5.2 In Silico Olefin Metathesis with Ru-Based Catalysts Containing N-Heterocyclic Carbenes Bearing C₆₀ Fullerenes


*J.P.M. participated in the design of the project, performed all the calculations, analyzed the results, and co-wrote the manuscript.*
In Silico Olefin Metathesis with Ru-Based Catalysts Containing N-Heterocyclic Carbenes Bearing C_{60} Fullerenes

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In memory of our colleague Yves Chauvin

Abstract: Density functional theory calculations have been used to explore the potential of Ru-based complexes with 1,3-bis(2,4,6-trimethylphenyl)imidazolin-2-ylidene (SIMes) ligand backbone (A) being modified in silico by the insertion of a C_{60} molecule (B and C), as olefin metathesis catalysts. To this end, we investigated the olefin metathesis reaction catalyzed by complexes A, B, and C using ethylene as the substrate, focusing mainly on the thermodynamic stability of all possible reaction intermediates. Our results suggest that complex B bearing an electron-withdrawing N-heterocyclic carbene improves the performance of unannulated complex A. The efficiency of complex B is only surpassed by complex A when the backbone of the N-heterocyclic carbene of complex A is substituted by two amino groups. The particular performance of complexes B and C has to be attributed to electronic factors, that is, the electronic-donating capacity of modified SIMes ligand rather than steric effects, because the latter are predicted to be almost identical for complexes B and C when compared to those of A. Overall, this study indicates that such Ru-based complexes B and C might have the potential to be effective olefin metathesis catalysts.

Introduction

Olefin metathesis is one of the most important tools for the formation of carbon–carbon bonds in modern synthetic chemistry.[1] Among its various industrial applications, the metathesis reaction is used mainly in the preparation of fine chemicals,[2] biologically active compounds,[3] new functionalized materials and polymers.[4] Although there exists other metal-based complexes, ruthenium has occupied a prominent role in olefin metathesis during the last decade. This preference for a second-row transition metal is due to the high reactivity and tolerance towards group functionalization that they offer.[5,6]

The metathesis reaction mechanism proposed by Chauvin in the early 1970s considers the metal carbene complex as the active catalyst and the respective four-membered metallacycle derivatives as the crucial intermediates leading to the desired products.[7] The presence of a ruthenacycle intermediate has been studied experimentally[8] and theoretically[9] since the late 1990s. In these studies, density functional theory (DFT) calculations have been extensively used to clarify many aspects of Ru-catalyzed olefin metathesis,[10,11] and efforts have been also made to achieve highly accurate and less expensive computational recipes to acquire new mechanistic knowledge to feed into catalyst design efforts.[12,13]

Focusing on the Ru-based systems, the activity of the “first-generation” phosphine-based catalysts was significantly improved with the discovery of a “second-generation” catalysts, in which an N-heterocyclic carbene (NHC) was used to replace one phosphine ligand.[14] In the last decade, many variants of the Ru-based catalysts have been disclosed.[5,15]

Despite the numerous studies in the past two decades,[5,14] there is still the absence of a “universal” catalyst for all olefin metathesis applications; however, there are smart particular solutions.[15] Additionally, there is no rule of thumb to predict exactly why Ru-based catalysts with certain NHCs and phosphine ligands show catalytic activity, whereas with other ligands (including variants of NHCs and phosphines) they display poor performance.[15]
Chapter 5. Metal-Catalyzed Reactions with Fullerene C\textsubscript{60}

Research and industrial interest in fullerenes has been translated into a recent high number of applications.\textsuperscript{[17]} Apart from being able to produce solar cells painting simply a surface, or store hydrogen as a green energy source or killers of bacteria in membranes in water systems, these nanotechnological species are prone to trap free radicals,\textsuperscript{[18]} thus are suitable to act as active agents to block the inflammation generated by an allergy, or to fight against the deterioration of motor function due to multiple sclerosis. Here we envisaged fullerenes as a new supporting ligand that could facilitate olefin metathesis processes. The combination of organometallic chemistry and fullerenes is relatively scarce.\textsuperscript{[19,20]} Very recently, Stana et al. have synthesized a series of supramolecular platinum(II) complexes in which the metal is attached to macrocycles containing pyridine rings that are connected to C\textsubscript{60}.\textsuperscript{[21]} To our knowledge, NHC ligands bearing fullerene moieties have not been reported yet,\textsuperscript{[22]} apart from a recent study bearing C\textsubscript{60}\textsuperscript{[23,24]}

In the present study, we use DFT calculations to explore the potential of Ru-based complexes with SIMes (SIMes = 1,3-bis[2,4,6-trimethylphenyl]imidazolin-2-ylidene) ligand backbone (A) being modified in silico by the insertion of a C\textsubscript{60} molecule (B and C), and its activity as an olefin metathesis catalyst (see Scheme 1). In principle, this modification of the SIMes ligand will increase its steric hindrance by either replacing the methylene H atoms by a fullerene (complex B) or replacing both methylene C and H atoms (complex C).

