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Mechanistic and Synthetic Studies in Catalytic Allylic Alkylation with Palladium Complexes of 1-(2-Diphenylphosphino-1-naphthyl)isoquinoline

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Abstract : The title complexes are highly reactive catalysts for the reaction between (E)-1,3-diphenyl-2-propenyl acetate and dimethyl malonate ion; the enantiomer excess varies between 67% and 98% depending on how the reaction is conducted, with the best result obtained in CH_3CN at -13°C in the presence of 15-crown-5. With 2-cyclohexenyl acetate the reaction was much slower and the best e.e. obtained was 67%. With 1,1,3-triphenyl-2-propenyl acetate, reaction was again much slower than in the first case, the best e.e. was 47%, and the configurational correlation between catalyst and reactant was in the opposite sense. Many of the trends can be satisfactorily rationalised by recourse to the NMR spectra of a series of Pd allyl complexes. In the case of the (E,E)-1,3-diphenylallyl complex, two diastereomers were observed and their configurations assigned with the aid of nOe experiments. The results are best interpreted if the reaction proceeds through a late transition-state with nucleophilic attack on the allyl trans- to the phosphorus of the ligand and preferentially on the predominant diastereomer.

Introduction.

Catalytic allylic alkylation[1] was one of the first organometallic reactions for which asymmetric induction was demonstrated[2], although progress towards a genuinely effective synthetic method has been slow. In an early example, Bosnich and co-workers showed that palladium complexes of 2S, 3S-bis(diphenylphosphino)butane catalysed the alkylation of di- and triphenylpropenyl acetates with malonates or with benzylamine in enantiomeric excesses of between 23% and 84%. Evidence that the reaction proceeded *via* a cationic diphosphine palladium allyl was obtained from a combination of crystallographic and ^{31}P NMR spectroscopic studies[3]. Kumada, Hayashi and co-workers demonstrated some interesting examples of alkylation of allylic acetates by β-diketonate anions, employing aminoalkylferrocene-based diphosphines[4]. In some cases kinetic resolution of the reactant could be achieved[5]. The most interesting example from their work is shown in Scheme 1, where the high level of asymmetric induction is attributed to a direct interaction between the nucleophile and an amino-group in the ferrocene side-chain. The possibility of reaction proceeding through a P-N chelate complex was not formally considered[6]. In recent work, Trost and co-workers have investigated new types of ligand for allylic alkylation based on heteroatomic frameworks, typified by the case illustrated in Scheme 2. An emphasis in this work is to apply allylic alkylation to synthetically useful cases, rather than formal exemplification[7]. The potential of ligands other than diphosphines has only been recognised recently. Thus Togni and Pastor showed that sparteine palladium complexes had some potential for catalytic allylic alkylation giving e.e.s of up to 77%[8]. A more impressive result was obtained by Pfaltz and co-workers using their bis-oxazoline ligands[9]. In the reaction between 1,3-diphenyl-2-propenyl acetate and diethyl malonate, where the nucleophile was generated *in situ* using

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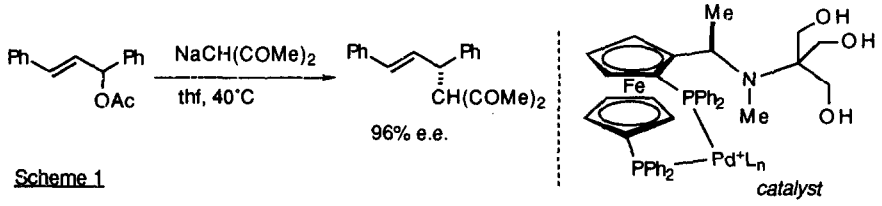
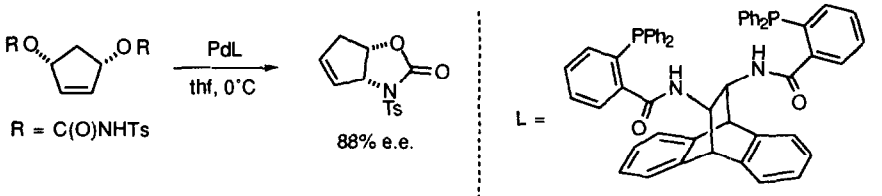
Dedicated to Professors Ryoji Noyori and Barry Sharpless on their award of the Tetrahedron Prize for Creativity in Organic Synthesis

N,O-bis(trimethylsilyl)acetamide as recommended by Trost[10], e.e.s of up to 98% were obtained under optimised conditions. The X-ray crystal structure of the resulting allyl complex demonstrates the configurational relationship between the coordinated allyl and product, consistent with exometallic nucleophilic attack.

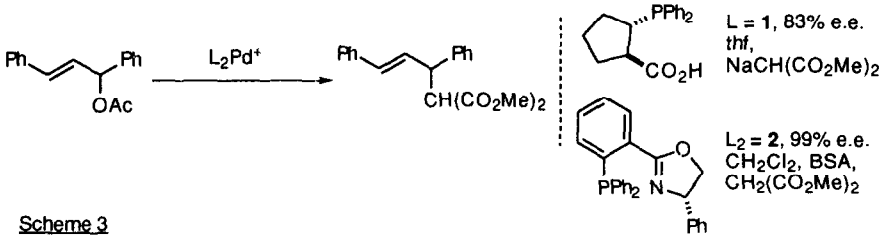
The potential of heterotopic chelate ligands has been noted more recently. Minami and co-workers[11] demonstrated that the reaction between 1,3-diphenyl-2-propenyl acetate and dimethyl malonate or triethyl phosphonoacetate occurred in up to 85% e.e. when catalysed by an *in situ* generated palladium complex of **1**. The best results to date have been obtained in related experiments carried out by Pfaltz[12], Helmchen[13], and Williams[14] and their respective co-workers, all using similar 2-(diphenylphosphino)aryloxazolines as the catalytic ligand. Of these, the most comprehensive study is due to von Matt and Pfaltz, who showed that complexes of ligand **2**, the most effective of a series of 4-substituted oxazoles, effected allylic alkylation in up to 99% e.e. with 1,3-diphenyl-2-propenyl acetate, and in up to 96% e.e. with 1,3-diisopropyl-2-propenyl acetate (Scheme 3).



Scheme 1



Scheme 2

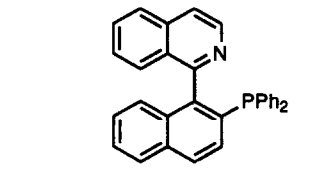


Scheme 3

Results and Discussion.

The preparation and resolution of 1-(2-diphenylphosphino-1-naphthyl)isoquinoline (QUINAP)[15], and application of its rhodium complexes in catalytic asymmetric hydroboration[16], have already been described; both enantiomers of the ligand are accessible on a multigram scale. The backbone of ligand **3** in its chelate metal complexes (P-C=C-C=N) is identical to that which pertains in **2** and its relatives, but the geometrical constraints are very different. The asymmetry of **3** derives from restricted rotation about the biaryl linkage and the inter-aryl dihedral angle in a crystallographically characterised Pd complex is 65°, similar to that observed in BINAP

complexes[17]. For the oxazole ligand **2**, the chelate ring is likely to be much closer to coplanarity. For this reason it was of interest to compare the effectiveness of the two types of complex in allylic alkylation.



