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Palladium-catalysed allylic alkylations and aminations with hetero- and homoannularly bridged bidentate ferrocene ligands

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Abstract

Sets of hetero- and homoannularly bridged ferrocenyl aminophosphine and diphosphine ligands were investigated in palladium-catalysed allylic alkylation and amination reactions ([1-PPh_2-2,1′-(α-R-$CH(CH_2)_2$)-ferrocene]: (R_c,R_p)-**1**: R = $N(CH_3)_2$; (R_c,R_p)-**4**: R = PPh_2; (R_c,R_p)-**5**: R = PCy_2; ([1-PPh_2-2,3-(α-R-$CH(CH_2)_3$)-ferrocene]: (R_c,R_p)-**2**: R = $N(CH_3)_2$; (S_c,R_p)-**3**: R = $N(CH_3)_2$; (S_c,R_p)-**6**: R = PPh_2; (S_c,R_p)-**7**: R = PCy_2). Diphenylprop-2-en-1-yl acetate and pent-3-en-2-yl acetate were used as the substrates and dimethyl malonate or benzylamine as the nucleophiles. Catalytic data were analysed and compared to those of PPFA (**8**) and Josiphos-type (**9**, **10**) ligands ([1-PPh_2-2-(α-R-$CHCH_3$)-ferrocene]: (S_c,R_p)-**8**: R = $N(CH_3)_2$; (S_c,R_p)-**9**: R = PPh_2; (S_c,R_p)-**10**: R = PCy_2). Correlations between changes in enantioselectivity or absolute configuration of product and changes in ligand backbones or functional groups were assessed. Cationic palladium(II) diphenylallyl complexes of ligands **1**, **4**, **5** and **7** were isolated and their conformational behaviour in solution was analysed both as the isolated complexes and under catalytic conditions. The molecular structure of complex **7C** (*endo syn*/*syn* form) was determined by X-ray diffraction.

Keywords: Ferrocene; Palladium; Phosphines; Allylic alkylation; Allylic amination

1. Introduction

Catalytic nucleophilic substitution reactions involving palladium-allyl intermediates are very powerful tools for the formation of carbon–carbon or carbon-heteroatom bonds [1–5]. Although such reactions have been investigated for more than two decades, interest in ligand development, synthetic applications and mechanistic considerations of enantioselective allylic alkylations and aminations remains high [6–14]. Several classes of ligands have been identified as being particularly able to promote such reactions with exceptionally high enantioselectivity. Amongst others, these classes include phosphinooxazolines, diphosphinodiamides, naphthylisoquinoline, binaphthoazepine and ferrocene derivatives [15–17]. 1,3-Diphenylallyl acetate or carbonate is frequently used as a first test substrate and, when reacted with a (usually bidentate) ligand and an appropriate palladium source, leads to a cationic intermediate (Scheme 1). In many cases, this intermediate palladium allyl cation is present in solution not only as a mixture of *exo* and *endo* isomers but it can also adopt different *syn*/*syn* and *syn*/*anti* structures. Addition of a soft nucleophile—such as deprotonated dimethyl malonate—to one of the coordinated allyl termini of this intermediate results in the final product. Several strategies to improve enantioselectivity by controlling both electronic and steric properties of the ligand (and as a consequence of the intermediate palladium allyl complex) have been studied, particularly with ferrocene ligands. Hayashi and Ito showed that the trajectory of the incoming nucleophile can be controlled by means of secondary interactions between the nucleophile and a non-coordinated functional group of the ligand [18–21]. In another approach, Togni made use of P,N-chelating pyrazole-modified ferrocenyl ligands and showed that, as with phosphinooxazolines [22–31] or naphthylquinolines [32], for electronic reasons the approach of the nucleophile—if not overruled by steric interactions

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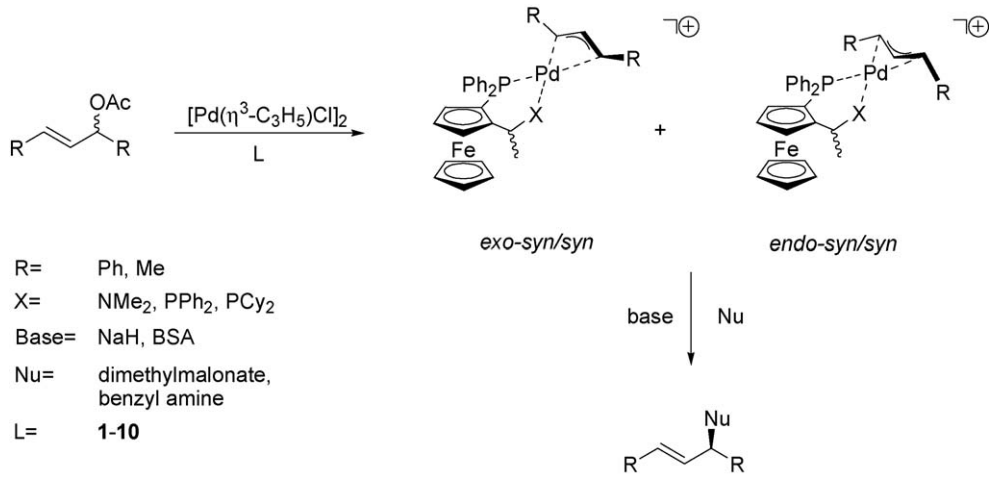

Scheme 1. Allylic alkylation and amination reactions: reaction 1: R = Ph, Nu = dimethyl malonate; reaction 2: R = Me, Nu = dimethyl malonate; reaction 3: R = Ph, Nu = benzylamine; product configuration shown: Nu = dimethyl malonate: (*S*), Nu = benzylamine: (*R*).

[11]—is likely to occur *trans* to phosphorus [17,33–36]. Togni also showed that even the use of simple ferrocenyl diphosphine ligands like Josiphos (Chart 1, **10**) can give a product with >90% e.e. [37]. In general, the course of the overall reaction is controlled not only by the electronic and steric properties of the palladium allyl intermediate but also depends on the type of substrate, the palladium source, the leaving group, the counteranion and the base, as well as on the presence of additives such as fluoride ions or crown ethers [38]. Furthermore, Pregosin pointed out that when rather flexible ligands are used in allylic alkylations, different chelate conformations may be populated and may alter the overall course of the reaction. A Josiphos allyl complex was given as an example of this phenomenon [39].

Some time ago we reported the synthesis of a number of aminophosphine and diphosphine ligands, all of which were based on either a heteroannularly or a homoannularly bridged ferrocenyl backbone (Chart 1, **1**–**7**) [40–43]. Applications of these systems in catalytic reactions, including hydrogenations, have also been reported [44]. As compared to Josiphos-type ligands, both the hetero- and the homoannularly bridged backbones are rather stiff and therefore limit the accessible segment of space for each functional group to a rather narrow volume. This restriction significantly reduces the problem of potential chelate flexibility. In addition, ferrocenes **1**–**10** constitute three groups of ligands that each have identical functional groups but slightly different backbones (aminophosphines **1**–**3** and

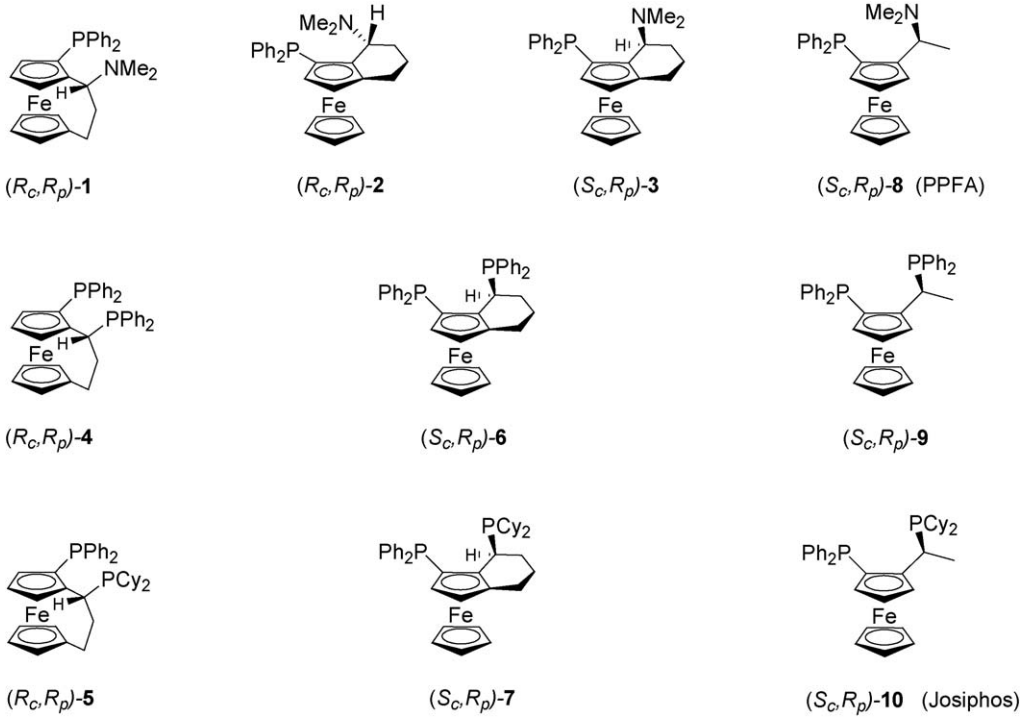

Chart 1.

