This is an Accepted Manuscript, which has been through the Royal Society of Chemistry peer review process and has been accepted for publication.

Accepted Manuscripts are published online shortly after acceptance, before technical editing, formatting and proof reading. Using this free service, authors can make their results available to the community, in citable form, before we publish the edited article. This Accepted Manuscript will be replaced by the edited, formatted and paginated article as soon as this is available.

You can find more information about Accepted Manuscripts in the Information for Authors.

Please note that technical editing may introduce minor changes to the text and/or graphics, which may alter content. The journal’s standard Terms & Conditions and the Ethical guidelines still apply. In no event shall the Royal Society of Chemistry be held responsible for any errors or omissions in this Accepted Manuscript or any consequences arising from the use of any information it contains.
A Theoretical Study of Dirhodium-Catalyzed Intramolecular Aliphatic C–H Bond Amination of Aryl Azides†

Huiying Xu, Xuepeng Zhang, Zhuofeng Ke* and Cunyuan Zhao*

School of Chemistry and Chemical Engineering, Sun Yat-sen University, Guangzhou 510275, P. R. China. E-mail: kezhf3@mail.sysu.edu.cn; ceszhcy@mail.sysu.edu.cn; Fax: +8620 8411 0523; Tel: +8620 8411 0523

† Electronic supplementary information (ESI) available: The Cartesian coordinates for the calculated stationary structures.

ABSTRACT: Dirhodium-contained catalysts mediated aliphatic C–H bond amination of aryl azides were studied using BPW91 functional. Calculations show the reactions with Rh2(esp)2 (esp=α,α,α’,α’-tetramethyl-1,3-benzenedipropionic acid) and the model compound Rh2(OCHO)4 as catalysts take place via similar mechanisms. Firstly, the dirhodium metal complex coordinates with the substrate and releases nitrogen gas. This rate-determining step results in the formation of the metal nitrene. Metal nitrene mediated intramolecular C–H bond amination is conducted via two alternative pathways, respectively. The singlet metal nitrene mediated intramolecular C–H bond amination occurs via a concerted and asynchronous pathway involving direct metal nitrene insertion into the C–H bond. The triplet metal nitrene case is a stepwise pathway involving a hydrogen transfer and then a diradical recombination. Our study suggests the triplet H-abstraction is more favorable than the singlet one. The resulted triplet intermediate would not go through the high-barrier diradical recombination process, but across to the singlet pathway via a MECP and form the final singlet product. The tethered esp ligands in Rh2(esp)2 provide steric effects to constrain the substrate-catalyst compound but indicates inconspicuous influence on the mechanisms of dirhodium catalyzed aliphatic C–H bond amination of aryl azides.
1. Introduction

C–H functionalization is an efficient approach to obtain natural or unnatural heteroatom-containing compound such as C–N bond formation among which metal nitrene mediated amination and aziridination have both attracted much attention.\textsuperscript{1-3} Nitrogen containing compound are widely used in drug synthesis because nitrogen generally exhibits ability to act as a hydrogen bond donor and/or acceptor which influences the interaction between the medicinal agent and its target significantly.\textsuperscript{4} Metal nitrane catalysis reaction can initiate amination to form C–N bond directly.\textsuperscript{5-9} Rhodium metal compounds are one of the effective and widely used catalysts to mediate C–H bond amination.\textsuperscript{10-13} For the C–N bond formation reaction from rhodium nitrane, concerted insertion via a singlet nitrane and radical recombination via a triplet nitrane are alternative pathways.\textsuperscript{14} Du Bois and co-workers have done many researches on dirhodium catalysts and found some of them, including Rh\textsubscript{2}(OAc)\textsubscript{4} and Rh\textsubscript{2}(esp)\textsubscript{2}, exhibit the catalysis with a concerted but asynchronous mechanism, just like Rh-catalyzed carbene insertion.\textsuperscript{15, 16} Our group and co-workers also reported the intramolecular amidation of carbamates prefers the singlet pathway rather than the triplet pathway according to the free energy of activation.\textsuperscript{17} And recently we have published further study on dirhodium mediated C–H bond amination mechanism and found the reaction takes place via triplet mecheanism.\textsuperscript{18, 19} However, the mechanisms of rhodium-catalyzed amination would be system-dependent and thus detailed explorations on various reactions should be paid attention to.