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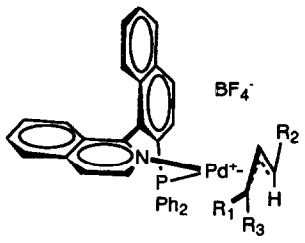
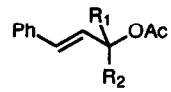
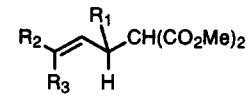


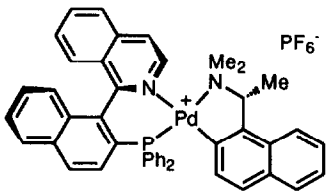
4a: $R_1 = R_2 = R_3 = H$
4b: R_1 =Ph, $R_2 = R_3 = H$
4c: $R_1 = R_2$ = Ph, $R_3 = H$
4d: $R_1 = R_2 = R_3$ = Ph



5a: R_1 = Ph, R_2 = H
5b: $R_1 = R_2$ = H
5c: $R_1 = R_2$ = Ph



6a: $R_1 = R_2$ = Ph, R_3 = H
6b: $R_1 = R_3$ = H, R_2 = Ph
6c: R_1 = Ph, $R_2 = R_3$ = H
6d: $R_1 = R_2 = R_3$ = Ph



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Allylpalladium complexes of ligand S-**3** were readily prepared by employing allylpalladium chloride and its mono-, 1,3-di-, and 1,1,3-triphenyl analogues, and reacting with one equivalent of ligand based on Pd. The resulting allyl complexes were isolated as BF_4^- salts. In all cases except the triphenylallyl complex **4d**, which was obtained analytically pure, the NMR spectra (vide infra) showed that a mixture of diastereomers prevailed in solution. In these cases the structure was confirmed by electrospray MS. Catalytic runs involving (E)-1,3-diphenyl-2-propenyl acetate **5a** and dimethyl malonate (Table 1) were initially carried out following the previously described method with N,O-bis(trimethylsilyl)acetamide; for the most part, reactions were carried out on an NMR scale so that monitoring was facilitated. It was found that the level of asymmetric induction was essentially independent of the solvent, varying between 75% and 79%, and that catalytic turnover generally occurred rapidly at ambient temperature. Since the starting material is racemic, the reaction was stopped at 50% completion and acetate **5a** reisolated and shown still to be a racemate; this suggests that the Pd-catalysed [1,3]-shift of acetate[18] which interconverts the R- and S-enantiomers of **5a** is fast compared to allylic alkylation, or that there is no discrimination between enantiomers. With 2 mol% catalyst, the reaction was complete in a period which depended on the solvent , with $CDCl_3$ the slowest and CD_2Cl_2 fastest. During catalytic turnover the solutions were yellow or orange in colour consistent with the appearance of the free allyl complex, apart from the reaction solution in $CDCl_3$ which was dark red. These results indicated substantially lower enantiomeric efficiency than the oxazoline-derived complexes under related conditions, and hence some optimisation was sought.

Solvent	CD_2Cl_2	$CDCl_3$	THF	Toluene	CD_3CN
E.e.% [a]	76[c,d]	75	75	75	78
Turnover rate[b]	0.4 min	60 min[e]	8 min	1.2 min	0.6 min

*Table 1. Allylic alkylation of (E)-1,3-diphenyl-2-propenyl acetate **5a** with dimethyl malonate and N,O-bis(trimethylsilyl)acetamide, 2 mol% catalyst; see Experimental Section. [a]Enantiomer excesses were measured with Eu(hfc)$_3$ in $CDCl_3$. [b] Estimated time for completion / 50. [c]E.e. = 79% at 0 °C. [d]E.e. = 79% using the palladium dichloride complex of ligand 3, turnover time = 4 min. [e]Probable catalyst deterioration.*

When the preformed sodium or lithium salts of dimethyl malonate were employed the e.e.s obtained were if anything marginally lower, but again not very sensitive to the solvent employed, even though the reaction was part heterogeneous in some cases. There was a weak trend of increased e.e. with increased solvent polarity. Since the sodium dimethyl malonate salt was incompletely soluble in CD_2Cl_2 under the reaction conditions, an equivalent of 15-crown-5 was added[19]. This had a significant effect in enhancing the e.e. to 90%. It was demonstrated that variations on reaction conditions (e.g. inverse addition, doubling reactant concentrations) had little effect on the enantiomeric purity of the product. In addition, the stoichiometric reaction between Pd allyl **4c** and sodium dimethyl malonate in the presence of 15-crown-5 occurred in 89% e.e. in CD_2Cl_2. The critical effect of the crown ether in complexing Na^+ was shown in two further experiments; it had little effect on the enantiomeric purity of product when Li^+ was the counter-ion (73% with vs. 67% without), but catalytic reaction of the Na^+ salt in neat 15-crown-5 occurred in 92% e.e.

Further improvement was effected by carrying out the reaction in acetonitrile, where an enantiomeric purity of 95% was obtained at ambient temperature in the presence of 15-crown-5, this being essentially insensitive to the concentration of the components. At 0°C, the e.e. was 97.8%, and at -13°C it was 98.2%. A preparative reaction using 2 mol% catalyst gave the diester R-**6a** in 95% yield, $[\alpha]_D^{23}$ = +17.9 (c = 1.1, EtOH) [Lit[12]. $[\alpha]_D^{23}$ = +18.4 (c = 1.1, EtOH) for enantiomerically pure material].

Reagent	$LiCH(CO_2Me)_2$			$NaCH(CO_2Me)_2$[a]			$NaCH(CO_2Me)_2$/15-crown-5[b]		
Solvent	THF	CD_2Cl_2	CH_3CN	THF	CD_2Cl_2	CH_3CN	$CDCl_3$	CD_2Cl_2	CH_3CN
E.e.% (temp. °C)	73(20)	67 (20)	82 (20)[c]	67 (20)	75 (20)	78 (20)	84 (20)	90 (20)	95 (20)
		73 (20)[c]		74(-15)					98 (0, -13)

*Table 2. Reagent and solvent effects on the enantioselectivity of allylic alkylation of acetate **5a**. [a]In other solvents: DMSO, 80% e.e., DMPU 81% e.e.; [b]92% e.e. in neat 15-crown-5, 20 °C; [c]15-crown-5 added.*

As anticipated, the reaction of allylic acetate **5b** under the N,O-bis(trimethylsilyl)acetamide conditions gave mainly the linear diester **6b** (~83:17, linear / branched), but the reaction was markedly slower than that of the diphenyl analogue, requiring 3h. for completion of 50 turnovers (Table 3).

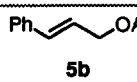
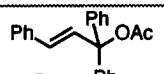
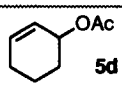
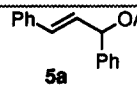
 **5b**	 **5c**	 **5d**	 **5a**
BSA / CD_2Cl_2 method 100% reaction in 3 h. ~83:17 **6b** / **6c** $NaCH(CO_2Me)_2$/15-crown-5/ CH_3CN 100% reaction in 1.5 h. ~85:15 **6b** / **6c**	BSA / CD_2Cl_2 method 85% reaction in 3.5 days E.e. = 34% (S-**6d**) $NaCH(CO_2Me)_2$/15-crown-5/ CD_2Cl_2 60% reaction in 4 days E.e. = 47% (S-**6d**)	BSA / CD_2Cl_2 method 90% reaction in 3 days E.e. = 42% (R) $NaCH(CO_2Me)_2$/15-crown-5 CH_3CN 68% reaction in 16 hours E.e. = 67% (R)	BSA / CD_2Cl_2 method With 2 mol% of (S)-BINAP / $(allylPdCl)_2$ complex. 85% reaction in 4 days E.e. = 90% (R-**6a**)[20]

Table 3. Other allylic alkylations with 2 mol% catalyst.

