Chelated Enolates of Amino Acid Esters − New and Efficient Nucleophiles for Isomerization-Free, Stereoselective Palladium-Catalyzed Allylic Substitutions

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Dedicated to Professor Barry M. Trost on the occasion of his 60th birthday

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Chelated amino acid ester enolates were found to be suitable nucleophiles for palladium-catalyzed allylic alkylations. Unlike stabilized soft nucleophiles, the chelated enolates react under very mild reaction conditions, even at −78 °C. If TFA-protected amino acid *tert*-butyl esters are used as nucleophiles, the *anti*-configured products are obtained in a highly diastereoselective fashion. This protocol is therefore a good supplement to the chelate enolate Claisen rearrangement, which gives rise to the corresponding *syn* products. Especially good results are obtained with allylic carbonates as substrates, as these are readily able to form the required π-allylpalladium complexes at temperatures as low as −78 °C. In this temperature range, π–σ–π isomerization of the π-allyl intermediates does not play a significant role, and so application of the highly reactive chelated enolates allows the use of C-nucleophiles in allylic alkylation of (*Z*)-allyl substrates with complete conservation of the olefin geometry for the first time. With (*Z*)-allyl carbonates bearing two identical substituents at the allyl termini, the attack of the nucleophile on the intermediate π-allylpalladium complex occurs exclusively at the *anti* position, giving rise to the (*E*)-configured substitution product. If optically active allyl carbonates are used, complete transfer of the chirality to the product is observed. These examples clearly indicate that the π–σ–π isomerization is completely suppressed under the reaction conditions used. This opens up new synthetic applications, which will be evaluated in the near future.

Introduction

Transition metal catalyzed reactions are becoming more and more popular in organic synthesis.[1] As many of these reactions tolerate a large number of functional groups, they are especially well suited for the synthesis of complex molecules. Palladium, which can be used for cyclizations, cross-coupling reactions, and allylic substitutions, occupies a predominant position among the transition metals.[2] In particular, palladium-catalyzed allylic alkylation has developed into one of the standard reactions in organic synthesis, not least because asymmetric variations of this reaction are possible.[3] Since it is mainly symmetric, stabilized carbanions such as malonates that are used as C-nucleophiles, only one stereogenic center, the configuration of which can be easily controlled, is generated in the allyl moiety in most cases.

When unsymmetrical C-nucleophiles − such as β-oxo esters[4] or imines of amino acid esters[5] − are used, mixtures of diastereomers are usually obtained. This is due to the configurational lability of the allylated nucleophiles. Thus, considerably better results are obtained with alkylated derivatives.[6] In contrast to the well-investigated reactions of stabilized "soft" carbanions, there exist only a few reports concerning unstabilized enolates (those of ketones or esters, for example), although the resulting products are often more interesting. The reactions of these enolates seem to be limited to only a few substrates. In the case of ketones, the best results are obtained with tin[7] and boron enolates.[8] The first asymmetric version of this technique, using chiral ligands, was reported very recently.[9] It was shown that the counterion of the enolate has a strong influence on the stereochemical outcome of the reaction. Whereas these ketone enolates attack the terminal position of the allyl moiety, lithium enolates of esters preferentially attack the central position, giving rise to cyclopropane derivatives.[10] The main problems involved in reactions of these unstabilized nucleophiles may arise from coordination of the enolates to the palladium center, which might result in inactivated complexes.

With respect to the reaction mechanism, palladium-catalyzed allylic alkylations proceed through π-allylpalladium complexes, and the configuration of the substitution products depends on the configuration of these π-allyl intermediates.[11] Thus, the oxidative addition of palladium(0) to (*E*)-allyl acetates and carbonates produces allyl complexes with *syn* configurations, which react with nucleophiles to provide the corresponding (*E*) substitution products (Scheme 1). The *anti* complexes are generated by an attack of the palladium complex on (*Z*) substrates. Reactions with nucleophiles would provide (*Z*)-configured products if π−σ−π-isomerization did not occur.[12] This isomerization causes a fast interconversion of the complexes, normally

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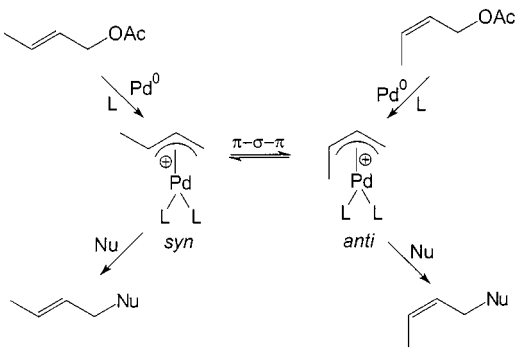
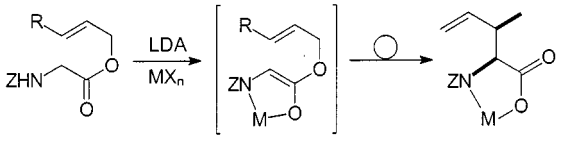


Scheme 1. π−σ−π isomerization of allylpalladium complexes

favoring the *syn* complex. Exceptions can be observed only if steric interactions either between the substituents in the allyl substrate[13] or between the allyl moiety and the ligands[14] destabilize the *syn* complex. This results in enrichment in the *anti* complex, and reactions with nucleophiles give rise to an increased amount of (*Z*) substitution product. However, selective palladium-catalyzed[15] conversions of (*Z*)-allyl substrates with retention of the olefin geometry remain an unsolved problem.[16] One key issue involved in the solution of this problem is probably the suppression of the π−σ−π-isomerization.

All this prompted us to investigate chelated enolates of amino acid esters as nucleophiles in palladium-catalyzed allylic substitutions. Chelation causes a marked enhancement in thermal stability without having any negative influence on the reactivity of these enolates. Because of the fixed enolate geometry, their transformations often proceed with high degrees of stereoselectivity. We have therefore been investigating transformations of these species, to provide non-natural amino acids, for a long time.[17] We are especially interested in reactions that cannot be carried out with non-chelated enolates. Thus, chelated enolates of amino acid esters undergo Claisen rearrangements when warmed to room temperature, providing γ,δ-unsaturated amino acids (Scheme 2).[18] When substituted (*E*)-allylic esters are used, products with *syn* configurations are obtained diastereoselectively, by way of the chair-like transition state. The *anti* products, however, cannot be obtained as easily from the corresponding (*Z*)-esters.[19]



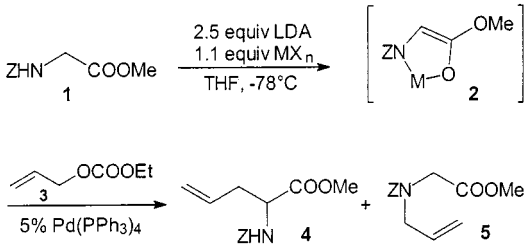
Scheme 2. Chelate Claisen rearrangement of glycine allyl esters

For that reason, we wanted to ascertain whether the *anti* products might be accessible through palladium-catalyzed allylic alkylation. Stabilization of the enolate by chelation should also diminish the tendency of the enolate to coordinate to the palladium − a solution of the "enolate problem"? Furthermore, we hoped to be able to circumvent the problems resulting from π−σ−π isomerization, because of the very high reactivity of the chelated enolates.

Results and Discussion

Initial Studies

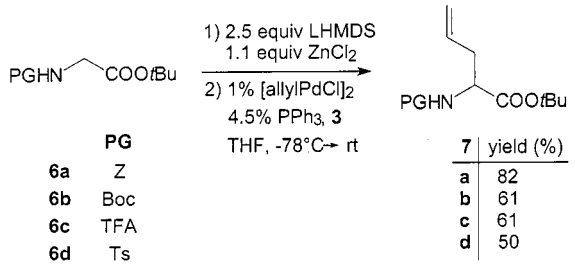
At the beginning of our investigations we used Z-protected methyl glycinate **1** as amino acid substrates (Scheme 3). Deprotonation of compounds **1** with excess LDA at −78 °C and addition of metal salts (MX_n) presumably results in the formation of the chelated enolates **2**. We found that these chelated enolates react with allyl carbonate (**3**) in the presence of palladium(0). *C*- or *N*-allylation in the products obtained was dependent on the metal salt used. Whereas zinc enolates exclusively gave rise to the *C*-allylated products **4**, Mg or Li enolates afforded mixtures of products containing *C*- and *N*-allylated species.



