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# Mechanistic aspects of C–C bond formation involving allylpalladium complexes: the role of computational studies

**Diego J. Cárdenas*** and **Antonio M. Echavarren***

*Departamento de Química Orgánica, Universidad Autónoma de Madrid, Cantoblanco, 28049, Madrid, Spain. E-mail: diego.cardenas@uam.es, anton.echavarren@uam.es;*
*Fax: +34 91 4973966; Tel: +34 91 4974358*

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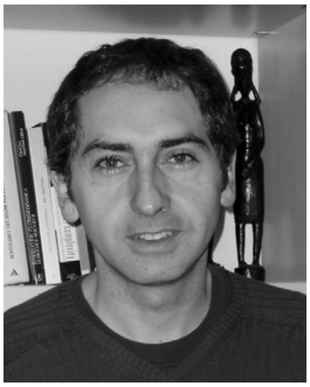
Computational studies have proven to be a useful tool for the study of mechanistic aspects of reactions involving allylpalladium complexes as intermediates. Previous work on the mechanisms of reactions involving such intermediates is discussed, as well as our contributions in this field. Thus, we report on the study of the mechanism of the insertion of alkenes into allylpalladium intermediates involved in the Oppolzer carbocyclization, the possible reaction pathways for the allylstannylation of alkynes, and the carbon-carbon reductive elimination from bis(allyl)palladium complexes. Structures for elusive intermediates, transition states, and even a novel mechanism for the reductive elimination in allyl-allyl cross-coupling reactions have been proposed.

## Introduction

Palladium is probably the most useful metal in organic synthesis. Many different complexes and salts may act as catalysts or pre-catalysts for a wide variety of transformations.[1–3] Reactions involving the formation of C–C bonds are, of course, of main interest. Allyl complexes are key intermediates in many of these reactions and have a major role in processes catalyzed by palladium. Advances in the understanding of the reaction mechanisms have been made by both experimental and computational means. Theoretical calculations allow the observed regio- and stereoselectivities to be rationalized and the structure of reaction intermediates and transition states to be determined. In the reactions that involve allylic electrophiles, $\eta^3$-allylpalladium complexes are the actual intermediates involved in catalytic cycles, although, depending on the ligands, they may be in equilibrium with $\eta^1$-allyl species.[4] These intermediates are usually formed by oxidative



**Diego J. Cárdenas**

*Diego J. Cárdenas was born in Jaén (Spain), in 1967. He graduated in Chemistry at the Universidad de Granada in 1990, and received his PhD in Organic Chemistry at the Universidad Autónoma de Madrid (UAM) in 1994, under the supervision of Prof. Antonio M. Echavarren. After a postdoctoral stay (1995–96) at the Université Louis Pasteur (Strasbourg, France) with Prof. Jean-Pierre Sauvage, he joined the Department of Organic Chemistry of the UAM as an Assistant Professor, and became Professor Titular in 2001. He is interested in the development of new synthetic methods based on the organometallic chemistry of transition metals, and on the experimental and computational study of metal-catalyzed reactions mechanisms.*

**Antonio M. Echavarren**

*Antonio M. Echavarren, born in 1955 in Bilbao, obtained his PhD in 1982 with Prof. Francisco Fariña (Universidad Autónoma de Madrid, UAM). After a postdoctoral stay at Boston College with Prof. T. Ross Kelly (1982–84), he joined the UAM as an Assistant Professor (1984–86). Following a two years period as a NATO-fellow at Colorado State University with Prof. John K. Stille (1986–88), he joined the Institute of Organic Chemistry (CSIC) in Madrid. In 1992 he returned to the UAM as a Professor of Organic Chemistry. In 2004, Antonio M. Echavarren will move to the Institute of Chemical Research of Catalonia (Tarragona, Spain) as a Senior Group Leader. His research focuses on the development of synthetic methods and the organometallic chemistry of the late transition metals, with projects including the synthesis of natural and non-natural products.*

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addition of allyl halides, esters or carbonates to Pd(0) precursors. They may also be generated by transmetallation from Grignard reagents, allylic deprotonation of coordinated olefins or by reaction of nucleophiles on Pd-coordinated dienes.[2,3] Allylsilanes have been recently used in palladium-catalyzed cyclizations in which the formation of the allylpalladium complex takes place by electrophilic displacement of the silyl group.[5] Allyl ligands usually show electrophilic character when being bound to Pd and may react in different ways to give C–C bonds. Thus, they may be intermolecularly attacked by external nucleophiles; undergo 1,2-insertion of alkenes or alkynes, and 1,1-insertion of CO.[3] Transmetallation of the allyl ligands from Pd to Zn gives nucleophilic allylzinc species, which results in the *umpolung* of the reactivity of the starting allyl electrophiles.[6] When a second carbon ligand is present in the coordination sphere, a C–C reductive elimination may take place, thus affording reduced species that can enter the catalytic cycle.[1,3]

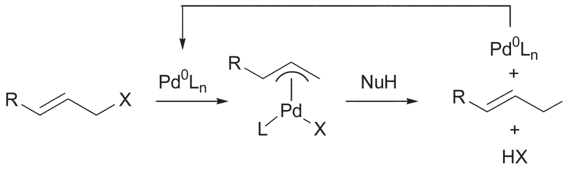
On the other hand, bis(allyl)palladium complexes show nucleophilic behaviour, and are able to react first with electrophiles. The resulting monoallyl derivatives can further react with nucleophiles, which make bis(allyl) complexes highly valuable for synthetic purposes. Reductive elimination from these intermediates to give C–C bonds is also possible. *Ab initio* and density functional theory (DFT) computational studies on reactions involving allylpalladium derivatives have provided useful information about the reaction mechanisms, especially in cases for which other types of studies are difficult. For example, the intramolecular character of many of these reactions preclude the acquisition of information by kinetic measurements. On the other hand, the actual structure of the elusive intermediates involved can be determined by calculations. Here we wish to review the role of theoretical calculations in the study of reactions involving the formation of carbon-carbon bonds with the intermediacy of allylpalladium complexes.

## C–C bond forming reactions involving allylpalladium complexes as intermediates

### External attack by carbon nucleophiles

Nucleophilic addition on (π-allyl)palladium complexes is a key process in several synthetically useful palladium-catalyzed reactions, such as allylic nucleophilic substitution, allylic acetoxylation and 1,4-oxidation of conjugated dienes. The most extensively used is the Tsuji–Trost reaction, which consists in the Pd catalyzed allylation of nucleophiles. In this case the allyl-Pd(II) intermediate is formed by oxidative addition of an allyl electrophile to a Pd(0) complex. Subsequent reaction of the electrophilic (π-allyl)palladium intermediate with soft carbon nucleophiles affords the allylation product and regenerates a Pd(0) species, thus allowing a catalytic process (Scheme 1).[7–9] Nitrogen, oxygen and sulfur nucleophiles also react with (π-allyl)palladium intermediates.[10]

The regiochemical outcome of the reaction for non-symmetric allyl moieties is governed by both steric and electronic factors, depending on the ancillary ligands on Pd. The reaction usually proceeds with retention of the configuration of the carbon atom bearing the leaving group, since both the oxidative addition and the nucleophilic attack take place with stereochemical inversion.[11] Hard carbon nucleophiles or organometallic compounds transmetallate with Pd and give C–C reductive elimination with retention, thus resulting in global inversion.[12] Nucleophiles prefer to react with the terminal carbons of the allyl moiety, although attack on the central carbon has also been reported (Scheme 2).[13,14]



