

[g011]

ON THE MECHANISM OF RHODIUM-CATALYZED [6+2] CYCLOADDITION OF 2-VINYLCYLOBUTANONES AND ALKENES

M. Merced Montero-Campillo^(a,), Enrique M. Cabaleiro-Lago^(b), Jesús Rodríguez-Otero^(a)*

(a) Dpto. de Química Física, F. de Química, Universidade de Santiago de Compostela
Avda. das Ciencias s/n, 15782 Santiago de Compostela (Spain)

(b) Dpto. de Química Física, F. de Ciencias, Universidade de Santiago de Compostela
Campus de Lugo, Avda. Alfonso X El Sabio s/n, 27002 Lugo (Spain)

^(*) gfmerche@usc.es

Abstract. The intramolecular [6+2] cycloaddition mechanism of 2-vinylcyclobutanones and alkenes catalyzed by the $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ dimer has been studied using density functional theory, comparing this multistep process with the one-step reaction in absence of catalyst. This possible mechanism agrees with what was previously experimentally suggested. Calculations have also allowed to explain the selectivity of the reaction.

Introduction. Carbocyclations are ring-forming processes that involve the formation of new carbon-carbon bonds via carbometallation. Transition metals, like rhodium, are of common use in these kind of reactions ⁽¹⁾; in concrete, the $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ dimer is an efficient catalyst for [5+2], [6+2] or [5+2+1] reactions ⁽²⁾.

Paul Wender and co-workers reported a new [6+2] cycloaddition of 2-vinylcyclobutanones and alkenes for the synthesis of eight-membered rings ⁽³⁾ (see **Figure 1**). They proposed the most probable mechanism considering some experimental evidences, although there are several mechanistic hypotheses for this transformation ^(3,4). This work presents density functional

calculations in order to study the mechanism of this [6+2] cycloaddition and to analyze the paper of the rhodium catalyst comparing with the same reaction in absence of catalyst. The study also tries to explain the selectivity of the reaction, because the product is obtained as a single *cis*-diastereomer.

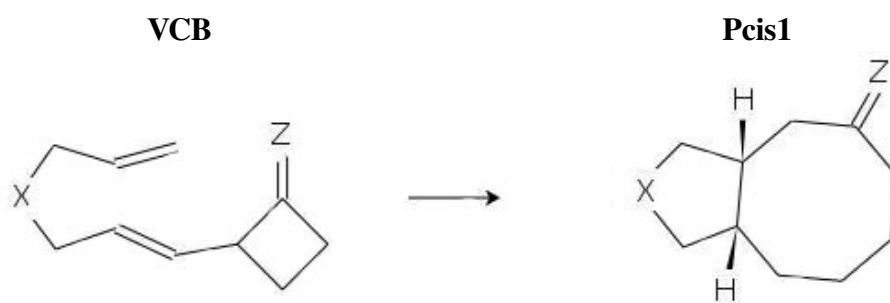


Figure 1. General [6+2] intramolecular cycloaddition ($Z=O$ for vinylcyclobutanones, **VCB**).

The product **Pcis1** is the obtained diastereomer. We labeled the other *cis*-diastereomer as **Pcis2**.

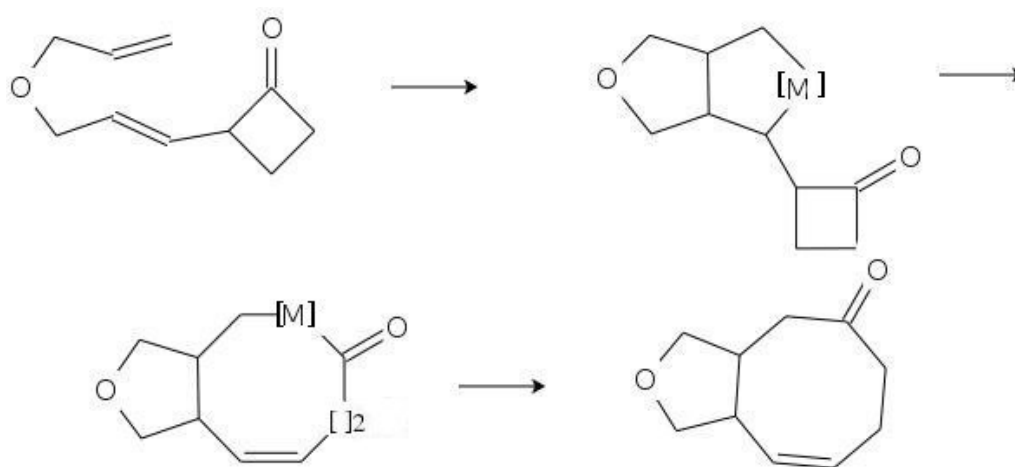
Computational details. Calculations were done employing B3LYP functional ⁽⁵⁾. 6-31G(d,p) Pople's basis set was used for C, O, H and Cl atoms, and the effective core potential LANL2DZ ⁽⁶⁾ was used for Rh atom. IRC ⁽⁷⁾ (intrinsic reaction path) was obtained at the same level. All the stationary points were characterized as minimum or transition state by the vibrational frequency analysis, using analytical second derivatives. All calculations were carried out with Gaussian03 program ⁽⁸⁾.

