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Ru-catalysed oxidative cyclisation of 1,5-dienes: an unprecedented role for the co-oxidant†

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The Ru-mediated oxidative cyclisation of 1,5-dienes to furnish 2,5-dihydroxyalkyl-substituted tetrahydrofuran-diols (THF-diols) represents a practical approach for the synthesis of many bioactive natural products. In the current study, we reported profound findings obtained by density functional theory (DFT) simulations, and they were consistent with the experimental conditions. The results set out a catalytic cycle within intermediacy of NaO_4 -complexed Ru(vi) species. Importantly, the co-oxidant played a critical role in the cyclisation step and subsequently the release of THF-diols. Following the formation of Ru(vi) glycolate, cyclisation and THF-diol release proceeded through NaO_4 -coordinated Ru(vi) intermediates, outpacing the Ru(viii) glycolate or THF-diolate intermediates and subsequently entering "second cycle" type pathways. The results indicated a cycle involving Ru(viii)/Ru(vi)/Ru(iv)/Ru(vi) rather than Ru(viii)/Ru(vi)/Ru(viii)/Ru(vi)/Ru(viii). Additionally, the existence of an electron-withdrawing group (EWG) on one of the double bonds of 1,5-dienes revealed that the regioselectivity of the Ru-catalysed oxidative cyclisation was predominantly initiated at the electron-rich alkene. Overall, this study offers new insights, which were ignored by earlier experimentalists and theoreticians, into the Ru-catalysed functionalizations of alkenes and 1,5-dienes.

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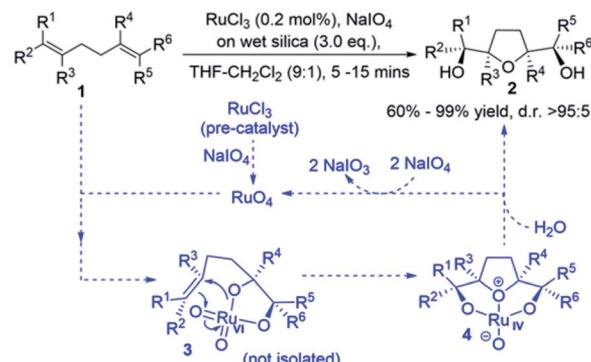
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Introduction

Many bioactive natural products such as polyether ionophore antibiotics and annonaceous acetogenins contain THF-diols.^{1,2} An important approach for the synthesis of THF-diols is the oxidative cyclisation of 1,5-dienes using transition-metal-oxo species (MnO_4^- , OsO_4 , and RuO_4). This approach has been shown to give structurally complex products,³ whereby up to four stereogenic centres can be formed with the control of relative stereochemistry in a single reaction.^{3–8} The synthesis of *cis*-THF-diols by the oxidative cyclisation of 1,5-dienes was first reported using potassium permanganate,⁹ which was followed by related stereoselective approaches using osmium and ruthenium.^{10,11} The first mechanistic proposal was set out for the permanganate-promoted reaction by Walba *et al.* and was based on the (2 + 2) suprafacial additions of metal-oxo species across the olefin double bonds. Baldwin proposed an alternative mechanism for Mn oxidative cyclisations based on (3 + 2) cycloadditions,^{6c,9a,12,13} which has become a general framework for oxidative cyclisations by Os and Ru-oxo species,^{3,10,11} and the Ru-catalysed version is the concern of this paper.¹⁴

Previous studies on the RuO_4 oxidative cyclisation of 1,5-dienes have reported mixtures of *cis* and *trans* THF-diol products.^{11a} However, developments by Stark *et al.* led to *cis*-THF diols with high yields and stereoselectivities (Scheme 1).^{5b,11b,11d} They suggested a mechanism analogous to the one presented by Baldwin.^{9a} It is basically believed that RuO_4 interacts with a double bond to form Ru(vi) glycolate 3, followed by cyclisation to give THF-diolate Ru(iv) 4 and subsequent hydrolysis to afford *cis*-THF-diol 2 (Scheme 1).

Mechanistic computational studies on the oxidative cyclisation of 1,5-dienes by metal-oxo species have been reported, but studies concerning Ru-mediated reactions have not been fully



Scheme 1 Ru-mediated oxidative cyclisation of 1,5-diene 1 to afford *cis*-THF-diol 2.

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† Electronic supplementary information (ESI) available: Additional calculated reaction pathways, cartesian coordinates, absolute energies for reported structures. See DOI: [10.1039/d0ra02303e](https://doi.org/10.1039/d0ra02303e)



investigated.^{13,15} Despite the reliable use of the reaction in the synthetic methods,^{11,14} only one step of the catalytic cycle, which is alkene oxidation to yield Ru(vi) dioxoglycolate, has been studied computationally.¹⁶ The mechanism of Ru-catalysed oxidative cyclisation involves several steps. These steps are as follows:

- alkene oxidation to generate Ru(vi) glycolate (the first reaction step, FRS);¹⁶
- cyclisation to form the Ru(iv) THF-diolate (the second reaction step, SRS);
- possible secondary reactions that may occur prior to cyclisation such as reoxidation, complexation with a co-oxidant, and hydration with water;
- hydrolysis to release the THF-diol; and
- other intermolecular (3 + 2) cycloaddition pathways that propagate the catalytic cycle (Fig. 1).

