Ring-Opening of Cyclohexene via Metathesis by Ruthenium Carbene Complexes. A Computational Study

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Cyclohexene (CH) metathesis reaction mediated by the second-generation ruthenium alkylidene catalyst $(IMesH_2)(PCy_3)CI_2Ru=CHPh$ (**1a**), ruthenium ester carbene complexes $(IMesH_2)(PCy_3)CI_2Ru=CHCOOMe$ (**1b**), and $(PCy_3)_2CI_2Ru=CHCOOMe$ (**1c**), where $IMesH_2$ is a 1,3-dimesityl-4,5-dihydroimidazol-2-ylidene group, has been modeled at the PBE0/LACV3P**++//PBE0/LACVP* level of theory. The calculations revealed that the necessary condition for the catalyst to be active in CH ring-opening is the existence of a high-energy π-complex. It has been shown that the complex **4b** complies with this condition, while the ruthenium alkylidene **4a** does not. The higher reactivity of **1b** compared to **1c** can be rationalized in terms of better stabilization of the Ru center in transition states by the $IMesH_2$ ligand.

Introduction

The ring-opening metathesis polymerization (ROMP) of many cyclic olefins is a thermodynamically controlled process, and thermodynamic data can be used for the prediction of cyclic olefin polymerizabilty via ring-opening metathesis. ROMP of three-, four-, eight-, and larger-membered cyclic olefins is thermodynamically favored and proceeds to form high molecular weight polyalkenamers.[1] On the other hand, six-membered rings do not undergo ROMP due to their low strain energy.[1] The computational modeling of the ring−chain equilibrium for the ring-opening cross-metathesis of cyclohexene (CH) with ethylene and carbonyl-containing olefins revealed that CH-ring-opened products equilibrium is shifted toward the thermodynamically stable six-membered ring.[2] Such unreactive-in-ROMP rings can be prepared via ring-closing metathesis (RCM) of the appropriate compounds. Thus, ROMP-nonpolymerizable 4-methylcyclohexene has been prepared by RCM degradation of highly alternated butadiene−propylene copolymer.[1,3] On the other hand, it is well-known that the free Gibbs energy for the ring−chain equilibrium process depends on many factors including temperature and substituents in the ring. Thus, there is evidence of CH ring-opening via metathesis to yield a small proportion of oligomers at low temperature and high monomer concentration.[1] It has been reported that thermodynamically stable CH can be ring-opened via metathesis in the presence of α-carbonyl-containing olefins using the second-generation ruthenium alkylidene catalyst.[4] Authors proposed that in this case the reaction proceeds via the formation of a very active Ru-ester (ether) carbene complex, which cleaved the thermodynamically stable CH. The synthesis of a variety of Ru-ester carbenes and their activity for the metathesis of challenging

olefins have also been reported.[5] Thus, it was shown that the Ru-ester carbene $(PCy_3)_2CI_2Ru=CHCOOMe$ reacted with excess CH, giving the ring-opening metathesis product.[5]

The second generation of ruthenium alkylidene catalysts opens vast opportunities to metathesize challenging olefins with sterically hindered or electronically deactivating ester and amide groups.[6] Recently, we reported a computational study of metathesis of ester- and halogen-containing olefins using the second-generation ruthenium alkylidene catalyst where the importance of steric factors for Ru-mediated metathesis of olefins has been shown.[7]

The aim of this study is to model CH ring-opening metathesis reaction pathways using second-generation ruthenium alkylidene catalysts $(IMesH_2)(PCy_3)CI_2Ru=CHPh$ (**1a**) and $(IMesH_2)$-$(PCy_3)CI2Ru=CHCOOMe$ (**1b**) and the first-generation $(PCy_3)_2$-$CI2Ru=CHCOOMe$ (**1c**) catalyst where $IMesH_2$ is 1,3-dimethyl-4,5-dihydroimidazol-2-ylidene.

Computational Details

All geometry optimizations were carried out with the Jaguar v 6.5 program[8] using the PBE0 functional in combination with the LACVP* basis set. The LACVP* basis set uses the standard 6-31G* basis set for light elements and the LAC pseudopotential[9] for third-row and heavier elements. It has been shown that the PBE0 functional significantly outperforms the popular B3LYP functional for Ru(II) complexes of general formula $[Ru(CO)_3(Ph_2Ppy)_2]$ (py

