

Article

A DFT Study on Sc-Catalyzed Diastereoselective Cyclization of 2-Picoline with 1,5-Hexadiene: Mechanism and Origins of Regio- and Stereoselectivity

 Guangli Zhou ¹ , Shuangxin Zhai ¹, Xia Leng ¹, Yunzhi Li ¹, Qiying Xia ^{1,*} and Yi Luo ^{2,3,*} 
¹ School of Chemistry and Chemical Engineering, Linyi University, Linyi 276000, China; zhouguangli@lyu.edu.cn (G.Z.); zhaishuangxin0626@163.com (S.Z.); lengxia@lyu.edu.cn (X.L.); liyunzhi@lyu.edu.cn (Y.L.)

² State Key Laboratory of Fine Chemicals, School of Chemical Engineering, Dalian University of Technology, Dalian 116024, China

³ PetroChina Petrochemical Research Institute, Beijing 102206, China

* Correspondence: xiaqiying@lyu.edu.cn (Q.X.); luoyi10@petrochina.com.cn (Y.L.)

Abstract

Density functional theory (DFT) calculations elucidate the mechanism of diastereoselective cyclization of 2-picoline with 1,5-hexadiene catalyzed by a cationic half-sandwich scandium complex. The catalytic cycle proceeds through four key stages: formation of active species, initial alkene insertion, *cis*-selective cyclization, and protonation. Central to the mechanism is the dual role of 2-picoline, which initially coordinates as a supporting ligand to facilitate C–H activation and regioselective 1,2-insertion but must dissociate to enable stereocontrol. The mono(2-picoline)-coordinated complex **C3** is identified as the thermodynamically favored active species. C–H activation reactivity follows the trend: *ortho*-C(sp²)–H (2-picoline-free) > *ortho*-C(sp²)–H (2-picoline-coordinated) > benzylic C(sp³)–H (2-picoline-free) > benzylic C(sp³)–H (2-picoline-coordinated), a preference governed by a wider C_α–Sc–C_{α'} angle and shorter Sc⋯X (X = C_α, C_{α'}, H) distances that enhance scandium–substrate interaction. Subsequent 1,5-hexadiene insertion proceeds with high 1,2-regioselectivity through a picoline-assisted pathway. The stereoselectivity-determining step reveals a mechanistic dichotomy: while picoline coordination is essential for initial activation, its dissociation is required for intramolecular cyclization. This ligand displacement avoids prohibitive steric repulsion in the transition state, directing the reaction exclusively toward the *cis*-cyclized product. The cycle concludes with a sterically accessible mono-coordinated protonation. This work establishes a “ligand-enabled then ligand-displaced” mechanism, highlighting dynamic substrate coordination as a critical design principle for achieving high selectivity in rare-earth-catalyzed C–H functionalization.

Keywords: rare-earth metal complex; density functional theory; C–H alkylation; reaction mechanism



Academic Editors: Francis Verpoort and Jean Pierre Djukic

Received: 26 November 2025

Revised: 27 December 2025

Accepted: 14 January 2026

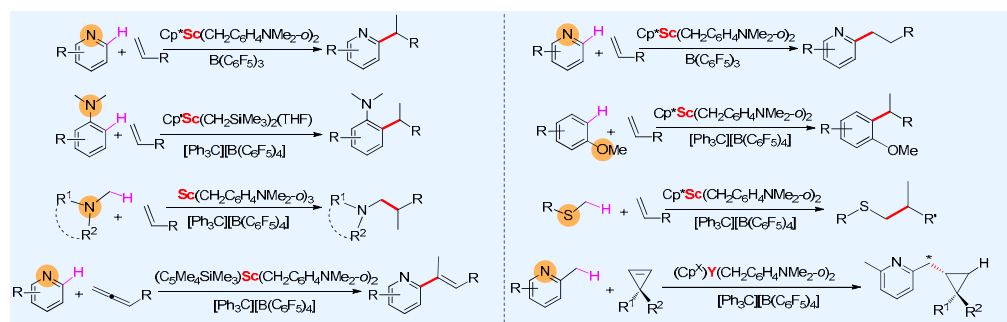
Published: 16 January 2026

Copyright: © 2026 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the [Creative Commons Attribution \(CC BY\)](https://creativecommons.org/licenses/by/4.0/) license.

1. Introduction

Cationic rare-earth metal complexes demonstrate high activity and stereoselectivity in the functionalization [1–7] of olefins with a variety of heteroatom-containing substrates (e.g., pyridines [8–19], anilines [20–27], amines [28–30] aldimines [31–39], quinolines [40–43], imidazoles [44,45], sulfides [46–48], anisoles [49–52]) due to their distinctive chemical properties (Scheme 1). Among these substrates, pyridine has been the

most extensively investigated due to its prevalence in functional molecules. The development of efficient synthetic pathways for pyridine-containing compounds is of considerable importance, as the pyridine motif is a key heterocyclic unit present in numerous natural products, pharmaceuticals, bioactive molecules, functional materials, and organic ligands. In this regard, direct catalytic C–H alkylation of pyridines with olefins represents a particularly attractive, 100% atom-economical route to valuable alkylated derivatives. While significant progress has been made in reactions with monoolefins like ethylene and styrene, the engagement of more complex substrates, such as non-conjugated dienes, remains less explored mechanistically [53,54].

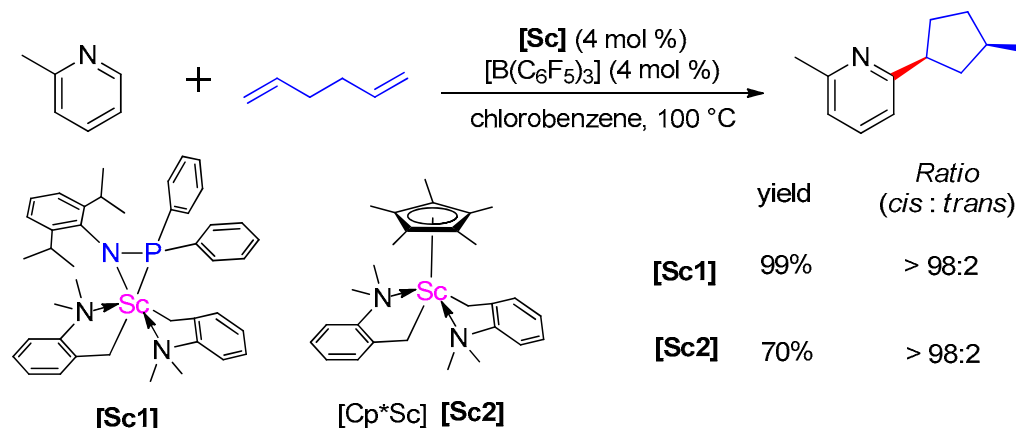


Scheme 1. Representative examples of rare-earth-catalyzed C–H functionalization of heteroatom-containing substrates with olefins by cationic half-sandwich rare-earth alkyl complexes.

Catalytic cyclizations of dienes offer efficient pathways for constructing cyclic frameworks, yet controlling stereochemistry, particularly toward the kinetically disfavored *cis* isomers from 1,5-dienes remains a significant synthetic challenge, as conventional post-transition-metal catalysts predominantly deliver the more thermodynamically stable *trans*-configured products [55–66]. In contrast to this context, rare-earth catalysts have emerged as versatile platforms capable of overriding inherent stereochemical preferences. For instance, Hou and co-workers have systematically demonstrated the stereochemical versatility of half-sandwich rare-earth complexes, employing scandium catalysts to achieve *trans*-selective [3+2] annulations via β' -allylic C–H activation, and utilizing cerium or yttrium catalysts to deliver *cis*-selective [4+2] annulations via γ -allylic or benzylic C–H activation [36,67]. The same group reported the first remarkable scandium-catalyzed diastereoselective cyclization of 1,5-hexadiene with 2-picoline that defies conventional selectivity patterns (Scheme 2) [68]. While their novel mono(phosphinoamido) (NP) ligand system achieved an excellent 99% yield with high *cis* selectivity (*cis/trans* > 98:2), the more conventional half-sandwich scandium alkyl catalyst (Cp^*) also successfully delivered the C–H addition/cyclization product in 70% yield while maintaining comparably high *cis* selectivity (*cis/trans* > 98:2). For our detailed computational mechanistic investigation, we strategically elected to employ the Cp -ligated system as our model. This decision is primarily motivated by the need to circumvent the significant conformational complexity introduced by the flexible, non-symmetric NP ligand. The high symmetry and rigid coordination sphere of the Cp^* (C_5Me_5) scaffold present a well-defined catalytic center, drastically reducing the number of low-energy conformers and enabling a more tractable and focused analysis of the core reaction pathway.

However, several fundamental questions about this transformation remain unanswered by experiment alone. What is the true catalytically active species? How does the number of coordinated 2-picoline molecules influence the reaction trajectory? Why does the reaction favor diastereoselective cyclization over simple mono-alkylation, and what is the electronic and steric origin of the overwhelming preference for the *cis* product? In particular, the role of the 2-picoline substrate itself, whether it acts merely as a reactant

or also as a critical coordinating ligand that modulates the catalyst's behavior, is a key open question.



Scheme 2. The *cis*-selective cyclization of 1,5-hexadiene with the *ortho*-C(sp²)-H bond of 2-picoline catalyzed by the [Sc]/B(C₆F₅)₃ combination.

Herein, we report a comprehensive DFT study to address these questions. Our investigation goes beyond mapping the energy profile. It aims to decipher the nuanced factors that control this unique selectivity. We identify a “ligand-enabled then ligand-displaced” mechanism, wherein 2-picoline coordination is essential to initiate the reaction, but its subsequent dissociation is imperative to achieve the high diastereoselectivity. This work not only refines the mechanistic picture of rare earth-catalyzed C–H functionalization with dienes, but also highlights the dynamic role of substrate coordination as a versatile design principle for selective catalysis.