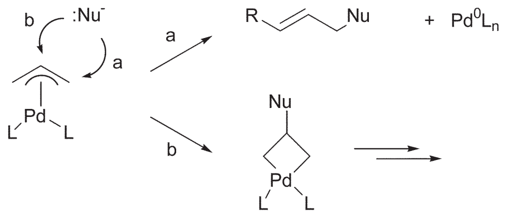
**Scheme 1** Mechanism of the Tsuji–Trost reaction

Central attack takes place when strong σ-donor ligands are present in the coordination sphere. Theoretical studies provide an explanation for this behaviour. In complexes containing strong σ-donor ligands, the allyl carbons participate in the LUMO through a symmetric combination in which the highest participation corresponds to the central atom. Thus, the functionalization is frontier orbital controlled. When π-acceptor ligands are present, an inversion of the energies of the lowest empty orbitals takes place and the LUMO now shows a higher participation of the terminal carbons. Besides, back-bonding from the metal to the π-acid ligands decreases the electron density on the allyl moiety, especially on the terminal carbons. Therefore, a charge control reinforces the orbital control in this case, both factors favouring the usually observed terminal attack.[13,15]

Regioselectivity has also been studied computationally for the non-equivalent reactions of carbons α and γ in the case of asymmetrical allyl derivatives.[16–18] In the case of allyl ligands substituted by alkyl or aryl groups, nucleophiles usually attack the less hindered carbon. Nevertheless, the situation is more complicated and electronic factors, depending on the ligands and the nucleophile, also play an important role. In general, acceptor ligands and non-stabilized nucleophiles favour attack at the most substituted carbon. When the substituents on the allyl show strong electron donor or acceptor properties, α- and γ-attack, respectively, are preferentially observed. Recent calculations on model systems using $NH_3$ as a nucleophile are in agreement with the experimental results. Silanes directly attached to terminal allyl carbons direct the attack to the γ-position (Scheme 3).[17,18]

The inclusion of solvent effects in the calculations leads to better agreement with the experimental evidence.[16] Moreover, introduction of solvent is necessary in order to locate transition states in the additions of cyanide and fluoride to $(\eta^3\text{-allyl})Pd(NH_3)_2$.[19] On the other hand, the regioselectivity of the intramolecular allylation of ketone and amide stabilized carbanions depends on the atoms of the tether, which influence the flexibility of the chain. DFT calculations are in agreement with the experimentally observed mixture of five- and seven-membered ring products.[20]

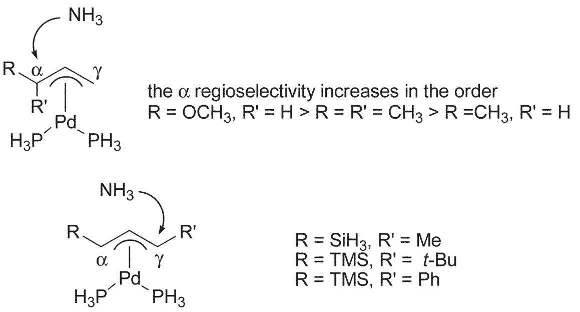
Simple models such as those shown above do not account for the influence of steric effects in these reactions. Since it may happen that steric and electronic effects favour the reaction at different allylic carbon atoms, the situation becomes more complicated and difficult to study. More realistic models that include larger ligands and different geometric isomers of



a: preferred pathway, (π-acceptor ligands, stabilized carbanions)

b: occurs when L is a strong σ-donor (TMEDA,bipy) and with less stabilized carbon nucleophiles

**Scheme 2** Terminal versus central nucleophilic attack on π-allyl-palladium complexes



**Scheme 3** Regioselectivity of the nucleophilic attack on model systems

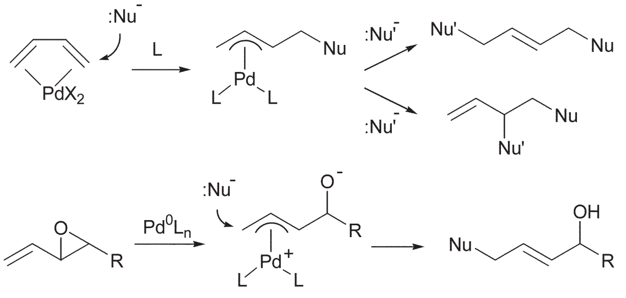
the allyl fragment must also be considered. Norrby *et al.* have developed a force field for ($\eta^3$-allyl)palladium complexes containing phosphorous and/or nitrogen ligands that may help to simplify problems regarding the stereochemistry of the reaction.[21] Recent DFT and HF calculations satisfactorily explain the stereoisomer distribution of allylpalladium complexes containing large bidentate P,N ligands.[22] On the other hand, the asymmetric induction observed in the alkylation of allylpalladium complexes containing such ligands has been modelled by a combination of DFT and molecular mechanics. The results show that the stereochemical outcome is not determined by electronic effects, but mainly by a delicate balance of steric repulsions.[23]

It has been shown that the presence of a substituent at the homoallylic position (β-position) has an important effect on both the reactivity and the stability of the allylpalladium intermediates.[24] These are important intermediates that can be generated by nucleophilic attack on coordinated dienes (in the first step of their oxidative functionalization) or by oxidative addition of diene epoxides to Pd(0) complexes (Scheme 4).

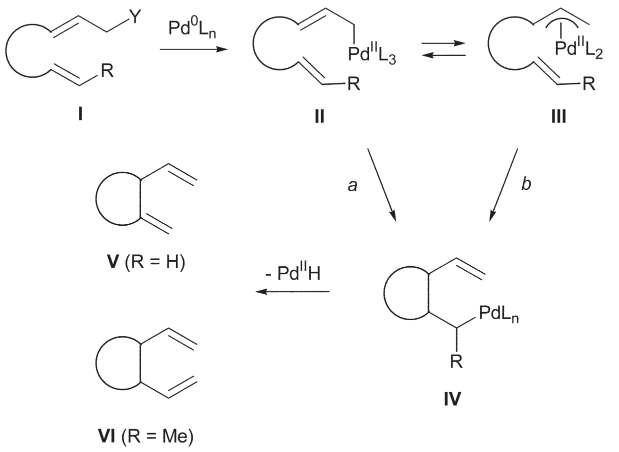
The presence of a substituent Y = OR, OCOR, $NR_2$, $NO_2$ in the homoallylic position has been calculated to stabilize the (π-allyl)palladium complexes by up to 8–10 kcal $mol^{-1}$. It also makes the complex more reactive towards nucleophiles and enhances the reactivity of the less substituted allyl terminus. The effect is stronger when the C–Y and Pd–C3 bonds are antiperiplanar and when at least one σ-donor or two moderately π-acceptor ligands are coordinated to Pd.[24]

### Insertion of alkenes into allylpalladium

The insertion of alkenes into π-allylpalladium is the key step in the carbocyclization of allyl electrophiles with alkenes (Oppolzer reaction), a powerful method for the construction of five- and six-membered carbo- and heterocycles.[25] This reaction was originally suggested to take place by a pericyclic-type pathway by analogy with the lithium and magnesium-ene reactions (Scheme 5, path *a*). Thus, the allyl electrophile **I** was proposed to react with a Pd(0) complex to form a σ-allylpalladium intermediate, which undergoes a palladium-ene reaction to give **IV**. A β-hydride elimination would afford either **V** or **VI**, depending on the group involved in the elimination of the hydrogen atom. Another possibility for the step involving the C–C bond formation is outlined in path *b* (Scheme 5), and involves the $\eta^3$-allylpalladium complex **III**. This might take place directly from the electrophile **I** or by associative displacement of two carbons of the allyl moiety by an external ligand. As a result of mechanistic work directed at the determination of the key intermediates of the Oppolzer reaction, we found experimental evidence suggesting that the cyclization proceeds through cationic ($\eta^3$-allyl)($\eta^2$-alkene)palladium(II) complexes.[26] Thus, complexes **2b** or **2c**, formed by oxidative addition of allylic trifluoroacetate **1** to a palladium(0) reactive intermediate, undergo the cyclization reaction to give dienes **3a** or **3b** (Scheme 6). Neutral complexes such as **2d** or **2e** fail to react. $PCy_3$ is also an adequate ligand for this transformation, whereas P(*o*-tol)$_3$, $AsPh_3$ or phosphites led to slower and/or less efficient cyclizations. Bidentate phosphines or phenanthroline give intermediates that are unproductive.

