ChemPubSoc Europe

DOI: 10.1002/ejic.201800720

EurJIC European Journal of Inorganic Chemistry

Full Paper

Chiral Metallocycles

Efficient Synthesis of Malonate Functionalized Chiral Phosphapalladacycles and their Catalytic Evaluation in Asymmetric Hydrophosphination of Chalcone

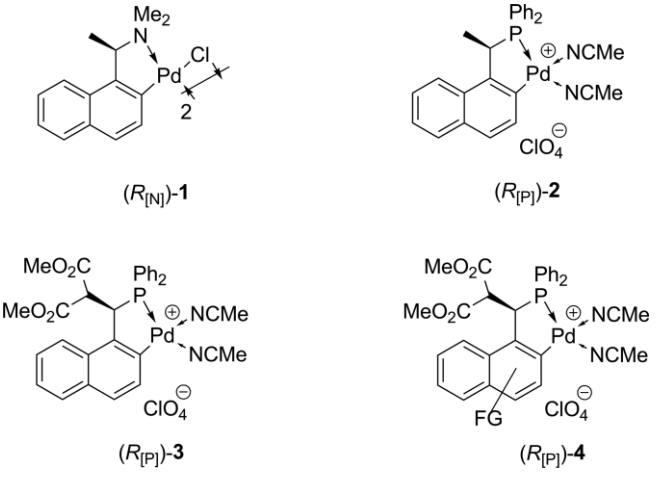
Xi-Rui Li,[a] Yu Chen,[b,c] Benjamin Piaoxiang Pang,[a] Jaeyu Tan,[a] Yongxin Li,[a] Sumod A. Pullarkat,[a] and Pak-Hing Leung*[a]

Abstract: Four chiral phosphapalladacycle complexes functionalized with the malonate moiety at the chiral carbon have been synthesized via a consecutive asymmetric hydrophosphination and cyclometallation protocol. High conversions were achieved in the P–H addition reaction, which was itself catalyzed by a phosphapalladacycle. Moderate to good enantioselectivities, were obtained for this step depending on the nature of the functional groups present on the naphthalene backbone. In contrast, the outcome of the subsequent cyclometallation reaction relies highly on the character of the functional groups. The catalytic potential of the synthesized phosphapalladacycle complexes was evaluated in the hydrophosphination reaction of chalcone with moderate results.

Introduction

The synthesis and application of *ortho*-palladated C-N complexes have been well established.[1-7] In particular, the N-donor palladacycle initially developed by Wild and co-workers[2] has been employed in a wide variety of catalytic asymmetric reactions, for example, as the catalyst in a overman-rearrangement reaction,[3] as either a catalyst precursor or promoter in hydrophosphination,[4] hydroamination,[5] Heck,[6] and Suzuki reaction and as an optical resolution reagent for various chiral ligands. In contrast to the predominately sigma donating effect of the nitrogen–metal bond in the azapalladacycle complexes, π back bonding effect is known to be present in the phosphapalladacycle complexes as seen from our earlier studies.[8] This in conjunction with other structural and electronic features is thought to be responsible for the different catalytic reactivity and selectivity of the resulting metal-phosphine complex when compared to the azapalladacycle. However, reports on chiral cyclopalladated C-P compounds, a congener of C-N complexes are relatively less,[9] though the phosphine palladium complexes have played an important role in various organic reactions, such as [4+2] cycloadditions,[10] Heck,[11] Suzuki[9c,12] Stille,[13] Sonogashira coupling,[14] Claisen rearrangements,[15] As/P–H addition reaction[4a,16] and medicinal chemistry.[17]

The application of cyclopalladated complex ($R_{[N]}$)-**1** (Figure 1) as catalysts in the synthesis of various chiral phosphine compounds via asymmetric hydrophosphination reactions of a variety of substrates including α,β- and α,β,γ,δ-unsaturated malonate esters,[18] α,β-unsaturated carbonyl compounds,[19] enones,[20] and α,β-unsaturated *N*-acylpyrroles[21] has been highlighted recently. The CP compound ($R_{[P]}$)-**2** is known as an excellent catalyst for asymmetric P–H addition reaction of 4-oxo-enamides,[22] *N*-enoyl phthalimides,[23] benzoquinones[24].



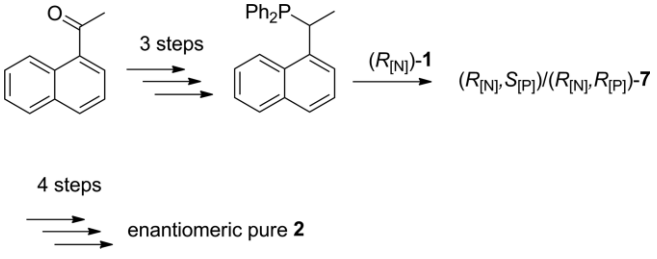
($R_{[N]}$)-**1** ($R_{[P]}$)-**2** ($R_{[P]}$)-**3** ($R_{[P]}$)-**4**

Figure 1. Example of selected existing cyclopalladated complexes (**1–3**) and their functionalized derivatives (**4**) developed in this study. [N] denotes a coordinated amine ligand and [P] represents a phosphine ligand.