Scheme 3. Allylic alkylations of glycine ester **1**

These observations prompted the development of selective *N*-allylation conditions, which we reported recently.[20] We also described intensive investigations into palladium-catalyzed allylic alkylation with the corresponding zinc enolates.[21]

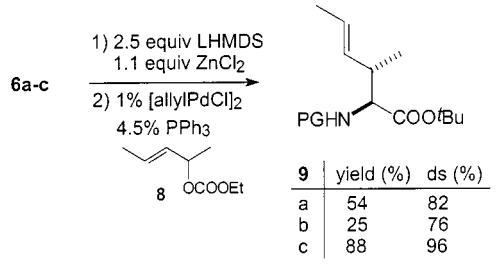
First of all, we examined the reaction behavior of different *N*-protected glycine esters **6** with allyl carbonate (**3**) (Scheme 4). The corresponding acetate or benzoate can also be used in place of the carbonate **3**, but the yields and selectivities are usually better with the more reactive carbonates. To avoid transesterifications by the liberated ethoxide, the *tert*-butyl esters were chosen. These esters were deprotonated with excess LHMDS, and the resulting lithium enolates were transmetallated to the corresponding chelated zinc enolates by addition of zinc chloride. After a short time, a solution of the allyl carbonate (**3**) and the palladium source were added. In general, the best results were obtained with $[allylPdCl]_2$ in the presence of triphenylphosphane. As a consequence of the high reactivity of the chelated enolates, the allylation takes place under very mild conditions at −78° C, giving rise to the desired allylated amino acid derivative **7**. Most common *N*-protecting groups (PGs) can be used with comparable success, although the Z-protected derivative was superior in this particular case.



Scheme 4. Influence of the protecting group on the allylic alkylation

Diastereoselectivity

On the basis of these encouraging results, we were now interested in seeing whether allylic alkylation with our nucleophiles could also be carried out diastereoselectively when substituted allyl substrates were used. We therefore investigated the influence of the *N*-protecting group in the reaction behavior of the 1,3-dimethylated allyl carbonate **8** (Scheme 5). We decided to use **8** because this compound generates a symmetrical π-allylpalladium complex, so regioselectivity problems can be ignored. The best results by far were obtained with the TFA-protected glycine ester **6c**. The yield was very good and the diastereoselectivity excellent. The diastereomerically pure product **9c** was accessible after a single crystallization step.



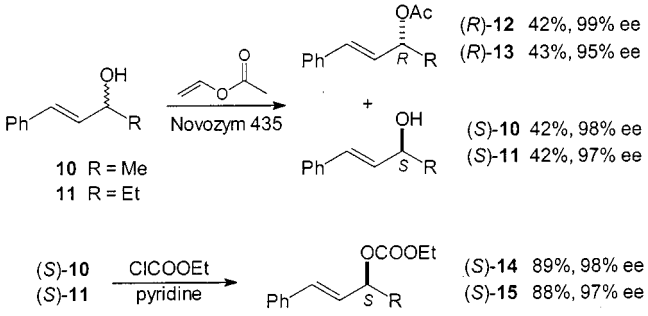
Scheme 5. Diastereoselective allylic alkylations

As confirmed by X-ray structure analysis, the product preferentially obtained from the palladium-catalyzed allylic alkylation was the *anti* one. Hence, two different, mutually complementary procedures for the synthesis of substituted γ,δ-unsaturated amino acids are available. We are now able to synthesize the *syn* diastereomer by ester enolate Claisen rearrangement,[17] and the *anti* diastereomer by palladium-catalyzed allylic substitution.[21]

This was the point at which we focused our investigations on an asymmetric version of this methodology. Depending on the allylic substrate used, two different strategies can be applied. Substrates such as **8**, with two identical substituents at the two allyl termini, form symmetrical, achiral π-allylpalladium complexes, and so the stereochemical outcome of the reaction can be controlled by means of chiral ligands on the palladium center.[3] This straightforward approach is very elegant, but unfortunately more or less limited to such symmetrical substrates. If, on the other hand, allyl derivatives with different substituents are used, unsymmetrical π-allylpalladium complexes are formed. In general, attack of nucleophiles on these complexes provides mixtures of regioisomers, depending on the substitution pattern of the allyl moiety. Although this can be problematic, these substrates also have a big advantage: if optically active allyl substrates are used, the π-allylpalladium complexes formed are chiral, and nucleophilic attack on these complexes provides optically active substitution products. On the basis of the reaction mechanism, stereochemical control in the allyl fragment is not a problem (double inversion), in contrast to chiral centers formed in the "nucleophile moiety". The good results obtained with ester **6c** and allylic carbonate **8** encouraged us to address this challenge, and to investigate reactions of chiral allylic substrates.

Synthesis of Optically Active Allyl Derivatives

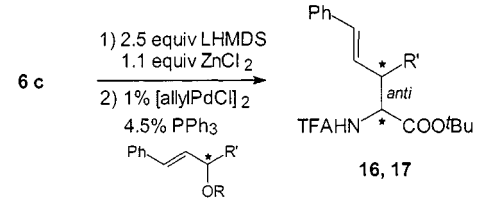
To avoid problems concerning regioselectivity, we decided to use chiral, phenyl-substituted derivatives as substrates. These compounds could easily be prepared by kinetic enzymatic resolution of the corresponding racemic allylic alcohols **10** and **11** with vinyl acetate[22] in the presence of Novozym 435®, an immobilized lipase from *Candida antarctica* (Scheme 6). Both the (*R*)-acetates **12** and **13** and the (*S*)-alcohols (*S*)-**10** and (*S*)-**11** were obtained in good yields and excellent enantiomeric excesses. Treatment of the (*S*)-alcohols with ethyl chloroformate in the presence of pyridine provided the (*S*)-carbonates **14** and **15** in good yields. For analytical purposes the racemic carbonates **14** and **15** were also prepared.



Scheme 6. Synthesis of optically active allyl derivatives

Reactions with Optically Active Allyl Derivatives

Allylic substitutions with these allyl substrates (Scheme 7) proceeded cleanly and in good yields. The only regioisomers obtained were those with the double bond in conjugation with the phenyl ring. The diastereoselectivities of the reactions were high, depending on the substitution patterns at the allyl moieties. The methyl derivative **14** was superior to the ethyl derivative **15**, probably for steric reasons. It was a striking feature that the diastereoselectivities obtained with the acetates were a little worse than those obtained with the carbonates. As we had hoped, the chirality could be transferred almost completely from the allyl derivative to the product. The results obtained are summarized in Table 1.



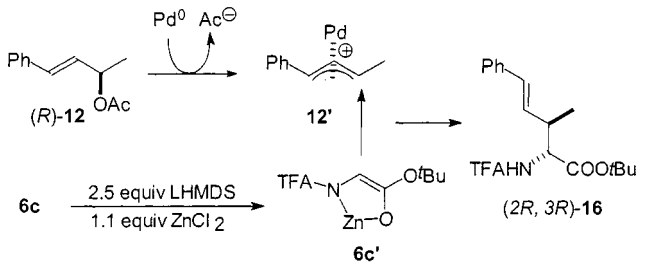
Scheme 7. Stereoselective allylic alkylations

Table 1. Allylic substitution with optically active allyl compounds

Allyl substrate	R	R′	Major product	Yield [%]	*ds* [%]	*ee*[a] [%]
rac-**14**	CO_2Et	Me	*rac*-**16**	71	92	–
(*S*)-**14**	CO_2Et	Me	(2*S*,3*S*)-**16**	76	89	96
(*R*)-**12**	Ac	Me	(2*R*,3*R*)-**16**	67	83	96
rac-**15**	CO_2Et	Et	*rac*-**17**	58	78	–
(*S*)-**15**	CO_2Et	Et	(2*S*,3*S*)-**17**	67	79	95
(*R*)-**13**	Ac	Et	(2*R*,3*R*)-**17**	67	74	93

[a] *ee* of major diastereomer.