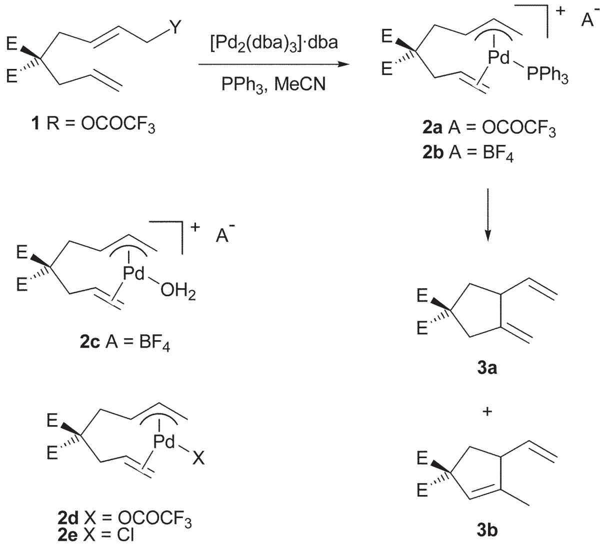


**Scheme 4** Allylpalladium intermediates containing a β-substituent



**Scheme 5** Proposed pathways for the Oppolzer reaction

Cationic ($\eta^3$-allyl)palladium complexes have been shown to be the actual intermediates in some other insertions of alkenes into ($\eta^3$-allyl)palladium species.[27] On the other hand, ($\eta^1$-allyl)palladium complexes have been proposed to be involved in the insertion of norbornene into ($\eta^3$-allyl)(hexafluoroacetylacetonate)palladium derivatives.[28] We studied computationally the key step of the Oppolzer reaction to determine if the insertion proceeds through $\eta^1$- or $\eta^3$-allylpalladium complexes and to get insight into the influence of the ligands on the insertion process.[29] Simplified systems were used and two possible

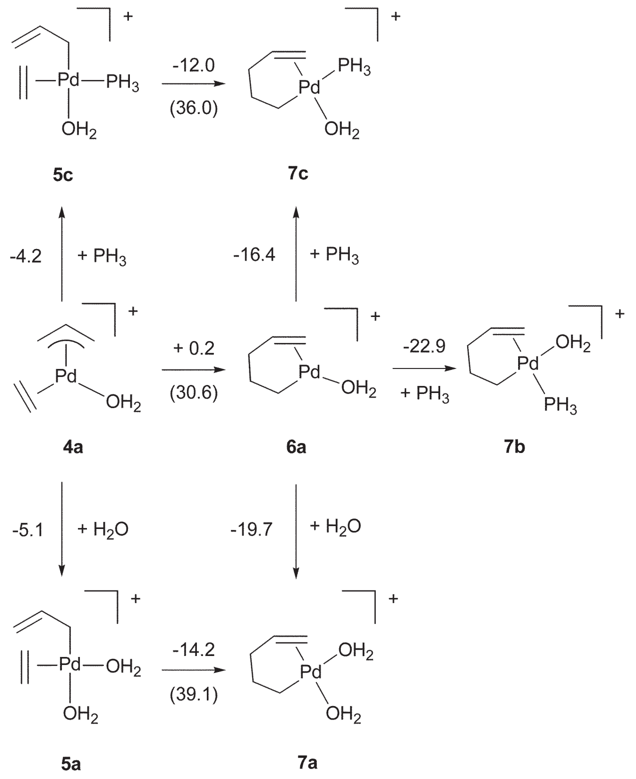


**Scheme 6**

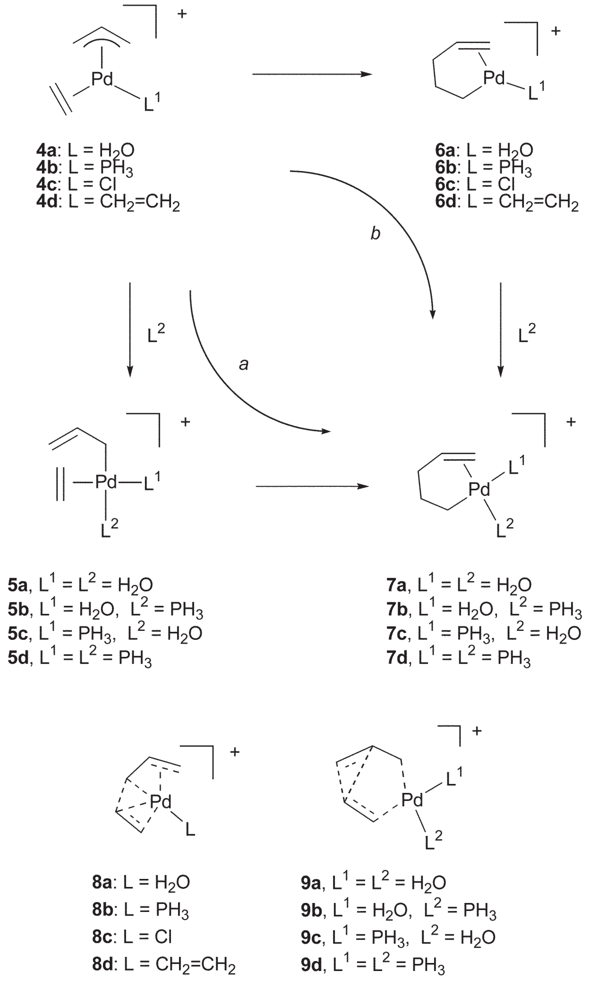
reaction mechanisms were modelled (Scheme 7, pathways *a* and *b*). Calculations were performed at the DFT level using the B3LYP hybrid functional.[30]

Complexes **5** result from reaction of the $\eta^3$-allyl species with an additional ligand. All possible combinations of $PH_3$ and $H_2O$ ligands were considered in **5a**–**d**, keeping the reacting carbon ligands in a cis arrangement. All complexes show the usual square planar coordination. The main structural difference occurs between **4a** and **4b**. In the former, the ethylene ligand lies perpendicular to the coordination plane, whereas in the latter, this ligand is coplanar, which makes this complex more similar to the transition state (**8b**) involved in this transformation. The reaction and activation energies for the processes starting from **4a** and **4b** are summarized in Schemes 8 and 9, respectively. In all cases, the direct insertion of ethylene into the ($\eta^3$-allyl)palladium bond through the transition state **8** shows a lower activation energy compared with the insertion in $\eta^1$-allyl intermediates and is approximately thermoneutral. Subsequent coordination of an additional ligand to the coordinatively unsaturated complexes **6** makes the global process significantly exothermic.

