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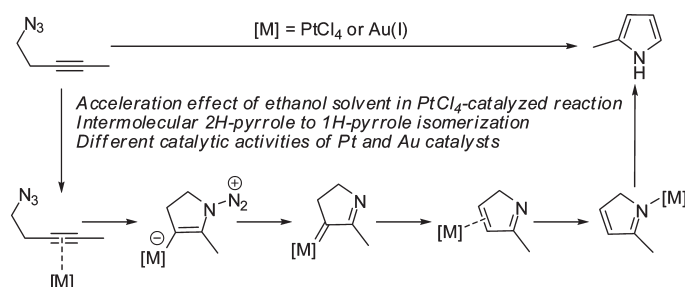
Mechanisms of the Au- and Pt-Catalyzed Intramolecular Acetylenic Schmidt Reactions: A DFT Study

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The reaction mechanisms of the PtCl₄- and Au(I)-catalyzed intramolecular acetylenic Schmidt reactions were analyzed by means of hybrid density functional calculations at the B3LYP/6-31G*(LANL2DZ) level of theory for better understanding of the acceleration effect of ethanol solvent in PtCl₄-catalyzed reaction and the different catalytic activities of Au and Pt catalysts. Calculations indicate the rate of the PtCl₄-catalyzed reaction in noncoordinative solvent of 1,2-dichloroethane is limited by isomerization of the relatively stable chelate complex to the reactive π -complex of PtCl₄ with the acetylenic moiety of homopropargyl azide substrate, which requires an activation energy of 29.6 kcal/mol. All nucleophilic cyclization, dinitrogen elimination, and 1,2-H shift of metal-carbene steps are quite facile. The generation of 2*H*-pyrrole intermediate in PtCl₄-catalyzed reaction is completed by a ligand substitution reaction, and the final 2*H*-pyrrole to 1*H*-pyrrole isomerization is an intermolecular process with another 2*H*-pyrrole as a proton shuttle. When in ethanol solution, the favorable coordination of solvent molecules with PtCl₄ could inhibit the chelation of PtCl₄ with the homopropargyl azide. Besides, the alcohol coordination also facilitates the generation of 2*H*-pyrrole intermediate and the intermolecular isomerization of 2*H*-pyrrole to 1*H*-pyrrole. Consequently, the overall activation barrier of PtCl₄-catalyzed reaction in ethanol solution is lowered to 21.5 kcal/mol, determined by the H-abstraction step of the intermolecular 2*H*-pyrrole to 1*H*-pyrrole isomerization. The basic steps in the Au(I)-catalyzed reaction are similar to those in the PtCl₄-catalyzed one. However, no chelate complex could be formed from PR₃AuSbF₆ and homopropargyl azide, and the 2*H*-pyrrole generation step is much more favorable, indicating weaker interactions of Au(I) catalyst with the homopropargyl azide and the C–C double bond of 2*H*-pyrrole.

1. Introduction

Pyrroles are one of the most important classes of heterocyclic compounds due to their wide appearance in medicinal

chemistry,¹ material science,² and polymer synthesis.³ Furthermore, they are useful building blocks in the synthesis of many physiologically interesting natural products as well as

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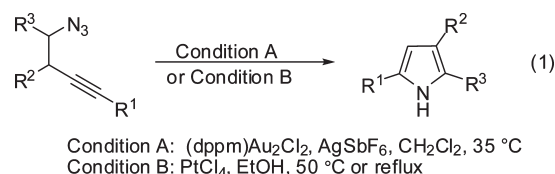
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in heterocyclic chemistry.⁴ Therefore, many methods exist for the organic synthesis of pyrrole derivatives. The classical methods for pyrrole synthesis include the Paal–Knorr condensation reaction,⁵ Knorr reaction,⁶ Hantzsch reaction,⁷ and Barton–Zard reaction.⁸ Recently, the development of metal-catalyzed one-, two-, or multi-component reactions for synthesis of highly substituted pyrroles has attracted tremendous interest.⁹

Over the past decade, organic chemists have witnessed a significant advance in the π -acidic transition metal-catalyzed

SCHEME 1



cyclization of unsaturated precursors for the synthesis of carbonyl and heterocycles,¹⁰ and new methodologies based on platinum and gold catalysis have grown into a major field of experimental¹¹ as well as theoretical research.¹² In this respect, a variety of methods for the synthesis of pyrroles are described by using gold catalysts,¹³ while the employment of platinum complexes is rare.¹⁴ The recent Schmidt reaction of homopropargyl azides from the Toste group and the Hiroya group represents a rare example of pyrrole synthesis in which both Au and Pt complexes are capable catalysts (Scheme 1).^{15a,b}

Despite the convenient synthesis of substituted pyrrole by both methods, it is interesting to find that different reaction conditions were employed in the reactions. While Toste et al. found that the combination of (dppm)Au₂Cl₂ with AgSbF₆ could efficiently promote the conversion of homopropargyl azide into substituted pyrrole in dichloromethane solution (Condition A), the efficiency of this transformation was more condition-dependent in the Pt-catalyzed reaction of Hiroya and co-workers. Namely, the PtCl₄-catalyzed reactions were rather sluggish in 1,2-dichloroethane solution. Interestingly, great improvement of the reaction rate was observed if the PtCl₄ catalyst was stirred in ethanol solution for 1 h at 50 °C before adding the substrate (Condition B). Different catalytic activities of Au and Pt complexes have been observed in many reactions, and the understanding of such difference from a mechanistic point of view is still highly desirable.¹⁶

The plausible mechanism of these metal-catalyzed Schmidt reactions is outlined in Scheme 2. In this mechanism, the carbophilic transition metal Pt or Au first activates the triple bond of **A** and triggers the intramolecular nucleophilic addition of the proximal nitrogen atom of the azide moiety to give cyclic intermediate **C**. Then the loss of dinitrogen from **C** leads to carbene intermediate **D**, which could produce the 2H-pyrrole (**E**) and regenerate the active catalyst via a formal 1,2-H shift.

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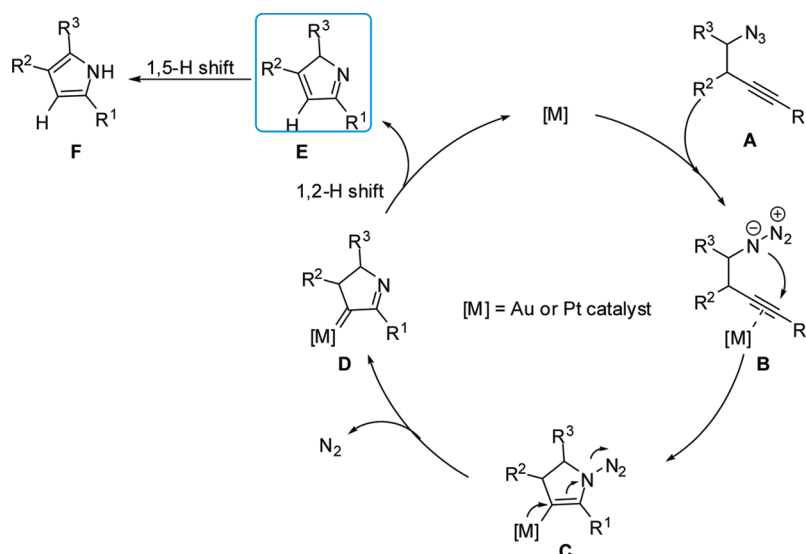
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SCHEME 2



Finally, the 1*H*-pyrrole product (**F**) is formed from the tautomerization of 2*H*-pyrrole. In addition, another possible mechanism initiated by metal-promoted decomposition of the azide for generation of a nitrene-like intermediate was not ruled out by the experiments.^{15a,b}

We are very interested in the different catalytic activity of Au and Pt catalysts in the intramolecular Schmidt reactions of homopropargyl azides, particularly how the PtCl₄-catalyzed reaction is accelerated in ethanol solution and why an induction period is necessary. According to the experimental facts and the possible mechanism, several aspects of these reactions are worthy of investigation. First, since ethanol is a coordinative solvent, we hypothesized that the first coordination of solvent molecule to the platinum catalyst may occur during the induction period. But why further reactions could be facilitated by the ethanol coordination is unknown. Second, the mechanism in Scheme 2 suggests that the 1,2-H shift is involved in **D** to **E** transformation, thus the possibility of ethanol-catalyzed H-shift should be considered. Several recent

studies of gold chemistry have revealed that such H migrations could be assisted by alcohol, water, or ligands.¹⁷ Third, the 2*H*-pyrrole (**D**) has been proposed as a key intermediate in many pyrrole syntheses;¹⁸ however, the tautomerization of 2*H*-pyrrole to 1*H*-pyrrole is difficult, as theoretical studies at different levels have shown the activation barrier is over 34 kcal/mol.¹⁹ The details of this tautomerization process in Au- and Pt-catalyzed intramolecular acetylenic Schmidt reactions are unclear. Moreover, an in-depth comparison of the mechanism of the Au-catalyzed reaction with that of the Pt-catalyzed one is important to understand the different catalytic activity of Au and Pt.

