

A Journal of the Gesellschaft Deutscher Chemiker A Deutscher Chemiker GDCh International Edition www.angewandte.org

Accepted Article

Title: A MnIIMnIII-peroxide complex capable of aldehyde deformylation

Authors: Adriana M. Magherusan, Subhasree Kal, Daniel N. Nelis, Lorna M. Doyle, Erik R. Farquhar, Lawrence Que, and Aidan Richard McDonald

This manuscript has been accepted after peer review and appears as an Accepted Article online prior to editing, proofing, and formal publication of the final Version of Record (VoR). This work is currently citable by using the Digital Object Identifier (DOI) given below. The VoR will be published online in Early View as soon as possible and may be different to this Accepted Article as a result of editing. Readers should obtain the VoR from the journal website shown below when it is published to ensure accuracy of information. The authors are responsible for the content of this Accepted Article.

To be cited as: Angew. Chem. Int. Ed. 10.1002/anie.201900717 Angew. Chem. 10.1002/ange.201900717

Link to VoR: http://dx.doi.org/10.1002/anie.201900717 http://dx.doi.org/10.1002/ange.201900717

WILEY-VCH

COMMUNICATION

A Mn^{III}Mn^{III}-peroxide complex capable of aldehyde deformylation

Adriana M. Magherusan,^a Subhasree Kal,^b Daniel N. Nelis,^a Lorna M. Doyle,^a Erik R. Farquhar,^c Lawrence Que, Jr.,^b Aidan R. McDonald^{*a}

Abstract: Ribonucleotide reductases (RNRs) are essential enzymes required for DNA synthesis. In class Ib Mn₂ RNRs superoxide (O₂*-) was postulated to react with the Mn^{II}₂ core to yield a Mn^{II}Mn^{III}-peroxide moiety. The reactivity of complex 1 ([Mn^{II}₂(O₂CCH₃)₂(BPMP)](ClO₄) (1, where HBPMP = 2,6-bis[(bis(2-pyridylmethyl)amino)methyl]-4methylphenol))) towards O₂⁻⁻ was investigated at -90 °C, generating a metastable species, 2. The electronic absorption spectrum of 2 displayed features (λ_{max} = 440, 590 nm) characteristic of a Mn^{II}Mn^{III}peroxide species, representing just the second example of such. Electron paramagnetic resonance and X-ray absorption spectroscopies, and mass spectrometry supported the formulation of 2 as a Mn^{III}Mn^{III}-peroxide complex. Unlike all other previously reported Mn₂-peroxides, which were unreactive, **2** proved to be a capable oxidant in aldehyde deformylation. Our studies provide insight into the mechanism of O₂-activation in Class Ib Mn₂ RNRs, and the highly reactive intermediates in their catalytic cycle.

Ribonucleotide reductases (RNRs) are essential enzymes that play a pivotal role in the regulation of DNA synthesis.^[1] Three different RNR classes have been reported (I, II, and III).^[2] Our attention is focused on class Ib Mn₂ RNRs, which use a Mn₂ cofactor for catalytic activity.^[3] Stubbe and co-workers have proposed that superoxide anion (O2^{•-}), rather than dioxygen, reacts with the Mn^{II}₂ core, to form a mixed valent Mn^{II}Mn^{III}-(hydro)peroxide adduct.^[3d] Mn-peroxide species have often been implicated as precursors to high-valent oxidants,[4] and the Mn^{III}-(hydro)peroxide was postulated to be a precursor to the active oxidant, a μ -O-Mn^{III}Mn^{IV} moiety. We expect a Mn^{II}Mn^{III}-(hydro)peroxide to be highly reactive, however, no insight into any Mn₂-peroxide reactivity is currently available. Exploring the reactivity of the peroxide core will provide information on how external stimuli (*i.e.* H⁺, electrophilies) activate the peroxide core in RNRs.