The approach to use computational techniques as a tool to screen new catalyst architectures more rapidly and examine their potential as efficient catalysts for a certain reaction is nowadays very popular. This can be understood if one considers the experimental exploration of the catalytic site to find new and better catalysts is a tedious task often driven by a trial and error approach. In this sense, Paater et al. recently reported the in silico prediction of new Fe- and Rh-based olefin metathesis catalyst activities.\textsuperscript{[25]} Additionally, this in silico approach has been extended to predict promising new starting materials as well.\textsuperscript{[26,27]}

Results and Discussion

For this study we computed the olefin metathesis reaction mechanism for the Ru-based complexes A, B, and C using ethylene as the substrate. The main focus is on the differential thermodynamic stability of the reaction intermediates of complexes A, B, and C. Figure 1 collects the Gibbs energies relative to species I for the studied olefin metathesis reaction catalyzed by Ru-based complexes A-C using ethylene as the substrate. L = NHC. Gibbs energies in CH\textsubscript{2}Cl\textsubscript{2} solvent are given in kcal mol\textsuperscript{-1}.

As can be seen in Figure 1, the rate-determining transition state\textsuperscript{[28]} in this process is the IV-V, corresponding to the breaking of the ruthenacyclobutane complex. Indeed, once species V is generated the Gibbs energy profile follows an energetically slight downhill trajectory without high-energy barriers or highly stabilized intermediates that follow the classical steps described in a number of previous reports.\textsuperscript{[29]} Overall, our results indicate that for the studied olefin metathesis reaction, complex B presents the lowest energy barrier (15.1 kcal mol\textsuperscript{-1}) followed by complex A (17.5 kcal mol\textsuperscript{-1}), whereas complex C has the highest energy barrier (20.5 kcal mol\textsuperscript{-1}).

The formation of a stable ruthenacyclobutane IV by the metathesis of ethylene with the Ru-allylidyne bond is considered fundamental to describe a successful olefin metathesis catalyst.\textsuperscript{[16,22]} The ruthenacyclobutane is a relatively stable key intermediate of each metathesis, and it has been characterized experimentally.\textsuperscript{[8]} Furthermore, the less substituted the metalacycle, the higher its stability is. Nolan et al. reported in a recent study that the substitution of the SIMes ligand in the Ru-based catalyst by a phosphine resulted in the destabilization of metalacyclic IV by 8.4 kcal mol\textsuperscript{-1} with respect to the previous ethylene coordination intermediate III,\textsuperscript{[30]} compared with just 0.4 kcal mol\textsuperscript{-1} for the system containing SIMes. The studied olefin metathesis reaction was with methyl vinyl ether as a substrate instead of ethylene. Experimentally, a Ru-based complex containing SIMes ligand was found to be catalytically
active, but it showed poor catalytic performance when substituted with phosphine. This poor catalytic activity observed was attributed to the low stability of ruthenacyclobutane IV. The possible difficulty in the evolution of the catalytic process can be also related to a high thermodynamic stability of the metalla-cyclopropane intermediate. Thus, Schrock catalysts with highly stable metalla-cyclopropanes showed poor catalytic performances. These insights allow us to confirm the relationship between the stability of the ruthenacyclobutane and the potential catalytic activity of the corresponding Ru-catalyst species. For the catalysts to be efficient, the ruthenacyclobutane should be moderately stable. Going back to the present study, for complexes B and C, the metalla-cyclopropane IV is 1.1 and 3.6 kcal mol\(^{-1}\) more stable than the former coordination intermediate III, respectively, and comparable to the relative stability of metalla-cyclopropane for complex A (0.9 kcal mol\(^{-1}\)), thus the values fit perfectly with the active catalysts in olefin metathesis. Thus, taking into account that a too high stability of the ruthenacyclobutane intermediate might be a bottleneck in olefin metathesis catalysis, this new family of catalysts overcomes this hurdle.

