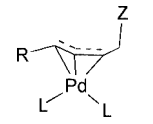
Nature of the interaction between β-substituents and the allyl moiety in (η³-allyl)palladium complexes



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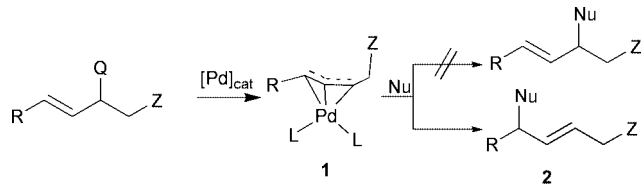
β-Substituted (η³-allyl)palladium complexes are key-intermediates in synthetically important highly selective palladium-catalyzed transformations. Recently, several studies have appeared on the investigation of the electronic interactions occurring between β-substituents and the allyl moiety in these complexes. The nature of these electronic interactions was explored by MP2 and DFT calculations, and it has been studied by X-ray crystallography, kinetic experiments and stoichiometric nucleophilic substitution of the β-substituted (η³-allyl)palladium complexes. These studies revealed a new type of σ–π electronic interaction between the β-substituents (Cl, OR, OAc and SiR_3) and the allyl–metal moiety. It was found that these electronic interactions influence: (i) the structure of (η³-allyl)palladium complexes; (ii) the kinetic and thermodynamic stability of these species; and (iii) the regiochemistry of the nucleophilic attack on the allyl moiety.

1 Introduction

Catalytic transformations involving (η³-allyl)palladium intermediates have been widely applied in a number of important chemical processes,[1,2] such as allylic substitution reactions,[3] allylic oxidation[4] and 1,4-oxidation of conjugated dienes.[5,6] One of the most important aspects of this allylpalladium chemistry is the possibility of controlling the chemo-, regio- stereo- and enantioselectivity of the nucleophilic attack on the allyl moiety through the appropriate choice of the reaction conditions and the ancillary ligands on palladium.[1–11] Accordingly, there is a considerable interest at the present time in investigating those electronic and steric interactions that govern the selectivity in catalytic transformations proceeding through (η³-allyl)palladium intermediates.

Catalytic procedures providing unsymmetrical 1,4-disubstituted alkenes are particularly interesting from a synthetic and mechanistic point of view (Scheme 1). These compounds are



Scheme 1

useful building blocks in organic synthesis since they can be selectively functionalized at either allylic position.[5] The key step in the palladium-catalyzed preparation of 1,4-disubstituted alkenes is the nucleophilic attack on an (η³-allyl)palladium complex bearing a substituent on the carbon atom adjacent (4- or β-position) to the allyl–palladium moiety (**1**). It has been recognized[2] that the electronic effects of certain β-substituents, such as Z = Cl, OH, OR, OAc, NR_2 and NO_2,[12–14] are capable of being transmitted to the allylic moiety, increasing the regioselectivity of the nucleophilic attack for formation of bis-allylic products (**2**). This regiochemistry is difficult to rationalize on steric grounds as isosteric alkyl groups do not exert nearly as effective regiocontrol.[2] On the other hand the observed regioselectivity cannot be simply explained by the electron-withdrawing effects of the β-substituent Z (Scheme 1), since the electron deficiency is created at the more substituted terminus of the allyl moiety.

Since the electronic interactions between a β-substituent and the allylic π-system lead to asymmetric distortion of the allyl–metal bonding in (η³-allyl)palladium complexes, the β-substituent effects can also influence the enantioselectivity of the nucleophilic attack. Pfaltz and co-workers[7,8,15] have shown that bulky chiral ligands significantly change the palladium–carbon bond lengths to the allylic termini (Pd–C1 and Pd–C3). The repulsive interaction between the chiral ligand and one of the allylic termini leads to elongation of the corresponding Pd–C bond. It was shown[7,8,15] that the nucleophile preferentially attacks the longer Pd–C bond, and, accordingly the asymmetric induction is governed by the allyl–metal bonding in the (η³-allyl)palladium intermediate.

The purpose of this review is to highlight structural and mechanistic studies on the nature of the interactions between the allylic β-substituents and the π-system in (η³-allyl)palladium

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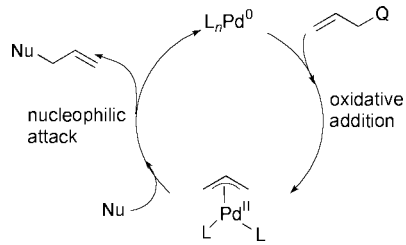
complexes. Since recognition of the β-substituent effects can provide significant help for the design and development of new selective palladium-catalyzed transformations, particular attention is paid to the synthetically important structural and reactivity features of these complexes.

2 β-Substituted (η³-allyl)palladium complexes as catalytic intermediates

The key steps of the Pd(0) catalyzed allylic substitution reaction are depicted in Scheme 2. A wide range of allylic substrates,

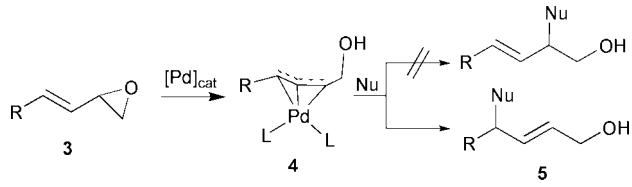


Scheme 2

such as halides, acetates, carbonates and carbamates (Q = X, OAc, OCOOR and OCONR respectively), undergo oxidative addition to palladium(0) to form (η³-allyl)palladium(II) complexes. The nucleophilic attack on the (η³-allyl)palladium complexes affords the allylic product and formation of palladium(0). The regenerated palladium(0) undergoes oxidative addition to allylic compounds starting a new catalytic cycle.