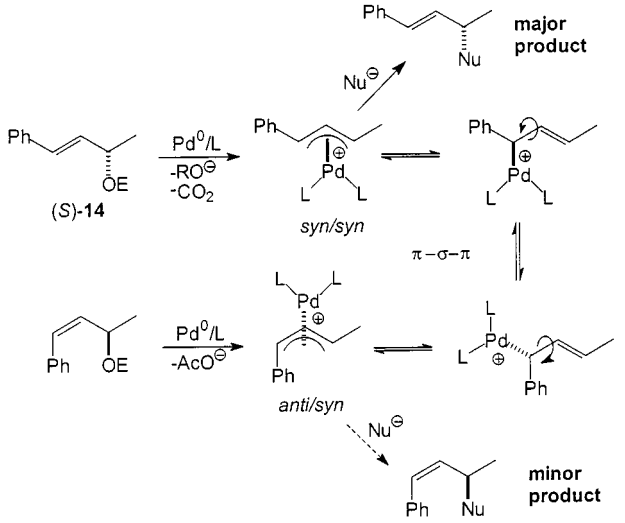
The stereochemical course of the reaction can be explained by the following model (Scheme 8). The π-allyl complex **12′** is formed by attack of palladium(0) on the allylic acetate **12** with inversion of the configuration. This complex subsequently reacts with the chelate enolate **6c′**. The attack of the nucleophile occurs in such a way that the resulting double bond is conjugated with the aromatic π-system. Because of the staggered arrangement of the substituents, steric interactions in the transition state between the π-allyl complex and the nucleophile are minimized. The bulky *tert*-butyl group is situated at the less hindered methyl-substituted side of the allyl complex. No significant interactions should be expected here either. Obviously, these interactions are more pronounced in the case of the corresponding ethyl-substituted derivatives, resulting in lower selectivities. This model is also in accordance with the observation that no significant diastereoselectivity can be obtained when the corresponding methyl glycinate is used.



Scheme 8. Explanation of the stereochemical outcome in the allylation step

π−σ−π Isomerization

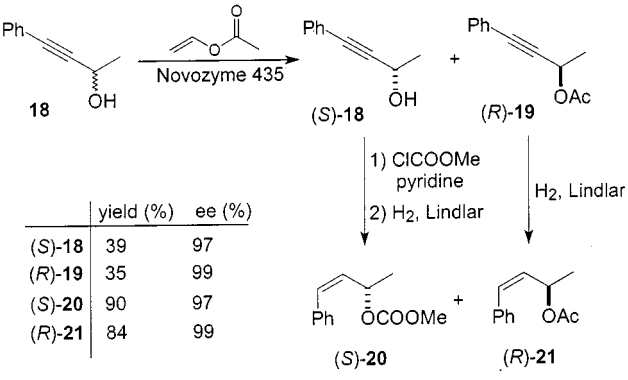
As mentioned above, π−σ−π isomerization is a significant feature of many palladium-catalyzed allylic alkylation reactions. Substituents in a 1,3-disubstituted allyl moiety preferentially occupy the most stable *syn*/*syn* orientation in the π-allyl intermediate (Scheme 9). Through π−σ−π isomerization, the substituents can switch from the *syn* to the *anti* position and vice versa. More or less the same reaction products are therefore normally obtained in palladium-catalyzed allylic substitutions, irrespective of the configuration of the allyl substrate.[3] While maintaining an (*E*)-olefin geometry during the reaction of substrates such as **14** is not a big problem, the corresponding (*Z*)-allylic derivatives and the resulting *anti*/*syn* intermediates fall victim to this isomerization.[23] If optically active compounds are used, the (*S*,*E*)-allyl substrates provide the same products as the (*R*,*Z*) derivatives. Transfer of the (*Z*) configuration from the allyl substrate to the product would only be possible if the reaction could be performed at temperatures at which isomerization reactions cannot take place. Since palladium-catalyzed allylic substitution with chelated ester enolates proceeds even at −78 °C, we saw a good chance of meeting these preconditions.



Scheme 9. π−σ−π Isomerization of (*Z*)- and (*E*)-allyl carbonates

Synthesis of (*Z*)-Allyl Esters

As substrates we chose the (*Z*) analogues of **12** and **14**. The racemic propargylic alcohol **18** was prepared from phenylacetylene and acetaldehyde. The corresponding optically active (*Z*)-allyl compounds were again synthesized by a kinetic enzymatic resolution (Scheme 10). The racemic



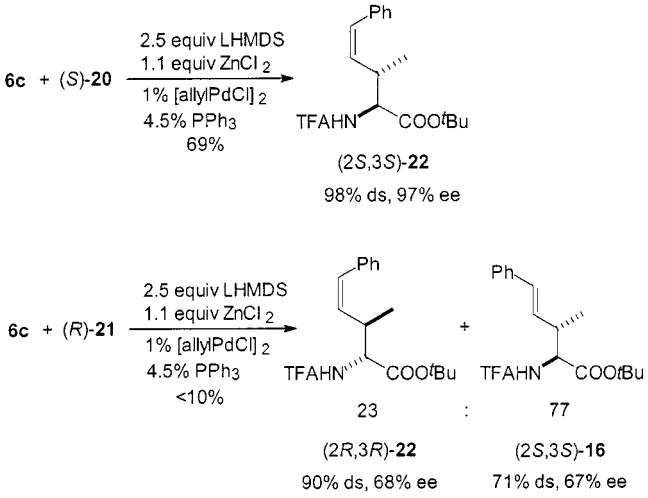
	yield (%)	ee (%)
(*S*)-**18**	39	97
(*R*)-**19**	35	99
(*S*)-**20**	90	97
(*R*)-**21**	84	99

Scheme 10. Preparation of (*Z*)-allyl derivatives

alcohol was therefore treated with vinyl acetate in the presence of Novozym 435®, providing the (*S*)-alcohol (*S*)-**18** and the (*R*)-acetate (*R*)-**19** in good yields and excellent enantiomeric excesses. Compound (*S*)-**18** was converted into the corresponding carbonate, and subsequent Lindlar hydrogenation[24] provided the (*Z*)-carbonate (*S*)-**20**. The (*Z*)-acetate (*R*)-**21** was also accessible by Lindlar hydrogenation of (*R*)-**19**.

C-Allylations with (*Z*)-Allyl Derivatives

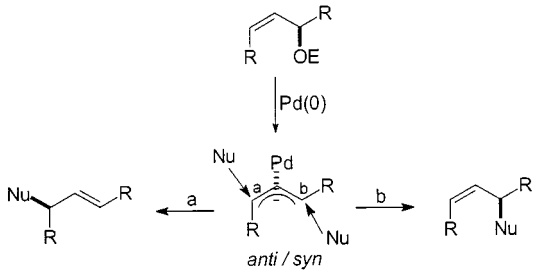
Treatment of these (*Z*) substrates with the glycine ester **6c** gave interesting results (Scheme 11). The reaction with the (*Z*)-carbonates (*S*)-**20** almost exclusively yielded the desired (*Z*) substitution product **22** [(*Z*)/(*E*) > 99:1]. The outstanding selectivities (98% ds, 97% *ee*) observed surpassed even the very good results of the reaction with the (*E*)-carbonate (*S*)-**14**. In contrast, the reaction with (*R*)-**21** furnished an (*E*)/(*Z*) mixture in a very low yield. The selectivities were markedly worse than those obtained with the carbonate. The major isomer was identical to the product resulting from the reaction with the (*E*)-carbonate (*S*)-**14**, which is in good agreement with the reaction mechanism discussed (Scheme 9).



Scheme 11. Reactions of (*Z*)-allyl carbonates

This difference in product formation can be explained by the higher reactivity of the allyl carbonate. Because this substrate can already react at −78 °C, π−σ−π isomerization obviously does not occur. In contrast, the reaction of the acetate takes place at a higher temperature, during the warmup. At the same time, the isomerization is setting in and a partial conversion of the primarily formed *anti*/*syn* complex into the more stable *syn*/*syn* complex can be observed (Scheme 9).[25] The same complex is also formed from the (*S*)-carbonate (*S*)-**12**.

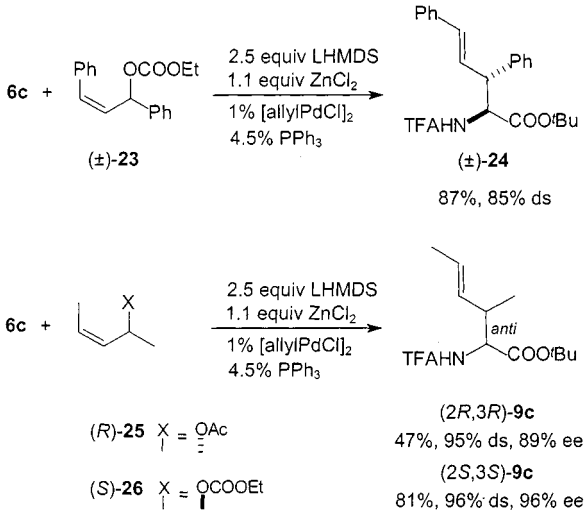
After we had succeeded in transferring the (*Z*) configuration from allyl derivatives to the substitution products by suppressing π−σ−π isomerization, we turned to the following interesting question. What would happen to allylic substrates with (*Z*) configuration and the same substituents at the allyl moiety? In principle, there are two different reaction pathways, because the *anti*/*syn*-π-allyl complex formed as an intermediate has two different allylic termini (Scheme 12). Nucleophilic attack at **a** (*anti* position) would provide a product with the (*E*) configuration at the double bond, whereas attack at **b** (*syn* position) would result in a (*Z*) double bond. Which position is the more reactive one: the *syn* or the *anti* position?