8, bisdiphenylphosphines **4**, **6** and **9**, and diphenylphosphinodicyclohexylphosphino derivatives **5**, **7** and **10**) and three groups of ligands with identical backbones but different sets of functional groups (**1**, **4**, **5**; **3**, **6**, **7**, and **8**–**10**; see Chart 1). It was anticipated that these sets of ligands would allow a study into the dependence of enantioselectivity on defined structural changes of the backbone and functional groups.

In this paper we describe allylic alkylations with ligands **1**–**7** and allylic aminations with ligands **4**–**7**. For the sake of comparison, allylic alkylations were also carried out with PPFA (**8**) and, in addition, the data previously reported for ligands **9** and **10** have been taken into account in the discussion [37]. It should be mentioned that we focused primarily on a qualitative comparison of ligands **1**–**10** rather than on mechanistic considerations. However, some of our experimental results will be discussed in terms of the reported mechanistic proposals.

2. Experimental

2.1. General methods

All manipulations were carried out under an atmosphere of argon using standard Schlenk techniques. Solvents were distilled from the appropriate drying agents and degassed before use. Elemental analyses were performed with a Thermo Quest FlashEA 1112 microanalyser. ^{1}H NMR and ^{31}P{^{1}H} NMR spectra were recorded on a Varian Unity 300 MHz spectrometer and ^{13}C{^{1}H} NMR spectra on an INOVA Varian 500 MHz or a Bruker 250 MHz spectrometer. For ^{1}H-^{13}C *g*-HSQC and *g*-HMQC spectra the standard VARIAN pulse sequences were used (VNMR 6.1 C software). The spectra were acquired using 7996 Hz (^{1}H) and 25133.5 Hz (^{13}C) widths; 16 transients of 2048 data points were collected for each of the 256 increments. Chemical shifts (ppm) are relative to TMS (^{1}H, ^{13}C) or 85% H_3PO_4 (^{31}P). Standard experimental conditions were employed. The NOE difference spectra were recorded with the following acquisition parameters: spectral width 5000 Hz, acquisition time 3.27 s, pulse width 90°, relaxation delay 4 s, irradiation power 5–10 dB, number of scans 240. COSY spectra: standard pulse sequence, acquisition time 0.214 s, pulse width 10 μs, relaxation delay 1 s, 16 scans, 512 increments. In the NMR data s, d, t, m and C_q refer to singlet, doublet, triplet, multiplet and quaternary carbon. The derivatives [Pd(η^3-1,3-$Ph_2C_3H_3$)Cl]$_2$ [45] and [Pd(η^3-C_3H_5)Cl]$_2$ [46] and ligands **1** [40,47], **2**–**3** [42,48], **4**–**7** [44] and **8** [49] were prepared according to published procedures. AgOTf (OTf = CF_3SO_3) was purchased from Aldrich. When referring to isomers, **M** and **m** stand for major and minor isomer, respectively (see Chart 2 for the atom numbering scheme). The cationic 1,3-diphenylallyl palladium complexes of ligands **1**, **4**, **5** and **7** (**1C**, **4C**, **5C** and **7C**) were prepared according to the following equation:

$$[Pd(PhCHCHCHPh)Cl]_2 + 2AgOTf + 2L \rightarrow 2[Pd(PhCHCHCHPh)(L)]OTf + 2AgCl \quad L = \mathbf{1}, \mathbf{4}, \mathbf{5}, \mathbf{7}$$

All complexes were characterised by NMR spectroscopy in $CDCl_3$ and elemental analysis. In addition, single crystals for X-ray diffraction were obtained for complex **7C**. The molecular structure of **7C** is shown in Fig. 1. For selected bond lengths and bond angles see the caption for Fig. 1. For crystallographic data, see below.

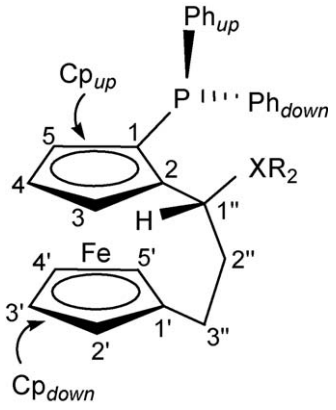

Chart 2. Atom numbering scheme for ligands **1**, **4** and **5**.

2.2. Standard procedure for the synthesis of 1,3-diphenylallyl complexes [Pd(η^3-1,3-$Ph_2C_3H_3$)(L)]OTf (L = **1**, **4**, **5**, **7**)

A solution of 1,3-diphenylallyl-palladiumchloride dimer [Pd($Ph_2C_3H_3$)Cl]$_2$ (67 mg, 0.1 mmol) and AgOTf (50.4 mg, 0.2 mmol) in dry THF (4 ml) was stirred for 4 h at room temperature. The precipitated AgCl was filtered off and the appropriate ligand **1**, **4**, **5** or **7** (0.2 mmol) was added to the filtrate. The mixture was stirred for a further 3 h at room temperature, the solvent was removed in vacuo and the residue was recrystallised from CH_2Cl_2/hexane.

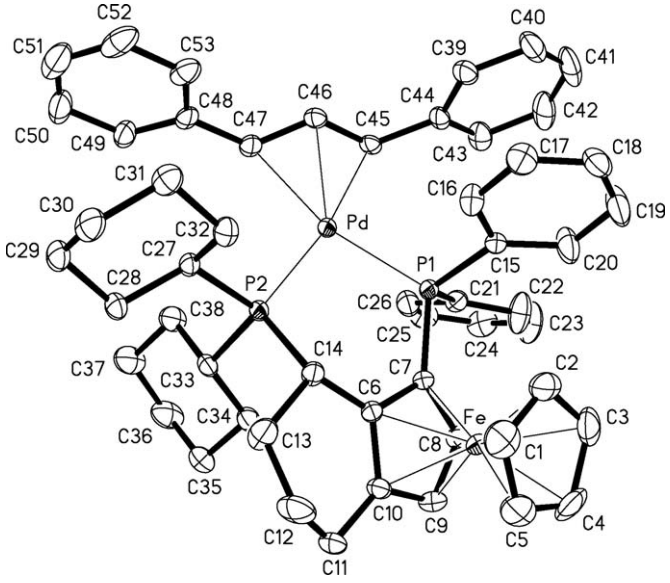

Fig. 1. Molecular structure of **7C** (complex 1); the anion has been removed for clarity; selected bond lengths (Å) and bond angles (°): Pd–P(1) 2.2936(12), Pd–P(2) 2.3228(12), Pd–C(45) 2.250(4), Pd–C(46) 2.206(4), Pd–C(47) 2.290(4), C(45)–C(46) 1.405(6), C(46)–C(47) 1.387(6), C(47)–C(48) 1.475(7), P(1)–Pd–P(2) 96.26(4), C(6)–C(7)–P(1) 126.4(3), C(6)–C(14)–P(2) 112.9(3).