We recently reported the first example of a $Mn^{II}Mn^{II}$ peroxide complex formed from the reaction of $O_2^{\bullet-}$ with $[Mn^{II}_2(O_2CCH_3)(N-Et-HPTB)](CIO_4)_2$ (N-Et-HPTB = N,N,N',N'tetrakis(2-(1-ethylbenzimidazolyl))-2-hydroxy-1,3-

diaminopropane, Figure 1).^[5] However, that complex proved to be unreactive as either an electrophilic or nucleophilic oxidant.^[5] All other reported Mn₂-peroxide complexes (one Mn^{III}₂- and one Mn^{IV}₂-peroxide)^[6] also displayed no reactivity towards external substrates. Herein, we report the preparation of the second example of a Mn^{III}Mn^{III}-peroxide complex and demonstrate it to be (to the best of our knowledge) the first example of a reactive Mn₂-peroxide.

- a] Adriana M. Magherusan, Daniel N. Nelis, Lorna M. Doyle, Dr. Aidan R. McDonald, School of Chemistry, Trinity College Dublin, The University of Dublin, College Green, Dublin 2, Ireland E-mail: aidan.mcdonald@tcd.ie
- [b] Subhasree Kal, Prof. Lawrence Que, Jr., Department of Chemistry and Centre for Metals in Biocatalysis, University of Minnesota, 207 Pleasant St. SE, Minneapolis, MN 55455, USA
- [c] Dr. Erik R. Farquhar, Case Western Reserve University Centre for Synchrotron Biosciences, National Synchrotron Light Source II, Brookhaven National Laboratory, Upton, NY 11973, USA.

Supporting information for this article is given via a link at the end of the document.

Results and discussion. [Mn^{II}₂(O₂CCH₃)₂(BPMP)](ClO₄) (**1**, where HBPMP = 2,6-bis[(bis(2-pyridylmethyl)amino)methyl]-4-methylphenol, Figure 1) was synthesised as previously described.^[7] To a solution of **1** at -90 °C was added KO₂ and 18-crown-6. An instantaneous reaction occurred (complete within 30 s), as evidenced by changes in the electronic absorption spectrum (Figure 2), resulting in the formation of a new species (**2**).







Figure 2. Electronic absorption spectra of 1 (black trace, 1.5 mM) and 2 (purple trace, from the reaction of 1 (1.5 mM) with KO₂ (1.25 equiv.) at -90 °C in 1:9 CH₃CN/THF). Inset: The ESI-MS spectrum showing the molecular ion for 2 ({[Mn₂(O₂)(BPMP)](ClO₄)}⁺).

The electronic absorption spectrum of **1** displayed no absorbance bands above 400 nm, whereas **2** displayed two low intensity features at $\lambda_{max} = 440$ and 590 nm (Figure 2). The electronic absorption features of **2** were remarkably similar to those of [Mn₂(O₂)(N-Et-HPTB)]²⁺ that we recently reported ($\lambda_{max} = 460, 610$ nm, Figure S1).^[5] Furthermore, such features are also characteristic of mononuclear Mn^{III}-peroxide complexes, which have been reported to display absorption bands at $\lambda_{max} = 400$ - 500 nm and 550 – 650 nm.^[8] This led us to conclude that species **2** was the second example of a Mn^{III}Mn^{III}-peroxide complex.

Cold injection electrospray ionisation mass spectrometry (ESI-MS) on a just-thawed solution of **2** revealed a peak at m/z =

COMMUNICATION

770.2933 with the appropriate isotope distribution pattern to be consistent with its formulation as the mono-cation $\{[Mn_2(O_2)(BPMP)](CIO_4)\}^{+[6a, 4a]}$ (Figures 2, S2). In this cation both acetate ligands from the precursor complex 1 were absent. This mirrors our observations made with $[Mn_2(O_2)(N-Et-HPTB)]^{2+}$ where the starting material contained an acetate ligand, but by ESI-MS we identified only the $[Mn_2(O_2)(N-Et-HPTB)]^{2+}$ dication.^[5]

