity of the Mn(V)O species would be enhanced compared to the *trans*-dioxo species.[18,19] To verify this, we attempted to calculate the rebound barrier for the acetonitrile substituted intermediate, $[(TF_4TMAP)(CH_3CN)Mn^{IV}OH]^{5+}$, in the presence of the xanthene substrate radical. However, despite orbital swapping efforts, these species were not obtained. Instead, $[(TF_4TMAP)(CH_3CN)Mn^{III}OH]^{4+}$ (**2**) and a substrate cation were obtained, indicating that a hydride transfer has occurred. This stands to reason considering that the charge of the catalyst is very high positive (+5, including the charge of the *meso*-groups), facilitating a second electron abstraction. It has indeed been shown experimentally that a hydride transfer can occur in (OMn^VO) systems, possibly preceded by a ((OH)Mn^VO) formation.[26] The calculated rebound barrier for the triplet **2** is 7.0 kcal/mol, considerably lower than that of **1** (14.5 kcal/mol). This lowers the energy gap between dissociation and rebound barrier to 8.7 kcal/mol, down from 13.9 kcal/mol with **1**. Hence, while the dissociation is still preferred, the rebound product is now more accessible compared to **1**. Further research is needed to explore whether a more charge-neutral environment (e.g. use of counter ions in the modelling[33]) would decrease the gap even further, favouring ORM over ONRM in **2**, but these results show clearly that the rebound reaction rate can be enhanced by less strong donating ligands. Presumably, protonation of **1** (i.e. creating a hydroxyl ligand) would lead to the same behaviour vis-à-vis **1**.

In conclusion, we have investigated the C-H bond activation of xanthene by the $[(TF_4TMAP)OMn^VO]^{3+}$ species theoretically. It is found that this reaction indeed should be possible without a prior protonation of one of the oxygen atoms. Care must be taken in determining the correct wave function, since multiple configurations are found within the same spin states. The possibility of a spin state crossing before the transition state cannot be excluded based on the B3LYP calculations, as the lowest barrier is obtained by the triplet state. Whether this is a result of B3LYP bias for higher spin states remains to be verified. Experiments and calculations do, however, agree that a spin state change has occurred by the time the reaction reaches the intermediate state. All the spin states exhibit energy barriers reasonably close to the experimentally determined one. In the following step, the rebound barriers are found to be clearly higher than the dissociation energies of the substrate radical, thus rendering the rebound step improbable. This is in agreement with our earlier experimental results for the current model system[27] and work of others.[18] It is also shown that less strong donor axial ligands have a lower rebound barrier.

The authors acknowledge financial support from the NRF of KOREA through the CRI (NRF-2012R1A3A2048842 to W.N.), GRL (NRF-2010-00353 to W.N.) and MSIP (NRF-2013R1A1A2062737 to K.-B.C.).