The slowest insertion in $\eta^1$-allyl intermediates is also exothermic. Interestingly, the transition states involved in these transformations (complexes **9a**–**d**) do not correspond to those expected for the previously proposed palladium-ene reaction.[25] In contrast, in the actual transition states the Pd atom approaches one of the ethylene carbons to give a Pd–C single bond, creating an electron deficiency on the other carbon that is stabilized by the allyl π-cloud (Fig. 1).



**Scheme 8** Calculated ZPE corrected activation energies (in parentheses) and reaction energies (in kcal $mol^{-1}$) at the B3LYP/6-31G(d)-LANL2DZ level

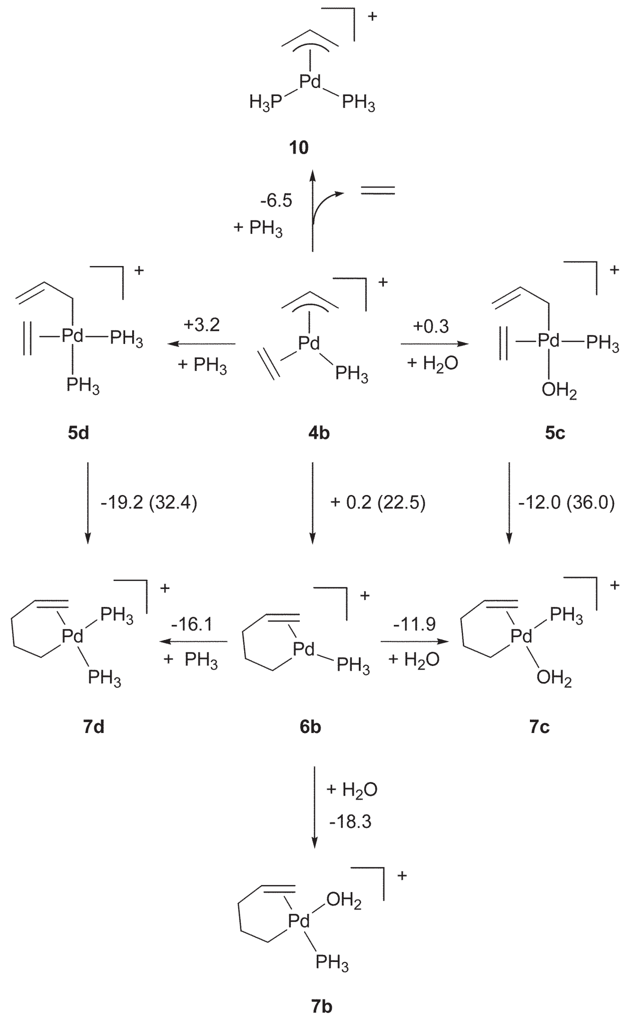


**Scheme 7**

The influence of the ligand on the activation barrier of the insertion was also studied and the energies of the reactions from $\eta^3$-allyl derivatives containing additional ethylene or chloride as ligands were also considered. Complexes **4a**–**d** follow the reactivity $PH_3$ > ethylene > Cl > $H_2O$ (Scheme 10). Analysis of the electron density in complexes **4a**–**d** and transition states **8a**–**d** led us to conclude that the reactivity is related to the differences in the electron richness of the metal in the starting complex. Thus, donor $PH_3$ increases back-bonding of Pd to the reacting ethylene, thus favouring a coplanar arrangement of this ligand with respect to the coordination plane and lowering the energy necessary to reach the transition state. In the case of the less donating water and chloride, back-bonding from the metal is not so important, which makes the ethylene ligand lie perpendicular to the coordination plane, further from the transition state geometry. The calculated energy for the formation of **10** (Scheme 9), which is exothermic and must proceed with a low barrier, also explains the lack of reactivity when bidentate phosphines are used. In that case, the bidentate ligands prevent coordination of the alkene moiety and the insertion reaction cannot take place. Interestingly, when the reaction was performed with 1,2-bis(diphenylphosphino)ethane under high dilution conditions, the insertion took place due to partial de-coordination of the phosphine.[26]

With regards to the stereoselectivity of C–C bond formation, the Oppolzer reaction is known to favour the formation of the more stable *trans*-dialkenyl five-membered cycles of type **VI** in most cases; this was proposed that be due to a cis-to-trans isomerization of derivatives of **VI** by a Pd(0) catalyzed Cope rearrangement (Scheme 11).[31] We prepared the cis compound **11**, which was recovered unchanged after having been exposed to typical conditions for the Oppolzer reaction. This result suggests that the configuration is settled in an irreversible insertion process. The previously observed apparent isomerization is probably a result of the selective decomposition of the cis product at long reaction times.

In conclusion, all the results exposed above led to a reformulation of the catalytic cycle for the Oppolzer reaction (Scheme 12), consisting in a reversible oxidative addition of the allyl



**Scheme 9** Calculated ZPE corrected activation energies (in parentheses) and reaction energies (in kcal mol$^{-1}$) at the B3LYP/6-31G(d)-LANL2DZ level

electrophile to a Pd(0) active complex to give intermediate **VII**, followed by coordination of the olefin and subsequent formation of a more reactive cationic complex **IX**, in which the insertion reaction takes place. After β-elimination of hydrogen and de-coordination, the final products **V** and **VI** are obtained.

## Reactions involving (alkyne)(allyl)palladium complexes

Few examples of reactions involving insertion of alkynes into π-allylpalladium bonds have been reported. The first known example was the intermolecular cloroallylation of alkynes catalyzed by Pd(MeCN)$_2$Cl$_2$.[32] A dimerization-allylation reaction of terminal alkynes[33] and several intramolecular reactions with concomitant carbonylation were also reported.[34] More recently, the insertion of alkynes into (η$^3$-allyl)palladium species has

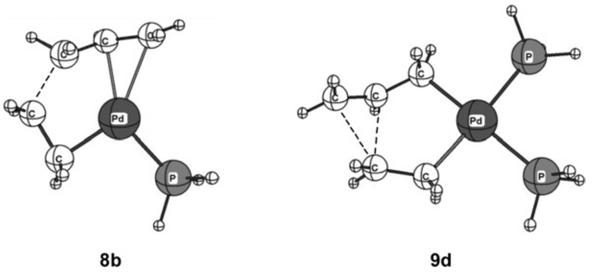
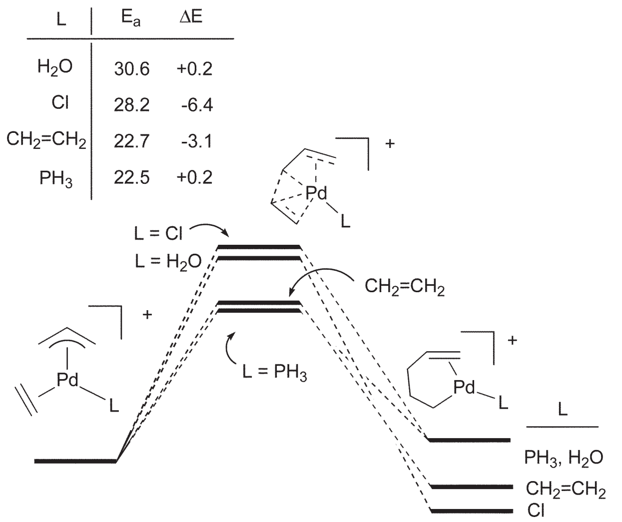
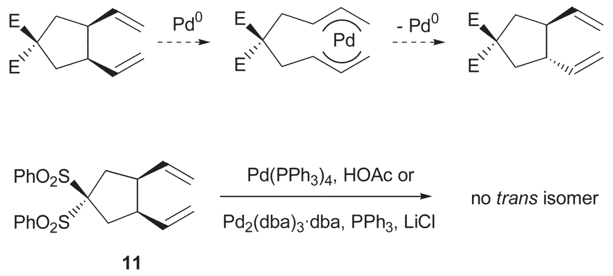


