JOC Article

Palladium-Catalyzed Electrophilic Substitution of Allyl Chlorides and Acetates via Bis-allylpalladium Intermediates

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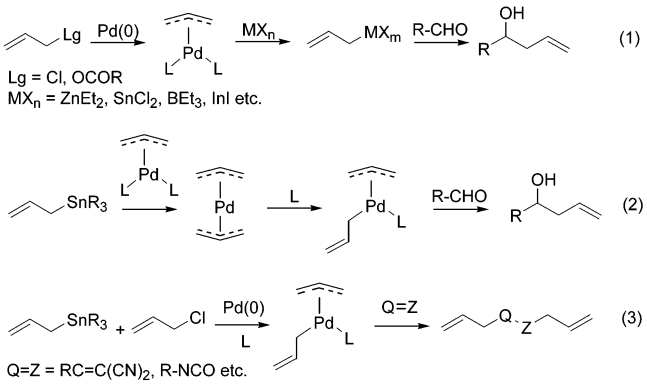
Palladium-catalyzed electrophilic allylic substitution of functionalized allyl chlorides and allyl acetates can be achieved in the presence of hexamethylditin under mild and neutral reaction conditions. This efficient one-pot procedure involves palladium-catalyzed formation of transient allylstannanes followed by generation of a bis-allylpalladium intermediate, which subsequently reacts with electrophiles. Using this catalytic transformation, various aldehydes and imines can be allylated providing highly functionalized homoallyl alcohols and amines. Furthermore, tandem bis-allylation reactions could be performed by employing tosyl isocyanate and benzylidenemalonitrile as substrates. A particularly interesting mechanistic feature of this reaction is that palladium catalyzes up to three different transformations in each catalytic cycle. Various allylic functionalities, including COOEt, $CONH_2$, $COCH_3$, CN, Ph, and CH_3, are tolerated in the catalytic reactions due to the application of neutral and mild reaction conditions. The substitution reaction occurs with very high regioselectivity at the branched allylic terminus. Moreover, in several reactions, a high stereoselectivity was observed indicating that this new catalytic process has a high potential for stereoselective synthesis. The regioselectivity of the reaction can be explained on the basis of DFT calculations. These studies indicate that the allylic substituent prefers the γ-position of the η^1-allyl moiety of the reaction intermediate.

Introduction

Palladium-catalyzed allylic substitution involving electrophilic reagents represents an attractive synthetic approach for stereo- and regioselective carbon−carbon bond formation.[1] This process may proceed through transformation of electrophilic (η^3-allyl)palladium intermediates into nucleophilic allylmetal species, which subsequently directly reacts with electrophiles (eq 1).[2−8] Another approach is based on generation of bis-allylpalladium intermediates from allyl stannanes[9] followed by the nucleophilic attack of the η^1-allyl moiety[10] on various types of electrophiles (eq 2).[11,12] This catalytic transformation can also be extended to tandem bisallylation reactions using appropriate electrophiles with a mixture of allylstannane and allyl chloride (eq 3).[13−16]



It is a particularly important difference that in the latter processes (eqs 2 and 3) the electrophile reacts directly with the allyl moiety of the bis-allylpalladium complex, while in the former case (eq 1) the highly reactive allyl-metal species attack the electrophile without any assistance of palladium. This mechanistic difference leads to a highly different reactivity and selectivity in catalytic applications.

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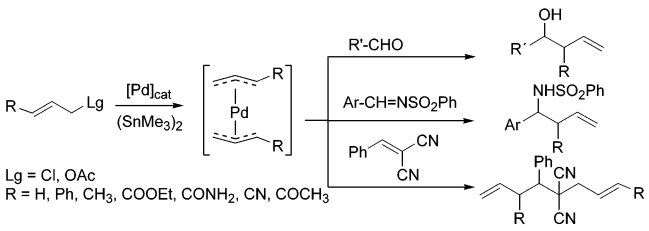
SCHEME 1



A wide range of electrophilic reagents can be employed in the catalytic reactions proceeding through bis-allylpalladium complexes (eqs 2 and 3) including aldehydes, imines,[11,12] isocyanates,[14,16,17] and Michael acceptors.[13,14] Furthermore, this process has a high potential for asymmetric catalysis by using chiral allylpalladium species.[18−20] On the other hand, employment of easily accessible allyl chloride and allyl acetate precursors allows a very broad synthetic scope in palladium-catalyzed processes involving highly reactive allylmetal species (eq 1).[1−8] However, the poor availability of functionalized allyl stannane substrates impose a limitation on the synthetic scope of the bis-allylpalladium (eqs 2 and 3) catalyzed reactions, which in its original form was mainly applied for alkylation of the parent or simple alkyl-substituted allylic precursors. Therefore, it would be highly desirable to conduct the bis-allylpalladium-catalyzed reactions starting from stable and readily available allyl substrates in place of the corresponding allylstannanes.

In a preliminary paper, we have presented a procedure based on the combination of the two above strategies (eqs 1−3) for palladium-catalyzed electrophilic substitution of allylic substrates.[21] This procedure involves palladium-catalyzed formation of the transient allylstannanes from hexamethylditin and allyl chlorides or allyl acetates followed by generation of a bis-allylpalladium intermediate reacting with electrophiles. Here we give a full account of our results on palladium-catalyzed allylic substitution of allyl chlorides and allyl acetates, and we also present an extension of the synthetic scope of this reaction to new types of allylic substrates and electrophiles (Scheme 1). Furthermore, we have studied the effects of the allylic functionalities on the reactivity and selectivity of the reaction as well as the functional group tolerance of the catalytic process.

Results and Discussion

Our results on the substitution of various allyl chloride and acetate substrates (**1**−**11**) with different electrophiles (**12**−**18**) in the presence of a stoichiometric amount of hexamethylditin (Scheme 1) and palladium catalysts (**19**−**21**) are given in Table 1.

Reactions with Aldehyde Electrophiles (Entries 1−9). The catalytic reactions with aldehyde electrophiles (**12**−**15**) proceed under mild conditions typically at 40 °C overnight leading to the corresponding homoallylic alcohol products. The regioselectivity of the reaction is very high. In the presented reactions, only a single regioisomer was formed, which corresponds to the branched allylic product (**24**−**30**). It is important to note that this regiochemistry is in sharp contrast with the regioselectivity of the nucleophilic attack on (η^3-allyl)palladium complexes, which usually takes place at the less substituted allylic terminus.[10,22−25]

The stereoselectivity of the reaction is dependent on the actual allyl chloride and electrophile combination. A precursor with a bulky allylic substituent, such as cinnamyl chloride (**3**), and *p*-nitrobenzaldehyde (**12**) reacts with a high diastereoselectivity (entry 4), and the stereoselectivity is still fairly good in the reaction of **4** with the same electrophile (entry 5). However, as the steric bulk of the allylic substituents decreases (**2**, **5**, and **6**) the stereoselectivity of the reaction is lowered. According to Table 1, the following trend can be envisaged for the influence of the allylic functionalities on the stereoselectivity of the reaction: Ph > COOEt > $COCH_3$ > CN ≈ CH_3. A similar trend was observed for the substituent effects of the aldehyde electrophiles. As one goes from the bulky aryl substituent (entry 5) to vinyl derivatives (entries 6 and 7) the stereoselectivity drops when **4** is used as allylic precursor.

In the above reactions (entries 1−9), 5 mol % of (η^3-allyl)palladium chloro dimer (**19**) was applied as the catalyst source. Accordingly, these reactions proceed under so-called "ligand free" conditions. Employment of monodentate phosphine ligands (such as PPh_3, PBu_3, $P(OPh)_3$) does not hinder the catalytic process; however, we could not find any clear advantage of using these ligands in the above reactions. The catalytic process is somewhat faster in the presence of phosphines; however, the stereoselectivity of the reaction is usually lowered.

