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Non-heme manganese(II) complex-catalysed oxidative cleavage of 1,2-diols *via* alcohol-assisted O_2 activation†

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Bio-inspired oxidation strategies are gaining increasing interest in the synthesis of fine and commodity chemicals. In particular, the development of catalytic oxidation systems with bio-relevant metal complexes capable of activating molecular oxygen (O_2) is of utmost interest. In this work, a well-defined non-heme Mn(II) complex is found to catalyse, under the irradiation of blue light, the efficient aerobic oxidative cleavage of 1,2-diols to afford valuable carbonyl compounds and five-membered heterocycles. The photo-promoted catalysis allows for aromatic, aliphatic as well as bio-derived 1,2-diols to be cleaved, while tolerating a broad range of functional groups. Preliminary mechanistic investigation suggests that the catalytic cycle features two sequential redox events, with the first involving one alcohol molecule reducing one oxygen atom of O_2 to water while promoting the formation of an active Mn-oxo species, which cleaves a second alcohol molecule in the subsequent event.

Introduction

Manganese is one of the most abundant, inexpensive and environmentally friendly metals on Earth. With readily accessible oxidation states ranging from II to VII, manganese has a rich redox chemistry, which has been exploited by nature in a number of important enzymatic reactions,[1] such as oxidation of water to form O_2,[2] disproportionation of toxic superoxide,[3] oxidation of oxalate for seed germination[4] and catabolism of xenobiotic aromatics.[5] Inspired by nature, a great number of manganese-based homogeneous catalysts have been developed for oxidation reactions over the past several decades. However, the vast majority of these catalysts necessitate the use of activated oxidants, such as H_2O_2, NaOCl/Br, PhIO and its derivatives,[6] eliciting cost, waste and/or environmental impact. Thus, manganese catalysts that enable more selective, milder and safer oxidation with cleaner and more economical oxidants are still highly sought after. Of particular interest is to develop bio-inspired Mn-catalysed oxidation strategies, in which the readily accessible, inexpensive, and clean O_2 is used as the oxidant.

Activation of O_2 is generally required for aerobic oxidation. The ground state of O_2 is a triplet diradical that is spin forbidden to react *via* common two-electron reaction mechanisms. Nature circumvents the spin state barrier and performs highly selective aerobic oxidations by employing redox-active metal ions (Fe^{II}, Mn^{II}, Cu^{I}, *etc.*) that are able to transfer a single electron to O_2.[7] Taking inspiration from nature, numerous biomimetic transition metal complexes bearing heme and non-heme polydentate ligands have been synthesized for studying O_2 activation in the past four decades or so.[7b,8] However, there are still relatively few well-defined Fe and Mn complexes that activate O_2 in a controlled manner and particularly, the use of benign and inexpensive O_2 for selective oxidation with such biologically relevant metal complexes remains "a significant challenge for the synthetic chemist".[7b] The main challenging issues are: (1) O_2 activation is not straightforward, as the redox potential for reduction of O_2 to superoxide is unfavorable;[7a] so specific ligands must be employed to promote the reduction process and stabilize the resulting metal-superoxide; (2) the metal-superoxide intermediate is too reactive to engage in a selective oxidation process and more prone to poorly controlled radical-type pathways;[9] (3) a reducing agent capable of donating two electrons at the right time is generally required to form high valent M=O species for subsequent substrate oxidation.[10] Few biomimetic metal complexes are known that can fulfil these roles, *i.e.* reduction of O_2 while abstracting electrons from a reducing agent.[11] Herein, we report a well-defined non-heme Mn(II) complex for oxidative cleavage of 1,2-diols *via* O_2 activation promoted by visible light, in which one diol (or cheap methanol) provides electrons and protons, leading to its oxidative cleavage while initiating the cleavage of a second diol molecule.

Oxidative C–C bond cleavage of 1,2-diols is an important reaction, finding countless applications in organic chemistry

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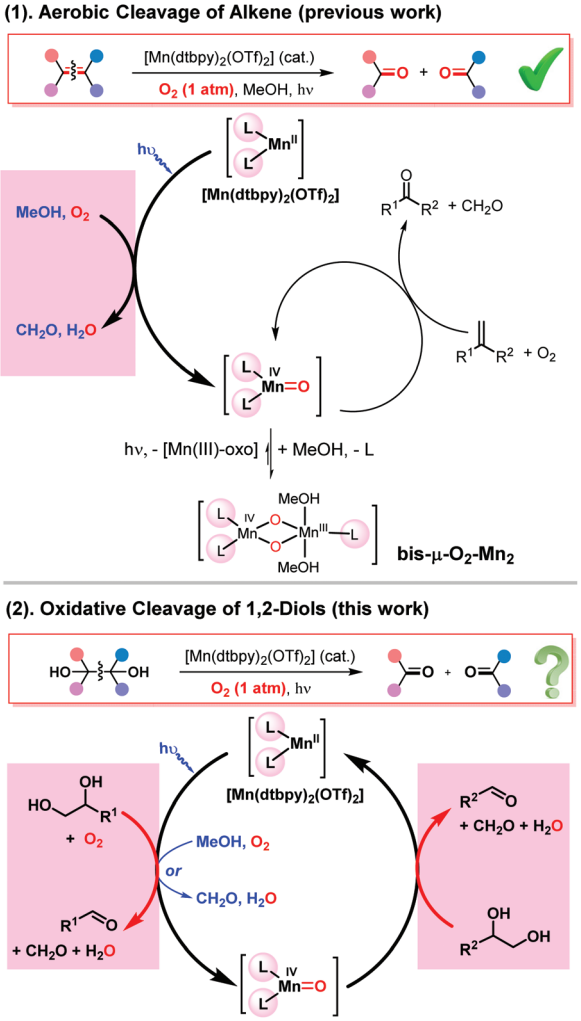
since its discovery by Malaprade and Criegee around the 1930s.[12] Although the original methods remain the most widely used for the cleavage of vicinal diols, the use of stoichiometric high-valent inorganic oxidants, mainly HIO_4 and analogues, $Pb(OAc)_4$ or $KMnO_4$,[12,13] brings about serious issues, such as high toxicity and copious amount of waste. Whilst the last three decades have witnessed the development of various catalytic methods and some significant advances in aerobic cleavage of 1,2-diols (Scheme 1),[14] developing novel, cheap and green catalysts for this cleavage reaction that shows a broad scope with O_2 or air under mild conditions remains highly necessary. In particular, the environmentally friendly, bio-relevant manganese has been much less studied for the aerobic oxidative cleavage of 1,2-diols, with the few reported Mn catalysts all showing limited substrate scope while requiring either a high temperature or a co-reductant (Scheme 1b).[14m,n,15] In continuing our study of catalytic oxidation,[6d,11b–d,16] this prompted us to develop an efficient, widely applicable non-heme Mn catalyst for this transformation (Scheme 1c).