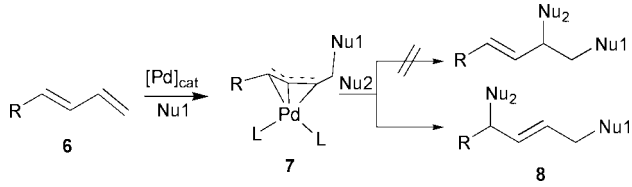
When the substrates of the allylic substitution reactions have functionalities (Z) in an allylic position (Scheme 1), the nucleophile can attack either the more or the less substituted allylic terminus of the allyl–palladium intermediate. A high level of regiocontrol is required to direct the nucleophilic attack to the less substituted allylic terminus affording bis-allylic compounds (**2**) as products. Very often a Z functionality is present in the allylic substrate, however in many cases it emerges during the catalytic procedure.[2]

In catalytic alkylation of 1,3-diene monoepoxides (**3**) the oxidative addition generates a Z = OH functionality (Scheme 3).[16] In this process the nucleophile selectively attacks the



Scheme 3

allylic carbon remote from the incipient hydroxy group. In the 1,4-oxidation of conjugated dienes (**6**) (Scheme 4) the asym-



Scheme 4

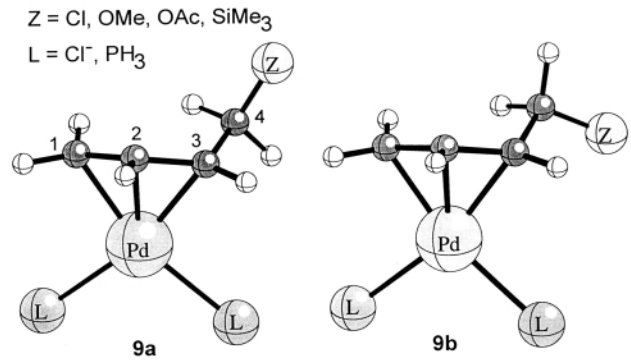
metrical (η³-allyl)palladium intermediate (**7**) is usually formed by the highly chemoselective attack of an O- or N-nucleophile (Z = Nu1) on a (η⁴-diene)palladium complex. Addition of a second nucleophile (Nu2) determines the regiochemistry of the reaction, which can give 1,2- or 1,4-disubstituted (**8**) products.[5,6] The synthetic value of this transformation arises from the very high 1,4 selectivity. Another interesting feature of the β-substituted (η³-allyl)palladium complexes is the possibility for the exchange of the substituent under catalytic conditions. In the 1,4-chloracetoxylation of conjugated dienes[5] the first nucleophile is always the acetate ion (Nu1 = OAc), since the β-chloro substituted intermediate (**7**, Nu1 = Cl) is kinetically unstable and easily decomposes to (η⁴-diene)palladium complex and chloride ion. This property forms the basis of the high chemoselectivity of the chloracetoxylation reaction.

3 Theoretical studies on the effects of β-substituents

The enormous progress in quantum chemical computational techniques over the past several years is also reflected by the increasing number of organometallic applications. In fact, employment of density functional theory (DFT)[17] has become a standard tool for exploration of the electronic structure and reactivity of transition metal complexes.[18] The theoretical aspects of palladium chemistry have attracted particular attention.[19] Recently, a number of theoretical studies have been published on the structure and properties of β-substituted (η³-allyl)palladium complexes.[20–23] These studies investigated the β-substituent effects on the allylpalladium system as a function of the substituent (Z) polarity and the electronic character of the ligand (L). Most of these calculations are performed using density functional theory with a relativistic small-core pseudopotential on Pd and a polarized basis set on the heavy atoms.[24–26]

3.1 Effects of electronegative substituents (Z = Cl, OMe, OAc) with σ-donor ligand (L = Cl)

Full geometry optimization of various β-substituted complexes leads to equilibrium structure **9a**, which shows some remarkable geometrical features (Scheme 5). The C4–Z bond, which is



Scheme 5

always antiperiplanar to the Pd–C3 bond (τ defined as Pd–C3–C4–Z is 170–180°), is longer than a usual C–Z bond (Table 1). Bonding between palladium and the allylic carbons is also influenced by the Z substituent. The Pd–C3 bond is invariably shorter than the Pd–C1 bond, *i.e.* the more substituted allylic terminus is closer to the palladium than the less substituted one. This is surprising in view of the fact that in allyl metal complexes there is a considerable repulsion between the metal atom and the *anti* functionality.

Rotation of the functional group by 90° (**9b**) leads to thermodynamic destabilization of the complexes by 15–30 kJ

Table 1 Geometrical parameters [Å], energies [kJ mol^{-1}] and force constants [mdyn Å^{-1}] for β-substituted (η^3-allyl)palladium complexes **9a** and **9b**[a]

	Z	L	Pd–C1	Pd–C3	Pd–C4	C3–C4	C4–Z	k_{C-Z}	q(Z)	E_{rel}
9a	Cl[b]	Cl	2.121	2.109	2.889	1.500	1.833	2.71	−0.194	
9b	Cl[b]	Cl	2.113	2.119	3.045	1.514	1.797	3.30	−0.130	33.9
9a	OMe	Cl	2.135	2.135	2.959	1.503	1.433	4.69	−0.331	
9b	OMe	Cl	2.139	2.155	3.069	1.511	1.411	5.38	−0.299	25.5
9a	OAc	Cl	2.142	2.127	2.962	1.499	1.466	3.96	−0.394	
9b	OAc	Cl	2.140	2.146	3.028	1.510	1.436	4.81	−0.359	14.2
9a	$SiMe_3$	Cl	2.133	2.147	3.003	1.512	1.899	2.72	0.430	
9b	$SiMe_3$	Cl	2.142	2.130	3.063	1.523	1.907	2.81	0.441	3.8
9a	Cl[b]	PH_3	2.223	2.220	2.971	1.512	1.795	3.30	−0.060	
9b	Cl[b]	PH_3	2.226	2.209	2.983	1.516	1.790	3.40	−0.080	−7.1
9a	OMe	PH_3	2.193	2.218	3.029	1.517	1.404	5.42	−0.259	
9b	OMe	PH_3	2.205	2.205	2.989	1.511	1.406	5.53	−0.273	−14.2
9a	OAc	PH_3	2.195	2.221	3.001	1.511	1.429	5.11	−0.300	
9b	OAc	PH_3	2.203	2.215	3.006	1.508	1.428	5.27	−0.310	−4.2
9a	$SiMe_3$	PH_3	2.180	2.299	3.029	1.486	1.950	2.26	0.538	
9b	$SiMe_3$	PH_3	2.191	2.270	3.059	1.513	1.920	2.60	0.506	25.5