Under these conditions, the triphenylpropenyl acetate **5c** reacted even more slowly, giving the malonate S-**6d** in 34% e.e.; increased to 47% when the 15-crown-5 conditions in CD_2Cl_2 were adopted. It is interesting to

note that in the earlier work of Bosnich and co-workers using CHIRAPHOS the conversion of **5c** into **6d** occurred with far greater enantiomeric efficiency than the transformation of **5a** into **6a**, and in that case the relative configuration of the two products was the same, rather than opposite as we observed. In prior work, the allylic alkylation of 2-cyclohexenyl acetate has never given particularly high e.e.s.[8,11,21] Under the optimum conditions described above the reaction is rather slow, and although the enantiomeric purity of the product is still modest (67%) it is as high as the best previously reported, leading to the isolation of dimethyl cyclohex-2-enylmalonate, $[\alpha]_D^{23}$ = 24.4 (c = 2.6, $CHCl_3$) [Lit . $[\alpha]_D^{23}$ = 15.6 (c = 2.6, $CHCl_3$) for 50% e.e.].

In summary, Pd complexes of the QUINAP ligand are comparable in reactivity and enantiomeric efficiency to those of the phosphinoaryloxazolines described above for the conversion of rac-**5a** into R-**6a**, albeit the conditions for highest enantioselectivity are rather distinct. Under conditions where a low steady-state concentration of malonate ion pertains in the BSA-promoted reaction, the solvent plays little part in determining the enantioselectivity, which is modest. When the pre-formed sodium salt is involved, there is a weak trend towards higher e.e.s as the solvent polarity[22] is enhanced. Only when ion-pairing and aggregation is broken by addition of crown ether is there a dramatic enhancement of enantioselectivity, and in that case the difference between dichloromethane and acetonitrile is quite marked. A reasonable inference is that solvation and ion-aggregation affect the structure of the transition-state for the C-C bond-forming step which leads to enantiomeric discrimination; the closer this is to an unencumbered allylpalladium-malonate ion pair, the higher the e.e.

NMR Spectra of palladium allyl complexes

The X-ray structure[15] of complex **7** derived from ligand **3** provides a set of geometric coordinates for other complexes. As in the case of BINAP, there is an expectation that the backbone will be relatively rigid, so that much of the coordination sphere is spatially defined, although the P-aryl bonds of the PPh_2 group are conformationally mobile. In order to form a chelate ring some distortion from ideal bond angles is required, and this is largely accommodated by shifting the vector of the N-Pd bond out of the isoquinoline ring mean plane, although some non-planar distortion of the biaryl linkage is also observed. The intention was to combine this crystallographic information with NMR studies to gain insight into the stereochemical course of allylic alkylation.

Structures and assignments: Experiments were first carried out with the simple allyl complex **4a**. A sharp ^1H NMR spectrum was only obtained below 220K, and revealed two diastereomeric complexes in 45:55 ratio. Assuming that the larger $^3J_{HH}$ coupling is associated with a trans-configuration, and that the protons trans to phosphorus are coupled to it, a complete assignment can be made (Figure 1). As the temperature is raised, broadening occurs and eventually the terminal protons collapse to a single envelope. which then gradually sharpens with increasing temperature; each terminal proton is in rapid dynamic interchange with the other seven. This observation requires that there are two separate processes leading to dynamic effects in the NMR. If as is widely assumed[23], these changes are due to σ–π–σ interchanges in the allylic fragment, the intermediate must have sufficient lifetime to undergo bond rotation about both single bonds in the Pd-C-C=C unit; either process leads to interconversion of the two diastereomers but with interchange of different pairs of protons (Figure 2).

For the phenylallyl complex **4b**, two main diastereomers (of a possible four with (E)-configuration) are again observed, but their interchange is slow on the NMR timescale at probe temperature (300K). Based on analysis of the chemical shifts (Table 4) it is apparent that both have the Ph-group disposed syn to the isoquinoline nitrogen. Several lines of evidence support this. Thus the PhCH proton is trans to phosphorus in both diastereomers, and there is a substantial difference between the chemical shifts of the distinctive 3-proton of the isoquinoline; in one

diastereomer it is at 8.84 ppm, whilst in the other it resonates at 7.82 ppm, consistent with the effects of intracomplex aromatic shielding in the latter. Molecular models based on the X-ray structure indicate the feasibility of this explanation.

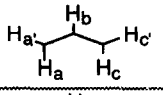
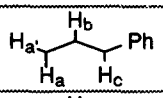
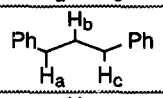
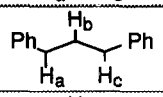
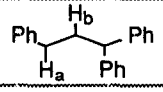
	P-------N	H_3	H_a	$H_{a'}$	H_b	H_c	$H_{c'}$
4a		8.82 8.97	2.97 3.53	3.85 3.77	6.19 5.75	3.96 4.18	5.17 5.03
4b		7.82 8.84	3.17 3.65	3.92 3.72	6.63 6.19	5.63 5.96	
4c		7.72‡ 8.99*	4.57✚ 5.56#		7.01 6.54	5.82 6.12	
4c (CD_2Cl_2)		7.66 8.69	4.64 5.39		6.89 6.64	5.89 5.75	
4d		8.51	4.49		6.90		

*Table 4. ^1H NMR Chemical shifts of allylic protons in complexes **4**, $CDCl_3$.The major diastereomer is shown above the minor in each case.* [a] *Proton α-to the isoquinoline nitrogen.* * *7.5% nOe on irradiation of H_c at 6.12 ppm.* ‡ *No detected nOe on irradiation of H_c at 5.82 ppm.* ✚ *7% nOe on irradiation of H_c at 5.82 ppm.* # *5% nOe on irradiation of H_c at 6.12 ppm.*

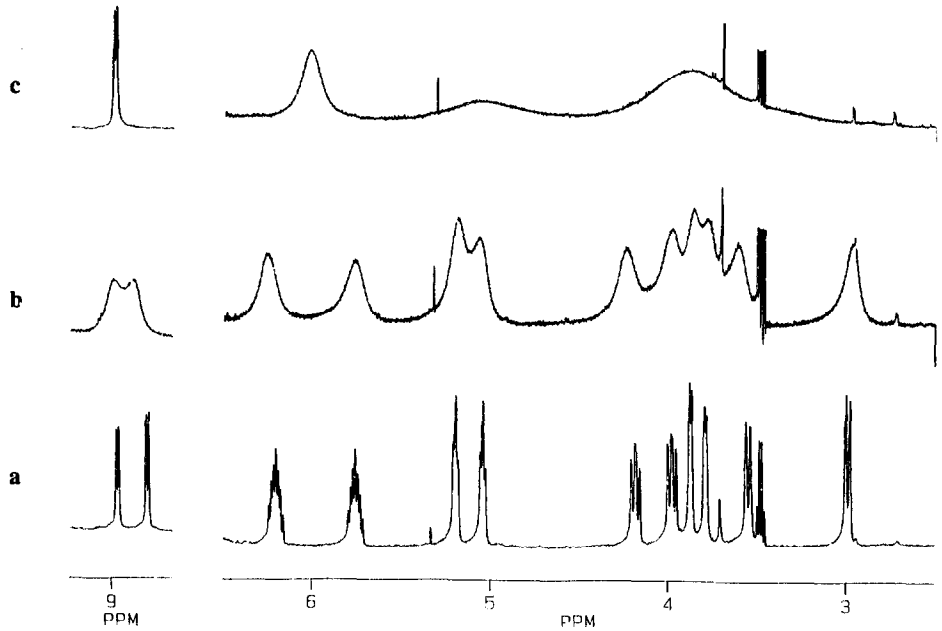


*Figure 1. ^1H NMR spectra of the allyl **4a** in $CDCl_3$ at (**a**) 218K (**b**) 258K and (**c**) 298K.*

