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REGULAR ARTICLE

Deactivation of Ru-benzylidene Grubbs catalysts active in olefin metathesis

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Abstract In this work, we explore the reactivity induced by coordination of a CO molecule trans to the Ru-benzylidene bond of a prototype Ru-olefin metathesis catalyst bearing a *N*-heterocyclic carbene (NHC) ligand. DFT calculations indicate that CO binding to the Ru center promotes a cascade of reactions with very low-energy barriers that lead to the final crystallographically characterized product, in which the original benzylidene group has attacked the proximal aromatic ring of the ligand leading to a cycloheptatriene ring through a Buchner ring expansion. In conclusion, the overall mechanism is best described as a carbene insertion into a C–C bond of the aromatic *N*-substituent of the NHC ligand, forming a cyclopropane ring. This cyclopropanation step is followed by a Buchner ring expansion reaction, leading to the experimentally observed product presenting a cycloheptatriene ring.

Keywords Homogeneous catalysis · Olefins metathesis · Deactivation · Cyclopropanation · *N*-heterocyclic carbene

Dedicated to Professor Vincenzo Barone and published as part of the special collection of articles celebrating his 60th birthday.

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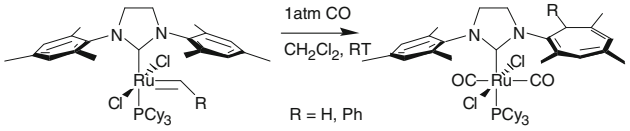
1 Introduction

Ru-catalyzed olefin metathesis is on the verge to make the big leap from a flexible synthetic tool in the academy to a variety of large-scale applications of great economic return in the industry [1]. However, one of the drawbacks slowing this step still is the scarce stability of otherwise quite active *N*-heterocyclic carbene (NHC)-based second-generation catalysts [2–5]. The greater activity of NHC-based catalysts is now rather well understood [3, 6–10], while knowledge about their stability is still scarce [11–16].

One of the reasons for this limited understanding is that academic groups usually focus on the more rewarding improvement of activity and/or selectivity of a catalyst, since more or less rational strategies can be followed, rather than investing resources to follow catalyst deactivation along unexplored pathways. Nevertheless, seminal computational efforts have confirmed experimental insights, such as that one deactivation pathway starts with the activation of an aromatic ortho C–H bond of the N-substituents of the NHC ligand [17–19]. The emerging picture is that stable catalysts must be protected in the ortho position to avoid this deactivation pathway. This immediately explains the increased stability of catalysts with mesityl N-substituents. However, the increased stability is accompanied by inferior performances in the formation of tetrasubstituted C=C bonds. A solution to this impasse has been the synthesis of catalysts with *o*-tolyl N-substituents. The single o-methyl stabilizes the catalyst without degrading performances in challenging synthesis [20–22]. Another solution is the synthesis of NHC ligands tetramethyl substituted on the saturated NHC skeleton, with the precise idea that the bulky NHC skeleton should prevent free rotation around the N-aryl bond, thus shutting off the C–H deactivation pathway [23].



Scheme 1 Sketch of the deactivation reaction promoted by CO

Broadly speaking, deactivation pathways are those chemical transformations of the (pre)catalyst or the active species that remove them from productive metathesis. In this sense, Diver, Keister, and coworkers [24, 25] have clearly shown that addition of π acids such as CO or isocyanides to a solution of typical second-generation catalysts can switch a metathesis catalyst into a cyclopropanation catalyst [26–31], by activating the Ru-ylidene bond to a carbene-like reactivity. This promotes ylidene attack to the proximal N-bonded aromatic ring of the NHC ligand, which results in a Buchner type ring expansion reaction; see Scheme 1.

