21. Enantioselective Allylic Substitution Catalyzed by Chiral [Bis(dihydrooxazole)]palladium Complexes: Catalyst Structure and Possible Mechanism of Enantioselection

by **Peter von Matt, Guy C. Lloyd-Jones, Alexander B. E. Minidis,** and **Andreas Pfaltz***

Institut für Organische Chemie, Universität Basel, St. Johanns-Ring 19, CH–4056 Basel

and **Ludwig Macko, Markus Neuburger,** and **Margareta Zehnder***

Institut für Anorganische Chemie, Universität Basel, Spitalstrasse 51, CH–4056 Basel

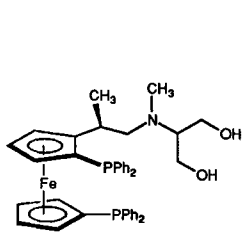
and **Heinz Rüegger** and **Paul S. Pregosin***

Laboratorium für Anorganische Chemie, ETH-Zentrum, CH–8092 Zürich

(8.XI.94)

Allylpalladium complexes with chiral bis(dihydrooxazole) ligands were studied as catalysts for the enantioselective allylic substitution reaction of *rac*-1,3-diphenylprop-2-enyl acetate (*rac*-**5**) with the anion of dimethyl malonate (*Scheme 1*). Using enantiomerically pure (*S,E*)-1-(4-tolyl)-3-phenylprop-2-enyl acatete ((*S*)-**25**) as substrate, the reaction was shown to proceed by a clean '*syn*' displacement of acetate by dimethyl malonate (*Scheme 6*). The [$Pd^{II}(\eta^3$-allyl)] complex **18** and the analogous [$Pd(\eta^3$-1,3-diphenylallyl)] complex **20**, both containing the same bis(dihydrooxazole) ligand, were characterized by X-ray structure analysis and by NMR spectroscopy in solution. The structural data reveal that steric interactions of the allyl system with the chiral ligand result in selective electronic activation of one of the allylic termini. The higher reactivity of one allylic terminus toward nucleophilic attack is reflected in a significantly longer Pd–C bond and a shift of the corresponding ^{13}C-NMR resonance to higher frequency.

1. Introduction. – Over the last years, considerable progress has been made in the development of enantioselective Pd catalysts for nucleophilic allylic substitution [1–8]. Various chiral ligands such as **1** [2c], **2** [3], **3** [4] [5], and **4** [6] [7] [8b] were described which induce high enantiomer excesses (ee's) in certain reactions of achiral or racemic allylic substrates with C- and N-nucleophiles. The best enantioselectivities were reported for *rac*-cyclopent-2-enyl acetate and analogous cyclohexenyl and cycloheptenyl derivatives as substrates (up to 98% ee with **2**) [3c] and for *rac*-1,3-diphenyl- and 1,3-diisopropylprop-2-enyl acetate (up to 99% ee with **4**; R = Ph) [6a]. There are, however, other classes



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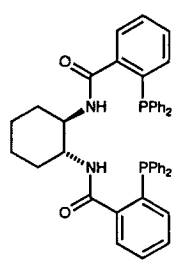

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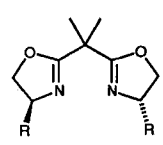

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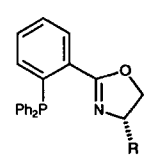

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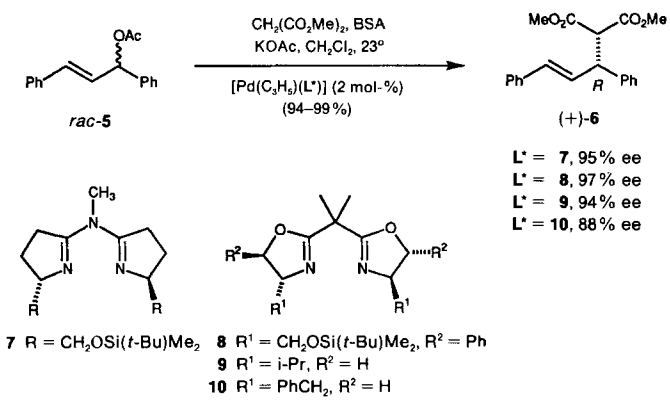
of substrates giving unsatisfactory ee's with the catalysts developed so far. For further catalyst improvement and the design of new ligands, it will be important to gain a better understanding of the mechanism of enantioselection in these reactions.

During the course of our work on chiral semicorrins and related C_2-symmetric N-ligands [4], we found that (η^3-allyl)palladium complexes of chiral azasemicorrins **7** and bis(dihydrooxazole) ligands[1]) such as **8**–**10** are efficient catalysts for allylic substitution, exerting effective enantiocontrol in the reaction of racemic 1,3-diphenylprop-2-enyl acetate *rac*-**5** with dimethyl malonate (*Scheme 1*) [4] [5] [9]. Here, we report the results of structural and mechanistic studies of these catalysts and propose a possible mechanism of enantioselection based on crystal-structure data.

Scheme 1

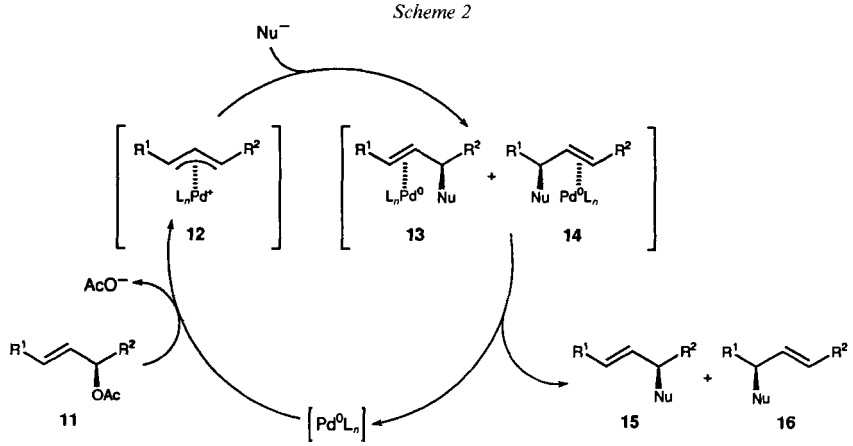


2. Allylic Substitution with [Bis(dihydrooxazole)]palladium Catalysts: Mechanism and Stereochemistry. – The generally accepted mechanism of Pd-catalyzed allylic substitution with 'soft' nucleophiles such as stabilized carbanions or amines is shown in *Scheme 2* [1]. First, the catalyst in the reduced Pd^0 state displaces the allylic leaving group in **11** to produce a [Pd^{II}(η^3-allyl)] complex **12**. Nucleophilic attack at the allyl system then leads – presumably *via* an unstable [Pd^0(olefin)] complex (see **13** and **14**) – to the substitution product **15** or the corresponding regioisomer **16** with concomitant regeneration of the catalytically active Pd^0 complex. Both formation of the [Pd(allyl)] intermediate **12** and the subsequent nucleophilic cleavage of one of the Pd–C bonds were shown to take place with inversion of configuration [1] [10].

Enantioselective allylic substitution by means of a chiral catalyst can be realized starting either from an achiral allyl derivative or from a chiral racemic substrate, provided that the two enantiomorphic reaction pathways merge at some point in the catalytic cycle. This condition is always met by substrates bearing identical substituents at the two allylic termini, as *e.g.* by *rac*-**5**, because in this case, both enantiomers are converted to the same [Pd(allyl)] intermediate **12** ($R^1 = R^2$). The enantioselectivity of the overall process is determined by the regioselectivity of nucleophilic attack at the allyl system leading to **15**

[1]) Systematic name of the ligand system of **3** and **8**–**10**: 2,2′-(1-methylethylidene)bis(4,5-dihydrooxazole).

Scheme 2

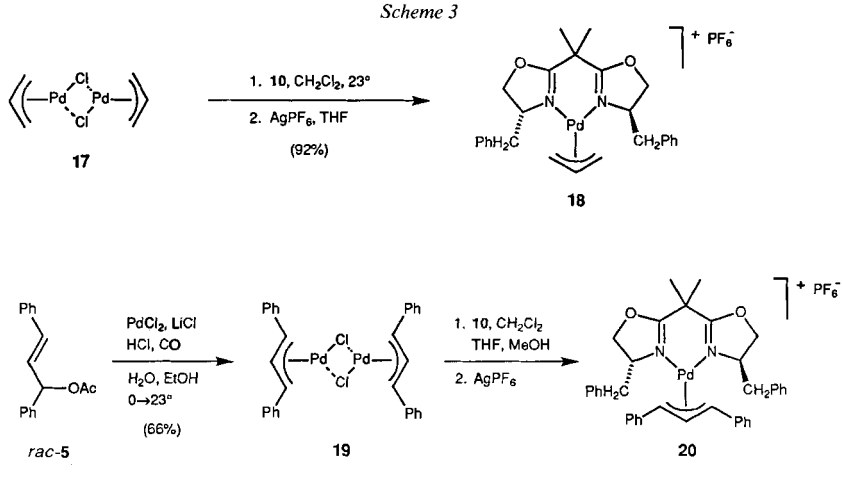


and **16** which, in this case, are enantiomers. Accordingly, both enantiomers of the chiral substrate can be converted to the same product enantiomer, as illustrated in *Scheme 1*.

To understand the source of the high enantioselectivity of [bis(dihydrooxazole)]palladium catalysts in the reaction shown in *Scheme 1*, a detailed knowledge of the structure and reactivity of the (allyl)palladium intermediate **12** ($R^1 = R^2 = Ph$) is crucial. Previously, we had generated the catalysts *in situ* from $[\{Pd(\eta^3\text{-}C_3H_5)Cl\}_2]$ (**17**) and a slight excess (1.1–1.3 equiv.) of the corresponding chiral ligand [5]. For the work described herein, we prepared the (allyl)palladium complexes **18** and **20** (*via* **19**) in analytically pure form (*Scheme 3*). The three-dimensional structure of the two complexes was analyzed by X-ray crystallography and NMR spectroscopy (see *Sections 3* and *4*).

When the crystalline hexafluorophosphate complex **20** was employed as catalyst, the enantiomeric excess and yield of product (+)-**6** were the same as with the corresponding chloro complex prepared *in situ* from $[\{Pd(\eta^3\text{-}C_3H_5)Cl\}_2]$ (**17**) and ligand **10**. The stoichiometric reaction of complex **20** with dimethyl malonate in the presence of *N,O*-

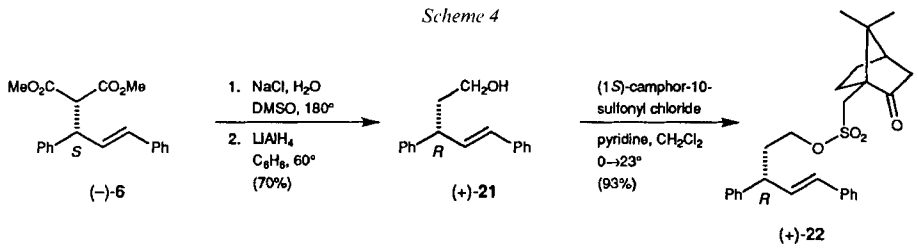
Scheme 3



bis(trimethylsilyl)acetamide (BSA) and KOAc (CH_2Cl_2, 23°) was somewhat less selective (75% ee instead of 88% ee), which is not surprising, because the conditions (concentration of the reactants, ionic strength, polarity) differ from those of the corresponding catalytic process.