*2.2.1. Synthesis of [Pd(η^3-1,3-$Ph_2C_3H_3$)(R_c,R_p-**1**)]OTf (**1C**)*

Compound **1** (90.6 mg, 0.2 mmol) gave **1C** (144 mg, 0.16 mmol, 80%). $C_{43}H_{41}F_3FeNO_3PS$ (795.71): Calc. C, 64.91; H, 5.19; N, 1.76. Found: C, 64.75; H, 5.38; N, 1.97. ^{1}H NMR (300 MHz, $CDCl_3$), **1C M**: δ some Ph signals have been identified: 8.21 (dd, 2H, $J_{H\text{-}P}$ = 12.0 Hz, $J_{H\text{-}H}$ = 7.3 Hz, CH_{ortho}Ph$_{down}$), 6.34 (dd, 2H, $J_{H\text{-}P}$ = 11.2 Hz, $J_{H\text{-}H}$ = 7.3 Hz, CH_{ortho}Ph$_{up}$), 7.8–6.6 (rest of Ph signals), 6.17–6.25 [2H, AB part of an ABX system; A and B: central and terminal (*trans* to P) allyl protons, X = P], 5.43 (d, 1H, $J_{H\text{-}H}$ = 9.8 Hz, H$_{allylic,transN}$), 4.34 (s, 1H, C*H*Cp$_{up}$), 4.20 (s, 1H, C*H*Cp$_{up}$), 4.01 (s, 1H, C*H*Cp$_{down}$), 3.87 (s, 1H, C*H*Cp$_{up}$), 3.74 (s, 1H, C*H*Cp$_{down}$), 3.64 (s, 1H, C*H*Cp$_{down}$), 2.68 (s, 3H, NMe$_{down}$), 2.30 (s, 3H, NMe$_{up}$), 2.07 (s, 1H, C$H^{5'}$ Cp$_{down}$), 3.1–1.7 (m, 5H, heteroannular chain). **1C m**: three signals have been identified, 5.55 (dd, 1H, $J_{H\text{-}H}$ = 13.7 Hz, $J_{H\text{-}P}$ = 7.8 Hz, H$_{allylic,transP}$), 4.43 (s, 1H, C*H*Cp), 4.26 (s, 1H, C*H*Cp). ^{13}C{^{1}H} NMR (125 MHz), **1C M**: 138–127 (Ph), 136.8 (d, $J_{C\text{-}P}$ = 14.9 Hz, CH_{ortho}Ph$_{down}$), 130.6 (d, $J_{C\text{-}P}$ = 11.2 Hz, CH_{ortho}Ph$_{up}$), 129.2 (d, $J_{C\text{-}P}$ = 11.3 Hz, CH_{meta}Ph$_{down}$), 128.4 (d, $J_{C\text{-}P}$ = 10.1 Hz, CH_{meta}Ph$_{up}$), 111.4 (d, $J_{C\text{-}P}$ = 6.5 Hz, C$H_{allyl,central}$), 99.7 (d, 1C, $J_{C\text{-}P}$ = 23.2 Hz, C$H_{allyl,transP}$), 89.5 (s, 1C, C_qCp), 88.2 (d, 1C, $J_{C\text{-}P}$ = 21.0 Hz, C_qCp), 76.2 (s, 1C, *C*HCp$_{up}$), 73.3 (s, 1C, C$^{5''}$ Cp$_{down}$), 73.0 (s, 1C, C$H_{allyl,transN}$), 72.7 (s, 1C, C$^{1''}$), 72.4 (d, $J_{C\text{-}P}$ = 9.9 Hz, 1C, *C*HCp$_{up}$), 72.1 (s, 1C, *C*HCp$_{down}$), 71.4 (s, 1C, *C*HCp$_{down}$), 70.4 (d, 1C, $J_{C\text{-}P}$ = 6.1 Hz, *C*HCp$_{up}$), 68.4 (s, 1C, *C*HCp$_{down}$), 54.6 (s, 1C, N*C*H$_{3,down}$), 50.5 (s, 1C, N*C*H$_{3,up}$), 43.0 (d, $J_{C\text{-}P}$ = 4.0, 1C, C$^{2''}$), 24.8 (s, 1C, C$^{3''}$). **1C m**: two signals have been identified: 53.1 (s, 1C, N*C*H$_{3,down}$), 51.6 (s, 1C, N*C*H$_{3,up}$). ^{31}P{^{1}H} NMR (121 MHz, $CDCl_3$), **1C M**: 21.81 (s). **1C m**: 18.02 (s).

*2.2.2. Synthesis of [Pd(η^3-1,3-$Ph_2C_3H_3$)(R_c,R_p-**4**)]OTf (**4C**)*

Ligand **4** (118.8 mg, 0.2 mmol) gave compound **4C** (183 mg, 0.17 mmol, 88%). $C_{53}H_{45}F_3FeO_3P_2S$ (936.82): Calc. C, 67.95; H, 4.84. Found: C, 67.78; H, 5.01. ^{1}H NMR (300 MHz, $CDCl_3$), **4C M**: δ some Ph signals have been identified: 8.17 (bs, 2H, CH_{ortho}Ph$_{down}$), 5.92 (dd, 2H, $J_{H\text{-}P}$ = 11.2 Hz, $J_{H\text{-}H}$ = 7.1 Hz, CH_{ortho}Ph$_{up}$), 7.8–6.6 (rest of Ph), 6.29 (t, 1H, H$_{allyl,central}$), 6.14 (ddd, 1H, $J_{H\text{-}H}$ = 13.7 Hz, $J_{H\text{-}Pchain}$ = 10.5 Hz, $J_{H\text{-}PCp}$ = 2.7 Hz, H$_{allyl,transPchain}$), 5.36 (td, 1H, $J_{H\text{-}PCp}$ = $J_{H\text{-}H}$ = 12.4 Hz, $J_{H\text{-}Pchain}$ = 2 Hz, H$_{allyl,transPCp}$), 3.96 (t, 1H, $J_{H\text{-}P}$ = 2.3 Hz, Cp$_{up}$), 3.89 (s, 1H, C*H*Cp$_{down}$); 3.71 (s, 1H, C*H*Cp$_{down}$), 3.51 (s, 1H, C*H*Cp$_{down}$), 2.11 (s, 1H, H$^{5'}$, Cp$_{down}$), Cp signals of either isomer: 4.30 (s), 4.12 (s), 3.89 (s), 3.79 (s), 3.71(s), 3.0–1.2 (heteroannular chain). **4C m**: some signals have been identified: 7.2 (1H, H$_{allyl,central}$, overlapped signal), 5.07 (t, 1H, $J_{H\text{-}P} \approx J_{H\text{-}H}$ = 13 Hz, H$_{allyl,transPCp}$), 4.09 (1H, H$_{allyl,transPchain}$, overlapped signal), 4.05 (t, 1H, $J_{H\text{-}P}$ = 2.4 Hz, C*H*Cp$_{up}$), 3.45 (s, 1H, C*H*Cp$_{down}$), 1.98 (s, 1H, H$^{5'}$,Cp$_{down}$). ^{13}C{^{1}H} NMR (62.9 MHz), **4C M**: 138–127 (Ph), 111.5 (s, C$H_{allyl,central}$), 94.5 (d, 1C, $J_{C\text{-}P}$ = 28.7 Hz, C$H_{allyl,\ terminal}$), 90.5 (d, 1C, C_qCp), 89.7 (d, 1C, $J_{C\text{-}P}$ = 25.6 Hz, C$H_{allyl,terminal}$), 87.5 (s, 1C, C_q-Cp), *C*H, Cp: 91.5–90.5, 76.3, 73.5, 73.3, 72.9, 72.4, 69.5 and 69.0; 41.6 (s, 1C, C$^{2''}$), 36.2 (d, $^1J_{C\text{-}P}$ = 24.0 Hz, C$^{1''}$), 25.2 (s, 1C, C$^{3''}$). ^{31}P{^{1}H} NMR (121 MHz, $CDCl_3$), **4C M**: 43.69 (d, $J_{P\text{-}P}$ = 76.9 Hz, P$_{chain}$), 15.29 (d, P$_{Cp}$). **4C m**: 47.64 (d, 1P, $J_{P\text{-}P}$ = 80.6 Hz, P$_{chain}$), 12.22 (d, 1P, P$_{Cp}$).

