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Catalytic oxidation of alcohols with novel non-heme N_4-tetradentate manganese(II) complexes†

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We report the preparation and characterisation of a series of novel non-heme N_4-tetradentate $Mn(OTf)_2$ complexes of the type, [(L)$MnOTf_2$], where L = *R*,*R* and *S*,*S* enantiomers of BPMCN, its 6-methyl and 6-bromo derivatives as well as the novel ligand BMIMCN (BPMCN = *N*,*N*′-dimethyl-*N*,*N*′-bis(2-pyridylmethyl)-(*R*,*R*/*S*,*S*)-1,2-diaminocyclohexane, BMIMCN = *N*,*N*′-dimethyl-*N*,*N*′-bis(1-methyl-2-imidazolemethyl)-(*R*,*R*/*S*,*S*)-1,2-diaminocyclohexane). Solid state structural analysis of the BMIMCN-ligated Mn-triflate complexes (***R*,*R*-C4** and ***S*,*S*-C4**) revealed opposite helicity but identical metal site accessibility. This feature was exploited in the catalytic oxidation of primary and secondary alcohols, with hydrogen peroxide as oxidant and acetic acid as co-catalyst. Complexes ***R*,*R*-C4** and ***S*,*S*-C4** displayed the highest activity in benzyl alcohol oxidation, attributed to the electron-donating property of the BMIMCN ligand. Complex ***S*,*S*-C4**, displayed high activity for a variety of primary alcohol substrates, but the reaction suffered from reduced selectivity and side-reactions due to the presence of acetic acid. In contrast, secondary alcohol substrates could be oxidised to the corresponding ketone products in excellent isolated yields under mild reaction conditions and short reaction times.

Introduction

The production of carbonyl compounds, *i.e.* aldehydes and ketones, has become an important research field in recent years due to their use in the pharmaceutical and perfume industry.[1,2] Although several effective processes have been utilised to produce them *via* the oxidation of alcohols, it requires the use of hazardous oxidisers (HNO_3, $KMnO_4$ and CrO_3)[3,4] and expensive metals (Au, Pt and Cr).[5,6] A greener alternative which utilises more benign conditions (lower temperatures and pressures), a cheaper metal (Mn) and an environmentally friendly oxidant (H_2O_2) has been found in the form of non-heme manganese(II) complexes. The catalytic oxidation of hydrocarbons with non-heme Mn(II)-complexes has received significant attention in the last few decades and has proved to show high activity, selectivity and versatility towards various alkane and alkene substrates.[7–14] Classic N_4-tetradentate ligands which have been employed include TMTACN, BPMCN, BQEN and TPA, with variations including the type of backbone and substituents on the heterocyclic ring. Advantages of using Mn(II)-complexes, is that they display higher activity compared to their Fe(II)-counterparts.[13,15,16] The only drawback is the necessity of an excess co-catalyst,[7,9,17] particularly a carboxylic acid such as acetic acid (AcOH), to facilitate catalyst activation[13] and suppress the disproportionation of H_2O_2.[9] Although catalytic oxidation studies of alkanes and alkenes have been numerous, the catalytic oxidation of alcohols with non-heme Mn(II)-complexes has received little attention.[3,11,17,18,19,20] In general, the reported activity and selectivity in alcohol oxidation is low, facilitating a need for Mn(II)-complexes capable of catalysing alcohol oxidation with high activity and selectivity. Herein, we report our contribution to the development of novel non-heme N_4-tetradentate $Mn(OTf)_2$ complexes, derived from the *R*,*R* and *S*,*S* enantiomers of BPMCN and its 6-substituted derivatives (***R*,*R*-C1–C3** and ***S*,*S*-C1–C3**, Scheme 1) as well as the novel BMIMCN ligand (***R*,*R*-C4** and ***S*,*S*-C4**, Scheme 1). Catalyst and reaction parameter optimisation was accomplished with benzyl alcohol (BnOH) as substrate, with H_2O_2 and AcOH serving as the oxidant and co-catalyst, respectively. Finally, the most active pre-catalysts, ***R*,*R*-C4** and ***S*,*S*-C4**, were evaluated against a variety of primary and secondary alcohol substrates, thereby establishing the substrate scope of our catalyst system.

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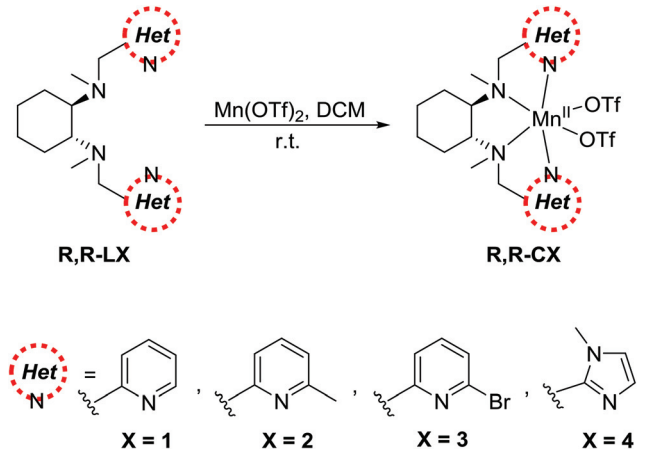
Experimental