Because of the mild reaction conditions, many different allylic functionalities are tolerated in these reactions. The reaction temperature is usually moderate. An exception is the reaction of crotyl chloride (**2**) with **12**, which proceeds at 60 °C. This reaction (entry 3) results in only traces of product (**24**) at 40 °C within 24 h. Application of the low reaction temperature and the strictly neutral reaction conditions are particularly important factors concerning the tolerance of the electron withdrawing allylic functionalities (**4**−**6**). Allylstannanes with electron-withdrawing substituents (which are also the transient intermediets of the reaction) are thermally unstable[26] and easily undergo polymerization reactions. Furthermore, the reaction products with electron-withdrawing allylic functionalities (**26**−**30**) are particularly sensitive to allylic deprotonation, which can lead to rearrangement or decomposition.

The tolerance of the allylic carbonyl functionality (entry 9) is particularly important. This functionality remains intact under the applied reaction conditions indicating

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TABLE 1. Palladium-Catalyzed Allylic Substitution of 1−11 in the Presence of Hexamethylditin

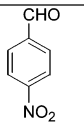
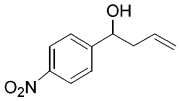
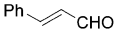
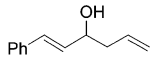
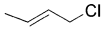
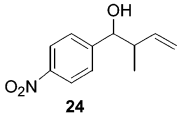
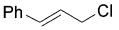
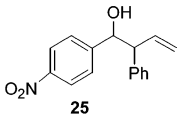
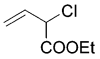
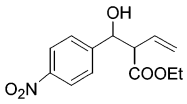
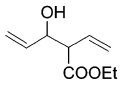
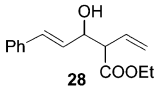
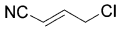
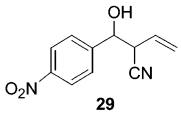
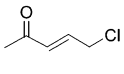
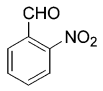
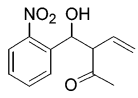
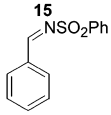
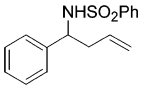
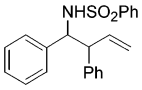
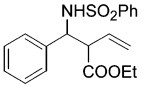
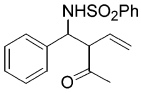
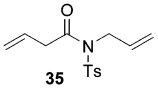
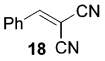
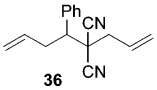
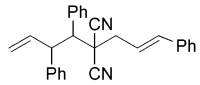
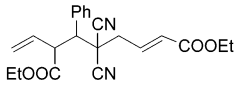
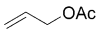
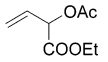
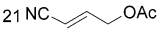
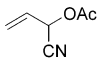
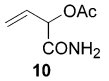
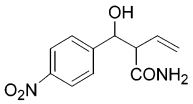
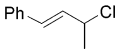
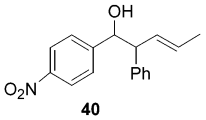
Entry	Allyl	Electrophile	Catalyst[a]	t [^{0}C]	Time [h]	Product	d.r.[b]	Yield[c]
1	 **1**	 **12**	 **19**	40	6	 **22**	-	86
2	**1**	 **13**	**19**	40	26	 **23**	-	67
3	 **2**	**12**	**19**	60	6	 **24**	1:1	55
4	 **3**	**12**	**19**	40	14	 **25**	10:1	87
5	 **4**	**12**	**19**	20	17	 **26**	4:1	88
6	**4**	 **14**	**19**	40	4	 **27**	1:1	60
7	**4**	**13**	**19**	40	15	 **28**	3:2	55
8	 **5**	**12**	**19**	40	14	 **29**	1:1	79
9	 **6**	 **15**	**19**	0	3	 **30**	2:1	57
10	**1**	 **16**	**19**	40	21	 **31**	-	67
11	**3**	**16**	**19**	40	16	 **32**	sd[d]	58
12	**4**	**16**	**19**	40	15	 **33**	sd[d]	57
13	**6**	**16**	**19**	0	30	 **34**	2:1	54
14	**1**	Ts-NCO **17**	**19** + PPh_3 **20**	60	24	 **35**	-	59
15	**1**	 **18**	**20**	40	14	 **36**	-	78

Table 1 (Continued)

Entry	Allyl	Electrophile	Catalyst[a]	t [^{0}C]	Time [h]	Product	d.r.[a]	Yield[c]
16	**3**	**18**	**20**	60	16	 **37**	2:1	60
17	**4**	**18**	$Pd(PPh_3)_4$ **21**	40	15	 **38**	2:1	70
18	 **7**	**12**	**20**	40	17	**22**	-	57
19	**7**	**16**	**20**	60	9	**31**	-	50
20	 **8**	**16**	**20**	40	16	**33**	3:2	40
21	 **9a**	**12**	**21**	40	4	**29**	1:1	58
22	 **9b**	**12**	**21**	40	6	**29**	1:1	61
23	 **10**	**12**	**21**[e]	25	4	 **39**	3:1	56
24	 **11**	**12**	**19**	20	14	 **40**	9:1	59

[a] All reactions were conducted using 5 mol% Pd-catalyst in (unless otherwise stated) THF solvent. [b] Diastereomer ratio. [c] Isolated yield. [d] A single diastereomer was obtained. [e] DMF was used as solvent.

that the catalytic transformation is highly chemoselective, since an aldehyde functionality (**15**) can be manipulated in the presence of an allylic keto group (**6**). Furthermore, it is well-known that in α,β-unsaturated ketons (such as in **6**) there is a strong conjugation between the carbon−carbon and carbon−oxygene double bonds.[27] Disconnection of this conjugation is, of course, energetically costly. However, the reaction of **6** with **15** results in the branched allylic product (**30**) in which this conjugation is broken. This also indicates that there is a pronounced electronic effect in the key intermediate of the reaction, which directs the regioselectivity toward formation of the branched regioisomer. It is interesting to note that **6** readily reacts with **12** as well; however, the reaction product partially decomposes under silica gel chromatography. This finding shows that these multifunctional compounds (such as **30**) are sensitive even for mild acidic conditions, and therefore, the employment of mild, neutral reaction conditions is a prerequisite of their preparation.

A further important aspect of the applied reaction conditions is that the organometallic reagent ($(SnMe_3)_2$) and the allylstannane intermediates contain tin in a high oxidation state, and accordingly, undesired reductive processes can easily be avoided. Therefore, we could use nitrobenzaldehyde (**12** and **15**) as electrophile, in which the nitro functionality is sensitive for reduction by low-valent metals (such as $SnCl_2$, eq 1). Furthermore, under basic conditions nitrobenzaldehydes easily undergo Canizzaro and Tischenko reactions[28] or other decomposition processes, which can be avoided under the above neutral reaction conditions.[29] Other aldehydes, such as cinnamyl aldehyde (**13**) and acrolein (**14**), reacts selectively at the carbonyl functionality, as reduction of the double bond due to attack at the γ-position was not observed (entries 2, 6, and 7).

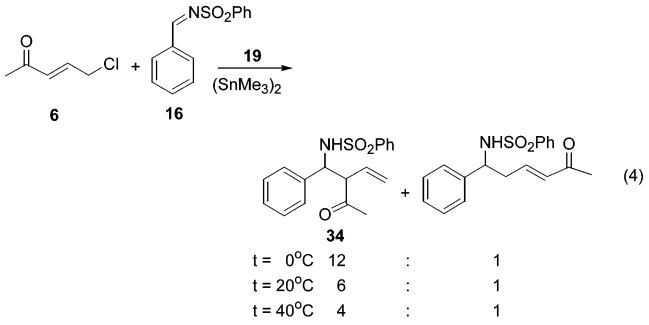
Reactions with Imine Electrophile (Entries 10−13). A great advantage of the allylation reactions proceeding through bis-allylpalladium intermediates is that imines can also be applied as highly reactive electrophiles.[11,12] We have found that *N*-benzylidenebenzenesulfonamide (**16**) reacts readily with allyl chloride (**1**) and its derivatives (**3**, **4**, and **6**) under mild reaction condi-

(27) Heatchcock, C. H. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: New York, 1991; Vol. 2, Chapter 1.5.