*2.2.3. Synthesis of [Pd(η^3-1,3-$Ph_2C_3H_3$)(R_c,R_p-**5**)]OTf (**5C**)*

Ligand **5** (124 mg, 0.2 mmol) gave complex **5C** (176 mg, 0.16 mmol, 80%). $C_{53}H_{57}F_3FeO_3P_2S$ (948.92): Calc. C, 67.09; H, 6.05. Found: C, 67.34: H, 6.16. ^{1}H NMR (500 MHz, $CDCl_3$), **5C M**: δ some Ph signals have been identified: 8.01 (mt, 2H, CH_{ortho}Ph$_{down}$), 6.31 (dd, 2H, $J_{H\text{-}P}$ = 10.7 Hz, $J_{H\text{-}H}$ = 7.4 Hz, CH_{ortho}Ph$_{up}$), 7.9–6.5 (rest of Ph signals), 6.02 (t, 1H, H$_{allylic,central}$), 5.72 (t, 1H, $J_{H\text{-}H}$ = 13.9 Hz, $J_{H\text{-}P}$ = 11.0 Hz, H$_{allylic,transPCy2}$), 5.42 (t, 1H, $J_{H\text{-}H}$ = 11.8 Hz, $J_{H\text{-}P}$ = 11.6 Hz, H$_{allylic,transPPh2}$), 4.45 (s, 1H, C*H*Cp$_{up}$), 4.19 (m, 1H, C*H*Cp$_{up}$), 4.01 (s, 1H, C*H*Cp$_{down}$), 3.89 (s, 1H, C*H*Cp$_{up}$), 3.83 (s, 1H, C*H*Cp$_{down}$), 3.79 (s, 1H, C*H*Cp$_{down}$), 2.79 (t, $J_{H\text{-}P}$ = $J_{H\text{-}H}$ = 13.0 Hz, H$^{1''}$), 1.82 (s, 1H, H$^{5'}$, Cp$_{down}$), 2.85–0.5 (Cy and heteroannular chain). **5C m**: ∼6.6 (1H, partially overlapped, H$_{allylic,central}$), 4.96 (t, 1H, $J_{H\text{-}H}$ = 13.7 Hz, $J_{H\text{-}P}$ = 12 Hz, H$_{allylic,transPPh2}$), 4.58 (s, 1H, C*H*Cp$_{up}$), 4.30 (m, 1H, C*H*Cp$_{up}$), 4.08 (s, 2H, C*H*Cp$_{up}$ + C*H*Cp$_{down}$), 3.85 (s, 1H, C*H*Cp$_{down}$), ∼3.8 (t, 1H, partially overlapped, H$_{allylic,transPCy2}$), 3.72 (s, 1H, C*H*Cp$_{down}$), 2.67 (t, $J_{H\text{-}P}$ = $J_{H\text{-}H}$ = 13.0 Hz, H$^{1''}$), 1.82 (s, 1H, H$^{5'}$, Cp$_{down}$), 2.85–0.5 (Cy and heteroannular chain). ^{13}C{^{1}H} NMR (125 MHz), **5C M**: 110.3 (t, J_{CP} = 6.9 Hz, C$H_{allylic,central}$), 95.1 (dd, $J_{C\text{-}P}$ = 26.6, 5.0 Hz, C$H_{allylic,transPCy2}$), 83.5 (d, $J_{C\text{-}P}$ = 27.4 Hz, C$H_{allylic,transPPh2}$), 77.4 (overlapped, *C*HCp$_{up}$), 73.7 (s, $C^{5'}$HCp$_{down}$), 73.2 (m, *C*HCp$_{up}$), 72.2 (s, *C*HCp$_{down}$), 71.2 *C*HCp$_{down}$), 69.3 (s, *C*HCp$_{up}$), 69.0 (s, *C*HCp$_{down}$), 28.6 (d, $J_{C\text{-}P}$ = 22.6 Hz, C$^{1''}$). **5C m**: 112.0 (b, C$H_{allylic,central}$), 91.5 (bd, C$H_{allylic,transPCy2}$), 88.7 (d, $J_{C\text{-}P}$ = 28.2 Hz, C$H_{allylic,transPPh2}$), 77.1 (overlapped, *C*HCp$_{down}$), 73.6 (m, *C*HCp$_{up}$), 73.4 (s, $C^{5'}$HCp$_{down}$), 72.5 (s, *C*HCp$_{down}$), 71.3 (s, *C*HCp$_{down}$), 69.8 (d, $J_{C\text{-}P}$ = 6.9 Hz, *C*HCp$_{up}$), 69.4 (s, *C*HCp$_{down}$), 29.8 (d, $J_{C\text{-}P}$ = 14.1, C$^{1''}$). **5C M + 5C m**: 138–127 (Ph), 130.4 (d, $J_{C\text{-}P}$ = 10.9 Hz, CH_{ortho}Ph$_{up}$), 90.0 (d, $J_{C\text{-}P}$ = 18.1 Hz, C_qCp), 86.4 (s, C_qCp), 74.0 (d, $J_{C\text{-}P}$ = 7.3 Hz, C_qCp), *C*H-Cy: 38.6 (d, $J_{C\text{-}P}$ = 18.9) and 36.0 (d, $J_{C\text{-}P}$ = 12.0); chain and Cy: 41.1 (d, $J_{C\text{-}P}$ = 11.2 Hz), 41.0 (d, $J_{C\text{-}P}$ = 11.2 Hz), 38.8 (d, $J_{C\text{-}P}$ = 19.3 Hz), 35.4 (d, $J_{C\text{-}P}$ = 12.4 Hz), 32.1 (s), 31.6 (s), 30.9 (s), 30.8–24.0. ^{31}P{^{1}H} NMR (121 MHz, $CDCl_3$), **5C M**: 58.97 (d, $J_{P\text{-}P}$ = 69.0 Hz, PCy_2), 17.38 (d, PPh_2). **5C m**: 59.34 (d, $J_{P\text{-}P}$ = 73.2 Hz, PCy_2), 14.74 (d, PPh_2).

*2.2.4. Synthesis of [Pd(η^3-1,3-$Ph_2C_3H_3$)(S_c,R_p-**7**)]OTf (**7C**)*

Compound **7** (124 mg, 0.2 mmol) gave complex **7C** (150 mg, 0.14 mmol, 70%). $C_{54}H_{59}F_3FeO_3P_2S$ (962.94): Calc. C, 67.36; H, 6.18. Found: C, 67.04; H, 6.35. ^{1}H NMR (300 MHz, $CDCl_3$), **7C M**: δ 6.30–7.75 (Ph), 6.60 (t, 1H, H$_{allyl,central}$), 4.95 (t, 1H, $J_{H\text{-}H} \approx J_{H\text{-}P}$ = 12.2 Hz, H$_{allyl,transPPh2}$), 4.32 (m, 1H, C*H*Cp), 4.25 (t, 1H, $J_{H\text{-}H} \approx J_{H\text{-}P}$ = 11.3 Hz, H$_{allyl,transPCy2}$), 3.91 (bs, 1H, C*H*Cp), 3.44 (s, 5H, C*H*Cp). **7C m**: some Ph signals have been identified: 7.91 (dd, 2H, $J_{H\text{-}P}$ = 12.7 Hz, $J_{H\text{-}H}$ = 7.3 Hz, CH_{ortho}Ph$_{down}$), 6.29 (dd, 2H, $J_{H\text{-}P}$ = 10.9 Hz, $J_{H\text{-}H}$ = 7.9 Hz,

$CH_{ortho}Ph_{up}$), 6.30–7.75 (rest of Ph signals), 6.33 (t, 1H, $H_{allyl,central}$), 5.38 (t, 1H, $J_{H\text{-}H} \approx J_{H\text{-}P} = 9$ Hz, $H_{allyl,transPCy2}$), 5.34 (t, 1H, $J_{H\text{-}H} \approx J_{H\text{-}P} = 11.7$ Hz, $H_{allyl,transPPh2}$), 4.34 (m, 1H, C*H*Cp), 3.94 (bs, 1H, C*H*Cp), 3.55 (s, 5H, C*H*Cp). For both isomers signals of Cy and the homoannular chain are at: 3.85–3.7 and 2.7–0.15. $^{13}C\{^1H\}$ NMR (62.9 MHz), **7C M + 7cm**: 138–118 (Ph), 113.7 (s, $CH_{allyl,central}$, **7C M**), 112.6 (s, $CH_{allyl,central}$, **7C m**), 91.5 (d, $J_{H\text{-}P} = 24.0$ Hz, $CH_{allyl,terminal}$, **7C M**), 91.4 (d, $J_{C\text{-}P} = 23.8$ Hz, $CH_{allyl,terminal}$, **7C M**), 90.0 (d, $J_{H\text{-}P} = 28.6$ Hz, $CH_{allyl,terminal}$, **7C m**), 88.9 (d, $J_{C\text{-}P} = 23.6$ Hz, C_q-Cp), 72.3 (s, C_5H_5), *C*H Cp: 72.9, 70.7 and 69.2; chain and Cy: 35–23 and 15.5. $^{31}P\{^1H\}$ NMR (121 MHz, $CDCl_3$), **7C M**: 49.10 (d, $J_{P\text{-}P} = 77.5$ Hz, PCy_2); 15.32 (d, PPh_2). **7C m**: 42.68 (d, $J_{P\text{-}P} = 80.6$ Hz, PCy_2); 13.84 (d, PPh_2).