The detailed catalytic cycle of Au and Pt catalysts and the solvent effect on Pt-catalyzed reaction are not easily accessible by experiment. Therefore, we report herein a DFT computational study on the Au- and Pt-catalyzed intramolecular acetylenic Schmidt reactions, aiming to better understand the experimental observations and to reveal the origin of different catalytic activity of the two catalysts at a molecular level. The experimental results are satisfactorily explained from the discussion of detailed potential energy surfaces and

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the geometric structures of intermediates and transition states involved in these transformations. While recent works mainly focused on the importance of alcohol (and water) in H-migrations in gold catalysis,¹⁷ the present study uncovered the significance of solvent coordination with catalyst in the PtCl₄-catalyzed reaction, that the precoordination of alcohol solvent could inhibit the chelation of PtCl₄ catalyst with homopropargyl azide substrate and thus facilitates the following intramolecular nucleophilic cyclization. The influence of alcohol ligand on other steps was also investigated. The computational results indicated the generation of 1*H*-pyrrole product from 2*H*-pyrrole intermediate is an intermolecular process in both Au- and Pt-catalyzed reactions, in which the 2*H*-pyrrole itself acts as proton shuttle to catalyze the 1,5-H shift, and greatly lowers the tautomerization barrier to about 20 kcal/mol. Furthermore, the feature of Au(I) catalyst in the concerned reaction was demonstrated by comparing the energy of each fundamental step with that of the Pt catalyst.

2. Computational Method

All of the DFT calculations were performed with the Gaussian 09 program package.²⁰ The geometry optimizations of all minima and transition states involved were performed at the B3LYP levels of theory.²¹ The 6-31G* basis set was used for C, H, O, P, Cl, and N atoms,²² while the LANL2DZ basis set was used for Pt and Au.²³ These methods have been proven reliable

in numerous theoretical simulations of the mechanisms of Pt- and Au-catalyzed reactions.^{12,17,24} The vibrational frequencies were computed at the same level of theory as that for the geometry optimization to check whether the optimized geometrical structure is at an energy minimum (no imaginary frequency) or a transition state (only one imaginary frequency). Intrinsic reaction coordinate (IRC) calculations were used to confirm that the transition states connected the related reactants and products.²⁵ Bulk solvent effects were computed by the Polarizable Continuum Model (PCM) with UAO radii at the B3LYP/6-31G*(LANL2DZ) level using the gas-phase optimized structures.²⁶ The dielectric constant in the PCM calculations was set to $\epsilon = 10.360$, 24.550, and 8.930 for simulation of dichloroethane (DCE), ethanol (EtOH), and dichloromethane (DCM), respectively, the solvents used in experiments. Solvation free energies (ΔG_{DCE} , ΔG_{EtOH} , and ΔG_{DCM}) were calculated by adding the solvation energies to the computed gas-phase relative free energies (ΔG_{298}). All relative energies were referred to the energy sum of free reactant and catalyst. Unless otherwise stated, only the energy and geometry of the lowest energy conformer were provided for a compound that had more than one conformation.

In the experiments of Toste et al. the bidentate phosphine digold(I) complexes (2.5% (dppm)Au₂Cl₂ and 5% AgSbF₆) were found to be the optimal catalysts; however, the combination of 5% PPh₃-AuCl and 5% AgSbF₆ could also produce the 2,5-disubstituted pyrrole in 72% yield.^{15a} Previous works considered cationic [PPh₃Au]⁺ species as the active catalyst in such systems,^{24a,b} whereas calculations indicated that the [PPh₃Au]⁺ moiety has strong interaction with the SbF₆[−] ligand in reactions.^{17b,c,g,27} The simplification of the experimentally used PPh₃ ligand to PH₃ was adopted in many theoretical studies.^{17a,b,24a,b} Thus, it is reasonable to use PH₃AuSbF₆ for simulation of the gold(I) catalyst in the present study. To fully understand the solvent effect in PtCl₄-catalyzed reactions, the possibilities of solvent molecules as ligands and as proton shuttles were considered. In these cases the explicit ethanol and dichloroethane solvents were modeled by methanol and chloromethane, respectively, for minimizing the CPU time.

3. Results and Discussion

In this section, we will first present the PtCl₄-catalyzed intramolecular Schmidt reaction of homopropargyl azides in 1,2-dichloroethane solution to reveal why the reaction was sluggish under this condition, and then the rate acceleration effect of ethanol solvent will be analyzed. Next, the details of 2*H*-pyrrole to 1*H*-pyrrole tautomerization will be discussed. Finally the potential energy surface of the PR₃AuSbF₆-catalyzed reaction is depicted and comparison is made to highlight the difference between Pt and Au catalysts.

3.1. Computational Results for the PtCl₄-Catalyzed Acetylenic Schmidt Reaction in 1,2-Dichloroethane Solution. According to the proposed mechanism in Scheme 2, the detailed potential energy surface of the PtCl₄-catalyzed Schmidt reaction of homopropargyl azide **1** in 1,2-dichloroethane solution is depicted in Figure 1. Geometric structures of selected transition states and intermediates are collected in Figure 2, and the computed structures for all other species are given in the Supporting Information. The possible nitrene pathway is higher in energy and is given in the Supporting Information.

This cyclization reaction starts with the coordination of PtCl₄ catalyst with substrate **1**. Figure 1 shows that the

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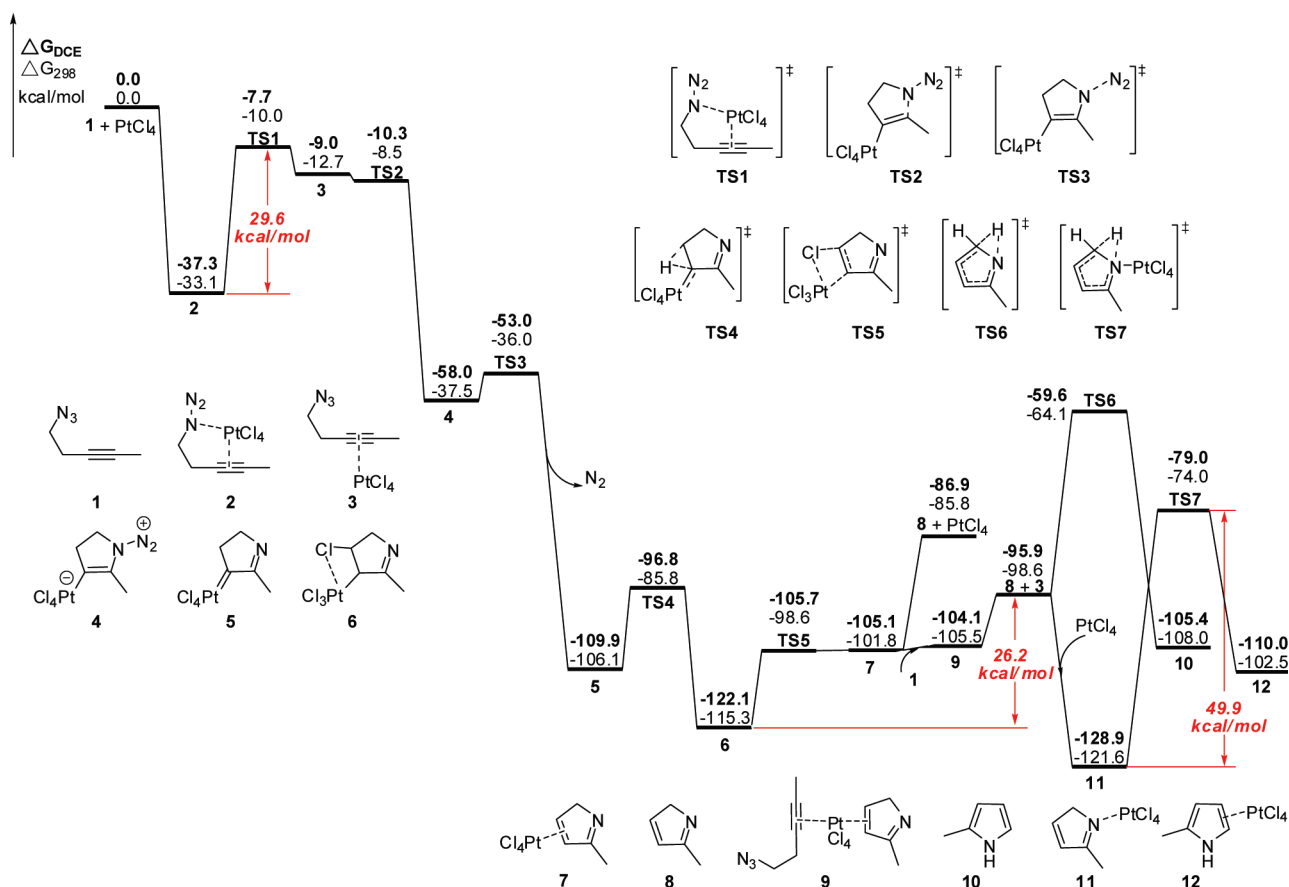


FIGURE 1. Potential energy surface for the PtCl₄-catalyzed acetylenic Schmidt reaction in 1,2-dichloroethane solution.

