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cis-Oxoruthenium complexes supported by chiral tetradeutate amine (N₄) ligands for hydrocarbon oxidations†

Chun-Wai Tse, a,b Yungen Liu, a,c Toby Tai-Shan Chow, a Chaoquun Ma, a Kam-Hung Low, a Jie-Sheng Huang a, d and Chi-Ming Che a,b

We report the first examples of ruthenium complexes cis-[N₄RuIIICl₂]⁺ and cis-[N₄RuII(OH₂)₂]²⁺ supported by chiral tetradeutate amine ligands (N₄), together with a high-valent cis-dioxo complex cis-[(N₄)RuIII(O)₂]²⁺ supported by the chiral N₄ ligand mcp (mcp = N,N'-dimethyl-N,N'-bis(pyridin-2-ylmethyl)cyclohexane-1,2-diamine). The X-ray crystal structures of cis-[(mcp)RuIIICl₂](ClO₄) (1a), cis-[(Me₂mcp)RuIIICl₂]ClO₄ (2a) and cis-[(pdp)RuIIICl₂](ClO₄) (3a) (Me₂mcp = N,N'-dimethyl-N,N'-bis[6-methylpyridin-2-ylmethyl]cyclohexane-1,2-diamine, pdp = 1,1'-bis(pyridin-2-ylmethyl)-2,2'-bipyridylidine) show that the ligands coordinate to the ruthenium centre in a cis-α configuration. In aqueous solutions, proton-coupled electron-transfer redox couples were observed for cis-[(mcp)RuII(O₂CCF₃)₂]ClO₄ (1b) and cis-[(pdp)RuII(O₂SCF₃)₂]CF₃SO₃ (3c). Electrochemical analyses showed that the chemically/electrochemically generated cis-[(mcp)RuIV(O)₂]²⁺ and cis-[(pdp)RuIV(O)₂]²⁺ complexes are strong oxidants with E° = 1.11–1.13 V vs. SCE (at pH 1) and strong H-atom abstractors with D(·H) = 90.1–90.8 kcal mol⁻¹. The reaction of 1b or its (R,R)-mcp counterpart with excess [NH₄]₂[CeIV(NO₃)₆] (CAN) in aqueous medium afforded cis-[(mcp)RuIV(O)₂]ClO₄ (1e) or cis-[(R,R)-mcp]RuIV(O)₂]ClO₄ (2e), respectively, a strong oxidant with E(RuIV/V) = 0.78 V (vs. Ag/AgNO₃) in acetonitrile solution. Complex 1e oxidized various hydrocarbons, including cyclohexene, in acetonitrile at room temperature, affording alcohols and/or ketones in up to 66% yield. Stoichiometric oxidations of alkenes by 1e or 1e⁺ in 1BuOH/H₂O (5 : 1 v/v) afforded diols and aldehydes in combined yields of up to 98%, with moderate enantioselectivity obtained for the reaction using 1e⁺. The cis-[(pdp)RuIV(OH₂)₂]²⁻ (3c) catalyst oxidation of saturated C–H bonds, including those of ethane and propane, with CAN as terminal oxidant was also demonstrated.

Introduction

The selective oxidations of hydrocarbons including alkanes and alkenes, and oxidation of alcohols, have been catalysed by metal complexes under mild conditions are important reactions in chemical synthesis. Iron and manganese complexes bearing tetradeutate pyridylmethyl amine or quinolylamine N₄ ligands constitute one of the platforms for performing efficient and selective C–H and C=C functionalizations, wherein the widely employed N₄ ligands include mcp, pdp and bqcn ligands and their derivatives (examples depicted in Fig. 1). These acyclic chiral tetradeutate amine (N₄) ligands, in most scenarios, coordinate to metal ions in a cis-α configuration to form octahedral metal complexes (Fig. 2), leaving a pair of H Bonds, including those of ethane and propane, with CAN as terminal oxidant was also demonstrated.

† Electronic supplementary information (ESI) available: Experimental procedures and characterization, Scheme S1, Tables S1–S6, Fig. S1–S20. CCDC 1589975 (1a), CCDC 1589976 (2a), CCDC 1589977 (3a), CCDC 1589978 (5d), CCDC 1589979 (6d). For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c7sc05224c.
extraordinary reactivity of high-valent iron–oxo complexes. A proposed cis-[(N₄)MnV(O)₂] intermediate, cis-[[((S,S)-bqcn)Mn(V)O₂] -isolation. While several cis-[(N₄)ReIV(O)₂]⁺ complexes and a cis-[(N₄)ReV(O)₂]²⁺ complex have been isolated and structurally characterized in our recent work,¹¹ the former were not reactive towards organic substrates, and concerning hydrocarbon oxidation reactivity, the latter only reacted with weak C–H bonds (bond dissociation energy: ~ 76 kcal mol⁻¹) of 1,4-cyclohexadiene, 9,10-dihydroanthracene and xanthene at 80 °C to give dehydrogenation or ketone products.

To search for isoal ale cis-dioxo metal complexes that are supported by the abovementioned chiral N₄ ligands and are reactive towards hydrocarbon oxidation, including the cis-dihydroxylation of alkenes and the oxidation of strong C–H bonds at room temperature, we directed our efforts to ruthenium systems. High-valent Ru–oxo complexes are generally more stable than their iron counterparts due to their lower redox potentials as well as substituential inertness of auxiliary ligands.¹² cis-Dioxoruthenium(v) complexes can have a delicate balance between stability and reactivity that allows them to be isolated/characterized¹⁵,¹¹ or even studied in reactions with organic substrates in a stoichiometric manner.¹⁴–¹⁶ Several cationic cis-dioxoruthenium(v) complexes, including cis-[(Tet-Me₆)RuVI(O)₂]²⁺ (Tet-Me₆ = N,N,N',N'-4,6-hexamethyl-3,6-diazaocetane-1,8-diamine),¹⁴a cis-[(Me₃tacn)RuVI(O)₂(O₂CCF₃)]⁻ (Me₃tacn = 1,4,7-trimethyl-triazacyclononane),¹⁶a cis-[(6,6'-Cl₂-bpy)₂RuVI(O)₂]²⁺ (6,6'-Cl₂-bpy = 6,6'-dichloro-2,2'-bipyridine),¹⁶b cis-[(bpy)₂RuVI(O)₂]²⁺ (bpy = 2,2'-bipyridine)³⁷ and cis-[(dmp)₂RuVI(O)₂]²⁺ (dmp = 2,9-dimethyl-1,10-phenanthroline)³⁸ have been isolated and/or spectroscopically characterized. Among them, cis-[(Me₃tacn)RuVI(O)₂(O₂CCF₃)]⁻ and cis-[(6,6'-Cl₂-bpy)₂RuVI(O)₂]²⁺ are known to react with simple saturated alkanes (e.g., cyclohexane) stoichiometrically.¹⁵,¹⁶ The related catalytic oxygenation of cyclohexene with 1BuOOH could be performed with [(Me₃tacn)Ru VI(Cl)₃]³⁹ and cis-[(Cl₂-bpy)₂Ru VI(OH)₂]⁺ as catalysts.¹⁶b Du Bois and co-workers recently demonstrated selective C–H functionalization catalysed by [(Me₃tacn)RuVICl₃] with ceric ammonium nitrate (CAN) as a terminal oxidant to give tertiary C–H hydroxylation products.²⁰ Using bis(bipyridine)Ru catalysts, the selective functionalization of amine derivatives was attainable with various oxidants and acid additives.²¹ These studies highlight the amendable oxidation capabilities of the cis-dioxoruthenium(v) moiety and the underdeveloped potential of ruthenium catalysts in C–H oxidation.

Thus far, studies on highly oxidizing cis-dioxoruthenium(v) complexes have focused on tridentate Me₃tacn and simple bidentate aromatic diimine ligands.¹⁵–¹⁸ The Me₃tacn ligand is not flexible for structure modification.²² Ruthenium complexes with aromatic diimine ligands may undergo cis–trans isomerization²² and ligand loss in a high oxidation state.²³ These difficulties can potentially be resolved by utilizing the above-mentioned chiral N₄ ligands: the first coordination sphere is highly tunable by ligand modification, as revealed by recent works from White,³¹ Costas,³²,³³,³⁸,³⁹ and their co-workers; the higher rigidity and denticity can provide better conformational stability under catalytic conditions.

