The Role of Xantphos in forming an Elusive dirhodium-η¹-allyl Intermediate in a Rh(II)-Catalyzed Allylic Alkylation: A Combined Computational and Experimental Study


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Abstract

The use of dirhodium tetracarboxylate catalysts in multicomponent reactions involving allylic alkylation has been a formidable challenge to synthetic chemists. A unique strategy by means of catalyst structure modification in the presence of an external ligand, Xantphos, has recently enabled their efficient use in one-pot reactions involving carbene insertion into X–H bonds followed by allylic alkylation. However, the origin of the novel reactivity and the mechanism of such reactions remains unclear. Herein, we report a combined computational and experimental mechanistic study to shed light on the ligand enabled catalyst structure modification and its implication in catalysis. This unique reactivity is enabled by the dissociation of an octanoate bridge driven by κ²-Xantphos ligation to the dirhodium core of the catalyst. This, in turn, allows for the hitherto unknown oxidative addition with a Rh(II) catalyst resulting in a dirhodium-η¹-allyl species. For the first time, we confirm the presence of such a species in solution through in situ NMR and cyclic voltammetry experiments in line with DFT calculations. Alongside, we study the role of the base and solvent in generating the nucleophilic partner that can trap the electrophilic allylic species. This study is expected to guide future catalyst design including chiral variants for exploring newer modes of reactivity and selectivity using dirhodium catalysis.
1 Introduction

Dirhodium tetracarboxylate-based paddlewheel complexes have found widespread utility in the functionalization of X–H (X = N, O, S, C) bonds with impressive regio-, chemo-, and stereoselectivities. The simple yet elegant two-component strategy has been further extended to MCRs (multicomponent reactions) where the reactive onium ylide intermediate traps an external electrophile. The capture of external electrophiles both in the form of Michael acceptors (prior to a delayed proton transfer) and electrophile transfer reagents or intermediates to yield valuable and diverse molecular scaffolds has been reported (Scheme 1).

Despite the burgeoning success of dirhodium tetracarboxylate-based catalysts for X–H insertion reactions, the catalysts of choice for another class of reactions involving allylic alkylation via metal-allyl intermediates largely remain monorhodium and palladium-based. This is due to the ease of formation of these intermediates through a facile oxidative addition process, which is typically not possible in the stable dirhodium tetracarboxylate architecture owing to the lack of two vacant adjacent coordination sites. Due to this, dirhodium tetracarboxylate-based catalysts are incapable of catalyzing the MCRs involving allylic reagents as electrophiles. This necessitates the use of two metal catalysts, one for the formation of the metal carbene and the other for that of the metal-allyl complex. In this context, the use of Rh and Pd has been a convenient strategy to form complex targets. However, an ideal scenario would be the use of single catalyst that can enable both carbene insertion followed by allylic alkylation or vice versa. Although monorhodium-based catalysts are also capable of X–H insertion reactions and can thereby in principle be used as the sole metal catalyst for MCRs, they fail to catalyze the MCR involving allylic alkylation most likely due to their tendency to easily form the metal-allyl intermediate through oxidative addition and the subsequent allylic alkylation of the X–H based nucleophile, precluding the metal carbene formation and X–H insertion, and instead affording the X-allylated product.