Results and Discussion.

A. Rhodium-catalyzed [6+2] cycloaddition in gas phase. In the first studies of the catalyzed intramolecular [5+2] cycloaddition of alkenes and vinylcyclopropanes ^(4c,4d) Paul Wender *et al.* proposed two main possibilities for the reaction mechanism, which translated to the present case, are showed in **Figure 2**. Attending to their arguments, and applying them to our [6+2] case, the most probable way seems to be the initial formation of a metallacyclopentene with the π -system ⁽⁹⁾,

and then to form a bicyclo interacting with the cyclobutanone (a-pathway in Figure 2).

a)



(b)

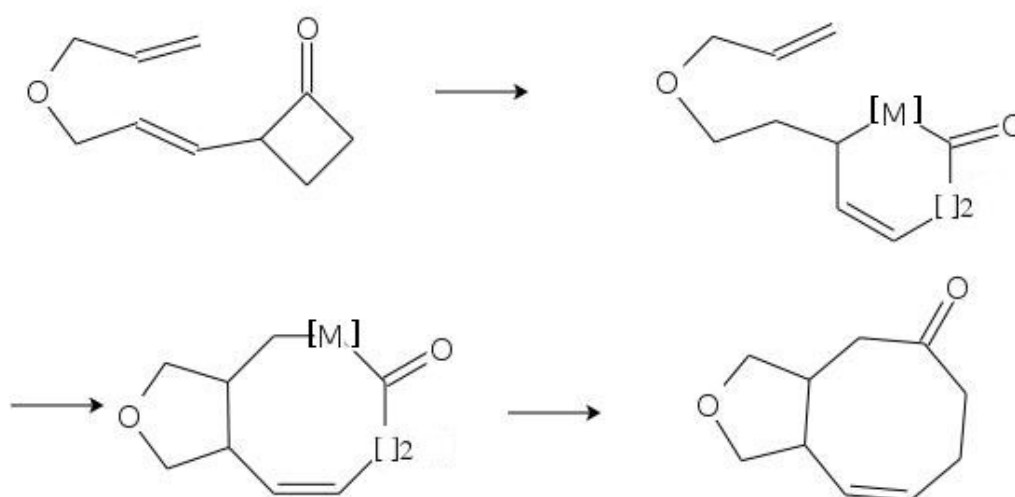


Figure 2. Two mechanistic possibilities proposed by Wender *et al.*

Figure 3 shows the intermediates and transition states geometries for the rhodium-catalyzed [6+2] cycloaddition in gas phase to obtain the diastereomer we have labeled as **Pcis1**. The $[\text{Rh}(\text{CO})_2\text{Cl}]_2$ dimer is in equilibrium with two monomeric units, and the rhodium atom bonded to two ligands, CO and Cl, is the active specie⁽¹⁰⁾. The complex **II** shows an arrangement in which the transition metal is coordinated to the two parallel double bonds. Considering those multiple bonds as two different ligands, rhodium adopts a planar-square geometry. From the point of view of the transition