(28) Parra, M.; Mestres, R.; Aparicio, D.; Durana, N.; Rubiales, G. *J. Chem. Soc., Perkin Trans. 1* **1989**, 327.

(29) Kisanga, P. B.; Verkade, J. G. *J. Org. Chem.* **2002**, *67*, 426.

tions. The regioselectivity of the reaction is still very high as the phenyl- (**3**) and carbethoxy-substituted (**4**) substrates give exclusively the branched product (entries 11 and 12). However, the reaction with **6** (entry 13) provides **34** and its allylic isomer in a ratio of 12:1 at 0 °C. Raising the reaction temperature leads to a decrease of the regioselectivity, however **34** still remains the major regioisomer (eq 4).



(4)

Comparison of entries 11 and 12 with entries 4 and 5 reveals that the imine electrophile **16** reacts with higher stereoselectivity than aldehyde **12**. Thus, reaction of **3** and **4** with **16** results in a single stereoisomer as product. Highly stereo- and regioselective formation of **33** is of particular interest, since this compound can be used as a building block in synthesis of β-amino acids.[30]

The high-level of functional group tolerance is also a preparatively useful feature of the reaction of **3**, **4**, and **6** with imine **16**. Similarly to the corresponding reaction with aldehyde **15** (entry 9) the allylic keto functionality is not affected in the reaction of **6** with **16** (entry 13) leading to an N-protected amino ketone as a product.

Tandem Bis-allylation Reactions (Entries 14−17). As mentioned above (eq 3), bis-allylpalladium intermediates display a unique ambiphilic reactivity under catalytic conditions.[13−16] Yamamoto and co-workers[13] have shown that this reaction proceeds through an initial *electrophilic* attack on one of the allyl moieties of the bis-allylpalladium intermediate followed by a *nucleophilic* attack on the mono-allylpalladium intermediate of the reaction.

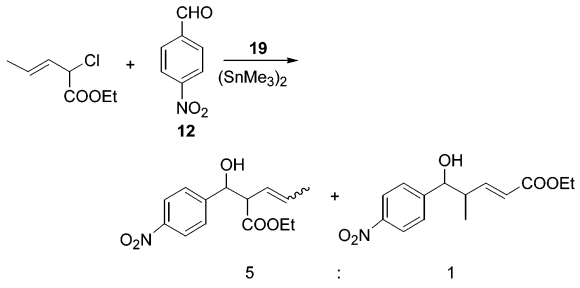
In previous applications, this reaction was performed by employing a 1:1 mixture of the allylstannane and allyl chloride components. However, using $(SnMe_3)_2$ as co-reactant, bis-allylation of tosyl isocyanate (**17**) and benzylidenemalonitrile (**18**) can be performed with allyl chloride alone (entries 14 and 15). Allyl-substituted derivatives **3** and **4** were reacted with **18** (entries 16 and 17), providing a single regioisomer (**37** and **38**, respectively) out of the four possible ones. The structure of these regioisomers (**37** and **38**) clearly demonstrates the contrasting regioselectivity of the initial electrophilic attack and the subsequent nucleophilic attack. The phenyl-substituted electrophilic carbon in **18** is attached to the *branched* allylic position of the substrate (**3** and **4**), while the nucleophlic dinitrile substituted carbon in **18** is bound to the *unsubstituted* allylic terminus of **3** and **4**. Thus, starting from a particular chloride precursor the two subsequent allylation processes occur with opposite regioselection providing a single regioisomer.

In this tandem allylation reaction, we used **19** together with 5 mol % of PPh_3 as cocatalyst (this catalyst system is denoted as **20**, entries 14−16) or $Pd(PPh_3)_4$ (**21**, entry 17). Without phosphine cocatalyst, the double allylation process does not occur. The reaction with **4** proceeds under mild conditions; however, the reaction with **1** and **3** requires relatively high reaction temperature (60 °C) and elongated reaction time (24 h). The phosphine cocatalyst is probably necessary for the activation of mono-allylpalladium intermediate in the nuclephilic attack of the reaction. This nucleophilic attack may also require high temperature under the applied reaction conditions.

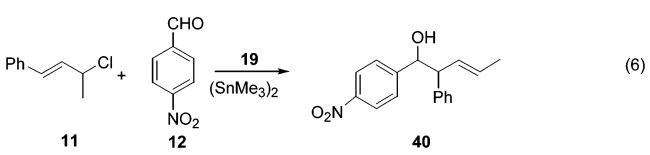
Allyl Acetates as Substrates (Entries 18−23). Allyl acetates react with aldehyde (**12**) and imine (**16**) electrophiles under mild conditions similarly to the allyl chloride precursors. The high regioselectivity of the reaction is maintained (entries 20−23) providing the branched allylic products. However, the stereoselectivity of the reactions and the isolated yields are usually lower with allyl acetate precursors than with allyl chlorides. For example, allyl chloride **4** reacts with imine **16** providing a single diastereomer of **33** (entry 12), while the corresponding reaction with the allyl acetate precursor **(8)** provides the same diastereomer as a major product with poor stereoselectivity (entry 20). On the other hand, substrate **10** with allylic amide functionality is formed with a fairly high stereoselectivity (entry 23). It is also interesting to note that in this reaction the amide functionality remains intact.

For allyl acetate substrates, it was necessary to use phosphine cocatalyst (**20** and **21**) in the reaction. In the absence of phosphine, colloidal palladium(0) was precipitated on addition of $(SnMe_3)_2$. As mentioned above, use of phosphine cocatalyst usually leads to lowering of the diastereoselectivity, which may explain the fact that the reaction with acetates proceeds with a low stereoselectivity.

Reactions with Disubstituted Allylic Precursors. We have also studied the selectivity of the electrophilic attack in the presence of two different allylic substituents. The catalytic reaction with the allyl chloride substrate functionalized with a methyl and a carbethoxy functionality at the two different allylic terminus leads to a complicated reaction mixture involving the two possible regioisomers and their diastereomers (eq 5).



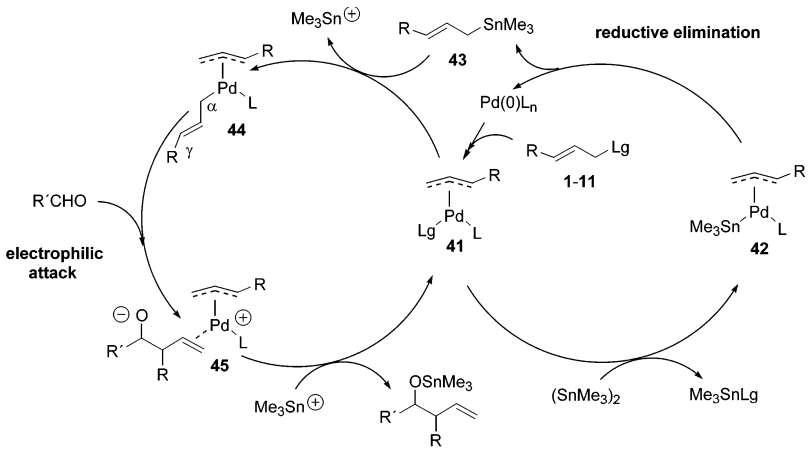
(5)



(6)

(30) Ruano, J. L. G.; Fernández, I.; Catalina, M. d. P.; Hermoso, J. A.; Sanz-Aparicio, J.; Martínez-Ripoll, M. *J. Org. Chem.* **1998**, *63*, 7157.

