



HAL
open science

Chirality Control in Planar Chiral Cobalt Oxazoline Palladacycles

Doyle Cassar, Hemin Roghzai, Didier Villemin, Peter Horton, Simon Coles, Christopher Richards

► **To cite this version:**

Doyle Cassar, Hemin Roghzai, Didier Villemin, Peter Horton, Simon Coles, et al.. Chirality Control in Planar Chiral Cobalt Oxazoline Palladacycles. *Organometallics*, 2015, 34 (12), pp.2953-2961. 10.1021/acs.organomet.5b00282 . hal-01829915

HAL Id: hal-01829915

<https://hal.science/hal-01829915v1>

Submitted on 11 Oct 2024

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Chirality Control in Planar Chiral Cobalt Oxazoline Palladacycles

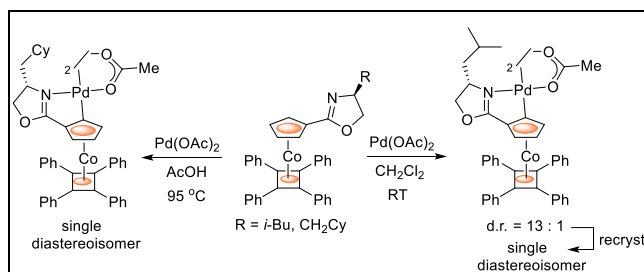
Doyle J. Cassar,[†] Hemin Roghzai,[†] Didier Villemin,[‡] Peter N. Horton,[§] Simon J. Coles[§] and
Christopher J. Richards^{†*}

[†]School of Chemistry, University of East Anglia, Norwich Research Park, Norwich, NR4
7TJ, U.K

[‡]Laboratoire de Chimie Moleculaire et Thioorganique, UMR CNRS 6507, INC3M, FR 3038,,
labex EMC3, ENSICAEN 14050 Caen, France

[§]EPSRC National Crystallography Service, School of Chemistry, University of Southampton,
Highfield, Southampton SO17 1BJ, UK

Graphic for Table of Contents and Abstract.

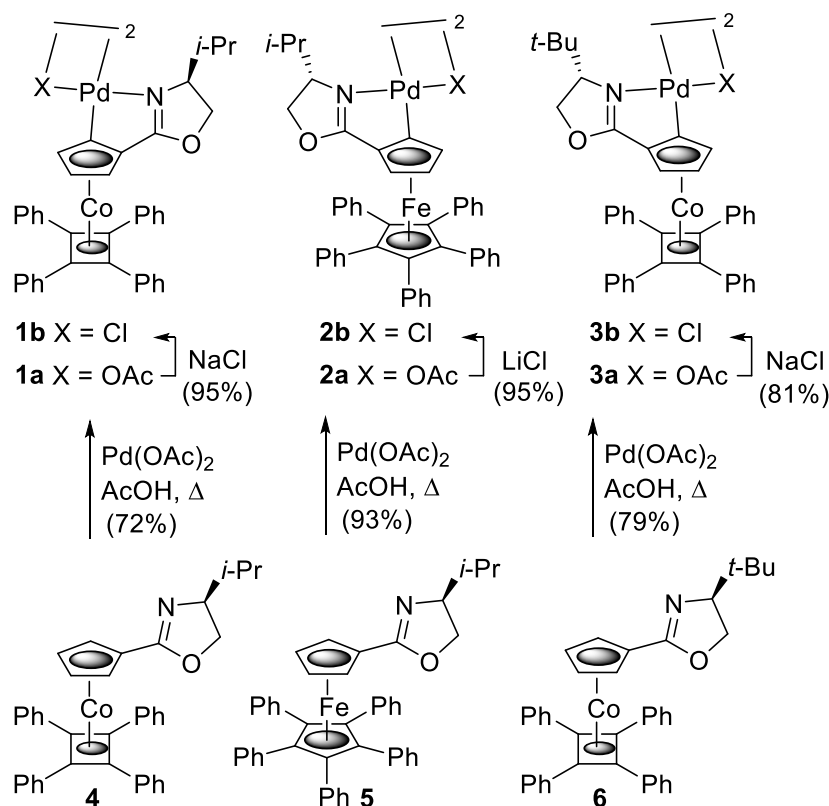


ABSTRACT: Palladation of $(\eta^5\text{-}(S)\text{-}2\text{-}(4\text{-R-substituted})\text{oxazolinylcyclopentadienyl})(\eta^4\text{-tetraphenylcyclobutadiene})\text{cobalt(I)}$ with $\text{Pd}(\text{OAc})_2$ ($\text{R} = \text{Me}, \text{CH}_2i\text{-Cy}, \text{CH}_2i\text{-Pr}, \text{CH}_2\text{Ph}$) resulted exclusively in formation of the (S,S_p) -palladacycle with $\text{R} = \text{CH}_2\text{Cy}$ (acetic acid solvent), and up to 13 : 1 selectivity in favour of the (S,S_p) -palladacycle with $\text{R} = \text{CH}_2i\text{-Pr}$ (CH_2Cl_2 solvent). In the latter case diastereomeric purity was achieved by recrystallisation, and the absolute configuration of the new element of planar chirality established by X-ray crystallography. These outcomes contrast with the opposite sense of diastereoselectivity observed for the corresponding $\text{R} = i\text{-Pr}$ substituted oxazoline which results in the palladacycle $(S,R_p)\text{-COP-OAc}$ (acetic acid solvent), these palladation reactions being under either kinetic (S,S_p) or thermodynamic (S,R_p) control. Following conversion to the chloride bridged (S,S_p) -palladacycle dimer ($\text{R} = \text{CH}_2\text{Cy}$), this was employed as a catalyst for the rearrangement of allylic trichloroacetimidates (0.25 mol% catalyst loading, up to 80% ee).

INTRODUCTION

Following the first report on the application of cobalt oxazoline palladacycle **1b** (COP-Cl) as a catalyst for the enantioselective rearrangement of *N*-aryltrifluoroacetimidates,¹ there have been many further publications on the successful use of COP complexes **1a/b** as either a catalyst² or reagent³ for other asymmetric transformations. Pentaphenylferrocene based oxazoline complex **2b**⁴ and related imidazolines^{4,5} have also highlighted the applicability to asymmetric synthesis of palladacycle catalysts based upon bulky ferrocene frameworks.⁶ Central to the success of these palladacycles is the high diastereoselectivity of C-H activation/palladium-carbon bond formation, as controlled by the heterocyclic auxiliary.⁷ A notable feature of these reactions is the formation of opposite elements of planar chirality from the *i*-Pr substituted oxazolines **4** and **5** under identical reaction conditions (Scheme 1).^{4,8} Furthermore, changing a stereogenic centre substituent from *i*-Pr to *t*-Bu in the cobalt-based

series also results in a switching of planar chirality, with **3a** generated from **6** under the same conditions used for the synthesis of **1a** and **2a**.⁹



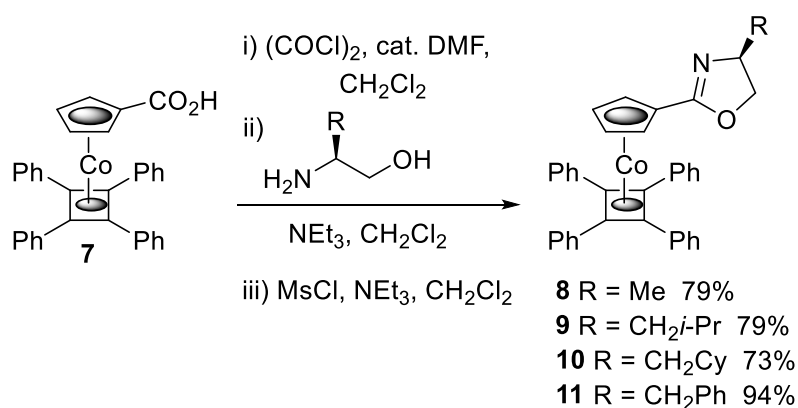
Scheme 1. Diastereoselective synthesis of known oxazoline-based bulky sandwich-complex based palladacycles.

In this paper we report in detail on the factors influencing the diastereoselectivity of palladation of chiral oxazoline-appended cobalt sandwich complexes, and methods are described for the synthesis of two new diastereomerically pure (*S,S_p*)-congeners related to **3**. These new catalysts, with the potential to be used in several asymmetric transformations, are exemplified by application to the rearrangement of trichloroacetimidates.

RESULTS AND DISCUSSION

Oxazoline synthesis and diastereoselective palladation: Starting from the carboxylic acid

7, and a series of commercially available (*S*)-amino alcohols, oxazolines **8–11** were synthesised using the same procedure reported previously for **4**.¹⁰ Following initial formation of an acid chloride with oxalyl chloride, amino alcohol addition gave intermediate hydroxyamides that underwent cyclisation to the required oxazoline moiety on addition of methanesulfonyl chloride (Scheme 2).



Scheme 2. Synthesis of chiral oxazoline-appended cobalt sandwich complexes.

The procedure utilised in the diastereoselective palladation of **4**, and also applied to the related oxazolines **5** and **6**, involved heating a solution of **4** and $\text{Pd}(\text{OAc})_2$ in acetic acid at 95 °C for 30 minutes which resulted in the precipitation of **1a** as a single diastereoisomer.⁸ Application of this protocol to oxazolines **8–11** resulted in the formation of a precipitate in all cases, but following isolation only the product arising from methylenecyclohexyl substituted oxazoline **10** proved to be a palladacycle (Scheme 3, Table 1). This was established readily by the presence of three cyclopentadienyl hydrogen signals in the ^1H NMR spectrum compared to the two sets of two diastereotopic cyclopentadienyl hydrogen signals observed in the spectrum of the starting oxazoline. The identity of an oxazoline coordinated palladium as the new cyclopentadienyl ring substituent was confirmed by the reduction in wavenumber of $\nu(\text{C}=\text{N})$ to 1606 cm^{-1} from the value of 1655 cm^{-1} measured for **10**, and by the single methyl singlet in the ^1H NMR spectrum arising from the acetate ligand. The configuration of

the new element of planar chirality was determined as S_p and thus the identity of the palladacycle as **18a** by the similarity of the CD spectrum (Figure 1) to that of (S,S_p) -**16a** for which the configuration of planar chirality was determined later by X-ray crystallography (*vide infra*).