At 2 K complex 2 displays a 22-line electron paramagnetic resonance (EPR) signal centered at g ~ 1.96 (Figure 3), which can be attributed to an $S = \frac{1}{2} \text{ Mn}^{\parallel}\text{Mn}^{\parallel}$ species.^[9] A 36-line spectrum would be expected assuming an isotropic g-tensor, however, the number of lines is expected to increase with anisotropy, but at the same time there is overlap, resulting in a 22-line spectrum for 2. The yield of 2 was determined by EPR integration to be ~50% (Figure S3). The EPR signal of 2 has a wide spectral width and is well-resolved below 10 K. Above 10 K the signal broadens, obscuring its characteristic 22-line pattern. Similar behavior was reported for the EPR signals of previously reported Mn^{II}Mn^{III} complexes, which exhibit well-resolved 24-29line signals but only at temperatures below 15 K.^[10a, 10b, 9, 10c, 10d] Furthermore, [Mn₂(O₂)(N-Et-HPTB)]²⁺, the only other Mn^{II}Mn^{III-} peroxide reported to date, also displayed a well-resolved 29-line EPR signal centered at g ~ 1.96 with a wide spectral width but was only well resolved below 10 K (Figures 3, S4).^[5] This temperature dependence is indicative of a weak coupling interaction between the Mn ions.[10c]



Figure 3. Perpendicular mode X-band EPR spectrum of 2 at 2 K (purple trace, obtained from the reaction of 1 (1.5 mM) and KO₂ in 1:9 CH₃CN/THF, 9.64 GHz, 0.2 mW microwave power) and $[Mn_2(O_2)(N-Et-HPTB)]^2$ (red trace, for comparison).

Hendrickson and co-workers previously reported a mixed valent form of complex **1** ([Mn^{II}Mn^{III}(O₂CCH₃)₂(BPMP)]²⁺) which displayed a 29-line signal centred at g ~ 2 at 7.5 K^[10a] and differs from the 22-line EPR spectrum exhibited by **2** at 2 K. Thus, we conclude that complex **2** represented a unique Mn^{II}Mn^{III} complex supported by the BPMP ligand. Furthermore, while the electronic absorption spectrum of **2** exhibited two weak absorption bands at λ_{max} = 440 and 590 nm, the Hendrickson complex displayed three absorption bands at λ_{max} = 427, 478 and 620 nm which were markedly more intense as well.^[7a] The different EPR and electronic absorption spectra support our postulate that complex **2** and [Mn^{III}Mn^{III}(O₂CCH₃)₂(BPMP)]²⁺ are different species, leading us to define complex **2** as [Mn^{II}Mn^{III}(O₂)(BPMP)]²⁺.

To gain better insight into the oxidation state of **2**, Mn K-edge X-ray absorption near edge spectroscopy (XANES) was carried out on frozen samples of **1** and **2**. The edge energy of **1** was found to be 6548.4 eV, while that of **2** was 6548.9 eV, an increase of 0.5 eV (Table S1, Figures 4, S5). Systematic studies of Mn coordination compounds have shown that each integer change in formal oxidation state elicits a blue-shift of 2-4 eV in K-edge inflection energy.^[11] For a mixed valent Mn₂ species, a shift of 1 eV would therefore be expected upon quantitative oxidation of a Mn^{II}Mn^{III} precursor (**1**) to a Mn^{II}Mn^{III}-peroxide (**2**) adduct. Here, the yield of **2** was only ~50%, according to EPR analysis, consistent with the observed blue-shift of 0.5 eV. For the previously reported peroxide complex [Mn₂(O₂)(N-Et-HPTB)]²⁺ we observed an ~1 eV shift upon conversion of the Mn^{III}₂ starting material to the Mn^{III}Mn^{III} species [Mn₂(O₂)(N-Et-HPTB)]²⁺ (obtained in 80% yield, Figure



Figure 4. Normalised XANES spectra of 1 (solid trace) and 2 (dashed trace). The inset shows an expansion of the pre-edge region.