2. Results and Discussion

Generation of Active Catalytic Species. The cationic scandium monoalkyl species **1** is generated via cationization of the rare-earth dialkyl precursor (C₅Me₅)Sc(CH₂C₆H₄NMe₂-*o*)₂ with one equivalent of [Ph₃C][B(C₆F₅)₄]. As depicted in Figure 1, two potential C–H bonds in 2-picoline (**a**) can be activated under the influence of the directing group, viz. *ortho*-C(sp²)-H and benzylic C(sp³)-H. The reaction initiates with coordination of 2-picoline to the Sc center in **1**, forming the more stable π-complex **A1**, which lies 12.3 kcal/mol (‡ = transition state) lower in energy. Subsequently, the π-complex **A1** then undergoes σ-bond metathesis (σ-BM) via transition state **TS1a** (path a), with a barrier of 23.7 kcal/mol, leading to the Sc-η²-picolyl species **B1** accompanied by a coordinated *o*-Me₂NC₆H₄Me (**b**). Dissociation of **b** from **B1** yields the proposed naked cationic scandium species **C1**, featuring a three-membered metallacycle. This step is endergonic by 6.2 kcal/mol. Alternatively, coordination of 2-picoline to species **1** can also form the thermodynamically stable adduct **A2** (ΔG = −13.9 kcal/mol). From **A2**, benzylic C(sp³)-H activation proceeds via transition state **TS1b** (path b), affording Sc-η²-picolyl species **B2**. Subsequent release of **b** gives the cationic four-membered scandium species **C2**. The computed free energy barriers reveal a definitive kinetic preference for *ortho*-C(sp²)-H activation. The barrier for this process in the absence of an additional picoline ligand (**TS1a**) is 23.7 kcal/mol, which is 2.5 kcal/mol lower than the barrier for the corresponding benzylic C(sp³)-H activation via **TS1b** (26.2 kcal/mol).

Given the heteroatom affinity of the rare-earth metal center, we further examined *ortho*-C(sp²)-H and benzylic C(sp³)-H activation in the presence of an additional coordinating 2-picoline ligand. Upon coordination of a second 2-picoline molecule, C(sp²)-H activation proceeds along **A3** → **TS1c** → **B3** (path c), whereas the benzylic C(sp³)-H activation follows

A4 → **TS1d** → **B4** (path d). This preference is maintained upon coordination of a second 2-picoline molecule, with the *ortho*-C(sp²)-H activation barrier via **TS1c** (24.7 kcal/mol) being 4.7 kcal/mol lower than the benzylic activation via **TS1d** (29.4 kcal/mol). While the barrier for the naked cation pathway (**TS1a**) is marginally the lowest, the resultant species **C1** is thermodynamically unstable ($\Delta G = +6.2$ kcal/mol). In contrast, dissociation of the amine byproduct from **B3** yields the mono(2-picoline)-coordinated complex **C3**, which is both kinetically accessible and the thermodynamic minimum of the system ($\Delta G = -11.7$ kcal/mol). Since **C3** can also be generated by coordination of 2-picoline to **C1**, consequently, **C3** is identified as the catalytically competent active species. Such a favorable activation manner has also been reported in previous theoretical study on cationic systems [2e, 9d].

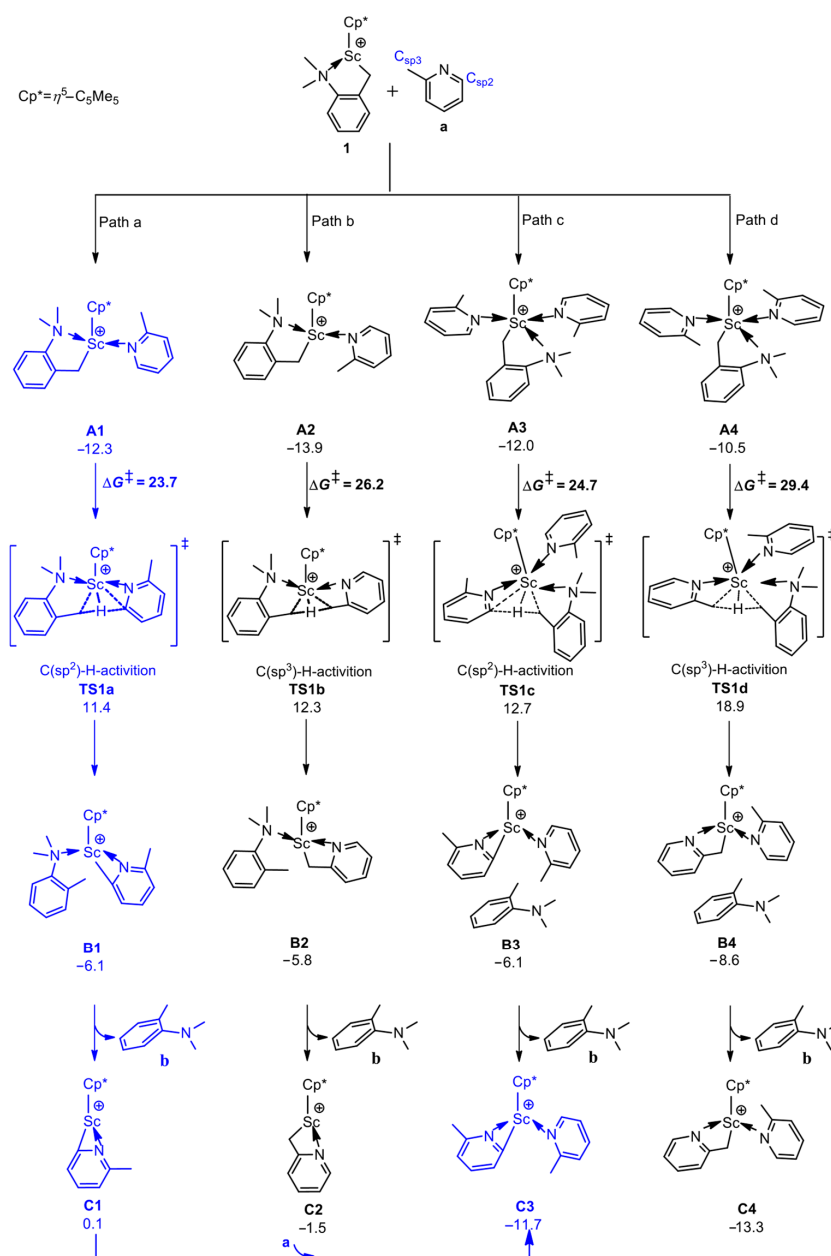


Figure 1. Free energy profile (kcal/mol) for the formation of potential active species C_i ($i = 1, 2, 3, 4$) via C-H activation of 2-picoline by cationic complex **1**.

Figure 2 provides a geometric and electronic rationale for the observed reactivity trends in C-H activation. The computed energy barriers for **TS1a–d** are markedly differ-

ent, with values of 23.7, 26.2, 24.7, and 29.2 kcal/mol, respectively. All transition states confirm a concerted σ -bond metathesis mechanism [69,70], characterized by their four-membered Sc-C $_{\alpha}$ -H-C $_{\alpha'}$ ring geometries, as supported by key interatomic distances: Sc-C $_{\alpha}$ (2.39~2.45 Å), Sc-C $_{\alpha'}$ (2.26~2.47 Å), C $_{\alpha}$ -H (1.40~1.46 Å), C $_{\alpha'}$ -H (1.43~1.46 Å), and Sc-H (1.86~1.92 Å). These parameters are consistent with geometries reported for scandium-alkyl-catalyzed reactions of 2-ethylpyridine or amines with olefins [71]. Further analysis revealed a strong negative correlation between the C $_{\alpha}$ -Sc-C $_{\alpha'}$ angle and the activation barrier: **TS1a** (76.1°, 23.7 kcal/mol) > **TS1c** (75.8°, 24.7 kcal/mol) > **TS1b** (72.1°, 26.2 kcal/mol) > **TS1d** (70.5°, 29.2 kcal/mol). The activation barrier decreases with an increasing C $_{\alpha}$ -Sc-C $_{\alpha'}$ angle. This angle was widest in the most favorable **TS1a** (76.1°) and most acute in the least favorable **TS1d** (70.5°). A wider angle facilitates shorter Sc...C/H distances, thereby enhancing the interaction between the metal center and the substrate. This geometric analysis was corroborated by Natural Bond Orbital (NBO) charge analysis. The natural population analysis (NPA) on the Sc center increases as follows: 1.20 (**TS1a**) < 1.29 (**TS1c**) < 1.32 (**TS1b**) < 1.43 (**TS1d**). This trend suggests that a reduced Lewis acidity at the metal center, likely due to enhanced charge transfer from the substrate and/or ligands, contributes to transition state stabilization. The increasing NBO charge on Sc from **TS1a** to **TS1d** reflects a greater degree of electron transfer from the substrate to the metal center during the C-H cleavage event. This enhanced charge transfer stabilizes the transition state, and the extent of this stabilization correlates with the lower barriers.

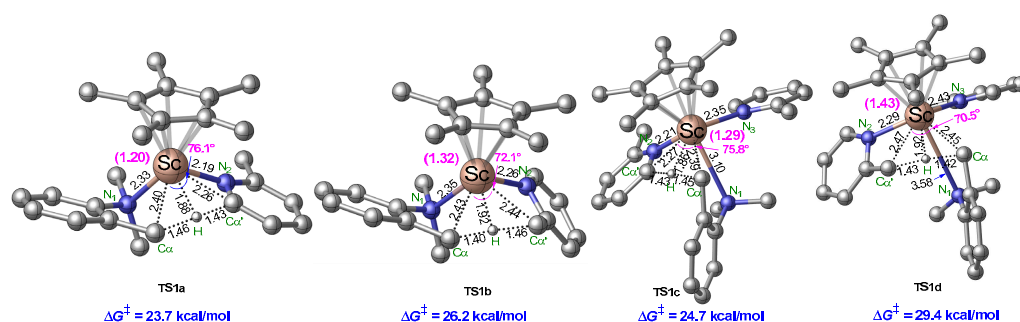


Figure 2. Optimized geometries of the key C-H activation transition states **TS1_i** (*i* = a, b, c, d). Selected distances are shown in Ångströms (Å) and angles in degrees (°). The natural bond orbital (NBO) charge on the Sc center is given in parentheses, with the corresponding free energy barrier ($\Delta G^{\ddagger}$, kcal/mol) listed below each structure. Hydrogen atoms, except for the transferring hydrogen, are omitted for clarity.