Recently, Du Bois and co-workers\textsuperscript{2, 8, 12, 13, 20-22} designed and synthesized a new catalyst Rh\textsubscript{2}(esp)\textsubscript{2}, a tethered dicarboxylate-derived complex for intramolecular C–H oxidation and this catalyst performed excellent C–H amination with low catalyst loading.\textsuperscript{23, 24} The chelating dicarboxylate ligand groups are resistant to ligand exchange and would shroud the dirhodium core even in oxidative conditions.\textsuperscript{20} Therefore, the unusual kinetic stability override other dirhodium tetracarboxylate complexes possibly has contributed to the high-efficiency of Rh\textsubscript{2}(esp)\textsubscript{2}.\textsuperscript{25} Though the use of Rh\textsubscript{2}(esp)\textsubscript{2} could
be converse C–H bond into C–N bond via amination effectively, the condensation
between the substrate and terminal oxidant is obviously limited for product purifying. The C–H oxidation (sulfamate, carbamate, sulfamide and guanidine, etc.) mediated by rhodium catalysts usually occur under oxidative conditions and require strong electron-withdrawing groups on the nitrene. These limitations are not favored for expanding the scale of potential substrates and the utility of the catalysis reaction. Recently, a new type of reactions with azides has been used for the synthesis of nitrogen heterocycles via intramolecular addition. Reactions with azides involve no oxidants and would release the only byproduct N₂ gas which is environmentally friendly.

Driver and co-workers have reported the preparation of indoles and carbazoles that involves the catalytic decomposition of aryl azides followed by sp² C–H bond amination reactions. On the basis of the sp² C–H bond amination reactions, Driver and co-workers reported a new type of reactions catalyzed by Rh₂(esp)₂ using aryl azides as the N-atom source and it has a high conversion up to 99% (see Scheme 1). These reactions could occur with aryl azides containing para-electron-releasing, -neutral, or –withdrawing groups rather than require an electron-withdrawing group on the nitrogen. Rh₂(esp)₂ is an unusual dirhodium catalyst that is clear of rapid carboxylate ligand exchange, namely, it exhibits high kinetic stability in reaction solution. In the metal catalyzed C–N bond formation with aryl azides, N₂ gas will be firstly released to form metal nitrene complex which undergoes subsequent nitrene transfer/insertion reaction. According to the related experiments, the diastereoisomers of products (dr 50:50) and intramolecular kinetic isotope effect (KIE) of 6.7 corroborate a stepwise C–H bond amination and the rate-determining step is the extrusion of N₂. Therefore, it is necessary to further analyze and understand Rh₂(esp)₂ mediated C–H bond amination reactions. In this paper, we report a density functional theory (DFT) computational study of the mechanisms of this dirhodium catalyzed intramolecular aliphatic C–H bond amination of aryl azides. Also, the catalysis nature
differences or similarities between Rh$_2$(esp)$_2$ (I in Figure 1) and other dirhodium catalysts with bridging tetracarboxylate ligand groups (Rh$_2$L$_4$) will be discussed.