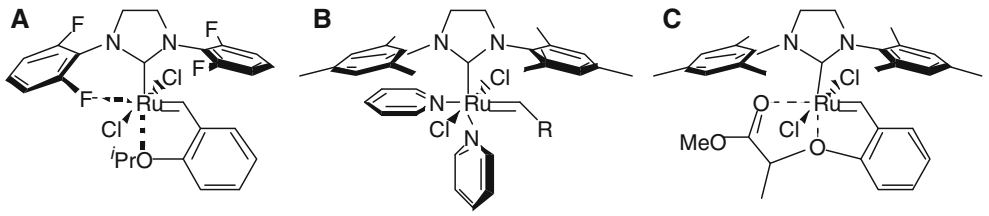
Focusing on the reactivity promoted by CO, for which accurate data are available, this decomposition reaction starts with coordination of a CO molecule trans to Ru-ylidene bond. In this respect, it is worth noting that the position trans to the Ru-ylidene bond has been scarcely considered during the years [24, 25, 32–34]. For example, Grubbs and coworkers have suggested that one of the ortho-F atoms of the NHC **A** shown in Scheme 2 could be engaged in an interaction with the Ru center that results in increased metathesis activity [35]. Furthermore, strategies for the synthesis of (pre)catalysts having labile ligands that could result in more stable and active catalysts, such as **B** and **C** of Scheme 2, have been also explored [36, 37]. In this framework, the deactivation reaction of Scheme 1 illustrates that the coordination position trans to the Ru-ylidene bond is not "innocent" and can trigger interesting reactivity. For this reason, we investigated the mechanism of deactivation shown in Scheme 1 in case of the Ru-methyidene bond [32].

Although it is difficult to call the reaction of Scheme 1 a deactivation reaction, since CO is not normally added during metathesis, understanding the chemistry behind this transformation is relevant for the following reasons. (1) π-acids are inevitably present during metathesis, and any organometallic textbook presents educative comparisons between the σ-basic/π-acid properties of CO, olefins, and phosphines. Clearly, olefins and phosphines are much weaker π-acids than CO, but a reduced acidity could still induce slow deactivation reactions as those shown in Scheme 1 for CO. (2) A clear understanding of the changes in the chemical behavior promoted by a σ-basic/π-acid ligand trans to the Ru-ylidene bond would expand our knowledge of the chemistry of Ru-based catalysts with possible consequences in the design of new ligands with tuned properties.

Along this line, we recently demonstrated that for a series of σ-basic/π-acid ligands coordinated trans to a Ru-methylidene bond of the systems, a quite acidic ligand was enough to produce such a decomposition of the olefin metathesis catalyst [24, 32]. To insert the methylidene moiety inside one of the aromatic rings of the SIMes ligand, the system must carry out a Buchner ring expansion reaction to allow the formation of a cycloheptatriene type ring. Calculations suggested that CO binding may weaken π-back-bonding between the Ru atom and the ylidene ligand [24, 32], making the latter more electrophilic and disengaging it from the metal center [38]. Electron density is donated from filled d orbitals on the Ru to the empty π orbital of the benzylidene. Differently, in the presence of the strong π-acid CO molecule, electron density from the Ru is more strongly donated to π-acid MOs of the CO. As suggested by Diver, this depletes electron density from the π orbital of the benzylidene, which is able to accept from the properly oriented π orbital of the C_{ipso} atom of the proximal ring, resulting in a very low barrier for formation of the $C_{benzylidene}$–C_{ipso} bond. However, this study was focused on the Ru-methylidene bond, which is known to be a rather reactive and unstable bond, while standard and commercial (pre)catalysts normally bear a Ru-benzylidene group. For this reason, we decided to extend our previous study to the reactivity induced by CO-coordinated trans to the Ru-benzylidene bond, see Scheme 1. Comparison between the behavior of the Ru-methylidene and Ru-benzylidene systems of Scheme 1 should increase our understanding of the basic properties of the Ru-ylidene bond and of the reactivity changes that could in principle be induced by changes in the nature of the ligands connected to the Ru atom. The only approximation we have made to the systems of Scheme 1 is replacing PCy_3 with PMe_3 to save computer time.

