Concave Reagents, 30[+]

Diastereoselective Generation of Quaternary Stereocenters by Ligand-Controlled Palladium-Catalyzed Allylations

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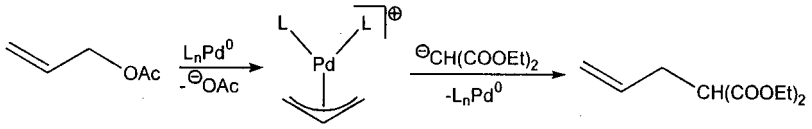
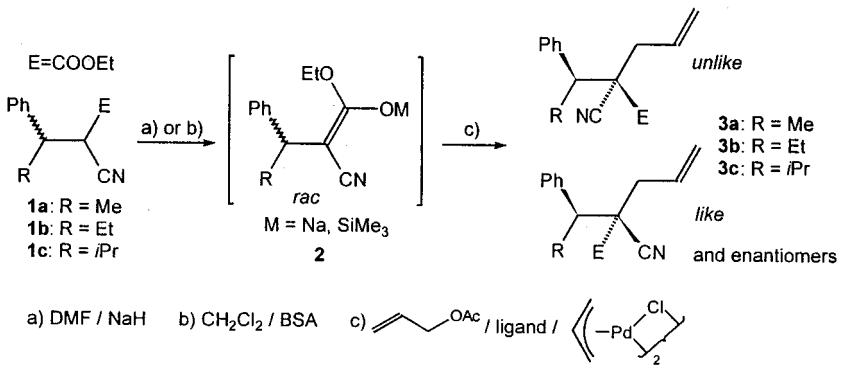
The 1,2-asymmetric induction in the formation of new quaternary centers by palladium-catalyzed allylation of substituted cyanoacetates **1a–c** was controlled by using 2,9-disubstituted 1,10-phenanthrolines as ligands, giving the allylated products **3a–c** with *like*/*unlike* diastereoselectivities up to 94:6. The increased selectivities were caused by a tight wrapping of the allyl unit in the intermediate complexes. Differences in stereoselectivity for varying substrates can be understood when modified Taft parameters, the homo-E_s values, are considered. The *like*/*unlike* isomers were assigned by using a combination of molecular modeling, NOE measurements and analyses of chemical shifts. An X-ray analysis of the acid **14** confirmed the structural assignment.

Palladium-catalyzed allylic substitutions are C−C bond-formation reactions with wide synthetic applications.[2] In Scheme 1 the general reaction with allyl acetate as the allyl source and diethyl malonate as the nucleophile is shown. The allyl compound may be substituted, and leaving groups other than acetate have also been used successfully; in addition, the nucleophile may be varied, too.

Depending on the substitution pattern of the allyl unit and the nucleophile, the formation of stereo- and regioisomers is possible. If substituted allyl units are employed, enantiomers may be formed.[3] The enantioselectivity can be controlled by the ligand L.[4] If the allyl unit is part of a cyclic molecule and the cycle carries at least one additional substituent, diastereomeric products are formed by 1,*n*-asymmetric induction.[2] If the nucleophile is unsymmetrically substituted (prochiral) and one substituent contains a chiral center, diastereomers will also be formed.[5] Here we demonstrate that for the latter systems the stereochemistry



Scheme 1. Palladium catalyzed allylation of diethyl malonate with allyl acetate; L = ligand



Scheme 2. The palladium-catalyzed allylation of substituted cyanoacetates **1** gives diastereomeric allyl cyanoacetates **3**

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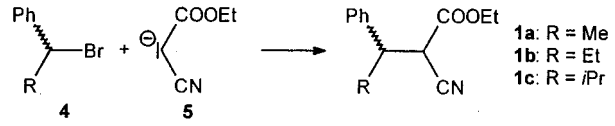


Scheme 3. Syntheses of the cyanoacetates **1**

of allyl-substituted quaternary stereocenters can be directed by appropriate ligands L in the palladium catalyst. For this purpose, cyanoacetates containing a chiral substituent have been synthesized and have been used as a substrate in this allylation.

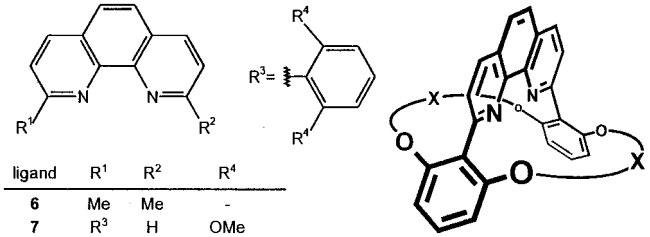
The substrates **1a–c** have been synthesized by alkylation of ethyl cyanoacetate with α-(bromoalkyl)benzenes **4** which are either commercially available or can be synthesized by a Ziegler NBS bromination[6] (Scheme 3).

Allylation of these substrates **1** gives the diastereomeric allylcyanoacetates **3** (Scheme 2). Such an allylation can be carried out with or without catalysis by palladium complexes. Without a catalyst a good leaving group such as bromide is necessary. With the help of palladium the reaction occurs in a smoother way; e.g. acetates react, and the diastereoselectivity of the palladium-catalyzed allylation can be directed by sterical shielding of the terminal carbon atoms of the allylpalladium unit when suitable ligands are chosen.

Triphenylphosphane is usually used as the ligand L for palladium,[2] but leads only to low selectivities. Åkermark et al. have demonstrated[7a,7b] that this palladium-catalyzed allylation can also be carried out with N,N-ligands such as substituted 1,10-phenanthrolines. Further N,N-ligands have been investigated by other groups.[7]

2,9-Dimethyl-1,10-phenanthroline (**6**, neocuproine) is the simplest of the 2,9-disubstituted 1,10-phenanthrolines. With other substituents in the 2- and 9-positions of the 1,10-phenanthroline, the sterical shielding of the terminal carbon atoms of the allyl moiety in an allylpalladium complex can be expanded. In the case of 2,9-diaryl-1,10-phenanthrolines, the allyl unit is pinched between the aryl rings (see Figure 1). The ligand wraps the allyl unit exactly and tightly and can be seen as "molecular earmuffs" for the allyl unit. Due to the sterical shielding of the allyl unit the differentiation between the two diastereotopic sides of the nucleophile **2** is enhanced, leading to higher diastereoselectivities. The aryl substituents of the 1,10-phenanthrolines **7–10** (Scheme 4) act as pseudosubstituents for the allyl unit. An additional shielding is achieved when the aryl rings are bridged, as in the concave 1,10-phenanthrolines **12** and **13**. Concave 1,10-phenanthrolines which represent one class of concave reagents[8] are molecules with a lamp-like geometry. The light bulb in its center, in this case the allylpalladium unit, is shielded from all sides but one. Such a shielding is very useful in other diastereoselective reactions such as copper(I)-catalyzed cyclopropanations[9] or transition-metal-catalyzed (Lewis acid catalyzed) Diels–Alder reactions.[10]

The catalytic allylations were carried out in dichloromethane using up to 2.5 mol-% of bis(μ-chloro)bis[(1,2,3-η)-propenyl]dipalladium (= $[AllylPdCl]_2$) (i.e. 5 mol-% of



ligand	R^1	R^2	R^4
6	Me	Me	-
7	R^3	H	OMe
8	R^3	R^3	Me
9	R^3	R^3	OMe
10	R^3	R^3	$O(CH_2)_2OMe$
11	R^3	R^3	OCO*t*Bu

Scheme 4. 1,10-Phenanthroline ligands **6–13**

Pd) and 1.5 equivalents of the bidentate ligands **6–13** per palladium. The catalyst was mixed with the allyl acetate and substrate **1**, which was deprotonated with sodium hydride in DMF, was added at −78°C. The reaction conditions are smoother when the cyanoacetates **1** are deprotonated in situ with *N*,*O*-bis(trimethylsilyl)acetamide (= BSA):[11] A solution of the catalyst, the allyl acetate and substrate **1** was cooled to −78°C before three equivalents of BSA were added.[12] In both cases, deprotonation by sodium hydride or by BSA, cooling was stopped after the addition of all reagents.[13]

The catalytic allylation of the substrates **1** gave diastereomeric products **3**. The stereoselectivities are listed in Table 1 as *unlike* (*R*,*S*/*S*,*R*) and *like* (*R*,*R*/*S*,*S*) ratios.[14]

Table 1 shows that 1,10-phenanthroline ligands at the palladium center (entries 1–7) can be used to increase the diastereoselectivities in comparison to conventional reactions (entries 9, 10). As shown in the experimental section for some relevant cases the yields are greater than 80%. With the substrates **1a** and **1b**, the 2,9-diaryl-substituted 1,10-phenanthrolines **9**, **10**, **12** and **13** were the most successful ligands (entries 3–6). The optimal ligand for these substrates was the tetramethoxy-substituted derivative **9** because it combines high selectivities with little synthetic effort. The use of the concave ligands **12** and **13** does not lead to a further increase of the selectivity. This is not surprising because the direct vicinity of the allyl unit is the same (see Figure 1).