We have studied in detail the steric and electronic properties of species I and II for complexes A, B, and C (see Figure 2). Focusing on the steric properties, we calculated the buried volume (\(V_{\text{bur}}\)) of the three NHC ligands A, B, and C using the Sambi\textit{c} package developed by Cavallo et al. This program analyzes the first coordination sphere around the metal, which is the place where catalysis occurs, and the buried volume is the amount of the first coordination sphere of the metal occupied by a given ligand. We performed also a more detailed analysis by evaluating the \(V_{\text{bur}}\) in the single quadrants around the Ru center and plotted them as steric contour steric maps (Figure 3 and Table 1), see the Supporting Information for further details. Splitting the total \(V_{\text{bur}}\) into quadrant contributions quantifies any asymmetry in the way the ligand wraps around the metal. Here, this analysis will show how the shape of the reactive pocket is modified when moving from A to B or C.

It is evident from Figure 3 that for the studied Ru-based complexes A–C, species I presents quite similar stericus, thus neither B nor C are significantly more sterically congested than A. In detail, the calculated percent buried volume (\(V_{\text{bur}}\)) for complexes B (32.5%) and C (33.3%) are comparable to the \(V_{\text{bur}}\) of A (32.8%) (see Table 1). Similarly, for species II, the predicted \(V_{\text{bur}}\) values are nearly the same despite the potential relaxation of NHC ligand after the dissociation of phosphate ligand. Nevertheless, species II of complex C displayed a somewhat more sterically hindered environment next to the metal, being three out of four quadrants generously occupied.

<table>
<thead>
<tr>
<th>Complex</th>
<th>Sterics (% (V_{\text{bur}}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>32.8 (41.0/31.3/29.3/26.7)</td>
</tr>
<tr>
<td>B</td>
<td>32.5 (44.3/32.3/27.3/26.4)</td>
</tr>
<tr>
<td>C</td>
<td>33.3 (40.0/34.5/29.8/28.6)</td>
</tr>
</tbody>
</table>

Table 1. Total \(V_{\text{bur}}\) and quadrant \(V_{\text{bur}}\) (numbers in brackets) values for species I and II for the considered Ru-based complexes A–C.

Taken together, these observations confirm that the sterics for the studied complexes A–C are quite similar and indeed none of them preclude coordination of bulky substrates.

To understand the effect of the bulky \(C_{60}\) fullerene on the binding of NHC to the Ru metal, we decomposed the total bond energy, \(BE\), of the NHC-Ru bond in species I for the studied Ru-complexes A–C as shown in Equation (1)

\[
BE = E_{\text{Dea}} + E_{\text{ex}}
\]

in which \(E_{\text{Dea}}\) is the deformation energy associated with the change in the geometry of the free NHC and of the Ru metal fragment, to the geometry they have in the complex, whereas \(E_{\text{ex}}\) is the interaction energy between the NHC and the metal fragment frozen at the geometry they have in the complex.

The \(E_{\text{ex}}\) is negative because it is the energy gain associated with placing together the two deformed fragments, whereas the \(E_{\text{Dea}}\) is positive as it corresponds to the energetic cost of deforming the two fragments to the geometry they have in
Chapter 5. Metal-Catalyzed Reactions with Fullerene C₆₀

Figure 3. Topographic steric maps of the NHC ligands of species I for the studied Ru complexes A–C. %VolBₐ is the percent of buried volume. The Ru atom is at the origin and the P atom is on the z axis. The isosurface curves of the steric maps are given in A.

The complex within this framework, the $E_{\text{int}}$ in species I is $-59.8$ kcal mol$^{-1}$ for A, whereas it is 3.7 and 2.0 kcal mol$^{-1}$ lower (in absolute value) in the cases of complexes B and C, respectively. The lower interaction energy for complexes B and C is likely due to the electron-withdrawing capacity of the C₆₀ group, which makes the electron pair of the NHC less available for the interaction with the metal. The lower NHC-Ru interaction energy of the B complex is attributed to the fact that the NHC moiety of B interacts with the π-system of C₆₀ through the C=C double bond more effectively than that of the A complex that does not have such a π-system. On the other hand, the $E_{\text{int}}$ of NHC with C₆₀ is similar in energy (2.8 and 2.1 kcal mol$^{-1}$ for complexes B and C, respectively) with respect to the standard NHC, that is, SIMes (1.9 kcal mol$^{-1}$ for complex A).

