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Enantioselective Synthesis and Application to the Allylic Imidate Rearrangement of Amine-Coordinated Palladacycle Catalysts of Cobalt Sandwich Complexes

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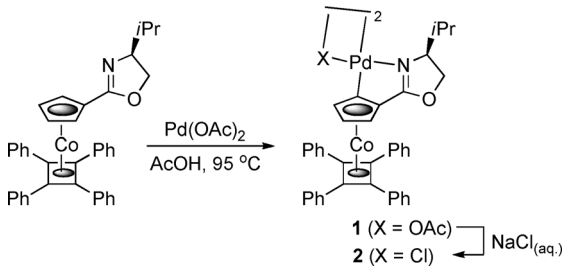
Abstract: The reaction of (η^5-(*N*,*N*-dimethylaminomethyl)cyclopentadienyl)(η^4-tetraphenylcyclobutadiene)cobalt with sodium tetrachloropalladate and (*R*)-*N*-acetylphenylalanine gave planar chiral palladacycle di-μ-chloridebis[(η^5-(S_p)-2-(*N*,*N*-dimethylaminomethyl)cyclopentadienyl,1-*C*,3′-*N*)(η^4-tetraphenylcyclobutadiene)cobalt]dipalladium [(S_p)-Me$_2$-CAP-Cl] in 92% *ee* and 64% yield. Enantiopurity (>98% *ee*) was achieved by purification of the monomeric (*R*)-proline adducts and conversion back to the chloride dimer. Treatment with AgOAc gave (S_p)-Me$_2$-CAP-OAc which was applied to asymmetric transcyclopalladation (up to 78% *ee*). The (*R*)-*N*-acetylphenylalanine mediated palladation methodology was applicable also to the corresponding *N*,*N*-diethyl (82% *ee*, 39% yield) and pyrrolidinyl (>98% *ee*, 43% yield) cobalt sandwich complexes. A combination of 5 mol% of the latter [(S_p)-Pyrr-CAP-Cl] and $AgNO_3$ (3.8 equiv) is a catalyst for the allylic imidate rearrangement of an (*E*)-*N*-aryltrifluoroacetimidate (up to 83% *ee*), and this catalyst system is also applicable to the rearrangement of a range of (*E*)-trichloroacetimidates (up to 99% *ee*). This asymmetric efficiency combined with the simplicity of catalyst synthesis provides accessible solutions to the generation of non-racemic allylic amine derivatives.

Keywords: asymmetric synthesis · catalysis · metallacycles · palladium · sandwich complexes

Introduction

There are three principal reasons to develop methods for the asymmetric synthesis of chiral palladacycles,[1] an area in which many examples are metallocene-based planar chiral complexes.[2] First is the use of these metallacycles as catalysts for the synthesis of non-racemic organic compounds.[3] Conspicuous success has been achieved in catalysis of the asymmetric allylic imidate rearrangement and closely related reactions using planar chiral palladacycles based upon bulky cobalt sandwich complexes (e.g., **1** and **2**) or related pentaphenylferrocene frameworks (Scheme 1).[4–6] In these reactions the palladium-carbon palladacycle bond is maintained throughout the catalytic cycle. Numerous other examples of chiral palladacycle-catalysed asymmetric transformations have been reported also.[7] Second is the use of palladacycles as precatalysts for the in situ generation of Pd^0 species.[8,9] Finally, the development of enantioselective methods for palladium catalysed asymmetric C–H activation is informed by the synthesis of complexes related closely to the intermediate chiral palladacycles generated in these reactions.[10]



Scheme 1. Diastereoselective synthesis of cobalt oxazoline palladacycle **1** [(S,R_p)-COP-OAc] and transformation into chloride-bridged dimer **2** [(S,R_p)-COP-Cl].[11]

Central to the synthesis of **1**, as with many related planar chiral metallocene-based palladacycles, is an auxiliary-mediated diastereoselective C–H activation step resulting in a new carbon–palladium bond.[2b,11] There are far fewer examples of planar chiral palladacycles derived from enantioselective C–H activation. Non-racemic planar chiral palladacycles have been generated from a limited number of enantioselective transcyclopalladation reactions,[12] and in 1979 Sokolov reported the *N*-acetyl amino acid mediated enantio-

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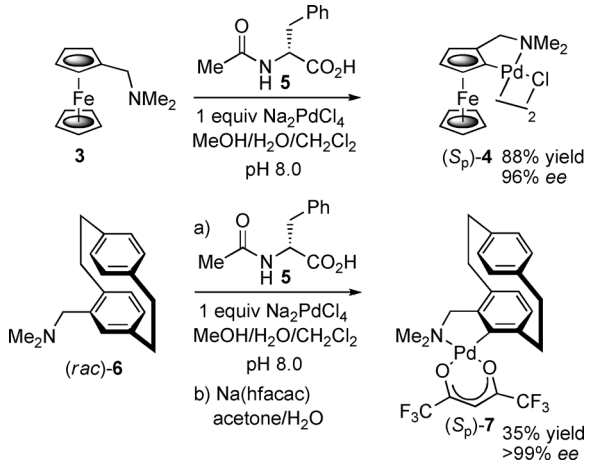
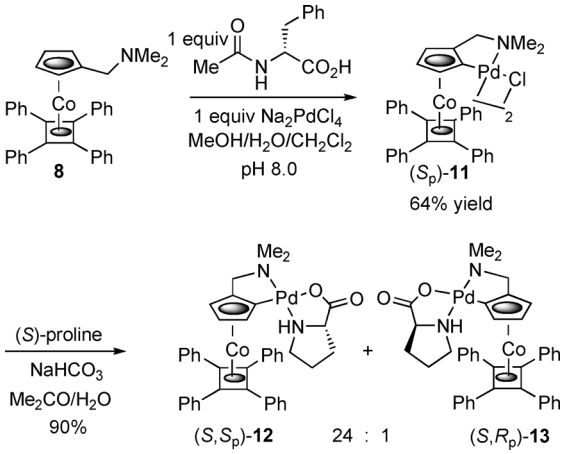


Scheme 2. Application of enantioselective palladation to the synthesis of planar chiral palladacycles.

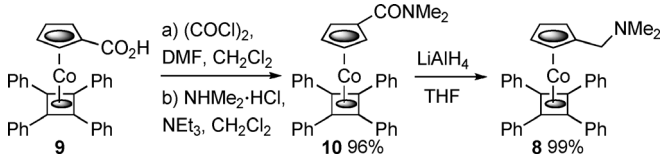


Scheme 4. Enantioselective palladation of **8** and derivatisation with (*S*)-proline.

selective palladation of *N*,*N*-dimethylaminomethylferrocene (**3**).[13] Recent re-investigation of this latter chemistry within our group identified conditions for the synthesis of palladacycle (S_p)-**4** in 96% *ee* using (*R*)-*N*-acetylphenylalanine (**5**),[14] and an extension of the methodology to the kinetic resolution of [2.2]paracyclophane (**6**) gave palladacycle (S_p)-**7** in more than 99% *ee* (Scheme 2).[15] In this study we report on the application of enantioselective palladation to the facile synthesis of non-racemic amine palladacycles containing a cobalt sandwich complex, and on the application of these to asymmetric transcyclopalladation and asymmetric allylic imidate rearrangement.

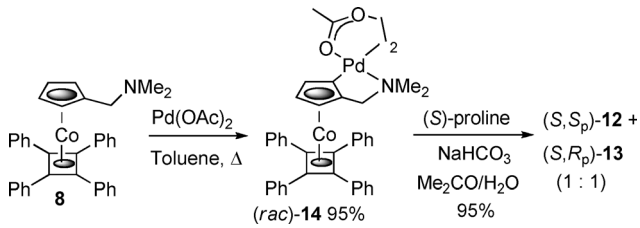
Results and Discussion

Amine **8**, a cobalt sandwich complex analogue of **3**, was first synthesised as previously reported from the Mannich-type reaction of (η^5-cyclopentadienyl)(η^4-tetraphenylcyclobutadiene)cobalt with bis(dimethylamino)methane.[16] The low yield of this reaction (typically ~40%) led us to an alternative and more productive procedure in which acid **9**[11,17] was converted to dimethylamide **10** followed by reduction (Scheme 3).



Scheme 3. Alternative synthesis of amine **8**.

The palladation of amine **8** has been reported previously with a mixture of lithium tetrachloropalladate and sodium acetate in methanol.[18] This result suggested that the prochiral cobalt complex **8** would be a suitable substrate for a chiral carboxylate mediated asymmetric palladation. Application of the room temperature conditions optimised previously for the enantioselective palladation of **3**, with a reaction time of 16 h, resulted in a new chloride bridged palladacycle **11** in 64% yield (Scheme 4). The product was determined to have an enantiomeric excess of 92% following treatment with (*S*)-proline and analysis of the resulting diastereomeric adducts **12** and **13**. Their ratio was determined readily by ^{1}H NMR spectroscopy, in particular by comparison of one of the base-line resolved methyl singlets [**12**: 2.31 ppm (3H, s), **13** 2.36 ppm (3H, s)], or by comparison of two of the signals arising from the cyclopentadienyl rings [(**12**: 4.26 ppm (1H, br s), **13** 4.30 ppm (2H, br s)]. Performing the palladation reaction at 0°C resulted in no change in enantioselectivity and a longer reaction time was required to ensure complete palladation. A racemic acetate-bridged palladacycle **14** was synthesised by heating together **8** and palladium acetate in toluene at reflux for 2 h (Scheme 5).



Scheme 5. Non-enantioselective palladation of **8** with $Pd(OAc)_2$.

Subsequent treatment with (*S*)-proline as before gave a 1:1 mixture of **12** and **13**, confirming that these proline adducts are planar chiral stereoisomers and not *cis*/*trans* coordination stereoisomers.