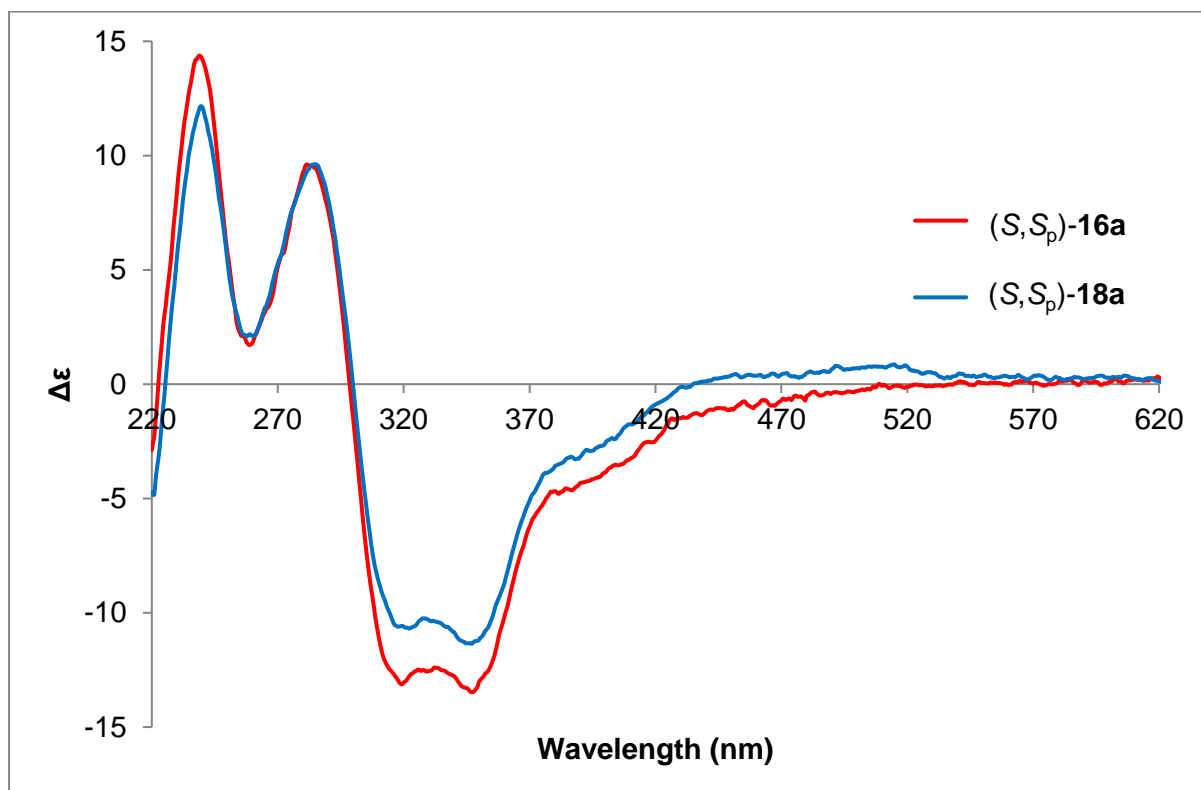
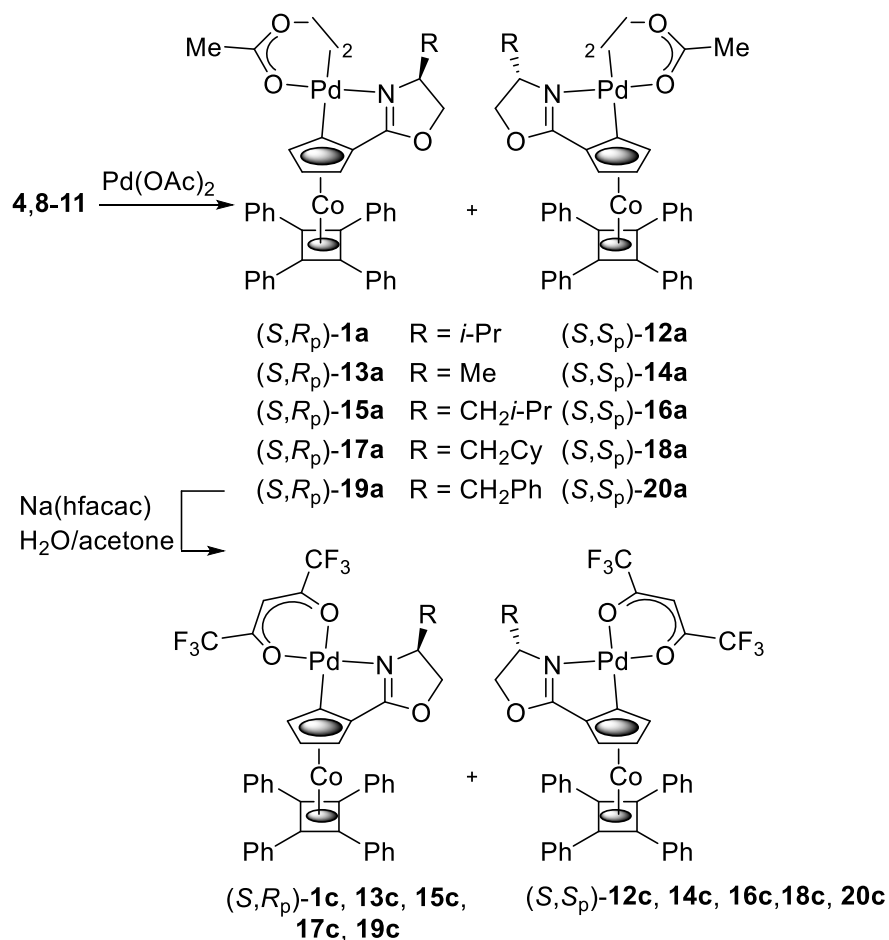


Figure 1. Circular dichroism spectra of (S,S_p) -**16a** and (S,S_p) -**18a**.



Scheme 3. Reaction of oxazolines **4** and **8-11** with palladium acetate and conversion to monomeric hfacac derivatives.

The precipitate obtained from the reaction of oxazoline **9** was identified as palladium acetate adduct **22** (Scheme 4), in part because of the similarity of the cyclopentadienyl region ^1H NMR to that of the related *trans*-chloride-adduct **24**⁹ for which two signals are significantly deshielded [5.79 (**22**) vs. 5.86 (**24**) and 6.05 (**22**) vs. 5.98 (**24**)]. From an examination of the X-ray crystal structure of **24** this may be due to the proximity of the diastereotopic cyclopentadienyl α -hydrogens to the palladium environment perpendicular to the square-plane. The structures of **21** and **23** were assigned by analogy. An attempt to convert an adduct into a palladacycle was performed by re-heating **22** in acetic acid at 95 °C for 30 minutes. This resulted only in oxazoline ring opening and isolation of **25**, an outcome consistent with the known Pd(II) promoted ring-opening of an oxazoline by acetate to form

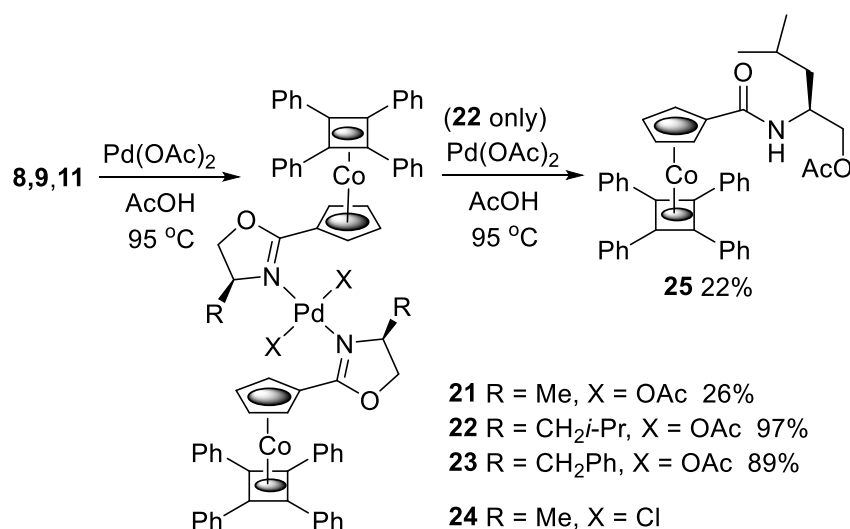
an acetate substituted amide.¹¹

Table 1. Reaction of cobalt metallocene oxazolines with palladium acetate.^a

Entry	Oxazoline (substituent)	Solvent	Major product	Diastereomeric Ratio (dr) ^b	Yield (%)
1	4 (<i>i</i> -Pr)	AcOH	(<i>S,R</i> _p)- 1a	>100:1	72
2	8 (Me)	AcOH	21	-	26
3	9 (CH ₂ <i>i</i> -Pr)	AcOH	22	-	97
4	10 (CH ₂ Cy)	AcOH	(<i>S,S</i> _p)- 18a	>100:1	70
5	11 (CH ₂ Ph)	AcOH	23	-	89
6	4 (<i>i</i> -Pr)	CH ₂ Cl ₂	(<i>S,S</i> _p)- 12a	2:1	nd
7	8 (Me)	CH ₂ Cl ₂	(<i>S,S</i> _p)- 13a	2.5:1 ^c	nd
8	9 (CH ₂ <i>i</i> -Pr)	CH ₂ Cl ₂	(<i>S,S</i> _p)- 16a	13:1 ^c	73% ^d
9	10 (CH ₂ Cy)	CH ₂ Cl ₂	(<i>S,S</i> _p)- 18a	1.5:1 ^c	nd
10	11 (CH ₂ Ph)	CH ₂ Cl ₂	(<i>S,S</i> _p)- 20a	1:1 ^{c, e}	nd

^a 95 °C, 30 min. in AcOH or R.T., 16 h. in CH₂Cl₂. ^b Determined by ¹H NMR spectroscopy. ^c

Determined following conversion to monomeric hfacac complexes. ^d Diastereomerically pure (*S,S*_p)-**16a** (>100:1) achieved by recrystallisation from CH₂Cl₂/hexane (73% yield). ^e The major product results from *exo*-palladation (2.3:1 *exo:endo*).



Scheme 4. Reaction of oxazolines **8**, **9** and **11** with palladium acetate in acetic acid.

Precipitation of these *trans*-bis(oxazoline) coordination complexes was avoided by carrying out the palladation reactions in dichloromethane at room temperature for 16 hours (Table 1, entries 6-10). Palladacycles were isolated in all cases, and the ratio of (*S,R_p*)-**1a** and (*S,S_p*)-**12a** (R = *i*-Pr) was determined directly by ¹H NMR. In all other cases the diastereoselectivities were determined by ¹H and ¹⁹F NMR spectroscopy following conversion to the corresponding hexafluoroacetylacetonate complexes **13c** – **20c** (Scheme 3). The absolute configuration of the element of planar chirality in the new complexes was made initially by comparison of the cyclopentadienyl proton signals in the mixture, with those observed for diastereomerically pure (*S,S_p*)-**18c** obtained for the reaction of (*S,S_p*)-**18a** with hexafluoroacetylacetonate, the (*S,R_p*) and (*S,S_p*) diastereoisomers each having a characteristic pattern in this region. Modest diastereoselectivities were observed with the Me (**8**), *i*-Pr (**4**) and CH₂Cy (**10**) substituted oxazolines. Palladation of the CH₂Ph oxazoline **11** resulted in the additional formation of a palladacycle containing an *ortho*-carbon/palladium bond on the oxazoline benzyl substituent. This is an example of competitive *exo* palladation (as opposed to the desired *endo* palladation), related to that observed previously in the palladation of (*R*)-

4-phenyl-2-oxazolines^{12a} and (*S*)-4-benzyl-2-methyl-2-oxazoline.^{12b} In contrast, the CH₂*i*-Pr substituted oxazoline **9** resulted in the predominant formation of **16a** which was obtained as a single diastereoisomer following recrystallisation from CH₂Cl₂/hexane. The *S_p* configuration of the new element of planar chirality was confirmed by an X-ray crystal structure determination (Figure 2).