Results and discussion

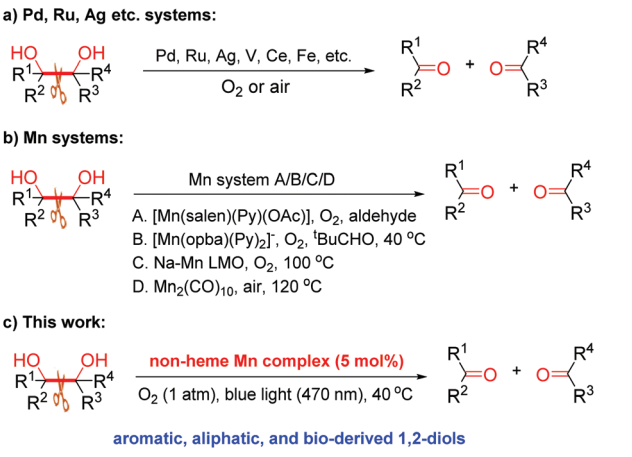
Method development

We recently reported a novel photo-Mn catalytic system for the oxidative cleavage of alkenes, in which MeOH acts as the electron and proton donor in the process of O_2 activation by Mn(II), leading to its oxidation to formaldehyde and the formation of a Mn(IV)=O species capable of catalytically cleaving olefins in a dioxygenase manner [Scheme 2(1)].[11b] Interestingly, the active oxo species is stabilized by forming a more stable **bis-μ-O_2-Mn_2** dimer, which is photoreversible, thus enhancing the catalyst lifetime. Building on this knowledge, we envisaged a substrate-promoted O_2 activation strategy for the oxidative cleavage of 1,2-diols [Scheme 2(2)]. First, a 1,2-diol substrate acts as a two-electron and two-proton donor, reducing one oxygen atom of O_2 to water while being cleaved, with the other oxygen atom oxidizing Mn(II) to a Mn(IV)-oxo species under blue light irradiation. As a highly reactive species, the oxo intermediate would then react with another 1,2-diol, leading to its cleavage. There are literature precedents regarding the cleavage of 1,2-diols by Mn-oxo species.[15,17] *The overall process thus involves the oxidative cleavage of two diol molecules with one O_2 molecule via two sequential two-electron steps, with water as the only by-product.* As indicated, methanol can also act as a reductant in forming the Mn(IV)=O species.

We set out to examine the oxidation of 1,2-diols by employing 1-phenyl-1,2-ethanediol (**1a**) as the model substrate (Table 1). As expected, under the irradiation of blue light (470 nm, 9 W), **1a** was successfully cleaved by O_2 with 5 mol% $[Mn(dtbpy)_2(OTf)_2]$ as the precatalyst in DCE, affording the desired carbonyl product **2a** in 67% yield (Table 1, entry 1). The $[Mn(dtbpy)_2(OTf)_2]$ prepared *in situ* by combining $Mn(OTf)_2$ and 4,4′-di-*tert*-butyl-2,2′-bipyridine (**L1**) displayed a

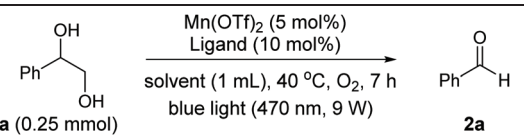


Scheme 2 (1) MeOH-promoted O_2 activation for the aerobic oxidation of alkenes by a non-heme Mn(II) complex; (2) schematic showing of a substrate or MeOH-promoted O_2 activation strategy for the aerobic cleavage of 1,2-diols (L = dtbpy).



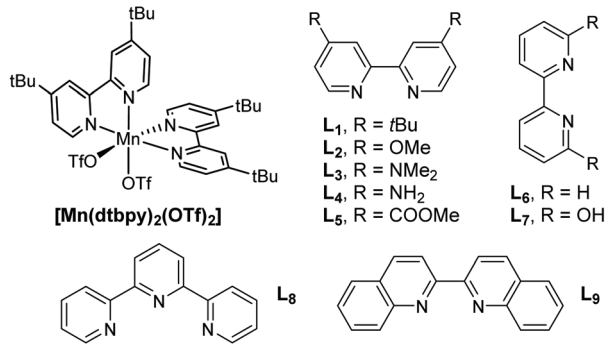
Scheme 1 Oxidative cleavage of 1,2-diols with molecular O_2.