Notes and references

1 J. T. Groves, *J. Inorg. Biochem.*, 2006, **100**, 434.
2 W. Nam, *Acc. Chem. Res.*, 2007, **40**, 522.
3 J. Hohenberger, K. Ray and K. Meyer, *Nature Commun.*, 2012, **3**, 720.
4 W. Nam, Y.-M. Lee and S. Fukuzumi, *Acc. Chem. Res.*, 2014, **47**, 1146.
5 S. A. Cook and A. S. Borovik, *Acc. Chem. Res.*, 2015, **48**, 2407.
6 M. Puri and L. Que Jr., *Acc. Chem. Res.*, 2015, **48**, 2443.
7 Z. Chen and G. Yin, *Chem. Soc. Rev.*, 2015, **44**, 1083.
8 J. T. Groves, *J. Chem. Educ.*, 1985, **62**, 928.
9 J. T. Groves and G. A. McClusky, *J. Am. Chem. Soc.*, 1976, **98**, 859.
10 S. Shaik, H. Hirao and D. Kumar, *Acc. Chem. Res.*, 2007, **40**, 532.
11 S. Shaik, S. Cohen, Y. Wang, H. Chen, D. Kumar and W. Thiel, *Chem. Rev.*, 2010, **110**, 949.
12 K.-B. Cho, X. Wu, Y. M. Lee, Y. H. Kwon, S. Shaik and W. Nam, *J. Am. Chem. Soc.*, 2012, **134**, 20222.
13 E. Kwon, K.-B. Cho, S. Hong and W. Nam, *Chem. Commun.*, 2014, **50**, 5572.
14 X. Wu, M. S. Seo, K. M. Davis, Y. M. Lee, J. Chen, K.-B. Cho, Y. N. Pushkar and W. Nam, *J. Am. Chem. Soc.*, 2011, **133**, 20088.
15 K.-B. Cho, S. Shaik and W. Nam, *J. Phys. Chem. Lett.*, 2012, **3**, 2851.
16 K.-B. Cho, H. Kang, J. Woo, Y. J. Park, M. S. Seo, J. Cho and W. Nam, *Inorg. Chem.*, 2014, **53**, 645.
17 S. N. Dhuri, K.-B. Cho, Y.-M. Lee, S. Y. Shin, J. H. Kim, D. Mandal, S. Shaik and W. Nam, *J. Am. Chem. Soc*, 2015, **137**, 8623.
18 W. Liu and J. T. Groves, *Acc. Chem. Res.*, 2015, **48**, 1727.
19 N. Jin, M. Ibrahim, T. G. Spiro and J. T. Groves, *J. Am. Chem. Soc.*, 2007, **129**, 12416.
20 W. J. Song, M. S. Seo, S. DeBeer George, T. Ohta, R. Song, M. J. Kang, T. Tosha, T. Kitagawa, E. I. Solomon and W. Nam, *J. Am. Chem. Soc.*, 2007, **129**, 1268.
21 F. Chen, S.-H. Cheng, C.-H. Yu, M.-H. Liu and Y. O. Su, *Electroanal. Chem.*, 1999, **474**, 52.
22 N. Jin, J. L. Bourassa, S. C. Tizio and J. T. Groves, *Angew. Chem. Int. Ed.*, 2000, **39**, 3849.
23 F. De Angelis, N. Jin, R. Car and J. T. Groves, *Inorg. Chem.*, 2006, **45**, 4268.
24 H.-B. Li, S. X. Tian and J. Yang, *J. Phys. Chem. B*, 2008, **112**, 15807.
25 N. Jin and J. T. Groves, *J. Am. Chem. Soc.*, 1999, **121**, 2923.
26 J. Y. Lee, Y.-M. Lee, H. Kotani, W. Nam and S. Fukuzumi, *Chem. Commun.*, 2009, 704.
27 C. Arunkumar, Y.-M. Lee, J. Y. Lee, S. Fukuzumi and W. Nam, *Chem. – A Eur. J.*, 2009, **15**, 11482.
28 K.-B. Cho, H. Hirao, S. Shaik and W. Nam, *Chem. Soc. Rev.*, 2015, submitted.
29 G. S. M. Tong, E. L.-M. Wong and C.-M. Che, *Chem. – A Eur. J.*, 2008, **14**, 5495.
30 D. Janardanan, D. Usharani and S. Shaik, *Angew. Chem. Int. Ed.*, 2012, **51**, 4421.
31 There are two studies using (Mn^VO) and (OMn^VO) where theoretical calculations show singlet transition states as energetically lowest, however, these studies did not use the lowest triplet configurations for the comparisons: *a*) K. A. Prokop, S. P. de Visser and D. P. Goldberg, *Angew. Chem. Int. Ed.*, 2010, **49**, 5091; *b*) S. P. de Visser, *J. Porphyrins Phthalocyanines*, 2013, **17**, 955.
32 Y. H. Kwon, B. K. Mai, Y.-M. Lee, S. N. Dhuri, D. Mandal, K.-B. Cho, Y. Kim, S. Shaik and W. Nam, *J. Phys. Chem. Lett.*, 2015, 1472.
33 D. Janardanan, D. Usharani, H. Chen and S. Shaik, *J. Phys. Chem. Lett.*, 2011, **2**, 2610.