Regioselectivity and the Facilitating Role of 2-Picoline in Alkene Insertion. Having established **C3** as the active species, DFT investigations were conducted to elucidate the origin of regioselectivity in the insertion of 1,5-hexadiene (c). As illustrated in Figure 3, coordination of **c** to **C3** forms the π -complex **D1**. Subsequent 1,2-insertion of 1,5-hexadiene into the Sc-C bond proceeds via a conventional four-center transition state [72–76], **TS2a**, yielding the more stable ring-expanded five-membered metallocycle intermediate **E1**. This step exhibits a free energy barrier of 17.9 kcal/mol. In contrast, the alternative 2,1-insertion pathway forms intermediate **E2**. Obviously, the 2,1-insertion transition state **TS2b** presents a barrier of 19.5 kcal/mol, which is 1.6 kcal/mol higher than that for the 2,1-insertion via **TS2a** (17.9 kcal/mol). Furthermore, the precursor coordination complex **D2** is less stable than **D1** by 1.6 kcal/mol. The computational results demonstrate that 1,2-insertion is both kinetically and thermodynamically favored over 2,1-insertion. Given that coordination of the C=C double bond in 1,5-hexadiene might induce dissociation of 2-picoline from **C3**, pathways involving the picoline-dissociated scandium center were also examined for comparison. The results revealed that the initial C=C bond insertion via 1,2-insertion on the ligand-

free pathway (**TS2c**) had a free energy barrier of 29.3 kcal/mol, while the corresponding 2,1-insertion via **TS2d** exhibited a prohibitively high barrier of 31.0 kcal/mol. Notably, the energy barriers for insertion were significantly lower via the 2-picoline-coordinated transition states **TS2a** or **TS2b** compared to their picoline-dissociated counterparts **TS2c** or **TS2d**. Consequently, terminal C=C bond 1,2-insertion through the 2-picoline-coordinated mechanism (via **TS2a**) represents the most favorable pathway among the four options, producing the thermodynamically stable exothermic insertion intermediate **E1** ($\Delta G = -21.9$ kcal/mol). The geometric structures and NBO analyses of the four key transition states (**TS2a**, **TS2b**, **TS2c**, and **TS2d**) were examined. Their free energy barriers were 17.9, 19.5, 29.3, and 31.0 kcal/mol, respectively. The NPA charges on Sc (Q_{Sc}) were 1.32, 1.34, 1.59, and 1.64, respectively. This underscores the indispensable role of 2-picoline coordination in stabilizing the Lewis acidic metal center and enabling the alkene insertion step.

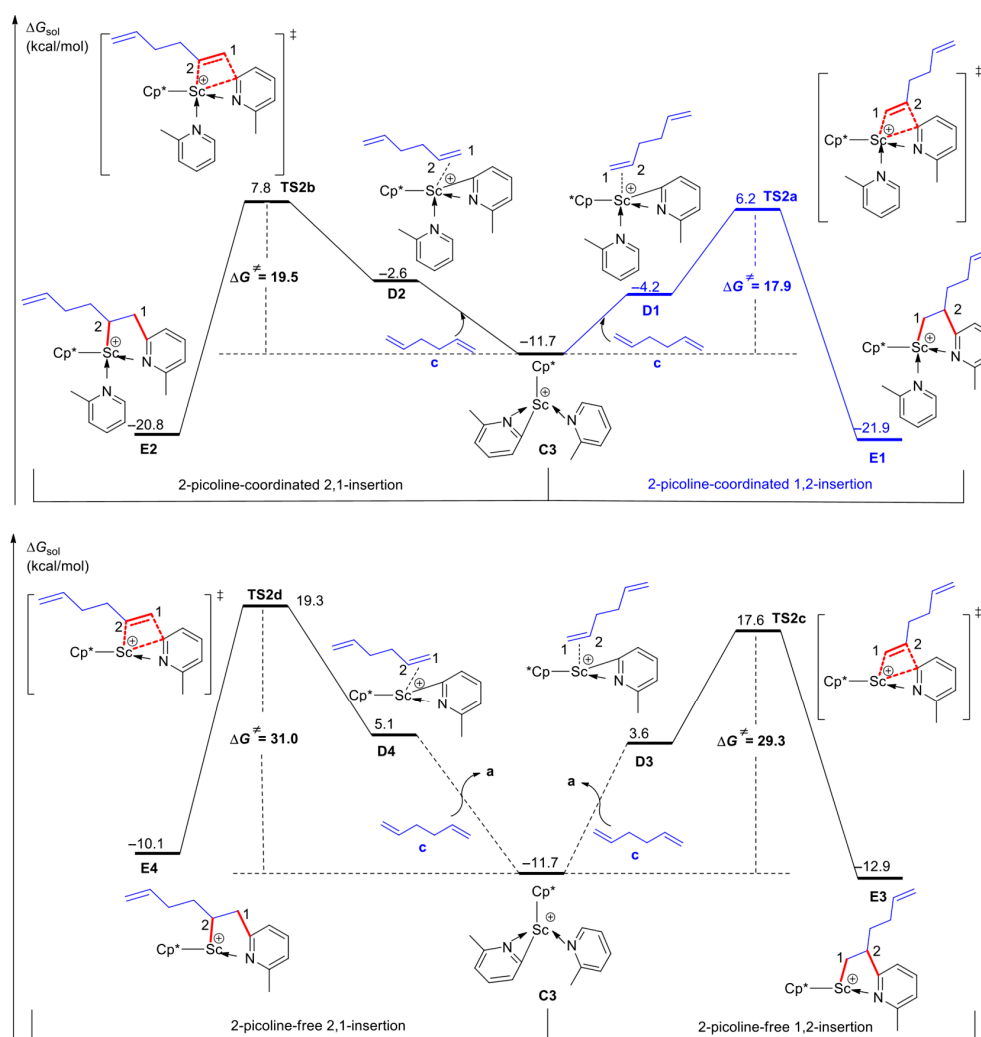


Figure 3. Computed free energy profile (kcal/mol) for the Sc-catalyzed 1,5-hexadiene insertion into the active species **C3** via 1,2- or 2,1-insertion manners along with 2-picoline-free or 2-picoline-coordinated fashion.

To elucidate the physical origin of the 1,2-regioselectivity, a distortion/interaction analysis (EDA) [77,78] was performed on the most favorable transition states **TS2a** and **TS2b** (Figure 4). Each transition state was divided into two fragments: the 1,5-hexadiene moiety (**F2**) and the remaining metal complex (**F1**). The total energy of the transition state (ΔE_{total}) relative to the separated fragments was decomposed into deformation and interaction components using single-point energy calculations. The deformation energy

for each fragment (ΔE_{def}) was defined as the energy difference between its geometry within the transition state and its fully optimized structure. The interaction energy (ΔE_{int}) was then evaluated as the difference between the single-point energy of the full transition state and the sum of the single-point energies of the individual fragments, each held in their transition-state geometries. This approach leads to the fundamental relationship: $\Delta E_{\text{total}} = \Delta E_{\text{def(F1)}} + \Delta E_{\text{def(F2)}} + \Delta E_{\text{int}}$, thereby quantitatively separating the intrinsic strain within the fragments from the energy associated with their interaction in the transition state. The results indicate that the total deformation energy required to achieve the 1,2-insertion geometry (**TS2a**) is 5.0 kcal/mol higher than for the 2,1-insertion (**TS2b**) (27.6 vs. 22.6 kcal/mol). However, this greater distortion is overcompensated by a significantly more favorable interaction energy in **TS2a** (−30.9 vs. −23.5 kcal/mol). The total electronic energy of **TS2a** (−3.3 kcal/mol) is thus lower than that of **TS2b** (−0.9 kcal/mol). This establishes that the regioselectivity is governed by superior stabilizing interactions in the 1,2-insertion transition state, rather than the strain required to form it.

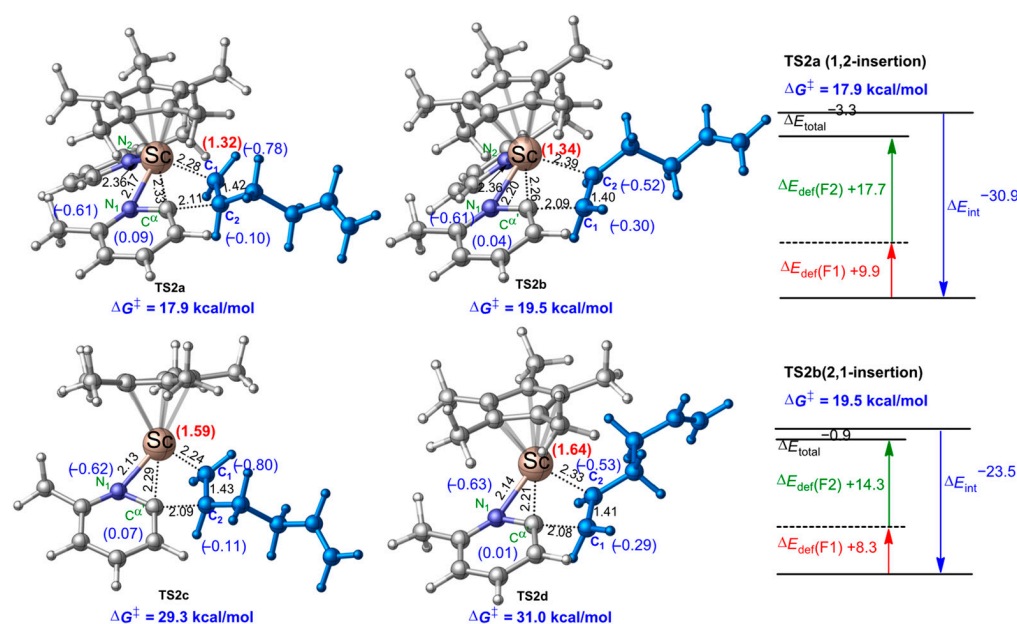


Figure 4. Optimized geometries of the 1,5-hexadiene insertion transition states **TS2i** ($i = a, b, c, d$) with key distances (Å) and angles (°). NBO charges are shown in parentheses and corresponding energy barriers ($\Delta G^\ddagger$) are shown below the structures. Energy decomposition analysis (EDA) for the competing 1,2- and 2,1-insertion transition states.

In addition, the 1,2-insertion of 1,5-hexadiene into the Sc–alkyl bond in complex **D3** assisted by an additional coordinated molecule was also considered. This process requires overcoming an energy barrier of 30.1 kcal/mol through transition state **TS2e** (Figure S1), which is significantly higher than that of the 2-picoline-coordinated pathway. Therefore, this process can be excluded due to its unfavorable relative energy.

Generation of Monoalkylation Product. Following the formation of the alkyl insertion intermediate **E1**, the reaction pathway diverges towards either monoalkylation or cyclization. It is worth noting that direct protonation of the Sc–alkyl bond in **E1** via hydrogen abstraction by coordinated specie **a** through transition state **TS3a** requires overcoming an energy barrier of 22.2 kcal·mol^{−1} (Figure 5, left). Subsequent coordination of an additional 2-picoline leads to the formation of complex **F2** at a higher energy level due to steric effects. From **F2**, the reaction proceeds via a σ -bond metathesis transition state (**TS3b**) to afford the monoalkylation product **G2** with two 2-picoline ligands. This pathway exhibits a higher energy barrier of 29.5 kcal·mol^{−1}.

