CHEMISTRY
A EUROPEAN JOURNAL

DOI: 10.1002/chem.200701332

Influences on the Regioselectivity of Palladium-Catalyzed Allylic Alkylations

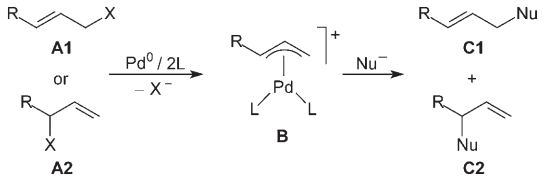
Uli Kazmaier,*[a] Daniel Stolz,[a] Katja Krämer,[a] and Franz L. Zumpe[b]

Abstract: Chelated amino acid ester enolates are excellent nucleophiles for palladium-catalyzed allylic alkylations. These enolates react rapidly at −78 °C and in general without isomerization of π-allyl palladium complexes. Therefore, they are good candidates for mechanistic studies and regioselective reactions. Terminal π-allyl palladium complexes are preferentially attacked at the least hindered position giving rise to linear products, as illustrated with several (*E*)-configured allylic substrates. Under isomerization free conditions the branched products are formed preferentially from the corresponding (*Z*)-allyl substrates. An interesting behavior is observed in the reaction of secondary allylic substrates. Aryl-substituted substrates show a significant memory effect which can be explained by an asymmetric π-allyl complex. For alkyl-substituted substrates a strong dependence of the regioselectivity on the leaving group is observed, which can be explained by different conformations in the ionization step. Under isomerization free conditions the product ratio gives important information about this step.

Keywords: allylation · amino acids · enolates · memory effect · palladium

Introduction

π-Allyl metal complexes play an important role in modern organic synthesis. Among the different metals used, palladium plays a dominant role,[1] and the allylic alkylation, also called the Tsuji–Trost reaction, is by far the most popular application.[2] During the last years with the development of suitable asymmetric ligands, especially asymmetric versions of this protocol became more and more important.[3] π-Allyl palladium complexes are formed from allylic substrates such as **A1** and **A2** via coordination of the alkene towards Pd^0 and subsequent internal nucleophilic attack of the electron-rich Pd at the allylic position (Scheme 1).[4] The π-allyl palladium intermediate **B** formed can be attacked by the nucleophile either at the terminal position (**C1**) or at the internal position (**C2**). In general, attack of the nucleophile occurs at the sterically least hindered position, and therefore the linear product **C1** is the preferred one.[2] According to this simplified model, one should expect the same product distribution, independent of the starting material (**A1** or **A2**) used, as long as the same π-allyl intermediate **B** can be formed. Interestingly, quite often this is not the case, and a substrate dependent product ratio is observed. Depending on the reaction conditions branched substrate **A2** can give a higher ratio of branched product **C2** than the linear substrate **A1**.[5–7] This so-called "memory effect" has intensively be studied, and several explanations were given, depending on the substrates and reaction conditions used.[8–11]



Scheme 1. Simplified mechanism of the Tsuji–Trost reaction.

Because in most cases symmetric nucleophiles such as malonates are used, only the branched product **C2** is of interest for an asymmetric version. Therefore, a lot of efforts have been made to get higher ratios of branched product. Big improvements have been made by Pfaltz et al. They could show, that the regioselectivity of the nucleophilic attack can be influenced by "tuning" the reaction mechanism.[12] If the nucleophile attacks in a S_N2 fashion, attack should occur preferentially at the terminal position (**D**), while reaction via a cationic S_N1 transition state **E** should

[a] Prof. Dr. U. Kazmaier, Dr. D. Stolz, Dipl.-Chem. K. Krämer
Institut für Organische Chemie
Universität des Saarlandes, Im Stadtwald, Geb. C4.2
66041 Saarbrücken (Germany)
Fax: (+49) 681-302-2409
E-mail: u.kazmaier@mx.uni-saarland.de

[b] Dr. F. L. Zumpe
Bayer HealthCare AG, BHC-GDD-CMC-GCD-PR&D
42096 Wuppertal (Germany)

preferentially provide the branched product (Figure 1). Transition state **E** can be favored by using electron-withdrawing groups in the ligand, for example, if phosphines are

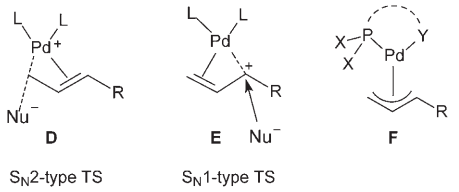
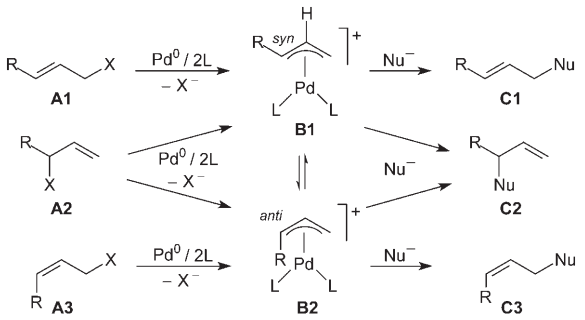


Figure 1. Possible transition states of allylic alkylation.

replaced by phosphites.[13] Based on that, Pfaltz et al. created unsymmetrical chiral ligands such as phosphitoxazolines.[12] Sterical hindrance favors transition state **F** where the substituent R on the allyl fragment is located *trans* to the bulky phosphorus ligand. Nucleophilic attack on the π-allyl system preferentially occurs *trans* to the P atom,[14] giving rise to the branched product with good chirality transfer.

Another important class of memory effects, also observed for unsymmetrical π-allyl groups, is more complex and can be found with achiral ligands as well. It is observed that the product distribution not only depends on the regio- but also the stereochemistry of the starting material.[7] This effect was recently investigated by Norrby et al.[15] Scheme 2 shows



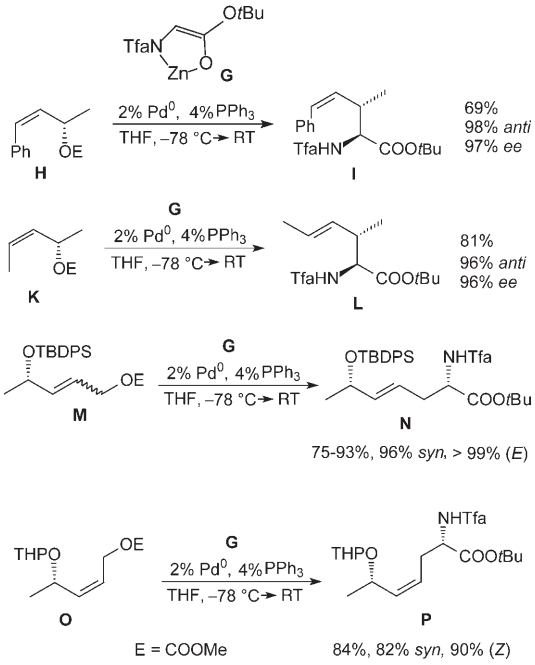
Scheme 2. Detailed mechanism of allylic alkylation

a more detailed mechanism of the allylation using unsymmetrical substrates **A1**–**A3**.