During the course of studying the asymmetric P–H addition, we found that minor modifications of the functional groups present on the phosphorus ligands backbone can help to tune

[a] *Division of Chemistry & Biological Chemistry, School of Physical and Mathematical Sciences, Nanyang Technological University, Singapore 637371, Singapore*
E-mail: pakhing@ntu.edu.sg
http://www.ntu.edu.sg/home/pakhing/
[b] *Department of Chemistry and Biochemistry Queens College of the City University of New York, 65-30 Kissena Blvd., Queens, New York 11367, United States*
[c] *Ph.D. Program in Chemistry, The Graduate Center of the City University of New York, 365 Fifth Ave., New York, New York 10016, United States*
Supporting information and ORCID(s) from the author(s) for this article are available on the WWW under https://doi.org/10.1002/ejic.201800720.

the catalytic properties of the catalyst. On the other hand, considering the laborious synthetic procedure towards complex ($R_{[P]}$)-**2** (Scheme 1), we decided to prepare its congeneric complexes ($R_{[P]}$)-**3** and derivatives represented by ($R_{[P]}$)-**4** by using a protocol that involved asymmetric hydrophosphination followed by regioselective cyclometallation.[16c] Besides being electronically different from the traditional methyl moiety, the presence of the diester group at the chiral center in the new complexes also results in greater steric hindrance in the cyclometallated ring system that may potentially be beneficial in enhancing stereocontrol during asymmetric synthesis. In addition to the aforementioned, the rationale behind our ligand design also took into account the potential electronic effects that can come into play by modification of the naphthalene ring system. We therefore planned to introduce different functional groups, including electron-withdrawing group (F), electron-donating groups (OMe, Me), and greater delocalization (phenanthrenyl), into the aromatic ring to synthesize complexes of the type depicted by **4**. These modifications are expected to have an impact on the nature of the C–Pd bond of the newly designed phosphapalladacycles. This study also has relevance in the greater context of cyclometallation reactions since for cyclopalladation reactions involving free phosphine ligands, there are only very few examples known in literature involving functionalized chiral aromatic ring-based substrates.[16c,25]



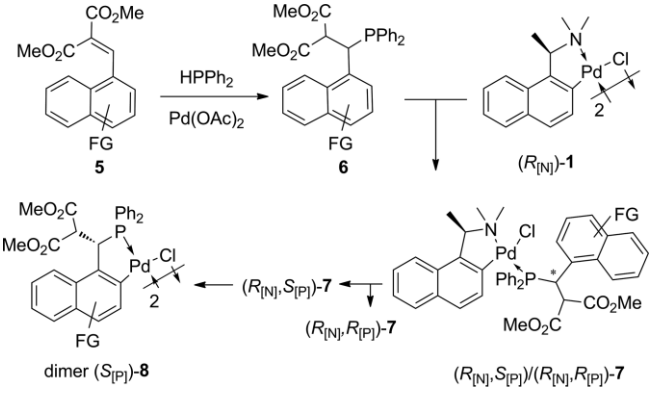
Scheme 1. Overview of the traditional procedure for the synthesis of phosphapalladacycle ($R_{[P]}$)-**2**.

We herein report the efficient synthesis of four chiral cyclophosphapalladated complexes with different steric and electronic properties. In this study, chalcone is used as a model substrate for comparison of the catalytic properties of these new complexes in asymmetric hydrophosphination reaction.

Results and Discussion

We initiated our preliminary investigations by using palladium acetate as the catalyst in the synthesis of the racemic ligands **6** via the hydrophosphination reaction between malonate activated substrates **5** and diphenylphosphine in methanol at room temperature (Scheme 2). It needs to be noted that based on our previous studies it has been established that the malonate moiety can sufficiently activate C=C bond of substrates such as **5** towards the P–H addition reaction.[26]

The conversions of this reaction were greater than 99 % as seen from the $^{31}P\{^{1}H\}$ NMR spectroscopy. Treatment of racemic phosphine ligands **6** with azapalladacycle ($R_{[N]}$)-**1** leads to the formation of diastereoisomers ($R_{[N]}$,$S_{[P]}$)/($R_{[N]}$,$R_{[P]}$)-**7**, which were



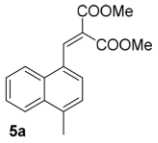
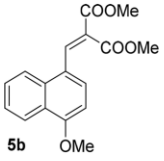
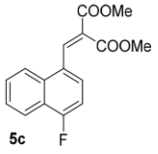
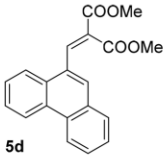
Scheme 2. Synthesis of ($S_{[P]}$)-**8** from racemic phosphine ligands.

then separated by either fractional crystallization or column chromatography. With ($R_{[N]}$,$S_{[P]}$)-**7** in hand, we subsequently explored the synthesis of dimeric phosphapalladacycles ($S_{[P]}$)-**8** by cyclometallation reaction (Table 1). Before the cyclometallation reaction of ($R_{[N]}$,$S_{[P]}$)-**7a**/**7b**, concentrated HCl was added to the solution of ($R_{[N]}$,$S_{[P]}$)-**7a**/**7b** in acetone at room temperature for 1 hour to remove the C–N auxiliary (Scheme 2). Sodium acetate was then added as a base, and C–Pd–P five-membered ring formation led to the dimeric product ($S_{[P]}$)-**8a**/**8b** at room temperature after 1 h and 3 h respectively, with a yields of 77 % and 72 %, respectively (Table 1, entry 1 and 2). When the solution of concentrated HCl and ($R_{[N]}$,$S_{[P]}$)-**7c** in acetone was refluxed for 40 minutes, the final product ($S_{[P]}$)-**8c** was obtained in 81 % yield (entry 3). On the other hand, dimeric ($S_{[P]}$)-**8d** was formed in 54 % yield upon treatment of ($R_{[N]}$,$S_{[P]}$)-**7d** with concentrated HCl at 40 °C for 1 hour, followed by treatment of NEt_3 in degassed DCM (entry 4).