[a] The Pd–C3–C4–Z angle in **9b** is frozen at 90°. Unless otherwise stated the calculations are carried out at the B3PW91/LANL2DZ + P level. [b] MP2/LANL2DZ + P calculations.

mol^{-1}. In **9b** the C–Z bond lengths are shorter than the corresponding bond lengths in the equilibrium form (**9a**). Another important geometrical effect is that the Pd–C3 bond is elongated on the **9a** → **9b** conversion, and thus the Pd–C1 and Pd–C3 bonds are approximately the same in **9b**.

As mentioned above the C4–Z bond is remarkably long in the equilibrium conformation **9a**. Weakening of the C4–Z bond is also reflected by its low stretching force constant (Table 1), which is smaller by up to 20% than the C–Z stretching force constant in the **9b** form. Accordingly, the C4–Z bond is the weakest in the equilibrium conformation, hence the electronic interactions thermodynamically stabilize the kinetically least stable conformation. Clearly, the intensity of the interactions between palladium and the C4–Cl bond in **9a** are determined by stereoelectronic effects.

3.2 Effects of the π-acceptor ligand (L = PH_3)

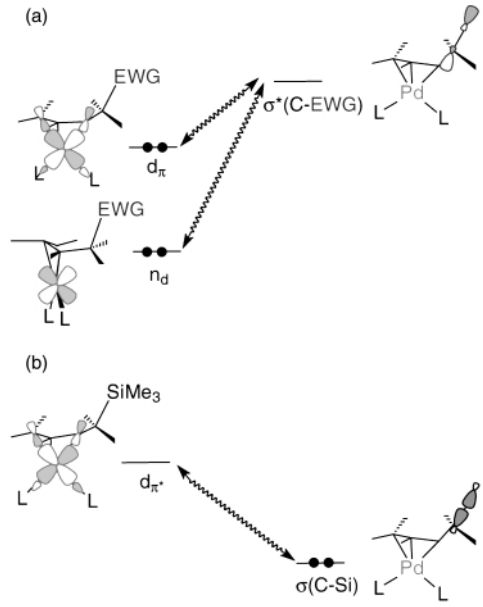
In complexes bearing an electronegative β-substituent (Z = Cl, OMe, OAc) replacement of the chloride ligands with phosphine ligands leads to lengthening of the palladium–carbon bonds, which can be attributed to the π-acceptor character of PH_3. Although the antiperiplanar conformation represents a local minimum on the potential energy surface, its geometry reflects very weak (if any) interactions between the β-substituent and palladium. In **9a**, the C4–Z bond is always shorter than this bond in the corresponding chloro complexes. Furthermore, rotation of the functional group (**9a** → **9b**) leads to stabilization of the phosphine complexes. The C–Z stretching force constants and C4–Z bond lengths are invariant to the rotation of the functional group.

3.3 Effects of the electropositive β-silyl substituent (Z = $SiMe_3$)

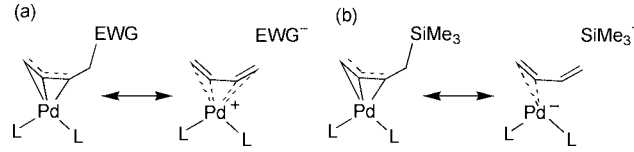
The ligand effects on the structure and stability of **9a** are reversed for the β-silyl substituent. The C4–Si bond is longer in the phosphine complex than in the corresponding chloro complex. Furthermore, rotation of the functional group (**9a** → **9b**) destabilizes the phosphine complex to a larger extent (25.5 kJ mol^{-1}) than the chloro complex (3.8 kJ mol^{-1}). In the equilibrium conformation (**9a**) the C–Si force constant in the phosphine complex is considerably smaller (2.26 mdyn Å^{-1}) than in case of a chloride ligand (2.72 mdyn Å^{-1}). These results indicate that the interactions between the allyl–metal complex and the β-silyl substituent are more pronounced in the phosphine complex.

3.4 MO interpretation of the β-substituent effects

The structural effects induced by OAc and other electron-withdrawing substituents were rationalized[20–22] by the electronic interactions shown in Schemes 6a and 7a using MO



Scheme 6



Scheme 7

formalism and resonance structures, respectively. Accordingly, partial coordination of C4 to palladium lends C1–C4 similarity to a butadiene moiety. Charge transfer from the high lying HOMO orbital (d_π) of the complex and a properly positioned lone-pair orbital of palladium (n_d) into the σ*(C-EWG) leads to weakening and elongation of the C–O single bond. The interaction between n_d and σ*(C-EWG) leads to partial coordination of C4 to palladium (*cf.* MO interactions in (η^4-butadiene)palladium complexes[27]), and therefore *shortening* of

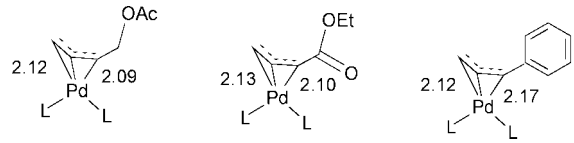
the Pd–C4 distance and the Pd–C3 bond length. The d_π level is lowered on coordination of π-acceptor ligands,[28] which causes the energy gap between d_π and σ*(C-EWG) to increase leading to decreased orbital interactions.