2.3. Allylic alkylation and amination reactions

All catalytic reactions with ligands **1**–**8** were carried out in situ according to standard protocols (see following paragraphs). In each case the allyl-palladiumchloride dimer $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ was used as the palladium source. For allylic alkylation reactions (*E*)-1,3-diphenylprop-2-en-1-yl acetate and (*E*)-pent-3-en-2-yl acetate were used as substrates and dimethyl malonate as the nucleophile (reactions 1 and 2, Scheme 1). In alkylations with (*E*)-pent-3-en-2-yl acetate NaH was used as the base, whereas with (*E*)-1,3-diphenylprop-2-en-1-yl acetate both NaH and *N*,*O*-bis(trimethylsilyl)acetamide (BSA) were used. Reactions were carried out in the presence of 1 mol% catalyst either in THF (NaH) or in CH_2Cl_2 (BSA) as the solvent. Amination reactions were performed with (*E*)-1,3-diphenylprop-2-en-1-yl acetate as the substrate and benzylamine as the nucleophile (reaction 3, Scheme 1) and again with a substrate to catalyst ratio of 100. The results of the allylic alkylation reactions are summarised in Tables 1 and 2 and the amination results are listed in Table 3.

2.3.1. General procedure for the allylic alkylation reaction using BSA as the base

To a degassed solution of $[Pd(\eta^3\text{-}C_3H_5)C1]_2$ (1.8 mg, 0.005 mmol) and the appropriate ligand (0.01 mmol) in CH_2Cl_2 were subsequently added the substrate [1 mmol, 252 mg in the case of (*E*)-1,3-diphenylprop-2-en-l-yl acetate, 128 mg in the

Table 1
Pd-catalysed allylic alkylation of (*E*)-1,3-diphenylprop-2-ene-1-yl acetate with dimethyl malonate

Entry	Ligand[a]	Base	T (°C)	React. time (h)	Isol. yield (%)	e.e. (%)[b] (config.)
1	(R_c,R_p)-**1**	NaH	RT	18	98	0
2	(R_c,R_p)-**2**	NaH	RT	18	92	66 (*S*)
3	(R_c,R_p)-**2**	BSA	RT	18	60	70 (*S*)
4	(R_c,R_p)-**2**	BSA*	RT	18	75	71 (*S*)
5	(R_c,R_p)-**2**	BSA	0	40	34	62 (*S*)
6	(R_c,R_p)-**2**	BSA	–20	70	26	61 (*S*)
7	(S_c,R_p)-**3**	NaH	RT	18	95	39 (*R*)
8	(S_c,R_p)-**3**	BSA	RT	18	65	45 (*R*)
9	(S_c,R_p)-**3**	BSA*	RT	18	83	41 (*R*)
10	(R_c,R_p)-**4**	NaH	RT	18	81	64 (*R*)
11	(R_c,R_p)-**4**	BSA	RT	18	94	61 (*R*)
12	(R_c,R_p)-**4**	BSA*	RT	18	83	64 (*R*)
13	(R_c,R_p)-**4**	BSA	0	40	90	66 (*R*)
14	(R_c,R_p)-**4**	BSA	–20	70	91	70 (*R*)
15	(R_c,R_p)-**5**	NaH	RT	18	99	61 (*R*)
16	(R_c,R_p)-**5**	BSA	RT	18	86	59 (*R*)
17	(R_c,R_p)-**5**	BSA*	RT	18	76	61 (*R*)
18	(R_c,R_p)-**5**	BSA	0	40	56	64 (*R*)
19	(R_c,R_p)-**5**	BSA	–20	70	52	69 (*R*)
20	(S_c,R_p)-**6**	NaH	RT	18	80	70 (*S*)
21	(S_c,R_p)-**6**	BSA	RT	18	92	76 (*S*)
22	(S_c,R_p)-**6**	BSA*	RT	18	80	69 (*S*)
23	(S_c,R_p)-**6**	BSA	0	40	72	72 (*S*)
24	(S_c,R_p)-**6**	BSA	–20	70	79	70 (*S*)
25	(S_c,R_p)-**7**	NaH	RT	18	92	38 (*S*)
26	(S_c,R_p)-**7**	BSA	RT	18	99	34 (*S*)
27	(S_c,R_p)-**7**	BSA*	RT	18	87	33 (*S*)
28	(S_c,R_p)-**7**	BSA	0	40	65	33 (*S*)
29	(S_c,R_p)-**7**	BSA	−20	70	62	19 (*S*)
30	(S_c,R_p)-**8**	BSA	RT	18	n.d.	54 (*R*)[c]
31	(S_c,R_p)-**9**	BSA	RT	18	n.d.	66 (*R*)[d]
32	(S_c,R_p)-**10**	BSA	RT	18	n.d.	93 (*R*)[d]

[a] Catalyst prepared in situ from $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ and the ligand; for details see Section 2.
[b] Determined by HPLC on Chiralcel OD (Daicel).
[c] Experiment was carried out with (R_c,S_p)-**8** and product of (*S*) configuration was obtained; for reasons of better comparison listed as (S_c,R_p)-**8**.
[d] Literature data; see [37].
* 2 mol.% catalyst.

Table 2
Pd-catalysed allylic alkylation of (*E*)-pent-3-ene-2-yl acetate with dimethyl malonate

Entry	Ligand[a]	*T* (°C)	React. time (h)	Isol. yield (%)	e.e. (%) (config.)[b]
33	(R_c,R_p)-**1**	RT	18	40	5 (*S*)
34	(R_c,R_p)-**4**	RT	18	66	35 (*R*)
35	(R_c,R_p)-**4**	0	40	87	39 (*R*)
36	(R_c,R_p)-**4**	−20	70	65	44 (*R*)
37	(R_c,R_p)-**5**	RT	18	82	55 (*R*)
38	(R_c,R_p)-**5**	0	40	47	46 (*R*)
39	(R_c,R_p)-**5**	−20	70	34	53 (*R*)
40	(S_c,R_p)-**6**	RT	18	91	17 (*S*)
41	(S_c,R_p)-**6**	0	40	88	20 (*S*)
42	(S_c,R_p)-**6**	−20	70	43	22 (*S*)
43	(S_c,R_p)-**7**	RT	18	54	43 (*S*)
44	(S_c,R_p)-**7**	0	40	84	34 (*S*)
45	(S_c,R_p)-**7**	−20	70	32	40 (*S*)

[a] Catalyst prepared in situ from $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ and the ligand; for details see Section 2.
[b] Determined by GC on a chiral stationary phase (50% Oktakis(6-*O*-methyl-2,3-di-*O*-pentyl)-γ-cyclodextrin).

case of (*E*)-pent-3-en-2-yl acetate, respectively], dimethyl malonate (396 mg, 340 μl, 3 mmol), BSA (610 mg, 741 μl, 3 mmol) and a catalytic amount of KOAc. The mixture was stirred at a defined temperature until the reaction was complete [in the case of (*E*)-l,3-diphenylprop-2-en-l-yl acetate as the substrate the progress of the reaction was monitored by TLC (silica, petroleum ether/ethyl acetate = 95/5)]. Diethyl ether (15 ml) was added in order to stop the reaction, the organic layer was washed twice with saturated aqueous NH_4Cl solution and was dried over Na_2SO_4. Evaporation of the solvent and chromatography on silica afforded the product.

(*E*)-l,3-Diphenylprop-2-en-l-yl acetate as the substrate: chromatography on silica, PE/CH_2Cl_2 = 50/50. Detection at 280 nm. The enantiomeric excess was determined by HPLC on a chiral column (Chiralcel OD, 2-propanol/*n*-hexane = 2/98, 0.5 ml/min), the absolute configuration of the product was determined by the sense of the optical rotation [29].

(*E*)-Pent-3-en-2-yl acetate as substrate: chromatography on silica, PE/Et_2O = 75/25. Detection at 214 nm. The enantiomeric excess was determined by GC on a chiral column [50% Octakis(6-*O*-methyl-2,3-di-*O*-pentyl)-γ-cyclodextrin, FS, 0.5 atm H_2, column temperature: 55 °C, injector temperature: 175 °C, split 1:100, sample concentration: 30 mg/ml CH_2Cl_2, 0.2 μl injected]. The absolute configuration of the product was determined by the sense of the optical rotation [28].

Table 3
Pd-catalysed allylic amination of (*E*)-1,3-diphenylprop-2-ene-1-yl acetate with benzylamine

Entry	Ligand[a] (config.)	*T* (°C)	Time (h)	Isol. yield (%)	e.e. (%) (config.)[b]
46	(R_c,R_p)-**4**	RT	70	75	44 (*S*)
47	(R_c,R_p)-**5**	RT	48	60	40 (*S*)
48	(S_c,R_p)-**6**	RT	48	46	61 (*R*)
49	(S_c,R_p)-**7**	RT	48	68	24 (*R*)

[a] Catalyst prepared in situ from $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ and the ligand; for details see Section 2.
[b] Determined by HPLC on Chiralcel OD (Daicel).