Following recrystallisation from CH_2Cl_2/hexane of the proline adducts derived from asymmetric palladation, a small quantity of the major diastereoisomer was obtained pure and the configuration of the element of planar chirality was determined as S_p by X-ray crystallography (Figure 1).[19]

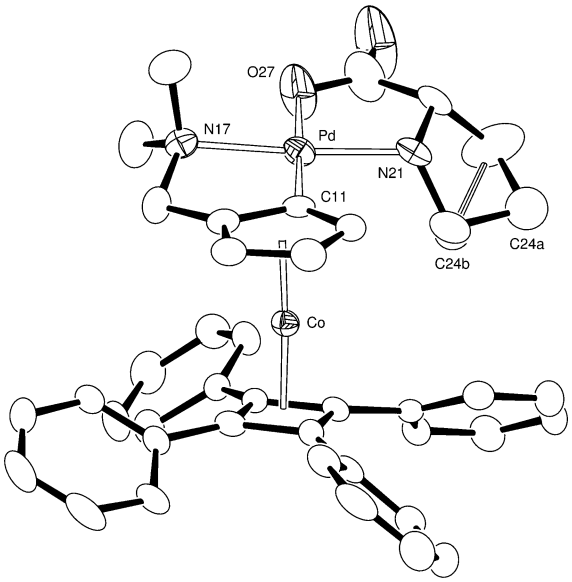
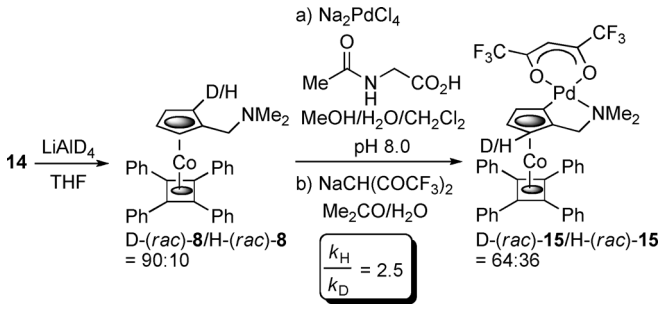


Figure 1. A molecule of (S,S_p)-**12** from the X-ray analysis. Principal bond lengths [Å] include: Pd–C(11) 1.973(4), Pd–N(17) 2.092(4), Pd–N(21) 2.023(4), Pd–O(27) 2.082(4); mean Co–C(C4 ring) 1.991(5), mean Co–C(cp) 2.07(2). Principal angles [°] include: C(11)-Pd-N(17) 82.68(18), N(21)-Pd-O(27) 82.50(16).

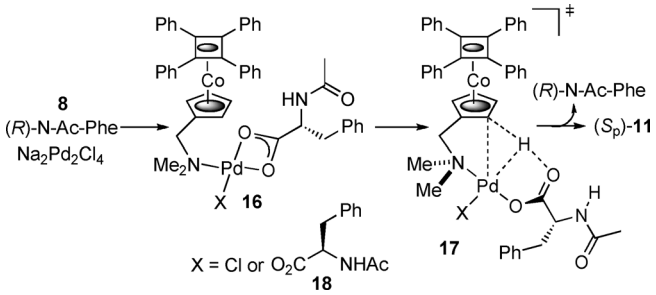
The pyrrolidine ring is disordered, with alternative sites for one methylene group, at C(24a) and C(24b). The other four members of this ring are approximately co-planar, so that the five-membered ring adopts an envelope shape with the flap on one side, for example, C(24a), or the other, C(24b).

The high enantioselectivity observed in the palladation reaction points to the involvement of a palladium intermediate containing a coordinated carboxylate ligand obtained by deprotonation of (*R*)-*N*-acetylphenylalanine. Palladation reactions with palladium acetate and other palladium(II)-carboxylate species have been shown to proceed by a concerted metallation-deprotonation (CMD) pathway, a mechanism consistent with a kinetic isotope effect of more than 1.[20] To determine if this mechanism may be operating in the *N*-acetyl amino acid mediated formation of **11**, a racemic 2-deutertated sample of the starting amine D-(*rac*)-**8** (90% deuterium incorporation) was synthesised by treatment of the racemic palladacycle **14** with $LiAlD_4$ (Scheme 6). Repetition of the Na_2PdCl_4/*N*-acetyl amino acid palladation conditions, with *N*-acetylglycine in place of (*R*)-*N*-acetylphenylalanine, followed by ligand substitution with sodium hexafluoroacetylacetonate, gave monomeric palladacycle D-(*rac*)-**15**/H-(*rac*)-**15** (64% deuterium incorporation). The intramolecular isotope effect of 2.5 is very similar to the value of 2.3 determined for the palladation of the ferrocene analogue **3** under the same conditions.[14] Furthermore, use of the same sample of D-(*rac*)-**8** in a reaction with palladium acetate in toluene at reflux followed by ligand substitution revealed an intramolecular isotope effect of 2.0 (D-(*rac*)-**15**/H-(*rac*)-**15** = 60:40). All of these values are consistent with a carboxylate ligand accelerated CMD pathway, with the reactions containing (*R*)-*N*-acetylphenylalanine resulting in the preferential formation of the (S_p)-palladacycle.



Scheme 6. Determination of the intramolecular isotope effect for the *N*-acetyl amino acid promoted palladation of **8**.

A pathway for the chiral carboxylate mediated palladation of **8** is outlined in Scheme 7. This is based on the DFT calculated mechanism of dimethylbenzylamine cyclometalation by palladium acetate,[21] and a suggested extension of this process to the *N*-acetylphenylalanine mediated enantioselective palladation of phosphines containing a 2-phenylferrocene substituent.[22] In this pathway an initially formed amine and η^2-carboxylate ligated complex **16** leads to transition state **17** with the carbonyl oxygen of the now η^1-carboxylate ligand participating in deprotonation simultaneously with the formation of the new carbon–palladium bond in the vacant coordination site. Replacement of ligand X in **17** by the nitrogen of the amino acid derived ligand to give a chelate would appear to be geometrically incompatible with the participation of the carbonyl group of this ligand as a base. Instead the conformational properties of the ligand are controlled by its dipeptide-like properties.[22] Variation of the *ee* of the (*R*)-*N*-acetylphenylalanine employed in cyclometallation resulted in a small positive non-linear effect with respect to the *ee* of metallacycle (S_p)-**11**, an outcome compatible with coordination of a second η^1-carboxylate **18** and chirality matched rate accelerated cyclometallation (Figure 2).



Scheme 7. A possible pathway for the enantioselective palladation of **8**.

Separation of the diastereoisomeric proline adducts was achieved readily by column chromatography. This was most conveniently performed by first treating (S_p)-**11** with (*R*)-proline as the major diastereoisomer (R,S_p)-**13** has a higher R_f (0.24) than the minor diastereoisomer (R,R_p)-**12** (0.16) in

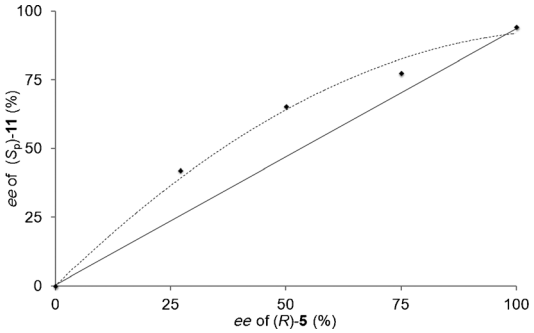
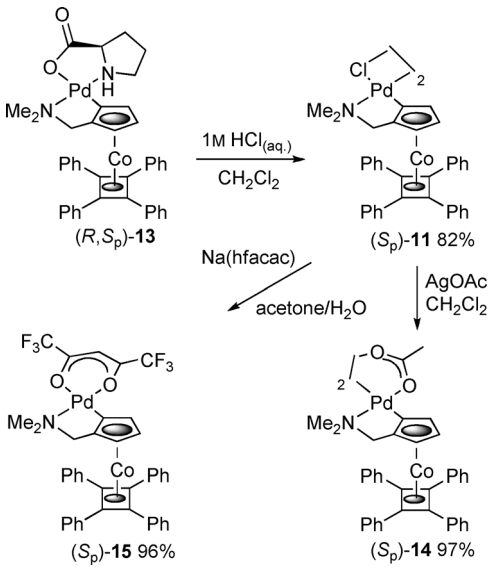


Figure 2. An investigation into the relationship between the *ee* of *N*-acetylphenylalanine and the *ee* of product palladacycle (S_p)-**11**.

2.5% MeOH/CH_2Cl_2, such that the majority of the former can be eluted with little or no contamination from the latter. If required, a subsequent recrystallisation can ensure diastereomeric purity (>99:1 as determined by ^{1}H NMR spectroscopy). The X-ray crystal structure of (R,S_p)-**13** (see the Supporting Information) confirmed further the absolute configuration and the *trans* nitrogen geometry.

Conversion back to the cobalt amine palladacycle (S_p)-**11** [(S_p)-Me_2-CAP-Cl] was carried out by stirring, overnight, a biphasic mixture of (R,S_p)-**13** in CH_2Cl_2 and aqueous 0.5 M HCl (Scheme 8).[23] The enantiopure chloride-bridged dimer



Scheme 8. Ligand exchange reactions starting from (R,S_p)-**13**.

is formed in good yield as an approximately 1:1 mixture of isomers with respect to the *cis*/*trans* arrangements of the two bridged C–N chelates. Addition of silver acetate to (S_p)-**11** resulted in the clean formation of acetate bridged dimer (S_p)-**14** [(S_p)-Me_2-CAP-OAc], and in common with other examples of planar chiral acetate-bridged palladacycles this is a single, presumably *trans*, stereoisomer.[24] Treatment of (S_p)-**11** with sodium hexafluoroacetylacetonate [Na-

