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Selectivity of the Ru(II)-Catalyzed [2+2+2] Cycloaddition of 1,6-Diynes and Tricarbonyl Compounds

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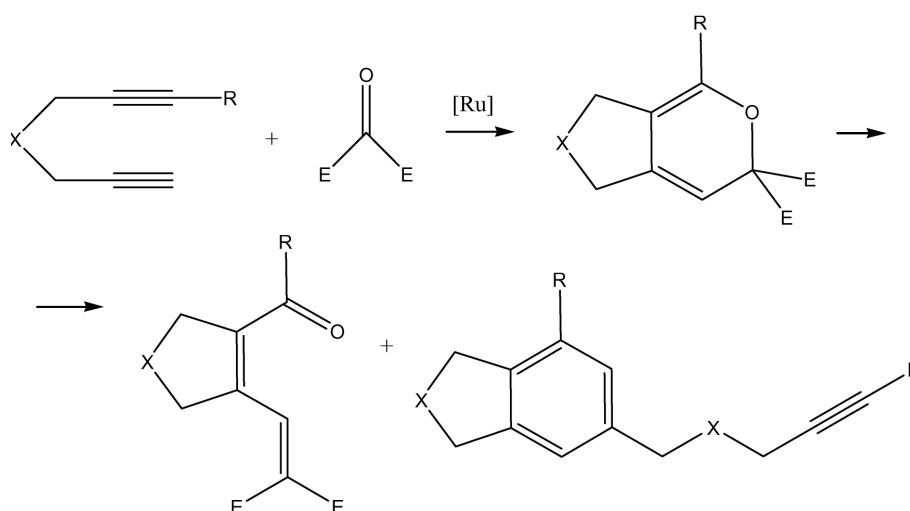
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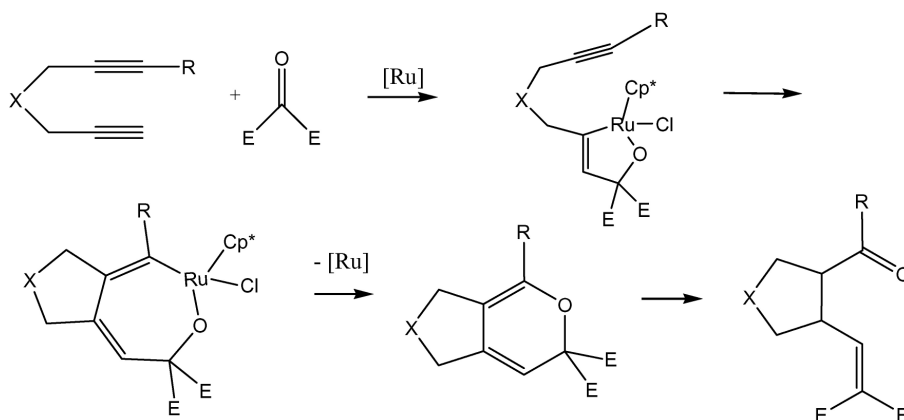
Density Functional Theory (DFT) has extensively been employed to study a large number of transition metal-catalyzed reactions during the last years. Several rhodium and ruthenium-catalyzed cycloaddition mechanisms have been studied in our group, being the Ru(II)-catalyzed [2+2+2] cycloaddition one of them.^{1,2} This cycloaddition was first reported by Yamamoto and co-workers which proposed a reasonable sketch of the mechanism (see Scheme 1).³