General considerations

All chemicals and reagents were obtained from commercial sources and used as received. Catalytic experiments were con-



Scheme 1 Synthesis of Mn(II)-triflate complexes, ***R,R*-C1–C4**. Complexes ***S,S*-C1–C4** prepared in an analogous fashion from the *S,S*-enantiomers.

ducted with 30% H_2O_2, containing an inhibitor to prevent disproportionation, and stored in a refrigerator when not in use. FT-IR spectra were recorded as neat samples on a BrukerAlpha-P range infrared spectrometer equipped with an ATR accessory in the range 400 cm^{-1} to 4000 cm^{-1}. GC and GC-MS analysis were both performed on an Agilent 6890 Series GC System equipped with a HP-5 column: 30 m × 0.320 mm × 0.25 mm. Rinsing solutions included MeCN (GC) or MeOH and DCM (GC-MS) with N_2 (GC) or He (GC-MS) serving as the carrier gas and biphenyl as an internal standard. ^1H and ^{13}C $\{^1H\}$ NMR spectra were recorded on a Bruker Ultrashield Plus (600 MHz and 151 MHz, respectively) in 5 mm cylindrical glass tubes. Magnetic susceptibility measurements were conducted using a Sherwood Scientific MK1 with sample tubes (4 mm diameter) containing 50 mM samples in acetonitrile. UV-vis spectroscopic analysis was performed on a Specord® s600 (AnalyticJena) at 298 K in 10 mm quartz cuvettes. Elemental analysis was carried out by the University of KwaZulu-Natal (UKZN) Mass Spectrometry Laboratory and the North-West University (NWU) Potchefstroom Laboratory for Analytical Services on a PerkinElmer 2400 Series II CHNS-O elemental analyser. Melting point analysis was performed on a Buchi Melting Point B-540. Catalytic reaction products were identified and characterised by GC and GC-MS while the isolated secondary alcohol oxidation products were confirmed with FT-IR, ^1H and ^{13}C $\{^1H\}$ NMR spectroscopy after isolation.

Non-heme N_4-tetradentate ligands, *R,R*-L1–L4 and *S,S*-L1–L4 and $Mn(OTf)_2$, R,R and *S,S*-C1–C4, complex synthesis

Resolution of the 1,2-diaminocyclohexane tartrate salt, synthesis of the non-heme N_4-tetradentate ligands and their $Mn(OTf)_2$ complexes was done using previously reported literature procedures.[10,21–23]

Synthesis of *N,N′*-dimethyl-*N,N′*-bis(2-pyridylmethyl)-(*R,R*)-1,2-diaminocyclohexane (*R,R*-BPMCN) (*R,R*-L1)

R,R-BPMCN-amine (136 mg, 0.4587 mmol) was dissolved in MeCN (5 ml). Whilst stirring, 35% formaldehyde (436 mg, 5.082 mmol) and glacial acetic acid (0.75 ml) was added to the solution. The solution was stirred for 30 min after which $NaBH_4$ (73 mg, 1.923 mmol) was added portion wise. The reaction mixture was stirred for 72 hours at ambient temperature where after the MeCN was removed *in vacuo*. KOH (2 M) was added to the oily residue to raise the pH of the solution above 10. The resulting aqueous solution was extracted with DCM (3 × 10 ml portions), separated and the organic layer washed with H_2O (2 × 10 ml portions) and saturated NaCl solution (1 × 10 ml portion). The organic layer was dried over Na_2SO_4 and the solvent removed *in vacuo* to obtain a brown oil (114 mg; 77%). FT-IR (ATR, ν, cm^{-1}): 3050, 2930, 2856, 2791, 1591, 1433, 1264, 732. ^1H NMR (600 MHz, $CDCl_3$, ppm) δ: 8.51 (d, J = 4.8 Hz, 2H), 7.60 (dd, J = 6.2, 1.6 Hz, 2H), 7.16–7.11 (m, 2H), 3.94 (d, J = 14.5 Hz, 2H), 3.82 (d, J = 14.6 Hz, 2H), 2.30 (s, 6H), 2.00 (dd, J = 10.6, 2.3 Hz, 2H), 1.85–1.70 (m, 2H), 1.34–1.27 (m, 2H), 1.23–1.12 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$, ppm) δ: 161.29, 148.63, 136.32, 122.92, 121.63, 64.53, 60.44, 36.68, 30.96, 25.84, 25.82. Experimental procedures for the preparation of ***R,R* and *S,S*-L1–L4** provided in the ESI.†