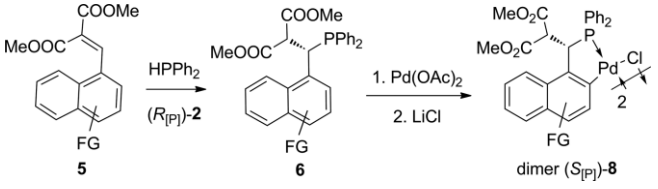
The final overall yields of enantiomerically pure dimer ($S_{[P]}$)-**8**, however, were very low (18–35 %, Table 1). In addition, the usage of stoichiometric amount of chiral reagent ($R_{[N]}$)-**1** is not economical. We, therefore, decided to explore a facile and efficient alternate route for synthesis of the dimer complexes ($S_{[P]}$)-**8** by phosphapalladacycle ($R_{[P]}$)-**2** catalyzed asymmetric hydrophosphination reaction followed by a cyclometallation step (Scheme 3).

Following the general conditions established from our previous work,[16c] we first examined the reactivity and enantioselectivity of various substrates catalyzed by ($R_{[P]}$)-**2** in the asymmetric P–H addition reaction, at –80 °C in the presence of NEt_3 (Table 2). Initial studies established that the use of a single solvent system resulted in either very low conversions, such as in the case of $CHCl_3$, THF, acetone, and toluene, or unaccepted enantioselectivities, such as in the case of MeOH. Therefore, a mixture of two different solvents was employed as shown in Table 2. The best reactivity and enantioselectivity were observed on substrate **5c** among the four substrates examined **5** (entry 1–4) (> 99 % yield, 88 % *ee*), hence it was selected as the sample substrate for further optimizing the asymmetric hydrophosphination reaction conditions. The mixture of MeOH and chloroform gave both excellent conversion and enantioselectivity (entry 3, 5–8). Different ratio of methanol and chloroform in the solvent system was also examined, which showed that

Table 1. Coordination reaction and optical resolution of palladacycles.

Entry	Substrate	Condition[a]	Yield of ($R_{[N]}$,$S_{[P]}$)-**7** from optical resolution[b]	Yield ($R_{[N]}$,$R_{[P]}$)-**7** from optical resolution[b]	Yield ($S_{[P]}$)-**8** from ($R_{[N]}$,$S_{[P]}$)-**7** (%)[b]	Overall yield of ($S_{[P]}$)-**8**
1	 **5a**	conc. HCl, RT, 1 h NaOAc, RT, 1 h	35	14	77	27
2	 **5b**	conc. HCl, RT, 1 h NaOAc, RT, 3 h	32	17	72	23
3	 **5c**	conc. HCl, reflux, 40 min	43	12	81	35
4	 **5d**	conc. HCl, 40 °C, 1 h degassed DCM, NEt_3	36	13	54	18

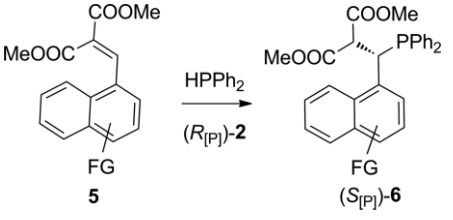
[a] Condition of the reaction from **7** to **8**. [b] Isolated yields.



Scheme 3. Stereoselective synthesis of ($S_{[P]}$)-**8** via ($R_{[P]}$)-**2** catalyzed asymmetric hydrophosphination and subsequent cyclometallation.

the best result was obtained when the volume ratio of the two was 1:1 (entry 3, 9–11). This was subsequently selected as the optimum solvent. With the free phosphine ligands **6** in hand, we then examined the yields of cyclometallation reaction with various palladium sources (Table 3). The reaction conditions and palladium sources employed differ depending on the various functional groups present on the aromatic rings. In general, the *ortho*-H on the aromatic ring is activated when the phosphorus ligand coordinates to the palladium center. $Pd(OAc)_2$, $Li_2[PdCl_4]$, and $PdCl_2(NCMe)_2$ are therefore usually used as the palladium sources for cyclometallation. On the other hand, the C–N palladated compounds similar to **1** can be the palladium source too, via metal transfer methods followed by removal of the C–N auxiliary. Palladium acetate proved to be the optimal palladium source for the cyclometallation reaction of **6a**–**d** (entry 1–3, 4–6). Although the enantioselectivities of **5a** and **5b** were only moderate (Table 2, entry 1 and 2, 58 % for **5a**, 61 % for **5b**), the yields of enantiomerically pure product ($S_{[P]}$)-**8** after cyclometallation reaction and fractional crystallization process were still acceptable and better than the one obtained by the previously adopted method (38 % and 42 % respectively)

Table 2. Screening of mixed solvent systems for the asymmetric P–H reaction catalyzed by ($R_{[P]}$)-**2**.