2.3.2. General procedure for the allylic alkylation reaction using NaH as the base

(*E*)-1,3-Diphenylprop-2-en-l-yl acetate (252 mg, 1 mmol), $[Pd(\eta^3\text{-}C_3H_5)C1]_2$ (1.8 mg, 0.005 mmol) and the appropriate ligand (0.01 mmol) were dissolved in THF (4 ml). The solution was degassed and was stirred for additional 15 min. To a degassed solution of dimethyl malonate (198 mg, 171 μl, 1.5 mmol) in THF (2 ml) was added NaH (63 mg, 1.5 mmol) in portions. This solution was stirred for 30 min and was then added at 0 °C to the solution containing the allylic acetate and the catalyst. The reaction mixture was stirred at room temperature until the reaction was complete. After quenching with a small amount of 2N HCl the mixture was extracted with Et_2O (3 × 10 ml). The combined organic phases were washed with brine and dried over $MgSO_4$. The solvent was evaporated and the residue was purified by chromatography as described in Section 2.3.1.

2.3.3. General procedure for the allylic amination reaction

A solution of (*E*)-l,3-diphenylprop-2-en-l-yl acetate (252 mg, 1 mmol), the ligand (0.01 mmol) and $[Pd(\eta^3\text{-}C_3H_5)C1]_2$ (1.8 mg, 0.005 mmol) in CH_2Cl_2 (1 ml) was degassed and stirred at room temperature for 15 min. Benzylamine (321 mg, 3 mmol) and a catalytic amount of KOAc were added and the reaction mixture was stirred at room temperature for 18 h. The reaction was monitored by TLC (PE/EE = 95/5). The solvent was evaporated and the residue was purified by chromatography on silica (PE/EE = 90/10). Detection at 280 nm. The enantiomeric excess was determined by HPLC on a chiral column (Chiralcel OD-H, 0.2% diethylamine, 0.25% 2-propanol in hexane, 0.5 ml/min) and the absolute configuration of the product was determined by the sense of optical rotation [27].

2.4. Determination of isomer ratios of complexes *1C*, *4C*, *5C* and *7C* under catalytic conditions

Allylic alkylations were carried out in CD_2Cl_2 as the solvent with 1,3-diphenylprop-2-en-1-yl acetate as the substrate, BSA as the base, deprotonated dimethyl malonate as the nucleophile and with complexes **1C**, **4C**, **5C** and **7C** as the catalyst precursors. The reactions were monitored by $^{31}P\{^1H\}$ NMR spectroscopy. The diastereomer ratios of allyl derivatives **1C**, **4C**, **5C** and **7C** under catalytic conditions were determined by $^{31}P\{^1H\}$ NMR spectroscopy and calculated on the basis of the relative integrations of the resonances after the preparation of the respective solutions. The following products were dissolved in CD_2Cl_2 (1 ml): 0.01 mmol of the corresponding complex, 252 mg of (*E*)-1,3-diphenylprop-2-en-1-yl acetate (1 mmol), 741 μl of BSA (610 mg, 3 mmol), 0.98 mg of KOAc (0.01 mmol) and 340 μl of dimethyl malonate (396 mg, 3 mmol). An aliquot of the reaction mixture was checked 10 min after the addition of the dimethyl malonate and a second aliquot was assessed after 10 h.

2.5. Crystal structure analysis of **7C**

Orange crystals of racemic **7C** in the form of a $CHCl_3$ solvate were obtained by diffusion of Et_2O into a $CHCl_3$ solution. The X-ray intensity data were collected at room temperature on a Bruker SMART CCD area detector system equipped with a normal focus molybdenum-target X-ray tube operated at 2.0 kW. A total of 2424 frames of data (complete sphere) were collected using the narrow frame method with scan widths of 0.3° in ω and exposure times of 15 s/frame by applying a detector-to-crystal distance of 5.0 cm. After data integration with the SAINT program, corrections for absorption and λ/2-effects were applied with the SADABS program. The structure was solved with direct methods and was then refined on F^2 with the program package SHELX97 [50,51]. The non-hydrogen atoms were refined with anisotropic thermal parameters and hydrogens were included in idealized positions. Complete structure data have been deposited. Salient crystal data are: $C_{53}H_{59}FeP_2Pd{\cdot}CF_3SO_3{\cdot}CHCl_3$, $M_r = 1188.63$, monoclinic, space group $P2_1/n$ (no. 14), $T = 299$ K, $a = 24.423(6)$ Å, $b = 18.232(6)$ Å, $c = 26.272(6)$ Å, $\beta = 112.78(1)°$, $V = 10786(5)$ Å^3, $Z = 8$, $\rho_{calc} = 1.464$ g/cm^3, λ(Mo-Kα) = 0.71073 Å, $\mu = 0.902$ mm^{-1}. Of 115303 reflections collected up to $\theta_{max} = 25°$, 18896 were independent, $R_{int} = 0.044$, and 14501 were observed ($I > 2\sigma(I)$); final R indices: $R_1 = 0.0495$ ($I > 2\sigma(I)$), $R_1 = 0.0719$ (all data), $wR_2 = 0.1318$ (all data).

The crystal structure contains two crystallographically independent Pd complexes, which are of similar dimensions and shape but show differences in conformation for their peripheral parts, in particular for the orientations of the P1-bound phenyl rings (rotations about P–C bonds resulting in relative positional differences of up to about 0.9 Å for the corresponding carbon atoms; the biggest differences are seen in the PPh_2 part). A view of the first complex together with important bond lengths and angles is shown in Fig. 1 and a superposition plot of both complexes is presented in Fig. 2. Pd–C bond lengths in both complexes are similar and are consistent with approximately symmetrically Pd-bound allyl groups, the bond lengths being Pd–C45 = 2.250/2.276 Å (complex 1/complex 2), Pd–C47 = 2.290/2.273 Å, and Pd–C46 = 2.206/2.196 Å. The Pd–P bonds for both types of phosphorus—aryl-bearing P1 and alkyl-bearing P2—are also quite similar, namely Pd–P1 = 2.294/2.302 Å and Pd–P2 = 2.323/2.328 Å, although for electronic reasons (PCy_2 being considered a stronger donor than PPh_2) one might expect the Pd–PCy_2 bond to be significantly shorter than the Pd–PCy_2 bond. However, despite this essentially symmetrical behaviour in bond lengths the spatial arrangement of P1 and P2 relative to the allyl system is notably asymmetric: the non-bonding intramolecular distance P1 − C45 = 3.317/3.387 Å (aryl-bound phosphorus) is notably shorter than the counterpart P2 − C47 = 3.653/3.567 Å (alkyl-bound phosphorus). The reason for this difference is attractive intramolecular phenyl–phenyl π-stacking interactions between ring C39-C44 and the P1-bound ring C15-C20 on one side of the complex, and sterically impeding interactions on the cyclohexyl side, namely the contact between cyclohexyl C27-H27

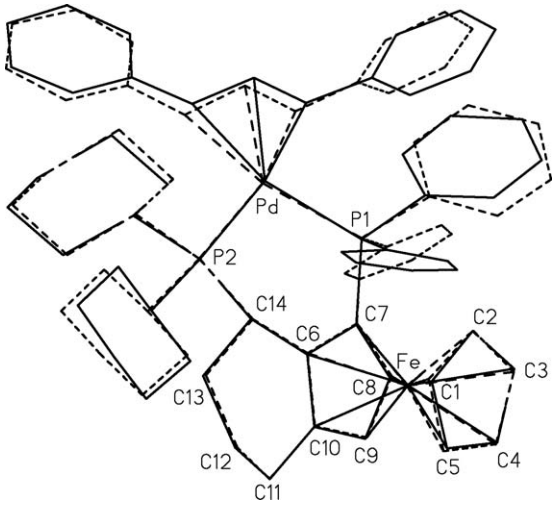

Fig. 2. Superposition of the two crystallographically independent complexes of **7C** mutually fitted via the labelled atoms. Positional differences between corresponding atom pairs are between 0.02 and 0.94 Å.

and phenyl ring C48-C53, specifically between H27 and C48 (2.64/2.59 Å). In summary, arene π-stacking on one side and C − H· · · · ·C contacts on the other side of the complex appear to be responsible for the asymmetry in the P ligand disposition relative to the allyl system. Together with different donor properties of the aryl- and alkyl-substituted phosphorus atoms this geometric feature may also influence the course of the asymmetric allylic alkylation (see below) [52].

