Asymmetric Synthesis. Asymmetric Catalytic Allylation Using Palladium Chiral Phosphine Complexes

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Abstract: The general characteristics of asymmetric catalytic allylation are analyzed in terms of the properties of the allyl acetate substrates and of the putative (π-allyl)palladium(II) intermediates. After examining the diastereomeric equilibria of a series of [Pd(chiral diphosphine)(chiral π-allyl)]$^+$ complexes, it was established that anti-disposed π-allyl substituents are the major source of discrimination and that aryl substituents cause an enhancement of the epimerization rate and also are responsible for the greatest discrimination. The π-allyl substituents appear to contribute additively to the discrimination, and a sector rule is proposed for predicting diastereomeric equilibrium constants. Under appropriate conditions, it is proposed that the optical yields of asymmetric catalytic allylation can be predicted from the chiral discrimination found for these π-allyl intermediates. These proposals were tested and optical yields of up to 86% are reported. Quantitative chemical yields were obtained, catalysis can be performed at 25 °C, and the products are readily transformed into useful chirons. The optical yields are sensitive to the chiral phosphine used but are insensitive to the nature of the nucleophiles that were used. There is an approximate correlation of the optical yield with the previously observed diastereomeric ratio of the corresponding (π-allyl)palladium intermediate. All of the reactions are completely regioselective, and all of the nucleophiles used gave the same prevailing enantiomer of the product for a given chiral phosphine.

The most important reaction of organic chemistry, carbon–carbon bond formation, ultimately requires two refinements, that it be enantioselective and be catalytic. There are at present many examples of asymmetric, but stoichiometric, carbon–carbon bond forming reactions which give high optical and chemical yields.[1-6] Some have the added advantage that the chiral-inducing entity can be recycled[1,2] but there appears to be no obvious simple way of making these reactions catalytic. Organometallic systems provide the possibility of achieving this twofold goal of asymmetric catalysis.[7]

Currently there are a number of viable catalytic organometallic carbon–carbon bond forming reactions which have been used for asymmetric catalytic synthesis: hydroformylation,[8] cyclopropanation,[9] Grignard (alkyl–vinyl) cross coupling,[10] olefin codimerization,[11] and allylic alkylation[12] (allylation). Although a number of these systems have given excellent optical yields, none as yet has consistently rivaled the spectacular results obtained for asymmetric hydrogenation[13,14] nor do they have the rational stereochemical[15] and mechanistic[16-18] underpinnings that are now recognized for the asymmetric hydrogenation of amino acid precursors.

Of these carbon–carbon bond forming reactions, it seemed to us that allylation was the most amenable to rational development for asymmetric catalytic synthesis. The refinement of this reaction owes much to the work of Trost,[19] who recognized the synthetic potential of earlier observations by Tsuji,[20] who described the first stoichiometric palladium allylation reaction and those of Walker[21] and Hata,[22] who discovered palladium-catalyzed allylation using various allylic leaving groups and nucleophiles. Among the characteristics investigated by Trost were the catalytic conditions, substrate and nucleophile tolerance, regioselectivity, and stereoselectivity. For the first reported asymmetric catalytic allylation reaction, Trost[23] obtained optical yields which ranged from 16% to 46% depending on the allylic substrate, the chiral phosphine and the nucleophile. Kagan[24] devised a different approach where he used a chiral phosphine palladium catalyst, an achiral allyl phenoxide substrate and a chiral carbanion. The optical yields were low, up to 10%. Other asymmetric catalytic allylic alkylations using allylic alcohols or phenoxides, alkyl Grignard reagents, and chiral nickel complexes, also give very low optical yields[25,26] except in a few notable exceptions.[27] Faller, however, has developed a remarkable chiral molybdenum system which stoichiometrically

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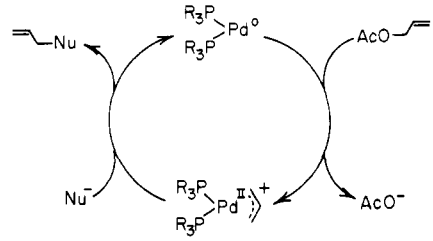

Figure 1. Catalytic cycle for palladium-catalyzed allylation.

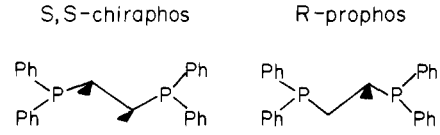

Figure 2. Preferred conformations of *S,S*-chiraphos and *R*-prophos when coordinated to a metal.

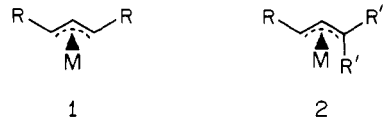

Figure 3. Structures of the type **1** and type **2** allyls when coordinated to a metal.

gives essentially optically pure products through stereo and electronic control.[28]

These previous catalytic studies were essentially exploratory and did not incorporate an overall strategy which clearly defined all of the factors governing asymmetric catalytic allylation, although they demonstrated the potential of the method. In this paper we describe our orchestration of the palladium system for asymmetric allylation.[29] We consider and incorporate certain crucial features required of the substrate and catalyst in order to obtain a viable asymmetric catalytic system and we also record the results of asymmetric catalysis. The assumptions inherent in the strategy are examined in detail in the following paper where we describe a detailed study of the mechanism of catalysis.

Catalyst and Substrate

The assumed catalytic cycle is shown in Figure 1. The cationic π-allyl–palladium(II)–diphosphine complex is susceptible to nucleophilic attack by soft (carbon) nucleophiles ($pK_a < 16$) to produce an allylic product and a palladium(0)–diphosphine complex which may be stabilized by coordination to an olefin of either the substrate or the product. An allylic acetate then oxidatively adds to the palladium(0) complex to regenerate the π-allyl–palladium(II)–diphosphine intermediate. Allylic acetates themselves do not react with soft (carbon) nucleophiles, and although acetates are not normally good leaving groups for oxidative addition, allylic acetates react readily with palladium(0)–diphosphine complexes presumably because of the intramolecular assistance provided by prior olefin coordination.

In order to make this catalytic system suitable for asymmetric synthesis, prochiral π-allylic intermediates are required and diastereomeric transition states need to be produced by incorporation of chiral phosphine ligands. The chiral ligand chosen for this study is *S,S*-chiraphos[15] which is depicted in Figure 2 in its preferred chelate ring conformation. As noted elsewhere[14,15,18] it is the chiral array of phenyl groups, held so as a consequence of the chelate ring conformation, which is the major source of dissymmetric discrimination of prochiral entities bonded to the other coordination sites of the phosphine complex.

The choice of the allylic substrate is crucial, however, since, as we will show, a general and versatile system requires that a number of stringent demands are met. In Figure 3 we depict two structurally simple (1,3-substituted) types of π-coordinated allyls

Figure 4. π–σ–π rearrangement process for a type **2** allyl.

Figure 5. Diastereomeric equilibrium for the [Pd(*S,S*-chiraphos)(type **2** allyl)]$^+$ intermediates.

which are capable of switching the face of coordination via the π–σ–π mechanism. The π–σ–π interconversion process[30] is shown in Figure 4 for the type **2** allyl. It will be noted that if the σ-bond is formed at the more substituted end of the allyl, rearrangement leads to inversion of the π-allyl chirality[30,31] and to concomitant interchange of the syn and anti dispositions of the R′ groups. Formation of a σ-metal–carbon bond at the less substituted end, followed by rearrangement, does not lead to inversion of the π-allyl chirality but rather it leads to an anti-disposed R group. Given this mechanism, it can be seen that 1,3-substitution patterns other than those shown in Figure 3 will lead to geometrical isomerism and, for certain kinds of substituted allyls no net inversion of the chirality can occur.[30,32] Thus the type **1** and **2** allyls obviate some of the potential complexities that could arise from geometrical isomerism and the inability of certain π-allyl systems to racemize. Whereas it is true that for the π-allyl types shown in Figure 3, isomers having the much less stable[30] anti-disposed R groups are possible, the type **2** structures examined here show no evidence for the existence of anti-disposed R groups.

For the purpose of asymmetric synthesis, type **1** and type **2** π-allyls present different features. Type **1** is achiral when bound to a metal with syn-disposed R groups and an asymmetric reaction would depend on the preference for nucleophilic attack at the two prochiral centers (1 and 3 positions). All of the dissymmetric discrimination of an asymmetric reaction would be determined in the transition state. Type **2** π-allyls, however, form chiral complexes, the enantiomers of which are interconverted by switching the π-face coordination (Figure 4). Thus type **2** π-allyl complexes incorporating the *S,S*-chiraphos ligand will give the interconvertable diastereomers shown in Figure 5. The prevailing chirality of the product of an asymmetric reaction would, unlike the type **1** case, be determined by the relative rates of reaction of the two four-coordinate diastereomers provided equilibration is rapid.

Enantioselection

Rather than performing asymmetric catalytic reactions using a variety of allylic substrates, it would be advantageous to find a semiempirical method for predicting the approximate optical yields using a given class of chiral phosphine ligand. One such approach depends on a number of assumptions and seeks to find a connection between the ground-state dissymmetric discrimination of the intermediate (Figure 5) and that of the diastereomeric transition states. In the case of type **1** π-allyls no such connection can exist because the π-allyl moiety is achiral but for type **2** π-allyls such a connection may be possible because both the intermediates and their corresponding transition states are diastereomeric.

If we can arrange by judicious choice of R′ groups that the epimerization of the palladium(II) intermediates (Figure 5) is much faster than the nucleophilic attack (Curtin–Hammett conditions[33]), then the oxidative addition step will be irrelevant in determing the optical yield. Under these conditions the enantiomeric excess will be determined by the relative rates of reaction of the two diastereomeric intermediates and, furthermore,

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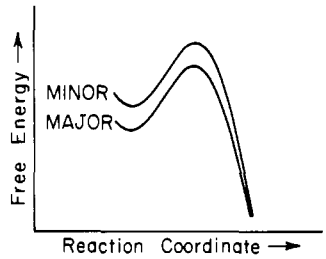


Figure 6. Exothermic rate profile assumed for the nucleophilic attack on the two four-coordinate diastereomeric intermediates via the corresponding transition states.

the stereochemistry of the allylic acetate substrate and stereoselectivity of the oxidative addition will be irrelevant, for all memory of the substrate structure and oxidative addition selectivity will be lost after epimerization.

In Figure 6 we show a reaction energy profile for the nucleophilic attack step which we assume is strongly exothermic. If we invoke an asymmetric variation of the Hammond postulate[34] then we may assume that the dissymmetric discrimination in the ground-state intermediates will to some extent be reflected in the corresponding diastereomeric transition states because the intermediates and the transition states are closer to each other in energy than are the transition states and the products; i.e., the lower energy diastereomer will also have a lower energy transition state. Thus, without dwelling on the difficulties associated with the Hammond postulate, the measurement of the equilibrium shown in Figure 5 may give an approximate indication of the optical yield as well as the chirality of the major enantiomer. Implicit in this assumption is that the prevailing chirality of the product originates in the major four-coordinate diastereomer. The observation that the opposite is the case for asymmetric hydrogenation of amino acid precursors[16,17] is not inconsistent with the present arguments because the crucial step in the hydrogenations is endothermic.[18]

Regioselectivity and Products

To complete the orchestration of the system we sought two further conditions. First, we required exclusive regioselectivity so that nucleophilic attack occurred only at the asymmetric center bearing the R group of a type **2** allyl (Figure 3). Second, it would be advantageous if the allylation products could be readily derivatized to useful chirons.

Under normal conditions nucleophilic attack at a *free* type **2** allyl would be expected to give a mixture of products resulting from S_N and S_N' attack. For the analogous coordinated type **2** allyl, however, the presence of the metal will change the regioselectivity. Trost[35] has shown that the regioselectivity can depend on a number of factors among which are the steric hindrance of the two allyl sites and the stability of the palladium–olefin bond that is developed during attack. For type **2** allyls, steric effects would tend to direct attack at the desired less substituted end of the allyl, but steric effects alone are unlikely to cause exclusive attack at this center. It is known[36] that palladium(0)–phosphine complexes coordinate more strongly with electron-deficient olefins than with those that are electron rich. Thus nucleophilic attack at the chiral center of a type **2** allyl bearing aryl-R′ groups will form a more electron-deficient olefin than if attack occurred at the other site. Since nucleophilic attack involves the simultaneous formation of a palladium(0) species and an olefin, we expected that this mutually stabilizing electronic effect would be the dominant contributor to the regioselectivity. As we show, type **2** allyls bearing aryl-R′ groups accept exclusive attack at the chiral allyl center for a range of nucleophiles even when the R group is an aryl substituent.

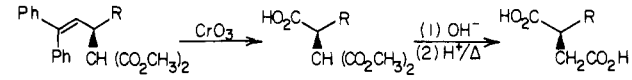


Figure 7. One method of derivatizing the allylation product derived from the reaction of sodium dimethyl malonate with a type **2** allyl.

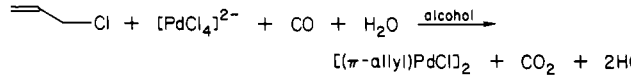
Given this exclusive regioselectivity, the products of allylation are easily derivatized. In Figure 7 we outline the method used for derivatizing the dimethyl malonate allylation products to give chiral substituted succinic acids. It is clear that other derivatives can also be obtained.

Thus the aryl-R′ groups of type **2** allyls serve to increase the rate of epimerization, enhance enantioselection, direct nucleophilic attack, and in the allylation product serve as (acid) protecting groups.

Synthesis of the π-Allyls

The diastereomeric complexes [Pd(*S*,*S*-chiraphos)(π-allyl)]ClO_4 incorporating various substituted allyls were prepared from the corresponding [Pd(π-allyl)Cl]$_2$ dimers. Most of these salts are highly crystalline materials but a number of the phenyl-substituted derivatives gave impure products when the corresponding dimers were allowed to react with chiraphos even under very mild conditions. These diastereomeric salts were prepared in solution by the addition of *S*,*S*-chiraphos to cold solutions of [Pd(π-allyl)-$(CH_3OH)_2$]ClO_4 complexes which were prepared from the corresponding chloro-bridged dimers by reaction with $AgClO_4$. Although spectroscopically (^1H and ^{31}P NMR) pure materials were thus obtained, the solid products deposited as amorphous powders and we were unable, in most cases, to obtain crystalline solids.