While **A1** on ionization gives rise to the *syn*-complex **B1**, the *anti*-complex **B2** is obtained from *cis*-substrate **A3**.[16] The branched substrate **A2** is able to form both, the *syn* and the *anti* complex, and the ratio depends on the conformation of the substrate in the ionization step. Therefore, a strong influence of the leaving group can be observed in certain cases.[15] Especially for terminal allyl complexes the intermediates **B1** and **B2** can equilibrate rapidly via π–σ–π isomerization.[17] If isomerization is fast compared with the nucleophilic attack, product distribution results from the equilibrium mixture in which the *syn* complex as the thermodynamically favored one is enriched. In this case the product ratio is nearly independent of the allylic substrate used (Scheme 1). On the other hand, if nucleophilic attack is faster than the equilibrium of the intermediates, or at least in the same range, one should observe memory effects based on the different ratio and reactivity of the allyl complexes **B1** and **B2**. Work carried out in the Åkermark group showed, that under certain circumstances isomerization can be slow enough, and pure *syn*- and *anti* complexes can be isolated.[7,18] They found that nucleophilic attack at the *syn*-position is disfavored, and therefore the linear *trans*-substrate **A1** gives predominantly the *trans* configured product **C1**. On the other hand, the *anti*-position is significantly more reactive, and therefore in *anti*-complex **B2** attack of the nucleophile occurs at both positions in a similar ratio. Depending on the substitution pattern, a mixture of branched (**C2**) and *cis* product (**C3**) is obtained.

Finally, the branched substrate should give a result in between that of the *cis* and the *trans* substrate, entirely dependent on the initial ionization preference (*anti* or *syn* complex). Norrby et al. carefully investigated reactions of all three allylic substrates to figure out if only the situation illustrated in Scheme 2 is responsible for the memory effect, or if there is also another contribution, for example, from halides. Halides have two effects on the outcome of the reaction. First, they increase the rate of isomerization,[19] and second, they can coordinate to the palladium giving rise to unsymmetrical π-allyl complexes.[14,20] Based on the strong *trans* effect of the P atom, the phosphine ligand should be located *trans* to the leaving group. Because nucleophilic attack occurs also preferentially *trans* to phosphorous, this *trans* effect can significantly contribute to the memory effect (regioretention).

For some time our group is investigating chelated amino acid ester enolates (**G**) as nucleophiles in palladium catalyzed allylic alkylations (Scheme 3).[21] These enolates react



Scheme 3. Allylic alkylations of chelated enolates (Tfa = trifluoroacetyl).

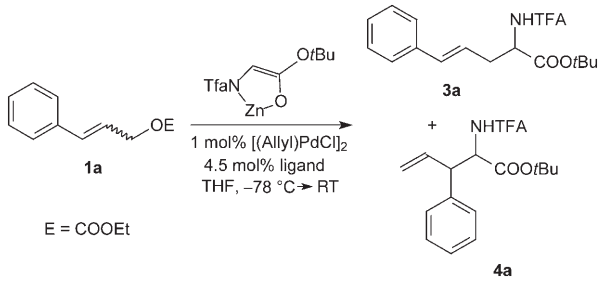
under much milder conditions (already at −78 °C) with π-allyl palladium complexes than the generally used nucleophiles such as malonates. As a result, these were the first *C*-nucleophiles showing no π–σ–π isomerization of complexes obtained from 1,3-disubstituted substrates.[22] For example, if *cis*-configured carbonate **H** was reacted, the substitution product **I** was obtained with perfect conservation of the olefin geometry (full stereoretention). With symmetrically substituted *cis* allyl substrates of type **K**, nucleophilic attack occurs selectively at the more reactive *anti*-position giving rise to **L** with excellent chirality transfer from **K** to **L**. This nicely correlates with the results described by Åkermark et al.[7] Very recently, we could also show that in reactions of chiral substrates **M** the nucleophilic attack on the terminal π-allyl intermediate could be controlled by the stereogenic center in the substrate.[23] With sterically demanding protecting groups the nucleophilic attack slows down and isomerization becomes dominant. Replacing the *tert*-butyldiphenylsilyl (TBDPS) group by a smaller one accelerates nucleophilic attack, and therefore with substrates such as **O** also a high degree of stereoretention was observed.[24]

This clearly indicates that with these enolates even terminal π-allyl–palladium complexes can react without significant isomerization, what makes them good candidates to investigate mechanistical details such as the memory effect. This is especially interesting, because with the terminal π-allyl complexes investigated so far, only the linear substitution products were obtained. From a synthetical point of view it is also important to get a suitable protocol which can provide the branched products. One possibility is to switch to other transition metals such as rhodium, which indeed can give access to branched products with excellent chirality transfer.[25] On the other hand, we were interested to see if we can modify the reaction conditions of the palladium-catalyzed version in such a way, that at least the ratio of the branched product could be increased.

Results and Discussion

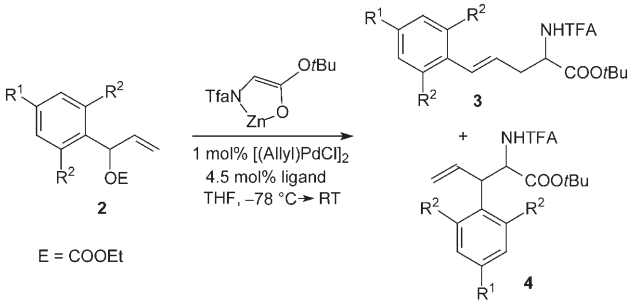
We became interested in this topic during our investigations on the regioselectivity of phenyl-substituted terminal π-allyl palladium complexes. While the cinnamyl carbonate (*E*)-**1a** gave rise to the linear substitution product **3a** as the sole regio- and stereoisomer [>99% *RS*, >99% (*E*)] in excellent yield (Table 1, entry 1), the corresponding *Z* isomer provided a 9:1 mixture of the branched product **4a** and the linear **3a** (entry 2). Surprisingly, (*E*)-configured **3a** was formed nearly exclusively [<1% (*Z*)], although the *anti*-complex had to be formed in the ionisation step. The high ratio of branched product indicates that the nucleophilic attack at the *anti* position of the *anti* complex is very fast—slightly faster than the isomerization (which occurs in part), but much faster than the attack at the terminal position. Therefore, we found only linear product **3a** after the isomerization. In principle, the amount of branched product should increase if the nucleophilic attack becomes faster, while a slower reaction should favor the formation of **3a**, because the intermediate π-allyl complex has more time for isomerization. Therefore, we varied the amount of nucleophile used. And indeed, with an excess of nucleophile (1.5 equiv) not only the yield increased, but also the ratio of branched product. On the other hand, if the allyl substrate was used in excess, significantly more linear product was formed, which nicely supports the mechanistic proposal.

Table 1. Allylic alkylations using linear aryl substituted allylic substrates **1**.