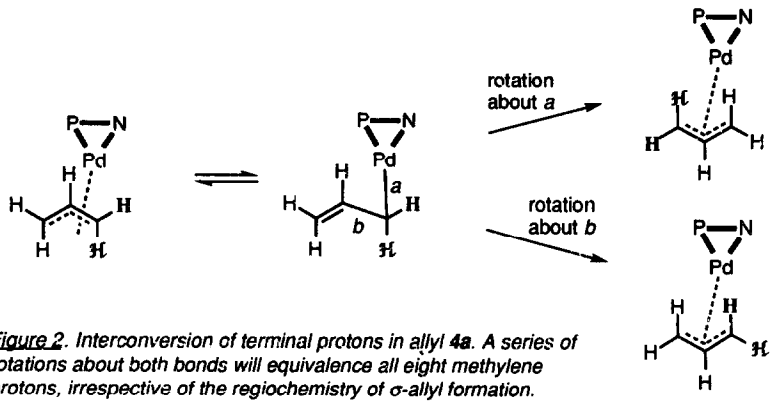
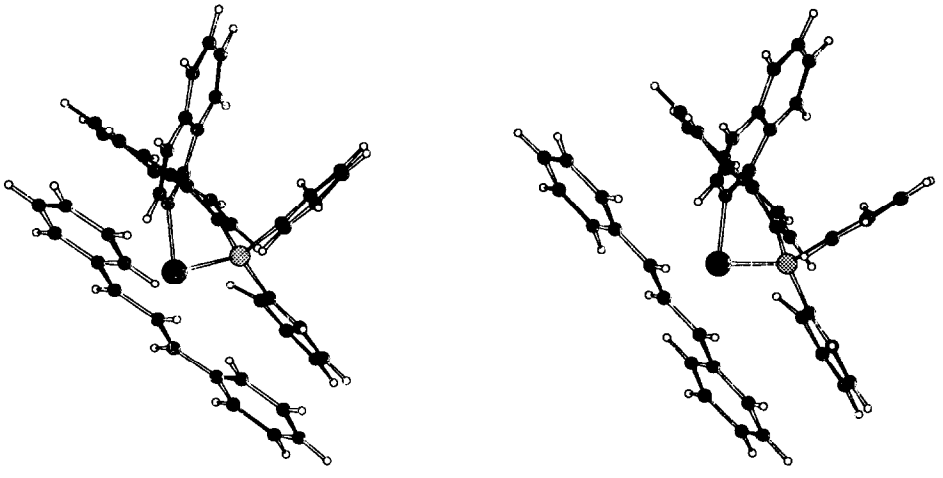


*Figure 2. Interconversion of terminal protons in allyl **4a**. A series of rotations about both bonds will equivalence all eight methylene protons, irrespective of the regiochemistry of σ-allyl formation.*

In the case of the diphenylallyl **4c**, two diastereomers are again apparent, both with E,E-configuration; no evidence was obtained for E,Z-isomers under any conditions. In CD_2Cl_2, these are in ratio 6:1 but 2:1 in the same sense in $CDCl_3$. There are also some interesting chemical shift differences between the two solvents, notably that in CD_2Cl_2 both the anti-protons of the allylic fragment of the minor diastereomer and also its isoquinoline H_3 are shielded relative to their $CDCl_3$ values; the major diastereomer is not much affected by solvent change. The relative configuration[24] of ligand and allyl was established by nOe experiments in both solvents, the results being shown schematically in Figure 3. The most critical observation is that the 3-proton of the isoquinoline has a distinct nOe to the endo-allyl proton trans to phosphorus in the minor diastereomer alone, leading to the configurations drawn. The two species interconvert on the timescale of the nOe, leading to negative adsorption in the proton connected to the site of excitation by rearrangement. These specifically link the trans-P allyl proton in one diastereomer with the trans-N allyl proton in the other, defining the interconversion as being due to a rotation about the Pd-C bond in a σ-allyl intermediate (path *a*). In more basic solvents like CD_3CN or DMSO-d_6 which may attack palladium reversibly the interconversion is much faster leading to dynamic broadening under ambient conditions.



A Major Isomer B Minor Isomer

*Figure 3. Configurations of allyls derived from the nOe data in $CDCl_3$. The observed effect between the isoquinoline H_3 and syn-allyl proton in (**B**) -predicted distance 2.3 A is absent in (**A**) - predicted distance 3.4 A The effect of intracomplex shielding of H_3 is evident in (**A**), δ = 7.72 ppm but not in (**B**) δ = 8.99 ppm.*

In contrast to these observations, the triphenylallyl complex **4d** is a single diastereomer in CD_2Cl_2, with the CPh_2 trans to phosphorus. Its configuration is not known.

In situ studies of catalysis : It was hoped that reaction of the diphenylallyl complex **4c** with malonate ion at low temperatures would reveal directly which of the two diastereomers was involved in catalytic turnover. The experiment was carried out by mixing the allyl and sodium dimethyl malonate at 203K in CD_2Cl_2. No reaction occurred, and on gradual warming the first signs of product formation were evident at 243K. By this temperature, it was also apparent that the presence of the nucleophile led to enhanced rates of interconversion of the two diastereomeric allyls, faster than the rate of nucleophilic attack by malonate ion. Although at this temperature the emergence of signals due to alkene **6a** were apparent, no Pd-bound intermediate could be detected.

Mechanism of allylic alkylation catalysed by QUINAP-Pd.

Several features of the chemistry described above permit a more revealing discussion of mechanism than has previously been possible. We shall address two specific questions - does the nucleophile attack trans to P or to N and can the observed high enantioselectivity be explained in terms of a reasonable transition-state model?

Taking the first of these, we have shown that the absolute configuration of the major diastereomer of allyl **4c** is as drawn in Figure 3. The atomic coordinates of the ligand-Pd component can be obtained from the previously solved X-ray structure[15]; noting that it is the opposite enantiomer to the one employed in catalysis. The implication of the NMR results is clear - either the nucleophile attacks trans to N in the minor diastereomer, or trans to P in the major diastereomer. We prefer the latter explanation for a variety of reasons, and note that Bosnich and co-workers came to a similar conclusion in that the major diastereomer of their Pd-allyl complex, defined by X-ray[3], was the one involved in the nucleophilic addition step. *Firstly*, the reaction of diphenylallyl acetate **5a** with dimethyl malonate and N,O-bis(trimethylsilyl)acetamide is substantially faster than that of either the monophenyl or triphenylallyl analogues **5b** and **5c** under the conditions described above. In both the latter cases **5b** and **5c**, the main product has the malonate entity bonded to the less substituted carbon, and we have shown that this is the carbon trans to the ligand nitrogen in both allylic intermediates. If the reactive allyl terminus must be trans to phosphorus, then an unfavourable equilibrium is traversed before the C-C bond forming step for Pd allyls **4b** (from **5b**) or **4d** (from **5c**) in order to place the reacting allyl terminus trans to P. These allylic alkylations are much slower than that of **5a** where no such pre-equilibrium is required. The cyclohexenyl acetate **5d** is less reactive than **5a**, and this is tentatively attributed to the relative stability's of the corresponding alkene complexes in a product-like transition-state (vide infra). *Secondly*, we note that the level of asymmetric induction in the BSA route is consistently 75% - 79%, independent of the solvent, whilst the equilibrium diastereomer ratio varies from 6:1 to 2:1. This indicates that the transition-state energetics are not influenced by whatever factors cause the discrimination between ground-state diastereomers. *Thirdly*, a comparison may be made between QUINAP and BINAP in catalytic allylic alkylation. The e.e.s are comparable and in the same sense, but the former Pd complex is much more reactive. A likely interpretation is that there is increased steric interaction along the potential energy surface of malonate attack, and that this is much lower in the former case, consistent with attack trans to phosphorus (and hence cis to the sterically less demanding nitrogen).