**Scheme 1.** Rh$_2$(esp)$_2$-Catalyzed Intramolecular Aliphatic C–H Bond Amination with Aryl Azides*

* Yield as isolated after silica gel chromatography: II 84%.39

2. **Computational Details**

Theoretical calculations were performed utilizing Gaussian 09 program.43 All geometries are fully optimized using DFT method BPW91 with the 6-31G(d) basis sets for C, H, O and N atoms while the 1997 Stuttgart relativistic small-core effective core-potential [Stuttgart RSC 1997 ECP]$^{44, 45}$ for Rh atoms, augmented with a 4f-function ($\xi(Rh) = 1.350$),46 which are donated as BPW91/BS1. BPW91 is a reliable method for metal nitrene mediated reactions, especially in describing the singlet–triplet energy difference ($E_{st}$) of dirhodium–nitrene complexes.17-19, 47-49 Intrinsic reaction coordinate (IRC)$^{50}$ calculations were done to confirm the reactant and product connecting the corresponding transition states. The energies were calculated at 393.15 K and 1 atm according to the experiment conditions.39 Natural bond orbital (NBO) analysis$^{51, 52}$ and Kohn-Sham frontier orbital analysis were done with the calculated level BPW91/BS1. Solvent effects (in toluene) were estimated using the polarizable continuum model (PCM) with radii and non-electrostatic terms for Truhlar and coworkers' SMD salvation model$^{53}$ with a larger basis set 6-311++G(d,p) for C, H, O and N atoms and the same Stuttgart basis sets as BS1 (RSCf) for Rh atoms, which are donated as BS2. Minimum-energy crossing points (MECPs) were located utilizing the MECP program developed by Harvey and co-workers.$^{54}$
In order to obtain accurate thermochemistry predictions and descriptions of weak interaction, we performed geometry optimization and energy calculations of selected important intermediates and transition states at the M06L (the pure functional of Truhlar and Zhao)/BS1 level of theory. Also, the composite basis sets (denoted as BS3) consisting of the basis set 6-311G(d,p) for C, H, O and N atoms and the same Stuttgart basis sets as BS1 for Rh atoms were also employed. These calculations have shown that the BPW91/BS1, M06L/BS1 and BPW91/BS3 optimized geometries are very close, while relative energies can vary by a few kcal/mol with solvent effects at BPW91/BS2 or M06L/BS2 included (see ESI), and they give the same conclusions. Therefore, below, in sake of consistency, we discuss the BPW91/BS1 calculated results unless otherwise specified.

3. Results and Discussions

Figure 1. Catalysts in the calculations of the intramolecular C–H bond amination with aryl azides: I = Rh$_2$(esp)$_2$, II = Rh$_2$(OCHO)$_4$.

Based on the survey of catalysts in the related experiments, the reaction yields in the presence of Rh$_2$(esp)$_2$, Rh$_2$(OAc)$_4$, Rh$_2$(O$_2$CC$_7$H$_{15}$)$_4$ and Rh$_2$(O$_2$CC$_3$F$_7$)$_4$ are 75%, 0%, 35% and 20%, respectively. As reported in previous literature, the tetracarboxylate
ligand groups are sensitive to ligand exchange which would inhibit the cycled catalysis of C−H bond amination.\textsuperscript{5, 25} However, this ligand exchange event is assumed to be inoperative in order to explore other factors that influence catalytic reactivity and reaction mechanism. To investigate the mechanistic similarities and differences between Rh\textsubscript{2}(esp\textsubscript{2}) (I in Figure 1) and the general dirhodium catalysts with bridging tetracarboxylate ligand (Rh\textsubscript{2}L\textsubscript{4}), in this paper, a model compound Rh\textsubscript{2}(OCHO)\textsubscript{4} (II in Figure 1) was used to model Rh\textsubscript{2}L\textsubscript{4}. Figure 1 shows the computed geometries of the catalysts I and II. Comparing the key bond lengths such as Rh−Rh and Rh−O bond distances in I and II, they have almost the same values, which indicates these two catalysts have a similar framework and bimetallic interactions.

