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Planar chiral palladacycle precatalysts for asymmetric synthesis†

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Chiral non-racemic palladacycles were employed as precatalysts for Pd(0) mediated asymmetric synthesis. Addition of $HPAr_2$/base to a ferrocenyloxazoline planar chiral palladacycle resulted in ligand synthesis and palladium capture to give a bidentate Phosferrox/Pd(0) complex. A series of these complexes were generated *in situ* and applied successfully as catalysts for asymmetric allylic alkylation.

Introduction

Air-stable palladacycles containing a bidentate carbon-heteroatom ligated palladium(II) core have been employed extensively in catalysis.[1] Following the discovery that high turn-over numbers may be achieved on application of the Herrmann complex to the Heck reaction,[2] this and other palladacycles have also found application in a number of cross-coupling processes including the Suzuki–Miyaura[3] and Buchwald–Hartwig amination reactions.[4] In addition, related chiral non-racemic palladacycles have been applied successfully to the catalysis of asymmetric reactions.[5] Examples include the allylic imidate rearrangement,[6] hydrophosphination,[7] imine arylation,[8] the aza-Morita–Baylis–Hillman reaction[9] and Michael type reactions.[10] Palladium(II) mediated activation of the substrate and retention of the palladacycle C–Pd bond in the chiral catalyst is either demonstrated[11] or invoked.[7–10] A recent report on palladacycle catalysed asymmetric Suzuki cross-coupling was explained by the operation of a Pd(II)/Pd(IV) catalytic cycle.[12] In contrast, the use of chiral non-racemic palladacycles as precatalysts for asymmetric reactions proceeding *via* a Pd(0)/Pd(II) catalytic cycle does not appear to have been demonstrated.[13]

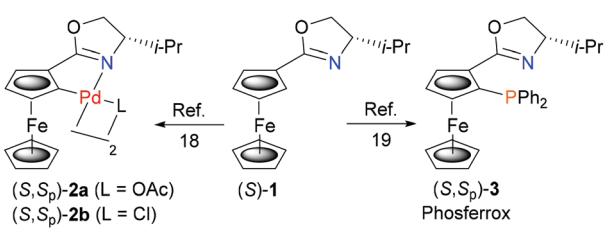
In this paper we describe the use of chiral non-racemic palladacycles as precatalysts for the formation of Pd(0)/chiral ligand coordinated complexes, followed by the application of these as catalysts in asymmetric synthesis. This first report on simultaneous bidentate ligand synthesis/palladium(0) capture provides a new and versatile approach to the generation of Pd/chiral ligand complexes, with potential applications across a range of palladium catalysed asymmetric transformations.[14]

Results and discussion

Palladacycles are known to undergo ligand phosphination on reaction with $MPPh_2$ (M = Li, K), where initial phosphide coordination to palladium followed by reductive elimination results in C–P bond formation.[15,16] In this way a number of N–P, S–P and P–P bidentate ligands have been synthesised from the corresponding S, N or P precursor palladacycles. Many of these product ligands are chiral, including planar chiral examples displaying stereospecific replacement of the C–Pd bond by a new C–P bond.[15a,b] Formation of these ligands also results in the generation of Pd(0), but as far as we are aware, isolation of a resulting ligated Pd(0) complex in this way has not been reported, let alone used subsequently in catalysis.

To address this challenge we chose to start with ferrocenyloxazoline (*S*)-**1**[17] as this may be transformed readily into planar chiral palladacycles (S,S_p)-**2a**/**b** (Scheme 1).[18] Furthermore, the Phosferrox ligand (S,S_p)-**3**[19] is also derived from (*S*)-**1**, this bidentate ligand having been applied successfully in several palladium catalysed asymmetric reactions.[20] It was anticipated that this would aid the identification and comparative application of a corresponding palladacycle derived Pd(0) complex of (S,S_p)-**3**.

We reasoned that identification of *in situ* formed P–N ligated Pd(0) would be aided by addition of a second ligand to



Scheme 1 Palladacycles and a chiral bidentate ligand derived from (*S*)-**1**.

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†Electronic supplementary information (ESI) available: Additional experimental detail, copies of the ^1H, ^{13}C and ^{31}P NMR spectra, HPLC traces and details of the X-ray crystal structure determination. CCDC 1983850. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/d0ob01331e