In this work, we aim to (i) isolate/generate cis-dioxoruthenium(v) complexes bearing chiral tetradeutate amine (N₄) ligands, (ii) study the redox potentials and hydrocarbon oxidation reactions of these cis-[(N₄)RuVI(O)₂]²⁺ complexes, and (iii) gain insight into the activity of chiral Ru(N₄) complex in asymmetric oxidation reactions. Until now, studies on rutenium complexes supported by chiral N₄ ligands (mcp, pdp, bqcn and their derivatives) have been limited,²¹–²⁵ including a report involving some data of [Ru⁶⁺(mcp)Cl₂]-catalysed oxidation of thioanisole with H₂O₂,²⁶ another report involving the synthesis and crystallographic characterization of [Ru⁶⁺(R,R)-pdp(NCMe)₂]²⁺,²⁷ and density functional calculations on a hypothetical monoxo ruthenium(v) species cis-[(bqcn)RuV²⁺(NCMe)₂]²⁺.²⁸ No examples of the corresponding cis-dioxo ruthenium chiral N₄ complexes have been reported.²³–²⁶ Herein, we describe the syntheses, characterization, and electrochemical and reactivity studies of a series of chiral Ru(N₄) complexes, including a highly reactive chiral cis-[(N₄)RuVI(O)₂]²⁺ complex that can perform dihydroxylation of alkenes and oxidation of strong C–H bonds of alkanes (including cyclohexane) and oxidation of alcohols at room temperature. The studies on cis-[(N₄)RuVI(O)₂]²⁺ complexes provide insight into the reactivity and electrochemical properties of the analogous highly oxidizing cis-[(N₄)M(O)₂]²⁺ (n = 1 or 2; M = Fe or Mn) species.⁶,¹⁰

**Results**

**Synthesis and characterization**

In this work, a series of ruthenium complexes bearing six chiral tetradeutate amine N₄ ligands (Fig. 1) and different auxiliary ligands were prepared (Schemes 1 and 2). The reaction of
K₂[Ru⁷Cl₃(OH₂)] with the mcp, Me₂mcp, pdp or Me₂pdp ligand in ethanol under refluxing conditions (Scheme 1) gave the corresponding cis-[N₄]Ru⁷Cl₃⁺ salt of cis-[N₄]Ru⁷Cl₃⁺ complex (1a, 2a, 3a or 4a) in 32–97% yield.⁷ The reaction of 1a with Zn/Hg in distilled water at 80 °C for 30 min, followed by subsequent treatment of the solution with AgOTf and 0.2 M CF₃CO₂H, afforded cis-[mcp]Ru⁷[O₂CCF₃]₂ClO₄ (1b) in 20% yield (Scheme 1). To prepare ruthenium complexes containing the bqcn ligand, an alternative synthetic method was developed. Treatment of bqcn or Me₂bqcn with a slight excess (1.2 equiv.) of [Ru⁷(OH₂)₆]OTs₂ under Ar in THF furnished the OTs⁻ salt of cis-[N₄]Ru⁷(OH₂)₂Cl²⁺ (5c or 6c) in good yield (up to 71%). A similar treatment using pdp or Me₂pdp gave the OTs⁻ salt of 3c or 4c. Recrystallization of 5c·OTs or 6c·OTs in acetonitrile in the presence of LiClO₄ caused cis-[bqcn]Ru⁷([NCMe]₂)[ClO₄]₂ (5d) and cis-[Me₂bqcn]Ru⁷([NCMe]₂)[ClO₄]₂ (6d), respectively (Scheme 2).

The structures of 1a, 2a, 3a, 5d and 6d (as ClO₄⁻ salts) were established by X-ray crystallography. All these complexes, except 5d, adopt a cis-α configuration (Fig. 3 and S1–S5, ESI†), where the two terminal pyridyl/quinolyl groups are positioned trans to each other. For 5d, its crystal structure showed that the cis-α and cis-β isomers are present in a 1:1 ratio in the unit cell.⁴ The two isomers could not be separated by repeated recrystallizations. Fig. 3a depicts the structure of cis-α-5d; its two methyl groups on the cyclohexane-1,2-diamine nitrogen atoms are oriented anti to each other (C40 and C47). In the cis-β isomer (Fig. 3b), the corresponding two methyl groups (C10 and C17) show the opposite (syn) orientation.

The ¹H NMR spectra of 3c, 4c (in CD₃CN) and 6d show signals indicative of a cis-α configuration (Fig. 2) with C₂ symmetry (see Experimental section); no interconversion to the cis-β conformer was observed by standing the solution at room temperature for days. In contrast, the ¹H NMR spectrum of 5d comprises a mixture of signals from the cis-α and cis-β isomers.

The UV-Vis absorption spectra of the cis-[N₄]Ru⁷Cl₃⁺ complexes (1a, 2a, 3a and 4a) in acetonitrile solution are characterized by p→(Cl)→Ru(II) LMCT transitions. The coupling constants (rubidium) complexes display diastereomeric isomers. Preparation of (1b) and (3) are different cyclic voltammetric behaviours in acetonitrile solutions (Fig. S9, ESI†). Complexes 1a and 3a display a reversible couple at E₁/₂ = ca. 0 V vs. SCE. This is assigned to the Ru⁷ᴵᴵᴵ/ᴵᴵ couple: cis-[N₄]Ru⁷ᴵᴵCl₂⁺ + e⁻ → cis-[N₄]Ru⁷ᴵᴵ(Cl)₂⁺. The Ru⁷ᴵᴵ⁺ couple was not observed at potentials up to 1.6 V vs. SCE. For 2a, where the N₄ ligand possesses a methyl substituent on the pyridyl moiety, the Ru⁷ᴵᴵ⁺ couple is irreversible. The irreversible reduction of cis-[N₄]Ru⁷Cl₃²⁻ occurs at Eₚₑ = −0.01 V; upon the reverse scan, an oxidation wave appears at Eₚₐ = 0.69 V, which is attributed to the oxidation of cis-[Me₂mcp]Ru⁷Cl(NCMe)²⁺ to cis-[Me₂mcp]Ru⁷Cl₂⁻⁺ after a ligand exchange reaction of cis-[Me₂mcp]Ru⁷Cl₃²⁻ with the solvent.⁴ The cyclic voltammograms of 5d and 6d in MeCN display reversible oxidation couples at E₁/₂ = 1.35 V and 1.36 V vs. SCE, respectively (Fig. S11, ESI†). The electrochemical reaction is assigned to cis-[N₄]Ru⁷([NCMe]₂)₃³⁻⁺ + e⁻ → cis-[N₄]Ru⁷([NCMe]₂)₃²⁺.