Table 1 Optimization of reaction conditions[a]



Entry	[Mn]	Ligand	Solvent	Yield of **2a**
1	$[Mn(dtbpy)_2(OTf)_2]$	—	DCE	67%
2	$Mn(OTf)_2$	L_1	DCE	69%
3	$Mn(OTf)_2$	—	DCE	8%
4	$Mn(OTf)_2$	L_2	DCE	58%
5	$Mn(OTf)_2$	L_3	DCE	46%
6	$Mn(OTf)_2$	L_4	DCE	10%
7	$Mn(OTf)_2$	L_5	DCE	34%
8	$Mn(OTf)_2$	L_6	DCE	59%
9	$Mn(OTf)_2$	L_7	DCE	35%
10	$Mn(OTf)_2$	L_8	DCE	36%
11	$Mn(OTf)_2$	L_9	DCE	21%
12	$Mn(OTf)_2$	L_1	*t*BuOH	76%
13	$Mn(OTf)_2$	L_1	PrOH	84%
14	$Mn(OTf)_2$	L_1	EtOH	60%
15	$Mn(OTf)_2$	L_1	Acetone	72%
16	$Mn(OTf)_2$	L_1	EA	67%
17	$Mn(OTf)_2$	L_1	2-Me-THF	82%
18	$Mn(OTf)_2$	L_1	CH_3CN	70%
19	$Mn(OTf)_2$	L_1	TFE	83%
20	**$Mn(OTf)_2$**	**L_1**	**DCE/tBuOH (1 : 3)**	**92% (90%)**
21	$[Mn(dtbpy)_2(OTf)_2]$	—	DCE/tBuOH (1 : 3)	90%
22[b]	$Mn(OTf)_2$	L_1	DCE/tBuOH (1 : 3)	0%

[a] Yield determined by ^1H NMR with mesitylene as the internal standard; isolated yield in parentheses. [b] Without blue light.



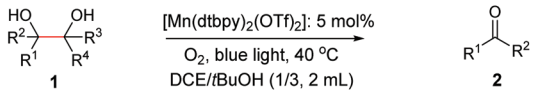
similar activity, which could afford **2a** in 69% yield (Table 1, entry 2). As is clear, both the ligand and blue light play important roles in this transformation; in their absence, a dramatically decreased yield or no target product was observed (Table 1, entries 3 and 22, also see Fig. S3 in the ESI†). The effect of the ligand was further explored by testing a range of substituted bipyridines (**L2–L9**), revealing **L1** to give the best yield (Table 1, entries 4–11). A variety of solvents, including those that are considered green[18] (Table 1, entries 12–19), were then screened. All of them afforded the desired product in good yields. In particular, for 1-propanol (PrOH), which is environmentally safe in the industrial SSGs and is at the top of the list of green chemicals,[19] a high yield of 84% was obtained. These results indicate that this reaction has excellent solvent compatibility. Furthermore, when the oxidation was performed at a 10 mmol scale, 46% isolated yield of **2a** could be obtained with 2 mol% Mn catalyst in propanol (4 mL) under an O_2 balloon at room temperature for 24 h, indicating the robustness of this protocol (see the ESI for more details†). A somewhat higher yield was obtained when the reaction was performed in a mixed solvent (1 : 3 DCE/*t*BuOH, Table 1, entries 20 and 21). Our subsequent study was therefore focused on the following reaction conditions: $Mn(OTf)_2$ (5 mol%) as the pre-catalyst, **L1** (10 mol%) as the ligand, O_2 as the oxidant in DCE/*t*BuOH (1 : 3) at 40 °C with blue light irradiation. We note, however, that the oxidative cleavage reactions could well be carried out in a green solvent, such as PrOH (see the ESI† for examples).

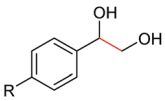
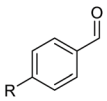
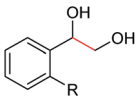
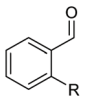
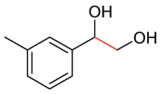
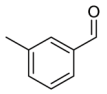
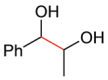
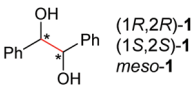
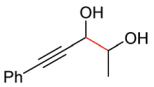
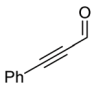
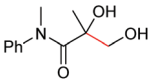
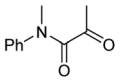
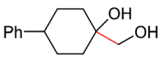
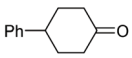
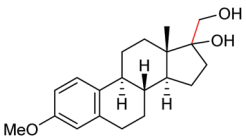
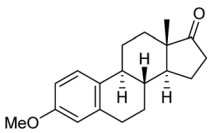
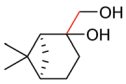
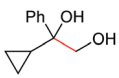
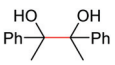
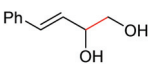
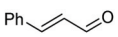
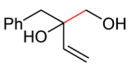
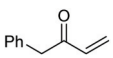
Substrate scope

Under the chosen reaction conditions, the scope of diols for the oxidative cleavage was investigated. As shown in Table 2, terminal aromatic 1,2-diols bearing electron-withdrawing or electron-donating groups are all suitable substrates, affording the corresponding aldehydes in good to excellent yields (**2b–2i**). Internal aromatic 1,2-diols, such as 1-phenylpropane-1,2-diol, (*S*,*S*)-(−)-hydrobenzoin, (*R*,*R*)-(+)-hydrobenzoin, and *meso*-hydrobenzoin were also tolerated in this transformation to give **2a** in 50%–80% yield (Table 2, entries 9–12). Notably, an unsaturated C≡C triple bond is compatible with this oxidation process, as is seen from the oxidation leading to **2j** in 62% yield. Two alkenyl 1,2-diols were also tested under the standard conditions, both of which could produce the desired cleavage product successfully (**2q** and **2r**). However, lower yields were obtained, which might be caused by the oxidation of the unsaturated C=C double bond. Furthermore, a 1,2-diol with an amide functional group was cleaved to afford the amido ketone **2k** in 83% yield. In addition, the natural product derivatives, 1-(hydroxymethyl)-4-phenylcyclohexan-1-ol, 2,10-pinanediol, and 17-hydroxy-3-methoxyestra-1,3,5(10)-triene-17-methanol, are all viable for this transformation, affording the ketone products with good to excellent yields (**2l–2n**). In the oxidation of a cyclopropyl-containing substrate, the cyclopropyl ring remained intact (**2o**). The viability of oxidative cleavage of tetra-substituted diols is demonstrated by the formation of **2p**.