Entry	Substrate	Equiv enolate	Yield [%]	Ratio **3**/**4**	Ratio **4** *anti*/*syn*
1	(*E*)-**1a**	1	89	>99:<1	n.d.
2	(*Z*)-**1a**	1	70	9:91	93:7
3	(*Z*)-**1a**	1.5	93	6:94	92:8
4	(*Z*)-**1a**	0.5	47	20:80	92:8

Table 2. Allylic alkylations via aryl substituted π-allyl complexes.



Entry	Substrate	R^1	R^2	Ligand	Yield [%]	Ratio **3**/**4**	Ratio **4** *anti*/*syn*
1	**2a**	H	H	PPh_3	77	60:40	93:7
2	**2a**	H	H	$P(OEt)_3$	69	60:40	92:8
3	**2a**	H	H	$P(OPh)_3$	60	60:40	89:11
4	**2b**	OMe	H	PPh_3	78	50:50	91:9
5	**2c**	Cl	H	PPh_3	74	93:7	85:15
6	**2d**	H	Cl	PPh_3	56	99:1	n.d.
7	**2a**	H	H	dppe	72	89:11	58:42

With these results at hand, we next focused on reactions of the corresponding branched substrate **2a** (Table 2). Interestingly, **2a** yielded a mixture of linear (**3a**) and branched product **4a** in a 6:4 ratio, whereby the branched product was again formed with a high *anti*/*syn* selectivity what is in good agreement with our previous results (entry 1). And again, the *E* isomer of **3a** was formed exclusively as with (*E*)-con-

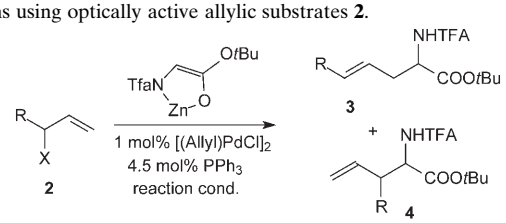
figured linear substrate **1a**. The relatively high amount of **4a** is surprising, because one might not expect, that **2a** is ionising to the *anti* complex, at least not in such a high ratio, and therefore this significant memory effect must have other reasons.

In a comparable study with malonates in the presence of chiral ligands Pfaltz proposed a S_N1-type transition state (**E**, Figure 1) for such phenyl-substituted π-allyl complexes.[12] They reported that an increase in the S_N1 character of the π-allyl intermediate resulted in a higher ratio of branched product, and proposed to favor the S_N1-type substitution by introducing electron-withdrawing groups into the phosphorous ligand. But in principle this should also be true for the linear substrate **1a**, which gave absolutely no branched product under our reaction conditions (contrary to malonates). Therefore, we investigated the influence of the ligands on the outcome of the reaction (Table 2). Replacing the originally used PPh_3 by the more electron-withdrawing phosphites $P(OEt)_3$ (entry 2) and $P(OPh)_3$ (entry 3) had no significant effect, neither on the regio- nor the diastereoselectivity. Only the yield dropped slightly. Obviously, it is not possible to take significant influence on the reaction via ligands. On the other hand, factors able to stabilize a benzylic carbenium ion should have some influence. Therefore, we varied the substitution pattern at the aromatic ring system. Introduction of electron-donating groups should stabilize the S_N1 transition state favoring the branched product, while electron-withdrawing groups should switch the mechanism towards S_N2, providing more linear product. That was exactly what we observed.

The *p*-methoxy derivative **2b** (entry 4) provided a 1:1 regioisomeric mixture with comparable yield and diastereoselectivity as the unsubstituted system. Unfortunately it was not possible to increase this effect via stronger donating groups (such as $R^1=NR_2$ or R^2, $R^2=OMe$) because the corresponding carbonates were not stable and isomerized rapidly to the linear substrates, which were unsuitable for our investigations. On the other hand, introduction of a chloride in *para*-position (**2c**) resulted in a strong preference for the linear product **3c**, while with the 2,6-dichloro derivative **2d** linear **3d** was produced exclusively. In addition to the "S_N1 effect" the chloride ions in solution can also have an effect on the regioselectivity, because they can generate asymmetric π-allyl complexes.[14,20] Starting from allyl substrate **2a** an intermediate can be proposed having only one phosphine ligand *trans* to the leaving group (*trans* effect). If nucleophilic attack is fast and no isomerization occurs, the nucleophile should come in again *trans* to phosphorus at the same position of the original leaving group. To prove the proportion of this "halide effect" to the regioselectivity we carried out the reaction in the presence of bidentate dppe (bisdiphenylphosphinoethane) which should not allow the formation of such an unsymmetric π-allyl complex. And indeed, in this case (Table 1, entry 7) the ratio of branched product dropped to 11%. Probably this is the pure S_N1 effect, while the regioselectivity observed previously was the sum of both effects (S_N1 + halide).

Based on this significant memory effect, we focused on another interesting question: What would happen with optically active allylic substrates? Is it possible to transfer (at least in part) the chiral information into the products? In principle, if ionization and nucleophilic attack is fast, and under consideration of the halide effect, optically active products should be obtained, especially for the branched products. Therefore, we subjected two aromatic, and for comparison also one aliphatic allyl substrate,[26] to our reaction conditions (Table 3). And indeed, an excellent chirality transfer was observed for (*S*)-**2a**, which gave the branched product **4a** with 90% *ee*. In contrast, the enantiomeric excess for the linear product was significantly lower (36% *ee*). Obviously, the memory effect supports the chirality transfer. To increase the selectivity we also carried out the reaction at −70°C (entry 2). In this temperature range one has a good chance to suppress π–σ–π isomerization, at least in part. The yield obtained was comparable to our standard condition (warming up from −78°C to RT), but the selectivity, especially for the linear product was better (61% *ee*). Replacing PPh_3 by phosphites had no effect on the chirality transfer. As a second example we chose the *p*-chlorophenyl derivative (*R*)-**2c**, which gave in the racemic version mainly linear product without significant memory effect. Obviously the halide effect is not operating in this case, or the halide accelerates isomerization.[19] In this case, the chirality transfer was significantly worse. Although the branched side product was obtained with 60% *ee*, the linear product showed only 21% enantiomeric excess. In this case, keeping the reaction at low temperature had no distinct effect. Obviously the degree of chirality transfer correlates with the memory effect. To prove this theory we also investigated the

Table 3. Allylic alkylations using optically active allylic substrates **2**.

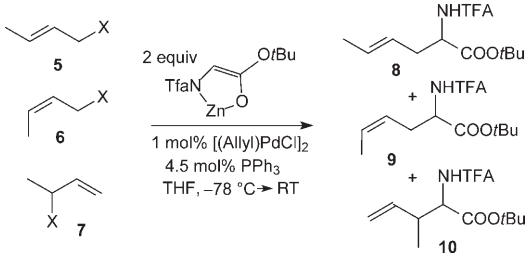


Entry	Substrate	R	X	Reaction conditions	Yield [%]	Ratio **3**/**4**	*ee* **3** [%]	*ee* **4** [%]	Ratio **4** *anti*/*syn*
1	(*S*)-**2a**	Ph	OCOOEt	−78°C→RT, 16 h	77	60:40	36	90	93:7
2	(*S*)-**2a**	Ph	OCOOEt	−70°C, 16 h	70	60:40	61	97	92:8
3	(*R*)-**2c**	*p*-ClPh	OAc	−78°C→RT, 16 h	62	95:5	21	60	78:22
4	(*S*)-**2e**	*i*Bu	OAc	−78°C→RT, 16 h	77	99:1	0	n.d.	n.d.

reaction of aliphatic substrate (*S*)-**2e**. In this case, the memory effect via a S_N1 transition state should not play any role and only the halide effect should be left over. In this case only the linear product was formed in completely racemic form.