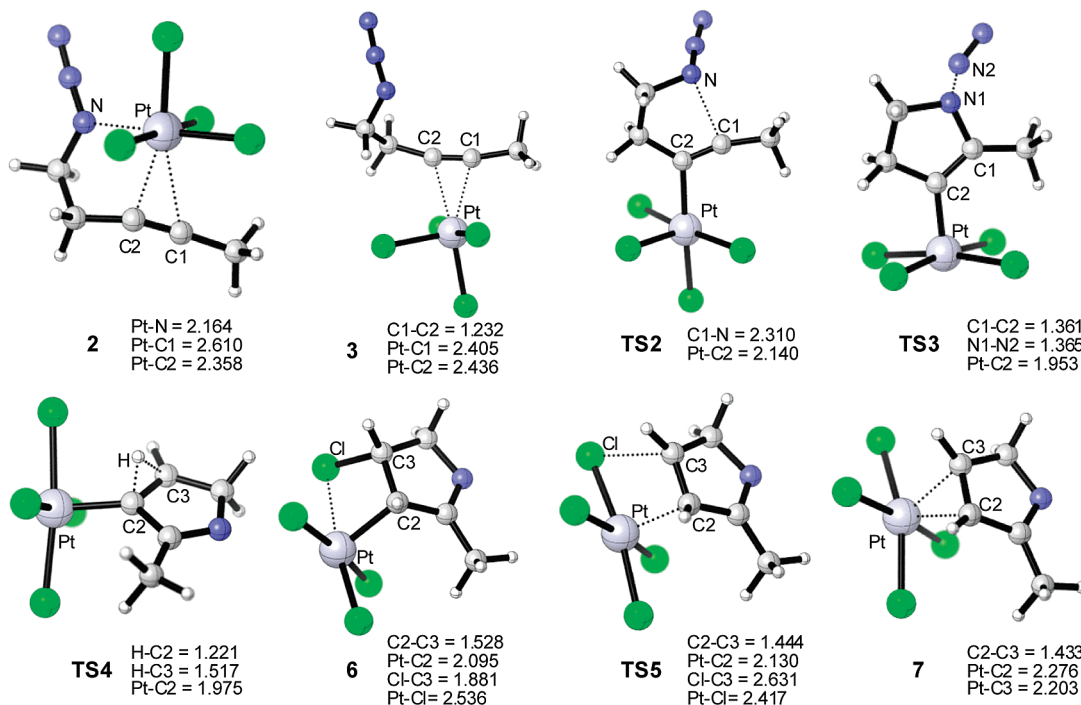
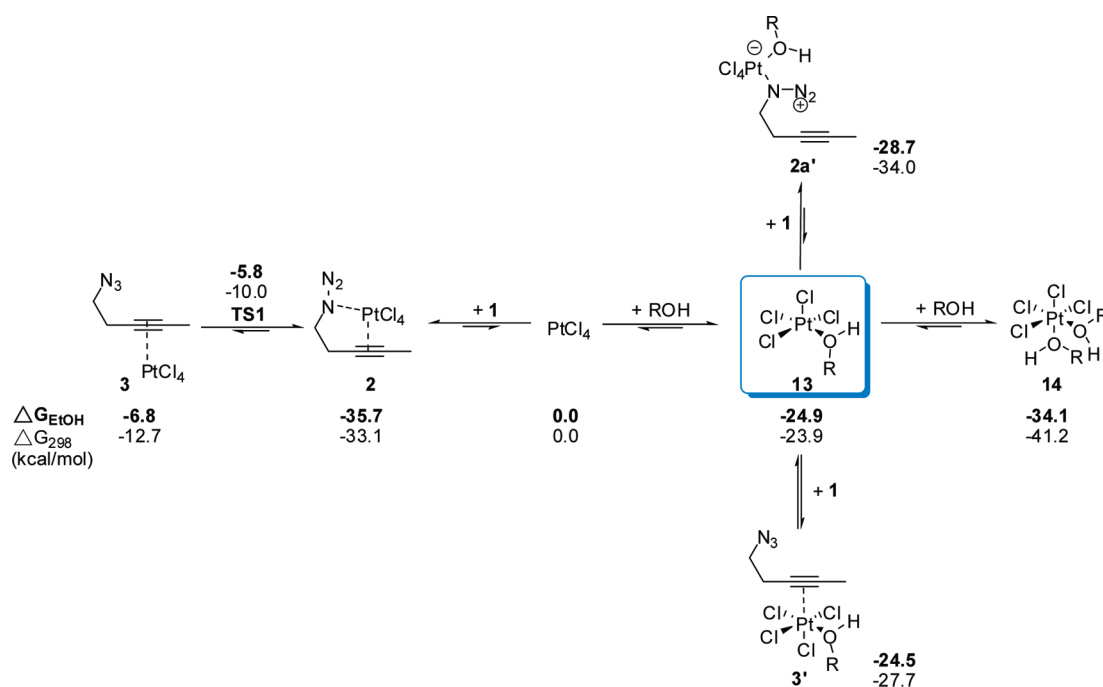


FIGURE 2. Geometric structures for selected intermediates and transition states of the PtCl₄-catalyzed reaction in 1,2-dichloroethane solution; selected distances are in angstroms.

formation of chelate complex 2 is exergonic by 37.3 kcal/mol. In this complex, both the carbon-carbon triple bond and the

proximal nitrogen atom of the homopropargyl azide are coordinated with the Pt center, and the Pt-N, Pt-C1, and Pt-C2

SCHEME 3



distances are 2.164, 2.610, and 2.358 Å, respectively. To effect the intramolecular cyclization, complex **2** could first rearrange into isomeric complex **3** via dissociation of the Pt–N coordination. The transition state corresponding to this process is **TS1**, which has a much more elongated Pt–N distance of 4.328 Å and is 29.6 kcal/mol higher in solvation free energy than **2**. The resulting intermediate **3** is a η^2 - π -complex of PtCl₄ with **1** with the distances between Pt and two sp-hybridized carbon atoms of 2.405 and 2.436 Å. The formation of **3** from **2** is endergonic by 28.3 kcal/mol in 1,2-dichloroethane solution. The subsequent intramolecular nucleophilic cyclization from **3** is quite facile with an activation energy of only 4.2 kcal/mol in the gas phase via transition state **TS2**, in which the forming Cl–N distance is 2.310 Å and Pt is connected to C2 with a distance of 2.140 Å. The generated cyclic intermediate **4** is about 50 kcal/mol lower in energy than **3**. In **4**, the Pt–C2 distance is shortened to 1.966 Å. The solvation free energy of the following dinitrogen elimination transition state **TS3** is only 5 kcal/mol higher than that of **4**. Upon the formation of Pt-carbene **5**, the exergonicity is increased to 109.9 kcal/mol, indicating the nucleophilic cyclization and dinitrogen elimination steps are highly energetically favorable. Geometries show that the breaking N–N distance in **TS3** is only slightly elongated by 0.11 Å compared to that distance in **4**, and the Pt–C2 distance is further shortened to 1.905 Å in **5**.

The following step is a formal 1,2-H migration in the Pt-carbene intermediate **5**. The activation barrier of this step (via **TS4**) is about 13.1 kcal/mol in 1,2-dichloroethane solution. In **TS4**, the shifting hydrogen atom is closer to C2, with the H–C2 and H–C3 distances of 1.221 and 1.517 Å, respectively. IRC calculation indicates the intermediate resulting from 1,2-H shift is **6**, which is 12.2 kcal/mol more stable than **5**. In intermediate **6**, C2 and C3 are σ -bonded with the Pt atom and one Cl ligand, respectively, with the C3–Cl and Pt–C2 distances of 1.881 and 2.095 Å, resulting from the addition of one Pt–Cl bond across the C2–C3 double bond.