In general, the [Pd(π-allyl)Cl]$_2$ dimers were made either from the corresponding allylic chlorides or from the corresponding allylic alcohols. For the allylic chlorides the reaction shown was followed.[37,38]



By this method high yields of the dimers containing, 1-methyl-, 1,1-dimethyl-, 1,1-dimethyl-3-methyl-, 1,1-diethyl-, 1-phenyl-, and 1,1-diphenyl-π-allyl ligands were prepared. The alcohol–water ratios were varied to ensure homogeneity, and in some cases gentle heating was required to complete the reaction.

For the dimers containing, 1,1-diphenyl-2-methyl-, 1,1-diphenyl-3-phenyl-, 1,1-diphenyl-3-methyl-, 1,1-di-*o*-tolyl-3-phenyl-, 1,1-di-*o*-anisyl-3-phenyl-, 1,1-di-3,5-dimethylphenyl-3-phenyl-π-allyl ligands, a similar procedure was used except that aqueous HCl was added to the homogeneous THF/ethanol/water reaction solutions. In the absence of HCl, palladium metal is formed in nearly quantitative amounts. By appropriate adjustment of the amount of HCl and the solvent mixture, very high yields of the dimers were obtained. There is evidence that the allylic alchol is not the reactive species but rather that it is the allylic ethyl ether, formed from these very reactive alcohols under the acid/ethanol conditions, that is the reactive organic moiety.

The only [Pd(*S*,*S*-chiraphos)(π-allyl)]ClO_4 complex that could not be prepared by the preceding procedures was the species containing the 1,1-diphenyl-2,3-cyclotetramethylene-π-allyl ligand because all attempts to make the corresponding dimer failed. The chiraphos complex was made directly by oxidative addition of the corresponding allylic acetate with the [(*S*,*S*-chiraphos)Pd^0] species which was generated in solution by reaction of sodium dimethyl malonate with the [Pd(*S*,*S*-chiraphos)(η^3-C_3H_5)]$^+$. We have found this to be a general method.

The synthesis of the allylic chlorides and alcohols followed standard procedures. The palladium dimers were obtained with equal facility from either of the allylic isomers or a mixture of these.

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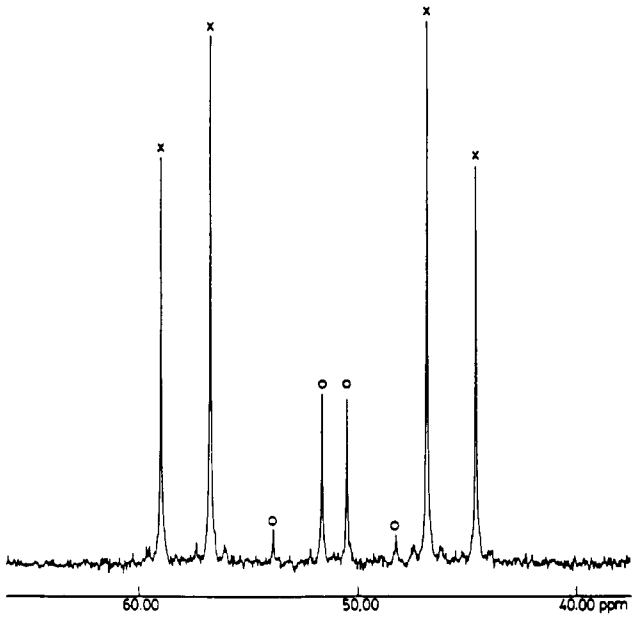


Figure 8. Equilibrium ^{31}P NMR spectrum of the [Pd(*S*,*S*-chiraphos)-(1,1,3-triphenylallyl)]ClO_4 complex in $CDCl_3$ solution at 35 °C.

Diastereomer Ratios

Solutions of the [Pd(*S*,*S*-chiraphos)(π-allyl)]ClO_4 complexes gave two AB quartets for their ^{31}P NMR spectra. These pairs of quartets were generally well separated (at 32.3 MHz) and represent the two four-coordinated diastereomers (Figure 5). A representative spectrum is shown in Figure 8 which refers to the 1-phenyl-3,3-diphenyl system. The ratio of the two diastereomers was determined by integration, the error being about ±10%. The chemical shifts and coupling constants for these ^{31}P NMR spectra are collected in Table I.

Table I also lists the diastereomer ratios for the various allyl complexes all of which can epimerize by the π–σ–π mechanism. Before we discuss these, it is important to establish that the ratios are indeed equilibrium values. For complexes bearing an allyl group for which one end of the allyl is devoid of substituents, the ^{31}P NMR spectra at 35 °C in DMF solution were either very broad or actually at the verge of coalescing into a single quartet. This suggests that at 35 °C the π-allyl complexes are undergoing rapid epimerization via the π–σ–π mechanism (Figure 4). Consistently, when the solutions were cooled to −20 °C, two sharp quartets were observed in all cases. In chloroform solutions, the epimerization of these complexes was not as fast at 35 °C; upon dissolution, sharp spectra were obtained which remained constant over a period of days and did not change upon heating suggesting that equilibration was established soon after dissolution.

Whereas the π-allyls with one end unsubstituted were found to equilibrate rapidly, equilibration of the 1,1,3-trimethylallyl complex was exceedingly slow at 35 °C. In order for epimerization to occur in this case, intermediate σ-bond formation has to occur at the disubstituted end of the allyl (Figure 4) and this, for dialkyl systems, has been shown to be a slow process.[30] Even in DMF solution the trimethyl derivative reached equilibrium only after 3 h at 60 °C.

Although the 1,1-diphenyl-3-substituted π-allyl complexes have the same type **2** allyl structure as the 1,1,3-trimethylallyl system, all of the former species were found to equilibrate rapidly at 35 °C. Equilibration was complete soon after dissolution at 35 °C. This is an important result because, as we have pointed out, rapid equilibration of the diastereomers may allow us to achieve Curtin–Hammett conditions for the catalytic reaction, a necessary but not sufficient condition for connecting the ground- and transition-state energies and for circumventing any problems associated with oxidative addition stereoselectivity.

The enhanced equilibration rates observed for the type **2** π-allyl complexes when the R′ groups are phenyl rather than alkyl groups, we believe, is connected with the enhanced stability that is provided

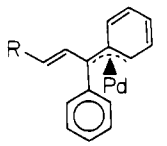


Figure 9. Proposed π-benzylic assisted π–σ–π rearrangement mechanism showing some of the important features.

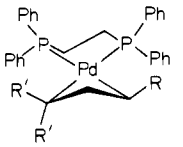


Figure 10. Absolute configuration of the major diastereomer of the [Pd(*S*,*S*,-chiraphos)(1,1-bis(3,5-dimethylphenyl)-3-phenylallyl))]$^+$ ion.

by π-benzyl formation which directs bond formation to the generally less favored end of the allyl. We depict the equilibration process involving π-benzyl participation in Figure 9. Complexes containing π-benzyl allyls are well-known and their mechanisms of rearrangement have been studied in detail.[39–41] The proposed mechanism depicted in Figure 9 is consistent with previous observations. Whether this rate enhancement is sufficient or otherwise for Curtin–Hammett conditions to obtain will be dealt with in the next paper.

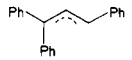
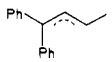
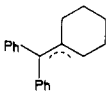
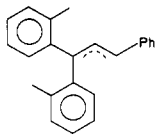
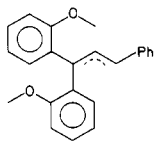
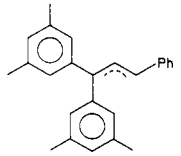
The results in Table I present a number of consistent patterns. Entries **1–3** establish the first observation, namely that syn-disposed groups produce little or no diastereomeric discrimination. Thus **2** and **3** give similar discrimination, of about 1.7:1, whereas **1** with only a syn-disposed methyl group gives a 1:1 ratio. Entry **4** suggests that increasing the bulk by the introduction of ethyl groups actually decreases the ratio. A six-membered ring, **5**, gives a similar discrimination as an anti-disposed methyl group.

A syn-disposed phenyl group, **6**, has no discernible discrimination but an anti-disposed phenyl group, **7**, gives considerable diastereomeric selection, 6:1 ($CDCl_3$, 35 °C) and almost 10:1 (DMF, −20 °C). As for the case of the methylated allyls, **1–3**, the ratio is insensitive to the syn-disposed group in **6–9** and all allyls with an anti-disposed phenyl group give very similar ratios, although there are solvent variations. Comparing **11** with **7**, we note that the discrimination for **11** is less than expected. Since the 2-methyl group is symmetrically disposed, it is not expected to contribute directly to the diastereomeric equilibrium. Presumably in this case the effect is indirect, the methyl group could cause the phenyl groups to orient in different rotameric populations from those that obtain for **7–9**. A similar effect might be expected to be present for **10**, although in this case the ring system can contribute to the discrimination as we have observed for **5**. Perhaps because of these rotameric effects the diastereomeric ratio is very sensitive to substituents on the phenyl rings. Thus **12** and **13** give low ratios whereas **14** gives the largest discrimination observed. Were this ground-state discrimination of **14** completely transferred to the diastereomeric transition states, optical yields of the order of 90% would be observed.

We have not established the chiral sense of the diastereomeric equilibrium except for the case of **14**. This was determined from a crystal structure[42] together with experiments which connect the solution and solid structures. We describe these experiments in the next paper. The preferred absolute configuration of the allyl in **14** is depicted in Figure 10. We think that the absolute configuration of the major diasteromer of **7–12**, is the same as **14** because the ^{31}P NMR spectra (Table I) of all of these systems show similar eight-line patterns with the outer quartets being more intense than the inner quartets as exemplified in Figure 8. Although this does not constitute proof of assignment, we are confident of the assignments for **8** and **9** because of the similarity of structural type and because **8**, **9**, and **14**, as we show presently,

(39) Becker, Y.; Stille, J. K. *J. Am. Chem. Soc.* **1978**, *100*, 845.
(40) Cotton, F. A.; Marks, T. J. J. *Am. Chem. Soc.* **1969**, *91*, 1339.
(41) Sonoda, A.; Mann, B. E.; Maitlis, P. M. *J. Chem. Soc., Chem. Commun.* **1975**, 108.
(42) Farrar, D. H.; Payne, N. C., personal communication.

Table I. ^{31}P NMR Chemical Shifts and Coupling Constants for the Major and Minor Diastereomers of the [Pd(*S,S*-chiraphos)(allyl)] ClO_4 Complexes and Their Diastereomer Ratios

compd	allyl	major minor diasteromer ^{31}P NMR[a] $\nu(P_1)$	$\nu(P_2)$	J	diastereomer ratios[b] $CDCl_3$	DMF
1		50.58 51.02	49.38 49.02	51.17 50.84	1:1	1:1 (−20 °C)f[e]
2		53.29 49.44	48.49 48.38	53.79 52.15	1.7:1	1.9:1 (−20 °C)f[e]
3		51.75 47.45	46.89 47.09	52.15 *c*		1.6:1 (60 °C)
4		53.42 48.78	47.52 47.12	55.76 54.45	1.2:1	f[e]
5		50.64 50.38	49.26 48.92	50.18 49.20	1.8:1	f[e]
6		52.26 52.34	50.20 48.50	59.04 58.38	1:1	1:1 (−20 °C)f[e]
7		55.75 51.28	44.47 50.56	64.62 *c*	6:1	9.7:1 (−20 °C)f[e]
8		57.74 52.33	45.84 49.81	73.80 73.47	5.5:1	6:1 (3.7:1 in THF)
9		55.60 50.86	42.22 50.36	67.57 *c*	4:1	6:1
10		53.78 49.52	42.60 48.62	61.01 *c*	5:1	7.4:1
11		54.74 50.32	44.86 48.72	58.38 *c*	3.1:1	f[e]
12		57.76 52.15	44.18 48.89	73.47 *c*	1.5:1	2.8:1 (1.6:1 in Me_2SO)
13		57.06 51.89	45.98 51.89	76.75 *c*	<2:1[d]	<2:1[d]
14		55.22 52.54	47.44 48.08	76.75 75.44	14:1	11.7:1 12.5:1 (Me_2SO) 11:1 (THF)

[a] Chemical shifts in ppm relative to 85% H_3PO_4; $\nu(P_1)$ and $\nu(P_2)$ are the chemical shifts of the phosphorus atoms of the major (top row) and minor (lower row) diastereomers; J is the coupling constant in Hz; spectra were run in $CDCl_3$ at 32.3 MHz and are proton decoupled. [b] Ratios were determined at 35 °C unless otherwise noted. [c] Only two peaks observed and are assumed to be the inner peaks of an AB quartet. The quoted chemical shifts are based on this assumption and on the assumption that the coupling constant is the same as that of the major diastereomer. [d] Large error. [e] f = fluxional at 35 °C.

give the same absolute configuration for the major product in the asymmetric synthesis.

The observation that syn-disposed groups have little effect on the discrimination could be an important finding if this insensitivity were transferred to the diastereomeric transition states. Thus for type **2** allyls the R′ groups could be varied to maximize the optical yields while at the same time any R group could be used to give, after asymmetric synthesis, a homologous series of chiral molecules of similar optical purity.

Sector Rule

A consideration of the results in Table I suggests that the discriminatory substituent effects are additive and that they may be used to predict the diastereomer ratios of other prochiral π-allyl diastereomers containing different permutations of substituents. Consider the coordinated *S,S*-chiraphos molecule in its preferred absolute configuration viewed in the manner shown in Figure 11. It will be noted that the chiral array of phenyl groups occupy mainly the "top-left" and "bottom-right" of the space about the palladium atom. A chiral π-allyl ligand coordinated to the palladium–*S,S*-chiraphos fragment would experience dissymmetric interactions from this chiral disposition of phenyl groups. It is convenient, therefore, to divide the space into quadrants of which, because of the twofold rotation axis, the diagonally disposed quadrants are of equivalent dissymmetric interaction. The bisector perpendicular to the mean molecular plane is a nodal plane,[43] in

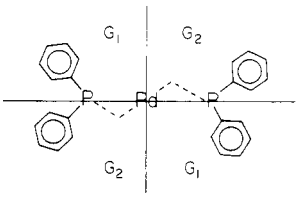


Figure 11. Quadrant space demarkation about the complexed *S,S*-chiraphos ligand. G_1 and G_2 are the *dissymetric* molar free energies of interaction which contribute to the displacement of the diastereomeric equilibrium. The chelate ring backbone is in the background.