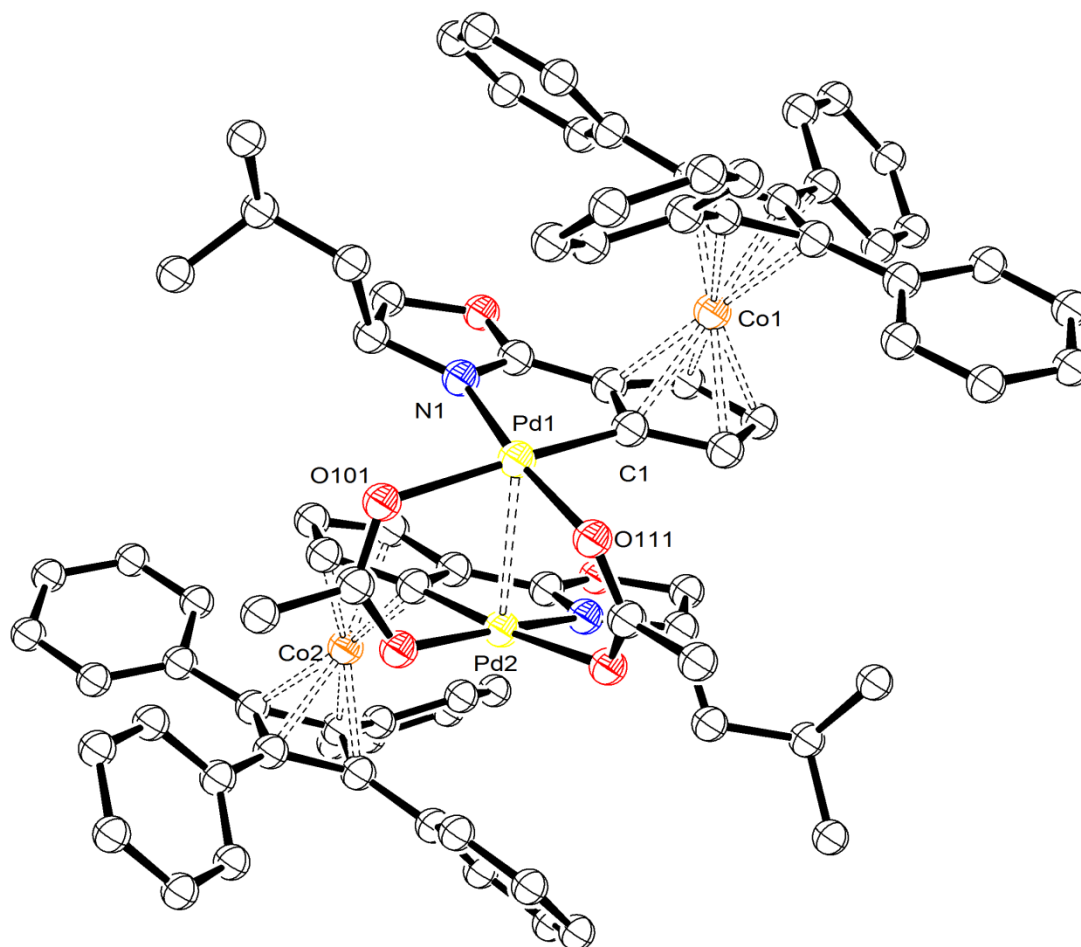


Figure 2. A molecule of (*S,S_p*)-**16a** from X-ray analysis. Principal bond lengths (Å) include: Pd(1)-C(1) 1.970(3), Pd(1)-N(1) 2.029(2), Pd(1)-O(101) 2.134(2), Pd(1)-O(111) 2.051(2). Pd(1)-Pd(2) 2.836(2). Principal angles (°) include: C(1)-Pd(1)-N(1) 80.73(13), O(101)-Pd(1)-O(111) 92.69(10).

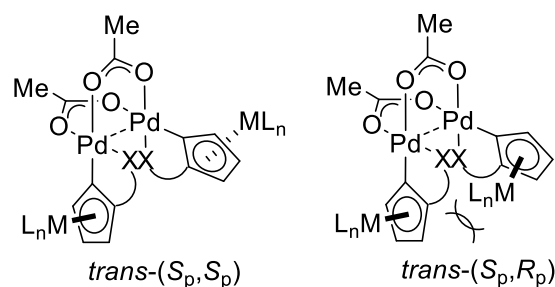


Figure 3. Generalised *trans*-configured acetate-bridged palladacycles containing the same (S_p,S_p) and mixed (R_p,S_p) elements of planar chirality.

The solid state structure of the acetate bridged palladacycle (S,S_p)-**16a** has a *trans* orientation of the two bidentate C-N ligands about the Pd₂(μ-OAc)₂ core. A search of the Cambridge Crystallographic Database revealed 96 palladacycle structures containing this unit, 86 of which are also *trans*-configured. Of the remaining 10 *cis*-dimers, 4 adopt this geometry due to geometrical constraints.¹³ The Pd₂(μ-OAc)₂ unit of **16a** has a Pd-Pd distance of 2.836(2) Å indicative of attractive d⁸-d⁸ interaction,¹⁴ and the ‘open-book’ or ‘clam’ shape resulting from the bridging ligands is a structural feature found in all acetate-bridged palladacycles. Coupled with the *trans* geometry, a planar chiral acetate-bridged palladacycle is only feasible with matched S_p,S_p or R_p,R_p configurations, a mixed S_p,R_p configuration resulting in a severe steric clash (Figure 3). In addition to **16a**, the 7 reported X-ray crystal structures of planar-chiral acetate-bridged palladacycles are all *trans*-S_pS_p or *trans*-R_pR_p,^{4, 15,16} *i.e.* consistent with this model. This self-recognition reduces the number of possible dimeric acetate-bridged palladacycles in the solid state, and may be an important factor in the selective precipitation of diastereomerically pure (S,R_p)-**1a** and (S,S_p)-**18a** from solution. Acetate-bridged palladacycles have been shown to be monomeric in solution.¹⁷ The relative simplicity of the NMR spectra of a mixture of diastereoisomers arising from palladation (*e.g.* the ratio of (S,R_p)-**1a** and (S,S_p)-**12a** was determined directly by ¹H NMR), is likely due to

these being monomeric in solution at the concentration studied (ca. 5 mM) rather than an extension of dimeric self recognition. For this to be the case, just two (*trans*- S_p,S_p , *trans*- R_p,R_p) and none of the remaining four (*trans*- S_p,R_p , *cis*- S_p,S_p , *cis*- R_p,R_p and *cis*- S_p,R_p), of the six possible dimeric structures would have to be present in solution.

A previous study on the palladation of *i*-Pr substituted oxazoline **4** in acetic acid at 95 °C revealed a 1:2 ratio of (S,R_p)-**1a** : (S,S_p)-**12a** after 5 minutes, as determined by ^1H NMR spectroscopy.¹⁸ This changed to >20 : 1 after 30 minutes, the isolation of **1a** under these conditions resulting from epimerisation and exclusive precipitation of the major thermodynamic diastereoisomer from solution, for which the *i*-Pr substituent is orientated away from the bulky tetraphenylcyclobutadiene moiety. In contrast, examination by ^1H NMR of the palladation of the CH_2Cy substituted oxazoline **10** in acetic acid at 95 °C after 5 minutes revealed the presence of (S,S_p)-**18a** (with no (S,R_p)-**17a**), and an additional complex for which the ^1H NMR data is consistent with a *trans*-bis(oxazoline) coordination complex. Pure (S,S_p)-**18a** precipitated from solution after 10 minutes. In this instance, and unlike the outcomes with oxazolines **8**, **9** and **11**, the presence of the CH_2Cy oxazoline substituent does not result in the precipitation from solution of an initially formed coordination complex. In addition, the conformationally more flexible CH_2Cy oxazoline substituent does not drive equilibration, unlike the *i*-Pr substituent of oxazoline **4**.

Further examination of the palladation of **4** in dichloromethane at room temperature again revealed a change in diastereoselectivity as a function of time, with the initial preference for **12a** (S,S_p) changing to **1a** (S,R_p) after prolonged stirring to give a 2:3 (S,S_p)/(S,R_p) thermodynamic ratio after approximately one day (Figure 4). In the early stages of this reaction a *trans*-bis(oxazoline) intermediate complex was again observed. Repetition, with the addition of approximately 0.6 eq. of dimeric (S,R_p)-**1a** into the reaction mixture after 3 hours, resulted in a switch in the (S,S_p)/(S,R_p) ratio from 7:3 to 3:7. Further stirring again

resulted in the formation of a 2:3 (*S,S*_p)/(*S,R*_p) thermodynamic ratio (Figure 5). Examination of the palladation of **10** (R = CH₂Cy) under these conditions revealed that the initial ~7 : 3 ratio of (*S,S*_p)-**18a** : (*S,R*_p)-**17a** determined within the first hour did not change significantly during a 6 day reaction. In contrast, examination of the palladation of CH₂*i*-Pr oxazoline **9** established that the initial ~4 : 1 ratio of (*S,S*_p)-**16a** : (*S,R*_p)-**15a** determined within the first hour increased over time to give an ~20 : 1 ratio after 30 hours. Although the reactions in dichloromethane avoid the precipitation of a coordination complex, and thus lead to the formation of a palladacycle, the diastereoselectivities observed are, for the most part, low. Selectivity is observed in the early stages of the reaction for the (*S,S*_p) diastereoisomer, although starting with the *i*-Pr containing oxazoline **4**, epimerisation is again observed resulting, in this instance, in a modest preference for the (*S,R*_p) diastereoisomer. In contrast the CH₂*i*-Pr substituted oxazoline **9** gives a sufficiently high selectivity that palladation followed by recrystallisation is a practical procedure for the generation of pure (*S,S*_p)-**16a**.