2 Computational details

All the DFT static calculations were performed at the GGA level with the Gaussian03 set of programs [39], using the BP86 functional of Becke and Perdew [40–42]. The electronic configuration of the molecular systems was described with the standard split-valence basis set with a polarization function of Ahlrichs and coworkers for H, C, N, O, P, F, and Cl (SVP keyword in Gaussian) [43]. For Ru, we used the small-core, quasi-relativistic Stuttgart/Dresden effective core potential, with an associated (8s7p6d)/[6s5p3d] valence basis set contracted according to a (311111/22111/411) scheme (standard SDD keywords in Gaussian03) [44–46]. The geometry optimizations were performed without symmetry constraints. The Synchronous Transit-Guided Quasi-Newton (STQN) Method, developed



Scheme 2 Representation of Ru-complexes presenting a ligand coordinated trans to the Ru-alkylidene bond

by H. B. Schlegel and coworkers, was used to calculate the transition states. This method is requested with the QST3 keyword [47]. The characterization of the located stationary points was performed by analytical frequency calculations. Solvent effects including contributions of non-electrostatic terms have been estimated in single-point calculations on the gas-phase optimized structures, based on the polarizable continuous solvation model PCM using CH_2Cl_2 as a solvent [48, 49]. In conclusion, the energies reported correspond to the "Total free energy in solution: with all non-electrostatic terms" value in the Gaussian output. Previous studies have revealed that this scheme of calculation provides excellent results [50–52].

3 Results

To get insight into the decomposition for the so-called benzylidene olefin metathesis precatalyst, complex **1**, induced by CO, we first optimized complex **7**, for which we had available X-ray structural data. Although the optimization suffered the simplification of the tricyclohexyl phosphine by trimethyl phosphine, the agreement was excellent, with a rmsd of 0.039 Å for distances and of 0.9° for angles [53–55].[1] This indicates that the sterically demanding PCy_3 phosphine can be replaced with the less bulkier PMe_3 phosphine to shed light on this kind of reactions. Since no intermediate between the starting species **1** and the product **7** was experimentally characterized, we assumed a decomposition pathway similar to that we calculated for the similar Ru-methylidene complex. The complete energy profile for the benzylidene complex is shown in Fig. 1.

The first step in Fig. 1 shows that the coordination of a CO molecule trans to the Ru-benzylidene bond of **1** is an exoergonic process releasing 25.7 kcal/mol. Linear transit calculations using the Ru–CO distance as reaction coordinate revealed the absence of a transition state between complexes **1** and **2**, demonstrating CO coordination to be a barrierless step in terms of potential energy. The vacant position trans to the ylidene group reveals no sterical hindrance for the entering CO molecule; however, after bonding, the metal the Ru-benzylidene bond elongates from 1.85 Å in **1** to 1 99 Å in **2** and pushes the phosphine almost perfectly trans to the NHC ligand, with a small elongation (less than 0.05 Å) of the Ru-NHC and Ru–P bonds. CO coordination also results in the remarkable reduction of the NHC-Ru-benzylidene angle from 103.3° in **1** to 96.1° in **2**. These structural rearrangements increase the proximity of the benzylidene group with the proximal aromatic ring of the SIMes ligand, with the a sensible reduction of the distance between the $C_{benzylidene}$ and C_{ipso} atoms from 3.11 Å in **1** to 2.82 Å in **2**.

Starting from **2,** the cyclopropanation reaction between the benzylidene group and one of the C_{ipso}–C_{ortho} bonds of the nearby mesityl ring occurs in two steps. The former corresponds to attack of the benzylidene group to the C_{ipso} atom, which requires overcoming a barrier of 7.1 kcal/mol and leads to **3**, which still presents a Ru-benzylidene bond and is 6.8 kcal/mol less stable than **2** (see Fig. 1). It is worth noting that in the absence of a CO molecule coordinated trans to the Ru-methylidene bond, that is, in system **1**, the metallacycle structure **3** of Fig. 1 is not stable. All our attempts to locate a metallacycle species similar to **3** in the absence of the CO ligand failed, and the geometry optimization collapsed into the starting species **1**. Then, the second step of the cyclopropanation reaction requires the complete rupture of the previous Ru-benzylidene bond with the concerted formation of a cyclopropane ring by attack of the $C_{benzylidene}$ atom to one of the C_{ortho} atoms of the mesityl ring. This step requires the overcoming of a negligible barrier of 0.9 kcal/mol, after which the system collapses into the intermediate **4**. This species **4** is 4.7 kcal/mol below in energy with respect to species **2**.

