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Palladium-Catalyzed Dienylations of Chelated Enolates

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Isomerization-free reactions of dienyl carbonates with chelated amino acid ester enolates at –78 °C provide important information concerning the mechanism of these dienylations. The formation of regioisomeric products can be explained by competing S_N2/S_N2' reactions, and the product distribution can be influenced by the proper choice of the reaction conditions. Chiral allylic substrates show a significant transfer of chirality.
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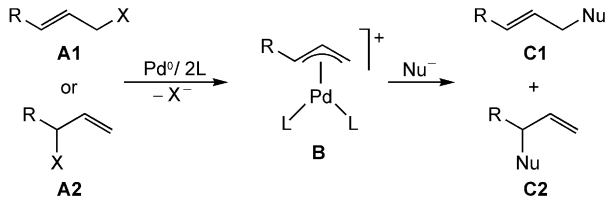
Introduction

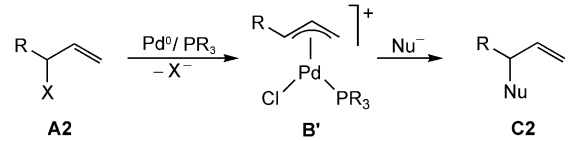
(π-Allyl)metal complexes are of significant importance in modern organic synthesis. Among the different metals used, palladium plays a dominant role,[1] and the allylic alkylation, also called the Tsuji–Trost reaction, is by far the most popular application.[2] (π-Allyl)palladium complexes **B** are formed from allylic substrates such as **A1** and **A2**,[3] which can be attacked in the next step either at the terminal position, giving rise to the linear product **C1**, or at the internal position, which provides the branched product **C2** (Scheme 1). In general, attack of the nucleophile occurs at the sterically least hindered position, and therefore the linear product **C1** is the preferred one.[2]



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

In general, for an asymmetric version the branched product **C2** is of greater interest, because the linear **C1** in most cases is achiral, as long as symmetric nucleophiles such as malonates are used. Therefore, much efforts have been made to obtain higher ratios of branched product. Pfaltz et al. could show, that the regioselectivity of the nucleophilic attack can be influenced by "tuning" the reaction mechanism.[4] Nucleophilic attacks in an S_N2-type fashion occurs preferentially at the terminal position, whereas reaction via a cationic S_N1 transition state should provide a higher ratio of the branched product. The S_N1 transition state can be favoured by using electron-withdrawing groups in the ligand, for example if phosphanes are replaced by phosphites.[5]

According to the simplified model shown in Scheme 1, one should expect more or less the same product distribution, independent of the starting material used, as long as the same π-allyl intermediate **B** is formed. Interestingly, quite often this is not the case. Especially with unsymmetric substrates, such as **A1** and **A2**, 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**.[6] This so-called "memory effect" has intensively be studied, and several explanations were given.[7] For example, in the presence of chloride ions an unsymmetrical π-allyl complex **B′** can be formed from substrates **A2** (Scheme 2). Based on the strong *trans* effect of the phosphorus atom, the phosphane ligand should be located *trans* to the leaving group. Because nucleophilic attack occurs also preferentially *trans* to the phosphorus atom, this *trans* effect can significantly contribute to the memory effect (regioretention).[8]



Scheme 2. Formation of unsymmetrical (π-allyl)palladium complexes.

Another important class of memory effects, also observed for unsymmetrical π-allyl complexes, is more complex. It is observed that the product distribution not only depends on the regio- but also the stereochemistry of the starting material.[6b] This effect was investigated by Norrby

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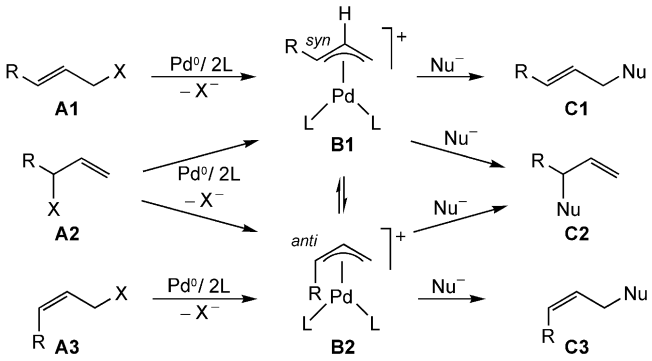
et al.[9] and recently also by our group.[10] Scheme 3 shows a more detailed mechanism of the allylation using unsymmetrical substrates **A1**–**A3**.



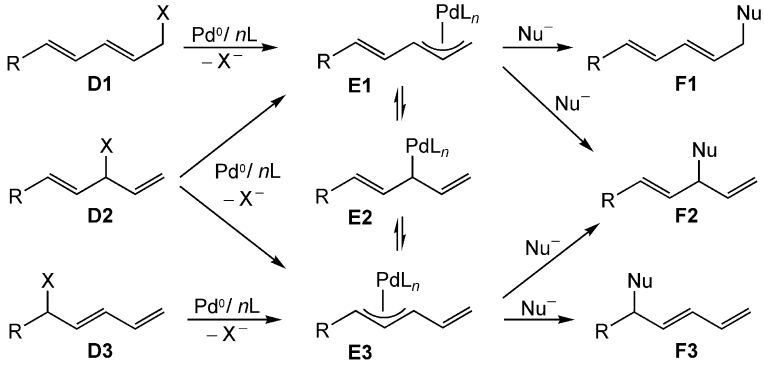
Scheme 3. Detailed mechanism of allylic alkylation.