Synthesis of [(*R,R*-L1)Mn(II)$(OTf)_2$], *R,R*-C1

To a stirring solution of $Mn(OTf)_2$ (165 mg, 0.443 mmol) in dichloromethane (2 ml) was added ***R,R*-L1** (155 mg, 0.478 mmol) in dichloromethane (2 ml). The reaction mixture was stirred for 1 hour. After the allotted time, the pale yellow solution was filtered to remove metallic manganese, the solvent reduced and Et_2O added. The pale-yellow/beige solid which formed was washed with Et_2O (2 × 20 ml portions), dried *in vacuo* to afford a beige solid (146 mg, 46%). UV/vis, nm (ε, A/mol dm^{-3}): 210.5 (3463), 263.5 (4082). Anal. calc. (found) for $MnC_{22}N_4O_6H_{28}F_6S_2$: C 38.99 (39.53); H 4.17 (3.84); N 8.27 (8.47); S 9.47 (9.14). μ_{eff} = 5.553 BM (297 K, MeCN). APCI-MS (m/z): 528.1214 $[M - OTf]^+$. Experimental procedures for the preparation of ***R,R*-C2–C4** and ***S,S*-C1–C4** provided in the ESI.†

X-ray crystal analysis

Single crystals of complexes ***R,R*-C4** and ***S,S*-C4** were mounted on a nylon loop and centred in a stream of cold nitrogen at 173(2) and 200(2) K respectively. Crystal evaluation and data collection were performed on a Bruker D8 Quest Eco diffractometer with Mo Kα radiation (λ = 0.71073 Å). Data collection, reduction and refinement were performed using SAINT[24] and SADABS,[25] which forms part of the APEX3 software package.[26] The structures were solved by direct methods and refined by full-matrix least-squares on F^2 using SHELX-2016[27] within the X-Seed graphic user interface.[28,29] All non-hydrogen atoms were refined anisotropically and all hydrogen atoms were placed using calculated positions and riding models.

Screening of complexes in benzyl alcohol oxidation

The Mn(II)-complex (2 μmol) was dissolved in MeCN (1.225 ml) along with BnOH (2 mmol) and AcOH (10 equivalents, 1.140 ml). Following dissolution, 4 equivalents (0.620 ml) of 30% H_2O_2 was added by syringe pump over a period of 30 minutes where after the reaction was stirred for an

additional 5 minutes. Final concentrations: complex (0.620 mM), BnOH (620 mM), AcOH (6.2 M) and H_2O_2 (2.5 M) The mixture was filtered through a silica plug and analysed by GC employing biphenyl as an internal standard. All catalytic runs were done in duplicate and are reported as the average of these independent runs. Additional experimental details are provided in the ESI.†

Results and discussion

Ligand and complex synthesis

The N_4-tetradendate ligands, ***R*,*R*-L1–L4** and ***S*,*S*-L1–L4**, were prepared according to a reductive amination of the condensation products formed between various carboxaldehydes and *R*,*R* or *S*,*S*-1,2-diaminocyclohexane tartrate salt (ESI, Scheme S1†). The ligands (***R*,*R*-L1–L4** and ***S*,*S*-L1–L4**) were isolated as yellow or brown oils in good to excellent yields. All the prepared ligands displayed solubility in polar protic and aprotic organic solvent and were insoluble in non-polar organic solvents and water. Spectroscopic characterisation by FT-IR and NMR spectroscopy confirmed the formation of the desired ligands. Finally, ***R*,*R*-L1–L2** and ***S*,*S*-L1–L2** (**BPMCN** and **BMPMCN**) have been reported previously,[12] whereas ***R*,*R*-L3–L4** and ***S*,*S*-L3–L4** (**BBPCM** and **BMIMCN**) are novel.

The Mn(II)-triflate complexes, ***R*,*R*-C1–C4** and ***S*,*S*-C1–C4**, were prepared by reacting $Mn(OTf)_2$ with a slight excess of the corresponding ligand (Scheme 1 and Fig. S1†).

The desired complexes were isolated, after reaction work-up, as pale-yellow/white or beige solids in moderate yields ranging between 46–74% (see ESI†). Complexes ***R*,*R*-C1–C4** and ***S*,*S*-C1–C4** were found to be fairly stable in air (up to one week) and displayed solubility in polar organic solvents while being insoluble in ethers and alkanes. The complexes were characterised by a range of spectroscopic and analytical techniques. Analysis by APCI-MS showed characteristic mass fragments corresponding to $[M - OTf]^+$, a common feature of these and analogous manganese(II)-triflate complexes.[8,9,20] Magnetic susceptibility values (μ_{eff}), recorded in acetonitrile solvent, were in the range 5.6–5.9 BM for both ***R*,*R*** and ***S*,*S*** configurations. The experimentally obtained values are in the range observed for previously reported Mn(II) complexes.[9,10,30] Finally, elemental analysis confirmed the bulk purity of the isolated complexes.