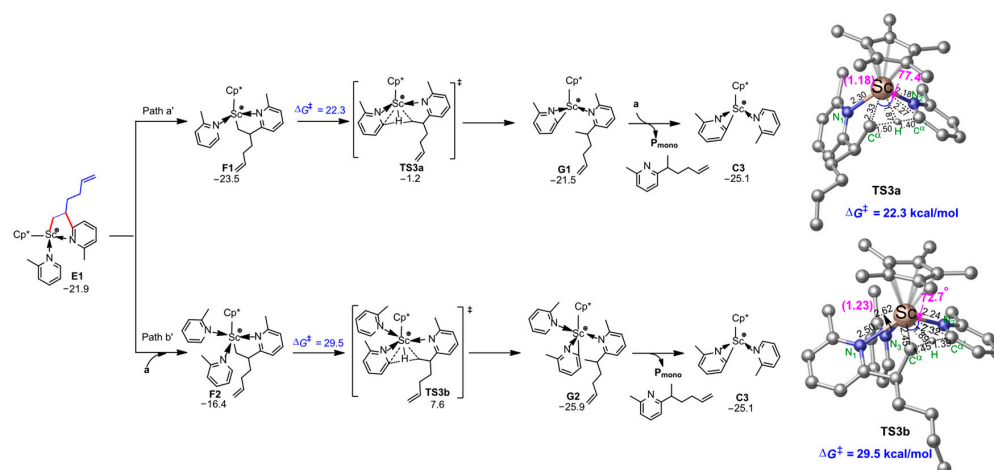


Figure 5. Free energy profile (kcal/mol) for the formation of the monoalkylated product P_{mono} via a protonation/reductive elimination pathway.

Comparison of the two C–H activation transition states revealed that **TS3a** has a significantly lower energy barrier than **TS3b** (22.2 vs. 29.5 kcal·mol^{−1}). Therefore, if a reductive elimination process were to take place, it would be more likely to proceed via the species with one coordinated ligand (**1a**) rather than the one with two ligands (**2a**).

Consistent with the trend observed for **TS1i**, both the Lewis acidity and the geometry of the metal center correlated well with the energy barriers. Specifically, the lower-barrier **TS3a** exhibited a lower NPA charge on Sc (1.18) compared to **TS3b** (1.23), and a wider $C_{\alpha}-Sc-C_{\alpha'}$ angle (77.4° in **TS3a** vs. 72.7° in **TS3b**). These structural and electronic features aligned with the relative activation energies of 22.2 and 29.5 kcal·mol^{−1} for **TS3a** and **TS3b**, respectively.

Ligand Dissociation and the Origin of Diastereoselectivity. As illustrated in Figure 6, following the coordination–insertion pathway, the subsequent intramolecular C=C insertion into the Sc–C bond of intermediate **E1**, assisted by one molecule of 2-picoline, affords the corresponding cyclization intermediate. The *cis*-cyclization proceeds via **H1** → **TS4a** → **J1** (Path a), whereas *trans*-cyclization follows **H2** → **TS4b** → **J2** (Path b). The *cis*-pathway exhibits a lower energy barrier (16.0 vs. 23.0 kcal·mol^{−1}), indicating that *cis*-cyclization is more favorable. For comparison, the decooordination of 2-picoline from **E1** was also examined. Upon ligand dissociation, the system rises in energy to form the less stable alkyl insertion intermediate **E3**. This is followed by energy stabilization through intramolecular C=C coordination of the 1,5-hexadien, yielding coordination complexes **H3** or **H4**. From **H3**, the reaction proceeds via transition state **TS4c** to form the thermodynamically more stable *cis*-cyclization product **J3**. Alternatively, **H4** undergoes *trans*-cyclization via **TS4d** to give **J4** in the absence of 2-picoline. To our surprise, in contrast to the initial insertion, the *cis*-cyclization pathway through the picoline-free transition state **TS4c** exhibits a barrier of only 12.0 kcal/mol. This is 4.0 kcal/mol lower than the *cis*-pathway with coordinated picoline (**TS4a**) and a substantial 14.8 kcal/mol lower than the picoline-free *trans*-cyclization via **TS4d** (26.8 kcal/mol). This identifies a “ligand-dissociation” mechanism for cyclization.

Overall, the results summarized in Figure 6 indicate that among the four possible insertion pathways (Paths a–d), the *cis*-cyclization mechanism without 2-picoline coordination proceeding through **TS4c** is the most favorable both kinetically and thermodynamically. This contrasts with the earlier first C=C insertion results (Figure 3), where the 2-picoline-coordinated mechanism was more advantageous. The origin of the high *cis*-diastereoselectivity is unambiguously steric. The dissociation of 2-picoline creates a sterically open coordination sphere, permitting the diene chain to cyclize via the least hindered *cis* trajectory. The persistence of the picoline ligand in other pathways exacerbates this steric congestion, rendering them non-competitive. This presents a mechanistic

dichotomy, the very 2-picoline coordination that is indispensable for the first insertion becomes detrimental in the cyclization step. This necessitates a ligand displacement event to unlock the observed high diastereoselectivity.

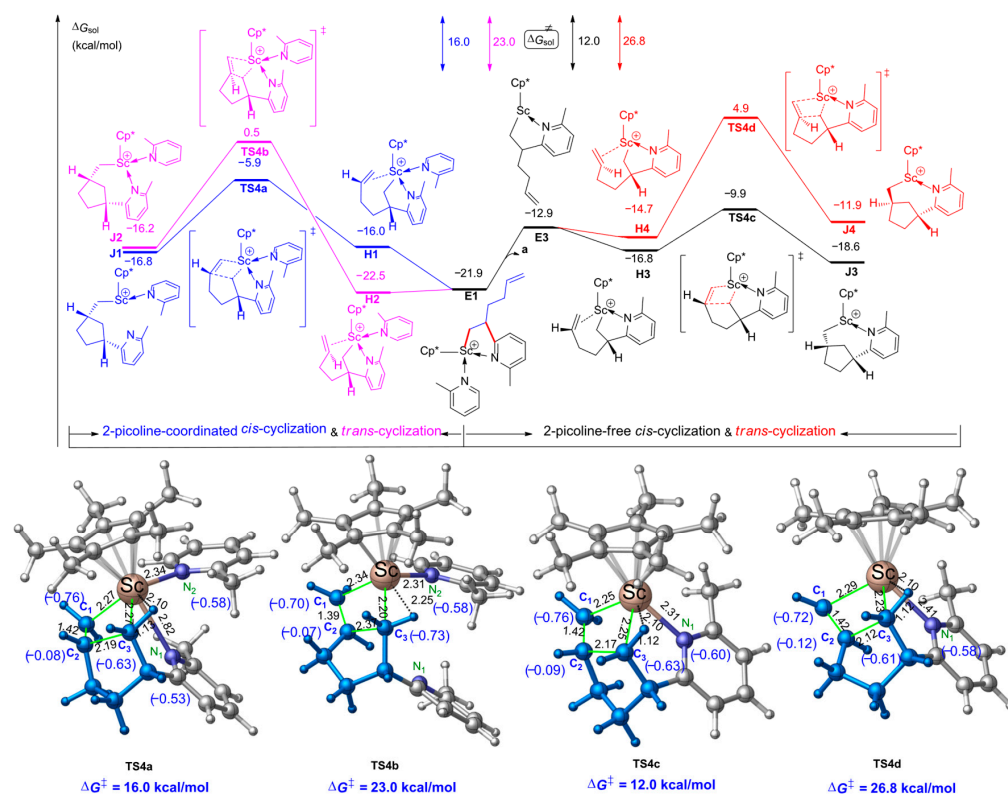


Figure 6. Computed energy profiles for the diastereoselective cyclization from intermediate **E1**. Pathways on *cis*-cyclization or *trans*-cyclization process with (TS4a, TS4b) and without (TS4c, TS4d) a coordinated 2-picoline molecule are compared.

A comparison between the *cis*-cyclization pathway (Figure 6) and the reductive elimination pathway (Figure 5) reveals that the energy barrier for monoalkylated reductive elimination is significantly higher than that for the corresponding cyclization process (22.3 vs. 12.0 kcal·mol^{−1}). This indicates that after the first C=C bond of 1,5-hexadiene inserts into the Sc–C bond, intramolecular *cis*-cyclization is strongly favored over alkyl elimination. These computational results are in excellent agreement with experimental observations, in which the *cis*-cyclization product was detected rather than a simple alkylated species.

Cycle Completion and Overall Mechanism. The catalytic cycle is concluded through protonolysis of the Sc–C bond in the cyclized intermediates. As shown in Figure 7, starting from the *cis*-cyclization intermediate **J3** and *trans*-cyclization intermediate **J4**, protonation of the Sc–C bond via C–H bond activation of coordinated 2-picoline yields the corresponding *cis*-cyclization product **P_{cis}** or *trans*-cyclization product **P_{trans}**, regenerating the active species **C3** to complete the catalytic cycle. Similar to **TS1**, the protonation transition states **TS5i** (*i* = a, b, c, d) represent typical σ-bond metathesis processes. The *cis*-cyclic pathway proceeds via **K1_{cis}** → **TS5a_{cis}** → **L1_{cis}**, while the *trans*-cyclic pathway follows **K2_{trans}** → **TS5b_{trans}** → **L2_{trans}**. Although the activation barriers for these two pathways are similar (20.3 kcal·mol^{−1} for *cis*-pathway and 20.2 kcal·mol^{−1} for *trans*-pathway), the *cis*-cyclization complex **K1_{cis}** is energetically more stable than **K2_{trans}** by 6.1 kcal·mol^{−1} (−24.5 vs. −18.4 kcal·mol^{−1}). A similar energy difference was observed between the transition states **TS5a_{cis}** and **TS5b_{trans}** (−4.3 vs. +1.8 kcal·mol^{−1}), indicating that the formation of the *cis*-cyclization product **P_{cis}** is strongly favored. Consistent with the preceding steps,

pathways involving a dicoordinated scandium center via **TS5c_{cis}** or **TS5d_{trans}** are disfavored due to their high energy barriers (29.3 and 24.5 kcal·mol^{−1}, respectively). This can be attributed to increased steric hindrance in **TS5c_{cis}** or **TS5d_{trans}** relative to **TS5a_{cis}** and **TS5b_{trans}**.