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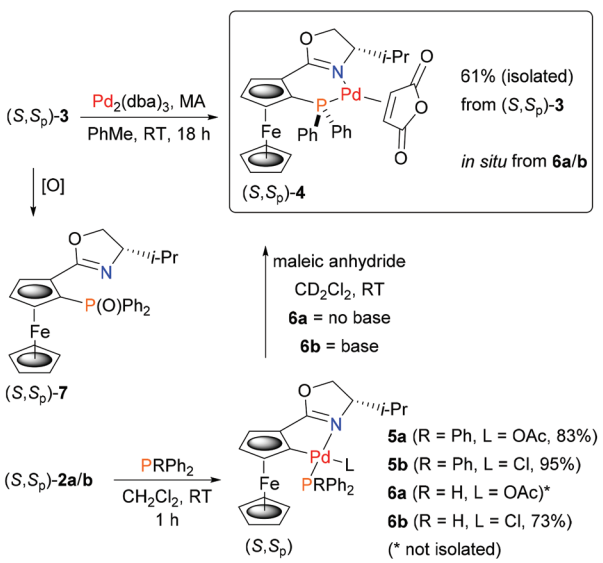
give a readily characterised complex. As maleic anhydride (MA) is known to result in stable low valent complexes of palladium,[21] we first used this electron deficient alkene with (S,S_p)-**3** and $Pd_2(dba)_3$ for the synthesis of (S,S_p)-**4** (Scheme 2). This air-stable Pd(0) complex was purified readily by column chromatography. Its ^{31}P NMR spectrum[22] contained characteristic major and minor signals at 14.39 and 15.81 ppm respectively due to the two possible (*exo*/*endo*) orientations of the cyclic unsaturated ligand.

Phosphine complexes of palladacycles (S,S_p)-**2a**/**b** were first investigated using triphenylphosphine. On combination in CH_2Cl_2 at room temperature monomeric adducts **5a**/**b** were formed cleanly (Scheme 2). The phosphine is assigned a *trans* to nitrogen orientation in the resulting complexes in accord with the geometry of related monomeric phosphine coordinated palladacycles.[15b,23] The ^{31}P NMR signals[22] observed for **5a** (36.5 ppm) and **5b** (37.5 ppm), compared to PPh_3 (−5.4 ppm), were used to aid the assignment of the corresponding adducts obtained from $HPPh_2$ (−40.1 ppm). Addition of this secondary phosphine to chloride ligated **2b** gave stable and isolable adduct **6b** (8.4 ppm). In contrast, addition to acetate ligated **2a** resulted in immediate darkening to brown/black of the initially orange solution, and after stirring for 1 hour, no phosphine adduct was obtained.

To investigate the possibility that this colour change was indicative of reductive elimination from an initially formed phosphine adduct, the experiment was repeated in CD_2Cl_2 and followed by ^{31}P NMR spectroscopy. Following addition of $HPPh_2$ to **2a** at room temperature, a major signal observed in the ^{31}P NMR spectrum obtained after *ca*. 10 minutes (7.5 ppm) is indicative of adduct **6a** (Fig. 1a). Significantly, following the addition of MA, subsequent NMR analysis revealed the disappearance of this complex and the formation of (S,S_p)-**4** (Fig. 1b).



Scheme 2 Synthesis of Pd(0) complex (S,S_p)-**4** by ligand exchange and ligand synthesis/palladium capture.

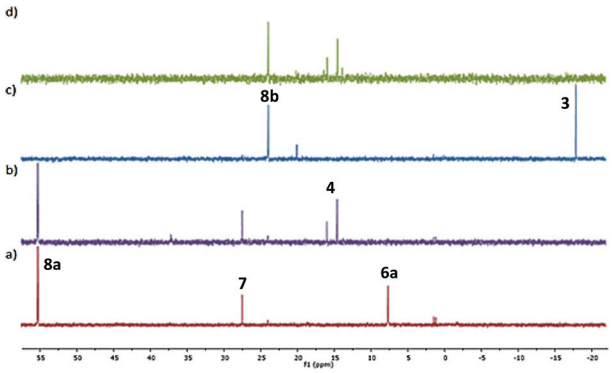


Fig. 1 ^{31}P NMR spectra (CD_2Cl_2): (a) following the addition of $HPPh_2$ (2 eq.) to **2a**, (b) *ca*. 10 minutes after the addition of MA (2 eq.), (c) following the addition of $NaCH(CO_2Me)_2$ (10 eq.) to **6b**, (d) *ca*. 1 h after the addition of MA (4 eq.).

Two other major signals at 27.3 and 55.2 ppm were observed in the ^{31}P NMR spectra obtained before and after the addition of MA. The first corresponds to (S,S_p)-**7**, a phosferrox derived phosphine oxide for which the identity was confirmed by independent synthesis. The second is assigned to a Pd(II)/PPh_2 complex (*vide infra*). Formation of **4** was not observed when MA was added to palladacycle **2a** before the addition of $PHPh_2$ due to fast competitive Michael addition.[24] The formation of **4** and **7**, as a single diastereoisomer in both cases, confirms that replacement of palladium by phosphorus proceeds with no erosion of stereochemical integrity.[25]

