Density functional theory investigation of the ruthenium-catalyzed cycloisomerization of silicon-tethered 1,7-enynes

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ABSTRACT

Density functional theory calculations at the M06-2X/6-31G(d,p) (RECPs for Ru) level of theory are performed to explore the reaction mechanism for the cycloisomerization of silicon-tethered 1,7-enynes using CpRuCl as a catalyst. The solvent effect is taken into account by M06-2X/6-311++G (d,p) single-point calculations with SMD solvation model in toluene. The calculation results indicate that the reactions of the ruthenium-catalyzed cycloisomerization of 1,7-enynes occur through the possible mechanisms and get five-membered ring or six-membered ring products, respectively. The process of forming six-membered ring product is more favored kinetically with the barrier of 13.6 kcal/mol for Ph group, while the energy barrier for five-membered ring product becomes relatively higher of 34.3 kcal/mol. The above reaction mechanism indicates that the ruthenium-catalyzed cycloisomerization of silicon connected 1,7-enynes has high regioselectivity, which is consistent with the experimental observations of Kaminsky and Clark.

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1. Introduction

Conjugated diene has some important biological activity in a wide variety of natural products [1,2]. These functions are mainly applied to the synthesis of naturally medicinal intermediates. Cycloisomerization of enynes as a very common synthetic method is to generate dienes. Because these reactions of cycloisomerization has many advantages, such as requiring few reagents and generating minimal byproducts [3,4], fast chemical reactions [5] and readily available starting materials [6].

Silicon tethers having highly functionalized systems in stereodefined manner and regioselectivity is widely used in organic synthesis, which have been found to apply to the different reactions including carbosilylation, carbocyclization, silylcyanation, silylcarbonylation, cross-coupling and metathesis [7]. In addition, this type of reaction can build the complex silanes to provide common functional groups in order to further synthesis. The field has attracted the interest of more and more researchers. Most of the work has focused on the study of hydrosilylation chemistry in this area [8]. In recent years, the different ruthenium catalysts have been successfully applied to catalyze intramolecular hydrosilation of alkynes and generate trisubstituted olefins [9–12]. Subsequently, Denmark and coworkers have explored the silylformylation of alkynes and six-membered rings and five-membered rings

could be formed easily [13,14]. Transition-metal-catalyzed the cycloisomerizations of enynes is an atom-economical and a simple method to form diene skeleton [15]. The ruthenium-catalyzed the cycloisomerization of 1,5- and 1,6-enynes has been thoroughly investigated [16–20]. For 1,7 enynes, Trost' group have explored the ruthenium-catalyzed cycloisomerization and acquired 1,4-dienes [21]. Specifically, subsequent studies on silylvinylation of alkynes also have been found that structure 2a is the major product and 3a is the minor byproduct by Clark and coworker (Scheme 1, Eq. (1)) [22].

Recently, Kaminsky and Clark reported the cycloisomerization of vinyl silicon-tethered 1,7-enynes to get exocyclic 1,3-dienes of CpRuCl(COD) catalyst in toluene at 70 °C (Scheme 1, Eq. (2)) [23]. As can be seen from the experimental results, six-membered silylcycles product 3a was only obtained efficiently as the single product by a endocyclic β-H elimination in this reaction system. Many ruthenium-catalyzed reaction mechanisms have been reported [24–32], we have also carried out the theoretical study of a series of metal-catalyzed reactions [33–38]. As far as we know, no relevant theoretical investigation for Ru-catalyzed cycloisomerization has been reported by Kaminsky and Clark. In this paper, we carry out a detailed mechanism investigation based on the computational results from density functional theory for the cycloisomerization of silicon-tethered 1,7-enynes using CpRuCl(COD) as activating reagents. Through mechanism research we hope to find the reasonable factors controlling the activation energy of the reaction in order to guide more efficient synthesis.