The nature of the electronic interactions is somewhat different for the electron supplying $SiMe_3$ group. It is well established that σ(C–Si) orbitals readily conjugate with low-lying unfilled π-levels. The interactions between σ(C–Si) and the p_π-orbital of carbocations are the basis of the well-known β-silicon effect.[29] The effects of β-silicon substituents in (η^3-allyl)palladium complexes, can also be ascribed to the electronic interactions between the unfilled LUMO of the allyl–palladium fragment (d_{π^*}) and the high-lying σ(C–Si) orbital (Scheme 6b). Delocalization of electrons from the bonding σ(C–Si) orbital leads to weakening of the C–Si bond. Since the d_{π^*} is Pd–C_t antibonding, the allyl–palladium bonding is also weakened. The σ(C–Si) orbital directly overlaps with the π-lobe of C3, and therefore the Pd–C3 bond is weakened to a much greater extent than the Pd–C1 bond. On the other hand, in-phase overlap between σ(C–Si) and d_{π^*} increases the C3–C4 bonding, leading to shortening of the C3–C4 bond. Coordination of π-acceptor ligands involves charge transfer from the metal to the ligand through back-donation, leading to orbital contraction and therefore lowering of the d_{π^*} level. Decreasing the energy of d_{π^*} causes the energy gap between d_{π^*} and σ(C–Si) to decrease, which leads to increased orbital interactions.

4 Experimental studies on the structure of β-substituted (η^3-allyl)palladium complexes

4.1 X-ray studies

Manchand and co-workers,[13] and Welch and co-workers[30,31] reported X-ray structures for β-substituted (η^3-allyl)palladium complexes (Scheme 8). These authors found that the allylic terminus which is closer to the O-functionality is "hinging



Scheme 8

towards" the metal.[30] However, when a bulky phenyl group is attached to the allyl moiety, the more substituted terminus is "hinging away" from palladium.[31] From the analysis of the contacts within and between molecules, Welch and co-workers[30] concluded that the asymmetrical metal–allyl bonding was electronically induced and not simply a consequence of the steric effects. Considering the theoretical results these electronic effects can be ascribed to the interactions between the electron-withdrawing β-substituents and the (η^3-allyl)palladium system.

Cyclic allylpalladium complexes are important intermediates in palladium-catalyzed regio- and stereoselective 1,4-oxidation of conjugated dienes.[5,6] In a recent publication[32] X-ray data have appeared for cyclic chlorodimers *trans*- and *cis*-**10** (Fig. 1). The cyclohexenyl rings in the dimeric (η^3-allyl)palladium complex *trans*-**10** possess a chair conformation rendering the OAc groups to an axial position. However, in *cis*-**10** the six-membered rings have a boat conformation and the OAc groups are in axial position. Another important structural feature of *trans*-**10** is the asymmetric allyl–palladium bonding. The palladium carbon bond to the C3–allylic terminal position (Pd–C3 = 2.145(9) and Pd–C3′ = 2.143(9) Å) is shorter than the other terminal palladium–carbon bond (Pd–C1 = 2.185(9) Å, Pd–C1′ = 2.187(10) Å). In contrast to *trans*-**10**, *cis*-**10** does *not* show a contracted Pd–C3 bond compared to the Pd–C1 bond but

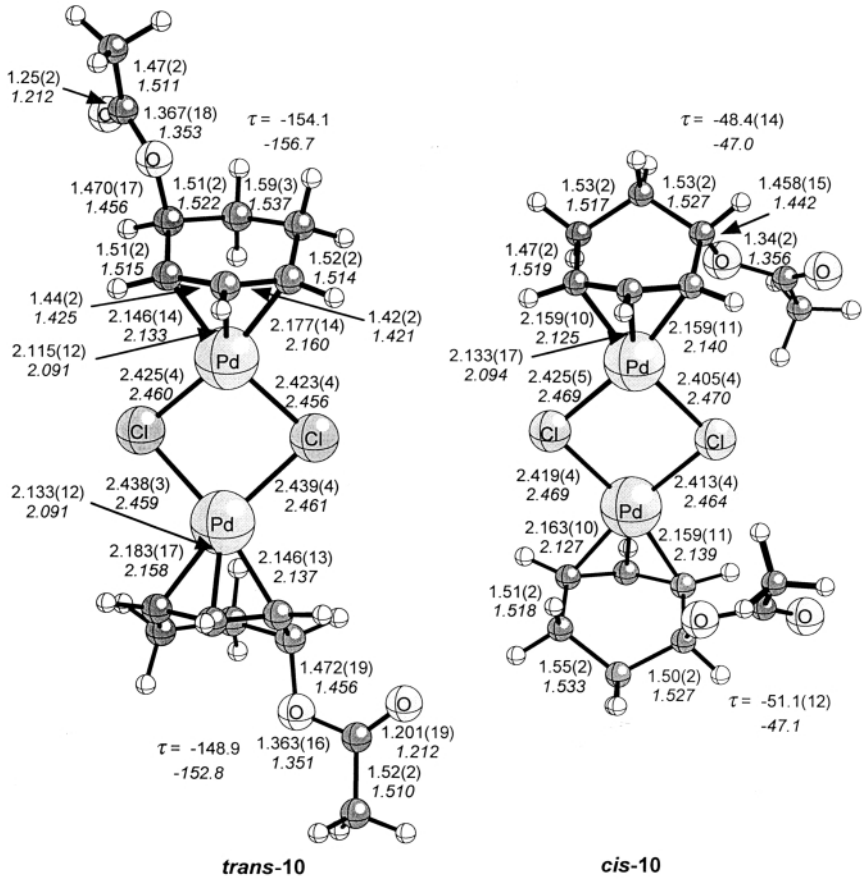


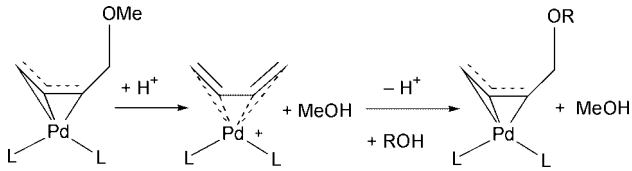
Fig. 1 Experimental and calculated (B3PW91/LANL2DZ + P) structure of *trans*- and *cis*-**10** (bond lengths in Å, and angles in deg.). The X-ray data are given in normal type face, and the calculated parameters are given in italic type face. τ refers to the Pd–C3–C4–O dihedral angle.