Scheme 12. Possible reaction pathways of *anti*/*syn* complexes

Clarification of this question is of major interest, because symmetrically substituted allyl derivatives are normally used in asymmetric catalyzed reactions. Irrespective of the configuration of the starting material, achiral *syn*/*syn*-π-allylpalladium complexes are generally formed and nucleophilic attack on complexes of this kind can be controlled by, for example, chiral ligands.[3] If, therefore, enantiomerically pure allyl substrates are used, the chiral information is lost during the reaction. If it is possible to suppress π−σ−π isomerization during the reaction of (*Z*)-configured substrates, however, and if one of the two allylic positions is markedly more reactive than the other, it should be possible to generate optically active compounds with these substrates as well.

Our first choice was the diphenyl-substituted derivative **23**, which was obtained in comparable fashion to the other (*Z*) substrates by Lindlar hydrogenation as described above. The resulting allylic alkylation with **23** was very pleasing. The only product isolated was the (*E*)-configured **24**, with a good yield and diastereoselectivity (Scheme 13). Keeping



Scheme 13. Regioselective allylic alkylations

in mind that π−σ−π isomerization does not play a significant role under these reaction conditions, we concluded that the *anti* position is much more reactive than the *syn* position.[14a] For that reason, our next goal was the investigation of a feasible transfer of chirality from optically active, symmetrically substituted (*Z*)-allyl substrates. Because we were unable to obtain optically active derivatives of **23** by kinetic enzymatic resolution, we synthesized (*R*)-**25** and (*S*)-**26** according to the methodology described above for substrates **19** and **20** (Scheme 10). Corresponding treatment of these allyl substrates also exclusively provided the (*E*)-configured substitution products **9c** in acceptable to very good yields. The selectivities with which the *anti* products were formed were excellent in these cases as well.[26] Moreover, the almost complete transfer of chirality shows that the reaction proceeds through the *anti*/*syn* complex and not by way of the *syn*/*syn* complex, which would inevitably produce racemization. Surprisingly, the *ee* was very high even with the acetate **25**, which clearly indicates that substrates with (*Z*) configurations are more reactive than their (*E*) counterparts, giving products without isomerization.

Conclusion

In conclusion, we have shown that chelated enolates of amino acid esters are highly suitable nucleophiles for palladium-catalyzed allylic alkylations. Because of their high reactivities, these enolates react under very mild conditions: at or even below −78 °C. This, for the first time, permits suppression of the π−σ−π isomerization, a typical side reaction of palladium-catalyzed allylations of C-nucleophiles. We were also able to show that *anti*/*syn* complexes obtained under these conditions react selectively at the *anti* position. These chelated enolates therefore enrich the field of palladium-catalyzed reactions. The methodology described is a valuable new tool for the stereoselective synthesis of amino acids and related structures.

Experimental Section

General: All reactions were carried out in oven-dried glassware (100 °C) under argon. All solvents were dried before use. THF was distilled from sodium/benzophenone, CH_2Cl_2 from CaH_2, and stored over molecular sieves. The products were purified by flash chromatography on silica gel (32−63 μm). Mixtures of EtOAc and hexanes were generally used as eluents. − TLC: Commercially precoated Polygram® SIL-G/UV 254 plates (Macherey−Nagel). Viewing was accomplished with UV light and $KMnO_4$ solution. − Melting points were determined with a Büchi melting point apparatus and are uncorrected. − ^1H and ^{13}C NMR: Bruker AC 300 or Bruker DRX 500 spectrometers. − Enantiomeric and diastereomeric excesses were determined with HP 5890 and HP 5890 Series II gas chromatographs with Chira-Si-L-Val and Permethyl-β-Cyclodextrin capillary columns. Helium was used as carrier gas. Diastereomeric ratios were also determined by analytical HPLC, using a Knauer Eurosphere column (250 × 4 mm, Si80, 5 μm, flow: 2 mL/min), and a Knauer UV detector. − Optical rotations were measured with a Perkin−Elmer polarimeter PE 241. − Elemental analyses were carried out at the Department of Chemistry, University of Heidelberg.

General Procedures

a) Kinetic Enzymatic Resolutions: The racemic allyl alcohol (10 mmol) was dissolved in vinyl acetate (10 mL), after which Novozym 435® (100 mg) was added. The reaction mixture was shaken at room temperature while the progress of the reaction was monitored by gas chromatography. After completion of the reaction, the solution was decanted and the residual immobilized enzyme washed repeatedly with diethyl ether. The formed (*R*)-acetates and the unchanged (*S*)-alcohols were separated and purified by silica gel column chromatography.

b) Synthesis of Allyl Carbonates: The carbonates were synthesized according to the technique of Xu et al.[27] The appropriate alcohol (10 mmol) was dissolved in dry CH_2Cl_2 (10 mL) and pyridine (24 mmol). After this had been cooled to 0 °C, ethyl or methyl chloroformate (12 mmol) was added dropwise. The reaction mixture was stirred overnight and then hydrolyzed with 1 N HCl solution. The organic layer was washed three times with 1 N HCl solution and subsequently dried with sodium sulfate. After filtration and evaporation of the solvent, the crude product was purified either by silica gel column chromatography or by kugelrohr distillation.

c) Lindlar Hydrogenations:[22] The substrate (1 mmol) was dissolved in hexane (1 mL), after which the Lindlar catalyst (5 mg) and quinoline (0.02 mL) were added. The flask was connected to a calibrated hydrogenation apparatus. During the reaction the mixture was stirred vigorously. After absorption of the calculated amount of hydrogen, the reaction was interrupted and checked for completion by gas chromatography. The solution was filtered through Celite. After evaporation of the solvent, the products were purified by silica gel column chromatography (eluent: hexanes/ethyl acetate or hexanes/ether).

d) Palladium-Catalyzed Allylic Alkylations: A solution of LHMDS at −20 °C, obtained from HMDS (111 mg, 0.69 mmol) and BuLi (1.6 M, 0.39 mL, 0.625 mmol) in THF (1 mL), was prepared. This solution was cooled to −78 °C and then added to a solution of 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 with vigorous stirring. After an additional 30 min, a solution of $[allylPdCl]_2$ (1 mg, 2.5 μmol, 1 mol %), PPh_3 (3 mg, 11.3 μmol, 4.5 mol %), and the appropriate allylic ester (0.5 mmol) in THF (3 mL) was added. The solution was stirred and allowed to warm to room temperature in the cooling bath overnight. (For monitoring the reaction, samples were taken during the warmup under argon by syringe.) The solution was subsequently diluted with diethyl ether and hydrolyzed with 1 N $KHSO_4$ solution. The aqueous phase 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 (eluent: hexanes/ethyl acetate).

***tert*-Butyl (±)-2-(Benzyloxycarbonyl)amino-4-pentenoate (7a):** By following General Procedure d), **7a** was obtained from **6a** (66 mg, 0.25 mmol) and allyl carbonate **3** (65 mg, 0.5 mmol) in 82% yield (63 mg, 0.21 mmol) as a colorless oil after flash chromatography (ethyl acetate/hexanes, 1:9). − ^1H NMR (300 MHz, $CDCl_3$): δ = 1.44 (s, 9 H), 2.31 (m, 2 H), 4.32 (m, 1 H), 5.06−5.12 (m, 4 H), 5.34 (d, *J* = 8.1 Hz, 1 H), 5.68 (m, 1 H), 7.26−7.34 (m, 5 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.80 (3 C), 36.77, 53.43, 66.62, 81.95, 118.85, 127.87 (2 C), 127.91, 128.28 (2 C), 132.00, 136.16,

155.47, 170.53. − $C_{17}H_{23}NO_4$ (305.37): calcd. C 66.86, H 7.59, N 4.59; found C 66.70, H 7.57, N 4.43.