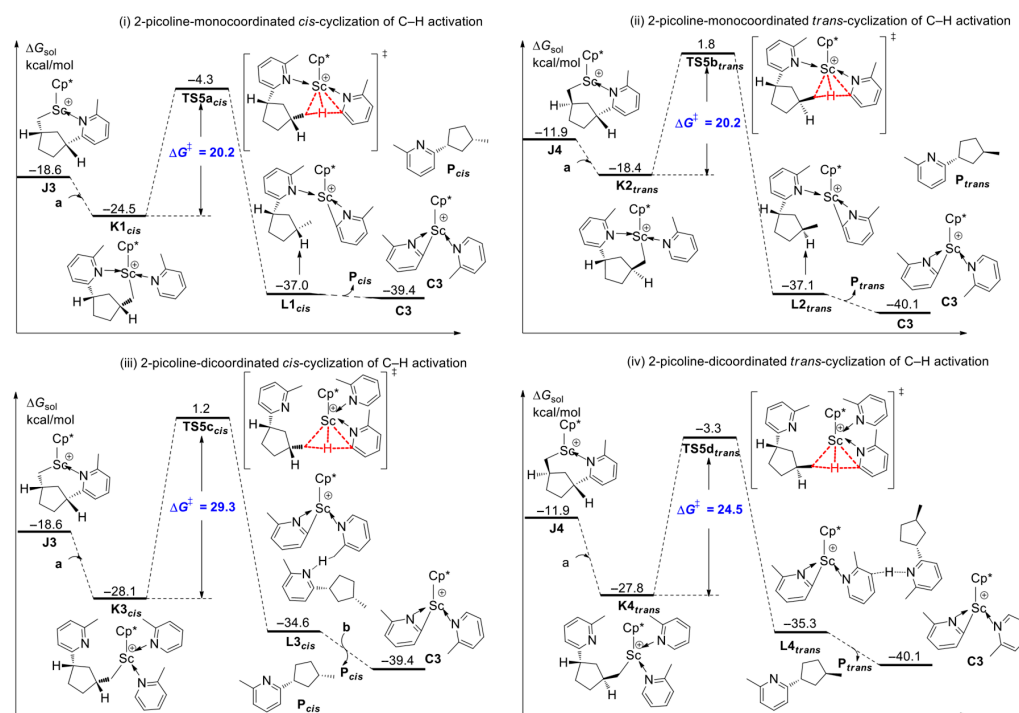


Figure 7. Free energy profile (kcal/mol) for the protonolysis step that concludes the catalytic cycle, regenerating the active species **C3** and releasing the final *cis*- or *trans*-cyclized product (**P_{cis}** or **P_{trans}**) via mono-coordinated pathways (i,ii) or dicoordinated pathways (iii,iv).

Notably, the energy barrier for the C–H activation step was significantly higher than that for the olefin insertion process. The overall energy profile confirms that the initial C–H activation is the rate-determining step, which is consistent with reported experimental kinetic isotope effects. Besides, in view of the gas phase statistical mechanic calculations of entropy are in error for solution state reactions, the entropies have also been further corrected [79–82]. A free energy of solvation calculated was added to the thermodynamic corrections for Gibbs free energy and 1.9 kcal/mol (accounting for the standard state change from 1 atm (gas) to 1 mol/L (solution) at 298.15 K to obtain the final solution-phase Gibbs free energies for all species. The final solution-phase Gibbs free energies, incorporating this correction and the solvation free energy, are summarized in Table S1. These corrected values confirm that all mechanistic conclusions, including the identity of the active species, the regioselectivity of insertion, and the stereoselectivity of cyclization, remain fully consistent with those derived from the uncorrected energies. The fully elucidated catalytic cycle, integrating all elementary steps, is depicted in Figure 8.

The mechanistic insights presented in this work establish a new paradigm for rare-earth catalysis based on hemilabile substrate coordination, wherein a substrate dynamically coordinates to and dissociates from the metal center. This dual role enables sequential functions, promoting challenging bond activations initially and then vacating the coordination sphere to achieve high stereoselectivity. Characterized by an initial heteroatom-assisted activation step followed by sterically driven ligand dissociation, this mechanistic model is anticipated to exhibit broad applicability in alkylation reactions involving diverse functional substrates (e.g., pyridines, anilines, amines, aldimines, quinolines, imidazoles, sulfides, anisoles) with alkenes. The governing principles of regioselectivity and steric modulation

are further extendable to a range of alkene and diene coupling partners. While energetic landscapes remain substrate-dependent, the deliberate utilization of dynamic substrate coordination as a stereocontrol strategy establishes a rational and generalizable framework for advancing rare-earth-catalyzed C–H functionalization. Moreover, this perspective offers valuable guidance for the design of coordination-auxiliary pendant ligands and for the controlled polymerization of polar monomers, thereby bridging molecular C–H activation with precision macromolecular synthesis.

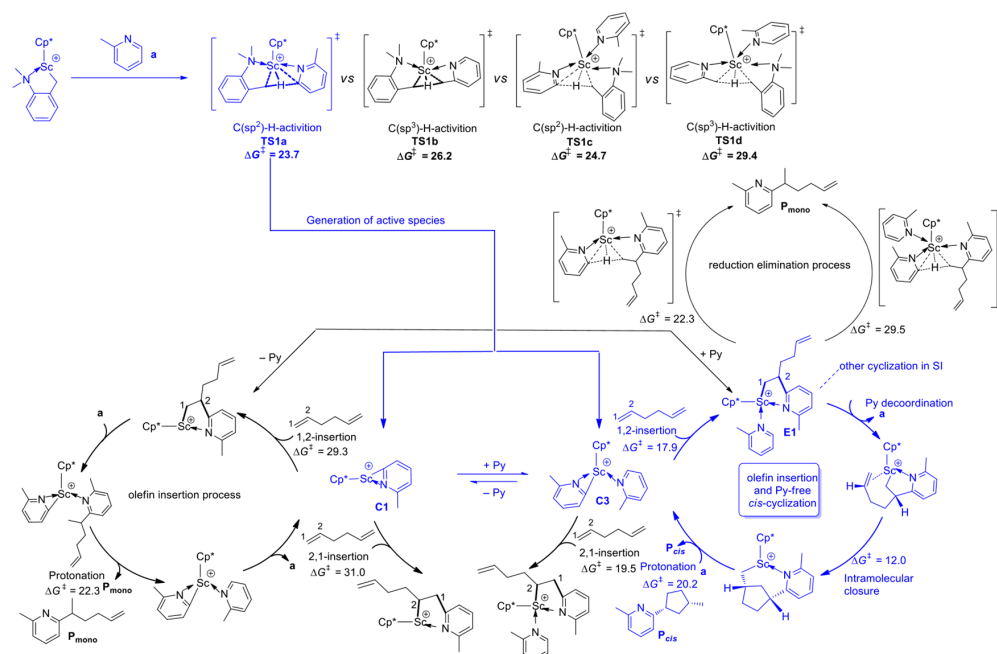


Figure 8. The complete catalytic cycle for the Sc-catalyzed diastereoselective cyclization of 2-picoline with 1,5-hexadiene.

3. Computational Details

All density functional theory (DFT) calculations were performed using the Gaussian 09 software package [83]. Geometry optimizations of all reactants, intermediates, transition states, and products were carried out in the gas phase using the B3PW91 hybrid functional [83–87]. The 6-31G(d) basis set was used for C, H, and N atoms, while the scandium atom was treated with the Stuttgart/Dresden effective core potential (ECP) and its associated basis set (SDD) [88]. No symmetry constraints were applied during the optimization process. Vibrational frequency calculations were performed at the same level of theory to confirm the nature of each stationary point: minima (zero imaginary frequencies) and transition states (one imaginary frequency). The obtained frequencies, unscaled, were also used to compute the thermodynamic corrections (enthalpy and Gibbs free energy) at 298.15 K and 1.0 atm. To achieve higher accuracy in the energetics, single-point energy calculations were conducted on the optimized geometries using the M06 meta-hybrid functional [89,90], which has been shown to perform well for organometallic thermochemistry and non-covalent interactions. For these calculations, a larger basis set, 6-311+G(d,p), was employed for C, H, and N atoms, while the SDD ECP and basis set were retained for Sc. To model the solvation effects of the experimental solvent, chlorobenzene ($\epsilon = 5.6968$), the conductor-like polarizable continuum model (CPCM), was employed during the single-point calculations [91–93]. The final reported solution-phase Gibbs free energies (G_{sol}) were calculated by combining the M06/6-311+G(d,p)/SDD/CPCM(chlorobenzene) single-point electronic energies with the thermal and entropic corrections obtained at the B3PW91/6-31G(d)/SDD level of theory: $G_{\text{sol}} = E_{\text{SP}}(\text{M06/CPCM}) + G_{\text{corr}}(\text{B3PW91})$. Intrinsic reaction coordinate

(IRC) calculations were performed for all transition states to verify that they correctly connect the intended reactants and products. All molecular structures depicted in this work were rendered using CYLview [94].

4. Conclusions

In conclusion, our DFT study unveils a sophisticated “ligand-enabled, then ligand-displaced” mechanism for the Sc-catalyzed diastereoselective cyclization of 2-picoline with 1,5-hexadiene. This mechanism resolves the apparent paradox of how 2-picoline acts as both a substrate and essential ligand, yet its dissociation is key to selectivity.

The catalytic cycle is initiated by the ligand-enabled phase. Here, the 2-picoline substrate coordinates to the metal center to form the active species **C3**, which is crucial for facilitating both the C–H activation and the regioselective 1,2-insertion of 1,5-hexadiene. During this phase, the ligand stabilizes the Lewis-acidic Sc center and enables superior orbital overlap that dictates regiochemistry.

The cycle then undergoes a decisive switch to the ligand-displaced phase for the critical diastereoselective controlling step. The dissociation of 2-picoline is mandatory to relieve steric congestion around the metal center, opening a low-energy pathway for *cis*-cyclization. This creates a powerful steric gating effect, where the bulky Cp* ligand selectively destabilizes the *trans*-cyclization transition state, thereby enforcing the high observed diastereoselectivity.