In this context, almost no details of the mechanism's steps have appeared in the literature. This lack of mechanistic understanding frequently impedes further improvements in the catalytic studies. Therefore, the present study reports a detailed description of these steps, which were ignored by previous researchers, both experimentalists and theoreticians, using computational investigations. Based on the results, we proposed a catalytic cycle and determined the important role of the co-oxidant in the Ru-catalysed oxidative cyclisation of 1,5-dienes. Subsequently, the regioselectivity of the reaction was evaluated when an EWG was found on one of the double bonds of 1,5-dienes.

Results and discussion

The computational approach to the oxidative cyclisation of 1,5-diene was performed using DFT simulations with the (SMD/THF)-M06/aug-cc-pVDZ/LANL2DZ/M06/cc-pVDZ/LANL2DZ level of theory at 298.15 K.¹⁷ All calculations considered here account for singlet spin multiplicity.¹⁸ The following sections explain the mechanism of Ru-catalysed oxidative cyclisation and the regioselectivity of the reaction.

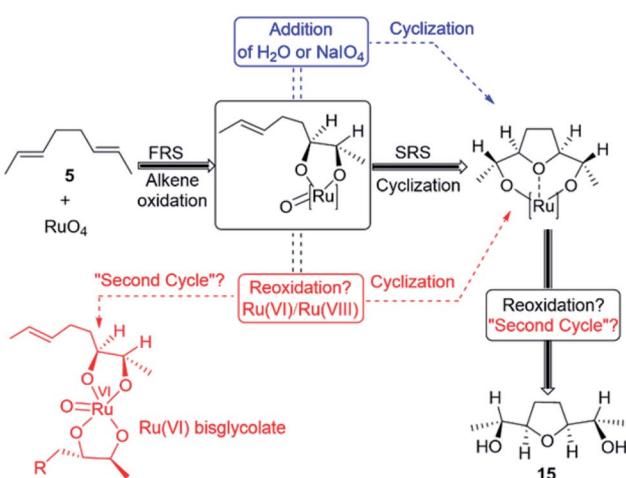


Fig. 1 Pathways obtained for the Ru-catalysed oxidative cyclisation of 1,5-diene (5) in this study.

Mechanism of Ru-catalysed oxidative cyclisation

The formation of THF-diolate from the oxidative cyclisation of 1,5-diene (5) has been realised through different reaction manifolds considered for SRS after the formation of the Ru(vi) dioxoglycolate intermediate 7 (Fig. 2). Generally, these manifolds either proceed without or with a co-oxidant (NaIO_4).

Oxidative cyclisation without a co-oxidant. The simplest pathway to form THF-diolate 9 was estimated without considering a co-oxidant (Fig. 2). Initially, the reaction of RuO_4 with the double bond of 1,5-diene (5) needed a remarkably low barrier of only 3.2 kcal mol⁻¹ through a tetrahedral (3 + 2) cycloaddition TS 6 to give a distorted tetrahedral Ru(vi) ruthenate ester 7 via a highly exergonic step ($\Delta G_r = -58.2$ kcal mol⁻¹).^{19,20} Without any additive, this intermediate dynamically cyclised to the square planar Ru(iv) diolate 9 ($\Delta G_r = -96.0$ kcal mol⁻¹).

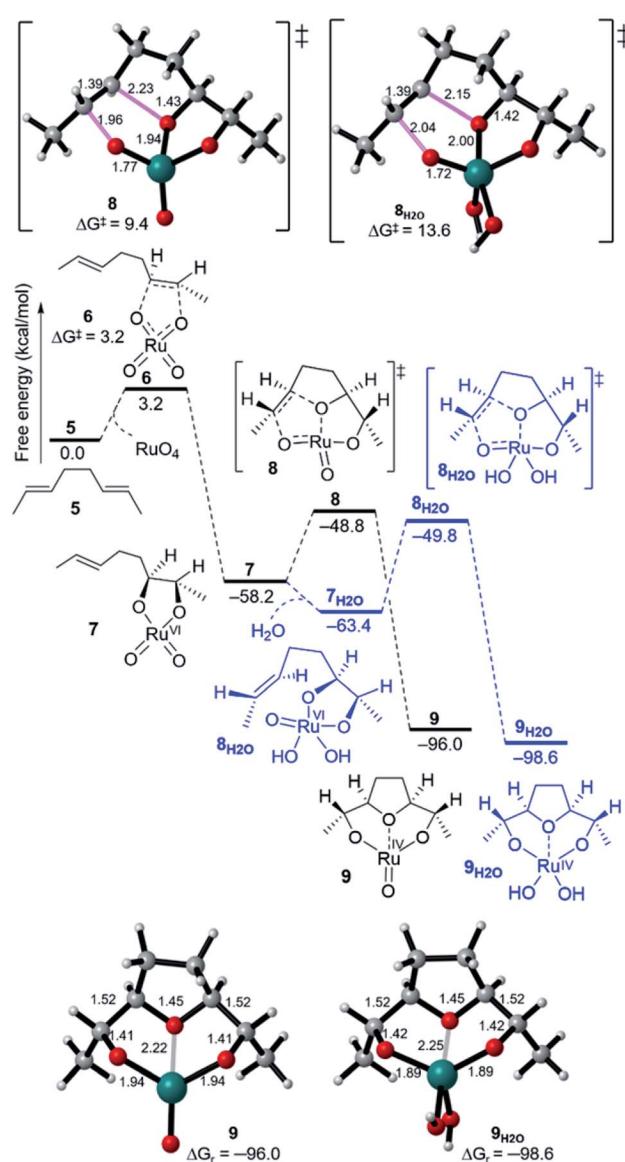


Fig. 2 Free energy profiles for the oxidative cyclisation of 1,5-diene 5 by RuO_4 , showing cyclisation pathways without water ($7 \rightarrow 9$) and with water ($7_{\text{H}_2\text{O}} \rightarrow 9_{\text{H}_2\text{O}}$).