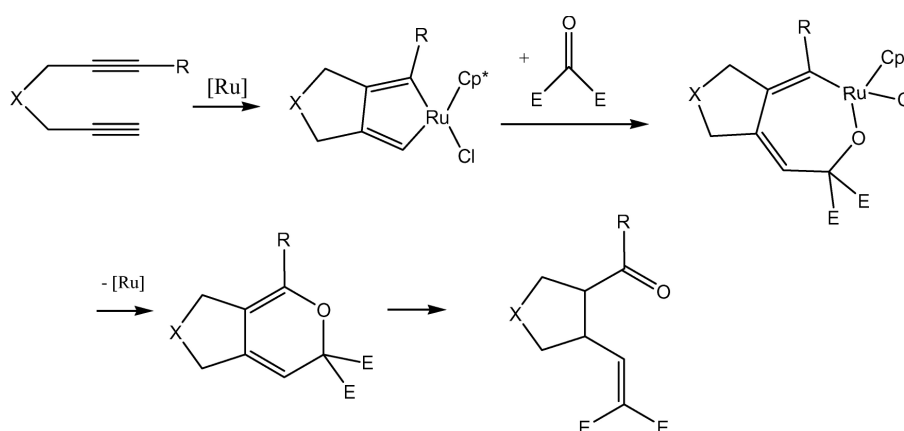
Scheme 1. The experimental Ru(II)-catalyzed [2+2+2] cycloaddition of 1,6-diynes and tricarbonyl compounds. The main product is the dienone, but it is also produced the 1,6-diyne dimer.³

A complete theoretical study of Yamamoto's mechanistical proposal and another alternative mechanism for the same reaction was previously carried out.² These two mechanisms are summarized in Scheme 2. It was found that the second mechanism (labeled “b”) has lower energy barriers (B3LYP/6-31G(d)+LANL2DZ level, at 90°C); the catalytic cycle begins with an oxidative coupling followed by the insertion of the central carbonyl group, being the last steps a reductive elimination and a electrocyclic ring opening.

(a)



(b)

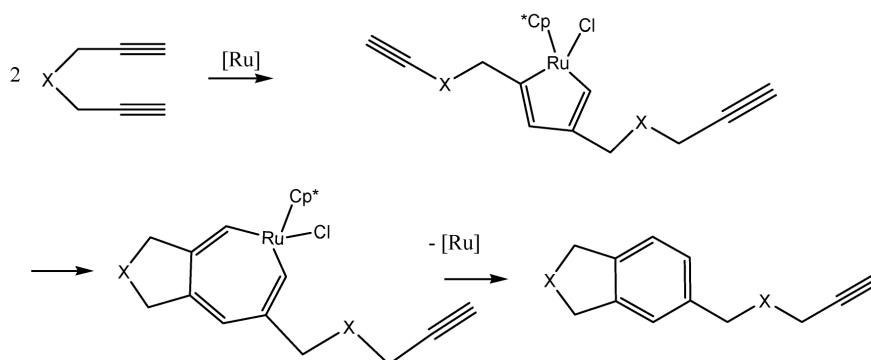


Scheme 2. Mechanisms to explain the cycloaddition: (a) Yamamoto's proposal; (b) an alternative mechanism. The (b) pathway is more favourable.²

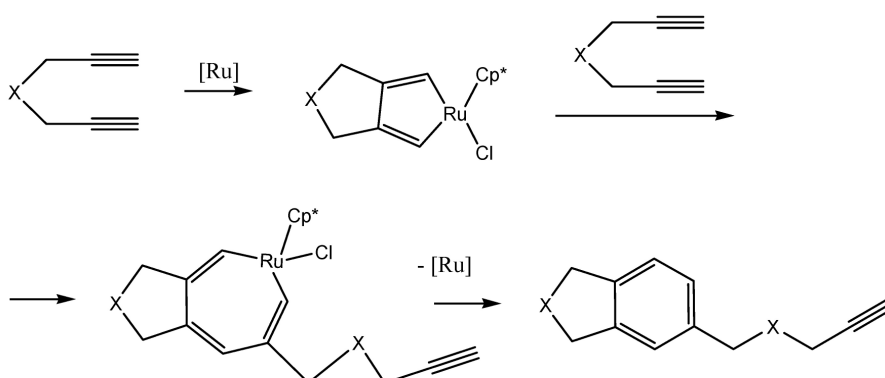
An important feature of this [2+2+2] cycloaddition is its selectivity. In this work two different possible mechanisms have been studied in order to explain the formation of the secondary product of the reaction. The comparison between the main and the minority pathways will be useful to study how selective the cycloaddition is. As it is said in the paper by the own authors,² changes in the diene's X group or the use of unsymmetrical diynes could be decisive to discriminating the competitive processes.