the Pd–C3 and Pd–C1 bond lengths are identical within the experimental error. The different Pd–C bonding in *trans*- and *cis*-**10** clearly indicates the stereoelectronic nature of the interactions between the acetate functionality and the allyl–palladium system.[32]

Complex *trans*-**10** represents a particularly suitable species for investigation of the structural consequences of the above electronic interactions, since the hindered rotation due to the six-membered ring framework locks the conformation of the 4-OAc group. Furthermore, in the chair form the conformation of the OAc group (τ = −149–154°, where τ is the Pd–C3–C4–O dihedral angle) stereoelectronically favours the π−σ* type interactions.[21,28] The geometrical parameters calculated for *trans*-**10** and *cis*-**10** (Fig. 1) are in good agreement with the values obtained by the X-ray studies verifying the presence of the β-substituent interactions.

4.2 Kinetic studies on the cleavage of the C–Z bond

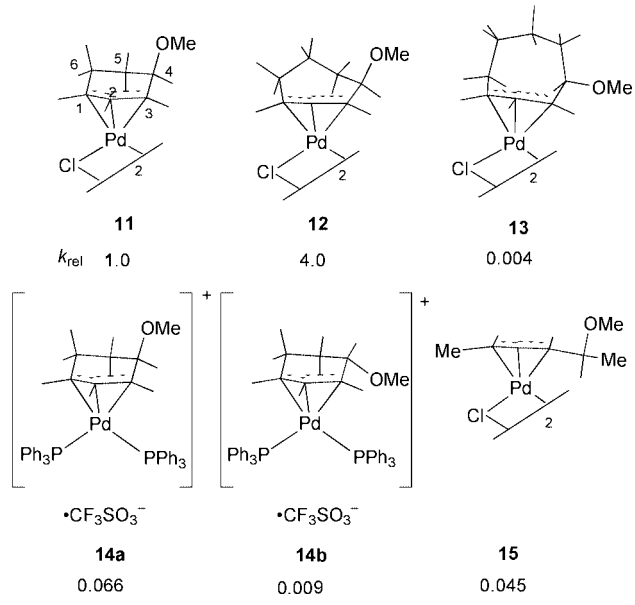
It is well established that the acid catalysed alcoholysis of β-methoxy substituted (η³-allyl)palladium complexes takes place through the breaking of the C4–O bond (Scheme 9).[33,34] This



Scheme 9

reaction can be carried out under mild conditions, since the palladium atom lends anchimeric assistance to the bond breaking process.[33] The anchimeric assistance is, in fact, a manifestation of the β-substituent effects[20] that weakens the C4–O bonding and, therefore, facilitates the breaking of the C4–O bond. Hence, the rate of alcoholysis will depend on the magnitude of the anchimeric assistance and, accordingly, on the intensity of the β-substituent effect.

Therefore the rate of the deuteromethanolysis was studied for various β-substituted (η³-allyl)palladium complexes (Scheme 10).[21] The observed rates of deuteromethanolysis span three orders of magnitude (Scheme 10). The reaction was fastest for the cycloheptylallyl complex **12**, followed by the cyclohexylallyl complex **11**. Interestingly, expansion of the seven membered ring with only a single methylene unit leads to a drastic change in the rate of reaction. The deuteromethanolysis of the cycloheptylallyl complex **12** proceeds about a 1000 times faster than that of the cyclooctylallyl complex **13**. This remarkable decrease of the reaction rate is indicative of a conformationally induced weakening of the β-substituent effects in **13**. When the σ-donor chloride ligands of **11** are exchanged with π-acceptor triphenyl phosphine (PPh_3) ligands (**14a**) the reaction rate is significantly decreased. Furthermore, when the ligand exchange is accompanied by a change of the *trans* configuration of the methoxy group to a *cis* configuration (**14b**) the reaction rate is reduced by more than two orders of

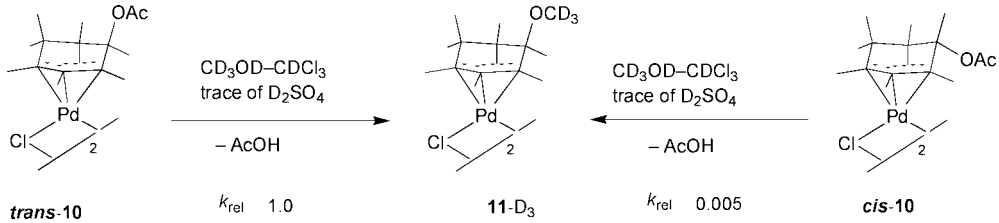


Scheme 10

magnitude. In **15** the methoxy group is attached to a secondary carbon atom (C4), such as in cyclic complexes **11**–**14**. However, in **15** the allylic $C4H_2OMe$ functionality occupies a *syn* configuration,[35] besides free rotation is allowed at the C3–C4 bond. Because of these differences, the cyclohexylallyl complex **11** reacts more than 20 times faster than **15**.