There is surprisingly little discussion in the literature about the pathway of nucleophilic allylic alkylation. It has not, for example, been the subject of high-level MO calculations[25]. Consider the reaction as illustrated in Figure 4. The trajectory of nucleophilic attack will be such as to form a new sp^3 carbon atom, along a vector in a plane orthogonal to the allyl plane and bisecting the terminal carbon. When the bond is formed, the geometry may

relax to give the most stable rotamer about the C-C bond adjacent to the coordinated double bond, but until that point the stereoelectronic constraints may engender unfavourable steric interactions between ligand and allyl. The later the transition state, the greater are those constraints, since the closer to sp^3 will the reacting terminus be. Some insight into the transition-state structure may be obtained by consideration of the reverse reaction, exemplified by the ionisation of a Pd-bound allylic acetate. This S_N1 step is much more favourable than for triphenylmethyl acetate[26], and a crude estimate is that coordination to palladium accelerates the reaction by about 10^{10}. This requires that the transition state has substantial positive charge on palladium, consistent with a reactant-like geometry which facilitates charge-transfer through vertical stabilisation. The corollary of this is that the nucleophilic attack on an allyl occurs via a late transition-state, and thus brings the steric interaction between ligand and allyl into play. This would further explain the fact that the asymmetric induction is much greater than the diastereomer ratio would predict.

On this basis, a model for the reaction transition-state can be constructed (Figure 4). In both diastereomers, a late transition state with attack trans to nitrogen brings about an unavoidable clash between the allyl and one phenyl group of the PPh_2 fragment, hence attack trans to phosphorus in a product-like geometry is assumed. This entails rotation and translation of the allyl so that it is η^2-bonded leaving the reaction site uncoordinated; partial bonding to the incoming nucleophile causes its rehybridisation towards sp^3. The trajectory of the nucleophile is orthogonal to the original η^3-allyl plane. In the minor diastereomer, (Figure 4 B) this engenders severe and unavoidable steric interactions between H_3 of the isoquinoline and the proximal phenyl group of the diphenylallyl moiety. For the major diastereomer, the related structure (Figure 4 A) is not sterically constrained.

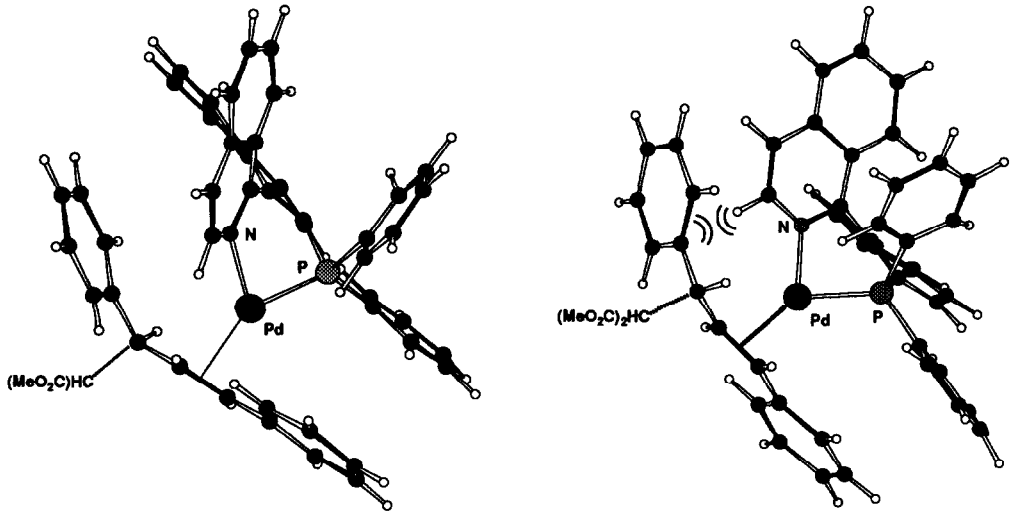


Figure 4. Chem 3-D molecular models of (A) the favoured diastereomer and (B) the disfavoured diastereomer at a late transition-state for malonate nucleophilic attack trans to phosphorus.

The less efficient BSA-derived results are insensitive to changes in solvent, concentration of reactants or the order of reactant and reagent addition; thus it is unlikely that factors such as the relative concentration of the two diastereomers under turnover conditions and the presence or absence of kinetic resolution of the acetate reactant

play a part. The 15-crown-5 reaction occurring *via* a desolvated malonate ion promotes a high level of discrimination between diastereomers.

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Experimental

General. NMR spectra were recorded on a Varian Gemini 200, Bruker AC 200, Bruker AM 250, or Bruker AM 500 spectrometer. ^1H chemical shifts are reported in δ ppm relative to $CHCl_3$ (7.27 ppm), ^{13}C chemical shifts are reported relative to the central peak of $CDCl_3$ (77.0 ppm), and ^{31}P chemical shifts are reported relative to 85% aqueous phosphoric acid (0.0 ppm). Elemental microanalyses were carried out using a Carlo Erba 1106 elemental analyser. Mass spectra were recorded on a BIO-Q spectrometer. IR spectra were recorded on a Perkin Elmer 1750 FT spectrometer. Optical rotations were recorded on a Perkin Elmer 241 polarimeter. Melting points were recorded on a Reichert-Kofler block, and are uncorrected. Solvents were dried immediately before use by distillation from standard drying agents. Sodium tetrafluoroborate, potassium acetate (BDH), silver tetrafluoroborate, dimethyl malonate, N,O-bis(trimethylsilyl)acetamide, 15-crown-5 and $Eu(hfc)_3$ (Aldrich Chemical Co.) were commercially available. Di-μ-chloro-bis(π-allyl)dipalladium[27], di-μ-chloro-bis(1-phenyl-π-allyl)dipalladium[3], di-μ-chloro-bis(1,3-diphenyl-π-allyl)dipalladium[6b], di-μ-chloro-bis(1,1,3-triphenyl-π-allyl) dipalladium[3], propenyl acetates (**5a**, **5b**, **5c**)[3], (S)-1-(2-diphenylphosphino-1-naphthyl)isoquinoline (S-**3**)[15] and cis-[(R)-dimethyl(1-(1-naphthyl)ethyl)aminato-C^2,N]-[(S)-1-(2-diphenylphosphino-1-naphthyl)isoquinoline] palladium (II) hexafluorophosphate[15] were prepared according to literature procedures.

[(S)-1-(2-Diphenylphosphino-1-naphthyl)isoquinoline]-[π-allyl]palladium (II) tetrafluoro borate, 4a.[28] Di-μ-chloro-bis(π-allyl)dipalladium (109.7 mg, 0.3 mmol), (S)-1-(2-diphenylphosphino-1-naphthyl)isoquinoline (263.7 mg, 0.6 mmol) and sodium tetrafluoroborate (197.6 mg, 1.8 mmol) were placed in a Schlenk tube under argon. Degassed chloroform (10 ml) was added *via* syringe to give a yellow suspension which was stirred for 1 day. The solid was removed by filtration, then the solvent was removed *in vacuo* to give [(S)-1-(2-diphenylphosphino-1-naphthyl)isoquinoline]-[π-allyl]palladium (II) tetrafluoroborate (391 mg, 96%) as a pale yellow solid, m.p. 177-182°C. ^1H NMR (500 MHz): δ ($CDCl_3$) 8.95 (d, 1H, J = 6.1 Hz, H_3), 8.08 (d, 1H, J = 8.5 Hz, $H_{4'}$), 8.00 (d, 1H, J = 8.3 Hz), 7.86 (d, 1H, J = 6.1 Hz, H_4), 7.7-7.2 (m, Ar-H), 6.95 (d, 1H, J = 8.7 Hz), 6.90 (br, s, Ph-H), 6.85 (d, 1H, J = 8.6 Hz), 5.97 (br, s, 1H, $CH(CH_2)_2$), 3.9 (vbr, s, 4H, $CH(CH_2)_2$); ^{13}C NMR (62.9 MHz): δ ($CDCl_3$) 157.5 (d, $J_{P,C}$ = 7.5 Hz, C_1), 144.9 (s, C_3), 139.9 (d, $J_{P,C}$ = 14.9 Hz, $C_{1'}$), 137-121 (Ar-C); ^{31}P NMR (101.3 MHz): δ ($CDCl_3$) 31.2 (br, s); λ_{max} (MeOH) 338 (ε/dm^3 mol^{-1} cm^{-1} = 7 400), 222 (72 100) nm; ν_{max} (KBr) 3055 (w) (Ar-H), 1621 (w) (conj C=C), 1591 (w) (conj C=C), 1501 (w) (Ar-H), 1437 (m) (P-Ph), 1059 (br, vs) (B-F), 821 (m) (Ar-H), 749 (s) (Ar-H) and 701 (s) (Ar-H) cm^{-1}; m/z (ES+) 586 (100%, M^+); $[\alpha]_D^{21}$ = -204 (c = 1, $CHCl_3$)

