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Asymmetric allylic alkylation catalyzed by Pd(II)-complexes with (*S*)-BINPO, a hemilabile axially chiral P,O-heterodonor inducer

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Abstract—A complex generated in situ from $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ and (*S*)-BINPO **1** is an active catalyst in the asymmetric allylic alkylation of 1,3-diphenyl-2-propenyl esters **6** via a malonate anion with ee's up to 81% being obtained. Rate and stereoselectivity of the reaction are dramatically influenced by the solvent. The Pd-complex [(*S*)-(BINPO)Pd(η^3-1,3-diphenylallyl)] **5** has been synthesized and its structure in the solid state determined by X-ray diffraction. The stoichiometric reaction of **5** with malonate anion affords the alkylated product of the same configuration as the one obtained in the catalytic reaction at room temperature in nearly identical enantiomeric purity (71%).

1. Introduction

Bidentate P,X-heterodonor ligands where the chelate coordination of a phosphino group (P) is supported by a different heteroatom (X) display a peculiar catalytic behaviour due to the presence of two donors of diverse ligating properties. Within this class of derivatives, mixed ligands with a phosphorus and an oxygen as substitutionally inert and labile donors, respectively, usually display a pronounced hemilabile character.[1]

Easily dissociable donors may readily provide vacant coordination sites around the metal. This fact may be useful whenever dissociation of an ancillary ligand to give a coordinatively unsaturated species is required for the complex to be catalytically active. Furthermore, the presence of a coordinative site in the proximity of the metal may be helpful in stabilizing, and possibly permitting the interception of otherwise labile short-lived intermediates involved in the catalytic cycle.

The P,O-association of donors is one of the most commonly exploited in the search for improved performances of a complex in a catalytic reaction where a dissociative step is critically involved at some stage of the process. This concept is illustrated at its best by the success encountered by the catalytic system utilized in the SHOP process more than 25 years ago.[2] Several additional examples of significant value of this strategy can be found in the recent literature.[3]

The advantage of the use of hemilabile ligands is not immediately apparent in the case of metal catalyzed asymmetric reactions. In these processes, strong donors, which tightly bind the metal seem better suited for steering the complex towards the rigid conformational arrays, which are considered appropriate for obtaining high enantioselectivities. This is probably one of the main reasons why the use of hemilabile ligands as chiral auxiliaries has been overlooked for so long.

Recently, however, an increased number of heterodonor ligands have been designed for the use in asymmetric catalysis with hemilability being more frequently encountered in this field.[4] Among chiral P,O-hemilabile derivatives, the binaphthalene-scaffolded axially chiral phosphinyl phosphane **1** (BINPO,[5] BINAP monophosphine oxide) has attracted the attention of several

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different research groups, which in recent years have repeatedly reported both on synthetic and applicative aspects of its chemistry.

BINPO provides moderate to good stereoselectivities in a variety of metal catalyzed asymmetric processes. In a range of addition reactions to styrene, for instance, the ee's fluctuated in between 70% (Pd-catalyzed hydrosilylation)[6] and 30% (hydroformylation with Pt–Sn catalysts)[7] and 40% (Rh-catalyzed hydroboration).[8] Higher stereoselectivities, up to 99%, have been more recently reported in the asymmetric Diels–Alder reaction of cyclopentadiene with methacrolein catalyzed by diastereomerically pure (η^6-cymene)Ru(BINPO) complexes.[9] BINPO itself, in the absence of any transition metal, can participate in promoting the nonenzymatic kinetic resolution of secondary alcohols.[10]

Over the course of these studies, several transition metal complexes incorporating BINPO have been prepared and structurally characterized. As a general trend, it has been observed that BINPO displays a sharp propensity towards bidentate binding to transition metal centres. Some derivatives of Pd(II)[6,11] and Rh(I)[12] where BINPO displays a 'normal' P,O-chelate coordination have been isolated and characterized by NMR and X-ray diffraction. The P,O-chelate coordination of BINPO to (η^6-cymene)Ru-complexes is remarkable in that it proceeds with complete stereoselectivity affording one single diastereomeric complex.[13]

The inherent electronic disparity of the donors of the chelating arms of BINPO is mainly responsible for the selectivity shown by some BINPO complexes in the oxidative addition of aryl iodide (Pd)[11] and in the insertion of tin chloride into the metal–chloride bond (Pt).[14] The formation of one single isomer in reactions such as these may have important bearings in addressing the selectivity of the reactions where these complexes are involved as catalysts.

In addition to the P,O-chelate binding mode, BINPO can display a different hapticity as has been noticed in the coordination to Pd(0)[11] and to some L_2Ru(II)-complexes (L_2 = bipy or phen).[15] Therein the ligand acts as a six-electron donor, adding to the P and O atoms, a η^2-arene coordination of the naphthyl group proximate to the oxidized P atom.

Direct experimental evidence of the hemilabile behaviour of BINPO has only been collected in the case of Pt(II)[7] and Pd(II)[11] derivatives where ^{31}P NMR monitoring clearly shows that opening of the chelate ring involving displacement of the oxygenated arm of BINPO readily takes place in the presence of competitive donors. The role, if any, of species such as these in the catalytic reactions supported by these complexes, that is, hydroformylation[7] and hydrosilylation,[6] is still to be cleared.