The differences in the methanolysis rates of **11**–**15** could also be explained on the basis of the electronic interactions of β-substituents and the allyl–palladium system.[21] The theoretical DFT studies have shown that a six- and a seven-membered ring framework (**11** and **12**) provides a *trans*-β-substituent conformation (τ = 159–200°) that is particularly favoured by the β-substituent effects. On the other hand, in the thermodynamically stable forms of the cyclooctylallyl complex (**13**) the *trans*-β-substituent conformation is not optimal for the conjugative interactions (τ = −120 −200°), which leads to a decrease of the intensity of the β-substituent effects. Similarly, the *cis*-β-substituent geometry (**14b**) and the acyclic framework (**15**) are typical structural factors, which lead to weakening of the interactions between a polar β-substituent and palladium. Ancillary ligands with a pronounced π-acceptor character also reduce the intensity of the interactions even in such cases when the stereoelectronic requirements of the β-substituent effects are satisfied (**14a** and **14b**).

A similar study[22] was conducted for β-acetoxy substituted complexes *trans*-**10** and *cis*-**10** (Scheme 11). The *trans* complex (*trans*-**10**) reacted very quickly and was completely converted to its deuteromethoxy analog **11**-D_3. Retention of the configuration of C4 is a direct consequence of the anchimeric assistance of palladium. The *cis* complex (*cis*-**10**) was significantly more stable than *trans*-**10** under the reaction conditions of the deuteromethanolysis. It was converted to **11**-D_3, about 200 times slower than *trans*-**10**. The rapid exchange of the β-substituent in *trans*-**10** arises from the acetoxy substituent being locked in a conformation (Fig. 1) that is favoured by the β-



Scheme 11

substituent effects. On the other hand, the *cis*-complex is more stable kinetically under the same reaction conditions, indicating the absence of the conjugative interactions between the palladium atom and the acetoxy functionality.

4.3 NMR studies of the β-silyl substituted complexes

β-Silyl substituted cyclic (η^3-allyl)palladium complex **16** (Scheme 12) was prepared by palladadesilylation of **17a** and the ancillary chloride ligand could be exchanged with dppe (**18**) and PPh_3 (**19**) by $AgBF_4$ in the presence of the corresponding phosphine. The ^{13}C NMR spectra of the allyl–palladium complexes showed some interesting features: the chemical shift of the allylic terminus (C_t) closer to the $SiMe_2Ph$ functionality (C3) was observed at a lower field than that of the remote allylic terminus (C1). Comparison of δ(C1) and δ(C3) in **16**, **18** and **19** with the allylic shift [δ(C1)] in the corresponding unsubstituted complex reveals that the 4-silyl substitution generates deshielding effects at the closer allylic terminus (C3). The differences in the chemical shift between C1 and C3 are also dependent on the ligand effects: the difference is rather small (3.6 ppm) for the σ-donor Cl^- ligand (**16**), somewhat larger (5.3 ppm) in the dppe complex (**18**) and a whole 11.8 ppm for **19**. As the palladium atom has a considerable shielding effect on the allylic carbons, partial deshielding of C3 arising from the presence of the β-silyl substituent is indicative of weakening of the Pd–C3 interactions.

A similar trend was found for the corresponding acyclic systems (Fig. 2).[36] Comparison of the ^{13}C NMR shifts of the allylic terminal carbons in **22** and **21a**–**b** reveals the perturbation effects of the $SiMe_2R$ group on the electronic structure of the allylic moiety. The chemical shift difference between the terminal carbons ($\Delta\delta_t$) increases in the presence of the silyl substituent. Furthermore, the chemical shift of the allylic terminus closer to the silyl functionality (C3) in **21a**–**b** is observed at a lower field than the corresponding ^{13}C shift in **22**, indicating a deshielding effect of the β-$SiMe_2R$ group on the C3 allylic position. The asymmetrizing effect of the silyl substituent on the electronic structure of the allylic moiety is also reflected by the ^{13}C shifts of **21c**. The presence of the silyl functionality leads to a difference of 6.7 ppm in the C_t shift values, and the closer allylic terminus (C3) is less shielded than the remote one. The same trend applies to the phosphine complexes. The $\Delta\delta_t$ values of **23a**–**b** and **24** differ even more than the corresponding values in the chloro complexes **21a**–**b** and **22**. Similarly, the perturbation effects of the silyl functionality on the allylic terminal carbons are stronger in the phosphine complex **23c** ($\Delta\delta_t$ = 10.4 ppm), than in the chloro-complex **21c** ($\Delta\delta_t$ = 6.7 ppm).