Scheme 1. Two- and three-component reactions catalysed by dirhodium carboxylates.
Despite the challenges discussed above, Wang and co-workers recently developed a MCR protocol for the construction of α-quaternary α-amino ester from an α-diazoester, amine, and allylic compound, involving a dirhodium tetracarboxylate/Xantphos-catalyzed carbene insertion and allylic alkylation relay (Scheme 2).⁵ The unique reactivity was a result of the combination of different factors that include the nature of the catalyst, external ligand, base, and solvent. Their synthesis design was based on the possible modification of the catalyst in the presence of the external Xantphos ligand where the choice of the solvent and base also played a crucial role. The modification of dirhodium catalysts in different ways has enabled newer reactivity in several other reactions. For instance, chiral carboxylate ligands have been incorporated into the catalyst framework for the development of asymmetric X–H insertion reactions.⁶ There have also been a number of attempts to tune the reactivity of dirhodium-based catalysts by the use of external and tethered axial ligands without modifying the paddlewheel framework.⁷ Although the use of external chiral ligands in this aspect has only resulted in modest enantioselectivities so far, the differential reactivities are of immense importance.⁷b In the work by Wang and coworkers, it was hypothesized that the external Xantphos ligand drives the dissociation of one of the carboxylate ligands. This in turn provides vacant adjacent sites necessary for the oxidative addition of the allyl substrate resulting in the formation of a hitherto unreported dirhodium-η¹-allyl species, which is postulated to serve as the active allylating agent in the reaction (Scheme 3). However, they were able to detect neither the cationic complex nor the Rh-allyl species. Numerous similar reports of carbene insertion and allylic alkylation relay utilizing this strategy have followed thereafter,⁸ making it necessary to establish the mechanistic details of this reaction. Recently, this strategy of ligand induced dirhodium catalyst modification has also been applied to a carbonyl arylation reaction involving external chiral ligands.⁹ This arylation reaction, supposedly proceeding via a similar modified catalyst, provides the motivation for developing asymmetric reactions for MCRs as well. Since there are no experimental or computational reports on the mechanistic front for this intriguing MCR, in this work, we attempt to delineate its mechanism and the key species involved via computational and experimental studies.

Scheme 2. General scheme for the synthesis of α-quaternary α-amino ester.

The work under investigation involves a relay pathway where the N–H insertion product (an α-amino ester) is formed, exits the catalytic cycle, and enters the subsequent catalytic cycle for allylic alkylation (Scheme 3). As shown by Wang and co-workers,⁵ when the N–H insertion product is subjected to the standard reaction conditions, the α-quaternary α-amino ester is formed in high yield, thus confirming the relay nature of this MCR. This relay reactivity is different from the other MCRs where the ylide/enol intermediate traps the external electrophile. Under these circumstances, there is competition between the formation
of the two- and three-component products. However, in the reaction under investigation, the two-component product is first formed, which then undergoes further reaction. In the absence of the Xantphos ligand, the reaction stops at the N–H insertion product, thereby indicating that the ligand is essential for the subsequent allylic alkylation. At the same time, deviations in the solvent and base also significantly affected the yield of the α-quaternary α-amino ester. We therefore set out to first investigate the role of Xantphos in the allylic alkylation of the α-amino ester. The primary goal is to establish the nature of the electrophilic and nucleophilic species participating in this allylic alkylation reaction. Our study provides the first explanation for the unique reactivity of the dirhodium/Xantphos system. We confirm our mechanistic model obtained through DFT calculations using in situ NMR and CV experiments.

Scheme 3. Proposed mechanism for dirhodium tetracarboxylate/Xantphos-catalyzed carbene insertion and allylic alkylation relay.

2 Results and Discussion

2.1 Search for the active catalyst

We begin our study by looking at the different possibilities for the most stable active form of the catalyst (Figure 1) at the SMD(acetonitrile)/B3LYP-D3(BJ)/6-311++G(d,p),SDD(Rh,Cs)//B3LYP-D3(BJ)/6-31G(d,p),SDD(Rh,Cs) level of theory. In the absence of the external Xantphos ligand, the complex A5 with one molecule each of Cs2CO3 coordinated axially to the two ends of dirhodium tetracarboxylate catalyst was found to be most stable. However, this diaxial mode of coordination blocks both ends of the catalyst and
prevents subsequent reactions, viz. N–H insertion and Rh association for allylic alkylation due to lack of any reactive sites and an over-stabilized complex, leading to a dead end. This phenomenon has been previously studied by Pirrung and co-workers for dirhodium tetracarboxylate catalyzed C–H insertion.\textsuperscript{10} A kinetic treatment in their report using different axial ligands revealed that axial ligand coordination in general slowed down the insertion reaction and that bis-coordination leads to a catalytic dead end. Therefore, the complex with Cs\textsubscript{2}CO\textsubscript{3} coordinating to one of the axial sites of the catalyst A\textsubscript{4} is most likely the active form of the catalyst in the absence of Xantphos.