3.1 Proposed Mechanism of dirhodium Catalyzed C−H Bond Amination with Aryl Azide 1

Scheme 2. Proposed Mechanisms of Rh\textsubscript{2}L\textsubscript{4} Promoted Intramolecular Aliphatic C−H Bond Amination with Aryl Azide 1

Step 1: extrusion of N\textsubscript{2}

Taking o-tert-butylaryl azide 1 in Scheme 1 as a sample substrate, Scheme 2 shows the proposed mechanisms of dirhodium complexes (Rh\textsubscript{2}L\textsubscript{4}) promoted intramolecular aliphatic C−H bond amination with aryl azides. In Scheme 2, [Rh\textsubscript{2}] denotes the
dirhodium paddlewheel catalysts. According to the investigations of related reactions mentioned above, the metal catalyst and the azides combine together via Rh–N bonding before N2 release.40 The intramolecular aliphatic C–H bond amination reaction might involve two steps (Scheme 2): i) the first step is extrusion of nitrogen gas from the precursor complex of the metal catalyst and substrate, ii) the second step is conversion of C–H bond into C–N bond, which might take place through singlet or triplet pathway. The concerted singlet pathway could form C–N and N–H bond spontaneously through C–H bond nitrogen insertion while the stepwise triplet pathway would go through H-abstraction followed by diradical recombination or intersystem crossing (ISC).47 Both the singlet and triplet pathways lead to the final product indolines and the catalyst is regenerated.

Scheme 3. Depicted are labels of the selected atoms in the reaction complexes. O1 and O2 refer to the oxygen atoms coordinated to Rh1 and Rh2 centers, respectively.

3.2. Rh2(esp)2 catalyzed amination of aryl azide 1.

As mentioned above, the purpose of this paper is to elucidate the reaction mechanism of dirhodium complex, Rh2(esp)2 and Rh2(tetracarboxylate)4 included, catalyzed amination which includes two basic steps: i) extrusion of N2, ii) nitrene insertion. In this section, the reaction with Rh2(esp)2 (I) as the catalyst is computed and compared with the case for Rh2(OCHO)4 (II). It should be mentioned that the computational data for Rh2(OCHO)4 are majorly presented in ESI. For clear descriptions, labels of the atoms in the active sites of reaction complexes are given in Scheme 3.
3.2.1. Metal nitrene formation from Rh$_2$(esp)$_2$ and aryl azide 1.

As reported in related investigations about metal nitrene catalyzed C–H bond
amination with azides, coordination of the metal core could be towards either the $\alpha$- or
$\gamma$-nitrogen of the azides. However, the $\gamma$-coordination complex may not directly
release nitrogen gas but transform into the $\alpha$- coordination complex which could trigger
amination reactions (see Figure S1 in ESI).

Figure 2. Possible coordination modes of Rh$_2$(esp)$_2$ and aryl azides.

The two rhodium centers in Rh$_2$(esp)$_2$ are in equal positions. As shown in Figure 2,
the centro-symmetric geometry of Rh$_2$(esp)$_2$ can provide four positions to recognize and
bond with the substrate aryl azide molecule. In order to diminish steric effects, the aryl
group and the tert-butyl group should be located near two out of the four “caves”
divided by the tethered ligands. And from the structure of the catalyst-substrate binding
complex in Figure 2a, the aryl azide molecule rotates along Rh–N bond anticlockwise
and forms the other three structures (Figures 2b, 2c and 2d). In Figures 2a and 2b, both
the aryl group and the tert-butyl group are positioned over the less crowded caves. In
Figures 2c and 2d, either the aryl group or the tert-butyl group is over the crowded cave
with a phenyl group pointing inside. On the other hand, the azide moiety (–N=N=N)
may be repulsed by the ligand, especially for the structure in Figure 2b.

The four coordination complexes of aryl azide 1 and Rh$_2$(esp)$_2$ shown in Figure 2 lead
to four pathways of metal nitrene formation (see Figure 3). Ac has almost the same
energy as Aa while Ab and Ad are 2.3 and 1.7 kcal/mol higher in free energy than Aa, respectively. The higher free energies might be mainly ascribed to the steric repulsion between the ligand of I and the tert-butyl group or the azide moiety of I. However, the energy differences are still acceptable and these four isomers could be interchanged with each other. Therefore, only the reaction from Aa is discussed in the present paper.

Figure 3. Reaction profiles of metal nitrenoid formation from Rh$_2$(esp)$_2$ and I. The relative Gibbs free energies and thermal energies are presented with Aa, Aa-TS and Ba as the zero points, respectively.