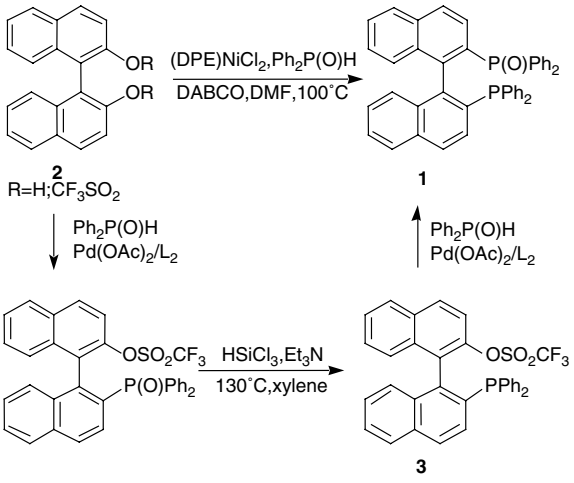
The results reported above stimulated us to expand the scope of this hemilabile ligand in asymmetric catalysis. Herein we report on the behaviour of BINPO in the Pd-catalyzed allylic alkylation of 1,3-diphenyl-2-propenyl esters by a malonate anion.

2. Results and discussion

2.1. Synthesis of BINPO

Although the first report on the isolation of enantiopure BINPO dates back to 1992, when the (*R*)-isomer was obtained as a co-product in the preparation of Pd(0)[(*R*)-BINAP]$_2$ from palladium(II) diacetate and (*R*)-BINAP,[16] the first preparation of any practical value of this ligand was reported by some of us in 1998.[6] Soon after, Grushin developed a simple and efficient synthesis of phosphine–phosphine oxides which relies on the Pd-catalyzed selective mono-oxidation of the homotopic P atoms of C_2-symmetrical bis-phosphines. Application of this procedure to enantiopure BINAP allows BINPO of the same configuration to be isolated in some 80% yield.[17]

In our original methodology,[6] racemic BINPO was synthesized from 2,2′-dihydroxy-1,1′-binaphthalene **2** (R = H; BINOL) through a four step reaction procedure involving the Pd-catalyzed sequential substitution of the homotopic triflate groups of the BINOL ditriflate **2** (R = SO_2CF_3) by diphenylphosphine oxide (Scheme 1).[18] Resolution of the racemate was accomplished by complexation to an enantiopure chloride-bridged C,N-cyclopalladated complex.



Scheme 1.

The same route can also be adopted for the preparation of enantiopure BINPO from enantiopure BINOL as we routinely did in the following years when enantiopure BINOL became more and more accessible.

For the preparation of BINPO congeners, we have now devised a novel and more expedient route relying on a Ni-catalyzed cascade reaction of the ditriflate **2** with a diarylphosphine oxide, which allows the homotopic triflate groups of the substrate to be sequentially

substituted in a single process affording the corresponding mono-phosphine oxide in a fair to good isolated yield.[19]

Although some details of this reaction are still to be cleared, ^{31}P NMR monitoring shows that the reaction proceeds through the intermediate formation of the phosphino triflate **3**, which undergoes the fast substitution of the second triflate by diphenylphosphine oxide. Small amounts of BINAP, arising from the reaction of **3** with diphenylphosphine are simultaneously formed. Evidence has been collected that suggests **3** originates from the reaction of the ditriflate **2** with diphenylphosphine and that this latter reagent is formed in the early stages of the reaction by disproportionation of diphenylphosphine oxide.

2.2. Synthesis of [Pd(η^3-C_3H_5)Cl(BINPO-κ^1P,O)] complex 4

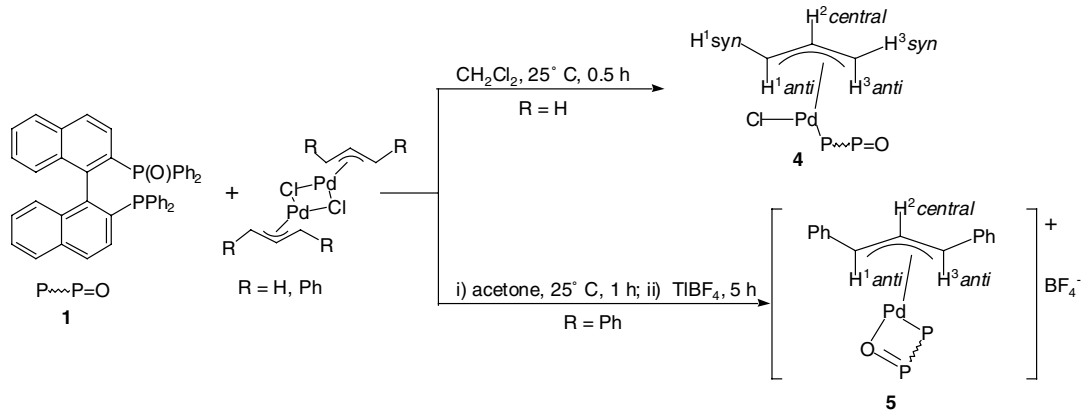
The synthesis of the [Pd(η^3-C_3H_5)Cl(BINPO-κ^1P,O)] complex was carried out by reacting the appropriate amount of [Pd((η^3-C_3H_5)Cl]$_2$ dimer with 2 equiv of the enantiopure, (*S*)-BINPO **1** ligand in CH_2Cl_2 at room temperature under a nitrogen atmosphere (Scheme 2). It is apparent from the ^{31}P NMR spectra of the isolated neutral complex **4** that the ligand is bound to the metal in a monodentate fashion. For free (*S*)-BINPO, ^{31}P NMR signals appear at $\delta = -16.3$ ppm (PPh_2) and 26.1 ppm ($OPPh_2$), while for complex **4** two different signals appear at 26.8 ppm ($OPPh_2$) and 25.0 ppm (PPh_2). The 41.3 ppm downfield shift observed for the PPh_2 phosphorous atom and the nearly unchanged position of the $OPPh_2$ resonance provide a strong indication that only the PPh_2 group is coordinated to the metal as observed for other complexes of this ligand.[7]