**Figure 1.** Possible active catalysts (relative free energies are in kcal mol\textsuperscript{-1}).

In the presence of Xantphos, the $\kappa^1$-mode of coordination of Xantphos to the catalyst (D\textsubscript{1}) leads to a stabilization of 18.3 kcal mol\textsuperscript{-1}. The bis-coordination of two Xantphos in the $\kappa^1$-mode to the two axial sites (D\textsubscript{2}) leads to a stabilization of 25.1 kcal mol\textsuperscript{-1}. However, this bis-coordinated form cannot function as the active catalyst as it blocks both the reactive axial sites, as discussed previously in the case of Cs\textsubscript{2}CO\textsubscript{3} coordination. These two geometries correspond to the crystal structures reported by Wang and co-workers.\textsuperscript{5} A third crystal structure reported by this group (D\textsubscript{7}) provides indirect evidence for the $\kappa^2$-Xantphos coordination to one of the rhodium centres by the dissociation of an octanoate bridge (D\textsubscript{4}), and they hypothesize this to be the active form of the catalyst.\textsuperscript{5,12} Recent reports in dirhodium catalysis have also invoked this hypothesis to explain the catalytic activity in their reactions.\textsuperscript{8,9} This complex D\textsubscript{4}, with the dissociated bridge octanoate now coordinating in a $\kappa^2$ fashion to the second rhodium centre, was found to be stabilized by 25.2 kcal mol\textsuperscript{-1} (the coordination of a Cs\textsubscript{2}CO\textsubscript{3} molecule to the opposite axial site D\textsubscript{6} was found to be further
stabilizing by 7.7 kcal mol\(^{-1}\), but was discarded as a dead end following the same reasoning as above).

With the active catalytic species in the absence and presence of the external Xantphos ligand established, we attempted to study the allylic alkylation of the N–H insertion product, \(i.e.,\) the \(\alpha\)-aminoester 3 (Scheme 3). The mechanism of X–H (X = N, O, S, C) insertion reactions catalyzed by dirhodium tetracarboxylate and other transition metal complexes have been well studied computationally and reported to proceed through metallocarbene, B formation from diazoesters followed by a nucleophilic attack to yield the ylide, C and subsequent proton transfer to yield the X–H insertion product, 3 (Scheme 3). Therefore, the first catalytic cycle for the N–H insertion reaction leading to the \(\alpha\)-aminoester, 3 has not been investigated computationally in this work. The nucleophile in this process is likely an enolate formed from the deprotonation of the \(\alpha\)-proton from the \(\alpha\)-aminoester by the Cs\(_2\)CO\(_3\). The enolization of the \(\alpha\)-aminoester by Cs\(_2\)CO\(_3\) in acetonitrile was confirmed by 42% deuterium incorporation using D\(_2\)O, as verified from \(^1\)H NMR (see Supporting Information Section C). This enolization was calculated to proceed with a free energy barrier of 7.8 kcal mol\(^{-1}\) and 8.9 kcal mol\(^{-1}\) to form (E)-enolate and (Z)-enolate respectively, thereby confirming the feasibility of such a process. All calculations presented hereafter have considered the kinetically more feasible (E)-enolate (calculations with the (Z)-enolate show similar trends, see Supporting Information Figure S1 and Figure S2 for details).