**Fig. 1** Calculated structures of **8b** and **9d** (DFT, B3LYP/6-31G(d)-LANL2DZ).

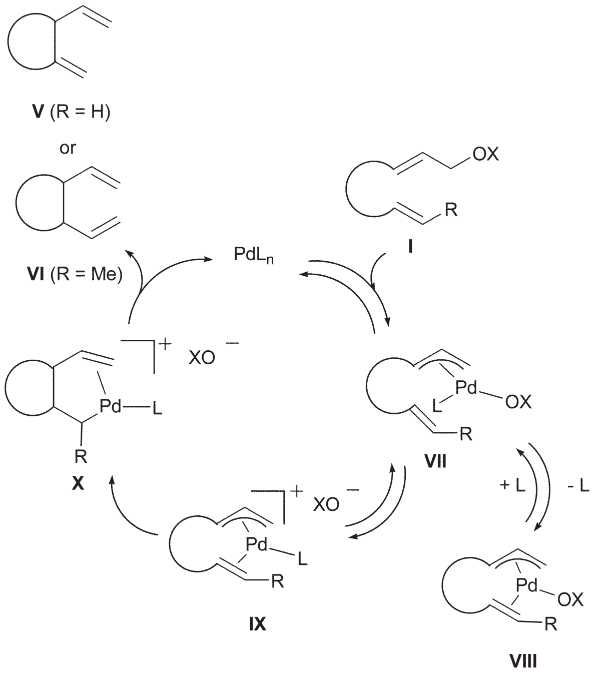


| L | E$_a$ | ΔE |
|---|---|---|
| $H_2O$ | 30.6 | +0.2 |
| Cl | 28.2 | -6.4 |
| $CH_2{=}CH_2$ | 22.7 | -3.1 |
| $PH_3$ | 22.5 | +0.2 |

**Scheme 10** Energy profiles for the insertion reaction of (η$^3$-allyl)-palladium complexes (E + ZPE in kcal mol$^{-1}$)



**Scheme 11** The Pd catalyzed Cope rearrangement does not take place, since **11** does not isomerize to the trans derivative

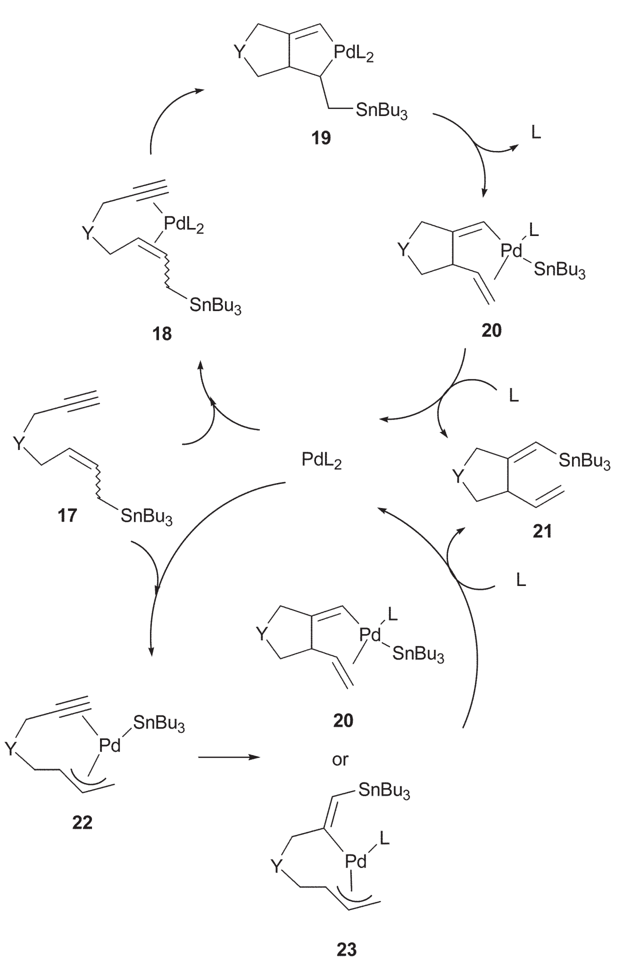


**Scheme 12** Complete catalytic cycle for the Oppolzer reaction

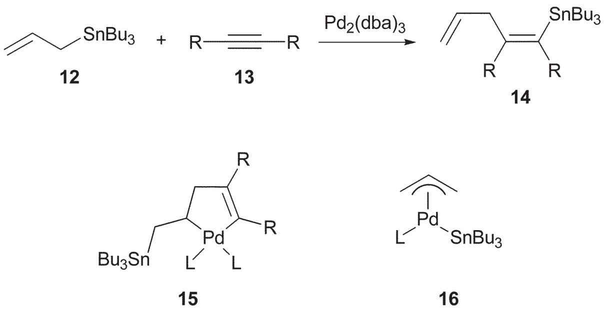
been proposed in the mechanism of a novel benzannulation from allyl tosylates and alkynes.[35] On the other hand, Shirakawa *et al.* have found that the Pd(0) catalyzed reaction of allylstannanes (**12**) with alkynes (**13**) affords allylstannylation products (**14**; Scheme 13).[36] This transformation is also catalyzed by Ni(COD)$_2$.[37] It was proposed that the palladium-catalyzed allylstannylation of alkynes could proceed by oxidative cyclometallation on an alkene-alkyne palladium complex to form a palladacyclopentene **15**, which would undergo β-tin elimination, followed by reductive elimination. An alternative mechanism would involve oxidative addition of the allyltin reagent to a Pd(0) complex to give a (η$^3$-allyl)palladium intermediate (**16**). The alkyne could also be bound to the Pd(0) complex or become ligated after the oxidative addition.

In order to get insight into the mechanism of this process, we studied the intramolecular reaction of several allylstannanes containing an alkyne catalyzed by Pd(II) and Pd(0) (Scheme 14).[38] Pd(II) pre-catalysts are reduced to Pd(0) by the stannane. Since the final stannanes suffered partial protodestannylation under chromatographic purification conditions, usually the products were treated with iodine and the corresponding alkenyl iodides were isolated with retention of the configuration at the exocyclic double bond. The reactions are stereoselective and afford carbocycles **XII**, which show an *E* configuration at the alkene. These results are consistent with a Pd(0) catalyzed reaction following the possible pathways proposed by Shirakawa *et al.* (Scheme 15). In the upper cycle, oxidative cyclometallation leads to **19**. Then, β-tin elimination and C–Sn reductive elimination from **20** would give product **21**. Alternatively, oxidative addition of **17** would afford complex **22**.