The Pt–Cl distance in **6** is 2.536 Å, being about 0.2 Å longer than the other three normal Pt–Cl distances. To generate the 2*H*-pyrrole intermediate, **6** could first isomerize to π complex **7** via **TS5**. This step requires an activation energy of 16.4 kcal/mol, and **7** is 17 kcal/mol less stable than **6**. In **TS5**, the Pt–Cl and C2–C3 distances are shortened to 2.417 and 1.444 Å, respectively, and the Pt–C2 and C3–Cl distances are elongated to 2.130 and 2.631 Å. The C2–C3 distance in **7** is 1.433 Å, significantly longer than the normal C–C double bond distance.²⁸ This implies the strong interaction between C2–C3 and PtCl₄. As a result, the dissociation of **7** into PtCl₄ and 2*H*-pyrrole **8** is endergonic by 18.2 kcal/mol. Thus, the direct formation of **8** is unfavorable due to the large energy gap (35.2 kcal/mol) from **6** to **8** and PtCl₄. We envisioned a ligand exchange reaction between substrate **1** and complex **7** to be more feasible. Indeed, the free energy is increased by only 1 kcal/mol for the formation of complex **9** from the coordination of **1** with **7**. The interaction between Pt and the C2–C3 double bond is weakened in complex **9**, as evidenced by the obviously elongated Pt–C2 and Pt–C3 distances of 2.547 and 2.465 Å, respectively. Then the dissociation of **9** into **8** and **3** is endergonic by 8.2 kcal/mol. Accordingly, the energy required for generation of 2*H*-pyrrole **8** from **6** is 26.2 kcal/mol via the intermediacy of complexes **7** and **9**.

The final step of the reaction is tautomerization of 2*H*-pyrrole **8** to 1*H*-pyrrole **10**. The 1,5-H shift transition state **TS6** is 62.5 kcal/mol higher in energy than intermediate **6**. Alternatively, the coordination of PtCl₄ with the N site of **8** is exergonic by 33 kcal/mol, leading to intermediate **11**, which is the global minimum on the potential energy surface. However, the activation barrier for the 1,5-H shift via **TS7** is still

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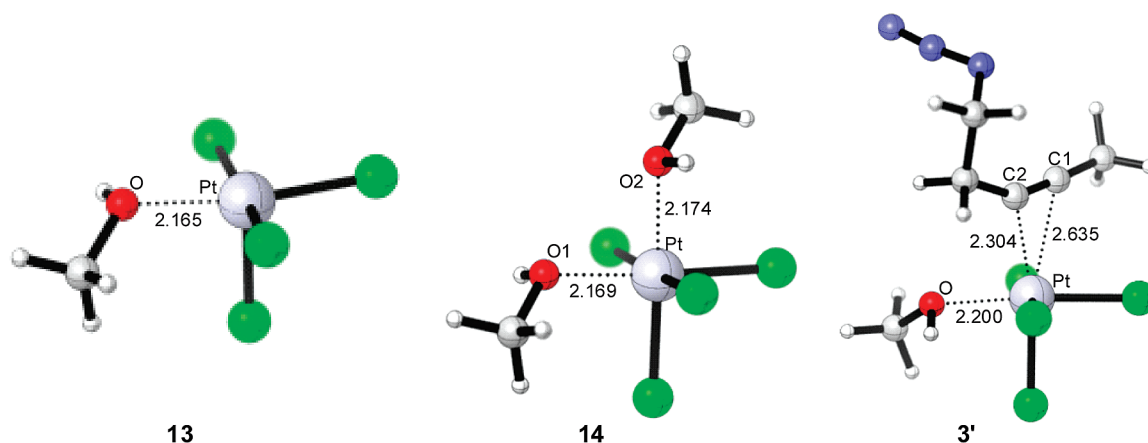
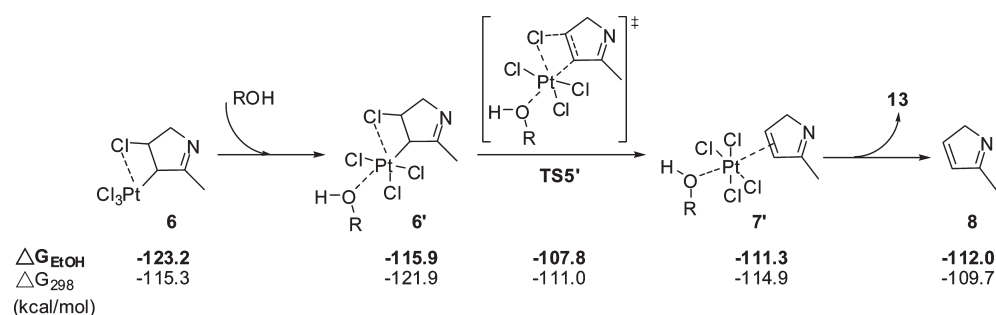


FIGURE 3. Geometric structures for complexes **13**, **14**, and **3'**; selected distances are in angstroms.

SCHEME 4



as high as 49.9 kcal/mol. These results indicate that the tautomerization of 2*H*-pyrrole **8** to 1*H*-pyrrole **10** via an intramolecular 1,5-H migration is not feasible kinetically.²⁹ In fact, later results of this study find the intermolecular H-migrations are more favorable, and the isomerization of chelate complex **2** to **3** is the rate-limiting step of the PtCl₄-catalyzed reaction in 1,2-dichloroethane solution.

Thus, the computational results in Figure 1 reveal that all the nucleophilic cyclization, dinitrogen elimination, and 1,2-H shift of Pt-carbene steps are relatively easy for the PtCl₄-catalyzed reaction in 1,2-dichloroethane solution. However, the reaction efficiency is limited by several factors, including (1) the formation of chelated complex **2** retards the following intramolecular cyclization, as the isomerization of **2** to **3** requires an activation energy of 29.6 kcal/mol, (2) the energy for generation of 2*H*-pyrrole **8** from σ -bonded complex **6** is about 26.2 kcal/mol, indicating this step is also energetically demanding, and (3) the intramolecular 1,5-H shift for converting 2*H*-pyrrole intermediate to 1*H*-pyrrole product is not possible due to the very high activation barrier of 49.9 kcal/mol of this process.

3.2. How Does Alcohol Solvent Accelerate the PtCl₄-Catalyzed Reaction? The above results disclose the factors that may influence the PtCl₄-catalyzed reaction in 1,2-dichloroethane. We next focus on the acceleration effect of alcohol solvent on the reaction. We first change the solvent to ethanol in the

PCM solvation model calculations. However, only marginal variation of the potential energy surface is detected. Considering the fact that an induction period was necessary for rate acceleration of Hiroya's reactions in ethanol solution, we propose the first complexation of PtCl₄ catalyst with alcohol solvent may occur during this period. Besides, the coordination of PtCl₄ with alcohol solvent may ease the 2*H*-pyrrole generation step, as Figure 1 has demonstrated the promoting effect of substrate coordination on this step. In addition, the presence of alcohol as proton shuttle to facilitate the 2*H*-pyrrole to 1*H*-pyrrole tautomerization is also possible. Therefore, the influences of alcohol solvent on the key steps of PtCl₄-catalyzed reaction are detailed here.