SCHEME 2

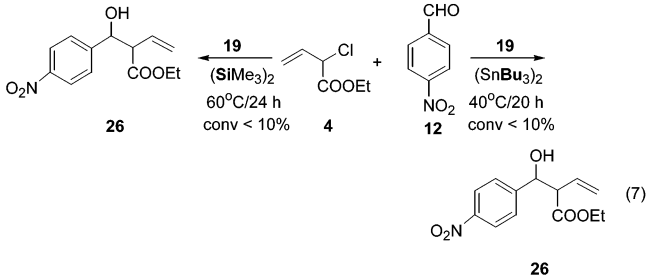


The major regioisomer was formed by substitution at the carbethoxy-functionalized carbon atom. In the reaction mixture, both the cis and the trans form of this product could be observed. However, when the carbethoxy group was exchanged to the bulkier phenyl functionality, the reaction gave only one regioisomer with high stereoselectivity, and the double bond was formed with trans selectivity (eq 6, entry 24). Comparison of these two processes (eqs 5 and 6) reveals that increase of the steric bulk of one of the allylic substituents increase the regiopreference toward the more hindered allylic terminus. This type of regioselectivity is also the opposite of that observed in palladium-catalyzed nucleophilic substitution reactions.[31]

Mechanistic Considerations. The catalytic process can be divided into two main cycles. The first cycle provides the transient allylstannane species, and the second cycle incorporates formation and reaction of the bis-allylpalladium intermediate (Scheme 2). In the catalytic reactions we have employed hexamethylditin and allyl chlorides/acetates for formation of the transient allylstannes. This reaction using simple allylic substrates (such as **1**, **3**, and **7**) was first reported by Bumagin and Beletskaya.[32]

Formation of the transient allylstannane is initiated by oxidative addition of the allylic substrate to the palladium(0) catalyst (**41**) followed by transmetalation with $(SnMe_3)_2$ to form **42**. This process is probably affected by the leaving group of the allylic substrate. In the case of allyl chlorides, intermediate complexes **41** and **42** are stabilized by chloride coordination. However, when allyl acetates are used as substrates these intermediates are probably unstable, which is indicated by precipitation of palladium-black immediately after addition of $(SnMe_3)_2$ to the corresponding reaction mixture. We have found that precipitation of amorphous palladium(0) can be avoided by addition of at least 5 mol % PPh_3 cocatalyst, which probably thermodynamically stabilizes **41** and **42**. A similar behavior has been reported for the allylpalladium intermediates formed in palladium-catalyzed synthesis of allyl silanes from allyl acetates and $(SiMe_3)_2$.[33,34] It was shown[33] that in this silylation process the silyl group coordinates to palladium followed by *cis*-migration to the η^3-allyl moiety. Formation of the allylstannane product **43** from **42** may proceed by the same mechanism.

Schwartz and Yamamoto have shown[9,12] that allylstannanes (e.g., **43**) undergo transmetalation with (η^3-allyl)palladium complexes, such as **41**. This transmetalation providing the bis-allylpalladium intermediate is a crucial reaction step, which is influenced by the steric and electronic properties of the stannane leaving group as well as the substituent effects of the allylic functionalities. The easy cleavage of the C−Sn bond can be ascribed to two important factors: the relatively low bond dissociation energy; and the small size of the $SnMe_3$ leaving group. When the electrophilic substitution of allyl chloride **4** (entry 5) was attempted using $(SnBu_3)_2$ or $(SiMe_3)_2$ in place of $(SnMe_3)_2$ a very slow reaction with a low conversion occurred (eq 7). The slow reaction is probably due to the more sluggish transmetalation by the transient tributyl allyl stannyl and trimethylsilyl allyl species. Use of mild reaction conditions allowed by aplication of $(SnMe_3)_2$ is particularly important, since employment of high temperature and elongated reaction time leads to lowering of the selectivity and decomposition of the reaction products.



Electron-withdrawing allylic substituents (such as CN, COOEt, $COCH_3$, and $CONH_2$) are expected to facilitate the transmetalation by stabilizing the transient carbanion species developed by heterolytic cleavage of the C−Sn bond. For example, compound **6** bearing an allylic $COCH_3$ substituent reacts with electrophiles **15** and **16** at 0 °C (entries 9 and 13). The low reaction temperature allowed

(31) Hayashi, T.; Yamamoto, A.; Hagihara, T. *J. Am. Chem. Soc.* **1986**, *51*, 723.
(32) Bumagin, N. A.; Kasatkin, A. N.; Beletskaya, I. P. *Izv. Akad. Nauk SSSR, Ser. Khim.* (*Engl. Transl.*) **1984**, 636.
(33) Tsuji, Y.; Funato, M.; Ozawa, M.; Ogiyama, H.; Kajita, S.; Kawamura, T. *J. Org. Chem.* **1996**, *61*, 5779.
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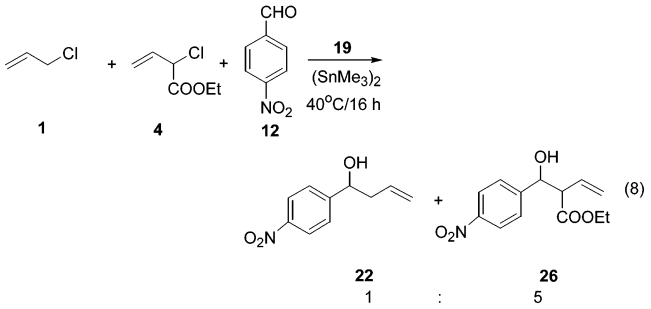
by the facile transmetalation is important to obtain a high regioselectivity in reaction of **6** with **16** (eq 4). On the other hand, electron-supplying groups, such as CH_3 (**2**), raise the activation barrier for transmetalation, which explains the high reaction temperature (60 °C) required in the catalytic substitution (entry 3).

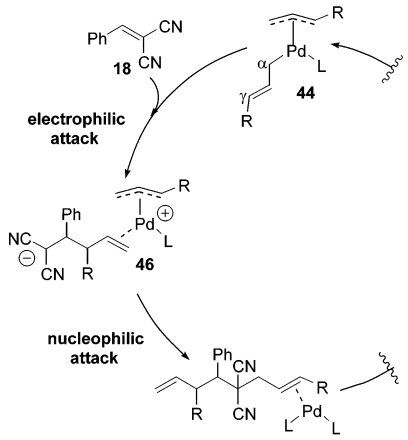
The acceleration effect of the electron-withdrawing substituents could also be demonstrated by competitive substitution reactions (eq 8). When a 1:1 mixture of allyl chloride (**1**) and its carbethoxy-substituted derivative (**4**) was reacted with **12**, a 1:5 mixture of the corresponding products was obtained, indicating that the substitution reaction of **4** is about five times as fast as the substitution of the parent compound (**1**).



The bis-allylpalladium complex formed (**44**) in the transmetalation step may exist in different isomeric forms (vide infra). It has been shown that bis-allylpalladium complexes readily react with electrophiles.[11,35] We have previously studied the mechanism of the electrophilic attack on bis-allylpalladium complexes.[36] These studies have revealed that the electrophilic attack takes place at the γ-position of the η^1-moiety of the complex (**44**) with a low activation barrier. The η^3-coordinated allyl moiety does not participate directly in the electrophilic attack, and therefore it can be considered as a π-donor spectator ligand. The electrophilic attack on **44** is probably the most important step of the entire catalytic cycle since this step determines the regio- and stereoselectivity of the catalytic process (*vide supra*). Electrophilic attack with aldehyde (**12**−**15**) and imine (**16**) electrophiles provides **45**, which after decomplexation gives the final reaction product (Scheme 2). In the case of the reaction with ambiphilic reagents (**17** and **18**) the electrophilic attack gives intermediate **46** (Scheme 3), which subsequently undergoes nucleophilic attack (cf. eq 3) and after dissociation provides the final product.

However, it should also be mentioned that under the applied reaction conditions the electrophilic attack on bis-allylpalladium complexes may compete with other reactions. For example, bis-allylpalladium complexes may undergo allyl-allyl (Stille) coupling, which is facilitated by addition of phosphine ligands.[37] According to recent mechanistic studies, the allyl−allyl coupling proceeds through η^1,η^1-coordinated complexes.[38] Comparison of the reactivity of the η^1,η^1-coordinated complexes toward

SCHEME 3



allyl−allyl coupling[38] with the reactivity of η^1,η^3-coordinated complexes toward electrophilic attack[36] reveals that the latter process requires somewhat lower activation energy. The allyl−allyl coupling in the above reactions (Table 1) can be avoided by a proper choice of the reaction conditions: employment of low phosphine concentration or, if it is possible, to conduct the reactions under phosphine free conditions[37] and by use of relatively reactive electrophiles.