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Scheme 1. Reaction Path of CH Metathesis by Ru Catalysts 1a−c

a: L=IMesH$_2$ R=Ph
b: L=IMesH$_2$ R=COOMe
c: L=PCy$_3$ R=COOMe
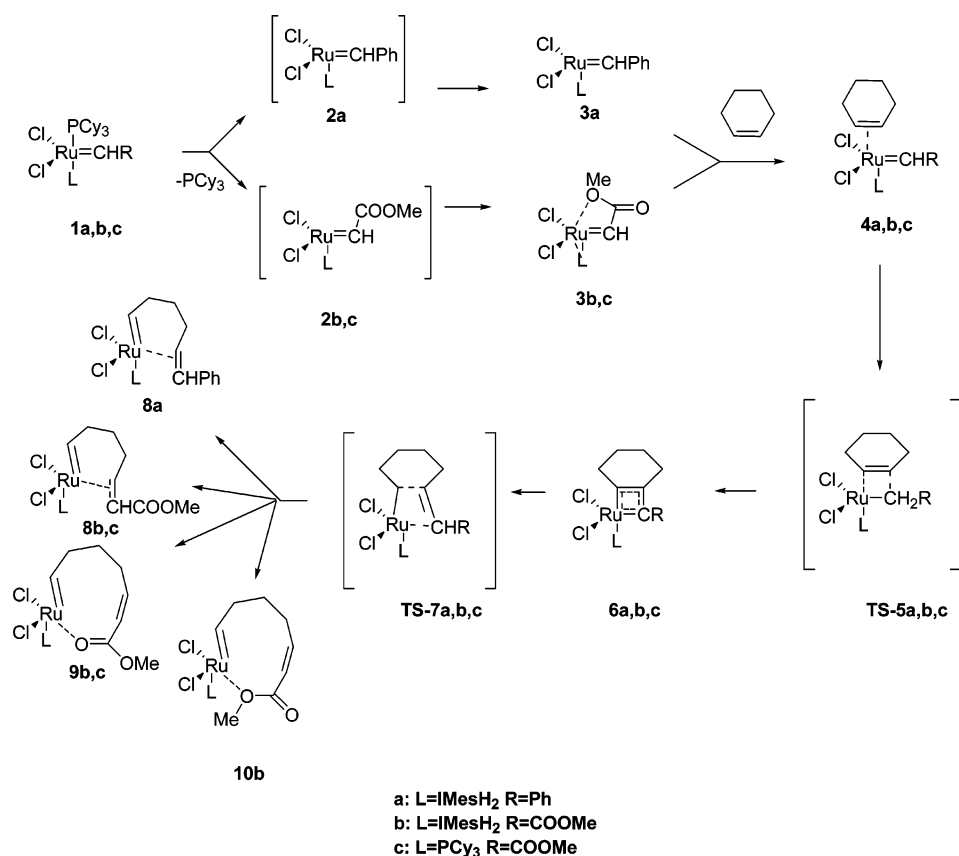
= pyridine).[10] Frequency calculations at 298.15 K were run for all structures at the same level of theory to make sure that a transition state (one imaginary mode) or minimum (zero imaginary modes) is located and to reach zero-point energy (ZPE) correction and thermodynamic properties. Single-point calculations were carried out using the larger LACV3P**++ basis set developed and tested at Schrodinger Inc. This is a triple-ζ contraction of the LACVP basis set using the 6-311++G** basis set for light elements.

The total Gibbs energies of all molecules (G) were calculated as follows: $G = E_t + \Delta G$, where E_t is the total electronic energy calculated at the PBE0/LACV3P**++ level using PBE0/LACVP*-optimized geometry and ΔG is the Gibbs energy correction calculated as the difference between the total electronic energy and the Gibbs energy estimated at the PBE0/LACVP* level using PBE0/LACVP*-optimized geometry.

Initial structures for calculations were obtained as follows; in the case of molecules **1a**, **1b**, **1c**, **3a**, **3b**, **3c 8b**, **8c**, **9b**, and **9c** structures were prepared using Titan builder.[11] Then a conformational search was carried out using the MonteCarlo program and the PM3(tm) method implemented in Titan. The energy of five lowest energy conformers was refined using PBE0/LACVP* single-point calculations, and the lowest energy conformer was taken as input for DFT geometry optimization. The initial structures of other molecules were located during the potential energy scans starting from optimized structures of **4a**, **4b**, and **4c**.

Since the PBE0 functional is not implemented directly in Jaguar 6.5, it was defined using the following keywords: idft=−1, xhf=0.25, xexnl9=0.75, xcornl9=1.0, xcorl4=1.0, which corresponds to the definition of the PBE0 functional in the original paper[12] as follows: 25% of exact HF exchange, 75% of PBE local

and nonlocal exchange functional, Perdew−Wang GGA-II 1991 local correlation functional, and PBE local and nonlocal correlation functional.

A few test runs were carried out to take into account solvent effects (1,2-dichloroethane) using a Poisson−Boltzmann solver[13,14] implemented in the Jaguar v 6.5 suite of programs. The difference between the gas and solution state free Gibbs energies was found to be within 1.5 kcal/mol. It has been shown earlier[15] that solvation energies of similar molecules in nonpolar solvents introduce smaller errors than the method itself. Therefore, all calculations were carried out in the gas phase.