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Scheme 1. Ruthenium catalyzed silylvinylation of alkynes.
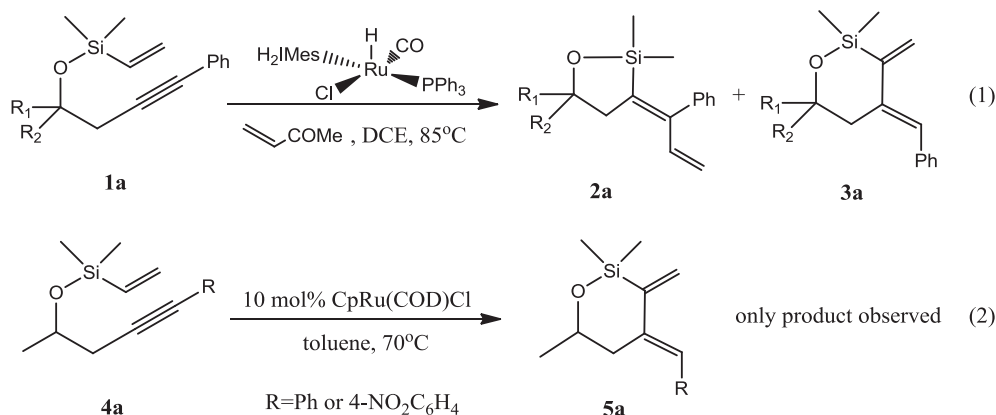
2. Computational methods

All molecular geometries and energies of the model complexes were fully optimized via DFT calculations [39] using the M06-2X hybrid functional [40]. The M06-2X method has been successfully applied in a variety of theoretical studies of metal-catalyzed reactions and given reliable energies [41–44]. The ruthenium atom was selected the basis set including the quasi relativistic effective core pseudo-potentials (RECPs) of the Stuttgart-Bonn group with a polarization function [45,46]. The 6-31G(d, p) basis set [47] was utilized for all other atoms. Vibrational frequency calculations were carried out at the M06-2X/6-31G(d,p) level to identify the computed stationary points as minima or transition states and to give the thermal correction to free energies at 298.15 K. The relative energies are corrected by the vibrational zero-point energies (ZPE). All transition states in the reaction channels were checked by using the intrinsic reaction coordinate (IRC) [48]. To obtain solvation energies, single-point energy calculations were done at the gas-phase optimized geometries using M06-2X/6-311++G(d,p) (RECPs for Ru) with the continuum solvent model SMD [49] in toluene, which was selected as solvent in the experiments. All theoretical calculations were completed with the Gaussian 09 program suites [50].

3. Results and discussion

For cycloisomerization of silicon-tethered 1,7-enynes by CpRuCl (COD), the mechanism have been investigated with CpRuCl as the most effective model catalyst [51,52], and the results have been confirmed in good consistent with the corresponding experimental facts. In these reactions, the relative energy and free energy changes corresponding to the starting materials (**a-IN₁** and **b-IN₁**) in the gas and solution phases are displayed in Table 1. The energy profiles for the ruthenium-catalyzed cycloisomerization channels a and b are presented in Fig. 1. Unless otherwise specified, free energies discussed in subsequent sections refer to the value in toluene solvent. The optimized stationary structures (the intermediates and the transition states) on the potential energy surfaces of the title reactions are depicted schematically in Figs. 2 and 3. The detailed energies and structural parameters for the selected stationary structures are gathered in the Supporting Information.