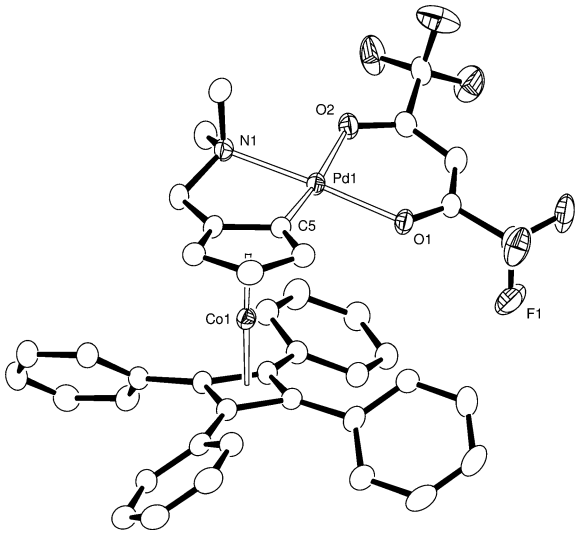
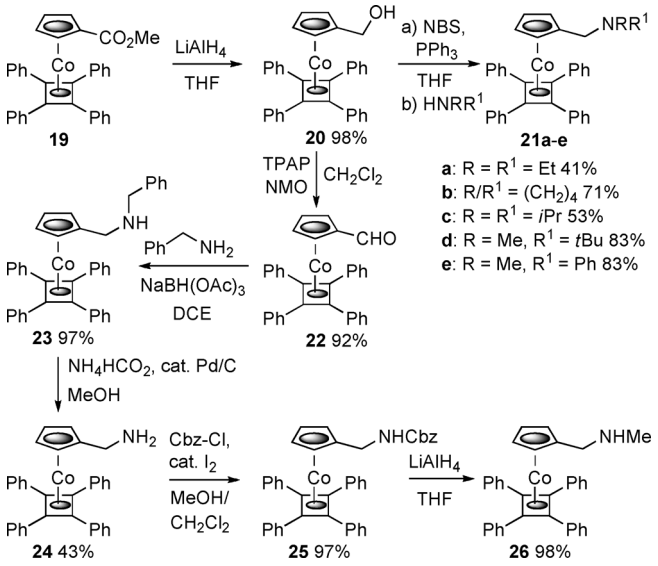


Figure 3. A molecule of (*rac*)-**15** from X-ray analysis. Principal bond lengths [Å] and angles [°] [corresponding data for (S,R_p)-COP-hfacac) in parenthesis][5c] include: C(5)–Pd 1.955(3) [1.962(6)], N(1)–Pd 2.085(3) [2.026(5)], O(1)–Pd 2.046(2) [2.020(4)], O(2)–Pd 2.119(2) [2.102(4)], C(5)-Pd-N(1) 81.87(12) [80.8(2)], O(1)-Pd-O(2) 91.33(9) [92.77(15)].

(hfacac)] gave (S_p)-**15** [(S_p)-Me_2-CAP-hfacac], although attempts to synthesise this directly from proline adduct (R,S_p)-**13** were unsuccessful.

A representation of the X-ray crystal structure of (*rac*)-**15** (obtained from (*rac*)-**14** and Na(hfacac)) is shown in Figure 3.[25] The hfacac ligand allows comparison of this structure with the hfacac derivative of palladacycles **1** and **2** [(S,R_p)-COP-hfacac].[5c] In common with that structure is the longer length of the O(2)–Pd bond compared to O(1)–Pd, indicative of the larger *trans* influence of the carbanion ligand compared to nitrogen. That both these bond lengths in **15** are longer than the corresponding bonds in the COP derivative point to more electron density on the palladium atom of **15** due to the greater basicity of the amine nitrogen compared to the oxazoline nitrogen,[26] and the presence of the electron-withdrawing oxazoline substituent in the COP derivative. This is supported further by the larger chemical shift of the methine proton in the hfacac ligand of the COP derivative (5.95 ppm) compared to that in **15** (5.87 ppm).

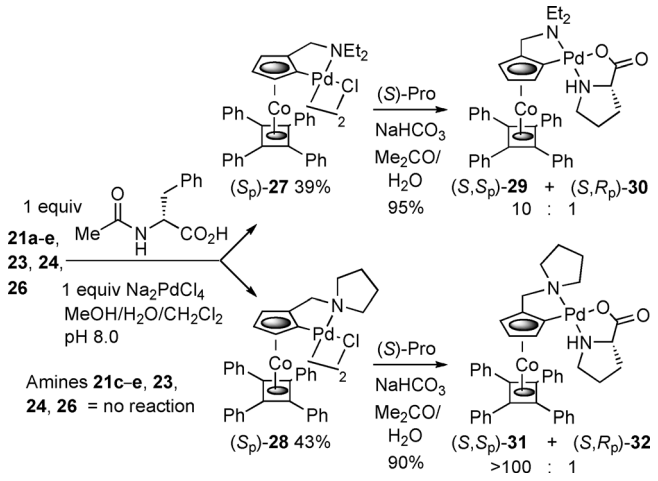
A number of amines related to the *N*,*N*-dimethylamino containing substrate **8** were synthesised to examine further the asymmetric palladation methodology. Following reduction of methyl ester **19**,[27] the alcohol **20** was converted in situ with *N*-bromosuccinimide/triphenylphosphine into the corresponding α-bromomethyl sandwich complex followed by treatment with a variety of secondary amines to give products **21a–e** (Scheme 9).[28] Oxidation of alcohol **20** to aldehyde **22**[27] followed by reductive amination with benzylamine gave secondary amine **23**. Hydrogenolysis of this resulted only in debenzylation to give the primary amine **24** with no formation of (η^5-methylcyclopentadienyl)(η^4-tetraphenylcyclobutadiene)cobalt, an alternative reduction product which would have resulted from hydrogenolysis of the



Scheme 9. Synthesis of further amine substrates **21a–e**, **23**, **24** and **26**.

nitrogen-C(α-sandwich complex) bond. Finally, introduction of a Cbz group followed by reduction of **25** with lithium aluminium hydride gave the *N*-methyl amine **26**.

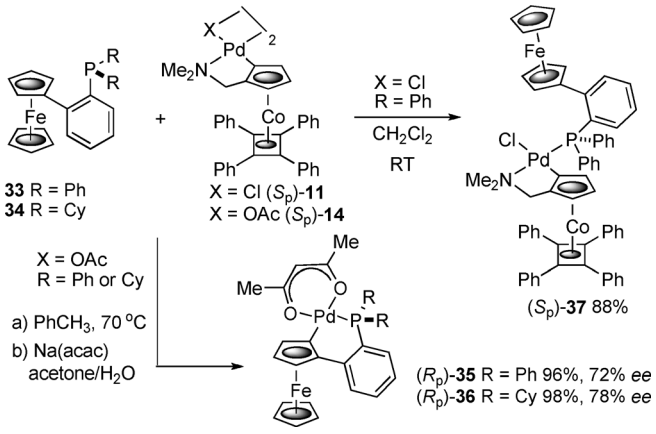
Application to these new amines of the standard asymmetric palladation conditions resulted in only two new palladacycles, (S_p)-**27** and (S_p)-**28** derived from the *N*,*N*-diethylamine **21a** and pyrrolidinyl complex **21b**, respectively (Scheme 10). (*S*)-Proline derivatisation revealed the *ee* of **27**



Scheme 10. Enantioselective palladation of additional amine substrates.

as 82% and **28** as more than 98%. In the latter case the minor diastereoisomer (*S*,R_p)-**32** could not be detected by ^{1}H NMR spectroscopy. The determination of the ratio of isomers as more than 100:1 was made following the synthesis of (*R*,S_p)-**32** from (*R*)-proline, and the use of this to spike the ^{1}H NMR sample. The absolute configuration of these new palladacycles was assigned initially by the sign of the specific rotation [(S_p) = −ve, (R_p) = +ve],[29] and confirmed by the correspondence between the CD spectra of (S_p)-**27** and (S_p)-**28** with that of (S_p)-**11** (see the Supporting Information). That the diethylamine and pyrrolidine derivatives are limiting substrates under these reaction conditions is revealed by the reduced yield obtained. The *N*,*N*-dimethyl, *N*,*N*-diethyl and pyrrolidinyl substrates appear to have the correct balance of nitrogen basicity and steric accessibility to permit palladation. It is significant that treatment of **21c–e** with $Pd(OAc)_2$ in toluene at either 70–80 °C, or heating at reflux, also did not result in palladation.

Preliminary investigations into the use of these new CAP complexes in asymmetric synthesis began with the *N*,*N*-dimethylamino derivatives obtained following proline-mediated purification. Transcyclometallation is a term coined to describe the exchange of cyclometalated ligands without the formation of dissociated metal salts.[30] Following a demonstration of asymmetric transcyclopalladation using palladacycles derived from (*R*)-3-amino-3-phenyl-2,2-dimethylpropane,[12a] one of us reported that the reaction between (*S*,R_p)-COP-OAc (**1**) and prochiral phosphines **33** or **34** resulted in the clean formation of phosphapalladacycles **35** and **36** in up to 95% *ee* (R = Cy).[12b] The applicability of CAP complexes to this reaction was investigated by combining (S_p)-Me_2-CAP-OAc and phosphine **33** (R = Ph) followed by heating at 70 °C in toluene for 24 h (Scheme 11). The ini-



Scheme 11. Asymmetric transcyclopalladation and a phosphine addition product.

tially formed acetate-bridged phosphapalladacycle was converted into the monomeric acac ligated complex **35** for which a 86:14 ratio of R_p and S_p enantiomers was determined by chiral HPLC analysis. In the same way phosphine **34** (R = Cy) gave a 89:11 ratio of R_p and S_p isomers of **36**.