### 2.2 Reaction pathways in absence of Xantphos

![Diagram of reaction pathways](image)

**Figure 2.** Transition states and the relative free energies (kcal mol\(^{-1}\)) with respect to the catalytic species A5 (left) and A1 (right) in the absence of Xantphos.
In the absence of Xantphos, we considered a Rh-associated enolate (H) as a possible intermediate effecting a nucleophilic attack on allyl carbonate. We also speculated the external attack of a nucleophile on a Rh-associated allyl carbonate (G). However, whether the nucleophile (generated by a proton abstraction from the N–H insertion product) is a Cs-enolate or a Cs-free enolate is dubious. The nucleophilic attack of the Cs-enolate on the Rh-associated allyl carbonate \( \text{TS}^{A4(G-P)}_{\text{Cs}} \) was found to have a barrier of 23.1 kcal mol\(^{-1}\), and the nucleophilic attack of the Rh-associated Cs-enolate on allyl carbonate \( \text{TS}^{A4(H-P)}_{\text{Cs}} \) to have a barrier of 22.6 kcal mol\(^{-1}\) (Figure 2, left). Such low free energy barriers indicate a facile reaction at room temperature (for reference, \( \text{N}_2 \) expulsion for metallocarbene formation, the typical rate-determining step for the N–H insertion pathway, has barriers of 22.3 kcal mol\(^{-1}\) and 14.7 kcal mol\(^{-1}\) with and without Xantphos, respectively, Figure S3), in stark contrast to experimental results where no allylic alkylation is observed in the absence of Xantphos.

Previous studies on the extent of ion-pairing in alkali enolates have revealed a decreasing trend of ion-pairing going from Li\(^+\) to Na\(^+\) to K\(^+\) (log \( K_{\text{assoc}} \) = 4.6, 3.3, 2.3 respectively for diethyl malonate in DMSO) showing an inverse relation with cation size.\(^{14}\) Based on the much larger size of the Cs\(^+\) cation and the polarity of the solvent, the Cs-enolate is expected to be in the completely solvent-separated form. In fact, the so-called “cesium effect” used in justifying the enhanced reactivity of cesium salts, cesium carbonate in particular, as compared to other alkali metal analogues is often explained in terms of the higher solubility of these salts on account of their greater solvation.\(^{15}\) Thus, incorporating a Cs-enolate species in our DFT calculations might be incorrect and leads to the unrealistically low free energy barriers stated above, causing us to exclude the Cs-bound enolate from our calculations. Therefore, expecting a similar behaviour of Cs in the current work, too, we, therefore incorporate the Cs-free enolate as the nucleophilic species in this reaction and find the nucleophilic attack of the enolate on the Rh-associated allyl carbonate \( \text{TS}^{A4(G-P)} \) to have a barrier of 38.2 kcal mol\(^{-1}\) and that of the Rh-associated enolate on allyl carbonate \( \text{TS}^{A4(H-P)} \) to have a barrier of 31.8 kcal mol\(^{-1}\) (Figure 2, left). The reaction pathways corresponding to the catalyst without axial Cs\(_2\)CO\(_3\) coordination were also studied and found to have a similar trend of free energy barriers (Figure 2, right).

\subsection*{2.3 Reaction pathways in presence of Xantphos}
Figure 3. Intermediates and transition states and their associated free energies for pathways involving Rh-associated allyl carbonate and Rh-associated enolates in presence of Xantphos (free energies relative to catalyst D4 are given in kcal mol\(^{-1}\)).

Having rationalized the reactivity in the absence of Xantphos, we investigated the potential reaction pathways in the presence of Xantphos (Figure 3). As discussed in Section 3.1, complex D4 with a \(\kappa^2\)-Xantphos coordination is considered to be the active form of the catalyst\(^{16}\) and all relative free energies are hereafter referenced to it. As the oxidative addition pathway\(^5\) has no literature precedence in the context of dirhodium catalysis, we looked at the possibility of a Rh-associated enolate as an intermediate with a subsequent nucleophilic attack on allylic carbonate, but each of these pathways TS\(^{D4}(H_X-P)\) (where \(X\) denotes the enolate binding site) was calculated to have a preventively high free energy barrier. The nucleophilic attack of the enolate on the Rh associated allyl carbonate TS\(^{D4}(G-P)\) was also found to have a very high barrier. (Note: In both the above possibilities, incorporating a Cs-enolate or a Rh-associated Cs-enolate as the nucleophile yields much lower barriers (Figure S5), but must be disregarded in accordance with our previous justification). The possibility of an allyl transfer from a Rh-associated allyl carbonate to the neighboring \(\kappa^1\)-octanoate (Figure S6) was also excluded based on high energy transition states.