With the coordination between the Rh-atom and $\alpha$-N-atom in Aa, the atomic charge on $\alpha$-N-atom decreases which could assist the N$_2$ loss. The N–N bond cleavage via the transition state Aa-TS requires a barrier of 19.2 kcal/mol. The elimination of nitrogen gas is an exothermic process that produces the singlet metal nitrene $^5$Ba. The structures located in the reaction pathway from Aa are shown in Figure 4. The coordination of Rh1–N1 (2.31 Å) in the reactant species Aa is relatively weak while it obviously becomes stronger in the transition state Aa-TS (Rh1–N1, 2.07 Å) with the elongation of N1–N2 bond distance (from 1.26 Å in Aa to 1.63 Å in Aa-TS). From the NBO charge
analysis, the rhodium centers would help to stabilize the negative-charged nitrogen atom N1 through the reaction process (see Figure 4).

**Figure 4.** Shown are selected optimized structures in the reaction of Rh₂(esp)₂ (I) and 1.
The tethered dicarboxylate ligands (esp) are simplified. Selected NBO charges are in parentheses and bond distances are in angstrom.

When comparing the mechanisms of nitrene formation mediated by Rh₂(esp)₂ (I) and Rh₂(OCHO)₄ (II) (see ESI), the whole reaction profiles of N₂ extrusion shown in Figures 3 and S1 exhibit identical patterns for the complete reaction pathway. What’s more, the geometric parameters in these two reaction systems are comparative in spite of a few differences. For instance, the Rh1–Rh2 bond is slightly longer in the reaction process of Rh₂(OCHO)₄ and 1 (Figure S3) than those of Rh₂(esp)₂ and 1 (Figure 4), which is probably due to the compacting enhancement from the “esp” ligand in Rh₂(esp)₂. From the aspect of energy, the activation energy of Aa-TS (19.2 kcal/mol) is
slightly lower than that of A-TS (20.0 kcal/mol). This could be ascribed to the weak electron-donating esp ligands.

3.2.2. Metal nitrene mediated amination in Ba.

Following the metal nitrene formation, the resulted active intermediates would undergo subsequent nitrene insertion/C–H bond amination. In consideration of the similar reaction mechanisms for the metal nitrenes Ba–d (Figure S5), only the reactions from Ba (see Figure 5) and the species on these reaction profiles (Figure 4) will be further discussed.

Figure 5. Reaction profiles of C–H bond amination mediated by Ba. Spin densities of Rh1-Rh2, N1, C1, Ph(C2–C7) are in parentheses.

As discussed above, the singlet metal nitrene $^S$Ba is formed in the extrusion of N$_2$ from Aa (Figure 3). However, the existence of a minimum energy crossing point (MECP1) between the singlet and the triplet profiles allows the formation of the triplet metal nitrene $^T$Ba. At the minimum energy crossing point MECP1 located before the reactants, the singlet nitrenoid and triplet one are quite close in energy. It should be mentioned that the relative free energies of MECPs are estimated taking the salvation effects into account. Thus, they represent the most possible location areas rather than the accurate crossing points (see Figure S6 in ESI). The triplet metal nitrene $^T$Ba is
more stable than the singlet nitrene $^S$Ba by 3.7 kcal/mol. This is different from the
previously reported conclusion obtained from similar reaction systems involving Rh$_2$L$_4$
that the ground triplet state of metal nitrene is estimated to be about 2 kcal/mol higher
than the singlet state and thus they could coexist with each other.$^{17}$ Comparing the
structures of the singlet and triplet metal nitrenes, $^S$Ba and $^T$Ba, not only the Rh1–Rh2
and Rh1–N1 bond distances are almost the same, but the dihedral angle $\chi$(O1, Rh1, N1, C2) is also comparable in $^T$Ba (51°) with that in $^S$Ba (48°). On the other hand, the spin
densities for Rh1, Rh2, N1 atoms and the phenyl ring (C2–C7) in $^T$Ba are 0.35, 0.18,
1.02 and 0.43, respectively (Figure 5 and Table S2). This means the two unpaired
electrons mainly reside on the Rh$_2$ and N1-Ph(C2–C7) moiety.