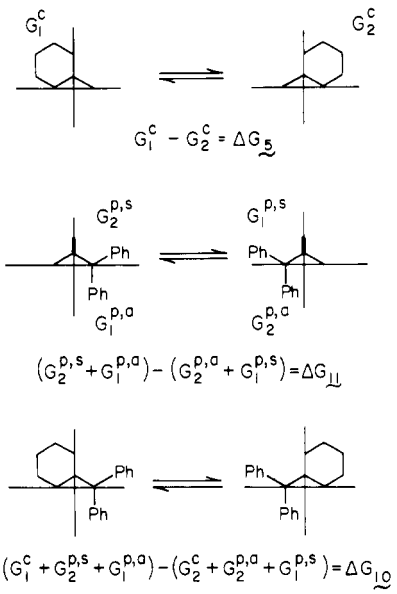


Figure 12. Pictorial representation of the quadrant sum rule using the free energy contribution of **5** and **11** to calculate the ΔG of **10**. The symbols are c = cyclic, p = phenyl, s = syn, a = anti, and 1 and 2 refer to the quadrants.

the sense that a π-allyl substituent which lies identically in this plane will have no *dissymmetric* interaction with the chiral phosphine. The other bisector, lying in the mean molecular plane, does not represent a nodal plane. It is drawn in recognition of the equivalence of the diagonal quadrants[44] and to accommodate the fact that an allyl can reside equivalently with its 3-carbon atom above and below this plane and be of the same chirality.

If we assume that the position of the diastereomeric equilibrium (Figure 5) will be determined by the additive dissymmetric free energy, G, contributions of the π-allyl substituents according to which of the quadrants they occupy, then for any number of substituents, the ΔG of equilibrium will be given by

$$\text{minor isomer} \rightleftharpoons \text{major isomer}$$

$$\sum G(\text{minor isomer}) - \sum G(\text{major isomer}) = \Delta G$$

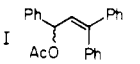
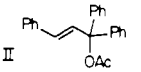
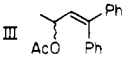
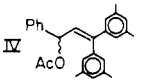
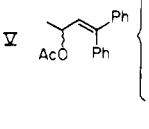
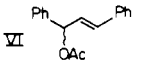
The value of G for any substituent is determined by experiment and will depend on whether it is syn- or anti-disposed in a particular quadrant, and its sign in the molecular conglomerate, will depend on the chiral sense in which it displaces the equilibrium.

We take as an example the prediction of the diastereomer ratio of **10** by use of the results obtained for **5** and **11** (Table I). The ratio for **11** was chosen in preference to **7** because, as we have noted, a substituent in the 2-allyl position has a secondary effect

(43) The nodal plane is determined by the reflection planes of the ligand. In this case it corresponds to the plane of symmetry that the unsubstituted π-allyl–palladium fragment possesses.

(44) A similar space demarkation has been used previously[13] in a qualitative way for assymmetric hydrogenation. In order to avoid confusion, we note that the quadrant shown in Figure 10 bears a superficial resemblance to the simplest pseudoscalar representation of the point group C_{2v} (see: Schellman, J. A. *J. Chem. Phys.* **1966**, *44*, 55). We do not imply any necessary connection between Figure 10 and a pseudoscalar.

Table II. Optical Yields for Asymmetric Catalytic Allylation Using Chiral (Phosphine)palladium Complexes

	Substrate	Nucleophile	Solvent, temp. C	Optical Yield S,S-chiraphos	Optical Yield R-prophos
I		$NaCH(CO_2CH_3)_2$	THF, 25°	84	
II		$NaCH(CO_2CH_3)_2$	THF, 25°	84	64
			DMF, 25°	86	
III		$NaCH(CO_2CH_3)_2$	THF, 25°	65	27
			DMF, 25°	67	
IV		$NaCH(CO_2CH_3)_2$	THF, 25°	64	59
V		$NaCH(SO_2(C_6H_4)CH_3)CO_2CH_3$	THF, 55°	65	
		$NaCH(COCH_3)CO_2C_2H_5$	THF, 25°	67	
		H_2N 	THF, 25°	63	
VI		$NaCH(CO_2CH_3)_2$	THF, 25°	22	

on the ratio. For clarity we present the argument pictorially in Figure 12. We have formally included the effect of syn-free energy contributions, although as the results in Table I show $G_2^{p,s} - G_1^{p,s} = 0$. Assuming additivity of the free energies of **5** and **11** as components of **10**, it is obvious that

$$\Delta G_5 + \Delta G_{11} = \Delta G_{10}$$

Since we do not know the chiral sense of induction for any of the systems, **5**, **10**, and **11**, ΔG_{10} could be either the sum or the difference of ΔG_5 and ΔG_{11}. At 35 °C, the difference gives a ratio of 1.7:1 whereas the sum gives a ratio of 5.6:1 for **10**. The actual ratio for **10**, Table I, is 5:1 which is well within experimental error and implies that the free energies of **5** and **11** contribute additively in **10**.

These additive free energy relationships can be applied to the other systems listed in Table I and all are consistent with the hypothesis. If these observations are of general validity, it is obvious how they could be applied in predicting diastereomer ratios for a variety of systems.

Substrates and Catalyst Precursors

The allylic acetate substrates that were investigated are shown in Table II. They were all made by conventional means from the corresponding alcohols. Compound II was converted to the thermodynamically more stable I in chloroform solution in the presence of a catalytic amount of acid. Compound IV was similarly obtained from the corresponding tertiary acetate.

For all of the catalytic reactions, we have used the [Pd(chiral phosphine)(η^3-C_3H_5)]ClO_4 complex as the catalyst precursor. This precursor reacts rapidly with the nucleophiles (Nu) to generate the "[Pd^0(chiral phosphine)]" species which, in turn, sets off the catalytic cycle.

$$[\text{Pd(chiral phosphine)}(\eta^3\text{-}C_3H_5)]^+ + \text{Nu} \rightarrow \text{"[Pd}^0\text{(chiral phosphine)]"} + C_3H_5\text{Nu}$$

The palladium(II) precursors are air-stable, nonlabile, well-defined crystalline compounds which are easy to handle whereas the "[Pd^0(chiral phosphine)]" species are labile, air-sensitive materials which in the absence of an excess of phosphine or of other stabilizing ligands soon deposit metal from solutions. Deposition of metal, however, is not a problem during the catalytic reactions; it is only after all of the allylic acetate has been consumed that metal may begin to deposit. The palladium(0) appears to be

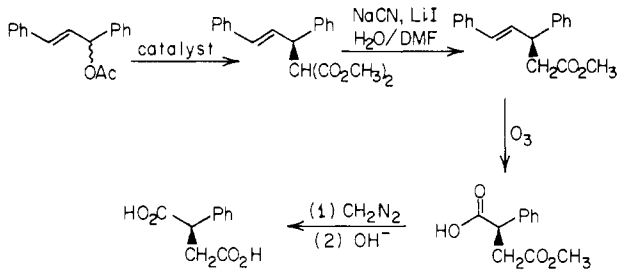


Figure 13. Outline of the transformation of the allylation product into phenylsuccinic acid.

stabilized by coordination to the substrate.

Asymmetric Catalytic Allylation

Most of the catalytic reactions were carried out in dry THF at 25 °C and in all cases oxygen was excluded. Usually 5 mol % of catalyst precursor was used to give convenient rates, although much lower concentrations can be used. With 5 mol % of catalyst the reaction times varied from 5 to 70 h depending on the nature of the substrate and on that of the nucleophile. As far as we could ascertain the catalytic activity did not diminish with time, the system appears to be capable of turning over indefinitely while the substrate is present. Furthermore, there are no detectable side products of reaction, and quantitative yields of allylation products are obtained. After the reactions were complete, the reaction mixtures were quenched with water and were extracted with ether. The presence of the "catalyst" does not interfere with the subsequent derivatization of the allylation products, although it is easily removed by means of short path chromatography.

For the dimethyl malonate anion reactions with the substrates I–IV, the allylation products were converted to the corresponding substituted succinic acids by the method outlined in Figure 7. The overall yields, including the catalytic reactions, were about 70%. For the dimethyl malonate reaction with substrate VI, the allylation product was also converted to the corresponding substituted succinic acid but by the route outlined in Figure 13. The optical yields and the chirality of the prevailing optical isomer of the substituted succinic acid were determined by optical rotation measurements,[45,46] the usual precautions being taken with regard to enrichment and concentration effects. The error from run to run was ±2%. The optical yield for the allylation product derived from dimethyl malonate anion and substrate III was checked by using the [Eu(hfc)$_3$] chiral shift reagent on the derivative shown in the box of Figure 14. The agreement was within experimental error. The absolute configuration of this derivative can therefore be correlated with that of methylsuccinic acid (Figures 7 and 14).

Knowing this, it was possible to determine the optical yields and absolute configurations of two other allylation reactions; the allylation of III with the monoanions of ethyl acetoacetate and of methyl 2-(*p*-tolylsulfonyl)acetate. The derivatization of these allylation products to a common derivative is outlined in Figure 14. Finally, the optical yield of the product of catalytic allylation of substrate III with benzylamine was determined by using the chiral shift reagent with methyl 2-(*N*-benzylsulfonamido)-propionate (Figure 15). The absolute configuration was correlated with that of alanine as outlined in Figure 15. The optical yield determined by rotation and by use of the chiral shift reagent agreed within 2%.

Except for the derivatization scheme shown in Figure 7, we have not sought to maximize the yields of the derivatization procedures for the materials in the other schemes. In these latter cases we were primarily interested in the optical yields and the absolute configurations of the allylation products.

Optical Yields

The results of the asymmetric allylation using the *S,S*-chiraphos and *R*-prophos palladium catalysts are listed in Table II. We deal

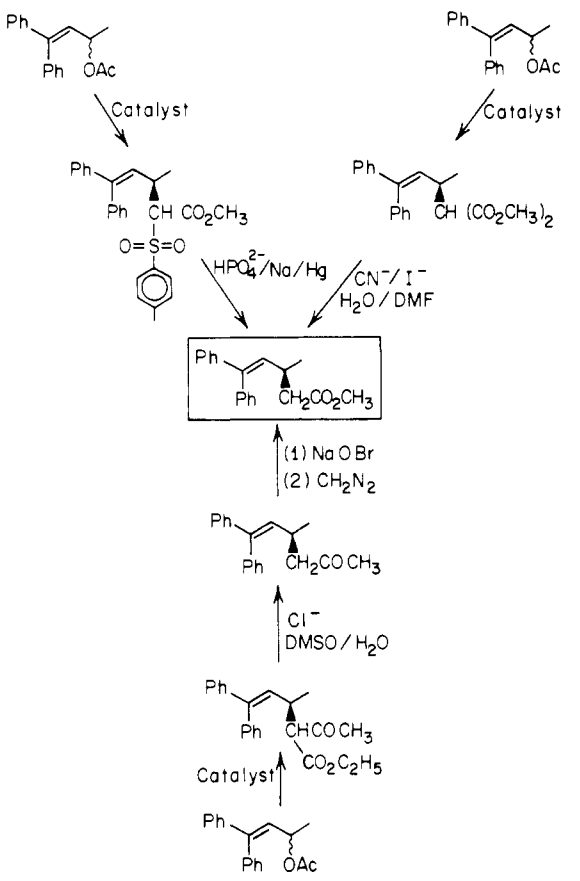


Figure 14. Outline of the transformation of three allylation products into a common product (shown in the box).

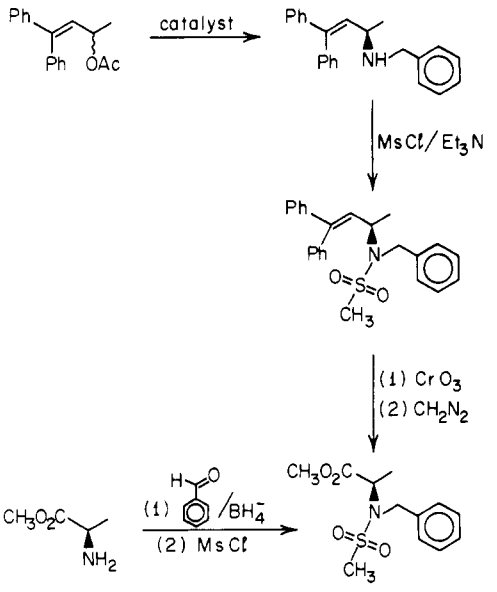


Figure 15. Outline of the transformations used for the establishment of the optical yield and absolute configuration of the product of asymmetric catalytic amination using benzylamine.

with the chiraphos results first. Taken as a whole the optical yields are much higher than have been reported previously for this catalytic reaction and, in some cases, approach practical levels of optical purity. Moreover, irrespective of nucleophile or of the substrate the *S,S*-chiraphos catalyst gives the same absolute configuration of the products.

Entries I and II represent an important result; despite the fact that the ^{1}H NMR spectra showed that no double bond migration occurred during catalysis, the same optical yield is observed starting from either the chiral substrate I or the corresponding

(45) Berner, V. E.; Leonardson, R. *Justus Liebigs Ann. Chem.* **1949**, *538*, 1.

(46) Wren, H.; Williams, H. *J. Chem. Soc.* **1916**, *109*, 572.

prochiral substrate II. As we hoped to contrive, this result suggests that the putative palladium(II)–π-allylic intermediate rapidly epimerizes so that memory of the stereochemistry of the substrate is lost before nucleophilic attack occurs. The validity and implications of this observation will be established and discussed in the following paper. We showed earlier that the diastereomeric equilibria of the [Pd(*S*,*S*-chiraphos)(π-allyl)]$^+$ cations for the π-allyls corresponding to the substrates shown in the entries I or II and III (Table II) were approximately the same and we argued that the optical yields would roughly parallel the diastereomeric ratios. This parallelism obtains approximately for entries III and I or II, but entry IV shows an optical yield which is lower than that expected from the observed diastereomeric ratio. If in the last case (entry IV), the thermodynamic diastereomeric ratio, of about 14:1 (Table I) were completely transferred to the diastereomeric transition states, the optical yield would be about 90%, the actual value is 64%. The important observation, however, is not that the thermodynamic–kinetic correlation is imprecise but rather that the correlation appears to exist to the extent that it does.