2.4 The oxidative addition pathway

Wang and co-workers have hypothesized the complete dissociation of the octanoate ligand from the \(\kappa^2\)-Xantphos dirhodium tetracarboxylate active catalyst along with a concomitant association of the allyl carbonate to the cationic dirhodium species (Scheme 3).\(^{5,16}\) Previous reports involving dirhodium carboxylate catalysts with and without external ligands have also
hypothesized the complete dissociation of a carboxylate ligand\textsuperscript{17} although the external ligand-free version has been challenged.\textsuperscript{18} We calculated the allyl carbonate associated dirhodium cation/octanoate ion pair E to be destabilized by 15.8 kcal mol\textsuperscript{-1} (Figure 4). However, the calculation of charged species, especially for an ion pair such as this, by even state-of-the-art DFT methods, has been previously noted to have errors up to five kcal mol\textsuperscript{-1} in general\textsuperscript{19} and more than seven kcal mol\textsuperscript{-1} in certain cases.\textsuperscript{20} In order to get a more accurate estimate, as outlined in previous protocols,\textsuperscript{20} we tried incorporating up to four explicit solvent (MeCN) molecules without seeing any additional stabilization. A solvent phase optimization at the SMD\textsubscript{acetonitrile}/B3LYP-D3(BJ)/6-31G(d,p),SDD(Rh,Cs)//SMD\textsubscript{acetonitrile}/B3LYP-D3(BJ)/6-31G(d,p),SDD(Rh,Cs) level of theory led to a reduced free energy of 14.1 kcal mol\textsuperscript{-1}.\textsuperscript{21}

Figure 4. Optimized geometries for the ion pairs following the complete octanoate dissociation with and without allyl carbonate association (free energies in parenthesis correspond to the gas-phase optimized geometry relative to D4, free energies in parenthesis correspond to the solvent-phase optimized geometry relative to D4, given in kcal mol\textsuperscript{-1}).

To ascertain the existence of such an intermediate, we therefore resorted to experimental methods. We first performed in situ \textsuperscript{1}H NMR experiments (Figure 5) under inert conditions. Upon addition of the commercially available allyl chloride to a mixture of dirhodium tetraacetate and Xantphos in acetonitrile-\textit{d3}, we observed an allyl species distinct from the allyl chloride to be present in 16-20\% relative yield (Figure 5(b)), which is absent in the control experiment without Xantphos (Figure 5(a)). Closer inspection revealed the allylic protons in the new allyl species to be in the form of a doublet of doublet of doublets at 4.41 ppm likely due to \textsuperscript{3}J\textsubscript{H-H} and \textsuperscript{2}J\textsubscript{H-Rh\textsubscript{1}}, and \textsuperscript{3}J\textsubscript{H-Rh\textsubscript{2}} coupling corresponding to \textsuperscript{103}Rh\textsubscript{2}–\textsuperscript{103}Rh\textsubscript{1} (J = 4.9 Hz, 6.9 Hz, 16.9 Hz) (Figure 5(c)), confirming the presence of a dirhodium-\textit{η}\textsuperscript{1}-allyl species in solution.
Figure 5. *in situ* $^1$H NMR spectra of (a) equimolar mixture of dirhodium tetraacetate and allyl chloride (b) equimolar mixture of dirhodium tetraacetate, Xantphos, and allyl chloride (c) spectrum (b) magnified to focus on the doublet of doublet of doublet at 4.41 ppm (d) equimolar mixture (stirred overnight) of dirhodium tetraacetate, Xantphos, allyl chloride, and cesium carbonate (1.5 equiv) (e) 1 equiv of $\alpha$-amino ester added to the solution in (d); all in acetonitrile-$d_3$. **Note:** Although the cartoon representation adopted here is the same as before, the rhodium complex being used here is dirhodium tetraacetate and not dirhodium tetraoctanoate.