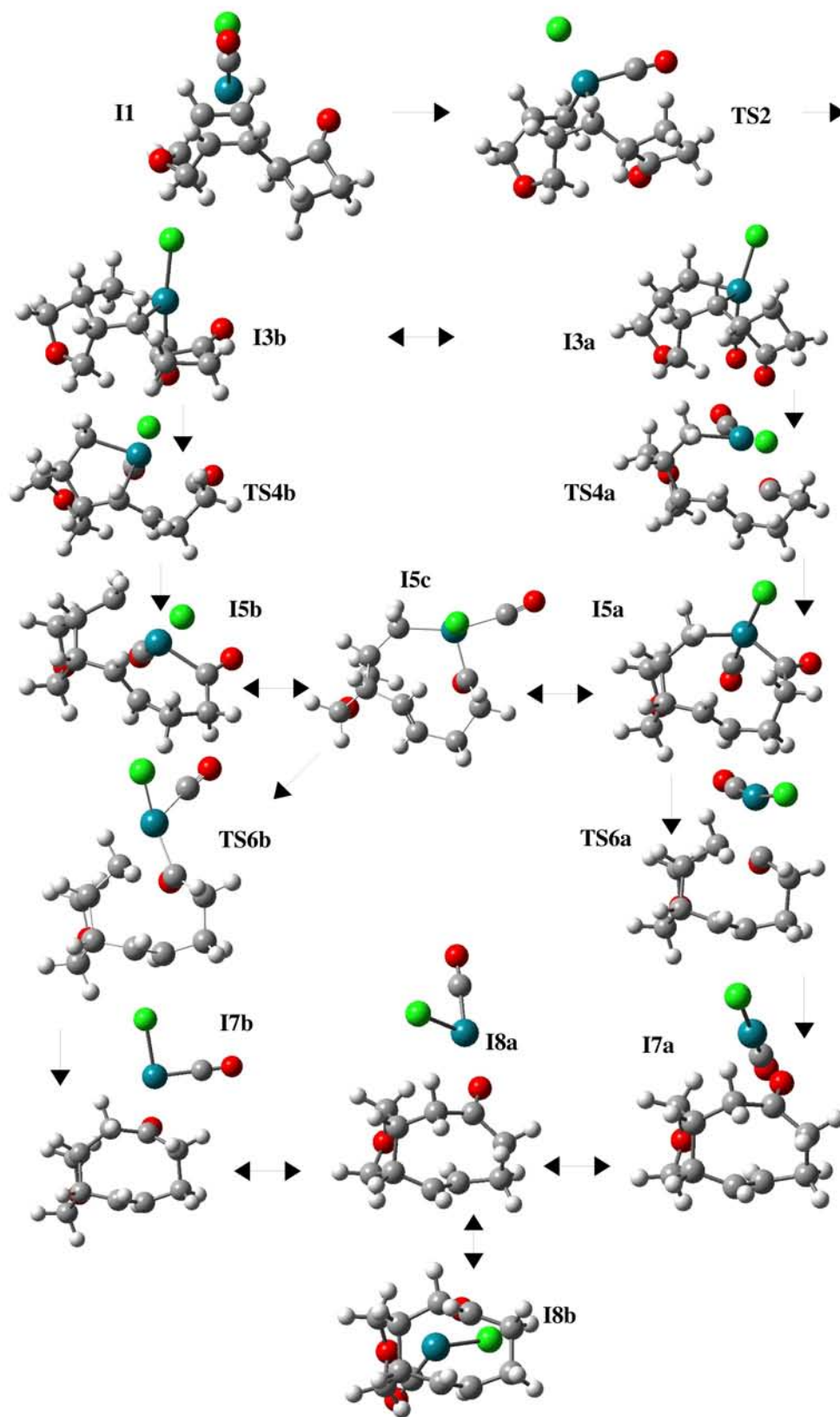


Figure 3. Intermediates and transition states for the rhodium-catalyzed cycloaddition.

metal, **I1** is a 16e⁻ complex. In spite of the known “18 electron rule”, is usual in Rh(I) and in other d⁸ metals from the 8-11 groups to adopt 16 e⁻ ⁽¹¹⁾.

Through the transition state **TS2** we reach to the intermediate **I3b**. **I3b** is a structure with two five-member cycles, one of them the mentioned metallacyclopentene. The disposition of the cyclobutanone is parallel to the metallacyclopentene's plane. This situation is more stable than in **I3a**, another conformer, in which the cyclobutanone's plane is perpendicular to the metallacycle's plane. From **I3b** to **I8b** the reaction goes through less stable intermediates than **I3b**, but with smaller barriers than from **I3a**. The metallacyclopentene is transformed into an eight-member one, more strained in the **I5b** case than in the **I5a** one. The conformer **I5c** connects the two pathways. In the intermediates **I7a** and **I7b** the rhodium was already almost eliminated. The rhodium atom is far away from the bicyclo in **I8a**, but the stablest complex is **I8b**, where it can interact with the two oxygen atoms of the **Pcis1** product. A new molecule of vinylcyclobutanone **VCBcis1** will interact with the rhodium catalyst beginning the catalytic cycle again. It is well-known the rhodium trend of forming strong bonds with oxygen.