[(S)-1-(2-Diphenylphosphino-1-naphthyl)isoquinoline]-[1-phenyl-π-allyl]palladium (II) tetrafluoroborate, 4b. Di-μ-chloro-bis(1-phenyl-π-allyl)dipalladium (25.9 mg, 0.05 mmol), (S)-1-(2-diphenylphosphino-1-naphthyl)isoquinoline (43.9 mg, 0.1 mmol) and silver tetrafluoroborate (39 mg, 0.2 mmol) were placed in a Schlenk tube under argon. Degassed dichloromethane (2 ml) was added *via* syringe to give a

yellow suspension which was stirred for 1 hour. The solid was removed by filtration, then diethyl ether added to precipitate a yellow solid. The solvent was removed *in vacuo* to give a pale yellow solid, [(S)-1-(2-diphenylphosphino-1-naphthyl)isoquinoline]-[1-phenyl-π-allyl]palladium (II) tetrafluoroborate (72 mg, 96%) as a mixture of at least four diastereomers (the two dominant isomers in a 3:2 ratio accounting for >90% of the mixture in $CDCl_3$), m.p. 202-208°C. ^1H NMR (500 MHz): δ ($CDCl_3$) (major isomer) 8.15 (d, 1H, J = 8.5 Hz, $H_{4'}$), 8.05 (d, 1H), 7.82 (d, 1H, J = 6.1 Hz, H_3), 7.7-6.7 (m, Ar-H), 6.63 (td, 1H, H_b), 5.63 (dd, 1H, $J_{H,H}$ = 13.4, $J_{P,H}$ = 9.5 Hz, H_c), 3.92 (d, 1H, J = 6.7 Hz, $H_{a'}$), 3.17 (d, 1H, J = 11.7 Hz, H_a), (minor isomer) 8.84 (d, 1H, J = 6.2 Hz, H_3), 8.06 (d, 1H), 7.99 (d, 1H, J = 8.3 Hz), 7.7-6.7 (m, Ar-H), 6.20 (td, 1H, J = 12.6, 6.9 Hz, H_b), 5.96 (dd, 1H, $J_{H,H}$ = 12.6, $J_{P,H}$ = 10.3 Hz, H_c), 3.72 (d, 1H, J = 6.2 Hz, $H_{a'}$), 3.17 (d, 1H, J = 12.3 Hz, H_a); ^{13}C NMR (62.9 MHz): δ ($CDCl_3$) 157.6 (d, C_1), 144.0 (s), 141.2 (s), 136.3 (s) 135-124 (Ar-C), 113.8, 101.1, 99.6, 99.1, 55.7, 53.1; ^{31}P NMR (101.3 MHz): δ ($CDCl_3$) 32.6 (s, major), 31.6 (s, minor), 30.4 (s), 27.3 (s); λ_{max} (MeOH) 337 (ε/dm^3 mol^{-1} cm^{-1} = 33 000), 225 (127 500) nm; ν_{max} (KBr) 3055 (w) (Ar-H), 1621 (w) (conj C=C), 1591 (w) (conj C=C), 1437 (m) (P-Ph), 1058 (br, vs) (B-F), 822 (m) (Ar-H), 749 (s) (Ar-H) and 697 (s) (Ar-H) cm^{-1}; m/z (ES+) 662 (100%, M$^+$); $[\alpha]_D^{23}$ = -247 (c = 1, $CHCl_3$).

[(S)-1-(2-Diphenylphosphino-1-naphthyl)isoquinoline]-[1,3-diphenyl-π-allyl]palladium (II) tetrafluoroborate, 4c. Di-μ-chloro-bis(1,3-diphenyl-π-allyl)dipalladium (67.0 mg, .1 mmol), (S)-1-(2-diphenylphosphino-1-naphthyl)isoquinoline (87.9 mg, 0.2 mmol) and silver tetrafluoroborate (77.9 mg, 0.4 mmol) were placed in a Schlenk tube under argon. Degassed dichloromethane (3 ml) was added *via* syringe to give an orange suspension which was stirred for 16 hours. The solid was removed by filtration, then the solution was concentrated *in vacuo* and diethyl ether added to precipitate a yellow solid. The solvent was removed *in vacuo* to give a yellow solid, [(S)-1-(2-diphenylphosphino-1-naphthyl)isoquinoline]-[1,3-diphenyl-π-allyl] palladium (II) tetrafluoroborate (143 mg, 87%) as a mixture of two diastereomers (~2:1 in $CDCl_3$), m.p. 235-238°C. ^1H NMR (500 MHz): δ ($CDCl_3$) (major isomer) 8.12 (d, 1H, J = 8.5 Hz, $H_{4'}$), 8.03 (d, 1H, J = 8.4 Hz, $H_{8'}$), 7.84 (d, 2H, J = 7.1 Hz, o-Ph_a), 7.72 (d, 1H, J = 6.2 Hz, H_3), 7.7-6.7 (m, Ar-H + H_b), 6.59 (d, 1H, J = 8.0 Hz, H_5), 5.82 (dd, 1H, $J_{H,H}$ = 12.1, $J_{P,H}$ = 10.0 Hz, H_c), 4.57 (d, 1H, J = 10.8 Hz, H_a), (minor isomer) 8.99 (d, 1H, J = 6.2 Hz, H_3), 7.98 (2d, 2H, $H_{4'}$ + $H_{8'}$), 7.77 (d, 1H, J = 6.2 Hz, H_4), 7.7-6.7 (m, Ar-H), 6.68 (d, 1H, J = 8.6 Hz, H_5), 6.61 (d, 1H), 6.54 (t, 1H, J = 12.2 Hz, H_b), 6.48 (dd, 2H, $J_{P,H}$ = 11.6, $J_{H,H}$ = 8.2 Hz, o-PhP), 6.12 (dd, 1H, $J_{P,H}$ = 10.0, $J_{H,H}$ = 12.1 Hz, H_c), 5.56 (d, 1H, J = 11.9 Hz, H_a); ^{13}C NMR (62.9 MHz): δ ($CDCl_3$) (major isomer) 157.6 (d, $J_{P,C}$ = 8 Hz, C_1), 141.5 (s, C_3), 140-121 (Ar-C), 112.0 (s, C_a), 98.4 (d, $J_{P,C}$ = 23 Hz, C_c), 72.9 (s, C_b), (minor isomer) 156.5 (d, C_1), 144.1 (s, C_3), 140-121 (Ar-C), 109.8 (s, C_a), 96.5 (d, $J_{P,C}$ = 22 Hz, C_c), 76.3 (s, C_b); ^{31}P NMR (101.3 MHz): δ ($CDCl_3$) 31.2 (s, major), 30.9 (s, minor); λ_{max} (MeOH) 341 (ε/dm^3 mol^{-1} cm^{-1} = 34 900), 224 (125 900) nm; ν_{max} (KBr) 3057 (w) (Ar-H), 1621 (w) (conj C=C), 1593 (w) (conj C=C), 1437 (m) (P-Ph), 1059 (br, vs) (B-F), 824 (m) (Ar-H), 749 (s) (Ar-H) and 696 (s) (Ar-H) cm^{-1}; m/z (ES+) 738 (100%, M$^+$); $[\alpha]_D^{23}$ = -579 (c = 1, $CHCl_3$).