The coordination energy of alcohol solvent (explicit solvent is exemplified by MeOH) to PtCl₄ catalyst is given in Scheme 3. The formation of **13** from PtCl₄ and one MeOH is exergonic by 24.9 kcal/mol, and the solvation free energy is further decreased to -34.1 kcal/mol upon the formation of hexacoordinated complex **14** (Figure 3). This energy is comparable to the formation energy of chelate complex **2**. Hence, it is most likely that complex **14** is formed first during the induction period. In reactions, equilibration of **14** to **13** by losing one alcohol ligand is a facile process with the solvation free energy increased by only 9.2 kcal/mol. Coordination of **13** to the carbon-carbon triple bond of substrate **1** is almost thermodynamically neutral, as **3'** is only 0.4 kcal/mol higher in energy than **13**. Then from **3'**, the following nucleophilic cyclization and dinitrogen elimination steps are quite facile and irreversible (vide infra). These results demonstrate that the precoordination of alcohol solvent prevents the

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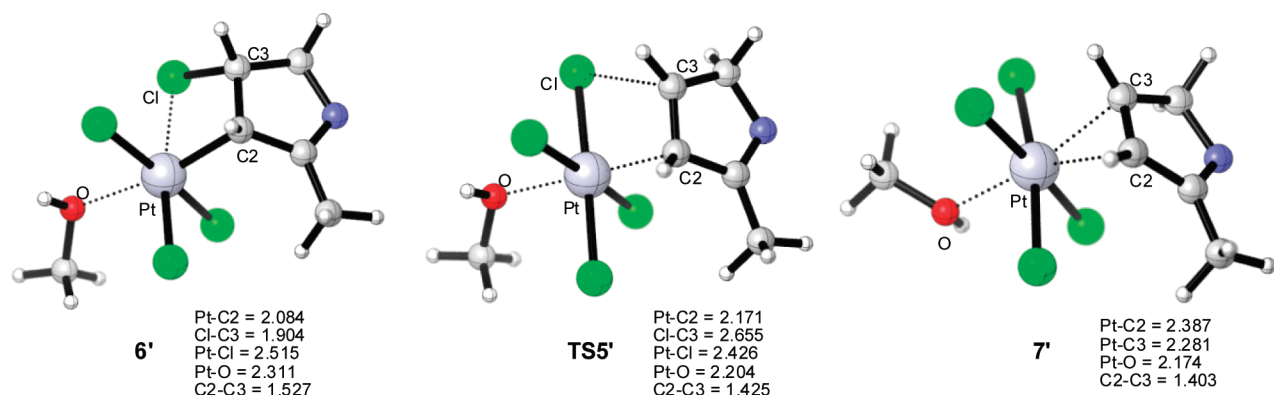
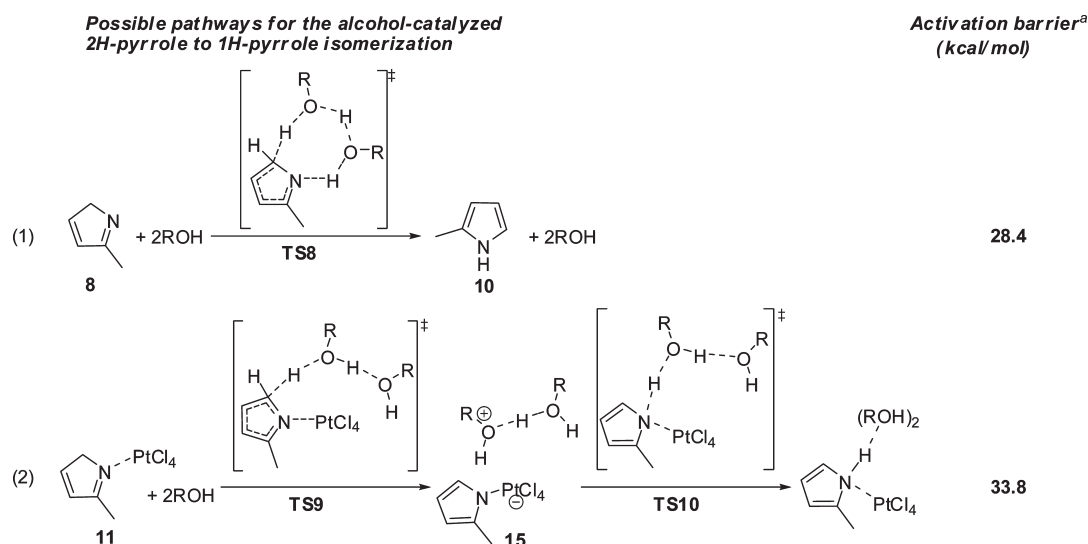


FIGURE 4. Geometric structures for 6', TS5', and 7'; selected distances are in angstroms.

SCHEME 5



^aActivation free energies in ethanol solution. Detailed potential energy surfaces are depicted in the Supporting Information.

chelation of PtCl₄ with homopropargyl azide **1**, and provides a low-energy-lying pathway to the reactive reactant complex 3'.³⁰ Although the coordination of **13** with the proximal nitrogen of **1** to give **2a'** is slightly exergonic, calculations suggest the following reaction from this intermediate is kinetically unfavorable.²⁷

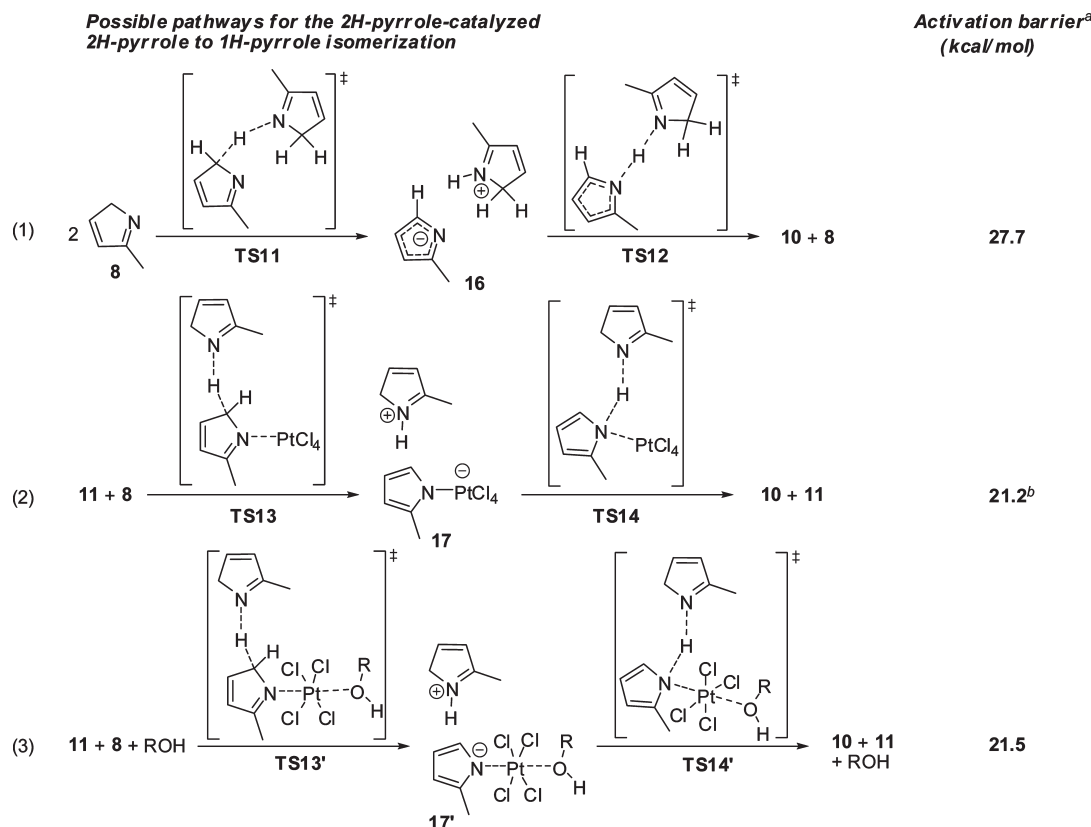
In 1,2-dichloroethane solution, the energy needed for generation of 2H-pyrrole **8** from **6** is about 26.2 kcal/mol via the ligand exchange reaction. The influence of alcohol ligand on this process is given in Scheme 4, and optimized geometries are depicted in Figure 4. The free energy is increased by 7.3 kcal/mol for the complexation of **6** with MeOH to give 6'. Then via TS5' the σ -bonded complex 6' is transformed to π -bonded complex 7'. Due to endergonic formation of 6' from **6** and MeOH, the activation energy for β -Cl elimination via TS5' is 15.4 kcal/mol, similar to that of the process without alcohol ligand. In contrast to the unfavorable dissociations of complexes **7** and **9**, the dissociation of 7'

into **13** and **8** is almost energetically neutral. Thus, the generation of 2H-pyrrole intermediate **8** from **6** is facilitated by the coordination of alcohol solvent, and the barrier of this process is decreased to 15.4 kcal/mol, which is determined by the energy gap between **6** and TS5'.