Aqueous electrochemistry of cis-[mcp]Ru⁷(O₂CCF₃)₂ClO₄ (1b) and cis-[pdp]Ru⁷(O₂CCF₃)₂CF₃SO₃ (3c)

The cyclic voltammogram of cis-[mcp]Ru⁷(O₂CCF₃)₂ClO₄ (1b) at pH 1 displays three reversible/quasi-reversible couples (i), (ii) and (iii) at E₁/₂ = 0.37, 0.92 and 1.11 V vs. SCE, respectively (Fig. 4a). Using rotating-disc electrode voltammetry, the coulombic stoichiometries of the redox couples were determined to be 1.0, 1.9 and 1.1 for couples (i), (ii) and (iii), respectively (Fig. 4b). With reference to previous work, these couples could be assigned to Ru⁷ᴵᴵ/ᴵᴵ, Ru⁷ᴵᴵ/ᴵ and Ru⁷ᴵ/ᴵ redox processes, and the electrochemical reactions (1)–(3) are
depicted in Scheme 3. At pH 5, the $E_{1/2}$ of couples (i) and (iii) shift to 0.25 and 0.98 V, respectively, and couple (ii) splits into two reversible one-electron couples (iv) and v at 0.65 and 0.77 V, respectively (Fig. S12, ESI†). Couples (iv) and (v) are assigned to Ru IV/III and Ru V/IV couples (eqn (4) and (5) in Scheme 3). The cathodic shift in the $E_{1/2}$ of couple (iii) with an increasing pH is in accordance with other dioxoruthenium(VI) complexes.\(^{14,32,33,34}\)

The electrochemical properties of cis-[(pdp)RuII(OH)2(OTs)2]CF3SO3 (3c′, Scheme S1, ESI†) in 0.1 M CF3SO3H at pH 1 are reminiscent of that of 1b. As depicted in Fig. 5a, 3c′ shows a reversible couple I at $E_{1/2} = 0.36$ V and a quasi-reversible couple III at $E_{1/2} = 1.13$ V ($E_{pa} = 1.19$ V) vs. SCE. Notably, at the foot of couple III, there is a less defined couple II at $E_{1/2} = 0.95$ V. Couple I ($\Delta E_p \approx 60$ mV; $i_{pa}/i_{pc} \approx 1$) is attributed to a Ru III/II couple (eqn (6) in Scheme 4). Couple II is assigned as a Ru IV/III couple (eqn (7)). Its much smaller current measured relative to the Ru III/II couple is attributed to the rate-determining deprotonation of [RuIII(OH)] or [RuIII(OH2)] prior to the oxidation of RuIII to RuIV.\(^{35}\) Couple III is assigned as a Ru V/IV couple (eqn (8)).\(^{36}\) The natures of couples I, II and III were examined by rotating-disk electrode voltammetry (Fig. 5b), showing that the limiting current/number of electrons involved in couples I and (II and III) has a ratio of 1 to 2.7.\(^{37}\)

The complex cis-[(bqcn)RuIII(OH2)]2OTs2 (5c·OTs) similarly shows a reversible couple at $E_{1/2} = 0.36$ V and an irreversible oxidation wave at $E_{pa} = 1.14$ V at pH 1 (Fig. S14a, ESI†). At pH 1, cis-[(bqcn)RuIII(OH2)]2OTs2 (5c·OTs) shows a reversible RuIII II couple at $E_{1/2} = 0.45$ V and a shoulder oxidation wave at $E_{pa} = 1.15$ V (Fig. S14b, ESI†), while cis-[(Me2bqcn)RuIII(OH2)]2OTs2 (6c·OTs) shows a reversible RuIII II couple at $E_{1/2} = 0.49$ V and a shoulder oxidation wave at $E_{pa} = 1.08$ V (Fig. S14c, ESI†). The σ-donating ability of the N4 ligands follows the order of mcp > pdp > bqcn > Me2bqcn, as revealed by the $E_{1/2}$ values of the Ru III/II couples (Table 1).\(^{39}\) However, varying the structure of the N4 ligand has a minor effect on the redox potentials of the electrochemically generated cis-dioxoruthenium(VI) complexes ($\Delta E_{pa} \approx 70$ mV).

Variable-pH cyclic voltammetry of 3c′ was conducted in Britton–Robinson buffer.\(^{40–42}\) Selected voltammograms at pH = 2.56, 5.02 and 6.37 are displayed in Fig. S15 (ESI†). Above pH 1.98, couple III splits into two one-electron couples (Ru V/IV and Ru IV/III); the former, which merges with couple II to form a new couple IV, can be assigned as a Ru V/IV couple (eqn (9)). The latter one is designated as couple V (eqn (10)). The Pourbaix diagram

![Chemical Science](https://example.com/chemical-science.png)

**Scheme 3** Proposed redox couples for cis-[(mcp)RuIII(O2CCF3)2]ClO4 (1b) in different pH buffer solutions. The cis-sign is omitted for clarity.

![Fig. 5](https://example.com/fig-5.png)

**Fig. 5** Cyclic voltamogram (a, upper) at 0.1 V s⁻¹ and rotating-disk-electrode voltammogram (b, lower) at 100 rpm of 3c′ in 0.1 M CF3SO3H (pH 1). Working electrode: edge-plane pyrolytic graphite for CV; glassy carbon for RDEV.
from pH 1 to 7.96 is shown in Fig. 6. For couple I (RuIII/II), there are two straight-line fragments with slopes of −56 and −122 mV per pH unit at 1 < pH < 6.37 and 6.37 < pH < 7.24, respectively, corresponding to the electrochemical reactions described in eqn (6) and (11). The breakpoint (pH = 6.4) of the plot for couple I is logically the pKₐ value of cis-[(pdp)RuIII(O)(OH)]²⁺, which is comparable to that of cis-[(Tet-Me₆)RuIII(O)(OH)]²⁺ (pKₐ = 6.5).¹⁴ For couple IV (RuVIII), three linear segments with slopes of −57, −85 and −52 mV per pH unit are found at 1.98 < pH < 5.72, 5.72 < pH < 6.37 and 6.37 < pH < 7.96, respectively. The corresponding electrochemical reactions are described in eqn (9), (12) and (13). For couple V (RuVII), its potential shifts cathodically with a slope of −51 mV pH⁻¹ at 1.98 < pH < 5.02. This is in line with its one-proton one-electron nature (equation (10)). At 5.02 < pH < 7.96, it becomes insensitive to pH, suggesting a one-electron process that does not involve proton loss (equation (14)). From this observation, together with the breakpoint of the plot of couple IV, the pKₐ value of cis-[(pdp) RuVII(O)(OH)]²⁺ is estimated to be 5.6.

With the above electrochemical information in hand, the bond dissociation energy (D₀–H) for cis-[(pdp)RuVII(O)(O–H)]²⁺ to form cis-[(pdp)RuVII(O)²⁺] can be obtained from eqn (15), based on the thermochemical method developed by Mayer and Bordwell.¹⁴,⁴⁴ The D₀–H value is calculated to be 90.8 kcal mol⁻¹ for cis-[(pdp)RuVII(O)²⁺] (Scheme 5) and 90.1 kcal mol⁻¹ for cis-[(mcp)RuVII(O)²⁺].

\[
D_{O-H} = 23.06E^0 + 1.37pK_a + C^{48}
\]

**Isolation or generation of cis-dioxoruthenium(VI) complexes via chemical oxidation**

Treatment of cis-[(mcp)RuVIII(O₂CCF₃)²⁺] (1b) with excess CAN in aqueous solution gave cis-[(mcp)RuVII(O)²⁺] (1c), which was isolated as a pale green perchlorate salt in 66% yield (Scheme 6, see Experimental section for details). The UV-visible absorption spectrum of a freshly prepared solution of cis-[(mcp)RuVII(O)²⁺] (Scheme 5) and 90.1 kcal mol⁻¹ for cis-[(mcp)RuVII(O)²⁺].

**Table 1** Redox potentials of ruthenium N₄ complexes in aqueous solution at pH 1 (ref. 39)

<table>
<thead>
<tr>
<th>Complex</th>
<th>E₁/₂ of RuVII⁺⁺⁺⁺⁺⁺⁺⁺ couple (V vs. SCE)</th>
<th>RuV⁺⁺⁺⁺⁺⁺⁺⁺⁺ oxidation (V vs. SCE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1b (N₄ = mcp)</td>
<td>0.37</td>
<td>1.11</td>
</tr>
<tr>
<td>3c (N₄ = pdp)</td>
<td>0.36</td>
<td>1.13</td>
</tr>
<tr>
<td>5c OTs (N₄ = bqcn)</td>
<td>0.45</td>
<td>1.15</td>
</tr>
<tr>
<td>6c OTs (N₄ = Me₂bqcn)</td>
<td>0.49</td>
<td>1.08</td>
</tr>
</tbody>
</table>