^1H NMR spectrum in $CDCl_3$ at 298 K showed several overlapping signals between 7.5 and 6.2 ppm corresponding to the 32 aromatic protons of (*S*)-BINPO ligand. Only a well defined triplet at 6.48 ppm ($J = 7.5$ Hz) and a doublet at 6.24 ppm ($J = 8.5$ Hz) were observed in the aromatic region. At higher fields the allylic protons showed a pseudoquintuplet at 5.28 ppm ($J = 10$ Hz) assigned to the central allylic hydrogen and a broad triplet at 4.42 ppm ($J = 7$ Hz) assigned to *syn*-hydrogen atom located in the carbon *trans* to the coordinated phosphorus atom of the (*S*)-BINPO ligand. The proposal was based on the ^1H–^{13}C heterocorrelation and on reported values for similar complexes.[20] Although only two broad signals at 3.30 and 2.81 ppm were observed, the peaks in between 3.70–2.40 ppm integrate three hydrogens corresponding to one *anti* proton *trans* to the P atom and to both the terminal protons in *cis* position respect to the P. This provides an indication of the dynamic behaviour of neutral compound **4** in solution. Accordingly, 2D NOESY experiment shows exchange signals between all terminal protons. This fact suggests that the two well documented dynamic processes of Pd-allyl complexes are operative:[21,22] the first is the apparent rotation around Pd-allylic bond exchanging *anti–anti* and *syn–syn* protons on different terminal carbon atom; the second being the π–σ–π mechanism exchanging *syn–anti* protons on the carbon atom that retains the σ bond with the palladium centre.

^{13}C NMR spectrum at 298 K shows three signals in the allylic region that can be unambiguously assigned to the three carbon atoms of the C_3H_5 ligand, central C^2 at 117.9 ppm, terminal carbon C^1 that appears as a doublet at 78.6 ppm ($J_{PC} = 31$ Hz) and a broad singlet at 63.9 ppm assigned to C^3. ^{13}C–^1H heterocorrelation allowed us to assign the H *anti trans* to the phosphorus atom to the broad signal at 3.3 ppm.

2.3. Variable temperature experiments

^1H NMR variable temperature experiments have been recorded within the range 223–323 K. A selection of the ^1H NMR spectra in the allylic region is shown in Figure 1 showing the broadening of the signals on lowering the temperature. At 238 K, the existence of two different isomers in a ratio 1/1 was evidenced. There are two isomers of complex **4** when considering the Pd(allyl)ClP fragment as shown in Scheme 3. Extending Cahn, Ingold, and Prelog rules to define the configuration in these systems and considering the metal as the stereogenic centre, we can design (*R*)-**4** or (*S*)-**4** owing to the clockwise or anticlockwise assignment of priorities as described by Faller et al.[22] The H *central* appears as two



Scheme 2.

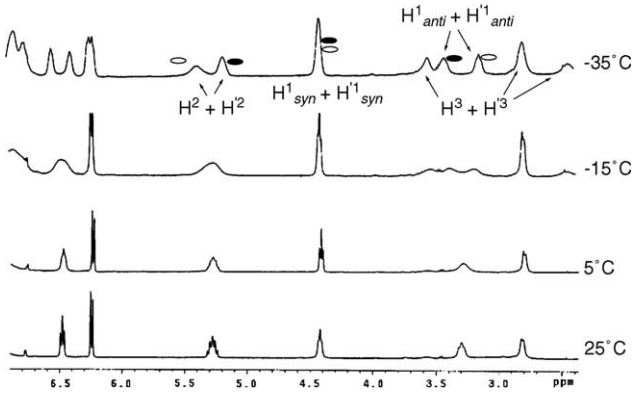
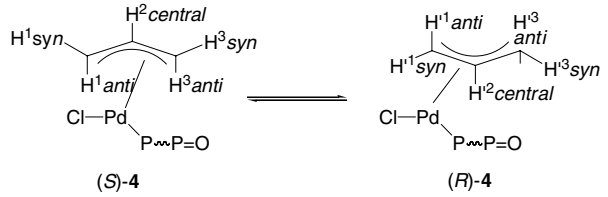


Figure 1. Selection of ^{1}H NMR spectra at different temperatures of compound **4**.



Scheme 3.

broad signals at 5.4 and 5.2 ppm and H*syn* at the *trans* position to the phosphorous atom as a single signal at 4.4 ppm. Moreover, two broad signals at 3.4 and 3.1 ppm are clearly defined and can be assigned to the H^1*anti* and H$^{1\prime}$ *anti* based on the heterocorrelation ^{1}H–^{13}C at 238 K. Terminal protons at the *cis* position to the P atom appear at 3.5 (1H), 2.8 (2H) and 2.5 (1H) ppm. 2D COSY experiment shows that signals at 5.4, 4.4 and 3.1 ppm belong to one isomer, while signals at 5.2, 4.4 and 3.4 to the other one. 2D ROESY experiment at 238 K only shows exchange signals between H^2*central*–H$^{2\prime}$*central* and H^1*anti*–H$^{1\prime}$*anti* suggesting that the predominant exchange mechanism between both isomers at 238 K may be a π–σ–π process, proceeding by opening the Pd–C allylic bond *trans* to the P atom. At this temperature, Pd–allylic rotation probably occurs at slower rates since exchange between H^1*anti* and H$^{3\prime}$*anti* is not observed.

^{31}P NMR was run at 238 K in $CDCl_3$ solution. Three different signals appear, one at 26.94 ppm assigned to $P(O)PPh_2$ not coordinated, that has the same chemical shift as observed at 298 K and two signals of the same intensity but lower than the first one at 25.73 and 25.4 ppm assigned to the P atom coordinated to the metal (PPh_2) of each one of the isomers.