According to Figure 1, the tautomerization of 2H-pyrrole to 1H-pyrrole via an intramolecular 1,5-H shift (TS6 or TS7) is unfeasible, thus the activation energies of possible intermolecular H migrations are calculated. The possible pathways of alcohol solvent-assisted H-migrations are illustrated in Scheme 5, which shows the involvement of two MeOH molecules could efficiently lower the activation barrier to around 30 kcal/mol. When starting from 2H-pyrrole **8**, the tautomerization could be realized via a seven-membered ring transition state (TS8) with an activation free energy of 28.4 kcal/mol. However, the formation of **8** from **6** with the assistance of alcohol coordination is endergonic by 11.2 kcal/mol (Scheme 4), thus making the tautomerization via TS8 unfavorable as the overall barrier is about 40 kcal/mol. Alternatively, the formation of **11** from 2H-pyrrole and PtCl₄ is highly exergonic in catalytic reaction (Figure 1). Calculations indicate the 1,5-H shift of **11** could be catalyzed by a

(30) As expected, the coordination of PtCl₄ with 1,2-dichloroethane solvent is rather weak. The exergonicities for formations of complexes PtCl₄(CH₃Cl) and PtCl₄(CH₃Cl)₂ from PtCl₄ and CH₃Cl are only 4.6 and 8.1 kcal/mol, respectively.

SCHEME 6



^aActivation free energies in ethanol solution. Detailed potential energy surfaces are depicted in Supporting Information. ^bActivation energy for the first step.

cluster containing two methanol molecules via a stepwise fashion (eq 2, Scheme 5). In this process, the H-abstraction transition state **TS9** is 31.1 kcal/mol higher in energy than **11**, leading to zwitterionic intermediate **15** endergonically, by 25.6 kcal/mol. The activation barrier is determined by the second step, and the free energy of the H-donation transition state **TS10** is 33.8 kcal/mol relative to that of **11**. Despite the dramatic lowering of the 2*H*-pyrrole to 1*H*-pyrrole tautomerization activation barrier by methanol cluster, the 33.8 kcal/mol activation energy is still too high, considering the reactions were carried out at 50 °C or in refluxing ethanol. Besides, how the reaction occurred in solvents other than ethanol is still unclear.

3.3. Intermolecular 2*H*-Pyrrole to 1*H*-Pyrrole Isomerization with a 2*H*-Pyrrole Proton Shuttle. The previous calculations indicate that 2*H*-pyrrole intermediate could be generated in both 1,2-dichloroethane and ethanol solutions. We hypothesize the final tautomerization of 2*H*-pyrrole to 1*H*-pyrrole could be realized via the 2*H*-pyrrole-assisted H migrations.³¹ Scheme 6 shows the activation energies of the pathways in which one 2*H*-pyrrole acts as a proton shuttle to facilitate the 1,5-H shift. The reaction between two 2*H*-pyrrole **8** is a two-step proton transfer process (eq 1, Scheme 6). The first step consists of the deprotonation of 2*H*-pyrrole via **TS11**, requiring an activation energy of 27.7 kcal/mol. In **TS11** the N'–H and C4–H distances are 1.175 and 1.567 Å, respectively (Figure 5). The free energy is increased by 24.5 kcal/mol for

generation of intermediate **16**. In this zwitterionic species the protonated 2*H*-pyrrole moiety interacts with the delocalized negative charge via H-bonding interactions. Geometries in Figure 5 show the H–C1, H–C2, H–C3, H–C4, and H–N distances in **16** are 2.396, 2.384, 2.093, 1.926, and 2.181 Å, respectively. As a result of the charge separation, intermediate **16** is highly unstable and could be transformed to **10** and **8** via **TS12** with an activation energy of only 0.8 kcal/mol. In fact, **TS12** is not a typical hydrogen transfer transition state. The imaginary vibrational mode shows in **TS12** the cationic moiety is moving toward the nitrogen atom of the pyrrole anion. The geometry of **TS12** reveals the H–C2, H–C3, and H–C4 are elongated to 2.548, 2.361, and 1.943 Å, respectively, while the H–C1 and H–N distances are shortened to 2.295 and 1.954 Å. As mentioned above, however, the formation of 2*H*-pyrrole **8** from intermediate **6** is endergonic by 11.2 kcal/mol with an alcohol solvent coordinated to PtCl₄, and even higher endergonicity is predicted without the alcohol ligand. Thus, in reactions the intermolecular tautomerization of 2*H*-pyrrole via **TS11** and **TS12** is not possible.

According to the favorable formation of **11** from the coordination of PtCl₄ with the nitrogen site of 2*H*-pyrrole, the 2*H*-pyrrole-assisted H migrations of **11** are shown in eq 2, Scheme 6, and the influence of alcohol solvent coordination on this process is given in eq 3. In eq 2, the H-abstraction by 2*H*-pyrrole via **TS13** has an activation energy of 21.2 kcal/mol, and the energy of the generated zwitterionic intermediate **17** is 5.7 kcal/mol higher than the energy sum of **11** and **8**.

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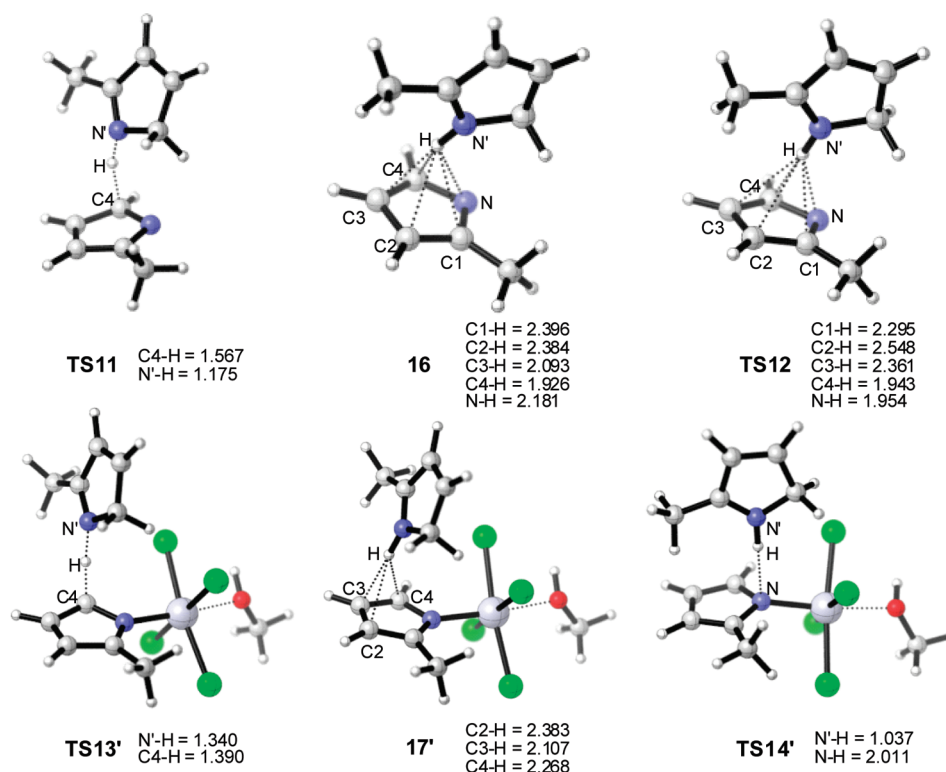


FIGURE 5. Geometric structures for selected intermediates and transition states in *2H*-pyrrole-catalyzed *2H*-pyrrole to *1H*-pyrrole isomerizations; selected distances are in angstroms.

All attempts to locate a transition structure corresponding to the H-donation (**TS14**) failed. This may be attributed to the decreased basicity of the nitrogen atom of pyrrole anion, which is coordinated to PtCl_4 in **17**. Such a problem is not encountered when one alcohol is incorporated as a ligand (eq 3, Scheme 6). Calculations indicate the complexation of MeOH with **11** to form **11'-b** is exergonic by about 10 kcal/mol (vide infra). The energy barrier for the H-abstraction via **TS13'** is 21.5 kcal/mol, which is similar to that without the MeOH ligand. Zwitterionic intermediate **17'** is 9.1 kcal/mol higher in energy than **11'-b**, and the activation energy for the H-donation via **TS14'** is 11.5 kcal/mol. Thus the activation free energy for *2H*-pyrrole-catalyzed H-migration of **11** in alcohol solution is 21.5 kcal/mol, determined by the H-abstraction transition state **TS13'**. The geometric structures of related intermediate and transition states are depicted in Figure 5.