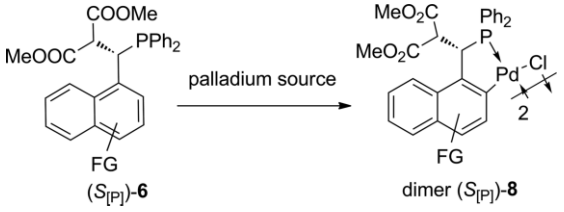


Entry	Substrate	Solvent	*t* [d]	Conversion [%][a]	*ee* [%][b]
1	5a	MeOH/$CHCl_3$ (v:v = 1:1)	4	> 99	58
2	5b	MeOH/$CHCl_3$ (v:v = 1:1)	4	> 99	61
3	5c	MeOH/$CHCl_3$ (v:v = 1:1)	1	> 99	88
4	5d	MeOH/$CHCl_3$ (v:v = 1:1)	5	> 99	78
5	5d	MeOH/acetone (v:v = 1:1)	5	14	35
6	5c	MeOH/THF (v:v = 1:1)	3	19	31
7	5c	MeOH/acetone (v:v = 1:1)	3	22	64
8	5c	EtOH/$CHCl_3$ (v:v = 1:1)	2	> 99	19
9	5c	MeOH/$CHCl_3$ (v:v = 2:1)	1	> 99	79
10	5c	MeOH/$CHCl_3$ (v:v = 3:2)	1	> 99	26
11	5c	MeOH/$CHCl_3$ (v:v = 1:2)	1	32	37

[a] The conversions were examined by $^{31}P\{^1H\}$ NMR. [b] The *ee* were examined by $^{31}P\{^1H\}$ NMR after coordinating of free phosphine ligands to ($R_{[N]}$)-**1**.

(Table 3, entry 7 and 1). To our delight, enantiomerically pure products ($S_{[P]}$)-**8c/8d** can also be prepared in good yields when **6c** and **6d** were treated with palladium acetate (Table 3, entry 4 and 8, 73 %, 65 % respectively). The molecular structure and the absolute stereochemistry of dimer ($S_{[P]}$)-**8a**–**c** were determined by X-ray crystallography (Figure 2, Figure 3 and Figure 4).

Table 3. The cyclometallation reaction of free ligands.



Entry	Substrate	Palladium source	Yield [%][a]
1	6b	$Pd(OAc)_2$	42
2	6b	$PdCl_2(NCMe)_2$	22
3	6b	$Li_2[PdCl_4]$	15
4	6c	$Pd(OAc)_2$	73
5	6c	$PdCl_2(NCMe)_2$	34
6	6c	$Li_2[PdCl_4]$	52
7	6a	$Pd(OAc)_2$	38
8	6d	$Pd(OAc)_2$	65

[a] The yields are the final yields of the enantiomeric pure product ($S_{[P]}$)-**8** after the fractional crystallization.

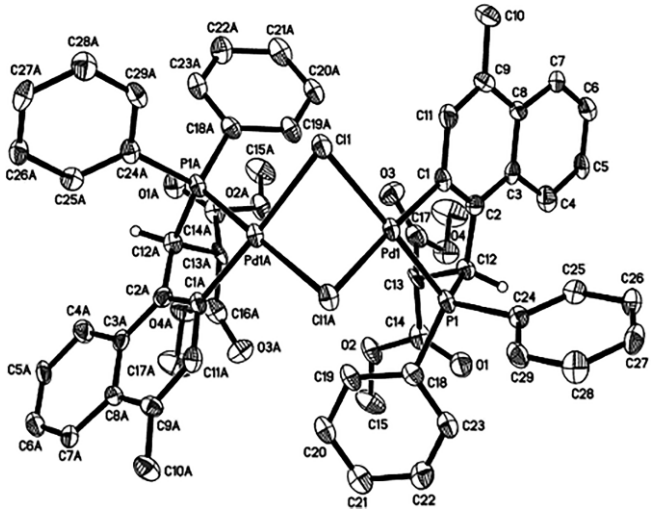


Figure 2. X-ray crystal structure of complex ($S_{[P]}$)-**8a** (CCDC 1835263). Selected bond lengths [Å] C2–C12 1.511(14); C12–P1 1.834(10); C1–C2 1.382(13); P1–Pd1 2.192(3); C1–Pd1 2.015(9); Cl1–Pd1 2.422(3); Cl1–Pd1 2.443(2). Selected bond angles [°] C2–C12–P1 103.3(6); C1–C2–C12 117.0(9); C12–P1–Pd1 104.0(4); C2–C1–Pd1 122.7(8); C1–Pd1–P1 80.5(3); Cl1–Pd1–Cl1 83.46(11); Pd1–Cl1–Pd1 74.09(7).

The enantiomeric purity of ($S_{[P]}$)-**8** was examined by exchanging the chloro bridge of the dimeric complex with *l*-proline to form two pairs of diastereoisomers. Treating racemic **8** with *l*-proline led to the formation of two pairs of diastereomeric regio-isomers ($S_{[P]}$,$S_{[O]}$)-**9a**, ($R_{[P]}$,$S_{[O]}$)-**9a** and ($S_{[P]}$,$S_{[O]}$)-**9b**, ($R_{[P]}$,$S_{[O]}$)-**9b**, which displayed four chemical shifts in $^{31}P\{^1H\}$ NMR (Scheme 4). On the other hand, there were only two chemical shifts observed in $^{31}P\{^1H\}$ NMR when we added