The absolute configuration of the product ((*R*) for (+)-**6**) was assigned from its optical rotation according to literature data based on degradation to dimethyl (+)-(*S*)-2-phenylsuccinate [2c]. This assignment was independently confirmed by X-ray structure analysis of (+)-**22**, obtained from (−)-**6** by de(alkoxycarbonylation) [11], subsequent reduction (→(+)-**21**), and esterification with (+)-(1*S*)-camphor-10-sulfonyl chloride (*Scheme 4* and *Fig. 1*).

Scheme 4



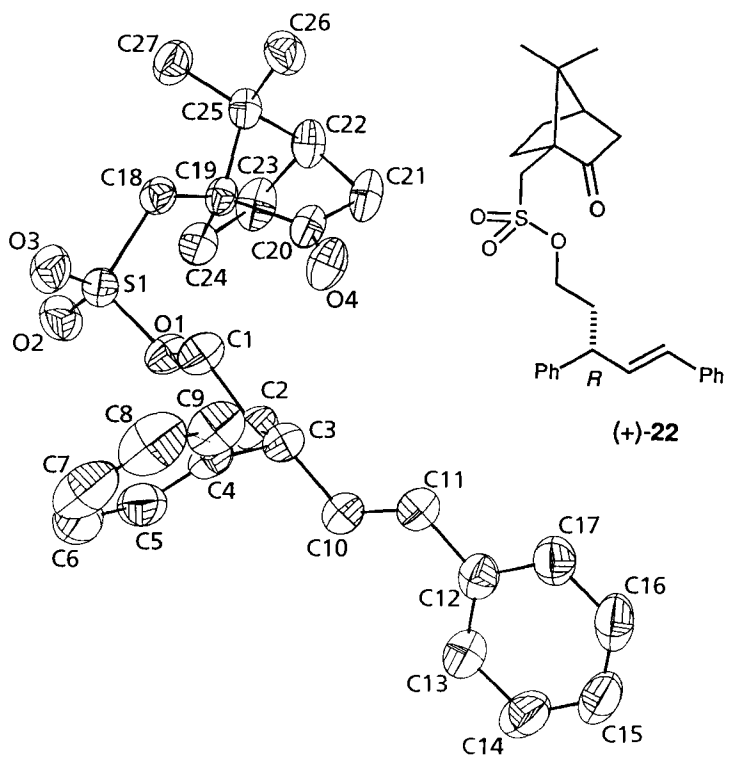
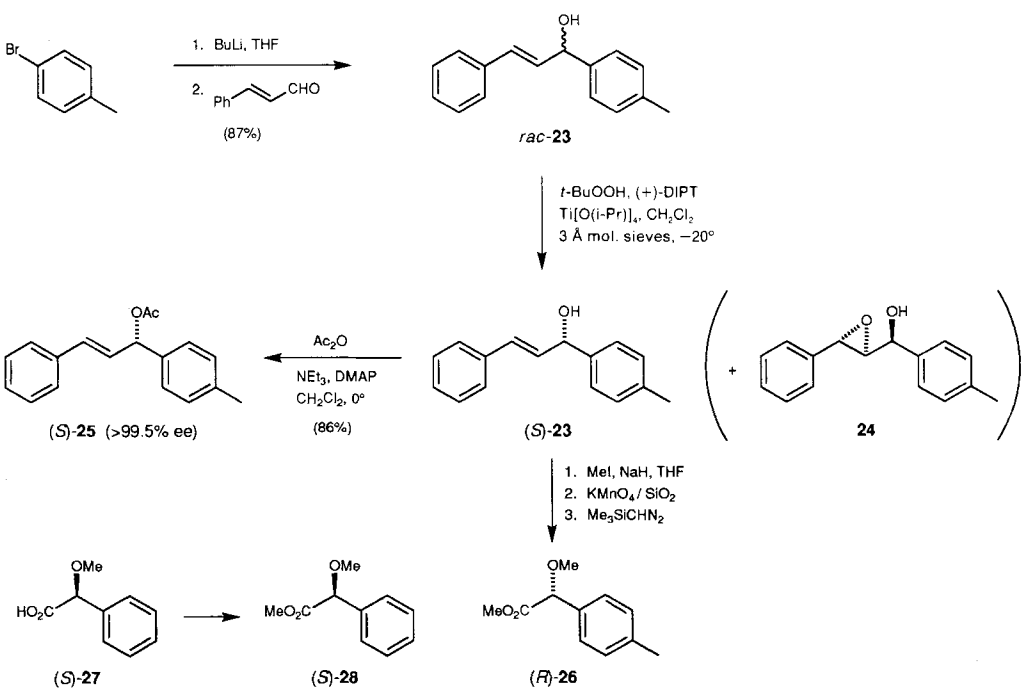


Fig. 1. *X-Ray structure of (+)-***22**. ORTEP Plot with 50% ellipsoids. Arbitrary numbering.

The stereochemical course ('*syn*' or '*anti*') of the overall reaction **5** → **6** (*Scheme 1*) cannot be determined, because the chirality information is lost upon conversion of (*R*)- or (*S*)-**5** to the [Pd(allyl)] intermediate. However, using enantiomerically pure 1-(4-tolyl)-3-phenylprop-2-enyl acetate (*S*)-**25** as a close analog of substrate *rac*-**5**, we could demonstrate that the reaction with [bis(dihydrooxazole)]palladium catalysts results in a clean '*syn*' displacement of acetate by dimethyl malonate (see below, *Scheme 6*), consistent with the findings reported for other Pd-catalyzed allylic alkylations [1] [10].

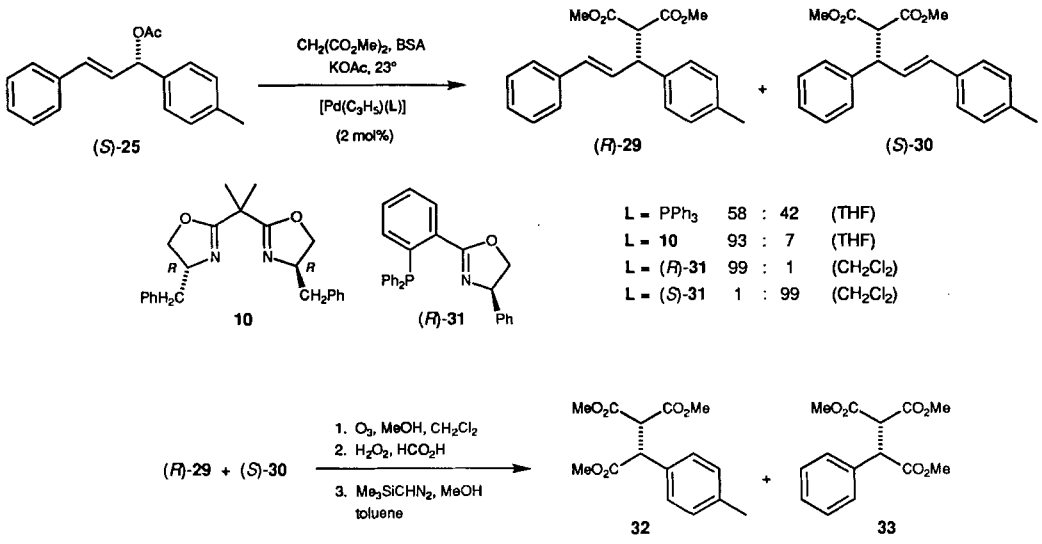
The substrate (*S*)-**25** was synthesized, as shown in *Scheme 5*, *via* the racemic allylic alcohol *rac*-**23** which was kinetically resolved using the *Sharpless* epoxidation method [12]. After *ca.* 60% conversion (→ **24**), the remaining allylic alcohol (*S*)-**23** was isolated with 97% ee. Recrystallization from Et_2O/hexane gave enantiomerically pure material (> 99.5% ee by HPLC on a chiral column). The (*S*)-configuration, which was assigned based on the results of analogous kinetic resolutions by the *Sharpless* method [12], was later confirmed by conversion to methyl (*R*)-2-methoxy-2-(4-tolyl)acetate ((−)-(*R*)-**26**) and CD-spectroscopic comparison with methyl *O*-methylmandelate ((+)-(*S*)-**28**) prepared from the corresponding acid (+)-(*S*)-**27** of known absolute configuration. The corresponding acetate (*S*)-**25** proved to be quite labile. Column chromatography on silica gel led to extensive isomerization, presumably by an acid-catalyzed ionic mechanism resulting in 1,3-migration of the AcO group and concomitant racemization. However, analytically pure (*S*)-**25** with an enantiomeric excess of > 99.5% ee could be obtained by chromatography on basic alumina.

Scheme 5



The Pd-catalyzed reaction of (*S*)-**25** with dimethyl malonate was carried out under standard conditions using triphenylphosphine, bis(dihydrooxazole) **10**, or phosphinodihydrooxazoles (*R*)-**31** and (*S*)-**31** as ligands (*Scheme 6*). The structures of the resulting regioisomers **29** and **30** were assigned by degradation to the triesters **32** and **33** which could be readily identified by GC/MS. The absolute configuration of **29** and **30** was determined by comparing their CD spectra with that of the diphenyl analog (−)-**6** of known absolute configuration (*S*). The spectra of **30** and (*S*)-**6** closely resembled each other, whereas the spectrum of **29** showed essentially the same bands, but of opposite sign.

Scheme 6



With the achiral (triphenylphosphine)palladium catalyst, product (*R*)-**29** was formed in slight excess over the regioisomer (*S*)-**30**, reflecting a weak electronic effect of the *p*-Me substituent. The chiral Pd complex with the bis(dihydrooxazole) **10** produced a 93:7 ratio of (*R*)-**29** and (*S*)-**30**. Using the more selective Pd-catalysts derived from phosphinodihydrooxazoles (*R*)- and (*S*)-**31**, each of the two regioisomers could be obtained in high purity. The high regioselectivities in this case parallel the high enantioselectivities observed in the corresponding reaction of diphenylprop-2-enyl acetate **5** (99% ee) [6a]. In all cases, the two products (*R*)-**29** and (*S*)-**30** were enantiomerically pure as shown by HPLC on a chiral column. This confirms that the overall reaction proceeds by clean '*syn*' displacement of acetate by dimethyl malonate. We, therefore, assume that the reactions shown in *Schemes 1* and *6* follow the pathway depicted in *Scheme 2*, and that the crucial, selectivity-determining step involves back-side attack of the nucleophile at the [Pd(η^3-allyl)] intermediate **12**.