–37.8 kcal mol^{–1}) through a tetrahedral (3 + 2) cycloaddition TS **8** with a barrier of 9.4 kcal mol^{–1}.^{21–23} Other possible pathways from Ru(vi) **7** are the addition of water (blue pathway, Fig. 2) and NaIO₄ or reoxidation (Fig. 3).

The addition of a water molecule stabilized Ru(vi) **7** by 5.2 kcal mol^{–1} to give a distorted square pyramid Ru(vi) glycolate **7**_{H2O} (Fig. 2, blue pathway). However, this raised the barrier of cyclisation to 13.6 kcal mol^{–1} via a distorted trigonal bipyramidal (3 + 2) cycloaddition TS **8**_{H2O} to form the trigonal bipyramidal Ru(iv) diolate **9**_{H2O} ($\Delta G_r = -35.2$ kcal mol^{–1}). The increased energy barrier can be understood by the effect of the decrease in the electrophilicity of the hydrated Ru(vi) glycolate **7**_{H2O} (see Fig. 4). The LUMO energy of **7**_{H2O} (LUMO = –3.7 eV, $E_{\text{gap}} = 3.1$ eV) has been calculated to be higher than that of the non-hydrated Ru(vi) **7** (LUMO = –4.2 eV, $E_{\text{gap}} = 2.6$ eV). The HOMO and LUMO orbitals are shown in Fig. 4.

Oxidative cyclisation with a co-oxidant. Now, the addition of NaIO₄ to Ru(vi) **7** forms the NaIO₄-complexed Ru(vi) glycolate **7**_{NaIO4}, which is either cyclised or reoxidized, Ru(vi) \rightarrow Ru(viii) (see Fig. 3). The effect of reoxidation Ru(vi) \rightarrow Ru(viii) on oxidative cyclisation was considered first through oxo-ligand transfer from NaIO₄ to Ru(vi) dioxoglycolate (right, Fig. 3). The TS of reoxidation was investigated as two elementary steps, which are NaIO₄-Ru(vi) complexation and oxo-transfer dissociation, and in an inner sphere manner.^{24,25} The formation of NaIO₄-complexed Ru(vi) **7**_{NaIO4} was exergonic by 6.3 kcal mol^{–1} and preceded the dissociation of the I–O bond to release Ru(viii) trioxoglycolate and NaIO₃ with a high energy barrier of 39.5 kcal mol^{–1} via TS **10** as an endergonic step ($\Delta G_r = 16.0$ kcal mol^{–1}). Although the barrier of reoxidation is

unfavourable, it was found that once **7**_[ox] was formed, Ru(vi) THF-diolate **9**_[ox] was directly generated through a barrierless and thermodynamic sink step (TS **8**_[ox], $\Delta G^\ddagger = 0.5$ and $\Delta G_r = -64.5$ kcal mol^{–1}).

A comparison between Ru(viii), hydrated Ru(vi), and naked Ru(vi) cyclisation is clearly evident. The Ru(vi) glycolates **7** and **7**_{H2O} have two d electrons, and these can lead to electronic repulsions with the two oxo ligands.²⁶ Consequently, this will decrease the electrophilicity and increase the cyclisation barrier. In contrast, this does not occur in **7**_[ox] and thus, a remarkable increase in the electrophilicity (LUMO = –4.6 eV, $E_{\text{gap}} = 2.2$ eV, Fig. 4) is seen to stimulate barrierless cycloaddition.

It is noteworthy to mention that reoxidation may be competitive when only alkenes are applied and not 1,5-dienes. However, whether the Ru(vii) intermediate is viable during the Ru-catalysed dihydroxylation of alkenes is still disputed.²⁷ In this work, DFT simulations showed that reoxidation was excluded due to the high barrier needed. Therefore, there is no possibility of entering a “second cycle” type pathway from the reaction of **7**_[ox] with another alkene to obtain the Ru(iv) bis-glycolate (see Fig. 1).^{4c,11f,28–30}

Cyclisation through NaIO₄-complexed Ru(vi) glycolate displayed a low barrier of 2.5 kcal mol^{–1} via distorted trigonal bipyramidal TS **8**_{NaIO4} and was a favourably exergonic step with $\Delta G_r = -43.1$ kcal mol^{–1} (Fig. 3, right).³¹ When the NaIO₄-complexed pathway (**7**_{NaIO4} \rightarrow **8**_{NaIO4} \rightarrow **9**_{NaIO4}) and the reoxidation pathway (**7**_{NaIO4} \rightarrow **7**_[ox] \rightarrow **8**_[ox] \rightarrow **9**_[ox]) were compared, the former was exceedingly preferred. Molecular orbital analysis revealed that although the energy gap for **7**_{NaIO4} was 2.7 eV