For the PtCl_4 -catalyzed reactions in 1,2-dichloroethane solution, another *2H*-pyrrole could coordinate to the Pt catalyst in place of alcohol solvent as a σ -ligand. In this case, the activation energy of the *2H*-pyrrole-assisted H-migration is about 24.9 kcal/mol.²⁷

3.4. Overall Catalytic Cycle of the PtCl_4 -Catalyzed Reaction in Ethanol Solution. The energy profile of the overall catalytic cycle of PtCl_4 -catalyzed reaction in ethanol solution is depicted in Figure 6. The reaction starts with the ligand exchange of complex $\text{PtCl}_4(\text{MeOH})_2$ **14** with substrate **1**, yielding reactant complex **3'** with an endergonicity of 9.6 kcal/mol. Intermediate **4'** could be formed easily from the intramolecular cyclization of **3'**. After an energetically favorable dissociation of the MeOH ligand, intermediate **4** undergoes a facile dinitrogen elimination step, leading to platinum-carbene **5** highly exergonic. The following 1,2-H shift of **5** has an

activation energy of only about 11 kcal/mol. This exergonic step leads to intermediate **6**, in which the Pt atom and one Cl ligand are σ -bonded with C2 and C3 of the heterocycle moiety, respectively. The generation of *2H*-pyrrole **8** from **6** is facilitated upon the incorporation of one MeOH ligand. In the process, a first formation of **6'** from the coordination of MeOH with **6** is slightly endergonic. Then π -complex **7'** is formed from a β -Cl elimination (via **TS5'**) and the liberation of **8** is realized by a ligand dissociation step. The final formation of *1H*-pyrrole product from *2H*-pyrrole intermediate is an intermolecular process featuring a *2H*-pyrrole proton shuttle to catalyze the H-migration. Coordination of **13** to the nitrogen site of **8** is exergonic by 23.9 kcal/mol, generating hexacoordinated complex **11'-a**. Prior to the incorporation of another *2H*-pyrrole, **11'-a** would isomerize to a more thermodynamically stable isomer **11'-b**, in which both *2H*-pyrrole and MeOH ligands occupy the axial positions.³² Formation of H-bonding complex **18'** from **11'-b** and **8** is endergonic by 14.3 kcal/mol. The H-abstraction by *2H*-pyrrole represents the rate-limiting step of the whole reaction, and transition state **TS13'** lies 21.5 kcal/mol above **11'-b**. The resulting zwitterionic intermediate **17'** is 9.1 kcal/mol less stable than **11'-b**. The catalytic cycle is completed by a relatively facile H-donation step (via **TS14'**), from which the *1H*-pyrrole product is formed in company

(32) The *2H*-pyrrole-assisted H-migration starting from **11'-a** is slightly higher in energy. The barrier for **11'-a** to **11'-b** isomerization is 18.9 kcal/mol. The detailed potential energy surfaces are given in the Supporting Information. Such isomerization is quite facile via a dissociation, isomerization, and recoordination process. See: (a) Braga, A. A. C.; Ujaque, G.; Maseras, F. *Organometallics* **2006**, 25, 3647. (b) Wang, M.; Cheng, L.; Hong, B.; Wu, Z. *Organometallics* **2009**, 28, 1506.

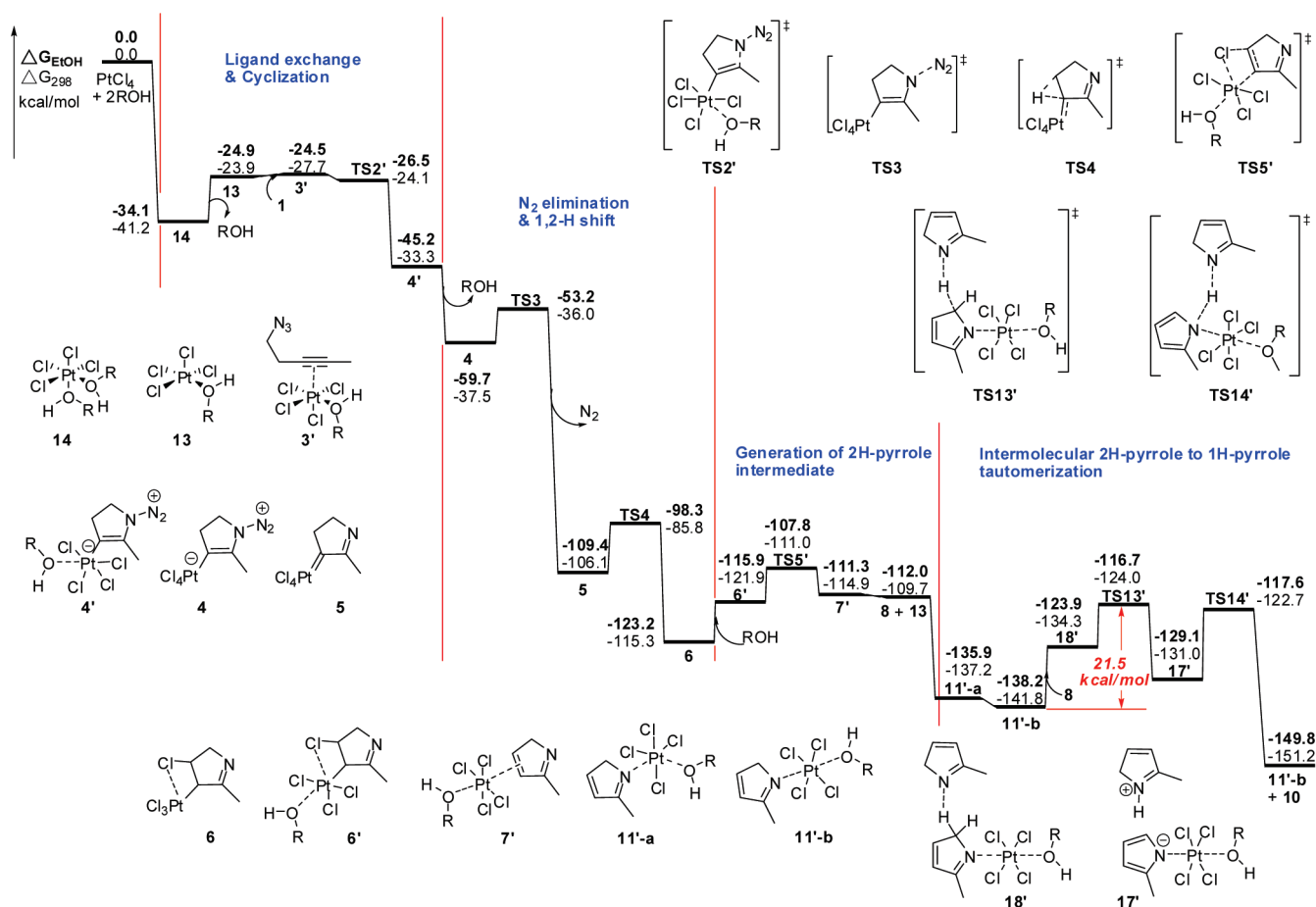


FIGURE 6. Potential energy surface for the overall catalytic cycle of PtCl_4 -catalyzed acetylenic Schmidt reaction in alcohol solution, $\text{R} = \text{Me}$.

with the regeneration of complex **11'-b**. The overall exergonicity of this reaction is about 150 kcal/mol.

3.5. Mechanism of the Au(I)-Catalyzed Acetylenic Schmidt Reaction. As shown in Figure 7, the mechanism of the Au(I)-catalyzed reaction is similar to that of the PtCl_4 -catalyzed reaction. The potential energy surface of the $\text{PH}_3\text{AuSbF}_6$ -catalyzed reaction indicates all the cyclization (via **TS15**), dinitrogen elimination (via **TS16**), and 1,2-H shift of Au-carbene intermediate (via **TS17**) steps are easy to occur with relatively low energy barriers. After the cyclization and dinitrogen elimination steps, carbene intermediate **21** is formed irreversibly with an exergonicity of 55.8 kcal/mol. The 1,2-H shift step leads to π complex **22**, further increasing the exergonicity to 80.4 kcal/mol. Dissociation of π complex **22** into $\text{PH}_3\text{AuSbF}_6$ and 2H-pyrrole **8** is exergonic by 6.5 kcal/mol, suggesting the interaction between Au(I) and the C–C double bond of 2H-pyrrole is rather weak. The coordination of 2H-pyrrole nitrogen site to Au(I) is quite favorable, and the resulting intermediate **23** is 101.3 kcal/mol lower than the energy sum of **1** and $\text{PH}_3\text{AuSbF}_6$. Similarly, the direct 1,5-H shift of **23** via **TS18** is unfeasible due to the insurmountable energy barrier, whereas the intermolecular process with the assistance of a 2H-pyrrole proton shuttle is more favorable. H-bonding complex **24** is first formed from intermediate **23** and 2H-pyrrole, followed by the H-abstraction and H-donation steps. The activation barrier of this process is 20.1 kcal/mol, corresponding to the energy difference between

the H-abstraction transition state **TS19** and intermediate **23**. This is also the highest energy barrier on the reaction pathway. The 1H-pyrrole product and intermediate **23** are generated with a relatively lower activation barrier by passing the final H-donation step, increasing the overall exergonicity to 112.6 kcal/mol.