3. Results and discussion

3.1. Results of the allylic alkylation and amination reactions

In the next few paragraphs some general comments are made on the results of the allylic alkylation and amination reactions (listed in Tables 1–3). When the reactions were carried out at room temperature, products were isolated in moderate to nearly quantitative yields. At lower temperatures the reactions slowed down significantly, with ligand **4** (entries 11, 13 and 14) being least affected. As observed frequently, allylic aminations with benzylamine as the nucleophile are significantly slower than comparable alkylation reactions with dimethyl malonate (entries 46–49 and e.g. 11, 16, 21, 26).

Enantioselectivities were found to be small to moderate. In the allylic alkylations the maximum e.e. values obtained were 76% and 55%, respectively, when 1,3-diphenylpropenyl acetate (ligand **6**, entry 21) or pentenyl acetate (ligand **5**, entry 37) were used. One exception was ligand **1**, which performed very poorly, giving racemic or nearly racemic products in both allylic alkylation reactions (entries 1 and 33). The influence of both temperature and the base/solvent system on enantioselectivity was rather small and was not uniform. As compared to NaH (THF) as the base, the use of BSA (CH_2Cl_2) and ligands **2**, **3** and **6** led to an increase of up to 6% whereas with ligands **4**, **5** and **7** the enantioselectivity decreased slightly. Interestingly, the influence of temperature on the enantioselectivity measured

Table 4
Selected data for the Pd-catalysed allylic alkylation of (*E*)-1,3-diphenylprop-2-ene-1-yl acetate with dimethyl malonate,[a] (entry, ligand, % e.e., absolute configuration of product)

Heteroannularly bridged ligands			Homoannularly bridged *endo*-ligand			Homoannularly bridged *exo*-ligand			Ppfa and Josiphos-type ligands		
1	(R_c,R_p)-**1**	0[b]	2	(R_c,R_p)-**2**	66 (*S*)[b]	7	(S_c,R_p)-**3**	39 (*R*)[b]	30	(S_c,R_p)-**8**	54 (*R*)
–			3	(R_c,R_p)-**2**	70 (*S*)	8	(S_c,R_p)-**3**	45 (*R*)	31	(S_c,R_p)-**9**	66 (*R*)[c]
11	(R_c,R_p)-**4**	61 (*R*)				21	(S_c,R_p)-**6**	76 (*S*)	32	(S_c,R_p)-**10**	93 (*R*)[c]
16	(R_c,R_p)-**5**	59 (*R*)				26	(S_c,R_p)-**7**	34 (*S*)			

[a] Data are arranged according to Chart 1; reaction conditions: RT, 18 h; BSA.
[b] NaH.
[c] Literature data; see [37].

between 25 and −20 °C was significantly higher (up to 15% e.e.) but again did not give a consistent trend. In the alkylation with 1,3-diphenylpropenyl acetate as the substrate an increase was seen for heteroannularly bridged ligands **4** and **5** (10%, entries 11, 14 and 16, 19) while for **2**, **6** and **7** a decrease of up to 15% e.e. was found (entries 3, 6; 21, 24; and 26, 29). In the reaction with pentenylacetate as the substrate the effects are rather small. A maximum increase of 9% e.e. was observed for ligand **4** (entries 34 and 36).

As mentioned above, ligands **1**–**10** can be classified in two ways: ligands having identical functional groups and ligands having an identical backbone, with aminophosphines **1**, **2**, **3** and **8** falling into the former group. With the exception of **1**, these aminophosphines were tested only in the allylic alkylation with 1,3-diphenylpropenyl acetate as the substrate (reaction 1, for a summary of these results see Table 4). The enantioselectivity varied over a wide range from 0 to 66% e.e., with ligand **2** giving the best performance. Whilst conformational changes in the chelate ring of the intermediate palladium diphenylallyl complex may, at least in part, be responsible for the poor performance of ligand **8**, such changes are expected to play only a minor role for ligands **1**–**3**. Other reasons seem to be responsible for the very poor performance of **1**. In the series of aminophosphine ligands **1**–**3** in particular the enantioselectivity depends quite markedly on backbone modification, which is expected to influence the *exo*/*endo* and *syn*/*syn syn*/*anti* ratio of the intermediate allyl complexes and, as a consequence, may lead to changes in the overall enantioselectivity. In principle, a very unfavourable ratio of palladium allyl intermediates could cause the formation of a racemic product (see below). However, for aminophosphine ligands, particularly ligands **1**, **2**, **3** and **8**, palladium bond rupture processes must also be taken into account. For example, for 2-methylallyl palladium complexes of **1**, **2** and **8** we have demonstrated that these processes are fast at room temperature, with activation energies increasing in the order **8** < **1** < **2** [53].

Like the aminophosphines discussed above, diphosphines **4**, **6**, and **9** as well as **5**, **7**, and **10** constitute groups of ligands with identical functional groups but different backbones. In allylic alkylations with 1,3-diphenylpropenyl acetate as the substrate e.e. values ranging from 34% (**7**) to 93% (Josiphos, **10** [37]) were found (Table 4). Interestingly, identical backbone changes in both series are reflected differently in terms of changes in the related e.e. values and these changes are clearly not directly correlated with each other. When the e.e. values obtained with the heteroannularly bridged ligands **4** and **5** are compared with those of their homoannularly bridged analogues **6** and **7** (as well as with those reported for Josiphos type ligands **9** and **10**), the following trends are seen: in series **4**, **6**, and **9** the enantioselectivity increases in the order **6** > **9** ≈ **4** [76% (**6**), 66% (**9** [37]), 61% (**4**)] while with **5**, **7**, and **10** an order of **10** > > **5** > **7** [93% (**10** [37]), 59% (**5**), 34% (**7**)] was found.

A comparison of ligands with identical backbones but different functional groups shows a similar picture. Identical changes in the functional groups on all three backbones did not parallel the observed changes in e.e. values. For example, replacing a diphenylphosphino group in **4**, **6**, or **9** with a dicyclohexyl group led either to higher (**9**/**10**), to lower (**6**/**7**) or to almost identical e.e. values (**4**/**5**). This lack of correlation clearly reflects the fact that even for one particular reaction—like the allylic alkylation with 1,3-diphenylpropenyl acetate as the substrate and dimethyl malonate as the nucleophile—a successful ligand optimization needs tuning of both the backbone and the functional groups.

Besides relating structural changes to e.e. values, it seemed to be of interest to analyse how structural changes in the ligands are reflected in changes in the absolute configuration of the products (Tables 1–3). The following brief discussion focuses first on the allylic alkylation with 1,3-diphenylpropenyl acetate since a full set of data is available for this reaction.

It can been seen from the results in Table 4 that changes in the absolute configuration of the product do not uniformly depend on changes in the absolute configurations of ligands **2**–**10**. For example, on changing aminophosphine ligand (R_c,R_p)-**2** to (S_c,R_p)-**3** the product configuration changes from (*S*) to (*R*). A similar trend is seen when diphosphines (R_c,R_p)-**4** and (R_c,R_p)-**5** are replaced by (S_c,R_p)-**6** and (S_c,R_p)-**7**, respectively. In these cases the product configuration changes from (*R*) to (*S*). However, when comparing the results obtained with ligands (S_c,R_p)-**6** and (S_c,R_p)-**7** with those for (S_c,R_p)-**9** and (S_c,R_p)-**10**, a change in product configuration is observed although the descriptors for the absolute configuration of ligands did not change at all. Within the small set of diphosphines (**4**–**7**, **9** and **10**) the replacement of a diphenylphosphino group with a dicyclohexylphosphino group did not lead to a change in the product configuration in any case. In summary, for the given set of ligands changes in the absolute configuration of the product can neither be consistently attributed to changes in the ferrocene configuration nor exclusively to configurational changes of the *pseudo*-benzylic carbon. If at all, such correlations seem to be useful only in cases of diastereomers such as **2** and **3**.