For the dirhodium reaction complex, the strong d-p orbital interactions between the
Rh$_2^{II,II}$ center and N1 could stabilize the radical species.$^{19}$ This would increase the
reaction barrier for the H-abstraction process and could possibly further improve the
reaction selectivity. This type of metal-metal bonded systems has been extensively
discussed in literature and they are suggested to exhibit exceptional efficiency in C–H
functionalization rather than mono-metal catalysts. The dirhodium d$^{14}$ electronic
configuration were highly effective at metal to ligand $\pi$ back-bonding and the filled $\pi^*$
orbital of Rh$_2$L$_4$ could donate electron-pair,$^{57}$ e.g. the $\pi$ and $\pi$(nb) bonding shown in
Figure S7. This indicates distinctive metal-metal synergism which endues a metal-metal
complex reactivity different from a mono-nuclear metal complex.$^{58}$ Furthermore, the
unique catalysis is attributed to the three-center/four-electron (3c/4e) bonds in
metal-metal bonded intermediates such as carbene and nitrene intermediates
Rh–Rh–C(or N) which is suggested to be described as superelectrophilic by virtue of
3c/4e Rh–Rh–C(or N) s and p bonds.$^{59}$

In the singlet pathway of C–H bond amination, the C–H bond cleavage, N–H and
C–N bond formation through the transition state $^S$TS1a requires an energy barrier of
13.5 kcal/mol relative to $^T$Ba. For Rh$_2$(OCHO)$_4$, the barrier is 12.0 kcal/mol relative to
$^T$B, respectively (Figure S2 in ESI). The vibration of the unique imaginary frequency
(-659.3 cm⁻¹) in $^{8}\text{TS1a}$ shows an evident H-abstraction process accompanied with an initial C–N bond formation. According to the IRC calculation (see Figure S9 in ESI), the concerted singlet pathway exhibits asynchronous characteristic that the hydride-like H1 is transferred prior to the formation of N1–C1 bond. This feature can be seen from the angle $\alpha(N1,H1,C1) = 133^\circ$, and the charge change of H-donor C1(sp³) from -0.69 for $^{8}\text{Ba}$ to -0.46 for $^{8}\text{TS1a}$. However, the weak electron-donating catalyst Rh₂(esp)₂ cannot stabilize a potential intermediate followed by H-abstraction step featuring a carbocation and a negative nitrogen center. Therefore, no intermediates or transition states are observed on the way from $^{8}\text{TS1a}$ to the final product $^{8}\text{Ca}$. Our previous study has proposed the nature of the singlet pathway is a stepwise process and the fast combination of a carbocation and an electron-sufficient nitrogen center is barrier-free or require an identifiable energy barrier.¹⁸