Results and Discussion

The experimental[16,17] and theoretical[15] studies clearly indicate that for ruthenium complexes with general formula L(PR$_3$)(X)$_2$-Ru=CHR[1] (R = Cy, Cp, and Ph; X = Cl, Br, and I; L = N-heterocyclic carbene ligand, NHC) initiation occurs via dissociative substitution of a phosphine ligand (PR$_3$) with an olefin substrate, giving a monoligand complex.

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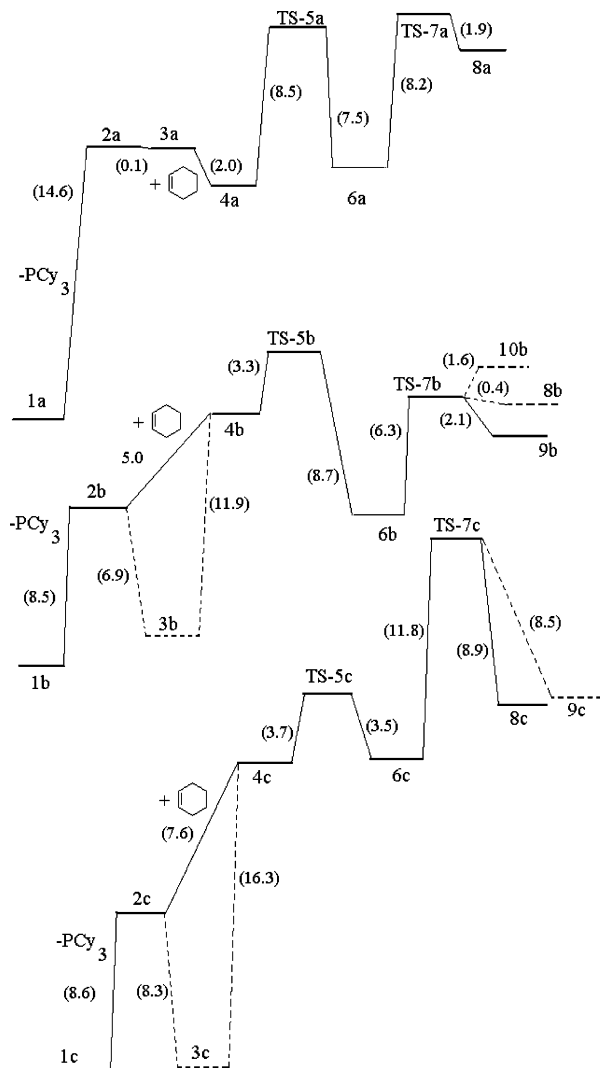
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Figure 1. Free Gibbs reaction energy profile of CH metathesis by **1a**, **1b**, and **1c**. The free Gibbs reaction energies of each step are given in parentheses.

Scheme 1 shows the ring-opening reaction pathways of CH by catalysts **1a**, **1b**, and **1c**.

Figure 1 shows the free Gibbs reaction energy profiles of CH ring-opening by catalysts **1a**, **1b**, and **1c**.

The experiments reveal that Ru-ester carbenes are very active in initiation of olefin metathesis, where they are significantly more active compared to Ru-alkylidene catalysts.[5] This feature could be related with the energy of Ru−P bond cleavage in **1b** and **1c**. The calculations show that ΔG of phosphine ligand dissociation for **1a**, **1b**, and **1c** is 14.4, 1.6, and 0.3 kcal/mol, respectively, reflecting a significant weakening of Ru−P binding in **1b** and **1c** compared to **1a**. The experimental dissociation enthalpy determined for catalyst **1a** (25 ± 4 kcal/mol)[16c] is in very good agreement with the theoretically calculated enthalpy value at the PBE0/LACV3P**++//PBE0/LACVP* level of theory (27.8 kcal/mol), validating the employed calculation method. Such a big difference in dissociation energies between **1a**, **1b**, and **1c** is related to the additional stabilization of the Ru center by sp^3 oxygen of the carbomethoxy group.[7c] To estimate this stabilization effect, all atoms belonging to the PCy$_3$ fragment were removed from the z-matrix of the corresponding optimized geometries of catalysts **1b** and **1c**. Then, a partial geometry optimization with frozen Ru and sp^3 O atoms was carried out and the difference between the total electronic energy

of obtained structures and that of **3b** and **3c** was taken as the Ru−O binding energy (−6.9 and −8.3 kcal/mol, respectively). As seen, the low binding energy between the phosphine ligand and Ru in **1b** and **1c** can be rationalized in terms of a "push−pull" mechanism, when Ru−P binding competes with Ru−O binding. Additional evidence for the interaction of the Ru center with a carbomethoxy group of the carbene fragments comes from the analysis of the electron density distribution. Thus, 4d level occupation at the Ru center in catalyst **1b** increases from 7.22 to 7.24, passing from a 14-electron intermediate with "frozen" carbometroxy group **2b** (Ru−O distance 3.41 Å) to relaxed structure (Ru−O distance 2.46 Å) **3b**.