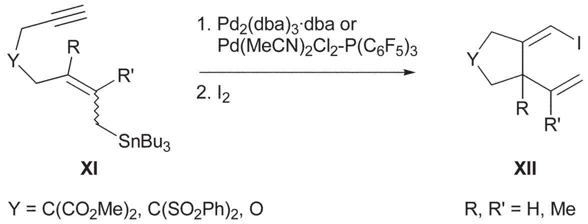
Besides the proposed insertion of the alkyne into the Pd–Sn bond to give **23**, we also considered the possibility of evolution of **22** by insertion of the alkyne into the allyl–Pd bonds to form **20**. C–C or C–Sn reductive elimination in each case, respectively, would lead to **21**. Interestingly, substrate **24** gave exclusively the six-membered carbocycle **25** with the opposite alkene configuration (Scheme 16). The possible intermediates that could be formed by reaction of **24** with a Pd(0) active catalyst (**26** or **27**) cannot evolve by the pathways outlined in Scheme 15, since neither β-tin elimination nor insertion of the alkyne (due to geometrical constraints) can occur. For this reaction we propose the Pd(II) catalyzed process outlined in Scheme 16, in which the formation of the C–C bond occurs by nucleophilic anti attack of the stannane on the (η$^2$-alkyne)palladium(II) complex, as shown in **28**, to give intermediate **29**. Cleavage of the Pd–C bond by electrophilic Bu$_3$SnCl affords the final product.



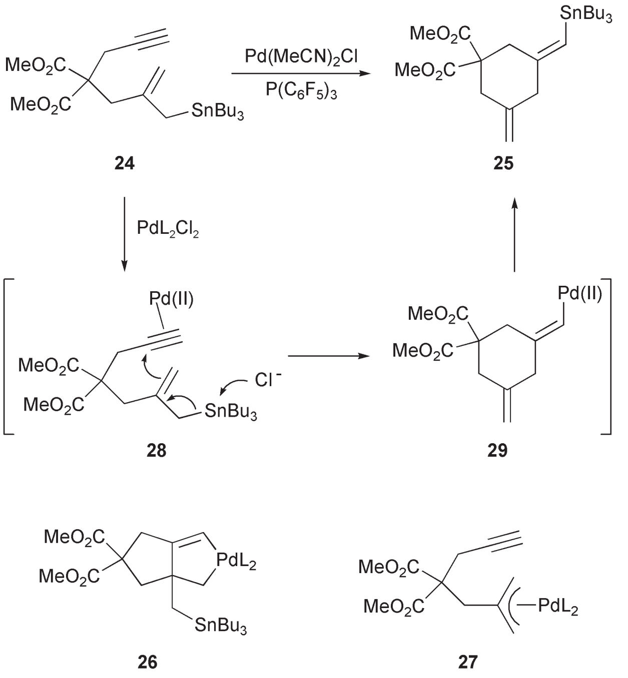
**Scheme 15**



**Scheme 13**



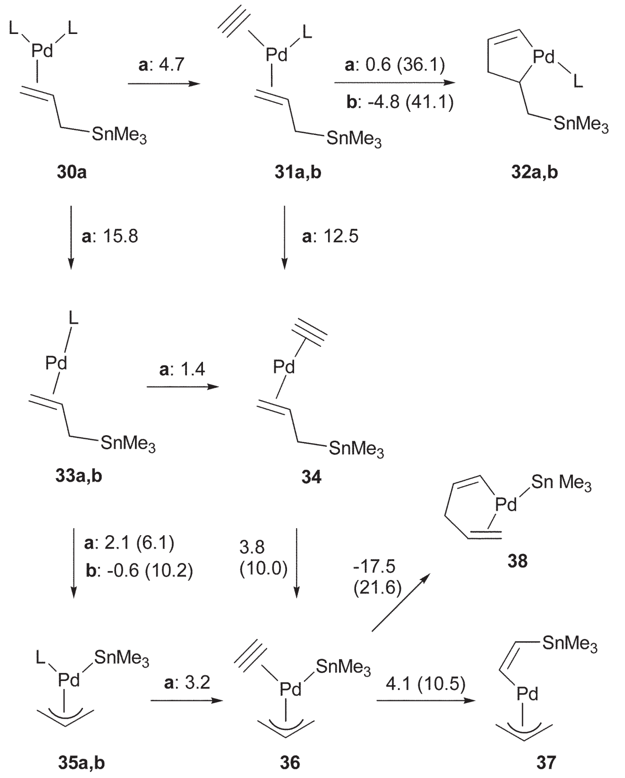
**Scheme 14**



**Scheme 16**

We determined the actual reaction pathway of those reactions shown in Scheme 15 by performing calculations at the DFT level on model substrates to compare the activation and reaction energies of the possible routes. Maleic anhydride and $PH_3$ were used as models of the ancillary ligands. We found that activation energies are significantly lower for the oxidative addition of the allyl–Sn bond compared with the alternative oxidative cyclometallation (Scheme 17). The fastest reaction corresponds to the oxidative addition from **33a** to **35a** ($E_a = 6.1$ kcal mol$^{-1}$), which is even lower than that corresponding to the $PH_3$ and acetylene derivatives ($E_a$ *ca.* 10 kcal mol$^{-1}$). These processes are slightly endothermic or practically thermoneutral. The oxidative cyclometallation would proceed with a much higher barrier (36–41 kcal mol$^{-1}$).

The structures of the transition states corresponding to the C–Sn oxidative addition from **34** (**TS$_{34–36}$**) and one for the oxidative cyclometallation (**TS$_{31a\text{-}32a}$**) are shown in Fig. 2. Concerning the subsequent insertion reactions, the energies of these processes were also calculated (Scheme 18). Insertion of the alkyne into the Pd–Sn bond is much more kinetically favoured compared with the insertion into the allyl–Pd bonds. *Albeit* its endothermic character, it would be the preferred pathway since the subsequent step (C–C reductive elimination) is strongly favoured. These results support a mechanism for the allylstannylation of alkynes consisting in Sn–C oxidative addition of the allylstannane to a Pd(0) precursor affording a ($\eta^3$-allyl)palladium complex. In the lowest energy pathway, the alkyne ligand would coordinate after the oxidative addition, then inserting into the Pd–Sn bond. Reductive elimination of the final product would re-generate the Pd(0) active catalyst. In conclusion, the reactivity of allylstannanes can be inverted by changing the oxidation state of the catalyst from Pd(II) to Pd(0), which has significant synthetic potential.