Comparing the selectivity increase by ligands with increasing steric demand (**6** vs. **9**), the gain in selectivity is larger for **1b** than for **1a** [from 54:46 to 91:9 ($\Delta\Delta G^{\neq}$ = 1.3 kcal mol^{-1}) as against from 75:25 to 93:7 ($\Delta\Delta G^{\neq}$ = 0.87 kcal mol^{-1})]. This gain is caused by the fact that an ethyl and a phenyl group (substrate **1b**) are more similar in size than a methyl and a phenyl group (substrate **1a**). For **1b** this results in a larger similarity of the diastereotopic sides of the ester enolate **2** which therefore are less easy to distinguish from one another. Thus, in the case of **1b** a smaller inherent asymmetric induction enables the system to gain more selectivity if appropriate ligands are found.

The influence of the 1,10-phenanthroline ligands on the stereoselectivity with substrate **1c** differs from that observed with **1a** and **1b**. The best selectivity was found with the dimethyl-substituted ligand **6** (entry 1). Using sterically more demanding ligands, the selectivity is lost. Remarkably, the

Table 1. *unlike/like* diastereoselectivities of the allylation reaction forming the products **3** as analyzed by GC and verified in some cases by NMR[a]

Entry	Ligand	*unlike*-**3a**/*like*-**3a**		*unlike*-**3b**/*like*-**3b**		*unlike*-**3c**/*like*-**3c**	
		BSA	NaH	BSA	NaH	BSA	NaH
1	**6**	75:25	–	54:46	55:45	7:93[b]	8:92
2	**8**	92:8	–	–	88:12	41:59	–
3	**9**	94:6	–	91:9	91:9	58:42	51:49
4	**10**	93:7	–	–	91:9	–	–
5	**12**	93:7	–	–	82:18	54:46	–
6	**13**	93:7	–	91:9	91:9	55:45	–
7	**7**	81:19	–	69:31	71:29	–	87:13
8	without	81:19	–	65:35	76:29	10:90	16:84
9	PPh_3	81:19	–	70:30	67:33	12:88	13:87
10	Allyl-Br[c]	–	84:16	–	71:29	–	15:85

[a] For detailed conditions see Experimental Section. – [b] For solubility reasons $[CrotylPdCl]_2$ was used instead of $[AllylPdCl]_2$. The initial crotyl catalyst did not alter the diastereoselectivities because after one catalytic cycle the selectivity-determining species were the same. The products did, however, contain some crotylated impurities. – [c] Allylation with allyl bromide without catalysis by palladium.

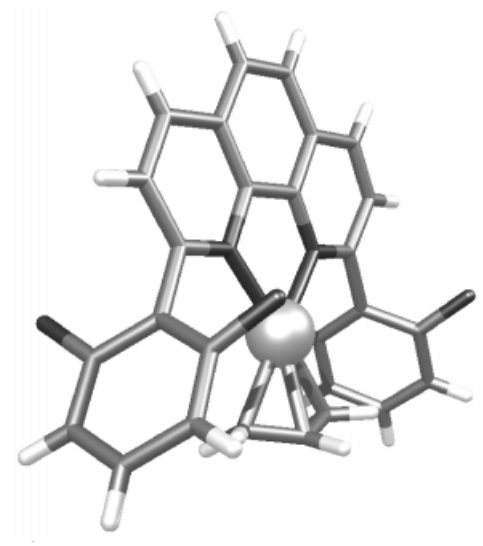


Figure 1. Structure of the complex [allyl-Pd·**11**]$^+$ as determined by X-ray analysis;[15] for clarity, the pivaloyl residues at the four oxygen atoms are omitted; the allyl unit is squeezed between the two aryl groups in 2- and 9-position of the 1,10-phenanthroline with **11** acting as a "molecular earmuff" for the allyl moiety

preferred selectivities for **1a** and **1b** favor the *unlike* product. In contrast, with substrate **1c** and ligand **6** the major compound is the *like* product.

This result can only be explained if one assumes that an isopropyl group is larger than a phenyl group. Consideration of the steric E_s parameter developed by Taft[16] indicates that a phenyl group is the largest group (comparing phenyl, methyl, ethyl and isopropyl, see Table 2, entry 1).

However, the reaction center in the allylation reaction is not next to the sterically demanding groups, the reaction takes place one carbon atom further away. Therefore in a first approximation, it is legitimate to compare homo-E_s values, e.g. phenylmethylene (CH_2Ph, benzyl) with isopropylmethylene (CH_2*i*Pr, isobutyl) rather than phenyl (Ph) with isopropyl (*i*Pr) (see Table 2, entry 2). Homo-E_S values have already successfully been applied to understand the selectivity in base-catalyzed addition of different alcohols to diphenylketene.[17]

Using such homo-E_s values, the selectivity observed for **1c** in combination with catalyst **6** can be explained qualitatively. The observations for the substrates **1a** and **1b** with ligand **6** are also in agreement with these homo-E_s values. In contrast, the selectivities obtained with other ligands, e.g. **9**, cannot be explained. In the case of **1a** and **1b**, the selectivities can be described much better by using the original Taft E_s values.

Neither the original Taft E_s values nor the homo-E_s values can, however, explain the selectivity for the allylation of **1c** in combination with ligand **9**. The gap between both sets of values can only be filled if these sets (E_s and homo-E_s) are regarded as extremes between which a continuous transition exists. A simplified linear transition is visualized in Figure 2.

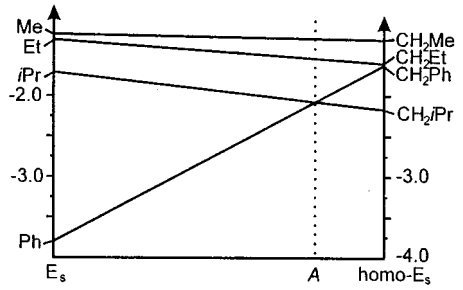


Figure 2. Steric Taft parameters E_s for groups R^1 and homo parameters homo-E_s for groups CH_2-R^1; all E_s values are normalized to H ($\equiv$ 0);[28] while the steric hindrance of the alkyl groups increases on insertion of a methylene group, the sterical influence of a phenyl group decreases; E_s and homo-E_s values are connected by straight lines suggesting a linear transition (for discussion see text); at point A such a process results in identical steric parameters for isopropyl and phenyl

Figure 2 shows clearly that between the extremes E_s and homo-E_s, a point A exists at which the difference between a phenyl and an isopropyl group becomes negligible as required for the selectivity for **1c** in combination with the catalyst **9**. Qualitatively the selectivities for ligand **9** in combination with the other substrates **1a**–**b** are also reflected correctly at this point A.

The transition between the two extremes in Figure 2 correlates with the radii of interaction of the ligands in the palladium catalysts. This is shown in Figure 3.

In the definition of Taft's steric parameters E_s, the voluminous substituent R^1 is next to the reaction center (Figure 3a). In contrast in the allylation reaction, a carbon atom separates R^1 and the carbanionic center (Figure 3c and 3d). A comparable situation for the ester hydrolysis is shown in Figure 3b, and the steric influences of various substituents R^1 in this case are better described when CH_2-modified Taft parameters, homo-E_s values, are used.

With increasing size of the phenanthroline ligands at the palladium center the radius of interaction of the ligand becomes larger and reaches beyond the allyl unit overcoming the separation of R^1 and the reagent. Consequently the influence of R^1 on the reaction rate cannot accurately be described for 2,9-diaryl-substituted phenanthroline ligands (Figure 3c) by the homo-E_s parameters as is possible for dimethylphenanthroline (**6**) (Figure 3d). For these ligands the steric parameters must be modified towards the original parameters E_s, as was done to reach point A in Figure 2.