This refined mechanistic understanding, which highlights the dynamic and context-dependent role of substrate coordination, provides a new design principle for rare-earth catalysis. It demonstrates that strategic ligand association and dissociation can be harnessed to sequentially control reactivity and selectivity, offering a versatile blueprint for developing next-generation catalysts for C–H functionalization and challenging diastereoselective transformations.

Supplementary Materials: The following supporting information can be downloaded at: <https://www.mdpi.com/article/10.3390/inorganics14010028/s1>, Figure S1: The computed energy profiles for 1,5-hexadiene insertion based on species **D1** with a coordinated 1,5-hexadiene; Figure S2: The computed energy profiles for *cis*-cyclization and *trans*-cyclization processes based on 1,5-hexadiene insertion intermediate; Table S1: Computed free energy ΔG (kcal/mol) for all the species including solution-phase single point energies, the gas phase zero-point correction, thermal correction to enthalpy, thermal correction to Gibbs free energy.

Author Contributions: Conceptualization, G.Z., S.Z., X.L. and Y.L. (Yunzhi Li) Methodology, G.Z., X.L., Y.L. (Yunzhi Li) and Y.L. (Yi Luo); Software, G.Z., S.Z., X.L. and Y.L. (Yunzhi Li); Formal analysis, G.Z. and Y.L. (Yi Luo); Investigation, G.Z., S.Z., X.L. and Y.L. (Yunzhi Li); Data curation, G.Z., Q.X. and Y.L. (Yi Luo); Writing—original draft, G.Z.; Writing—review & editing, G.Z., Q.X. and Y.L. (Yi Luo); Supervision, G.Z., Q.X. and Y.L. (Yi Luo). All authors have read and agreed to the published version of the manuscript.

Funding: This work was supported by the National Natural Science Foundation of China (No. 22003021), the Natural Science Foundation of Shandong Province (Nos. ZR2021QB153 and ZR2022QB043), the Key Research and Development Program of Shandong Province (No. 2025TS-GCCZZB0827), and the Open Funding Project of Key Laboratory of Functional Polymer Materials, Ministry of Education, Nankai University (KLFP202301).

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: The original contributions presented in the study are included in the article/Supplementary Materials, further inquiries can be directed to the corresponding authors.

Conflicts of Interest: The authors declare no conflicts of interest.

References

- Nishiura, M.; Guo, F.; Hou, Z. Half-Sandwich Rare-Earth-Catalyzed Olefin Polymerization, Carbometallation, and Hydroarylation. *Acc. Chem. Res.* **2015**, *48*, 2209–2220. [\[CrossRef\]](#)
- Seth, K. Recent Progress in Rare-Earth Metal-Catalyzed sp^2 and sp^3 C–H Functionalization to Construct C–C and C–Heteroelement Bonds. *Org. Chem. Front.* **2022**, *9*, 3102–3141. [\[CrossRef\]](#)
- Su, J.; Xu, X. Rare-Earth Metal-Catalyzed C–H Functionalization. *J. Chin. Soc. Rare Earths* **2021**, *39*, 171–180.
- Murakami, K.; Yamada, S.; Kaneda, T.; Itami, K. C–H Functionalization of Azines. *Chem. Rev.* **2017**, *117*, 9302–9332. [\[CrossRef\]](#) [\[PubMed\]](#)
- Cong, X.; Huang, L.; Hou, Z. C–H Functionalization with Alkenes, Allenes, and Alkynes by Half-Sandwich Rare-Earth Catalysts. *Tetrahedron* **2023**, *135*, 133323. [\[CrossRef\]](#)
- Sun, Q.; Xu, X.; Xu, X. Recent Advances in Rare-Earth Metal-Catalyzed C–H Functionalization Reactions. *ChemCatChem* **2022**, *14*, e202201083. [\[CrossRef\]](#)
- Wang, S.; Ning, L.; Mao, T.; Zhou, Y.; Pu, M.; Feng, X.M.; Dong, S.X. Anti-Markovnikov Hydroallylation Reaction of Alkenes via Scandium-Catalyzed Allylic C–H Activation. *Nat. Commun.* **2025**, *16*, 1423. [\[CrossRef\]](#) [\[PubMed\]](#)
- Guan, B.T.; Hou, Z. Rare-Earth-Catalyzed C–H Bond Addition of Pyridines to Olefins. *J. Am. Chem. Soc.* **2011**, *133*, 18086–18089. [\[CrossRef\]](#)
- Guan, B.T.; Wang, B.; Nishiura, M.; Hou, Z. Yttrium-Catalyzed Addition of Benzylic C–H Bonds of Alkyl Pyridines to Olefins. *Angew. Chem., Int. Ed.* **2013**, *52*, 4418–4421. [\[CrossRef\]](#)
- Song, G.; Wylie, W.N.O.; Hou, Z. Enantioselective C–H Bond Addition of Pyridines to Alkenes Catalyzed by Chiral Half-Sandwich Rare-Earth Complexes. *J. Am. Chem. Soc.* **2014**, *136*, 12209–12212. [\[CrossRef\]](#)
- Luo, Y.; Teng, H.-L.; Nishiura, M.; Hou, Z. Asymmetric Yttrium-Catalyzed $C(sp^3)$ –H Addition of 2-Methyl Azaarenes to Cyclopropenes. *Angew. Chem. Int. Ed.* **2017**, *56*, 9207–9210. [\[CrossRef\]](#)
- Wu, P.; Cao, F.; Zhou, Y.; Xue, Z.; Zhang, N.; Shi, L.; Luo, G. Substrate Facilitating Roles in Rare-Earth-Catalyzed C–H Alkenylation of Pyridines with Allenes: Mechanism and Origins of Regio- and Stereoselectivity. *Inorg. Chem.* **2022**, *61*, 17330–17341. [\[CrossRef\]](#)
- Zhou, G.; Luo, G.; Kang, X.; Hou, Z.; Luo, Y. Origin of Product Selectivity in Yttrium-Catalyzed Benzylic C–H Alkylations of Alkylpyridines with Olefins: A DFT Study. *Organometallics* **2018**, *37*, 2741–2748.
- Song, G.; Wang, B.; Nishiura, M.; Hou, Z. Catalytic C–H Bond Addition of Pyridines to Allenes by a Rare-Earth Catalyst. *Chem. Eur. J.* **2015**, *21*, 8394–8398.
- Kundu, A.; Inoue, M.; Nagae, H.; Tsurugi, H.; Mashima, K. Direct *ortho*-C–H Aminoalkylation of 2-Substituted Pyridine Derivatives Catalyzed by Yttrium Complexes with N,N' -Diarylethylenediamido Ligands. *J. Am. Chem. Soc.* **2018**, *140*, 7332–7342.
- Ye, P.; Shao, Y.; Zhang, F.; Zou, J.; Ye, X.; Chen, J. Rare-Earth-Metal-Catalyzed Synthesis of Azaindoles and Naphthyridines via C–H Cyclization of Functionalized Pyridines. *Adv. Synth. Catal.* **2020**, *362*, 851–857.
- Li, D.; Ning, L.; Luo, Q.; Wang, S.; Feng, X.-M.; Dong, S.-X. C–H Alkylation of Pyridines with Olefins Catalyzed by Imidazolin-2-Iminato-Ligated Rare-Earth Alkyl Complexes. *Sci. China Chem.* **2023**, *66*, 1804–1813. [\[CrossRef\]](#)
- Luo, Y.; Jiang, S.; Xu, X. Yttrium-Catalyzed *ortho*-Selective C–H Borylation of Pyridines with Pinacolborane. *Angew. Chem. Int. Ed.* **2022**, *61*, e202117750.
- Zhan, G.; Jiao, T.; Lou, S.; Wang, S.; Luo, G.; Nishiura, M.; Hou, Z. Regioselective Hydropyridylation of Heteroatom-Functionalized Internal Alkenes by Half-Sandwich Rare-Earth Catalysts. *J. Am. Chem. Soc.* **2025**, *147*, 22092–22103. [\[CrossRef\]](#) [\[PubMed\]](#)
- Song, G.; Luo, G.; Oyamada, J.; Luo, Y.; Hou, Z. *Ortho*-Selective C–H Addition of N,N -Dimethyl Anilines to Alkenes by a Yttrium Catalyst. *Chem. Sci.* **2016**, *7*, 5265–5270.
- Gao, H.; Su, J.; Xu, P.; Xu, X. Scandium-Catalyzed $C(sp^3)$ –H Alkylation of N,N -Dimethyl Anilines with Alkenes. *Org. Chem. Front.* **2018**, *5*, 59–63. [\[CrossRef\]](#)
- Su, J.; Cai, Y.; Xu, X. Scandium-Catalyzed para-Selective Alkylation of Aromatic Amines with Alkenes. *Org. Lett.* **2019**, *21*, 9055–9059. [\[CrossRef\]](#) [\[PubMed\]](#)
- Su, J.; Luo, Y.; Xu, X. Benzylic C–H Addition of Aromatic Amines to Alkenes Using a Scandium Catalyst. *Chem. Commun.* **2021**, *57*, 3688–3691.
- Xu, X.; Zheng, X.; Xu, X. Synthesis of Tetrahydroquinolines by Scandium-Catalyzed [3+3] Annulation of Anilines with Allenes and Dienes. *ACS Catal.* **2021**, *11*, 14995–15003.
- Xu, X.; Sun, Q.; Xu, X. Scandium-Catalyzed Benzylic $C(sp^3)$ –H Alkenylation of Tertiary Anilines with Alkynes. *Org. Lett.* **2022**, *24*, 3970–3975. [\[CrossRef\]](#)
- Zhou, W.; Cong, X.; Nishiura, M.; Hou, Z. Synthesis of Allylanilines via Scandium-Catalyzed Benzylic $C(sp^3)$ –H Alkenylation with Alkynes. *Chem. Commun.* **2022**, *58*, 7257–7260. [\[CrossRef\]](#) [\[PubMed\]](#)