**Scheme 17** Calculated ZPE corrected activation energies (in parentheses) and reaction energies (in kcal mol$^{-1}$) at the B3LYP/6-31G(d)-LANL2DZ level

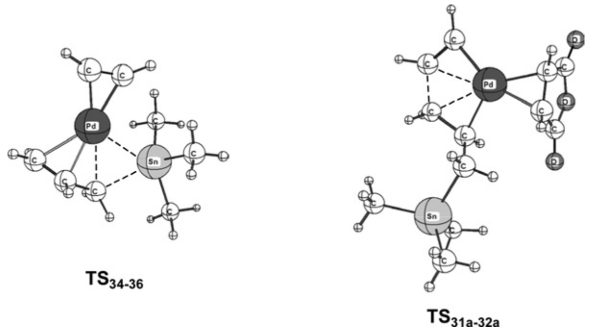
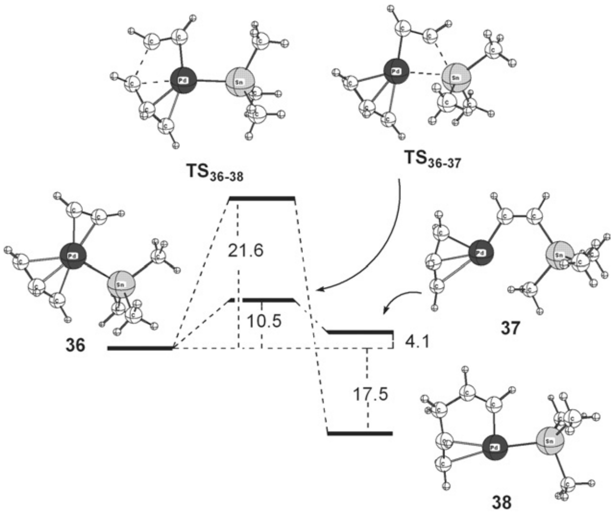


**Fig. 2** Calculated structures for the transition states at the B3LYP/6-31G(d)-LANL2DZ level

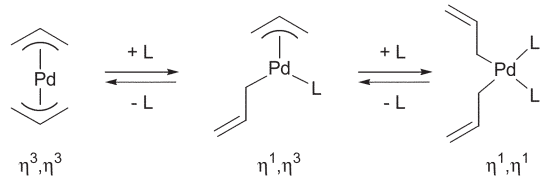


**Scheme 18** Possible insertion pathways from intermediate **36**. Calculated ZPE corrected activation energies and reaction energies are given in kcal mol$^{-1}$ at the B3LYP/6-31G(d)-LANL2DZ level

## Reactions involving bis(allyl)palladium complexes

Bis(allyl)palladium complexes are intermediates in some synthetically useful transformations. For example, the Stille coupling of allylstannanes with allyl carboxylates[39,40] or bromides[41,42] is used to synthesize 1,5-dienes. The clean allylic inversion observed in the allylstannane led to the proposal that this reaction might proceed by an external attack of the tin reagent on the intermediate ($\eta^3$-allyl)palladium complex, such as occurs for the reactions of this type of complex with soft nucleophiles.[2] Allylic inversion has also been demonstrated in the coupling with allylsilanes.[43] A different reaction pathway involving bis($\eta^3$-allyl)palladium complexes has been proposed in the coupling reactions of allylic species in the absence of phosphine ligands.[44] Bis($\eta^3$-allyl)palladium species have been shown to be intermediates in the allylation of aldehydes[45,46] and in the bis(allylation) of Michael acceptors[47,48] and isocyanates.[49] These reactants display amphiphilic allylating character, since they can also act as nucleophiles in the reaction with aldehydes and some other electrophiles to give mono allyl species capable of reacting with nucleophiles, as it has been shown above. Both coordination modes for the allyl ligand are possible in bis(allyl)palladium complexes, which results in the formation of several species in equilibrium (Scheme 19).

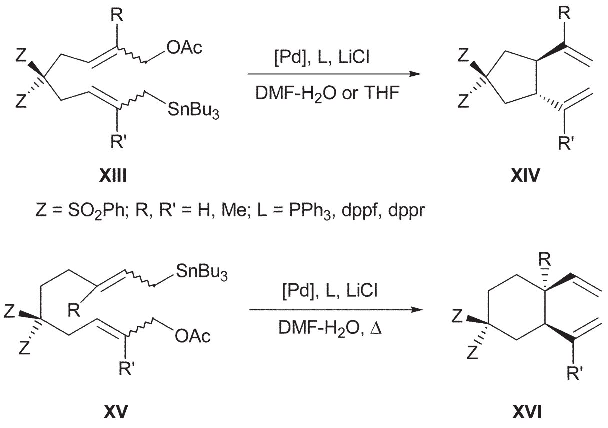
Theoretical studies at the DFT level have shown that the lowest energy pathways for the reactions involving bis(allyl)palladium intermediates with aldehydes and isocyanates involve ($\eta^1$,$\eta^3$) species. The formation of these complexes is favoured by hyperconjugative $d_\sigma$-$\pi^*$ type interactions of the free C–C double bond of the $\eta^1$-allyl ligand with the metal atom, which is also responsible for the high regioselectivity observed in the reactions with electrophiles.[46,48] We studied



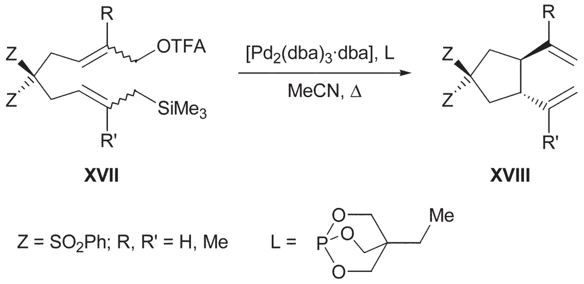
Scheme 19

the Pd catalyzed intramolecular reaction of allylstannanes with allyl acetates, as well as the analogous process of substrates containing both an allylsilane and an allyl trifluoroacetate within the same molecule. Substituted substrates can also be employed.[50] This intramolecular Stille coupling is stereoselective, regardless of the configuration of the double bonds in the starting compounds. Depending on the chain length, five- or six-membered carbocycles can be formed. The reaction leading to five-membered ring products (**XIV**) is trans stereoselective and, except for the simplest substrate[51] (Scheme 20), the trans-fused compound is the exclusive product. On the other hand, six-membered rings show cis configuration, except when using 1,1′-bis(diphenylphosphino)ferrocene or 1,1′-bis(diphenylphosphino)ruthenocene as the ligands for palladium. In these cases, the trans stereoisomer is also formed.[52] The reaction can be extended to allylsilanes, but in this case only trifluoroacetates are reactive and a bicyclic phosphite was the only suitable ligand (Scheme 21). Intramolecular transmetallation of the ($\eta^3$-allyl)palladium complexes formed by oxidative addition of the allyl electrophiles to a Pd(0) precursor would afford bis(allyl)palladium species like those shown in Scheme 19.

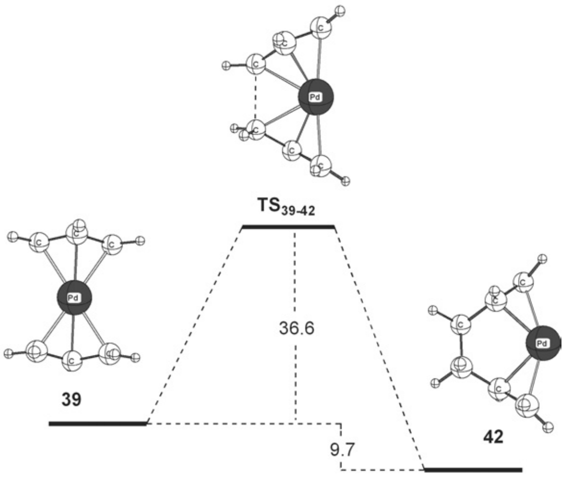
We studied the possible pathways leading to the formation of C–C bonds by reductive elimination for the three types of bis(allyl)palladium complexes that may be involved in these reactions. Some years ago it was reported that the reductive elimination from bis($\eta^3$-allyl)palladium complexes was triggered by the addition of diphosphines through bis($\eta^1$-allyl)palladium species.[53] We determined the reaction and activation energies for the reductive elimination from complexes **39–41** at the DFT level. These complexes are suitable models for the several possible intermediate complexes. The reductive elimination from the bis($\eta^3$-allyl)palladium complex **39** to give **42** has a high activation energy ($E_\mathrm{a} = 36.6$ kcal mol$^{-1}$) and a relatively low exothermic character (Scheme 22). All six carbons remain coordinated in the transition state. On the other hand, a faster elimination would take place from the monophosphine ($\eta^1$-allyl)($\eta^3$-allyl)palladium complex **40** ($E_\mathrm{a} =$ 23.4 kcal mol$^{-1}$, Scheme 23).[54] The resulting compound **43** contains only one double bond coordinated to Pd. The lowest activation barriers correspond to elimination reactions from bis($\eta^1$-allyl)palladium complex **41** (Scheme 24). In this case, several pathways can be envisaged, depending on which carbon atoms are involved in the C–C bond formation. Due to the nature of the allyl ligand, the reductive elimination could involve C1–C1′, C1–C3′, and C3–C3′. Additionally, two