Notably, there was a significant increase in the pre-edge area from 5.8 to 9.4 units upon conversion of 1 to 2, respectively (Figure 4, S7, Table S1). The increased pre-edge area is indicative of a decrease in symmetry from octahedral Mn sites in 1 to a lower degree of symmetry (possibly 5-coordinate Mn site(s)) in $\mathbf{2}^{[11b,\ 12]}$ The pre-edge peak of $\mathbf{1}$ can be constructed as a combination of two independent peaks at 6540.0 eV and 6540.8 eV (Figures S7-S9). The weighted average of these two transitions give a pre-edge energy of approximately 6540.3 eV, which is identical to that of 2 (also 6540.3 eV, Table S1). This is not unexpected, as appreciable changes in pre-edge energy are generally not found until the Mn^{IV} state is achieved.^[11c] It has been shown that octahedral Mn^{II} complexes exhibit two 1s \rightarrow 3d transitions of similar energy (1s \rightarrow 3d(e_g) and 1s \rightarrow 3d(t_{2g})), separated by ~ 0.8 - 1 eV.^[13, 11b] We assume that the two features observed derive from the octahedral nature of the Mn sites in 1. The observation of a loss of symmetry in the pre-edge feature for 2, upon conversion of 1 to 2, indicates a change in coordination environment at the metals. The loss of an electron, through Mn oxidation, could lead to an increase in the number of vacant valence *d*-orbitals present, thus affecting the $1s \rightarrow 3d$ transitions. This would in turn increase the area of the pre-edge feature, as is observed. $^{\left[11b,\ 12\right] }$ A change comparable to this was reported by Kovacs, DeBeer, and co-workers, wherein a 5-coordinate starting

COMMUNICATION

Mn^{II} complex was oxidised to a 6-coordinate Mn^{III}₂-peroxide complex, leading to a *decrease* in the pre-edge area, providing support for our interpretation.^[14] The shift of the edge energy by 0.5 eV as well as the changes to pre-edge area and decreased site symmetry support our assignment of **2** as a Mn^{II}Mn^{III} species. Extended X-ray absorption fine structure (EXAFS) analysis on **2** was not carried out due to the low yield obtained (~ 50%). Based on the spectroscopic results along with the mass spectrometric evidence, we concluded that **2** was a Mn^{II}Mn^{III}-peroxide complex.

At -90 °C, **2** displayed a $t_{1/2} = 2$ h, but decayed fully within 180 s upon warming to room temperature. The electronic absorption spectrum of **2** at -90 °C remained unchanged upon the addition of triphenylphosphine (PPh₃), cyclohexene, or substrates containing weak X–H bonds (all added in 100-fold excess, including 1-methyl-1,4-cyclohexadiene, 9,10-dihydroanthracene, and 2,4-di*tert*-butylphenol). Hence, **2** was determined to be a poor electrophilic oxidant. This observation was consistent with our observations for [Mn₂(O₂)(N-Et-HPTB)]^{2+,[5]} which was also unreactive towards such substrates.

In contrast, at -90 °C in 1:9 CH₃CN/THF 2 reacted readily with aldehyde substrates including 2-phenylpropionaldehyde (PPA), cyclohexanecarboxaldehyde (CCA), and para-substituted benzaldehydes (p-X-C₆H₄C(H)O). The reactions with PPA and CCA (Figures S10-S17) afforded acetophenone and cyclohexanone, respectively. as evidenced by gas chromatography mass spectrometry. By plotting the change in the absorbance of the λ_{max} = 440 nm feature of **2** against time and fitting the resulting curve, first order rate constants (k_{obs}) for the reaction with PPA or CCA were determined (Figures S10, S14). To calculate a second order rate constant (k_2) we plotted k_{obs} against [substrate] for a series of [substrate] (Figures S12, S16). At low [substrate] the relationship appeared to be linear allowing for an estimation of k_2 values (Table 1). However, and surprisingly, at higher [substrate] the rate at which 2 reacted increased exponentially.^[21]

We believe that, as typical for Baeyer-Villiger oxidations (Scheme 1),^[15] the reaction between 2 and aldehyde involves initial reversible nucleophilic attack of the peroxide on the electrophilic aldehyde C-atom, followed by Criegeerearrangement (where the C-atom α to the aldehyde C-atom attacks the distal O-atom resulting in O-O bond scission, which is irreversible, Scheme 1).^[16] The latter is normally ascribed as the rate-limiting step in such reactions. We postulate that at low [substrate] the kinetic results provide insight into the reversible nucleophilic attack, and at high [substrate] the kinetic results are likely associated with the Criegee rearrangement.



Scheme 1. Nucleophilic attack of 2 on aldehyde substrates followed by irreversible Criegee rearrangement.