This clearly indicates that alkyl- and aryl-substituted substrates behave differently, and therefore we also investigated reactions of substrates **5** to **7** giving rise to methyl-substituted π-allyl complexes (Table 4). With these small substituents steric effects should be minimized and therefore the formation of *syn*/*anti*-π-allyl complexes can contribute to the memory effect. We checked the influence of the leaving group on the selectivity of the reaction, including the new leaving groups introduced by Norrby.[15] They introduced isoureas as well as trichloroimidates as new leaving groups for allylic alkylation and reported on a different ionization behavior. While imidates (**5c**) give mainly the thermodynamically more stable *syn* complexes, isoureas (**5b**) show a relatively strong tendency towards the *anti* complex. In addition, these leaving groups seem to favor isomerizations. Although we were mainly interested in more or less isomerization free reactions, from a mechanistic point of view it was interesting to have a look on these leaving groups. We started our investigations with the linear acetate **5a**, which gave the linear (**8**) as well as the branched product (**10**) in good yield and selectivity. The results obtained are summarized in Table 4.

Table 4. Influence of the leaving group (X) on the allylations using substrates **5**–**7**.



Entry	Substrate	X	Yield [%]	**8** [%]	**9** [%]	**10** [%]	Ratio **10** *anti*/*syn*	Complex *syn*/*anti*	**10** [%] calcd
1	**5a**	OAc	81	77	1	22	91:9		
2	**5b**	OC(=N*i*Pr)NH*i*Pr	85	82	1	17	92:8		
3	**5c**	$OC(=NH)CCl_3$	71	77	<1	23	87:13		
4	**5d**	$OPO(OEt)_2$	84	88	<1	12	95:5		
5	**6a**	OAc	71	2	36	62	76:24		
6	**6b**	OC(=N*i*Pr)NH*i*Pr	82	14	38	48	89:11		
7	**6c**	$OC(=NH)CCl_3$	91	2	43	55	87:13		
8	**6d**	$OPO(OEt)_2$	87	1	44	55	88:12		
9	**7a**	OAc	68	66	6	28	85:15	85:15	25
10	**7b**	OC(=N*i*Pr)NH*i*Pr	75	32	23	45	86:14	40:60	41
11	**7c**	$OC(=NH)CCl_3$	84	82	4	14	92:8	90:10	23
12	**7d**	$OPO(OEt)_2$	85	27	31	42	88:12	30:70	44
13	**7e**	$OPO(OPh)_2$	57[a]	41	23	36	91:9	50:50	37
14	**7f**	$OPOPh_2$	64[a]	45	24	31	90:10	50:50	37
15	**7g**	OTs	60[a]	54	14	32	85:15	70:30	30
16	**7h**	OCO*t*Bu	79[a]	66	10	24	93:7	80:20	27

[a] 1.2 equiv of enolate were used.

An excess of enolate was used to guarantee fast and complete conversion. Only traces of *cis*-configured product **9** were observed, which clearly indicates, that isomerization does not play a significant role. While imidate **5c** gave the same product ratio, with isourea **5b** the linear product **8** was formed to a slightly higher extend. The best results with respect to regio- and diastereoselectivity were obtained with the phosphate leaving group (**5d**). This can probably be explained by the higher reactivity of the phosphates, which allows the reaction to proceed at lower temperature. Here, the different reactivities of the branched and the linear position of the *syn* complex became more significant. The higher *anti*/*syn* selectivity is also in good agreement with previous investigations.

Next we investigated the reaction of *cis*-configured substrates **6**. It was interesting to see if the olefin geometry can be transferred into the product, or if the π–σ–π isomerization is faster. Recently, we could show that with our highly reactive enolate nucleophiles even with substrates giving terminal π-allyl complexes, the isomerization can be suppressed, at least in part. Interestingly, with acetate **6a** as well as imidate **6c** and phosphate **6d**, branched product **10** and *cis*-product **9** were obtained but no *trans* product **8**. Only with the isourea **6b** a significant rate of isomerization (15–20%) was observed. The branched product **10** was obtained with good selectivity and slight excess compared to **9**, which illustrates the especially high reactivity at the *anti* position, which is obviously higher than at the terminal position. With these relative reactivities in hand (Figure 2) we next focused on the branched substrates **7**.

Under the assumption that with these substrates isomerization can be suppressed (except for the isourea derivative) one should be able to calculate the ratio of *syn* and *anti* complex formed in the ionization step from the product distribution. While the *trans*-product **8** can only be obtained from the *syn* complex, the *cis*-product **9** must result from

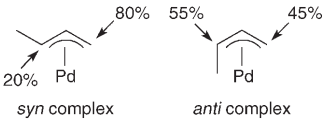
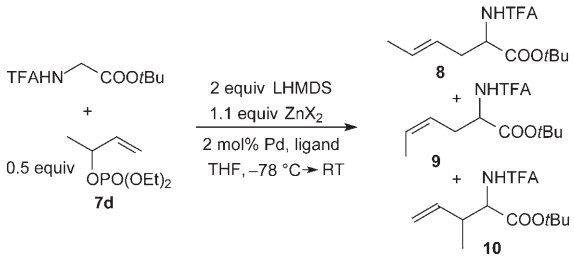


Figure 2. Estimated relative reactivities of *syn* and *anti* complexes.

the *anti* complex. The comparison of the four leaving groups clearly demonstrates, that the leaving group has a very strong influence on the *syn*/*anti*-complex ratio, and therefore also on the regioselectivity of the nucleophilic attack. While the acetate **7a** and especially the imidate **7c** show a high preference for the *syn* complex, the isourea **7b** and the phosphate **7d** favor the *anti* complex. These results are in good agreement with those obtained by Norrby et al. The diethylphosphate group seems to be superior to other leaving groups, both with respect to yield and selectivity. The memory effect observed is the strongest of all leaving groups investigated so far. Some further examples are collected in Table 4 (entries 13–16). Even replacing the ethoxy groups on the phosphorus by other aryloxy groups resulted in a decrease of *anti* complex coming close to a 1:1 mixture. Other leaving groups such as tosyl (**7g**, entry 15) or carbonate **7h** show a much higher tendency towards the *syn* complex.

Table 5. Allylic alkylations using optically active allylic substrates **7d**.