***tert*-Butyl (±)-2-(*tert*-Butyloxycarbonyl)amino-4-pentenoate (7b):** Starting from ester **6b** (58 mg, 0.25 mmol), **7b** was obtained according to General Procedure d) in 61% yield (42 mg, 0.15 mmol) as a colorless oil after flash chromatography (ethyl acetate/hexanes, 1:9). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.40 (s, 9 H), 1.43 (s, 9 H), 2.45 (m, 2 H), 4.21 (m, 1 H), 5.00−5.11 (m, 3 H), 5.67 (m, 1 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.79 (3 C), 28.08 (3 C), 36.81, 53.10, 79.34, 81.63, 118.46, 132.32, 154.94, 170.87. − $C_{14}H_{25}NO_4$ (271.36): calcd. C 61.97, H 9.29, N 5.16; found C 61.87, H 9.02, N 4.87.

***tert*-Butyl (±)-2-(Trifluoroacetyl)amino-4-pentenoate (7c):** Ester **7c** was obtained from ester **6c** (47 mg, 0.25 mmol) according to General Procedure d), in 61% yield (41 mg, 0.15 mmol) after flash chromatography (ethyl acetate/hexanes, 1:9) as a colorless, amorphous solid, m.p. 36−37 °C. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.45 (s, 9 H), 2.53 (m, 1 H), 2.65 (m, 1 H), 4.52 (m, 1 H), 5.07−5.15 (m, 2 H), 5.62 (m, 1 H), 6.94 (br s, 1 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.68 (3 C), 35.71, 52.14, 83.22, 115.42, 119.71, 130.77, 156.28, 168.98. − $C_{11}H_{16}F_3NO_3$ (267.25): calcd. C 49.44, H 6.03, N 5.24; found C 49.81, H 6.34, N 5.18.

***tert*-Butyl (±)-2-(4-Toluenesulfonyl)amino-4-pentenoate (7d):** According to General Procedure d), **7d** was obtained from **6d** (71 mg, 0.25 mmol) in 59% yield (48 mg, 0.148 mmol) after flash chromatography (ethyl acetate/hexanes, 12:88) as a colorless solid, m.p. 93−94 °C. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.22 (s, 9 H), 2.36 (s, 3 H), 2.41 (m, 2 H), 3.85 (m, 1 H), 5.02−5.08 (m, 2 H), 5.23 (d, *J* = 9.0 Hz, 1 H), 5.62 (m, 1 H), 7.24 (d, *J* = 8.1 Hz, 2 H), 7.69 (d, *J* = 8.3 Hz, 2 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.37, 27.65 (3 C), 37.85, 55.49, 82.52, 119.26, 127.24 (2 C), 129.54 (2 C), 131.52, 136.96, 143.45, 169.81. − $C_{16}H_{23}NO_4S$ (325.43): calcd. C 59.05, H 7.12, N 4.32, S 9.85; found C 59.10, H 7.04, N 4.26, S 9.88.

***tert*-Butyl (±)-(*E*)-2-(Benzyloxycarbonyl)amino-3-methyl-4-hexenoate (9a):** According to General Procedure d), ester **9a** was obtained from **6a** (66 mg, 0.25 mmol) and carbonate **8** (79 mg, 0.5 mmol) in 54% yield (54 mg, 0.13 mmol) as a colorless oil (after flash chromatography, ethyl acetate/hexanes, 1:9). Ratio *anti*/*syn* 82:18; HPLC (ethyl acetate/hexanes, 5:95): $t_{R(anti)}$ = 12.12 min, $t_{R(syn)}$ = 14.54 min. − ***anti* Diastereomer:** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.04 (d, *J* = 6.9 Hz, 3 H), 1.44 (s, 9 H), 1.62 (d, *J* = 6.3 Hz, 3 H), 2.69 (m, 1 H), 4.19 (dd, *J* = 8.9, 4.5 Hz, 1 H), 5.09 (br s, 2 H), 5.14−5.29 (m, 2 H), 5.48 (m, 1 H), 7.29−7.35 (m, 5 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 16.74, 17.92, 28.02 (3 C), 39.40, 58.81, 66.86, 81.79, 127.21, 128.06 (2 C), 128.46 (3 C), 130.35, 136.39, 156.26, 170.67. − ***syn* Diastereomer:** ^{1}H NMR (300 MHz, $CDCl_3$; selected signals): δ = 2.52 (m, 1 H), 4.14 (m, 1 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 16.42, 27.83 (3 C), 40.22, 58.66, 126.49, 131.15. − $C_{19}H_{27}NO_4$: calcd. C 68.45, H 8.16, N 4.20; found C 68.26, H 8.14, N 4.22.

***tert*-Butyl (±)-(*E*)-2-(*tert*-Butyloxycarbonyl)-3-methyl-4-hexenoate (9b):** Ester **9b** was obtained from ester **6b** (59 mmol, 0.25 mmol) and carbonate **8** (79 mg, 0.5 mmol) according to General Procedure d), in 25% yield (19 mg, 0.06 mmol) (after flash chromatography, ethyl acetate/hexanes, 5:95). Ratio *anti*/*syn* 76:24. − ***anti* Diastereomer:** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.02 (d, *J* = 6.8 Hz, 3 H), 1.41, 1.43 (2s, 18 H), 1.63 (d, *J* = 6.1 Hz, 3 H), 2.63 (m, 1 H), 4.09 (dd, *J* = 8.8, 4.6 Hz, 1 H), 4.89 (d, *J* = 8.8 Hz, 1 H), 5.24 (dd, *J* = 15.2, 7.6 Hz, 1 H), 5.45 (dq, *J* = 15.2, 6.3 Hz, 1 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 16.61, 17.68, 27.84 (3 C), 28.09 (3 C), 39.37, 58.20, 81.32 (2 C), 126.66, 130.52, 156.31, 170.84. − ***syn* Diastereomer:** ^{1}H NMR (300 MHz, $CDCl_3$; selected signals): δ = 1.00 (d, *J* = 6.8 Hz, 3 H), 1.44 (s, 9 H), 2.47 (m, 1 H), 4.19 (m, 1 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 16.18, 17.72, 40.02, 131.44. − HRMS (EI) calcd. for $C_{16}H_{29}NO_4$ [M^+ − isobutene] 243.14706; found 243.14547.

***tert*-Butyl (*E*)-3-Methyl-2-(trifluoroacetyl)amino-4-hexenoate (9c):** According to General Procedure d), *rac*-**9c** was obtained from **6c** (57 mg, 0.25 mmol) and **8** in 88% yield (65 mg, 0.22 mmol) as a colorless solid (after flash chromatography, ethyl acetate/hexanes, 1:9). Ratio *anti*/*syn* 96:4. Recrystallization from diethyl ether/hexanes provided diastereomerically pure, colorless, rhombic crystals of the *anti* stereoisomer, m.p. 62−63 °C. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.03 (d, *J* = 6.9 Hz, 3 H), 1.45 (s, 9 H), 1.65 (d, *J* = 6.3 Hz, 3 H), 2.75 (m, 1 H), 4.42 (dd, *J* = 8.7, 4.7 Hz, 1 H), 5.24 (dd, *J* = 15.3, 7.7 Hz, 1 H), 5.52 (dqd, *J* = 15.3, 6.3, 1.0 Hz, 1 H), 6.65 (br s, 1 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 16.36, 17.63, 27.75 (3 C), 39.37, 56.96, 82.83, 115.56, 128.03, 129.30, 156.74, 168.83. − The optically active derivatives were obtained from (*R*)-**25** and (*S*)-**26**, respectively. − **(2*R*,3*R*)-9c:** Oil. − $[\alpha]_D^{20}$ = −18.1 (*c* = 1.1, $CHCl_3$, 95% *ds*, 89% *ee*). − **(2*S*,3*S*)-9c:** Oil. − $[\alpha]_D^{20}$ = +21.7 (*c* = 1.0, $CHCl_3$, 96% *ds*, 96% *ee*). − GC (Chira-Si-L-Val, 80 °C, isothermic): $t_{R(2R,3R)}$ = 17.39 min, $t_{R(2R,3S)}$ = 17.95 min, $t_{R(2S,3S)}$ = 23.21 min, $t_{R(2S,3R)}$ = 24.60 min. − $C_{13}H_{20}F_3NO_3$ (295.30): calcd. C 52.88, H 6.83, N 4.74; found C 52.85, H 6.60, N 4.71.