2 also reacted with electron-poor p-X-C₆H₄C(H)O (X = H, Cl, CF₃, CN, NO₂, Figures S15-S20). The products of the oxidation of these substrates were the respective benzoic acids. No reaction was observed when **2** was reacted with p-OCH₃-C₆H₄C(H)O or p-

CH₃-C₆H₄C(H)O (~3000 equiv.). k_2 values were determined for the substrates that did react. Importantly, exponential changes to k_{obs} were not observed for the benzaldehyde substrates (to the limits of [substrate] before precipitation of the substrate). This suggests that for the *p*-X-C₆H₄C(H)O substrates the kinetic results provide insight into the initial nucleophilic attack, while the subsequent Criegee rearrangement does not influence the kinetics. This observation is consistent with Criegee rearrangement being slower for the electron-poor α -C atom (relative to the aldehyde ketone) benzaldehydes than for the electron-rich α -C PPA and CCA. Overall, this indicates that at low [PPA] or low [CCA], and for all [*p*-X-C₆H₄C(H)O], nucleophilic attack is rate limiting. While at high [PPA] or [CCA] Criegee rearrangement is rate limiting.



Figure 5. Hammett plot for the reaction between **2** and p-X-C₆H₄C(H)O (X = H, Cl, CF₃, CN, NO₂).

A Hammett plot of the log(^R k_2 /^H k_2) versus the *para*-substituent (σ_p) was linear and resulted in a positive ρ value of 0.64 (Figure 5). Previous reports showed that the nucleophilic character of the {M^{III}O₂} unit (M = Mn, Ni, Co) could be confirmed by using *p*-X-PhC(O)H. For these metal-peroxides a Hammett plot was always linear with a positive ρ value in the range of 1.7-2.5.^[17] The slightly higher ρ values were obtained for mononuclear complexes and when compared to the ρ value of 0.64 obtained for 2 indicate that the electronic influence of the substrate on the rate of nucleophilic attack may be diminished for 2. Nonetheless, these results confirm that the rate limiting step in the reaction of 2 and *p*-X-C₆H₄C(H)O was nucleophilic attack. 2 was thus a capable aldehyde deformylating oxidant, and the first Mn₂-peroxide to display reactivity towards external substrates.

Previously reported *mononuclear* Mn^{III}-peroxide complexes also proved to be competent PPA and CCA deformylating oxidants (both TMC- (tetramethylcyclam)^[18, 17b, 8d] and polypyridine-^[19] supported complexes, Table 1). For PPA, at -90 °C **2** displayed a relatively low estimated k_2 compared to k_2 values determined for those Mn^{III}-peroxide complexes. It is important, however, to consider the different temperatures these measurements were performed at: -90 °C for **2**; 0 °C for [Mn^{III}(O₂)(Pro3Py)]⁺; +20 °C for TMC-supported complexes. In contrast, **2** oxidised CCA at -90 °C at rates comparable to those determined for TMCsupported complexes at significantly higher temperatures (+10 °C, Table 1), while still displaying lower reactivity than polypyridinesupported complexes (-40 °C). Overall, **2** proved to be an effective deformylating oxidant considering the low temperature the

COMMUNICATION

reactivity was performed under.^[18, 17b, 8d] The reactivity properties of previously reported Mn2-peroxide complexes were not addressed.^[6] The lower metal oxidation state in 2 with respect to the other examples (Mn^{III}₂- and Mn^{IV}₂-peroxide complexes) could enhance its nucleophilic reactivity.^[6] We believe that 2 was more reactive than [Mn₂(O₂)(N-Et-HPTB)]²⁺ due to the presence of less steric bulk in 2 allowing for more facile access to the peroxide core. That aldehydes reacted with 2 demonstrates that an electrophile is required to activate the Mn^{II}Mn^{III}-peroxide core, as in the RNRs where H⁺ is postulated to activate the core.