The $E_{\text{int}}$ of the metal fragment is not significant (for complex A just 0.1 kcal mol$^{-1}$ more distorted). Overall, the calculated BE is 4.5 and 2.2 kcal mol$^{-1}$ less stabilizing for complexes B and C, respectively, than for complex A. To summarize, the presence of the C₆₀ molecule reduces the strength of the Ru-NHC bond, and this observation is further supported by the shorter Ru–C₆₀ bond length for complex A when compared with those of complexes B and C (see Figure 3).

The activation strain model (ASM)$^{98}$ was also used to analyze the first steps of the reaction. Basically, this model establishes the desired causal relationship between reaction barriers, on one hand, and the properties of reactants and characteristics of reaction mechanisms, on the other hand. Here the ASM cannot be applied to the rate-determining step described by IV–V because of the too different nature of the latter transition state with respect to II,$^{98}$ but only to the barrier described by the closure of the metallacycle, that is, III–IV, to provide insight about how the balance between steric and electronic factors drives the reaction to the metallacycle. Following the same Scheme for the energy decomposition given by Equation (1), the energy data for transition state III–IV, together with the corresponding values for the former intermediate III, referred to II, are collected in Table 2. Fragments considered are the incom-

<table>
<thead>
<tr>
<th>Species</th>
<th>BE</th>
<th>$E_{\text{int}}$</th>
<th>$E_{\text{int}}$</th>
<th>$E_{\text{int}}$</th>
<th>$E_{\text{int}}$</th>
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<tbody>
<tr>
<td>A</td>
<td>0.3</td>
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<td>0.5</td>
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<td>10.7</td>
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<tr>
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<td>11.5</td>
<td>3.8</td>
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<tr>
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<td>-24.3</td>
<td>30.8</td>
<td>19.3</td>
<td>11.5</td>
</tr>
<tr>
<td>C</td>
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<td>-15.9</td>
<td>20.0</td>
<td>16.0</td>
<td>4.0</td>
</tr>
<tr>
<td>III–IV</td>
<td>0.8</td>
<td>-23.5</td>
<td>26.3</td>
<td>17.4</td>
<td>9.9</td>
</tr>
</tbody>
</table>

Table 2. Energy decomposition analysis of reaction intermediates III plus the transition state III–IV relative to that of species II for the studied olefin metathesis reaction catalyzed by complex A and its analogues with the C₆₀ annulated NHC backbone. B and C. Gibbs energies in CH₂Cl₂ solvent are given in kcal mol$^{-1}$.

Because of slight differences in the charge analysis (see the Supporting Information, Table S1)$^{98}$ we envisaged an additional conceptual DFT analysis to get more insights into the electronic contribution of the NHCs. The electrophilicity of the complexes was evaluated as the Parr electrophilicity index shown in Equation (2)$^{98}$

$$\omega = \frac{\mu^2}{2\eta}$$

in which $\mu$ and $\eta$ are the chemical potential and the molecular hardness, respectively. In the framework of DFT,$^{98}$ $\mu$ and $\eta$ for a N-electron system with total electronic energy $E$ are defined as the first and second derivatives of the energy with respect to $N$ at a fixed external potential$^{98}$ in numerical applications, $\mu$ and $\eta$ are calculated with the finite difference formulas of Equations (3) and (4), which are based on Koopmans’ approximation$^{98}$

$$\mu \approx \frac{1}{2}(\epsilon_{l} + \epsilon_{h})$$

and

$$\eta \approx \frac{1}{2}(\epsilon_{l} - \epsilon_{h})$$
in which $\epsilon_H$ and $\epsilon_L$ are the energies of the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO), respectively.