3. Crystal Structures (X-Ray) of Palladium Complexes 18 and 20. – Hexafluorophosphate complexes **18** and **20** (*Scheme 3*) which are both derived from the bis(dihydrooxazole) ligand **10** were recrystallized from EtOH/$CHCl_3$/AcOEt and THF/AcOEt/Et_2O,

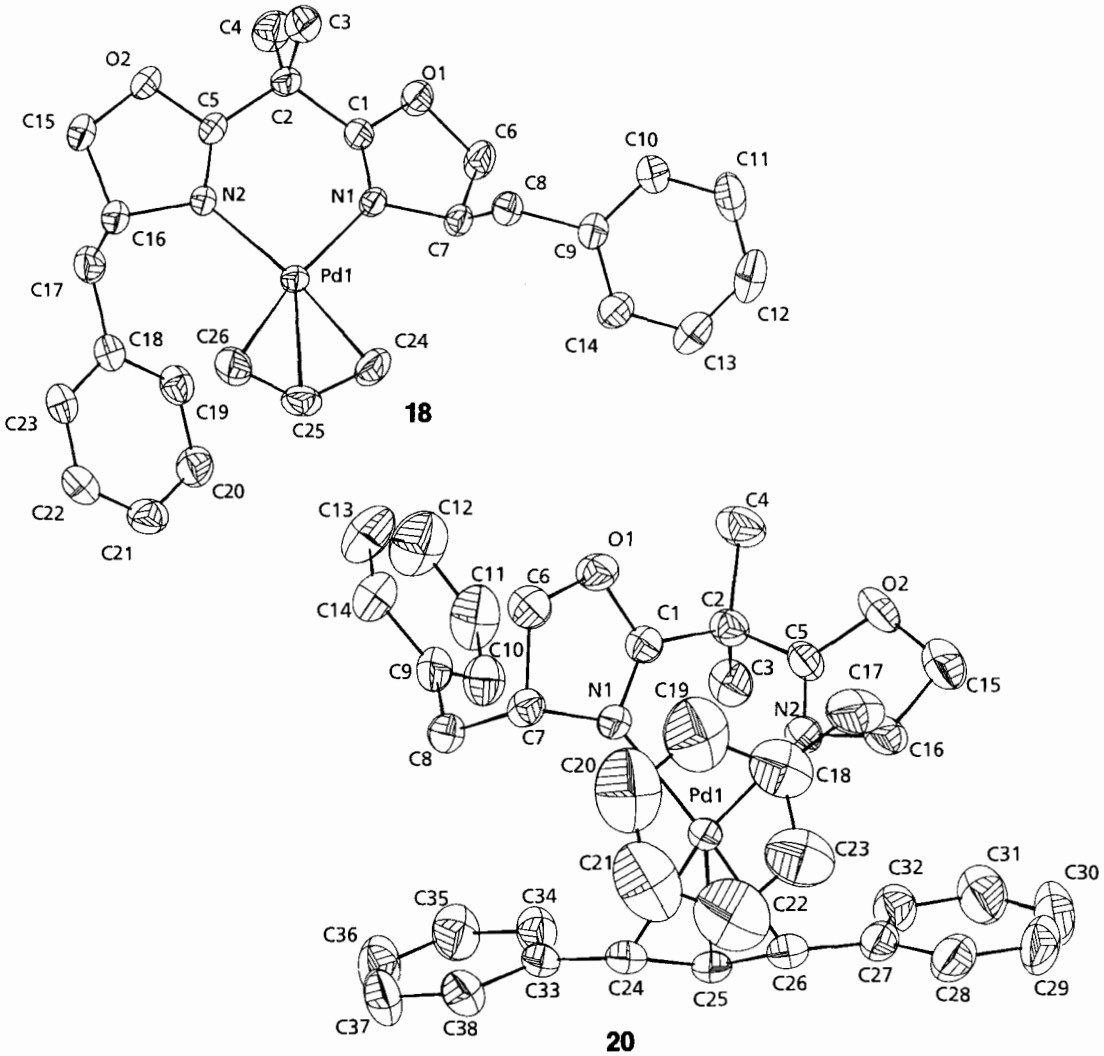


Fig. 2. *X-Ray structures of complexes* **18** *and* **20**. ORTEP Plots with 50% ellipsoids. Arbitrary numbering.

respectively, to give yellow prisms. The crystal structures of the two compounds were determined by X-ray analysis at −23° (*Fig. 2*). Both structures are of good quality with weighted *R* values of less than 2% (for a more detailed description of the X-ray analyses, see [13]). The allyl ligand in **18** was found to be disordered and was refined with the central C atom C(25) in a second position designated C(125). The resulting occupancies of these two positions were 0.74 for C(25) and 0.26 for C(125). The following discussion refers to the predominating allyl structure C(24)–C(25)–C(26) shown in *Figs. 2* and *3*. In complex **20**, the benzyl group at C(16), which is pointing toward the Pd-atom, changes its conformation even at −23° in the crystal, resulting in large thermal ellipsoids for the aromatic C-atoms.

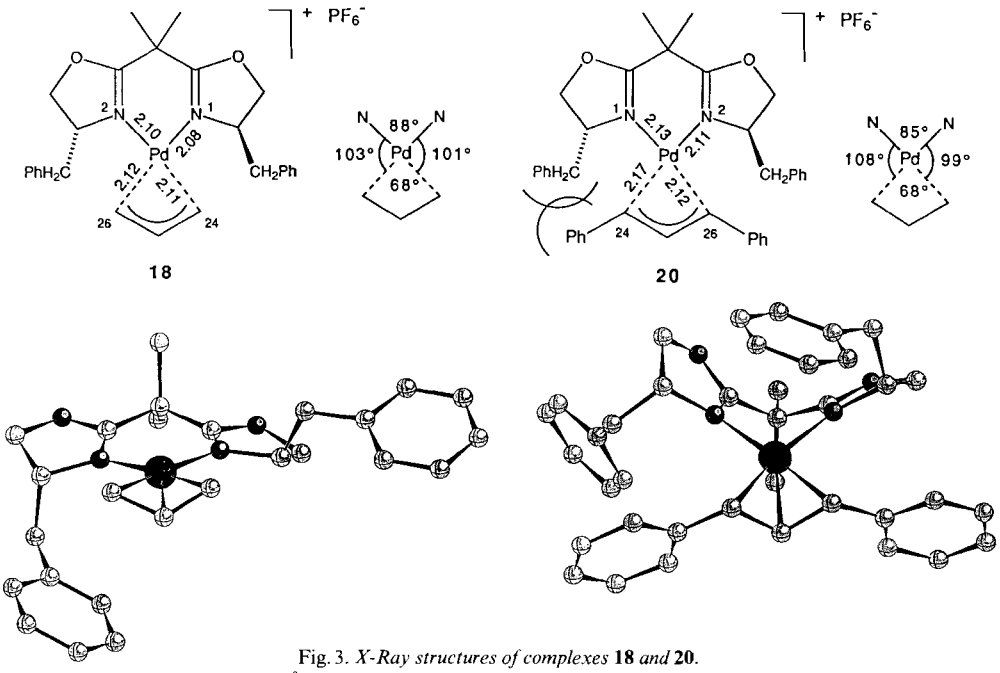


Fig. 3. *X-Ray structures of complexes* **18** *and* **20**.
Selected bond lengths [Å] and bond angles. Ball-and-stick representation. Arbitrary numbering.

Table 1. *Selected Structural Parameters for Complexes* **18** *and* **20** [13]

		18	**20**
Bond lengths	Pd(1)–N(1)	2.075(3)	2.130(3)
[Å]	Pd(1)–N(2)	2.099(3)	2.105(3)
	Pd(1)–C(24)	2.110(4)	2.169(3)
	Pd(1)–C(26)	2.117(4)	2.118(3)
	C(24)–C(25)	1.327(6)	1.405(5)
	C(25)–C(26)	1.387(6)	1.400(5)
Bond angles	N(1)–Pd(1)–N(2)	87.6(1)	84.5(1)
[°]	C(24)–Pd(1)–N(1)	101.3(1)	108.0(1)
	C(26)–Pd(1)–N(2)	102.8(1)	99.3(1)
	C(26)–Pd(1)–C(24)	68.2(2)	68.3(1)
Deviation from the N–Pd–N plane	C(24)	0.045	–0.088
[Å]	C(25)	–0.511	0.679
	C(26)	0.118	0.072

As expected for [Pd^{II}(allyl)] complexes of this type [14] [15], the coordination geometry of **18** and **20** is pseudo-squareplanar, with the four coordination sites occupied by the two N-atoms and the allylic termini C(24) and C(26). Maximum deviations from the best plane defined by Pd, N(1), N(2), C(24), and C(26) are 0.030 Å in **18** and 0.046 Å in **20**. The dihedral angle between the N–Pd–N plane and C(24)–Pd–C(26) plane is 3.2° in **18** and 3.8° in **20**. The plane defined by the three allylic C-atoms and the N–Pd–N plane form an angle of 117° in **18** and 107° in **20**. The bond lengths and bond angles of the [PdN_2(allyl)]

core (*Fig. 3*, *Table 1*) are in the expected range for [Pd(allyl)] complexes with N-ligands [14] [15].

In complex **18** with the unsubstituted allyl ligand, the conformation of the methylenebis(dihydrooxazole) ligand framework is almost planar. The structure of the corresponding (1,3-diphenylallyl)palladium complex **20**, which is the actual intermediate in the catalytic reaction (*Scheme 1*), is strikingly different. Presumably as a consequence of the steric repulsion between the allylic Ph group and the adjacent benzyl substituent of the chiral ligand, the methylenebis(dihydrooxazole) ring system has a strongly distorted non-planar shape with the six-membered chelate ring in a boat-like conformation (see *Fig. 3*). The repulsive interaction between the chiral ligand and one of the allylic termini is also reflected in the bond lengths and bond angles in the [PdN_2(allyl)] core (see *Fig. 3*). In **20**, the Pd–C bond to the allylic terminus C(24) interacting with the adjacent benzyl group is *ca.* 0.05 Å longer than the Pd–C(26) bond and the analogous bond in complex **18**. Further, the corresponding N–Pd–C angle is widened from 103° in **18** to 108° in **20**. These differences are well out of the 3σ range of e.s.d. and, therefore, can be considered significant. The Pd–C(26) bond in complex **20**, on the other hand, has essentially the same length as the two Pd–C bonds to C(24) and C(26) in complex **18**. Interestingly, the lengths of the two allylic C–C bonds in complex **20** are almost identical, despite the nonsymmetrical binding of the allyl system to the Pd-atom. However, the distinct differences in the Pd–C bond lengths and angles clearly demonstrate that the interaction between the chiral ligand and the symmetric 1,3-diphenylallyl system results in an effective electronic differentiation of the two allylic termini. Therefore, C(24) and C(26) in complex **20** are expected to exhibit distinctly different reactivity towards nucleophiles (see *Sect. 5*).

4. NMR Studies of (Allyl)palladium Complexes 18 and 20. – *Assigments.* The combined use of two-dimensional ^{13}C,^1H heteronuclear correlation and ^1H-NOESY experiments resulted in the assignment of all relevant ^1H- and ^{13}C-signals of complexes **18** and **20**, with the results summarized in *Table 2*.

Table 2. *^1H- and ^{13}C-NMR Data* (δ in ppm, J in Hz) *of Palladium Complexes* **18** *and* **20**[a])

	^{13}C	^1H (J(H,H))		^{13}C	^1H (J(H,H))
Complex **18**					
C(1)	172.91[b])		C(5)	173.00[b])	
C(2)	40.28				
CH_3(3)	24.34	1.28	CH_3(4)	25.28	1.23
CH_2(6)	72.62[b])	4.43	CH_2(15)	72.56[b])	4.52 (9.0, 9.2)
		4.45			4.41 (4.4, 9.0)
CH(7)	69.63	4.55 (4.6, 4.9, 7.2, 8.3)	CH(16)	69.48	4.67 (4.4, 4.4, 7.1, 9.2)
CH_2(8)	40.12	2.86 (7.0, 14.2)	CH_2(17)	39.86	2.77 (7.1, 14.2)
		3.00 (4.6, 14.2)			2.93 (4.3, 14.2)
C(9)	134.98		C(18)	134.71	
CH(10), CH(14)	129.98	7.22	CH(19), CH(23)	129.89	7.14
CH(11), CH(13)	128.88[b])	7.31	CH(20), CH(22)	128.90[b])	7.29
CH(12)	127.44[b])	7.22	CH(21)	127.44[b])	7.22
CH_2(24)	60.13[c])	4.01 (2.0, 6.9)	CH_2(26)	62.03[d])	4.05 (2.0, 6.9)
		2.89 (12.2)			3.20 (12.4)
CH(25)	116.97[g])	5.64 (6.9, 6.9, 12.3, 12.3)			

Table 2 (cont.)