**Scheme 5** Thermochemical cycle of cis-[(pdp)RuVII(O)²⁺].
symmetric and asymmetric stretches of the cis-dioxoruthenium(vi) moiety. Complex 1e is diamagnetic, as revealed by its $^1$H NMR signals. Notably, 1e is stable at $-15^\circ C$ under argon for a few hours but decomposes in aqueous tert-butanol or acetonitrile within 30 min to give a dark brown solution, while the ESI-MS analysis of this solution showed peaks centred at $m/z = 460.1$, which corresponds to $[[\text{mcpRu(OH)}_2]]^+$ in aqueous tert-butanol, and $m/z = 254.1$, which corresponds to $[[\text{mcpRu(NCMe)}_2]]^+$ in acetonitrile. In aqueous solution at pH 1, cis$-[[\text{mcpRu}^{\text{VI}}(O)_2]^{2+}}$ shows an identical cyclic voltammogram as that as 1b. The cyclic voltammogram of 1e in acetonitrile shows a reversible one-electron couple at $E_{1/2} = 0.78$ V vs. Ag/AgNO$_3$. Similar oxidation of cis$-[[\text{pdpRu}^{\text{III}}(O)_2]^{2+}}$ (3c) or in situ generated cis$-[[\text{pdpRu}^{\text{IV}}(OH)_2]^{2+}}$ by CAN did not furnish isolable cis$-[[\text{pdpRu}^{\text{IV}}(O)_2]^{2+}}$ (Scheme 6). Upon addition of the CAN solution into an ice-cooled solution of cis$-[[\text{Tet-Me}_6]^{2+}}$ (Lower) Experimental ESI-MS signals for a reaction mixture of 3c$-\text{CF}_3\text{SO}_3$ and 6 equiv. of $\text{Ce}^{\text{IV}}(\text{ClO}_4)_4$ [Ru] was $1 \times 10^{-4}$ M.

**Table 2** Stoichiometric oxidation of alkenes by cis$-[[\text{R}(\text{R})-\text{mcp}]^{\text{IV}}(O)_2]^{2+}}$ in aqueous tert-butanol

<table>
<thead>
<tr>
<th>Entry</th>
<th>Alkene substrate</th>
<th>Product(s)</th>
<th>% Yield$^a$ (% ee)</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>PhCHO</td>
<td>cis-Diol</td>
<td>70$^a$</td>
</tr>
<tr>
<td>2</td>
<td>PhCHO</td>
<td>syn-Diol</td>
<td>20 (24)</td>
</tr>
<tr>
<td>3</td>
<td>PhCHO</td>
<td>anti-Diol</td>
<td>28 (35)</td>
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<tr>
<td>4</td>
<td>PhCHO</td>
<td>syn-Diol</td>
<td>21 (30)</td>
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<tr>
<td>5</td>
<td>PhCHO</td>
<td>anti-Diol</td>
<td>25 (36)</td>
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<tr>
<td>6</td>
<td>PhCHO</td>
<td>39 (33)</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>PhCHO</td>
<td>51$^b$</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>PhCHO</td>
<td>43 (28)</td>
<td></td>
</tr>
</tbody>
</table>

$^a$ Reaction conditions: 1e$^+$ (0.3 mmol), substrate (30 mmol), tert-BuOH/H$_2$O (5:1 v/v, 12 mL), under argon, room temperature, and 30 min.

$^b$ Isolated yield, calculated as mmol of product per mmol of 1e.

$^c$ Determined by GC.
A cis-dioxo-Ru(v) species was also detected at m/z = 456.10 (Fig. S19a, ESI†), with its signal intensity remaining constant for at least 3 min (Fig. S19b†). At a higher concentration of 3c·CF$_3$SO$_3$ ($[\text{Ru}] = 1 \times 10^{-3}$ M), a complicated spectrum dominated by noise signals was obtained with just 4 equiv. of Ce$^{IV}$(ClO$_4$)$_3$. Most likely, the decomposition of Ru(pdp) complexes under oxidizing condition is significantly fast with $[\text{Ru}] \geq 1$ mM. This may account for the difficult isolation of cis-$[(\text{pdp})\text{Ru}^{IV}(O)_{2}]\text{ClO}_4$ in the large-scale preparative experiment.

**Stoichiometric oxidation of hydrocarbons by cis-$([(\text{mcp})\text{Ru}^{IV}(O)_{2}]\text{ClO}_4)_2$ (1e)**

The results of the electrochemical studies suggest that cis-$[(\text{mcp})\text{Ru}^{IV}(O)_{2}]\text{ClO}_4)_2$ (1e) is a strong oxidant ($E^o = 1.11$ V vs. SCE at pH 1). In aqueous tert-butanol, freshly prepared 1e could stoichiometrically oxidize cyclooctene to give a mixture of cis-cyclooctane-1,2-diol (27%) and 1,8-octanedialdehyde (70%) (Table 2, entry 1). Compared with our previous works, cis-$[(\text{mes})\text{Ru}^{IV}(O)_{2}(O_2\text{CF}_3)]\text{ClO}_4$ oxidized cyclooctene stoichiometrically to give cis-cyclooctane-1,2-diol and 1,8-octanedialdehyde in 85% and 5% yields, respectively, whereas use of cis-$[(\text{Tet-Me})\text{Ru}^{IV}(O)_{2}]\text{ClO}_4)_2$ gave 22% cis-cyclooctane-1,2-diol and 60% 1,8-octanedialdehyde. Alternatively, a green ruthenium compound was isolated at the end of the reaction of 1e with cyclooctene. ESI-MS analysis revealed a prominent ion peak at $m/z = 460.1$; its $m/z$ ratio and isotopic distribution pattern are consistent with a $[(\text{mcp})\text{Ru}^{III}(\text{OH})_2]^+$ formulation.

Using chiral (R,R)-mcp as a ligand, the chiral cis-dioxidiruthenium(v) complex, cis-$[(\text{R,R})\text{mcp}\text{Ru}^{IV}(O)_{2}]\text{ClO}_4)_2$ (1e*), was prepared. Several stoichiometric alkene oxidation reactions were performed by reacting 1e* (0.3 mmol) with excess alkene substrate (30 mmol, 100 equiv.) in a degassed (5 : 1 v/v) tert-butanol/H$_2$O mixture (12 mL) under argon at room temperature for 30 min (Table 2). Aryl alkenes were oxidized to their corresponding diols (39–48% yields) with ee values ranging from 24 to 36%, accompanied by the formation of C=C bond cleavage products in considerable amounts (45–53%). In the reaction of 1e* with styrene, for instance, a 42% yield of styrene glycol (27% ee) and 50% yield of benzaldehyde were obtained (entry 5, Table 2). Similarly, trans-β-(trimethylsilyl)styrene reacted with 1e* to afford a 19% yield of syn-diol (28% ee) and 26% yield of anti-diol (33% ee) along with a 53% yield of benzaldehyde (entry 4, Table 2). There is no major difference in the reactions of 1e* with trans-β-methylstyrene and with cis-β-methylstyrene, which afforded the enantio-enriched syn-diol in 20% yield (24% ee) and 21% yield (30% ee), anti-diol in 28% yield (35% ee) and 25% yield (36% ee), benzaldehyde in 45% and 52% yields, respectively (entries 2 and 3, Table 2). The effects of para-substituents on the enantioselectivity of p-substituted styrenes in the reaction with 1e* were examined (entries 5–8, Table 2); the para-substituents CH$_3$, Cl and Br had no significant effect on either the yields (39–45%) or ee (28–34%) of the diol products.