(2*S*,3*E*)-4-Phenyl-3-buten-2-ol [(*S*)-10]:[22] According to General Procedure a), (*S*)-**10** was obtained on a 20-mmol scale in 42% yield (1.257 g, 8.4 mmol, 98% *ee*) after flash chromatography (ethyl acetate/hexanes, 1:9) as a colorless solid, m.p. 58−59 °C. − $[\alpha]_D^{20}$ = −32.1 (*c* = 1.8, $CHCl_3$, 98% *ee*) {ref.[22] $[\alpha]_D^{20}$ = −29.2 (*c* = 2.00, $CHCl_3$, > 95% *ee*)}. − ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.35 (d, *J* = 6.4 Hz, 3 H), 1.69 (br s, 1 H), 4.46 (dqd, *J* = 6.4, 6.4, 0.9 Hz, 1 H), 6.23 (dd, *J* = 15.9, 6.4 Hz, 1 H), 6.54 (d, *J* = 15.9 Hz, 1 H), 7.21 (t, *J* = 7.8 Hz, 1 H), 7.29 (dd, *J* = 7.8, 7.3 Hz, 2 H), 7.34 (d, *J* = 7.3 Hz, 2 H). − ^{13}C NMR (125 MHz, $CDCl_3$): δ = 23.38, 68.90, 126.42 (2 C), 127.60, 128.55 (2 C), 129.35, 133.54, 136.66. − GC (β-CD, 115 °C, isothermic): $t_{R(R)}$ = 33.25 min, $t_{R(S)}$ = 33.48 min.

(1*E*,3*S*)-1-Phenyl-1-penten-3-ol [(*S*)-11]:[28] Enzymatic kinetic resolution [General Procedure a)] provided (*S*)-**11** on a 16.25-mmol scale in 45% yield (1.18 g, 7.31 mmol, 97% *ee*), as a colorless oil after flash chromatography (ethyl acetate/hexanes 1:9). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.96 (t, *J* = 7.5 Hz, 3 H), 1.62 (m, 2 H), 1.74 (br s, 1 H), 4.20 (m, 1 H), 6.21 (dd, *J* = 15.9, 6.7 Hz, 1 H), 6.57 (d, *J* = 16.0 Hz, 1 H), 7.20−7.39 (m, 5 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 9.49, 30.03, 74.15, 126.24 (2 C), 127.38, 128.35 (2 C), 130.20, 132.12, 136.59. GC (β-CD, 120 °C, isothermic): $t_{R(R)}$ = 46.17 min, $t_{R(S)}$ = 46.41 min.

(1*E*,3*R*)-3-Acetoxy-1-phenyl-1-butene [(*R*)-12]:[29] According to General Procedure a), (*R*)-**12** was obtained on a 20-mmol scale in 42% yield (1.69 g, 8.4 mmol, 99% *ee*) as a colorless oil after flash chromatography (ethyl acetate/hexanes, 1:9). − $[\alpha]_D^{20}$ = +142.2 (*c* = 1.0, $CHCl_3$, 99% *ee*) {ref.[29] $[\alpha]_D^{20}$ = +59 (*c* = 0.93, CCl_4, 44% *ee*)}. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.40 (d, *J* = 6.5 Hz, 3 H), 2.06 (s, 3 H), 5.52 (dqd, *J* = 6.7, 6.5, 1.0 Hz, 1 H), 6.18 (dd, *J* = 15.9, 6.7 Hz, 1 H), 6.59 (d, *J* = 15.9 Hz, 1 H), 7.20−7.39 (m, 5 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.34, 21.34, 70.95, 126.53 (2 C), 127.86, 128.53 (2 C), 128.81, 131.51, 136.33, 170.28. − GC (β-CD, 115 °C, isothermic): $t_{R(S)}$ = 31.14 min, $t_{R(R)}$ = 35.72 min.

(1*E*,3*R*)-3-Acetoxy-1-phenyl-1-pentene [(*R*)-13]:[30] Enzymatic kinetic resolution [General Procedure a)] provided (*R*)-**13** on a 16.25-

mmol scale in 48% yield (1.59 g, 7.8 mmol, 95% *ee*) as a colorless oil after flash chromatography (ethyl acetate/hexanes, 1:9). − $[\alpha]_D^{20}$ = +114.9 (*c* = 1.1, $CHCl_3$, 95% *ee*) {ref.[29] $[\alpha]_D^{20}$ = 120.1}. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.93 (t, *J* = 7.5 Hz, 3 H), 1.74 (m, 2 H), 2.07 (s, 3 H), 5.33 (m, 1 H), 6.11 (dd, *J* = 15.9, 7.3 Hz, 1 H), 6.59 (d, *J* = 15.9 Hz, 1 H), 7.20−7.39 (m, 5 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 9.32, 21.07, 27.40, 75.77, 126.34 (2 C), 127.35, 127.65, 128.33 (2 C), 132.35, 136.21, 170.18. − GC (β-CD, 120 °C, isothermic): $t_{R(S)}$ = 37.17 min, $t_{R(R)}$ = 39.05 min.

Ethyl (2*S*,3*E*)-(4-Phenyl-3-buten-2-yl)carbonate [(*S*)-14]: Carbonate (*S*)-**14** was obtained from alcohol (*S*)-**10** (1.26 g, 8.48 mmol) according to General Procedure b), in 89% yield (1.67 g, 7.55 mmol, 98% *ee*) and as a colorless oil after flash chromatography (ethyl acetate/hexanes, 15:85). − $[\alpha]_D^{20}$ = −117.4 (*c* = 1.0, $CHCl_3$, 98% *ee*). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.30 (t, *J* = 7.1 Hz, 3 H), 1.46 (d, *J* = 6.4 Hz, 3 H), 4.19 (q, *J* = 7.1 Hz, 2 H), 5.36 (dqd, *J* = 7.0, 6.4, 1.0 Hz, 1 H), 6.19 (dd, *J* = 15.9, 7.0 Hz, 1 H), 6.64 (d, *J* = 15.9 Hz, 1 H), 7.21−7.39 (m, 5 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.23, 20.46, 63.78, 74.97, 126.61 (2 C), 127.98, 128.13, 128.54 (2 C), 132.14, 136.17, 154.48. − $C_{13}H_{16}O_3$ (220.27): calcd. C 70.89, H 7.32; found C 70.89, H 7.35.

Ethyl (1*E*,3*S*)-(1-Phenyl-1-penten-3-yl)carbonate [(*S*)-15]: According to General Procedure b), (*S*)-**15** was obtained from alcohol (*S*)-**11** (1.18 g, 7.26 mmol) in 88% yield (1.50 g, 6.39 mmol, 97% *ee*) as a colorless oil after flash chromatography (ethyl acetate/hexanes, 15:85). − $[\alpha]_D^{20}$ = −97.5 (*c* = 1.0, $CHCl_3$, 97% *ee*). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.96 (t, *J* = 7.4 Hz, 3 H), 1.30 (t, *J* = 7.1 Hz, 3 H), 1.78 (m, 2 H), 4.18 (q, *J* = 7.1 Hz, 2 H), 5.15 (m, 1 H), 6.13 (dd, *J* = 16.0, 7.6 Hz, 1 H), 6.65 (d, *J* = 16.0 Hz, 1 H), 7.20−7.40 (m, 5 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 9.26, 14.04, 27.46, 63.58, 79.90, 126.43 (2 C), 126.70, 127.77, 128.34 (2 C), 132.99, 136.05, 154.48. − $C_{14}H_{18}O_3$ (234.30): calcd. C 71.77, H 7.74; found C 71.61, H 7.68.

