J|A|C|S
COMMUNICATIONS

The Elusive Mechanism of Olefin Metathesis Promoted by (NHC)Ru-Based Catalysts: A Trade between Steric, Electronic, and Solvent Effects

Andrea Correa and Luigi Cavallo*

Dipartimento di Chimica, Università di Salerno, Via Salvador Allende, Baronissi (SA), I-84081, Italy

Received July 11, 2006; E-mail: lcavallo@unisa.it

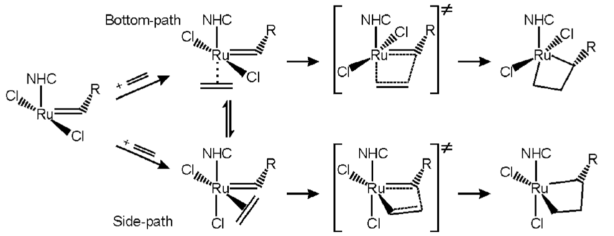
It took only a few years to elevate olefin metathesis as one of the most versatile tools for the synthesis of $C{=}C$ double bonds. The giant step was possible when a detailed comprehension of the chemical mechanics at work with these systems was achieved. This understanding was key to the rational design of a large number of more active and, in the broadest sense, better performing catalysts.[1−5] Nevertheless, the exact mechanism operative in the case of the (NHC)Ru-based catalysts still is a matter of debate (NHC = N-heterocyclic carbene). Postulated substrate binding can be preferentially trans to the NHC ligand (bottom path in Scheme 1) or cis to this ligand with a simultaneous shift of a halogen group to a trans position (side path in Scheme 1).

In previous papers,[6,7] consistently with other theoretical studies,[8−15] we reported that olefin metathesis with Ru-catalysts starts from a bottom-bound olefin complex, and this geometry is retained also at the transition state for metallacycle formation. We based this conclusion on the relatively high energy of the possible side-bound olefin complexes. This mechanism is also supported by a NMR study of Piers and co-workers that evidenced a bottom-bound geometry for a Ru-cyclobutane model compound.[16] Differently, a paper by Grubbs and co-workers supported the side-bound pathway. NMR and X-ray analysis of the model compound **1** revealed the presence of two structures.[17] One of them with the N atom of the pyridine-based ligand bottom-bound to Ru **(1a)** while, somewhat surprisingly, the other geometry presented the N atom side-bound to Ru (**1b**) (Scheme 2).

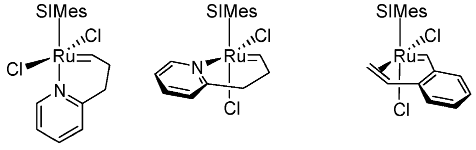
Subsequent DFT calculations of Goddard and co-workers indicated clearly that solvent effects were of paramount relevance to the high stability of **1b**.[18] In fact, in the gas-phase **1a** was predicted to be about 7 kcal/mol more stable than **1b**, whereas in CH_2Cl_2 **1b** is favored by about 1 kcal/mol relative to **1a**. This remarkable solvent effect was ascribed to the much larger dipole moment of **1b** (12.4 D) relative to that of **1a** (1.5 D).[18] More recently, Grubbs and co-workers reported the X-ray structure of the model compound **2**, which clearly indicates that the olefin is side-bound to Ru.[19] On this basis, it is reasonable they wondered about the actual reaction pathway in olefin metathesis catalyzed by (NHC)Ru-based catalysts. In this Communication we contribute to the discussion using a DFT approach.[20]

Besides complex **2**, as a test case of the computational approach, we considered the systems shown in Chart 1: briefly, the simple model system **3**, to investigate electronic effects; system **4**, with a more complex and representative substrate, to investigate steric effects; and finally system **5**, the actual system used for asymmetric metathesis.[21,22] We focused on the relative stability of the side- and bottom-bound coordination intermediates and the stability of the corresponding transition states for metallacycle formation. The solvent effect of CH_2Cl_2 were also considered.

Scheme 1

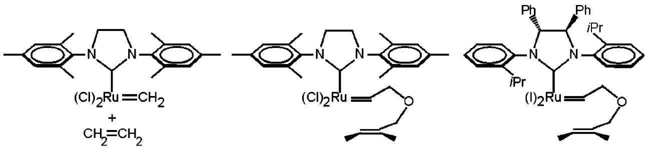


Scheme 2



1a **1b** **2**

Chart 1



3 **4** **5**

Table 1. BP86 Free Energy Differences, in kcal/mol, between the Best Side-Bound and Bottom-Bound Geometries[a]

	coordination intermediate		transition state	
	ΔG (gas)	ΔG (CH_2Cl_2)	ΔG (gas)	ΔG (CH_2Cl_2)
2[b]	1.2	−5.1		
2	−1.4	−7.5		
3	3.4	−2.8	11.3	3.8
4	7.6	0.4	18.9	12.0
5	6.8	−2.2	20.2	14.1

[a] Positive values mean that the bottom-down geometry is favored. [b] Calculated with the B3LYP functional.