Whereas **A1** gives rise to the *syn* complex **B1**, the *anti* complex **B2** is obtained from *cis* substrate **A3**.[11] 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.[9] Especially for terminal allyl complexes the intermediates **B1** and **B2** can equilibrate rapidly by π-σ-π isomerization.[12] If isomerization is fast compared to nucleophilic attack, product distribution results from the equilibrium mixture in which the *syn* complex as the thermodynamically favoured 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, or at least in the same range, one can observe memory effects based on the different ratio and reactivity of the allyl complexes **B1** and **B2**.[10,13]

Even more complicated is the situation if higher unsaturated substrates such as **D** are used. Early investigations by Trost et al. using dienyl substrate **D1** and amines or sodium malonates as nucleophiles showed that in the palladium-catalyzed reaction nucleophilic attack occurred preferentially at the least hindered terminal position (**F1**),[14] while with tungsten complexes the branched product **F2** was obtained preferentially.[15] The same regioselectivity is also observed with other transition metals such as molybdenum,[16] and iridium.[17] In principle, this result can be explained by the formation of (π-allyl)palladium complex **E1**, which can be attacked at the two different allylic positions giving rise to products **F1** and **F2**. More detailed investigations by Trost et al.[18] and simultaneously by Bäckvall et al.[19] indicated, that with these substrates **D** the situation is much more complex. With respect, that with sodium malonates a mixture of substitution products **F1** and **F2** (not **F3**) is formed from **D1** in a ratio of 2–4:1 (depending on the malonate), one might expect a product mixture **F2/F3** from substrate **D3** (via **E3**). Dienyl substrate **D2** should be able to form both π-allyl complexes **E1** and **E3**, and therefore, all three products **F** can be expected. In addition, **D2** should be able to form an allyl *anti*-vinyl complex,[9] analogous to **B2** (not shown here for clarity reasons), which should favor the formation of **F2**.[6b] But the results obtained are quite different. Both, **D1** and **D2** give rise to **F1** (major product) and **F2** (minor product), while **D3** provided all three products (**F2** as major isomer). This clearly indicates that the initially formed π-allyl complex **E3** can isomerize (at least in part) to π-allyl complex **E1**, probably via the σ-allyl intermediate **E2** (π-σ-π isomerization). Interestingly, not only the structure of the malonate has an influence on the regioselectivity, but also the counterion.[18] Replacement of the sodium ion by caesium or tetrahexylammonium gave a completely different result. All these substrates **D1**–**D3** gave more or less the same product ratio **F1**–**F3**, indicating that under these conditions all (allyl)palladium intermediates **E1**–**E3** are in full equilibrium (Scheme 4).

Another explanation for the product ratio formed from **D3** might be S_N2'-type processes. Both steps, the oxidative addition (on substrates **D1** and **D3**, but not **D2**) as well as the nucleophilic attack, can also occur in an S_N2'-type fashion. In addition to the "normal" allylic alkylation, this might explain the formation of all three products,[18b] and it is extremely difficult to differentiate between these mechanistic options. Under certain circumstances, also isomerization of the products can be observed.[14]

An interesting observation was made by Bäckvall et al.,[19] that PBu_3 instead of PPh_3 gives a significantly higher ratio of linear product **F1**. This was explained by a diminished carbenium ion character at the π-allyl carbon atom in



Scheme 4. Allylic alkylations with dienyl substrates **D**.

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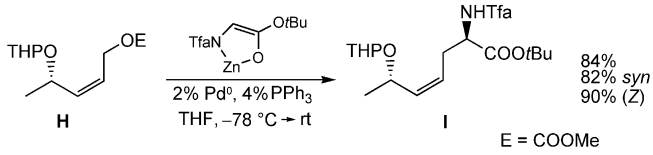
the π-allyl complex, which favours attack at the terminal position via an S_N2-type transition state.[14] On the other hand, replacement of the phosphanes by phosphites or related ligands gives preferentially rise to branched product as illustrated by a recent example using a chiral 1-oxazolinyl-1′-phosphanylferrocene complex.[20]

In all examples investigated so far, either symmetrical C-nucleophiles or amines were used, generating only one stereogenic center in the allyl fragment if branched products are obtained (**F2**, **F3**; R ≠ H). To the best of our knowledge, there is no report on diastereoselective reactions using unsymmetrical nucleophiles.

For some time, our group is investigating chelated amino acid ester enolates **G** as nucleophiles in transition-metal-catalyzed allylic alkylations (Scheme 5).[21] The great advantage of these nucleophiles is their high reactivity. Therefore, they react under much milder conditions (already at –78 °C) 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, *cis*-configured substrates can react either with conservation of the olefin geometry (stereoretention), or selectively at the more reactive *anti* position,[13] depending on the substrate used. Very recently, we could also show that in reactions of chiral substrates **H** the nucleophilic attack on the terminal π-allyl intermediate could be controlled by the stereogenic centre in the substrate.[23] This clearly indicates, that with these enolates even terminal (π-allyl)palladium complexes can react without significant isomerization[24] which makes them good candidates to investigate mechanistical details such as the memory effect,[10] or to differentiate between S_N2'-type reactions and π-σ-π isomerization of type **E** allyl complexes.[25]



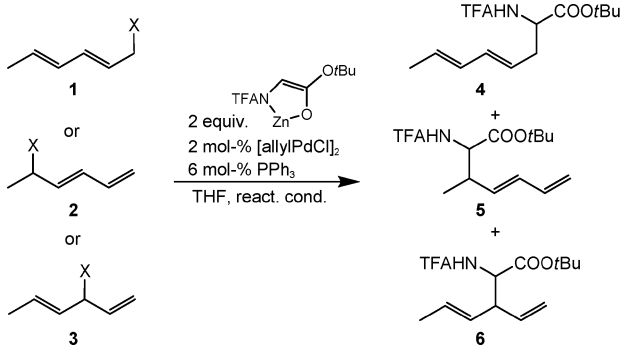
Scheme 5. Allylic alkylations of chelated enolate **G** (Tfa = trifluoroacetyl).