Table 5
Selected data obtained with ligands **4**–**7** in reactions 1–3 (entry, % e.e., absolute configuration of product)

Ligand	Reaction 1		Reaction 2		Reaction 3	
(R_c,R_p)-**4**	11	61 (*R*)	31	35 (*R*)	43	44 (*S*)
(R_c,R_p)-**5**	16	59 (*R*)	34	55 (*R*)	44	40 (*S*)
(R_c,R_p)-**6**	21	76 (*S*)	37	17 (*S*)	45	61 (*R*)
(R_c,R_p)-**7**	26	34 (*S*)	40	43 (*S*)	46	24 (*R*)

Data for allylic alkylations with pentenyl acetate (reaction 2, Table 2) and for allylic aminations with 1,3-diphenylpropenyl acetate as the substrate (reaction 3, Table 3) were collected only for ligands **4**–**7**. A comparison of the results obtained with these four ligands shows (for a summary see Table 5) that (i) for all three reactions the absolute configuration of products obtained with the heteroannularly bridged ligands **4** and **5** is identical but opposite to those of **6** and **7**; and (ii) from a structural point of view the products obtained with each individual ligand are identical. For example, ligand **4** gave a product of (*R*) configuration in both alkylation reactions and a product of (*S*) configuration in the allylic amination reaction; hence, from a topological point of view, all three products are identical. [Note: as depicted in Scheme 1, replacing the malonic ester unit by an amino substituent changes only the descriptor of the absolute configuration from e.g. (*S*) to (*R*) but not its topology].

Based on these results, it seemed to be of interest to rationalise, at least in part, both experimentally observed features—the surprisingly identical stereochemical course of all three reactions as well as changes in the absolute configuration of the product.

*3.2. Analysis of (1,3-diphenylallyl)palladium complexes of ligands **1**, **4**, **5**, and **7***

As discussed extensively before, under certain conditions both the absolute configuration and the enantioselectivity of such reactions is controlled by the ratio of *exo/endo* as well as *syn/syn* and *syn/anti* structures of the intermediate palladium allyl complexes (Scheme 1) [32,38,53]. One could, for example, imagine that on changing the heteroannularly bridged backbone of **5** to the homoannularly bridged unit of **7** the *exo/endo* ratio of the intermediate allyl complexes, and therefore the absolute configuration of the product, changes. Based on such considerations we synthesised and isolated the diphenylallyl complexes of diphosphine ligands **4**, **5** and **7** along with that of aminophosphine **1** (which in reactions 1 and 2 led to exceptionally poor results). The structural behaviour of these complexes in solution was studied by NMR both as isolated complexes and under catalytic conditions (see Section 2.4). Structural assignments were mainly based on NOE measurements and typical sets of coupling constants. The *exo* orientation of the allyl group in the respective isomers was deduced from the NOE found between the terminal allylic proton *cis* to the PPh_2 group (bonded to Cp_{up}) and the *ortho* protons of the phenyl group oriented downwards. The latter protons were identified from the NOEs observed with protons Cp_{down}. In all cases only *exo syn/syn* and *endo syn/syn* complexes were identified. The ratios of these compounds measured at 25 °C in $CDCl_3$, CD_2Cl_2 and under catalytic conditions are listed in Table 6.

It was very interesting to find that in $CDCl_3$ the *exo/endo* ratio was opposite for complexes of the heteroannularly bridged ligands **4** and **5** (**4C** and **5C**) as compared to that of the homoannularly bridged ligand **7** (**7C**). Furthermore, the solid state structure of **7C** (the *endo* isomer) was found to be identical to that of the major isomer in solution. However, as one might expect, in CD_2Cl_2 the *exo/endo* ratios change slightly in comparison to $CDCl_3$ and for **5C** the *endo* isomer even becomes predominant. Under catalytic conditions the *exo/endo* ratios change again and, with the exception of **5C**, continue to change with time as long as the reactions evolve. Interestingly, for complexes **5C** and **7C** the *exo/endo* ratio not only changed very significantly, but was also reversed (**5C**: from 44:56 to 100:0; **7C**: from 42:58 to 56:44 finally evolving to 71:29).

In principle, based on a number of assumptions [for example: (i) the attack of the nucleophile is rate determining; (ii) the ground state energy differences of the palladium allyl intermediates are also reflected in the transition states of the nucleophilic substitution step, and hence the major diastereomer determines the absolute configuration of the predominant product enantiomer] and with a knowledge of the absolute configuration of both ligand and product, the allyl terminus at which the nucleophilic substitution takes place can be determined. The *exo syn/syn* arrangement of the diphenylallyl unit always predominates under catalytic conditions for all of the investigated complexes (Table 6) and so for **4C** and **5C** such an analysis would lead to the conclusion that the nucleophile had to react at the allyl terminus *trans* to the diphenylphosphino group attached to the heteroannular bridge of **4C** (Chart 3) and *trans* to the dicyclohexylphosphino group of **5C**. This would be in agreement with the view that the nucleophilic substitution takes place *trans* to the phosphino unit that has the strongest *trans* influence. On employing identical assumptions, in the case of the *syn/syn* complex **7C** a correlation of the *exo/endo* ratio with the

Table 6
Exo/endo ratio of the palladium diphenylallyl intermediates **1C**, **4C**, **5C**, and **7C**, {[(PhCHCHCHPh)Pd(L)]SO_3CF_3, L = **1**, **4**, **5**, **7**} at 25 °C

Complex	*exo/endo* ratio in $CDCl_3$	*exo/endo* ratio in CD_2Cl_2	*exo/endo* ratio; catalytic conditions; after 10 min	*exo/endo* ratio; catalytic conditions; after 10 h
1C	91:9	87:13	88:12	91:9
4C	66:34	63:37	73:27	100:0
5C	53:47	44:56	100:0	100:0
7C	44:56	42:58	56:44	91:29

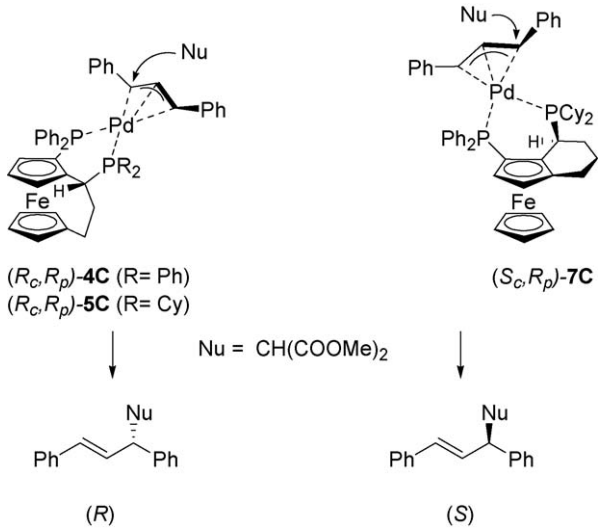

Chart 3.

absolute (*S*) configuration of the product would, however, lead to opposite conclusions as far as the attack of the nucleophile is concerned. Contrary to **5C**, in this case the data would predict attack at the allyl carbon *cis* to the cyclohexyl group (Chart 3). The aminophosphine complex **1C** constitutes an extreme example since, although under catalytic conditions the *exo/endo* ratio is always strongly in favour of the *exo* form, the reaction lacks any selectivity and *racemic* product is formed. In conclusion, even when taking into account the *exo/endo* ratios measured under catalytic conditions, the simplified analysis used above would only predict correctly the absolute configuration of products obtained with **4C** and **5C** but not with **1C** and **7C**. These results, and particularly the fact that in reaction 1 the closely related complexes **5C** and **7C** both preferentially adopt the *exo syn/syn* configuration of the diphenyl allyl unit but give the product of opposite configuration, indicate that at least some of the assumptions used in the analysis do not apply to the set of ligands investigated here.

4. Conclusions

Sets of ferrocenyl aminophosphine and diphosphine ligands having either identical backbones and varying functional groups or identical functional groups and varying backbones have been investigated in asymmetric allylic alkylation and partly in allylic amination reactions. It was found for these sets of ligands that the observed enantioselectivity does not uniformly depend on either changes in the ligand backbone or on changes in the functional groups. This clearly shows that even for one particular reaction, such as the allylic alkylation with 1,3-diphenylpropenyl acetate as the substrate and dimethyl malonate as the nucleophile, successful ligand optimization is hardly predictable and both the functional groups and the backbone need to be tuned. Similarly, changes in the absolute configuration of product do not consistently correspond to changes in the ligand configuration, changes of the ferrocene configuration or to configurational changes of the *pseudo*-benzylic carbon. Finally, an NMR investigation of isolated diphenylallyl palladium complexes (**1C**, **4C**, **5C**, and **7C**) showed that in solution the diphenylallyl unit adopts *exo syn/syn* or *endo syn/syn* arrangements exclusively, with the *exo syn/syn* always predominating. It was found that the measured *exo/endo* ratios neither corresponded to the measured e.e. values nor correlated uniquely with the absolute configuration of product. This finding indicates that some of the assumptions frequently used in the analysis of such complexes do not apply to the full set of ligands investigated here.

Supporting information available

CCDC 293100 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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