Another problem is that bis-allylpalladium complexes easily undergo protonation by water.[39] Therefore, moisture must be strictly excluded from the reactions. We found that the protonation reaction particularly easily occurs for allylic substrates with electron withdrawing functionality (**4**−**6** and **8**−**10**). This side reaction resulting in allyl cyanide, 3-butenoic acid ethylester or amide as byproducts lowers the yield for the corresponding substitution reactions. The protonations can be largely avoided by using of carefully dried solvents in combination with addition of 4 Å molecular sieves.

Development of the Regioselectivity. As mentioned above, the discussed electrophilic allylic substitution and the palladium-catalyzed nucleophilic allylic substitution reaction are regiocomplementary. The opposite regioselectivity is due to the different reaction mechanism of the allylation process. The nucleophilic attack takes place at the terminal position of the η^3-allyl moiety,[40−42] while the electrophilic attack takes place at the γ-position of the η^1-allyl moiety.[15,36] Therefore, the structure and stability of the substituted η^1,η^3-bis-allylpalladium complexes has a great influence on the regioselectivity of the latter process.[15,36] To study the substituent effects on the stability of the isomeric η^1,η^3-bis-allylpalladium species we carried out density functional calculations at the B3PW91/LANL2DZ(P) level of theory (Figure 1).

We chose complexes **47** and **48** as model systems, in which both allyl moieties are substituted with phenyl groups. These types of complexes occur as reaction intermediates in case of using cinnamyl chloride (**3**) as allylic precursor (entries 4, 11, and 16). In the model calcula-

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(39) Jolly, P. W. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 283.
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(42) Branchadell, V.; Moreno-Mañas, M.; Pajuelo, F.; Pleixats, R. *Organometallics* **1999**, *18*, 4934.

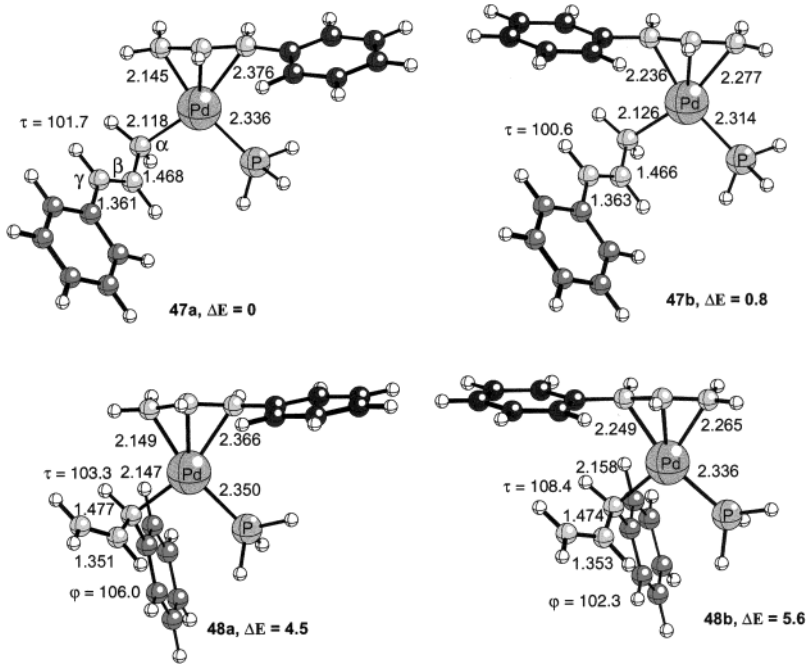

FIGURE 1. B3PW91/LANL2DZ(P) geometries and relative energies for η^1,η^3-bis-allylpalladium complexes (bond lengths in Å, dihedral angles in deg, and energies in kcal mol^{-1}).

tions we employed phosphine ligand to model PPh_3 which is used as ancillary ligand in the experimental studies (entry 16). DFT calculations on the four isomeric η^1,η^3-bis-allylpalladium complexes clearly show that the most stable form bears the phenyl substituent at the γ-position of the η^1-allyl moiety (**47a**), while the other phenyl substituent is located at the *trans*-η^3-allyl carbon. Complexes with α-phenyl substituent at the η^1-allyl moiety (**48a**,**b**) have much higher (4−6 kcal mol^{-1}) relative energy. Considering that the γ-phenyl-substituted form (**47a**) is the most stable one, and that the electrophilic attack occurs at γ-carbon atom of the η^1-allyl moiety, this model predicts the formation of the branched allylic product in agreement with the experimental findings. Formation of the unbranched regioisomer should proceed through the highly unstable α-substituted complexes **48a**,**b**.

The η^1-moiety of the complexes shows some interesting structural features. The $C_\alpha-C_\beta$ bond is shorter (1.46−1.48 Å) than an ordinary C−C single bond, and the $C_\beta-C_\gamma$ bond (1.35−1.36 Å) is somewhat longer than a usual C=C double bond. Furthermore, the $Pd-C_\alpha$ and $C_\beta-C_\gamma$ bonds are closely orthogonal (τ = 100−108°). All these structural features indicate the presence of hyperconjugative interactions between the $d_\sigma(Pd-C_\alpha)$ and $\pi^*(C_\beta-C_\gamma)$ molecular orbitals.[15,36,43] This electronic interaction greatly facilitates electrophilic attack at the γ-carbon of the η^1-moiety. The η^1-moiety exerts a considerable trans influence on the η^3-moiety elongating the Pd−C bond (2.27−2.38 Å).

The phenyl groups on the η^3-moiety and at the γ-position of the η^1-moiety (**47a**,**b**) are in the plane of the allylic carbons, indicating the presence of π-conjugative electronic interactions. However, in case of α-phenyl substitution (**48a**,**b**) the phenyl group is perpendicular to the plane of the allyl moiety (φ = 102−106°, where φ is defined as CC(Ph)-C_αPd). This also indicates that the α-phenyl group in **48a**,**b** avoids the conjugation with the η^1-allyl moiety to hinder electron transfer from the electron-rich phenyl functionality to the negatively charged metalated α-carbon. Accordingly, the destabilization by the α-phenyl group is due to unfavorable steric and electronic interactions between the allylic substituents and the metal atom. It is interesting to note that in the presence of electron withdrawing α-substituents, at least the electronic interactions are less unfavorable, which can explain the lowering of the regioselectivity at higher reaction temperatures (eq 4). Under phosphine-free conditions, the corresponding electrophiles (**12**−**16**) coordinate to palladium, which probably does not change significantly the above structural and energetic features.

Conclusions

In this study, we have shown that palladium-catalyzed electrophilic substitution of easily available allyl chlorides and acetatates can be achieved in the presence of hexamethylditin. In this one-pot reaction, various electrophiles, such as aldehydes, imines, isocyanates, and Michael acceptors, can be employed to prepare highly functionalized allylic products. These reactions proceed under neutral reaction conditions without addition of external base or Lewis acid cocatalyst. Many allylic functionalities, such as COOEt, $CONH_2$, $COCH_3$, CN, Ph, and CH_3, are tolerated in the catalytic transformations. The substitution reactions of functionalized allylic substrates occur with very high regioselectivity at the branched allylic terminus. This can be explained by the fact that the most stable η^1,η^3-bis-allylpalladium intermediate is substituted at the γ-postition of the η^1-allyl moiety, which is attacked by the electrophile. In several cases, the reaction proceeds with high stereoselectivity, and therefore, this catalytic process has a high potential

(43) Solin, N.; Szabó, K. J. *Organometallics* **2001**, *20*, 5464.

for stereoselective synthesis. A particularly interesting mechanistic feature of the reaction is that palladium catalyzes up to three different reactions in each catalytic cycle.