This indicates the oxidative addition of the allylating agent (allyl carbonate, allyl chloride, etc.) across the rhodium centre to which it is associated (in intermediate E) to form the detected dirhodium-η¹-allyl intermediate. Encouraged by this observation, we attempted to computationally examine the pathway of formation of this dirhodium-η¹-allyl intermediate.
(Figure 6). As the energy penalty of the ion pair E with respect to the neutral system cannot be accurately captured by our calculations (discussed above), we consider all subsequent free energies relative to this intermediate. The oxidative addition pathway TS(E-F) was found to be most favourable, possessing an activation free energy barrier of 17.2 kcal mol$^{-1}$ with respect to the intermediate E, leading to the dirhodium-$\eta^1$-allyl intermediate F with a free energy of 14.9 kcal mol$^{-1}$ with respect to E (calculations using dirhodium tetraacetate and allyl chloride, which are used for all experiments, show similar trends; Figure S7). It must be noted here that the Rh “enyl” intermediate K (proposed by Evans and co-workers in the case of Rh(I)/Rh(III) catalysis) was calculated to be 28.7 kcal mol$^{-1}$ higher in energy than the dirhodium-$\eta^1$-allyl intermediate F and was therefore discarded as a possible intermediate. Additionally, the direct Rh-allylation by allyl carbonate (formally, a nucleophilic displacement or the first step of a stepwise oxidative addition pathway; Figure S6) was calculated to have a preventively high barrier. For the sake of completeness, we also considered the exchange of the non-bridging octanoate ligand with the enolate and a subsequent inner sphere allylic alkylation by a Rh-associated allyl carbonate but found these pathways to possess insurmountable barriers (Figure S8).

In order to confirm that the oxidative addition pathway is indeed taken, CV (cyclic voltammetry) measurements were performed under inert conditions in acetonitrile with tertbutylammonium hexafluorophosphate as the supporting electrolyte (see Section 2.3 for details). Dirhodium tetraacetate showed the reported reversible one-electron oxidation/reduction wave at 1.18 V (Figure 7(a) and 7(b)), while Xantphos exhibited three separate quasireversible oxidation/reduction waves at 1.13 V, 1.48 V, and 1.98 V (Figure S9). When dirhodium tetraacetate and Xantphos were taken together in solution, a nearly irreversible hump near 0.94 V was observed and the wave corresponding to one-electron oxidation/reduction of dirhodium tetraacetate turned quasireversible without any shift in potential (Figure 7(c) and 7(d)). This further supported the complexation of Xantphos with dirhodium tetraacetate. Upon adding allyl chloride along with dirhodium tetraacetate and Xantphos in solution, new quasireversible reduction/oxidation waves near -1.38 V and -1.58 V were observed (Figure 7(e) and 7(f)), likely corresponding to the two-electron reduction of the oxidative addition product, i.e., $[\text{Rh}_2]^{4+}$ to $[\text{Rh}_2]^{4+}$. These waves were absent in all control experiments (Figure S9). Thus, it was confirmed that the product observed through in situ $^1$H NMR results from oxidative addition.