Scheme 3 describes two different pathways to obtain the secondary product of the reaction. This product is due to the dimerization of the 1,6-diyne reactant. In order to explore the dimerization mechanism, the corresponding calculations were carried out with DFT employing B3LYP functional. 6-31G(d) Pople's basis set was used for C, O, H and Cl atoms and the effective core potential LANL2DZ was used for Ru atom. All the stationary points were characterized as minima or transition states by the vibrational frequency analysis.⁴

(a)



(b)



Scheme 3. Two different pathways for the dimerization mechanism, which origin the secondary product of the [2+2+2] cycloaddition. The main pathway and also this dimerization pathway have been modeled choosing $X=O$, $R=H$ and $E=COH$ in Scheme 1.²

The dimerization reaction is also a [2+2+2] Ru(II)-catalyzed cycloaddition. The main difference between the two proposed pathways is the way in which the coupling takes place: in the first one, the ruthenium catalyst forms a complex with two molecules of 1,6-diyne; in the second one, an oxidative coupling between the two alkynes of one molecule reactant is followed by the insertion of a second 1,6-diyne molecule. In the two cases the last steps involves a reductive elimination of the catalytic species. The obtained structures for the first pathway are shown are in Figure 1. The first step, **II-TS2-I3**, is the oxidative coupling. **II** is characterized by the parallel disposition of the two alkyne groups (each one from different molecules), which are complexed with the ruthenium atom because of the trend of olefines of forming strong bonds with transition metals by back-donation. The geometry of the formed complex is

tetrahedral. The coupling takes place in **TS2**, where two of the carbons are being brought closer. The resulting **I3** has a conformer, **I4**, in which the atom arrangement is more favourable for the following alkyne insertion (**TS5**), being **I6** the structure previous to the last step (**I7-TS8-I9**). This reductive elimination has a three-center transition state (**TS8**), where the two carbons of the main ring are being got closer and the transition metal is being moved away. Note that the **I9** structure is just the dimerization product plus the catalyst, which will react again to starting the catalytic cycle one more time.