As proposed in Scheme 2, two diols are cleaved in one catalytic cycle. Since the Mn(II) and Mn(IV) species are expected to have different catalytic activities, diols of different reactivities could be cleaved in one-pot. Thus, as exemplified in Table 3, the oxidation of a 1 : 1 mixture of **1a** with 1-(3,4-dimeth-oxyphenyl)ethane-1,2-diol, 2-phenylpropane-1,2-diol, 1-phenylcyclohexane-1,2-diol, cyclooctane-1,2-diol, or 4,5-dihydroxy-1-phenylpentan-1-one afforded **2a** and the other corresponding cleavage products in a one-pot, highly selective manner (Table 3, entries 1, 2 and 5–7). Note that only a trace amount of **2s**, **2p** and **2t** and none of **2u** and **2v** were observed when those oxidation reactions were performed in the absence of **1a** under the same conditions. Meanwhile, the product yield from 2,3-diphenylbutane-2,3-diol and 1-cyclopropyl-1-phenylethane-1,2-diol was also improved in the presence of **1a** (*c.f.* Table 3, entries 3, 4 with Table 2, entries 18 and 19). These obser-

Table 2 Substrate scope of the Mn-catalysed aerobic oxidation of 1,2-diols[a]



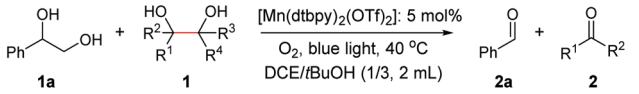
Entry	Substrate	Product	Yield[b]
1			**2b**, R = Cl, 82%
2			**2c**, R = F, 85%
3			**2d**, R = CF_3, 90%
4			**2e**, R = COOMe, 81%
5			**2f**, R = OMe, 86%
6			**2g**, R = Cl, 86%
7			**2h**, R = Br, 87%
8			**2i**, 84%
9			**2a**, 51%
10			**2a**, 77%
11	(1*R*,2*R*)-**1**		**2a**, 80%
12	(1*S*,2*S*)-**1** *meso*-**1**		**2a**, 78%
13			**2j**, 62%
14			**2k**, 83%
15			**2l**, 86%
16			**2m**, 76%
17			**2n**, 92%
18			**2o**, 54%
19			**2p**, 59%
20			**2q**, 25%
21			**2r**, 26%

[a] All of the reactions were performed with *in situ* prepared $[Mn(dtbpy)_2(OTf)_2]$ and **1** (0.5mmol) in DCE/tBuOH (1/3, 2 mL) at 40 °C under O_2 (1 atm) and blue light for 13 h. [b] Yield of the isolated product.

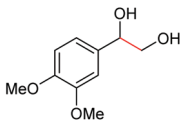
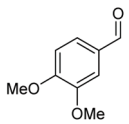
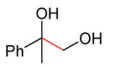
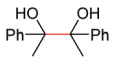
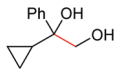
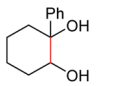
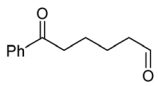
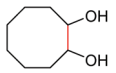
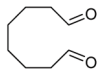
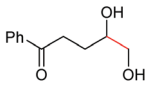
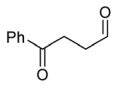
vations show that diols of lower reactivities can be oxidatively cleaved with a more active diol in a one-pot fashion. The oxidation of the latter presumably activates O_2, giving rise to a highly active Mn(IV)-oxo species that cleaves the former.

The more challenging aliphatic diols can be more easily dealt with when the oxidation is carried out in methanol, where the resulting more active carbonyls are protected, being converted *in situ* into the corresponding acetals. This strategy

Table 3 Mn-catalysed aerobic cleavage of two diols in one pot[a]



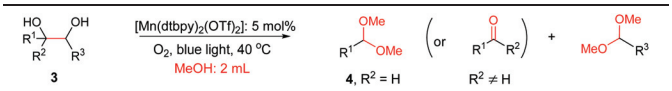
1a 1 2a 2

Entry	Substrate 1	Product 2[b] (yield)	Yield of 2a[c]
1		 (2s, trace)[d] (2s, 93%)	2a, 93%
2		 (2p, trace)[d] (2p, 75%)	2a, 65%
3		 (2p, 88%)	2a, 87%
4		 (2o, 87%)	2a, 64%
5		 (2t, trace)[d] (2t, 83%)	2a, 80%
6		 (2u, 0%)[d] (2u, 46%)	2a, 51%
7		 (2v, 0%)[d] (2v, 49%)	2a, 71%

[a] All of the reactions were performed with *in situ* prepared $[Mn(dtbpy)_2(OTf)_2]$ (5 mol%), **1a** (0.5 mmol), and **1** (0.5 mmol) in DCE/*t*BuOH (1/3, 2 mL) at 40 °C under O_2 (1 atm) and blue light for 13 h. [b] Yield of isolated product. [c] Yield was obtained by ^1H NMR with mesitylene as internal standard. [d] Without **1a**.