The solid state structures of ***R*,*R*-C4** and ***S*,*S*-C4** were unambiguously established by X-ray analysis. Suitable crystals were grown by slow diffusion of diethyl ether into concentrated acetonitrile solutions of the complexes. The ellipsoid diagrams for ***R*,*R*-C4** and ***S*,*S*-C4** are shown in Fig. 1a and b respectively, while crystallographic data and selected bond lengths and angles appear in Tables S2 and S3.† For both complexes, the coordination geometry about the metal centre is distorted octahedral in which the respective ligands adopt a *cis*-α topology. Complexes ***R*,*R*-C4** and ***S*,*S*-C4** are enantiomers of each other in the solid state, crystallising in the enantiomeric space groups $P4_12_12$ and $P4_32_12$ respectively. In the case of ***R*,*R*-C4** this results in a Δ helical chirality of the complex, whereas in the case of ***S*,*S*-C4** it results in a Λ helical chirality of the complex. In both instances the nitrogen atoms of the *N*-methylimidazole moieties (N1 and N1′) are situated *trans* to each other, whereas the aliphatic nitrogen atoms (N3 and N3′) are situated *cis* to each other. A comparison of the Mn–N bond lengths reflect the different chemical nature of the donor atoms. In both cases, the Mn–N1 bond lengths are significantly shorter [~2.143(6) Å] than the corresponding Mn–N3 bond lengths [~2.373(6) Å].

In general, the Mn–N distances for complexes ***R*,*R*-C4** and ***S*,*S*-C4** are in the range observed for analogous high spin Mn(II) complexes with N_4-tetradentate ligands reported in literature.[10,31–35] As expected, comparative space-filling structural analysis shows the same degree of accessibility of the binding sites (represented by the triflate O-atoms) to the bulk (Fig. 2a and b). This observation suggests that, all other factors

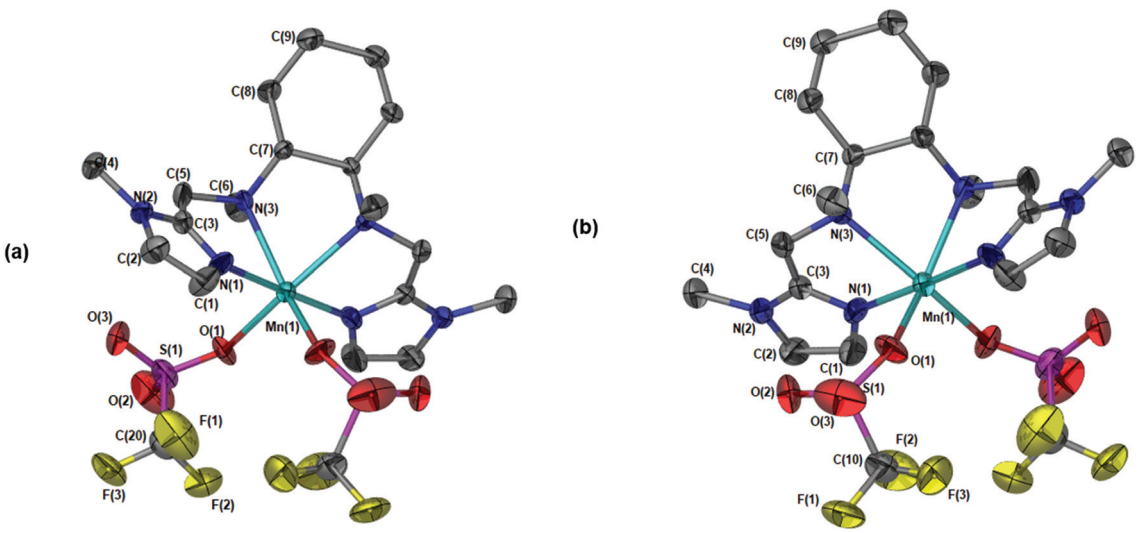


Fig. 1 Ellipsoid diagrams of (a) ***R*,*R*-C4** and (b) ***S*,*S*-C4** drawn at 50% probability.

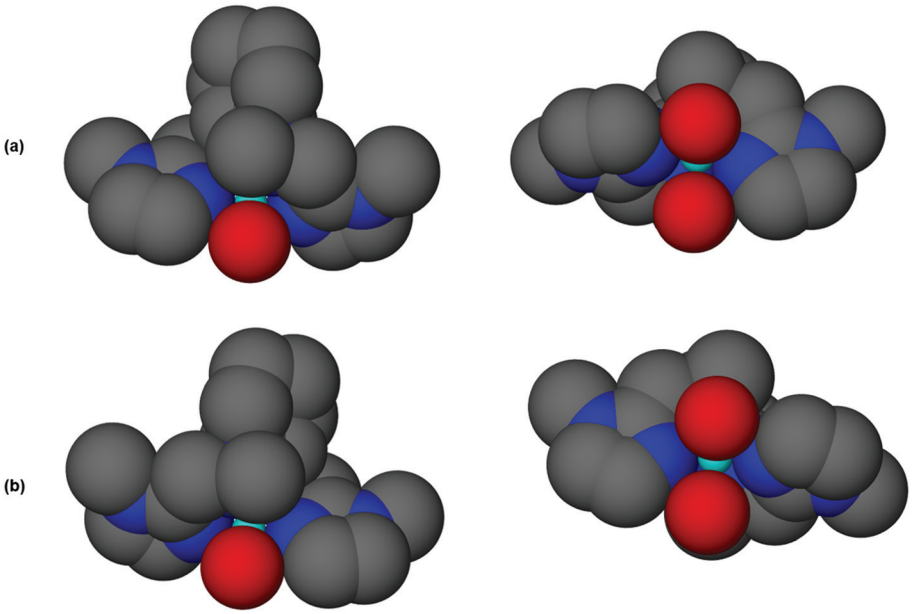


Fig. 2 Space-filling diagrams of (a) ***R,R*-C4** and (b) ***S,S*-C4**. The trifluoromethanesulfonate groups and hydrogen atoms have been omitted for clarity, but the O-atoms directly bound to the manganese centre have been retained. Colour code: grey (C), turquoise (Mn), blue (N) and red (O).

being equal, both ***R,R*-C4** and ***S,S*-C4** should display similar catalytic activity.