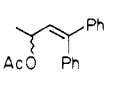
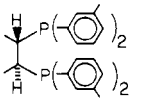
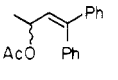
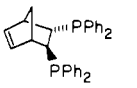
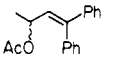
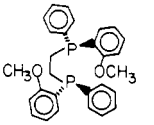
We note that the optical yields are largely insensitive to the reaction solvent, entries II and III. Similarly, the optical yields are only slightly sensitive to the nature of the nucleophile at least for the 1-methyl-3,3-diphenylallyl system. Thus, the four nucleophiles possessing different steric and nucleophilic characteristics, entries III and V, all give products with similar optical yields, suggesting that the stabilities of the diastereomeric transition states are determined mainly by the nature of the allyl. The potential utility of asymmetric allylation is greatly expanded if this result is general for the types of substrates we have chosen.

Entry VI is an example of a type **1** allyl for which no diastereomers can exist for the corresponding [Pd(*S*,*S*-chiraphos)(π-allyl)]$^+$ cations, only diastereomeric transition states are produced. Previously we observed that only anti-disposed groups contributed to the thermodynamic diastereomeric equilibria (Table I) and, in connection with the relationship between diastereomer ratios and optical yields, it was of interest to determine if syn-disposed groups would affect the diastereomeric transition-state stabilities. Given the different optical yields found for the substrates shown in entries I or II and III (Table II) which give similar diastereomeric ratios, it is not surprising that syn-disposed phenyl groups have an effect. It is small and it fortunately induces chirality in the same absolute sense as anti-disposed phenyl groups. Thus comparing the optical yields for entries I or II with that of entry VI, it is clear that an anti-disposed phenyl group has a much larger contribution to the optical yield assuming that in these compounds the syn- or anti-disposed substituents contribute to the optical yield roughly additively.

We now compare the results of using *R*-prophos (Figure 2) as the inducing phosphine. The favored conformation of the *R*-prophos chelate ring is enantiomeric to that of *S*,*S*-chiraphos (Figure 2). We therefore predict, on the basis of arguments we have given elsewhere,[14] that the prevailing enantiomeric products produced for the *R*-prophos catalyst should be opposite to those by the *S*,*S*-chiraphos catalyst. Indeed they are, but the optical yields are lower for the *R*-prophos catalyst (Table II). We point out, however, that [Pd(*R*-prophos)(chiral-π-allyl)]$^+$ complexes are stereochemically more complex than the corresponding complexes of *S*,*S*-chiraphos. Whereas *S*,*S*-chiraphos produces only two diastereomers for the palladium type **2** allyls, *R*-prophos gives, in addition, two geometric isomers for each of its two diastereomers, a total of four isomers. Thus there are potentially four energetically different diastereomeric transition states for the *R*-prophos catalyst. Even so, it is not clear to us how precisely this isomeric complexity might affect the optical yields.

Finally, we include some of the results obtained by using three other phosphines, metachiraphos, norphos, and dipamp (Table III). The first two phosphines give optical yields which are somewhat better than those observed for chiraphos but dipamp gives negligible optical yields. This last result does not occasion surprise since the chiral conformation of dipamp is not as strongly enforced as that for the other ligands discussed here. Moreover, as our previous arguments would infer, the [Pd(*R*,*R*-dipamp)(1,1,3-triphenylallyl)]$^+$ complex is found to have a 1:1 ratio for its diastereomers.

Table III. Optical Yields for Asymmetric Catalytic Allylation Using Chiral (Phosphine)palladium Complexes in THF at 25 °C

Substrate	Phosphine	Optical yield %
	 S,S-metachiraphos	72
	 S,S-norphos	76
	 R,R-DIPAMP	1

Discussion

The optical yields reported here demonstrate that asymmetric catalytic allylation is a practical method for asymmetric carbon–carbon bond formation provided that the system is properly orchestrated and its inherent limitations are recognized and circumvented. The strategy we have adopted represents one solution to the palladium-mediated asymmetric catalytic allylation problem. It largely depended on selecting substrates which embodied most of the desired features. Thus, with the present substrates, we have obtained the correct and exclusive regioselectivity for all nucleophiles, for all phosphines, and for the two R-groups of the type **2** allyl we have studied. This regioselectivity, we believe, is driven mainly by the electronic effects emanating from the 1,1-diaryl substituents. These aryl substituents also appear to enhance the π-allylic epimerization rate of the itermediate sufficiently to allow the use of either achiral or chiral allylic substrates in the asymmetric synthesis. This observation greatly expands the generality of the system. Further, an anti-disposed aryl substituent gives strong chiral induction whereas syn-disposed substituents, whether aryl or otherwise, appear to have a secondary effect on the chiral induction. This observation is also important for it suggests that high optical yields might be obtained for a range of type **2** allyl R groups and thus a homologous series of chiral products of similar optical purities is potentially available by relying on the chiral induction of the same pair of R′ groups. The generality of this system is further enhanced by the observation that the optical yield does not depend on the nature of the nucleophile. Thus it is possible to vary both the R group and the nucleophile without greatly altering the optical yields. Finally, the 1,1-diaryl groups act as readily removed protecting groups and allow for sequential derivatization of the products.

Although we consider that the major problems of palladium-mediated asymmetric catalytic allylation have been addressed and solved in principle, there remains the question of raising the optical yields of the reaction. This, of course, can only be done by changes in either the phosphine or the substrate or both. We have shown that, for the present substrates, the five chiral phosphines tried gave optical yields within a narrow range, except for the case of dipamp. Four of these phosphines are structurally and substitutionally similar and if the present substrates were to be used for raising the optical yields, new types of phosphines may be required. Conversely, new substrates having varying arrays of substituents on the R′-aryl groups could be introduced while retaining the present set of phosphines. Because of the ready synthesis of the present substrates, this second approach may give the more rapid results. There is, however, no systematic method of predicting the outcome of such manipulation. In the present

work we have adopted a quasi-empirical approach which involved the measurement of ground-state diasteromeric equilibria. We argued that, under appropriate circumstances, a large ground-state discrimination would also give a large transition-state discrimination. As we have seen, this strategy was useful for the present systems, although the correlations were inexact, some substrates increased whereas others decreased in discrimination when transferring from the ground to transition states. This is not surprising because of the assumptions involved, but it does suggest that using this method for surveying new substrates for *higher* optical yields may not be as useful as it was for the initial selection of substrates.

Aside from these questions, there remain a number of subtle problems which require resolution. Asymmetric catalysis is fundamentally a kinetic phenomenon and implicit in our strategy were certain suppositions about the kinetic relationships in the catalytic allylation cycle. We require to establish that these mechanistic assumptions are correct even though our results so far appear to be consistent with them. These mechanistic questions are addressed in the following paper.

Experimental Section

(A) Allylic Alcohols. 3-Hydroxy-1-phenylprop-1-ene was purchased. 4-Hydroxy-2-methylpent-2-ene was prepared[47] by LAH reduction of the corresponding ketone. 3-Ethyl-3-hydroxypent-1-ene,[48] 3,3-diphenyl-3-hydroxyprop-1-ene,[48] and (*E,Z*)-4,4-diphenyl-4-hydroxybut-2-ene were synthesized[49] by reaction of the appropriately substituted alkenylmagnesium bromide reagent with the corresponding ketone. Similarly, cyclohex-1-enyldiphenylcarbinol was prepared[50] from cyclohexenyllithium and benzophenone. 4,4-Diphenyl-2-hydroxybut-3-ene[51] was prepared by reduction of the corresponding α,β-unsaturated ketone[52] with sodium borohydride.

3,3-Diphenyl-3-hydroxy-2-methylprop-1-ene and the remaining allylic alcohols, all 3,3-diaryl-3-hydroxy-1-phenylprop-1-ene compounds, were obtained by the reaction of the appropriately substituted acrylate esters with the corresponding aryllithium reagent.[53] The general procedure is exemplified below.

3,3-Diphenyl-3-hydroxy-1-phenylprop-1-ene.[53] Bromobenzene (131.7 g, 0.839 mol) in dry ether (200 mL) was added dropwise to thin strips of lithium (12.2 g, 1.76 mol) suspended in dry ether (100 mL) at such a rate that gentle reflux was maintained. After the addition was complete (~1 h), the solution was refluxed for a further 0.5 h. The dark-brown solution was cooled to −20 °C and methyl cinnamate (64.8 g, 0.4 mol) in dry ether (200 mL) was added dropwise to the cold lithio reagent over 0.5 h. The resultant mixture was allowed to warm to 25 °C. After remaining at 25 °C for 15 min, the mixture was quenched with a saturated aqueous solution of ammonium chloride (100 mL). The ether layer was separated and was washed twice with water and once with brine and was dried ($MgSO_4$). Removal of the $MgSO_4$ followed by rotary evaporation left a red-brown oil which was dissolved in hot methanol (100 mL) and the solution was decolorized with activated charcoal. After removal of the methanol a light yellow oil remained which was taken up in hot benzene (200 mL). Slow addition of hexane (800 mL) to this solution induced the product to deposit as colorless needles. After the mixture was allowed to stand at 0 °C for 24 h, the crystals were collected, washed with hexane, and dried. A second crop of crystals was obtained from the filtrate. A total of 92.5 g was obtained of the alcohol which was contaminated with 3% of the ketone that results from 1,4-addition. The impurity does not affect the subsequent reactions. ^{1}H NMR ($CDCl_3$): δ 7.30 (m, 15 H), 6.65 (AB quartet, 2 H), 2.4 (s, 1 H).

3,3-Bis(*o*-anisyl)-3-hydroxy-1-phenylprop-1-ene. This compound was prepared by the reaction of methyl cinnamate with *o*-anisyllithium, following the procedure described above. The crude product, a white powder, was crystallized from chloroform by the addition of hexane: yield, 77%; ^{1}H NMR ($CDCl_3$) δ 6.4–7.6 (m, 15 H), 4.8 (br s, 1 H), 3.5 (s, 6 H). Anal. Calcd for $C_{23}H_{22}O_3$: C, 79.7; H, 6.4. Found: C, 79.7; H, 6.4.

3,3-Bis(*o*-tolyl)-3-hydroxy-1-phenylprop-1-ene. The reaction of methyl cinnamate with *o*-tolyllithium by the above procedure gave comparable amounts of the saturated ketone and the desired allylic alcohol. Crystallization of the crude product from chloroform by the addition of hexane gave white needles of the allylic alchol (25%). ^{1}H NMR ($CDCl_3$): δ 7.05 (m, 9 H), 6.65 (AB quartet, 2 H), 2.27 (s, 1 H), 2.02 (s, 6 H). Anal. Calcd for $C_{23}H_{22}O$: C, 87.9; H, 7.1. Found: C, 88.1; H, 7.0.

3,3-Bis(3,5-dimethylphenyl)-3-hydroxy-1-phenylprop-1-ene. This compound was made by the reaction of methyl cinnamate with 3,5-dimethylphenyllithium. 3,5-Dimethyl-1-bromobenzene was obtained by diazotization of the corresponding aniline in 48% HBr followed by the addition of copper powder under the usual conditions (yield, 40%). This somewhat unreactive bromo compound was lithated by using the "Ventron" dispersion (Li powder activiated with 2% Na in mineral oil) and the reaction was performed as above. The crude allylic alchol, which was contaminated with the saturated ketone (~15%) and mineral oil, was purified by chromatography. The crude product, a yellow oil (40 g), was loaded onto a 500-g alumina column in hexane. The column was eluted, in order, with hexane, 0.5% ethyl acetate/hexane, 1% ethyl acetate/hexane, and 2% ethyl acetate/hexane, and finally it was eluted with 4% ethyl acetate/hexane. This gave 16 g (47%) of pure allylic alcohol as an oil. ^{1}H NMR ($CDCl_3$): δ 6.7–7.6 (m, 13 H, aromatic + vinylic), 2.3 (s, 13 H, methyl + hydroxyl proton).

3,3-Diphenyl-3-hydroxy-2-methylprop-1-ene.[53] This compound was obtained as an oil from the reaction of methyl methacrylate with phenyllithium. A quantitative yield of essentially pure product was obtained from the reaction mixture. It was used without further purification. ^{1}H NMR ($CDCl_3$): δ 7.23 (m, 10 H), 5.05 (br q, J = 1 Hz, 1 H), 4.73 (br s, 1 H), 2.62 (br s, 1 H), 1.75 (br s, 3 H).

(B) Allylic Chlorides. The allylic chlorides, 3-chloroprop-1-ene, 4-chlorobut-2-ene, and 4-chloro-2-methylbut-2-ene, were purchased and distilled before use.

1-Chloro-3-ethylpent-2-ene.[54] Thionyl chloride (11.9 mL, 0.165 mol) was added dropwise to stirred (neat) 1-hydroxy-3-ethylpent-2-ene (18.5 g, 0.162 mol) at 0 °C over 15 min. After 45 min at 0 °C, gas evolution had ceased and the solution was pink. The solution was then stirred at 25 °C for 30 min. Distillation through a vacuum-jacketed 15-cm Vigreux column at 15 mm pressure gave a fraction (bp 30–48 °C, 12 g) which by ^{1}H NMR consisted of a 65:35 mixture of 1-chloro-3-ethylpent-2-ene and 3-chloro-3-ethylpent-1-ene, respectively, either of which can give the desired $[Pd(1,1\text{-diethylallyl})Cl]_2$ dimer.

4-Chloro-2-methylpent-2-ene. By a similar procedure to that described above, reaction of 4-hydroxy-2-methylpent-2-ene gave, after distillation, a 75% yield of an 80:20 mixture of 4-chloro-2-methylpent-2-ene and 4-chloro-4-methylpent-2-ene which was used for the preparation of $[Pd(1,1,3\text{-trimethylallyl})Cl]_2$.

1-Chloro-3-phenylprop-2-ene.[55] Concentrated aqueous HCl (50 mL) was added over 1 min to a stirred solution of cinnamyl alcohol (21 g) in THF (50 mL), whereafter the solution became heterogeneous. The mixture was vigorously stirred for 15 min and was then poured into water and was extracted with CH_2Cl_2. The CH_2Cl_2 was washed twice with water, once with aqueous $NaHCO_3$, with water again, and dried ($MgSO_4$). On removal of the solvent, a yellow oil remained which was distilled at 45 mm (bp 105 °C) through a 15-cm vacuum-jacketed Vigreux column to give 20.4 g of pure cinnamyl chloride.

1,1-Diphenyl-3-chloroprop-2-ene. This compound was prepared by the reaction of 3,3-diphenyl-3-hydroxyprop-1-ene with HCl in THF as described above except that, after the addition, the mixture was heated at 50 °C for 30 min. The solvent was removed to give essentially pure product in quantitative yield. ^{1}H NMR ($CDCl_3$): δ 7.23 (s, 10 H), 6.15 (t, 1 H), 4.05 (d, 2 H).