allows acetals as latent aldehydes to be readily synthesized through the oxidative cleavage of diols. As shown in Table 4, this aerobic oxidation method shows high chemoselectivity as well as an excellent functional group compatibility. For example, internal diols derived from methyl oleate, methyl *cis*-13-docosenoate and methyl 12-hydroxy-9-octadecenoate are viable substrates, producing the corresponding protected mono and di-carbonyl compounds in good yields (Table 4, entries 1–3). Thus, this method could be applied, in a two-step fashion, to the cleavage of unsaturated fatty acids that are challenging, *i.e.* oxidation to a diol followed by oxidative cleavage of the diol to the desired carbonyls. We notice that the oxidative cleavage of the C=C double bonds in unsaturated fatty acids into carbonyls is a reaction of current interest in biomass valorization.[20] Those carbonyl products from fatty acids, currently produced on an industrial scale by means of ozonolysis, are value-added commodity chemicals, such as plasticizers and polymer precursors. 1,2-Diols bearing acid, *tert*-butyldiphenylsilyl (TBDPS), ester, carbamate, urea or ketone functionalities are all suitable, affording the desired products in moderate to good yields (**4e** and **4h–4l**). Both benzylic C–H bonds and isolated alcohol units, which are prone to oxidation, were also tolerated during the oxidation (**4f**, **4g**, **4o** and **4p**), showing the high chemoselectivity of this oxidation protocol. Meanwhile, long chain 1,2-diols without

Table 4 Scope of the Mn-catalysed aerobic oxidation of aliphatic 1,2-diols[a]



3 4, R^2 = H $R^2 \neq H$

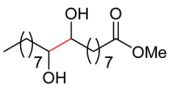
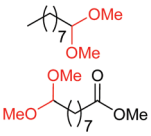
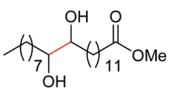
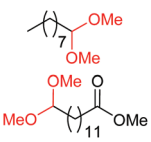
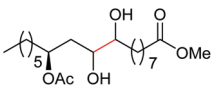
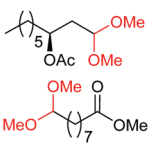
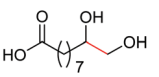
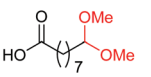
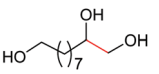
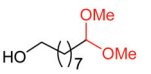
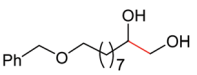
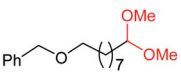
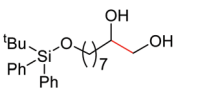
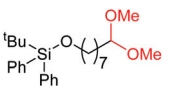
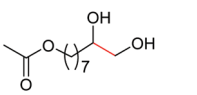
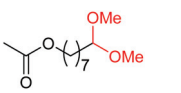
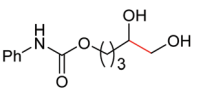
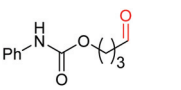
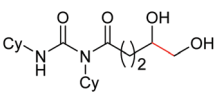
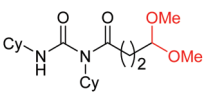
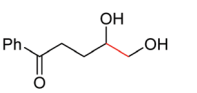
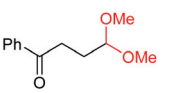
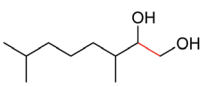
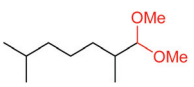
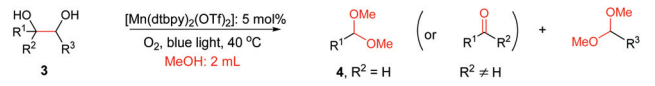
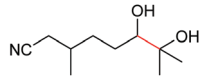
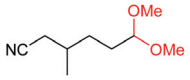
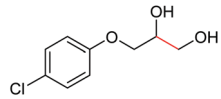
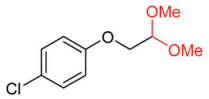
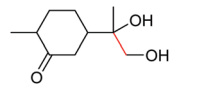
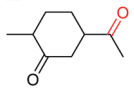
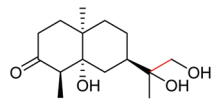
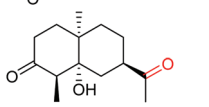
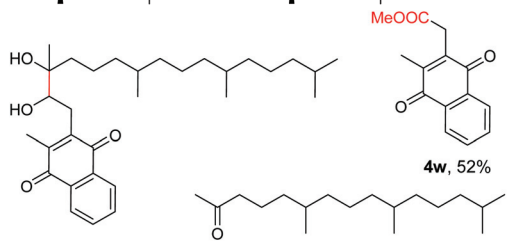
Entry	Substrate	Product	Yield[b]
1[c]			4a, 76% 4b, 70%
2[c]			4a, 60% 4c, 72%
3[c]			4d, 51% 4b, 73%
4			4e, 83%
5			4f, 84%
6			4g, 55%
7			4h, 61%
8			4i, 75%
9			4j, 58%
10			4k, 76%
11			4l, 74%
12			4m, 66%
13			4n, 53%
14[d] 15[d]			4o, n = 1, 70% 4p, n = 2, 73%
16[d] 17[d]			4a, n = 7, 74% 4q, n = 13, 70%
18			4r, 53%

Table 4 *(Contd.)*



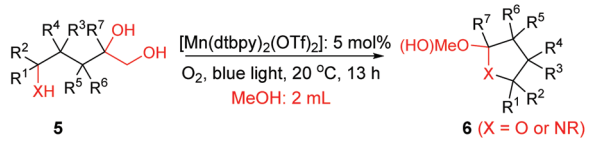
Entry	Substrate	Product	Yield[b]
19			**4s**, 37%
20			**4t**, 81%[e]
21			**4u**, 47%
22			**4v**, 92%
23		**4w**, 52% **4x**, 57%	