	^{13}C	^{1}H (J(H,H))		^{13}C	^{1}H (J(H,H))
Complex **20**					
C(1)	173.42		C(5)	173.42	
C(2)	39.76				
CH_3(3)	26.23	1.33	CH_3(4)	23.63	1.29
CH_2(6)	72.76	4.35 (8.8, 9.0)	CH_2(15)	72.81	4.17 (3.9, 9.0)
		4.06 (4.8, 8.8)			3.94 (9.0, 9.2)
CH(7)	65.65	4.14 (3.9, 4.8, 7.9, 9.0)	CH(16)	64.01	3.24 (3.9, 5.9, 6.7, 9.2)
CH_2(8)	38.70	2.10 (3.9, 14.5)	CH_2(17)	39.82	2.61 (6.7, 14.2)
		1.67 (7.9, 14.5)			2.67 (5.9, 14.2)
C(9)	135.20		C(18)	135.38	
CH(10), CH(14)	129.47	6.78	CH(19), CH(23)	129.90	7.05
CH(11), CH(13)	128.38	7.16	CH(20), CH(22)	128.69	7.31
CH(12)	128.38	7.13	CH(21)	127.12	7.23
CH(24)	81.80[e])	5.04 (12.2)	CH(26)	74.17[f])	4.17 (10.9)
CH(25)	108.05[h])	6.27 (10.9, 12.2)			
C(33)	137.55		C(27)	138.38	
CH(34), CH(38)	128.47	7.76	CH(28), CH(32)	128.10	7.59
CH(35), CH(37)	129.95	7.29	CH(29), CH(31)	129.81	7.36
CH(36)	129.30	7.33	CH(30)	128.85	7.43

[a]) Recorded at 500.13 MHz in $CDCl_3$ at r.t. Numbering scheme as in *Fig. 2*. For *cis*/*trans*, see legend to *Fig. 4*. [b]) Assignment could be reversed. [c]) J(C,H) = 161.3 (*cis*), 157.3 (*trans*). [d]) J(C,H) = 160.2 (*cis*), 158.6 (*trans*). [e]) J(C,H) = 156.3. [f]) J(C,H) = 156.5. [g]) J(C,H) = 163.5. [h]) J(C,H) = 161.3.

In particular, it proved possible to specifically assign the ^{1}H-signals of the two diastereoisotopic benzyldihydrooxazole units from NOE spectroscopy. This is illustrated for **18** in *Fig. 4*: one of the allylic *cis*-protons, H_{cis}–C(26) exhibits spatial closeness to both protons of one of the benzylic CH_2 groups, *i.e.*, CH_2(17) (*cis* refers to the relation of *H*–C(26) to *H*–C(25)). With this assignment, the ring protons at C(16) and C(15), and in an analogous fashion C(7) and C(6), are readily recognized.

For the diphenyl-substituted complex **20**, key NOE's arise from the two geminal Me groups at C(2): one of these NOE's, to the central proton of the allyl moiety, assigns Me–C(3), as the Me group proximate to the Pd-atom and in a pseudoaxial position (see *Fig. 5a*). Further, this same Me group shows NOE's to the H_o and H_m of one of the benzylic Ph groups, *i.e.*, H–C(10), H–C(14) and H–C(11), H–C(13) (of the four relatively intense aromatic signals, the two lowest in frequency) thereby assigning these protons.

For both complexes, **18** and **20**, a chain of uninterrupted NOE's or scalar couplings relates the now specifically assigned benzyl groups to the adjacent dihydrooxazole ring, whereas the remaining allyl protons can be assigned in the usual way from coupling constants, concluding the assignment procedure.

Solution Structures and Dynamics. Chiral chelating phosphine ligands at a Pd-atom generally tend to induce specific distortions in allyl ligands such as out-of-plane rotations, and these, as well as other distorted coordination modes, can usually be characterized in solution using two-dimensional NOE spectroscopy [16]. As the distance constraints obtained by this method only allow the description of relative mutual orientations of groups, one generally employs a group, a so-called 'reporter' ligand [14] [17] having a

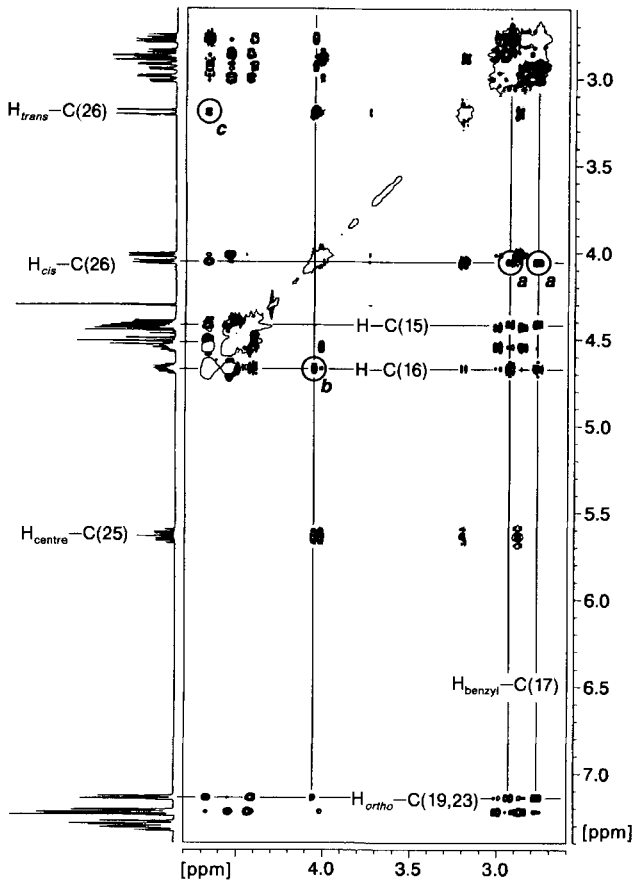


Fig. 4. *Section of the ^{1}H-NOESY spectrum of* **18**. Note the circled cross-peaks: *a*) NOE between H$_{cis}$–C(26) and H–C(17), *b*) NOE between H_{cis}–C(26) and *H*–C(16), and *c*) NOE between H_{trans}–C(26) and *H*–C(16). *cis*/*trans* refers to the relation of *H*–C(26) to *H*–C(25).

fixed conformation, to determine subtle aspects of the conformation of a second ligating group. In contrast to many of the chiral chelating N-ligands or chelating phosphine ligands currently in use, the bis(dihydrooxazole) ligand **10** should not be considered as a rigid group in the above sense as will be shown for complex **20**.

The solution data for the 1,3-diphenylallyl complex **20** suggest that this complex exists in at least two rapidly interconverting conformations. In the first of these, one of the geminal Me groups of the bis(dihydrooxazole) ligand is found to be in proximity to the central allyl proton and the two *cis*-Ph groups (*cis* with respect to *H*–C(25)) of the allyl moiety from 2D-NOE spectroscopy (see *Fig. 5a*). Such interactions can be explained by assuming a boat-like conformation for the chelate ring with this Me group in a pseudo-axial position, as shown in the stereopicture above the corresponding NOE spectrum. This conformation prevails in the solid state (see *Fig. 3*). Naturally, this would bring the second Me group into a pseudoequatorial position away from the metal and any allyl

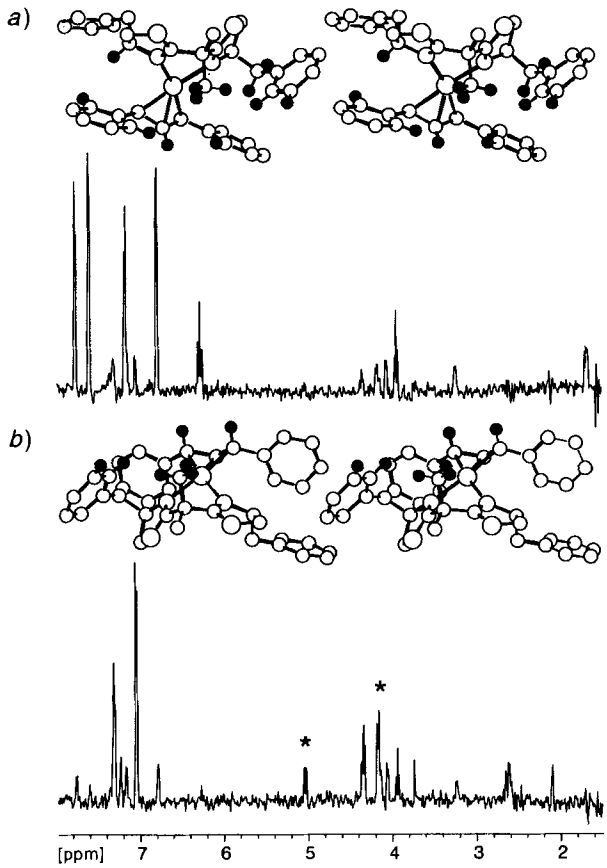


Fig. 5. *Slices through the* ^{1}*H-NOESY spectrum of* **20** *for* a) $CH_3(3)$ *and* b) $CH_3(4)$. This presentation is related to 1D difference NOE spectroscopy in that each signal corresponds to a NOE from the respective Me group. In *a*), the *t* at 6.27 ppm corresponds to the central allyl proton. In *b*), one finds NOE's from $CH_3(4)$ to both *trans*-protons (marked with asterisks; for *trans*, see *Fig. 4*) as well as NOE's to the relatively intense H_o and H_m of one benzyl group.

protons, so that no inter-ligand NOE's are expected for this second Me group. That this is *not* the case can be seen from *Fig. 5b*. Specifically, there is proximity of this second Me group to the *trans*-protons of the allyl moiety and the H_o and H_m of one of the benzyl groups. These observations can be rationalized by invoking a second conformation in which the boat-like chelate ring is inverted. A corresponding stereostructure is also shown above the appropriate trace from the NOESY spectrum. There exists no single static structure which would be consistent with the constraints implied by the observed NOE's, and the results are, therefore, best explained by assuming two chelate ring conformations and fast mutual interconversion on the NMR time-scale.

For the allyl protons in the cationic complex **18**, a number of interesting contacts are observed, *e.g.*, between H_{cis}–C(26) (*cis* to *H*–C(25)) and *H*–C(16) of the bis-(dihydrooxazole) (*b* in *Fig. 4*). There is only a weak NOE between H_{trans}–C(26) and *H*–C(16) (cross-peak *c*). In the crystal structure, C(16) lies below the coordination plane

defined by the two N-atoms and the metal. Further, due to the puckering of the five-membered ring, H–C(16) is pulled toward this plane and, accordingly, toward H_{cis}–C(26). This specific conformation of the dihydrooxazole ring seen in the X-ray structure, combined with the known bending of allyl *trans*-protons away from the Pd-atom, is sufficient to rationalize the two NOE's mentioned. We cannot exclude some small allyl-ligand rotation, but we have no evidence for this.

Both complexes **18** and **20** show an additional slow dynamic process in solution which leads to mutual exchange of the two diastereoisotopic benzyldihydrooxazole units. It is not clear by which mechanism this occurs, *e.g.*, dissociation of one of the Pd–N bonds and rearrangement of the three-coordinate complex, or rotation of the allyl ligand, or perhaps even an η^3–η^1 rearrangement. However, there is precedence for such behavior in [Pd(allyl)] chemistry [7b] [14a] [18]. This process is degenerate, *i.e.*, it leads to the same form after the exchange has taken place and possibly has no consequences for the catalytic reactions discussed in *Sections 1* and *2*.

In concluding this section, we reiterate that the bis(dihydrooxazole) ligand should be considered as a non-rigid ligand. Its shape (and preferred conformation) in solution might change as a function of the substituent pattern at the allyl system[2]). Hence, this ligand could well adapt to the varying space requirements during the course of a catalytic allylic substitution.