Entry	X	Catalyst	Ligand	Yield [%]	**8** [%]	**9** [%]	**10** [%]	Ratio **10** *anti*/*syn*
1	Cl	$[(allyl)PdCl]_2$	4.5% PPh_3	85	27	31	42	88:12
2	OAc[a]	$[Pd(PPh_3)_4]$	–	71	7	32	61	50:50
3	OBz[b]	$[Pd(PPh_3)_4]$	–	81	11	25	64	67:33
4	Cl	$[(allyl)PdCl]_2$	2.5% dppe	48	80	3	17	85:15
5	Cl	$[(allyl)PdCl]_2$	2.5% **L1**	50	28	17	55	72:28
6	Cl	$[(allyl)PdCl]_2$	2.5% **L2**	14	36	2	62	82:18

[a] Because of the low solubility of $Zn(OAc)_2$ in THF, the enolate solution has to be warmed up to room temperature to form the chelate complex. At lower temperatures side reactions such as *N*-alkylation or double allylation were observed. [b] Reaction conditions: 1.1 equiv $ZnEt_2$, 2.2 equiv BzOH.

If no isomerization occurs, the rate of branched product can be calculated from the *syn*/*anti*-complex ratio and the estimated relative reactivities (Figure 2). These calculated values are also incorporated in Table 4. And indeed, the measured and calculated rates are in relatively good agreement, except for the imidate **7c**. Here, the amount of branched product was significantly lower than expected. Obviously, in this case isomerization might play a role,[15] although in case of the linear substrate **6c** no isomerization was observed. This might be caused by the large excess of chloride (100-fold compared with Pd) in solution, although the "halide effect" on the regioselectivity was not significant. This is different to the situation observed with the aryl-substituted substrates, where Cl^- made a significant contribution to the memory effect. In no example the ratio of the branched product was significantly higher than expected. This is in contrast to the results obtained by Norrby in their studies with malonates. Here already traces of Cl^- showed a significant effect *via* the formation of unsymmetrical π-allyl complexes.

To prove if unsymmetrical π-allyl complexes might help to increase the rate of branched product, we investigated the reaction of phosphate **7d** (44% calculated **10**) under chloride free conditions (Table 5) and in the presence of bidentate ligands. While with $Zn(OTf)_2$ as chelating metal salt only decomposition was observed, with $Zn(OAc)_2$ an acceptable yield was obtained, with a high preference (71%) for the branched product. This was quite surprising, and probably acetate also forms an unsymmetrical π-allyl complex

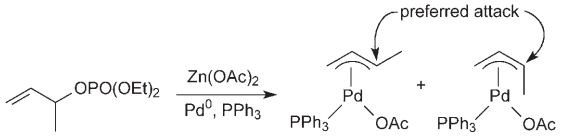


Figure 3. Unsymmetrical π-allyl complexes.

(Figure 3) showing a strong *trans* effect. To prove, if this is also valid for other carboxylates we investigated Zn-benzoate, which was generated in situ from Et_2Zn and benzoic acid. In this case the yield was much better and the reaction also showed a high ratio of branched product.

Obviously, the coordination of the carboxylate to the palladium is weaker than the coordination of chloride. In principle, such an unsymmetrical allyl complex can also be formed if allyl carboxylates such as **7a** are used as substrates. But in this case the ratio of branched product was only slightly increased. Probably acetate competes with the chloride and PPh_3 for the coordination side on the palladium. The formation of such an unsymmetrical complex should be completely suppressed in the presence of symmetrical bidentate ligands such as bis(diphenylphosphino)-ethane (dppe). And indeed, in this case the linear *trans*-product **8** was the predominant product (table 5, entry 4). Only 3% of *cis* product was formed, indicating that under these reaction conditions isomerization occurred nearly completely. The ratio of linear to branched product was close to 80:20, the estimated relative reactivities of the different allylic positions of the *syn* complex (Figure 2). Obviously, the halide effect on the product distribution can be neglected under our reaction conditions.

On the other hand, bidentate ligands which support the *trans* effect via different coordinating groups should increase the rate of **10**. Therefore, we synthesized achiral bidentate phospite oxazolines **L1** and **L2** (Figure 4), comparable li-

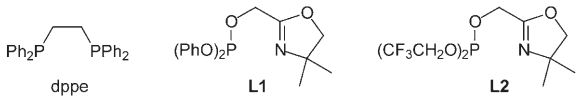


Figure 4. Bidentate ligands used.

gands as those used by Pfaltz during his investigations of asymmetric allylations.

As expected, with these ligands the branched product **10** was the major one. The relatively high amount of *trans* product **8** in relation to **9** indicates that some isomerization occurs. This is especially true for ligand **L2** with electron-withdrawing groups on the phosphorus. Here nearly no *cis* product was obtained, but more branched product as with phosphite **L1**. The electron withdrawing groups should shift the reaction mechanism more to S_N1-type, which should also favor the branched product.

Conclusion

In summary, we could show that several factors influence the product ratios of allylic alkylations. By using highly reactive chelated enolates, these influences could be investigated in detail, because isomerization processes which complicate such studies can be suppressed in most cases. The product distribution strongly depends on the substrates used.

Experimental Section

General remarks: All air- or moisture-sensitive reactions were carried out in oven-dried glassware (60 °C) under an atmosphere of argon. Dried solvents were distilled before use: THF was distilled from $LiAlH_4$, CH_2Cl_2 was dried with CaH_2 before distillation. The products were purified by flash chromatography on silica gel columns (Macherey-Nagel 60, 0.063–0.2 mm). Mixtures of ethyl acetate and hexane were generally used as eluents. Analytical TLC was performed on pre-coated silica gel plates (Macherey-Nagel, Polygram SIL G/UV_{254}). Visualization was accomplished with UV-light, $KMnO_4$ solution or iodine. Melting points were determined with a MEL-TEMP II apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were recorded with Bruker AC-400 [400 MHz (^1H) and 100 MHz (^{13}C)] or Bruker DRX-500 [500 MHz (^1H) and 125 MHz (^{13}C)] spectrometers in $CDCl_3$. Chemical shifts are reported in ppm (δ) with respect to TMS, and $CHCl_3$ was used as the internal standard. Selected signals for the minor diastereomers are extracted from the spectra of the diastereomeric mixture. Diastereomeric or enantiomeric excesses were determined by GC on a Varian Chrompack CP-3380 instrument equipped with a chiral Permabond-L-Chirasil-Val column. Optical rotations were measured with a Perkin-Elmer 341 polarimeter at the sodium D line (589 nm). Mass spectra were recorded with a Finnigan MAT 95 spectrometer using the CI technique. Elemental analyses were performed at the Saarland University.

General procedure for palladium-catalyzed allylic alkylations: LHMDS in THF (1 mL) was prepared by slowly addition of 1.6 M *n*BuLi (0.39 mL, 0.625 mmol) to HMDS (111 mg, 0.69 mmol) at −20 °C. This solution was cooled to −78 °C before it was added to the protected amino acid ester (0.25 mmol) in THF (1 mL). After 20 min at −78 °C a solution of $ZnCl_2$ (38 mg, 0.275 mmol) in THF (1 mL) was added under vigorous stirring. After additional 30 min a mixture of $[allylPdCl]_2$ (1 mg, 2.5 μmol, 1 mol %), PPh_3 (3 mg, 11.3 μmol, 4.5 mol %) and the corresponding allylic substrate in THF (2 mL) was added. The solution was stirred and warmed up to room temperature in the cooling bath overnight (for GC measurements, samples were taken after warm up by syringe under argon). Subsequently, the solution was diluted with diethyl ether and hydrolyzed with 1 N $KHSO_4$ solution. The aqueous layer was extracted twice with diethyl ether, and the combined organic phases were dried with anhydrous Na_2SO_4. After evaporation of the solvent the crude product was purified by silica gel column chromatography.