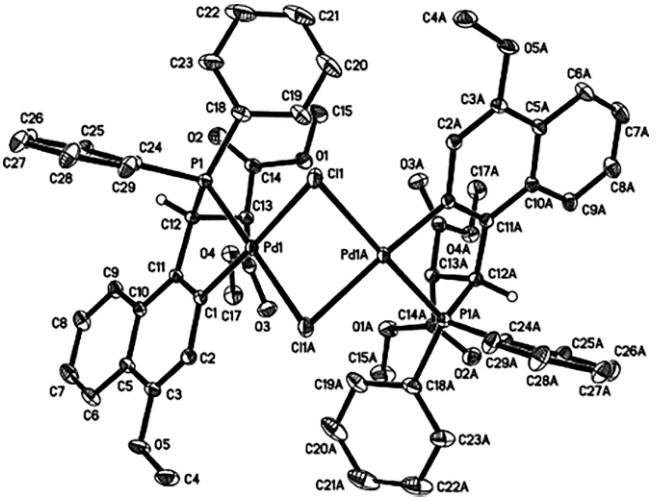


Figure 3. X-ray crystal structure of complex ($S_{[P]}$)-**8b** (CCDC 1835218). Selected bond lengths [Å] C12–P1 1.8456(14); C1–Pd1 2.0105(14); P1–Pd1 2.1914(4); C11–C12 1.5131(19); C1–C11 1.388(2). Selected bond angles [°] C1–Pd1–P1 79.83(4); C12–P1–Pd1 103.39(5); C11–C1–Pd1 121.78(10); Cl1–Pd1–Cl1A 84.17(7); Pd1–Cl1–Pd1A 75.40(5); C1–C11–C12 117.5(5); C11–C12–P1 101.2(4).

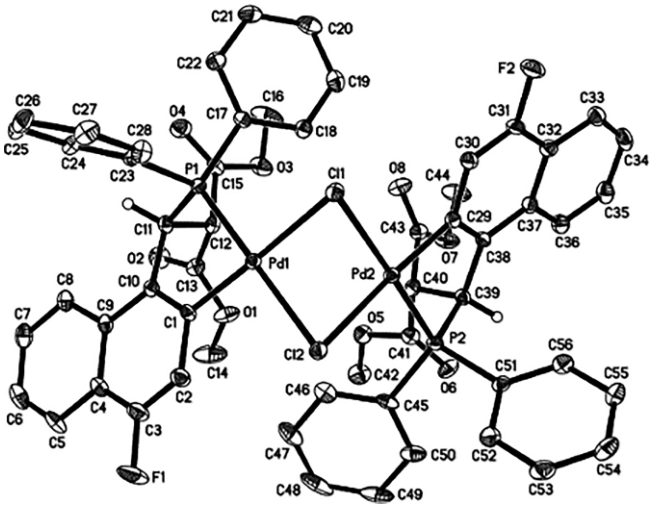
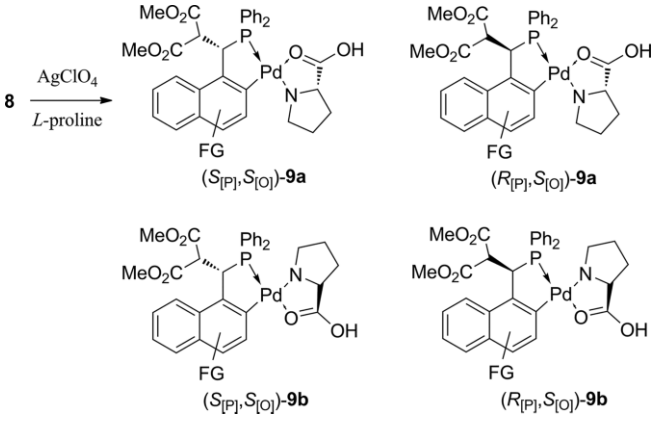


Figure 4. X-ray crystal structure of complex ($S_{[P]}$)-**8c** (CCDC 1835219). Selected bond lengths [Å] C11–P1 1.846(5); Pd1–C1 2.001(5); Pd1–P1 2.1926(12); C10–C11 1.516(7); C1–C10 1.391(6). Selected bond angles [°] C1–Pd1–P1 80.70(13); C10–C11–P1 103.0(3); C11–P1–Pd1 103.98(16); C10–C1–Pd1 123.2(3); Cl1–Pd1–Cl2 83.57(4); Pd1–Cl1–Pd2 73.57(3); Pd1–Cl2–Pd2 73.68(3); C10–C1–Pd1 123.2(3); C1–C10–C11 116.7(4).

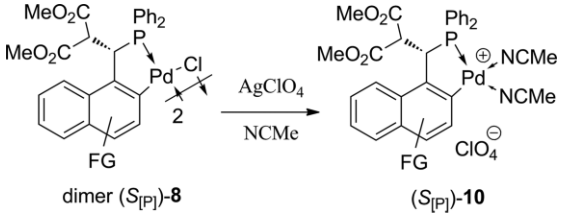
l-proline into the CP dimer products **8**, which was obtained after the asymmetric P–H addition reaction and cyclometallation reaction.

Derivatives of **10** incorporating an easily leaving moiety such as acetonitrile, suitable for catalytic applications were prepared by removing the chloro bridges with $AgClO_4$ (Scheme 5). In the absence of the inert Pd–Cl bond, catalysts **10** were more active than **8**.

The newly synthesized phosphapalladacycles **10** were subsequently applied in the hydrophosphination reaction and the results showed that all four catalysts gave complete conversions whilst catalyst **10b** gave the best enantioselectivity (Table 4).



