

View Article Online View Journal

# ChemComm

# Accepted Manuscript

This article can be cited before page numbers have been issued, to do this please use: T. Lau, M. Chen, Y. Pan, H. Kwong, R. J. Zeng and K. Lau, *Chem. Commun.*, 2015, DOI: 10.1039/C5CC03636D.



This is an *Accepted Manuscript*, which has been through the Royal Society of Chemistry peer review process and has been accepted for publication.

Accepted Manuscripts are published online shortly after acceptance, before technical editing, formatting and proof reading. Using this free service, authors can make their results available to the community, in citable form, before we publish the edited article. We will replace this Accepted Manuscript with the edited and formatted Advance Article as soon as it is available.

You can find more information about *Accepted Manuscripts* in the **Information for Authors**.

Please note that technical editing may introduce minor changes to the text and/or graphics, which may alter content. The journal's standard <u>Terms & Conditions</u> and the <u>Ethical guidelines</u> still apply. In no event shall the Royal Society of Chemistry be held responsible for any errors or omissions in this *Accepted Manuscript* or any consequences arising from the use of any information it contains.



www.rsc.org/chemcomm



# COMMUNICATION

# Catalytic oxidation of alkanes by a (salen)osmium(VI) nitrido complex using $H_2O_2$ as the terminal oxidant

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

Man Chen,<sup>a,b,c</sup> Pan Yi,<sup>b</sup> Hoi-Ki Kwong,<sup>b</sup> Raymond J. Zeng,<sup>a,c</sup> Kai-Chung Lau<sup>\*b</sup> and Tai-Chu Lau<sup>\*a,b</sup>

DOI: 10.1039/x0xx00000x

www.rsc.org/

The osmium(VI) nitrido complex,  $[Os^{VI}(N)(L)(CH_3OH)]^+$  (1, L = N,N'bis(salicylidene)-o-cyclohexyldiamine dianion) is an efficient catalyst for the oxidation of alkanes at ambient conditions using H<sub>2</sub>O<sub>2</sub> as the oxidant. Alkanes are oxidized to the corresponding alcohols and ketones, with yields up to 75% and turnover number up to 2230. Experimental and computational studies are consistent with a mechanism that involves O-atom transfer from  $H_2O_2$  to  $[Os^{VI}(N)(L)]^+$  to generate an  $[Os^{VIII}(N)(O)(L)]^+$  active intermediate.

The selective oxidation of alkanes under mild conditions continues to be an important research area.<sup>1</sup> A variety of enzymes, such as cytochrome P-450 and methane monooxygenase, are able to catalyze selective alkane oxidation.<sup>2</sup> On the other hand, relatively few chemical systems are able to oxidize alkanes efficiently under mild conditions, especially using green terminal oxidants such as  $H_2O_2$  or  $O_2$ . Transition metal complexes in oxidation states II or III are commonly used as catalysts for alkane oxidation. On the other hand, we recently demonstrated that high-valent d<sup>2</sup> metal nitrido species can function as highly efficient alkane oxidation catalysts; they can accept an O-atom from an oxidant such as  $H_2O_2$  to generate a d<sup>0</sup> metal nitrido oxo species as the active oxidant. For example, we have reported that the d<sup>2</sup>  $[Os^{VI}(N)Cl_4]^-$  and  $[Mn^{V}(N)(CN)_4]^{2-}$  complexes are highly efficient catalysts for alkane oxidation by H2O2.4,5 These square pyramidal nitrido species possess a vacant site that can readily bind and activate  $H_2O_2$ . In the case of  $[Os^{VI}(N)Cl_4]^{-}$ , its catalytic activity can be greatly accelerated by Lewis acids such as FeCl<sub>3</sub> or Sc(CF<sub>3</sub>SO<sub>3</sub>)<sub>3</sub>, which readily bind to the nitrido ligand and exert an electrophilic effect on the catalyst.<sup>4</sup>

states, moreover steric and electronic effects can be readily tuned by varying substituents on the ligand.<sup>6-9</sup> Herein we report the catalytic oxidation of alkanes by a (salen)osmium(VI) nitrido complex  $[Os^{VI}(N)(L)(CH_3OH)]^+$  (1, L = N,N'-bis(salicylidene)-o-cyclohexyldiamine dianion; Fig. 1),<sup>10</sup> using the environmentally benign hydrogen peroxide as the terminal oxidant.