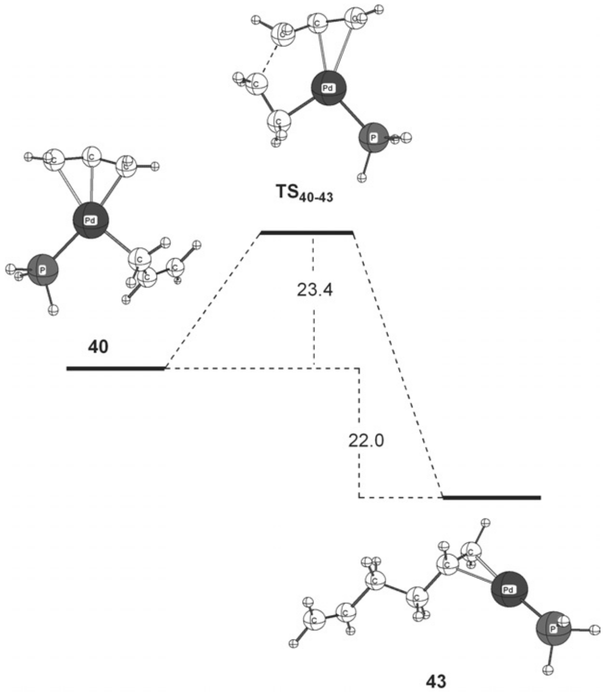
Scheme 20



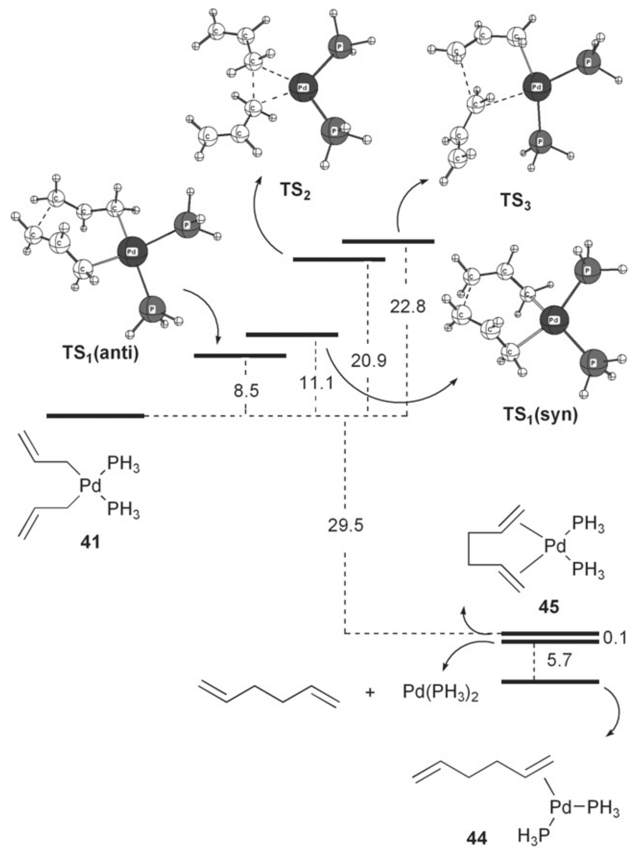
Scheme 21



Scheme 22 Calculated ZPE corrected activation and reaction energies for the reductive elimination from **39** (in kcal mol$^{-1}$) at the B3LYP/6-31G(d)-LANL2DZ level



Scheme 23 Calculated ZPE corrected activation and reaction energies for the reductive elimination from **40** (in kcal mol$^{-1}$) at the B3LYP/6-31G(d)-LANL2DZ level



**Scheme 24** Calculated ZPE corrected activation and reaction energies for the reductive elimination from bis($\eta^1$-allyl)palladium complex **41** (in kcal mol$^{-1}$) at the B3LYP/6-31G(d)-LANL2DZ level

possible conformations (anti or syn) are possible for the C3–C3′ coupling. The resulting 1,5-hexadiene can be obtained mono-coordinated to Pd (**44**), bis-coordinated (**45**) or free, depending on the particular case. Since these species would be in rapid equilibria, the most stable complex **44** would be the thermodynamic product, regardless of the actual mechanism involved.

The four possible transition states have the ligands in an arrangement lying between the square-planar geometry of the starting Pd(II) species and the usual tetrahedral geometry of the final Pd(0) complexes. The formation of the C3–C3′ bond is strongly preferred, with slightly lower activation energy for the anti isomer compared to the syn one ($E_a$ = 8.5 and 11.1 kcal mol$^{-1}$, respectively). Transition states involving C1–C1′ (**TS$_2$**)[55] and C1–C3′ (**TS$_3$**) lie 20.9 and 22.8 kcal mol$^{-1}$, respectively, above the starting complex **41**. Natural bond orbital (NBO) analysis of transition states **TS$_1$(anti)** and **TS$_1$(syn)** shows that the preference for their formation is related to the interaction of the emerging double bonds between C1–C2, and C1′–C2′, with palladium. Interaction of the incipient π-clouds with one of the Pd lone pairs stabilizes these species. The relatively high activation energy for the reductive elimination from complex **40** explains why this type of derivative prefers to react with electrophiles in reactions having lower computed activation energies.[46,48] Our calculations show that the formation of **41** by coordination of PH$_3$ to **40**, and the formation of **40** from **39**, are slightly endothermic processes (+2.4 and +0.4 kcal mol$^{-1}$, respectively). Considering the reaction energies for these equilibria and the differences between the computed activation energies for the possible mechanisms, we propose an unprecedented pathway for the reductive elimination from bis($\eta^1$-allyl)palladium derivatives involving the carbon atoms furthest from the metal. However, in the absence of phosphines or other donor ligands, different mechanisms could be operative.

## Conclusions and outlook

Computational studies are a valuable tool for the study of metal-catalyzed reactions. The structure and reactivity of allylpalladium complexes has been extensively studied. The influence of steric and electronic factors due to both the allyl substituents, and the ancillary ligands on palladium have been evaluated. Calculations are especially useful for the determination of the structure of elusive intermediates and transition states. In this sense, they can provide evidence to propose unprecedented mechanisms or to discern among several reaction pathways, provided that the energy differences are high enough to shed no doubt on the validity of the conclusions. For the cases in which kinetic studies are difficult to perform (heterogeneous reactions, for instance), or give limited information (as occurs for intramolecular reactions), theoretical studies may be indispensable. The currently available methods, especially DFT calculations, allow relatively large molecules to be studied with high accuracy. For these reasons, computational studies are an increasingly important tool for the study of organometallic reaction mechanisms.

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