	PPA		CCA	
	<i>k</i> ₂ [M⁻¹s⁻¹] (T [°C])	Ref	<i>k</i> ₂ [M⁻¹s⁻¹] (T [°C])	Ref
2	0.0006 (-90)		0.014 (-90)	
[Mn ^{III} (O ₂)(12-TMC)] ⁺	0.04 (20)	[8d]	0.3 (0)	[18]
[Mn ^{III} (O ₂)(13-TMC)] ⁺	0.03 (20)	[8d]	0.02 (10)	[17b]
[Mn ^{III} (O ₂)(14-TMC)] ⁺	0.04 (20)	[8d]	0.04 (10)	[17b]
[Mn ^{III} (O ₂)(Pro3Py)] ⁺	0.003 (0)	[19]	-	-
[Mn ^{III} (O ₂)(L ⁷ py ₂ ^{6-Me})] ⁺	-		0.32 (-40)	[20]
[Mn ^{III} (O ₂)(L ⁷ py ₂ ^{4-Me})] ⁺	-		0.40 (-40)	[20]
[Mn ^{III} (O ₂)(L ⁸ py ₂ ^H)] ⁺	-		0.19 (-40)	[20]

Table 1. Rate constants for deformylation by Mn-peroxide complexes.

12-TMC = 1,4,7,10-tetramethyl-1,4,7,10-tetraazacyclododecane; 13-TMC = 1,4,7,10-tetramethyl-1,4,7,10-tetraazacyclotridecane; 14-TMC = 1,4,8,11tetramethyl-1,4,8,11-tetraazacyclotetradecane. L⁷py2^{6-Me} = 1,4-bis(6-methyl-2pyridylmethyl)-1,4-diazepane; L⁷py2^{4-Me} = 1,4-bis(4-methyl-2-pyridylmethyl)-1,4diazepane; L⁸py₂^H = 1,5-bis(2-pyridylmethyl)-1,5-diazacyclooctane.

Conclusions. We prepared and characterized a meta-stable Mn^{III}Mn^{III}-peroxide complex from the reaction between a Mn2^{II} complex and superoxide anion, mimicking the postulated biochemistry of the class Ib Mn₂ RNRs. The complex displayed features typical of a Mn^{II}Mn^{III}-peroxide complex by electronic absorption, EPR, and XAS spectroscopies, and mass spectrometry. Interestingly, 2 was found to be an efficient nucleophilic aldehyde deformylation reagent, exhibiting comparable reaction rates to previously reported mononuclear Mn-peroxide complexes. To the best of our knowledge this is the first example of a reactive Mn₂-peroxide entity, and furthermore demonstrates that an electropositive species (H⁺ for RNRs. electrophilic aldehyde for 2) is required to activate the peroxide core in RNRs.

Ackowledgments: This publication has emanated from research supported by the Irish Research Council (IRC) under Grant GOIPG/2014/942 Numbers to Α. Magherusan and GOIPG/2017/525 to D. Nelis. Research in the McDonald lab is supported in part by the European Union (ERC-2015-STG-678202) and research grants Science Foundation Ireland (SFI/15/RS-URF/3307, SFI/17/RS-EA/3470). Support for this research in the Que lab has been provided by the US National Institutes of Health (GM38767). XAS measurements benefited from support of SSRL by the U.S. Department of Energy, Office of Science, Office of Basic Energy Sciences under Contract No. DE-AC02-76SF00515, as well as support of the SSRL Structural Molecular Biology Program through the DOE Office of Biological

and Environmental Research and the National Institutes of Health (P41-GM-103393). E.R.F. is supported by NIH grant P30-EB-009998.

Keywords: ribonucleotide reductases • Mn^{III}Mn^{III}-peroxide • superoxide activation • nucleophilic reactivity • aldehyde deformylation