As seen from the free Gibbs reaction energy profiles when starting from monoligand complexes **3a**, **3b**, **3c**, and CH, the ΔG of the CH ring-opening is quite positive for the three catalysts. This conclusion seems to differ from the experiment.[5] The ring-opening of CH on catalysts **1b** and **1c** can be understood only assuming that high-energy π-complexes **4b** and **4c** are generated somehow in the reaction mixture. The efficient generation of the Ru-ester carbene (enoic carbene) *in situ* with catalyst **1a** and successful ring-opening metathesis of thermodynamically stable CH were reported by Grubbs et al.[4]

Figure 2 shows optimized geometries of catalysts **1a** and **1b** and the corresponding monoligand complexes **3a,b**. As seen, there is a significant difference between them. In the case of **1a** the cleavage of the P−Ru bond does not affect the conformation of the carbene fragment, while in the case of **1b** the elimination of the PCy$_3$ molecule results in drastic changes in carbene moiety conformation due to interaction between the sp^3 oxygen and the Ru center. It has been shown previously[7c] that sp^3 and not sp^2 oxygen forms the most stable complex with the Ru center. The CH ring-opening is thermodynamically possible when a π-complex is formed from a 14-carbene intermediate *before* the formation of the internal Ru−O complex. In other words, the formation of π-complex **4b** is faster than the coordination of the sp^3 oxygen with the Ru center and the reaction path goes through intermediate **2b**, not **3b**, where the CHCOOMe group maintains the configuration of **1b**. This mechanism will be favored by high CH concentration. Assuming this mechanism, the formation of π-complex **4b** is an only moderately endothermic process with $\Delta G = 5.0$ kcal/mol.

Once π-complex **4b** is formed, there is a straightforward explanation for the ability of catalyst **1b** to cleave the CH cycle. As seen from Figure 1 the free Gibbs reaction energy of the π-complex transformation to the final open-chain carbene **9b** is negative (−1.2 kcal/mol). It is noteworthy that the ring-opening of CH in the case of catalyst **1b** leads to the formation of three different complexes: **8b**, **9b**, and **10b**. In the former a double bond forms a π-complex with the Ru center, in the second one a carbonyl oxygen is interacting with the Ru atom, and in the third a methoxy oxygen is bound to a transition metal. As seen from the reaction profile, the second complex is 2.1 kcal/mol more stable compared to the first one and even more stable compared to **10b**. Moreover, the possibility of CH ring-opening on catalyst **1b** is directly related with a Ru−carbonyl interaction in the final complex since considering the π-complex **8b** as the reaction product, the total free Gibbs reaction energy would be positive (+0.5 kcal/mol). It is noteworthy that unlike **1b**, where an sp^3 oxygen stabilizes the Ru center better compared to carbonyl,[7c] in the case of cyclohexene metathesis products **8b**, **9b**, and **10b** carbonyl complex **9b**, stabilized by a carbonyl group, is the lowest in energy. This is easy to understand taking into account steric factors. Complex **9b** is less demanding sterically compared to **10b** (see Supporting Information).
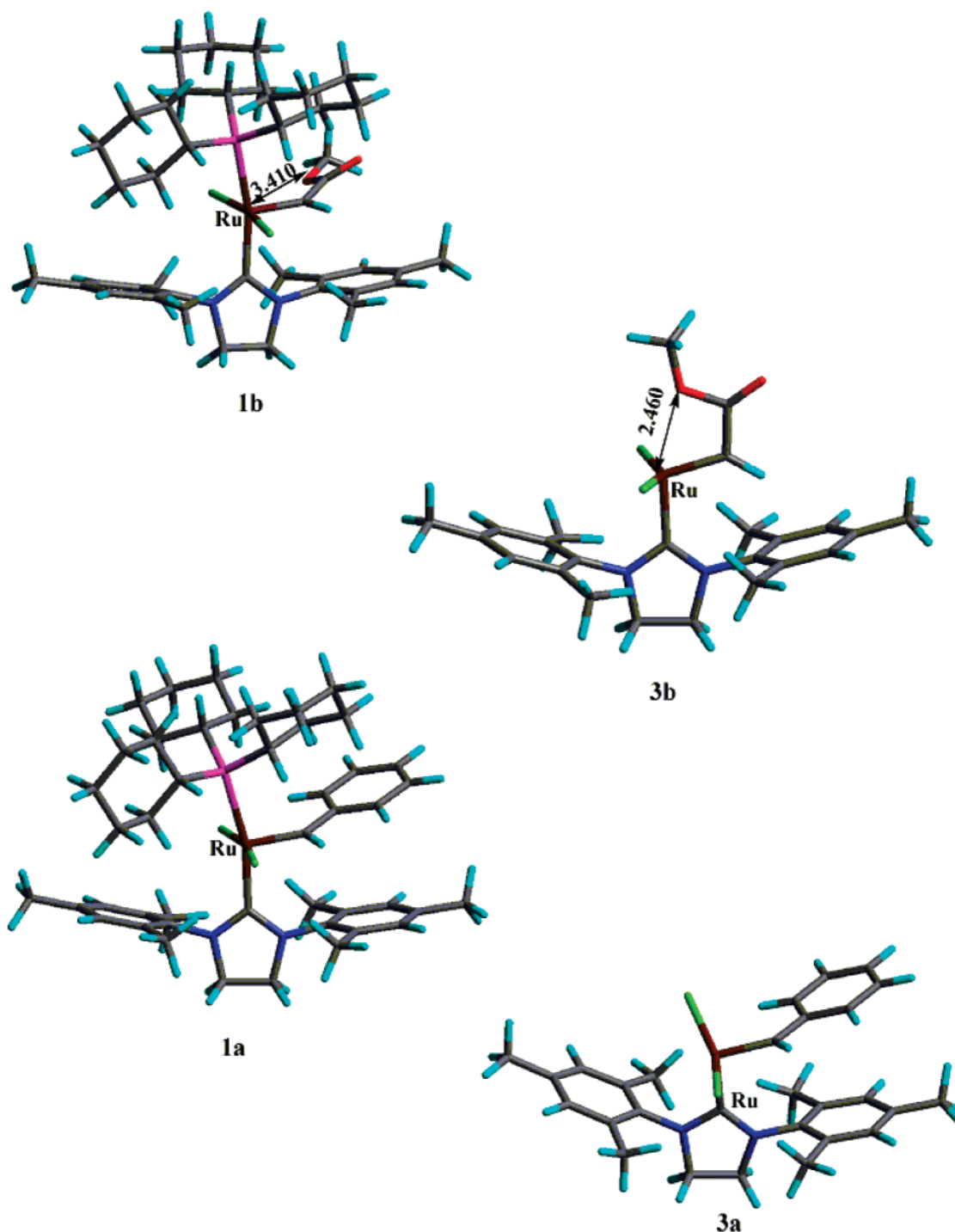
Figure 2. Fully optimized geometries of **1a,b** and partially optimized structures of the corresponding 14-electron intermediates **3a,b**.