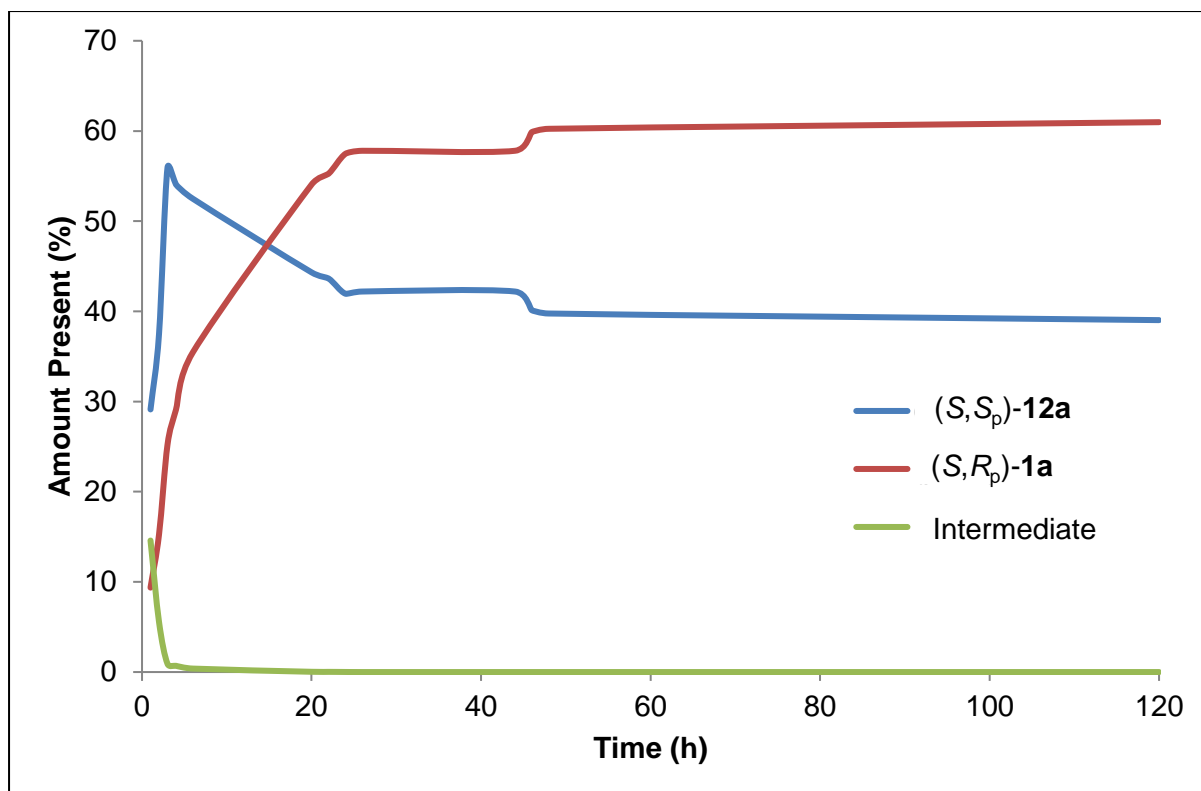


Figure 4. Reaction mixture composition vs. time following the addition of Pd(OAc)₂ to oxazoline **4** in CH₂Cl₂ to room temperature.

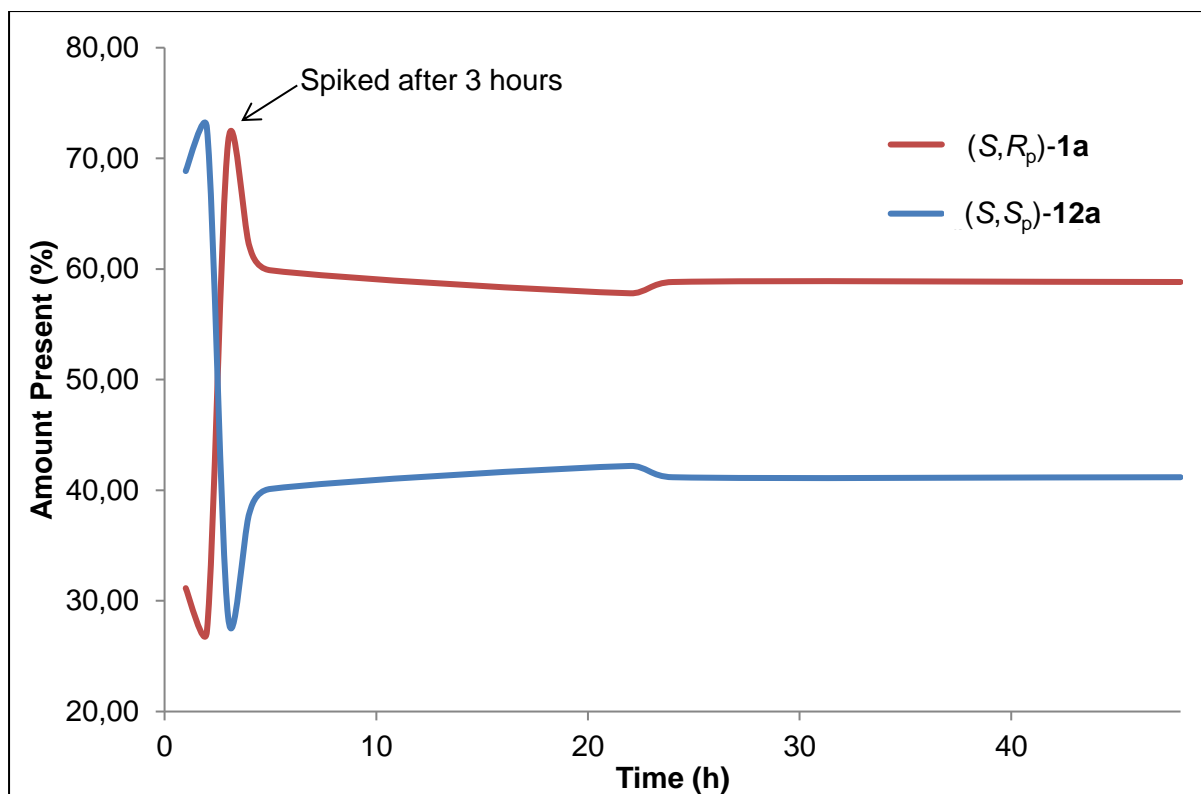


Figure 5. Reaction mixture composition vs. time following the addition of Pd(OAc)₂ to oxazoline **4** in CH₂Cl₂ to room temperature followed by spiking with additional (*S,R_p*)-**1a** after 3 hours.

The conversion of the palladium acetate adducts **21-23** into palladacycles, and the avoidance of oxazoline ring opening, was achieved by heating these in toluene at reflux (Table 2). Complexes **21** and **23**, containing the methyl and benzyl oxazoline substituents respectively, resulted in modest selectivity for the *S_p* diastereoisomer, although in this instance no *exo*-palladation by-product was formed from the benzyl-substituted oxazoline. The *S_p* selectivity again predominated with the CH₂*i*-Pr oxazoline containing complex **22** to give (*S,S_p*)-**16a**/*(S,R_p)*-**17a** in a ratio of 8:1, recrystallisation again resulting in the isolation of the major product as a single diastereoisomer.

Table 2. Conversion of palladium acetate adducts **21-23** into palladacycles^a

Entry	Complex (substituent)	Solvent	Major product	Diastereomeric Ratio (dr) ^b
1	21 (Me)	PhMe	(<i>S,S</i> _p)- 14a	1.5:1
2	22 (CH ₂ <i>i</i> -Pr)	PhMe	(<i>S,S</i> _p)- 16a	8:1 ^c
3	23 (CH ₂ Ph)	PhMe	(<i>S,S</i> _p)- 20a	1.8:1

^a Heated at reflux, 2 h. in PhMe. ^b Determined following conversion to monomeric hfacac complexes. ^c Diastereomeric purity (>100:1) achieved by recrystallisation from CH₂Cl₂/hexane.

Palladation with palladium acetate has been shown to occur by acetate-assisted concerted metallation deprotonation (CMD).¹⁹ The kinetic preference for the formation of (*S,S*_p)-palladacycles is the same sense of selectivity observed in the lithiation²⁰ and palladation²¹ of related ferrocenyloxazolines, and is also observed for the lithiation²² and palladation⁴ of pentaphenylferrocenyloxazoline **5**.²³ In the latter reaction, precipitation of this kinetic product from the reaction mixture prevents the possibility of isomerisation to the alternative (*S,R*_p)-isomer. The faster formation of the (*S,S*_p)-diastereoisomers may be accounted for by a transition state model in which formation of the palladium-carbon bond by *exo* approach of the metal is not restricted by the oxazoline substituent, as represented by **25** (Figure 6). This contrasts with **26**, the transition state leading to the (*S,R*_p)-diastereoisomers, in which the oxazoline 4-substituent is now proximate to the forming palladium-carbon bond, increasing the energy of this step. The palladation reaction is reversible in both acetic acid and dichloromethane, a viable pathway for this process being an acetate-mediated retro-CMD step followed by repalladation. Only in the case of the isopropyl substituted oxazoline does this result in reversal of the initial kinetic selectivity, and with acetic acid as solvent this is

sufficiently pronounced that, following precipitation, (*S,R*_p)-**1a** is isolated as a single diastereoisomer. Only for the palladation of the oxazolines containing a CH₂Cy substituent (**10**) or a CH₂*i*-Pr substituent (**9**), can this kinetic selectivity lead to the isolation of a pure diastereoisomer, albeit in different solvents. This further illustrates that achieving high diastereoselectivity in these palladation reactions is a subtle balance between kinetic and thermodynamic control, coupled with the differences in the solubility of the product, and that of the initially formed *trans*-bis(oxazoline) coordination complex.

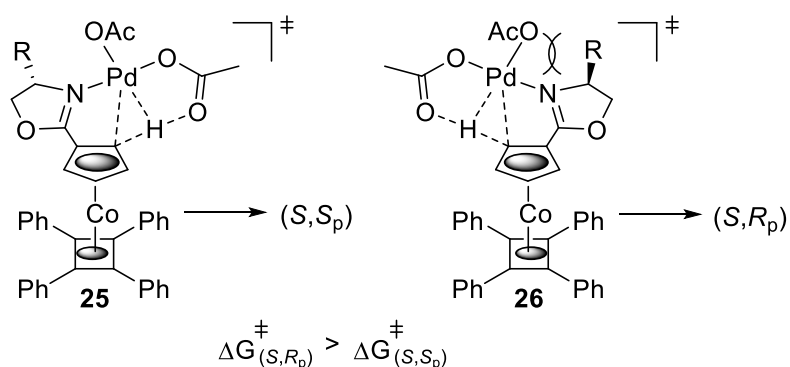
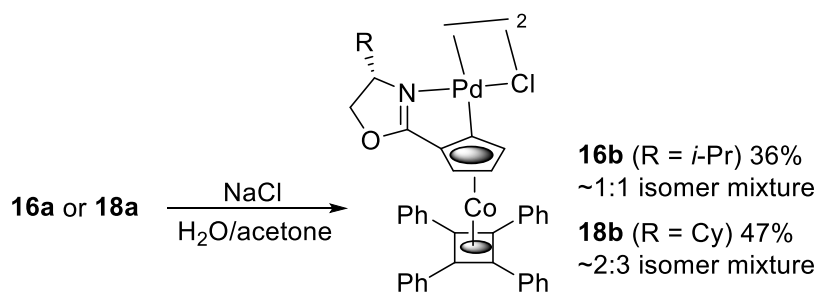
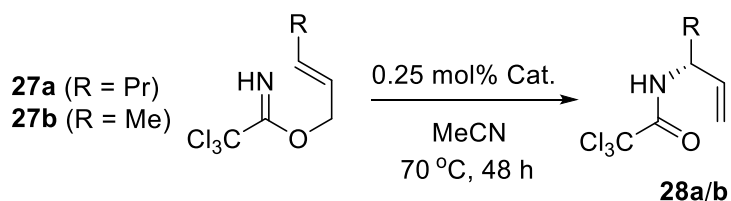


Figure 6. The basis of kinetic control *via* diastereomeric transition states **25** and **26**.

Asymmetric catalysis: As chloride-bridged complex (*S,R*_p)-**1b** has been applied successfully as a catalyst for the enantioselective rearrangement of trichloroacetimidates, comparison to at least one of the new palladacycles generated in this work required the conversion of (*S,S*_p)-**16a** and (*S,S*_p)-**18a** into the corresponding chloride-bridged palladacycles, (*S,S*_p)-**16b** and (*S,S*_p)-**18b** respectively. This was achieved readily by stirring the acetate-bridged palladacycles with an aqueous acetone solution of sodium chloride (Scheme 5). Both were obtained as a mixture of isomers containing *cis* and *trans* orientations of the two bidentate C-N ligands about the Pd₂(μ-Cl)₂ core, a dimeric structure which is maintained in solution.