The initial reaction between a phosphine substrate and the amine-coordinated palladacycle results in the formation of a monomeric adduct, as revealed by the synthesis of (S_p)-**37** from **33** and (S_p)-**11** (Scheme 11). A representation of the X-ray crystal structure of (S_p)-**37** is shown in Figure 4.[31] In common with most other nitrogen ligand based palladacycles, the added phosphine is incorporated *trans* to nitrogen, the thermodynamic ligand substitution product.[32] The

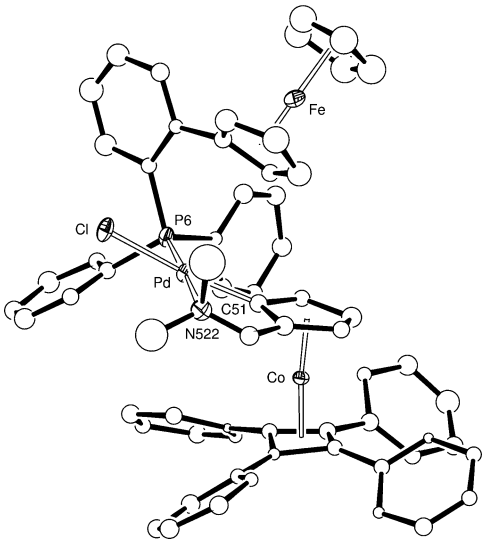
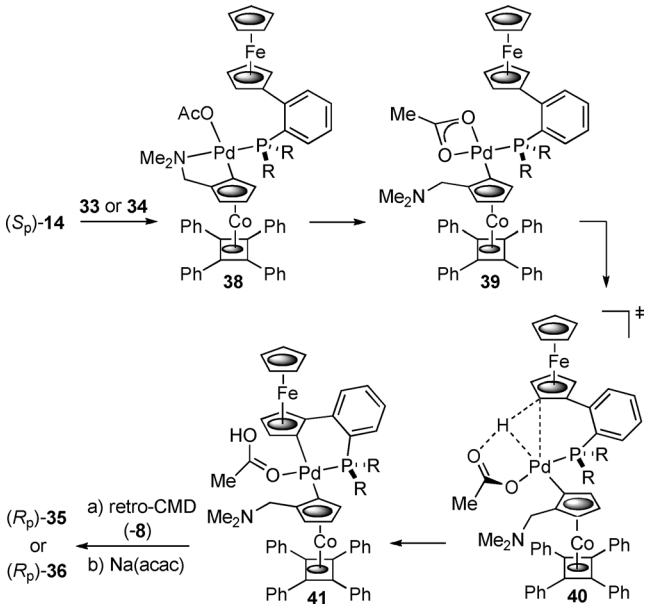


Figure 4. A molecule of (S_p)-**37** from X-ray analysis. Principal bond lengths [Å] include: Pd–Cl 2.383(4), Pd–C(51) 2.004(16), Pd–N(522) 2.193(10), Pd–P(6) 2.271(4), mean Co–C(C4 ring) 1.97(4), mean Co–C(cp) 2.05(7), mean Fe–C(substd-cp) 2.00(4), Fe–C(cp) 2.03(4). Principal angles [°] include: C(51)-Pd-N(522) 80.9(6), P(6)-Pd-Cl 87.8(2).

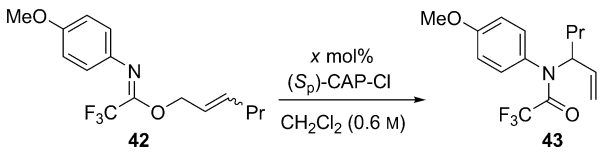


Scheme 12. Mechanism and origin of enantioselection in asymmetric transcyclopalladation.

triarylphosphine ligand displays an induced *P* configuration, and the tetraphenylcyclobutadiene moiety is *M*. This latter configuration is also displayed in the solid state structure of (*rac*)-**15** (relative to S_p), but (S,S_p)-**12** and (R,S_p)-**13** are *P*, revealing no correlation between the planar and induced propeller chirality of the η^4-tetraphenylcyclobutadiene group.[33]

The X-ray crystal structure of (S_p)-**37** also reveals the orientation of the ferrocenyl group above the palladium centred square-plane, as beneath lie phenyl groups attached to the η^4-cyclobutadiene moiety. This and the *trans* to nitrogen coordination geometry are instrumental in controlling the enantioselectivity of palladium transfer. A pathway for this process is outlined in Scheme 12 based, as before, on dimethylbenzylamine cyclopalladation and related studies.[21,22] Following formation of **38**, dissociation of the amine ligand by formation of the η^2-acetate complex **39** is followed by acetate assisted concerted metalation-deprotonation (CMD) via transition state **40** to give **41**. Subsequent protonolysis of the cobalt complex carbon–palladium bond by retro-CMD releases amine **8** and gives an acetate ligated phosphapalladacycle, replacement of which on addition of Na(acac) results in isolated complexes (R_p)-**35** or (R_p)-**36**. Although rotation is possible about the carbon–palladium bond in **39**, the conformer drawn is favoured by the orientation of the coordinated phosphine away from the dimethylaminomethyl moiety. Thus the planar chirality of this monodentate species is also a factor in controlling the enantioselectivity.

Kinetic and molecular modelling studies on the COP-Cl catalysed allylic imidate rearrangement revealed that the planar chirality is also the key factor in controlling the facial selectivity of nitrogen addition to the alkene moiety, this being bound *trans* to the oxazoline nitrogen in the rate and enantioselectivity determining *anti*-amino palladation step.[5e] Given the similarity of the coordination site *trans* to the amine nitrogen, it was anticipated that CAP catalysis of the allylic imidate rearrangement by this pathway would result in usable levels of enantioselectivity, and a predictable correspondence between the configurations of planar and product chirality (S_p gives *R*). This was investigated first with the allylic imidate rearrangement of representative (*E*)- and (*Z*)-*N*-(*para*-methoxyphenyl)trifluoroacetimidate substrates **42** (Scheme 13, Table 1). The reactions were performed first with 5 mol% of (S_p)-**11** at room temperature, which resulted in modest conversions for the formation of (*R*)-**43** (75% *ee*) and (*S*)-**43** (20% *ee*) from *E* and *Z* substrates, respectively (entries 1 and 2). Similar results were obtained with catalyst (S_p)-**28**, the *E* substrate also resulting in higher conversion and enantioselectivity (entries 3 and 4). Focusing on substrate (*E*)-**42**, and increasing the reaction temperature to 38 °C with the addition of proton sponge, improved the *ee* to 86% but the conversion was still modest (entry 5). Under similar conditions 5 mol% of (S,R_p)-COP-Cl (**1**) resulted in essentially complete conversion, and up to 92% *ee*.[5a]



Scheme 13. Use of (*S*)-CAP-Cl in catalysis of the rearrangement of (*E*)- and (*Z*)-*N*-(*para*-methoxyphenyl)trifluoroacetimidates (**42**).

Assuming a correlation between conversion and the rate of catalysis, the reduced activity observed with the CAP cat-

Table 1. Use of (S_p)-CAP-Cl in catalysis of the rearrangement of (*E*)- and (*Z*)-*N*-(*para*-methoxyphenyl)trifluoroacetimidates (**42**).[a]

Entry	Cat. (S_p)	*x* [mol%]	*T* [°C]	Config. **42**	Conv. [%][c]	*ee* **43** [%][d]	Config. **43**[d]
1	**11**[b]	5	RT	*E*	50	75	*R*
2	**11**[b]	5	RT	*Z*	54	20	*S*
3	**28**	5	RT	*E*	48	75	*R*
4	**28**	5	RT	*Z*	26	43	*S*
5	**28**[e]	5	38	*E*	43	86	*R*
6	**28**[f]	5	38	*E*	>99[g]	81	*R*
7	**28**[e,f]	5	38	*E*	>99[h]	83	*R*
8	**28**[e,f]	0.5	38	*E*	33	65	*R*

[a] 0.6 M **42** in CH_2Cl_2, reaction time 60 h at RT or 24 h at 38 °C. [b] Catalyst *ee* more than 98%. [c] Determined by ^{1}H NMR spectroscopy. [d] Determined by chiral HPLC of the secondary amine following trifluoroacetate removal. [e] With 4*x* mol% 1,8-bis(dimethylamino)naphthylene. [f] With 3.8*x* mol% $AgNO_3$. [g] Isolated yield = 80%. [h] Isolated yield = 80%.

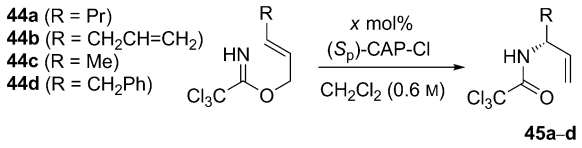
Table 2. Use of (S_p)-CAP-Cl in catalysis of the rearrangement of (*E*)-trichloroacetimidates (**44**).[a]

Entry	Cat. (S_p)	*x* [mol%]	Substrate (R)	Conv. [%][c] (yield [%])	Product[d]	*ee* [%][d]
1	**11**[b]	1	**44a** (Pr)	25	(*R*)-**45a**	51
2	**11**[b]	2	**44a** (Pr)	32	(*R*)-**45a**	68
3	**11**[b]	5	**44a** (Pr)	51	(*R*)-**45a**	72
4	**28**	5	**44a** (Pr)	51	(*R*)-**45a**	86
5	**28**[e]	5	**44a** (Pr)	>99 (77)	(*R*)-**45a**	73
6	**28**[e,f]	5	**44a** (Pr)	>99 (78)	(*R*)-**45a**	99
7	**28**[e,f]	0.5	**44a** (Pr)	7	(*R*)-**45a**	64
9	**28**[e,f]	5	**44b** (allyl)	58 (55)	(*R*)-**45b**	71
8	**28**[e,f]	5	**44c** (Me)	68 (66)	(*R*)-**45c**	91
10	**28**[e,f]	5	**44d** (Bn)	>99 (70)	(*R*)-**45d**	87

[a] 0.6 M **44** in CH_2Cl_2, reaction time 39 h at 38 °C. [b] Catalyst *ee* more than 98%. [c] Determined by ^{1}H NMR spectroscopy; yield = isolated yield. [d] Determined by chiral HPLC. [e] With 3.8*x* mol% $AgNO_3$. [f] With 4.0*x* mol% 1,8-bis(dimethylamino)naphthylene.

alysts is attributed to the increased electron density on the palladium of the amine coordinated complex. Related chloride-bridged ferrocene imidazoline palladacycles are essentially inactive as catalysts for the allylic imidate rearrangement due the electron-donating properties of the iron containing metallocene.[6] Activation is required by the addition of silver salts, a recent study having identified the resultant catalyst as a Pd^{III} species obtained by initial chloride ligand abstraction followed by oxidation.[34] Addition of 3.8 equivalents with respect to (S_p)-**28** of $AgNO_3$ prior to the introduction of the substrate (*E*)-**42** resulted in complete conversion to give (*R*)-**43** in 81% *ee* (entry 6). Essentially the same outcome was obtained on addition of proton sponge (entry 7), though a tenfold reduction in catalyst loading to 0.5 mol% led to the erosion of enantioselectivity and yield (entry 8).