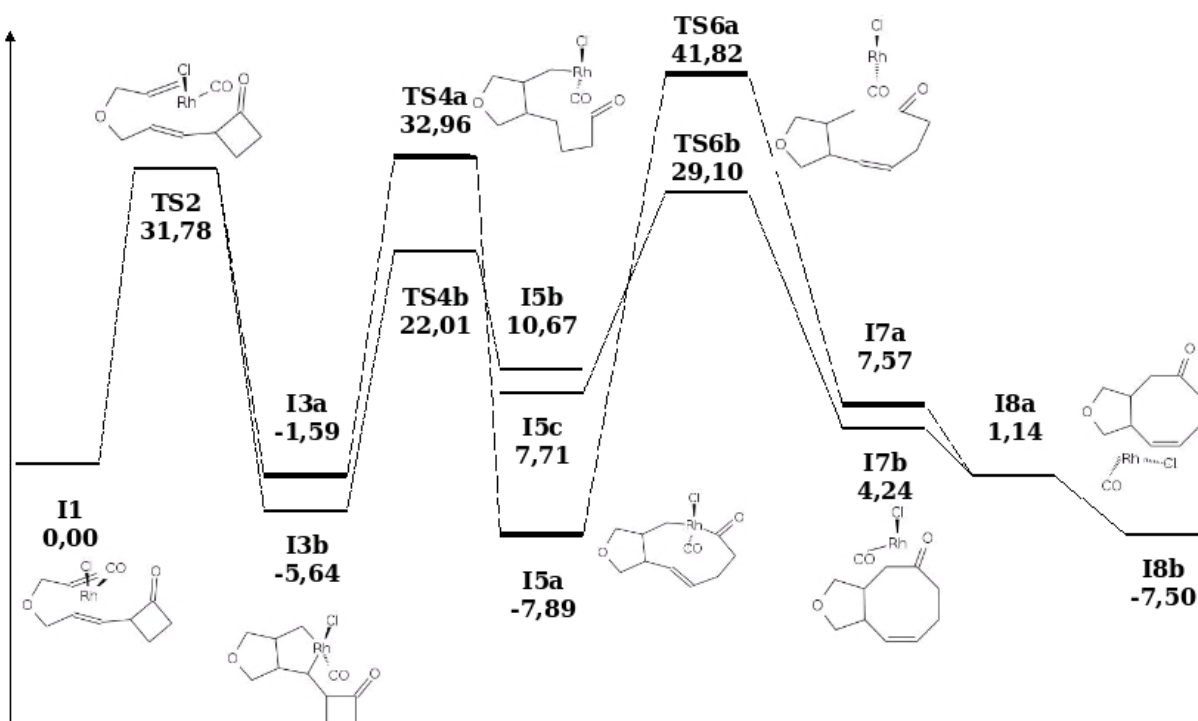


Figure 4. Relative energies (kcal/mol) for the structures showed in Figure 3.

Figure 4 shows the energy barriers obtained at B3LYP/6-31G(d,p)+LANL2DZ level. It is obvious that the reaction will probably go through the b-pathway, since the rate limiting steps (RLS) of “a” and “b” are really different. It is not only that in the a-pathway **I5a** is more stable than the product; moreover, the energy barrier of **TS6a** from **I5a** is almost 50 kcal/mol. The highest barrier in the b-pathway is less than 32 kcal/mol (the first transition state of the path) and the RLS corresponds with the way from the **I3b** to **TS6b**. However, this [6+2] cycloaddition is an expensive process from the energetic point of view, even going through the most favorable pathway.

The alternative mechanism is to form first a rhodacycle with the vinylcyclobutanone (b-pathway in Figure 2). Note that if the first intermediate of the reaction was a structure of this type (see Figure 5) then it would be possible to form at least a part of trans-diastereomer product. In the other mechanism rhodium interacts over or below the plane of the two double bonds, but here the olefin is free for bonding in different ways. However, only the *cis*-diastereomer is observed, so the conclusion is that this alternative mechanism is not viable.