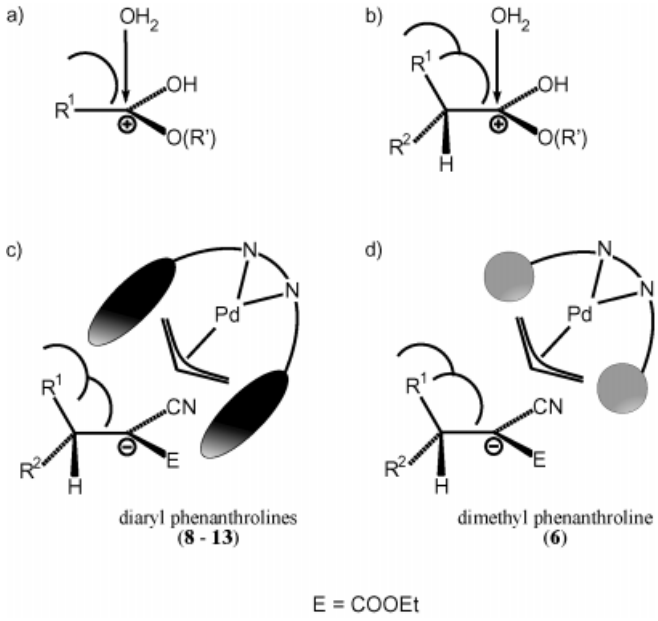


Figure 3. (a) Definition of Taft's E_s parameter; the rate of the attack of a water molecule onto a protonated ester is retarded by the steric interactions between R^1 (R^1 = Me, Et, *i*Pr, Ph) and the attacking water molecule; (b) by insertion of a carbon center CHR^2 between the protonated ester function and substituent R^1 the distance between R^1 and the approaching water molecule becomes larger; (c) and (d) allylation of a deprotonated cyanoacetate nucleophile by two different allylpalladium complexes. In the allylation reaction, the reaction center, a carbanion, is separated from the substituent R^1 by a carbon atom suggesting homo-E_s values should be used for this reaction instead of E_s values (compare Figures 3a and 3b); in Figures 3b and 3d the differences between the Taft and the homo Taft situation are indicated by two half circles; however, when a 2,9-diaryl-substituted phenanthroline ligand is attached to the allylpalladium unit (Figure 3c) it "reaches forward" resulting in an earlier, more intense interaction with R^1; although the reacting carbanion and R^1 are still separated by a carbon atom the distance between reagent and R^1 is smaller; therefore, with increasing radius of interaction of a ligand the homo-E_s values must be corrected in the direction of the original E_s values, see Figure 2

Is it legitimate to use homo-E_s values which are derived from the original Taft values by the insertion of an unsubstituted methylene group? In the substrates **1a–c**, substituted carbon atoms ($R^2 \neq H$), not methylene groups ($R^2 = H$), are inserted between the reaction center and the substituents R^1. The answer is yes because a comparison for other homo parameters shows similar trends (insertion of CHMe, CHEt or CHPh, Table 2, entries 3–5). Unfortunately values for *i*Pr are not known for these cases. For all homo-E_s values, however, phenyl is rarely larger than ethyl and there is a large increase in the E_s values when the ethyl value is substituted by one of the homo-E_s values. Therefore also the homo-E_s values for *i*Pr should be larger than the *i*Pr E_s value itself.

Table 2. Comparison of Taft and analogous homo Taft constants[28] (E_s and homo-E_s values)

Entry	Inserted group	Me	Et	*i*Pr	Ph
1	–	−1.24	−1.31	−1.71	−3.8
2	CH_2	−1.31	−1.60	−2.17	−1.62
3	CHMe	−2.17	−2.37	–[a]	−2.43
4	CHEt	−2.37	−3.22	–[a]	−2.74
5	CHPh	−2.43	−2.74	–[a]	−3.0

[a] Not available in cited references.

If these considerations are correct, the selectivities found with substrate **1c** and ligand **6** should be reversed favoring *unlike*-**3c** if the radius of interaction of the ligand could be further increased.

Stereochemical Analyses

The *like*/*unlike* ratios of the products **3a–c** were determined by GC and were confirmed by ^{1}H-NMR spectroscopy. However, the determination of the relative configuration of the isomers was not straightforward because one stereocenter is a quaternary carbon atom and the rotational barrier around the bond between the stereocenters is low, as was shown by conformational analyses using molecular mechanics[18] and semiempirical methods.[19]

According to the isolated spin-pair approximation (ISPA),[20] NOE crosspeak volumes are inversely proportional to the sixth power of the distance between the correlated nuclei. In contrast to common practice we did not scale the distances with respect to the known distance of geminal protons. Instead we correlated similar crosspeaks (distance > 2 to < 4 Å, similar framework between H atoms[21]) with H–H distances in a linear regression which was optimized by molecular modeling.

Instead of a time-consuming separation of the isomers of **3b**, NOE measurements were undertaken in different solvents and for different *like*/*unlike* mixtures, thus maximizing the number of utilizable NOE crosspeaks. The measurements of a 69:31 mixture of *unlike*/*like*-**3b** in [D_6]benzene gave 6 separated[22] crosspeaks for the minor product. In a molecular mechanics geometry optimization[18] starting with three fixed distances of H nuclei (Figure 4: solid lines: 2-4, 4-5, 6-7) the three other distances (Figure 4: open lines: 1-3, 2-3, 3-6) were determined. The fixed distances were chosen in such a way that the molecule could relax by changing only dihedral angles. The linear correlation of the

sixth root of the inverted crosspeak volumes with these six distances was then optimized by varying the fixed distances. Figure 4 shows the linear regression of that correlation for the minor product of **3b**. The rotamer shown is the result of this procedure and represents the time-averaged rotamer observed in the NOE experiments.

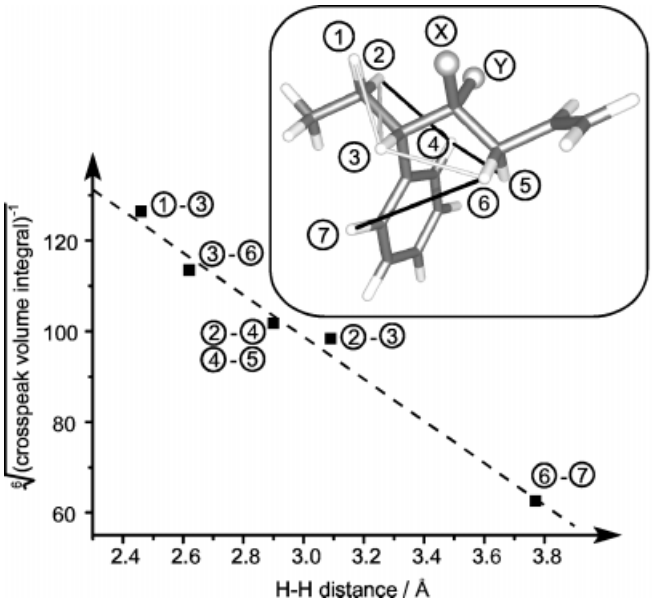


Figure 4. Conformation of minor product **3b** determined by NOE experiments; correlation between the NOE crosspeak volumes and the H−H distance for the minor product of **3b**

For the major product of **3b** the number of utilizable NOE crosspeaks was best for a 91:9 mixture in [D_6]acetone. Six separated crosspeaks could be used for the linear regression (Figure 5). In the measurements in benzene not all these crosspeaks were resolved for the major isomer, but the utilizable crosspeaks matched the distances obtained from the experiment in acetone proving that the conformations in both solvents were almost identical.

Figures 4 and 5 show the NOE-derived conformational orientations of the frameworks of the minor and major diastereoisomers of **3b**. Because the position for the cyano and the ester group could not be assigned by NOE experiments, chemical shifts of the ester and of the allyl protons were compared (Table 3). Figure 6 shows the two possible assignments of the isomers based on the two conformers determined by the NOE experiments.

In pair A the ester group is close to the aryl ring in the major product while in the minor product the distance between the phenyl ring and the ester group is large. Therefore, a high-field shift is expected for the ester protons of the major isomer with respect to the signals of the minor isomer. Such a difference is not expected in pair B because the dihedral angle between ester and phenyl group in both conformers is ca. 77°. Table 3 shows a considerable high-field shift for the major product. Therefore the major and minor conformers of **3b** must be *unlike*-**3b** and *like*-**3b,** respectively, as shown in pair A.

Table 3 also compares the NMR data of the ethyl compounds **3b** with those of the methyl and isopropyl derivatives **3a** and **3c** allowing the same assignment for the *like* and *unlike* isomers. Conformational studies[18][19] show similar conformations for **3a−c**.