Following the verification of the existence of the dirhodium-$\eta^1$-allyl intermediate and establishing the pathway of its formation, we turned to examine its fate in the presence of the $\alpha$-amino ester. We again performed the in situ $^1$H NMR of a mixture of dirhodium tetraacetate, Xantphos, cesium carbonate, and allyl chloride in acetonitrile-$d_3$, shaking the solution overnight to ensure maximum formation of the desired dirhodium-$\eta^1$-allyl complex. The $^1$H peaks corresponding to the dirhodium-$\eta^1$-allyl species were reproduced, indicating 38-40% relative yield (Figure 5(d)). Upon addition of the $\alpha$-amino ester, the above-mentioned peaks disappear completely, and a new set of allyl peaks appear, corresponding to the product, i.e., $\alpha$-quaternary $\alpha$-amino ester (Figure 5(e)). This further validates the idea that this dirhodium-$\eta^1$-allyl intermediate, in fact, leads to product formation by the nucleophilic attack of the deprotonated $\alpha$-amino ester.
Figure 6. Reaction profile for the possible oxidation pathways of allyl carbonate (free energies relative to D4 are given in kcal mol$^{-1}$). $^a$TS(F-P) and TS(L-P) are only representative; they could not be located. However, TS(F-P) is expected to be barrierless.
Figure 7. CV of (a), (b) dirhodium tetraacetate (c), (d) equimolar mixture of dirhodium tetraacetate and Xantphos (e), (f) equimolar mixture of dirhodium tetraacetate, Xantphos, and allyl chloride (1.25 mM in 0.1 M tetrabutylammonium hexafluorophosphate in CH$_3$CN; scan rate = 0.1 V s$^{-1}$). **Note:** Although the cartoon representation adopted here is the same as before, the rhodium complex being used here is dirhodium tetraacetate and not dirhodium tetraoctanoate.

Two potential pathways for allylic alkylation of the α-amino ester through this dirhodium-η$^1$-allyl species are most likely (Figure 6) – (1) the external nucleophilic attack of the enolate, here an SN2′-like pathway via TS(F-P) is likely favoured over an SN2-like pathway, as indicated by the deuterium labelling experiments by Wang and co-workers$^5$ as well as...
previous reports for rhodium based allylic alkylation reactons;\textsuperscript{24} (2) the exchange of the κ\textsuperscript{1}-octanoate with the enolate (L) followed by a reductive elimination via TS(L-P) to yield the α-quaternary α-amino ester. However, numerous attempts to locate the transition states for both the $S_N2'$-like and reductive elimination pathways were unsuccessful. A previous DFT study by Sunoj and co-workers\textsuperscript{25} indicates a nearly barrierless allylic alkylation transition state from a rhodium-η\textsuperscript{3}-allyl intermediate. We attempted to generate the potential energy surface for the $S_N2'$-like pathway using a reduced system (acetate in place of octanoate and two trimethyl phosphine molecules in place of Xantphos), but no saddle point was seen in the relaxed energy scan (Figure 8), indicating a nearly barrierless transition state for this reaction.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure8.png}
\caption{1-dimensional Relaxed Potential Energy Surface (PES) scan. The distance being varied is highlighted in the representative TS(F-P). Scan coordinate is in angstroms and Total Energy is in hartree.}
\end{figure}

### 3 Conclusion

In this work, we have unraveled the mechanistic possibilities for a dirhodium tetracarboxylate/Xantphos-catalyzed carbene insertion and allylic alkylation relay. Through computational studies, \textit{in situ} NMR, and cyclic voltammetry experiments, we confirmed the existence of a dirhodium-η\textsuperscript{1}-allyl species as a reactive intermediate in this reaction. We have discussed the reactivity of this allylic species with nucleophilic components, with the Cs-free enolate species determined to be the probable nucleophile in solution. Furthermore, our combined study sheds light on the individual roles of the Xantphos ligand, the Cs\textsubscript{2}CO\textsubscript{3} base, and the polar solvent. The ability of Xantphos to completely dissociate a carboxylate bridge, thereby bringing this interesting mechanistic paradigm into the picture, is expected to have serious implications in inducing new modes of reactivity utilizing dirhodium tetracarboxylate catalysts. Confirmation of the κ\textsuperscript{2}-Xantphos dirhodium tetracarboxylate active catalytic species is anticipated to pave the way for utilizing chiral bulky external ligands for efficient stereoinduction at the axial position. Recent reports on the use of chiral bisphosphine ligands such as DIOP\textsuperscript{8b} and Josiphos\textsuperscript{9} in dirhodium-catalyzed transformations illustrate this through good to excellent enantioselectivities for allylic alkylation and carbonyl addition respectively.
This κ²-mode of coordination is therefore expected to serve as a launchpad for the development of asymmetric reactions for achieving challenging transformations.