Only the diastereomer **Pcis1** is obtained as product. We performed the *cis2*-pathway at the same level to compare with the *cis1*-pathway and to analyze the diastereoselectivity of the reaction. Table 1 shows the energies for the calculated structures. The energy barriers are similar or lower than in the *cis1* case. A more detailed analysis reveals that even the *cis2* product **I8a** is more stable than the **I1** starting complex, the **I5a** (for the a-pathway) and **I3b** (for the b-pathway) energies are below the energy product. That is, the last steps of the reaction are endothermic in the *cis2*-pathway. But, moreover, **Pcis2** is less stable than **Pcis1** (absolute energies: **Pcis1** = -1222.75281 a.u., **Pcis2** = -1222.75231 a.u.).

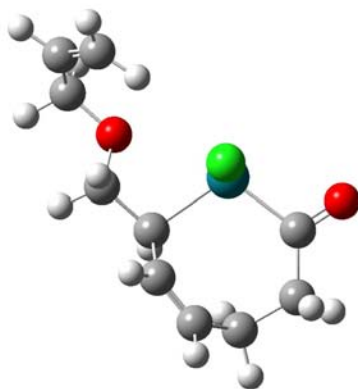


Figure 5. Alternative rhodacycle.

	Relative energy (kcal/mol)
I1	0.00
TS2	20.26
I3a	-16.99
I3b	-20.84
TS4a	7.70
TS4b	17.79
I5a	-25.49
I5b	-6.85
TS6a	19.30
TS6b	9.18
I7a	6.44
I7b	-14.42
I8	-18.11

Table 1. Relative energies in kcal/mol in the *cis2*-pathway.

Figure 6 shows the structures of the last complex in *cis1* and *cis2* pathways, which are **I8b** for *cis1* and **I8** for *cis2*. While in **I8b-cis1** the rhodium atom adopts a planar-square geometry bonding with the two oxygen atoms of the bicyclo, in the **I8-cis2** case this possibility does not exist. The oxygen from the ether group is far away from the catalyst, and rhodium can only bond with the oxygen from the carbonyl group.

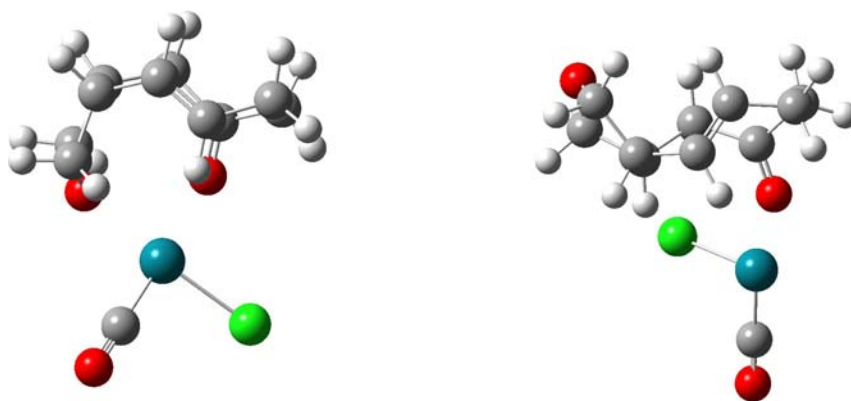
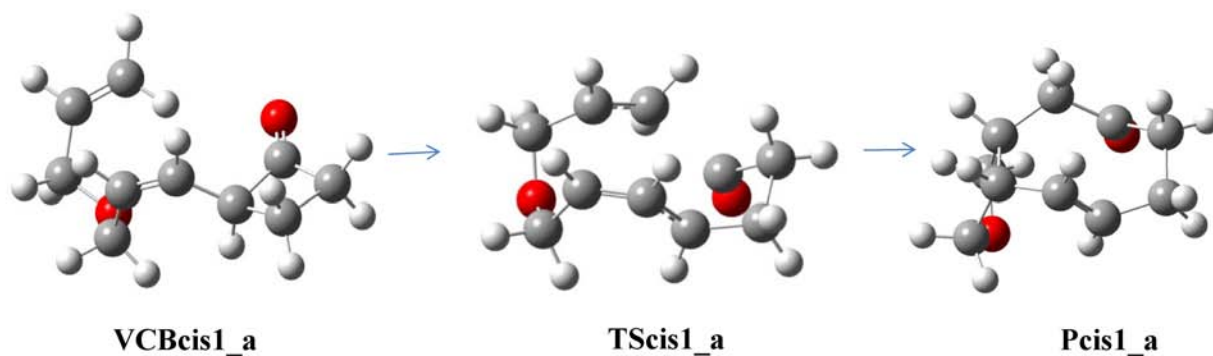
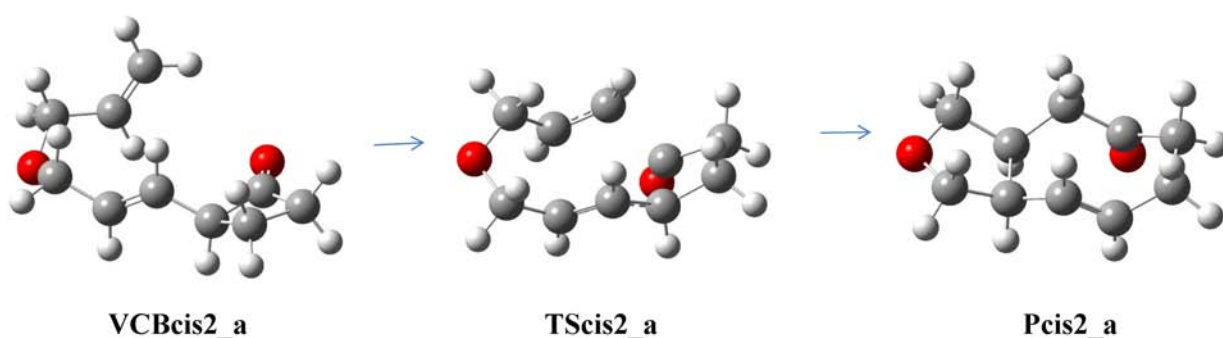