- [1] J. A. Cotruvo, J. Stubbe, Annu. Rev. Biochem. 2011, 80, 733-767.
- a) A. Jordan, P. Reichard, Annu. Rev. Biochem. 1998, 67, 71-98; b) M. [2] Kolberg, K. R. Strand, P. Graff, K. K. Andersson, Biochim. Biophys. Acta 2004, 1699, 1-34; c)P. Nordlund, P. Reichard, Annu. Rev. Biochem. 2006, 75, 681-706.
- a) A. K. Boal, J. A. Cotruvo, Jr., J. Stubbe, A. C. Rosenzweig, *Science* **2010**, 329, 1526-1530; b) J. A. Cotruvo, Jr., J. Stubbe, *Biochemistry* [3] 2010, 49, 1297-1309; c) N. Cox, H. Ogata, P. Stolle, E. Reijerse, G. Auling, W. Lubitz, *J. Am. Chem. Soc.* 2010, *132*, 11197-11213; d) J. *A* Cotruvo, Jr., T. A. Stich, R. D. Britt, J. Stubbe, J. Am. Chem. Soc. 2013, 135, 4027-4039
- [4] a) S. Groni, G. Blain, R. Guillot, C. Policar, E. Anxolabehere-Mallart, Inorg. Chem. 2007, 46, 1951-1953; b) M. Gennari, D. Brazzolotto, J. Pecaut, M. V. Cherrier, C. J. Pollock, S. DeBeer, M. Retegan, D. A. Pantazis, F. Neese, M. Rouzieres, R. Clerac, C. Duboc, J. Am. Chem. Soc. 2015, 137, 8644-8653; c) D. Brazzolotto, F. G. Cantu Reinhard, J. Smith-Jones, M. Retegan, L. Amidani, A. S. Faponle, K. Ray, C. Philouze, S. P. de Visser, M. Gennari, C. Duboc, Angew. Chem. Int. Ed. Engl. 2017, 56, 8211-8215.
- [5] A. M. Magherusan, A. Zhou, E. R. Farquhar, M. Garcia-Melchor, B. Twamley, L. Que, Jr., A. R. McDonald, *Angew. Chem. Int. Ed. Engl.* 2018, 57, 918-922.
- a) T. W. U. Bossek, K. Wieghardt, B. Nuber, J. Weiss, J. Am. Chem. [6] Soc. 1990, 112, 6387-6388; b) M. K. Coggins, X. Sun, Y. Kwak, E. I. Solomon, E. Rybak-Akimova, J. A. Kovacs, J. Am. Chem. Soc. 2013, 135, 5631-5640.
- a) M. Suzuki, M. Mikuriya, S. Murata, A. Uehara, H. Oshio, S. Kida, K. [7] Saito, Bull. Chem. Soc. Jpn. 1987, 60, 4305-4312; b) S. Blanchard, G. Blondin, E. Riviere, M. Nierlich, J. J. Girerd, Inorg. Chem. 2003, 42, 4568-4578.
- [8] a) D. R. Gamelin, M. L. Kirk, T. L. Stemmler, S. Pal, W. H. Armstrong, J. E. Penner-Hahn, E. I. Solomon, J. Am. Chem. Soc. 1994, 116, 2392-2399; b) R. L. Shook, W. A. Gunderson, J. Greaves, J. W. Ziller, M. P. Hendrich, A. S. Borovik, J. Am. Chem. Soc. 2008, 130, 8888-8889; c) J. Cho, R. Sarangi, W. Nam, Acc. Chem. Res. 2012, 45, 1321-1330; d) H. Kang, J. Cho, K. B. Cho, T. Nomura, T. Ogura, W. Nam, *Chem. Eur. J.* **2013**, *19*, 14119-14125; e) D. F. Leto, S. Chattopadhyay, V. W. Day, T. A. Jackson, *Dalton Trans.* **2013**, *42*, 13014-13025; f) D. F. Leto, T. A. Jackson, J. Biol. Inorg. Chem. 2014, 19, 1-15; g) N. Saravanan, M. Sankaralingam, M. Palaniandavar, RSC Advances 2014, 4, 12000.
- H. Diril, H. R. Chang, M. J. Nilges, X. Zhang, J. A. Potenza, H. J [9] Schugar, S. S. Isied, D. N. Hendrickson, J. Am. Chem. Soc. 1989, 111, 5102-5114