Results and Discussion

To obtain results comparable to those previously obtained with malonates, we first investigated the reaction of the three isomeric allyl substrates **1**–**3** (Table 1).[25] According to Scheme 4, these substrates should form the three different products **4**–**6** in different ratios, depending on the π-allyl complexes **E1**–**E3** (R = Me) involved. An excess of nucleophile was used to obtain high reaction rates and to suppress isomerization as much as possible.[26] We started our investigation with the linear acetate **1a** which gave the allylation products in high yield as a mixture of all three isomers. The linear product was formed as a single isomer [both double bonds (*E*)]. Interestingly, the branched isomers **5** and **6** were formed in equal amounts which indicates that either π-σ-π isomerization occurs or the nucleophilic attack occurs in an S_N2'-type fashion.

In general, allylic carbonates are more reactive than carboxylates, and in our previous investigations isomerization

Table 1. Allylic alkylations of dienyl substrates **1**–**3**.



Entry	Substrate	X	Reaction conditions	Yield [%]	Ratio **4/5/6**	*dr* (*anti*/*syn*)[a] **5**	**6**
1	**1a**	OCOMe	–78 °C to room temp., overnight	89	46:26:28	92:8	65:35
2	**1b**	OCOOEt	–78 °C, 16 h	92	57:22:21	97:3	65:35
3	**2b**	OCOOEt	–78 °C, 16 h	64	54[b]:31:15	90:10	33:67
4	**3b**	OCOOEt	–78 °C, 16 h	87	36:13:51	95:5	50:50
5	**1b**	OCOOEt	room temp.	83	37:20:43	92:8	61:39
6	**2b**	OCOOEt	room temp.	25	35[c]:16:49	88:12	42:58
7	**3b**	OCOOEt	room temp.	41	31:12:57	94:6	35:65

[a] Diastereomeric ratio determined by GC of the crude product mixture. [b] Product contains 36% (*E*/*Z*) isomer **4′** (GC). [c] Product contains 12% (*E*/*Z*) isomer **4′** (GC).

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could mostly be suppressed by using carbonates, while with acetates isomerization (at least in part) was observed. Therefore, we next allowed allylic carbonate **1b** to react at –78 °C (Entry 2). Again, the yield was excellent, which indicates that the reaction proceeds very well at this low temperature. The selectivity towards the linear product **4** was increased, but surprisingly the branched products **5** and **6** again were formed as a 1:1 mixture. Interestingly, under these conditions product **5** was obtained nearly as a single diastereomer (97% *ds*), while the isomeric products **6** were formed in a 2:1 ratio. The lower selectivity in this case is not surprising, because for a nucleophilic attack at the central position, the two substituents at this allylic carbon atom are too similar for significant stereodifferentiation.

Next, we switched to the regioisomeric substrate **2b** and subjected it to the same reaction conditions (Entry 3). The yield was lower with this substrate, but the linear product **4** was again obtained as the major product, surprisingly in this case as a 2:1 mixture of **4** and the (*Z*) isomer **4′** (Figure 1); **5** was formed as the major isomer of the two branched products, again with good selectivity.

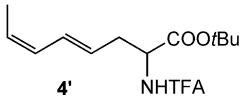
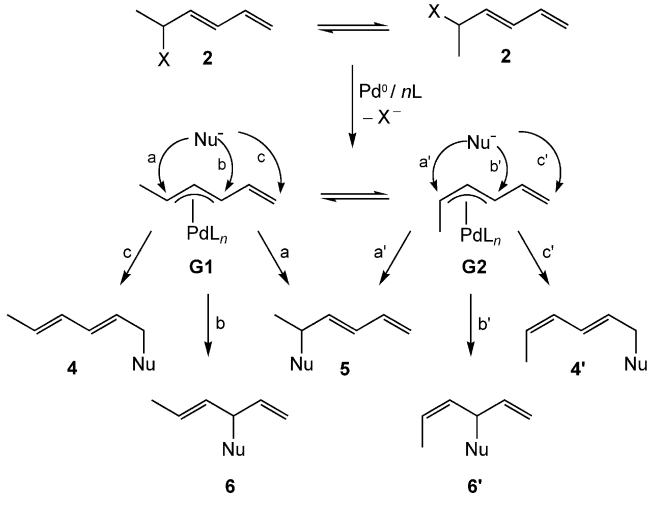


Figure 1. Minor linear product **4′**.

The relatively high amount of **5** (compared to **6**) might result (at least in part) from the memory effect, but on the other hand it might also be the result of the reaction mechanism (Scheme 6). Previous investigations by Norrby[9] and our group[10] showed that especially methyl-substituted allylic substrates can give significant amounts of *anti* complexes,[11] depending on the leaving groups used.



Scheme 6. Formation of isomeric products **4**–**6** from allylic substrate **2**.

With this in mind one can propose a similar situation also for dienyl substrates such as **2**. Depending on the conformation in the ionization step, both π-allyl complexes **K1** (*syn*/*syn*) and **K2** (*anti*/*syn*) can be formed, with **K1** expected to be the thermodynamical one. In principle, especially at higher temperature these two complexes can equilibrate by π-σ-π isomerization, and the equilibrium probably is on the side of **K1**. Both complexes can be attacked at the two allylic positions (a,b) and as proposed by Trost, also at the S_N2' position (c).

Nucleophilic attack at the positions a and a′ provide both the same product **5**, whereas attacks b and b′ should give rise to branched products **6** and **6′**. The formation of **6** [with an (*E*) double bond] is a result of attack b, whereas the product **6′** from attack b′ with a (*Z*)-configured double bond is not observed. But this is not surprising. Work by Åkermark et al. clearly indicates, that the *anti* position (attack a′) is the more reactive one,[13] and in our case, the S_N2' attack (c′) at the terminal position is obviously significantly favoured over b′. This explains the relatively high amount of (*Z*)-configured product **4′**. The major product **4** is obtained from the analogous attack c on the thermodynamical complex **K1**. The high amount of **5** (obtained from both complexes **K1** and **K2**) and of **4′** (obtained only from **K2**) indicates that the complexes **K1** and **K2** are formed in comparable amounts, and that isomerization under our reaction conditions is slow compared to nucleophilic attack.