We started with the relative stability of the side- and bottom-bound geometries of **2**. In agreement with the DFT results of Grubbs and co-workers,[19] the B3LYP functional predicts that the side-bound geometry is not favored in the gas-phase, but it becomes the most stable when the solvent effect is introduced, see Table 1. Differently, the BP86 functional predicts the side-bound geometry to be favored both in the gas phase and in CH_2Cl_2. In the remainder of this work we will use the computationally much less expensive BP86 functional that, if wrong, is biased in favor of the side-bound geometry. The different performances of the two functionals are outside the scope of the present paper.

Moving to **3**, a system representative of degenerate ethene metathesis, and where steric effects are less relevant, the side-bound coordination intermediate is about 3 kcal/mol higher in energy than the bottom-bound intermediate in the gas-phase. This energy preference increases to roughly 11 kcal/mol at the transition state

10.1021/ja064924j CCC: $33.50 © 2006 American Chemical Society

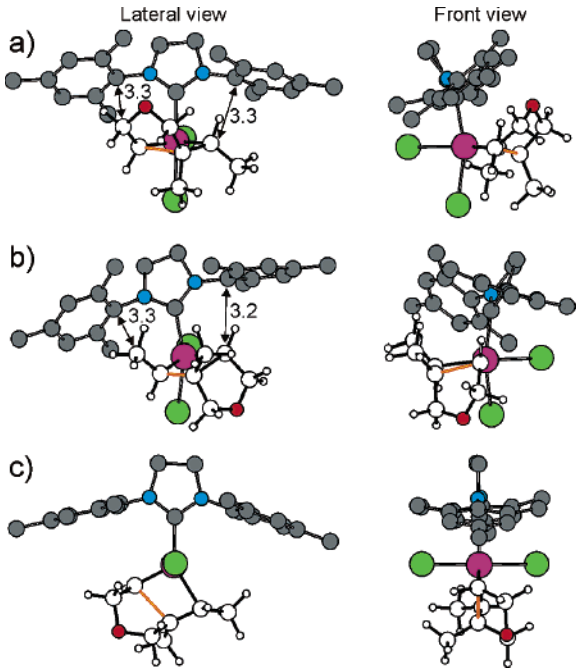


Figure 1. Geometries of the three transition states for system **4**. Distances are in Å. The forming C−C bond is colored in yellow.

for metallacycle formation. The increased preference for the bottom-bound geometry at the transition state is explained by the different orientation of ethene in the side-bound geometries. In the side-bound coordination intermediate the C═C double bond of ethene is almost perpendicular to the Ru═CH$_2$ bond, to minimize steric interaction with the mesityl groups. At the side-bound transition state, instead, ethene is forced to be parallel to the Ru═CH$_2$ bond. This increases steric interaction between ethene and the mesityl groups (see the Supporting Information). Nevertheless, steric pressure is not strong enough, and solvent effect effectively counterbalances the electronic/steric preference for the bottom-bound geometry. In CH$_2$Cl$_2$ the side-bound geometry is favored at the coordination intermediate, whereas it is unfavored at the transition state.

When a bulkier and "real life" substrate is considered, system **4**, increased steric pressure results in increased preference for the bottom-bound geometry at the coordination intermediate (about 8 kcal/mol). Nevertheless, solvent effect is strong enough to almost overturn the order of stability, and the side-bound coordination intermediate becomes competitive in CH$_2$Cl$_2$. However, at the transition state the bottom-bound geometry is favored by more than 15 kcal/mol. Of course, in this case the solvent effect can only reduce the preference for the bottom-bound geometry, which is with no doubt favored also in CH$_2$Cl$_2$. The sharp increase of selectivity in favor of the bottom-bound geometry is clearly understood by looking at the two possible side-bound transition states of Figure 1. In the structure of Figure 1a the O−CH$_2$ group of the substrate is pushed toward the nearby mesityl ring, and very short distances evidence strong steric stress. Similarly, in the structure of Figure 1b, the CH$_3$ groups on the C═C double bond are pushed toward the mesityl rings. In both structures the SIMes ligand is remarkably bent away from the substrate, and the Ru atom is about 0.6 Å out of the mean NHC plane. This clearly weakens the NHC−Ru σ-bond relative to that present in the undeformed bottom-bound transition state of Figure 1c.

The case of system **5**, which presents a chiral ligand and it is active in the desymmetrization of achiral trienes,[21,22] is consistent with that of the achiral system **4**. That is, the bottom-bound transition state is so strongly favored that even considering any source of error (functional, basis set, solvent model) it can be reasonably concluded that the bottom reaction pathway is favored.