The free Gibbs activation energies are low for both catalysts (**1a,b**), being 8.5 and 3.3 kcal/mol for the metalcyclobutane formation, **6a** and **6b**, respectively. Thus, it is thermodynamics that controls the ring-opening of CH. On the other hand, complex **1a** is unable to cleave CH, as seen from the free Gibbs energy reaction profile. The initial π-complex **4a** is 7.3 kcal/mol more stable than the final **8a**. In the case of catalyst **1a** the "relaxation" energy caused by the PCy$_3$ molecule loss is negligible, reaching only 0.1 kcal/mol.

As seen from the comparison of the reaction profiles for **1b** and **1c**, the catalyst **1c** is much less effective in CH ring-opening compared to **1b**. First, π-complex **4c** lies 3.1 kcal/mol below

the metathesis product **8c**, making this reaction thermodynamically less favorable compared to the **4b** → **9b** transformation. Second, the free Gibbs activation energies for the conversion of the metallocyclobutane intermediate **6c** to the metathesis product is almost twice as high (11.8 kcal/mol) as for **6b** (6.3 kcal/mol), in agreement with higher catalytical activity of Ru-alkylidene catalysts with N-heterocyclic carbene ligands. The higher activity of **1b** can be understood considering the ability of a ligand to stabilize the Ru center in transition states. When analyzing the natural charges at the Ru atom in different reaction intermediates, there is a clear correlation between the free Gibbs activation energies and the difference between natural charges
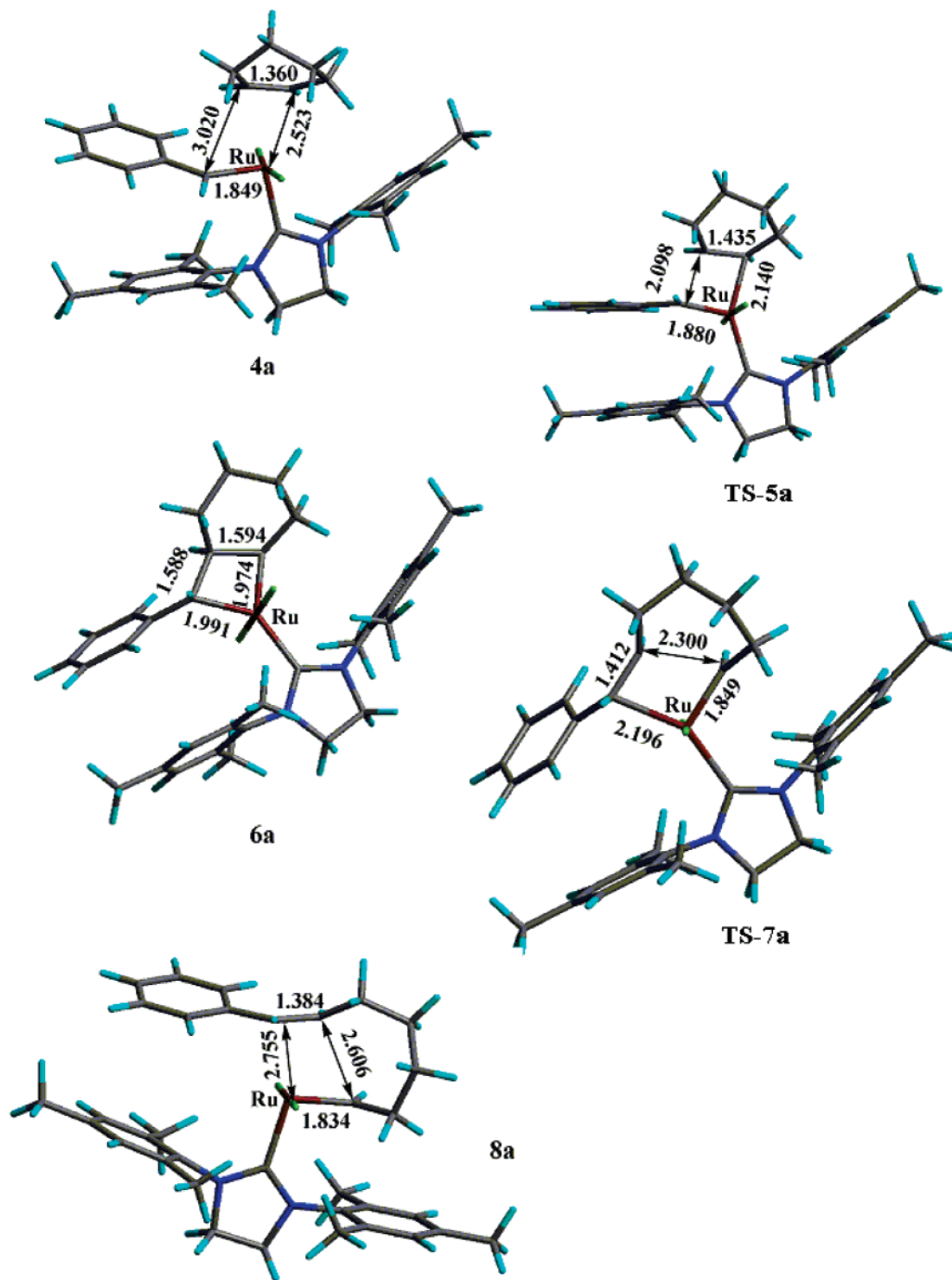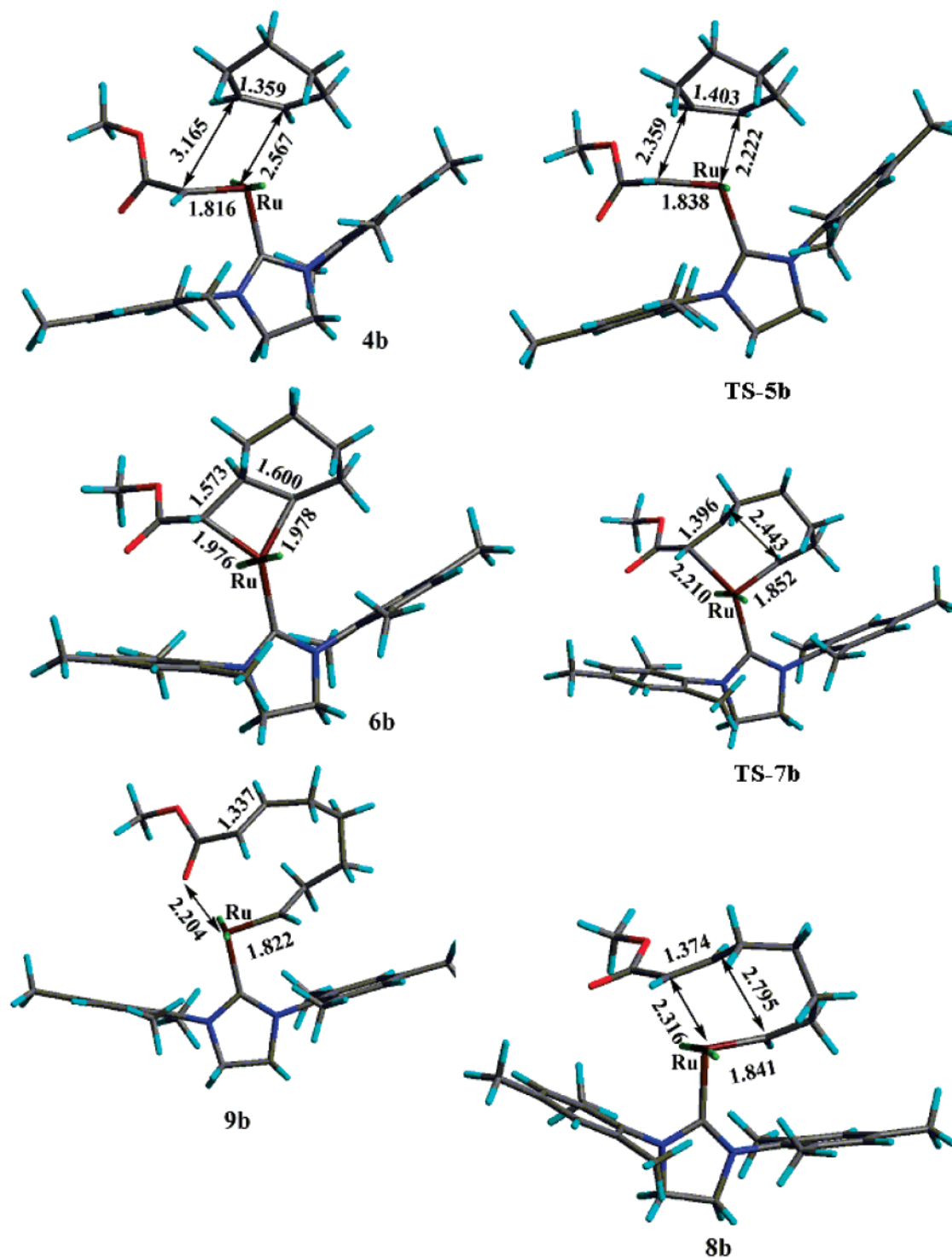
Figure 3. Optimized geometries of reaction intermediates for CH metathesis by **1a**.