^{1}H NMR spectra at 323 K was also run. The central proton appears as a well defined quintuplet suggesting equivalency of the four terminal allylic hydrogen atoms but the signals of the terminal allylic protons appear as broad signals between 4.8–2.5 ppm indicating rapid interconversion between them, probably through both π–σ–π and Pd–allyl rotation mechanisms.

2.4. Reaction of 4 with $TlBF_4$

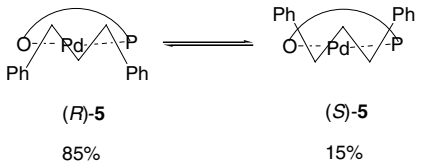
Reaction of neutral complex **4** with a stoichiometric amount of $TlBF_4$ for 30 min at room temperature in $CDCl_3$ led to a suspension that decomposed after 1 h. Nevertheless the reaction was followed by ^{1}H and ^{31}P NMR spectroscopy. ^{31}P NMR spectrum shows one sharp signal at 26 ppm (PPh_2) and a broad one centered at 31.8 ppm ($OPPh_2$). The 5 ppm shift downfield of the $OPPh_2$ phosphorous atom is indicative of the presumed formation of a cationic complex through chelate coordination of BINPO via P and O donor atoms; however this species is not stable in these conditions. The appearance of the broad signal at 31.8 ppm suggests that the oxygen atom may be involved in a continuous coordination–decoordination process. The ^{1}H NMR spectrum shows in the allylic region a pseudoquintuplet at 5.35 ppm (H*central)*, a broad signal at 4.53 ppm (H*syn trans* P), a broad triplet at 3.44 ppm (H*anti trans* P) and a very broad signal between 3.4–2.6 ppm (H*syn* and H*anti cis* P). The last very broad signals suggest a rapid interconversion of the two protons at the *cis*-position with respect to the coordinated P atom, through the π–σ–π mechanism that is favoured when the Pd–C bond *trans* to the P atom is open.

2.5. Synthesis of $[Pd(\eta^3\text{-}Ph_2C_3H_5)(BINPO\text{-}\kappa^2P,O)]BF_4$ ionic complex 5

The synthesis of **5** was carried out via reaction of 1,3-diphenylallylpalladium chloride dimer with stoichiometric amounts of (*S*)-BINPO and $TlBF_4$ in acetone at room temperature to produce [Pd(η^3-1,3-diphenylallyl)((*S*)-BINPO-κ^2P,O)]BF_4 (Scheme 2). The preparative reaction was monitored by ^{31}P. No cleavage of the chloro bridge took place in the absence of $TlBF_4$.

Due to the presence of two isomers in solution, the ^{31}P NMR spectrum in $CDCl_3$ of complex **5** showed four signals, at 40.7 and 25.9 ppm for the major isomer and at 42.5 and 27.2 ppm for the minor one. It is readily apparent from these chemical shifts that the diarylphosphinyl and diarylphosphine groups are both coordinated, with the signals at lower fields being assigned to the $OPPh_2$ and those at higher fields to the PPh_2 groups, respectively. ^{31}P NMR in CD_3COCD_3 at room temperature only shows one slightly broad signal at 20.0 ppm and a very broad signal at 40.0 ppm. This fact suggests that the coordinating solvent exchanges rapidly with the $OPPh_2$ group in the coordination sphere, leading to a broadening of the phosphorus resonance as previously observed with Pt(II) complexes with BINPO ligand.[7]

^{1}H NMR spectra of **5** in $CDCl_3$ solution were also consistent with the existence of two isomers in a 85/15 ratio (Scheme 4). The allylic protons of the major isomer appeared as a doublet at 4.58 ppm ($J_{(HH)} = 10.5$ Hz) and two pseudotriplets at 5.60 ppm ($J_{(HH)} = 10.0$ Hz) and 6.03 ppm ($J_{(HH)} = 11.5$ Hz). At 273 K, the pseudotriplet at 5.60 was separated into a doublet of doublets, $J_{(PH)} = 8.7$ and $J_{(HH)} = 12.9$ Hz, suggesting a location



Scheme 4.

trans to the P atom. Taking into account the values of the coupling constants between vicinal protons and reported data,[23] we assigned the doublet at 4.58 ppm to the terminal allylic H atom *cis* to the phosphorus, the triplet at 6.03 ppm to the central allylic H atom and the geometry of the 1,3-diphenylallyl system assumed to be *syn*/*syn*.

The allylic protons of the minor isomer appeared as broad signals centered at 4.14, 5.87 and 6.30 ppm. According to their chemical shifts (similar to those of the major isomer) we proposed a *syn*/*syn* structure for the allyl group and assigned them to the H atom *cis* and *trans* to the phosphorus, and central, respectively. The analysis of the signals thus indicate that the two *syn*/*syn* isomers differ in the orientation of the 1,3-diphenylallyl group respect the Pd-(*S*)-BINPO fragment. As shown in Scheme 4 and following Faller et al. nomenclature[22] we can design (*R*)-**5** and (*S*)-**5** each one of the isomers.

The aromatic region showed a complex pattern, with two groups of multiplets between 6.43–7.60 and 8.08–8.13 ppm and two well separated doublets at 5.78 and 8.60 ppm for the major isomer. COSY experiments allow us to identify five contiguous aromatic protons of the same phenyl ring (5.78, 6.51, 7.40, 8.10, 8.60 ppm).