The stoichiometric oxidations of alcohols and alkanes by 1e* were studied. When 1e was treated with benzyl alcohol (100 equiv.) in acetonitrile at room temperature for 30 min, benzaldehyde was formed in 90% yield (Table 3, entry 1). Similarly, other primary alcohols such as 1-heptanol and 1-octanol were oxidized by 1e to give a mixture of aldehyde and carboxylic acid (entries 2 and 3, Table 3). Under these conditions, cyclooctene reacted with 1e to afford cyclooctene oxide and 1,8-octanediol in 30% and 58% yields, respectively (entry 4, Table 3). Complex 1e could also oxidize saturated C–H bonds. For instance, ethylbenzene (BDE$_{C-H}$ = 85.4 kcal mol$^{-1}$) was oxidized by 1e to benzaldehyde in 62% yield (entry 5, Table 3). When 1e was treated with benzyl alcohol (100 equiv.) in acetonitrile at room temperature for 30 min, benzaldehyde was formed in 90% yield (Table 3, entry 1). Similarly, other primary alcohols such as 1-heptanol and 1-octanol were oxidized by 1e to give a mixture of aldehyde and carboxylic acid (entries 2 and 3, Table 3). Under these conditions, cyclooctene reacted with 1e to afford cyclooctene oxide and 1,8-octanediol in 30% and 58% yields, respectively (entry 4, Table 3). Complex 1e could also oxidize saturated C–H bonds. For instance, ethylbenzene (BDE$_{C-H}$ = 85.4 kcal mol$^{-1}$) was oxidized by 1e to benzaldehyde in 62% yield (entry 5, Table 3).
oxidized by 1e in acetonitrile to give acetonophene (55% yield) and 1-phenylethanol (26% yield) (entry 5, Table 3). Notably, cyclohexane (BD<sub>Δ</sub>-H = 99.5 kcal mol<sup>-1</sup>)<sup>6</sup> was oxidized to give cyclohexanone in 62% yield (entry 6, Table 3). Similar to the reported cis-dioxoruthenium(vi) complexes,<sup>14a,15a</sup> when adamantane was employed as a substrate, C–H oxidation occurred primarily at the 3<sup>°</sup> carbon; 1-adamantanone was formed as the sole product in 58% yield (entry 7, Table 3). The oxidation of cis-4-methylcyclohexyl benzoate afforded the tertiary alcohol product revealed no kinetic resolution effect (<2%). These organic transformations were accompanied by the production of cis-1,2-Dimethylcyclohexane (S1) as a byproducts (entry 8, Table 3). Reaction of 1e<sup>+</sup> with the two racemic substrates in entries 9 and 10 (Table 3) predominantly gave oxygenated products at the tertiary C–H bonds; however, chiral HPLC analysis of the tertiary alcohol product revealed no kinetic resolution effect (ee <2%). These organic transformations were accompanied by the reduction of cis-dioxoruthenium(vi) to cis-[Ru<sup>II</sup>(NCH<sub>3</sub>)<sub>2</sub>(ClO<sub>4</sub>)<sub>2</sub>] (1d), which was isolated and characterized (ESI′).<sup>†</sup>

**Catalytic oxidation of alkanes with CAN mediated by cis-[{pdp}<br>Ru<sup>III</sup>(OH<sub>2</sub>)<sub>6</sub>]<sup>−</sup> (3c)**

The catalytic activities of the cis-[{mcp}Ru<sup>III</sup>[O<sub>2</sub>CCF<sub>3</sub>]<sub>2</sub>]<sup>−</sup> (1b) and cis-diaquiruthenium(ii) complexes (3c–6c) towards the hydroxylation of C(sp<sup>3</sup>)–H bonds were examined using CAN as a terminal oxidant. cis-1,2-Dimethylcyclohexane (S1) was chosen as an initial test substrate (Table 4). The reaction of S1 with 2 mol% 3c-OTs and 3 equiv. of CAN for 15 min at room temperature in aqueous tert-butanol afforded a tertiary alcohol product (P1) in 64% yield based on 80% conversion (entry 2, Table 4).<sup>49</sup> The stereogenic centres are retained in the alcohol product, indicating that the hydroxylation reaction does not involve long-lived carbon-based radicals that can epimerize. Among the screened ruthenium catalysts, 3c-OTs showed the highest catalytic activity. When 4c-OTs or 6c-OTs was employed as the catalyst, particularly, the substrate conversion was <10% (entries 3 and 5, Table 4).<sup>49</sup> Therefore, subsequent studies focused on the use of 3c-OTs as a catalyst. In a control experiment, in which the ruthenium catalyst was replaced by [Ru<sup>III</sup>(OH<sub>2</sub>)<sub>6</sub>][OTs]<sub>2</sub>, S1 remained intact for a 30 min reaction (Table 5, entry 2). Subsequent addition of 3c-OTs to this reaction mixture followed by stirring for 15 min afforded P1 in 64% yield based on 61% conversion.

Oxidation of methylcyclohexane (S2) gave a tertiary alcohol product (P2) with high selectivity (96%) based on 52% conversion (Table 5, entry 3). Similarly, S3 was oxidized to P3 with good selectivity (entry 4, Table 5). For the oxidation of adamantanone (S4), apart from ordinary oxygenated products, such as Ad-1-ol (P4a, 47% yield) and “Ad-2-ol + Ad-2’-one” (P4b, 3% yield), adamantan-1,3-diol (P4c) was also formed in 32% yield (entry 5, Table 5). Most likely, the initial hydroxylation of S4 gives P4a; the latter, being more soluble, was efficiently further hydroxylated to yield P4c.<sup>24</sup> The normalized 3º/2º selectivity is as high as 79 : 1, showing the strong preference of the active oxidant to attack 3º over 2º C–H bonds. Following this preference, the oxidation of racemic S5 produced P5 in 48% isolated yield (entry 6, Table 5).<sup>22</sup> Compound S6 has two possible sites (C3 and C7) for tertiary C–H hydroxylation. Analysis of the crude reaction mixture by 1H NMR spectroscopy revealed the C7 : C3 selectivity to be a ratio of >10 : 1. After purification, a C7-hydroxylated product (P6) was obtained in 80% yield (entry 7, Table 5). Reactions of S7 and S8 similarly occurred at the 3º C–H bond which were remote from the electron-withdrawing ester/amide group.

### Table 5 Oxidation of tertiary and benzylic C–H bonds with CAN catalysed by 3c-OTs<sup>a</sup>

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Reaction time</th>
<th>Conversion (%)</th>
<th>Products (yield in % based on conversion)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>S1</td>
<td>15 min</td>
<td>80</td>
<td>P1 (64)</td>
</tr>
<tr>
<td>2b</td>
<td>S1</td>
<td>30 min</td>
<td>&lt;1</td>
<td>—</td>
</tr>
<tr>
<td>3c</td>
<td>S2</td>
<td>45 min</td>
<td>51</td>
<td>P2 (96)</td>
</tr>
<tr>
<td>4d</td>
<td>S3</td>
<td>1 h</td>
<td>52</td>
<td>P3 (84)</td>
</tr>
<tr>
<td>5e</td>
<td>S4</td>
<td>1.5 h</td>
<td>74</td>
<td>P4a (47), P4b (3), P4c (32)</td>
</tr>
<tr>
<td>6d</td>
<td>S5</td>
<td>1 h</td>
<td>59</td>
<td>P5 (83)</td>
</tr>
<tr>
<td>7</td>
<td>S6</td>
<td>1.5 h</td>
<td>40</td>
<td>P6 (88)</td>
</tr>
<tr>
<td>8</td>
<td>S7</td>
<td>1 h</td>
<td>60</td>
<td>P7 (85)</td>
</tr>
<tr>
<td>9</td>
<td>S8</td>
<td>1 h</td>
<td>65</td>
<td>P8 (89)</td>
</tr>
<tr>
<td>10</td>
<td>S9</td>
<td>15 min</td>
<td>28</td>
<td>P9 (91)</td>
</tr>
<tr>
<td>11</td>
<td>S10</td>
<td>40 min</td>
<td>84</td>
<td>P10 (89)</td>
</tr>
</tbody>
</table>

<sup>a</sup> Reaction conditions: substrate (0.25 mmol), catalyst (2 mol%), CAN (0.75 mmol), Bu<sub>4</sub>NH/H<sub>2</sub>O (1 : 1 v/v, 4 mL), and room temperature. <sup>b</sup> [Ru<sup>III</sup>(OH<sub>2</sub>)<sub>6</sub>][OTs]<sub>2</sub> was used as the catalyst. <sup>c</sup> Bu<sub>4</sub>NH/H<sub>2</sub>O (3 : 1 v/v, 4 mL) was used as the solvent. <sup>d</sup> CF<sub>3</sub>CH<sub>2</sub>OH/H<sub>2</sub>O (3 : 1 v/v, 4 mL) was used as the solvent. <sup>e</sup> 1.5 mmol CAN was used.
acetone with a TON of 9 (entry 2, Table 7). The reaction of 2-propanol with CAN catalysed by 3c·OTs afforded acetic acid with a TON = 3 (entry 4, Table 7). 