Encouraged by these results we applied the CAP catalysts to the rearrangement of (*E*)-trichloroacetimidates **44** (Scheme 14). Compared to *N*-aryltrifluoroacetimidates these



Scheme 14. Use of (S_p)-CAP-Cl in catalysis of the rearrangement of (*E*)-trichloroacetimidates **44a–d**.

are simpler to synthesise, and the products of rearrangement require only a single deprotection step to release an allylic amine building block. Initial experiments with 1, 2 and 5 mol% of (S_p)-**11** gave a higher *ee* value with each increase in catalyst loading (entries 1–3), and use of 5 mol% of (S_p)-**28** further increased the *ee* to 86% (Table 2). As these reactions all resulted in incomplete conversion to the product, the palladacycle (S_p)-**28** was again activated by the addition of 3.8 equivalents of $AgNO_3$ prior to the addition of the substrate. This gave complete conversion and an *ee* of 73% (entry 5), which on repetition in the presence of proton sponge increased to 99% *ee* (entry 6). Decreasing the catalyst loading to 0.5 mol% again eroded significantly the *ee* and yield (entry 7), and so a small range of additional substrates were examined at 5 mol% loading (entries 8–10). The allyl containing trichloroacetimidate **44b**, which due to the additional alkene functionality capable of competitive palladium coordination is a challenging substrate for this reaction, resulted in (*R*)-**45b** in 71% *ee*. In contrast, methyl and benzyl containing substrates **44c/d** reacted smoothly to give (*R*)-**45b** and (*R*)-**45c**, in 91 and 87% *ee*, respectively. These results are comparable to (S,R_p)-COP-Cl catalysed rearrangement of trichloroacetimidates,[5b,d] but now using a catalyst available readily from highly enantioselective palladation of a simple prochiral substrate.

Conclusions

Enantioselective palladation of *N,N*-dimethylaminomethyl-appended cobalt sandwich complex **8** with Na_2PdCl_4 mediated by (*R*)-*N*-acetylphenylalanine gave the chloride-bridged palladacycle (S_p)-**11** in 92% *ee*. The intramolecular isotope effect ($k_H/k_D = 2.5$) is consistent with a concerted metallation–deprotonation pathway mediated by a chiral η^1-carboxylate ligand. The enantiopurity of (S_p)-**11** may be increased to more than 98% *ee* by chromatographic separation of the minor diastereoisomer formed on addition of (*R*)-proline followed by treatment of the major diastereoisomer with aqueous HCl. A number of related aminomethyl-substituted cobalt complexes were synthesised readily, but this enantioselective palladation protocol is limited to *N,N*-diethyl- (82% *ee*) and pyrrolidinyl (>98% *ee*) substituents. Combining this enantioselective palladation with subsequent enantioselective transcyclopalladation enables the synthesis of ferrocene-based phosphapalladacycles in up to 78% *ee*. The activity and enantioselectivity of a cobalt amine palladacycle catalyst for the allylic imidate rearrangement is increased

significantly following the addition of 3.8 equivalents of silver nitrate. The catalyst generated from (S_p)-**28** results in the rearrangement of (*E*)-trichloroacetimidates with high enantioselectivity (up to 99% *ee*). Combined with the simple highly enantioselective generation of (S_p)-**28**, this methodology enables the straight-forward generation of highly scalemic allylic amine derivatives for application in organic synthesis.

Experimental Section

General: Thin layer chromatography (TLC) was performed on Merck Silica Gel 60 F254 and was visualised with UV light, iodine or potassium permanganate stain. NMR spectra were measured at 500 or 400 MHz for ^{1}H and 126 or 100 MHz for ^{13}C. The residual solvent protons (^{1}H) or the solvent carbons (^{13}C) were used as internal standards for chemical shift determinations. IR spectra were recorded on a Fourier transform interferometer; only diagnostic and/or intense peaks are reported. Melting points were measured in a melting point apparatus and are uncorrected. All reagents and solvents were purchased from commercial sources and were purified using standard methods where required. Toluene and THF were dried over sodium and benzophenone ketal. Dichloromethane was dried over $CaCl_2$. Methanol was dried over 4 Å molecular sieves. Complexes **9**,[17] **19**,[27] **20**[27] and **22**[27] were prepared as previously described. All imidate substrates used were synthesised according to the literature procedures from the corresponding allylic alcohols.[5a,b,d]

Synthesis of (η^5-*N*,*N*-dimethylcarboxamidocyclopentadienyl)(η^4-tetraphenylcyclobutadiene)cobalt (10): A flask was charged with **9** (1.00 g, 1.91 mmol) and it was then dissolved in CH_2Cl_2 (20 mL). Oxalyl chloride (0.33 mL, 3.8 mmol) and dimethylformamide (3 drops) were added sequentially. After 30 min the solution was concentrated in vacuo re-dissolved in CH_2Cl_2 and re-concentrated in vacuo to give the crude acid chloride as a red/brown solid. A solution of the crude acid chloride in CH_2Cl_2 (30 mL) was added via cannula to a solution of dimethylamine hydrochloride (0.311 g, 3.81 mmol) and triethylamine (2.30 mL, 16.5 mmol) in CH_2Cl_2 (20 mL). The resulting solution was stirred at room temperature. After 16 h the solution was washed with water (50 mL) and brine (50 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was dissolved in a minimum volume of CH_2Cl_2 and purified by column chromatography (SiO_2, 7:3 hexanes/ethyl acetate) to give the product **10** as an orange solid (1.01 g, 96%). M.p. 249 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.55–7.44 (m, 8H, Ar-*H*), 7.32–7.18 (m, 12H, Ar-*H*), 5.16 (brs, 2H, Cp-*H*), 4.75 (brs, 2H, Cp-*H*), 2.79 (brs, 3H, C*H*$_3$), 2.64 ppm (brs, 3H, C*H*$_3$); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 135.64, 129.04, 128.12, 126.64, 85.46, 84.89, 77.36, 76.26 ppm (C=O and 2×CH3 not observed); IR (neat): $\tilde{\nu}$ = 3052, 2923, 1967, 1609, 1596, 1496, 1388, 1267, 1162, 1027 cm^{-1}; HRMS (ESI$^+$): *m*/*z* calcd for $C_{36}H_{31}CoNO$: 552.1732 [*M*+H]$^+$; found 552.1726.

Alternative synthesis of (η^5-*N*,*N*-dimethylaminomethylcyclopentadienyl)(η^4-tetraphenylcyclobutadiene)cobalt (8):[16] A flask was charged with **10** (0.986 g, 1.78 mmol) and it was then dissolved in THF (20 mL). The flask was cooled in an ice-water bath and lithium aluminium hydride (0.214 g, 5.63 mmol) was added in two portions. The reaction was left to stir, overnight. On completion, water (20 mL) was added and the aqueous layer was extracted with CH_2Cl_2 (3×20 mL). The organic layer was dried over $MgSO_4$, filtered and concentrated in vacuo to give the product **8** as an orange solid (0.959 g, 99%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.51–7.40 (m, 8H, Ar-*H*), 7.33–7.21 (m, 12H, Ar-*H*), 4.73 (t, *J* = 2.0 Hz, 2H, Cp-*H*), 4.68 (d, *J* = 2.1 Hz, 2H, Cp-*H*), 2.90 (s, 2H, C*H*$_2$), 2.24 ppm (s, 6H, 2×C*H*$_3$); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 136.42, 128.95, 128.10, 126.30, 93.84, 84.21, 83.66, 74.89, 56.53, 44.95 ppm.

Synthesis of di-μ-chlorobis[(η^5-(S_p)-*N*,*N*-dimethylaminomethylcyclopentadienyl,1-*C*,3′-*N*)(η^4-tetraphenylcyclobutadiene)cobalt]dipalladium (11): A solution of (*R*)-*N*-acetylphenylalanine (0.740 g, 3.57 mmol) and NaOH (0.066 g, 1.65 mmol) in water (15 mL) was added to a solution of $Na_2Pd_2Cl_4$ (0.439 g, 1.49 mmol) in MeOH (50 mL). The pH of the mixture was adjusted to 8.0 using either aqueous 50% $NaOH_{(aq.)}$ or conc. $HCl_{(aq.)}$ as required and the mixture was allowed to stir for 20 min. A solution of **8** (0.800 g, 1.49 mmol) in MeOH/CH_2Cl_2 (75/15 mL) was then added in portions over 5 min. The solution was allowed to stir for 16 h at RT. On completion, the reaction mixture was diluted with CH_2Cl_2 (150 mL) and washed with brine (2×100 mL). The organic phase was dried over $MgSO_4$, filtered and the solvent was removed in vacuo. Purification by column chromatography (SiO_2, 4:1 hexanes/EtOAc) gave the product (S_p)-**11** as an orange solid (0.650 g, 64%), *ee* = 92% as determined by formation of the proline adducts. M.p. 143–145 °C; $[\alpha]_D^{21} = -289$ (c = 1.1 mg mL^{-1} in CH_2Cl_2). Further characterisation data below.

Synthesis of proline adduct (*S*,S_p)-12: A solution of (S_p)-**11** (0.050 g, 0.04 mmol) in acetone (1 mL) was added to a solution of $NaHCO_3$ (0.031 g, 0.37 mmol) and (*S*)-proline (0.043 g, 0.37 mmol) in water (0.5 mL). During the addition a copious amount of precipitate was formed. The reaction was vigorously stirred for 16 h at RT and then diluted with CH_2Cl_2 (50 mL). The phases were separated and the aqueous phase was washed with further portions of CH_2Cl_2 (2×25 mL). The organic phases were combined, dried over $MgSO_4$, filtered and solvent was removed in vacuo yielding the product as an orange solid (0.050 g, 90%). Ratio of (*S*,S_p)-**12**/(*S*,R_p)-**13** = 24:1. Crystals of (*S*,S_p)-**12** suitable for X-ray crystallography were obtained by slow diffusion of hexane into CH_2Cl_2 solution (~50:1 hexane/CH_2Cl_2). M.p. 190–192 °C; $[\alpha]_D^{20} = -99$ (c = 1.29 mg mL^{-1} in CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.58–7.56 (m, 8H, Ar-*H*), 7.26–7.22 (m, 12H, Ar-*H*), 4.36 (brs, 2H, Cp-*H*), 4.15 (t, *J* = 2 Hz, 1H, Cp-*H*), 3.93 (app. q, *J* = 7.6 Hz, 1H, NHC*H*), 3.20 (d and brs, *J* = 13.2 Hz, 2H, C*H*HNMe$_2$ and N*H*), 2.87 (d, *J* = 13.2 Hz, 1H, CH*H*NMe$_2$), 2.65 (s, 3H, C*H*$_3$), 2.50–2.40 (m, 1H, NHC*H*H), 2.38 (s, 3H, C*H*$_3$), 2.20–2.00 (m, 3H, 3×C*H*), 1.60–1.50 (m, 1H, C*H*H), 1.24–1.18 ppm (m, 1H, CH*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 136.72, 129.05, 128.23, 126.25, 103.75, 101.58, 84.33, 82.67, 77.85, 74.01, 64.28, 52.60, 51.70, 51.17, 29.89, 26.10 ppm (*C*=O not observed); IR (neat): $\tilde{\nu}$ = 2450, 2919, 1597, 1496, 1443, 1379, 1366, 1259, 1152, 1066, 1018, 845, 803, 740, 697 cm^{-1}; HRMS (EI): *m*/*z* calcd for $C_{41}H_{40}CoN_2O_2Pd$: 757.1466 [*M*+H]$^+$; found 757.1468.