Scheme 5. Synthesis of chloride-bridged dimers **16b** and **18b**.



Scheme 6. Catalyst comparison in the rearrangement of (*E*)-trichloroacetimidates **27a/b**.

Table 3. Catalyst comparison in the rearrangement of (*E*)-trichloroacetimidates **27a/b**.

Entry	Substrate	Catalyst	Product/ Yield ^a	Config.	ee ^b
1	27a	(<i>S,S</i> _p)- 18b	28a 79%	(<i>R</i>)	72
2	27a	(<i>R,S</i> _p)- 1b	28a 93%	(<i>R</i>)	92
3	27b	(<i>S,S</i> _p)- 18b	28b 81%	(<i>R</i>)	80 ^c
4	27b	(<i>R,S</i> _p)- 1b	28b 93%	(<i>R</i>)	89

^a Isolated by column chromatography. ^b Determined by chiral HPLC. ^c Determined by chiral HPLC following trichloroacetamide hydrolysis and reaction of the resulting allylamine with *p*-BrC₆H₄COCl.

The conditions used for the catalysed rearrangement of trichloroacetimidates **27a/b** were

those developed previously in the group using just 0.25 mol% of catalyst in acetonitrile at 70 °C for 48 hours (Scheme 6).^{2g} Under these conditions with substrate **27a**, catalyst (*S,S*_p)-**18b** resulted in a lower yield and ee compared to (*R,S*_p)-**1b** (Table 3, entries 1 and 2), results mirrored with a second trichloroacetimidate substrate **27b** (entries 3 and 4). That all the rearranged products had the same configuration (*R*) confirmed that the element of planar chirality (*S*_p for both catalysts) dominates the stereocontrol, as required by the model of the origin of enantioselectivity in these reactions.^{2f} As (*S,S*_p)-**18b** and (*R,S*_p)-**1b** are not diastereoisomers, due to their different oxazoline substituents, the terms matched and mismatched must be used with caution. However, when considered with the results of a previous study on the comparison of catalysts derived by treatment of (*R,S*_p)-**1b** or (*S,S*_p)-**3b** with silver trifluoroacetate for the rearrangement of *N*-(4-methoxyphenyl)trifluoroacetimidates⁹ [(*R,S*_p)-**1b**: 72-78% yield, 81-95% ee. (*S,S*_p)-**3b**: 24-64% yield, 36-58% ee], there is a clear trend in favour of the (*R,S*_p) diastereoisomer with respect to both yield and enantioselectivity. Whether this is the case for other palladacycle catalysed reactions remains an area of ongoing study.

CONCLUSION

For a range of chiral oxazoline-appended cobalt sandwich complexes of *S*-configuration, reaction with palladium acetate in acetic acid at 95 °C results in a diastereomerically pure (*S,S*_p)-palladacycle where the oxazoline substituent is CH₂Cy, With oxazolines containing Me, *i*-Bu or Bn substituents palladation was not observed due to the precipitation of the corresponding *trans*-bisoxazoline palladium diacetate complexes. On changing the reaction solvent to dichloromethane, palladation at room temperature was observed with all the (*S*)-oxazolines used (substituents = Me, *i*-Pr, *i*-Bu, CH₂Cy, Bn), but high selectivity was observed in only one case (*i*-Bu, dr = 13 : 1). Recrystallisation gave the diastereomerically pure (*S,S*_p)-

palladacycle. Examination of the palladation reactions in CH₂Cl₂ revealed epimerisation from (*S,S*_p) to (*S,R*_p) with time, consistent with the (*S,S*_p) isomer being kinetically preferred, and (*S,R*_p) being thermodynamically preferred. The two new (*S,S*_p)-palladacycles add to the two known cobalt oxazoline palladacycles (R = *i*-Pr = *S,R*_p and R = *t*-Bu = *S,S*_p) aiding the determination of potential matched and mismatched pairings in palladacycle catalysed reactions. Examination of the rearrangement of the allylic trichloroacetimidates points to (*S,R*_p) and (*S,S*_p)-systems being the matched and mismatched pairing respectively, with chirality control dominated by the element of planar chirality.

EXPERIMENTAL SECTION

General Remarks: All reactions were carried out under an argon atmosphere unless otherwise stated. Toluene was dried over sodium and benzophenone ketyl. Dichloromethane was dried over CaCl₂. (η^5 -Carboxycyclopentadienyl)(η^4 -tetraphenylcyclobutadiene)cobalt(I) was prepared as reported previously.¹⁰ Oxazolines **4** and **8** have been reported previously.^{8,9}

General method for oxazoline ligand preparation: A flask was charged with (η^5 -carboxycyclopentadienyl)(η^4 -tetraphenylcyclobutadiene)cobalt(I) (1 eq.) and dissolved in CH₂Cl₂ (10 mL/mmol). Oxalyl chloride (2 eq.) and dimethylformamide (3 drops) were added sequentially. After 30 minutes the solution was concentrated *in vacuo*, redissolved in CH₂Cl₂ and re-concentrated *in vacuo* to give the crude acid chloride. To a solution of amino alcohol (1.4 eq.) and triethylamine (6 eq.) in CH₂Cl₂ (5 mL/mmol) was added a solution of the crude acid chloride in CH₂Cl₂ (10 mL/mmol) *via* cannula. The resulting solution was maintained at rt and after 2 h the mixture was cooled to 0 °C in an ice bath. Methanesulfonyl chloride (2.5 eq.) was then added in one portion and the resulting solution was allowed to warm to rt. After 16 h the solution was washed with saturated aqueous sodium bicarbonate and then with brine. The organic layer was separated, dried over MgSO₄, filtered, and

concentrated *in vacuo*. Purification by column chromatography on silica eluting with hexanes/EtOAc (9:1) yielded the required product.

η^5 -(*S*)-2-(4-Isobutyl)oxazolinylcyclopentadienyl)(η^4 -tetraphenylcyclobutadiene)cobalt(I)

9: General method followed using (η^5 -carboxycyclopentadienyl)(η^4 -tetraphenylcyclobutadiene)cobalt(I) (2.65 g, 5.05 mmol) and (*S*)-leucinol (0.90 mL, 7.04 mmol). Purification by column chromatography on silica eluting with hexanes/EtOAc (9:1) gave the product as a gold coloured solid (2.43g, 79 %).

Mp: 116 °C. $[\alpha]_D^{23}$ -114 (*c* 0.14, CH₂Cl₂). IR (film): ν_{\max} = 1655 (C=N) cm⁻¹. ¹H NMR (δ , 500 MHz, CDCl₃): 7.42-7.32 (8H, m, ArH), 7.21-7.07 (12H, m, ArH), 5.09 (1H, brs, CpH), 5.02 (1H, brs, CpH), 4.70 (1H, brs, CpH), 4.62 (1H, brs, CpH), 3.70-3.60 (2H, m, CH), 3.30-3.20 (1H, m, CH), 1.63-1.53 (1H, m, CH), 1.36-1.26 (1H, m, CH), 0.95-0.88 (1H, m, CH), 0.83 (3H, d, *J* 6.3, CH₃), 0.81 (3H, d, *J* 6.3, CH₃). ¹³C NMR (δ , 126 MHz, CDCl₃): 135.4 (ArC) 128.9 (ArC), 127.9 (ArC), 126.4 (ArC), 86.4 (CpC), 85.0 (CpC), 84.6 (CpC), 84.5 (CpC), 82.1 (CpC), 76.0 (C₄Ph₄), 72.1 (CH), 64.6 (CH), 45.3 (CH), 25.5 (CH), 23.1 (CH), 22.8 (CH), (C=N not observed). High-resolution MS (*m/z*, ESI⁺) found for MH⁺ = 606.2197, calcd for C₄₀H₃₇CoNO 606.2202.

η^5 -(*S*)-2-(4-Cyclohexylmethyl)oxazolinylcyclopentadienyl)(η^4 -

tetraphenylcyclobutadiene)cobalt(I) 10: General method followed using (η^5 -carboxycyclopentadienyl)(η^4 -tetraphenylcyclobutadiene)cobalt(I) (0.965 g, 1.84 mmol) and (*S*)-cyclohexylalaninol (0.406 g, 2.58 mmol). Purification by column chromatography on silica eluting with hexanes/EtOAc (9:1) gave the product as an orange solid (0.868 g, 73%).

Mp: 175 °C. $[\alpha]_D^{21}$ -33 (*c* 0.06, CH₂Cl₂). IR (film): ν_{\max} = 1656 (C=N) cm⁻¹. ¹H NMR (δ , 500 MHz, CDCl₃): 7.39–7.32 (8H, m, ArH), 7.17-7.05 (12H, m, ArH), 5.06 (1H, brs, CpH), 4.99 (1H, brs, CpH), 4.66 (1H, brs, CpH), 4.58 (1H, brs, CpH), 3.72–3.64 (1H, m, CH), 3.64–3.58 (1H, m, CH), 3.21 (1H, t, *J* 7.5, CH), 1.66–1.52 (4H, m, CH), 1.30–1.02 (7H,

m, CH), 0.83–0.72 (2H, m, CH); ^{13}C NMR (δ , 126 MHz, CDCl_3): 159.4 (C=N), 134.3 (ArC), 127.9 (ArC), 126.9 (ArC), 125.4 (ArC), 85.4 (CpC), 83.6 (CpC), 83.4 (CpC), 81.0 (CpC), 74.9 (C_4Ph_4), 71.2 (CH), 63.0 (CH), 43.0 (CH), 33.8 (CH), 32.4 (CH), 32.4 (CH), 25.9 (CH), 25.6 (CH), 25.2 (CH). High-resolution MS (m/z , ESI^+) found for $\text{MH}^+ = 646.2506$, calcd for $\text{C}_{43}\text{H}_{41}\text{CoNO}$ 646.2515.

η^5 -(S)-2-(4-Benzyl)oxazolinylcyclopentadienyl)(η^4 -tetraphenylcyclobutadiene)cobalt(I)

11: General method followed using (η^5 -carboxycyclopentadienyl)(η^4 -tetraphenylcyclobutadiene)cobalt(I) (1.01 g, 1.93 mmol) and (S)-phenylalaninol (0.409 g, 2.70 mmol). Purification by column chromatography on silica eluting with hexanes/EtOAc (9:1) gave the product as a yellow solid (1.16 g, 94 %).

Mp: 131 °C. $[\alpha]_{\text{D}}^{19} -66$ (c 0.10, CH_2Cl_2). IR (film): $\nu_{\text{max}} = 1655$ (C=N) cm^{-1} . ^1H NMR (δ , 500 MHz, CDCl_3): 7.49-7.41 (8H, m, ArH), 7.33-7.17 (15H, m, ArH), 7.17-7.12 (2H, d, J 7.1, ArH), 5.18 (1H, brs, CpH), 5.10 (1H, brs, CpH), 4.81 (1H, brs, CpH), 4.73 (1H, brs, CpH), 4.07-3.92 (1H, m, CH), 3.62-3.42 (2H, m, CH), 3.00 (1H, dd, J 13.7, 4.9, CHHPh), 2.25 (1H, dd, J 13.7, 9.5, CHHPh). ^{13}C NMR (δ , 126 MHz, CDCl_3): 161.4 (C=N), 138.7 (ArC), 135.4 (ArC), 129.1 (ArC), 129.1 (ArC), 128.6 (ArC), 128.1 (ArC), 126.6 (ArC), 126.4 (ArC), 86.6 (CpC), 84.8 (CpC), 84.8 (CpC), 82.2 (CpC), 76.1 (C_4Ph_4), 71.3 (CH), 67.8 (CH), 41.8 (CH). High-resolution MS (m/z , ESI^+) found for $\text{MH}^+ = 640.2043$, calcd for $\text{C}_{43}\text{H}_{35}\text{CoNO}$ 640.2045.