(C) $[Pd(\pi\text{-Allyl})Cl]_2$ Complexes from Allylic Chlorides. $[Pd(1\text{-Methylallyl})Cl]_2$.[37] Palladium chloride (1 g) and lithium chloride (0.8 g) were dissolved by heating in water (1.5 mL). Methanol (30 mL) and 1-chlorobut-2-ene (1.5 g) were then added and carbon monoxide was bubbled through the stirred solution at a rate of 2 L h^{-1}. After 10 min, the color of the solution had changed from deep red-brown to lemon yellow and, shortly after, a yellow precipitate began to form. After a total of 30 min, the mixture was poured into water (1 L) and the product was extracted with chloroform. The combined yellow extracts were dried ($MgSO_4$) and upon evaporation gave a yellow powder. This was dissolved in a minimum volume of CH_2Cl_2 and was precipitated by the addition of hexane (3 volumes). After 3 h at 25 °C, the mixtures was left to stand at 0 °C for 16 h. The yellow crystals (0.84 g, 76%) were collected, washed with hexane, and dried. ^{1}H NMR ($CDCl_3$): δ 5.28

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(m, 1 H), 3.61–4.17 (complex multiplet, 2 H), 2.82 (d, J = 12 Hz, 1 H), 1.35 (d, J = 7 Hz, 3 H).

[Pd(1,1-Dimethylallyl)Cl]$_2$.[56] The same procedure as given above was used to prepare this compound from 1-chloro-3-methylbut-2-ene. It formed yellow-orange crystals from ether/hexane (86%). ^{1}H NMR ($CDCl_3$): δ 5.17 (dd, J = 8 Hz, J = 13 Hz, 1 H), 3.86 (d, J = 8 Hz, 1 H), 3.10 (d, J = 13 Hz, 1 H), 1.46 (s, 3 H), 1.26 (s, 3 H).

[Pd(1,1-Diethylallyl)Cl]$_2$. This compound was prepared from 1-chloro-3-ethylpent-2-ene by a procedure similar to that given for the synthesis of [Pd(1-methylallyl)Cl]$_2$ except that the ratio of allylic chloride/$PdCl_2$ was 4:1, the solvent was water (1.5 mL)/methanol (20 mL)/ethanol (5 mL) and the temperature of the reaction was 45 °C. The product was crystallized from hot hexane and then by cooling for 16 h at −20 °C. Orange-yellow crystals were obtained (88%). ^{1}H NMR ($CDCl_3$): δ 5.07 (dd, J = 8 Hz, J = 13 Hz, 1 H), 3.82 (d, J = 8 Hz, 1 H), 3.08 (d, J = 13 Hz, 1 H), 0.9–2.0 (m, 10 H).

[Pd(1,1,3-Trimethylallyl)Cl]$_2$. Palladium chloride (1.77 g) and lithium chloride were dissolved in hot water (1.5 mL). Ethanol (25 mL) and an 80:20 mixture of 4-chloro-2-methylpent-2-ene and 4-chloro-4-methylpent-2-ene (5 g) were added and the resultant solution was warmed to 45 °C. At this temperature carbon monoxide was passed through the solution and 50% water–ethanol (1 mL) was added every 15 min. After 90 min, the mixture was poured into water (1 L) and was extracted with CH_2Cl_2; the extracts were dried, and upon removal of the solvent a red-brown oil remained. This was dissolved in benzene (10 mL) and passed through a Florisil column (5 cm × 1 cm), to give a clear yellow eluent which was evaporated and the residue was taken up in hot benzene (10 mL) and diluted with hexane (40 mL). After this mixture was allowed to stand at 25 °C for 1 h and at 0 °C for 16 h, the yellow-orange crystals were collected and were washed with hexane and dried (1.5 g, 66%). ^{1}H NMR ($CDCl_3$): δ 4.92 (d, J = 12 Hz, 1 H), 3.99 (q, J = 7 Hz, 1 H), 1.38 (s, 3 H), 1.32 (d, J = 7 Hz, 3 H), 1.20 (s, 3 H).

[Pd(1-Phenylallyl)Cl]$_2$.[57] Palladium chloride (1.77 g) and lithium chloride (1.77 g) were dissolved in hot water (2.5 mL) and then cinnamyl chloride (6.2 g) in ethanol (20 mL) was added. Carbon monoxide was bubbled through the solution at 25 °C and after 15 min orange crystals began to form and after a total of 3 h, the carbon monoxide flow was discontinued and the mixture was stirred under carbon monoxide for 20 h at 25 °C and for a further 24 h at 0 °C. The product was then filtered and was washed with methanol followed by ether. The orange powder was recrystallized from chloroform by the addition ether (2.3 g, 90%). ^{1}H NMR (Me_2SO-d_6): δ 7.0–7.8 (m, 5 H), 6.40 (dt, J = 12 Hz, J = 10 Hz, 1 H), 5.13 (d, J = 12 Hz, 1 H), 3.83 (d, J = 10 Hz, 2 H).

[Pd(1,1-Diphenylallyl)Cl]$_2$. This compound was prepared from 3-chloro-1,1-diphenylprop-1-ene following the procedure given for [Pd(1-phenylallyl)Cl]$_2$ except that a ratio of allylic chloride to $PdCl_2$ was 3:1 and the organic solvent was a 1:1 mixture of ethanol and acetone in order to obtain homogeneity. The product was recrystallized from chloroform/hexane (1:5) giving yellow-orange crystals (2.95 g, 88%). ^{1}H NMR ($CDCl_3$): δ 7.18–7.55 (m, 10 H), 5.57 (dd, J = 7 Hz, J = 12 Hz, 1 H), 4.07 (d, J = 7 Hz, 1 H), 3.24 (d, J = 12 Hz, 1 H). Anal. Calcd for $C_{30}H_{26}Cl_2Pd_2$: C, 53.8; H, 3.9; Cl, 10.6. Found: C, 53.5; H, 4.1; Cl, 10.8.

[Pd(allyl)Cl]$_2$. This was prepared from allyl chloride by the literature method.[29]

(D) Allylic Alcohol Reactions. [Pd(1,1,3-Triphenylallyl)Cl]$_2$. Palladium chloride (1.77 g) and lithium chloride (1.77 g) were dissolved in hot water (9 mL) and to this solution were added in the following order: ethanol (18 mL), 1,3,3-triphenyl-3-hydroxyprop-1-ene (6.29 g) in tetrahydrofuran (90 mL) and aqueous hydrochloric acid (3.54 mL, 12 N). Carbon monoxide was passed through the solution at 25 °C and, after 2 h, a clear yellow orange solution was obtained. The reaction mixture was heated to 40 °C under carbon monoxide. Shortly thereafter, the product began to precipitate as iridescent orange-red crystals. After 16 h at 40 °C under carbon monoxide, the solvents were removed under reduced pressure and the residue was dissolved in CH_2Cl_2 which was washed with water, separated, and dried ($MgSO_4$). The volume of CH_2Cl_2 was adjusted to 100 mL and pentane (1 L) was added. Crystallization was slow, but after the solution was allowed to stand at 25 °C for 3 h and then at 0 °C for 24 h, the brick-red crystals were collected and were washed with pentane and air-dried (3.6 g, 88%). ^{1}H NMR (pyridine-d_5): δ 6.77–8.13 (m, phenyl + pyridyl), 6.40 (d, J = 12 Hz, 1 H), 5.13 (d, J = 12 Hz, 1 H). Anal. Calcd for $C_{42}H_{34}Cl_2Pd_2$: C, 61.3; H, 4.2; Cl, 8.6. Found: C, 61.2; H, 4.3; Cl, 8.3.

[Pd(1,1-Diphenyl-3-methylallyl)Cl]$_2$. This compound was prepared from a 1:1 mixture of E and Z isomers of 1,1-diphenyl-1-hydroxybut-2-ene following the procedure outlined for the synthesis of [Pd(1,1,3-triphenylallyl)Cl]$_2$. The product was crystallized from $CHCl_3$ by the addition of hexane to give orange crystals (83%). ^{1}H NMR ($CDCl_3$): δ 6.63–7.73 (m, 10 H), 5.43 (d, J = 12 Hz, 1 H), 3.93–4.47 (m, 1 H). Anal. Calcd for $C_{32}H_{30}Cl_2Pd_2$: C, 55.0; H, 4.3. Found: C, 54.6; H, 4.4.

[Pd(1,1-Bis(o-tolyl)-3-phenylallyl)Cl]$_2$. This compound was prepared from 3,3-bis(o-tolyl)-3-hydroxy-1-phenylprop-1-ene as described for the triphenyl analogue. In this case, following an initial period at 25 °C, the reaction temperature was raised to reflux and then water (0.5 mL) was added every 30 min. After a total of 5 h, the reaction mixture was worked up and the product was crystallized from $CHCl_3$ by the addition of hexane to give burgundy-red crystals (75%). ^{1}H NMR ($CDCl_3$): δ 6.60–8.20 (m, 13 H), 6.07 (d, J = 12 Hz, 1 H), 4.80 (d, J = 12 Hz, 1 H), 2.50 (s, 3 H), 2.10 (s, 3 H). Anal. Calcd for $C_{46}H_{42}Cl_2Pd_2$: C, 62.9; H, 4.8; Cl, 8.1. Found: C, 62.4; H, 5.0; Cl, 8.5.

Pd(1,1-Bis(o-anisyl)-3-phenylallyl)Cl]$_2$. This compound was prepared from 3,3-bis(o-anisyl)-3-hydroxy-1-phenylprop-1-ene following the procedure given for the o-tolyl analogue. It was recrystallized from $CHCl_3$ by the addition of hexane and was obtained as rust-colored crystals (85%) containing 0.5 $CHCl_3$ of crystallization (confirmed by ^{1}H NMR) which was removed by vacuum drying. ^{1}H NMR ($CDCl_3$): δ 6.73–8.20 (m, 13 H), 6.07 (d, J = 12 Hz, 1 H), 4.80 (d, J = 12 Hz, 1 H), 2.50 (s, 3 H), 2.16 (s, 3 H). Anal. Calcd for $C_{46}H_{42}O_4Cl_2Pd_2$: C, 58.6; H, 4.5; Cl, 7.5. Found: C, 58.5; H, 4.5; Cl, 7.9.

[Pd(1,1-Bis(3,5-dimethylphenyl)-3-(phenylallyl)Cl]$_2$. This compound was prepared from 3,3-bis(3,5-dimethylphenyl)-3-hydroxy-1-phenylprop-1-ene by a procedure similar to the one described for the triphenyl analogue, except that $CHCl_3$ and ethanol were added periodically to ensure homogeneity. (The starting allylic alcohol is converted to the corresponding ethyl ether in the acidic medium and it is the ether, continuously formed during the reaction, that requires to be solubilized.) The crude product, an oil initially, was crystallized by the addition of hexane and was recrystallized from $CHCl_3$/hexane as rust colored crystals (76%). ^{1}H NMR ($CDCl_3$): δ 6.43–7.70 (m, 11 H), 5.90 (d, J = 12 Hz, 1 H), 4.90 (d, J = 12 Hz, 1 H), 2.24 (s, 12 H).

[Pd(1,1-Diphenyl-2-methylallyl)Cl]$_2$. This compound was prepared from 3,3-diphenyl-2-hydroxy-2-methylprop-1-ene by a procedure similar to that given for the triphenyl analogues. It was recrystallized from $CHCl_3$ by the addition of ether followed by hexane and gave yellow crystals (72%). ^{1}H NMR (Me_2SO-d_6): δ 6.67–8.0 (m, 10 H), 3.40–4.43 (broad double hump-fluxional) 2.0 (s, 3 H).

(E) Preparation of [Pd(S,S-chiraphos)(π-allyl)]ClO$_4$ Complexes. Direct Reactions. General Procedure. The dimer (1.00 mmol) was triturated with solid S,S-chiraphos[15] (2.00 mmol) in methanol (6.5 mL). The solids dissolved after 10 min and gave faintly yellow or colorless solutions. After filtration through a 2-cm Celite plug and washing with methanol (2.5 mL), $LiClO_4$ (1 g, 35% H_2O) in methanol (2 mL) was added dropwise to the combined filtrates. After 1 h, more $LiClO_4$ (1 g) in methanol (1 mL) was added. The mixtures were allowed to stand for 4 h at 25 °C and then at 0 °C for 16 h. The precipitate was collected and was washed first with ethanol/water (1:1) and then with ether.

This procedure gave crude yields of 90% for all of the complexes except the 1,1-diethylallyl compound. This complex did not spontaneously crystallize after the addition of $LiClO_4$, addition of small amounts of water/methanol (1:1) and warming were required (70% recovery).

The complexes prepared by this procedure are listed below.

[Pd(S,S-Chiraphos)(1-methylallyl)]ClO$_4$: recrystallized from methanol. Anal. Calcd for $C_{32}H_{35}P_2O_4ClPd$: C, 55.9; H, 5.1; P, 9.0. Found: C, 56.0; H, 5.4; P, 9.1.

[Pd(S,S-Chiraphos)(1,1-dimethylallyl)]ClO$_4$: recrystallized from acetone/ether. Anal. Calcd for $C_{33}H_{37}P_2O_4ClPd$: C, 56.5; H, 5.3; P, 8.8. Found: C, 56.6; H, 5.1; P, 8.7.

[Pd(S,S-Chiraphos)(1,1,3-trimethylallyl)]ClO$_4$: recrystallized from acetone/ether. Anal. Calcd for $C_{34}H_{39}P_2O_4ClPd$: C, 57.1; H, 5.5; P, 8.7. Found: C, 57.3; H, 5.5; P, 8.5.

[Pd(S,S-Chiraphos)(1,1,-diethylallyl)]ClO$_4$: recrystallized from acetone/ether. Anal. Calcd for $C_{35}H_{41}P_2O_4ClPd$: C, 57.6; H, 5.7; P, 8.5; Cl, 4.9. Found: C, 57.4; H, 5.7; P, 8.8; Cl, 5.1.

[Pd(S,S-Chiraphos)(1,2-tetramethyleneallyl)]ClO$_4$·CHCl$_3$:[58] recrystallized from chloroform/hexane. Anal. Calcd for $C_{36}H_{40}P_2O_4Cl_4Pd$: C, 51.1; H, 4.8; P, 7.3. Found: C, 51.0; H, 4.8; P, 7.1.