Synthesis of proline adduct (*R*,S_p)-13: A solution of (S_p)-**11** (0.050 g, 0.04 mmol) in acetone (10 mL) was added to a solution of $NaHCO_3$ (0.088 g, 1.04 mmol) and (*R*)-proline (0.085 g, 0.74 mmol) in water (5 mL). During the addition a copious amount of precipitate was formed. The reaction was vigorously stirred for 16 h at RT and then diluted with CH_2Cl_2 (50 mL). The phases were separated and the aqueous phase was washed with further portions of CH_2Cl_2 (2×25 mL). The organic phases were combined, dried over $MgSO_4$, filtered and solvent was removed in vacuo yielding the crude product. Ratio of (*R*,R_p)-**12**/(*R*,S_p)-**13** = 1:33. Purification by column chromatography eluting with (SiO_2, 97:3 CH_2Cl_2/MeOH) gave exclusively (*R*,S_p)-**13** as an orange/red solid (0.045 g, 81%). Crystals suitable for X-ray crystallography were obtained by slow diffusion of hexane into CH_2Cl_2 solution (~50:1 hexane/CH_2Cl_2). M.p. 236 °C; $[\alpha]_D^{21} = +26$ (c = 0.5 mg mL^{-1} in CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.78–7.38 (m, 8H, Ar-*H*), 7.35–6.99 (m, 12H, Ar-*H*), 4.37 (t, *J* = 2.4 Hz, 1H, Cp-*H*), 4.26 (d, *J* = 1.9 Hz, 1H, Cp-*H*), 4.11 (brs, 1H, Cp-*H*), 3.27 (dd, *J* = 13.7, 8.6 Hz, 1H, NHC*H*), 3.10 (d, *J* = 13.2 Hz, 1H, C*H*HNMe$_2$), 3.06–2.94 (m, 1H, NHC*H*H), 2.90–2.78 (m, 1H, NHCH*H*), 2.74 (d, *J* = 13.2 Hz, 1H, CH*H*NMe$_2$), 2.53 (s, 3H, C*H*$_3$), 2.36 (s, 3H, C*H*$_3$), 2.15–1.96 (m, 2H, C*H*H and N*H*), 1.85 (ddt, *J* = 13.3, 8.9, 4.7 Hz, 1H, CH*H*), 1.79–1.69 (m, 1H, C*H*H), 1.43–1.28 ppm (m, 1H, CH*H*); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 180.42, 136.85, 128.96, 128.39, 126.26, 104.29, 97.65, 84.79, 84.03, 79.69, 73.86, 66.28, 63.57, 53.07, 51.43, 50.79, 29.74, 25.53 ppm; IR (neat): $\tilde{\nu}$ = 3056, 2917, 2849, 2160, 1972, 1655, 1596, 1498, 1446, 1373, 1263, 1113, 1067, 1017, 823, 778, 694 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{41}H_{40}O_2N_2PdCo$: 757.1466 [*M*+H]$^+$; found: 757.1467.

Conversion of (*R*,S_p)-13 into (S_p)-11: Dilute hydrochloric acid (0.64 mL of a 0.5 M solution) was added to a solution of (*R*,S_p)-**13** (0.100 g, 0.13 mmol) in CH_2Cl_2 (2 mL) and the mixture was stirred vigorously for 16 h. The solution was diluted with CH_2Cl_2 (5 mL) and washed with brine (3×5 mL). The organic layer was collected, dried over $MgSO_4$, fil-

tered and concentrated in vacuo. Purification by column chromatography (SiO_2, 4:1 hexanes/EtOAc) gave the product (S_p)-**11** as an orange solid (0.073 g, 82%). M.p. 191°C (decomp.); $[\alpha]_D^{21} = -310$ ($c = 0.5$ mg mL^{-1} in CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$), 1:0.9 mixture of isomers: $\delta = 7.77$–7.53 (m, 32H, Ar-*H*), 7.37–7.09 (m, 48H, Ar-*H*), 4.53 (d, $J = 1.2$ Hz, 2H, Cp-*H*), 4.38 (d, $J = 1.5$ Hz, 2H, Cp-*H*), 4.33 (br s, 4H, Cp-*H*), 4.19 (t, $J = 2.4$ Hz, 2H, Cp-*H*), 4.09 (t, $J = 2.4$ Hz, 2H, Cp-*H*), 3.18 (d, $J = 13.4$ Hz, 2H, C*H*HNMe$_2$), 3.13 (d, $J = 13.3$ Hz, 2H, C*H*HNMe$_2$), 2.81 (d, $J = 13.4$ Hz, 2H, CH*H*NMe$_2$), 2.77 (d, $J = 13.2$ Hz, 2H, CH*H*NMe$_2$), 2.67 (s, 6H, C*H*$_3$), 2.62 (s, 6H, C*H*$_3$), 2.19 (s, 6H, C*H*$_3$), 2.02 ppm (s, 6H, C*H*$_3$); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 136.83$, 136.78, 129.42, 129.36, 128.09, 128.06, 125.95, 125.87, 103.09, 102.71, 102.31, 101.91, 85.03, 83.46, 81.07, 80.36, 77.73, 74.84, 74.81, 64.64, 64.55, 53.57, 52.21, 51.87, 51.52 ppm; IR (neat): $\tilde{\nu} = 3056$, 2886, 1659, 1597, 1498, 1446, 1389, 1352, 1266, 1155, 1067, 1024, 984, 957, 910, 842, 809, 780, 739, 697, 563 cm^{-1}; elemental analysis calcd (%) for $C_{72}H_{62}Cl_2Co_2N_2Pd_2$: C 63.73, H 4.61, N 2.07; found C 63.75, H 4.55, N 2.16.

Synthesis of di-μ-acetatobis[(η^5-(S_p)-*N*,*N*-dimethylaminomethylcyclopentadienyl,1-*C*,3′-*N*)(η^4-tetraphenylcyclobutadiene)cobalt]dipalladium (14): Silver acetate (0.005 g, 0.03 mmol) was added to a solution of (S_p)-**11** (0.020 g, 0.02 mmol) in acetone (1 mL). The solution was stirred vigorously, overnight, and then it was filtered through a short pad of Celite, and eluted with CH_2Cl_2. The solvent was then removed in vacuo to give the product (S_p)-**14** as an orange solid (0.020 g, 97%). M.p. 162–164°C; $[\alpha]_D^{18} = -155$ ($c = 2.6$ mg mL^{-1}, in CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.71$–7.60 (m, 16H, Ar-*H*), 7.25–7.14 (m, 24H, Ar-*H*), 4.22 (d, $J = 1.3$ Hz, 2H, Cp-*H*), 4.06 (t, $J = 2.2$ Hz, 2H, Cp-*H*), 4.02 (br s, 2H, Cp-*H*), 3.05 (d, $J = 13.9$ Hz, 2H, C*H*HNMe$_2$), 2.76 (d, $J = 13.9$ Hz, 2H, CH*H*NMe$_2$), 2.30 (s, 6H, NC*H*$_3$), 2.15 (s, 6H, 2×O$_2$CC*H*$_3$), 1.71 ppm (s, 6H, NC*H*$_3$); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 179.70$, 135.96, 128.15, 126.78, 124.60, 102.08, 100.39, 83.06, 79.13, 74.10, 73.46, 64.11, 52.95, 50.78 24.14 ppm; IR (neat): $\tilde{\nu} = 3055$, 2920, 1577, 1498, 1412, 1261, 1176, 1023, 957, 740, 692, 617 cm^{-1}; elemental analysis calcd (%) for $C_{76}H_{68}Co_2N_2O_4Pd_2$: C 65.01, H 4.88, N 2.00; found C 65.18, H 4.96, N 2.04.

Synthesis of (*rac*)-14: A solution of **8** (0.050 g, 0.09 mmol) and Pd(OAc)$_2$ (0.021 g, 0.09 mmol) in toluene (1 mL) was heated at reflux for 2 h. After being cooled to room temperature the solvent was removed in vacuo to give the product (*rac*)-**14** as an orange solid (0.062 g, 95%). The spectral data matched that of (S_p)-**14**.