General method for palladation of oxazoline ligands: A flask was charged with the oxazoline ligand (1 eq.) and dissolved in the required solvent (5 mL/mmol). To this solution palladium(II) acetate (1 eq.) was added in one portion. The flask was sealed and the solution was stirred at the required temperature for the allotted time. The products were isolated either by filtration or by removal of the solvent *in vacuo*.

Di- μ -acetatobis[(η^5 -(*S*)-(*S_p*)-2-(2'-4'-isobutyl)oxazoliny)cyclopentadienyl, 1-C, 3'-N)(η^4 -tetraphenylcyclobutadiene)cobalt(I)]dipalladium(II) **16a:**

General method for palladation was followed using η^5 -(*S*)-2-(4-*iso*-butyl)oxazolinylcyclopentadienyl)(η^4 -tetraphenylcyclobutadiene)cobalt(I) **9** (0.050 g, 0.08 mmol) and palladium(II) acetate (0.019 g, 0.08 mmol) in CH₂Cl₂ (0.5 mL). The solution was stirred at rt for 16h. The solvent was removed *in vacuo* to yield the crude product as an orange solid, for which the ration of *S_p*:*R_p* was determined in a separate experiment as 13:1 by conversion to the corresponding hfacac monomer (see below). Recrystallisation from CH₂Cl₂/hexane gave **16a** as a single diastereoisomer (0.046 g, 73%).

Mp: 266 °C. Anal. Found: C 65.59; H 5.04; N 1.91. Calcd for C₈₄H₇₆Co₂N₂O₆Pd₂: C 65.50; H 4.98; N 1.82. [α]¹⁹_D -721 (*c* 0.12, CH₂Cl₂). IR (film): ν_{\max} = 1605 (C=N) cm⁻¹. ¹H NMR (δ , 500 MHz, CDCl₃): 7.67–7.60 (16H, m, ArH), 7.24–7.19 (24H, m, ArH), 4.65 (2H, brs, CpH), 4.49 (2H, brs, CpH), 4.07 (2H, t, *J* 2.4, CpH), 4.00–3.92 (2H, m, CH), 3.54 (2H, t, *J* 7.7, CH), 3.05–2.95 (2H, m, CH), 2.00 (6H, s, CH₃), 1.41–1.31 (2H, m, CH), 1.15–1.04 (2H, m, CH), 0.71 (6H, d, *J* 6.6, CH₃), 0.67 (6H, d, *J* 6.6, CH₃), 0.19 (2H, ddd, *J* 13.6, 11.3, 4.7, CH). ¹³C NMR (δ , 126 MHz, CDCl₃): 180.9 (MeCO₂), 172.1 (C=N), 135.9 (ArC), 129.2 (ArC), 128.0 (ArC), 126.4 (ArC), 97.7 (CpC), 86.9 (CpC), 85.7 (CpC), 83.3 (CpC), 76.9 (CH), 76.5 (C₄Ph₄), 59.7 (CH), 42.8 (CH), 25.4 (CH), 24.0 (CH), 23.4 (CH), 21.8 (CH).

Formation of *trans*-bis(oxazoline) coordination complex **22:** The general method for palladation was followed using η^5 -(*S*)-2-(4-*iso*-butyl)oxazolinylcyclopentadienyl)(η^4 -tetraphenylcyclobutadiene)cobalt(I) **9** (0.500 g, 0.83 mmol) and palladium(II) acetate (0.186 g, 0.83 mmol) in acetic acid (1 mL). Heating the solution at 95 °C for 30 minutes followed by cooling and isolation by filtration gave the product as an orange solid (0.573 g, 97 %).

Mp: 188-190 °C. Anal. Found: C 70.08; H 5.35; N 1.85. Calcd for C₈₄H₇₈Co₂N₂O₆Pd: C 70.27; H 5.48; N 1.95. [α]²⁴_D +151 (*c* 0.2, CH₂Cl₂). IR (film): ν_{\max} = 1634 (C=N) cm⁻¹. ¹H

NMR (δ , 500 MHz, CDCl₃): 7.46–7.33 (16H, m, ArH), 7.24–7.12 (24H, m, ArH), 6.05 (2H, vbrs, CpH), 5.79 (2H, brs, CpH), 4.90–4.57 (4H, m, CpH), 3.75–3.64 (2H, m, CH), 3.63–3.56 (2H, m, CH), 3.27–3.18 (2H, m, CH), 3.08–2.96 (2H, m, CH), 2.05 (6H, brs, CH₃), 1.58–1.42 (4H, m, CH), 1.02–0.86 (12H, m, CH₃). ¹³C NMR (δ , 126 MHz, CDCl₃): 175.6 (MeCO₂), 165.5 (C=N), 135.5 (ArC), 129.0 (ArC), 128.0 (ArC), 126.6 (ArC), 86.2 (CpC), 85.4 (CpC), 84.1 (CpC), 76.4 (C₄Ph₄), 72.4 (CH), 43.2 (CH), 26.0 (CH), 23.9 (CH), 22.4 (CH), 21.7 (CH), 21.0 (CH).

Conversion of *trans*-bis(oxazoline) coordination complex **22 into amide **25**:** A flask charged with **22** (0.080 g, 0.06 mmol) dissolved in AcOH (5 mL) and was heated to 90 °C for 4 h. On completion, the solvent was removed *in vacuo*. The crude residue was redissolved in CH₂Cl₂ (5 mL) and washed with aqueous sodium hydrocarbonate solution (5 mL). The organic layer was collected, dried over MgSO₄ and the solvent was removed *in vacuo*. Purification by column chromatography on silica eluting with CH₂Cl₂/EtOAc (9:1) gave the product as an orange oil (0.016 g, 22 %).

$[\alpha]_D^{26} +24.4$ ($c = 0.16$, CH₂Cl₂). IR (film): $\nu_{\max} = 1739$ (C=O), 1644 (C=O) cm⁻¹. ¹H NMR (δ , 500 MHz, CDCl₃): 7.45 (8H, d, J 7.3, ArH), 7.32–7.19 (12H, m, ArH), 5.22 (1H, brd, J 8.4, NH), 5.01 (2H, brs, CpH), 4.67 (2H, brs, CpH), 4.09–4.03 (1H, m, CH), 3.92 (1H, dd, J 11.2, 5.6, CH), 3.67 (1H, dd, J 11.2, 4.7, CH), 2.01 (3H, s, CH₃), 1.49–1.38 (1H, m, CH), 1.11–1.02 (1H, m, CH), 0.99–0.91 (1H, m, CH), 0.87 (3H, t, J 7.0, CH₃), 0.85 (3H, t, J 7.0, CH₃). ¹³C NMR (δ , 126 MHz, CDCl₃): 171.3 (C=O), 165.8 (C=O), 135.4 (ArC), 128.9 (ArC), 128.3 (ArC), 126.9 (ArC), 90.8 (CpC), 86.9 (CpC), 86.6 (CpC), 82.3 (CpC), 82.0 (CpC), 76.3 (C₄Ph₄), 66.0 (CH), 47.0 (CH), 40.5 (CH), 24.8 (CH), 22.9 (CH), 22.7 (CH), 21.1 (CH). High-resolution MS (m/z , ESI⁺) found for MH⁺ = 666.2413, calcd for C₄₂H₄₁CoNO₃ 666.2413.

Conversion of *trans*-bis(oxazoline) coordination complex 22 into 16a: A flask was charged with complex **22** (0.500 g, 0.35 mmol) dissolved in toluene (2 mL). The solution was heated at reflux for 2 h. On completion, the solution was cooled and the solvent was removed *in vacuo* to yield the product as an orange solid (0.252 g, 94 %). The 10:1 ratio of isomer was determined following conversion to the corresponding hfacac complexes. Recrystallisation from CH₂Cl₂/hexane gave diastereomerically pure **16a**.

Di- μ -acetatobis[(η^5 -(*S*)-(S_p)-2-(2'-4'-cyclohexylmethyl)oxazoliny)cyclopentadienyl, 1-C, 3'-N](η^4 -tetraphenylcyclobutadiene)cobalt(I)]dipalladium(II) 18a: General method for palladation was followed using η^5 -(*S*)-2-(4-cyclohexylmethyl)oxazoliny)cyclopentadienyl-(η^4 -tetraphenylcyclobutadiene)cobalt(I) **10** (0.419 g, 0.65 mmol) and palladium(II) acetate (0.146 g, 0.65 mmol) in acetic acid (1 mL). Heating the solution at 95 °C for 30 minutes yielded the product (after filtration) as an orange solid (0.370 g, 70 %).

Mp: 248 °C (dec.). Anal. Found: C 66.77; H 5.04; N 1.91. Calcd for C₉₀H₈₄Co₂N₂O₆Pd₂: C 66.71; H 5.23; N 1.73. [α]¹⁹_D -407 (*c* 0.10, CH₂Cl₂). IR (film): ν_{\max} = 1606 (C=N) cm⁻¹. ¹H NMR (δ , 500 MHz, CDCl₃): 7.63–7.56 (16H, m, ArH), 7.23–7.12 (24H, m, ArH), 4.55 (2H, brs, CpH), 4.39 (2H, brs, CpH), 3.96 (2H, brs, CpH), 3.88 (2H, t, *J* 8.5, CH), 3.47 (2H, t, *J* 7.5, CH), 3.02–2.86 (2H, m, CH), 1.92 (6H, s, CH₃), 1.72–1.17 (12H, m, CH), 1.15–0.90 (6H, m, CH), 0.84–0.49 (6H, m, CH), 0.14–0.02 (2H, m, CH). ¹³C NMR (δ , 126 MHz, CDCl₃): 180.9 (MeCO₂), 172.1 (C=N), 135.9 (ArC), 129.2 (ArC), 128.0 (ArC), 126.3 (ArC), 86.7 (CpC), 85.7 (CpC), 83.3 (CpC), 77.1 (CH), 76.5 (C₄Ph₄), 59.2 (CH), 41.2 (CH), 34.8 (CH), 33.8 (CH), 32.2 (CH), 26.4 (CH), 25.9 (CH), 24.0 (CH).