***tert*-Butyl (4*E*)-3-Methyl-5-phenyl-2-(trifluoroacetyl)amino-4-pentenoate (16):** Ester *rac*-**16** was obtained from ester **6c** (57 mg, 0.25 mmol) and *rac*-**14** (55 mg, 0.25 mmol) according to General Procedure d) in 71% yield (64 mg, 0.18 mmol) and as a colorless solid (after flash chromatography, ethyl acetate/hexanes, 1:9). Ratio *anti*/*syn* 92:8. Recrystallization from diethyl ether/hexanes provided a diastereomerically pure, white powder, m.p. 93−95 °C. − ***anti* Diastereomer:** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.17 (d, *J* = 6.9 Hz, 3 H), 1.47 (s, 9 H), 3.00 (m, 1 H), 4.59 (dd, *J* = 8.4, 4.7 Hz, 1 H), 6.04 (dd, *J* = 15.9, 7.8 Hz, 1 H), 6.46 (dd, *J* = 15.9, 1.0 Hz, 1 H), 6.90 (d, *J* = 8.0 Hz, 1 H), 7.20−7.33 (m, 5 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 16.16, 27.96 (3 C), 39.99, 57.26, 83.43, 115.73, 126.24 (2 C), 128.50, 128.59 (2 C), 127.70, 132.18, 136.67, 157.00, 169.58. − ***syn* Diastereomer:** ^{1}H NMR (300 MHz, $CDCl_3$; selected signals): δ = 1.20 (d, *J* = 6.9 Hz, 3 H), 1.46 (s, 9 H), 2.87 (m, 1 H), 4.56 (m, 1 H), 6.02 (dd, *J* = 15.9, 7.8 Hz, 1 H), 6.41 (d, *J* = 15.9 Hz, 1 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 16.29, 28.00 (3 C), 40.53, 57.05, 83.50, 127.62, 131.87, 168.87. − The optically active derivatives were obtained under the same conditions from (*R*)-**12** and (*S*)-**14**, respectively. − **(2*R*,3*R*)-16:** $[\alpha]_D^{25}$ = −12.5 (*c* = 1.2, $CHCl_3$, 83% *ds*, 96% *ee*). − **(2*S*,3*S*)-16:** $[\alpha]_D^{23}$ = +18.2 (*c* = 1.1, $CHCl_3$, 89% *ds*, 96% *ee*). − GC (Chira-Si-L-Val, 145 °C, isothermic): $t_{R(2R,3R)}$ = 17.92 min, $t_{R(2R,3S)}$ = 18.30 min, $t_{R(2S,3S)}$ = 19.96 min, $t_{R(2S,3R)}$ = 20.67 min. − $C_{18}H_{22}F_3NO_3$ (357.37): calcd. C 60.50, H 6.20, N 3.92; found C 60.50, H 6.39, N 3.82.

***tert*-Butyl (4*E*)-3-Ethyl-5-phenyl-2-(trifluoroacetyl)amino-4-pentenoate (17):** Ester *rac*-**17** was obtained from ester **6c** (57 mg, 0.25 mmol) and *rac*-**15** (59 mg, 0.25 mmol) according to General Procedure d) in 58% yield (54 mg, 0.15 mmol) and as a colorless oil (after flash chromatography, ethyl acetate/hexanes, 1:9), in an *anti*/*syn* ration of 78:22. − ***anti* Diastereomer:** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.94 (t, *J* = 7.3 Hz, 3 H), 1.40 (m, 1 H), 1.47 (s, 9 H), 1.63 (m, 1 H), 2.68 (m, 1 H), 4.66 (dd, *J* = 8.6, 4.4 Hz, 1 H), 5.88 (dd, *J* = 15.8, 9.2 Hz, 1 H), 6.46 (d, *J* = 15.8 Hz, 1 H), 6.81 (d, *J* = 8.2 Hz, 1 H) 7.22−7.33 (m, 5 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.61, 23.87, 27.84 (3 C), 47.75, 56.05, 83.17, 115.56, 126.07 (2 C), 126.62, 127.54, 128.39 (2 C), 133.82, 136.34, 156.83, 168.83. − ***syn* Diastereomer:** ^{1}H NMR (300 MHz, $CDCl_3$; selected signals): δ = 1.45 (s, 9 H), 2.50 (m, 1 H), 4.56 (m, 1 H), 6.41 (d, *J* = 15.8 Hz, 1 H), 6.91 (br s, 1 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.48, 28.04 (3 C), 48.54, 56.21, 83.47, 127.29, 133.92, 168.80. − The optically active derivatives were obtained from (*R*)-**13** and (*S*)-**15**, respectively. − **(2*R*,3*R*)-17:** Oil. − $[\alpha]_D^{20}$ = −3.6 (*c* = 1.1, $CHCl_3$, 74% *ds*, 93% *ee*). − **(2*S*,3*S*)-17:** Solid, m.p. 59−60 °C (diethyl ether/hexanes). − $[\alpha]_D^{25}$ = +34.5 (*c* = 0.7, $CHCl_3$, 97% *ds*, 99% *ee*). − GC (Chira-Si-L-Val, 140 °C, isothermic): $t_{R(2R,3R)}$ = 27.06 min, $t_{R(2R,3S)}$ = 27.67 min, $t_{R(2S,3S)}$ = 31.45 min, $t_{R(2S,3R)}$ = 32.69 min. − $C_{19}H_{24}F_3NO_3$ (371.40): calcd. C 61.45, H 6.51, N 3.77; found C 61.38, H 6.68, N 3.67.

(2*S*)-4-Phenyl-3-butyn-2-ol [(*S*)-18]:[22] According to General Procedure a), (*S*)-**18** was obtained from alcohol *rac*-**18** on a 10-mmol scale in 39% yield (0.56 g, 3.9 mmol, 97% *ee*) as a colorless oil after flash chromatography (ethyl acetate/hexanes, 15:85). − $[\alpha]_D^{20}$ = −33.9 (*c* = 1.1, $CHCl_3$, 97% *ee*) {ref.[20] $[\alpha]_D^{25}$ = −50.6 (*c* = 1.5, ether, > 95% *ee*)}. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.54 (d, *J* = 6.6 Hz, 3 H), 2.20 (d, *J* = 3.8 Hz, 1 H), 4.75 (m, 1 H), 7.26−7.50 (m, 5 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.17, 58.63, 83.80, 90.77, 122.38, 128.06, 128.14, 131.44. − GC (Chira-Si-L-Val, 80 °C, isothermic): $t_{R(S)}$ = 33.02 min, $t_{R(R)}$ = 33.78 min.

(3*R*)-3-Acetoxy-1-phenyl-1-butyne [(*R*)-19]:[22] According to General Procedure a), (*R*)-**19** was obtained from *rac*-**18** (1.46 g, 10 mmol) in 35% yield (0.67 g, 3.5 mmol, 99% *ee*) as a colorless oil (after flash chromatography, ethyl acetate/hexanes, 15:85). − $[\alpha]_D^{20}$ = +188 (*c* = 1.1, $CHCl_3$, 99% *ee*). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.57 (d, *J* = 6.7 Hz, 3 H), 2.09 (s, 3 H), 5.68 (q, *J* = 6.7 Hz, 1 H), 7.27−7.34 (m, 3 H), 7.39−7.43 (m, 2 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.87, 21.29, 60.58, 84.34, 87.20, 122.06, 128.01 (2 C), 128.36, 131.64 (2 C), 169.68. − GC (β-CD, 120 °C, isothermic): $t_{R(S)}$ = 34.76 min, $t_{R(R)}$ = 36.34 min.

Methyl (2*S*,3*Z*)-4-Phenyl-3-buten-2-ylcarbonate (20): According to General Procedures b) and c), carbonate **20** was obtained from alcohol (*S*)-**18** (500 mg, 3.41 mmol) in 90% overall yield (633 mg, 3.07 mmol, 97% *ee*) as a colorless oil after flash chromatography (ethyl acetate/hexanes, 1:9). − $[\alpha]_D^{20}$ = +45.8 (*c* = 1.1, $CHCl_3$, 97% *ee*). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.43 (d, *J* = 6.2 Hz, 3 H), 3.74 (s, 3 H), 5.64−5.72 (m, 2 H), 6.57 (d, *J* = 10.5 Hz, 1 H), 7.25−7.38 (m, 5 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.76, 54.54, 71.77, 127.46, 128.43 (2 C), 128.56 (2 C), 130.72, 131.42, 136.15, 154.98. − GC (β-CD, 125 °C, isothermic): $t_{R(R)}$ = 17.97 min, $t_{R(S)}$ = 18.55 min. − $C_{12}H_{14}O_3$ (206.24): calcd. C 69.89, H 6.84; found C 69.88, H 6.92.