***tert*-Butyl (2*S*,*E*)-5-phenyl-2-(trifluoroacetyl)amino-4-pentenoate (3a) and *tert*-butyl (2*R*,3*S*)-3-phenyl-2-(trifluoroacetyl)-amino-4-pentenoate (4a)**: According to the general procedure for palladium-catalyzed allylic alkylations TFA-protected *tert*-butylglycinate (57 mg, 0.25 mmol) was reacted with allyl carbonate (*S*)-**2a** (51 mg, 0.25 mmol). Flash chromatography (silica gel, hexanes/ethyl acetate 9:1) gave rise to an inseparable mixture of **3a** and **4a** (ratio **3a**/**4a** 6:4) as a colorless oil (66 mg, 0.19 mmol, 77 %). (2*S*,*E*)-**3a**: 36 % *ee*; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 1.47$ (s, 9H; CH_3), 2.77 (m, 2H; CH_2), 4.61 (dt, $J = 7.2$, 5.6 Hz, 1H; CHN), 6.02 (m, 1H; CH_2CH), 6.46 (d, $J = 15.7$ Hz, 1H; PhCH), 7.01 (brs, 1H; NH), 7.20–7.34 ppm (m, 5H; ArH); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 27.7$ (CH_3), 35.1 (CH_2), 53.6 (CHN), 83.3 (CCH_3), 115.5 ($J_F = 291$ Hz; CF_3), 122.1 (CH_2CH), 126.0, 127.5, 128.4 (ArCH), 134.6 (PhCH), 138.1 (ArCC), 156.0 ($J = 38$ Hz; CF_3CO), 169.0 ppm (COO); GC (Chirasil-Val, 145 °C, isothermic): $t_{R(2R)} = 19.03$ min, $t_{R(2S)} = 21.60$ min; (2*R*,3*S*)-**4a**: *anti*/*syn* 93:7, 90 % *ee*; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 1.22$ (s, 9H; CH_3), 3.65 (dd, $J = 8.7$, 8.7 Hz, 1H; PhCH), 4.57 (dd, $J = 8.6$, 8.6 Hz, 1H; CHN), 5.15–5.20 (m, 2H; $CHCH_2$), 6.02 (m, 1H; CH_2CH), 6.86 (brs, 1H; NH), 7.20–7.34 ppm (m, 5H; ArH); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 27.4$ (CH_3), 52.6 (PhCH), 56.5 (CHN), 83.5 (CCH_3), 115.5 ($J_F = 291$ Hz; CF_3), 118.5 (CH_2CH), 127.37, 127.43, 128.0 (ArCH), 135.8 (CH_2CH), 136.4 (ArCC), 156.4 ($J = 38$ Hz; CF_3CO), 168.6 ppm (COO); (2*R*,3*R*)-**4a** (selected signals): ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 27.6$ (CH_3), 51.6 (PhCH), 56.3 (CHN), 118.3 (CH_2CH), 134.9 ppm (CH_2CH); GC (Chirasil-Val, 145 °C, isothermic): $t_{R(2R,3R)} = 6.89$ min, $t_{R(2S,3S)} = 7.23$ min, $t_{R(2R,3S)} = 8.05$ min, $t_{R(2S,3R)} = 9.12$ min; elemental analysis calcd (%) for $C_{17}H_{20}F_3NO_3$ (343.35): C 59.47, H 5.87, N 4.08; found: C 59.29, H 6.12, N 4.08.

***tert*-Butyl (*E*)-2-(trifluoroacetyl)amino-4-hexenoate (8)**: According to the general procedure for palladium-catalyzed allylic alkylations TFA-protected *tert*-butylglycinate (114 mg, 0.5 mmol) was treated with (*E*)-crotyl phosphate **5d** (52 mg, 0.25 mmol). Flash chromatography (silica gel, hexanes/ethyl acetate 9:1) gave rise to an inseparable mixture of **8** and **10** (ratio **8**/**10** 88:12) as a colorless oil (59 mg, 0.21 mmol, 84 %). **8**: ^1H NMR (500 MHz, $CDCl_3$): $\delta = 1.45$ (s, 9H; CCH_3), 1.63 (dd, $J = 6.6$, 1.5 Hz, 3H; $CHCH_3$), 2.51 (m, 2H; CH_2), 4.46 (m, 1H; CHN), 5.24 (m, 1H; CH_2CH), 5.52 (m, 1H; CH_3CH), 6.88 ppm (brs, 1H; NH); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 17.6$ ($CHCH_3$), 27.7 (CCH_3), 34.6 (CH_2), 52.5 (CHN), 82.97 (CCH_3), 115.9 ($J_F = 287$ Hz; CF_3), 123.1 (CH_3CH), 130.6 (CH_2CH), 156.2 ($J = 37$ Hz; CF_3CO), 169.2 ppm (COO); GC (Chirasil-Val, 80 °C, 30 min; 1 °C min^{-1}; 100 °C, 20 min): $t_{R(R)} = 38.56$ min, $t_{R(S)} = 39.87$ min; HRMS (CI): *m*/*z*: calcd for $C_{12}H_{18}NO_3F_3$: 281.1239, found: 281.1213 $[M]^+$; elemental analysis calcd (%) for $C_{12}H_{18}NO_3F_3$ (281.27): C 51.24, H 6.45, N 4.98; found: C 51.32, H 6.33, N 4.64.

***tert*-Butyl (*Z*)-2-(trifluoroacetyl)amino-4-hexenoate (9) and *tert*-butyl 3-methyl-2-(trifluoroacetyl)amino-4-pentenoate (10)**: According to the general procedure for palladium-catalyzed allylic alkylations TFA-protected *tert*-butylglycinate (114 mg, 0.5 mmol) was treated with (*Z*)-crotyl phosphate **6d** (52 mg, 0.25 mmol). Flash chromatography (silica gel, hexanes/ethyl acetate 9:1) gave rise to an inseparable mixture of **9** and **10** (ratio **9**/**10** 44:55) as a colorless oil (61 mg, 0.22 mmol, 87 %). **9**: ^1H NMR (400 MHz, $CDCl_3$): $\delta = 1.48$ (s, 9H; CCH_3), 1.60 (dd, $J = 6.9$, 1.5 Hz, 3H; $CHCH_3$), 2.55 (m, 1H; CH_2), 2.74 (m, 1H; CH_2), 4.55 (td, $J = 7.2$, 5.3 Hz,1H; CHN), 5.25 (m, 1H; CH_2CH), 5.69 (m, 1H; CH_3CH), 6.93 ppm (brs, 1H; NH); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 12.9$ ($CHCH_3$), 27.9 (CCH_3), 28.9 (CH_2), 52.7 (CHN), 83.3 (CCH_3), 115.8 ($J_F = 288$ Hz; CF_3), 122.3 (CH_3CH), 129.2 (CH_2CH), 156.7 ($J = 37$ Hz; CF_3CO), 169.4 ppm (COO); GC (Chirasil-Val, 80 °C, 30 min; 1 °C min^{-1}; 100 °C, 20 min): $t_{R(R)} = 42.04$ min, $t_{R(S)} = 43.12$ min; *anti*-**10**: ^1H NMR (500 MHz, $CDCl_3$): $\delta = 1.07$ (d, $J = 7.0$ Hz, 3H; $CHCH_3$), 1.46 (s, 9H; CCH_3), 2.82 (dqdt, $J = 7.5$, 7.0, 4.5, 1.0 Hz, 1H; CH_3CH), 4.47 (dd, $J = 8.5$,