NOESY spectra at 500 MHz, in $CDCl_3$ showed NOE contacts between terminal allylic H *trans* P, central allylic H and aromatic protons at 7.6 ppm (presumably two *ortho* hydrogens of the phenyl allylic group *trans* to P atom). Besides strong NOE contacts between the two *anti* protons of the allyl group of the major isomer, exchange signals between allylic protons of both isomers are observed. The dynamic process was consistent with a pseudorotation through the Pd–allylic bond. ^{13}C NMR spectrum shows chemical shifts similar to those reported for P,N-ligands[24] at 109.4 (*central*, s) ppm, 103.8 (*trans* P, d, $J_{PC} = 14$ Hz) and 67.3 (*cis* P, s) ppm for the major isomer.

Crystals suitable for X-ray determinations were obtained after crystallization from CH_2Cl_2–hexane. A view of the allylic cation and the most representative parameters of the structure are reported in Figure 2 and Table 1.

The crystal contained discrete units of **5** in which (*S*)-BINPO acts as a bidentate ligand providing an eight-membered chelate ring with an irregular, partly boat-like conformation. The palladium coordination sphere was closely square planar (the distances of Pd, C(3), C(1), O and P from the mean plane defined by these atoms are small, less than 0.040 Å). The structure shows

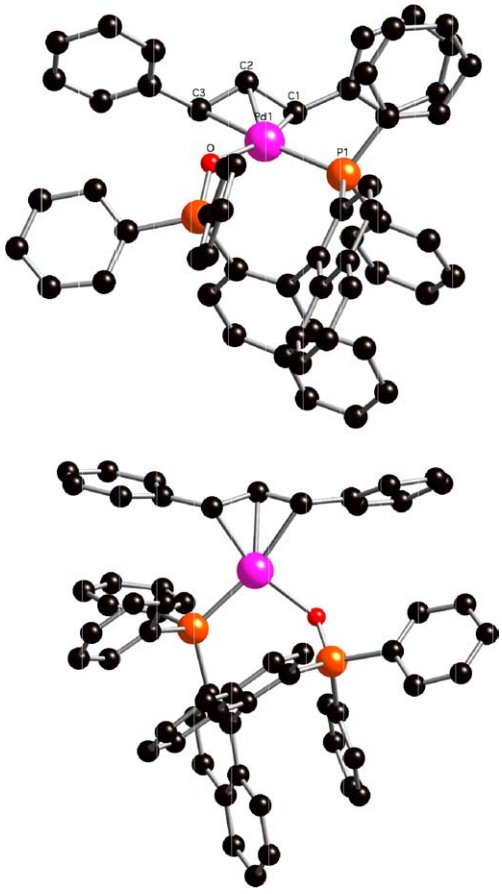


Figure 2. Representation of the cationic fragment of **5** with the numbering scheme emphasizing the geometry of the coordination sphere.

Table 1. Selected bond lengths (Å) and bond angles (°) for **5** [Pd(η^3-$Ph_2C_3H_3$)((*S*)-BINPO–*P*,*O*)]BF_4·CH_2Cl_2

	Bond lengths		Bond angles
Pd–O	2.101(6)	P(1)–Pd–O	98.46(16)
Pd–P(1)	2.3214(19)	C(1)–Pd–C(3)	67.1(3)
Pd–C(1)	2.113(9)	C(1)–Pd–P(1)	100.0(2)
Pd–C(2)	2.139(8)	C(3)–Pd–O	94.4(3)
Pd–C(3)	2.253(7)		
C(1)–C(2)	1.447(12)		
C(2)–C(3)	1.364(12)		

that the diphenylallyl group adopts a *syn*/*syn* configuration and that the phenyl groups of the allyl ligand and the naphthyl groups of the (*S*)-BINPO ligand are located at the opposite side of the coordination plane as described in Scheme 2. The formation enthalpy of both diasteromers were studied by means of theoretical calculations at PM3 (tm) level [255.138 Kcal/mol for the (*R*)-**5** isomer and 257.355 Kcal/mol for the (*S*)-**5** one] showing that the (*R*)-**5** disposition was more stable. The bond lengths are within the reported values,[6] but the Pd–P bond is longer than reported for similar complexes with P,N-ligands.[24a] Furthermore, the C(1)–Pd bond (2.113(9) Å) was significantly shorter than the C(3)–Pd bond [2.253(7) Å] according to the stronger *trans* influence of the phosphorus atom compared with oxygen atom. The terminal allylic carbons C(1) and C(3) were 0.069(7) and 0.157(7) Å below the P(1)–Pd–O

plane. The allyl group was bound rather asymmetrically to the Pd-atom. The allylic C–C bond *trans* to P was closer to the double bond 1.364(12) Å than the C–C bond *trans* to O 1.447(12) Å as reported for nonsubstituted allylic complexes.[25] The chelate bond angle O–Pd–P(1) was 98.46(16)° rather than 90.9(1)° as reported in cyclometallated Pd(II) complexes with a BINPO ligand.[24b] A similar trend was detected when comparing the chelate angles of a cyclometallated Pd(II) complex and a diphenylallyl Pd(II) complex with the same P,N-ligand (1-methyl-2-diphenylphosphino-3-(1′-isoquinolyl)-indole).[26]