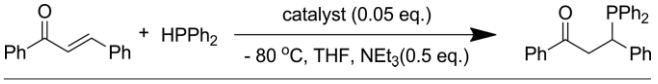
Scheme 4. Treatment of the **8** with *l*-proline to examine the enantiomeric purity.



Scheme 5. Synthesis of the CP catalyst ($S_{[P]}$)-**10**.

However, their performance, in terms of enantioselectivity was moderate when compared to ($R_{[P]}$)-**2** and ($R_{[P]}$)-**3** catalysts developed by us previously. We are currently in the process of screening these new complexes for other asymmetric reaction scenarios.

Table 4. The application of complexes **10** in catalytic hydrophosphination of chalcone.



Entry	Catalyst	Yield [%][a]	*ee* [%][b]
1	($R_{[P]}$)-**2**	> 99	>99
2	10a	> 99	64
3	**10b**	> 99	78
4	**10c**	> 99	70
5	**10d**	> 99	53
6	($R_{[P]}$)-**3**	> 99	77

[a] The yield were determined by $^{31}P\{^1H\}$ NMR spectrum. [b] The *ee* were determined by $^{31}P\{^1H\}$ NMR spectrum after the product coordinated to the chiral palladated complexes ($R_{[N]}$)-**1**.

Conclusions

Four functionalized chiral phosphapalladacycle complexes have been efficiently prepared by consecutive asymmetric hydrophosphination (P–H reaction) and cyclometallation reaction. The impact of installation of malonate moiety at the chiral carbon as well as the modification of the naphthalene ring system was studied for the asymmetric hydrophosphination reaction. These preliminary results will serve as a guide for the rational design of other functionalized phosphapalladacycles using this alternate synthetic methodology.

Experimental Section

General Information: All reactions including the air-sensitive complexes diphenylphosphine and free ligands **5** were carried out under an inert atmosphere of nitrogen employing Schlenk Line and two-neck round-bottomed flask, and all the solvent contacted the air-sensitive complexes were degassed by blowing with nitrogen. NMR spectra were recorded on Bruker AV 300, AV400, AV 500, and BBFO 400 spectrometers. Chemical shifts were reported in ppm and referenced to an internal $SiMe_4$ standard (δ =0 ppm) for ^1H NMR, [D]chloroform (δ =77.16 ppm) for ^{13}C NMR, and Dimethyl [D_6]sulfoxide (δ =39.6 ppm) for ^{13}C NMR spectroscopy. Dichloromethane, chloroform, tetrahydrofuran, acetone and methanol were purchased from their respective companies and used as supplied. Tetrahydrofuran was distilled from sodium/benzophenone prior to use. Solvents were degassed when necessary. A Low Temp Parr stirrer PSL-1800 was used for controlling low temperature reactions. Column chromatography was carried out with Silica gel 60 (Merck). Melting points were measured using SRS Optimelt Automated Point System SRS MPA100. Optical rotation was measured with JASCO P-1030 Polarimeter in the specified solvent in a 0.1 dm cell at 22.0 °C. Substrates **5** was prepared according to literature procedures.[27]

Optical Resolution and Preparation of ($R_{[N]}$,$S_{[P]}$)-7 from 5: To a solution of diphenylphosphine (10.0 mmol, 1.8619 g, 1.0 equiv.) in the degassed methanol (30 mL) in the two-neck round-bottomed flask was added substrate **5** (10.5 mmol, 1.05 equiv.) and catalyst $Pd(OAc)_2$ (0.5 mmol, 0.1123 g, 0.05 equiv.), and the resulting mixture was stirred at room temperature for 2 h to generate the air-sensitive crude products **6** (yield > 99 %). The diastereomeric isomers ($R_{[N]}$,$S_{[P]}$)/($R_{[N]}$,$R_{[P]}$)-**7** were generated by treating the resulting racemic ligand **6** with stoichiometric amount of chiral reagent ($R_{[N]}$)-**1** (5.0 mmol, 3.4016 g, 0.5 equiv.). The diastereomers ($R_{[N]}$,$S_{[P]}$)-**7** and ($R_{[N]}$,$R_{[P]}$)-**7** were separated into their isomeric pure forms by column chromatography on silica gel. The isolated yields were listed in Table 1.

Preparation of Dimer ($S_{[P]}$)-8a/b from Optical Resolution: Complex ($R_{[N]}$,$S_{[P]}$)-**7a/b** (1.0 mmol) was dissolved in acetone (50 mL) and treated with conc. HCl (2.2 mL). The reaction mixture was stirred at room temperature for 1 h to liberated the C–N auxiliary. The reaction mixture was poured into water (500 mL) and the intermediate compound was filtered and subsequently converted to dimer ($S_{[P]}$)-**8a/b** by the treatment with NaOAc (1.6210 g) for 1 h. Complex ($S_{[P]}$)-**8a/b** was purified by column chromatography on silica gel (elution: DCM). The isolated yields were listed in Table 1.

Preparation of Dimer ($S_{[P]}$)-8c from ($R_{[N]}$,$S_{[P]}$)-7c: The mixture of ($R_{[N]}$,$S_{[P]}$)-**7c** (1.0 mmol) and conc. HCl was heated in acetone (50 mL) at 60 °C for 40 min. The reaction mixture was cooled to room temperature and then poured into water (500 mL). The crude product was filtered followed by purification with column chromatography on silica gel (elution: DCM) to get the ($S_{[P]}$)-**8c**. The isolated yield was listed in Table 1.