Di- μ -chlorobis[(η^5 -(*S*)-(S_p)-2-(2'-4'-isobutyl)oxazoliny)cyclopentadienyl, 1-C, 3'-N](η^4 -tetraphenylcyclobutadiene)cobalt(I)]dipalladium(II) 16b:

A flask was charged with di- μ -acetatobis[(η^5 -(*S*)-(S_p)-2-(2'-4'-isobutyl)oxazoliny)cyclopentadienyl, 1-C, 3'-N](η^4 -tetraphenylcyclobutadiene)cobalt(I)]-

dipalladium(II) **16a** (0.020 g, 0.01 mmol) dissolved in acetone (0.5 mL). To this solution was added a 2M NaCl solution (0.06 mL, 0.12 mmol) and the solution was vigorously stirred at rt for 4 h, after which time a precipitate had formed. The precipitate was collected by filtration, washed with water and acetone and dried under *vacuum* to yield the product as a yellow solid (0.007 g, 36 %).

Mp: 183-185 °C. Anal. Found: C 62.81; H 5.15; N 1.76. Calcd for C₈₀H₇₀Cl₂Co₂N₂O₂Pd₂·2H₂O: C 62.84; H 4.88; N 1.83. [α]_D²⁵ -1222 (*c* 0.19 CH₂Cl₂). IR (film): ν_{\max} = 1601 (C=N) cm⁻¹. ¹H NMR (δ , 500 MHz, CDCl₃, ~1:1 ratio of *cis/trans* isomers): 7.72–7.65 (16 H m, ArH), 7.64–7.57 (16H, m, ArH), 7.31-7.16 (48H, m, ArH), 4.77 (2H, dd, *J* 2.5, 1.1, CpH), 4.71 (2H, dd, *J* 2.8, 1.0, CpH), 4.70–4.66 (4H, m, CpH), 4.58 (2H, t, *J* 7.8, CH), 4.52 (2H, t, *J* 8.7, CH), 4.46 (2H, t, *J* 2.5, CpH), 4.32 (1H, t, *J* 2.5, CpH), 3.93 (2H, dd, *J* 8.3, 6.4, CH), 3.89–3.72 (6H, m, CH), 1.81 (2H, ddd, *J* 12.9, 10.1, 2.3, CH), 1.55–1.48 (2H, m, CH), 1.37–1.24 (4H, m, CH), 0.94–0.77 (24H, m, CH₃), 0.43-0.32 (4H, m, CH). ¹³C NMR (δ , 126 MHz, CDCl₃): 173.8 (C=N), 173.7 (C=N), 135.8 (ArC), 135.8 (ArC), 129.5 (ArC), 129.4 (ArC), 128.2 (ArC), 128.1 (ArC), 126.6 (ArC), 126.5 (ArC), 100.1 (CpC), 99.9 (CpC), 89.0 (CpC), 88.8 (CpC), 83.2 (CpC), 82.0 (CpC), 77.7 (CH), 76.7 (CH), 76.5 (C₄Ph₄), 76.3 (C₄Ph₄), 60.8 (CH), 60.6 (CH), 43.6 (CH), 43.3 (CH), 25.7 (CH), 25.6 (CH), 23.8 (CH), 23.7 (CH), 21.5 (CH), 21.4 (CH).

Di- μ -chlorobis[(η^5 -(*S*)-(S_p)-2-(2'-4'-cyclohexyl)oxazolinylmethyl)cyclopentadienyl, 1-C, 3'-N](η^4 -tetraphenylcyclobutadiene)cobalt(I)]dipalladium(II) **18b:**

A flask was charged with di- μ -acetatobis[(η^5 -(*S*)-(S_p)-2-(2'-4'-cyclohexylmethyl)oxazolinyl)cyclopentadienyl, 1-C, 3'-N](η^4 -tetraphenylcyclobutadiene)-cobalt(I)]dipalladium(II) **18a** (0.050 g, 0.03 mmol) dissolved in acetone (1 mL). To this solution was added a 2M NaCl solution (0.2 mL, 0.4 mmol) and the solution was vigorously stirred at rt for 4 h after which time a precipitate had formed. The precipitate was collected by

filtration, washed with water and acetone and dried under *vacuum* to yield the product as a yellow solid (0.024 g, 47 %).

Mp: 203 °C. Anal. Found: C 64.35; H 4.74; N 1.88. Calcd for C₈₆H₇₈Cl₂Co₂N₂O₂Pd₂·2H₂O: C 64.19; H 5.14; N 1.74. [α]_D²⁵ -1113 (c 0.34, CH₂Cl₂). IR (film): ν_{\max} = 1601 (C=N) cm⁻¹. ¹H NMR (δ , 500 MHz, CDCl₃, ~2:3 ratio of isomers): 7.71–7.65 (13H, m, ArH), 7.64–7.58 (19H, m, ArH), 7.28–7.16 (48H, m, ArH), 4.76 (1.6H, dd, *J* 2.3, 1.1, CpH), 4.71 (2.4H, dd, *J* 2.8, 1.0, CpH), 4.71–4.65 (4H, m, CpH), 4.63–4.55 (2.4H, m, CH), 4.52 (1.6H, t, *J* 8.7, CH), 4.46 (2.4H, t, *J* 2.5, CpH), 4.34 (1.6H, t, *J* 2.6, CpH), 3.93 (1.6H, dd, *J* 8.3, 6.4, CH), 3.89–3.74 (6.4H, m, CH), 1.95–0.78 (48H, m, CH), 0.44–0.25 (4H, m, CH). ¹³C NMR (δ , 126 MHz, CDCl₃): 173.8 (C=N), 173.7 (C=N), 135.8 (ArC), 135.8 (ArC), 129.5 (ArC), 129.4 (ArC), 128.2 (ArC), 128.1 (ArC), 126.6 (ArC), 126.5 (ArC), 99.9 (CpC), 99.4 (CpC), 89.2 (CpC), 89.1 (CpC), 85.9 (CpC), 85.4 (CpC), 83.3 (CpC), 82.1 (CpC), 77.4 (CH), 77.3 (CH), 76.4 (C₄Ph₄), 76.3 (C₄Ph₄), 60.4 (CH), 60.2 (CH), 42.3 (CH), 41.9 (CH), 35.1 (CH), 34.2 (CH), 32.2 (CH), 31.1 (CH), 26.7 (CH), 26.7 (CH), 26.6 (CH), 26.5 (CH), 26.4 (CH), 26.2 (CH).

Hexafluoroacetylacetonate[(η^5 -(*S*)-(S_p)-2-(2'-4'-*iso*-butyl)oxazoliny]cyclopentadienyl, 1-*C*, 3'-*N*)(η^4 -tetraphenylcyclobutadiene)cobalt(I)]palladium(II) **16c:** A flask was charged with di- μ -acetatobis[(η^5 -(*S*)-(S_p)-2-(2'-4'-*iso*-butyl)oxazoliny]cyclopentadienyl, 1-*C*, 3'-*N*)(η^4 -tetraphenylcyclobutadiene)cobalt(I)]dipalladium(II) **16a** (0.010 g, 0.01 mmol) and sodium hexafluoroacetylacetonate (0.014 g, 0.06 mmol) in acetone/water (2:1 solution, 2 mL). The solution was stirred vigorously for 16 h after which time a precipitate had formed. The solution was diluted with CH₂Cl₂ (5 mL) and washed with water (5 mL). The organic layer was collected, dried over MgSO₄ and the solvent was removed *in vacuo* to yield the product as an orange solid (0.010 g, 83%).

Mp: 253 °C. Anal. Found: C 58.71; H 4.05; N 1.68. Calcd for C₄₅H₃₆CoF₆NO₃Pd: C 58.87; H 3.96; N 1.53. [α]_D²⁵ -919 (*c* 0.16, CH₂Cl₂). IR (film): ν_{\max} = 1600 (C=N) cm⁻¹. ¹H NMR (δ , 500 MHz, CDCl₃): 7.63–7.57 (8H, m, ArH), 7.27–7.22 (4H, m, ArH), 7.21–7.15 (8H, m, ArH), 5.92 (1H, s, CH), 4.97 (1H, dd, *J* 2.3, 0.9, CpH), 4.80 (1H, dd, *J* 2.6, 0.8, CpH), 4.64 (1H, t, *J* 2.5, CpH), 4.59 (1H, t, *J* 8.3, CH), 3.91–3.75 (2H, m, CH), 1.85–1.72 (1H, m, CH), 1.40–1.30 (1H, m, CH), 0.84 (6H, d, *J* 7.0, CH₃), 0.57–0.46 (1H, m, CH). ¹³C NMR (δ , 126 MHz, CDCl₃): 174.8 (C=N), 174.1 (CO, app d, *J*_{C-F} 4.7), 173.8 (CO, app d, *J*_{C-F} 4.8), 135.8 (ArC), 129.2 (ArC), 127.9 (ArC), 126.6 (ArC), 118.9 (CF, app d, *J*_{C-F} 55.7), 116.7 (CF, app d, *J*_{C-F} 55.1), 100.0 (CpC), 90.2 (CpC), 88.4 (CpC), 86.6 (CpC), 81.7 (CpC), 77.2 (CH), 76.5 (C₄Ph₄), 60.3 (CH), 43.8 (CH), 25.4 (CH), 23.6 (CH), 21.3 (CH). ¹⁹F NMR (δ , 471 MHz, CDCl₃): -74.69, -75.63.

Hexafluoroacetylacetonate[(η^5 -(*S*)-(S_p)-2-(2'-4'-

cyclohexylmethyl)oxazoliny]cyclopentadienyl, 1-C, 3'-N)(η^4 -tetraphenylcyclo-

butadiene)cobalt(I)]palladium(II) 18c: A flask was charged with di- μ -acetatobis[(η^5 -(*S*)-(S_p)-2-(2'-4'-cyclohexylmethyl)oxazoliny]cyclopentadienyl, 1-C, 3'-N)(η^4 -tetraphenylcyclobutadiene)cobalt(I)]dipalladium(II) **18a** (0.030 g, 0.02 mmol) and sodium hexafluoroacetylacetonate (0.043 g, 0.19 mmol) in acetone/water (2:1 solution, 2 mL). The solution was stirred vigorously for 16 h after which time a precipitate had formed. The solution was diluted with CH₂Cl₂ (5 mL) and washed with water (5 mL). The organic layer was collected, dried over MgSO₄ and the solvent was removed *in vacuo* to yield the product as an orange solid (0.031 g, 86%).

Mp: 204 °C. Anal. Found: C, 60.25; H, 4.36; N 1.81. Calcd for C₄₈H₄₀CoF₆NO₃Pd: C, 60.16; H, 4.22; N, 1.46. [α]_D²⁵ -532 (*c* 0.52, CH₂Cl₂). IR (film): ν_{\max} = 1601 (C=N) cm⁻¹. ¹H NMR (δ , 500 MHz, CDCl₃): 7.62–7.54 (8H, m, ArH), 7.25–7.20 (4H, m, ArH), 7.19–7.13 (8H, m, ArH), 5.88 (1H, s, CH), 4.94 (1H, dd, *J* 2.3, 1.0, CpH), 4.77 (1H, dd, *J* 2.6, 1.0, CpH), 4.60

(1H, t, J 2.6, CpH), 4.60–4.53 (1H, m, CH), 3.91–3.81 (1H, m, CH), 3.80–3.73 (1H, m, CH), 1.90–1.80 (1H, m, CH), 1.76–1.57 (3H, m, CH), 1.52–1.44 (1H, m, CH), 1.37–0.78 (7H, m, CH), 0.51–0.40 (1H, m, CH). ^{13}C NMR (δ , 126 MHz, CDCl_3): 174.7 (C=N), 174.0 (CO, app d, $J_{\text{C-F}}$ 10.0), 173.8 (CO app d, $J_{\text{C-F}}$ 10.6), 135.8 (ArC), 129.2 (ArC), 127.9 (ArC), 126.6 (ArC), 118.9 (CF, app d, $J_{\text{C-F}}$ 54.9), 116.7 (CF, app d, $J_{\text{C-F}}$ 53.9), 100.0 (CpC), 90.2 (CpC), 88.4 (CpC), 86.6 (CpC), 81.7 (CpC), 76.5 (C_4Ph_4), 59.9 (CH), 42.0 (CH), 34.9 (CH), 34.2 (CH), 32.0 (CH), 31.1 (CH), 26.5 (CH), 26.0 (CH). ^{19}F NMR (δ , 471 MHz, CDCl_3): -74.69, -75.56.