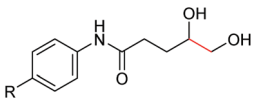
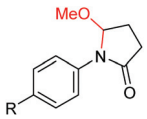
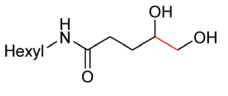
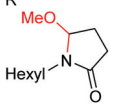
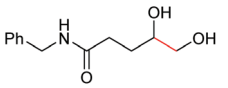
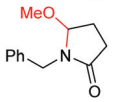
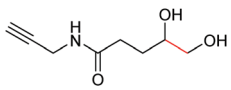
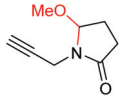
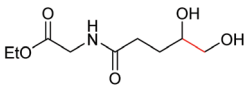
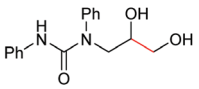
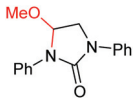
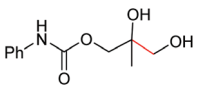
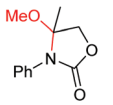
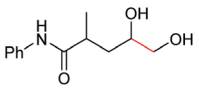
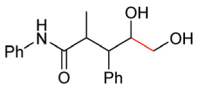
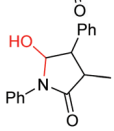
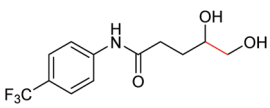
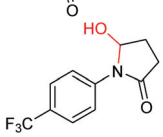
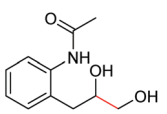
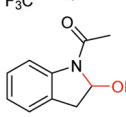
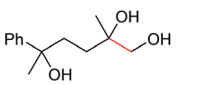
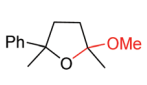
[a] All of the reactions were performed with *in situ* prepared [Mn(dtbgpy)$_2$(OTf)$_2$] (5 mol%) and **3** (0.5 mmol) in MeOH (2 mL) at 40 °C under O_2 (1 atm) and blue light (470 nm, 9 W) for 13 h. [b] Yield of the isolated product. [c] 24h. [d] TFA (30 mol%) was added as the co-catalyst. [e] Yield was determined by ^{1}H NMR with mesitylene as the internal standard.

other functional groups were also oxidatively cleaved to furnish the target carbonyls in good yields (Table 4, entries 12, 13, 16 and 17). Note that the relatively active tertiary C–H bonds in **4m** remained intact. Chlorphenesin, which is a preservative and cosmetic biocide, could be oxidized selectively to 1-chloro-4-(2,2-dimethoxyethoxy)benzene **4t** in 81% NMR yield. The acetal **4t** appears to be unstable in a silica gel column, undergoing decomposition during isolation to afford 2-(4-chlorophenoxy)acetaldehyde in 71% yield. Several other natural product-derived diols, such as sulcatone, citronellylnitrile, dihydrocarvone, α-cyperone and vitamin K1 derivatives, were also studied and shown to be suitable, giving the corresponding carbonyl compounds in moderate to excellent yields (**4r**, **4s** and **4u–4x**).

Interestingly, during the examination of the substrate scope, we noticed that a cyclization reaction occurred in nearly quantitative yield after the expected C–C bond cleavage process, when 4,5-dihydroxy-*N*-phenylpentanamide was employed (Table 5, entry 1). The formation of cyclic 5-methoxy-1-phenylpyrrolidin-2-one (**6a**) prompted us to further investigate the substrate scope, since 2-pyrrolidinones are important building blocks for a range of heterocyclic compounds,[21] as well as the key subunit in many pharmaceuticals and bioactive compounds.[22] As can be seen in Table 5, both

Table 5 Mn-Catalysed aerobic oxidation of diols for the synthesis of five-membered heterocycles[a]



Entry	Substrate	Product	Yield[b]
1			**6a**, R = H, 99%
2			**6b**, R = OMe, 74%
3			**6c**, R = CN, 88%
4			**6d**, 60%
5			**6e**, 74%
6			**6f**, 85%
7			**6g**, 65%
8			**6h**, 48%
9			**6i**, 60%
10			**6j**, 97%
11			**6k**, 92%
12			**6l**, 62%
13			**6m**, 30%
14			**6n**, 78%

[a] All of the reactions were performed with *in situ* prepared [Mn(dtbpy)$_2$(OTf)$_2$] (5 mol%) and **5** (0.5 mmol) in MeOH (2 mL) at 20 °C under O_2 (1 atm) and blue light for 13 h. [b] Yield of the isolated product.

N-aryl and *N*-alkyl substituted 4,5-dihydroxypentanamides are viable, giving the corresponding 2-pyrrolidinones in good to excellent yields (**6a–6d**). Notably, both benzylic C–H and C≡C triple bonds, usually sensitive to oxidation conditions, were

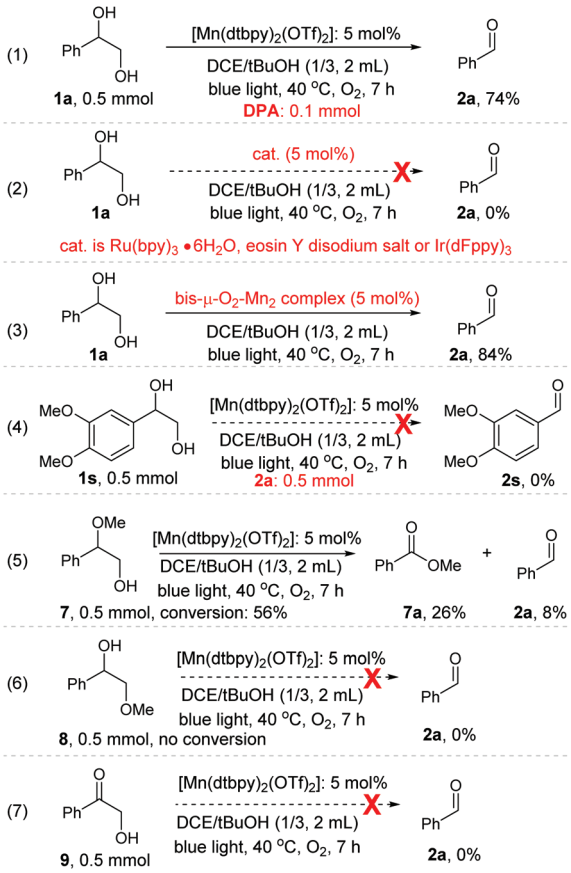
well tolerated (**6e** and **6f**). Amino acid, urea, and carbamate-containing diols could be oxidized selectively as well (**6g–6i**), showing potential applications in bio-conjugate chemistry. 4,5-Dihydroxy-2-methyl-*N*-phenylpentanamide, 4,5-dihydroxy-2-methyl-*N*,3-diphenylpentanamide and 5-dihydroxy-*N*-(4-(trifluoromethyl)phenyl)pentanamide were also viable for this transformation (**6j**, **6k** and **6l**). In the case of the latter two, the analogous 5-hydroxy-functionalized cyclic amides were isolated (Table 5, entries 11 and 12). Furthermore, *N*-(2-(2,3-dihydroxypropyl)phenyl)acetamide and 2-methyl-5-phenylhexane-1,2,5-triol could successfully be oxidized, furnishing important indoline and tetrahydrofuran products (**6m** and **6n**).