4 Methods

4.1 Computational Details

All calculations were done using Gaussian 16 suite of quantum chemical programs. The hybrid density functional B3LYP along with the D3(BJ) version of Grimme’s dispersion correction was used for geometry optimization with 6-31G(d,p) basis set for all atoms except Rh and Cs. For Rh and Cs, the SDD basis set with effective core potential (SDD) was chosen. The stationary points were characterized by frequency calculations. The transition states were verified by the unique imaginary frequency calculation concerning the desired reaction coordinate. Moreover, intrinsic reaction coordinate (IRC) calculations were carried out to verify the correctness of the transition states obtained. For all stationary points single calculations were performed using higher basis set 6-311++g(d,p) and all sorts of dispersion interaction were taken into account using the D3(BJ) version of Grimme’s dispersion correction. To take into the effect of solvent the keyword SCRF is used which performs calculations in the presence of a solvent by placing the solute in a cavity within the solvent reaction field, and herein solvent model density (SMD) with acetonitrile (ε = 35.688) was used. The ZPE (zero point energy), thermal, and entropic corrections obtained at 298.15 K and 1 atm pressure calculated in the gas phase at B3LYP-D3(BJ)/6-31G(d,p),SDD(Rh,Cs) level of theory were added to the ‘bottom-of-the-well’ energies obtained from single point calculations at the SMD_{acetonitrile}/B3LYP-D3(BJ)/6-311++G(d,p),SDD(Rh,Cs) level of theory. All the values mentioned in this work, unless mentioned otherwise, correspond to free energies obtained at the SMD_{acetonitrile}/B3LYP-D3(BJ)/6-311++G(d,p),SDD(Rh,Cs) level of theory.

4.2 NMR Spectroscopy

¹H NMR spectra were measured on an Avance Bruker 500 MHz NMR spectrometer at RT. Chemical shifts were reported in ppm with respect to SiMe₄ by referencing the solvent peak to SiMe₄. All in situ NMR experiments were set up inside an N₂-filled glove box using an airtight screw cap NMR tube.

4.3 Cyclic Voltammetry

Cyclic Voltammetry was performed using 12 mL dried and distilled acetonitrile solutions containing 0.1 M tertbutylammonium hexafluorophosphate with 0.00125 M analyte under a nitrogen atmosphere. The electrodes consisted of a glassy carbon working electrode, a Pt wire counter electrode, and an Ag/AgCl reference electrode. Measurements were taken using a Biologic SP-150 potentiostat. Prior to the measurement, all components of the analyte were taken inside the electrochemical cell and degassed before introducing it to nitrogen flow in order to ensure completely inert conditions.

4.4 Synthesis
The α-amino ester (3) was prepared according to a previously reported procedure. All other chemicals were purchased commercially and used without further purification.

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(11) The reaction catalysed by D7 was earlier to have a reduced rate and was thus not taking into consideration as the active catalytic species.


(16) See Figure S4 for the calculated reaction profile for the formation of the κ²-Xantphos dirhodium tetracarboxylate active catalyst D4 and the complete dissociation of the octanoate
ligand from D4 followed along with the concomitant association of the allyl carbonate to form E.


(21) See Table S1 and Table S2 for a comparision of the gas phase and solvent phase optimized separated ion pair (E) energy at different levels of theory.