In contrast to **6a**, the corresponding experiment with chloride complex **6b** (formed *in situ* from (S,S_p)-**2b** and $HPPh_2$) required the addition of a base to promote reductive elimination and formation of the MA adduct **4**. Nitrogen bases were employed initially, with triethylamine resulting in the highest conversion (14%) as determined by ^{31}P NMR spectroscopy.[26] With *N*,*O*-bis(trimethylsilyl)acetamide (BSA) the conversion was improved (23%), and the best result (29%) was obtained with sodium dimethyl malonate. Following addition of this base ^{31}P NMR spectroscopy revealed two major signals at −18.1 and 23.8 ppm (Fig. 1c). The former corresponds to Phosferrox ligand **3**, and on addition of MA this signal disappeared and was replaced predominantly by a corresponding amount of **4** (Fig. 1d). Following isolation of the other complex by column chromatography it was identified by X-ray crystallography as Pd(II)/PPh_2 dimer **8b** (Scheme 3 and Fig. 2).[27] Addition of silver acetate to **8b** gave **8a** (^{31}P NMR = −55.6 ppm), revealing that this corresponding acetate-bridged dimer is formed from the addition of $HPPh_2$ to **2a** (Fig. 1a and b). Addition of maleic anhydride to a solution of **8b** in CD_2Cl_2 did not result in the formation of **4**. Dimerisation to give **8a**/**b** is an alternative and apparently irreversible pathway to reductive elimination and formation of ligand **3**. It is of note that Pd(0) does not complex with **3** to a significant extent until maleic anhydride is added, an outcome consistent with initial and reversible formation of palladium nanoparticles.[28] No oxidation to phosphine oxide (S,S_p)-**7** was observed, in contrast to

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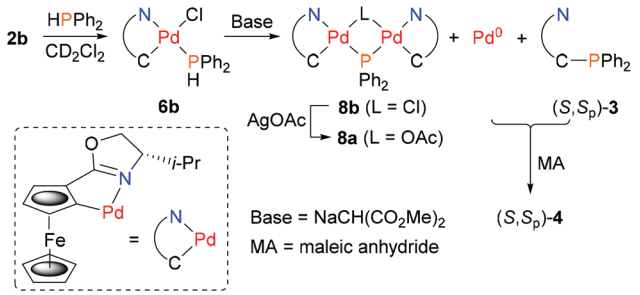


Scheme 3 The generation of (S,S_p)-**4**. by ligand synthesis/palladium capture from palladacycle **2b**.

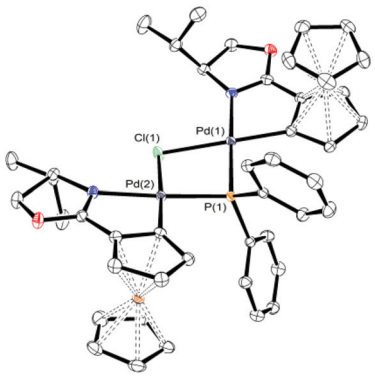
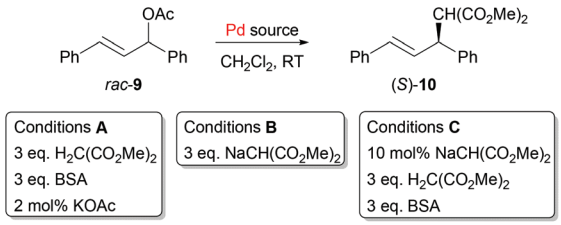


Fig. 2 A representation of the X-ray structure of **8b** (hydrogen atoms omitted for clarity). Principal bond lengths [Å] include: Pd(1)–Cl(1) = 2.4308(6), Pd(2)–Cl(1) = 2.4366(6), Pd(1)–P(1) = 2.2447(6), Pd(2)–P(1) = 2.2457(6). Principal bond angles [deg] include: Pd(1)–Cl(1)–Pd(2) = 86.641(18), Pd(1)–P(1)–Pd(2) = 96.09(2). Thermal ellipsoids are drawn at the 50% probability level. Flack parameter = −0.002(5).

the appreciable formation of this compound from acetate-bridged palladacycle **2a**, revealing a significant advantage of starting with chloride-bridged palladacycle **2b**.[29]

The successful formation of (S,S_p)-**4** from palladacycle precursors prompted us to investigate the use of these as precatalysts in asymmetric synthesis. The allylic alkylation of *trans*-1,3-diphenylallyl acetate **9** was chosen as an exemplar reaction due to its experimental simplicity and the potential to employ the basic reaction conditions for *in situ* ligand/Pd(0) generation (Table 1). Furthermore, ligand (S,S_p)-**3** is known to promote high enantioselectivity in this reaction, and in our hands repetition of conditions reported previously[20a] using BSA as base (3 eq.) gave (*S*)-**10** in 95% ee (conditions **A**, Table 1, entry 1). Replacing $[Pd(C_3H_5)Cl]_2$ with preformed Pd(0) complex (S,S_p)-**4** resulted in some loss of enantioselectivity, and a very significant reduction in activity due to inhibition by maleic anhydride (entry 2). This precluded the use of this π-acidic ligand in any subsequent runs. Instead, a catalytic asymmetric allylic alkylation was attempted directly following the addition of $HPPh_2$ to **2a**, and after stirring for 10 minutes, to resulting *in situ* generated **6a** was added sequentially *rac*-**9**, dimethyl malonate, BSA and KOAc (entry 3). Although slow, we

Table 1 Comparative catalysis of asymmetric allylic alkylation with preformed and palladacycle generated Phosferrox/Pd(0) complexes[a]