Mn(II)-Catalysed benzyl alcohol oxidation

A series of control experiments were conducted prior to screening the complexes, ***R,R*-C1–C4** and ***S,S*-C1–C4** in benzyl alcohol oxidation. Performing the oxidation reaction in the presence and absence of a manganese(II) salt, $Mn(OTf)_2$ or $MnCl_2{\cdot}4H_2O$, with 1.2 equivalents of hydrogen peroxide as oxidant showed no catalytic activity (Table 1, entries 1–3). The addition of 10 equivalents of AcOH as co-catalyst in the presence of $Mn(OTf)_2$ (Table 1, entry 4) or $MnCl_2{\cdot}4H_2O$ (Table 1, entry 5) resulted in no improvement in conversion. These results established that the metal precursor, in the absence of ligand, or the oxidant on its own does not catalyse the oxidation reaction.

Employing complex ***R,R*-C1** as catalyst, in the absence of acetic acid, resulted in no conversion (Table 1, entry 6). On the other hand, the inclusion of acetic acid resulted in 19% conversion of benzyl alcohol to benzaldehyde, confirming the importance of using a ligated Mn(II) complex (Table 1, entry 7) and AcOH as co-catalyst. No significant increase in conversion was seen when the oxidant concentration was increased (Table 1, entries 8 and 12).

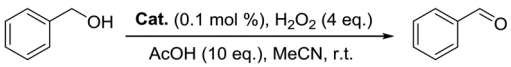
Screening of complexes in benzyl alcohol oxidation

To evaluate the effect of ligand substituents and N-donors on activity, the complexes were subjected to oxidation of benzyl alcohol (BnOH) with H_2O_2 serving as the oxidant along with AcOH as co-catalyst (Scheme 2). Low conversions not exceeding 30% were observed for all the complexes (Fig. 3). The chirality of the complexes tested did not have any significant effect on conversion which is attributed to the occurrence of dynamic interchangeability between different ligand topologies (*cis*-α and *cis*-β) in solution, and the fact that the product formed is achiral. In addition, solid state structural analysis confirms that the active site accessibility is the same in both

Table 1 Preliminary screening conditions for benzyl alcohol oxidation

Entry	Catalyst (mol%)	H_2O_2 (equivalents)	AcOH (equivalents)	Conversion[a] (%)	Aldehyde selectivity (%)
1	—	1.2	—	0.0	—
2	0.1 (**$Mn(OTf)_2$**)	1.2	—	0.0	—
3	0.1 (**$MnCl_2{\cdot}4H_2O$**)	1.2	—	0.0	—
4	0.1 (**$Mn(OTf)_2$**)	1.2	10	0.0	—
5	0.1 (**$MnCl_2{\cdot}4H_2O$**)	1.2	10	0.0	—
6	0.1 (***R,R*-C1**)	1.2	—	0.0	—
7	0.1 (***R,R*-C1**)	1.2	10	18.6	92
8	0.1 (***R,R*-C1**)	4.0	10	20.6	93

Reaction conditions: A manganese salt or ***R,R*-C1** (2 μmol) was dissolved in acetonitrile with benzyl alcohol (2 mmol) and AcOH (0 or 1.140 ml). H_2O_2 (0.19 or 0.620 ml) was added by syringe pump over 30 min at 25 °C (total volume = 3.19 ml) and stirred for an additional 5 min. [a] Conversions and aldehyde selectivity was determined by GC against an internal standard (biphenyl).



Scheme 2 General procedure used for screening Mn(II)-complexes against benzyl alcohol oxidation.

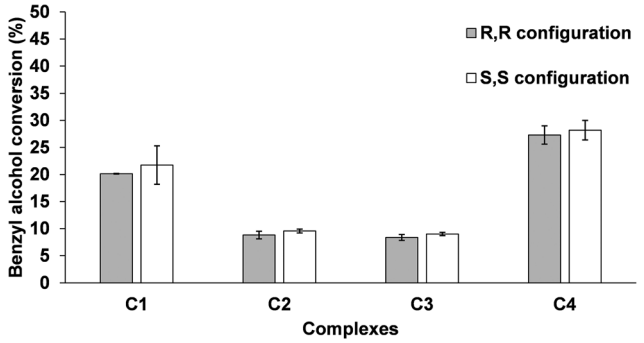


Fig. 3 Screening of Mn(II)-complexes ***R,R*-C1–C4** and ***S,S*-C1–C4**. Reaction conditions: A complex (0.1 mol%) was dissolved in acetonitrile (1.225 ml) with BnOH (2 mmol), AcOH (20 mmol) and H_2O_2 (8 mmol) at 298 K for 35 min.