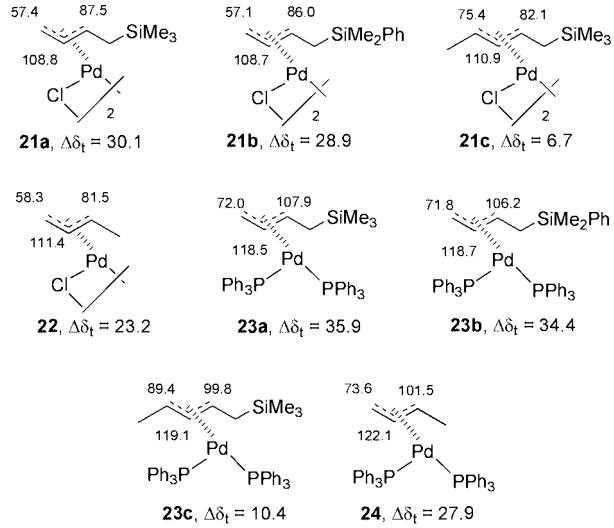
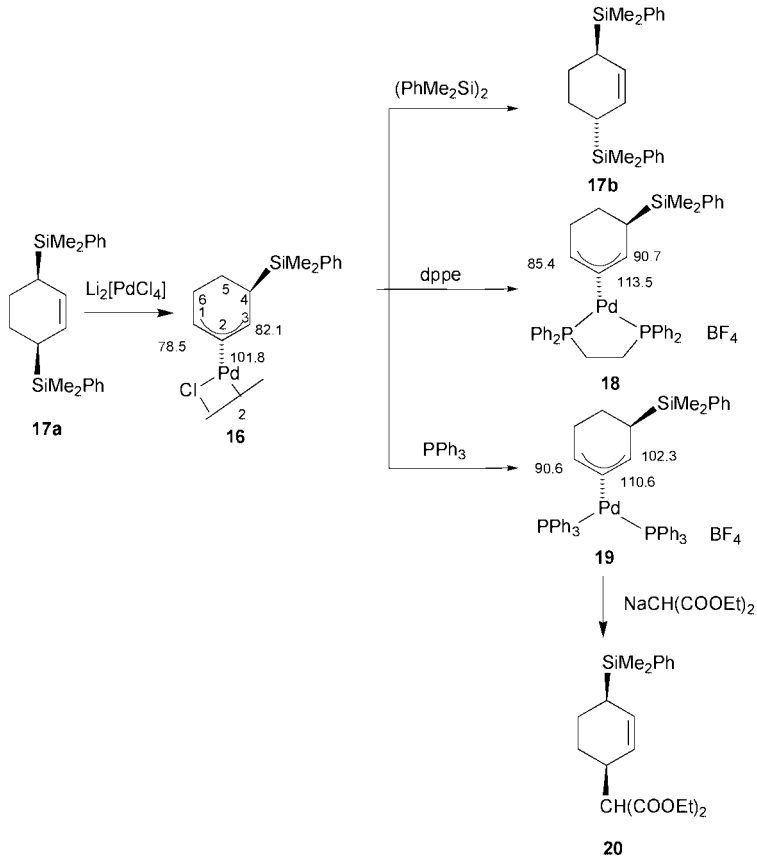


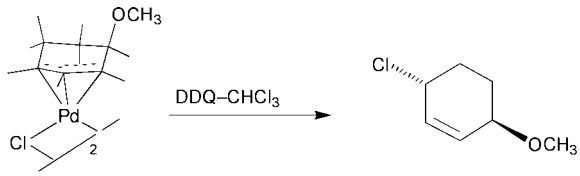
Fig. 2 ^{13}C NMR shifts (ppm) in $CDCl_3$ of the allylic carbons. $\Delta\delta_t$ denotes the chemical shift differences between C3 and C1 ($\Delta\delta_t = \delta C3 - \delta C1$).



Scheme 12

4.4 Stoichiometric reactions on the selectivity of the nucleophilic attack

Several mechanistic studies have appeared on the reactivity of β-substituted (η^3-allyl)palladium complexes. Bäckvall and coworkers[37] studied the regio- and stereoselectivity of the nucleophilic attack on the key intermediate (**7**) of the bis-oxidation of conjugated dienes (Scheme 4). It was found that the regioselectivity of the nucleophilic attack is very high in case of β-methoxy substituents (**7**, Nu1 = OMe). In these reactions exclusively the less substituted allylic position was attacked by the nucleophiles. The same regioselectivity was found for the DDQ (2,3-dichloro-5,6-dicyanobenzoquinone) mediated chloride migration in **11** (Scheme 13).[38]



11

Scheme 13

The regiochemistry of the nucleophilic attack was also studied for β-silyl substituted (η^3-allyl)palladium complexes.[23,36] Complex **19** was reacted with sodium diethyl malonate (Scheme 12), providing the 1,4-substituted product **20** with very high regio- and stereoselectivity. Since the external attack by the malonate proceeds by a *trans* mechanism,[37] it also involves steric influence of the 4-$SiMe_2Ph$ group. In order to investigate the effects of purely electronic factors on the regiochemistry of the nucleophilic attack, the Cl^- ligands of **16** were exchanged to OAc^- and the acetate complex was reacted with $(PhMe_2Si)_2$. It was shown[39] that allyl–palladium complexes react with alkyl- and aryl-disilanes through *cis*-migration of the silyl nucleophile from palladium to allyl. Transformation of **16** afforded *trans*-1,4-disilyl compound **17b** indicating that the nucleophilic attack is selective even in the absence of the steric influence of the silyl functionality. Similar results were found for acyclic silanes **21a–c** and **23a–c**.[36] The external attack with malonates proceeds with very high selectivity providing functionalized allylsilanes. The internal nucleophiles also predominantly attack at the less substituted allylic position, however the regioselectivity is somewhat lower than for the external attack.

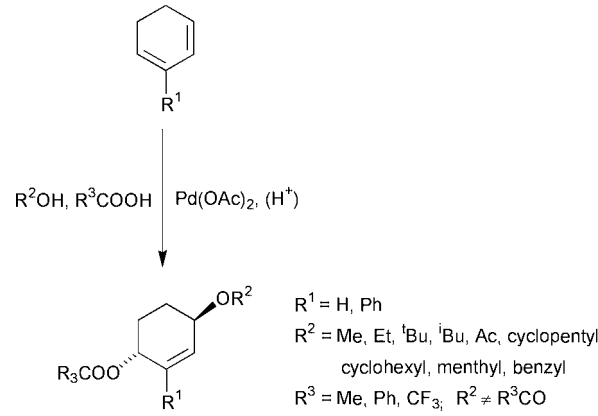
The high regioselectivity of the nucleophilic attack can also be explained on the basis of the β-substituent effects. In the presence of electron withdrawing or silyl substituents the C–Z bond is involved in conjugative interactions with the (η^3-allyl)palladium moiety (Schemes 6 and 7). This conjugation is extended to the C1–C4 fragment and the β-substituent. A nucleophilic attack at the C3 position would interrupt this conjugation, so the C1 terminus is preferentially attacked. Furthermore, the electronic interactions stabilize such conformations where the functional group is *trans* to palladium and the C–Z bond is perpendicular to the plane of allyl moiety ($\tau \approx 180°$), the steric effects will also improve the 1,4-selectivity of the external nucleophilic attack.