(1*Z*,3*R*)-3-Acetoxy-1-phenyl-1-butene [(*R*)-21]:[23] Acetate (*R*)-**21** was obtained from (*R*)-**19** (282 mg, 1.50 mmol) according to General Procedure c) in 84% yield (241 mg, 1.26 mmol, 99% *ee*) and as a colorless oil after flash chromatography (ethyl acetate/hexanes, 12:88). − $[\alpha]_D^{20}$ = −34.5 (*c* = 1.1, $CHCl_3$, 99% *ee*) {ref.[21] $[\alpha]_D^{20}$ = −75.3 (*c* = 0.5, CCl_4, 73% *ee*)}. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.36 (d, *J* = 6.3 Hz, 3 H), 2.01 (s, 3 H), 5.64 (dd, *J* = 11.6, 9.2 Hz, 1 H), 5.79 (dqd, *J* = 9.2, 6.3, 1.1 Hz, 1 H), 6.52 (d, *J* =

11.6 Hz, 1 H), 7.17−7.36 (m, 5 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.60, 21.09, 67.65, 127.14, 128.17 (2 C), 128.38 (2 C), 130.72, 131.11, 136.09, 169.94. − GC (β-CD, 110 °C, isothermic): $t_{R(R)}$ = 21.30 min, $t_{R(S)}$ = 22.43 min.

***tert*-Butyl (2*S*,3*S*,4*Z*)-3-Methyl-5-phenyl-2-(trifluoroacetyl)amino-4-pentenoate [(2*S*,3*S*)-22]:** Allylation product (2*S*,3*S*)-**22** was obtained from ester **6c** (57 mg, 0.25 mmol) and carbonate (*S*)-**20** (41 mg, 0.2 mmol) according to General Procedure d) in 69% yield (49 mg, 0.138 mmol, 98% ds, 97% *ee*) and as a colorless solid (after flash chromatography, ethyl acetate/hexanes, 5:95). Recrystallization from diethyl ether/hexanes furnished an enantiomerically pure, white, amorphous solid, m.p. 78−79 °C. − $[\alpha]_D^{23}$ = +3.5 (*c* = 2.6, $CHCl_3$, 99% ds, 99% *ee*). − The reaction products from (*R*)-**21** were not isolated. − ***anti* Diastereomer:** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.21 (s, 9 H), 1.66 (d, *J* = 4.7 Hz, 3 H), 3.59 (m, 1 H), 4.74 (dd, *J* = 8.6, 8.6 Hz, 1 H), 5.60−5.69 (m, 2 H), 6.88 (d, *J* = 8.6 Hz, 1 H), 7.19−7.34 (m, 5 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.54, 27.36 (3 C), 52.86, 56.75, 82.84, 115.52, 126.05, 127.18 (2 C), 127.49, 128.20 (2 C), 129.49, 138.83, 156.37, 168.80. − The signals of the *syn* diastereomer could not be found in the spectra. − GC (Chira-Si-L-Val, 140 °C, isothermic): $t_{R(2R,3S)}$ = 11.03 min, $t_{R(2S,3R)}$ = 11.84 min, $t_{R(2R,3R)}$ = 12.96 min, $t_{R(2S,3S)}$ = 15.09 min. − $C_{18}H_{22}F_3NO_3$ (357.37): calcd. C 60.50, H 6.20, N 3.92; found C 60.42, H 6.44, N 3.99.

Ethyl (2*Z*)-1,3-Diphenylpropenylcarbonate (23): According to General Procedure b), carbonate **23** was obtained from (2*Z*)-1,3-diphenyl-2-propen-1-ol[31] (866 mg, 4.12 mmol) in 86% yield (996 mg, 3.54 mmol) as a colorless oil after flash chromatography (ethyl acetate/hexanes, 1:9). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.27 (t, *J* = 7.1 Hz, 3 H), 4.15 (m, 2 H), 5.99 (dd, *J* = 11.6, 9.5 Hz, 1 H), 6.52 (d, *J* = 9.5 Hz, 1 H), 6.73 (d, *J* = 11.6 Hz, 1 H), 7.25−7.44 (m, 10 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.19, 64.00, 75.96, 126.99 (2 C), 127.64, 128.11, 128.35, 128.42 (2 C), 128.55 (2 C), 128.61 (2 C), 132.42, 135.96, 139.17, 154.27. − $C_{18}H_{18}O_3$ (282.34): calcd. C 76.57, H 6.43; found C 76.46, H 6.38.

(±)-[*tert*-Butyl (4*E*)-3,5-Diphenyl-2-(trifluoroacetyl)amino-4-pentenoate] (24): Allylic alkylation using **23** (56 mg, 0.2 mmol) and **6c** (57 mg, 0.25 mmol) according to General Procedure d) provided **24** in 87% yield (73 mg, 0.17 mmol), as a colorless solid (after flash chromatography, ethyl acetate/hexanes, 5:95). Ratio *anti*/*syn* 85:15. Recrystallization from diethyl ether/hexanes provided a diastereomerically pure, white powder, m.p. 113−115 °C. − ***anti* Diastereomer:** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.25 (s, 9 H), 3.84 (dd, *J* = 8.8, 8.5 Hz, 1 H), 4.89 (dd, *J* = 8.6, 8.5 Hz, 1 H), 6.37 (dd, *J* = 15.7, 8.8 Hz, 1 H), 6.52 (d, *J* = 15.7 Hz, 1 H), 6.89 (d, *J* = 8.6 Hz, 1 H), 7.19−7.37 (m, 10 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.62 (3 C), 52.99, 56.86, 83.20, 115.44, 126.20, 127.06, 127.60, 128.07, 128.34, 128.41, 128.57, 133.23, 136.26, 138.24, 156.46, 168.53. − ***syn* Diastereomer:** ^{1}H NMR (300 MHz, $CDCl_3$; selected signals): δ = 1.35 (s, 9 H), 4.01 (m, 1 H), 4.95 (m, 1 H), 6.32−6.54 (m, 2 H), 6.71 (d, *J* = 8.5 Hz, 1 H), 7.21−7.36 (m, 10 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.44, 51.45, 56.74, 83.38, 126.37, 133.26, 138.09.). − GC (Chira-Si-L-Val, 165 °C, isothermic): $t_{R(syn)}$ = 48.99 min, $t_{R(syn)}$ = 52.57 min, $t_{R(anti)}$ = 57.57 min, $t_{R(anti)}$ = 64.31 min. − $C_{23}H_{24}F_3NO_3$ (419.44): calcd. C 65.86, H 5.77, N 3.34; found C 65.81, H 6.01, N 3.24.

(2*Z*,3*R*)-3-Acetoxy-2-pentene [(*R*)-25]:[32] Subjection of 3-pentyn-2-ol[33] (2.15 g, 25.6 mmol) to General Procedures a) and c) gave rise to (*R*)-**25** in 27% yield (890 mg, 6.92 mmol, 99% *ee*), as a colorless oil (after flash chromatography, diethyl ether/hexanes, 1:9). − $[\alpha]_D^{25}$ = −18.1 (*c* = 0.9, $CHCl_3$, 99% *ee*) {ref.[32] [(*S*)-acetate]: $[\alpha]_D^{20}$ = +20.3 (*c* = 1.01, EtOH)}. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.25 (d, *J* = 6.4 Hz, 3 H), 1.68 (dd, *J* = 6.9, 1.6 Hz, 3 H), 2.00 (s, 3 H), 5.34 (m, 1 H), 5.49−5.68 (m, 2 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.99, 20.36, 21.09, 66.59, 126.91, 130.11, 170.12. − GC (β-CD, 50 °C, isothermic): $t_{R(S)}$ = 12.56 min, $t_{R(R)}$ = 13.26 min.

Ethyl (3*Z*)-3-Penten-2-ylcarbonate [(*S*)-26]: According to General Procedures a) to c), (*S*)-**26** was obtained from 3-pentyn-2-ol[33] on a 5-mmol scale in 31% yield (99% *ee*) and as a colorless oil (after flash chromatography, diethyl ether/hexanes, 1:9). − $[\alpha]_D^{20}$ = +25.1 (*c* = 1.0, $CHCl_3$, 99% *ee*). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.27 (t, *J* = 7.2 Hz, 3 H), 1.31 (d, *J* = 6.4 Hz, 3 H), 1.70 (dd, *J* = 6.9, 1.7 Hz, 3 H), 4.14 (q, *J* = 7.2 Hz, 2 H), 5.54−5.63 (m, 3 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.19, 14.23, 20.56, 63.61, 70.61, 127.60, 129.83, 154.59. − GC (β-CD, 70 °C, isothermic): $t_{R(R)}$ = 12.14 min, $t_{R(S)}$ = 12.76 min. − $C_8H_{14}O_3$ (158.20): calcd. C 60.74, H 8.92; found C 60.98, H 9.05.

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