In the triplet pathway, two steps are involved: H-abstraction and C–N bond formation. In the H-abstraction step, the activation energy of the transition state $^{7}\text{TS1a}$ is 10.8 kcal/mol. For Rh₂(OCHO)₄, the barrier is 9.1 kcal/mol relative to $^{7}\text{B}$ (Figure S2 in ESI). The spin density for H-donor (C1) increases significantly from 0.02 in $^{7}\text{Ba}$ to 0.62 in the triplet transition state $^{7}\text{TS1a}$ while the spin density for N1 atom decreases from 1.02 to 0.67. The vibration of the unique imaginary frequency (-1136.1 cm⁻¹) in $^{7}\text{TS1a}$ and the IRC calculation for $^{7}\text{TS1a}$ (see Figure S10 in ESI) shows this is a complete hydrogen-migration process and no signs of C–N bond formation. This C–H homolytic cleavage mediated by Rh₂(esp)₂ results in the intermediate $^{7}\text{IM1a}$. The spin densities for Rh1, Rh2, N1, C1 atoms and the phenyl ring (C2–C7) in $^{7}\text{IM1a}$ are 0.24, 0.12, 0.42, 0.98 and 0.33, respectively. It means the two unpaired electrons mainly reside on the C1, Rh₂ core and N1-Ph(C2–C7) moiety. The intermediate $^{7}\text{IM1a}$ on the triplet reaction profile is close to the triplet transition state $^{7}\text{TS1a}$ in energy. This could be attributed to the relatively small geometry change from the transition state to the corresponding reactive intermediate. The diradical intermediate $^{7}\text{IM1a}$ rebound in a subsequent step via the radical coupling transition state $^{7}\text{TS2a}$ requiring a high barrier (from $^{7}\text{Ba}$ to
$^{\text{TS2a}}$, 23.5 kcal/mol; from $^{\text{IM1a}}$ to $^{\text{TS2a}}$, 14.2 kcal/mol). For Rh$_2$(OCHO)$_4$, the barrier of the radical coupling is 23.4 kcal/mol relative to $^{\text{B}}$ and 15.4 kcal/mol relative to $^{\text{IM1}}$ (Figure S2 in ESI). As we previously reported, this type of diradical recombination step requires an identifiable energy barrier (~15 kcal/mol). However, this radical recombination may not be observed, because there exists a spin crossing via MECP2 between the triplet and singlet energy profiles. After spin crossover to the singlet pathway, the final product $^{\text{Ca}}$ is reached. Therefore, the overall energy barrier of the triplet pathway is determined by the relative energy of MECP2. It should be mentioned that our previous studies on the reactions of dirhodium tetracarboxylate (Rh$_2$(formate)$_4$ and Rh$_2$(OAc)$_4$) catalyzed nitrene insertion into C–H bonds generally suggest the closed-shell singlet transition state is lower in energy than the open-shell triplet transition state in the H-abstraction step. Also, we have done calculations of MECPs in amination reactions catalyzed by dirhodium tetracarboxylate and basically MECP is located on the way from the triplet reactant complex to the triplet H-abstraction transition state which suggests a spin crossover to the closed-shell singlet energy profile.

In order to understand the triplet pathway in depth, the Mulliken spin distribution along the reaction coordinate for the triplet states is presented in Figure 6. In the H-abstraction step, the spin density on the Rh$_2$ center in the triplet reactant complex $^{\text{Ba}}$ is significantly less than 1.0. With the spin on N1, Rh$_2$, Ph moieties partially transferred to C1 via $^{\text{TS1a}}$, the spin densities on the Rh$_2$ center decreases further in $^{\text{IM1a}}$. In the subsequent C–N bond formation step, the spin density on the Rh$_2$ center increases to larger than 1.0 in $^{\text{TS2a}}$ and the triplet product complex $^{\text{Ca}}$ holds the major spin density on the Rh$_2$ center. As we previously reported, the Rh$_2^{\text{II,II}}$ dimer in $^{\text{TS2a}}$ would be oxidized to a mixed-valent Rh$_2^{\text{II,III}}$ dimer and a NR radical. This spin-orbital coupling in the Rh$_2$ center forming C–N bond is an energy-consuming process.
Figure 6. Mulliken spin distribution along the reaction coordinate for the triplet states in reaction of Rh$_2$(esp)$_2$ and 1.

From the metal nitrenes $^t$S$^t$Ba to the transition states $^t$S$^t$TS1a, the Rh1–N1 bond elongates slightly and the charge of N1 atom becomes more negative (see Figure 4). It is worth noting that the dihedral angle $D$(O1, Rh1, N1, C2) is much smaller in $^t$TS1a (19°) than that in $^s$Ba (51°) but the values in $^t$TS1a (50°) and $^t$Ba (48°) are identical.

Comparing the singlet and triplet transition states, $^s$TS1a and $^t$TS1a, the distance of N1–H1 in $^t$TS1a is longer and C1–H1 shorter. As seen in the geometry of the final product-catalyst complex $^s$Ca, the distance of Rh1–N1 elongates to 2.25 Å which is close to that in Aa (2.31 Å); and Rh1 charge reduces to 0.43 which equals that in Aa.