at the Ru center in a transition state and in a preceding minimum. Thus, for catalyst **1c** natural charges at Ru centers in the initial π-complex (**3c**), first transition state (**TS-5c**), metallocyclobutane (**6c**), and second transition state (**TS-7c**) are +0.18, +0.16, +0.22, and +0.23. In the case of **1b** the corresponding charges are +0.33, +0.30, +0.35, and +0.29. Thus, in the case of the **6c** → **TS-7c** transformation the Ru center is destabilized, becoming more positive, while for the **6b** → **TS-7b** process the Ru atom is stabilized by the IMesH$_2$ ligand in transition state **TS-7b** compare to **6b**, thus reducing the activation energy. As seen, a strong difference in activation

energies of decomposition of a metallocyclobutane intermediate can be related with the fact that the IMesH$_2$ ligand stabilizes the transition state **TS-7** better than the PCy$_3$ ligand. Unlike **1b**, **1c** does not form a complex similar to **10b**. This is due to the fact that, as seen from the charge distribution analysis, PCy$_3$ is a stronger donor compared to IMesH$_2$, decreasing the binding energy of the Ru center with electron-donating atoms.

Figures 3, 4, and 5 show optimized geometries of reaction intermediates for CH ring-opening on different Ru catalysts. There is an important point to mention: in π-complexes **4a–c**
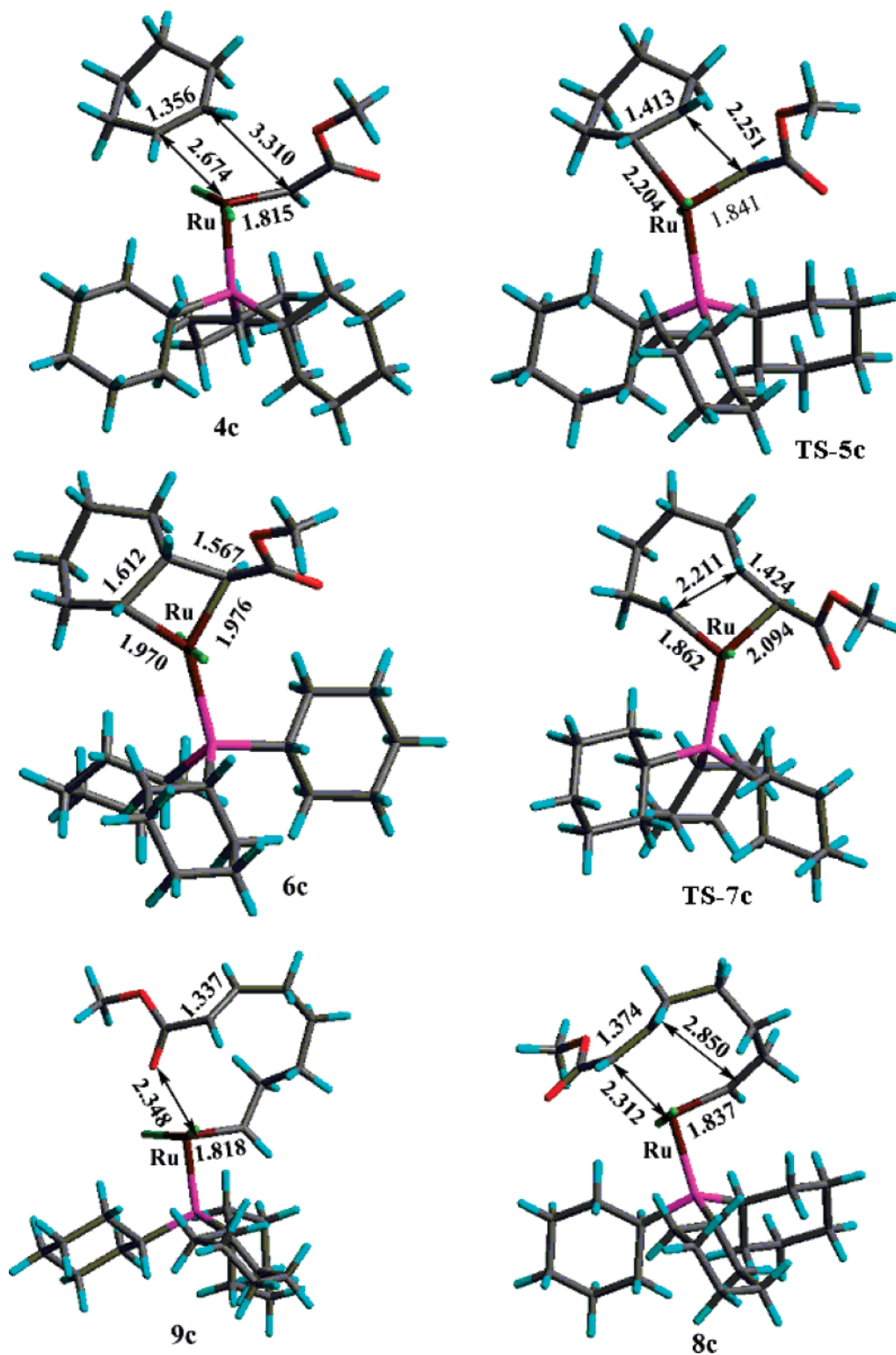
Figure 4. Optimized geometries of reaction intermediates for CH metathesis by **1b**.

and **8a−c** the olefin−Ru and olefin−carbene distances increase from **a** to **c** (Figure 1). We believe that this difference is due to steric rather than electronic factors. The dissimilarity in geometry between **4a** and **4b** is explained by the effect of the methoxy group in **4b**. The closest distance between the hydrogen atom of