[(S)-1-(2-Diphenylphosphino-1-naphthyl)isoquinoline]-[1,1,3-triphenyl-π-allyl] palladium (II) tetrafluoroborate, 4d. Di-μ-chloro-bis(1,1,3-triphenyl-π-allyl)dipalladium (41.1 mg, 0.05 mmol), (S)-1-(2-diphenylphosphino-1-naphthyl)isoquinoline (43.9 mg, 0.1 mmol) and sodium tetrafluoroborate (33 mg, 0.3 mmol) were placed in a Schlenk tube under argon. Degassed dichloromethane (2 ml) was added *via* syringe to give an orange suspension which turned yellow on stirring for 1 hour. The solid was removed by filtration, then the solvent was removed *in vacuo* to give [(S)-1-(2-diphenylphosphino-1-naphthyl)isoquinoline]-[1,1,3-triphenyl-π-allyl]palladium (II) tetrafluoroborate (90 mg, 100%) as a yellow solid. The solid was crystallised from chloroform / diethyl ether to give the chloroform solvate as dark orange crystals, m.p. 242-244°C. Found: C, 62.3; H, 3.7; N, 1.3. $C_{53}H_{40}NPPdCl_3BF_4$ requires C, 62.3; H, 3.8; N, 1.4%; ^1H NMR (500 MHz): δ ($CDCl_3$) 8.51 (d, 1H, J = 6.0 Hz, H_3), 8.12 (d, 1H, J = 8.3 Hz, H_5), 8.05 (d, 1H, J = 8.4 Hz,

$H_{4'}$), 7.87 (d, 1H, J = 6.2 Hz, H_4), 7.75 (d, 2H, J = 8 Hz, o-Ph_c), 7.70 (t, 1H), 7.69 (d, 1H, J = 8.0 Hz), 7.56 (m, 3H), 7.5-7.25 (m, 8H), 7.19 (t, 1H, J = 8 Hz), 7.06 (d, 1H, J = 8.6 Hz), 7.0-6.93 (m, Ar-H), 6.90 (d, 1H, J = 11.3 Hz, H_b), 6.82 (br, s, 2H, Ph-H), 6.77 (d, 1H, J = 8.7 Hz), 6.70 (dd, 2H, $J_{H,H}$ = 8.7, $J_{P,H}$ = 11.5 Hz, o-PhP), 6.40 (t, 2H, J = 7.4 Hz), 4.49 (d, 1H, J = 11.2 Hz, C_a); ^{13}C NMR (62.9 MHz): δ ($CDCl_3$) 157.3 (d, $J_{P,C}$ = 8.5 Hz, C_1), 142.7 (s, C_3), 139.7 (d, $J_{P,C}$ = 15.1 Hz, $C_{1'}$), 138-123 (Ar-C), 116.1 (d, $J_{P,C}$ = 13.7 Hz, C_c), 110.2 (d, $J_{P,C}$ = 6.0 Hz, C_a), 72.1 (d, $J_{P,C}$ = 5.4 Hz, C_b); ^{31}P NMR (101.3 MHz): δ ($CDCl_3$) 31.8 (s); λ_{max} (MeOH) 342 (ε/dm^3 mol^{-1} cm^{-1} = 17 100) nm; ν_{max} (KBr) 3055 (m) (Ar-H), 1622 (w) (conj C=C), 1592 (w) (conj C=C), 1438 (m) (P-Ph), 1056 (br, vs) (B-F), 750 (s) (Ar-H) and 702 (s) (Ar-H) cm^{-1}; m/z (ES+) 814 (100%, M^+); $[\alpha]_D^{21}$ = -609 (c = 1, $CHCl_3$).

[(S)-1-(2-diphenylphosphino-1-naphthyl)isoquinoline]palladium (II) dichloride. Concentrated hydrochloric acid (5 ml) was added to a solution of cis-[(R)-dimethyl(1-(1-naphthyl) ethyl)aminato-C^2,N]-[(S)-1-(2-diphenylphosphino-1-naphthyl)isoquinoline] palladium (II) hexafluorophosphate (373 mg, 0.42 mmol) in dichloromethane (5 ml) and the mixture stirred for 2 hours. The solvent was removed *in vacuo* to leave an orange solid. The solid was dissolved in dichloromethane (20 ml) then washed with water (20 ml), 10% hydrochloric acid (20 ml), water (20 ml) and saturated brine (20 ml). The solution was dried over magnesium sulphate then the solvent removed *in vacuo* to give [(S)-1-(2-diphenylphosphino-1-naphthyl)isoquinoline] palladium (II) dichloride (214 mg, 83%) as a yellow solid, m.p. 288-290°C. ^1H NMR (500 MHz): δ ($CDCl_3$) 9.58 (d, 1H, J = 6.6 Hz, H_3), 8.12 (dd, 1H, $J_{3',4'}$ = 8.5, $J_{P,H}$ = 2.0 Hz, $H_{4'}$), 8.03 (d, 1H, J = 8.3 Hz, $H_{8'}$), 7.73 (d, 1H, J = 8.2 Hz, H_8), 7.66 (d, 1H, J = 6.6 Hz, H_4), 7.65 (t, 1H, H_7), 7.64 (t, 1H, $H_{7'}$), 7.62 (m, Ph-H), 7.55-7.48 (m, Ph-H), 7.33 (t, 1H, J = 7.8 Hz, $H_{6'}$), 7.30 (t, 1H, J = 8.6 Hz, $H_{3'}$), 7.27 (t, 1H, J = 7.6 Hz, H_6), 7.05 (d, 1H, J = 8.7 Hz, $H_{5'}$), 7.01 (t, Ph-H), 6.95 (d, 1H, J = 8.7 Hz, H_5); ^{13}C NMR (62.9 MHz): δ ($CDCl_3$) 156.0 (d, $J_{P,C}$ = 11 Hz, C_1), 145.6 (s, C_3), 141.4 (d, $J_{P,C}$ = 15 Hz, $C_{1'}$), 137-123 (Ar-C), 121.6 (d, $J_{P,C}$ = 61 Hz, $C_{2'}$); ^{31}P NMR (101.3 MHz): δ ($CDCl_3$) 30.4 (s); λ_{max} (MeOH) 225 (ε/dm^3 mol^{-1} cm^{-1} = 77 300) nm; ν_{max} (KBr) 3056 (w) (Ar-H), 1620 (m) (conj C=C), 1592 (m) (conj C=C), 1436 (s) (P-Ph), 749 (s) (Ar-H), 704 (s) (Ar-H) and 694 (s) (Ar-H) cm^{-1}; m/z (ES+) 580 (100%, M-Cl); $[\alpha]_D^{22}$ = -361.5 (c = 1, $CHCl_3$).