Entry	Pd source (mol%)	Conditions	Time (h)	Con. (%)	ee (%)
1	(S,S_p)-**3** (2.5) + $[Pd(C_3H_5)Cl]_2$ (1)	**A**	<1	100	95[b]
2	(S,S_p)-**4** (1)	**A**	96	6	86
3	(S,S_p)-**2a** (1) + $HPPh_2$ (2)	**A**	96	51	85
4	(S,S_p)-**2b** (1) + $HPPh_2$ (2)	**A**	96	77	85
5	(S,S_p)-**2b** (1) + $HPPh_2$ (2)	**A**[c,d]	96	20	94
6	(S,S_p)-**2a** (1) or (S,S_p)-**2b** (1)	**A**	96	0	na
7	(S,S_p)-**3** (2.5) + $[Pd(C_3H_5)Cl]_2$ (1)	**B**	3.5	100	88
8	(S,S_p)-**2b** (1) + $HPPh_2$ (2)	**B**	2.5	100	77
9	(S,S_p)-**2b** (1) + $HPPh_2$ (2)	**C**	1	99	86
10	**8b** (1)	**A**	24	0	na
11	(S,S_p)-**2b** (1) + **11a** (2)	**C**	24	18	85
12	(S,S_p)-**2b** (1) + **11b** (2)	**C**	24[e]	100	84
13	(S,S_p)-**2b** (1) + **11c** (2)	**C**	24[e]	100	83

[a] 1 mmol *rac*-**9** (0.6 M) unless otherwise stated. [b] Lit. value 90% ee.[20a] [c] 0.33 mmol scale. [d] No KOAc. [e] Reaction essentially complete within 1 h (tlc).

noted with interest the formation of product **10**, subsequently isolated as the *S* enantiomer in 85% ee. Use in the same way of chloride **2b** resulted in a similar outcome (entry 4), and on repetition in the absence of KOAc the product ee increased to 94% (entry 5). No product was formed in the absence of added $PHPh_2$ (entry 6). These initial results are consistent with the *in situ* formation of (S,S_p)-**3** ligated Pd(0) as the sole catalytically active species, albeit in low concentration. Replacement of CH_2Cl_2 as solvent with THF or toluene resulted in no product formation.

As sodium dimethyl malonate gave the highest and cleanest conversion to (S,S_p)-**4**, this was employed next as both a base and a nucleophile, and the process referenced initially by use of (S,S_p)-**3**/$[Pd(C_3H_5)Cl]_2$ (3 fold excess, conditions **B**). The lower product ee, compared to that obtained from the use as base of BSA (95% – entry 1 *vs.* 88% – entry 7) is consistent with the superiority of the former conditions noted previously.[30] Significantly, addition of a three-fold excess of sodium dimethyl malonate to *rac*-**9** and 2 mol% of *in situ* generated **6b** resulted in complete conversion within 2.5 h to allylic alkylation product (*S*)-**10** formed in 77% ee (entry 8). Modifying these conditions further (conditions **C**) to the use sodium dimethyl malonate (10 mol%) as the base for *in situ* catalyst formation, and then the addition of BSA/dimethyl malonate (3 equivalents of each) further decreased the reaction time to 1 hour and increased the ee of (*S*)-**10** to 86% (entry 9). The use of conditions **C** provided an *in situ* generated catalyst with

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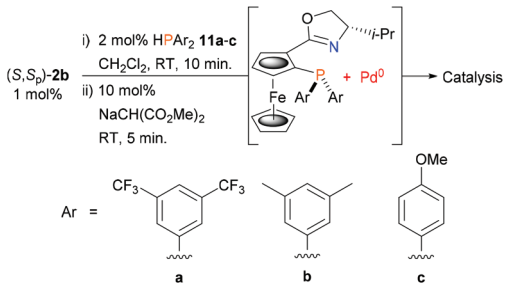

Scheme 4 Phosphine variation for *in situ* ligand synthesis/Pd(0) capture from palladacycle (S,S_p)-**b2**.

comparable activity and selectivity to that obtained using a preformed ligand, and consistent with this outcome is the absence of any catalysis with Pd(II) complex **8b** (entry 10).

Finally, this led us to explore the use of asymmetric allylic alkylation to test the viability of using electronically contrasting diarylphosphines in the ligand synthesis/Pd(0) capture protocol (Scheme 4). For this reaction previous work with related PHOX ligands containing PAr_2 units with various *para* substituents revealed little difference in enantioselectivity compared to the parent PPh_2 containing ligand,[31] albeit with faster conversion with electron-withdrawing substituents.[31a] Accordingly, secondary phosphines **11a–c** were added separately to palladacycle (S,S_p)-**2b** followed by sodium dimethyl malonate, and to the resulting solutions were added *rac*-**9** (50 equivalents w.r.t. Pd) and dimethyl malonate/BSA (*i.e.* conditions **C**). Use of electron-deficient phosphine **11a** resulted in a similar level of product enantioselectivity albeit in reduced yield (Table 1, entry 11). Further examination by ^{31}P NMR spectroscopy (CD_2Cl_2) of the addition of **11a** (−40.8 ppm) to **2b** confirmed the formation of the phosphine coordinated adduct (10.9 ppm), but little Pd^0 complex was observed following the addition of sodium dimethyl malonate and MA. In this instance catalyst formation appears to be limited by the inefficiency of reductive elimination.[32] In contrast, the catalysts derived from phosphines **11b** (entry 12) and **11c** (entry 13) gave essentially complete conversion after 1 h and ee values very similar to that obtained from diphenylphosphine.