Starting from intermediate **4**, with the newly formed cyclopropane ring, the next step involves the cleavage of the C_{ipso}–C_{ortho} bond of this tensioned small ring, evolving to intermediate **5** with a formal cycloheptatriene ring, with a small energy barrier, 4.6 kcal/mol, separating **4** from **5**. At this point, the decomposition reaction has completed, and the only steps required to reach the crystallographically characterized product are a rotation of nearly 180° around

[1] Standard deviations for distances and angles: $S_{n-1} = \sqrt{\frac{\sum_{i=1}^{N}(CV-EV)^2}{N-1}}$ where CV means calculated value, EV experimental value (X-ray data), and N is the number of distances or angles taken into account.

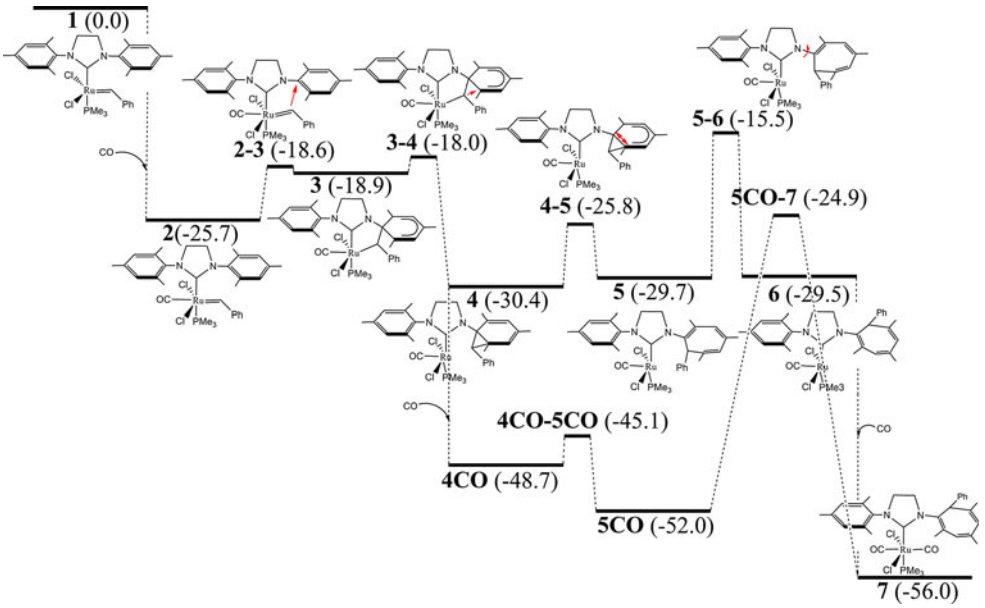


Fig. 1 Energy diagram of the complete **1**–**7** deactivation pathway. In *parentheses* is the energy of the various species, in kcal/mol, relative to the (pre)catalyst **1**

the N-cycloheptatriene bond, to reach a conformation in which the Ph substituent on the cycloheptatriene ring points away from the Ru atom, and coordination of a second CO molecule. Starting with the rotation around the *N*-cycloheptatriene bond, which corresponds to a conformational change from **5** to **6**, the transition state reported in Fig. 2 shows both the NHC and heptatriene rings almost coplanar. This transition state is 14.2 kcal/mol above **5**. It is worthy to note that this energy barrier could be somewhat higher when the model phosphine used in this work, PMe_3, is replaced by the experimentally used, and bulkier, PCy_3. Interestingly, intermediates **4**, **5,** and **6** are nearly isoenergetic with energy differences less than 1 kcal/mol. Coordination of a second CO molecule to the Ru atom of **6** leads to the experimental product **7** by release of 26.5 kcal/mol. This remarkable increase in the energy required for cycloheptatirene rotation is a consequence of the steric hindrance of the second CO molecule, which is coordinated just below the cycloheptatirene ring.