It is worth pointing out that although both aromatic and aliphatic 1,2-diols can be cleaved selectively with the reported catalysts in the presence of oxygen or air (Scheme 1a and b),[14] most of those methods are limited to substrates without any functional groups, especially functionalities usually sensitive to oxidation conditions. To the best of our knowledge, there appears to be only two reports in which a few functionalized diols feature using 3 equiv. of base[14a] or high temperature (130 °C).[14h] Our protocol overcomes the disadvantage of functionality limitation under mild conditions, which should make it more applicable in organic synthesis. For example, alkyne, amide, acid, TBDPS, ester, carbamate, urea, ketone and even alcohol functionalities, which are often presented in pharmaceuticals and natural products, are tolerated in our protocol, but are barely seen in the previous reports of aerobic oxidation.[14]

Preliminary mechanistic investigation

While the detailed mechanism of the oxidation remains largely speculative, we have performed a range of experiments, aiming to gain further understanding of this transformation. As we proposed above (Scheme 2), Mn-oxygen species from O_2 activation, instead of singlet oxygen ($^1O_2$) which is known to cleave diol derivatives,[23] is likely to be the active species for the oxidative cleavage of 1,2-diol. Our control experiments appear to support this conjecture. The $^1O_2$ trap, 9,10-diphenylanthracene (DPA), is known to react rapidly with $^1O_2$ to give an endoperoxide product ($k \approx 1.3 \times 10^6$ M^{-1} s^{-1}).[24] When **1a** was subjected to the standard oxidation conditions but in the presence of DPA as a $^1O_2$ trap, no endoperoxide was detected, and importantly, the expected cleavage product **2a** was formed in 74% yield (Scheme 3, eqn. (1)). In addition, when three well-known photosensitizers, eosin Y disodium salt, [Ru(bpy)$_3$·6H$_2$O], and [Ir(dFppy)$_3$], which are all known to be capable of producing $^1O_2$ under blue light irradiation,[25] were used individually as a replacement catalyst for the oxidative cleavage of **1a**, none were found to catalyse the reaction under the conditions employed (Scheme 3, eqn. (2)). These results support the proposition above.

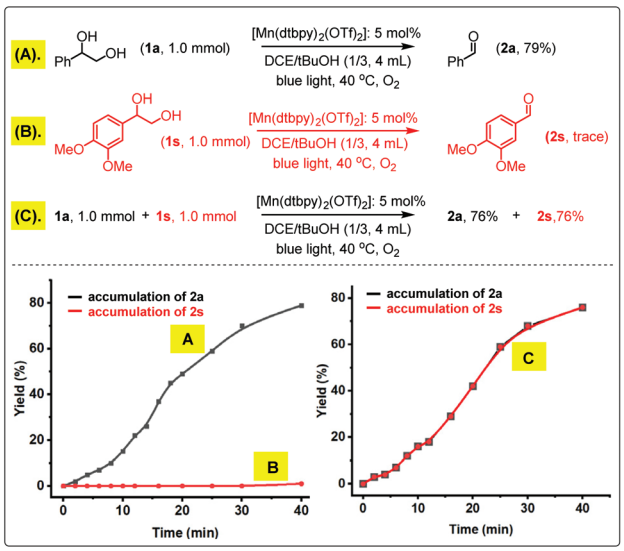
The **bis-μ-O$_2$-Mn$_2$** complex turned out to be active, catalysing the oxidation of **1a** to **2a** in 84% yield in the mix solvent of DCE/*t*BuOH (Scheme 3, eqn. (3)). However, light was still required; in its omission, the oxidation stalled. This is not surprising, as the oxo dimer is an off-cycle species.[11b] Aldehyde **2a**, which could be autoxidized to produce a peroxide under



Scheme 3 Control experiments to shed light on the mechanism.

O_2, was unable to replace **1a** to promote the oxidation of less reactive **1s** (Scheme 3, eqn. (4); also see Table 3, entry 1). In fact, when **1a** was subjected to the standard conditions but in the presence of peroxides like *m*CPBA, TBHP, DTBP, H_2O_2, or benzoyl peroxide as the oxidant, only a small amount of **2a** was obtained (see Table S2 in the ESI†). These observations make the possibility of an autoxidation pathway involving peroxides unlikely. When one of the –OH groups in **1a** was protected or pre-oxidized, the desired C–C bond cleavage process became difficult as well as less selective (Scheme 3, eqn. (5), (6) and (7)). These results appear to indicate that the cleavage of the C–C bond of diols proceeds *via* a concerted, rather than stepwise, process.

Further insight was gained by following the kinetic time course of the oxidation of **1a**, **1s** and their mixture. As shown in Scheme 4, **1a** could be smoothly oxidized to **2a** by O_2 with [Mn(dtbpy)$_2$(OTf)$_2$] as the catalyst in DCE/*t*BuOH, whilst **1s** was inactive under the same conditions. However, when an equal molar **1a** and **1s** were mixed together and subjected to the same oxidation conditions, **2a** and **2s** were formed in an identical yield, and remarkably, by the same rate, suggesting that **1a** and **1s** are oxidized in the same catalytic cycle. As proposed in Scheme 2(2), **1a** could promote O_2 activation by Mn(II) to form **2a** as well as a more active Mn(IV)-oxo species, which then oxidizes the less reactive **1s** to **2s** while regenerating Mn(II). Unfortunately, we failed to detect the possible



Scheme 4 Kinetic behaviors of the oxidation of **1a**, **1s** and their mixture.