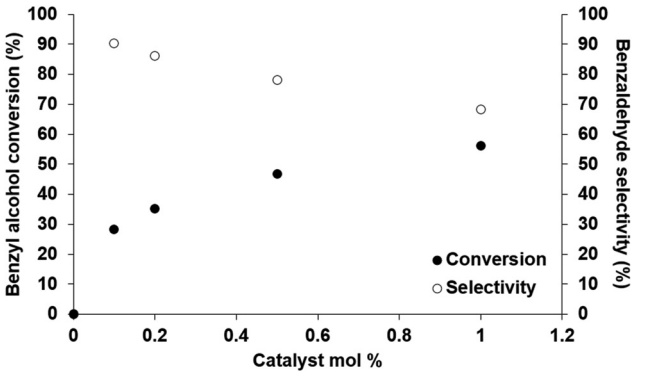


Fig. 4 Optimisation of catalyst concentration. Reaction conditions: Complex ***S,S*-C4** (0.1–1 mol%) in acetonitrile (1.225 ml) with BnOH (0.8 mmol), AcOH (8 mmol) and H_2O_2 (3.2 mmol) at 298 K for 35 min. All values are the average of a duplicate set of runs.

configurations, which would preclude any differential effect on activity.

Higher benzyl alcohol conversions were observed for complexes **C1** and **C4** (both ***R,R*** and ***S,S*** configurations) compared to those which had methyl- (**C2**) and bromo-substituents (**C3**) on the C6 position of the pyridine donor. This is due to the substituents exerting a stronger steric rather than electronic effect during the reaction and substituents in the 6-position resulting in an elongation of the Mn–$N_{pyridine}$ bond.[12] This elongation leads to a reduction in the thermodynamic stability of the active catalyst and potential demetallation.[36] No significant difference emerged when the methyl and bromo substituted complexes were compared to each other. The higher conversions for complex **C4** compared to complex **C1** can be attributed to its higher basicity (higher pK_a value) resulting in a stronger electron donor.[37] This is advantageous to the stabilisation of high valent manganese intermediate species and in doing so increases its lifetime.[16] The higher conversion may also be attributed to a more facile approach of substrate to the sterically accessible catalytic centre in complex **C4** compared to the bulkier **C1**.

Optimisation of reaction parameters

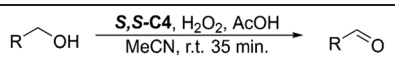
After screening of the different complexes, complex ***S,S*-C4** was chosen for further optimisation of reaction parameters, *i.e.* catalyst, AcOH and H_2O_2 concentrations. From preliminary studies, it was determined that temperature variation (−5 °C to 25 °C) and reaction time (35 min to 190 min) had no beneficial effect on the oxidation of benzyl alcohol (ESI, Table S1†). The latter observation may be attributed to catalyst decomposition. The observed effect of variations in catalyst, H_2O_2 and AcOH concentrations was found to be similar. An increase in the concentration of each parameter led to an increase in the percentage conversion of benzyl alcohol with a concomitant decrease in benzaldehyde selectivity due to over-oxidation (Fig. 4, ESI, Fig. S2 and S3†).[3] In addition, increasing H_2O_2 and AcOH concentrations above 2 equivalents had no beneficial effect on activity, likely due to active site saturation.[38]

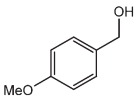
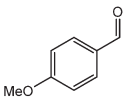
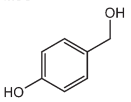
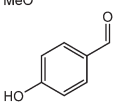
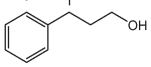
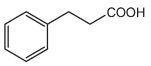
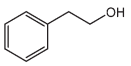
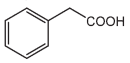
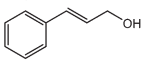
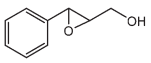
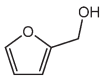
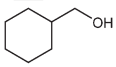
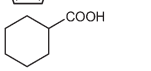
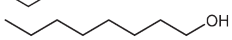
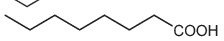
Catalytic oxidation of primary alcohols