In an attempt to design more robust catalysts, we plan to

replace the four monodentate ligands in these metal nitrido

catalysts with a quadridentate ligand such as salen or its

derivatives. Salen ligands are known to stabilize high oxidation

1 was found to readily catalyze the oxidation of cyclohexane in  $CH_2Cl_2/CH_3CO_2H$  (5:2, v/v) with  $H_2O_2$  at room temperature under argon (Table 1). Using excess cyclohexane, a mixture of cyclohexanol (61%) and cyclohexanone (12%) was obtained (Entry 1). There is also a small amount of chlorocyclohexane (2%), which probably came from the reaction of cyclohexyl radicals with CH<sub>2</sub>Cl<sub>2</sub>. The total yield is 75%, which corresponds to a turnover number (TON) of 60. Other solvents such as CF<sub>3</sub>CH<sub>2</sub>OH or CH<sub>3</sub>CN give lower yields (Table S1). By lowering the concentration of 1 and adding  $H_2O_2$ slowly using a syringe pump, a maximum TON of 2230 could be achieved (Table S2, entry 1). The observed higher TON when H<sub>2</sub>O<sub>2</sub> is added slowly suggests that the active intermediate can also oxidize H<sub>2</sub>O<sub>2</sub>, hence keeping [H<sub>2</sub>O<sub>2</sub>] low would minimize its decomposition. When the reaction was carried out in air, the yield increased from 75% to 82% (Table 1, entry 2). On the other hand, when the alkyl radical scavenger BrCCl<sub>3</sub> was added to the system, 6% of bromocyclohexane could be detected (Entry 3). These results indicate that some freely diffusing cyclohexyl radicals are formed in the system, which can abstract halogen atoms from the solvent CH<sub>2</sub>Cl<sub>2</sub> or from added

<sup>&</sup>lt;sup>a.</sup> Advanced Laboratory for Environmental Research & Technology (ALERT), USTC-CitvU, Suzhou 215123, China.

Email: bhtclau@cityu.edu.hk

<sup>&</sup>lt;sup>b.</sup> Department of Biology and Chemistry and Institute of Molecular Functional Materials, City University of Hong Kong, Tat Chee Avenue, Kowloon Tong, Hong Kong SAR, Ching

<sup>&</sup>lt;sup>2</sup> Department of Chemistry, University of Science & Technology of China, Hefei 230026, China

<sup>+</sup> Electronic Supplementary Information (ESI) available: experimental details and catalysis results. See DOI: 10.1039/x0xx00000x

Fig. 1 Structure of 1

### COMMUNICATION

Published on 20 July 2015. Downloaded by University of Arizona on 27/07/2015 03:18:33.

BrCCl<sub>3</sub>. The cyclohexyl radical can also react with O<sub>2</sub> to generate a mixture of cyclohexanol and cyclohexanone.<sup>11</sup> By using an equimolar mixture of C<sub>6</sub>H<sub>12</sub> and C<sub>6</sub>D<sub>12</sub> as substrate, a deuterium isotope effect of 4.2 was obtained, suggesting that the rate-limiting step in the oxidation of cyclohexane by the active intermediate involves C-H bond cleavage. Although we previously found that the catalytic oxidation of alkanes by  $[Os(N)Cl_4]$  is greatly accelerated by Lewis acids,<sup>4</sup> no enhancement of catalytic activity was found in this case when Lewis acids such as BF<sub>3</sub>, FeCl<sub>3</sub> and Sc(OTf)<sub>3</sub> were added to the system (Table 1, entries 4-6). This result is perhaps not surprising, since 1 is a cationic species and its affinity for Lewis acids is expected to be low. The UV/Vis spectrum of the catalyst is also not affected by the presence of various Lewis acids.