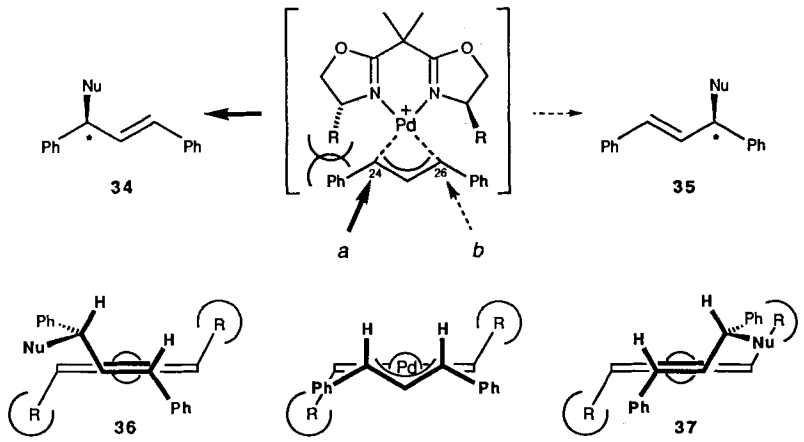
It is normal to use ^{13}C-NMR chemical shifts of the terminal allyl C-atoms as a yardstick for the *trans*-influence of a donor ligand, although this 'influence' may have both electronic and steric contributions. For complex **18**, the terminal C-atoms appear at 60.13 and 62.03 ppm, in good agreement with the values found by *Åkermark et al.* [20] for simple allyl complexes of TMEDA (*N,N,N′,N′*-tetramethylethylenediamine) and pyridine, so that there is no evidence for any special donor or acceptor properties of the bis(dihydrooxazole) ligand system. We do note, however, that the ^{13}C signals of the terminal allyl C-atoms for **20** are found at 74.17 and 81.80 ppm, *ca.* 7.6 ppm apart. Since such $\Delta\delta(^{13}C)$'s are known to indicate changes in the allyl bonding [16] [17] [20], we interpret this *electronic difference* as arising from the selective steric effects imposed by the bis(dihydrooxazole) ligand that weaken the Pd–C(24) bond relative to the Pd–C(26) bond, and we shall expand on this subject, in detail, separately [21].

5. Mechanistic Implications. – According to the generally accepted mechanism of Pd-catalyzed allylic alkylation (see *Scheme 2*), the enantioselectivity of the overall reaction *rac*-**5** → **6** (*Scheme 1*) is determined by the regioselectivity of nucleophilic attack at the (η^3-allyl)palladium intermediate. In this process, one of the Pd–C bonds is cleaved with inversion of configuration [1] [10]. The question is, how can the chiral ligand influence the reactivity of the allyl system such that the nucleophile preferentially attacks one of the two allylic termini (see *Scheme 7*).

Some clues are provided by the crystal structure and the NMR data of the (allyl)palladium complex **20**, the actual intermediate in the catalytic process. As discussed above, the steric repulsion between the allylic Ph group at C(24) and the adjacent benzyl substituent at the dihydrooxazole ring results in a strongly distorted ligand conformation and significant lengthening of the Pd–C(24) bond (see *Fig. 3*). The corresponding ^{13}C-

[2]) For an NMR investigation of the influence of bis(dihydrooxazole) ligands **3** on the stereoselectivity of coordination and the *cis*/*trans*-equilibrium of monosubstituted allyl ligands, see [19].

Scheme 7



NMR resonance is shifted to higher frequency indicative of a weakening of this Pd–C interaction. The Pd–C(26) bond, on the other hand, has the normal length observed in the unstrained complex **18**. From the absolute configuration of the product, we know that the nucleophile preferentially attacks the longer and, accordingly, more reactive Pd–C(24) bond (*Scheme 7*, *Pathway a*), suggesting that the sterically induced activation of this bond and the release of strain associated with the bond-breaking process, may be factors responsible for enantioselection.

This concept of regioselective Pd–C bond activation differs from previously developed concepts based on direct interactions between the chiral ligand and the nucleophile [2ac] [3d] [22]. Another factor that could contribute to the observed selectivity may be related to the thermodynamic stability of the resulting [Pd^0(olefin)] complexes which are postulated as primary products [1]. Assuming a pseudo square planar coordination geometry [23], the Pd^0 complex **36** (corresponding to the major product enantiomer **34**) is expected to be more stable than **37** (corresponding to **35**), based on steric considerations. Analogous steric interactions between the chiral ligand and the coordinated substrate should also be present in the corresponding transition states leading to **36** and **37**.

It can be dangerous to extrapolate from crystal-structure data to solution chemistry, especially as we know nothing of the dynamics in solution (*e.g. cis/trans* isomerization [18] [24]) under the conditions of the catalytic process. However, as shown by NMR spectroscopy (see *Sect. 4*), the crystal and solution structures of complex **20** are of the same type. Further, the higher reactivity at the allylic position *a* over *b* (see *Scheme 7*) is also reflected in the ^{13}C-NMR data (81.8 *vs.* 74.2 ppm for C(*a*) and C(*b*), resp., see *Sect. 4*).

The qualitative model shown in *Scheme 7* should also be useful for predicting the regioselectivity of other catalyst systems. Recently, *Tanner et al.* [2n] and *Koga et al.* [2i] reported two examples of enantioselective allylic alkylations catalyzed by Pd complexes of C_2-symmetric diamines which both can be rationalized by this model. *Koga et al.* also determined the structure of the intermediate (1,3-diphenylallyl)palladium complex by X-ray analysis and found similar differences in Pd–C bond lengths as in complex **20**.

Financial support of this work by the *Swiss National Science Foundation* and *F. Hoffmann-La Roche AG*, Basel, is gratefully acknowledged. *G.C.L.-J.* thanks the *Royal Society*, London, for a postdoctoral fellowship (1992–1994).

Experimental Part

General. Quality of solvents and reagents: see [6b]. Reactions were carried out under N_2 or Ar using dried glassware. Flash column chromatography (FC): *Chemie-Uetikon-C560* silica gel (35–70 μm) and *Fluka* aluminium oxide *5016A* (basic). TLC: 0.25 mm, *Merck* silica gel *60 F254* and *Macherey-Nagel* alox-*25* UV_{254}, visualizing at 254 nm or with 2% $KMnO_4$ soln. HPLC: *Daicel Chiralcel OJ* and *OD* columns (25 × 0.46 cm) with pre-column (5.0 cm); detection at 254 nm. GC/MS: *HP 5890 II* GC (FID); *HP 5971* MS (EI); column: *HP-Ultra* (12 m, dimethyl silicone). Optical rotations: *Perkin-Elmer-141* polarimeter; *c* in g/100 ml, $CHCl_3$, 23°; estimated accuracy ± 5%. CD Spectra: *JASCO-J-720* spectropolarimeter, Ar-sat. MeOH, scan-rate 50 nm/min, λ in nm ($\Delta\varepsilon$). Routine NMR spectra: chemical shifts δ (ppm) rel. to residual $CHCl_3$ (7.27 ppm, ^1H, 300 MHz) and to $CDCl_3$ (77.0 ppm, ^{13}C, 75 MHz). NMR Spectra in *Section 4*: measured as described in [16c] [17]. MS: 3-nitrobenzyl alcohol (fast-atom bombardment) for FAB.

(R,R)-2,2'-(1-Methylethylidene)bis(5-benzyl-4,5-dihydrooxazole) (**10**). Ligand **10** was prepared according to procedures described for analogous bis(dihydrooxazoles) [4] [9] [26]. A soln. of (+)-(*R*)-2-amino-3-phenylpropan-1-ol (D-phenylalaninol; *Fluka, purum*; 3.0 g, 20 mmol) and Et_3N (5.0 g, 50 mmol) was cooled to 0° under N_2. After dropwise addition of malonyl dichloride [25] (1.7 g, 10 mmol) in CH_2Cl_2 (5 ml), the mixture was stirred for 30 min at 0° and for an additional 2 h at 23°. The soln. was diluted with CH_2Cl_2 and poured into ice water and the org. phase separated, washed with 1M HCl, sat. aq. $NaHCO_3$, and sat. aq. NaCl soln., dried ($MgSO_4$), and evaporated: 3.8 g (97%) of *(R,R)-N,N'-bis(1-benzyl-2-hydroxyethyl)-2,2-dimethylpropane-1,3-diamide*; white solid which was used in the next step without purification. M.p. 94°. $[\alpha]_D = +3.1$ (*c* = 1.6). ^1H-NMR: 7.27–7.14 (*m*, 10 arom. H); 6.64 (br. *d*, *J* = 8.7, 2 NH); 4.5–4.4 (br., 2 OH); 4.30–4.16 (*m*, 2 CHN); 3.71, 3.46 (*AB* of *ABX*, $J_{AB} = 10.9$, $J_{AX} = 7.8$, $J_{BX} = 2.8$, 2 CH_2O); 2.78, 2.64 (*AB* of *ABX*, $J_{AB} = 13.7$, $J_{AX} = 8.2$, $J_{BX} = 6.1$, 2 $PhCH_2$); 1.20 (*s*, 2 Me). CI-MS (NH_3): 399 (100, $[M + H]^+$), 381 (37).

To a suspension of this diamide (3.8 g, 9.7 mmol) in benzene (80 ml) at 0° was slowly added $SOCl_2$. The mixture was heated to reflux for 7 h. The resulting clear soln. was evaporated to give an oil which was cooled to 0°, diluted with CH_2Cl_2, and poured into ice water. Washing with sat. aq. $NaHCO_3$ and sat. aq. NaCl soln., drying ($MgSO_4$), and evaporation afforded 3.9 g (93%) of *(R,R)-N,N'-bis(1-benzyl-2-chloroethyl)-2,2-dimethylpropane-1,3-diamide*, pale yellowish solid which was used in the subsequent reaction without purification. M.p. 145°. $[\alpha]_D = +28.8$ (*c* = 0.9). ^1H-NMR: 7.33–7.20 (*m*, 10 arom. H); 6.73 (br. *d*, *J* = 8.1, 2 NH); 4.45–4.34 (*m*, 2 CHN); 3.62, 3.50 (*AB* of *ABX*, $J_{AB} = 11.3$, $J_{AX} = 3.6$, $J_{BX} = 4.3$, 2 CH_2Cl); 2.88 (δ, *J* = 7.5, 2 $PhCH_2$); 1.35 (*s*, 2 Me). FAB-MS: 435 (100, M^+).

This product (3.9 g, 9.0 mmol) was dissolved in THF (100 ml) and treated with NaOH (0.9 g, 22.5 mmol) in EtOH (50 ml) under N_2. After refluxing for 3 h, the mixture was cooled to r.t. and evaporated. Addition of sat. aq. NaCl soln., extraction with Et_2O, drying ($MgSO_4$), evaporation, and FC (silica gel, 5 × 25 cm, AcOEt/EtOH 40:1) gave a colorless oil which was crystallized from Et_2O/hexane at −30° to afford 1.6 g (48%) of **10**. M.p. 52–53°. R_f (AcOEt/EtOH 40:1) 0.29. $[\alpha]_D = +44.3$ (*c* = 0.88). IR: 3090*w*, 3070*w*, 2985*m*, 2975*m*, 2860*w*, 1655*s*, 1610*w*, 1500*m*, 1475*m*, 1455*m*, 1390*m*, 1355*m*, 1275*w*, 1250*m*, 1245*m*, 1150*s*, 1120*s*, 1095*m*, 975*m*, 935*m*, 910*w*. ^1H-NMR: 7.30–7.18 (*m*, 10 arom. H); 4.42–4.38 (*m*, 2 CHN); 4.16, 4.00 (*AB* of *ABX*, $J_{AB} = 8.5$, $J_{AX} = 7.0$, $J_{BX} = 9.3$, 2 CH_2O); 3.08, 2.66 (*AB* of *ABX*, $J_{AB} = 13.7$, $J_{AX} = 8.5$, $J_{BX} = 4.9$, 2 $PhCH_2$); 1.50 (*s*, Me). ^{13}C-NMR: 169.3 (C=N); 137.6 (arom. C); 129.4, 128.3, 126.4 (arom. CH); 71.9 (CH_2O); 66.9 (CHN); 41.2 ($PhCH_2$); 38.5 (Me_2C); 24.7 (Me). EI-MS: 363 (3), 362 (12, $M^{+\cdot}$), 272 (18), 271 (100), 137 (36), 117 (13), 111 (8), 110 (23), 105 (12). Anal. calc. for $C_{23}H_{26}N_2O_2$: C 76.21, H 7.23, N 7.73; found: C 76.04, H 7.35, N 7.76.