Conclusion

We have established that ferrocenyloxazoline-based planar chiral palladacycles **2a**/**b**, on combination with diphenylphosphine (and for **2b** a base), are viable precatalysts for *in situ* catalyst generation using a new ligand synthesis/palladium(0) capture approach. This was demonstrated by formation of a stable Phosferrox/maleic anhydride coordinated Pd(0) complex (S,S_p)-**4a**, and by application of Phosferrox/Pd(0) as a catalyst for asymmetric allylic alkylation in the absence of maleic anhydride. The other palladium(II) complex formed in this process is not a competitive catalyst or catalyst precursor. Product configuration and enantioselectivity using a palladacycle derived catalyst are similar to that obtained using a preformed Phosferrox ligand and a source of Pd(0). In addition to being a precursor to an active and selective catalyst generated in one step, palladacycle **2b** may also be used for multiple catalyst generation with other diarylphosphines. It is anticipated that this approach will aid significantly the generation and identification of palladium based catalysts for application in other areas of asymmetric synthesis.

Experimental

General information

Tetrahydrofuran was distilled over sodium and benzophenone ketyl and dichloromethane distilled over calcium hydride. All reactions were carried out under an inert atmosphere of either nitrogen or argon. Silica gel (60 Å pore size, 40–63 μm technical grade) was used for chromatography. All starting materials not commercially available are specifically referenced.

Synthesis of (S,S_p)-4

(S,S_p)-**3**[19] (0.087 g, 0.18 mmol), tris(dibenzylideneacetone)-dipalladium(0) (0.076 g, 0.08 mmol) and maleic anhydride (0.024 g, 0.24 mmol) were added to a flame dried Schlenk tube and dissolved in toluene (15 mL). The resulting deep purple solution was stirred vigorously overnight resulting in the formation of a dark suspension. The reaction was filtered through Celite™ using toluene as the eluent and the solvent removed *in vacuo*. Purification by column chromatography (SiO_2, 40% EtOAc/hexane) yielded an orange solid (0.07 g, 61%); mp decomposed ~200 °C (under argon); HRMS (AS) $[M + H]^+$ anal. calcd for $C_{32}H_{31}FeNO_4PPd$ 686.0389, found 686.0389; $[\alpha]_D^{20.5°C}$ = −538 (c = 0.46, $CHCl_3$); ν_{max} (film)/cm^{-1} 3056, 3016, 2960, 2923, 2873, 1790, 1723, 1626; ^{1}H NMR (500 MHz, $CDCl_3$) major isomer (ratio of isomers = 1.6 : 1) δ 7.80 (2H, ddd, J = 11.6, 7.8, 1.5 Hz), 7.56–7.46 (3H, m), 7.33–7.27 (3H, m), 7.08 (2H, ddd, J = 11.0, 6.6, 3.2 Hz), 5.04 (1H, brs), 4.70 (1H, t, J = 2.6 Hz), 4.41–4.38 (1H, m), 4.35 (1H, t, J = 3.7 Hz), 4.33–4.21 (3H, m), 4.07 (1H, dd, J = 10.5, 3.8 Hz), 3.96 (5H, s), 2.80 (1H, dtd, J = 13.8, 6.9, 3.3 Hz), 1.07 (3H, d, J = 7.1 Hz), 0.99 (3H, d, J = 6.9 Hz); minor isomer 7.76–7.68 (2H, m), 7.56–7.46 (3H, m), 7.33–7.27 (3H, m), 7.21–7.14 (2H, m), 5.04 (1H, brs), 4.72 (1H, t, J = 2.6 Hz), 4.50–4.46 (1H, m), 4.33–4.21 (3H, m), 3.86 (5H, s), 3.87–3.79 (2H, m), 2.67 (1H, dtd, J = 13.7, 6.9, 3.4), 1.04 (3H, d, J = 7.0 Hz), 0.95 (3H, d, J = 6.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) major isomer δ 172.6 (d, J = 2.0 Hz), 171.5 (d, J = 5.2 Hz), 169.1, 135.5 (d, J = 36.7 Hz), 134.9 (d, J = 16.7 Hz), 134.7 (d, J = 40.1 Hz), 131.6 (d, J = 13.3 Hz), 131.2 (d, J = 2.0 Hz), 129.4 (d, J = 1.6 Hz), 128.6 (d, J = 10.8 Hz), 128.5 (d, J = 9.7 Hz), 75.5 (d, J = 2.6 Hz), 74.0 (d, J = 2.3 Hz), 73.5 (d, J = 46.2 Hz), 73.4 (d, J = 1.5 Hz), 73.1, 71.8 (d, J = 0.5 Hz), 71.4, 67.7, 47.4 (d, J = 31.7 Hz), 46.4 (d, J = 1.8 Hz), 29.2, 19.2, 14.7; minor isomer 172.9 (d, J = 1.5 Hz), 171.2 (d, J = 5.0 Hz), 169.1, 137.3 (d, J = 37.8 Hz), 135.1 (d, J = 16.6 Hz), 133.7 (d, J = 40.2 Hz), 131.4 (d, J = 13.1 Hz), 131.4 (d, J = 2.1 Hz), 129.1 (d, J = 1.5 Hz), 128.8 (d, J = 11.2 Hz), 128.5 (d, J = 9.7