Table 6 Oxidation of pharmaceutical ingredients and natural product derivatives with CAN catalysed by 3c·OTs

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Reaction time (h)</th>
<th>Conversion (%)</th>
<th>Products (yield in % based on conversion)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>S11</td>
<td>40 min</td>
<td>50</td>
<td>P11 (84)</td>
</tr>
<tr>
<td>2</td>
<td>S12</td>
<td>40 min</td>
<td>82</td>
<td>P12 (93)</td>
</tr>
<tr>
<td>3</td>
<td>S13</td>
<td>20 min</td>
<td>68</td>
<td>P13 (55)</td>
</tr>
<tr>
<td>4</td>
<td>S14</td>
<td>13 h</td>
<td>73</td>
<td>P14 (78)</td>
</tr>
</tbody>
</table>

a Reaction conditions: substrate (0.2 mmol), catalyst (5 mol%), CAN (1.2 mmol), BuOH/H2O (1 : 1 v/v, 4 mL), and room temperature.

Lastly, oxidation of ethane (BDEC-H = 100.5 kcal mol⁻¹) afforded acetic acid with a TON = 3 (entry 4, Table 7).

General remarks/discussion

General properties of the ruthenium N₄ complexes

Two series of ruthenium complexes, cis-[[N₄]Ru₄HCl₂]⁺ (1a–4a) and cis-[[N₄]Ru₄(μ-OH)₂]²⁺ (3c–6c), were prepared. Owing to the lability of aqua ligands, [Ru⁴(H₂O)₆][OTs]₂ is an efficient precursor for the synthesis of cis-[[N₄]Ru₄(μ-OH)₂]²⁺ complexes (3c–6c). The cis-diaquoruuthenium(II) complexes were isolated as ditosylate (OTs⁻) salts and are air sensitive. In aqueous solutions under aerobic conditions, they are susceptible to oxidation, as determined by the depletion of the characteristic MLCT transition band at 360–480 nm. Accompanying the UV-Vis spectral changes, the predominant species observed in ESI-MS analysis changed from [[N₄]Ru⁴(μ-OH)₄]⁻ to [[N₄]Ru⁴(μ-OH)₂]²⁻. Complexes without ortho-methyl substituents on the pyridyl/quinolyl moieties (3c and 5c) are less prone to aerobic oxidation; the process requires hours to complete. In contrast, complexes 4c and 6c are readily oxidized to Ru(m) species within 1 h.

The structural analyses of the cis-[[N₄]Ru₄HCl₂]⁺ complexes by X-ray crystallography show that the cis-alla configuration is the predominantly preferred geometry. ¹H NMR spectroscopy of the cis-[[N₄]Ru⁴(μ-OH)₂]²⁺ complexes in CD₂CN or the bis(acetonitrile)ruthenium(II) complex revealed that the coordination geometry depends on the ligand structure. In particular, the bqcn ligand coordinates to the ruthenium centre in an unselective manner affording a mixture of cis-alla and cis-β isomers, which do not interconvert in acetonitrile solution. In the X-ray crystal structures of cis-alla-5d and cis-β-5d, the N-methyl groups have different orientations (anti or syn). Thus, interconversion between the two isomers requires (i) breakage of the Ru-
N(quinolyl) bond, (ii) breakage of the Ru–N(amine) bond, and (iii) epimerization of the N-methyl group followed by migration of the acetonitrile ligand. These are expected to have large kinetic barriers, therefore, interconversion between the two isomeric forms is slow, and the ligand topology is likely determined at the synthetic stage of 5c-OTs. Similar arguments have been addressed by Nam, Shin and co-workers; they found that cis-$\alpha$ or cis-$\beta$-[(bqcn)Fe$^2$(NCMe)$_2$]$_2$ could be independently obtained with different synthetic methods and that these isomers do not interconvert in solution at room temperature.\textsuperscript{77}

### Electrochemistry/reduction potentials

Aqueous electrochemical measurements (at pH 1) of cis-[(mpc)Ru$^{	ext{III}}$(O$_2$CF$_3$)$_2$]ClO$_4$ (1b) and cis-[(dpdp)Ru$^{	ext{III}}$(O$_2$SCF$_3$)$_2$]CF$_3$SO$_3$ (3e) revealed the strong oxidizing powers of their corresponding cis-dioxoruthenium($\nu$) species. The highly anodic redox potentials ($E^\circ = 1.11–1.13$ V vs. SCE) are comparable to those of cis-[(6,6'-Cl$_2$ppy)Ru$^{	ext{V}}$(O)]$^{2+}$ (1.17 V)$^{58}$ and electrochemically generated cis-[(TPA)Ru$^{	ext{VI}}$(O)$_2$]$^{2+}$ (1.1 V, TPA = tris(2-pyridyldimethyl)amine).\textsuperscript{42}

The aqueous electrochemical data allow the determination of the hydrogen-atom affinity of the cis-dioxoruthenium($\nu$) complexes. The $D_{\text{H}}$ values are calculated to be 90.8 kcal mol$^{-1}$ for cis-[(dpdp)Ru$^{	ext{III}}$(O$_2$SCF$_3$)$_2$]$^{2+}$ and 90.1 kcal mol$^{-1}$ for cis-[(mpc)Ru$^{	ext{III}}$(O)$_2$]$^{2+}$. Referring to Table 8, these values are comparable to those of cis-[(bpy)Ru$^{	ext{V}}$(O)$_2$]$^{2+}$ (93.5 kcal mol$^{-1}$)$^{17}$ and [(TSMP)Fe$^{	ext{V}}$(O)] (90 kcal mol$^{-1}$, $E_{1/2}$ = 0.76 V, pH 4.1, for example, the potential of the redox couple 

$$\text{Fe}^{	ext{IV}}(\text{OH})_2^+ + 2\text{e}^- + 2\text{H}^+ \rightarrow \text{Fe}^{	ext{IV}}(\text{OH})_2^+$$

at 0.76 V.

### Reactivity of cis-dioxoruthenium($\nu$)

The results presented in this work show the strong oxidizing power of cis-dioxoruthenium($\nu$) complexes containing chiral $N_4$ ligands by electrochemical analysis and their reactivity with hydrocarbons. Although several cis-dioxoruthenium($\nu$) complexes are known,\textsuperscript{16a,15a,16c,17} chiral ones have not been reported in the literature to the best of our knowledge. In this work, we isolated and spectroscopically characterized the chiral complex cis-[(R,R)-mcp]Ru$^{	ext{VI}}$(O)$_2$][ClO$_4$]$_2$ (1e$^*$). Complex 1e$^*$ could exhibit the stoichiometric oxidations of alcohols, alkanes and alkenes, as was found for other cis-dioxoruthenium($\nu$) complexes. In the reaction of 1e$^*$ with alkenes, considerable amounts of dihydroxylation products were obtained with moderate enantioselectivities ($\sim$30% ee, Table 2), albeit with the predominant products being C=C bond cleavage ones, such as carbonyl compounds. In addition, a mixture of syn- and anti-diols was obtained, which possibly indicates the nonconcerted nature of the dihydroxylation reaction.\textsuperscript{72,73}