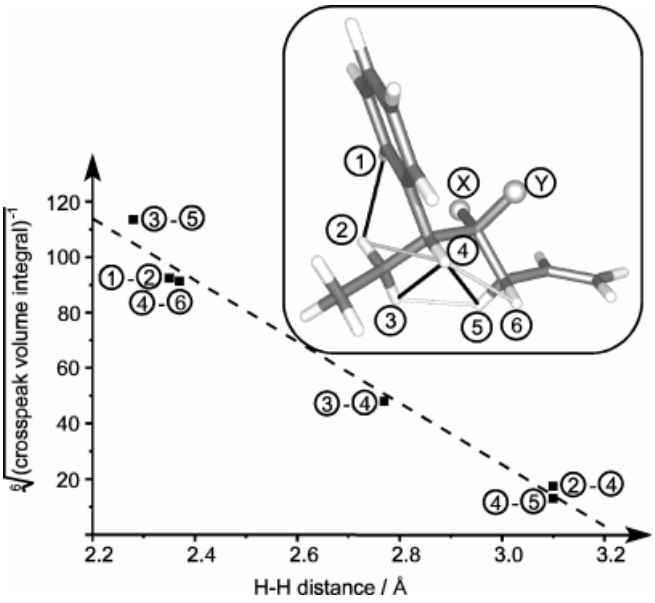


Figure 5. Conformation of major product **3b** determined by NOE; correlation between the NOE crosspeak volumes and the H−H distance for the major product of **3b**

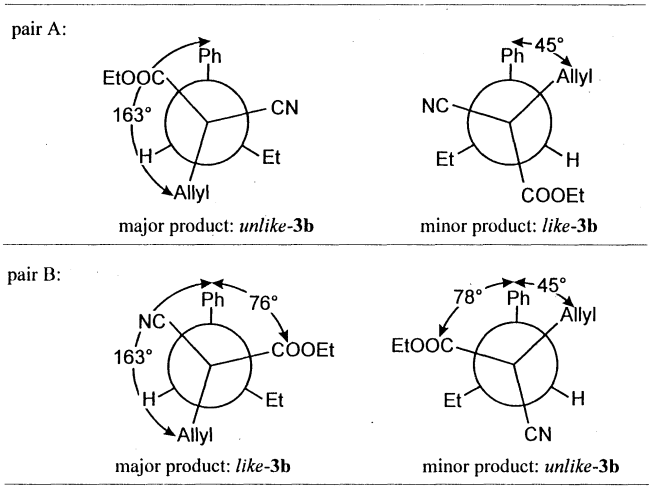


Figure 6. Newman projections of the two conceivable diastereoisomer pairs A and B for *unlike*-**3b** and *like*-**3b**

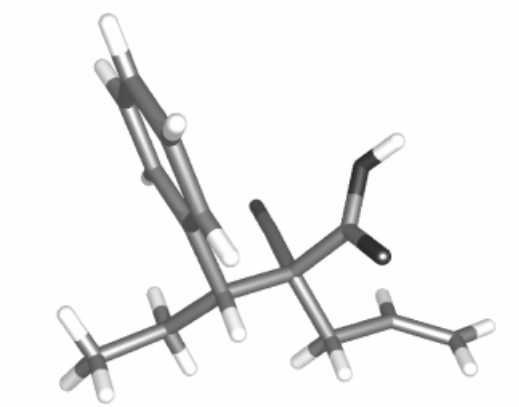
The structural assignment of the diastereoisomers obtained by the NOE measurements and chemical-shift studies was confirmed by an X-ray structure analysis of the saponification product of *unlike*-**3b**, acid *unlike*-**14** (see Figure 7).

Conclusion

The incorporation of 2,9-disubstituted 1,10-phenanthroline ligands into palladium catalysts allowed the control of the 1,2-asymmetric induction in the palladium-catalyzed allylation of the cyano esters **1a−c**. Quaternary stereocenters

Table 3. Selected ^{1}H-NMR signals for the *like* and *unlike* isomers of **3a−c** (high-field shifted signals are printed in bold-italic)

	unlike-**3a** (major product)	*unlike*-**3b**	*unlike*-**3c**	*like*-**3a** (minor product)	*like*-**3b**	*like*-**3c**
$-COOCH_2CH_3$	***3.91***	***3.86***	***3.83***	4.31	4.29	4.27
	3.90	***3.85***				
$-COOCH_2CH_3$	***0.94***	***0.91***	***0.91***	1.34	1.35	1.34
$-CH^aH^b-CH=CH_2$	2.72	2.72	2.69	***2.49***	***2.42***	***2.17***
$-CH^aH^b-CH=CH_2$	2.75	2.81	2.92	***2.10***	***2.04***	***1.92***
$-CH_2-CH=CH_2$	5.81	5.81	5.82	***5.69***	***5.68***	***5.68***
$-CH=CH^{syn}H^{anti}$	5.22	5.22	5.22	***5.12***	***5.11***	***5.07***
$-CH=CH^{syn}H^{anti}$	5.27	5.26	5.24	***5.10***	***5.08***	***5.00***



***unlike*-14**

Figure 7. Structure of acid *unlike*-**14** as determined by X-ray analysis

were formed diastereoselectively with selectivities up to 94:6. Besides the residue bearing the inducing chiral center the quaternary centers are substituted with a cyano, an ester and an allyl group. Using standard transformations of organic chemistry, a large number of selective transformations of these groups should be possible without isomerization, the saponification of *unlike*-**3b** to *unlike*-**14** being the first example.[23]

Experimental Section

General: Dichloromethane was distilled from $K_2CO_3/CaCl_2$ and was stored over molecular sieves (4 Å). DMF (> 99.5%), BSA and NBS were purchased from Fluka, 1-bromo-1-phenylethane (**4a**) and AIBN from Aldrich. Capillary column: Optima1/25 m, Fa. Macherey-Nagel; GC MS column: DB5/30 m, Fa. J+W. All NMR spectra were recorded at 25°C with TMS as internal standard.

General Procedure for the Synthesis of the Bromides 4b and 4c: 17.8 g (100 mmol) of *N*-bromosuccinimide (NBS) was added to a solution of 100 mmol of alkylbenzene in 100 mL of dry carbon tetrachloride. Then 0.20 g (1.2 mmol) of azobis(isobutyronitrile) (AIBN) was added and the reaction was started by careful initial heating. The reaction was controlled by cooling in such a way that the mixture refluxed gently. After the reaction ceased, refluxing was continued for 1 h. Precipitated succinimide was filtered off and was washed with carbon tetrachloride. After evaporation of the solvent, the product was purified by distillation in vacuo.

1-Bromo-1-phenylpropane (4b):[24] Yield: 17.3 g (81%), b. p. 98−100°C/ca. 14 Torr. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.00 (t, *J* = 7.3 Hz, C*H*$_3$, 3 H), 2.17 (dqd, *J* = 13.9, 7.2, 6.8 Hz, C*H*^{a}H^b, 1 H), 2.30 (ddq, *J* = 13.9, 8.1, 7.3 Hz, CH^a*H*^{b}, 1 H), 4.88 (dd, *J* = 8.1, 6.8 Hz, PhC*H*, 1 H), 7.25−7.41 (m, Ar*H*, 5 H). − IR (film): $\tilde{\nu}$ = 1494 cm^{-1}, 1454, 756, 696 (arom.). − MS (EI, 70 eV); *m/z* (%): 119 [M$^+$ − Br] (19), 105 [M$^+$ − CH_2Br] (100), 91 [PhCH_2^+] (24). − MS (CI, isobutane); *m/z* (%): 119 [M$^+$ − Br] (100).

1-Bromo-2-methyl-1-phenylpropane (4c):[25] Yield: 14.2 g (67%), b. p. 92−94°C/8 Torr. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.86 (d, *J* = 6.7 Hz, C*H*$_3$, 3 H), 1.19 (d, *J* = 6.5 Hz, C*H*$_3$, 3 H), 2.32 (dsept, *J* = 8.5, 6.6 Hz, $(CH_3)_2$C*H*, 1 H), 4.72 (d, *J* = 8.5 Hz, PhC*H*, 1 H), 7.20−7.40 (m, Ar*H*, 5 H). − IR (film): $\tilde{\nu}$ = 1491 cm^{-1}, 1454, 746, 697 (arom.). − MS (EI, 70 eV); *m/z* (%): 133 [M$^+$ − Br] (67), 91 [PhCH_2^+] (100). − MS (CI, isobutane); *m/z* (%): 133 [M$^+$ − Br] (100).