4.5 Hz, 1H; C*H*N), 5.12 (dd, $J=17.0$, 1.0 Hz, 1H; CH_2), 5.25 (dd, $J=11.0$, 1.0 Hz, 1H; CH_2), 5.67 (ddd, $J=17.5$, 10.5, 7.5 Hz, 1H; CH_2CH), 6.67 ppm (br s, 1H; N*H*); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta=15.8$ ($CHCH_3$), 28.0 (CCH_3), 40.2 (CH_3CH), 56.8 (*C*HN), 83.3 (CCH_3), 115.8 ($J_F=286$ Hz; CF_3), 117.4 (CH_2), 136.9 (CH_2CH), 157.0 ($J=38$ Hz; CF_3CO), 168.9 (*C*OO); *syn*-**10** (selected signals): ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=1.09$ (d, $J=7.0$ Hz, 3H; $CHCH_3$), 2.72 (m, 1H; CH_3CH), 5.07 (dd, $J=17.0$, 1.0 Hz, 1H; CH_2), 6.80 ppm (br s, 1H; N*H*); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta=15.3$ ($CHCH_3$), 40.6 (CH_3CH), 56.5 (*C*HN), 83.5 (CCH_3), 116.9 (CH_2), 137.5 (CH_2CH), 168.7 ppm (*C*OO); GC (Chirasil-Val, 80 °C, 30 min; 1 °C min^{-1}; 100 °C, 20 min): $t_{R(2R,3R)}=26.55$ min, $t_{R(2R,3S)}=t_{R(2S,3S)}=27.71$ min, $t_{R(2S,3R)}=28.82$ min; HRMS (CI): *m*/*z*: calcd for $C_{12}H_{18}NO_3F_3$ $[M]^+$: 281.1239, found: 281.1213; elemental analysis calcd (%) for $C_{12}H_{18}NO_3F_3$ (281.27): C 51.24, H 6.45, N 4.98; found: C 51.32, H 6.33, N 4.64.

Acknowledgements

Financial support by the Deutsche Forschungsgemeinschaft (Ka 880/6) and the Fonds der Chemischen Industrie is gratefully acknowledged.

[1] a) L. S. Hegedus, *Organische Synthese mit Übergangsmetallen*, VCH, Weinheim, **1995**; b) U. Kazmaier, M. Pohlman, "Cross Coupling Reactions via π-Allyl-Intermediates" in *Metal Catalyzed C–C and C–N Coupling Reactions* (Eds.: A. de Meijere, F. Diederich), Wiley-VCH, Weinheim, **2004**, pp. 531–583, and references therein.

[2] a) G. Consiglio, R. M. Waymouth, *Chem. Rev.* **1989**, *89*, 257–276; b) B. M. Trost, D. L. Van Vranken, *Chem. Rev.* **1996**, *96*, 395–422; c) G. Helmchen, *J. Organomet. Chem.* **1999**, *576*, 203–214; d) A. Pfaltz, M. Lautens in *Comprehensive Asymmetric Catalysis I–III* (Eds.: E. N. Jacobsen, A. Pfaltz, H. Yamamoto), Springer, Berlin, **1999**, pp. 833–884; e) L. Acemoglu, J. M. J. Williams in *Handbook of Organopalladium Chemistry for Organic Synthesis, Vol. 2* (Eds.: E.-I. Negishi, A. de Meijere), Wiley, New York, **2002**, pp. 1689–1705; f) J. Tsuji in *Handbook of Organopalladium Chemistry for Organic Synthesis, Vol. 2* (Eds.: E.-I. Negishi, A. de Meijere), Wiley, New York, **2002**, pp. 1669–1688; g) B. M. Trost, M. L. Crawley, *Chem. Rev.* **2003**, *103*, 2921–2944; h) B. M. Trost, C. Jiang, *Org. Lett.* **2003**, *5*, 1563–1565; i) B. M. Trost, J. Xu, *J. Am. Chem. Soc.* **2005**, *127*, 2846–2847; j) B. M. Trost, M. K. Brennan, *Org. Lett.* **2006**, *8*, 2027–2030.

[3] a) S. Ramdeehul, P. Dierkes, R. Aguado, P. C. J. Kamer, P. W. N. M. van Leeuwen, J. A. Osborn, *Angew. Chem.* **1998**, *110*, 3302–3304; *Angew. Chem. Int. Ed.* **1998**, *37*, 3118–3121; b) P. Dierkes, S. Ramdeehul, L. Barloy, A. D. Cian, J. Fischer, P. C. J. Kamer, P. W. N. M. van Leeuwen, J. A. Osborn, *Angew. Chem.* **1998**, *110*, 3299–3301; *Angew. Chem. Int. Ed.* **1998**, *37*, 3116–3118; c) B. M. Trost, J. Dudash, Jr., E. J. Hembre, *Chem. Eur. J.* **2001**, *7*, 1619–1629; d) B. M. Trost, H. C. Shen, L. Dong, J.-P. Surivet, *J. Am. Chem. Soc.* **2003**, *125*, 9276–9277; e) L. G. Bonnet, R. E. Douthwaite, B. M. Kariuki, *Organometallics* **2003**, *22*, 4187–4189; f) W.-H. Zheng, B.-H. Zheng, Y. Zhang, X.-L. Hou, *J. Am. Chem. Soc.* **2007**, *129*, 7718–7719.

[4] a) G. Poli, G. Giambastiani, A. Heumann, *Tetrahedron* **2000**, *56*, 5959–5989; b) J. W. Faller, J. C. Wilt, J. Parr, *Org. Lett.* **2004**, *6*, 1301–1304.

[5] A. J. Blacker, M. L. Clarke, M. S. Loft, J. M. J. Williams, *Org. Lett.* **1999**, *1*, 1969–1971.

[6] a) T. Hayashi, A. Yamamoto, T. Hagihara, *J. Org. Chem.* **1986**, *51*, 723–727; b) T. Hayashi, M. Kawatsura, Y. Uozumi, *J. Am. Chem. Soc.* **1998**, *120*, 1681–1687.