(η^3-Allyl)[(R,R)-2,2'-(1-methylethylidene)bis(5-benzyl-4,5-dihydrooxazole)-N,N']palladium(II) Hexafluorophosphate (**18**). A soln. of $[\{Pd^{II}(C_3H_5)Cl\}_2]$ [27] (**17**; 40 mg, 0.11 mmol) and **10** (82 mg, 0.23 mmol) in CH_2Cl_2 (6 ml) was stirred at r.t. for 1 h and then treated with $AgPF_6$ (60 mg, 0.24 mmol) in THF (5 ml). After 10 min, the mixture was filtered through a pad of *Celite* and the filtrate washed with aq. sat. NaCl soln., dried ($MgSO_4$), and evaporated: 132 mg (92%) of **18**. White powder. M.p. 178°. $[\alpha]_D = -47.8$ (*c* = 0.3). IR (KBr): 3030*m*, 2915*w*, 1655*s*, 1600*w*, 1495*w*, 1480*m*, 1450*s*, 1390*m*, 1130*s*, 960*m*, 910*s*. ^1H- and ^{13}C-NMR: *Table 2*. FAB-MS: 509 (100, $[M - PF_6]^+$, ^{106}Pd); isotope cluster 505–514, calc. (obs.) 2.9 (2.5), 0.9 (1.7), 31.9 (34.7), 73.9 (78.1), 100.0 (100.0), 27.3 (28.2), 81.4 (81.5), 24.0 (23.8), 37.9 (37.7), 10.8 (9.7). Anal. calc. for $C_{26}H_{31}F_6N_2O_2PPd$: C 47.68, H 4.77, N 4.28; found: C 47.59, H 4.77, N 4.25.

After a preliminary crystallization (CH_2Cl_2/Et_2O), single crystals suitable for X-ray diffraction were grown by isothermal distillation of AcOEt into a $CHCl_3$/EtOH soln. of **18**.

Di-μ-chlorobis{[(1,2,3-η)-1,3-diphenylallyl]palladium(II)} (**19**). A mixture of $PdCl_2$ (45 mg, 0.25 mmol) and LiCl (45 mg, 1.06 mmol) was stirred in H_2O (0.3 ml) for 30 min. The resultant dark brown suspension was treated with EtOH (0.5 ml) and then with a soln. of *rac*-**5** (107 mg, 0.51 mmol) in THF (1.5 ml). After cooling to 0°, conc. HCl soln. (0.1 ml) was added and, with stirring, CO bubbled through the soln. After 5 min, a further portion of conc. HCl soln. (0.1 ml) was added and stirring continued for 30 min (→light orange precipitate). The mixture was stirred for a further 7 h under a static CO atmosphere. After addition of CH_2Cl_2 (100 ml), the soln. was washed with H_2O, dried ($MgSO_4$), and evaporated. The resulting solid was suspended in CH_2Cl_2 (200 ml). After sonication, hexane (40 ml) was added and the suspension kept at −14° for several h. Filtration afforded **19** (112 mg, 66%). Orange-yellow powder. M.p. > 250° (dec.). IR (KBr): 3070*m*, 3020*m*, 1950*w*, 1880*w*, 1520*w*, 1480*s*, 1460*s*, 1380*m*, 1300*w*, 1070*s*, 1030*m*, 765*s*. ^{1}H-NMR ((D$_6$)DMSO): 7.76 (*d*, *J* = 6.6, 8 arom. H); 7.44–7.33 (*m*, 12 arom. H); 6.95 (*t*, *J* = 11.8, 2 $H_{cent.}$); 5.24 (*d*, *J* = 11.8, 4 H_{trans}). ^{13}C-NMR ((D$_6$)DMSO): 137.2 (arom. C); 128.6, 128.3, 128.0 (arom. CH); 107.2, 83.3 (allylic CH). Anal. calc. for $C_{30}H_{26}Cl_2Pd_2$: C 53.75, H 3.91; found: C 53.86, H 3.91.

[(1,2,3-η)-1,3-Diphenylallyl][(R,R)-2,2′-(1-methylethylidene)bis(5-benzyl-4,5-dihydrooxazole)-N,N′]palladium(II) Hexafluorophosphate (**20**). A soln. of **19** (62.3 mg, 0.09 mmol) and **10** (75.7 mg, 0.21 mmol) in CH_2Cl_2/THF/MeOH 6:5:5 (16 ml) was stirred at 50° for 3 h, cooled to r.t., and treated with $AgPF_6$ (50.6 mg, 0.2 mmol) in THF (3 ml). After 15 min, the mixture was filtered through a pad of *Celite* and the filtrate washed with aq. sat. NaCl soln., dried ($MgSO_4$), and evaporated: **20** (159 mg, *ca.* 100%). Orange solid. The product was recrystallized from THF/AcOEt. Single crystals suitable for X-ray diffraction were finally obtained by isothermal distillation of Et_2O into a THF soln. of **20**. M.p. 233°. $[\alpha]_D = -166$ (*c* = 0.11). IR (KBr): 3090*w*, 3065*w*, 3030*m*, 2960*s*, 2910*m*, 1650*s*, 1600*m*, 1540*w*, 1490*m*, 1480*w*, 1465*w*, 1425*w*, 1385*w*, 1260*s*, 1250*s*, 1130*m*, 1100*m*, 1015*m*, 960*w*. ^{1}H- and ^{13}C-NMR: *Table 2*. FAB-MS: 661 (100, $[M - PF_6]^+$), ^{106}Pd); isotope cluster 657–667, calc. (obs.) 2.6 (1.7), 1.2 (1.0), 29.1 (30.2), 70.9 (71.3), 100.0 (100.0), 37.7 (36.6) 77.9 (77.5), 32.0 (30.3), 38.0 (36.5), 14.7 (12.8), 3.2 (1.7). Anal. calc. for $C_{38}H_{39}F_6N_2O_2PPd$: C 56.55, H 4.87, N 3.47; found: C 56.37, H 4.92, N 3.45.

*Conversion of (−)-***6** *to (+)-***22**. A degassed soln. of (−)-**6** (98% ee; 1.59 g, 4.9 mmol) in DMSO (5 ml) containing NaCl (0.57 g, 9.8 mmol) and H_2O (0.18 g, 10 mmol) was heated in an ampoule to 180° for 6 h. After cooling to r.t., the mixture was diluted with Et_2O, washed with H_2O, dried ($MgSO_4$), and evaporated. FC (silica gel, 5 × 32 cm, hexane/AcOEt 4:1; R_f 0.42). afforded *methyl (R,E)-3,5-diphenylpent-4-enoate* (1.09 g, 83%). Colorless oil. $[\alpha]_D = +7.2$ (*c* = 1.4). IR: 3085*m*, 3065*m*, 2955*m*, 1950*w*, 1875*w*, 1735*s*, 1600*m*, 1495*s*, 1450*m*, 1140*s*, 1360*m*, 1330*m*, 1255*s*, 1160*s*, 1080*w*, 1030*m*, 985*m*, 965*s*, 910*m*. ^{1}H-NMR: 7.33–7.15 (*m*, 10 arom. H); 6.42 (*d*, *J* = 15.8, H–C(5)); 6.32 (*dd*, *J* = 6.9, 15.8, H–C(4)); 4.03 (br. *q*, *X* of *ABX*, *J* ≈ 7.4, H–C(3)); 3.59 (*s*, CO_2Me); 2.85, 2.79 (*AB* of *ABX*, J_{AB} = 15.1, J_{AX} = 7.4, J_{BX} = 8.0, 2 H–C(2)). ^{13}C-NMR ($CDCl_3$): 172.1 (C=O); 142.5, 137.0 (arom. C); 131.8, 130.1, 128.6, 128.4, 127.4, 127.3, 126.7, 126.2 (arom. C, CH=CH); 51.5 (MeO); 44.9 (H–C(3)); 40.4 (CH_2(2)). CI-MS (NH_3): 284 (100), 267 (13), 235 (10), 193 (10).

A soln. of the methyl ester (1.08 g, 4.1 mmol) in benzene (30 ml) was added slowly to a suspension of $LiAlH_4$ (160 mg, 4.2 mmol) in benzene (30 ml) at 5°. After complete addition, the mixture was heated to 60° for 16 h, then quenched with MeOH at 5°. The mixture was partitioned between Et_2O and ice-cold 1M HCl, the aq. phase further extracted with Et_2O, the combined org. phase washed with sat. aq. NaCl soln., dried ($MgSO_4$), and evaporated, and the crude product purified by FC (silica gel, 5 × 28 cm, hexane/AcOEt 1:1; R_f 0.42): *(R,E)-3,5-diphenylpent-4-enol* (+)-**21**; (0.816 g, 84%). Colorless oil. $[\alpha]_D = +17.8$ (*c* = 2.0). IR ($CHCl_3$): 3700–3200 (br.), 3620*m*, 3085*m*, 3060*m*, 2940*s*, 2885*m*, 1950*w*, 1880*w*, 1805*w*, 1730*w*, 1645*w*, 1600*m*, 1495*s*, 1450*s*, 1390*m*, 1155*m*, 1405*s*, 965*s*, 860*m*. ^{1}H-NMR: 7.14–7.33 (*m*, 10 arom. H); 6.42 (*d*, *J* = 15.9, H–C(5)); 6.31 (*dd*, *J* = 7.4, 15.9, H–C(4)); 3.57–3.65 (*m*, 2 H–C(1), H–C(3)); 1.96–2.12 (*m*, 2 H–C(2)); 1.73 (br. *s*, OH). ^{13}C-NMR: 143.6, 137.1 (arom. C); 133.4, 129.5, 128.5, 128.3, 127.5, 127.0, 126.3, 126.0 (arom. CH, CH=CH); 60.7 (CH_2(1)); 45.4 (H–C(3)); 38.3 (CH_2(2)). CI-MS (NH_3): 256 (100), 238 (4), 221 (9), 193 (22).