### Table 8 Hydrogen-atom affinity of selected metal–oxo complexes

<table>
<thead>
<tr>
<th>Complex</th>
<th>$D_{\text{H}}$ (kcal mol$^{-1}$)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>cis-[(bpy)Ru$^{	ext{V}}$(O)$_2$]$^{2+}$</td>
<td>93.5$^a$</td>
<td>17</td>
</tr>
<tr>
<td>cis-[(dpdp)Ru$^{	ext{V}}$(O)$_2$]$^{2+}$</td>
<td>90.8</td>
<td>This work</td>
</tr>
<tr>
<td>cis-[(mpc)Ru$^{	ext{V}}$(O)$_2$]$^{2+}$</td>
<td>90.1</td>
<td>This work</td>
</tr>
<tr>
<td>[(TSMP)Fe$^{	ext{V}}$(O)]</td>
<td>90</td>
<td>59, 60</td>
</tr>
<tr>
<td>cis-[(Me$_2$tnac)Ru$^{	ext{V}}$(O)$_2$(OCCF$_3$)$_2$]$^{2+}$</td>
<td>87.5$^a$</td>
<td>65</td>
</tr>
<tr>
<td>[(N4Py)Ru$^{	ext{V}}$(O)(OH)$_2$]$^{2+}$</td>
<td>84.8</td>
<td>62</td>
</tr>
<tr>
<td>cis-[(pdp)Ru$^{	ext{V}}$(O)$_2$]$^{2+}$</td>
<td>84</td>
<td>61</td>
</tr>
<tr>
<td>trans-[(N$_2$O$_2$)Ru$^{	ext{V}}$(O)$_2$]$^{2+}$</td>
<td>82.8</td>
<td>63</td>
</tr>
<tr>
<td>[(TPA)Ru$^{	ext{VI}}$(O)(OH)$_2$]$^{2+}$</td>
<td>82.7</td>
<td>62</td>
</tr>
<tr>
<td>[(Me$_2$BEC)Mn$^{	ext{II}}$(O)(OH)]$^+$</td>
<td>84.3</td>
<td>66, 67</td>
</tr>
<tr>
<td>Mn$^{	ext{IV}}$(O)</td>
<td>80</td>
<td>68</td>
</tr>
<tr>
<td>[(phen)Mn$^{	ext{IV}}$(μ-O)Mn$^{	ext{III}}$(phen)$_2$]$^{2+}$</td>
<td>79</td>
<td>69</td>
</tr>
<tr>
<td>trans-[(14-TMC)Ru$^{	ext{VI}}$(O)$_2$]$^{2+}$</td>
<td>76.3</td>
<td>64</td>
</tr>
</tbody>
</table>

$^a$ Calculated from the reported electrochemical data.
scission of aryl alkenes to carbonyl compounds (Table S5, ESI†, 6 examples). At a catalyst loading of 1 mol%, aryl C=C bonds are cleaved to aldehydes or ketones in high conversions (83–100%) and high yields (89–100%).[24] Over-oxidation of aldehydes to carboxylic acids was not observed by controlling the stoichiometry of NaIO4 (10% excess). The timespan of the reaction (1 h) is comparable to that (30 min) reported by Bera and co-workers using an abnormal-NHC–Ru(II) catalyst.[75]

Using cis-[(mpc)RuIIICl3]2ClO4 (1b) as a catalyst and H2O2 as a terminal oxidant, we also developed a catalytic protocol for the oxidation of alcohols (Table S6, ESI†, 14 examples). Alcoholic substrates were effectively oxidized to carbonyl compounds or carboxylic acids in yields up to 98% [see the ESI† for a more detailed description]. ESI-MS analysis of a mixture of 1b and H2O2 did not reveal formation of 1e or other high-valent ruthenium–oxo complexes. The active intermediate could be hydroperoxy- or peroxo-Ru(III) species, which has yet to be clarified.

Reports on the oxidation of alkane catalysed by ligand-supported ruthenium complexes are sparse in the literature.[76] In 2010, Du Bois and co-workers developed a RuCl3/pyridine/KBrO3 protocol for the hydroxylation of various substituted alkane substrates;[77] in 2012, they improved the yield and allowed a lower catalyst loading by employing [Me3tacn]RuIII[O2CCF3]ClO4 as a catalyst in combination with AgClO4 as an additive and CAN as a terminal oxidant.[28] Using desorption electrospray ionization mass spectrometry (DESI-MS), cis-[[Me3tacn]RuVI(O)2(O2CCF3)]2+ was identified as a plausible reactive hydroxylation agent, but the possible involvement of Ru(II) and/or Ru(III) species could not be discounted.[78] In this work, stoichiometric reactions between 1e and several alkane substrates (Table 3) provided direct evidence that cis-dioxoruthenium(IV) preferentially oxidizes the tertiary C–H bonds in hydrocarbons. The same selectivity was observed in catalytic experiments. Aqueous electrochemical and ESI-MS experiments showed that cis-[[dpdp]RuIV(O2CCF3)]2+ is accessible via the successive oxidative deprotonation of a low-valent precursor, such as 1c or 1c’. The D0–H values of cis-[[Me3tacn]RuIV(OR)2(O2CCF3)]2+ and cis-[[dpdp]RuIV(O2CCF3)]2+ are calculated to be 87.5 and 98.8 kcal mol−1, respectively [vide supra]. We anticipate that the Ru(dpdp) complex, with an additional driving force of 3.3 kcal mol−1, would be as reactive as the Ru(Me3tacn) complex in alkane oxidation reactions. Additionally, the use of a chiral N4 supporting ligand might incorporate chirality into the oxygenated products.[28–31] A catalytic system for the oxidation of alkynes by cis-[[dpdp]RuIV(OH2)2]2+ (3e) with CAN is herein reported. Compared to the [Me3tacn]RuIVCl2/AgClO4/CAN system, our system avoids the use of a Ag+ salt as a chloride scavenger, and the C–H oxidative process was decomposed almost completely. A likely deactivation pathway of the catalyst is the oxidation of the ligand by the strongly oxidizing Ru–oxo intermediate. Indeed, it was noted that complexes 4e and 6e showed much poorer activities than 3e and 5e (Tables 4 and S4, ESI†), presumably due to the intramolecular oxidation of the ortho-Me group by the Ru–oxo moiety.[28] Although our recent work on the Fe(N4)-catalysed AD reaction showed that installation of an ortho-Me group could substantially improve the catalyst activity (particularly the enantioselectivity),[28] this strategy cannot be directly transferred to the ruthenium chemistry. For the Fe((R,R)-Me)2bqcn)-catalysed AD reaction, the active intermediate was proposed to be [[(R,R)-Me2bqcn]FeIV(OOH)]2+ rather than dioxorhodium(IV).[29] From ESI-MS experiments, it was also demonstrated that the decomposition of Ru(dpdp) complexes under oxidizing condition is considerably fast when [Ru] ≥ 1 mM. Thus, a delicate balance between the oxidizing power and stability of the active intermediate is yet to be achieved for efficient ruthenium-catalysed C–H oxidation. Moreover, either stoichiometrically or catalytically, the studied chiral ruthenium complexes (1e, 3c–6c) did not show noticeable enantioselectivity in reactions with racemic tertiary alkane substrates (e.g., entries 9, 10, Table 3; entry 6, Table 5). This suggests, without any directing group,[30] there is