Ethyl 2-Cyano-3-phenylbutyrate (1a):[26] 0.690 g (30.0 mmol) of sodium was dissolved in 40 mL of dry ethanol. Then 3.39 g (30.0 mmol) of ethyl cyanoacetate was slowly added first, followed by 5.55 g (30.0 mmol) of 1-bromo-1-phenylethane (**4a**). The mixture was refluxed for 2 h, the majority of the ethanol was distilled off and the mixture was hydrolyzed with ca. 50 mL of ice/water. The organic layer was separated, and the water layer was extracted three times with ca. 20 mL of diethyl ether. The combined organic layers were dried with $MgSO_4$ and the solvents were removed in vacuo. Distillation (117−121°C/0.1 Torr) gave 3.96 g (61%) of **1a**. The *like*/*unlike* ratio of ca. 1:1 was estimated from the NMR signals at δ = 1.16 and 1.21 which were not baseline-separated. − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.16, 1.21 (t, *J* = 7.1 Hz; t, *J* = 7.1 Hz, CH_2C*H*$_3$, 3 H), 1.52 (d, *J* = 7.1 Hz, CHC*H*$_3$, 3 H), 3.53 (m$_c$, PhC*H*, 1 H), 3.67, 3.70 [d, *J* = 8.4 Hz; d, *J* = 8.6 Hz, (CN)C*H*, 1 H], 4.14, 4.18 (q, *J* = 7.0 Hz; q, *J* = 7.1 Hz, OC*H*$_2$, 2 H), 7.2−7.4 (m, Ar*H*, 5 H). − IR (Film): $\tilde{\nu}$ = 2248 cm^{-1} (CN), 1743 (C=O). − MS (EI, 70 eV); *m/z* (%): 217 [M$^+$] (9), 105 [M$^+$ − CH(COOEt)(CN)] (100). − MS (CI, isobutane); *m/z* (%): 218 [M$^+$ + 1] (100), 105 [M$^+$ − CH(COOEt)(CN)] (33).

Ethyl 2-Cyano-3-phenylpentanoate (1b):[26] Synthesized by analogy to **1a**. Yield: 4.92 g (71%) of **1b**, b.p. 125−128°C/0.07 Torr, the diastereomeric ratio was determined from the ^{1}H-NMR signals at δ = 3.65 and 3.81: 1:1.2. − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.89, 0.82 (t, *J* = 7.3 Hz; t, *J* = 7.3 Hz, C*H*$_3$, 3 H), 1.16, 1.10 (t, *J* = 7.1 Hz; t, *J* = 7.1 Hz, C*H*$_3$, 3 H), 1.21−1.76 (m, C*H*$_2$CH$_3$, 2 H), 3.15−3.29 (m, PhC*H*, 1 H), 3.65 [d, *J* = 7.0 Hz, (CN)C*H*, 0.55 H], 3.81 [d, *J* = 6.5 Hz, (CN)C*H*, 0.45 H], 4.13, 4.09 (q, *J* = 7.1 Hz; q, *J* = 7.2 Hz, OC*H*$_2$, 2 H), 7.21−7.40 (m, Ar*H*, 5 H). − IR (film): $\tilde{\nu}$ = 2248 cm^{-1} (CN), 1744 (C=O). − MS (EI, 70 eV); *m/z* (%): 231 [M$^+$] (16), 119 [M$^+$ − CH(COOEt)(CN)] (100), 91 [PhCH_2^+] (86). − MS (CI, isobutane); *m/z* (%): 231 [M$^+$ + 1] (100), 119 [M$^+$ − CH(COOEt)(CN)] (18).

Ethyl 2-Cyano-4-methyl-3-phenylpentanoate (1c):[27] Synthesized by analogy to **1a** on a 24.8-mmol scale. Yield: 2.55 g (42%) of **1c**,

Table 4. Reaction conditions, reaction times and yields[a] of the palladium-catalyzed allylation of substituted cyanoacetates **1a–c** to give **3a–c** using BSA or NaH for the deprotonation of **1a–c**; the diastereoselectivities are listed in Table 1

Ligand	**3a** BSA	NaH	**3b** BSA	NaH	**3c** BSA	NaH
6	A 6 h compl.	–	C 6 h compl.	C 6 h compl.	C crotyl-Pd[b] 6 h compl.	C 24 h compl.
	D 24 h compl. 79% isol.	–	–	–	C allyl-Pd > 24 h compl.	–
8	B 6 h compl.	–	–	C 6 h compl.	C 24 h compl.	–
9	A 6 h compl.	–	G 3 h compl. 90% isol.	C 6 h compl.	C 24 h compl.	C 24 h compl.
	E 3 h compl. 84% isol.	–	–	–	F 89% isol.	–
10	B 6 h compl.	–	–	C 24 h compl.	–	–
12	B 6 h compl.	–	–	C 24 h compl.	C >24 h compl.	–
13	C 24 h compl.	–	C 6 h compl.	C 24 h compl.	C 24 h compl.	–
7	A 6 h compl.	–	D 24 h compl. 82% isol.	C 6 h compl.	–	C 24 h compl.
PPh_3	A 6 h compl.	–	C 6 h compl.	C 6 h compl.	C 6 h compl.	C 24 h compl.
No additional ligand	C little conv. after 6d	–	C little conv. after 6d	C 24 h compl.	C little conv. after 6d	C little conv. after 24h
Allyl-Br[c]	–	small scale without Pd	–	small scale without Pd	–	small scale without Pd

[a] Abbreviations: compl.: reaction completed within the reaction time; isol.: isolated yield; conv.: conversion; A: small scale, 5 mol-% Pd; B: small scale, 4 mol-% Pd; C: small scale, 3 mol-% Pd; D: large scale (= 0.72 mmol of substrate), solutions of substrate and BSA added simultaneously during 6 h by syringe pump, 1.1 mol-% Pd; E: large scale, batch, 5 mol-% Pd; F: see D but 5 mol-% Pd; G: large scale, batch at −78°C, thawing during 3 h, 3 mol-% Pd. – [b] See footnote[b] of Table 1. – [c] Allylation with allyl bromide without catalysis by palladium.

b.p. 113–116°C/0.03 Torr, the diastereomeric ratio was determined from the ^{1}H-NMR signals at δ = 0.78 and 0.83: 3:1. – ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.78 (d, *J* = 6.6 Hz, CHC*H*$_3$, 2.25 H), 0.83 (d, *J* = 6.7 Hz, CHC*H*$_3$, 0.75 H), 0.99, 0.99 (t, *J* = 7.2 Hz, CH_2C*H*$_3$; d, *J* = 6.7 Hz, CHC*H*$_3$, 3 H), 1.14, 1.15 (t, *J* = 7.1 Hz, d, *J* = 6.5 Hz, CH_2C*H*$_3$, 3 H), 2.31 (dqq, *J* = 10.7, 6.6, 6.6 Hz, Me_2C*H*, 0.75 H), 2.42 (dqq, *J* = 7.8, 6.7, 6.7 Hz, Me_2C*H*, 0.25 H), 2.90 (dd, *J* = 10.7, 5.5 Hz, PhC*H*, 0.75 H), 3.18 (dd, *J* = 7.8, 6.9 Hz, PhC*H*, 0.25 H), 3.82 [d, *J* = 6.7 Hz, (CN)C*H*, 0.25 H], 3.96, 3.99, 4.01 [dq, *J* = 10.7, 7.1 Hz, OC*H*$_2$; dq, *J* = 10.7, 7.2, OC*H*$_2$; d, *J* = 5.5 Hz, (CN)CH; 2.25 H], 4.10, 4.13 (dq, *J* = 10.8, 7.1 Hz, OC*H*$_2$; dq, *J* = 10.8, 7.2 Hz, OC*H*$_2$; 0.5 H), 7.2–7.4 (m, Ar*H*, 5H). – IR (film): $\tilde{\nu}$ = 2249 cm^{-1} (CN), 1744 (C=O). – MS (EI, 70 eV); *m/z* (%): 245 [M^+] (10%), 202 [$M^+ - C_3H_7$] (39), 133 [M^+ – CH(COOEt)(CN)] (67), 91 [$PhCH_2^+$] (100). – MS (CI, isobutane); *m/z* (%): 246 [$M^+ + 1$] (100), 132 (34).