Entry	Catalyst	Product yield <sup>b</sup>			Total
		Cy-OH	Cy=O	Cy-Cl	yield
1	1	61%	12%	2%	75%
2	1 <sup>c</sup>	68%	12%	2%	82%
3	$1^{d}$	63%	8%	2%	73%
4	$1/BF_3$	63%	12%	2%	77%
5	1/FeCl₃	58%	12%	4%	74%
6	1/Sc(OTf) <sub>3</sub>	59%	11%	3%	73%

<sup>*a*</sup>Reaction conditions: **1** (0.625 mM), Lewis acid (1.25 mM), cyclohexane (1.2 M), CH<sub>2</sub>Cl<sub>2</sub>/CH<sub>3</sub>CO<sub>2</sub>H (5:2, v/v), H<sub>2</sub>O<sub>2</sub> (50 mM, 80 equiv), T = 23 <sup>o</sup>C, time = 3h, under argon. <sup>*b*</sup>Products yields were calculated based on H<sub>2</sub>O<sub>2</sub> acting as a two-electron oxidant. <sup>*c*</sup>Reaction in air. <sup>*d*</sup>Reaction in the presence of BrCCl<sub>3</sub> (50 mM), 6% bromocyclohexane could also be detected.

The catalytic oxidation of various other alkanes by  $1/H_2O_2$  has also been investigated (Table 2). As in the case of cyclohexane, good yields were obtained and the major products are the corresponding alcohols. Oxidation of linear alkanes occurs only at the secondary C-H bonds (Entries 4-5). On the other hand, oxidation of 1,2-dimethylcyclohexanes occurs predominantly at the tertiary C-H bonds (Entries 6-7), hence for this catalytic system the reactivity order is  $3^0>2^0>>1^0$ . Around 5% of epimerized products were observed in the oxidation of 1,2-dimethylcyclohexanes, implying that the tertiary alkyl radical is sufficiently long-lived to undergo some

epimerization. The alcohol/ketone ratio increases when [cyclohexane] increases or when  $[H_2O_2]$  decreases (Table S4), suggesting that the ketone is derived from further oxidation of the initial alcohol product by the active intermediate.

A metal catalyst may react with ROOH via homolytic (equation 1) or heterolytic (equation 2) pathways to generate species that can abstract H–atoms from RH.

$M^{n+} + ROOH \longrightarrow M^{n+1}-OH + RO^{\bullet}$	(1)
---	-----

 $M^{n+} + ROOH \longrightarrow M^{n+2} = O + ROH$  (2)

 $PhCH_2C(CH_3)_2O^{\bullet} \longrightarrow PhCH_2^{\bullet} + (CH_3)_2CO$ (3)

One way to distinguish between these two possibilities is to use PhCH<sub>2</sub>C(CH<sub>3</sub>)<sub>2</sub>OOH (MPPH) as the oxidant.<sup>12-14</sup> If MPPH undergoes homolytic O-O bond cleavage on interaction with the metal catalyst (equation 1), the resulting tert-alkoxyl radical PhCH<sub>2</sub>C(CH<sub>3</sub>)<sub>2</sub>O• would undergo very rapid  $\beta$ -scission (equation 3); thus H-atom abstraction from the alkane by PhCH<sub>2</sub>C(CH<sub>3</sub>)<sub>2</sub>O• cannot occur. Subsequent reactions of PhCH<sub>2</sub>• would result in products such as PhCH<sub>2</sub>OH and PhCHO. On the other hand, heterolytic cleavage of MPPH would produce PhCH<sub>2</sub>C(CH<sub>3</sub>)<sub>2</sub>OH (MPPOH) and M=O (equation 2), the latter species may oxidize RH to give ROH. When cyclohexane oxidation was carried out using 1/MPPH, the major products are those derived from heterolytic cleavage of MPPH and subsequent alkane oxidation by the M=O species, including 89% MPPOH, 40% cyclohexanol, 3% cyclohexanone and 3% chlorocyclohexane. There are also minor products derived from homolytic cleavage of MPPH, including 2% benzaldehyde, 7% benzyl alcohol and 1% benzyl chloride. We conclude that MPPH undergoes predominantly heterolytic cleavage on interaction with 1.