It is worthy to note that this conclusion cannot be generalized to the first generation Grubbs catalysts, although there are experimental indications that the bottom-path may be favored in this case.[23] Instead, calculations indicate that the preferred reaction pathway is a delicate balance between electronic, steric, and solvent effects. Each of them seems to be so strong that it is a hazard to generalize conclusions. As a rule of thumb, and as already pointed out by Goddard, polar solvents should push toward the side reaction pathway and can easily overturn an electronic preference for the bottom reaction pathway.[18] Thus, in the absence of strong steric effects, that is, with less bulky ligands and/or substrates, the side reaction pathway, as suggested by Grubbs and co-workers,[17,19] can be indeed competitive. However, steric effects owing to interaction between bulky NHC ligands (and SIMes already is a bulky NHC ligand)[24,25] and bulky substrates (as rather simple trienes) easily overcome other effects and push strongly toward the bottom reaction pathway.

Acknowledgment. We thank the MIUR of Italy (Grant PRIN-2004) for financial support.

Supporting Information Available: Computational details, energies, and Cartesian coordinates. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) Hoveyda, A. H.; Schrock, R. R. *Chem.*−*Eur. J.* **2001**, *7*, 945.
(2) Schrock, R. R.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2003**, *42*, 4592.
(3) Fürstner, A. *Angew. Chem., Int. Ed.* **2000**, *39*, 3012.
(4) Trnka, T. M.; Grubbs, R. H. *Acc. Chem. Res.* **2001**, *34*, 18.
(5) Grubbs, R. H. *Handbook of Olefin Metathesis*; Wiley-VCH: Weinheim, Germany, 2003.
(6) Cavallo, L. *J. Am. Chem. Soc.* **2002**, *124*, 8965.
(7) Costabile, C.; Cavallo, L. *J. Am. Chem. Soc.* **2004**, *126*, 9592.
(8) Aagaard, O. M.; Meier, R. J.; Buda, F. *J. Am. Chem. Soc.* **1998**, *120*, 7174.
(9) Adlhart, C.; Chen, P. *J. Am. Chem. Soc.* **2004**, *126*, 3496.
(10) Adlhart, C.; Chen, P. *Angew. Chem., Int. Ed.* **2002**, *41*, 4484.
(11) Adlhart, C.; Hinderling, C.; Baumann, H.; Chen, P. *J. Am. Chem. Soc.* **2000**, *122*, 8204.
(12) Vyboishchikov, S. F.; Bühl, M.; Thiel, W. *Chem.*−*Eur. J.* **2002**, *8*, 3962.
(13) Fomine, S.; Martinez Vargas, S.; Tlenkopatchev, M. A. *Organometallics* **2003**, *22*, 93.
(14) Suresh, C. H.; Koga, N. *Organometallics* **2004**, *23*, 76.
(15) Occhipinti, G.; Bjorsvik, H. R.; Jensen, V. R. *J. Am. Chem. Soc.* **2006**, *128*, 6952.
(16) Romero, P. E.; Piers, W. E. *J. Am. Chem. Soc.* **2005**, *127*, 5032.
(17) Ung, T.; Hejl, A.; Grubbs, R. H.; Schrodi, Y. *Organometallics* **2004**, *23*, 5399.
(18) Benitez, D.; Goddard, W. A., III. *J. Am. Chem. Soc.* **2005**, *127*, 12218.
(19) Anderson, D. R.; Hickstein, D. D.; O'Leary, D. J.; Grubbs, R. H. *J. Am. Chem. Soc.* **2006**, *128*, 8386.
(20) The GGA BP86 calculations have been performed with the Gaussian 03 package. The PCM solvation model has been used to simulate CH$_2$Cl$_2$ as solvent. See the Supporting Information for details.
(21) Seiders, T. J.; Ward, D. W.; Grubbs, R. H. *Org. Lett.* **2001**, *3*, 3225.
(22) Funk, T. W.; Berlin, J. M.; Grubbs, R. H. *J. Am. Chem. Soc.* **2006**, *128*, 1840.
(23) Tallarico, J. A.; Bonitatebus Jr., P. J.; Snapper, M. L. *J. Am. Chem. Soc.* **1997**, *119*, 7157.
(24) Dorta, R.; Stevens, E. D.; Scott, N. M.; Costabile, C.; Cavallo, L.; Hoff, C. D.; Nolan, S. P. *J. Am. Chem. Soc.* **2005**, *127*, 2485.
(25) Viciu, M. S.; Navarro, O.; Germaneau, R. F.; Kelly, R. A.; Sommer, W.; Marion, N.; Stevens, E. D.; Cavallo, L.; Nolan, S. P. *Organometallics* **2004**, *23*, 1629.

JA064924J