27. Cao, F.; Wu, P.; Zhou, Y.; Zhang, N.; Xue, Z.; Shi, L.; Zhou, G.; Luo, G. Mechanism and Origin of Site Selectivity and Regioselectivity of Scandium-Catalyzed Benzylic C–H Alkylation of Tertiary Anilines with Alkenes. *Inorg. Chem.* **2023**, *62*, 979–988.
28. Nako, A.; Oyamada, J.; Nishiura, M.; Hou, Z. Scandium-Catalysed Intermolecular Hydroaminoalkylation of Olefins with Aliphatic Tertiary Amines. *Chem. Sci.* **2016**, *7*, 6429–6434. [[CrossRef](#)]
29. Luo, G.; Liu, F.; Luo, Y.; Zhou, G.; Kang, X.; Hou, Z.; Luo, L. Computational Investigation of Scandium-Based Catalysts for Olefin Hydroaminoalkylation and C–H Addition. *Organometallics* **2019**, *38*, 1887–1896. [[CrossRef](#)]
30. Li, D.; Wang, Y.; Wang, S.; Dong, S.-X. The Effect of Basic Ligands and Alkenes on the Regioselectivity of C–H Additions of Tertiary Amines to Alkenes. *Chem.–Eur. J.* **2024**, *30*, e202401014.
31. Cong, X.; Zhan, G.; Mo, Z.; Nishiura, M.; Hou, Z. Diastereodivergent [3+2] Annulation of Aromatic Aldimines with Alkenes via C–H Activation by Half-Sandwich Rare-Earth Catalysts. *J. Am. Chem. Soc.* **2020**, *142*, 5531–5537. [[CrossRef](#)]
32. Cong, X.; Zhuo, Q.; Hao, N.; Mo, Z.; Zhan, G.; Nishiura, M.; Hou, Z. Regio- and Diastereoselective [3+2] Annulation of Aliphatic Aldimines with Alkenes by Scandium-Catalyzed β -C(sp³)–H Activation. *Angew. Chem., Int. Ed.* **2022**, *61*, e202115996. [[CrossRef](#)]
33. Wang, P.; Luo, G.; Yang, J.; Cong, X.; Hou, Z.; Luo, Y. Theoretical Studies of Rare-Earth-Catalyzed [3+2] Annulation of Aromatic Aldimine with Styrene: Mechanism and Origin of Diastereoselectivity. *J. Org. Chem.* **2021**, *86*, 4236–4244. [[CrossRef](#)] [[PubMed](#)]
34. Hu, J.; Tan, X.; Li, Y.; Luo, L.; Wang, X.; Cao, D.; Luo, G. Theoretical Insights into Rare-Earth Catalyst Controlled Diastereo- and Enantioselective [3+2] Annulation of Aromatic Aldimines with Styrenes. *Inorg. Chem.* **2025**, *64*, 3120–3128. [[CrossRef](#)]
35. Mishra, A.; Cong, X.; Nishiura, M.; Hou, Z. Enantioselective Synthesis of 1-Aminoindanes via [3+2] Annulation of Aldimines with Alkenes by Scandium-Catalyzed C–H Activation. *J. Am. Chem. Soc.* **2023**, *145*, 17468–17477. [[CrossRef](#)] [[PubMed](#)]
36. Cong, X.; Zhuo, Q.; Hao, N.; Mishra, A.; Nishiura, M.; Hou, Z. Divergent Synthesis of Multi-Substituted Aminotetralins via [4+2] Annulation of Aldimines with Alkenes by Rare-Earth-Catalyzed Benzylic C(sp³)–H Activation. *Angew. Chem. Int. Ed.* **2024**, *63*, e202318203. [[CrossRef](#)] [[PubMed](#)]
37. Mishra, A.; Lin, X.; Maji, K.; Nishiura, M.; Cong, X.; Hou, Z. Diastereo- and Enantioselective Synthesis of Polycyclic Amines by Cascade Cyclization of Aromatic Aldimines with Tethered Alkenes via Scandium-Catalyzed C–H Activation. *J. Am. Chem. Soc.* **2025**, *147*, 26116–26123. [[CrossRef](#)]
38. Sun, Q.; Feng, X.; Wang, X.; Shi, H.; Su, J.; Wang, M.; Luo, G.; Xu, X. Enantioselective ortho-C–H Addition of Aromatic Amines to Alkenes by Bulky Chiral Anilido-Oxazoline Scandium Complexes. *J. Am. Chem. Soc.* **2025**, *147*, 13658–13666. [[CrossRef](#)]
39. Zhang, Y.; Wang, Y. Elucidating the mechanism and origin of diastereoselectivity in scandium-catalyzed β -C(sp³)–H activation and transformation of an aliphatic aldimine. *Org. Chem. Front.* **2024**, *11*, 4391–4401. [[CrossRef](#)]
40. Lou, S.J.; Zhang, L.; Luo, Y.; Nishiura, M.; Luo, G.; Luo, Y.; Hou, Z. Regiodivergent C–H Alkylation of Quinolines with Alkenes by Half-Sandwich Rare-Earth Catalysts. *J. Am. Chem. Soc.* **2020**, *142*, 18128–18137. [[CrossRef](#)]
41. Lou, S.J.; Luo, G.; Yamaguchi, S.; An, K.; Nishiura, M.; Hou, Z. Modular Access to Spiro-dihydroquinolines via Scandium-Catalyzed Dearomative Annulation of Quinolines with Alkynes. *J. Am. Chem. Soc.* **2021**, *143*, 20462–20471. [[CrossRef](#)]
42. Lou, S.J.; Zhuo, Q.; Nishiura, M.; Luo, G.; Hou, Z. Enantioselective C–H Alkenylation of Ferrocenes with Alkynes by Half-Sandwich Scandium Catalyst. *J. Am. Chem. Soc.* **2021**, *143*, 2470–2476. [[CrossRef](#)] [[PubMed](#)]
43. Lou, S.; Wang, P.; Wen, X.; Mishra, A.; Cong, X.; Zhuo, Q.; An, K.; Nishiura, M.; Luo, Y.; Hou, Z. (Z)-Selective Isomerization of 1,1-Disubstituted Alkenes by Scandium-Catalyzed Allylic C–H Activation. *J. Am. Chem. Soc.* **2024**, *146*, 26766–26776.
44. Lou, S.-J.; Mo, Z.; Nishiura, M.; Hou, Z. Construction of All-Carbon Quaternary Stereocenters by Scandium-Catalyzed Intramolecular C–H Alkylation of Imidazoles with 1,1-Disubstituted Alkenes. *J. Am. Chem. Soc.* **2020**, *142*, 1200–1205.
45. Guo, J.; Yang, W.; Zhang, D.; Wang, S.-G.; Wang, X. Mechanistic Insights into Formation of All-Carbon Quaternary Centers via Scandium-Catalyzed C–H Alkylation of Imidazoles with 1,1-Disubstituted Alkenes. *J. Org. Chem.* **2021**, *86*, 4598–4606.
46. Luo, Y.; Ma, Y.; Hou, Z. α -C–H Alkylation of Methyl Sulfides with Alkenes by a Scandium Catalyst. *J. Am. Chem. Soc.* **2018**, *140*, 114–117. [[CrossRef](#)]
47. Zhou, Y.; Wu, P.; Cao, F.; Shi, L.; Zhang, N.; Xue, Z.; Luo, G. Mechanistic Insights into Rare-Earth-Catalysed C–H Alkylation of Sulfides: Sulfide Facilitating Alkene Insertion and Beyond. *RSC Adv.* **2022**, *12*, 13593–13599.
48. Shi, L.; Zhang, N.; Xue, Z.; Luo, G. Mechanistic Insights into Rare-Earth Catalyzed Alternating Copolymerization through C–H Polyaddition of Functionalized Organic Compounds to Unconjugated Dienes. *Inorg. Chem.* **2024**, *63*, 8079–8091. [[CrossRef](#)] [[PubMed](#)]
49. Oyamada, J.; Hou, Z. Regioselective C–H Alkylation of Anisoles with Olefins Catalyzed by Cationic Half-Sandwich Rare Earth Alkyl Complexes. *Angew. Chem. Int. Ed.* **2012**, *51*, 12828–12832. [[CrossRef](#)]
50. Wang, S.; Zhu, C.; Ning, L.; Li, D.; Feng, X.M.; Dong, S.X. Regioselective C–H Alkylation of Anisoles with Olefins by Cationic Imidazolin-2-Iminato Scandium (III) Alkyl Complexes. *Chem. Sci.* **2023**, *14*, 3132–3139. [[CrossRef](#)] [[PubMed](#)]
51. Mishra, A.; Wu, P.; Cong, X.; Nishiura, M.; Luo, G.; Hou, Z. Exo-Selective Intramolecular C–H Alkylation with 1,1-Disubstituted Alkenes by Rare-Earth Catalysts: Construction of Indanes and Tetralins with an All-Carbon Quaternary Center. *ACS Catal.* **2022**, *12*, 12973–12983. [[CrossRef](#)]