But if isomerization of the complexes **K1** and **K2** can be neglected, one should not expect a significant isomerization between the two regioisomeric π-allyl complexes **E1** and **E3** (Scheme 4). Therefore, allylic substrate **3b** was investigated next (Entry 4), because this substrate should give rise to a mixture of these complexes (which might be close to the equilibrium mixture). In high yield the branched product **6** was formed as the major isomer (51%). In addition to a potential memory effect, this product can be obtained by direct nucleophilic attack on both isomeric complexes **E1** and **E3**.

Because this product mixture probably arises from a mixture of regioisomeric complexes, one might expect similar results under conditions where isomerization occurs. Therefore, all these substrates were allowed to react also at room temperature (Entries 5–7). And indeed, the results obtained are relatively similar. Only the yields differ significantly, which is the result of several side reactions occurring at higher temperature. But these reactions were not optimized, because we were only interested in mechanistical information. Obviously, at room temperature all π-allyl complexes are more or less in equilibrium. This assumption is also supported by the observation that the amount of linear product **4** as well as the (*Z*) isomer **4′** is significantly reduced (Entry 6 vs. 3). The fact that **4′** still is observed indicates that even at room temperature isomerization is not complete and not so much faster than nucleophilic attack. Therefore, isomerization of the π-allyl intermediates can be ruled out at temperatures as low as –78 °C. The somewhat lower selectivities observed with allylic acetate **1a** (Entry 1) might be caused by a competing isomerization, based on an ionization of acetates at higher temperatures.

Because the leaving group obviously might have an influence, not only on the ratio isomerization/nucleophilic attack, but also on the mode of ionization, we investigated

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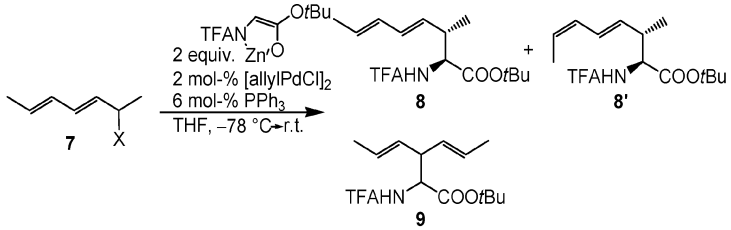
Table 2. Influence of the leaving group on the product distribution.



Entry	Substrate	*ee* [%]	X	Yield [%]	Ratio **8/8′/9**	*dr*[a] (*anti*/*syn*)	*ee* [%][a] *anti*-**8**	*syn*-**8**	**9**
1	**7a**	–	–OCOOMe	88	84:9:7	91: 9	–	–	–
2	**7b**	–	–OCOOEt	89	82:9:9	92: 8	–	–	–
3	**7c**	–	–OCOO*t*Bu	81	81:6:13	92: 8	–	–	–
4	**7d**	–	–OCO*t*Bu	79	60:3:37	90:10	–	–	–
5	**7e**	–	–OCOMe	82	70:4:26	90:10	–	–	–
6	**7f**	–	–OCOPh	67	66:5:29	90:10	–	–	–
7	**7g**	–	–OCOAr[b]	68	81:5:14	87:13	–	–	–
8	(*R*)-**7e**	66	OCOMe	81	63:3:34	90:10	0	0	0
9	(*S*)-**7b**	91	OCOOEt	80	81:10:9	93: 7	31	75	39

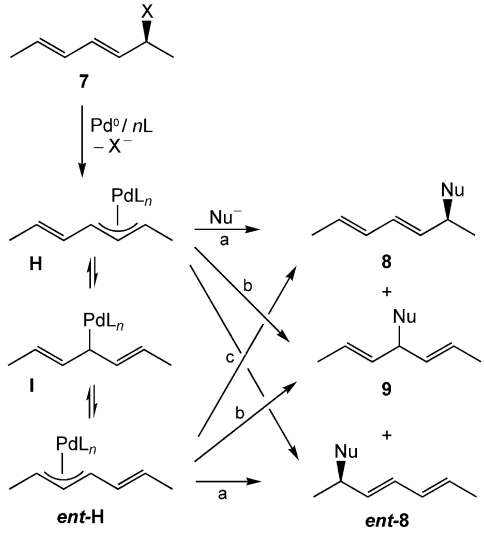
[a] Diastereomeric ratio and enantiomeric excess determined by GC after catalytic hydrogenation. [b] Ar: 2,4-dichlorophenyl.

this influence more detailed in reactions of substrates **7**. These substrates have the great advantage that in principle only two products should be obtained resulting from a nucleophilic attack at either the external position (giving rise to conjugated diene **8**) or internal, providing product **9** with only one stereogenic center at the α-position. Attack under S_N2 conditions also gives rise to **8**, although in this case the formation of (*Z*) product **8′** can be expected. The results obtained from the different leaving groups are summarized in Table 2.

As expected, the carbonates **7a**–**c** were superior to carboxylates, while the differences between the carbonates were minimal. The selectivity slightly decreased with the electron-donor ability of the alkyl group, and best results were obtained with the methyl carbonate. More obvious was the effect for the carboxylates, and the selectivity directly correlated with the pK_a value of the corresponding carboxylic acid. Whereas the 2,4-dichlorobenzoate **7g** (pK_a = 2.67) gave results very close to the carbonates (Entry 7), the pivaloate **7d** (pK_a = 5.05) showed a mixture of isomers which is close to the results obtained at room temperature (Entry 4). Probably with this leaving group isomerization occurs (at least in a significant ratio). The acetate (pK_a = 4.76) and benzoate (pK_a = 4.20) gave results between these extremes.

Unfortunately, we were not able to introduce better leaving groups, such as phosphates, because the required substrates were not stable and decomposed immediately. It should also be mentioned, that the substrates **7** are relatively sensitive. For example, during purification of **7b** by silica gel chromatography, we observed scrambling of the leaving group, presumably by an ionic mechanism.[26] Fortunately, there was no scrambling of the leaving group in the crude substrate, and it was found sufficiently pure by NMR spectroscopy. Therefore, we decided to use these crude substrates without purification.