Experimental Section

Allylic chlorides **4**−**6** and **11** and allylic acetates **8**, **9a**, and **10** were prepared using standard literature procedures.[21,44−48] All solvents used in the reactions were freshly distilled prior to use, and the reactions were conducted under argon atmosphere by employing standard manifold techniques. NMR spectra were recorded in $CDCl_3$ (unless stated otherwise) on Varian spectrometers with ^1H at 300 or 400 MHz and ^{13}C at 75 or 100.5 MHz with $CDCl_3$ ($\delta(^1H) = 7.26$, $\delta(^{13}C) = 77.36$) as internal standard. Mass spectra were recorded on a Finnigan Thermoquest 2000A spectrometer. For column chromatography, Merck silica gel 60 (230−400 mesh) was used. All eluents for silica gel chromatography are given in volume/volume ratios.

General Procedure A. Allylation with Allyl Chlorides. The corresponding electrophile (0.30 mmol) and catalyst **19** was dissolved in THF (3.0 mL) containing 4 Å molecular sieves (0.07 g). After addition of the corresponding allyl chloride (0.36 mmol), the reaction mixture was stirred for 10 min, and then $(SnMe_3)_2$ (0.118 g, 0.36 mmol) was added. This reaction mixture was stirred for the alloted times and temperatures (Table 1). After evaporation of the solvent, the crude product was purified by silica gel chromatography.

1-(4-Nitrophenyl)-3-buten-1-ol (22). This compound was obtained by general procedure A. The NMR spectrum is identical with that reported in the literature.[49]

1-Phenylhex-1,5-dien-3-ol (23). This compound was obtained by general procedure A. The NMR spectrum is identical with that reported in the literature.[50]

1-(4-Nitrophenyl)-2-methylbut-3-en-1-ol (24). This compound was obtained by general procedure A. The NMR spectrum is identical with that reported in the literature.[51]

1-(4-Nitrophenyl)-2-phenylbut-3-en-1-ol (25). The product obtained by procedure A was purified by silica gel chromatography using pentane/ethyl acetate (3:1) as eluent giving a mixture of diastereomers in a ratio of 10:1. NMR data given for the major diastereomer. ^1H NMR: δ 8.06−8.02 (m, 2H), 7.30−7.18 (m, 5H), 7.06−7.02 (m, 2H), 6.23 (ddd, 17.0 Hz, 10.1 Hz, 9.1 Hz, 1H), 5.32 (d, 10.1 Hz, 1H), 5.27 (d, 17.0 Hz, 1H), 4.93 (dd, 7.8 Hz, 2.3 Hz, 1H), 3.48 (bt, 8.5 Hz, 1H), 2.48 (t, 2.3 Hz, 1H). ^{13}C NMR: δ 149.5, 139.8, 137.2, 129.1, 128.5, 127.8, 127.5, 123.4, 119.9, 76.7, 59.9. On the basis of comparison of the NMR data with literature values[52] given for closely similar compounds, this major diastereomer is identified as the anti isomer. Anal. Calcd for $C_{16}H_{15}NO_3$: C, 71.36; H, 5.61; N, 5.20. Found: C, 71.27; H, 5.68; N, 5.09.

Ethyl 2-(Hydroxy(4-nitrophenyl)methyl)but-3-enoate (26). The product obtained by procedure A was purified by silica gel chromatography using pentane/ethyl acetate (4:1) as eluent giving a mixture of diastereomers in a ratio of 4:1. Diastereomer A. ^1H NMR: δ 8.18−8.14 (m, 2H), 7.52−7.46 (m, 2H), 5.87 (ddd, 17.4 Hz, 10.2 Hz, 9.0 Hz, 1H), 5.23 (dd, 10.2 Hz, 1.0 Hz, 1H), 5.16 (dd, 5.0 Hz, 2.6 Hz, 1H), 5.07 (dt, 17.4 Hz, 1.0 Hz, 1H), 4.11 (q, 7.1 Hz, 2H), 3.46 (d, 2.6 Hz, 1H), 3.28 (dd, 9.0 Hz, 5.0 Hz, 1H), 1.17 (t, 7.1 Hz, 3H). Diastereomer B. ^1H NMR: δ 8.18−8.14 (m, 2H), 7.52−7.46 (m, 2H), 5.70 (ddd, 17.2 Hz, 10.3 Hz, 8.6 Hz, 1H), 5.12 (d, 10.3 Hz, 1H), 4.99−5.05 (m, 2H), 4.15 (q, 7.1 Hz, 2H), 3.50 (d, 5.5 Hz, 1H), 3.36 (bt, 8.5 Hz, 1H), 1.21 (t, 7.1 Hz, 3H). ^{13}C NMR for diastereomers A and B: δ 172.7, 148.8, 148.3, 147.8, 147.7, 131.7, 130.7, 127.8, 127.6, 123.7, 123.7, 121.7, 120.7, 74.5, 73.1, 61.7, 58.0, 57.8, 14.3, 14.3. MS (EI): *m*/*z* (rel int) 265 (M^+, 2), 248 (6), 152 (18), 114 (46), 86 (100). Anal. Calcd for $C_{13}H_{15}NO_5$: C, 58.86; H, 5.70, N, 5.28. Found: C, 58.71; H, 5.89; N, 5.14.

3-Hydroxy-2-vinylpent-4-enoic Acid Ethyl Ester (27). This compound was obtained by general procedure A. The NMR spectrum is identical with that reported in the literature.[53]

Ethyl (*E*)-3-Hydroxy-5-phenyl-2-vinylpent-4-enoate (28). The product obtained by procedure A was purified by silica gel chromatography using pentane/ethyl acetate (5:1) as eluent giving a mixture of diastereomers in a ratio of 3:2. Diastereomer A. ^1H NMR: δ 7.39−7.35 (m, 2H), 7.34−7.29 (m, 2H), 7.27−7.22 (m, 1H), 6.65 (d, 15.9 Hz, 1H), 6.20 (dd, 15.9 Hz, 6.4 Hz, 1H), 5.88 (ddd, 17.4 Hz, 10.0 Hz, 8.9 Hz, 1H), 5.35−5.24 (m, 2H), 4.61−4.54 (m, 1H), 4.21 (q, 7.1 Hz, 2H), 3.29−3.23 (m, 1H), 2.69 (d, 6.4 Hz, 1H), 1.27 (t, 7.1 Hz, 3H). Diastereomer B. ^1H NMR: δ δ 7.39−7.35 (m, 2H), 7.34−7.29 (m, 2H), 7.27−7.22 (m, 1H), 6.65 (d, 15.9 Hz, 1H), 6.19 (dd, 15.9 Hz, 6.6 Hz, 1H), 5.98 (ddd, 17.1 Hz, 10.2 Hz, 9.0 Hz, 1H), 5.35−5.24 (m, 2H), 4.61−4.54 (m, 1H), 4.17 (q, 7.1 Hz, 2H), 3.29−3.23 (m, 1H), 2.73 (d, 3.7 Hz, 1H), 1.24 (t, 7.1 Hz, 3H). ^{13}C NMR for diastereomers A and B: δ 172.9, 172.8, 136.8, 136.8, 132.6, 132.5, 132.2, 132.1, 129.2, 128.9, 128.9, 128.5, 128.2, 126.9, 126.9, 120.8, 120.1, 73.5, 73.2, 61.4, 57.0, 56.9, 14.5. MS (EI): *m*/*z* (rel int) 246 (M^+, 1), 228 (7), 202 (24), 133 (22).

1-(Hydroxy(4-nitrophenyl)methyl)allylcyanide (29). The product obtained by procedure A was purified by silica gel chromatography using pentane/ethyl acetate (7:1) as eluent giving a mixture of diastereomers in a ratio of 1:1. ^1H NMR: δ 8.29−8.25 (m, 2H), 7.63−7.59 (m, 2H), 5.78−5.68 (m, 1H), 5.59−5.42 (m, 2H), 5.06−5.00 (m, 1H), 3.69−3.64 (m, 1H), 2.74−2.47 (bs, 1H). ^{13}C NMR: δ 148.3, 146.7, 146.5, 128.2, 127.9, 127.7, 127.6, 124.1, 124.0, 122.4, 122.2, 117.6, 117.3, 73.4, 73.3, 44.9, 44.4. MS (EI): *m*/*z* (rel int) 218 (M^+, 3), 201 (51), 152 (100), 122 (20), 77 (41).