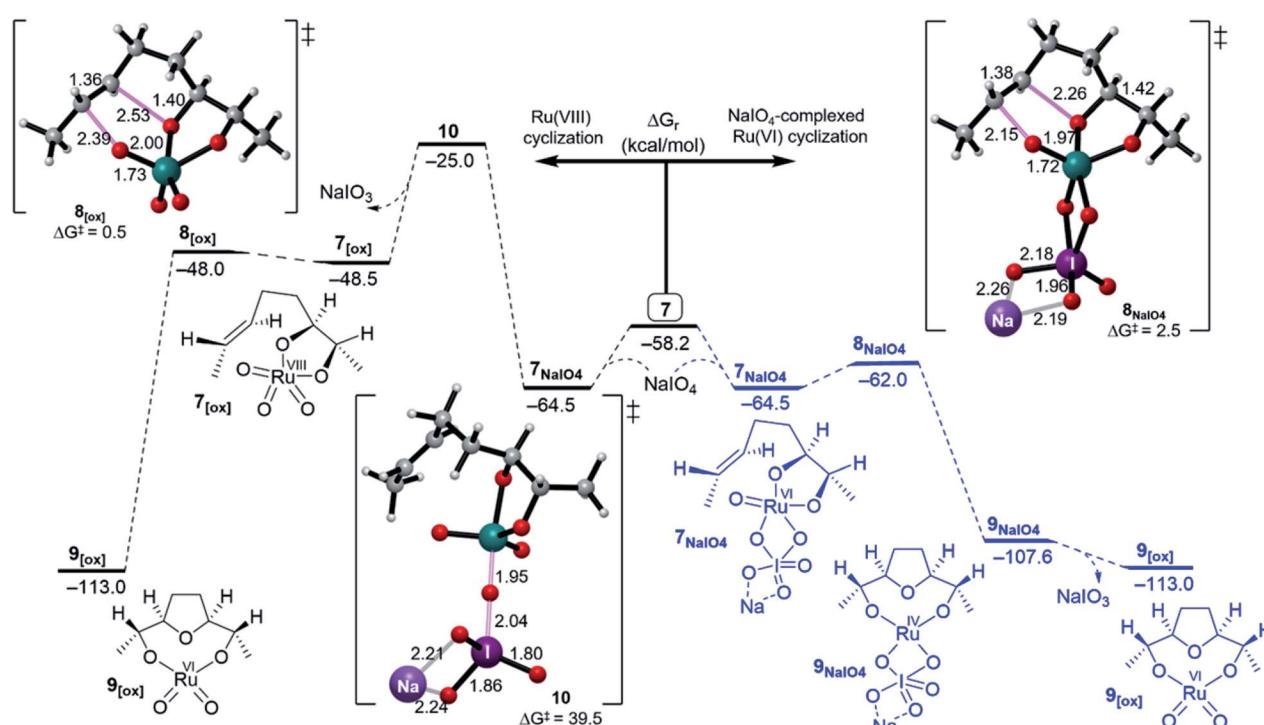


Fig. 3 Free energy profiles for the Ru(viii) (right) and NaIO₄-complexed Ru(vi) (left) cyclisation pathways.



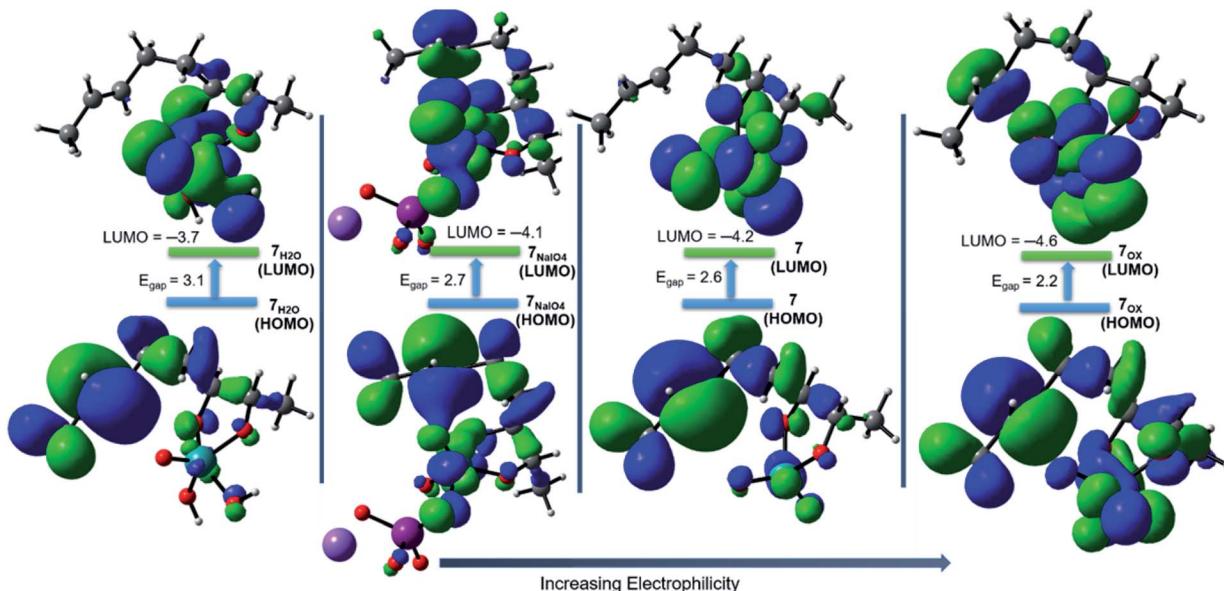


Fig. 4 Visualization (0.02 isovalue surface) of the HOMO (located on the alkene site) and LUMO (located on the Ru site) orbitals of Ru(vi) 7, 7_{H2O}, and 7_{NaIO4} and Ru(viii) 7_{ox} glycolates during the oxidative cyclisation of 1,5-diene (5) by RuO₄.