To investigate whether the acetate undergoes isomerization, we repeated our experiments with optically active substrates **7b** and **7e**. If isomerization occurs, one should observe a complete loss of chirality, because the σ-allyl intermediate **M** is achiral (Scheme 7). Nucleophilic attack a then provides a 1:1 mixture of the two enantiomers **8** and *ent*-**8**. If no isomerization occurs, loss of chirality can also be expected by nucleophilic attack in an S_N2-type fashion (c), but attacks a and c should show different kinetics, and therefore at least in part a chirality transfer should be observed.



Scheme 7. Formation of isomeric products from optically active **7**.

To prove this option, we subjected the corresponding allyl alcohol to an enzymatic kinetic resolution by using an immobilised *Candida antarctica* lipase (Novozym 435). In vinyl acetate we obtained the required acetate (*R*)-**7e** with 66% *ee*. The remaining alcohol (91% *ee*) was esterified with ethyl chloroformate to (*S*)-**7b** and was used without further purification. And indeed, as expected, the acetate (*R*)-**7e**

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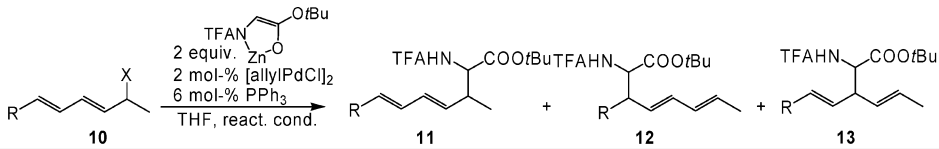
Table 3. Allyic alkylations with various dienyl substrates **10**.



10 **11** **12** **13**

Entry	Substrate	*ee* [%]	R	X	React. cond.	Yield [%]	Ratio [%] **11/12/13**	*dr*[a] **11** (*anti*/*syn*)	**12**	**13**	*ee* [%][a] **11** (*anti*)	**12**	**13**
1	**10a**	–	Et	–OCOOEt	–78 °C to r.t., overnight	85[b]	76:15:8	91:9	>97	n.d.	–	–	–
2	**10a**	–	Et	–OCOOEt	r.t.	60	48:15:37	77:23	92	n.d.	–	–	–
3	(*S*)-**10a**	97	Et	····OCOOEt	–78 °C to r.t., overnight	91[c]	76:17:7	90:10	>97	n.d.	92	79	n.d.
4	(*S*)-**10a**	97	Et	····OCOOEt	–78 °C, 21h	81[d]	75:18:7	90:10	>97	n.d.	95	83	n.d.
5	(*R*)-**10b**	53	Et	◀OCOMe	–78 °C to r.t., overnight	87	61:15:24	87:13	95	n.d.	44	34	n.d.
6	**10c**	–	Ph	–OCOOEt	–78 °C to r.t., overnight	96	78:12:10	87:13	>97	56:44	–	–	–
7	**10c**	–	Ph	–OCOOEt	r.t.	45	49:5:46	84:16	>97	33:67	–	–	–
8	(S)-**10c**	99	Ph	····OCOOEt	–78 °C to r.t., overnight	91	82:9:9	90:10	>97	51:49	>97	99	n.d.
9	(S)-**10c**	99	Ph	····OCOOEt	–78 °C, 23h	95	85:7:8	93: 7	>97	57:43	>97	99	n.d.
10	(R)-**10d**	97	Ph	◀OCOMe	–78 °C to r.t., overnight	65	55:7:38	85:15	>97	71:29	95	88	n.d.
11	**10e**	–	*p*-MeOC$_6$H$_4$	–OCOOEt	–78 °C to r.t., overnight	53	56:17:27	87:13	91	57:43	–	–	–
12	**10e**	–	*p*-MeOC$_6$H$_4$	–OCOOEt	r.t.	28	29:8:63	83:17	n.d.	35:65	–	–	–
13	**10e**	–	*p*-MeOC$_6$H$_4$	–OCOOEt	–78 °C, 21h	49	70:11:19	89:11	n.d.	49:51	–	–	–
14	**10f**	–	*p*-FC$_6$H$_4$	–OCOOEt	–78 °C to r.t., overnight	54	82:6:12	90:10	>95	51:49	–	–	–
15	**10g**	–	2-furyl	–OCOOEt	–78 °C to r.t., overnight	45	61:13:26	80:20	n.d.	70:30	–	–	–
16	**10g**	–	2-furyl	–OCOOEt	–78 °C, 20h	69	69:8:23	86:14	n.d.	71:29	–	–	–
17	**10g**	–	2-furyl	–OCOOEt	r.t.	27	25:8:68	80:20	n.d.	78:22	–	–	–

[a] Diastereomeric ratio and enantiomeric excess determined by GC of the crude product mixture. [b] Product contains less than 2% (*E*/*Z*) isomer **12a′** (GC). [c] Product contains 2–3% (*E*/*Z*) isomer **12a′** (GC). [d] Product contains 3% (*E*/*Z*) isomer **12a′** (GC).

yielded the allylation products in complete racemic form (Entry 8), whereas the corresponding carbonate (*S*)-**7b** gave enantiomerically enriched products (Entry 9).

A relatively high *ee* was obtained for the minor *syn* diastereomer (*syn*-**8**). Probably, this isomer is formed from the corresponding *anti*/*syn* complex **K2** (Scheme 6). The higher reactivity of the *anti* position should favour this position vs. the S_N2' position, which should result in a higher *ee*. The moderate *ee* for the branched product **9** results from the unselective attack at the internal position, comparable to the low diastereoselectivities obtained with substrates **1**–**3**.