[Pd(S,S-Chiraphos)(1,1-diphenyl-2-methylallyl)]ClO$_4$: recrystallized from chloroform/hexane. Anal. Calcd for $C_{44}H_{43}P_2O_4ClPd$: C, 62.9; H, 5.2; P, 7.4; Cl, 4.2. Found: C, 62.7; H, 5.1; P, 7.1; Cl, 4.3.

[Pd(S,S-Chiraphos)(allyl)]ClO$_4$·0.5(CH$_3$)$_2$CO: recrystallized from acetone/ether. Anal. Calcd for $C_{32.5}H_{36}P_2O_{4.5}ClPd$: C, 55.6; H, 5.2; Cl, 5.1; O, 10.3. Found: C, 55.7; H, 5.2; Cl, 5.4; O, 10.2. All solvents

(56) Powell, J.; Shaw, B. L. *J. Chem. Soc.* **1967**, 1839.
(57) Papdimitriou, V.; Paraskevas, S. *Chem. Chron.* **1974**, *3*, 113.
(58) Prepared by S. B. Wild who made the dimer according to the method in ref 12 and used a similar method for the S,S-chiraphos reaction.

of crystallization were identified by ^1H NMR.

Silver Perchlorate Reactions. Most of the arylallyl complexes were prepared by the following general procedure.

Procedure. The finely ground dimer (1.00 mmol) was dissolved in a minimum volume of CH_2Cl_2 and than an equivalent volume of methanol was added, followed immediately by the addition of a solution of $AgClO_4$ (2.00 mmol) in methanol (20 mL). The mixture was stirred in the absence of light for 30 min, then was filtered through Celite (4 × 8 mm column) to remove the AgCl. The column washed with 1:1 CH_2Cl_2/methanol and a clear yellow filtrate resulted. This solution was cooled to 5 °C and solid *S,S*-chiraphos (2.00 mmol) was added portion wise over 1 min to the stirred solution. After all of the phosphine had dissolved, the solution was allowed to warm to room temperature. Removal of the solvents under reduced pressure gave yellow oils which were shown to be pure materials by ^1H NMR and ^{31}P NMR but only the [Pd(*S,S*-chiraphos)(1,1-bis(3,5-dimethylphenyl)-3-phenylallyl)]ClO_4 salt crystallized (acetone/hexane). The others could be obtained as powders but not as well-formed crystals.

The above method gave the following compounds: [Pd(*S,S*-chiraphos)(1,1-diphenylallyl)]ClO_4, [Pd(*S,S*-chiraphos)(1,1,3-triphenylallyl)]ClO_4, [Pd(*S,S*-chiraphos)(1,1-diphenyl-3-methylallyl)]ClO_4, [Pd(*S,S*-chiraphos)(1,1-bis(*o*-tolyl)-3-phenylallyl)]ClO_4, [Pd(*S,S*-chiraphos)(1,1-bis(*o*-anisyl)-3-phenylallyl)]ClO_4, and [Pd(*S,S*-chiraphos)(1,1-bis(3,5-dimethylphenyl)-3-phenylallyl)]ClO_4.

(F) Other Reactions. [Pd(*S,S*-Chiraphos)(1-phenylallyl)]ClO_4. Solid *S,S*-chiraphos (0.426 g) was added to a stirred suspension of $Ni(OAc)_2$ (0.3 g) in methanol (5 mL). A dark red solution was produced. (Nickel ions are used to moderate the concentration of the phosphine which, in the free uncomplexed form, reacts with allyl ligand.) A solution of $[Pd(1\text{-phenylallyl})Cl]_2$ (0.259 g) in CH_2Cl_2 was added to the nickel solution and the mixture was refluxed for 1 h. The CH_2Cl_2 was removed leaving a green methanol solution which was filtered. The methanol filtrate was concentrated to 5 mL and $LiClO_4$ (0.45 g) in methanol (1 mL) was added dropwise with stirring. A gum formed. This was redissolved by warming, and on cooling, a yellow crystalline precipitate formed. After 2 days at 25 °C, these crystals were collected and were washed with ethanol/ether (4:1) and with ether (0.73 g, 97%). The product was recrystallized from acetone by the addition of ether. Anal. Calcd for $C_{37}H_{37}P_2O_4ClPd$: C, 59.3; H, 5.0; P, 8.3; Cl, 4.7. Found: C, 59.1; H, 5.0; P, 8.6; Cl, 4.9.

[Pd(*S,S*-Chiraphos)(1,1-diphenyl-2,3-tetramethyleneallyl)]ClO_4. A mineral oil dispersion of sodium hydride (57% NaH, 0.04 g, 1.1 mmol) was washed with pentane to remove the mineral oil. Cyclohex-1-enyldiphenylcarbinol (0.264 g, 1.00 mmol) in dry DME (10 mL) was added to the NaH and the mixture heated under reflux for 3 h. The mixture was then cooled to 25 °C and acetic anhydride (0.94 mL, 1.0 mmol) was added. The mixture was stirred for 16 h at 25 °C and then was refluxed for 10 min. It was allowed to cool and set aside.

A solution of $NaCH(CO_2CH_3)_2$ in DME was then prepared by the addition of dimethyl malonate (0.51 mL, 0.60 mmol) to a suspension of NaH (0.021 g, 0.50 mmol) in DME (5 mL). [Pd(*S,S*-Chiraphos)(allyl)]ClO_4·0.5acetone (0.34 g, 0.48 mmol) was added to this solution with stirring at 25 °C. The complex dissolved over 4 min to give a dark red-brown solution. After a total of 12 min, this solution was added to the previously prepared solution of the allylic acetate using 8 mL of DME to complete the transfer.

The resultant red-brown mixture was stirred at 25 °C for 30 min and then was poured into water (150 mL). The product was extracted with CH_2Cl_2, and upon removal of the CH_2Cl_2 an orange oil remained. This was dissolved in methanol (5 mL) and upon the careful addition of $LiClO_4$ (1 g), yellow crystals formed. These were collected after 24 h and were washed with methanol/water (1:1) followed by ether. The product was recrystallized from acetone by the addition of hexane (0.175 g, 40%). Anal. Calcd for $C_{47}H_{47}P_2O_4ClPd$: C, 64.2; H, 5.4; P, 7.0; Cl, 4.0. Found: C, 64.2; H, 5.5; P, 7.0; Cl, 4.3.

(G) Substrates. 1,1,3-Triphenylprop-2-enyl Acetate. 1,3,3-Triphenyl-3-hydroxyprop-1-ene (28.6 g, 0.10 mol) was allowed to react with sodium hydride (5.8 g, 0.12 mol; a 50% mineral oil dispersion which was washed with dry pentane, 3 × 75 mL) in 100 mL of refluxing DME (distilled from Na/benzophenone) for 3 h. The mixture was then cooled to 5 °C and acetyl chloride (7.8 mL, 0.11 mol) in DME (50 mL) was added over 10 min. The cooling was removed and the mixture was allowed to rise to room temperature at which temperature it was stirred for 17 h.

The mixture was then slowly poured into an ice-cold mixture of 200 mL of ether, 1.5 L of an aqueous buffer (KH_2PO_4/NaOH, pH 7), and 500 mL of brine. The mixture was transferred to a separatory funnel and was shaken. The aqueous layer was removed, and the ether layer was washed once with cold brine, dried over Na_2SO_4, and filtered. Removal of the solvent under reduced pressure at 40 °C left a red-brown oil. This was dissolved in 200 mL of boiling pentane and the resulting solution was filtered. Upon standing at room temperature, the filtrate deposited light-brown, granular crystals. After 24 h, these crystals were collected, washed once with cold pentane, and air-dried. Several more crops of crystals were recovered from the filtrate, a total of 21.0 g (64%) were obtained.

^1H NMR ($CDCl_3$): δ 7.48 (d, *J* = 16 Hz, 1 H), 7.50–7.07 (m, 15 H), 6.05 (d, *J* = 16 Hz, 1 H), 2.18 (s, 3 H).

This compound is difficult to purity because of its instability. Traces of acid in chloroform lead to rapid rearrangement to the isomeric allylic acetate, 1,3,3-triphenylprop-2-enyl acetate. In the absence of acid, isomerization is slow unless the compound is heated at about 60 °C in solution. The crystalline compound turns into an oil if left at 25 °C for several weeks, although it is indefinitely stable at −20 °C. Both alumina and silica columns cause isomerization, and in alcohol solutions rapid reactions occur to produce the rearranged allylic ether corresponding to the alcohol solvent.

1,3,3-Triphenylprop-2-enyl Acetate. 1,1,3-Triphenylprop-2-enyl acetate (1 g) was dissolved in $CHCl_3$ (5 mL) and glacial acetic acid (0.5 mL) was added. After 1.5 h, toluene (15 mL) was added and the solvents were removed under reduced pressure to give an oil from which the last traces of acetic acid were removed by reduced pressure azeotropic distillation with toluene. The product could not be induced to crystallize and was subsequently used as an oil. ^1H NMR ($CDCl_3$): δ 7.60–6.78 (m, 15 H), 6.20 (s, 2 H), 1.98 (s, 3 H) (vinylic and benzylic protons have the same chemical shift at 60 MHz). This acetate also reacts rapidly with alcohols to produce the corresponding allylic ether.

1,1-Bis(3,5-dimethylphenyl)-3-phenylprop-2-enyl Acetate. This compound was prepared from the corresponding alylic alcohol following the same procedure as that given above for the preparation of 1,1,3-triphenylprop-2-enyl acetate. The same isolation procedure gave a 50% yield of the product as light-brown crystals, mp 124–126 °C. ^1H NMR ($CDCl_3$): δ 7.40 (d, *J* = 16 Hz, 1 H), 7.38–6.65 (m, 11 H), 5.98 (d, *J* = 16 Hz, 1 H), 2.30 (s, 12 H), 2.10 (s, 3 H).

3,3-Bis(3,5-dimethylphenyl)-1-phenylprop-2-enyl Acetate. This compound was prepared by acid-catalyzed rearrangement of 1,1-bis(3,5-dimethylphenyl)-3-phenylprop-2-enyl acetate following the same procedure as that given above for the production of 1,3,3-triphenylprop-2-enyl acetate. The resultant oil was pure but could be obtained as clumps of light tan crystals by dissolution in hexane (1 g/10 mL) and then by allowing the solution to stand for several weeks at −20 °C. ^1H NMR ($CDCl_3$): δ 7.28 (s, 5 H), 7.10–6.60 (m, 6 H), 6.20 (s, 2 H), 2.32 (s, 6 H), 2.26 (s, 6 H), 2.00 (s, 3 H).

4,4-Diphenylbut-3-enyl Acetate.[59] 4,4-Diphenylbut-3-en-2-ol (19.1 g) was allowed to react with acetic anhydride (9.30 mL) in pyridine (40 mL). After 72 h at 25 °C, the pyridine was removed under reduced pressure, water was added, and the product was extracted with ether. The combined ether extracts were washed twice with water, once with brine, dried over Na_2SO_4, and then filtered. The ether was removed leaving a yellow oil which was distilled (0.5 mm, 116–118 °C) giving a clear liquid, 21.5 g (94%). ^1H NMR ($CDCl_3$): δ 7.22 (s, 10 H), 6.02 (d, *J* = 9 Hz, 1 H), 5.33 (d of q, *J* = 9 Hz, *J* = 6 Hz, 1 H), 1.99 (s, 3 H), 1.13 (d, *J* = 6 Hz, 1 H).

(H) Catalyst Precursors. The phosphine *R*-prophos was prepared by methods given elsewhere[15] as was *S,S*-chiraphos.[15] *S,S*-Norphos was obtained by a modification of the method described by Brunner;[60] the Diels–Alder reaction was carried out at 160 °C in *o*-dichlorobenzene for 3 h, the resolved phosphine oxide was reduced according to the method of Knowles,[61] and the free phosphine was first complexed to $Ni(NCS)_2$ and removed by CN^-. *R,R*-Dipamp was a gift from Dr. W. S. Knowles.[61]

***S,S*-Metachiraphos.** The phosphine, tris(3-methylphenylphosphine), was obtained in 75% yield from the reaction of the Grignard reagent of 3-bromotoluene with trichlorophosphine in ether solution. The product was crystallized from methanol.

S,S-Metachiraphos was prepared by a procedure almost identical with that described for the synthesis of *S,S*-chiraphos.[15] The product was obtained as white crystals from ethanol solution in 35% yield: mp 98–100 °C; $[\alpha]^{22}$ −170° (*c*1, acetone). Anal. Calcd for $C_{32}H_{36}P_2$: C, 79.6; H, 7.5; P, 13.0. Found: C, 79.8; H, 7.8; P, 13.0.

[Pd(*R*-prophos)(η^3-C_3H_5)]ClO_4. *R*-Prophos (0.412 g) was triturated with $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (0.183 g) in methanol (10 mL). Both solids dissolved within 15 min to give a pale yellow solution which was filtered through Celite. Solid $LiClO_4$ (0.4 g) was added to the filtrate followed by water (40 mL) which caused the product to precipitate as a white

(59) Cheminat, B. *Bull. Soc. Chim. Fr.* **1972**, 3415.
(60) Brunner, H.; Pieronczyk, W. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 620.
(61) Vineyard, B. D.; Knowles, W. S.; Sabacky, H. J.; Bachman, G. L.; Weinkaoff, D. J. *J. Am. Chem. Soc.* **1977**, *99*, 5946.

powder. After this mixture was stirred for 15 min, the solid was collected and was washed with water followed by ether. The dried product was twice recrystallized from acetone–ether. White needles were obtained, 0.5 g (77%). Anal. Calcd for $C_{30}H_{31}ClO_4P_2Pd$: C, 54.7; H, 4.7; Cl, 5.4; O, 9.7; P, 9.4. Found: C, 54.9; H, 4.9; Cl, 5.3; O, 9.6; P, 9.5.

[Pd(*R*,*R*-Dipamp)(η^3-C_3H_5)]ClO$_4$. A solution of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (0.16 g) in CH_2Cl_2 (2 mL) under argon was treated with a solution of $AgClO_4$ (0.18 g) in acetone (3 mL). Silver chloride precipitated at once. The mixture was allowed to stir for 30 min, after which the mixture was filtered through Celite. The pale yellow solution thus obtained was cooled to −78 °C and was treated with *R*,*R*-dipamp (0.38 g) in acetone (6 mL). The resulting solution was allowed to warm slowly to 25 °C. The solvents were removed under reduced pressure giving a white solid which was then dissolved in a minimum volume of methanol at 25 °C. Dropwise addition of water to this solution caused the precipitation of a fine white powder. After the mixture was stirred for 30 min, and then was allowed to stand at 5 °C for 12 h, the solid was collected. It was washed with ether and dried, 0.5 g (80%). Anal. Calcd for $C_{31}H_{33}ClO_6P_2Pd$: C, 52.8; H, 4.7; P, 8.8. Found: C, 52.6; H, 4.8; P, 8.8.