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Hz), 75.9 (d, J = 2.7 Hz), 75.1 (d, J = 1.8 Hz), 74.0 (d, J = 33.0 Hz), 74.0 (d, J = 2.1 Hz), 73.4 (d, J = 1.3 Hz), 73.1, 71.6, 67.7, 47.8 (d, J = 1.7 Hz), 46.7 (d, J = 32.7 Hz), 29.2, 19.2, 14.9; ^{31}P NMR (202 MHz, $CDCl_3$) major isomer δ 14.39; minor isomer 15.81.

General procedure for the synthesis of 5a, 5b and 6b

(S,S_p)-**2a** [18a,b] or (S,S_p)-**2b** [18b] (0.029 mmol) and either triphenylphosphine or diphenylphosphine (0.057 mmol) were added to a flame dried Schlenk tube and dissolved in dichloromethane (1 mL) and stirred at room temperature for 1 hour. The solvent was removed *in vacuo* yielding the product.

5a. Obtained as a deep orange solid (0.034 g, 83%): mp 136–137 °C (under argon), MS (EI) $[M]^+$ anal. calcd for $C_{36}H_{36}FeNO_3PPd$ 723.1, found 723.1; $[\alpha]_D^{23.5°C}$ = −572 (c = 0.55, MeCN); ν_{max} (film)/cm^{-1} 3052, 2961, 2925, 2871, 1615, 1582, 1499; ^{1}H NMR (500 MHz, MeCN-d^3) δ 7.78–7.72, (6H, m), 7.52–7.48 (3H, m), 7.46–7.41 (6H, m), 4.63 (1H, t, J = 9.5 Hz), 4.59–4.55 (1H, m), 4.45 (1H, d, J = 1.9 Hz), 4.07 (1H, ddd, J 10.0, 7.5, 4.2 Hz), 4.02 (1H, t, J = 2.2 Hz), 3.90 (5H, s), 3.30 (1H, d, J = 2.2 Hz), 2.34–2.26 (1H, m), 1.25 (3H, s), 1.03 (3H, d, J = 6.9 Hz), 0.88 (3H, d, J = 7.2 Hz); ^{13}C NMR (125 MHz, MeCN-d^3) δ 179.8, 176.3, 135.7 (d, J = 12.0 Hz), 132.1 (d, J = 50.3 Hz), 131.5 (d, J = 2.4 Hz), 129.1 (d, J = 10.7 Hz), 90.2 (d, J = 8.6 Hz), 77.3 (d, J = 9.0 Hz), 73.8 (d, J = 1.3 Hz), 73.1 (d, J = 3.0 Hz), 70.9, 69.7 (d, J = 2.6 Hz), 68.3 (d, J = 3.3 Hz), 65.6, 29.3, 23.9, 19.3, 15.7; ^{31}P NMR (202 MHz, MeCN-d^3) δ 36.48.

5b. Purified by column chromatography (SiO_2, 20% EtOAc/hexane) to give the product as a deep orange solid (0.038 g, 95%): mp decomposed ~230 °C (under argon); HRMS (AS) $[M\text{-}Cl]^+$ anal. calcd for $C_{34}H_{33}FeNOPPd$ 664.0699, found 664.0711; $[\alpha]_D^{22.8°C}$ = −825 (c = 0.26, MeCN); ν_{max} (film)/cm^{-1} 3077, 3052, 2958, 2925, 2867, 1618, 1503; ^{1}H NMR (500 MHz, MeCN-d^3) δ 7.78–7.72 (6H, m), 7.53–7.49 (3H, m), 7.48–7.43 (6H, m), 4.67–4.57 (2H, m), 4.47 (1H, d, J = 1.9 Hz), 4.18 (1H, ddd, J = 10.2, 6.3, 4.2 Hz), 4.02 (1H, t, J = 2.1 Hz), 3.97 (5H, s), 3.04 (1H, brs), 2.87 (1H, brs), 1.06 (3H, d, J = 6.9 Hz), 0.92 (3H, d, J = 7.2 Hz); ^{13}C NMR (125 MHz, MeCN-d^3) δ 179.9, 135.6 (d, J = 11.7 Hz), 132.9 (d, J = 51.3 Hz), 131.6, 129.1 (d, J = 10.8 Hz), 94.6, 75.9 (d, J = 8.7 Hz), 74.2, 73.3, 70.9, 69.4, 68.0 (d, J = 3.1 Hz), 65.6, 29.4, 19.2, 15.5; ^{31}P NMR (202 MHz, MeCN-d^3) δ 37.49.