- [10] a) H. Diril, H. R. Chang, X. Zhang, S. K. Larsen, J. A. Potenza, C. G. Pierpont, H. J. Schugar, S. S. Isied, D. N. Hendrickson, J. Am. Chem. Soc. 1987, 109, 6207-6208; b) R. M. Buchanan, K. J. Oberhausen, J. F. Richardson, Inorg. Chem. 1988, 27, 971-973; c) N. Cox, W. Ames, B. Epel, L. V. Kulik, L. Rapatskiy, F. Neese, J. Messinger, K Wieghardt, W. Lubitz, *Inorg. Chem.* 2011, *50*, 8238-8251; d) Y. Sano, A. C. Weitz, J. W. Ziller, M. P. Hendrich, A. S. Borovik, *Inorg. Chem.* 2013. 52. 10229-10231.
- [11] a) T. C. Weng, W. Y. Hsieh, E. S. Uffelman, S. W. Gordon-Wylie, T. J. Collins, V. L. Pecoraro, J. E. Penner-Hahn, J. Am. Chem. Soc. 2004, 126, 8070-8071; b) F. Farges, Phys. Rev. B 2005, 71; c) R. E. Schreiber, H. Cohen, G. Leitus, S. G. Wolf, A. Zhou, L. Que, Jr., R. Neumann, J. Am. Chem. Soc. 2015, 137, 8738-8748.
- [12] M. Roemelt, M. A. Beckwith, C. Duboc, M. N. Collomb, F. Neese, S. DeBeer, Inorg. Chem. 2012, 51, 680-687.
- [13] G. Dräger, T. Kirchner, S. Bocharov, C. C. Kao, Appl. Phys. A Mater. Sci. Process 2001, 73, 687-691.
- J. A. Rees, V. Martin-Diaconescu, J. A. Kovacs, S. DeBeer, Inorg. [14] Chem. 2015, 54, 6410-6422.
- [15] G. Strukul, Angew. Chem. Int. Ed. 1998, 37, 1198-1209
- [16] P. Pirovano, A. M. Magherusan, C. McGlynn, A. Ure, A. Lynes, A. R. McDonald, Angew. Chem. Int. Ed. 2014, 53, 5946-5950.
- [17] a) Y. Jo, J. Annaraj, M. S. Seo, Y. M. Lee, S. Y. Kim, J. Cho, W. Nam, J. Inorg. Biochem. 2008, 102, 2155-2159; b) J. Annaraj, J. Cho, Y. M. Lee, S. Y. Kim, R. Latifi, S. P. de Visser, W. Nam, Angew. Chem. Int. Ed. 2009, 48, 4150-4153; c) J. Cho, R. Sarangi, J. Annaraj, S. Y. Kim, M. Kubo, T. Ogura, E. I. Solomon, W. Nam, Nat. Chem. 2009, 1, 568; d) J. Cho, R. Sarangi, H. Y. Kang, J. Y. Lee, M. Kubo, T. Ogura, E. I. Solomon, W. Nam, J. Am. Chem. Soc. 2010, 132, 16977-16986
- [18] M. S. Seo, J. Y. Kim, J. Annaraj, Y. Kim, Y. M. Lee, S. J. Kim, J. Kim,
- W. Nam, Angew. Chem. Int. Ed. 2007, 46, 377-380. [19] J. Du, D. Xu, C. Zhang, C. Xia, Y. Wang, W. Sun, Dalton. Trans. 2016, 45, 10131-10135.



[20] R. A. Geiger, S. Chattopadhyay, V. W. Day, T. A. Jackson, *Dalton Trans.* 2011, *40*, 1707-1715.
[21] k_{obs} measurements at very high [substrate] were too fast to perfrom accurate kinetic analysis.

COMMUNICATION

Entry for the Table of Contents:

COMMUNICATION

Nucleophilic reactivity: The reaction of a Mn^{II}₂ complex with superoxide yielded Mn^{II}Mn^{III}а peroxide complex which mimics intermediates in class lb Mn₂ ribonucleotide reductases. The Mn^{III}Mn^{III}-peroxide species displayed an unexpected nucleophilic character in aldehyde deformylation.



Adriana M. Magherusan,^a Subhasree Kal,^b Daniel N. Nelis,^a Lorna Doyle,^a Erik R. Farquhar,^c Lawrence Que, Jr.,^b Aidan R. McDonald*^a

Page No. – Page No.

A Mn^{III}Mn^{III}-peroxide complex capable of aldehyde deformylation