3-(Hydroxy(2-nitrophenyl)methyl)pent-4-en-2-one (30). The product obtained by procedure A was purified by silica gel chromatography using pentane/ethyl acetate (4:1) as eluent. Using this eluent system the two diastereomers of **30** could be completely separated. Diastereomer A. ^1H NMR: δ 8.00−7.97 (m, 1H), 7.78−7.74 (m, 1H), 7.64−7.59 (m, 1H), 7.44−7.39 (m, 1H), 5.89 (ddd, 17.2 Hz, 10.1 Hz, 9.6 Hz, 1H), 5.78 (d, 2.0 Hz, 1H), 5.25 (dd, 10.1 Hz, 1.3 Hz, 1H), 4.97 (d, 17.2 Hz, 1H), 3.81 (bs, 1H), 3.66 (dd, 9.6 Hz, 2.0 Hz, 1H), 2.27 (s, 3H). ^{13}C NMR: δ 211.2, 147.3, 136.9, 133.5, 130.3, 130.2, 128.5, 124.8, 122.9, 68.6, 62.2, 29.6. Diastereomer B. ^1H NMR: 7.90−7.87 (m, 1H), 7.72−7.68 (m, 1H), 7.65−7.60 (m, 1H), 7.45−7.40 (m, 1H), 5.72 (ddd, 17.1 Hz, 10.1 Hz, 9.6 Hz, 1H), 5.66 (dd, 7.2 Hz, 5.4 Hz, 1H), 5.15 (dd, 10.1 Hz, 1.2 Hz, 1H), 5.09 (d, 17.1 Hz, 1H), 3.75 (bd, 5.4 Hz, 1H), 3.64 (dd, 9.6 Hz, 7.2 Hz, 1H), 2.17 (s, 3H). ^{13}C NMR: δ 210.1, 137.1, 133.6, 132.1, 129.4, 128.9, 124.7, 121.6, 70.6, 64.3, 30.7.

***N*-(1-Phenyl-3-butenyl)benzenesulfonamide (31).** This compound was obtained by general procedure A. The NMR spectrum is identical with that reported in the literature.[54]

***N*-(1,2-Diphenylbut-3-enyl)benzenesulfonamide (32).** The product obtained by procedure A was purified by silica gel chromatography using pentane/diethyl ether (2:1) as eluent yielding a single diastereomer. ^1H NMR: δ 7.51−7.47 (m, 2H),

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7.42−7.37 (m, 1H), 7.25−7.22 (m, 5H), 7.13−7.06 (m, 3H), 6.99−6.95 (m, 2H), 6.92−6.88 (m, 2H), 5.79 (ddd, 17.0 Hz, 10.2 Hz, 8.3 Hz, 1H), 5.00 (d, 10.2 Hz, 1H), 4.98 (d, 7.4 Hz, 1H), 4.88 (dt, 17.0 Hz, 1.3 Hz, 1H), 4.59 (dd, 7.4 Hz, 6.7 Hz, 1H), 3.55 (bt, 8.0 Hz, 1H). ^{13}C NMR: δ 140.4, 139.3, 138.5, 136.7, 132.4, 129.1, 128.9, 128.7, 128.2, 128.1, 127.7, 127.6, 127.3, 118.5, 62.0, 56.8.

Ethyl 2-((Phenyl(phenysulfonyl)amino)methyl)but-3-enoate (33). The product obtained by procedure A was purified by silica gel chromatography using pentane/ethyl acetate (4:1) as eluent providing a single diastereomer. ^{1}H NMR: δ 7.65−7.61 (m, 2H), 7.40−7.36 (m, 1H), 7.29−7.23 (m, 2H), 7.13−7.09 (m, 3H), 7.04−7.00 (m, 2H), 6.24 (d, 9.4 Hz, 1H), 5.73 (ddd, 17.5 Hz, 10.0 Hz, 8.5 Hz, 1H), 5.10 (m, 2H), 4.77 (dd, 9.4 Hz, 6.5 Hz, 1H), 4.06 (q, 7.1 Hz, 2H), 3.41 (dd, 8.5 Hz, 6.5 Hz, 1H), 1.15 (t, 7.1 Hz, 3H). ^{13}C NMR: δ 172.0, 141.0, 138.2, 132.4, 132.2, 128.8, 128.6, 127.9, 127.2, 127.0, 120.4, 61.5, 59.6, 56.6, 14.3. MS (EI): *m*/*z* (rel int) 359 (M^+, 4), 246 (100), 141 (43), 77 (45). Anal. Calcd for $C_{19}H_{21}NO_4S$: C, 63.49; H, 5.89; N, 3.90. Found: C, 63.38; H, 5.81; N, 3.79.

***N*-(2-Acetyl-1-phenylbut-3-enyl)benzenesulfonamide (34).** This product was obtained by a slight modification of procedure A involving an additional portion of hexamethylditin (0.03 g, 0.1 mmol) which was added to the reaction mixture after 24 h. The product was purified by silica gel chromatography using pentane/ethyl acetate (7:1) as eluent giving a mixture of diastereomers in a ratio of 2:1. Diastereomer A. ^{1}H NMR: δ 7.64−7.58 (m, 2H), 7.44−7.35 (m,1H), 7.32−7.22 (m, 2H), 7.13−6.98 (m, 5H), 6.35 (d, 9.3 Hz, 1H), 5.71−5.59 (m, 1H), 5.14 (d, 16.3 Hz, 1H), 5.13 (d, 11.1 Hz, 1H), 4.73 (dd, 9.3 Hz, 6.5 Hz, 1H), 3.56 (dd, 8.9 Hz, 6.5 Hz, 1H), 2.03 (s, 3H). Diastereomer B. ^{1}H NMR: δ 7.64−7.58 (m, 2H), 7.44−7.35 (m,-1H), 7.32−7.22 (m, 2H), 7.13−6.98 (m, 5H), 6.35 (d, 9.3 Hz, 1H), 5.71−5.59 (m, 1H), 5.28 (d, 9.6 Hz, 1H), 5.27 (d, 17.1 Hz, 1H), 4.64 (dd, 9.3 Hz, 7.1 Hz, 1H), 3.51 (bt, 9.3 Hz, 1H), 1.83 (s, 3H). ^{13}C NMR for diastereomers A and B: δ 208.8, 206.6, 140.9, 140.5, 138.6, 138.4, 133.2, 132.6, 132.4, 132.4, 128.9, 128.9, 128.6, 128.0, 127.8, 127.4, 127.2, 127.2, 122.2, 121.2, 64.5, 63.3, 59.6, 58.8, 30.5, 30.3. Anal. Calcd for $C_{18}H_{19}NO_3S$: C, 65.63; H, 5.81; N, 4.25. Found: C, 65.40; H, 5.88; N, 4.07.

General Procedure B. Tandem Bis-allylation Reactions. This procedure is identical with procedure A with the exception that triphenylphosphine (5 mol %) was used as a cocatalyst together with **19** (this catalyst combination is referred as **20**) and that 0.66 mmol of the corresponding allyl chloride was employed.