[7] a) M. P. T. Sjögren, S. Hansson, B. Åkermark, A. Vitagliano, *Organometallics* **1994**, *13*, 1963–1971.

[8] a) G. C. Lloyd-Jones, S. C. Stephen, *Chem. Eur. J.* **1998**, *4*, 2539–2549; b) G. C. Lloyd-Jones, S. C. Stephen, M. Murray, C. P. Butts, S. Vyskocil, P. Kocovsky, *Chem. Eur. J.* **2000**, *6*, 4348–4357; c) G. C. Lloyd-Jones, *Synlett* **2001**, 161–183; d) I. J. S. Fairlamb, G. C. Lloyd-Jones, S. Vyskocil, P. Kocovsky, *Chem. Eur. J.* **2002**, *8*, 4443–4453; e) L. Gouriou, G. C. Lloyd-Jones, S. Vyskovil, P. Kocovsky, *J. Organomet. Chem.* **2003**, *687*, 525–537.

[9] J. W. Faller, N. Sarantopoulos, *Organometallics* **2004**, *23*, 2179–2185.

[10] G. Poli, C. Scolastico, *Chemtracts* **1999**, *12*, 837–845.

[11] a) B. M. Trost, R. C. Bunt, *J. Am. Chem. Soc.* **1996**, *118*, 235–236; b) B. J. Lussem, H.-J. Gais, *J. Org. Chem.* **2004**, *69*, 4041–4052.

[12] a) R. Prétôt, A. Pfaltz, *Angew. Chem.* **1998**, *110*, 337–339; *Angew. Chem. Int. Ed.* **1998**, *37*, 323–325; b) G. Helmchen, A. Pfaltz, *Acc. Chem. Res.* **2000**, *33*, 336–345.

[13] J. Ansell, M. Wills, *Chem. Soc. Rev.* **2002**, *31*, 259–268.

[14] B. Goldfuss, U. Kazmaier, *Tetrahedron* **2000**, *56*, 6493–6496.

[15] P. Fristrup, T. Jensen, J. Hoppe, P.-O. Norrby, *Chem. Eur. J.* **2006**, *12*, 5352–5360.

[16] The *syn*/*anti* terminology is used to describe the orientation of the substituent R relative to the hydrogen atom at the central position of the allyl complex.

[17] a) P. R. Auburn, P. B. Mackenzie, B. Bosnich, *J. Am. Chem. Soc.* **1985**, *107*, 2033–2046; b) P. B. Mackenzie, J. Whelan, B. Bosnich, *J. Am. Chem. Soc.* **1985**, *107*, 2046–2054; c) P. Corradini, G. Maglio, A. Musco, G. Paiaro, *J. Chem. Soc. Chem. Commun.* **1996**, 618–619; d) N. Solin, K. J. Szabo, *Organometallics* **2001**, *20*, 5464–5471; e) J. Yu, M. J. Gaunt, J. B. Spencer, *J. Org. Chem.* **2002**, *67*, 4627–4629; f) M. Ogasawara, K.-i. Takizawa, T. Hayashi, *Organometallics* **2002**, *21*, 4853–4861.

[18] a) B. Åkermark, S. Hansson, A. Vitagliano, *J. Am. Chem. Soc.* **1990**, *112*, 4587–4588; b) M. Sjögren, S. Hansson, P.-O. Norrby, B. Åkermark, M. E. Cucciolito, A. Vitagliano, *Organometallics* **1992**, *11*, 3954–3964; c) P.-O. Norrby, B. Åkermark, F. Hæffner, S. Hansson, M. Blomberg, *J. Am. Chem. Soc.* **1993**, *115*, 4859–4867.

[19] K. Vrieze in *Dynamic Nuclear Magnetic Resonance Spectroscopy* (Eds.: L. M. Jackman, F. A. Cotton), Academic Press, New York, **1975**.

[20] a) J. Sprinz, M. Kiefer, G. Helmchen, M. Reggelin, G. Huttner, O. Walter, L. Zsolnai, *Tetrahedron Lett.* **1994**, *35*, 1523–1526; b) J. M. Brown, D. I. Hulmes, P. J. Guiry, *Tetrahedron* **1994**, *50*, 4493–4506; c) P. E. Blöchl, A. Togni, *Organometallics* **1996**, *15*, 4125–4132; d) T. Hayashi, M. Kawatsura and Y. Uozumi, *Chem. Commun.* **1997**, 561–562; e) G. C. Lloyd-Jones, S. C. Stephen, *Chem. Commun.* **1998**, 2321–2322; f) K. Fagnou, M. Lautens, *Angew. Chem.* **2002**, *114*, 26–49; *Angew. Chem. Int. Ed.* **2002**, *41*, 26–47.

[21] a) U. Kazmaier, F. L. Zumpe, *Angew. Chem.* **1999**, *111*, 1572–1574; *Angew. Chem. Int. Ed.* **1999**, *38*, 1468–1470; b) U. Kazmaier, S. Maier, F. L. Zumpe, *Synlett* **2000**, 1523–1535; c) T. D. Weiss, G. Helmchen, U. Kazmaier, *Chem. Commun.* **2002**, 1270–1271; d) U. Kazmaier, *Current Org. Chem.* **2003**, 317–328; e) U. Kazmaier, J. Deska, A. Watzke, *Angew. Chem.* **2006**, *118*, 4973–4976; *Angew. Chem. Int. Ed.* **2006**, *45*, 4855–4858; f) J. Deska, U. Kazmaier, *Chem. Eur. J.* **2007**, *13*, 6204–6211; g) J. Deska, U. Kazmaier, *Angew. Chem.* **2007**, *119*, 4654–4657; *Angew. Chem. Int. Ed.* **2007**, *46*, 4570–4573.

[22] a) U. Kazmaier, F. L. Zumpe, *Angew. Chem.* **2000**, *112*, 805–807; *Angew. Chem. Int. Ed.* **2000**, *39*, 802–804; b) U. Kazmaier, F. L. Zumpe, *Eur. J. Org. Chem.* **2001**, 4067–4076; c) U. Kazmaier, M. Pohlman, *Synlett* **2004**, 623–626; d) U. Kazmaier, M. Pohlmann, T. Lindner, *J. Org. Chem.* **2004**, *69*, 6909–6912.

[23] a) U. Kazmaier, T. Lindner, *Angew. Chem.* **2005**, *117*, 3368–3371; *Angew. Chem. Int. Ed.* **2005**, *44*, 3303–3306; b) T. Lindner, U. Kazmaier, *Adv. Synth. Catal.* **2005**, *347*, 1687–1695.

[24] U. Kazmaier, K. Krämer, *J. Org. Chem.* **2006**, *71*, 8950–8953.

[25] U. Kazmaier, D. Stolz, *Angew. Chem.* **2006**, *118*, 3143–3146; *Angew. Chem. Int. Ed.* **2006**, *45*, 3072–3075, and references therein.

[26] The optically active substrates were obtained from the racemic allylic alcohols via enzymatic kinetic resolution with Novozyme 435.

Received: August 27, 2007
Published online: November 15, 2007