Figure 6. Last structure for *cis1*-pathway (left) and for *cis2*-pathway (right).

1)



2)



3)

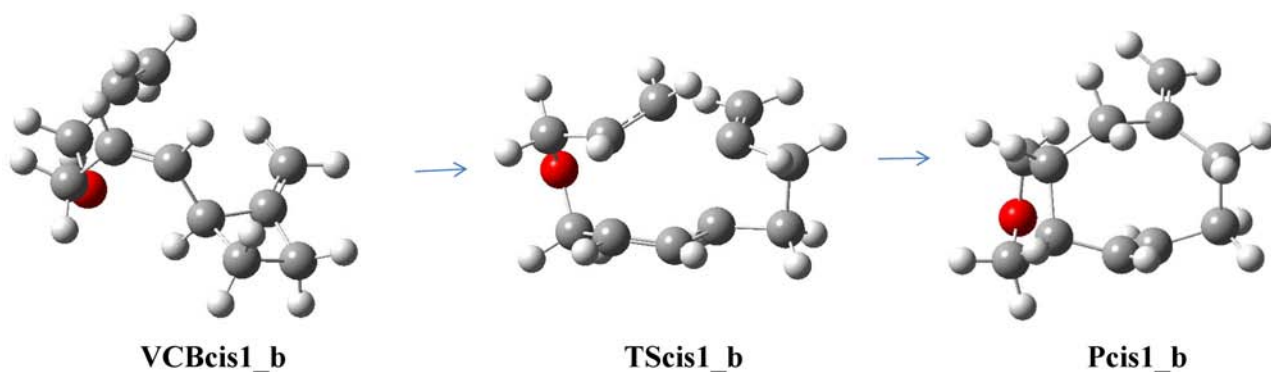


Figure 7. Reactants, transition states and product energies for the non-catalyzed [6+2] cycloaddition in gas phase using B3LYP/6-31G(d,p) in three different cases: **1)** to obtain **Pcis1** product starting from **VCBCis1**: VCBCis1a 0.00 kcal/mol, TScis1a 45.29 kcal/mol, Pcis1a -18.24 kcal/mol; **2)** to obtain **Pcis2** product starting from **VCBCis2**: VCBCis2a 0.00 kcal/mol, TScis2a 43.79 kcal/mol, Pcis2a -17.28 kcal/mol; **3)** to obtain the analogue to **Pcis1** but with vinylcyclobutane: VCBCis1b 0.00 kcal/mol, Tscis1b 58.60 kcal/mol, Pcis1b -18.89 kcal/mol.