Preparation of Dimer ($S_{[P]}$)-8d from ($R_{[N]}$,$S_{[P]}$)-7d: The mixture of ($R_{[N]}$,$S_{[P]}$)-**7d** (1.0 mmol) and conc. HCl was heated in acetone (50 mL) at 60 °C for 1 h. The resulting mixture was poured into water (500 mL) and the intermediate complex was filtered. The crude product was then stirred with NEt_3 (0.6 mmol) in degassed DCM at room temperature for 1 h. The crude mixture was extracted with DCM/H_2O and dried with $MgSO_4$, followed by purifying with

column chromatography on silica gel (elution: DCM), giving the pure ($S_{[P]}$)-**8d**. The isolated yield was listed in Table 1.

Catalytic Synthesis of ($S_{[P]}$)-8 from Chiral Phosphine 6: Substrate **5** (1.05 mmol, 1.05 equiv.) and the chiral catalyst ($R_{[P]}$)-**2** were added a solution of diphenylphosphine (1.0 mmol, 0.1862 g, 1.0 equiv.) in the degassed solvent (55 mL) in a 100 mL two-neck round-bottomed flask. The reaction mixture was then kept in the low temperature bath at the selected temperature for 30 min The external base NEt_3 (1.0 equiv.) in degassed solvent (0.5 mL) was added dropwise into the two-neck round-bottomed flask. The reaction mixture was then kept at the selected temperature for the duration listed in Table 2. The palladium source was then added into the resulting chiral phosphine ligand. The crude cyclopalladated dimer ($S_{[P]}$)-**8** thus obtained was purified by column chromatography on silica gel (elution: DCM). Enantiomerically pure product ($S_{[P]}$)-**8** could be further purified by recrystallization. The isolated yields were listed in Table 3.

Preparation of Complex 9: A mixture of *l*-proline (1.05 mmol) and KOH (1.05 mmol) in degassed water was added into a solution of **8** (1.0 mmol) in DCM. The resulting mixture was stirred at room temperature for 1 h, The structural isomeric complex **9** was thus obtained in quantitative yield.

Preparation of 10: The substrate **8** (1.0 mmol) and $AgClO_4$ (1.05 mmol) was added to the round-bottomed flask with acetonitrile (10 mL) as the solvent and stirred for 1 h. After the workup process, the cationic complex **10** was obtained quantitatively.

CCDC 1835263 [for ($S_{[P]}$)-**8a**], 1835218 [for ($S_{[P]}$)-**8b**], 1835219 [for ($S_{[P]}$)-**8c**] contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.

Acknowledgments

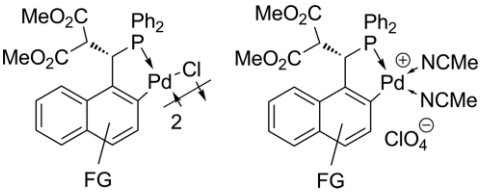
This work was supported by the Ministry of Education Academic Research Fund (AcRF-RG108/15). Xi-Rui Li is also grateful to Nanyang Technological University for the award of a research scholarship.

Keywords: Catalytic · Hydrophosphination · Isomers · Synthesis design · Transition metals