(Fig. 4), which was slightly lower than that for 7, its TS 8_{NaIO4} had a significantly lower barrier. This may be attributed to the favourable interactions between the reacting moieties with less geometrical changes or reorganizations around the Ru centre due to the exchangeable oxo ligands between the I and Ru centres that lead to a more stabilized TS to give Ru(iv) THF-diolate 9_{NaIO4}. The calculations show that Ru(iv) THF-diolate 9_{NaIO4} is simultaneously dissociated to Ru(vi) dioxodiolate 9_[ox] in a favoured step ($\Delta G_r = -6.6$ kcal mol⁻¹) (Fig. 3, right).

In summary, in the presence of NaIO₄, cyclisation through NaIO₄-coordinated Ru(vi) glycolate 7_{NaIO4} outpaces cyclisation *via* hydrated Ru(vi) 7_{H2O} and reoxidized Ru(viii) 7_{ox}. In this regard, the simulations showed that reoxidation was energetically unfavourable and thus, the formation of a “second cycle” type pathway product, Ru(vi) bisglycolate, was totally outpaced.

THF-diol release. The calculations reported above support the cyclisation of periodate-complexed Ru(vi) to give an Ru(iv) THF-diolate product. The completion of a catalytic cycle to furnish THF-diol 15 and regenerate a Ru(viii) species capable of propagating ruthenylation is important. Now, the Ru(vi) dioxodiolate 9_[ox] entails pathways toward either oxidation/hydrolysis or hydrolysis/oxidation while bearing in mind that 9_[ox] can engage in the ruthenylation of another 1,5-diene molecule (Fig. 5).

First, the oxidation of Ru(iv) THF-dioxodiolate 9_[ox] to Ru(viii) trioxodiolate 9_{[ox][ox]} is considered with an overall endergonicity of 13.5 kcal mol⁻¹ (Fig. 5, blue pathway).³² In this regard, Ru(viii) THF-trioxodiolate 9_{[ox][ox]} can overcome a barrier of 21.1 kcal mol⁻¹ *via* TS 12 to break the first O-[Ru] diolate in a modestly exergonic step ($\Delta G_r = -6.5$ kcal mol⁻¹, see 13, Fig. 5), which is followed by the release of THF-diol 15 as an overall exergonic hydrolysis pathway ($\Delta G_r = -20.9$ kcal mol⁻¹). Instead, DFT simulations indicate that Ru(vi) THF-dioxodiolate 9_[ox] coordinates with NaIO₄ and then H₂O to yield 16 *via* a low

endergonic step ($\Delta G_r = 3.4$ kcal mol⁻¹, Fig. 5). Also, 16 needs a comparatively low barrier of 10.7 kcal mol⁻¹ *via* a TS 17 to give intermediate 18 *via* an exergonic process ($\Delta G_r = -3.4$ kcal mol⁻¹). In the opposite mode to the hydrolysis of Ru(viii), the hydrolysis of the second O-[Ru] diolate in intermediate 18 was calculated to be unfavourable when compared to the experimental conditions. The located TS 22, shown in ESI Fig. 4,† requires a high energy barrier of 21.7 kcal mol⁻¹ to transfer the proton from the oxo ligand [HO-[Ru]] to the second O-[Ru] diolate bond although it is an exergonic step ($\Delta G_r = -7.6$ kcal mol⁻¹). Obviously, proton transfers involving electronegative atoms are known to be fast and diffusion controlled and therefore, getting intermediate 19 *via* a slightly endergonic step ($\Delta G_r = 6.3$ kcal mol⁻¹) is suggested. At this point, hydrolysis through Ru(vi) followed by oxidation to regenerate RuO₄ is more accessible than reoxidation, *i.e.*, Ru(vi) \rightarrow Ru(viii) followed by hydrolysis.

Second, it is interesting to note that Ru(vi) dioxodiolate 9_[ox] is a competent ruthenylating agent in the hydrolysis pathway and is capable of reacting with another alkene *via* a so-called “second cycle” type pathway (Fig. 5, left pathway).³³ The energy barrier of the (3 + 2) cycloaddition of 9_[ox] with E-but-2-ene was found to be 15.4 kcal mol⁻¹ *via* TS 19 to afford a tetraester 20 *via* an exergonic reaction ($\Delta G_r = -50.5$ kcal mol⁻¹). This would reveal a barrier difference of 1.3 kcal mol⁻¹ between intermolecular ruthenylation and hydrolysis with the hydrolysis being predominant.

Finally, based on the above-mentioned results, a catalytic cycle for the Ru-catalysed oxidative cyclisation of 1,5-diene 5 was proposed (Fig. 6). The complexation of Ru(vi) glycolate 7 with a co-oxidant (NaIO₄) is an essential feature found for SRS. The reoxidation of NaIO₄-coordinated Ru(iv) THF-diolate 9_{NaIO4} to Ru(vi) THF-dioxodiolate 9_[ox] followed by another coordination