To show the generality of these observations, we investigated a range of other substrates. The results obtained are collected in Table 3. With the methyl/ethyl-substituted substrate **10a** the results were comparable to those obtained with the dimethylated substrates. But in this case, the S_N2 and the S_N2' attacks gave different products, and therefore a high degree of chirality transfer was observed, especially under "isomerization-free" conditions (Entry 4). At higher temperature, again the relative amount of the branched product **13** was increased. Probably because of a conjugation effect, the amount of the S_N2' products **12** is slightly reduced in reactions of the phenyl-substituted substrates **10c** and **10d**. Especially with the chiral carbonates, the selectivities and the chirality transfers were excellent. Aryl substrates are best suited to vary the electronic properties of the substrates. While electron-donating groups on the aromatic ring should favour an S_N1-type reaction by stabilizing a potential carbeniumion intermediate, electron-withdrawing groups should destabilize these intermediates, preferring an S_N2-type reaction. Therefore, we also investigated the *p*-methoxy derivative **10e** as well as the *p*-fluoro substrate **10f**. Compared to the unmodified substrate **10c**, the electron-rich derivative **10e** gave a higher ratio of branched product as well as S_N2', while the electron-poor substrate **10f** provided the conjugated diene **11f** preferentially, but the effects are only moderate. With electron-rich heterocyclic systems, such as the furane derivative, a similar situation is found as with the *p*-methoxy substrate **10e**.

Conclusions

We have shown that in dienylations of chelated enolates isomerization processes of the (π-allyl)palladium complexes involved can be suppressed and that the formation of isomeric products is the result of competing S_N2/S_N2' reactions. By choosing proper reaction conditions (kinetic or thermodynamic control) the product ratio can be manipulated, at least in part. A high degree of chirality transfer can be observed in reactions of chiral allylic substrates.

Experimental Section

General Remarks: All reactions were carried out in oven-dried glassware (100 °C) under argon or nitrogen. All solvents were dried before use. THF, diethyl ether, hexane and toluene were distilled from sodium/benzophenone, CH_2Cl_2 from P_2O_5, MeOH from activated Mg, and stored over molecular sieves. Et_3N and pyridine were distilled from KOH. The products were purified by flash chromatography on silica gel (32–63 μm). Mixtures of EtOAc and hexane or diethyl ether were generally used as eluents. Analysis by TLC was carried out on commercially precoated Polygram® SIL-G/UV 254 plates (Macherey–Nagel). Visualization was accomplished with UV light, $KMnO_4$ solution or iodine. Melting points were determined with a Büchi melting point apparatus and are uncorrected. ^1H and ^{13}C NMR spectroscopic analysis was performed

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with Bruker AC-400 or DRX-500 spectrometers. Chemical shifts are reported in ppm relative to $CHCl_3$ as an internal reference. If selected signals are provided for the other isomeric products, these signals are extracted from the NMR spectra of the isomeric mixtures. Enantiomeric and diastereomeric excesses were determined with Varian Chrompack CP 3380 and GC 3400 gas chromatographs with a Chira-Si-L-Val (25 m × 0.25 mm) and an FS-Cyclodex-β-I/P capillary column (25 m × 0.25 mm), respectively. Helium was used as carrier gas. Enantiomeric excesses were also determined by analytical HPLC with a Trentec Reprosil-100 Chiral-NR 8 μm column (flow rate: 1–2 mL/min) and a Shimazu diode-array UV detector. HRMS analyses were performed with a Finnigan MAT 95S. Elemental analyses were carried out at the Institute of Organic Chemistry, Saarland University, Germany.

General Procedure for Palladium-Catalyzed Dienylations: Hexamethyldisilazane (225 mg, 1.40 mmol) was dissolved in dry THF (2 mL) in a Schlenk flask under Ar or N_2. To this solution *n*BuLi (1.6 M in hexane, 0.80 mL, 1.25 mmol) was added dropwise at –78 °C. The reaction mixture was stirred at this temperature for 30 min, before the cooling bath was removed. Stirring was continued for further 15 min. In a second Schlenk flask, $ZnCl_2$ (102 mg, 0.74 mmol) was carefully dried in vacuo with a heat gun. After cooling to room temperature, it was dissolved in dry THF (2 mL), and a solution of *tert*-butyl *N*-(trifluoroacetyl)glycinate (114 mg, 0.50 mmol) in dry THF (2 mL) was added. This mixture was cooled to –78 °C, the freshly prepared cooled LHMDS solution was added dropwise, and stirring was continued for 45 min. In a third flask $[Pd(allyl)Cl]_2$ (1.8 mg, 5.0 μmol, 2 mol-%) and PPh_3 (3.9 mg, 14.87 μmol) were dissolved in dry THF (0.5 mL). After this solution was stirred at room temperature for 15 min, it was added to the chelated enolate at –78 °C, followed by a cold solution of the conjugated dienyl substrate (0.25 mmol) in dry THF (1 mL). The mixture was warmed slowly to room temperature overnight. The solution was diluted with diethyl ether, and 1 M aq. $KHSO_4$ solution was added. The layers were separated, and the aqueous layer was extracted with diethyl ether. The combined organic extracts were dried (Na_2SO_4), and the solvent was evaporated under reduced pressure. The crude product was purified by flash chromatography on silica gel (hexane/ethyl acetate).