Catalytic cyclohexane oxidation under argon using  $H_2^{\ 18}O_2$ in  $H_2^{\ 16}O$  was also carried out. The cyclohexanol product was found to be 100%  $^{\ 18}O$ -labeled, while the cyclohexanone was 12%  $^{\ 18}O$ -labeled (Table S5). O-exchange between alcohol and water is known to be very slow while O-exchange between ketone and water occurs readily at room temperature.<sup>4</sup> This result indicates that the oxygen source in the organic products came from  $H_2O_2.$ 

All the experimental results are consistent with a

<b>Table 2.</b> Catalytic oxidation of alkanes by $1/H_2O_2^{a}$						
Entry	Substrate	Products (% yield) <sup>b</sup>	Total yield			
1	cyclohexane	cyclohexanol (61%), cyclohexanone (12%), chlorocyclohexane (2%)	75%			
2	cycloheptane	cycloheptanol (60%), cycloheptanone (10%)	70%			
3	cyclooctane	cyclooctanol (65%), cyclooctanone (6%)	71%			
4	<i>n</i> -hexane	2-hexanol (24%), 3-hexanol (28%), 2-hexanone (7%), 3-hexanone (8%)	67%			
5	<i>n</i> -heptane	2-heptanol (23%), 3-heptanol (23%), 4-heptanol (12%),	<u> </u>			
		2-heptanone (5%), 3-heptanone (4%), 4-heptanone (2%)	69%			
6	cis-1,2- dimethylcyclohexane	cis-1,2-dimethylcyclohexanol (68%), trans-1,2-dimethylcyclohexanol (5%),	750/			
		cis-2,3-dimethylcyclohexanol (1%), cis-3,4-dimethylcyclohexanone (1%)	/5%			
7	trans-1,2- dimethylcyclohexane	trans-1,2-dimethylcyclohexanol (48%), cis-1,2-dimethylcyclohexanol (4%)	70%			
		trans-2,3-dimethylcyclohexanol (8%), trans-2,3-dimethylcyclohexanone (3%),				
		trans-3 A-dimethylovclobexanol (5%) trans-3 A-dimethylovclobexanone (2%)				

<sup>a</sup>Reaction conditions: 1 (0.625 mM), alkane (1.2 M), CH<sub>2</sub>Cl<sub>2</sub>/CH<sub>3</sub>CO<sub>2</sub>H (5:2, v/v), H<sub>2</sub>O<sub>2</sub> (50 mM, 80 equiv.), under argon, T = 23 °C, t = 3h. <sup>b</sup>Products yields were calculated based on H<sub>2</sub>O<sub>2</sub> acting as a two-electron oxidant.

This journal is C The Royal Society of Chemistry 20xx

Published on 20 July 2015. Downloaded by University of Arizona on 27/07/2015 03:18:33.

### se ChemCommargins

# Journal Name

## COMMUNICATION



Scheme 1. Reaction mechanism (H<sub>2</sub>O<sub>2</sub> is *cis* to the nitrido ligand) obtained at B3LYP level. ΔG (298K) free energies are in kcal/mol. Basis sets: LanL2DZ for Os and Fe, 6-31G(d) for non-metal atoms. Solvent: CH<sub>3</sub>CO<sub>2</sub>H.

heterolytic mechanism that involves O-atom transfer from  $H_2O_2$  to **1**,  $[(L)OS^{VI}(N)]^*$ , to generate an osmium(VIII) nitride oxo species,  $[(L)OS^{VIII}(N)(O)]^*$ , as the active intermediate which oxidizes RH via a H-atom abstraction/O-rebound mechanism in the rate-limiting step to generate ROH, i.e.  $OS^{VIII}=O + RH \rightarrow OS^{VII}-OH + R\bullet \rightarrow OS^{VI} + ROH$ . The alcohol is then further oxidized by the active intermediate to generate the corresponding ketone. The alkyl radicals generated from the initial H-atom abstraction process are sufficiently long-lived to cause epimerization of 1,2-dimethylcyclohexane or to diffuse from the solvent cage to react with solvent,  $O_2$  or BrCCl<sub>3</sub>.