B. Non-catalyzed [6+2] cycloaddition in gas phase. The first attempts to achieve the product of the cycloaddition using vinylcyclobutanones were unsuccessful ⁽³⁾. Moreover, even the reaction using vinylcyclobutanones is forbidden or require forcing conditions, that's why the use of catalyst is essential in this case. **Figure 7** shows the reactants, transition states and products for the non-catalyzed [6+2] cycloaddition in gas phase using B3LYP/6-31G(d,p) in three different cases: 1) to obtain **Pcis1** product starting from **VCBcis1**; 2) to obtain **Pcis2** product starting from **VCBcis2**; 3) to obtain the analogue to **Pcis1** but with vinylcyclobutane. Relative energies are showed in text of the figure.

The comparison between them shows clearly why the attempts with vinylcyclobutane were impossible. The barrier decreases more than 13 kcal/mol changing the functional group of the reactant. But the most interesting is to check that in absence of catalyst products **Pcis1** and **Pcis2** would be almost equally probable to obtain attendint to their similar activation energies; that means, the rhodium catalyst not only transforms a one-step reaction in a multiple-step reaction with lower barriers, but also in a completely selective process for sterical reasons.

Conclusions. The study about the [6+2] rhodium-catalyzed cycloaddition of 2-vinylcyclobutanone and alkene point to a reaction mechanism in which the rhodium catalyst interacts first with the π - system, forming then a metallacyclopentene intermediate. This five-member ring reacts to get a nine-member metallacycle. The eight-member ring of the final product is obtained by elimination of the rhodium catalyst. The reaction mechanism in which the rhodium catalyst interacts first with the vinylcyclobutanone is ruled out for experimental and theoretical results. Calculations show why in this reaction *cis1*-product is formed exclusively. Comparison of the catalyzed and non-catalyzed cycloaddition shows how a forbbiden pericyclic cycloaddition is transformed into a viable formal cycloaddition by using a transition-metal catalyst.

Bibliography.

- 1) (a) I. Ojima, M. Tzamarioudaki, Z. Li, R.J. Donovan. *Chem. Rev.* **1996**, *96*, 635-662.
(b) M. Lautens, W. Klute, W. Tam. *Chem. Rev.* **1996**, *96*, 49-92.
- 2) See for example (a) P.A. Wender, N.M. Deschamps, R. Sun. *Angew. Chem. Int.Ed.* **2006**, *45*, 3957-3960 and references inside. (b) P.A. Wender, G.G. Gamber, R.D. Hubbard, L. Zhang. *J. Am. Chem. Soc.* **2002**, *124*, 2876.
- 3) P.A. Wender, A.G. Correa, Y. Sato, R. Sun. *J. Am. Chem. Soc.* **2000**, *122*, 7815-7816.
- 4) a) P.A. Wender, H. Takahashi, B. Witulski. *J. Am. Chem. Soc.* **1995**, *117*, 4720-4721. b) Z. Yu, P.A. Wender, K.N. Houk. *J. Am. Chem. Soc.* **2004**, *126*, 9154-9155. c) P.A. Wender, C.O. Husfeld, E. Langkopf, J. A. Love. *J. Am. Chem. Soc.* **1998**, *120*, 1940-1941. d) P.A. Wender, C.O. Husfeld, E. Langkopf, J.A. Love. *J. Am. Chem. Soc.* **1998**, *120*, 10976-10977.
- 5) C. Lee, W. Yang, R. J. Parr. *Phys. Rev. B* **1988**, *37*, 785. b) A.D. Becke, *J. Chem. Phys.* **1993**, *98*, 5648.
- 6) P. J. Hay, W. R. Wadt. *Chem. Phys.* **1985**, *82*, 299.
- 7) (a) K. Fukui. *Acc. Chem. Res.* **1981**, *14*, 363. (b) C. González, H.B. Schlegel. *J. Phys. Chem.* **1989**, *90*, 2154. (c) C. González, H.B. Schlegel. *J. Phys. Chem.* **1990**, *94*, 5223.
- 8) Gaussian 03, Revision C.01, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery, Jr., T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev,

A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez, and J. A. Pople, Gaussian, Inc., Wallingford CT, 2004.

9) See “The metallacycle pathway”, page 815 in C. Aubert, O. Buisine, M. Malacria. *Chem. Rev.* **2002**, *102*, 813-834.

10) M. R. Wilson, A. Prock, W. P. Giering. *Organometallics* **2002**, *21*, 2758.

11) “The Organometallic Chemistry of the Transition Metals”, chapter 2, Robert H. Crabtree, forth edition, ed. Wiley.