To this end, we obtained the values of chemical hardness ($\eta$) and Parr electrophilicity index ($\omega$) for the species I and II. For A, $\omega$ was calculated from the HOMO and LUMO orbital energies (see Figure 4). Whereas for a direct comparison between

A and C$_{60}$-based complexes B and C, we had to look for the appropriate frontier molecular orbitals of the former complexes (see the Supporting Information, Figure S1 for further details). For the studied Ru-based complexes A–C, the predicted $\eta$ values are quite constant and do not show a clear trend (see Table 3), whereas the predicted $\omega$ values increase (166.2, 179.3, and 181.1 kcal mol$^{-1}$, respectively, for species I for the considered Ru-complexes A–C) with significant quantitative differences. The reason for the high electrophilicity of B and C has to be attributed mainly to their larger chemical potential, that is, the energy released when the number of electrons increases as a result of a more accessible LUMO. Moreover, the predicted higher $\omega$ values for complexes B and C than for that of A suggest that the former complexes will be more prone to nucleophilic substrate attacks, and thus more reactive than A. In summary, our results indicate that a reduced electron-donating capability of the SiMes ligand with a backbone annulated by a C$_{60}$ molecule together with higher $\omega$ values make complexes B and C potentially more active catalysts for olefin metathesis.

Finally, to better understand the electronic properties of the C$_{60}$-based NHCs in complexes B and C, we replaced the methylen H atoms in complex A by either NH$_2$ or NO$_2$ groups to simulate NHCs with different electron-donor capabilities.

Table 4 reports the Gibbs energies relative to species I of intermediates II–VIII and the key transition structures for the studied Ru-complex A and its derivatives, A+2NH$_2$, A+2NO$_2$, and A+4NO$_2$. The catalyst with lowest barriers is A+2NH$_2$. This catalyst shows a performance similar to that of complex B.

### Conclusion

We have used DFT calculations to explore the potential of Ru-based complexes having SiMes ligand (complex A) and C$_{60}$ annulated SiMes ligand (complexes B and C) as olefin metathesis catalysts using ethylene as the substrate. Our results show that for complexes B and C, the thermodynamic stability of the reaction intermediates is similar to the respective intermediates of complex A, being the maximum energy difference $\leq$ 6.0 kcal mol$^{-1}$. However, for the studied olefin metathesis reaction, complex B presented the lowest energy barriers (15.1 kcal mol$^{-1}$) followed by complex A (17.5 kcal mol$^{-1}$), whereas complex C presented the highest energy barriers (20.5 kcal mol$^{-1}$). The predicted steric properties are almost similar for the studied complexes A–C, suggesting that sterics have no significant role in the observed differential catalytic activity of the Ru-based complexes under study. On the other hand, the lower electron-donating nature of the C$_{60}$ annulated SiMes ligand, revealed by a significant increase of electrophilicity of complexes B and C, change the nature of the available olefin metathesis catalysts, making the catalysis more efficient in the case of complex B. Therefore, our results show that the tuning of the electron-donating capacity of the NHC ligand by annulation at the NHC backbone substantially modifies the catalytic activity of Ru-based catalysts. The inclusion of C$_{60}$ into the structure of the NHC provides a potential path to be explored in the quest for more effective catalysts for olefin metathesis. Overall, this type of work might guide catalyst design efforts. In as such, this contribution aims to inspire and provoke interest in this specific catalyst architecture.
Experimental Section

All DFT static calculations were performed with the Gaussian set of programs.[48] The electronic configuration of the molecular systems was described with the standard split-valence basis set with a polarization function of Ahlrichs and co-workers for H, C, N, and Cl (SVP keyword in Gaussian 09). For Ru we used the small-core, quasi-relativistic Stuttgart-Dresden effective core potential, with an associated valence basis set contracted (standard SDD keywords in Gaussian 09).[49] The geometry optimizations were carried out without symmetry constraints, and the characterization of the located stationary points was performed by analytical frequency calculations. The M06L functional was employed in geometry optimizations and frequency calculations. Gibbs' energies, $\Delta G$, were built through single-point energy calculations on the M06/SVP geometries using the M06 functional[49] and the triple-$\zeta$ valence plus polarization on main group atoms (TZ2P keyword in Gaussian).[49] Solvent effects were included with the PCM model using CH$_2$Cl$_2$ as the solvent.[50] To these M06/TZ2P electronic energies in solvent, zero point energy and thermal and entropic corrections were included from the gas phase frequency calculations at the M06L/SVP level of theory.

% Your Calculations

The buried volume calculations were performed with the SambVca package developed by Cavallo et al.[51] The radius of the sphere around the metal center was set to 3.5 Å, whereas for the atoms we adopted the Bondi radii scaled by 1.17, and a mesh of 0.1 Å was used to scan the sphere for buried voxels. The static maps were evaluated with a development version of the SambVca package.[52]

Acknowledgements

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Olefin Metathesis by Ru-NHC-C\textsubscript{60} Based Catalysts