6b. Obtained as a deep orange solid (0.025 g, 73%): mp 110–112 °C (under argon), MS (EI) $[M]^+$ anal. calcd for $C_{28}H_{29}ClFeNOPPd$ 623.0, found 623.0; $[\alpha]_D^{22.8°C}$ = −882 (c = 0.20, MeCN); ν_{max} (film)/cm^{-1} 3077, 3055, 2961, 2929, 2871, 1615, 1503; ^{1}H NMR (500 MHz, MeCN-d^3) δ 8.05 (2H, dd, J = 12.0, 7.4 Hz), 7.88 (2H, dd, J = 12.7, 7.3 Hz), 7.58–7.49 (4H, m), 7.47 (2H, td, J = 7.3, 2.0 Hz), 6.56 (1H, d, J = 388.9 Hz), 4.64 (1H, dd, J = 9.0, 6.2 Hz), 4.57 (1H, t, J = 9.7 Hz), 4.54 (1H, d, J = 2.2 Hz), 4.45 (1H, brs), 4.37 (1H, t, J = 2.4 Hz), 4.17–4.12 (1H, m), 4.07 (5H, s), 2.90 (1H, brs), 1.04 (3H, d, J = 5.9 Hz), 0.90 (3H, d, J = 7.0 Hz); ^{13}C NMR (125 MHz, MeCN-d^3) δ 179.9, 135.2 (d, J = 11.1 Hz), 134.8 (d, J = 11.4 Hz), 132.2 (d, J = 2.6 Hz), 132.0 (d, J = 2.6 Hz), 129.9 (d, J = 10.8 Hz), 129.7 (d, J = 11.0 Hz), 129.5 (d, J = 51.2 Hz), 129.5 (d, J = 52.8 Hz), 91.6 (d, J = 8.0 Hz), 74.8 (d, J = 1.0 Hz), 73.8 (d, J = 15.7 Hz), 73.2 (d, J = 3.2 Hz), 70.7, 70.2 (d, J = 4.5 Hz), 68.0 (d, J = 3.4 Hz), 66.8, 29.2, 19.1, 15.1; ^{31}P NMR (202 MHz, MeCN-d^3) δ 8.44.

Synthesis of (S,S_p)-7

(S)-**1** [17] (0.059 g, 0.2 mmol) was added to a flame dried Schlenk tube under an atmosphere of argon and dissolved in dry THF (5 mL). The resulting orange solution was cooled to −78 °C and stirred for 5 min after which *n*-butyl lithium (2.5 M in hexanes) (0.11 mL, 0.28 mmol) was added slowly. After stirring for 2 hours the mixture was warmed to 0 °C and chlorodiphenylphosphine oxide (0.076 mL, 0.4 mmol) was added and the reaction was allowed to warm to room temperature. After an additional 15 min, the reaction was diluted with diethyl ether and then quenched with saturated sodium hydrogen carbonate solution. The organics were separated with H_2O, washed with brine, dried over $MgSO_4$ and the solvent removed *in vacuo* giving a crude product containing a 2 : 1 mixture of diastereoisomers. The diastereoisomers were separated by column chromatography (SiO_2, 2% MeOH/Et_2O) yielding the desired product as a yellow brown solid (0.0255 g, 26%): mp 197–198 °C; HRMS (ES) $[M + H]^+$ anal. calcd for $C_{28}H_{29}FeNO_2P$ 498.1280, found 498.1263; $[\alpha]_D^{19.4°C}$ = +114 (c = 0.2, $CHCl_3$); ν_{max} (film)/cm^{-1} 3080, 3062, 2963, 2930, 2871, 1648, 1120; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76–7.71 (2H, m), 7.69–7.64 (2H, m), 7.50–7.46 (1H, m), 7.45–7.36 (5H, m), 5.06 (1H, dt, J = 2.6, 1.4 Hz), 4.49 (5H, s), 4.45 (1H, dd, J = 4.4, 2.4 Hz), 4.22–4.18 (1H, m), 3.93 (1H, dd, J = 3.9, 2.5 Hz), 3.72 (1H, td, J = 9.3, 6.3 Hz), 3.13 (1H, t, J = 8.8 Hz), 1.53–1.47 (1H, m), 0.81 (3H, d, J = 6.8 Hz), 0.61 (3H, d, J = 6.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.6, 134.86 (d, J = 107 Hz), 134.8 (d, J = 110.4 Hz), 131.6 (d, J = 9.3 Hz), 131.4 (d, J = 9.7 Hz), 131.3 (d, J = 2.6 Hz), 131.0 (d, J = 2.9 Hz), 128.2 (d, J = 4.3 Hz), 128.1 (d, J = 4.8 Hz), 78.5 (d, J = 14.6 Hz), 75.7 (d, J = 109.9 Hz), 74.5 (d, J = 9.1 Hz), 73.5 (d, J = 8.2 Hz), 72.4, 71.5 (d, J = 10.9 Hz), 71.4, 70.1, 32.3, 19.2, 18.0; ^{31}P NMR (202 MHz, $CDCl_3$) δ 26.40.