[1] a) A. C. Cope, E. C. Friedrich, *J. Am. Chem. Soc.* **1968**, *90*, 909–913; b) A. C. Cope, R. W. Siekman, *J. Am. Chem. Soc.* **1965**, *87*, 3272–3273; c) P. Pregosin, R. Rüedi, *J. Organomet. Chem.* **1984**, *273*, 401–413.
[2] a) H.-K. Nguyen, U. Asseline, D. Dupret, N. T. Thuong, *Tetrahedron Lett.* **1997**, *38*, 4083–4086; b) D. G. Allen, G. M. McLaughlin, G. B. Robertson, W. L. Steffen, G. Salem, S. B. Wild, *Inorg. Chem.* **1982**, *21*, 1007–1014; c) S. B. Wild, *Coord. Chem. Rev.* **1997**, *166*, 291–311.
[3] D. F. Fischer, A. Barakat, Z. q. Xin, M. E. Weiss, R. Peters, *Chem. Eur. J.* **2009**, *15*, 8722–8741.
[4] a) Y. Huang, S. A. Pullarkat, Y. Li, P.-H. Leung, *Chem. Commun.* **2010**, *46*, 6950–6952; b) K. Chen, S. A. Pullarkat, M. Ma, Y. Li, P.-H. Leung, *Dalton Trans.* **2012**, *41*, 5391–5400.
[5] F. E. Michael, B. M. Cochran, *J. Am. Chem. Soc.* **2006**, *128*, 4246–4247.
[6] a) M. Ohff, A. Ohff, D. Milstein, *Chem. Commun.* **1999**, 357–358; b) M. Nowotny, U. Hanefeld, H. van Koningsveld, T. Maschmeyer, *Chem. Commun.* **2000**, 1877–1878; c) X. Gai, R. Grigg, M. I. Ramzan, V. Sridharan, S. Collard, J. E. Muir, *Chem. Commun.* **2000**, 2053–2054.
[7] O. N. Gorunova, I. M. Novitskiy, Y. K. Grishin, I. P. Gloriozov, V. A. Roznyatovsky, V. N. Khrustalev, K. A. Kochetkov, V. V. Dunina, *Organometallics* **2016**, *35*, 75–90.
[8] Y.-X. Jia, B.-B. Li, Y. Li, S. A. Pullarkat, K. Xu, H. Hirao, P.-H. Leung, *Organometallics* **2014**, *33*, 6053–6058.
[9] a) V. V. Dunina, *Curr. Org. Chem.* **2011**, *15*, 3415–3440; b) O. N. Gorunova, M. V. Livantsov, Y. K. Grishin, N. A. Kataeva, K. A. Kochetkov, A. V. Churakov, L. G. Kuz'mina, V. V. Dunina, *Polyhedron* **2012**, *31*, 37–43; c) O. Gorunova, Y. K. Grishin, M. Ilyin, K. Kochetkov, A. Churakov, L. Kuz, V. V. Dunina, *Russ. Chem. Bull.* **2017**, *66*, 282–292.
[10] H. Wang, W. Lu, J. Zhang, *Chem. Eur. J.* **2017**, *23*, 13587–13590.
[11] W.-J. Lin, K.-S. Shia, J.-S. Song, M.-H. Wu, W.-T. Li, *Org. Biomol. Chem.* **2016**, *14*, 220–228.
[12] M. Loubidi, A. Moutardier, J. F. Campos, S. Berteina-Raboin, *Tetrahedron Lett.* **2018**, *59*, 1050–1054.
[13] T. Castanheiro, A. Schoenfelder, J. Suffert, M. Donnard, M. Gulea, *C. R. Chim.* **2017**, *20*, 624–633.
[14] B. A. Rizkin, R. L. Hartman, *Reaction Chemistry & Engineering* **2018**, *3*, 251–257.
[15] P. Koukal, H. Dvořáková, D. Dvořák, T. Tobrman, *Chem. Pap.* **2013**, *67*, 3–8.
[16] a) W. S. Tay, X.-Y. Yang, Y. Li, S. A. Pullarkat, P.-H. Leung, *Chem. Commun.* **2017**, *53*, 6307–6310; b) R. J. Chew, Y. Huang, Y. Li, S. A. Pullarkat, P. H. Leung, *Adv. Synth. Catal.* **2013**, *355*, 1403–1408; c) X.-R. Li, X.-Y. Yang, Y. Li, S. A. Pullarkat, P.-H. Leung, *Dalton Trans.* **2017**, *46*, 1311–1316; d) X.-Y. Yang, W. S. Tay, Y. Li, S. A. Pullarkat, P.-H. Leung, *Chem. Commun.* **2016**, *52*, 4211–4214.
[17] E. G. Rodrigues, L. S. Silva, D. M. Fausto, M. S. Hayashi, S. Dreher, E. L. Santos, J. B. Pesquero, L. R. Travassos, A. C. Caires, *Int. J. Cancer* **2003**, *107*, 498–504.
[18] a) X.-Y. Yang, W. S. Tay, Y. Li, S. A. Pullarkat, P.-H. Leung, *Organometallics* **2015**, *34*, 5196–5201; b) X.-Y. Yang, J. H. Gan, Y. Li, S. A. Pullarkat, P.-H. Leung, *Dalton Trans.* **2015**, *44*, 1258–1263.
[19] C. Li, Q.-L. Bian, S. Xu, W.-L. Duan, *Org. Chem. Front.* **2014**, *1*, 541–545.
[20] J.-J. Feng, X.-F. Chen, M. Shi, W.-L. Duan, *J. Am. Chem. Soc.* **2010**, *132*, 5562–5563.
[21] D. Du, W.-L. Duan, *Chem. Commun.* **2011**, *47*, 11101–11103.
[22] R. J. Chew, X. R. Li, Y. Li, S. A. Pullarkat, P. H. Leung, *Chem. Eur. J.* **2015**, *21*, 4800–4804.
[23] R. J. Chew, Y. Lu, Y. X. Jia, B. B. Li, E. H. Y. Wong, R. Goh, Y. Li, Y. Huang, S. A. Pullarkat, P. H. Leung, *Chem. Eur. J.* **2014**, *20*, 14514–14517.
[24] Y. Huang, Y. Li, P.-H. Leung, T. Hayashi, *J. Am. Chem. Soc.* **2014**, *136*, 4865–4868.
[25] a) J. K.-P. Ng, G.-K. Tan, J. J. Vittal, P.-H. Leung, *Inorg. Chem.* **2003**, *42*, 7674–7682; b) J. Albert, R. Bosque, J. M. Cadena, S. Delgado, J. Granell, G. Muller, J. I. Ordinas, M. Font Bardia, X. Solans, *Chem. Eur. J.* **2002**, *8*, 2279–2287; c) V. V. Dunina, N. G. Ol'ga, L. G. Kuz'mina, M. V. Livantsov, Y. K. Grishin, *Tetrahedron: Asymmetry* **1999**, *10*, 3951–3961; d) J. M. Longmire, X. Zhang, M. Shang, *Organometallics* **1998**, *17*, 4374–4379.
[26] C. Xu, G. Jun Hao Kennard, F. Hennersdorf, Y. Li, S. A. Pullarkat, P.-H. Leung, *Organometallics* **2012**, *31*, 3022–3026.
[27] X. Zhu, S. Chiba, *Chem. Commun.* **2016**, *52*, 2473–2476.

Received: June 8, 2018

Chiral Metallocycles



Four new chiral phosphapalladacycles with designed stereo- and electronic properties were prepared by catalysis and by optical resolution and comprehensively characterised. The impact of incorporation of malonate moiety at the chiral carbon and modification of the naphthalene system was studied for the asymmetric hydrophosphination of chalcone.

DOI: 10.1002/ejic.201800720