It should be mentioned that the unstable triplet intermediate $^t$IM1a would possibly go through two alternative C–N formation pathways. One is direct recombination of diradical via $^t$TS2a which is discussed above. Another pathway is a N–H swing/diradical recombination process (see Figure S8 in ESI). Calculations show that these two pathways in the triplet mechanisms are competitive. Therefore, the N–H swing process could possibly lead to racemic products.
3.3. Key Mechanistic Features of Dirhodium Catalyzed C–H Bond Amination with Aryl Azides.

From results above, Rh$_2$(esp)$_2$ and Rh$_2$(OCHO)$_4$ (see ESI) catalyzed C–H amination majorly share an identical mechanism, including the PES pattern and the structure features of the reactants, transition states and products. The whole PES for the Rh$_2$(esp)$_2$ case is shown in Figure 7. The tethered ligands esp of Rh$_2$(esp)$_2$ would not obviously affect the amination reaction mechanism. Based on the experimental observations,$^{39}$ esp ligand can prevent oxidation in the reaction solution and protect the geometry of the dirhodium complex which increases the conversion of the catalytic reaction cycle. On the other hand, reactions with mononuclear catalysts known to catalyze N-atom-transfer reactions, such as [Rh(cod)$_2$]SO$_3$CF$_3$, [Rh(PPh$_3$_)$_3$]Cl and [Rh(cod)OMe]$_2$ (cod =1,5-cyclooctadiene), are unsuccessful in producing indoline product.$^{39}$ And as we discussed above, the strong d-p orbital interactions between the Rh$_2$$^{II,II}$ center and nitrene N could stabilize the radical species and could possibly further enhance the
reaction selectivity. Therefore, the combination of Rh$_2$^{II,II} dimer and ligands as “security
guard” is the key to success of the aliphatic C–H amination involved in this paper.

4. Conclusions

In conclusion, dirhodium catalysts Rh$_2$L$_m$, such as Rh$_2$(esp)$_2$ and Rh$_2$(OCHO)$_4$, mediated aliphatic C–H bond amination of aryl azides show a general mechanism. Firstly, the dirhodium complex coordinates with the substrate leading to the extrusion of nitrogen gas to produce metal nitrene. This is the rate-determining step and significantly exothermic. A minimum energy crossing point is located in this step and leads to the singlet metal nitrene or the triplet metal nitrene. Secondly, the dirhodium metal nitrene forms C–N bond via intramolecular nitrene insertion to C–H bond through two possible reaction pathways. One is the singlet concerted asynchronous pathway which results in direct insertion of metal nitrene into C–H bond. Another one is the triplet stepwise pathway in which hydrogen atom transfer followed by diradical combination. However, calculations show the diradical recombination requires a relatively high barrier more than 20 kcal/mol. There is a minimum energy crossing point located between the singlet and triplet pathways which leads the reaction towards the singlet pathway. The tethered ligands joined to the rhodium centers of Rh$_2$(esp)$_2$ give aid to stabilize the substrate-catalyst complex and play a role as “security guard” to protect the dirhodium core, but they do not indicate significant influence on the reaction mechanisms of metal nitrene catalyzed amination of aliphatic C–H bond of aryl azides.

Acknowledgements

The authors gratefully acknowledge the National Natural Science Foundation of China (Grant Nos. 21173273, 21203256, 21373277, 21473261, 21573292) and the Guangdong Provincial Natural Science Foundation (Nos. 2015A030313185, 2015A030306027). This work was partially sponsored by the high-performance grid computing platform of
Sun Yat-sen University and supported in part by the Guangdong Province Key Laboratory of Computational Science and the Guangdong Province Computational Science Innovative Research Team.

References


16 59 J. F. Berry, *Dalton Trans.*, 2012, **41**, 700-713.
An in-depth DFT study on the dirhodium-catalyzed intramolecular aliphatic C–H bond amination of aryl azides considering ISC.