(±)-*tert*-Butyl (4*E*,6*E*)-2-(Trifluoroacetamido)-4,6-octadienoate (4): According to the general procedure, **4** was obtained as major product from allylic carbonate **1b** (42.5 mg, 0.25 mmol) in an overall yield (mixture of isomers) of 92% (70 mg, 0.23 mmol) as a colourless oil after flash chromatography (hexanes/EtOAc, 98:2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.87 (br. s, 1 H, N*H*), 6.16–6.01 (m, 1 H, C*H*=CH), 6.10–5.94 (m, 1 H, C*H*=CH), 5.71–5.59 (m, 1 H, C*H*=CH), 5.38–5.27 (m, 1 H, C*H*=CH), 4.58–4.48 (m, 1 H, C*H*N), 2.75–2.50 (m, 2 H, CHCH_2), 1.74 (d, *J* = 6.8 Hz, 3 H, CHCH_3), 1.48 [s, 9 H, C(CH_3)$_3$] ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.2 (s, *C*OO), 156.4 (q, *J* = 37.4 Hz, *C*ON), 135.4 (d, *C*H=CH), 130.6 (d, *C*H=CH), 129.7 (d, *C*H=CH), 122.3 (d, *C*H=CH), 115.6 (q, *J* = 286 Hz, *C*F_3), 83.4 [s, *C*(CH$_3$)$_3$], 52.8 (d, *C*HN), 34.8 (t, CH*C*H$_2$), 27.9 [q, C(*C*H$_3$)$_3$], 18.0 (q, CH*C*H$_3$) ppm. GC [Chirasil-L-Val, T_0 (30 min) = 80 °C, 1 °C/min to T = 180 °C]: t_R(**4**) = 72.04 min, t_R(**4**) = 72.73 min, t_R(**4′**) = 72.91 min, t_R(**4′**) = 73.43 min. HRMS (mixture of isomers) (CI): calcd. for $C_{14}H_{20}NO_3F_3$ $[M]^+$ 307.1395, found 307.1407; calcd. for $C_{14}H_{21}NO_3F_3$ $[M + 1]^+$ 308.1473, found 308.1484. $C_{14}H_{20}NO_3F_3$ (307.31) (mixture of isomers): calcd. C 54.72, H 6.56, N 4.56; found C 54.55, H 6.66, N 4.80.

(±)-*tert*-Butyl (4*E*)-3-Methyl-2-(trifluoroacetamido)-4,6-heptadienoate (5): Ester **5** was obtained as one of the minor products in the allylic alkylation using **1b** as a diastereomeric mixture. *anti*-**5** (selected signals): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.71 (br. s, 1 H, N*H*), 6.29 (dt, *J* = 16.8, 10.4 Hz, 1 H, C*H*=CH$_2$), 6.16–6.04 (m, 1 H, *C*H=CH), 5.53 (dd, *J* = 15.6, 8 Hz, 1 H, *C*H=CH), 5.22–5.06 (m, 2 H, CH=CH_2), 4.58–4.48 (m, 1 H, C*H*N), 2.96–2.82 (m, 1 H, C*H*CH$_3$), 1.10 (d, *J* = 6.8 Hz, 3 H, CHCH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.7 (s, *C*OO), 136.2 (d, *C*H=CH$_2$), 133.2 (d, *C*H=CH), 132.2 (d, *C*H=CH), 117.4 (t, CH=*C*H$_2$), 57.1 (d, *C*HN), 39.5 (d, *C*HCH$_3$), 16.0 (q, CH*C*H$_3$) ppm. *syn*-**5** (selected signals): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.14 (d, *J* = 6.8 Hz, 3 H, CHCH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 35.9 (d, *C*HCH$_3$), 16.0 (q, CH*C*H$_3$) ppm. GC [Chirasil-L-Val, T_0 (30 min) = 80 °C, 1 °C/min to T = 180 °C]: t_R(*anti*-**5**) = 58.28 min, t_R(*anti*-**5**) = 59.13 min, t_R(*syn*-**5**) = 59.57 min, t_R(*syn*-**5**) = 60.41 min.

(±)-*tert*-Butyl (4*E*)-2-(Trifluoroacetamido)-3-vinyl-4-hexenoate (6): Ester **6** was obtained as one of the minor products in the allylic alkylation using **1b** as a diastereomeric mixture. Selected signals: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.71 (br. s, 1 H, N*H*), 5.83–5.70 (m, 1 H, C*H*=CH$_2$), 5.63–5.49 (m, 1 H, C*H*CH$_3$), 5.42–5.31 (m, 1 H, C*H*=CH), 5.22–5.06 (m, 2 H, CH=CH_2), 4.58–4.48 (m, 1 H, C*H*N), 3.32–3.17 (m, 1 H, C*H*CH), 1.70 (d, *J* = 6.8 Hz, 3 H, CHCH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.4 (s, *C*OO), 135.3 (d, *C*H=CH$_2$), 126.9 and 126.8 (2 d, *C*H=CH), 120.0 and 119.9 (2 t, CH=*C*H$_2$), 55.95 and 55.92 (2 d, *C*HN), 49.7 and 49.6 (2 d, *C*HCH), 17.9 (q, CH*C*H$_3$) ppm. GC [Chirasil-L-Val, T_0 (30 min) = 80 °C, 1 °C/min to T = 180 °C]: t_R(**6**, diast. 1) = 50.97 min, t_R(**6**, diast. 2) = 51.31 min, t_R(**6**, diast. 1) = 51.93 min, t_R(**6**, diast. 2) = 52.20 min.