General Procedure for the Palladium-Catalyzed Allylations (Large and Small Scale, see table 4): The catalyst solution containing 1.5 equiv. of ligand **6–13** (or 3 equiv. of PPh_3) per mol of palladium was prepared by mixing equal aliquots of a 54 mM (small scale: 39 mM or 78 mM for PPh_3) solution of the ligand in CH_2Cl_2 with a 18 mM (small scale: 13 mM) solution of bis(μ-chloro)bis[(1,2,3-η)-propenyl]dipalladium (= [AllylPdCl]$_2$) in CH_2Cl_2. To 1.1–5 mol-% of the resulting palladium complex in solution, 1.2 equiv. (small scale: 1.1) of allyl acetate was added, the mixture was cooled to −78°C, and then 1 equiv. of the substrate **1a–c**, dissolved as a 720 mM (small scale: 870 mM) solution in CH_2Cl_2, was added followed by the addition of 3 equiv. of *N*,*O*-bis(trimethylsilyl)acetamide (BSA). The mixture was slowly warmed to room temp. The conversion was checked by taking a 50-μL aliquot which was hydrolyzed with ca. 0.3 mL of water. After extraction with diethyl ether, the organic layer was filtered through silica gel with diethyl ether and analyzed by GC.

Work Up of Large-Scale Experiments: The reaction mixture was hydrolized with 2 mL of water. The layers were separated and the water layer was extracted three times with 2 mL of diethyl ether. The combined organic layer was concentrated to dryness, dissolved in 2 mL of diethyl ether and filtered through silica gel with ca. 5 mL of diethyl ether. After evaporation of the solvent, the product was purified by distillation (kugelrohr).

Deprotonation by Sodium Hydride (Small Scale Only). – (a) Preparation of the Substrate Solution: Avoiding moisture (argon), 21 mg (0.53 mmol) of a sodium hydride suspension in mineral oil (60%) was washed twice with dry *n*-pentane. After addition of 0.60 mL of dry DMF, 0.60 mL of a 0.87 M solution of the substrate **1a–c** (0.52 mmol) in DMF was added slowly while stirring. After ca. 1 h, the developed hydrogen was exchanged by argon.

(b) Allylation: 11 μL of allyl acetate (96 μmol) was added to a mixture of 0.10 mL of a 0.013 mM (1.3 μmol) solution of bis(μ-chloro)bis[(1,2,3-η)-propenyl]dipalladium (= [AllylPdCl]$_2$) in CH_2Cl_2 and 0.10 mL of a 0.039 mM (0.078 mM for PPh_3) solution of the ligand **6–13** (3.9 μmol) in CH_2Cl_2. After cooling to −78°C,

Table 5. ^{1}H-NMR spectra (500 MHz, $CDCl_3$) of the products **3**; the chemical shifts δ and the multiplicities are listed in each top row, the coupling constants *J* (in Hz) in the lower rows

Protons	*like*-**3a** (R = Me)	*unlike*-**3a** (R = Me)	*like*-**3b** (R = Et)	*unlike*-**3b** (R = Et)	*like*-**3c** (R = *i*Pr)	*unlike*-**3c** (R = *i*Pr)
−Ph	7.2−7.4 m	7.2−7.4 m	7.2−7.4 m	7.2−7.4 m	7.2−7.4 m	7.2−7.4 m
$-CH_2-CH=CH_2$	5.694 dddd 6.3, 8.2, 10.3, 16.7	5.811 dddd 6.8, 7.7, 11.0, 17.0	5.679 dddd 6.4, 8.4, 10.3, 16.6	5.809 dddd 6.7, 7.7, 10.0, 16.9	5.677 dddd 6.0, 8.8, 10.2, 16.9	5.821 dddd 6.7, 7.9, 10.2, 16.9
$-CH=CH^{anti}H^{syn}$	5.121 dddd 0.9, 0.9, 1.8, 10.3	5.224 dddd 0.9, 0.9, 1.6, 9.3	5.106 dddd 0.8, 1.2, 1.8, 10.2	5.220 dddd 0.8, 0.8, 1.7, 10.2	5.069 dddd 0.6, 1.8, 1.8, 10.2	5.220 dddd 0.9, 0.9, 1.8, 10.2
$-CH=CH^{anti}H^{syn}$	5.103 dddd 1.2, 1.2, 1.2, 16.9	5.266 dddd 1.5, 1.5, 1.5, 17.0	5.077 dddd 1.0, 1.5, 1.5, 16.8	5.258 dddd 1.3, 1.3, 1.4, 16.9	5.004 dddd 1.0, 1.7, 1.7, 16.9	5.243 dddd 1.5, 1.5,1.5,17.0
$-CH^aH^bCH=CH_2$	2.485 dddd 0.9, 0.9, 8.2, 13.7	2.750 dddd 1.2, 1.2, 6.8, 13.5	2.416 dddd 1.0, 1.0, 8.4, 13.7	2.810 dddd 1.2, 1.2, 6.7, 13.6	2.165 dddd 0.9, 0.9, 8.8, 13.7	2.919 dddd 1.3, 1.3, 6.6, 13.6
$-CH^aH^bCH=CH_2$	2.098 dddd 1.3, 1.3, 6.4, 13.7	2.717 dddd 1.0, 1.0, 7.6, 13.5	2.042 dddd 1.0, 1.0, 6.4, 13.7	2.717 dddd 1.0, 1.0, 7.7, 13.6	1.917 dddd 1.4, 1.4, 5.9, 13.7	2.685 dddd 1.0, 1.0, 7.9, 13.6
$-COOCH^aH^bCH_3$	br. q together with $-COOCH^aH^bCH_3$	3.912 qd 7.2, 10.0	4.315 qd 7.2, 10.7	3.856 qd 7.2, 10.7	4.266 q 7.1	3.828 q 7.1
$-COOCH^aH^bCH_3$	4.307 br. q 7.1	3.895 qd 7.1, 9.9	4.294 qd 7.2, 10.7	3.848 qd 7.2, 10.7	together with $-COOCH^aH^bCH_3$	together with $-COOCH^aH^bCH_3$
$-COOCH_2CH_3$	1.344 t 7.2	0.939 t 7.1	1.347 t 7.2	0.906 t 7.2	1.344 t 7.2	0.910 t 7.1
−CRH−Ph	3.276 q 7.2	3.220 q 7.2	3.018 dd 3.5, 11.9	2.871 dd 4.4, 11.4	2.997 d 9.8	2.875 d 5.6
$-CH_3$ (of R)	1.457 d 7.1	1.552 d 7.2	0.733 t 7.2	0.769 t 7.4	1.025 d 6.7 0.762 d 6.6	0.947 d 6.8 1.053 d 6.8
$-CH^aH^bCH_3$ (of R)−	−	−	2.073 dddd 7.2, 11.9, 13.6	2.024 dqd 4.4, 7.2, 13.4	−	−
$-CH^aH^bCH_3$ (of R)−	−	−	1.670 dqd 3.7, 7.4, 13.6	1.989 qdd 7.2, 11.4, 13.4	−	−
$-CH(CH_3)_2$ (of R) −	−	−	−	−	2.320 septd 6.7, 9.8	2.383 dsept 5.5, 6.8

0.20 mL of the substrate solution (0.435 M, 0.087 mmol) was added. For reaction control and analysis see general procedure.

Ethyl 2-Cyano-2-(1-phenylethyl)pent-4-enoate (3a): Yield: 72% [catalysis by palladium complex of **9**, *unlike*/*like* = 95:5, purity (*unlike*- and *like*-**3a**, GC) > 96%], b.p. ca. 120°C/0.3 Torr. − ^{1}H NMR: see Table 5. − ^{13}C NMR (75 MHz, $CDCl_3$, *l* = signal of *like*-**3a**, *u* = signal of *unlike*-**3a**): δ = 168.62 (C=O, *l*), 167.61 (C=O, *u*), 140.18 (ArC^1, *u*), 139.08 (ArC^1, *l*), 130.77 (*C*H=CH_2, *l*), 130.74 (*C*H=CH_2, *u*), 128.56 (Ar, *l* §), 128.53 (Ar, *l* §), 128.34 (Ar, *u*), 128.02 (Ar, *u*), 127.72 (ArC^4, *u*), 127.94 (ArC^4, *l* §), 120.74 (CH=*C*H_2, *u*),120.32 (CH=*C*H_2, *l*), 117.90 (CN, *u*), 117.81 (CN, *l*), 62.72 (O*C*H_2CH_3, *l*), 62.09 (O*C*H_2CH_3, *u*), 56.32 (*C*CN, *u*), 55.81 (*C*CN, *l*), 45.63 (CHPh, *u*), 45.44 (CHPh, *l*), 40.89 (*C*H_2CH, *l*), 40.46 (*C*H_2CH, *u*), 17.82 (CH*C*H_3, *l*), 16.54 (CH*C*H_3, *u*), 14.09 (CH_2*C*H_3, *l*), 13.57 (CH_2*C*H_3, *u*), §difficult to assign due to low intensity. − IR (film): $\tilde{\nu}$ = 2241 cm^{-1} (CN), 1740 (C=O). − GC MS (start temp. 80°C, hold 0 min, heat with 10°C/min to 250°C): *unlike*-**3a**: R_t = 18.1 min; MS (CI, isobutane); *m/z* (%): 258 [M^+ + 1]; *like*-**3a**: R_t = 18.2 min; MS (CI, isobutane); *m/z* (%): 258 [M^+ + 1]. − MS (EI, 70 eV); *m/z* (%): 257 [M^+] (3), 105 [M^+ − C(C_3H_5)(COOEt)(CN)] (100). − HRMS: $C_{16}H_{19}NO_2$: calcd. 257.14157, found 257.14150; $C_{15}{}^{13}CH_{19}NO_2$: calcd. 258.14493, found 258.14480.