Alcohol (+)-**21** (138 mg, 0.58 mmol) was dissolved in CH_2Cl_2 (5 ml) containing pyridine (240 mg, 3 mmol), cooled to 0°, and then treated dropwise with a soln. of (+)-camphor-10-sulfonyl chloride (*Fluka, puriss.*) in CH_2Cl_2 (2 ml). After complete addition, the mixture was stirred for 18 h, then diluted with Et_2O, and washed with sat. aq. NH_4Cl, sat. aq. $NaHCO_3$, and sat. aq. NaCl, soln., dried ($MgSO_4$), and evaporated. The crude product was purified by FC (silica gel, 1 × 24 cm, hexane/AcOEt 4:1; R_f 0.2): *(R,E)-3,5-diphenylpent-4-enyl camphor-10-sulfonate* (+)-**22**; (244 mg, 93%). Colorless oil, which was crystallized from CH_2Cl_2/hexane at −14°. M.p. 88°. $[\alpha]_D = +24.4$ (*c* = 1.5). IR: 3085*m*, 3060*m*, 3030*m*, 2960*s*, 1950*w*, 1880*w*, 1800*w*, 1745*s*, 1600*m*, 1495*s*, 1470*m*, 1455*s*, 1415*s*, 1360*s*, 1280*m*, 1175*s*, 1130*w*, 1070*m*, 1055*s*, 1030*m*, 965*s*, 930*s*. ^{1}H-NMR: 7.36–7.19 (*m*, 10 arom. H); 6.47 (*d*, *J* = 15.6, H–C(5′)); 6.30 (*dd*, *J* = 7.7, 15.6, H–C(4′)); 4.31–4.26 (*m*, 2 H–C(1′)); 3.66 (*q*, *J* = 7.8, H–C(3′)); 3.56 (*d*, *J* = 15.0, H–C(10)); 2.94 (*d*, *J* = 15.0, H–C(10)); 2.52–2.33 (*m*, H–C(4), H_{exo}–C(5 or 6)); 2.25 (*dq*, *J* = 1.5, 7.4, 2 H–C(2′)); 2.10 (*t*, *J* = 4.4, H–C(3)); 2.07–1.96 (*m*, H_{exo}–C(5 or 6)); 1.93 (*d*, *J* = 18.6, H–C(3)); 1.69–1.57, 1.46–1.37 (2*m*, H_{endo}–C(5), H_{endo}–C(6)); 1.09 (*s*, Me); 0.84 (*s*, Me). ^{13}C-NMR: 214.0 (C=O); 142.5,

136.9 (arom. C); 132.0, 130.4, 128.6, 128.3, 127.4, 127.2, 126.6, 126.1 (arom. CH, H–C(4'), H–C(5')); 68.5 (CH_2(1')); 57.8 (C(1)); 47.9 (C(7)); 46.7 (CH_2(10)); 42.7, 45.0 (H–C(3'), H–C(4)); 42.5 (CH_2(3)); 34.9 (CH_2(2')); 26.9 (CH_2(6)); 24.9 (CH_2(5)); 19.8, 19.7 (2 Me). CI-MS (NH_3): 470 (100), 221 (32), 193 (8), 117 (8). Anal. calc. for $C_{27}H_{32}O_4S$: C 71.65, H 7.13; found: C 71.59, H 6.93.

Single crystals suitable for X-ray diffraction were grown by isothermal distillation of pentane into a $CHCl_3$ soln. of (+)-**22** at −14°.

(S,E)-1-(4-Methylphenyl)-3-phenylprop-2-enol ((*S*)-**23**). At −78°, 4-bromotoluene (14.0 g, 81.8 mmol) in THF (200 ml) under N_2 was treated with 2.0M BuLi in hexane (58 ml) resulting in the precipitation of a white solid. The mixture was allowed to warm to −10°, stirred until all the precipitate dissolved, re-cooled to −78°, and treated with a soln. of cinnamaldehyde (7.45 g, 56.4 mmol) in THF (30 ml). After stirring for 2 h, the reaction was quenched with a sat. aq. NH_4Cl soln. (200 ml). The mixture was warmed to r.t. and the THF removed *in vacuo*. The residue was extracted with Et_2O, the combined extract washed with sat. aq. solns. of NH_4Cl and NaCl, dried ($MgSO_4$), and evaporated, and the residue crystallized from Et_2O/hexane: *rac*-**23** as a white solid (11.0 g, 87%). M.p. 76–77°.

Kinetic resolution [12]: *rac*-**23** (12.35 g, 55.3 mmol) in CH_2Cl_2 (220 ml) under N_2 was treated with (+)-(*R,R*)-diisopropyl tartrate ((+)-DIPT; 2.17 g, 9.26 mmol, 17 mol-%) and molecular sieves (3 Å, freshly activated; 6.62 g) and then cooled to −20°. After addition of Ti(i-PrO)$_4$ (1.57 g, 5.53 mmol, 10 mol-%), the mixture was stirred for 30 min and then treated with 3.0M *tert*-butyl hydroperoxide in isooctane (13 ml, 39 mmol), and stirring was continued for 19 h at −20°. The reaction was quenched by addition of an aq. soln. (55.5 ml) containing 18.3 g of $FeSO_4 \cdot H_2O$ and 6.1 g of citric acid monohydrate. After vigorous stirring for 30 min, the org. phase was separated, the aq. phase twice extracted with CH_2Cl_2, and the combined org. extract stirred vigorously with an aq. soln. (55.5 ml) containing NaOH (18.5 g) and NaCl (3.1 g). After separation of the org. phase, the aq. layer was twice extracted with CH_2Cl_2, the combined org. phase washed with a sat. NaCl soln., dried ($MgSO_4$), and evaporated, and the residue purified by FC (silica gel, 4 × 50 cm, hexane/AcOEt 4:1; R_f 0.27): (*S*)-**23** (3.58 g, 29%) in 97% ee. White solid. Crystallization from Et_2O/hexane gave enantiomerically pure product (2.55 g, 21%). M.p. 67–68°. HPLC (*OJ*, hexane/i-PrOH 93:7): t_R 78.8 (*S*), 90.8 min (*R*); > 99.5% ee. $[\alpha]_D = -35.3$, $[\alpha]_{578} = -37.3$, $[\alpha]_{546} = -44.8$, $[\alpha]_{436} = -101$, $[\alpha]_{365} = -243$ (*c* = 1.03). IR (KBr): 3555*s* (br.), 3082*w*, 3052*w*, 3025*m*, 2919*w*, 1654*w*, 1577*w*, 1508*s*, 1495*m*, 1458*m*, 1400*m*, 1352*m*, 1266*m*, 1171*m*, 1093*m*, 1017*s*, 965*s*, 884*w*, 812*m*, 758*s*, 741*s*, 691*s*. ^{1}H-NMR: 7.41–7.18 (*m*, 9 arom. H); 6.70 (*d*, *J* = 15.9, PhC*H*=CH); 6.39 (*dd*, *J* = 15.9, 6.4, PhCH=C*H*); 5.37 (*dd*, *J* = 6.4, 3.6, C*H*OH); 2.36 (*s*, Me); 1.97 (*d*, *J* = 3.6, OH). ^{13}C-NMR: 139.8, 137.5, 136.6 (arom. C); 131.6, 130.2, 129.3, 129.2, 128.5, 127.7, 127.1, 127.0, 126.6, 126.3 (arom. CH, *C*H=*C*H); 74.9 (CHOH); 21.1 (Me). EI-MS: 224 (17, M^+), 209 (13), 119 (100), 105 (14), 91 (24), 77 (12). Anal. calc. for $C_{16}H_{15}O$: C 86.06, H 6.77; found: C 85.90, H 6.81.

(S,E)-1-(4-Methylphenyl)-3-phenylprop-2-enyl Acetate ((*S*)-**25**). A soln. of (*S*)-**23** (115.5 mg, 0.52 mmol) in CH_2Cl_2 (8.0 ml) containing 4-(dimethylamino)pyridine (2 mg) and Et_3N (105 mg, 1.03 mmol) at 0° under N_2 was treated dropwise with Ac_2O (79 mg, 0.77 mmol). The mixture was warmed to r.t. and stirred for 4.5 h. After quenching with ice-cold sat. NH_4Cl soln., the aq. phase was further extracted with CH_2Cl_2 and the combined extract dried (Na_2SO_4) and evaporated. FC (basic Al_2O_3, 1.5 × 30 cm, hexane/AcOEt 9:1; R_f 0.54) afforded (*S*)-**25** (117 mg, 86%). Colorless oil. HPLC (*OD*, hexane/i-PrOH 99.5:0.5): t_R 38.8 (*S*), 42.4 min (*R*); > 99.5% ee. IR ($CHCl_3$): 3005*m*, 2978*m*, 2928*w*, 1732*s*, 1704*s*, 1602*w*, 1514*w*, 1495*w*, 1450*w*, 1371*s*, 1327*w*, 1018*m*, 965*m*, 915*w*. ^{1}H-NMR: 7.43–7.21 (*m*, 9 arom. H); 6.62 (*d*, *J* = 15.4, PhC*H*=CH); 6.43 (*d*, *J* = 6.8, C*H*OAc); 6.36 (*dd*, *J* = 15.4, 6.8, PhCH=C*H*); 2.35 (*s*, *Me*C$_6$H$_4$); 2.12 (*s*, MeO). ^{13}C-NMR: 169.9 (C=O); 139.4, 138.0, 136.2 (arom. C); 132.3, 129.3, 128.5, 128.0, 127.8, 127.5, 127.0 (arom. CH, *C*H=*C*H); 76.6 (*C*HOAc); 21.3, 21.2 (2 Me). EI-MS: 266 (24, M^+), 224 (36), 206 (100), 191 (73), 165 (18), 129 (22), 115 (47), 105 (41), 91 (26), 77 (20). Anal. calc. for $C_{18}H_{18}O_2$: C 81.17, H 6.81; found: C 81.08, H 7.01.

Methyl (R)-2-Methoxy-2-(4-methylphenyl)acetate ((*R*)-**26**). A soln. of (*S*)-**23** (141 mg, 0.63 mmol) in THF (5 ml) was treated with NaH (25.5 mg, 1.06 mmol) and stirred at r.t. for 1 h. After addition of MeI (709 mg, 5 mmol) and further NaH (19.3 mg, 0.8 mmol), the resulting suspension was stirred overnight. The mixture was treated with 2.8M aq. NH_4Cl (5 ml) and extracted with CH_2Cl_2 (3 × 10 ml), the combined extract dried (Na_2SO_4) and evaporated, and the residue purified by FC (silica gel, 1.5 × 25 cm, hexane/AcOEt 9:1, 12 × 16 ml fractions; R_f 0.40): *(S)-1-(4-methylphenyl)-3-phenylprop-2-enyl methyl ether* (143 mg, 96%). Colorless oil. $[\alpha]_D = -35.9$ (*c* = 1.0). IR (NaCl): 3026*m*, 2925*m*, 2820*m*, 1677*w*, 1601*w*, 1512*s*, 1494*m*, 1306*w*, 1186*m*, 1092*vs*, 967*vs*, 816*s*, 766*m*, 744*s*, 694*s*. ^{1}H-NMR: 7.41–7.18 (*m*, 9 arom. H); 6.63 (*d*, *J* = 15.9, PhC*H*=CH); 6.29 (*dd*, *J* = 6.9, 15.9, PhCH=C*H*); 4.78 (*d*, *J* = 6.9, MeOC*H*); 3.38 (*s*, MeO); 2.36 (*s*, *Me*C$_6$H$_4$). ^{13}C-NMR: 138.0, 137.4, 136.7 (arom. C); 131.2, 130.3, 129.2, 128.5, 127.6, 126.8, 126.6 (arom. CH, *C*H=*C*H); 84.1 (MeO*C*H); 56.3 (MeO); 21.1 (*Me*C$_6$H$_4$). EI-MS: 238 (68, M^+), 223 (100), 207 (39), 191 (24), 135 (20), 129 (24), 119 (73), 115 (49), 105 (33), 91 (60).