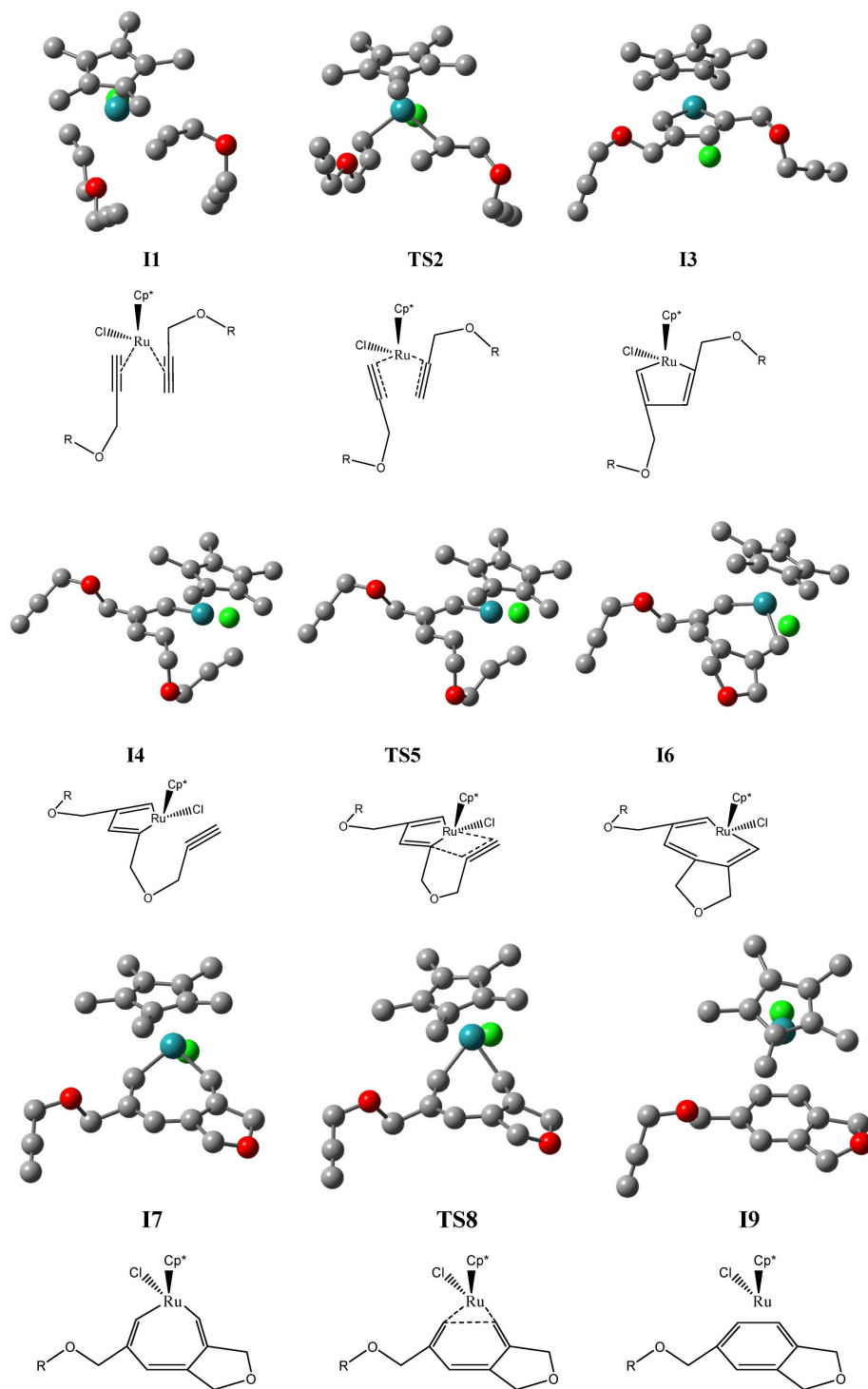


Figure 1. Structures related to dimerization mechanism (a).

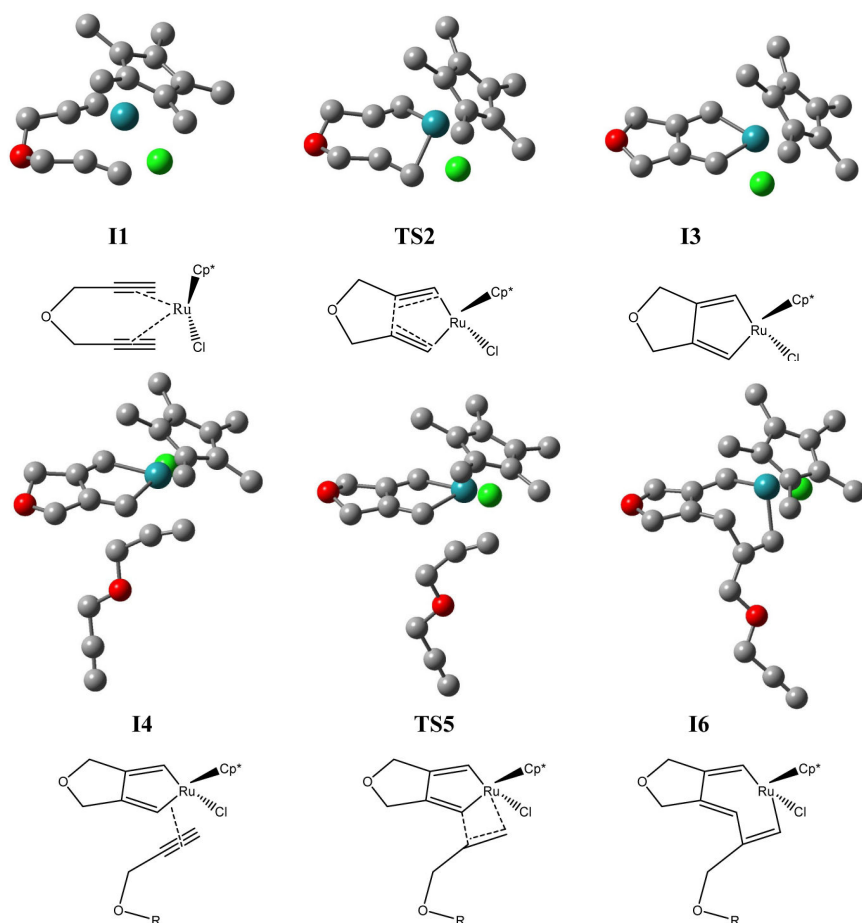


Figure 2. Dimerization mechanism (b). The remaining structures (**I7-TS8-I9**) are the same as in the mechanism (a).