S1 to P1 in Table 5, S11 to P11 in Table 6), which is a fundamentally defining feature in C–H functionalization rendering this method of synthetic value. When the substrate contains multiple tertiary C–H bonds (S8–S10, Table 5), hydroxylation preferentially occurs at the most electron-rich site, as was also observed in other Fe/Mn-catalysed C–H hydroxylation systems (e.g., cis-[[dpdp]FeIV(CNCMe3)2]2+/H2O2/AcOH).[28,32] This similar reactivity pattern implies the common electrophilic nature of cis-dioxoruthenium(IV) and the active oxidant in Fe(dpdp)-catalysed reactions. In literature, the identity of the latter was investigated by multiple research groups which has led to different formulations.[28,32–34] Talsi, Bilyiakov and co-workers identified an S = 1/2 species by EPR and assigned it to [[dpdp]FeV(O)(OAc)]2+. Based on computational results, Wang, Que, Shaik and co-workers suggested a cyclic Fe(III) peracetae complex that undergoes O–O bond cleavage to a transient oxirorh(IV)–AcO′ species which performs efficient C–H hydroxylations.[7] We also demonstrated the strong oxidizing power of this catalytic system in the reaction with propane and ethane (Table 7). Although the turnover numbers are not impressive, identification of appreciable amounts of the various oxidation products is significant, as light alkanes often exhibit resistance to functionalization. To the best of our knowledge, this represents a rare example of ruthenium-catalysed/mediated oxidation of light alkanes (<C4), except Drago’s reported work on the cis-[[dpdp]RuIV(S)2]2+ (S = MeCN or H2O)-catalysed hydroxylation of methane with H2O2.[80] Some issues remain to be resolved/explored that are worth being addressed. First, the stability/robustness of the highly oxidizing cis-dioxoruthenium(IV) species is of concern. In CAN-driven catalytic oxidation of alkanes, the turnover number based on 3c is typically less than 30. Post-reaction analysis of the mixture revealed that the catalyst had degraded/decomposed almost completely. A likely deactivation pathway of the catalyst is the oxidation of the ligand by the strongly oxidizing Ru–oxo intermediate. Indeed, it was noted that complexes 4c and 6c showed much poorer activities than 3e and 5e (Tables 4 and S4, ESI†), presumably due to the intramolecular oxidation of the ortho-Me group by the Ru–oxo moiety.[28] Although our recent work on the Fe(N4)-catalysed AD reaction showed that installation of an ortho-Me group could substantially improve the catalyst activity (particularly the enantioselectivity),[28] this strategy cannot be directly transferred to the ruthenium chemistry. For the Fe((R,R)-Me)2bqcn)-catalysed AD reaction, the active intermediate was proposed to be [[(R,R)-Me2bqcn]FeIV(OOH)]2+ rather than dioxorhodium(IV).[29] From ESI-MS experiments, it was also demonstrated that the decomposition of Ru(dpdp) complexes under oxidizing condition is considerably fast when [Ru] ≥ 1 mM. Thus, a delicate balance between the oxidizing power and stability of the active intermediate is yet to be achieved for efficient ruthenium-catalysed C–H oxidation. Moreover, either stoichiometrically or catalytically, the studied chiral ruthenium complexes (1e, 3c–6c) did not show noticeable enantioselectivity in reactions with racemic tertiary alkane substrates (e.g., entries 9, 10, Table 3; entry 6, Table 5). This suggests, without any directing group,[30] there is
not sufficient chiral differentiation between the two isomeric forms by kinetic resolution at the chiral ruthenium centre.

Conclusions

In this work, we reported the preparation and electrochemical oxidation of several ruthenium complexes bearing tetradentate N₄ ligands including cis-[(mcp)Ru(H)(O3SCF₃)₂]ClO₄ (1b) and cis-[(pdp)Ru(H)(O3SCF₃)₂]ClO₄ (3c). Complex cis-[(mcp)Ru(V)(O)₂]ClO₄ (1e) was obtained from CAN oxidation of 1b in aqueous solution. Complex 1e is a powerful oxidant with E(RuIV) = 0.78 V (vs. Ag/AgNO₃) in acetonitrile or E° = 1.11 V vs. SCE at pH 1. In aqueous tert-butanol, cis-[(R,R)-mcp]Ru(V)(O)₂]ClO₄ (1e) underwent stoichiometric alkene cis-dihydroxylation to afford cis-diol in 24% ee for trans-β-methylstyrene oxidation. With high hydrogen-atom affinities (D₀H is 90.1–90.8 kcal mol⁻¹), 1e and chemically generated cis-[(pdp)Ru(V)(O)₂]²⁺ are active oxidants for C–H oxidation. cis-[(pdp)Ru(III)(OH₂)]²⁺ (3c), in combination with CAN as a terminal oxidant, catalysed the oxidation of unactivated C–H bonds including those of some pharmaceutical ingredients and natural product derivatives. This work demonstrates that efficient oxidation catalysts can be constructed based on the cis-dioxoruthenium(vi) moiety on a N₄ ligand platform. The diversity and flexibility of chiral N₄ ligand design will direct subsequent efforts to improve the reaction selectivities. Further studies are also directed to gain a better understanding of the reaction mechanism in hydrocarbon oxidations and to explore other catalytic activities of chiral Ru(N₄) complexes.

Conflicts of interest

There are no conflicts to declare.

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Notes and references


6 Mn examples on C=C functionalization: (a) A. Murphy, G. Dubois and T. D. P. Stack, J. Am. Chem. Soc., 2003, 125, 5250; (b) T. W.-S. Chow, Y. Liu and C.-M. Che, Chem. Commun., 2011, 47, 11204; (c) O. Cussó, I. Garcia-Bosch,


28 Attempts to prepare the analogous complex [(Me2mcp)RuIII(O2CCF3)2]ClO4 (2b) by a similar protocol was unsuccessful. Treatment of 2a with Zn/Hg at 80 °C in water, followed by metathesis with AgOTf afforded a light green solution. However, the corresponding trifluoroacetato complex 2b was not isolated upon addition of NaClO4.

29 Remark: due to the small size of crystal sample (0.2 × 0.4 × 0.01 mm), the data were collected at a low resolution of 1 Å.

30 A similar scenario is also observed for 4a although the RuIII/II couple (E1/2 = −0.01 V) is quasi-reversible instead of irreversible. The oxidation of cis-[(Me2pdp)RuIIICl(NCMe)]+ to cis-[(Me2pdp)RuIIIICl(NCMe)]2+ occurs at Epa = 0.64 V.

31 The reversibility of the reduction wave of 2a in acetonitrile is partially restored at high scan rates (Fig. S10, ESIF).


34 Attempts were made to study in details the effect of pH on the redox couples of 1b over the pH range of 1–10. However, ill-defined/irreversible redox couples were recorded at pH 3 and 4 in alkaline medium.


36 In the presence of organic substrates such as ethanol or propan-2-ol (0.4–2.0 M), couple III of 3c is replaced by a large catalytic oxidative wave at ca. 1.2 V. A mild catalytic current was observed in the case of tosyl acid (0.4 M) (Fig. S13, ESIF).

37 Couples II and III, having a potential difference of <200 mV at pH 1, are not well-separated in rotating-disk electrode voltammetric measurement.

38 The return wave of couple III of 3c·OTs is less reversible, attributed to the oxidation of the benzylc C–H bonds in the tosylate anion (OTs−) by the electrochemically generated high-valent cis-dioxoruthenium(Ⅴ) species. See also ref. 36.

39 Well-defined redox couples have not been observed for 4c·OTs.


45 D0-H is the bond dissociation free energy of the O–H bond of [MeOH]−, E0 is the standard 1e− reduction potential of...
(M_{ox} = O)/(M_{red} = O^-) couple, pK_a is the acid dissociation constant of [M_{ox} = OH], and C is a constant of 63.1 kcal mol^{-1} (foraq. solution with E' vs. SCE).

No change in product yields or product distribution was observed when the reaction was conducted under air.


48 The remaining mass balance is ascribed to the formation of secondary C–H oxidation products such as 2,3-dimethylcyclohexanone and 3,4-dimethylcyclohexanone where the yields were estimated to be 20–30% by GC analysis.

49 We examined a reaction mixture of 4c-OTs (0.1 mM) and CAN (10 equiv.) in water and observed a new species at m/z 483.2, attributable to an intramolecularly oxidized Ru(Me_2pdp) species (see Fig. S20, ESI† for details).

50 In a control experiment where the substrate (adamantane) was replaced by adamant-1-ol (P4a), P4c was formed in 79% yield based on 83% conversion. A yet to be confirmed highly polar side product was also obtained in ca. 15%. This side product has a m/z value of 184 in GC-MS analysis and is likely adamantan-1,3,5-triol.

51 As was found in stoichiometric oxidation by 1e*, no kinetic resolution effect was observed by chiral HPLC analysis (ee < 1%).


54 Attempts to extend the substrate scope to more complex hydrocarbon artemisinin only afforded small amount of oxygenated products based on <5% conversion.

55 In these reactions, the corresponding alcohol product could not be detected.


65 Alkyl alkenes preferentially undergo epoxidation instead of C–C oxidative scission by the “1b + NaIO_4” protocol. For example, reaction of cis-cyclooctene oxide gave 95% cis-cyclooctene oxide based on 100% conversion.


70 During the course of our study, Du Bois, Sigman, and co-workers recently reported a bis(bipyridine)Ru-catalysed process where cis-[Ru^{II}(ligand)]_2Cl_2 could be directly used as catalyst without Ag^+ pre-treatment (see ref. 21).