X-ray details A suitable crystal of (*S,S*_p)-**16a** was selected and data collected following a standard method,²⁴ on a Rigaku AFC12 goniometer at 100K equipped with an enhanced sensitivity (HG) Saturn724+ detector mounted at the window of an FR-E-Superbright molybdenum anode generator with HF Varimax optics (100 μm focus). Cell determination, data collection, data reduction, cell refinement and absorption correction were carried out using CrystalClear.²⁵ Structure solution and refinement using SHELX programs.²⁶

Crystal data for (*S,S*_p)-**16a** : $\text{C}_{84}\text{H}_{76}\text{Co}_2\text{N}_2\text{O}_6\text{Pd}_2 \cdot 0.5(\text{H}_2\text{O})$, $M = 1549.13$, red blade, $a = 10.333(9)$, $b = 11.314(2)$, $c = 16.307(13)$ Å, $\alpha = 71.68(5)^\circ$, $\beta = 88.83(4)^\circ$, $\gamma = 76.54(4)^\circ$, $V = 1757(2)$ Å³, $T = 100(2)$ K, space group *PI*, $Z = 1$, $\mu = 1.025$ mm⁻¹, reflections collected = 19659, independent reflections = 12074, Flack parameter = 0.018(6), $R1 = 0.0221$, $wR2 = 0.0529$ [$F^2 > 2\sigma(F^2)$], $R1 = 0.0227$, $wR2 = 0.0533$ (all data).

ASSOCIATED CONTENT

Supporting Information. CCDC1055821 contains supplementary X-ray crystallographic data for (*S,S*_p)-**16a**. This data can be obtained free of charge via <http://www.ccdc.cam.ac.uk/conts/retrieving.html>, or from the Cambridge Crystallographic Data Centre, Union Road, Cambridge, CB2 1EZ; fax(+44) 1223-336-033 or email:

deposit@ccdc.cam.ac.uk. Methods for the determination of palladation diastereoselectivities and catalysis product enantioselectivities, $^1\text{H}/^{13}\text{C}/^{19}\text{F}$ spectra, and details of the X-ray structure search on $\text{Pd}_2(\mu\text{-OAc})_2$ containing palladacycles. This material is available free of charge via the Internet at <http://pubs.acs.org>.

AUTHOR INFORMATION

Corresponding Authors

*E-mail: Chris.Richards@uea.ac.uk

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

For financial support we thank the ISCE-Chem & INTERREGIVa programme (D.C.). We thank Niccole L. Sanders (UEA) for preliminary experiments, Myles Cheesman (UEA) for assistance with the CD spectra, and Laszlo Fabian (UEA) for the CCDC search. We also thank the EPSRC National Mass Spectrometry Centre (University of Wales, Swansea).

REFERENCES

- (1) Overman, L. E.; Owen, C. E.; Pavan, M. M.; Richards, C. J. *Org. Lett.* **2003**, *5*, 1809-1812.
- (2) (a) Anderson, C. E.; Overman, L. E. *J. Am. Chem. Soc.* **2003**, *125*, 12412-12413. (b) Kirsch, S. F.; Overman, L. E. *J. Am. Chem. Soc.* **2005**, *127*, 2866-2867. (c) Kirsch, S. F.; Overman, L. E. *J. Org. Chem.* **2005**, *70*, 2859-2861. (d) Lee, E. E.; Batey, R. A. *J. Am. Chem. Soc.* **2005**, *127*, 14887-14893. (e) Kirsch, S. F.; Overman, L. E.; White, N.

- S. *Org. Lett.* **2007**, *9*, 911-913 (f) Watson, M. P.; Overman, L. E.; Bergman, R. G. *J. Am. Chem. Soc.* **2007**, *129*, 5031-5044. (g) Nomura, H.; Richards, C. J. *Chem. Eur. J.* **2007**, *13*, 10216-10224. (h) Overman, L. E.; Roberts, S. W.; Sneddon, H. F. *Org. Lett.* **2008**, *10*, 1485-1488. (i) Rodrigues, A.; Lee, E. E.; Batey, R. A. *Org. Lett.* **2010**, *12*, 260-263. (j) Cannon, J. S.; Kirsch, S. F.; Overman, L. E. *J. Am. Chem. Soc.* **2010**, *132*, 15185-15191. (k) Cannon, J. S.; Kirsch, S. F.; Overman, L. E.; Sneddon, H. F. *J. Am. Chem. Soc.* **2010**, *132*, 15192-15203. (l) Cannon, J. S.; Olson, A. C.; Overman, L. E.; Solomon, N. S. *J. Org. Chem.* **2012**, *77*, 1961-1973. (m) Mingat, G.; MacLellan, P.; Laars, M.; Clayden, J. *Org. Lett.* **2014**, *16*, 1252-1255.
- (3) Roca, F. X.; Motevalli, M.; Richards, C. J. *J. Am. Chem. Soc.* **2005**, *127*, 2388-2389.
- (4) Fischer, D. F.; Barakat, A.; Xin, Z.; Weiss, M. E.; Peters, R. *Chem. Eur. J.* **2009**, *15*, 8722-8741.
- (5) Weiss, M. E.; Fischer, D. F.; Xin, Z.; Jautze, S.; Schweizer, W. B.; Peters, R. *Angew. Chem. Int. Ed.* **2006**, *45*, 5694-5698.
- (6) For a review see: Nomura, H.; Richards, C. J. *Chem. Asian J.* **2010**, *5*, 1726-1740.
- (7) For other planar chiral palladacycles synthesised by diastereoselective palladation see:
(a) Richards, C. J. In *Chiral Ferrocenes in Asymmetric Catalysis; Synthesis and Applications*, Dai, L.-X.; Hou, X.-L., Eds.; Wiley-VCH: Weinheim, 2010; pp 337-368. (b) Gan, K.; Sadeer, A.; Xu, C.; Li, Y.; Pullarkat, S. A. *Organometallics* **2014**, *33*, 5074-5076.
- (8) Stevens, A. M.; Richards, C. J. *Organometallics* **1999**, *18*, 1346-1348.
- (9) Prasad, R. S.; Anderson, C. E.; Richards, C. J.; Overman, L. E. *Organometallics* **2005**, *24*, 77-81.
- (10) Anderson, C. E.; Overman, L. E.; Richards, C. J.; Watson, M. P.; White, N. *Org. Synth.* **2007**, *84*, 139-147.

- (11) Kazi, A. B.; Jones, G. D.; Vicic, D. A. *Organometallics* **2005**, *24*, 6051-6054.
- (12) (a) Gorunova, O. N.; Keuseman, K. J.; Goebel, B. M.; Kataeva, N. A.; Churakov, A. V.; Kuz'mina, L. G.; Dunina, V. V.; Smoliakova, I. P. *J. Organomet. Chem.* **2004**, *689*, 2382-2394. (b) Mawo, R. Y.; Johnson, D. M.; Wood, J. L.; Smoliakova, I. P. *J. Organomet. Chem.* **2008**, *693*, 33-45.
- (13) A list of structures and references is given in the supporting information.
- (14) Bercaw, J. E.; Durrell, A. C.; Gray, H. B.; Green, J. C.; Hazari, N.; Labinger, J. A.; Winkler, J. R. *Inorg. Chem.* **2010**, *49*, 1801-1810.
- (15) (a) Blanco, J.; Gayoso, E.; Vila, J. M.; Gayoso, M.; Maichle-Mössmer, C.; Strähle, J. *Z. Naturforsch.* **1993**, *48b*, 906-910. (b) Freiesleben, D.; Polborn, K.; Robl, C.; Sünkel, K.; Beck, W. *Can. J. Chem.* **1995**, *73*, 1164-1174. (c) Zhao, G.; Yang, Q.-C.; Mak, T. C. W. *Organometallics* **1999**, *18*, 3623-3636. (d) Mercier, A.; Wagschal, S.; Guénée, L.; Besnard, C.; Kündig, E. P. *Organometallics* **2013**, *32*, 3932-3942.
- (16) The *trans*-configured pivalate-bridged derivative of **1a** has also been reported: Olson, A. C.; Overman, L. E.; Sneddon, H. F.; Ziller, J. W. *Adv. Synth. Catal.* **2009**, *351*, 3186-3192.
- (17) Panchal, K.; Amin, J.; Roca, F. X.; Motevalli, M.; Horton, P.N.; Coles S. J.; Richards, C. J. *J. Organomet. Chem.* **2015**, *775*, 12-19.
- (18) Yeamine, M. R.; Richards, C. J. *Tetrahedron: Asymmetry* **2007**, *18*, 2613-2616.
- (19) (a) Lafrance, M.; Rowley, C. N.; Woo, T. K.; Fagnou, K. *J. Am. Chem. Soc.* **2006**, *128*, 8754-8756. (b) García-Cuadrado, D.; de Mendoza, P.; Braga, A. A. C.; Maseras, F.; Echavarren, A. M. *J. Am. Chem. Soc.* **2007**, *129*, 6880-6886. (c) Gorelsky, S. I.; Lapointe, D.; Fagnou, K. *J. Am. Chem. Soc.* **2008**, *130*, 10848-10849.

- (20) (a) Sammakia, T.; Latham, H. A.; Schaad, D. R. *J. Org. Chem.* **1995**, *60*, 10-11. (b) Richards, C. J.; Damalidis, T.; Hibbs, D. E.; Hursthouse, M. B. *Synlett* **1995**, 74-76. (c) Nishibayashi, Y.; Uemura, S. *Synlett* **1995**, 79-81.
- (21) Xia, J.-B.; You, S.-L. *Organometallics* **2007**, *26*, 4869-4871.
- (22) Garcia, M. A.; Frey, W.; Peters, R. *Organometallics* **2014**, *33*, 1068-1078.
- (23) The diastereoselectivity of lithiation of a ferrocenyloxazoline and a pentaphenylferrocenyloxazoline, both derived from (*S*)-valine, is reversed with use of bis(2-*tert*-butoxyethyl)ether as an additive. See reference 22 and: Herbert, S. A.; Castell, D. C.; Clayden, J.; Arnott, G. E. *Org. Lett.* **2013**, *15*, 3334-3337.
- (24) Coles, S. J.; Gale, P. A. *Chem. Sci.* **2012**, *3*, 683-689.
- (25) Rigaku, CrystalClear- SM Expert 3.1 b27, **2013**.
- (26) Sheldrick, G.M., *Acta Cryst.* **2015**, *C71*, 3-8.