Ethyl 2-Cyano-2-(1-phenylpropyl)pent-4-enoate (3b): Yield: 82%*, purity (*unlike*- and *like*-**3b**, GC) > 96%; 90%$, purity (*unlike*- and *like*-**3b**, GC) > 99%, b.p. ca. 82°C/0.08 Torr. − ^{1}H NMR: see Table 5. − ^{13}C NMR (75 MHz, $CDCl_3$, *l* = signal of *like*-**3b**, *u* = *unlike*-**3b**): δ = 168.90 (C=O, *l*), 167.53 (C=O, *u*), 137.91 (ArC^1, *u*), 137.00 (ArC^1, *l*), 130.83 (*C*H=CH_2, *u*), 130.73 (*C*H=CH_2, *l*), 129.12 br. (Ar, *l*), 128.83 (Ar, *u*), 128.66 (Ar, *l*), 128.32 (Ar, *u*), 127.95 (ArC^4, *l*), 127.74 (ArC^4, *u*), 120.75 (CH=*C*H_2, *u*), 120.29 (CH=*C*H_2, *l*), 118.31 (CN, *l*), 118.14 (CN, *u*), 62.73 (O*C*H_2CH_3, *l*), 62.07 (O*C*H_2CH_3, *u*), 55.75 (*C*CN, *u*), 55.27 (*C*CN, *l*), 53.32 (CHPh, *u*), 52.88 (CHPh, *l*), 41.14 (*C*H_2CH, *l*), 40.61 (*C*H_2CH, *u*), 25.12 (CH*C*H_2CH_3, *l*), 23.30 (CH*C*H_2CH_3, *u*), 14.13 (*C*H_3, *l*), 13.54 (*C*H_3, *u*), 11.98 (*C*H_3, *l*), 11.92 (*C*H_3, *u*). − IR* (film): $\tilde{\nu}$ = 2242 cm^{-1} (CN), 1740 (C=O). − GC MS* (start temp. 120°C; hold 0 min; heat with 10°C/min to 250°C): *unlike*-**3b**: R_t = 17.1 min; MS (CI, isobutane); *m/z*: 272 [M^+ + 1]; *like*-**3b**: R_t = 17.2 min; MS (CI, isobutane); *m/z*: 272 [M^+ + 1]. − MS$ (EI, 70 eV); *m/z* (%): 271 [M^+] (5), 119 [M^+ − C(C_3H_5)(COOEt)(CN)] (100), 91 [$PhCH_2^+$] (75). − HRMS$: $C_{17}H_{21}NO_2$: calcd. 271.15723, found 271.15710; $C_{16}{}^{13}CH_{21}NO_2$: calcd. 272.16058, found 272.16040. − * Catalysis by palladium complex of **7**: *unlike*/*like* = 68:32; $ catalysis by palladium complex of **9**: *unlike*/*like* = 91:9.

Ethyl 2-Cyano-2-(2-methyl-1-phenylpropyl)pent-4-enoate (3c): Yield: 89% (catalysis by palladium complex of **9**, *unlike*/*like* = 58:42, purity (*unlike*- and *like*-**3c**, GC) > 98%, b.p. ca. 76°C/0.05 Torr. − ^{1}H NMR: see Table 5. − ^{13}C NMR (75 MHz, $CDCl_3$, *l* = signal of *like*-**3c**, *u* = *unlike*-**3c**§): δ = 169.63 (C=O, *l*), 167.77 (C=O, *u*), 138.89 (ArC^1, *l*), 137.55 (ArC^1, *u*), 130.80 (*C*H=CH_2, *u*), 130.73 (*C*H=CH_2, *l*), 129.68 br. (Ar, *u* + *l*), 128.70 br. (Ar), 127.92 (Ar), 127.61 (ArC^4, *l*), 127.41 (ArC^4, *u*), 120.80 (CH=*C*H_2, *u*), 120.04 (CH=*C*H_2, *l*), 119.38 (CN, *u*), 118.67 (CN, *l*), 62.64 (O*C*H_2CH_3, *l*), 62.14 (O*C*H_2CH_3, *u*), 57.58 (CHPh, *u*), 57.14 (CHPh, *l*), 53.68 (*C*CN, *u*), 52.58 (*C*CN, *l*), 43.33 (*C*H_2−CH, *l*), 41.76 (*C*H_2−CH, *u*), 32.34 (*C*H(CH_3)$_2$, *l*), 29.71 (*C*H(CH_3)$_2$, *u*), 23.52 (CH*C*H_3, *u*),

21.84 ($CHCH_3$, *l*), 20.81 ($CHCH_3$, *l*), 19.75 ($CHCH_3$, *u*), 13.95 ($OCHCH_3$, *l*), 13.50 (OCH_2CH_3, *u*); [§] assignment supported by HSQC. – IR (film): $\tilde{\nu}$ = 2242 cm^{-1} (CN), 1741 (C=O). – GC MS (start temp. 130°C; hold 0 min; heat with 3°C/min to 270°C): *unlike*-**3c**: R_t = 29.3 min; MS (CI, isobutane); *m/z*: 286 [M^+ + 1]; *like*-**3c**: R_t = 29.4 min; MS (CI, isobutane); *m/z*: 286 [M^+ + 1]. – MS (EI, 70 eV); *m/z* (%): 285 [M^+] (7), 133 [M^+ – $C(C_3H_5)(COOEt)(CN)$] (100), 91 [$PhCH_2^+$] (77). – HRMS: $C_{18}H_{23}NO_2$: calcd. 285.17288, found 285.17290; $C_{17}{}^{13}CH_{23}NO_2$: calcd. 286.17624, found 286.17600.