[Pd(*S*,*S*-Norphos)(η^3-C_3H_5)]ClO$_4$. This compound was prepared in a manner analogous to that given for the dipamp analogue except that ether was added to precipitate the product at 0 °C. The crude material was recrystallized from acetone–ether to give an off-white solid (78%). Anal. Calcd for $C_{34}H_{33}ClO_4P_2Pd$: C, 57.6; H, 4.7; P, 8.7. Found: C, 57.6; H, 4.8; P, 8.9.

[Pd(*S*,*S*-Metachiraphos)(η^3-C_3H_5)]ClO$_4$. *S*,*S*-Metachiraphos (0.48 g) and $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (0.18 g) were triturated in methanol (3 mL) and the resulting solution was filtered through Celite. The filtrate was treated with a solution of $LiClO_4$ (0.5 g) in methanol (0.5 mL). A white solid separated immediately. The mixture was digested on a steam bath for a few minutes and then was allowed to stand at 5 °C for 12 h. The solid was collected and was washed with water, then with cold methanol, and finally with ether. It was recrystallized from hot methanol and formed white crystals, 0.6 g (87%). Anal. Calcd for $C_{35}H_{41}ClO_4P_2Pd$: C, 57.6; H, 5.7; P, 8.5. Found: C, 57.1; H, 5.6; P, 8.7.

(I) Catalytic Allylation Reactions. The preparation of the nucleophile and the catalytic reactions were carried out under nitrogen and in dry solvents, THF(Na) and DMF(CaH_2). The procedure used for the catalytic reactions is exemplified by that given below for the palladium chiraphos catalyzed reaction of 1,3,3-triphenylprop-3-enyl acetate with $NaCH(CO_2CH_3)_2$ in THF solution.

Methyl 2-Carbomethoxy-3,5,5-triphenylpent-2-enoate. A mineral oil dispersion of NaH (50% NaH, 0.22 g, 4.6 mmol) was washed free of the oil with dry pentane (3 × 15 mL). The oil free NaH was suspended in THF (25 mL) and dimethyl malonate (0.53 mL, 6.1 mmol) was added dropwise to the stirred suspension. After the reaction was complete, the resulting solution was cannulated through a glass wool plug into a 125-mL flask containing 1,3,3-triphenylprop-2-enyl acetate (1.0 g, 3.0 mmol) and the catalytic precursor $[Pd(S,S\text{-chiraphos})(\eta^3\text{-}C_3H_5)]ClO_4$·acetone (0.10 g, 0.14 mmol, 5 mol %). Five milliliters of THF was used to complete the transfer. Upon stirring of the catalytic reaction, the substrate dissolved at once but the catalyst precursor dissolved in 3–4 min. A clear orange solution was obtained initially, but after 10–15 min NaOAc began to deposit.

The progress of the reaction was monitored by the singlet due to the vinylic and benzylic (degenerate at 60 mHz) protons of the allylic acetate substrate and by the vinylic proton doublet of the product. The reaction was essentially complete after 5 h; after 8 h palladium metal had deposited.

After a total of 20 h, acetic acid (1 mL) was added and the reaction mixture was poured into water (200 mL). The product was extracted with ether which was washed with brine, dried ($MgSO_4$), and filtered. The resulting clear yellow solution was evaporated under reduced pressure; the remaining dimethyl malonate was removed by several additions of acetic acid and vacuum evaporation. Benzene and CCl_4 were similarly added and removed to give a clear yellow oil. The yellow material can be removed by passing a benzene solution of the product through an alumina plug or simply by dissolving the oil in ether and filtering off the yellow residue. The resultant product is pure and the yield is quantitative. ^{1}H NMR ($CDCl_3$): δ 7.90–6.60 (m, 15 H), 6.41 (d, *J* = 10 Hz, 1 H, vinylic proton), 4.30 (asymmetric triplet, *J* = 10 Hz, 1 H, benzylic proton), 3.88 (d, *J* = 10 Hz, 1 H, malonate proton), 3.62 (s, 3 H), 3.38 (s, 3 H), assignments confirmed by decoupling.

The other two substrates were reacted similarly, except that the 3,5-dimethylphenyl substrate required 48–72 h for completion. All of the products were pure oils displaying the following ^{1}H NMR data.

Methyl 2-Carbomethoxy-3-phenyl-5,5-bis(3,5-dimethylphenyl)pent-4-enoate. ^{1}H NMR ($CDCl_3$): δ 7.60–6.38 (m, 11 H), 6.25 (d, *J* = 10 Hz, 1 H), 4.19 (t, *J* = 10 Hz, 1 H), 3.82 (d, *J* = 10 Hz, 1 H), 4.65 (s, 3 H), 3.29 (s, 3 H), 2.30 (s, 6 H), 2.10 (s, 6 H).

Methyl 2-Carbomethoxy-3-methyl-5,5-diphenylpent-4-enoate. ^{1}H NMR ($CDCl_3$): δ 7.15 (s, 10 H), 5.99 (d, *J* = 9 Hz, 1 H), 3.62 (s, 6 H), 3.55–3.00 (m, 2 H), 1.13 (d, *J* = 5 Hz, 3 H).

Substrate–Nucleophile Stability. In THF solutions, the substrate 1,1,3-triphenylprop-2-enyl acetate was observed to slowly rearrange to the isomeric allylic acetate in the presence of $NaCH(CO_2CH_3)_2$ under the same concentration conditions as used for the catalytic reaction. After 25 h, at 25 °C, approximately 10% of the substrate had isomerized and another 5–10% had reacted to give unidentified species. The catalytic reaction for this substrate, however, is complete in less than 5 h. In DMF solution, no reaction was observed after 24 h. The isomeric acetate, 1,3,3-triphenylprop-2-enyl acetate, is much more stable and is inert to $NaCH(CO_2CH_3)_2$ in THF for 12 days.

(J) Conversion of Allylation Products to Succinic Acid Derivatives. Oxidation. The allylation product (3.0 mmol) was dissolved in acetic acid (4 mL) and the solution was cooled to 10 °C and was stirred as a chromic acid solution (1.0 g of CrO_3, 10 mmol in 0.5 mL of H_2O and 6 mL of acetic acid) was added dropwise over 5 min. The resulting solution was stirred for 2 h, at 25 °C and was then poured into 10 mL of water and 40 mL of ether. The aqueous layer was extracted several times with ether. The combined ether extracts were evaporated under reduced pressure. The remaining greenish oil was taken up in ether and was washed twice with water to remove the remaining Cr^{3+} salts. Upon evaporation, the ether extract left a yellow oil which contained the product and benzophenone.

Saponification and Decarboxylation. The oil obtained from the oxidation was dissolved in methanol (10 mL) and to this solution was added sodium hydroxide (1.4 g) in water (10 mL). The mixture was refluxed for 1 h and then was cooled and partially neutralized with HCl (2.5 mL, 12 N in 7.5 mL of H_2O). This solution was evaporated to a small volume under reduced pressure and the residue was diluted with water and the resulting aqueous mixture was acidified (HCl) to pH 2. It was extracted with dichloromethane (4 × 50 mL). The aqueous layer was evaporated under reduced pressure to 20 mL and the solution was refluxed (4 h for the phenylsuccinic acid precursor, 10 h for the methylsuccinic acid precursor) in order to decarboxylate the triacid.

The cooled solution was extracted with ether (4 × 75 mL) and the combined ether extracts were dried (Na_2SO_4). Upon removal of the ether, an off-white solid remained. This was dissolved in methanol (15 mL) and decolorized with charcoal. After filtration and evaporation, a pure white powder remained which was dried at 60 °C in vacuo for 30 min. Both the phenyl- and methylsuccinic acids obtained in this way were pure. The overall yield was 70% in both cases. Anal. Calcd for $C_{10}H_{10}O_4$, phenylsuccinic acid (recrystallized): C, 61.9; H, 5.2; O, 33.0. Found: C, 61.9; H, 5.2; O, 32.9. Anal. Calcd for $C_5H_8O_4$, methylsuccinic acid (recrystallized): C, 45.5; H, 6.1; O, 48.4. Found: C, 45.5; H, 6.1; O, 48.5.

Optical Rotations. *R*-(−)-Phenylsuccinic acid obtained from the catalytic reaction using *S*,*S*-chiraphos had $[\alpha]^{25}$ −121.8° (absolute EtOH, *c* 1.3). After two crystallizations from hot water, a constant value of $[\alpha]^{25}$ −145.5° (absolute EtOH, *c* 1.3) was obtained. This value was used to determine the optical purity. The literature value of the optical rotation[45] was used for *S*-(−)-methylsuccinic acid. The optical yields were determined from the rotations observed for the powders obtained after the decarboxylation procedure.

We have checked the optical stabilities of the two succinic acids in boiling water. We find that the methylsuccinic acid is stable in boiling water for at least 36 h but that the phenyl analogue does racemize slowly. For the 4-h decarboxylation procedure we estimate that about 3% racemization may have occurred so that the optical yields quoted in Table I may be a little higher than quoted for the phenylsuccinic acid reactions.

(K) Reactions in Figure 13. 1,3-Diphenylprop-2-en-1-ol. To a stirred solution of phenylmagnesium bromide, prepared from Mg (6.07 g) and bromobenzene (39.3 g), in dry ether (300 mL) was added dropwise a solution of cinnamaldehyde (33 g) in dry ether (50 mL) over 15 min. The mixture was allowed to stir for an additional hour at 25 °C and then was quenched with saturated NH_4Cl. The aqueous layer was extracted once with ether and the combined ether extracts were washed twice with water, twice with brine, and dried over Na_2SO_4. Removal of the ether in vacuo afforded the alcohol (50.6 g) as a low-melting solid which was used directly in the next step. ^{1}H NMR ($CDCl_3$): δ 2.39 (s, 1 H), 5.25 (d, *J* = 5 Hz, 1 H), 6.3–6.55 (m, 2 H), 7.22–7.40 (m, 10 H).

1,3-Diphenylprop-2-enyl Acetate. A solution of the above alcohol (25 g) in acetic anhydride (12.4 mL) and pyridine (50 mL) was stirred for 3 days at 25 °C. The solvent was removed in vacuo and the residue was diluted with water which was extracted three times with ether. The combined ether extracts were washed with water and then with brine and were dried over Na_2SO_4. After removal of the ether the desired acetate (21.6 g) was distilled at 136–140 °C (0.2 mm). ^{1}H NMR ($CDCl_3$): δ 2.10 (s, 3 H), 6.4–6.52 (m, 2 H), 7.2–7.35 (m, 10 H).

Methyl 2-Carbomethoxy-3,5-diphenylpent-4-enoate. 1,3-Diphenylprop-2-enyl acetate (0.8 g) was catalytically reacted with sodium dimethyl malonate in THF (25 °C) using the palladium chiraphos catalyst. After 12 h, the reaction was worked up to give the product as a yellow oil which after chromatography over silica gel using hexane/ethyl acetate afforded the pure allylation product (0.9 g, 96%) as a colorless oil. ^{1}H NMR ($CDCl_3$): δ 3.45 (s, 3 H), 3.61 (s, 3 H), 4.13 (m, 2 H), 6.33 (m, 2 H), 6.9 (br s, 10 H).

Dimethyl Phenylsuccinate. A solution of methyl (3,5-diphenyl)-pent-4-enoate (0.5 g) in CH_2Cl_2 (5 mL) and methanol (10 mL) was ozonized at −70 °C until a pale blue color developed (~70 min). The system was flushed with oxygen and the solvents were removed in vacuo while maintaining the solution at less than 0 °C. A pale yellow oil resulted which was treated with formic acid (6 mL, 90%) followed by H_2O_2 (3 mL, 30%). The resulting solution was cautiously warmed until a vigorous reaction began (70 °C). The bath was removed until the reaction had subsided. The process was repated and then the solution was held at 100–120 °C for 45 min. After cooling and removal of the solvents, an orange oil (0.78 g) was obtained containing the product, benzoic acid, and formic acid. The product is difficult to separate from this mixture and, in order to obtain separation, the whole mixture was esterified.

An ether solution of diazomethane, generated from Diazald (8.6 g) was distilled directly into an ether solution of the above product mixture. The resulting yellow solution was allowed to stand at 25 °C for 2 h and then was quenched with acetic acid, washed with several portions of water, and dried over Na_2SO_4. Removal of the solvents in vacuo followed by chromatography over silica gel with benzene/ethyl acetate afforded the diester (0.2 g, 48%) as an oil which slowly solidified on standing. ^{1}H NMR ($CDCl_3$): δ 2.4–3.23 (m, 2 H), 3.67 (s, 6 H), 4.08 (d of d, J = 10 Hz, J = 5 Hz, 1 H), 7.25 (s, 5 H).

Phenylsuccinic Acid. To a stirred solution of phenylsuccinic acid dimethyl ester (0.2 g) in methanol (7 mL) was added a solution of NaOH (0.95 g) in water (7 mL). The resulting solution was refluxed for 1 h. After cooling, the solution was partially neutralized with 3 N HCl (6.7 mL). The solvents were removed in vacuo and the residue was dissolved in water and acidified to pH 1.5 with HCl. The aqueous mixture was extracted three times with ether. The extracts were dried over Na_2SO_4 and after the removal of the solvent, phenylsuccinic acid (0.15 g) remained as white flakes. The rotations of this material were used to determine the optical yield.

(L) Reactions in Figure 14. Methyl 2-Carbomethoxy-3-methyl-5,5-diphenylpent-4-enoate. The catalytic reaction was carried out in the usual way using, sodium dimethyl malonate, the *S,S*-chiraphos palladium catalyst and the substrate 3,3-diphenyl-1-methylprop-2-enyl acetate (1.1 mL, 4.3 mmol) in THF. After 10 h the reaction was worked up and the product was chromatographed over silica gel with hexane/ethyl acetate. The desired product was obtained as a clear oil (1.4 g, 96%). ^{1}H NMR ($CDCl_3$): δ 1.13 (d, J = 6 Hz, 3 H), 3.1–3.53 (m, 2 H), 3.63 (s, 6 H), 6.0 (d, J = 10 Hz, 1 H), 7.2 (br s, 10 H).