Although in our previous study on the CO-promoted decomposition in the presence of the Ru-methylidene group indicated that coordination of a second CO molecule is not needed to reach the experimental decomposition product, a result that is supported by the results presented in Fig. 1, we also investigated the energy profile in case the second CO molecule coordinates to the Ru atom of **4**, which means before the Buchner ring expansion step. Calculations indicate that CO coordination to 4, leading to **4CO**, releases 18.3 kcal/mol. This value is quite smaller than the energy gain associated with coordination of CO to **1** and **6**, 25.7 and 36.5 kcal/mol, respectively. From **4CO**, the next barrier corresponding to the opening of the cyclopropane ring, leading to structure **5CO**, is only

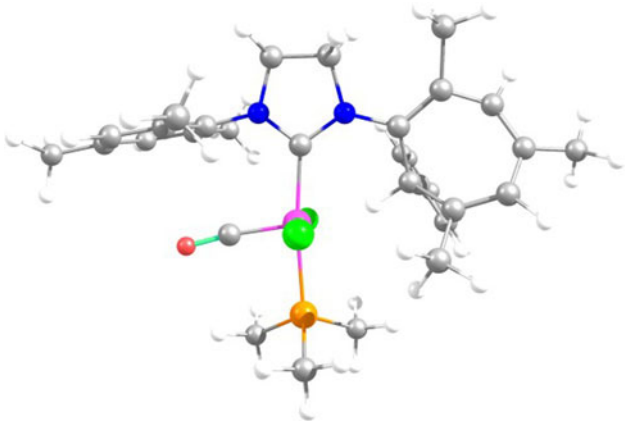


Fig. 2 DFT optimization of transition state **5**–**6**

1.9 kcal/mol. However, the barrier corresponding to a rotation of 180° around the N-cycloheptatriene bond, to reach the experimentally characterized conformer **7**, is now 27.1 kcal/mol. Thus, considering the small energy barrier for the **4** to **5** step, and the rather high barrier for the **5CO** to **7** step, it is likely that coordination of the second CO molecule might occur after the ring expansion step. This conclusion is also supported by considering that coordination of a second CO molecule would be further disfavored by an entropic contribution not included explicitly in the reported energy values. Comparison between these results and our previous results on the decomposition pathway in the presence of the Ru-methylidene bond indicates the nature of the Ru-ylidene bond has a very minor impact on the energetics of cyclopropane formation and of the following Buchner type ring expansion. Rather, that the main difference is in the rotation of 180° around the *N*-cycloheptatriene bond that, in case of the

Ru-benzylidene bond, is needed to place the Ph substituent on the cycloheptatriene ring away from the metal center.

4 Conclusions

In this contribution, we evaluated the complete energy profile corresponding to the deactivation, promoted by coordination of a CO molecule, of a NHC-Ru catalyst for olefins metathesis presenting a Ru-benzylidene bond. Consistent with our previous work on the deactivation of a similar NHC-Ru precatalyst presenting a Ru-methylidene bond, after CO coordination trans to the Ru-ylidene bond, the overall decomposition energy profile is characterized by very low-energy barriers. These results indicate that the nature of the Ru-ylidene bond has a minor impact on the energetics of this deactivation pathway. The main difference between the two decomposition mechanisms is that in case of the Ru-benzylidene system, an additional step, corresponding to rotation around the *N*-cycloheptatriene bond is needed in order to orientate the Ph substituent on the cycloheptatriene ring away from the metal atom.

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