Synthesis of hexafluoroacetylacetonate[(η^5-(S_p)-*N*,*N*-dimethylaminomethylcyclopentadienyl,1-*C*,3′-*N*)(η^4-tetraphenylcyclobutadiene)cobalt]palladium (15): Sodium hexafluoroacetylacetonate (0.007 g, 0.03 mmol) was added to a solution of (S_p)-**11** (0.020 g, 0.02 mmol) in acetone/water (2:1 mL). The solution was stirred vigorously for 16 h. On completion, the solution was diluted with CH_2Cl_2 (5 mL) and washed with water (5 mL). The organic layer was collected, dried over $MgSO_4$, filtered and concentrated in vacuo to give the product (S_p)-**15** as an orange solid (0.012 g, 96%). M.p. 219°C; $[\alpha]_D^{19} = -160$ ($c = 1.0$ mg mL^{-1} in CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.71$–7.47 (m, 8H, Ar-*H*), 7.34–7.08 (m, 12H, Ar-*H*), 5.87 (s, 1H, C*H*CO), 4.62 (dd, $J = 2.3$, 1.0 Hz, 1H, Cp-*H*), 4.50 (d, $J = 1.5$ Hz, 1H, Cp-*H*), 4.37 (t, $J = 2.4$ Hz, 1H, Cp-*H*), 3.41 (d, $J = 13.9$ Hz, 1H, C*H*HNMe$_2$), 2.92 (d, $J = 13.9$ Hz, 1H, CH*H*NMe$_2$), 2.76 (s, 3H, NC*H*$_3$), 2.48 ppm (s, 3H, NC*H*$_3$); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 174.40$ (q, $J_{C-F} = 8.0$ Hz), 174.12 (q, $J_{C-F} = 7.4$ Hz), 136.77, 129.14, 127.92, 126.15, 118.95 (q, $J_{C-F} = 38.9$ Hz), 116.68 (q, $J_{C-F} = 38.6$ Hz), 102.94, 101.83, 90.23, 84.49, 79.55, 75.44, 74.87, 65.71, 53.53, 51.12 ppm; IR (neat): $\tilde{\nu} = 3056$, 2928, 2160, 1623, 1597, 1545, 1498, 1481, 1458, 1253, 1195, 1144, 1024, 950, 779, 695 cm^{-1}; elemental analysis calcd (%) for $C_{41}H_{32}CoF_6NO_2Pd{\cdot}2H_2O$: C 55.58, H 4.10, N 1.58; found C 55.54, H 3.90, N 1.80. Crystals of (*rac*)-**15** for X-ray analysis, generated in the same way from (*rac*)-**14**, were obtained by slow diffusion of hexane into CH_2Cl_2 solution (~50:1 hexane/CH_2Cl_2).

Synthesis of (η^5-*N*,*N*-diethylaminomethylcyclopentadienyl)(η^4-tetraphenylcyclobutadiene)cobalt (21a): A solution of **20** (0.100 g, 0.20 mmol) and PPh_3 (0.051 g, 0.20 mmol) in THF (3 mL) was cooled to −20°C and NBS (0.035 g, 0.30 mmol) was added in one portion. The mixture was stirred for 10–15 min and Et_2NH (20 μL, 0.2 mmol) was added in one portion. The reaction was then allowed to warm to RT and was then heated at reflux for 1 h. The reaction mixture was cooled to RT and diluted with CH_2Cl_2 (15 mL). The mixture was washed with 10% HCl (10 mL), dried over $MgSO_4$, filtered and concentrated in vacuo. Purification by column chromatography (SiO_2, 19:1 CH_2Cl_2/MeOH) gave the product **21a** as a yellow solid (0.045 g, 41%). M.p. 140–142°C; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.52$–7.40 (m, 8H, Ar-*H*), 7.31–7.18 (m, 12H, Ar-*H*), 4.57 (s, 4H, Cp-*H*), 2.92 (s, 2H, C*H*$_2$NEt$_2$), 2.25 (q, $J = 7.2$ Hz, 4H, C*H*$_2$CH$_3$), 0.88 ppm (t, $J = 7.2$ Hz, 6H, CH$_2$C*H*$_3$); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 136.34$, 128.82, 127.98, 126.19, 84.14, 83.67, 74.74, 49.07, 11.84 ppm; IR (neat): $\tilde{\nu} = 3057$, 2966, 2921, 1597, 1499, 1446, 1068, 1020, 814, 780, 743, 698, 589, 564 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{38}H_{36}CoN$: 565.2180 $[M]^+$; found 565.2170.

Synthesis of (η^5-(1-pyrrolidinyl)methylcyclopentadienyl)(η^4-tetraphenylcyclobutadiene)cobalt (21b): The same method as described for **21a** was followed starting with **20** (0.127 g, 0.25 mmol). The product was isolated by column chromatography (SiO_2, 19:1 CH_2Cl_2/MeOH) to give product **21b** as a yellow solid (0.100 g, 71%). M.p. 180–182°C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.52$–7.40 (m, 8H, Ar-*H*), 7.31–7.18 (m, 12H, Ar-*H*), 4.75–4.70 (m, 2H, Cp-*H*), 4.62–4.58 (m, 2H, Cp-*H*), 2.84 (s, 2H, C*H*$_2$NMe$_2$), 2.34–2.26 (m, 4H, N(C*H*$_2$CH$_2$)$_2$), 1.70–1.64 ppm (m, 4H, N-(CH$_2$C*H*$_2$)$_2$); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 136.35$, 128.92, 128.08, 126.31, 84.06, 83.75, 74.93, 53.68, 52.60, 23.41 ppm; IR (neat): $\tilde{\nu} = 2924$, 1596, 1497, 1446, 1261, 1023, 816, 781, 746, 701, 589, 564 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{38}H_{35}CoN$: 564.2096 $[M+H]^+$; found 564.2094.

Synthesis of (η^5-*N*-benzylaminomethylcyclopentadienyl)(η^4-tetraphenylcyclobutadiene)cobalt (23): 1,2-Dichloroethane (35 mL) was added to a mixture of **22** (2.61 g, 5.13 mmol) and benzylamine (0.55 g, 5.13 mmol) and then sodium triacetoxyborohydride (1.72 g, 8.12 mmol) was added in one portion. The mixture was stirred at room temperature for 1.5 h. On completion, the reaction mixture was quenched by adding saturated aqueous $NaHCO_3$ solution (50 mL) and the product was extracted with EtOAc (2×40 mL). The EtOAc extract was dried over $MgSO_4$, filtered and the solvent was removed in vacuo to give the crude product, which was purified by column chromatography (SiO_2, 19:1 CH_2Cl_2/EtOAc) to give product **23** as a yellow solid (3.00 g, 4.45 mmol, 97%). M.p. 145–147°C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.43$ (dd, $J = 8.0$, 1.4 Hz, 8H, Ar-*H*), 7.33–7.11 (m, 17H, Ar-*H*), 4.66 (t, $J = 1.8$ Hz, 2H, Cp-*H*), 4.57 (t, $J = 1.9$ Hz, 2H, Cp-*H*), 3.52 (s, 2H, C*H*$_2$Ph), 3.13 ppm (s, 2H, C*H*$_2$NH); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 136.33$, 135.43, 129.01, 128.88, 128.14, 128.10, 126.62, 83.68, 82.56, 74.89, 53.56, 45.38 ppm; IR (neat): $\tilde{\nu} = 3080$, 3059, 3028, 2924, 2823, 2246, 1597, 1499, 1449, 1379, 909, 733, 697 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{41}H_{35}NCo$: 600.2102 $[M+H]^+$; found: 600.2093.

Synthesis of (η^5-aminomethylcyclopentadienyl)(η^4-tetraphenylcyclobutadiene)cobalt (24): Anhydrous ammonium formate (1.80 g, 28.5 mmol) was added in a single portion to a stirred suspension of **23** (3.00 g, 5.00 mmol) and an equal weight of 10% Pd/C in methanol (20 mL). The resulting reaction mixture was stirred at reflux for 2 h. On completion, the solution was filtered through a pad of Celite and then washed with chloroform (20 mL). The combined organic filtrate was evaporated in vacuo and purified by column chromatography (SiO_2, 3:2 CH_2Cl_2/EtOAc) to give the product **24** as a yellow solid (1.09 g, 2.05 mmol, 43%). M.p. 116°C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.49$–7.42 (m, 8H, Ar-*H*), 7.25–7.18 (m, 12H, Ar-*H*), 4.63 (t, $J = 2.0$ Hz, 2H, Cp-*H*), 4.57 (t, $J = 2.0$ Hz, 2H, Cp-*H*), 3.27 ppm (br s, 2H, C*H*$_2$NH$_2$); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 136.22$, 128.75, 128.09, 126.37, 83.57, 81.84, 74.85, 53.54 ppm; IR (neat): $\tilde{\nu} = 3052$, 2923, 2162, 1610, 1596, 1573, 1453, 1497, 1453, 1387, 1267, 1231, 1106, 1054 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{34}H_{28}NCoNa$: 532.1451 $[M+Na]^+$; found: 532.1438.

Synthesis of (η^5-*N*-(benzyloxycarbonyl)aminomethylcyclopentadienyl)(η^4-tetraphenylcyclobutadiene)cobalt (25): Iodine (0.006 g, 0.02 mmol) was added to a stirred mixture of **24** (0.610 g, 1.20 mmol) and benzylchloroformate (0.205 g, 1.20 mmol) in 1:1 methanol/dichloromethane (5 mL). After being stirred for 2 h at RT, diethyl ether (10 mL) was added. The reaction mixture was washed with 5% $Na_2S_2O_3$ solution (5 mL) and saturated $NaHCO_3$ (5 mL), dried over $MgSO_4$, filtered and the solvent was removed in vacuo. Purification by column chromatogra-

phy (SiO_2, CH_2Cl_2/EtOAc 4:1) gave the product as a yellow/brown solid (0.750 g, 97%). M.p. 88–90°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.45 (d, J = 6.4 Hz, 8H, Ar-*H*), 7.41–7.17 (m, 17H, Ar-*H*), 5.03 (s, 2H, OCH_2Ph), 4.63 (brs, 2H, Cp-*H*), 4.58 (d, J = 1.8 Hz, 2H, Cp-*H*), 4.31 (brs, 1H, N*H*Cbz), 3.77 ppm (d, J = 5.6 Hz, 2H, CH_2NH); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 156.23, 136.78, 136.18, 128.77, 128.54, 128.27, 128.09, 127.09, 126.56, 96.05, 83.61, 81.87, 75.04, 69.75, 66.58, 65.46, 54.97 ppm; IR (neat): $\tilde{\nu}$ = 3416, 3080, 3059, 3030, 2954, 2247, 1723, 1597, 1499, 1444, 1269, 1026, 735, 697 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{42}H_{35}CoNO_2$: 644.2000 [*M*+H]$^+$; found: 644.1990.