CH and the O atom of the methoxy group is only 2.287 Å, while in **4a** the closest distance between the hydrogen atom of CH and the phenyl carbon is 2.666 Å. Additional steric hindrances in **4c** are due to the PCy₃ ligand. The PCy₃ ligand is more bulky compared to IMesH₂, as follows from the comparison of ClRuCl angles for **3a−c**. These angle are 143° and 150° for **3c** and **3a,b**, respectively. This is also confirmed

by the molecular volume calculations. Thus, calculated molecular volumes for PCy₃ and IMesH₂ were found to be 300.0 and 291.1 Å³, respectively.

Conclusions

The calculations reveal that the ability of **1b** to cause CH ring-opening is due to the fact that the process **4b → 9b** is thermodynamically favorable, while **4a → 8a** is not. According to the proposed mechanism, the formation of complex **4b** is feasible when olefin Ru complexation occurs faster than the formation of an intramolecular complex between the sp³ oxygen

Figure 5. Optimized geometries of reaction intermediates for CH metathesis by **1c**.

and the Ru center. The additional stabilization of **9b** by the interaction of a carbonyl oxygen with the Ru center contributes significantly to the possibility of the **4b → 9b** transformation. On the other hand, excessive stabilization of complex **4a** disfavors the **4a → 8a** process. The free Gibbs activation energies for CH ring-opening are consistently higher for the catalyst **1c** than for **1b**, which is related with better transition state stabilization by the IMesH$_2$ ligand compared to PCy$_3$.

Supporting Information Available: Cartesian coordinates, total electronic and free Gibbs energies, gradients, and displacements. This material is available free of charge via the Internet at http://pubs.acs.org.

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