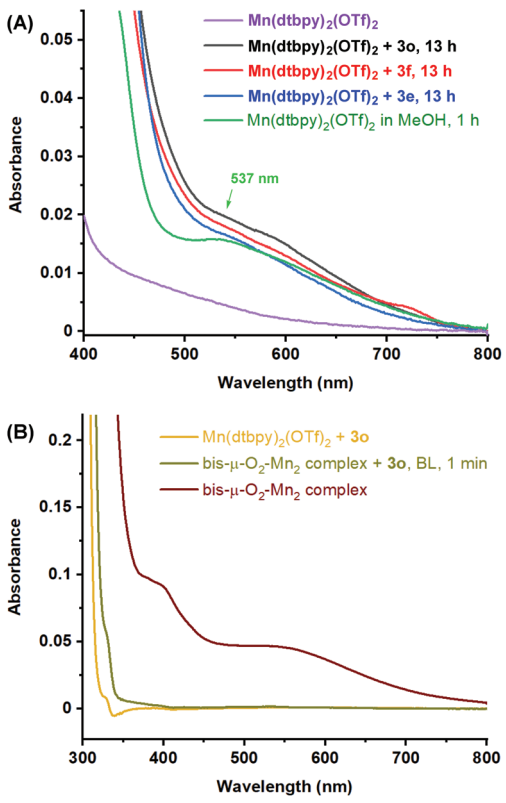


Fig. 1 (A) UV-Vis spectra of $[Mn(dtbpy)_2(OTf)_2]$, the reaction mixture of $[Mn(dtbpy)_2(OTf)_2]$ with **3e**/**3f**/**3o** in MeOH under O_2 after blue light (BL) irradiation for 13 h, and MeOH solution of $[Mn(dtbpy)_2(OTf)_2]$ under O_2 after BL irradiation for 1 h; (B) UV-Vis spectra of the **bis-μ-O_2-Mn_2** complex, the mixture of **bis-μ-O_2-Mn_2** and **3o** under N_2 after BL irradiation for 1 min, and the mixture of $[Mn(dtbpy)_2(OTf)_2]$ and **3o** in the absence of BL. The concentration of [Mn] for UV-Vis measurement was 0.25 mM in MeOH.

Mn(IV)-oxo species or the oxo dimer *via* UV-Vis spectroscopy under the conditions employed. Only the signals of $[Mn(dtbpy)_2(OTf)_2]$ were observed during the oxidation (Fig. S1A in the ESI†). Indeed, when the **bis-μ-O_2-Mn_2** complex was mixed with **1a** or **1s** under blue light, the greenish brown solution of **bis-μ-O_2-Mn_2** immediately changed to colorless, and the UV-Vis absorption of **bis-μ-O_2-Mn_2** disappeared concomitantly (Fig. S1B in the ESI†).

We then followed the oxidation of 9,10-dihydroxydecanoic acid (**3e**), decane-1,2,10-triol (**3f**) and 3-phenylpropane-1,2-diol (**3o**) in MeOH by UV-Vis spectroscopy. Similar to the oxidation of **1a** in DCE/*t*BuOH, no color change was observed during the reaction. As shown in Fig. S2,† although *ca.* 15% of the desired cleavage product was detected in the oxidation of **3e** or **3o** after 4 h, no obvious UV-Vis absorption arising from possible Mn-oxygen species was observed, which is in line with the observation of no color change. However, after the completion of the oxidation of **3e**, **3f**, or **3o**, an identical color change to greenish brown was noted, and revealingly, all of three solutions showed a UV-Vis absorption at around 537 nm [Fig. 1(A)], which can be assigned to the MeOH-coordinated **bis-μ-O_2-Mn_2** complex generated from O_2 activation by $[Mn(dtbpy)_2(OTf)_2]$ in MeOH [Fig. 1(A) and 1(B)].[11b] Of further note is that when the **bis-μ-O_2-Mn_2** complex was mixed with **3o** under blue light, the greenish brown solution immediately turned to colorless, accompanied with the disappearance of the absorption at 537 nm [Fig. 1(B)]. These observations indicate that the active Mn-oxygen species are too reactive to be observed by UV-Vis spectroscopy during the diol oxidation in either DCE/*t*BuOH or MeOH, although the more stable oxo dimer was observable in MeOH.

Conclusions

In conclusion, a well-defined, biologically relevant Mn(II) complex has been identified as an efficient catalyst for the aerobic oxidative cleavage of a wide range of diverse 1,2-diols under irradiation of visible light. Both aromatic and aliphatic diols are shown to be viable substrates, affording valuable carbonyl compounds and five-membered heterocycles with a broad range of functional groups tolerated in this oxidase-like system. Preliminary mechanistic investigations suggest that the reaction follows the pathway outlined in Scheme 2(2), in which two alcohol molecules are sequentially oxidized in one turnover, with the first alcohol reducing one oxygen atom to water while promoting the formation of an active Mn-oxo species that cleaves the second alcohol (also see Scheme S1 in the ESI† for a more detailed proposal). Further mechanistic studies and application of the catalytic system are underway in our laboratory and will be reported in the future.

Author contributions

J.X. conceptualized the project. Z.H., R.G., and E.B. performed the experiments, analyzed the data, and discussed the results.

Z.H. and J.X. wrote the paper. Z.H. wrote the ESI† and contributed to other related materials.

Conflicts of interest

There are no conflicts to declare.

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