3.1. Silicon-tethered 1,7-enynes of the phenyl moiety on the alkyne terminus

The path a where the alkenyl and alkynyl π electrons of phenyl substituted alkyne substrate first attacks d orbital of the catalyst CpRuCl, which generates the ruthenium complex **a-IN₁** as a precur-

Table 1
The relative energies and free energies in the gas phase and in solution of the structures (a: R = Ph and b: R = 4-NO₂C₆H₄) in the title reactions.[a]

Species	ΔE_{gas}^{rel}	$\Delta E_{gas}^{\ddagger}$	ΔE_{sol}^{rel}	$\Delta E_{sol}^{\ddagger}$	ΔG_{gas}^{rel}	$\Delta G_{gas}^{\ddagger}$	ΔG_{sol}^{rel}	$\Delta G_{sol}^{\ddagger}$
a-IN₁	0.0		0.0		0.0		0.0	
a-TS₁₋₂	13.3	13.3	13.6	13.6	14.5	14.5	13.6	13.6
a-IN₂	−3.2		−1.2		−4.4		−2.1	
a-TS₂₋₃	2.7	5.9	7.0	8.2	3.4	7.8	6.5	8.6
a-IN₃	−5.2		−4.1		−4.9		−4.8	
a-TS₁₋₄	33.7	38.9	34.6	38.7	34.5	39.4	34.3	39.1
a-IN₄	10.1		10.6		10.3		10.3	
a-TS₄₋₅	29.3	19.2	29.4	18.8	30.3	20.0	29.3	19.0
a-IN₅	−17.4		−16.1		−15.4		−16.0	
a-TS₅₋₆	−2.3	15.1	−2.0	14.1	−3.4	12.0	−2.3	13.7
a-IN₆	−21.0		−20.7		−20.0		−20.3	
b-IN₁	0.0		0.0		0.0		0.0	
b-TS₁₋₂	13.4	13.4	13.9	13.9	14.3	14.3	13.8	13.8
b-IN₂	−2.3		−1.1		−2.2		−1.9	
b-TS₂₋₃	4.6	6.9	8.6	9.7	5.8	8.0	8.1	10.0
b-IN₃	−3.8		−3.5		−3.2		−4.1	
b-TS₁₋₄	35.1	38.9	35.5	39.0	36.5	39.7	35.2	39.3
b-IN₄	10.8		10.5		12.1		10.3	
b-TS₄₋₅	30.9	20.1	31.2	20.7	31.7	19.6	31.1	20.8
b-IN₅	−16.9		−16.1		−14.8		−16.0	
b-TS₅₋₆	−3.0	13.9	−2.6	13.5	−4.3	10.5	−2.7	13.3
b-IN₆	−20.5		−20.7		−18.7		−20.4	

[a] These values, in kcal/mol, were calculated at the M06-2X level of theory and included the zero-point energy correction, using single point integral equation formalism polarizable continuum model (IEFPCM) calculations at the M06-2X/6-311++G(d,p) (RECPs for Ru) level of theory to model the effect of the solvent (toluene).

sor complex throughout the course of the reaction. The energy profile for the mechanism of the pathway a is shown in Fig. 1. The selected stationary structures with the key geometry parameters on the potential energy surfaces of this channel are described in Fig. 2. In **a-IN₁**, the distances of Ru—C^1, Ru—C^2, Ru—C^3 and Ru—C^4 are 2.218, 2.251, 2.251 and 2.285 Å, respectively. Due to form a six-membered ring structure, structure **a-IN₁** is then converted to the intermediate **a-IN₂** via the C^2—C^3 bond formation transition structure **a-TS₁₂**. Vibrational analysis shows that the **a-TS₁₂** structure has only one imaginary frequency of 222.6 i cm^{-1}, and IRC calculations confirmed that this TSs connects the corresponding precursor complex and intermediate. The transition vector is obtained for **a-TS₁₂** by the C_2—C_3 distance. Fig. 2 shows that the C^1 and C^4 atom are completely connected with the ruthenium atom (the bond distances Ru—C^1 and Ru—C^4 are 2.077 and 2.039 Å, respectively) in **a-TS₁₂**, and the C^2—C^3 bond length is 2.038 Å. Furthermore, the bond of the C^1—C^2 and C^3—C^4 change from 1.397 to 1.455 Å and from 1.244 to 1.282 Å. From the changes in the bond lengths, we can see that this transition state has similar structure