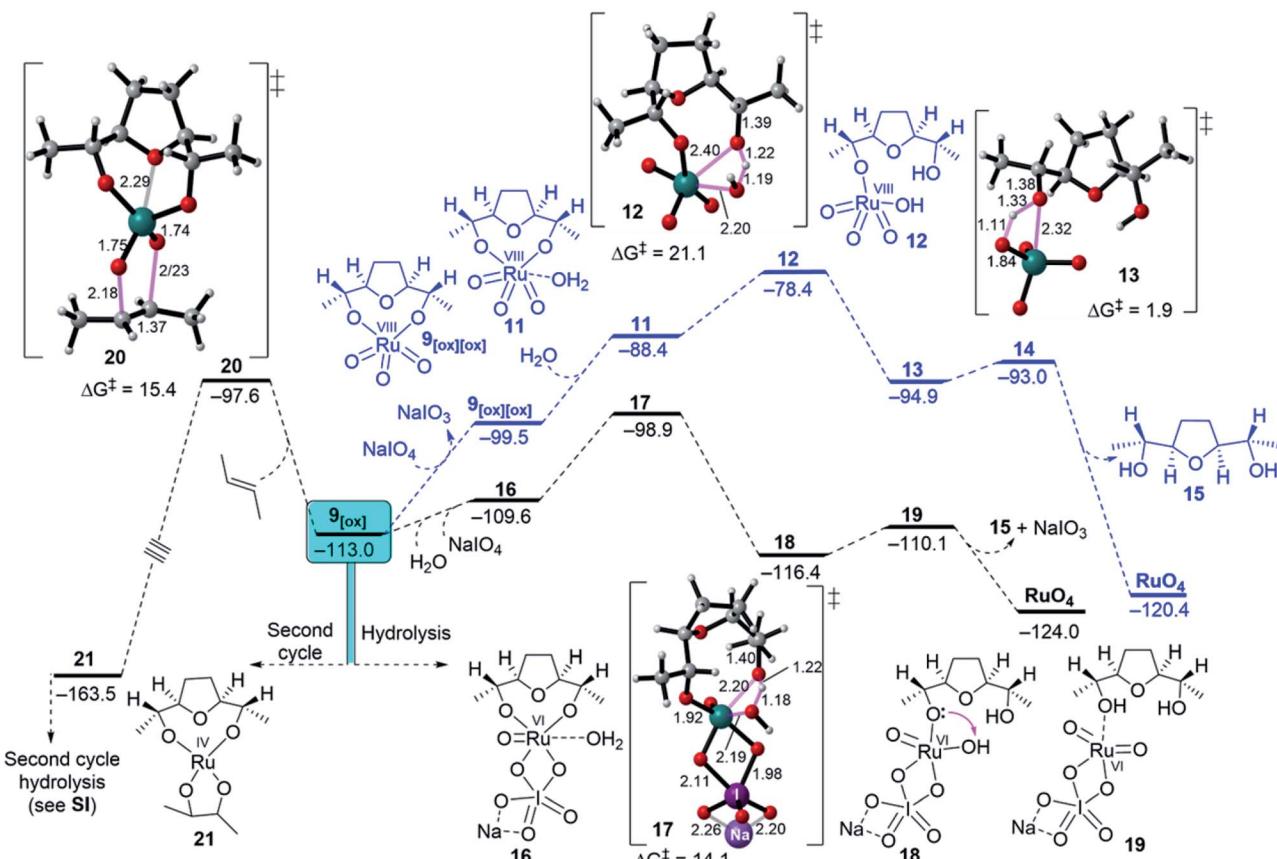


Fig. 5 Free energy evaluations for divergent reactions of 9_{ox} , showing hydrolysis via Ru(vi) or Ru(viii) or entering a second cycle through another ruthenylation. *E*-But-2-ene was used as a model for 5 to reduce the computational cost.

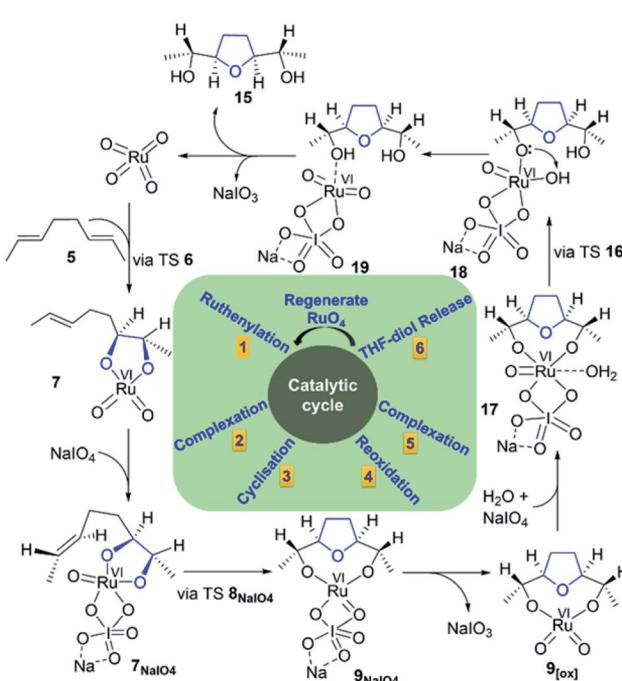


Fig. 6 Proposed catalytic cycle for Ru-catalysed oxidative cyclisation of 1,5-diene 5.

with both water and NaIO_4 gives **17**, releasing its THF-diol **15** and regenerating RuO_4 to continue the iterative cycle.

Regioselectivity of the Ru-catalysed oxidative cyclisation

The regioselectivity of RuO_4 is considered when an EWG such as a methyl ester group is found on one of the double bonds of 1,5-diene, as indicated in methyl dienoate **5a** shown in Fig. 7.^{11b} Based on the aforementioned findings, DFT calculations have been performed for FRS and SRS (Fig. 7). For FRS, the favourability of RuO_4 to initiate the electron-rich alkene (ERA) pathway over the electron-deficient alkene (EDA) pathway is highly evident. For instance, the ERA Ru(vi) glycolate **7a** ($\Delta G_r = -62.4 \text{ kcal mol}^{-1}$) is formed *via* a barrierless (3 + 2) cycloaddition TS **6a** of $\Delta G^\ddagger = 1.7 \text{ kcal mol}^{-1}$ (Fig. 7, right), whereas the formation of the EDA Ru(vi) glycolate **d-7a** requires a higher barrier of $4.9 \text{ kcal mol}^{-1}$ *via* TS **d-6a** *via* a slightly less exergonic step ($\Delta G_r = -55.1 \text{ kcal mol}^{-1}$ (Fig. 7, left)).³⁴ Thus, the ERA product is kinetically ($\Delta \Delta G^\ddagger = -3.2 \text{ kcal mol}^{-1}$) and thermodynamically ($\Delta \Delta G_r = -7.3 \text{ kcal mol}^{-1}$) favoured with a greater development of the C–O bond formation for ERA TS **6a** over EDA TS **d-6a**.