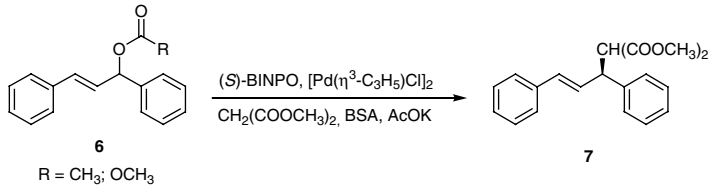
The naphthyl rings of the binaphthyl framework showed a torsion angle, C(28), C(37), C(38), C(47) of 73.916°. A significant-stacking interaction involves one of the phenyl substituents on each P atom and the phenyl ring, which is more remote from the metal of each naphthyl group of the binaphthalene template. The dihedral angles between the mean planes of the stacked aromatic rings are 13.6(4)° and 11.9(5)° for the interaction involving the naphthyl rings C(31)–C(36) and C(39)–C(44) and the distances between the centre of the aromatic rings being of 3.649 and 3.58 Å, respectively. Moreover the phenyl allylic group on C(1) and one of the phenyl's of the PPh_2 substituent adopt a nearly parallel stacked configuration. The dihedral angles between the mean planes of the aromatic rings C(4)–C(9) and C(16)–C(21) was 2.7(6)°. The distance between the center of both rings was 3.876 Å. This third interaction probably contributed to the adoption of an ideal square planar geometry as reported.[27]

2.6. Catalytic allylic alkylation of 1,3-diphenyl-2-propenyl esters

The Pd-catalyzed asymmetric allylic substitution of 1,3-diphenyl-2-propenyl esters **6** with the dimethyl malonate–BSA–potassium acetate system was successfully carried out in the presence of the catalyst generated in situ from $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ and (*S*)-BINPO (Scheme 5).

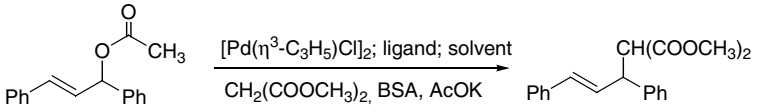
Rate and stereoselectivity of the reaction are strongly dependent on the solvent (Tables 2 and 3) and for a complete conversion to be achieved quite different reaction times were required. Chlorinated solvents performed far better than hydrocarbon or oxygenated counterparts, chloroform being the most effective of the list. The solvent effect was as pronounced as to be the cause of a switch of handness from the (*S*)- to the (*R*)-configured product in moving from the chlorinated solvents to toluene (Table 2, entry 3).

The stereoselectivities were almost identical for both the acetate (R = Me) and the carbonate (R = OMe) esters and improve slightly when decreasing the temperature in the range 298–223 K. The best ee (81%) was obtained in chloroform at 0 °C. At lower temperatures (−40 °C), the reaction was sluggish while after 12 h, the catalyst apparently underwent an irreversible deactivation. Notably, in this reaction BINAP was by far less stereoselective (25–35% ee depending on the conditions) and led to the alkylated product of opposite configuration.[28]



Scheme 5.

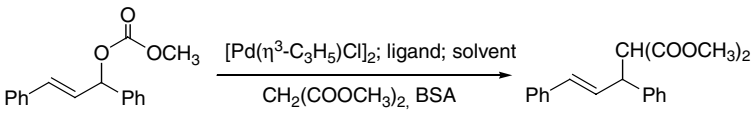
Table 2. Allylic alkylation of 1,3-diphenylallyl acetate by in situ Pd/(*S*)-BINPO catalyst



Solvent	*T* °C	*t*	Ee%	Configuration
THF	25	15 m	10	*S*
DMF	25	7 h	0	—
Toluene	25	1.5 h	6	*R*
$ClCH_2CH_2Cl$	25	40 m	48	*S*
CH_2Cl_2	25	20 m	47	*S*
CH_2Cl_2	0	1 h	50	*S*
CH_2Cl_2	−40	2 h	51	*S*
CH_2Cl_2	−50	2.5 h	51	*S*
$CHCl_3$	25	1.5 h	72	*S*
$CHCl_3$	0	4	81	*S*
CH_2Cl_2[a]	25	3.2 h	32	*R*
THF[a]	25	70 h	35	*R*

[a] Chiral ligand (*S*)-BINAP.

Table 3. Allylic alkylation of 1,3-diphenylallyl carbonate by in situ Pd/(*S*)-BINPO catalyst



Solvent	*T* °C	*t*	Ee%	Configuration
CH_2Cl_2	25	20 m	47	*S*
CH_2Cl_2	0	1.5 h	48	*S*
CH_2Cl_2	−20	2 h	56	*S*
CH_2Cl_2	−40	2.5 h	60	*S*
THF	25	15 m	32	*S*
CH_2Cl_2[a]	25	1.5 h	25.5	*R*

[a] Chiral ligand (*S*)-BINAP.

It is well known that the enantioselectivity in Pd-catalyzed allylic alkylation with soft reagents is controlled by nucleophilic attack at the more electrophilic terminal allylic carbon atom in Pd(II) intermediate **5**.[29] As described above, **5** is a 85:15 mixture of two isomers (*R*)-**5** and (*S*)-**5**, the former being the major one. The stereochemical outcome and the observed enantiomeric excess [72% in (*S*)] can be rationalized if we assume that the nucleophilic attack proceeds at similar rates onto the allylic carbon of the two isomers *trans* to the P-donor. This is the more electrophilic carbon as inferred by the longer bond length C^3–P and higher ^{13}C chemical shift.

2.7. Stoichiometric allylic alkylation

In order to confirm the source of enantioselectivity, we carried out the stoichiometric allylic alkylation of the preformed complex **5**. The reaction was run in $CHCl_3$ at room temperature with stoichiometric amounts of the nucleophile under basic conditions as used for the catalytic process. The change in colour was immediate, indicating a fast reaction. The enantiomeric excess of the alkylation product (71%) was close to the value observed in the catalytic reaction in the same solvent. This result provides further support to the reaction path formulated above.