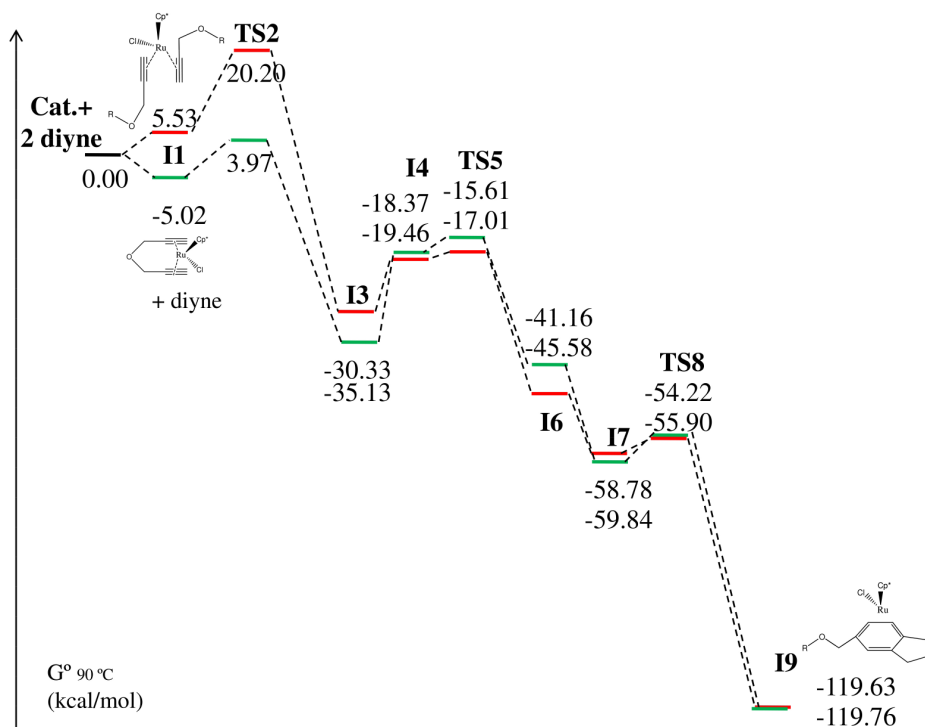


Figure 3. Comparison between dimerization mechanisms (a) and (b): Free energy profile ($T = 90\text{ }^\circ\text{C}$) at B3LYP/6-31G(d) +LANL2DZ level (Cat.= catalyst).

Figure 2 shows the second option: one molecule of 1,6-diyne forms a ruthenacycle (I1-TS2-I3) and then an alkyne of a second molecule is added to this ruthenacycle (I4-TS5-I6); the remaining part of the mechanism is the same as in the first option, the reductive elimination. The two pathways can be compared looking at Figure 3, which summarize the corresponding free energy profile at 90°C. The key step is clearly the first one since the coupling is easier between two triple bonds of the same molecule than from different molecules. So the dimerization pathway (b) will be preferred to the (a) one. It is also interesting noting that the reductive elimination is especially favoured in this catalytic cycle, with a very low energy barrier. The insertion of the third alkyne unity (I3-I4) is also a crucial step in both cases.

Conclusions. After a comprehensive study of the possible pathways to understand the mechanism of the Ru(II)-catalyzed [2+2+2] cycloaddition, the selectivity of the reaction has also been studied. The secondary product of the reaction is obtained via a dimerization of one of the reactants (1,6-diyne) in three steps: an oxidative coupling, an alkyne insertion and the reductive elimination of the catalyst. Although the information about those mechanisms is complementary to the main pathway, they have their own interest because they also are good examples of [2+2+2] transition-metal catalyzed cycloadditions and it could help to understand those reactions in which similar unsaturated reactants are involved. The pathway in which the first monomer forms a bicyclic structure followed by the insertion of the second monomer was founded most favourable than the other option, the simultaneous addition of the monomers.

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