(±)-*tert*-Butyl (4*E*,6*E*)-3-Methyl-2-(trifluoroacetamido)-4,6-nonadienoate (11a): According to the general procedure, **11a** was obtained as major product from allylic carbonate **10a** (50 mg, 0.25 mmol) in an overall yield (mixture of isomers) of 85% (71 mg, 0.21 mmol) as a colourless oil after flash chromatography (hexanes/EtOAc, 98:2). *anti*-**11a**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.67 (br. d, *J* = 8.0 Hz, 1 H, N*H*), 6.07 (ddd, *J* = 14.8, 10.1, 0.8 Hz, 1 H, C*H*=CH), 6.11–5.93 (m, 1 H, C*H*=CH), 5.71 (dt, *J* = 14.8, 6.4 Hz, 1 H, C*H*=CH), 5.37 (dd, *J* = 14.8, 7.5 Hz, 1 H, C*H*=CH), 4.49 (dd, *J* = 8.4, 4.4 Hz, 1 H, C*H*N), 2.95–2.80 (m, 1 H, C*H*CH$_3$), 2.09 (dqd, *J* = 7.5, 7.4, 1.0 Hz, 2 H, CH_2CH$_3$), 1.48 [s, 9 H, C(CH_3)$_3$], 1.09 (d, *J* = 6.8 Hz, 3 H, CHCH_3), 1.00 (t, *J* = 7.5 Hz, 3 H, CH$_2$CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.9 (s, *C*OO), 157.0 (q, *J* = 37.4 Hz, *C*ON), 136.8 (d, CH$_2$*C*H), 132.9 (d, *C*H=CH), 128.8 (d, *C*H=CH), 128.4 (d, *C*H=CH), 115.7 (q, *J* = 286 Hz, *C*F_3), 83.2 [s, *C*(CH$_3$)$_3$], 57.2 (d, *C*HN), 39.4 (d, *C*HCH$_3$), 27.9 [q, C(*C*H$_3$)$_3$], 25.5 (t, *C*H$_2$CH$_3$), 16.33 (q, CH*C*H$_3$), 13.3 (q, CH$_2$CH_3) ppm. *syn*-**11a** (selected signals): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.78 (br. d, 1 H, N*H*), 4.46 (dd, *J* = 8.4, 5.2 Hz, 1 H, C*H*N), 2.77–2.62 (m, 1 H, C*H*CH$_3$), 1.49 [s, 9 H, C(CH_3)$_3$], 1.12 (d, *J* = 6.8 Hz, 3 H, CHCH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 40.0 (d, *C*HCH$_3$), 16.37 (q, CH*C*H$_3$) ppm. GC (Chirasil-L-Val, 100 °C, isothermic): t_R(*anti*-**11a**) = 111.20 min, t_R(*anti*-**11a**) = 115.24 min, t_R(*syn*-**11a**) = 117.25 min, t_R(*syn*-**11a**) = 121.01 min. HRMS (mixture of isomers) (CI): calcd. for $C_{16}H_{25}NO_3F_3$ $[M + 1]^+$ 336.1786, found 336.1819. $C_{16}H_{24}NO_3F_3$ (335.37) (mixture of isomers): calcd. C 57.30, H 7.21, N 4.18; found C 56.96, H 7.33, N 4.34.

(±)-*tert*-Butyl (4*E*,6*E*)-3-Ethyl-2-(trifluoroacetamido)-4,6-octadienoate (12a): Ester **12a** was obtained as one of the minor products in the allylic alkylation using **10a**. ^{1}H NMR (400 MHz, $CDCl_3$) (selected signals): δ = 6.67 (br. d, *J* = 8 Hz,1 H; N*H*), 5.76–5.62 (m, 1 H, C*H*CH$_3$), 5.21 (dd, *J* = 14.8, 9.2 Hz, 1 H, C*H*=CH), 4.58 (dd, *J* = 8.8, 4.4 Hz, 1 H, C*H*N), 2.62–2.46 (m, 1 H, C*H*CH$_2$), 1.75

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(d, J = 6.4 Hz, 3 H, CHCH_3), 1.47 [s, 9 H, C(CH_3)$_3$], 1.41–1.20 (m, 2 H, CH_2CH$_3$), 0.91 (t, J = 7.3 Hz, 3 H, CH$_2$CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) (selected signals): δ = 169.08 (s, COO), 134.5 (d, *C*H=CH), 130.7 (d, *C*H=CH), 129.7 (d, *C*H=CH), 126.9 (d, *C*H=CH), 56.15 (d, *C*HN), 47.4 (d, *C*HCH$_2$), 24.1 (t, *C*H$_2$CH$_3$), 17.9 (q, CH*C*H$_3$), 11.7 (q, CH$_2$*C*H$_3$) ppm. GC (Chirasil-L-Val, 100 °C, isothermic): t_R(*anti*-**12a**) = 85.79 min, t_R(*anti*-**12a**) = 89.49 min, t_R(*syn*-**12a**) = 89.49 min, t_R(*syn*-**12a**) = 93.23 min.

(±)-*tert*-Butyl (4*E*,6*E*)-3-Ethyl-2-(trifluoroacetamido)-4,6-octadienoate (12a′): Ester **12a′** was obtained as one of the minor products in the allylic alkylation using **10a**. ^{1}H NMR (400 MHz, $CDCl_3$) (selected signals): δ = 6.39 (dd, J = 15.2, 11.2 Hz, C*H*=CH), 5.90 (dd, J = 15.2, 15.2 Hz, C*H*=CH), 5.59–5.43 (m, C*H*=CH), 5.34–5.28 (m, C*H*=CH), 2.22–2.14 (m, 2 H, CH_2CH$_3$) ppm. GC (Chirasil-L-Val, 100 °C, isothermic): t_R(**12′**) = 101.95 min, t_R(**12′**) = 105.23 min.

(±)-*tert*-Butyl (4*E*)-3-[(1*E*)-1-Propenyl]-2-(trifluoroacetamido)-4-heptenoate (13a): Ester **13a** was obtained as one of the minor products in the allylic alkylation using **10a**. ^{1}H NMR (400 MHz, $CDCl_3$) (selected signals): δ = 6.78 (br. d, 1 H, N*H*), 5.61–5.44 (m, 1 H, C*H*CH$_3$), 4.46 (dd, J = 8.4, 5.2 Hz, 1 H, C*H*N), 3.25–3.10 (m, 1 H, C*H*CH), 2.14–1.99 (m, 2 H, CH_2CH$_3$), 1.69 (d, J = 6.2 Hz, 3 H, CH CH_3), 1.46 [s, 9 H, C(CH_3)$_3$] ppm. GC (Chirasil-L-Val, 100 °C, isothermic): t_R(**13a**, diast. 1) = 59.37 min, t_R(**13a**, diast. 2) = 60.48 min, t_R(**13a**, diast. 1) = 61.23 min, t_R(**13a**, diast. 2) = 62.13 min.

Supporting Information (see footnote on the first page of this article): Experimental details and analytical data of all new compounds.

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