3. Experimental

3.1. General methods

All compounds were prepared under a purified nitrogen atmosphere using standard Schlenk and vacuum-line techniques. $[Pd(\eta^3\text{-}C_3H_5)(\mu\text{-}Cl)_2]$[30] and $[Pd(\eta^3\text{-}Ph_2C_3H_3)(\mu\text{-}Cl)]_2$[31] were prepared as described previously. NMR spectra were recorded on a Bruker DRX 500 (^1H, standard $SiMe_4$, 2D NMR experiments), Bruker Unity 300 (^{13}C, standard $SiMe_4$) and Bruker DRX 250 (^1H, ^{13}C standard $SiMe_4$, ^{31}P standard H_3PO_4) spectrometers in $CDCl_3$ unless otherwise cited. Chemical shifts were reported downfield from standards. IR spectra were recorded on a FTIR Nicolet Impact 400 spectrometers. FAB mass chromatograms were obtained on a Fisons V6-Quattro instrument. Enantiomeric excesses were determined by HPLC on a CHIRACEL OD column using hexane–*i*-PrOH, 99:1, as eluent, at a flow rate of 0.3 $cm^3\,min^{-1}$ and pressure 10 bar. Elemental analyses were carried out by the Serveis Cientifico-Tècnics de la Universitat de Barcelona in an Eager 1108 microanalyzer.

3.2. Synthesis of (*S*)-BINPO 1

A solution of diphenylphosphinoxide (1.84 g, 9.1 mmol) in DMF was added to a solution of $NiCl_2$ (dppe) (0.1 g, 0.182 mmol) in DMF (5 mL) under nitrogen. The mixture was stirred at 100 °C for 30 min, then a solution of (*S*)-BINOL ditriflate (1 g, 1.82 mmol) and DABCO (0,82 g, 7.32 mmol) in DMF (10 mL) were added. The mixture was stirred at 100 °C for 12 h. After cooling to room temperature, degassed water was added and the resulting yellow solid filtered off. After washing several times with water, the precipitate was dissolved in CH_2Cl_2, dried and evaporated. The residue was purified by flash chromatography on silica gel using petroleum ether–ethyl acetate (3:2) as eluent to give BINPO (45%) and BINAP (20%). BINPO: mp 230–233 °C; ^1H NMR ($CDCl_3$): δ(ppm) = 6.63 (d, J = 8.1 Hz, Ar, 1H), 6.72 (dt, J = 1.2, 6.6 Hz, Ar, 1H), 6.81–7.43 (series of m, Ar, 23H), 7.60 (m, Ar, 3H), 7.69 (d, J = 8.1 Hz, Ar, 1H), 7.74 (d, J = 8.4 Hz, Ar, 1H), 7.82 (d, J = 7.8 Hz, Ar, 1H), 7.93 (dd, J = 2.4, 8.4 Hz, Ar, 1H); ^{31}P NMR ($CDCl_3$): δ(ppm) = −14.25 (s), 28.51 (s); $[\alpha]_D^{20} = -92.2$ (*c* 1.02, $CHCl_3$). BINAP: ^1H NMR ($CDCl_3$): δ(ppm) = 7.0–8.0 (series of m, Ar, 23H), ^{31}P NMR ($CDCl_3$): δ(ppm) = −13.04.

3.3. Synthesis of $[Pd(\eta^3\text{-}C_3H_5)Cl(BINPO\text{-}\kappa^1P,O)]$ 4

A mixture of $[Pd(\eta^3\text{-}C_3H_5)(\mu\text{-}Cl)]_2$ (28 mg, 0.078 mmol) and (*S*)-BINPO (100 mg, 0.156 mmol) was stirred in dichloromethane (10 cm^3) under nitrogen for 1 h at room temperature. The solvent was removed under reduced pressure, affording a pale yellow solid. Recrystallization from dichloromethane/diethylether (1/1). Yield 77 mg (60%). Anal. Found: C, 67.99; H, 4.59. Calcd for $PdClC_{47}H_{37}OP_2C$, 68.71 ; H, 4.54. MS (FAB positive). m/z 785 ($[M-Cl]^+$). NMR data ($CDCl_3$ 298 K): 1H (500 MHz): 8.04–6.09 ppm (32H aromatic); 5.28 ppm (pq, J = 10 Hz, 1H); 4.42 ppm (pt, J = 7 Hz, 1H) ; 3.70–2.40 ppm (3H); ^{31}P NMR (101 MHz): 26.8 ppm (s);

25.0 ppm (s); ^{13}C NMR (75 MHz): allylic carbons: 117.9 ppm (s), 78.6 ppm (d, $J_{(PC)} = 31$ Hz); 63.9 ppm (s).