After optimisation of reaction parameters, the following reaction conditions were chosen to achieve high conversion but minimize over-oxidation: 0.5 mol% ***S,S*-C4**, 4 equivalents of H_2O_2 and 10 equivalents of AcOH. Under these conditions, various primary alcohol substrates were evaluated to establish the scope of Mn(II)-catalysed alcohol oxidation (Table 2). The addition of electron-donating groups on the benzene ring, *i.e.* amino (Table 2, entry 2), methoxy (Table 2, entry 3), resulted in increased conversion.[17] A drawback was the formation of dimers from 2-aminobenzaldehyde as soon as it formed due to self-condensation in the presence of a Mn(II)-complex and dilute acidic solutions.[39] Insertion of a *para*-hydroxy group (Table 2, entry 4) resulted in a low conversion due to its lack of solubility in MeCN, while the addition of an iodine group (Table 2, entry 5) on the *ortho*-position decreased the conversion, again illustrating the influence that steric pressure has on catalytic activity. Increasing the aliphatic chain length by employing 3-phenyl-1-propanol as substrate led to a 20% increase in conversion, albeit with over-oxidation to the carboxylic acid (Table 2, entries 6 *vs.* entry 1). In contrast, employing 2-phenylethanol as substrate decreased the conversion (Table 2, entry 7 *vs.* entry 1). The α and β carbons in the alcohol are both activated which under catalytic conditions can generate α-ketoaldehydes or α-ketocarboxylic acids as products. These have the potential to ligate to the metal, resulting in competitive inhibition and a decrease in conversion.[40] Over-oxidation towards the carboxylic acid resulted in an esterification reaction with the alcohol substrate to produce phenethyl phenylacetate as the product.

Evaluation of cinnamyl alcohol (Table 2, entry 8) resulted in the epoxide as major product rather than an aldehyde or car-

Table 2 Catalytic oxidation of primary alcohols with ***S,S*-C4** [a]



Entry	Substrate	Major product	Conversion[b]/%	TON[c]	Aldehyde selectivity (%)
1			47	97	79
2			77	155	55
3			69	140	80
4			22	45	74
5			22	45	96
6			67	134	13
7			38	76	43
8			82	170	22
9			51	105	94
10			97	195	57
11			80	163	11
12			72	149	5

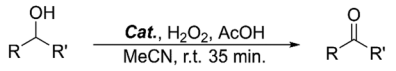
[a] Reaction conditions: Complex ***S,S*-C4** (0.5 mol%) in acetonitrile with alcohol (0.8 mmol), AcOH (8 mmol) and H_2O_2 (3.2 mmol) at 298 K for 35 min. [b] Conversions were determined by GC against an internal standard (biphenyl). [c] Turnover number (TON) = mol substrate converted per mol complex used.

boxylic acid which is attributed to the higher reactivity of non-heme Mn(II)-complexes towards alkene oxidation compared to alcohol oxidation.[41] Insertion of a heteroatom into the phenyl ring had no significant effect on the conversion compared to benzyl alcohol (Table 2, entry 9 *vs*. entry 1). In contrast, a significant increase in conversion was observed when a furan ring was used as the heterocycle due to the increased reactivity of furan (Table 2, entry 10). Another problem was the rapid decomposition of furfural in the presence of an acid, transition metal and H_2O_2 which explains the high percentage conversion.[42] Maleic anhydride was observed as one of the decomposition products. High catalytic activity towards the oxidation of cyclic and linear aliphatic primary alcohols was observed, in which 80% of the cyclohexanemethanol (Table 2, entry 11) and 72% of the 1-octanol (Table 2, entry 12) was converted. Removing the aromaticity from the ring increases the electron density at the α-carbon resulting in a higher conversion. This is in contrast to previous studies where benzylic alcohols were more reactive than their aliphatic counterparts.[40,43] Both cyclohexanemethanol and 1-octanol, however, over-oxidises to the carboxylic acid but contrary to a previous study, a higher percentage 1-octanol was converted in our study using a lower substrate concentration and much shorter reaction time.[18]

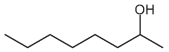
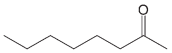
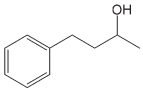
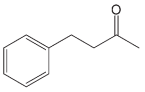
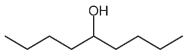
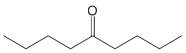
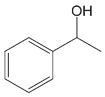
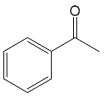
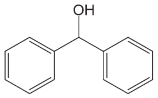
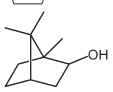
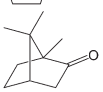
Catalytic oxidation of secondary alcohols

Due to the selectivity problems encountered during the oxidation of primary alcohols, it was decided to extend the study towards secondary alcohol substrates (Table 3). The oxidation of 2-octanol and 4-phenyl-2-butanol (Table 3, entries 1 and 2) were conducted with both ***S,S*-C4** and ***R,R*-C4** as catalysts with identical results being obtained, providing further evidence that the configuration and ultimately topology of the complex does not have an effect during alcohol oxidation. In general,

Table 3 Catalytic oxidation of secondary alcohols[a]



Cat. = R,R-C4 or S,S-C4

Entry	Substrate	Major product	Isolated yield[b] (%)
1			51 (81)
2			64 (68)
3*			67 (70)
4*			84 (100)
5*		—	—
6*			10 (96)
7*			7 (87)
8*			86 (>99)

[a] Reaction conditions: Complex ***R,R*-C4** and***S,S*-C4** (0.5 mol%) in acetonitrile with alcohol (0.8 mmol), AcOH (10 eq.) and H_2O_2 (4 eq.) at 298 K for 35 min. Conversions were determined by GC against an internal standard (biphenyl). [b] Numbers in parentheses indicate the average percentage substrate conversion from a duplicate set of runs. For entries 3–8 the asterisk denotes that ***R,R*-C4** was employed as catalyst precursor.