On the cyclisation step, the ERA Ru(vi) glycolate **7a_{NaIO4}** cyclises, *via* TS **8a_{NaIO4}** with a barrier of $\Delta G^\ddagger = 8.6$ kcal mol⁻¹, and this is slower than cyclisation through EDA Ru(vi) glycolate

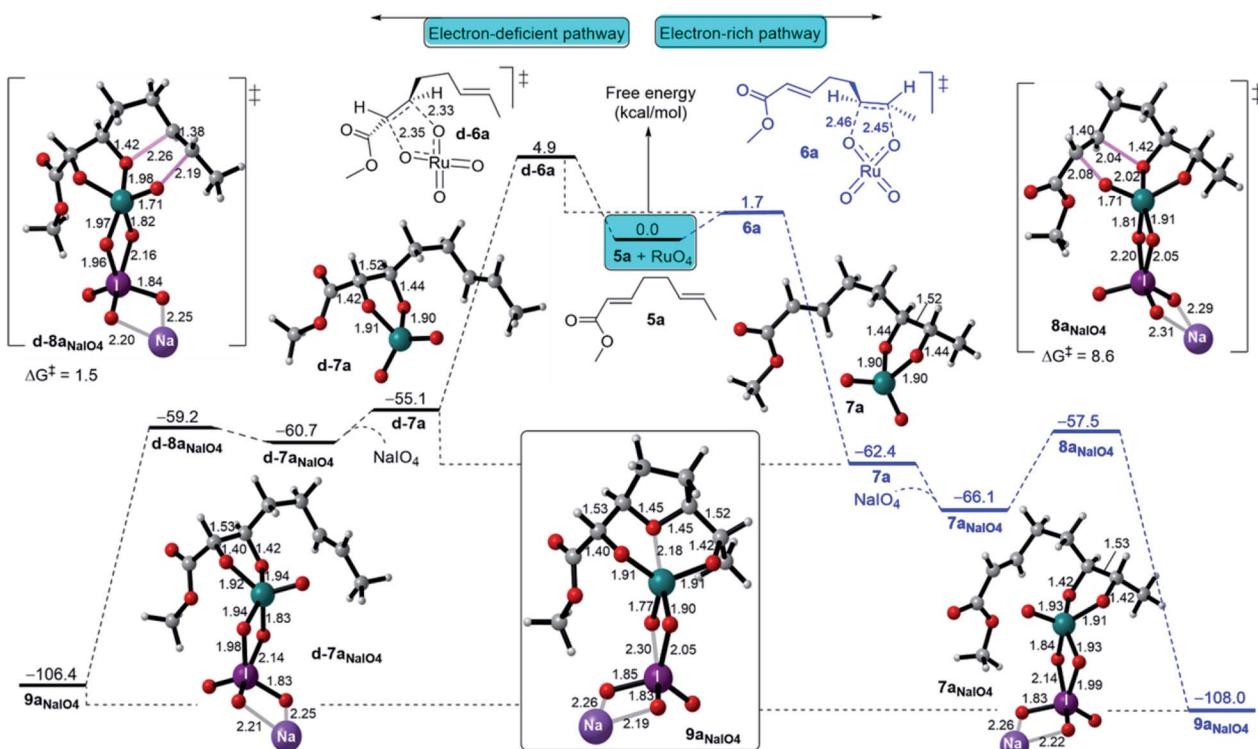


Fig. 7 Free energy bifurcation for the regioselectivity of the Ru-catalyzed oxidative cyclisation of methyl 1,5-dienoate (5a) initiated at the electron-rich and electron-deficient alkenes.

pathway (TS **d-8a**_{NaIO4}, $\Delta G^\ddagger = 1.5$ kcal mol⁻¹). A reasonable explanation for this is that the oxo ligands in **d-7a**_{NaIO4} are more electrophilic than those in **7a**_{NaIO4} mainly due to the electron-withdrawing nature of the carbonyl group with a possible minor contribution from complexation with NaIO₄. This would lead to a lower barrier for cyclisation because it has lower LUMO energy on the Ru site and higher HOMO energy on the alkene site. However, in the ERA Ru(vi) glycolate **7a**_{NaIO4}, cyclisation occurs from the highly electron-deficient alkene site to the slightly electron-deficient Ru site, subsequently ensuring that the cyclisation has a higher barrier. In comparison with the symmetric 1,5-diene (5), the cyclisation *via* the ERA NaIO₄-complexed Ru(vi) glycolate requires a three-fold higher energy barrier than the cyclisation with the symmetric 1,5-diene (5). Overall, the existence of an EWG on one of the alkenes in the 1,5-diene structure results in the Ru-catalysed oxidative cyclisation being predominantly initiated at the electron-rich alkene.

Conclusions

The first detailed mechanistic study on the Ru-catalysed oxidative cyclisation of 1,5-dienes has been performed with the (SMD/THF)-M06/aug-cc-pVDZ/LANL2DZ//M06/cc-pVDZ/LANL2DZ level of theory. The DFT simulations are in excellent agreement with the experimental conditions and consequently, complications accompanied throughout the Ru-catalysed oxidative cyclisation of 1,5-dienes are resolved.