3.4. Synthesis of [Pd(η³-$Ph_2C_3H_3$)(BINPO-κ²O,P)]BF_4 5

A mixture of [Pd(η³-$Ph_2C_3H_3$)(μ-Cl)]$_2$ (67 mg, 0.1 mmol) and (*S*)-BINPO (130 mg, 0.2 mmol) was stirred in acetone (25 cm^3) under nitrogen for 1 h. The resulting suspension was treated with $TlBF_4$ (58 mg, 0.2 mmol). After 5 h, the mixture was filtered through a pad of Celite and the solution concentrated in vacuo to leave a yellow solid. Recrystallization from dichloromethane–diethylether (1:5), gave 125 mg (61% yield) of a mixture of two isomers (85:15) followed by ^1H NMR in $CDCl_3$. Crystals suitable for X-ray analysis were obtained from CH_2Cl_2–hexane. Anal. Found: C, 66.57; H, 4.76. Calcd for $C_{59}H_{45}BF_4OP_2Pd{\cdot}CH_2Cl_2$: C, 64.92; H, 4.27. MS (FAB positive). *m/z* 938 ([M−BF_4]$^+$). NMR data ($CDCl_3$ 298 K): 1H (500 MHz): major isomer: 4.58 ppm [d, $^3J_{(HH)} = 10.5$, 1H], 5.60 ppm (pt, $J_{(HH)} = 10.0$ Hz, 1H), 5.78 ppm [d, $J^3_{(HH)} = 8.5$ Hz 1H), 6.03 ppm (pt, $J_{(HH)} = 11.5$ Hz, 1H), 6.43–7.60 ppm (40H), 8.08–8.13 ppm (m, 2H), 8.60 ppm (d, $^3J_{(HH)} = 7.5$ Hz, 1H); minor isomer (allylic protons): 4.14 (br s), 5.87 (br s), 6.30 (br s), ^{31}P NMR (101 MHz): major isomer: 40.7 ppm (s, $OPPh_2$), 25.9 ppm (s, PPh_2), minor isomer: 42.5 (s, $OPPh_2$), 27.2 ppm (s, PPh_2); ^{13}C NMR (63 MHz): allylic carbons major isomer: 109.4 ppm (s), 103.8 ppm (d, $J_{(P,C)} = 14$ Hz); 67.3 ppm (s).

3.5. Crystallography

The crystallographic data are summarized in Table 1. Yellow crystals of [Pd(η³-$Ph_2C_3H_3$)(BINPO-κ²O,P)]BF4 **3** were obtained by slow diffusion of *n*-pentane over dichloromethane solution of the ionic complex. The complex crystallizes with one molecule of dichloromethane.

A prismatic crystal (0.1 × 0.1 × 0.2 mm) was selected and mounted on a MAR345 diffractometer with a image plate detector. Unit-cell parameters were determined from automatic centering of 14381 reflections ($3< \theta <31$) and refined by least-squares method. Intensities were collected with graphite monochromatized Mo-K_α radiation($\lambda = 0.71069$ Å). 22086 reflections were measured in the range 2.43–25.00°. 4606 of which were nonequivalent by symmetry (R_{int} (on I) = 0.088). 3568 reflections were assumed as observed applying the condition $I > 2\sigma(I)$. Lorentz-polarization but no absorption corrections were made. The structure was solved by direct methods, using the SHELXS computer program[32] and refined by the full-matrix least-squares method with SHELX 97 computer program,[33] using 4606 reflections, (very negative intensities were not assumed). The function minimized was $\Sigma w||F_o|^2 - |F_c|^2|^2$, where $w = [\sigma^2(I) + (0.1217P)^2]^{-1}$, and $P = (|F_o|^2 + 2|F_c|^2)/3$, values of f, f' and f'' were taken from Ref. 34. The absolute configuration of the structure was defined from the Flack coefficient, which it is equal to 0.07(5) for the given results.[35] All H atoms were computed and refined, using a riding model, with an isotropic temperature factor equal to 1.2 time the equivalent temperature factor of the atom which are linked. The final *R* (on *F*) factor was 0.054, wR (on $|F|^2$) = 0.141 and goodness of fit = 0.950 for all observed reflections. The number of refined parameters was 615. Max. shift/esd = 0.0, Mean shift/esd = 0.0. Max. and min. peaks in final difference synthesis were 0.899 and −0.538 e$Å^{-3}$, respectively (CCDC 231370).

3.6. General procedure for palladium-catalyzed allylic alkylation

A solution of [Pd(η³-C_3H_5)Cl]$_2$ (2 mg, 0.01 mmol) and the free ligand (13 mg; 0.02 mmol) in CH_2Cl_2 (1 mL) was stirred at rt under nitrogen. After 30 min a solution of 1,3-diphenylprop-2-enyl acetate (50 mg, 0.2 mmol) in CH_2Cl_2 (0.5 mL) was added. Dimethyl malonate (80 mg, 0.6 mmol), *N*,*O*-bis(trimethylsilyl)acetamide (BSA) (122 mg, 0.6 mmol) dissolved in CH_2Cl_2 (1.5 mL) and potassium acetate (0.6 mg, 0.006 mmol) were added to the reaction mixture. Stirring continued at the required temperature until complete conversion was attained. The reaction mixture was diluted with ether (25 mL) and washed with saturated NH_4Cl. The organic phase was dried over Na_2SO_4, concentrated under reduced pressure and the residue purified by flash chromatography (light petroleum–ether, 3:1) to give dimethyl[(*S*)-1,3-diphenylprop-2-enyl]malonate. Ee's were determined from the integrals of the methoxy groups of (1,3-diphenylprop-2-enyl)malonate, as split by the chiral shift reagent europium tris[3-(trifluoromethylhydroxymethylene)-(+)-camphorate].

3.7. Stoichiometric allylic alkylation

Ionic complex **3** (75 mg, 0.073 mmol), was dissolved in 0.7 mL of $CHCl_3$ and stirred at room temperature under nitrogen for 30 min. Dimethyl malonate (29 mg, 0.219 mmol), BSA [*N*,*O*-bis(trimethylsilyl)acetamide] (45 mg, 0.219 mmol) and a catalytic amount of potassium acetate were added with 2 mL of $CHCl_3$. The mixture was stirred at room temperature for 45 min. The solution was then diluted with diethyl ether (8 mL) and washed with an aqueous solution of NH_4Br (10%) and water (3 × 10 mL). The organic phase was dried over anhydrous Na_2SO_4, filtered and the solvent removed under reduced pressure. The product was purified by column chromatography (SiO_2; ethyl acetate–hexane, 1:5) to give dimethyl [(*S*)-1,3-diphenylprop-2-enyl]malonate in 71% ee.

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