2-Cyano-2-(1-phenylethyl)pent-4-enoic Acid (14): One pellet of KOH (124 mg, 2.21 mmol) was dissolved in 17.7 mL of dry ethanol. 3.0 mL of this solution and 91 mg (0.34 mmol) of the ester **3b** (*unlike*/*like* = 95:5) were heated to reflux for 3 h. After most of the ethanol was evaporated, 2 mL of water was added, and the water layer was extracted three times with diethyl ether. The combined organic layers were dried with $MgSO_4$ and concentrated in vacuo. Ca. 1.5 mL of *n*-pentane and as little diethyl ether as possible were added to complete dissolvation. Colorless crystals suitable for X-ray analysis grew after *n*-pentane was allowed to diffuse into the solution for 15 h at +4°C. Yield: 53 mg (0.22 mmol, 64%), m.p. 141–143°C. – ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.77 (t, *J* = 7.3 Hz, CH_3, 3 H), 1.97, 2.03 (ddq, *J* = 13.5, 11.8, 7.3 Hz, $CH^aH^bCH_3$; dqd, *J* = 13.5, 7.4, 3.8 Hz, $CH^aH^bCH_3$; 2 H), 2.64 (dddd, *J* = 13.7, 7.8, 1, 1 Hz, $CH^aH^b–CH=CH_2$, 1 H), 2.82 (dddd, *J* = 13.6, 6.7, 1, 1 Hz, $CH^aH^b–CH=CH_2$, 1 H), 2.88 (dd, *J* = 11.8, 3.8 Hz, PhC*H*, 1 H), 5.24, 5.25 (dddd, *J* = 10.2, 1.4, 1, 1 Hz, $CH=CH^aH^b$; dddd, *J* = 16.9, 1.4, 1, 1 Hz, $CH=CH^aH^b$, 2 H), 5.80 (dddd, *J* = 16.9, 10.2, 7.8, 6.7 Hz, $CH=CH^aH^b$, 1 H), 7.2–7.4 (m, Ar*H*, 5 H). – IR (KBr): $\tilde{\nu}$ = 3423, 3066 cm^{-1} (OH), 2246 (CN), 1734 (C=O). – MS (EI, 70 eV); *m/z* (%): 243 [M^+] (2), 119 [M^+ – $C(C_3H_5)(COOH)(CN)$] (92), 91 [$PhCH_2^+$] (100). – (CI, isobutane); *m/z* (%): 244 [M^+ + 1] (8), 200 [M^+ – COOH] (100), 119 [M^+ – $C(C_3H_5)(COOH)(CN)$] (23). – HRMS: $C_{15}H_{17}NO_2$: calcd. 243.12593, found 243.12590; $C_{14}{}^{13}CH_{17}NO_2$: calcd. 244.12929, found 244.12920. – X-ray analysis of **14**: Crystallographic data (excluding structure factors) for the structure reported in this paper has been deposited with the Cambridge Crystallographic Data Centre (CCDC-127298). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk]. $C_{15}H_{17}NO_2$, M_r = 243.3 g/mol. Crystal data: monoclinic space group $P2_1/n$ (International Tables No.14), *Z* = 4, unit cell: *a* = 11.452(2), *b* = 7.038(1), *c* = 18.09(1) Å, β = 106.41(3)°, *V* = 1399(1) $Å^3$, calcd. density *d* = 1.155 g/cm^3. Data collection: Enraf–Nonius CAD4 four-circle diffractometer, graphite-monochromated, Mo-K_α radiation; colorless crystal, 0.6 × 0.6 × 0.2 mm, *T* = 200 K, ω-scans in the 2θ range 2–45°, index ranges $-12 \le h \le 5$, $-1 \le k \le 7$, $-19 \le l \le 19$; total of 3603 reflections, 1833 independent (R_{int} = 0.0424), μ = 0.08 mm^{-1}, structure solution by direct methods (SHELXS-94), structure refinement: full-matrix least squares on F^2 (SHELXL-93), *GoF* = 1.036, *R*1 for 979 $F_o > 4\sigma(F_o)$ = 0.0358, *wR*2 for all reflections = 0.0958, largest difference peak and hole: 0.15 and –0.20 e $Å^{-3}$.

[1] U. Lüning, T. Marquardt, *J. Prakt. Chem. Chem.-Ztg.* **1999**, *341*, 222–227.
[2] S. A. Godleski, *Comprehensive Organic Synthesis*, vol. 4 (Eds.: B. M. Trost, I. Flemming, M. F. Semmelhack), Pergamon Press, New York, Oxford, **1991**, pp. 585–661.
[3] B. M. Trost, D. L. van Vranken, *Chem. Rev.* **1996**, *96*, 395–422.
[4] [4a] R. Prétôt, G. C. Lloyd-Jones, A. Pfaltz, *Pure Appl. Chem.* **1998**, *70*, 1035–1040. – [4b] S. Kudis, G. Helmchen, *Angew. Chem.* **1998**, *110*, 3210–3212; *Angew. Chem., Int. Ed.* **1998**, *37*, 3047–3050.
[5] [5a] K. Voigt, A. Stolle, J. Salaün, A. de Meijere, *Synlett* **1995**, 226–228. – [5b] K. Hiroi, J. Abe, K. Suya, S. Sato, T. Koyama, *J. Org. Chem.* **1994**, *59*, 203–213.
[6] *Organikum*, 18th ed., Deutscher Verlag der Wissenschaften, Berlin, **1990**, p. 167.
[7] [7a] M.P.T. Sjögren, S. Hansson, B. Åkermark, A. Vitagliano, *Organometallics* **1994**, *13*, 1963–1971. – [7b] E. Peña-Cabrera, P.-O. Norrby, M. Sjögren, A. Vitagliano, V. De Felice, J. Oslob, S. Ishii, D. O'Neill, B. Åkermark, P. Helquist, *J. Am. Chem. Soc.* **1996**, *118*, 4299–4313. – [7c] G. Chelucci, A. Saba, *Tetrahedron: Asymmetry* **1998**, *9*, 2575–2578. – [7d] K. Nordström, E. Macedo, C. Moberg, *J. Org. Chem.* **1997**, *62*, 1604–1609. – [7e] D. Tanner, A. Harden, F. Johansson, P. Wyatt, P. G. Andersson, *Acta Chem. Scand.* **1996**, *50*, 361–368. – [7f] P. von Matt, G. C. Lloyd-Jones, A. B. E. Minidis, A. Pfaltz, L. Macko, M. Neuburger, M. Zehnder, H. Rüegger, P. S. Pregosin, *Helv. Chim. Acta* **1995**, *78*, 265–284. – [7g] A. Gogoll, H. Grennberg, A. Axén, *Organometallics* **1998**, *17*, 5248–5253.
[8] U. Lüning, *Top. Curr. Chem.* **1995**, *175*, 57–99.
[9] M. Hagen, U. Lüning, *Chem. Ber.* **1997**, *130*, 231–234.
[10] [10a] M. Gelbert, U. Lüning, *Supramolecular Chemistry*, Gordon & Breach, Newark, in press. – [10b] M. Gelbert, Ph. D. thesis, Freiburg University, **1995**.
[11] [11a] B. M. Trost, D. J. Murphy, *Organometallics* **1985**, *4*, 1143. – [11b] See also ref.[7b]
[12] The initial addition of catalytic amounts of KOAc to activate BSA (see ref.[11]) was not necessary in our experiments.
[13] In large-scale experiments the mixture of all reagents was allowed to warm up to 0°C.
[14] The *like*/*unlike* nomenclature suggested by Seebach is used because the *syn*/*anti* nomenclature is ambiguous: [14a] S. Masamune, S. A. Ali, D. L. Snitman, D. S. Garvey, *Angew. Chem.* **1980**, *92*, 573–575; *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 557. – [14b] E. L. Eliel, S. H. Wilen, *Organische Stereochemie* (Eds.: H. Hopf, J. Mulzer), Wiley-VCH, Weinheim, **1998**.
[15] [15a] B. Meynhardt, Ph. D. thesis, Kiel University, **1999**. – [15b] Crystallographic data has been deposited with the Cambridge Crystallographic Data Centre (CCDC-127299).
[16] [16a] R. W. Taft, Jr., *J. Am. Chem. Soc.* **1952**, *74*, 3120–3128. – [16b] S. H. Unger, C. Hansch, *Prog. Phys. Org. Chem.* **1976**, *12*, 91–118.
[17] W. Schyja, S. Petersen, U. Lüning, *Liebigs Ann.* **1996**, 2099–2105.
[18] J. J. Gajewski, K. E. Gilbert, *PCMODEL for Windows, Molecular Modeling Software for IBM and Compatible PCs under the Windows Operating System*, Serena Software, Bloomington, **1993**.
[19] [19a] AM1 in MOPAC 7.0, *QCPE*, Indiana University, Bloomington, **1994**. – [19b] M. J. S. Dewar, E. G. Zoebisch, E. F. Healy, J. P. Stewart, *J. Am. Chem. Soc.* **1985**, *107*, 3902–3909.
[20] B. A. Borgias, M. Gochin, D. J. Kerwood, T. L. James, *Prog. NMR Spec.* **1990**, *22*, 83–100.
[21] Crosspeaks of protons with conjugated framework are inapplicable because of scalar interactions.
[22] 2D-NOESY spectra were measured with 2 K points in the t_2 dimension and 512 experiments in t_1. Linear prediction to 1 K point and zero filling up to 2 K were applied for improving the resolution.
[23] Other example: Reduction with $LiAlH_4$ gives allyl-substituted amino alcohols: see ref.[15a]
[24] Compound **4b** has already been characterized in part and is commercially available: H. Pines, F. Schappell, *J. Org. Chem.* **1964**, *29*, 1503–1507.
[25] Compound **4c** has already been characterized in part: [25a] S. V. Truksa, A. Nibler, B. S. Schatz, K. W. Krosley, G. J. Gleicher, *J. Org. Chem.* **1992**, *57*, 2967–2970. – [25b] J. B. Conant, A. H. Blatt, *J. Am. Chem. Soc.* **1928**, *50*, 551–558.
[26] K. Nanjo, K. Suzuki, M. Sekiya, *Chem. Pharm. Bull.* **1977**, *25*, 2396–2400.
[27] Compound **1c** has already been characterized in part: E. P. Kohler, M. Reimer, *Am. Chem. J.* **1905**, *33*, 333–356.
[28] While in the original definiton of Taft's E_S values[16a] the standard was methyl, hydrogen is now often used as the standard, resulting in negative E_s values for *all* substituents.[16b]

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