Accordingly, the different catalytic activity of Au(I) and PtCl_4 catalysts originates from the different coordination behavior of the two catalysts with the substrate and the intermediates. The PtCl_4 catalyst is inclined to form a stable hexacoordinated complex with homopropargyl azide **1**, in non-coordinating solvent, thus retarding the following reactions. Whereas the Au(I) is more selective to the C–C triple bond of substrate **1**, forming complex **19** with the solvation free energy increased by 4.0 kcal/mol. No chelate complex like **2** could be formed from $\text{PH}_3\text{AuSbF}_6$ and **1**.³³ In PtCl_4 -catalyzed reaction, a relatively stable organometallic intermediate **6** is generated from the 1,2-H shift of Pt-carbene. This makes the generation of 2H-pyrrole intermediate difficult, because the barrier required for isomerization of **6** to π complex **7** and the following dissociation of **7** is 35.2 kcal/mol (Figure 1). In contrast, the generation of 2H-pyrrole intermediate in Au(I)-catalyzed reaction is quite facile. Dissociation of π complex **22** to $\text{PH}_3\text{AuSbF}_6$ and 2H-pyrrole is energetically favorable.

(33) The coordination of Au(I) to the proximal nitrogen of the azide is unfavorable, see the Supporting Information for details.

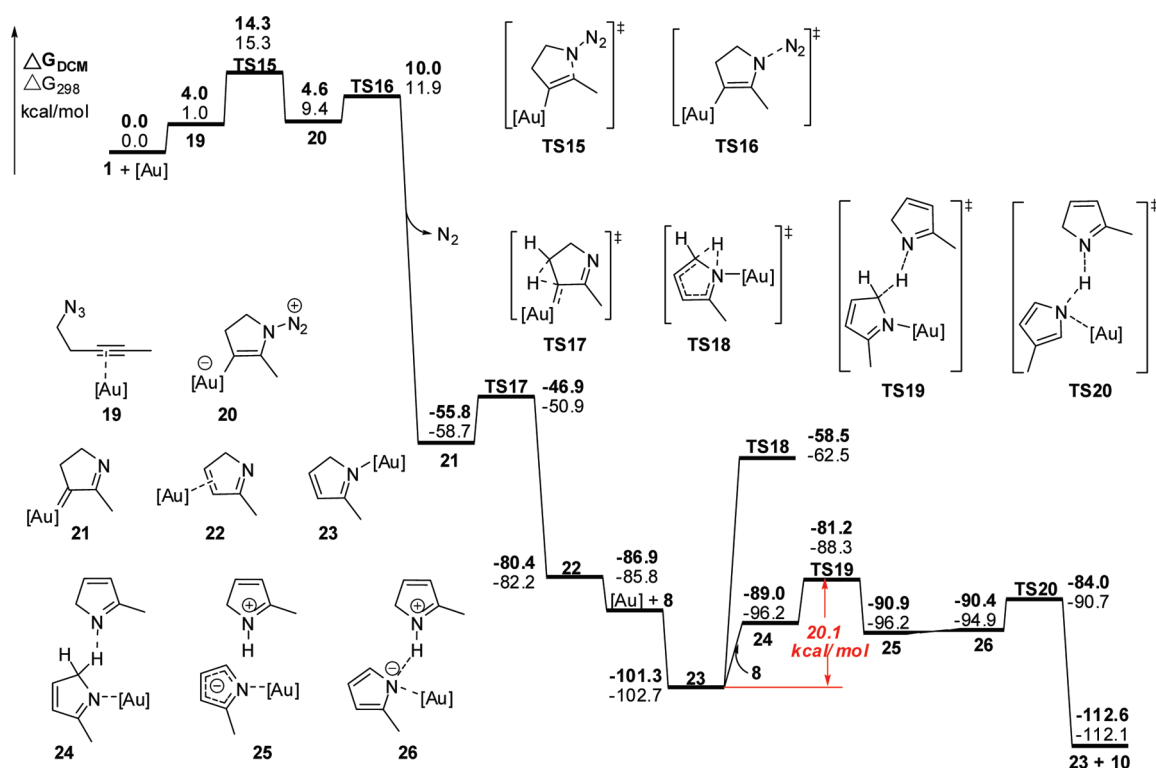


FIGURE 7. Potential energy surface for the Au(I)-catalyzed acetylenic Schmidt reaction in dichloromethane solution, [Au] = $\text{PH}_3\text{AuSbF}_6$.

4. Conclusions

In summary, the reaction mechanisms of PtCl_4 - and Au(I)-catalyzed intramolecular acetylenic Schmidt reaction have been studied with the DFT method at the B3LYP/6-31G*-(LANL2DZ) level of theory. The PtCl_4 -catalyzed reactions in 1,2-dichloroethane and ethanol solutions, acceleration effect of ethanol solvent, details of the intermolecular 2*H*-pyrrole to 1*H*-pyrrole isomerization, and the different catalytic activity of Au and Pt catalysts are presented. These results will provide guidance for the future design of new cyclization reactions in the ever-growing field of gold- and platinum-based catalysis.^{10–12,16}

For the PtCl_4 -catalyzed reaction in 1,2-dichloroethane solution, a relatively stable chelate complex is formed irreversibly from PtCl_4 and homopropargyl azide. The rate of the whole reaction is limited by isomerization of this complex to the reactive π complex, which requires an activation barrier of 29.6 kcal/mol. Via the following facile steps of nucleophilic cyclization, dinitrogen elimination, and 1,2-H shift of Pt-carbene, a σ -adduct from the addition of one Pt–Cl bond to the C–C double bond of 2*H*-pyrrole is obtained highly exergonically. Because this σ -adduct is 17 kcal/mol more stable than the π -complex of 2*H*-pyrrole and PtCl_4 and the dissociation of the latter via an initial incorporation of another substrate is endergonic by 9.2 kcal/mol, the energy required for generation of 2*H*-pyrrole intermediate is 26.2 kcal/mol. While the activation energy for the intramolecular 1,5-H shift of 2*H*-pyrrole is too high to overcome, the intermolecular processes with a 2*H*-pyrrole proton shuttle are more favorable. The energy for the isomerization of 2*H*-pyrrole to 1*H*-pyrrole in 1,2-dichloroethane solution is 24.9 kcal/mol,

in the presence of one 2*H*-pyrrole proton shuttle and one 2*H*-pyrrole σ -ligand.

When the solvent is changed to ethanol and an induction period is used, formation of hexacoordinated complex $\text{PtCl}_4(\text{ROH})_2$ is exergonic by 34.1 kcal/mol. Then the energy required for the formation of the reactive π complex is only 9.6 kcal/mol, via substitution of one alcohol ligand by the C–C triple bond of homopropargyl azide substrate. The involvement of one alcohol ligand to PtCl_4 does not affect much the kinetic and thermodynamic parameters of the nucleophilic cyclization, dinitrogen elimination, and 1,2-H shift of Pt-carbene steps. However, the activation energies for the generation of 2*H*-pyrrole from the σ -adduct and the intermolecular 2*H*-pyrrole to 1*H*-pyrrole isomerization are reduced to 15.4 and 21.5 kcal/mol, respectively. Thus, the acceleration effect of ethanol solvent in PtCl_4 -catalyzed reaction is the result of solvent coordination to the catalyst.

The mechanism of the Au(I)-catalyzed reaction is similar to that of the PtCl_4 -catalyzed one. However, much weaker interactions of $\text{PR}_3\text{AuSbF}_6$ with homopropargyl azide and the C–C double bond of 2*H*-pyrrole are calculated, as no chelate complex could be formed from Au(I) and substrate and the generation of 2*H*-pyrrole by dissociation of the π complex is much easier. This accounts for the different catalytic activity of Au(I) and PtCl_4 in noncoordinative solvents. The final isomerization of 2*H*-pyrrole to 1*H*-pyrrole in Au(I)-catalyzed reaction is also assisted by a 2*H*-pyrrole proton shuttle. The H-abstraction step of this intermolecular process is the rate-controlling step of the overall reaction, with an activation energy of 20.1 kcal/mol.

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Supporting Information Available: Energies and Cartesian coordinates of all stationary points, energetic profiles for

the possible nitrene pathways, the intermolecular *2H*-pyrrole to *1H*-pyrrole isomerizations, and Au(PH₃)⁺-catalyzed reactions, geometries in the PtCl₄⁻ and Au(I)-catalyzed reaction, validation of computational method, and IRC plots for selected transition states. This material is available free of charge via the Internet at <http://pubs.acs.org>.