On the other hand steric and electronic factors decreasing the intensity of the β-substituent effects leads to lowering of the regioselectivity of the nucleophilic attack. For example the eight membered ring framework (**13**) or *cis* geometry in cyclic systems (*cis*-**10**) displace the β-substituent from the antiperiplanar conformation leading to decrease of the β-substituent effects. As a consequence the nucleophilic attack on such complexes proceeds with a poor regioselectivity.[6,40,41] Strong π-acceptor ligands reduce the intensity of the β-effects of *electronegative* substituents (*vide supra*). Since π-acceptor ligands that are usually employed to activate (η^3-allyl)palladium complexes toward nucleophilic attack also decrease the intensity of the β-substituent effects, the activating ligand has to be carefully chosen when a high degree of regioselectivity is desired. The best compromise is to employ ligands with both π-acceptor and a fairly good σ-donor ability.

For β-silyl substituents the hyperconjugation involves the C1–C4 fragment and the C4–Si bond (Schemes 6 and 7). This hyperconjugation can be maintained, when the nucleophile attacks at the C1 terminus. The steric effects of the bulky silyl group also facilitate the nucleophilic attack at the C1 position of the allyl. Since the hyperconjugative interactions stabilize such conformations where the silyl group is *trans* to palladium and the C–Si bond is perpendicular to the plane of the allyl moiety, the steric effects will also improve the 1,4-selectivity of the external nucleophilic attack even for acyclic systems. On the other hand the electronic interactions involve weakening of the Pd–C3 bond. Since the nucleophilic attack on the allyl moiety involves Pd–C bond breaking, a weak Pd–C3 bond facilitates the C3 attack. This effect may lead to lowering the regioselectivity for internal nucleophilic attack, where the steric effects of the silyl functionality do not influence the regiochemistry of the reaction.

4.5 Recent examples of the employment of the β-effects in palladium-catalyzed transformations

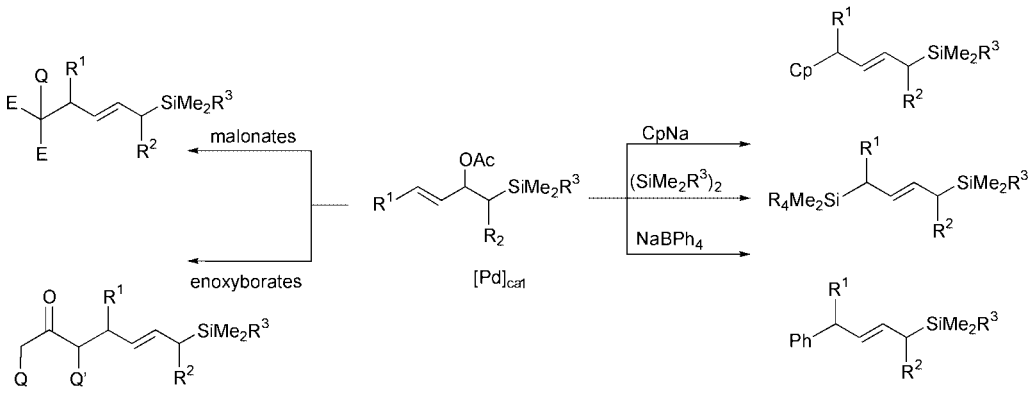
Having a deeper understanding of the nature of β-substituent effects permitted the design of a new type of chemo-, regio- and stereoselective 1,4-oxidation reaction of cyclic 1,3-dienes (Scheme 14).[42,43] Thus utilisation of the β-substituent effects in



Scheme 14

1,4-oxidation of conjugated dienes afforded a new synthetically useful procedure which has been employed for the preparation of new stereodefined 1,4-disubstituted alkenes from inexpensive starting materials.[42,43] For example, the highly stereo- and regioselective 1,4-acyloxy-alkoxylation of conjugated dienes (Scheme 14) used the fact that β-substituent in *trans*-**10** can be exchanged more easily than the corresponding functionality in complex **11**.

Functionalized allylsilanes have proven to be an exceedingly useful class of organometallic reagents and they continue to show enormous potential in regio- and stereocontrolled C–C bond formation reactions.[44] Regioselective catalytic transformations involving β-silyl substituted (η^3-allyl)palladium complexes, such as **18**, **19**, **21** and **23**, proved to be an efficient route to functionalized allylsilanes (Scheme 15).[23,36] An excellent regioselectivity was obtained, when external nucleophiles, such as malonates and enoxyborates, were employed,



Scheme 15

and useful levels of regiochemistry can be achived using internal nucleophiles such as disilanes and $NaBPh_4$.

5 Conclusions

The application of allylpalladium chemistry to organic synthesis has made remarkable progress in recent decades.[1–3] By a proper choice of the reaction conditions palladium-catalyzed transformations involving (η^3-allyl)palladium intermediates proceed with a high level of selectivity. Understanding of the fundamental steric and electronic effects between the (η^3-allyl)palladium moiety, spectator ligands and substituents is a prerequisite for designing new selective catalytic procedures. Recent studies described and characterized a new type of electronic interaction, which occurs between the allylic β-substituents (Z) and palladium in allylpalladium complexes. These interactions influence the structure of (η^3-allyl)palladium complexes; the kinetic and thermodynamic stability of these species; and the regiochemistry of the nucleophilic attack on the allyl moiety. The structural changes involve the antiperiplanar Pd–C3 bond and weakening of the C4–Z bond length. The β-substituent effects stabilize the (η^3-allyl)palladium complexes by up to 35 kJ mol^{-1}. Weakening of the C–Z bond as shown by the C–Z stretching force constants (Table 1), facilitates its heterolytic fission and therefore the β-substituent effects lead to a decrease of the kinetic stability of the complexes. The β-substituent effects can be influenced by: the polarity of the C4–Z bond, the relative conformation of the Pd–C3 and C4–Z bonds (value of τ), and the choice of the ancillary ligands on palladium.

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