The proposed mechanism is also supported by DFT calculations. The potential energy surface (PES) for catalytic oxidation of cyclohexane by  $1/H_2O_2$  in  $CH_3CO_2H$  is shown in Scheme 1.  $[Os^{VI}(N)(L)]^+$  first binds with one  $H_2O_2$  and one  $CH_3CO_2H$  molecule to form  $[Os^{VI}(N)(L)(H_2O_2)]^+$ · $CH_3CO_2H$  (INT1).  $H_2O_2$  is a very poor ligand,<sup>15</sup> however, in the presence of  $CH_3CO_2H$  the Os-(HOOH) intermediate is stabilized by hydrogen bonding. This explains the activating effects of  $CH_3CO_2H$  and similar molecules such as  $CF_3CH_2OH$  in catalytic oxidation by  $H_2O_2$ .<sup>5,16</sup> In INT1,  $H_2O_2$  is *cis* to the nitrido ligand. INT1 then undergoes proton transfer from  $H_2O_2$  to  $CH_3CO_2H$  to generate an Os-OOH species (INT2) *via* TS1 with a barrier height ( $\Delta G_{298}^{2}$ ) of 28.4 kcal mol<sup>-1</sup>. O-O bond elongation with concomitant proton rebound then occurs to produce  $H_2O_2$ .

CH<sub>3</sub>CO<sub>2</sub>H, and an Os(VIII) nitrido oxo complex, cis- $[Os^{VIII}(N)(O)(L)]^{+}$  (INT3) via TS2 ( $\Delta G_{298}^{+} = 29.6 \text{ kcal mol}^{-1}$ ). The oxo ligand in Os(VIII) then abstracts a H-atom from cyclohexane followed by O-rebound to give  $[Os^{VI}(N)(L)(C_6H_{11}OH)]^+$  (INT4) via TS3 ( $\Delta G_{298}^{\mp} = 23.3 \text{ kcal mol}^{-1}$ ). The weakly bound cyclohexanol is then released from INT4 to yield  $[Os^{VI}(N)(L)]^{\dagger}$  and  $C_6H_{11}OH$ . The  $\Delta G_{298}^{\dagger}$  of **TS3** for the oxidation of  $C_6D_{12}$  has also been computed and is found to be 24.1 kcal/mol, this yields a theoretical value of 3.9 for deuterium isotope effect, which is in good agreement with the experimental value of 4.2.

The possible effects of a Lewis acid such as FeCl<sub>3</sub> on the catalytic reaction were also investigated by DFT calculations (Scheme S1). The mechanism is similar to that without FeCl<sub>3</sub>. The barrier heights of the O-O cleavage are almost the same (via **TS2a**,  $\Delta G_{298}^{+} = 29.6$  kcal mol<sup>-1</sup> without FeCl<sub>3</sub> vs.  $\Delta G_{298}^{-} = 29.7$  kcal mol<sup>-1</sup> with FeCl<sub>3</sub>); this means that FeCl<sub>3</sub> has no effect on the catalytic oxidation, which is consistent with our experimental observations. We have also studied the reaction pathways with the H<sub>2</sub>O<sub>2</sub> initially bound to osmium *trans* to the nitrido ligand, which forms *trans*-[Os<sup>VIII</sup>(N)(O)(L)]<sup>+</sup> as the active intermediate (Scheme S2). The reaction mechanism is also similar, however in this case the barrier for the O-O cleavage process (39.1 kcal mol<sup>-1</sup>) is much higher than that of the pathway with initial *cis* binding of H<sub>2</sub>O<sub>2</sub> (29.6 kcal mol<sup>-1</sup>).

DOI: 10.1039/C5CC03636D

Scheme 1). The barrier for subsequent H-atom abstraction from cyclohexane by *trans*- $[Os^{VIII}(N)(O)(L)]^+$  (31.5 kcal mol<sup>-1</sup>) is also much higher than that by *cis*- $[Os^{VIII}(N)(O)(L)]^+$  (23.3 kcal mol<sup>-1</sup>).

In conclusion, we have demonstrated that the d<sup>2</sup> (salen)osmium(VI) nitrido complex **1** is a robust and efficient catalyst for alkane oxidation by  $H_2O_2$ . Our work suggests that a new class of oxidation catalysts may be designed based on the d<sup>2</sup> metal nitrido platform with a variety of multidentate ancilliary ligands.

The work described in this paper was supported by Hong Kong University Grants Committee Area of Excellence Scheme (AoE/P-03-08), the Research Grants Council of Hong Kong (CityU 101713 and CityU 101512), the Shenzhen Science and Technology Research Grant (JCYJ20120613115247045) and the Shenzhen Research Institute, City University of Hong Kong.