The results set out the catalytic cycle for THF-diol formation through the intermediacy of Ru(vi) with RuO₄ as the active catalytic species. Importantly, the co-oxidant NaIO₄ has been evidently shown to play a critical role in the cyclisation and hydrolysis steps through complexation with Ru rather than reoxidation to a higher oxidation state. Following the initially formed Ru(vi) dioxoglycolate, the cyclisation overcomes a favourable NaIO₄-coordinated TS to give the THF-diolate ring, excluding the cyclisation or entering the second cycle through the intermediacy of Ru(viii) trioxoglycolate **7_[ox]**. Thereafter, the dissociation of the NaIO₄-coordinated Ru(iv) THF-diolate **9_{NaIO4}** to Ru(vi) THF-dioxodiolate **9_[ox]** was calculated to undergo hydrolytic release to give THF-diol **15** and RuO₄ to continue the iterative cycle. The release of THF-diol **15** from Ru(vi) THF-dioxodiolate **9_[ox]** was found to be favourable over reoxidation to Ru(viii) THF-trioxodiolate **9_{[ox][ox]}** or entering the so-called “second cycle” type pathway. This protocol has evidently conducted a cycle of Ru(viii)/Ru(vi)/Ru(iv)/Ru(vi) rather than Ru(viii)/Ru(vi)/Ru(viii)/Ru(vi)/Ru(viii).

Furthermore, DFT simulations on asymmetric 1,5-dienes, such as methyl 1,5-dienoate (5a), have provided further mechanistic descriptions when an electron-withdrawing group is attached to one of the alkenes. The calculations revealed that the Ru-catalysed oxidative cyclisation is predominantly initiated at the electron-rich alkene. The cyclisation from the ERA NaIO₄-complexed Ru(vi) glycolate was shown to be slower than the cyclisation from an electron-deficient Ru(vi) intermediate. In comparison with symmetric 1,5-diene (5), the barrier for



cyclisation from an asymmetric 1,5-diene was calculated to be more than three times higher than the barrier for symmetric cyclisation.

Overall, this computational study gives significantly important insights into this key synthetic method, which may offer a viable pathway towards advancing an efficient protocol for alkene oxidation.

Computational details

All calculations were performed using Gaussian 09 (ref. 35) with the global hybrid functional approximations M06 (ref. 36) used with the augmented correlation-consistent polarized valence double- ζ (DZ) basis set (cc-pVDZ and aug-cc-pVDZ)³⁷ for C, H, O, Si, and Na, whereas an effective core potential basis step LANL2DZ³⁸ was used for Ru and I. All geometry optimisations, even for triplet and quintet spin multiplicities, shown in the ESI,[†] were performed with the basis set cc-pVDZ/LANL2DZ, in which all minima intermediates were verified by the absence of negative eigenvalues in the vibrational frequency analysis. Restricted spin Hartree–Fock calculations were used for singlet spin multiplicity, whereas unrestricted spin calculations were used for triplet and quintet spin multiplicity. All of the transition state structures were found using the Berny algorithm,³⁹ verified by vibrational analysis, and visualised by animating the negative eigenvector coordinate. In order to account for the effect of the solvent, single-point energies of the optimised geometries were evaluated with the M06/aug-cc-pVDZ/LANL2DZ level of theory in tetrahydrofuran (THF) as a representative solvent medium *via* the solvation model based on density (IEFPCM-SMD).⁴⁰ To obtain the free energies at 298.15 K and 1 atm, the thermal corrections were evaluated from the unscaled vibrational frequencies at the M06/cc-pVDZ/LANL2DZ level of theory and were then added to the electronic energies calculated from the M06/aug-cc-pVDZ/LANL2DZ level of theory. Intrinsic reaction coordinate (IRC) calculations were performed for the identified transition states to confirm the reaction path proceeding in both directions (reactant and product), in which the Hessian was recomputed every 3 predictor steps with a step size along the reaction path of 0.05 Bohr.⁴¹ All activation free energies are quoted relative to infinitely separated reagents and the optimised structures were illustrated using CYLview.⁴²

Conflicts of interest

There are no conflicts to declare.

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22 It is very desirable to mention that Ru(vi) complex $[(\text{Me}_3\text{tacn})(\text{CF}_3\text{CO}_2)\text{RuO}_2]\text{ClO}_4$ was isolated by Che *et al.* and used in *cis*-dihydroxylation of alkenes in which they also isolated the (3 + 2) cycloadduct intermediate Ru(iv) glycolate. (See ref. 23).

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33 In comparison to Ru(vi) glycolate **7**, the Ru(vi) glycolate **7** did not undergo intermolecular ruthenylation and this is believed due to the geometrical difference, especially angle in $\text{O}=\text{Ru}=\text{O}$, between **7** and $9_{[\text{ox}]}$. The angle of $\text{O}=\text{Ru}=\text{O}$ in Ru(vi) diolate $9_{[\text{ox}]}$ is 119.4° and Ru(vi) glycolate **7** is 125.7°.

34 Due to the difficulty in locating the TS **6a** using the DFT functional M06 (M06/cc-pVDZ/LANL2DZ), both TSs **6a** and **d-6a** have been optimised in gas phase with M06-2X (M06-2X/cc-pVDZ/LANL2DZ) followed by single point energy calculations in THF with the M06 functional ((SMD)-M06//aug-cc-pVDZ/LANL2DZ).

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