52. Tan, X.; Hu, J.; Li, Y.; Luo, L.; Wang, X.; Cao, D.; Luo, G. Mechanisms and Origins of Regioselectivity in Rare-Earth-Catalyzed C–H Functionalization of Anisoles and Thioanisoles. *Inorg. Chem.* **2025**, *64*, 5778–5788. [\[CrossRef\]](#)
53. Tang, B.; Hu, X.; Liu, C.; Jiang, T.; Alam, F.; Chen, Y. Tandem Cyclization/Hydroarylation of α,ω -Dienes Triggered by Scandium Catalyzed C–H Activation. *ACS Catal.* **2019**, *9*, 599–604. [\[CrossRef\]](#)
54. Shi, X.; Nishiura, M.; Hou, Z. C–H Polyaddition of Dimethoxyarenes to Unconjugated Dienes by Rare Earth Catalysts. *J. Am. Chem. Soc.* **2016**, *138*, 6147–6150. [\[CrossRef\]](#)
55. Xu, Z.; Tang, Y.; Shen, C.; Zhang, H.; Gan, Y.; Ji, X.; Tian, X.; Dong, K. Nickel-Catalyzed Regio- and Diastereoselective Hydroarylation and Hydroalkenylative Cyclization of 1,6-Dienes. *Chem. Commun.* **2020**, *56*, 7741–7744. [\[CrossRef\]](#) [\[PubMed\]](#)
56. Tanaka, K.; Hattori, H.; Yabe, R.; Nishimura, T. Ir-Catalyzed Cyclization of α, ω -Dienes with an N-Methyl Group via Two C–H Activation Steps. *Chem. Commun.* **2022**, *58*, 5371–5374. [\[CrossRef\]](#) [\[PubMed\]](#)
57. Widenhoefer, R.A.; Decarli, M.A. Tandem Cyclization/Hydrosilylation of Functionalized 1,6-Dienes Catalyzed by a Cationic Palladium Complex. *J. Am. Chem. Soc.* **1998**, *120*, 3805–3806. [\[CrossRef\]](#)
58. Pei, T.; Widenhoefer, R.A. Use of Pentamethyldisiloxane in the Palladium-Catalyzed Cyclization/Hydrosilylation of Functionalized Dienes. *Org. Lett.* **2000**, *2*, 1469–1471. [\[CrossRef\]](#)
59. Molander, G.A.; Schmitt, M.H. Organoyttrium-Catalyzed Sequential Cyclization/Silylation Reactions of Nitrogen-Heteroaromatic Dienes Demonstrating “Aryl-Directed” Regioselectivity. *J. Org. Chem.* **2000**, *65*, 3767–3770. [\[CrossRef\]](#)
60. Perch, N.S.; Widenhoefer, R.A. Mechanism of Palladium-Catalyzed Diene Cyclization/Hydrosilylation: Direct Observation of Intramolecular Carbometalation. *J. Am. Chem. Soc.* **2004**, *126*, 6332–6346. [\[CrossRef\]](#)
61. Molander, G.A.; Dowdy, E.D. Catalytic Cyclization/Silylation of Dienes Containing 1,1-Disubstituted Olefins Using Organolanthanide and Group 3 Organometallic Complexes. *J. Org. Chem.* **1998**, *63*, 3386–3396. [\[CrossRef\]](#)
62. Molander, G.A.; Nichols, P.J.; Noll, B.C. Stereoselective Synthesis of Carbobicyclics via Organoyttrium-Catalyzed Sequential Cyclization/Silylation Reactions. *J. Org. Chem.* **1998**, *63*, 2292–2306. [\[CrossRef\]](#)
63. Molander, G.A.; Pfeiffer, D. Organolanthanide-Catalyzed Cyclization/Boration of 1,5- and 1,6-Dienes. *Org. Lett.* **2001**, *3*, 361–363. [\[CrossRef\]](#) [\[PubMed\]](#)
64. Molander, G.A.; Hoberg, J.O. Organoyttrium-catalyzed cyclization of substituted 1,5- and 1,6-dienes. *J. Am. Chem. Soc.* **1992**, *114*, 3123–3125. [\[CrossRef\]](#)
65. Widenhoefer, R.A.; Vadehra, A.; Cheruvu, P.K. Cyclization/Hydrogermylation of Functionalized 1,6-Dienes Catalyzed by Cationic Palladium Complexes. *Organometallics* **1999**, *18*, 4614–4618. [\[CrossRef\]](#)
66. Negishi, E.M.; Jensen, D.; Kondakov, D.Y.; Wang, S. Titanium-Catalyzed Cascade Carboalumination of Dienes and Trienes. *J. Am. Chem. Soc.* **1994**, *116*, 8404–8405. [\[CrossRef\]](#)
67. Cong, X.; Hao, N.; Mishra, A.; Zhuo, Q.; An, K.; Nishiura, M.; Hou, Z. Regio- and Diastereoselective Annulation of α,β -Unsaturated Aldimines with Alkenes via Allylic C(sp³)-H Activation by Rare-Earth Catalysts. *J. Am. Chem. Soc.* **2024**, *146*, 10187–10198. [\[CrossRef\]](#)
68. Chen, Y.; Song, D.; Li, J.; Hu, X.; Song, D.; Bi, X.; Jiang, T.; Hou, Z. Diastereoselective cyclization of 1,5-dienes with the C–H bond of pyridine catalyzed by a cationic mono(phosphinoamide) alkyl scandium complex. *ChemCatChem* **2018**, *10*, 159–164. [\[CrossRef\]](#)
69. Luo, G.; Luo, Y.; Zhang, W.; Qu, J.; Hou, Z. DFT Studies on the Methane Elimination Reaction of a Trinuclear Rare-Earth Polymethyl Complex: σ -Bond Metathesis Assisted by Cooperation of Multimetal Sites. *Organometallics* **2014**, *33*, 1126–1134. [\[CrossRef\]](#)
70. Luo, G.; Luo, Y.; Hou, Z. E–H (E = N and P) Bond Activation of PhEH₂ by a Trinuclear Yttrium Methylidene Complex: Theoretical Insights into Mechanism and Multimetal Cooperation Behavior. *Organometallics* **2017**, *36*, 4611–4619. [\[CrossRef\]](#)
71. Liu, F.; Luo, G.; Hou, Z.; Luo, Y. Mechanistic Insights into Scandium-Catalyzed Hydroaminoalkylation of Olefins with Amines: Origin of Regioselectivity and Charge-Based Prediction Model. *Organometallics* **2017**, *36*, 1557–1565. [\[CrossRef\]](#)
72. Niu, S.; Hall, M.B. Theoretical Studies on Reactions of Transition-Metal Complexes. *Chem. Rev.* **2000**, *100*, 353–406. [\[CrossRef\]](#) [\[PubMed\]](#)
73. Luo, Y.; Luo, Y.; Qu, J.; Hou, Z. QM/MM Studies on Scandium-Catalyzed Syndiospecific Copolymerization of Styrene and Ethylene. *Organometallics* **2011**, *30*, 2908–2919. [\[CrossRef\]](#)
74. Kang, X.; Song, Y.; Luo, Y.; Li, G.; Hou, Z.; Qu, J. Computational Studies on Isospecific Polymerization of 1-Hexene Catalyzed by Cationic Rare Earth Metal Alkyl Complex Bearing a C3ⁱPr-trisox Ligand. *Macromolecules* **2012**, *45*, 640–651. [\[CrossRef\]](#)
75. Luo, G.; Luo, Y.; Hou, Z.; Qu, J. Intermetallic Cooperation in Olefin Polymerization Catalyzed by a Binuclear Samarocene Hydride: A Theoretical Study. *Organometallics* **2016**, *35*, 778–784. [\[CrossRef\]](#)
76. Zhou, G.; Kang, X.; Wang, X.; Hou, Z.; Luo, Y. Theoretical Investigations of Isoprene Polymerization Catalyzed by Cationic Half-Sandwich Scandium Complexes Bearing a Coordinative Side Arm. *Organometallics* **2018**, *37*, 551–558. [\[CrossRef\]](#)
77. Bickelhaupt, F.M.; Baerends, E.J.; Lipkowitz, K.B.; Boyd, D.B. Kohn-Sham Density Functional Theory: Predicting and Understanding Chemistry. *Rev. Comput. Chem.* **2007**, *15*, 1–86.

78. Kitaura, K.; Morokuma, K. A New Energy Decomposition Scheme for Molecular Interactions within the Hartree-Fock Approximation. *Int. J. Quantum Chem.* **1976**, *10*, 325–340. [[CrossRef](#)]
79. Rusdipoetra, R.A.; Suwito, H.; Tripuspaningsih, N.N.; Haq, K.U. Theoretical investigation of the anti-nitrosant mechanism of syringol and its derivatives. *RSC Adv.* **2025**, *15*, 33936–33945. [[CrossRef](#)]
80. Chen, X.Y.; Pu, M.; Cheng, H.G.; Sperger, T.; Schoenebeck, F. Arylation of axially chiral phosphorothioate salts by dinuclear Pd catalysis. *Angew. Chem. Int. Ed.* **2019**, *58*, 11395–11399. [[CrossRef](#)] [[PubMed](#)]
81. Zhu, L.; Luo, Y.; Wen, X.; Zhang, W.; Zhou, G. Theoretical investigations of para- methoxystyrene/styrene polymerization catalyzed by cationic methyl- and dibenzobarrelene-based α -diimine palladium complexes. *Inorganics* **2024**, *12*, 315. [[CrossRef](#)]
82. Liu, C.; Qin, Z.X.; Ji, C.L.; Hong, X.; Szostak, M. Highly-chemoselective step-down reduction of carboxylic acids to aromatic hydrocarbons via palladium catalysis. *Chem. Sci.* **2019**, *10*, 5736–5742. [[CrossRef](#)] [[PubMed](#)]
83. Frisch, M.J. *Gaussian 09*, Revision A. 02; Gaussian, Inc.: Wallingford, CT, USA, 2009.
84. Lee, C.T.; Yang, W.T.; Parr, R.G. Development of the Colle-Salvetti Correlation-Energy Formula into a Functional of the Electron Density. *Phys. Rev. B* **1988**, *37*, 785–789. [[CrossRef](#)]
85. Perdew, J.P.; Wang, Y. Accurate and Simple Analytic Representation of the Electron-gas Correlation Energy. *Phys. Rev. B Condens. Matter Mater. Phys.* **1992**, *45*, 13244–13249. [[CrossRef](#)]
86. Beck, A.D. Density-Functional Thermochemistry. III. The Role of Exact Exchange. *J. Chem. Phys.* **1993**, *98*, 5648–5652. [[CrossRef](#)]
87. Perdew, J.P.; Burke, K.; Wang, Y. Generalized Gradient Approximation for the Exchange–Correlation Hole of a Many-Electron System. *Phys. Rev. B* **1996**, *54*, 16533–16539. [[CrossRef](#)] [[PubMed](#)]
88. Dolg, M.; Wedig, U.; Stoll, H.; Preuss, H. Energy-Adjusted ab initio Pseudopotentials for the First Row Transition Elements. *J. Chem. Phys.* **1987**, *86*, 866–872. [[CrossRef](#)]
89. Gusev, D.G. Assessing the Accuracy of M06-L Organometallic Thermochemistry. *Organometallics* **2013**, *32*, 4239–4243. [[CrossRef](#)]
90. Zhao, Y.; Truhlar, D.G. Density Functionals with Broad Applicability in Chemistry. *Acc. Chem. Res.* **2007**, *41*, 157–167. [[CrossRef](#)]
91. Barone, V.; Cossi, M. Quantum Calculation of Molecular Energies and Energy Gradients in Solution by a Conductor Solvent Model. *J. Phys. Chem. A* **1998**, *102*, 1995–2001. [[CrossRef](#)]
92. Cossi, M.; Rega, N.; Scalmani, G.; Barone, V. Energies, Structures, and Electronic Properties of Molecules in Solution with the C-PCM Solvation Model. *J. Comput. Chem.* **2003**, *24*, 669–681. [[CrossRef](#)]
93. Marenich, A.V.; Cramer, C.J.; Truhlar, D.G. Universal Solvation Model Based on Solute Electron Density and on a Continuum Model of the Solvent Defined by the Bulk Dielectric Constant and Atomic Surface Tensions. *J. Phys. Chem. B* **2009**, *113*, 6378–6396. [[CrossRef](#)]
94. Legault, C.Y. *CYLview*, 1.0b; Université de Sherbrooke: Sherbrooke, QC, Canada, 2009. Available online: <http://www.cylview.org> (accessed on 10 January 2020).

Disclaimer/Publisher’s Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.