### References

Published on 20 July 2015. Downloaded by University of Arizona on 27/07/2015 03:18:33.

- (a) E. Shilov and G. B. Shul'pin, Activation and Catalytic Reactions of Saturated Hydrocarbons in the Presence of Metal Complexes, Kluwer, Boston, 2000; (b) K. I. Goldberg and A. S. Goldman, Activation and Functionalization of C-H Bonds, ACS Symposium Series 885, American Chemical Society, Washington, DC, 2004.
- 2 (a) P. R. Ortiz de Montellano, Cytochrome P450. Structure, Mechanism and Biochemistry, Plenum Press, New York, 2005;
  (b) J. L. McLain, J. Lee and J. T. Groves, in Biomimetic Oxidations Catalyzed by Transition Metal Complexes, ed. B. Meunier, Imperial College Press, London, 2000, pp. 91- 170;
  (c) M.-H. Baik, M. Newcomb, R. A. Friesner and S. J. Lippard, Chem. Rev., 2003, 103, 2385.
- 3 (a) K. Kamata, K. Yonehara, Y. Nakagawa, K. Uehara and N. Mizuno, *Nature Chem.*, 2010, **2**, 478; (b) G. B. Shul'pin, Y. N. Kozlov, L. S. Shul'pina, A. R. Kudinov and D. Mandelli, *Inorg. Chem.*, 2009, **48**, 10480; (c) L. Gomez, I. Garcia-Bosch, A. Company, J. Benet-Buchholz, A. Polo, X. Sala, X. Ribas and M. Costas, *Angew. Chem. Int. Ed.*, 2009, **48**, 5720; (d) M. S. Chen and M. C. White, *Science*, 2007, **318**, 783; (e) A. M. Kirillov, M. N. Kopylovich, M. V. Kirillova, M. Haukka, M. F. C. Guedes da Silva and A. J. L. Pombeiro, *Angew. Chem. Int. Ed.*, 2005, **44**, 4345; (f) C. Kim, K. Chen, J. Kim and L. Que, Jr., *J. Am. Chem. Soc.*, 1997, **119**, 5964.
- 4 S. M. Yiu, W. L. Man and T. C. Lau, J. Am. Chem. Soc., 2008, 130, 10821.
- 5 L. Ma, Y. Pan, W. L. Man, H. K. Kwong, W. W. Y. Lam, G. Chen, K. C. Lau and T. C. Lau, J. Am. Chem. Soc., 2014, **136**, 7680.
- 6 E. G. Samsel, K. Srinivasan and J. K. Kochi, J. Am. Chem. Soc., 1985, 107, 7606.
- 7 K. Srinivasan, P. Michaud and J. K. Kochi, J. Am. Chem. Soc., 1986, 108, 2309.
- 8 W. Zhang, J. L. Loebach, S. R. Wilson and E. N. Jacobsen, J. Am. Chem. Soc., 1990, **112**, 2801.
- R. Irie, K. Noda, Y. Ito and T. Katsuki, *Tetrahedron Lett.*, 1991, 32, 1055.
- 10 W. L. Man, G. Chen, S. M. Yiu, L. Shek, W. Y. Wong, W. T. Wong and T. C. Lau, *Dalton Trans.*, 2010, **39**, 11163.
- 11 R. A. Sheldon and J. K. Kochi, *Metal-Catalyzed Oxidations of Organic Compounds*, Academic Press, New York, 1981, pp. 17-32.
- 12 I. W. C. E. Arends, K. U. Ingold and D. D. M. Wayner, J. Am. Chem. Soc., 1995, 117, 4710.

- 14 K. U. Ingold and P. A. MacFaul, in *Biomimetic Oxidations Catalyzed by Transition Metal Complexes*, ed. B. Meunier, Imperial College Press, London, 2000, pp. 45-89.
- 15 A. G. DiPasquale and J. M. Mayer, *J. Am. Chem. Soc.*, 2008, **130**, 1812.
- 16 H. K. Kwong, P. K. Lo, K. C. Lau and T. C. Lau, *Chem. Commun.*, 2011, **47**, 4273.

<sup>13</sup> P. A. MacFaul, K. U. Ingold, D. D. M. Wayner and L. Que, Jr., J. Am. Chem. Soc., 1997, **119**, 10594.