Methyl 3-Methyl-5,5-diphenylpent-4-enoate. The diester (1.4 g) was decarboxylated in DMF (9 mL) using NaCN (0.28 g) in H_2O (1 mL) and LiI (4.2 g) for 10 h at 120 °C. The desired monester was obtained as an oil (1.2 g, 100%). The enantiomeric purity was determined by the chiral shift reagent Eu(hfc)$_3$ in benzene-d_6. Upon addition of the shift reagent the cis-ortho aromatic proton signals separated as a pair of doublets, J = 7 Hz. These were used to determine the ee. Spectra were run at 360 MHz. ^{1}H NMR ($CDCl_3$): δ 1.05 (d, J = 6 Hz, 3 H), 2.32 (d, J = 7 Hz, 2 H), 3.5 (s, 3 H), 6.83 (d, J = 10 Hz, 1 H), 7.18 (br s, 10 H).

Ethyl 2-Acetyl-3-methyl-5,5-diphenylpent-4-enoate. In a manner similar to that described for the sodium dimethyl malonate reaction, sodium ethyl acetoacetate, from NaH and ethyl acetoacetate in THF, was catalytically reacted with 3,3-diphenyl-1-methylprop-2-enyl acetate (2.5 mL, 9.8 mmol) using the *S,S*-chiraphos palladium catalyst. After stirring for 10 h at 25 °C, the reaction was worked up. The (diasteromeric) product was obtained as an oil (3.25 g, 99%) after chromatography over silica gel with benzene/ethyl acetate. ^{1}H NMR ($CDCl_3$, a mixture of diastereomers): δ 1.02–1.4 (m, 6 H), 2.0, 2.12 (s, 3 H), 2.87–3.4 (m, 2 H), 3.92–4.33 (m, 2 H), 5.82, 5.98 (d, J = 10 Hz, 1 H), 7.2 (br s, 10 H).

4-Methyl-6,6-diphenylhex-5-en-2-one. To a stirred solution of ethyl 2-acetyl-3-methyl-5,5-diphenylpent-4-enoate (3.25 g) in Me_2SO (10 mL) and water (0.53 mL) was added sodium chloride (0.74 g). The substrate was decarboxylated by heating this solution at 165 °C for 10 h. After cooling, the reaction mixture was diluted with water and was extracted three times with ether. The combined ether layers were washed with water and then with brine and were dried over Na_2SO_4. Removal of the solvents followed by chromatography over silica gel with hexane/ethyl acetate gave the desired ketone (1.5 g, 58%) as an oil. ^{1}H NMR ($CDCl_3$): δ 1.05 (d, J = 6 Hz, 3 H), 1.94 (s, 3 H), 2.36 (br d, J = 7.5 Hz, 2 H), 2.57–3.06 (m, 1 H), 5.85 (d, J = 10 Hz, 1 H), 7.38 (br s, 10 H).

3-Methyl-5,5-diphenyl-4-pentenoic Acid. To a stirred solution of the above ketone (0.5 g) in dioxane (25 mL) and water (7.5 mL) at 0 °C was added a cold solution of freshly prepared hypobromite (15 mL, prepared from 10 g of NaOH, 3.3 mL of Br_2 in 85 mL of H_2O and 55 mL of dioxane). The solution was stirred at 0 °C for 3 h and then was quenched by the addition of a 10% solution of sodium sulfite (2 mL). The mixture was allowed to warm to 25 °C and then was acidified with HCl (2 mL, 12 N) and extracted with ether. Upon removal of the ether an oil remained which was chromatographed over silica gel with benzene/ethyl acetate. The pure product (0.35 g, 69%) was an oil. ^{1}H NMR ($CDCl_3$): δ 1.04 (d, J = 6 Hz, 3 H), 2.3 (d, J = 7 Hz, 2 H), 2.58–3.16 (m, 1 H), 5.85 (d, J = 9 Hz, 1 H), 7.3 (br s, 10 H), 10.38 (br s, 1 H).

Methyl 3-Methyl-5,5-diphenylpent-4-enoate. The acid from above was esterified in ether using diazomethane in a manner described earlier. An oil (85%) was obtained. The optical yield was determined by using Eu(hfc)$_3$ as described before.

Methyl 3-Methyl-5,5-diphenyl-2-(*p*-toluenesulfonyl)pent-4-enoate. Sodium methyl (α-*p*-toluenesulfonyl)acetate was prepared by reaction of NaH with methyl (α-*p*-toluenesulfonyl)acetate[62] in THF and reacted with 3,3-diphenyl-1-methylprop-2-enyl acetate in the presence of the palladium *S,S*-chiraphos catalyst. The reaction is slower than the others and it was carried out at 55 °C for 12 h. After the usual workup and chromatography over silica gel with benzene/ethyl acetate the product was obtained as an oil in 95% yield. ^{1}H NMR ($CDCl_3$, a mixture of diastereomers): δ 1.13, 1.33 (d, J = 7 Hz, 3 H), 2.33, 2.38 (s, 3 H), 2.67–3.30 (m, 1 H), 3.48, 3.56 (s, 3 H), 3.88, 4.05 (d, J = 3 Hz, 2 H), 5.70, 5.86 (d, J = 10 Hz, 1 H), 6.90–7.70 (m, 14 H).

Methyl 3-Methyl-5,5-diphenylpent-4-enoate. To a stirred solution of methyl 3-methyl-5,5-diphenyl-2-(*p*-toluenesulfonyl)pent-4-enoate (0.39 g) in a mixture of methanol (8 mL) and THF (2 mL) was added K_2HPO_4 (0.53 g). The resulting slurry was cooled to −20 °C and then finely ground 3% Na/Hg (2.32 g) was added. The reaction was stirred at −20 °C for 8 h. The mixture was then filtered through Celite and the filtrate was diluted with water. It was extracted with ether and these extracts were backwashed with water until a neutral aqueous phase was obtained. After removal of the ether and chromatography the pure product was obtained (0.13 g, 60%). Its optical purity was determined by the shift reagent as described before.

(M) Reactions in Figure 15. *N*-Benzyl-1-methyl-3,3-diphenyl-2-propenamine. To a stirred slurry of [Pd(*S,S*-chiraphos)(η^3-C_3H_5)]-ClO_4·$^1/_2$acetone (0.3 g, 0.4 mmol) in dry, degassed THF (12 mL) under nitrogen were added in sequence, 1-methyl-3,3-diphenylprop-2-enyl acetate (2.2 mL, 8.6 mmol) and benzylamine (9.6 mL, 89 mmol). The solution became yellow within 30 min and then red after 16 h. The reaction was allowed to stir at 25 °C for 3 days and then was poured into water and the product was extracted with ether. The organic phase was washed with water until a neutral aqueous phase was obtained. The ether was dried over Na_2SO_4 and upon removal of the solvents in vacuo, the desired amine was obtained as a yellow oil (2.5 g, 93%). Less benzylamine can be used for this reaction without diminution of optical or chemical yield but the reaction is inconveniently slow at 25 °C under these conditions. ^{1}H NMR ($CDCl_3$): δ 1.12 (d, J = 7 Hz, 3 H), 1.43 (br s, 1 H), 3.13–3.63 (m, 1 H), 3.98 (d, J = 4 Hz, 2 H), 5.95 (d, J = 9 Hz, 1 H), 7.15 (br s, 10 H).

***N*-Benzyl-1-methyl-3,3-diphenylprop-2-enesulfonamide.** To a stirred solution of the above benzylamine compound (1.3 g) and triethylamine (0.69 mL) in dry CH_2Cl_2 (100 mL) at −20 °C was added dropwise a solution of mesyl chloride (0.36 mL) in CH_2Cl_2 (5 mL). The resulting solution was allowed to warm to 25 °C and was stirred for 12 h, after which it was quenched with water. The organic layer was separated and washed with water. After removal of the solvent, the sulfonamide was obtained as an oil (1.6 g, 98%).

The enantiomeric purity of this species was determined at 200 MHz. Successive additions of Eu(hfc)$_3$ to a benzene-d_6 solution of the sulfonamide caused the allylic methyl proton signal to appear as a pair of doublets. The optical yield was found to be 63%. The major absolute configuration of the enantiomer was established by the experiments which follow. ^{1}H NMR (C_6D_6): δ 1.30 (d, J = 7 Hz, 3 H), 2.37 (s, 3 H), 4.20 (d, J = 7 Hz, 2 H), 4.40–4.80 (m, 1 H), 6.40 (d, J = 10 Hz, 1 H), 7.10 (br s, 10 H).

Methyl 2-(*N*-Benzylsulfonamido)propionate. To a stirred solution of the above sulfonamide (3.3 g) in cold acetic acid (16 mL) was added dropwise a solution of CrO_3 (1.7 g) in water (1.3 mL) and acetic acid (9.3 mL). The resulting solution was stirred at 0 °C for 1 h and then at 25 °C for 12 h. The reaction mixture was extracted three times with ether. The combined ether extracts were washed with small portions of

(62) Beck, G.; Gunther, D. *Chem. Ber.* **1973**, *106*, 2758.

water until a colorless aqueous layer was obtained. The organic phase was extracted once with aqueous sodium hydroxide and the alkaline aqueous phase was extracted with ether (benzophenone). The aqueous phase was then acidified and again extracted with ether. The combined ether extracts were dried and, after removal of the solvent, the desired product was obtained as an orange oil (1.4 g).

This oil (1.4 g) was taken up in ether (20 mL) and esterified by using diazomethane in ether as described before. The product was chromatographed over silica gel with benzene/ethyl acetate giving the pure compound as an oil (0.45 g, 20% for two steps). The optical rotation of this compound was measured at five wavelengths (see later). ^{1}H NMR ($CDCl_3$): δ 1.30 (d, J = 8 Hz, 3 H), 2.86 (s, 3 H), 3.62 (s, 3 H), 4.32-4.86 (m, 3 H), 7.26 (s, 5 H).

***N*-Benzyl-D-alanine.** This compound was prepared from D-alanine by a method previously described.[63]

Methyl D-2-(*N*-Benzylsulfonamido)propionoate. A solution of *N*-benzyl-D-alanine (3.1 g) in methanol (30 mL) was saturated with dry HCl during which time a white solid precipitated from solution. The resultant mixture was allowed to stir for 12 h and then the solvent was removed in vacuo to give the ester hydrochloride (3.6 g, 98%) as a white solid.

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This solid (3.6 g) was suspended in dry CH_2Cl_2 (200 mL) and triethylamine (5.3 mL) was added. The mixture was cooled to -78 °C and a solution of mesyl chloride (1.47 mL) in CH_2Cl_2 (20 mL) was added. The mixture was allowed to warm to 25 °C and was stirred at this temperature for 12 h, after which it was quenched with water. The organic layer was washed with water, followed by dilute acid and again with water, and was dried over Na_2SO_4. On removal of the solvent, the resulting oil was chromatographed as before to give (0.63 g, 14%) of the pure product having an identical ^{1}H NMR with that observed for the material obtained from allylation.

The absolute configuration of the prevailing enantiomer of the product of allylation was determined from the rotations of the D-alanine derived product. The rotations at 25 °C in $CHCl_3$, c 1.6 were $[\alpha]_{589}$ +43.21°, $[\alpha]_{578}$ +45.28°, $[\alpha]_{546}$ +51.50°, $[\alpha]_{436}$ +89.36° and $[\alpha]_{365}$ +144.42°. The values of the optical purity obtained from rotation measurements and from chiral shift experiments corresponded within 2%.

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Asymmetric Synthesis. Mechanism of Asymmetric Catalytic Allylation

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Abstract: The mechanism of palladium-assisted asymmetric catalytic allylation has been investigated. It is found that the process involves two primary steps: the oxidative addition of a palladium(0)-phosphine species with an allyl acetate to form diastereomeric π-allyl intermediates which are then attacked by the nucleophile. Both steps proceed with inversion of configuration and the irreversible oxidative addition is much faster than the nucleophilic attack. The π-allyl intermediates epimerize between 10 and 10^2 times faster than nucleophilic attack occurs. The nucleophilic attack is the turnover limiting step as well as being the enantioselective step. The *major* π-allyl diastereomeric intermediate produces the *major* product enantiomer.

Homogeneous catalytic allylation with palladium complexes is a facile transformation of wide applicability.[1] The catalytic process is believed to involve two major steps. The first step is the oxidative addition of an allylic acetate (or an other suitable substrate) to a palladium(0)-phosphine complex to produce a phosphine-palladium(II)-π-allylic intermediate. This intermediate is then attacked by a "soft" nucleophile to give the allylic product with the regeneration of the palladium(0) catalyst. It has been established that, with both cyclic[2] and acyclic[3] allyl acetates, the oxidative addition step as well as the nucleophilic attack step proceed with inversion of configuration. That is, the overall process is one of net retention, although complications have been noted. Apart from this stereochemical information, little more is known quantitatively about the mechanism of this important reaction. In order to convert this catalytic process rationally for asymmetric synthesis, however, a detailed knowledge of the mechanism is required.

In the preceding paper[4] we described our attempts at orchestrating this system for asymmetric catalysis. We showed that, of all of the possible π-allyl substitution patterns, systems with the type **1** and type **2** structures (Figure 1) were the least complicated. All other 1,3-substitution patterns either possess isomeric complexity or are incapable of racemizing via the π-σ-π mechanism.[5,6] Type **1** allyls form achiral intermediates in the catalytic cycle and asymmetric synthesis occurs by enantiocenter(1,3) discrimination. The type **2** coordinated π-allyls are chiral and invert their chirality by formation of a σ-bond at the disubstituted end of the allyl during the π-σ-π process. Formation of a σ-bond at a tertiary center, however, is generally an unfavorable process when the R′ substituents are alkyl groups.[5] Such species racemize exceedingly slowly at 25 °C. Type **2** π-allyl intermediates can be derived by oxidative addition to either prochiral or chiral allyl acetates (Figure 2) and if the type **2** π-allyl intermediate were incapable of inverting its absolute configuration during its lifetime in the catalytic cycle, the optical yields for asymmetric catalysis would depend on whether a prochiral or chiral substrate were used. In the absence of epimerization of the intermediate, the optical yield would be determined at the oxidative addition stage for a type **2** prochiral substrate; i.e., oxidative addition would represent the enantioselective step. Without epimerization of the intermediate, a type **2** chiral (racemic) allyl substrate would give zero optical yield in the product. For both cases we assume that the

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