***N*-But-3-enoyl(*N*-prop-2-en)tolylsulfonamide (35).** This compound was prepared by general procedure B in a sealed vessel. The NMR spectrum is identical with that reported in the literature.[14,16]

4,4-Dicyano-5-phenyl-1,7-octadiene (36). This compound was obtained by general procedure B. The NMR spectrum is identical with that reported in the literature.[13]

4,4-Dicyano-1,5,6-triphenyl-1,7-octadiene (37). The product obtained by procedure B was purified by silica gel chromatography using pentane/ethyl acetate (10:1) as eluent. Using this eluent system, the two diastereomers of **37** could be completely separated. Diastereomer A. ^{1}H NMR: δ 7.44−6.97 (m, 15H), 6.44 (d, 15.7 Hz, 1H), 6.32 (dt, 17.0 Hz, 10.0 Hz, 1H), 6.18 (dt, 15.7 Hz, 7.4 Hz, 1H), 5.66 (d, 17.0 Hz, 1H), 5.36 (dd, 10.0 Hz, 1.3 Hz, 1H), 4.10 (t, 11.2 Hz, 1H), 3.48 (d, 11.2 Hz, 1H), 2.55 (ddd, 14.0 Hz, 7.6 Hz, 1.2 Hz, 1H), 2.46 (ddd, 14.0 Hz, 7.1 Hz, 1.2 Hz, 1H). ^{13}C NMR: δ 141.2, 138.6, 138.0, 136.3, 135.9, 129.2, 129.0, 128.9, 128.8, 128.6, 127.9, 127.0, 127.0, 120.2, 119.6, 116.8, 115.1, 57.1, 56.2, 42.2, 41.2. Diastereomer B. ^{1}H NMR: δ 7.46−7.27 (m, 15H), 6.36 (dt, 15.6 Hz, 1.1 Hz, 1H), 6.08 (dt, 15.6 Hz, 7.4 Hz, 1H), 5.88 (ddd, 16.8 Hz, 10.2 Hz, 8.9 Hz, 1H), 5.01 (dt, 16.8 Hz, 1.2 Hz, 1H), 4.97 (m, 1H), 4.19 (t, 9.3 Hz, 1H), 3.38 (d, 9.3 Hz, 1H), 2.41 (dt, 7.4 Hz, 1.4 Hz, 2H). ^{13}C NMR: δ 140.8, 138.0, 137.8, 136.2, 135.8, 129.7, 129.5, 129.4, 129.2, 129.0, 128.9, 128.6, 128.4, 119.6, 118.4, 115.3, 114.8, 56.4, 54.1, 42.1, 41.9. MS (EI): *m*/*z* (rel int) 388 (M^+, 10), 361 (4), 297 (8), 207 (9), 117 (100). Anal. Calcd for $C_{28}H_{24}N_2$: C, 86.56; H, 6.23; N, 7.21. Found: C, 86.40; H, 6.39; N, 7.10.

Diethyl 5,5-Dicyano-6-phenyl-7-vinyloct-2-enedioate (38). This compound was obtained by general procedure B except that **21** was employed as catalyst source (5 mol %). The product was purified by silica gel chromatography using pentane/ethyl acetate 7:1 as eluent giving a mixture of diastereomers in a ratio of 2:1. Diastereomer A. ^{1}H NMR: δ 7.41−7.30 (m, 5H), 6.86 (dt, 15.5 Hz, 7.8 Hz, 1H), 5.95 (dt, 15.5 Hz, 1.4 Hz, 1H), 5.57 (dt, 17.0 Hz, 9.9 Hz, 1H), 5.22 (d, 17.0 Hz, 1H), 5.11 (dd, 9.9 Hz, 0.9 Hz, 1H), 4.24−4.16 (m, 4H), 3.96−3.79 (m, 1H), 3.69 (d, 9.2 Hz, 1H), 2.55 (m, 2H), 1.31−1.24 (m, 6H). Diastereomer B. ^{1}H NMR: δ 7.41−7.30 (m, 5H), 6.82 (dt, 15.4 Hz, 7.4 Hz, 1H), 6.06 (dt, 16.7 Hz, 10.0 Hz, 1H), 5.89 (dt, 15.4 Hz, 1.3 Hz, 1H), 5.74 (d, 16.7 Hz, 1H), 5.51 (dd, 10.0 Hz, 1.0 Hz, 1H), 4.24−4.16 (m, 4H), 3.96−3.79 (m, 1H), 3.59 (d, 11.4 Hz, 1H), 2.43 (m, 2H), 1.31−1.24 (m, 6H). ^{13}C NMR for diastereomers A and B: δ 171.7, 170.5, 165.1, 136.9, 136.9, 134.5, 133.3, 132.7, 132.6, 130.2, 129.8, 129.7, 129.5, 129.1, 128.9, 124.2, 121.3, 115.4, 114.4, 114.1, 114.0, 62.3, 61.5, 61.2, 61.2, 57.3, 53.3, 52.3, 52.1, 41.1, 40.5, 40.1, 39.4, 14.5, 14.2, 14.0. MS (EI): *m*/*z* (rel int) 381 ($M^+ + 1$, 6), 307 (30), 261 (36), 157 (43), 129 (100). Anal. Calcd for $C_{22}H_{24}N_2O_4$: C, 69.46; H, 6.36; N, 7.36. Found: C, 69.31; H, 6.39; N, 7.27.

General Procedure C. Allylation with Allyl Acetates. This procedure is identical with procedure A with the exception that 5 mol % of **20** or **21** (Table 1) was used as catalyst. Isolation and identification of the products from entries 18−22 are given above.

2-(Hydroxy(4-nitrophenyl)methyl)but-3-enamide (39). General procedure C was followed using catalyst **21**; however, DMF was used as solvent instead of THF. The product was purified by silica gel chromatography using toluene:methanol 10:1 as eluent giving a mixture of diastereomers in a ratio of 3:1. Diastereomer A. ^{1}H NMR (CD_3OD, ref 3.34 ppm): δ 8.23−8.20 (m, 2H), 7.65−7.59 (m, 2H), 6.06 (ddd, 17.2 Hz, 10.3 Hz, 9.0 Hz, 1H), 5.23 (d, 10.3 Hz, 1H), 5.17 (d, 17.2 Hz, 1H), 5.11 (d, 6.8 Hz, 1H), 3.32 (m, 1H). Diastereomer B. ^{1}H NMR (CD_3-OD, ref 3.34 ppm): δ 8.23−8.20 (m, 2H), 7.65−7.59 (m, 2H), 5.77 (ddd, 17.2 Hz, 10.4 Hz, 9.2 Hz, 1H), 5.05−4.99 (m, 2H), 4.96 (d, 17.2 Hz, 1H), 3.32−3.24 (m, 1H). ^{13}C NMR for diastereomers A and B (CD_3OD, ref 49.86 ppm): δ 178.1, 177.6, 152.6, 152.5, 149.5, 135.9, 135.6, 130.0, 129.7, 125.0, 125.0, 120.9, 120.4, 75.9, 75.3, 61.4, 61.2. MS (EI): *m*/*z* (rel int) 237 ($M^+ + 1$, 5), 223 (18), 205 (16), 149 (100).

(*E*)-1-(4-nitrophenyl)-2-phenylpent-3-en-1-ol (40). The product obtained by general procedure A was purified by silica gel chromatography using pentane/ethyl acetate 5:1 as eluent giving a mixture of diastereomers in a ratio of 9:1. NMR data given for the major diastereomer. ^{1}H NMR: δ 8.07−8.04 (m, 2H), 7.33−7.29 (m, 2H), 7.25−7.19 (m, 3H), 7.09−7.06 (m, 2H), 5.92−5.76 (m, 2H), 4.91 (d, 7.5 Hz, 1H), 3.84 (dd, 9.6 Hz, 7.5 Hz, 1H), 2.50 (bs, 1H), 1.61 (dd, 6.6 Hz, 1.5 Hz, 3H). ^{13}C NMR: δ 149.8, 147.4, 140.6, 129.4, 129.0, 128.6, 128.5, 127.7, 127.3, 123.3, 77.5, 52.5, 13.6. On the basis of comparison of the NMR data with literature values[52] given for closely similar compounds, this major diastereomer is identified as the anti isomer.

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Supporting Information Available: ^{13}C NMR spectra for compounds **25**, **26**, **28**−**30**, **32**−**34**, and **37**−**40** as well as computational details for **47** and **48**. This material is available free of charge via the Internet at http://pubs.acs.org.

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