The product (125 mg, 0.447 mmol) was dissolved in benzene (5 ml) and filtered through a column of $KMnO_4$ on silica gel (20% *w/w* $KMnO_4$, 1.7 × 3 cm) [28]. After recycling the filtrate and washing the column with benzene (9 ml), the column was dried under a gentle flow of N_2. Elution with H_2O (30 ml) and collecting the eluate directly in a mixture of 1M HCl (20 ml) and $Na_2S_2O_5$ (5.0 g) afforded a colorless soln. which was extracted with CH_2Cl_2. After drying (Na_4SO_4) and evaporation, the resulting white solid was dissolved in MeOH/toluene 2:5 (7 ml), treated with 2.0M Me_3SiCHN_2 in hexane (0.5 ml) and stirred for 15 min [29]. Excess Me_3SiCHN_2 was destroyed with AcOH, and the volatiles were removed *in vacuo*. The residue was purified by FC (silica gel, 2.5 × 15 cm, hexane/AcOEt 9:1; R_f 0.11): (*R*)-**26** (15.2 mg, 18%). Very pale yellow oil. $[\alpha]_D = -125$ (*c* = 1.03). CD (0.373 mM, 24°): 222 (−11), 226 (−12), 250 (0). IR (NaCl): 2953*w*, 1753*vs* (br.), 1455*m*, 1261*m* (br.), 1198*s*, 1108*s*, 1013*m*, 732*m*, 698*m*. ^{1}H-NMR: 7.33 (*d*, *J* = 8.0, 2 arom. H); 7.19 (*d*, *J* = 8.0, 2 arom. H); 4.75 (*s*, MeOC*H*); 3.72 (*s*, CO_2Me); 3.39 (*s*, MeO); 2.35 (*s*, *Me*C_6H_4). ^{13}C-NMR: 171.3 (C=O); 138.7, 133.2 (arom. C); 129.4, 127.2 (arom. CH); 82.4 (MeO*C*H); 57.2 (MeO); 52.2 (CO_2*Me*); 21.2 (*Me*C_6H_4). CI-MS: 212 (83, $[M + NH_4]^+$), 180 (100), 163 (11), 135 (10). Anal. calc. for $C_{11}H_{14}O_3$: C 68.02, H 7.27; found: C 68.20, H 7.25.

Methyl (S)-2-Methoxy-2-phenylacetate ((*S*)-**28**). (+)-(*S*)-2-Methoxy-2-phenylacetic acid (*Fluka, purum*; 50 mg, 0.30 mmol) in MeOH/toluene 2:5 (7 ml) was treated with 2.0M Me_3SiCHN_2 [29] in hexane (0.5 ml). The resulting yellow soln. was stirred for 15 min, excess Me_3SiCHN_2 quenched with AcOH, the mixture evaporated and the residue purified by FC (silica gel, 2.5 × 15 cm, hexane/AcOEt 9:1; R_f 0.11): (*S*)-**28** (48 mg, 89%). Colorless oil. $[\alpha]_D = +125$ (*c* = 0.97). CD (0.369 mM, 24°): 213 (+8), 223 (+12), 252 (0). IR (NaCl): 3032*w*, 2996*w*, 2952*w*, 2829*w*, 1753*vs* (br.), 1494*w*, 1455*m*, 1436*m*, 1351*w* (br.), 1261*m* (br.), 1198*s* (br.), 1175*s*, 1109*s* (br.), 785*w*, 732*m*, 699*m*. ^{1}H-NMR: 7.46–7.36 (*m*, 5 arom. H); 4.78 (*s*, MeOC*H*); 3.73 (*s*, CO_2Me); 3.41 (*s*, MeO). ^{13}C-NMR: 171.1 (C=O); 138.7 (arom. C); 128.8, 128.6, 127.2 (arom. CH); 82.6 (MeO*C*H); 57.3 (*Me*OCH); 52.3 (CO_2*Me*). CI-MS: 198 (100, $[M + NH_4]^+$), 166 (26), 121 (15). Anal. calc. for $C_{10}H_{12}O_3$: C 66.65, H 6.71; found: C 66.68, H 6.63.

Palladium-Catalyzed Allylic Alkylation. General Procedure. In a 30-ml ampoule equipped with magnetic stirring bar and *Young*-valve™, under N_2, [{Pd(η^3-C_3H_5)}$_2$] [27] (2.34 mg, 6.4 μmol, 1.1 mol-%) was treated with **10** (6.34 mg, 17.5 μmol, 2.9 mol-%) in THF (0.7 ml). The soln. was degassed (three freeze-thaw cycles) and the ampoule sealed at 0.01 Torr. After stirring at 50° for 2 h, the ampoule was opened under N_2 and the soln. treated sequentially with (*S*)-**25** (155.0 mg, 0.58 mmol) in THF (2.2 ml), dimethyl malonate (231.5 mg, 1.75 mmol), *N,O*-bis(trimethylsilyl)acetamide (356 mg, 1.75 mmol), and KOAc (2 mg) and then degassed (three freeze-thaw cycles). The ampoule was resealed (0.01 Torr) and the soln. stirred at r.t. for 48 h after which the mixture was diluted with Et_2O and then extracted with two portions of ice-cold sat. aq. NH_4Cl soln. Drying ($MgSO_4$), evaporation, and FC (silica gel, 4 × 30 cm, hexane/AcOEt 3:1) afforded the product as a colorless oil (185.7 mg, 94.3%). GC-MS (50→270°, 20°/min): t_R 8.24 (**29**), 8.36 min (**30**); **29**/**30** 93.1:6.9. HPLC (*OJ*, hexane/i-PrOH 99:1): t_R 22.5 (*R*), 24.8 min (*S*; not detected); > 99% ee.

Dimethyl 2-[(R,E)-1-(4-Methylphenyl)-3-phenylprop-2-enyl]propanedioate ((*R*)-**29**): Obtained from a reaction in CH_2Cl_2 using ligand (*R*)-**31**. M.p. 69–70°. R_f (hexane/AcOEt 3:1) 0.30. $[\alpha]_D = +20.8$, $[\alpha]_{578} = +24.3$, $[\alpha]_{546} = +24.5$, $[\alpha]_{436} = +27.8$, $[\alpha]_{365} = -12.7$ (*c* = 0.63). HPLC (*OJ*, hexane/i-PrOH 99:1): t_R 22.7 (*R*), 24.8 min (*S*); > 99.5% ee. CD (0.434 mM, 23°): 215 (+33), 222 (+46), 237 (0), 253 (−13), 259 (−15), 265 (−12). IR (KBr): 3022*w*, 2955*w*, 1750*s*, 1729*m*, 1511*w*, 1433*m*, 1317*m* (br.), 1261*m*, 1144*m*, 967*m*, 827*m*, 750*w*, 694*w*, 581*w*. ^{1}H-NMR: 7.33–7.11 (*m*, 9 arom. H); 6.47 (*d*, *J* = 15.7, PhC*H*=CHCH); 6.32 (*dd*, *J* = 15.7, 8.5, PhCH=C*H*CH); 4.26 (*dd*, *J* = 10.9, 8.51, PhCH=CHC*H*); 3.94 (*d*, *J* = 10.9, *H*C(CO_2Me)$_2$); 3.70 (*s*, MeO); 3.56 (*s*, MeO); 2.32 (*s*, *Me*C_6H_4). ^{13}C-NMR: 168.1, 167.7 (C=O); 137.1, 136.9, 136.7 (arom. C); 131.6, 129.4, 129.3, 128.4, 127.7, 127.5, 126.3 (arom. CH, *C*H=*C*H); 57.6 (*C*H(CO_2Me)$_2$); 52.5, 52.3 (MeO); 48.7 (*C*HCH=CH); 21.1 (*Me*C_6H_4). EI-MS: 338 (2, M^+), 219 (47), 218 (26), 207 (100), 206 (15), 192 (15), 191 (14), 129 (34), 128 (13), 115 (52), 91 (14), 77 (6). Anal. calc. for $C_{21}H_{22}O_4$: C 74.54, H 6.55; found: C 74.30, H 6.52.

Dimethyl 2-[(S,E)-3-(4-Methylphenyl)-1-phenylprop-2-enyl]propanedioate ((*S*)-**30**): Obtained from a reaction in CH_2Cl_2 using ligand (*S*)-**31**. M.p. 69–70°. R_f (hexane/AcOEt 3:1) 0.30. $[\alpha]_D = -15.0$, $[\alpha]_{578} = -14.3$, $[\alpha]_{546} = -15.6$, $[\alpha]_{436} = -14.6$, $[\alpha]_{365} = +26.5$ (*c* = 0.63). HPLC (*OJ*, hexane/i-PrOH 99:1): t_R 25.0 (*S*), 23.3 min (*R*); > 99.5% ee. CD (0.435 mM, 23°): 217 (−32), 223 (−44), 234 (0), 252 (+7), 258 (+10), 262 (+12), 267 (+11), 270 (+12). IR (KBr): 3033*w*, 2956*w*, 1756*s*, 1736*s*, 1511*w*, 1433*m*, 1311*m* (br.), 1261*m*, 1179*m*, 1138*m*, 983*m*, 806*m*, 761*m*, 699*m*, 579*w*, 500*m*. ^{1}H-NMR: 7.33–7.07 (*m*, 9 arom. H); 6.45 (*d*, *J* = 15.7, C_6H_4C*H*=CHCH); 6.27 (*dd*, *J* = 15.7, 8.6, C_6H_4CH=C*H*CH); 4.25 (*dd*, *J* = 10.9, 8.5, C_6H_4CH=CHC*H*); 3.95 (*d*, *J* = 10.9, *H*C(CO_2Me)$_2$); 3.70 (*s*, MeO); 3.52 (*s*, MeO); 2.31 (*s*, *Me*C_6H_4). ^{13}C-NMR: 168.2, 167.8 (C=O); 137.1, 136.9, 136.7 (arom. C); 131.6, 129.4, 129.3, 128.4, 127.7, 127.5, 126.3 (CH); 57.7 (*C*H(CO_2Me)$_2$); 52.6, 52.4 (MeO); 48.8 (CH=CH*C*H); 21.0 (*Me*C_6H_4). EI-MS: 338 (4, M^+), 219 (49), 218 (36), 207 (100), 206 (36), 192 (16), 191 (15), 129 (37), 128 (13), 115 (59), 91 (18), 77 (6). Anal. calc. for $C_{21}H_{22}O_4$: C 74.54, H 6.55; found: C 74.30, H 6.45.

Dimethyl 2-[(S,E)-1,3-Diphenylprop-2-enyl]propanedioate ((−)-**6**): Obtained from a reaction of *rac*-**5** in CH_2Cl_2 using ligand (*S*)-**31** [6a] [9]. Anal. data: see [5] [9]. CD (0.433 mM, 23°): 215 (−37), 221 (−51), 232 (0), 250 (+10), 257 (+12), 260 (+11), 263 (+12), 267 (+10), 269 (+11).

*X-Ray Structure Analysis of (+)-***22** (*Fig. 1*). Crystal data and parameters of the data collection are compiled in *Table 3*. Unit-cell parameters were determined by accurate centering of 25 strong independent reflections by the least-squares method. Reflection intensities were collected at r.t. on a four-circle diffractometer (*Enraf-Nonius CAD4*) equipped with a graphite monochromator and using MoK_α radiation. Three standard reflections monitored every h during data collection showed no intensity loss. The usual corrections were applied. Diffraction absorption direct-method strategies using the program SHELXS-86 [30]. Anisotropic least-squares refinement was carried out on all non-H-atoms using the program CRYSTALS [31]. Positions of H-atoms were calculated. Scattering factors were taken from the International Tables of Crystallography, Vol. IV. Fractional coordinates are deposited in the *Cambridge Crystallographic Data Base*.

Table 3. *Crystallographic Data and Parameters of Data Collection for* (+)-**22**

Molecular formula	$C_{27}H_{32}O_4S$	Crystal dimensions [mm]	0.2 × 0.4 × 0.8
Crystal system	monoclinic	Temperature [K]	293
Space group	$P2_1$	Θ_{max} [°]	26.32
a [Å]	11.690(2)	Radiation	MoK_α, 0.71069 Å
b [Å]	6.382(1)	Scan type	$\omega/2\Theta$
c [Å]	16.198(2)	No. of independent refl.	2674
α [°]	90(0)	No. of refl. in refinement	2284
β [°]	90.355(12)	No. of variables	289
γ [°]	90(0)	Final *R*	3.91
V [Å^3]	1208.47(38)	Final R_w	4.33
Z	2	Weighting scheme	weight·$[1-(\Delta F/6\sigma F)^2]^2$

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