excellent conversions and isolated yields were obtained for all the alcohols evaluated. Specifically, the addition of a methyl group on the α-carbon had no effect on catalytic activity, evident when comparing 4-phenyl-2-butanol (Table 3, entry 1) and 4-phenyl-1-butanol (Table 3, entry 2). In both instances comparable conversions and isolated yields were obtained. Employing 1-phenylethanol as substrate resulted in 100% conversion and 84% isolated yield of acetophenone (Table 3, entry 4). The addition of a methyl group therefore, in this case, has an electron donating effect, increasing the oxidation activity.[11,20] In contrast, changing the methyl group on the α-carbon to a phenyl substituent resulted in no conversion, attributed to increased steric bulk hindering substrate approach (Table 3, entry 5).[17] In contrast, employing an aliphatic derivative such as 5-nonanol yielded the ketone product in 67% isolated yield. This is significantly higher to that reported in a previous study.[43]

Cyclic aliphatic alcohols, cyclohexanol and cyclopentanol, were oxidised in good conversions of 96% and 87% respectively (Table 3, entries 6 and 7). Unfortunately, very low isolated yields were obtained for the cyclic ketones due to a higher distribution of the ketones in the water phase compared to the organic phase and high volatility.[43] Other solvents, *i.e.* $CHCl_3$ and Et_2O, were also utilised for extraction and salting out methods were employed but no improvement was seen. Finally, a bicyclic aliphatic alcohol, *i.e.* isoborneol, was also oxidized in near quantitative conversion and 86% isolated yield (Table 3, entry 8). In the context of manganese(II)-catalysed secondary oxidation, the reported catalytic activity (conversions and isolated yields) for the substrates in Table 3 are comparable and in some cases better than literature precedent. Bhat *et al.* reported a Mn(II)/terpyridine-ligated complexes, which with a catalyst concentration of 0.5 mol% was capable of oxidising 2-phenylethanol and cyclohexanol to the corresponding ketone in 11% and 38% GC yield respectively *vs*. 10% and 84% isolated yield when employing our catalyst system.[44] Gao and co-workers reported a porphyrin-inspired Mn(II) complex which operated as an alcohol oxidation catalyst at a catalyst concentration of 1 mol%. Operating under these conditions cyclohexanol and 2-octanol was oxidised to the ketones in 38% and 25% GC yield respectively. In comparison isolated yields of 10% and 51% were obtained for these substrates when employing our catalyst system.[45] Nam, Sun and co-workers evaluated non-heme Mn(II) complexes, operating at catalyst concentrations of 0.3 mol%, in the oxidation of secondary alcohols.[46] Under these conditions 2-phenylethanol and cyclohexanol were oxidised to the ketones in 93% and 86% isolated yield respectively. This example is the most efficient Mn(II) catalyst for alcohol oxidation reported to date. Our catalyst system also outperforms analogous Fe(II) catalyst systems reported in literature. Sato and co-workers evaluated iron-picolinate complexes as alcohol oxidation catalysts, operating at 5 mol% Fe. Under these conditions, their catalyst oxidised 2-phenylethanol to 2-phenylethanone in 64% GC yield (*vs*. 84% isolated yield for our catalyst system).[47] Olivo and co-workers applied an iron-base imine complex, with a catalyst concentration of 3 mol% and hydrogen peroxide as oxidant, to the oxidation of alcohols.[48] Under their operating conditions, 2-phenylethanol was oxidised to the ketone in 9% GC yield. On the other hand, their catalyst system could oxidise cyclopentanol and cyclohexanol to the corresponding ketones in 54% and 70% GC yields respectively. Our Mn(II) complexes are outperformed by the current state of the art in alcohol oxidation catalysis: a Cu(I)/ABNO (ABNO = 9-azabicyclo [3.3.1]nonane *N*-oxyl, a nitroxyl radical) catalyst system reported by Stahl and co-workers.[49] Operating at a copper concentration of 5 mol%, 2-octanol and 4-phenyl-1-butanol could be oxidised to the ketone products in isolated yields of 96% and 95% respectively.

Conclusions

A series of ***R,R*-** and ***S,S*-**Mn(II) complexes, bearing BPMCN ligands and their derivatives (***R,R*-C1–C4** and ***S,S*-C1–C4**), were successfully applied as alcohol oxidation catalysts. In particu-

lar, complexes bearing the novel BMIMCN ligand, ***R*,*R*-C4** and ***S*,*S*-C4**, were found to be the most active. This highlighted the stabilising effect that this ligand has on the catalytically active species. While high activity was observed for primary alcohol oxidation, acid-mediated over-oxidation and side-reactions proved problematic. In contrast, secondary alcohols had no such limitations and could be oxidised to the corresponding ketones in excellent isolated yields at short reaction times. Current work in our laboratory is directed toward elucidating the mechanistic features of the oxidation reaction.

Conflicts of interest

There are no conflicts of interest to declare.

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