Synthesis of (S,S,S_p,S_p)-8b

To a flame dried Schlenk tube (tube-1) was added sodium *tert*-butoxide solution (2 M in THF) (0.05 mL, 0.10 mmol) followed by a solution of dimethyl malonate (22.6 μl, 0.20 mmol) in THF (1 mL) at 0 °C. After stirring for 30 min the solvent was removed under high vacuum to give a beige residue. In a separate flame dried Schlenk tube (tube-2), (S,S_p)-**6b** (0.0125 g, 0.020 mmol) was dissolved in CH_2Cl_2 (1.7 mL) and then the contents of Schlenk tube (2) were transferred to Schlenk tube (1) and stirred at room temperature for 10 min. The solvent was then removed *in vacuo* and the residue purified by column chromatography (SiO_2, 10% EtOAc/hexane) to give an orange solid (0.007 g, 70%): mp > 230 °C (under argon); HRMS (AS) $[M - Cl]^+$ anal. calcd for $C_{44}H_{46}Fe_2N_2O_2PPd_2$ 991.0103, found 991.0093; $[\alpha]_D^{20.1°C}$ = −2000 (c = 0.23, $CHCl_3$); ν_{max} (film)/cm^{-1} 3096, 2958, 2923, 2967, 1617, 1495; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12–8.05 (4H, m), 7.38–7.34 (6H, m), 4.49–4.47 (4H, m), 4.36 (2H, d, J = 1.8 Hz), 4.08 (2H, td, J = 8.0, 4.6 Hz), 4.04 (10H, s), 4.02 (2H, t, J = 2.3 Hz), 3.22 (2H, d, J = 1.6 Hz), 2.51–2.43 (2H,

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m), 1.06 (6H, d, J = 6.8 Hz), 0.97 (6H, d, J = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.9, 137.2 (d, J = 32.8 Hz), 135.4 (d, J = 12.7 Hz), 128.8, 127.8 (d, J = 10.5 Hz), 91.4 (d, J = 2.9 Hz), 75.1 (d, J = 8.6 Hz), 73.3 (d, J = 1.6 Hz), 72.2, 70.0, 69.0, 66.9, 64.5, 29.3, 19.6, 16.0; ^{31}P NMR (202 MHz, $CDCl_3$) δ 23.40.

Synthesis of (S,S,S_p,S_p)-8a

Addition of excess AgOAc to an NMR tube containing (S,S,S_p, S_p)-**8b** showed the formation of acetate bridged palladacycle (S, S,S_p,S_p)-**8a**; ν_{max} (film)/cm^{-1} 3096, 2958, 2919, 2849, 1621, 1556, 1495; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12–7.97 (4H, m), 7.33–7.27 (6H, m), 4.51–4.46 (4H, m), 4.34 (2H, brs), 4.09–4.03 (2H, m), 4.00 (10H, s), 3.97 (2H, brs), 3.00 (2H, brs), 2.70–2.60 (2H, m), 2.01 (3H, brs), 1.04 (6H, d, J = 6.8 Hz), 0.95 (6H, d, J = 7.1 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 55.63.

Phosphine insertion studies

Using a glove box, 0.01 mmol of either (S,S_p)-**2a** or (S,S_p)-**2b** was dissolved in CD_2Cl_2 (0.7 mL) in an NMR tube fitted with a J. Young valve under an inert atmosphere. After addition of the reagents approximately 10 minutes elapsed before the first NMR spectrum was recorded.

In situ catalyst preparation and asymmetric allylic alkylation (conditions C)

To a flame dried Schlenk tube (tube-1) was added sodium *tert*-butoxide solution (2 M in THF) (0.05 mL, 0.10 mmol) followed by a solution of dimethyl malonate (22.6 μl, 0.20 mmol) in THF (1 mL) at 0 °C. After stirring for 30 min the solvent was removed under high vacuum to give a beige residue. In a separate flame dried Schlenk tube (tube-2), (S, S_p)-**2b** (0.0088 g, 0.010 mmol) was dissolved in CH_2Cl_2 (1.7 mL) and phosphine (0.020 mmol) was added and stirred for 10 min. 1,3-Diphenylallyl acetate (0.252 g, 1.0 mmol) was dissolved in CH_2Cl_2 (1.7 mL) and then added to Schlenk tube (2) followed by dimethyl malonate (0.34 mL, 3.0 mmol). The contents of Schlenk tube (2) were transferred to Schlenk tube (1) and stirred for 5 min after which *N*,*O*-bis(trimethylsilyl) acetamide (0.74 mL, 3.0 mmol) was added and the reaction allowed to stir at room temperature. After completion or 24 hours (whichever came first), the reaction was quenched with saturated ammonium chloride, separated with diethyl ether, dried with magnesium sulphate and the solvent removed *in vacuo*. A ^{1}H NMR was performed at this point to determine the conversion. Purification by column chromatography (SiO_2, 5% EtOAc/hexane) gave the product (S)-**10** as a colourless oil for which the ^{1}H/^{13}C NMR spectra matched previously reported data.[33] The enantiomeric excess was determined by HPLC analysis using a CHIRALCEL OD-H column; eluent = 98 : 2 (hexane : IPA); flow rate = 0.5 mL min^{-1}; concentration = 0.0015 g mL^{-1}, injection volume = 5 μl, wavelength = 254 nm. (S)-Enantiomer RT = 20.5 min, (R)-enantiomer RT = 18.9 min.

Conflicts of interest

There are no conflicts to declare.

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