Allylation Procedures. The reactions were carried out using two different procedures; using the preformed malonate ion or generating it *in situ* using BSA / dimethyl malonate. The preformed catalyst **4a** was used in most cases, but similar results were obtained by forming the catalyst *in situ* using (S)-1-(2-diphenylphosphino-1-naphthyl)isoquinoline (S-**3**) and di-μ-chloro-bis(π-allyl)dipalladium. The e.e. of the product was determined by ^1H nmr using the chiral shift reagent Eu(hfc)$_3$ (typically 100 μl of a 0.1M solution in $CDCl_3$ added to the diester (2 mg) in $CDCl_3$ (0.4 ml)). Illustrative reactions are given below:

BSA Procedure. A solution of [(S)-1-(2-diphenylphosphino-1-naphthyl)isoquinoline]-[π-allyl]palladium (II) tetrafluoroborate (3.4 mg, 0.005 mmol) in d_2-dichloromethane (.5 ml) was added to potassium acetate (0.5 mg, 0.005 mmol) in a 5mm nmr tube. The solution was degassed (freeze-thaw), then 1,3-diphenyl-2-propenyl acetate (60 μl, 0.25 mmol), dimethyl malonate (31.5 μl, 0.275 mmol) and N,O-bis(trimethylsilyl)acetamide (68 μl, 0.275 mmol) were added sequentially *via* syringe. The tube was stoppered and shaken to give an orange solution, then the reaction was monitored by ^1H nmr. After 15 minutes the reaction was complete, giving methyl 2-carbomethoxy-3,5-diphenylpent-4-enoate as the only observed product. After 1 hour acetic acid (0.1 ml) was added, then the reaction mixture poured into water (25 ml), extracted into diethyl ether (25 ml), then washed with water (25 ml) and saturated brine (25 ml). The solution was dried over magnesium sulphate, then the solvent removed *in vacuo* to give a yellow oil. Prep. t.l.c. on silica (1:2, diethyl ether / 40-60 petrol) gave (R)-methyl 2-carbomethoxy-3,5-diphenylpent-4-enoate **6a** (42 mg, 52%) as a clear oil, e.e. = 76%. ^1H NMR (500 MHz): δ ($CDCl_3$) 7.4-7.1 (m, 10H, Ph-H), 6.48 (d, 1H, J = 15.8 Hz, H_5), 6.33 (dd, 1H, $J_{3,4}$ = 8.6, $J_{4,5}$ = 15.8 Hz,

H_4), 4.27 (dd, 1H, $J_{2,3}$ = 8.6, $J_{3,4}$ = 10.9 Hz, H_3), 3.95 (d, 1H, J = 10.9 Hz, H_2), 3.70 (s, 3H, OMe), 3.52 (s, 3H, OMe).

Malonate Ion Procedure. Sodium dimethyl malonate (42 mg, 0.275 mmol) was placed in a small vial, acetonitrile (0.3 ml) and 15-crown-5 (55 µl, 0.275 mmol) were added and the resultant white suspension degassed. A solution of 1,3-diphenyl-2-propenyl acetate (63 mg, 0.25 mmol) and [(S)-1-(2-diphenylphosphino-1-naphthyl)isoquinoline]-[π-allyl] palladium (II) tetrafluoroborate (3.4 mg, 0.005 mmol) in acetonitrile (0.1 ml) was added *via* syringe to the vigorously stirred suspension. The yellow suspension was stirred for 1 hour to give a viscous orange suspension. Acetic acid (0.1 ml) was added then the solvent removed *in vacuo*. The reaction mixture was poured into water (25 ml), extracted into diethyl ether (25 ml), then washed with water (25 ml) and saturated brine (25 ml). The solution was dried over magnesium sulphate, then the solvent removed *in vacuo* to give a yellow oil. ^{1}H nmr on the crude product showed complete reaction. Prep. t.l.c. on silica (1:2, diethyl ether / 40-60 petrol) gave (R)-methyl 2-carbomethoxy-3,5-diphenylpent-4-enoate (45 mg, 56%) as a clear oil, e.e. = 95%.When the reaction was carried out on a 10 x scale at 0°C and the product isolated by column chromatography on silica (1:3 diethyl ether / 40-60 petrol) a 95% yield of **6a** was obtained, e.e. = 98%; $[\alpha]_D^{23}$ = +17.9 (c = 1.1, EtOH) [Lit[20]. $[\alpha]_D^{23}$ = +18.4 (c = 1.1, EtOH for enantiomerically pure material)].

Reaction of 1,1,3-triphenyl-2-propenyl acetate **5c** with sodium dimethyl malonate in CD_2Cl_2 over 4 days (60% reaction) gave a 45% yield of (S)-methyl 2-carbomethoxy-3,5,5-triphenylpent-4-enoate **6d**, e.e. = 47%. ^{1}H NMR (250 MHz): δ ($CDCl_3$) 7.5-7.0 (m, 15H, Ph-H), 6.34 (d, 1H, J = 10.6 Hz, H_4), 4.23 (t, 1H, J = 10.4 Hz, H_3), 3.89 (d, 1H, J = 10.3 Hz, H_2), 3.69 (s, 3H, OMe), 3.47 (s, 3H, OMe); $[\alpha]_D^{22}$ = +17.9 (c = 2, $CHCl_3$).

Reaction of 3-phenyl-2-propenyl acetate **5b** with sodium dimethyl malonate in CH_3CN over 1.5 hours (100% reaction) gave a mixture of **6b** and **6c** (~85:15) which was not separated. Methyl 2-carbomethoxy-5-phenylpent-4-enoate **6b**, ^{1}H NMR (250 MHz): δ (CD_2Cl_2) 7.4-7.1 (m, 5H, Ph-H), 6.47 (d, 1H, J = 15.8 Hz, H_5), 6.15 (dt, 1H, J = 15.8, 7.2 Hz, H_4), 3.70 (s, 6H, OMe), 3.53 (t, 1H, J = 7.5 Hz, H_2), 2.77 (t, 2H, J = 7.3 Hz, H_3). Methyl 2-carbomethoxy-3-phenylpent-4-enoate **6c**, ^{1}H NMR (250 MHz): δ (CD_2Cl_2) 7.4-7.1 (m, 5H, Ph-H), 5.98 (ddd, 1H, J = 17.0, 10.1, 8.2 Hz, H_4), 5.10 (d, 1H, J = 17.0 Hz, H_5), 5.06 (d, 1H, J = 10.1 Hz, H_5), 4.07 (dd, 1H, J = 11.1, 8.2 Hz, H_3), 3.87 (d, 1H, J = 11.1 Hz, H_2), 3.45 (s, 3H, OMe), 3.37 (s, 3H, OMe).

Reaction of 2-cyclohexenyl acetate **5d** (175 mg, 1.25 mmol) with sodium dimethyl malonate in CH_3CN over 16 hours (68% reaction) and isolation of the product by column chromatography on silica (1:3 diethyl ether / 40-60 petrol) gave a 60% yield of (R)-dimethyl cyclohex-2-enylmalonate, e.e. = 67%. ^{1}H NMR (250 MHz): δ ($CDCl_3$) 5.79 (m, 1H, =CH), 5.54 (m, 1H, =CH), 3.75 (s, 3H, OMe), 3.74 (s, 3H, OMe) 3.30 (d, 1H, J = 9.5 Hz, $C\underline{H}(CO_2Me)_2$), 2.92 (m, 1H, CH), 2.00 (m, 2H, CH_2), 1.9-1.5 (m, 3H, CH_2), 1.40 (m, 1H, CH_2); $[\alpha]_D^{23}$ = 24.4 (c = 2.6, $CHCl_3$) [Lit[8]. $[\alpha]_D^{23}$ = 15.6 (c = 2.6, $CHCl_3$) for 50% e.e.].

Stoichiometric Reaction. [(S)-1-(2-Diphenylphosphino-1-naphthyl)isoquinoline]-[1,3-diphenyl-π-allyl]palladium (II) tetrafluoroborate (20.6 mg, 0.025 mmol) was placed in a 5mm nmr tube and d_2-dichloromethane (0.2 ml) added and degassed to give an orange solution. A solution of sodium dimethyl malonate (4.2 mg, 0.0275 mmol) and 15-crown-5 (110 µl, 0.0275 mmol) in d_2-dichloromethane (0.2 ml) was added *via* syringe and whirlimixed to give a deep purple solution. ^{1}H nmr after 5 minutes showed that the reaction was complete. After 30 minutes the reaction mixture was worked up as described in the BSA procedure to give methyl 2-carbomethoxy-3,5-diphenylpent-4-enoate (6.0 mg, 74%) as a clear oil, e.e. = 89%.

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