Synthesis of (η^5-*N*-methylaminomethylcyclopentadienyl)(η^4-tetraphenylcyclobutadiene)cobalt (26): A stirred suspension of $LiAlH_4$, (0.090 g, 2.37 mmol) in THF (30 mL) was cooled to 0°C in an ice-water bath. To this was added a solution of **25** (0.700 g, 1.09 mmol) in THF (40 mL) and the mixture was heated to reflux for 1.5 h. After being cooled the reaction was quenched with saturated Na_2SO_4 solution (5 mL), filtered through a pad of Celite and extracted with EtOAc (2×30 mL). The combined organic extracts were concentrated under reduced pressure to give a crude solid, which was purified by column chromatography (SiO_2, CH_2Cl_2/EtOAc 7:3) to give the product **26** as yellow solid (0.560 g, 98%). M.p. 177–179°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.45 (dd, J = 7.2, 1.9 Hz, 8H, Ar-*H*), 7.22–7.26 (m, 12H, Ar-*H*), 4.66 (s, 2H, Cp-*H*), 4.57 (s, 2H, Cp-*H*), 3.07 (s, 2H, CH_2NHMe), 2.14 ppm (s, 3H, NHCH_3); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 136.29, 128.85, 128.19, 126.45, 84.26, 83.76, 83.64, 82.82, 74.99, 48.34 ppm; IR (neat): $\tilde{\nu}$ = 3080, 3028, 2938, 2787, 1597, 1499, 1444, 1025, 909, 733, 697 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{35}H_{31}CoN$: 524.1778 [*M*+H]$^+$; found: 524.1789.

Synthesis of di-μ-chlorobis[(η^5-(S_p)-*N*,*N*-diethylaminomethylcyclopentadienyl,1-*C*,3′-*N*)(η^4-tetraphenylcyclobutadiene)cobalt]dipalladium (27): A solution of (*R*)-*N*-acetylphenylalanine (0.250 g, 1.21 mmol) and NaOH (0.039 g, 0.98 mmol) in water (15 mL) was added to a solution of $Na_2Pd_2Cl_4$ (0.263 g, 0.89 mmol) in MeOH (50 mL). The pH of the mixture was adjusted to 8.0 using either aqueous NaOH or HCl as required and the mixture was allowed to stir for 20 min. A solution of **21a** (0.500 g, 0.88 mmol) in 5:1 MeOH/CH_2Cl_2 (90 mL) was then added in portions over 5 min. The solution was allowed to stir for 16 h at RT. On completion, the reaction mixture was diluted with CH_2Cl_2 (100 mL) and washed with brine (2×100 mL). The organic phase was dried over $MgSO_4$, filtered and the solvent was removed in vacuo. Purification by column chromatography (SiO_2, 4:1 hexanes/EtOAc) gave the product (S_p)-**27** as an orange solid (0.244 g, 39%), *ee* = 82% as determined by formation of the proline adducts. M.p. >200°C (decomp); $[\alpha]_D^{24} = -618$ (c = 0.5 mg mL^{-1} in CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) 1:0.6 mixture of isomers: δ = 7.70–7.60 (m, 32H, Ar-*H*), 7.29–7.15 (m, 48H, Ar-*H*), 4.47 (dd, J = 2.3, 1.1 Hz, 2H, Cp-*H*), 4.32 (t, J = 2.2 Hz, 4H, Cp-*H*), 4.30–4.27 (m, 2H, Cp-*H*), 4.24 (t, J = 2.4 Hz, 2H, Cp-*H*), 4.17 (t, J = 2.4 Hz, 2H, Cp-*H*), 3.29 (d, J = 13.9 Hz, 2H, C*H*HNEt$_2$), 3.22 (d, J = 13.9 Hz, 2H, C*H*HNEt$_2$), 2.75 (d, J = 13.9 Hz, 4H, CH*H*NEt$_2$), 2.68–2.43 (m, 16H, CH_2CH$_3$), 1.52 (t, J = 7.1, Hz, 6H, CH_2CH_3), 1.52 (t, J = 7.1, Hz, 6H, CH_2CH_3), 0.92–0.84 ppm (m, 12H, CH_2CH_3); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 136.74, 136.68, 129.32, 129.26, 127.95, 127.92, 129.79, 125.76, 84.27, 82.65, 79.50, 79.44, 77.24, 76.45, 75.55, 60.41, 57.44, 57.28, 55.39, 55.33, 54.32, 53.22, 14.53, 14.22, 10.01, 9.80 ppm; IR (neat): $\tilde{\nu}$ = 3056, 2971, 2929, 1596, 1498, 1444, 1387, 909, 734, 695 cm^{-1}; elemental analysis calcd (%) for $C_{76}H_{70}Cl_2Co_2N_2Pd_2$: C 64.60, H 4.99, N 1.98; found C 64.70, H 4.89, N 2.04.

Synthesis of proline adducts (*S*,S_p)-29 and (*S*,R_p)-30: A solution of (S_p)-**27** (0.020 g, 0.014 mmol) in acetone (1 mL) was added to a solution of $NaHCO_3$ (0.003 g, 0.04 mmol) and (*S*)-proline (0.003 g, 0.03 mmol) in water (0.5 mL). During the addition a copious amount of precipitate was formed. The reaction was then vigorously stirred for 16 h at RT and then diluted with CH_2Cl_2 (5 mL). The phases were separated and the aqueous phase was washed with further portions of CH_2Cl_2 (2×2 mL). The organic phases were combined, dried over $MgSO_4$, filtered and the solvent was removed in vacuo yielding the product as an orange solid (0.021 g, 95%). M.p. 206–208°C; $[\alpha]_D^{21} = -104$ (c = 0.7 mg mL^{-1} in CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.55 (dd, J = 6.6, 3.0 Hz, 8H, Ar-*H*), 7.25–7.21 (m, 12H, Ar-*H*), 4.40 (t, J = 2.4 Hz, 1H, Cp-*H*), 4.34 (d, J = 1.6 Hz, 1H, Cp-*H*), 4.13 (d, J = 1.5 Hz, 1H, Cp-*H*), 3.92 (dd, J = 15.2, 7.6 Hz, 1H, NC*H*), 3.29 (d, J = 13.9 Hz, 2H, 2×C*H*H), 2.88 (d, J = 13.7 Hz, 2H, 2×C*H*H), 2.78–2.55 (m, 3H, 3×C*H*H), 2.49–2.27 (m, 2H, 2×C*H*H), 2.17–2.06 (m, 3H, C*H*H), 1.40–1.31 (m, 3H, CH_2CH_3), 0.94 ppm (t, J = 7.4 Hz, 3H, CH_2CH_3); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 180.08, 136.79, 129.01, 128.20, 126.21, 84.38 84.0, 81.39, 79.62 74.82, 73.96, 66.17, 58.09, 54.23, 53.31, 52.52, 29.97, 26.07, 13.52, 9.84 ppm; IR (neat): $\tilde{\nu}$ = 3453, 2929, 2852, 1725, 1594, 1492, 1446, 1381, 1255, 1179, 1156, 1122, 1071, 1021, 804, 778, 740, 699 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{43}H_{44}CoN_2O_2Pd$: 785.1780 [*M*+H]$^+$; found: 785.1773. Ratio of isomers obtained from integration of signals at 4.40 (t, J = 2.4 Hz, 1H, (*S*,S_p)-Cp-*H*) and 4.42 ppm (t, J = 2.4 Hz, 1H, (*S*,R_p)-Cp-*H*).

Synthesis of di-μ-chlorobis[(η^5-(S_p)-(1-pyrrolidinyl)methylcyclopentadienyl,1-*C*,3′-*N*)(η^4-tetraphenylcyclobutadiene)cobalt]dipalladium (28): A solution of (*R*)-*N*-acetylphenylalanine (0.251 g, 1.21 mmol) and NaOH (0.039 g, 0.98 mmol) in water (15 mL) was added to a solution of $Na_2Pd_2Cl_4$ (0.263 g, 0.89 mmol) in MeOH (50 mL). The pH of the mixture was adjusted to 8.0 using either aqueous NaOH or HCl as required and the mixture was allowed to stir for 20 min. A solution of **21b** (0.500 g, 0.89 mmol) in 5: 1 MeOH/CH_2Cl_2 (90 mL) was then added in portions over 5 min. The solution was allowed to stir for 16 h at RT. On completion, the reaction mixture was diluted with CH_2Cl_2 (150 mL) and washed with brine (2×100 mL). The organic phase was dried over $MgSO_4$, filtered and the solvent was removed in vacuo. Purification by column chromatography (SiO_2, 4:1 hexanes/EtOAc) gave the product (S_p)-**28** as an orange solid (0.270 g, 43%), *ee* >98% as determined by formation of the proline adducts M.p. >200°C (decomp); $[\alpha]_D^{24} = -266$ (c = 0.5 mg mL^{-1} in CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) 1:1 mixture of isomers: δ = 7.72–7.63 (m, 32H, Ar-*H*), 7.28–7.16 (m, 48H, Ar-*H*), 4.53–4.50 (m, 2H, Cp-*H*), 4.38–4.35 (m, 2H, Cp-*H*), 4.31 (d, J = 1.5 Hz, 2H, Cp-*H*), 4.26 (d, J = 1.5 Hz, 2H, Cp-*H*), 4.23 (t, J = 2.4 Hz, 2H, Cp-*H*), 4.15–4.09 (m, 2H, Cp-*H*), 3.44–3.32 (m, 4H, CpC*H*HN), 3.08–2.81 (m, 16H, CpCH*H*N and NCH_2), 2.32–2.23 (m, 2H, NCH_2), 2.08–2.03 (m, 2H, NCH_2), 1.81 (ddd, J = 9.3, 6.2, 3.5 Hz, 4H, NCH$_2$CH_2), 1.76–1.60 (m, 8H, NCH$_2$CH_2), 1.53–1.45 ppm (m, 4H, NCH$_2$CH_2); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 136.75, 136.68, 129.34, 129.28, 127.94, 125.79, 125.72, 103.20, 102.85, 102.75, 102.31, 84.84, 82.99, 80.55, 79.96, 77.60, 76.71, 75.25, 74.68, 74.66, 60.46, 60.38, 60.28, 60.22, 59.67, 30.95, 22.00, 21.65, 21.55, 21.30 ppm; IR (neat): $\tilde{\nu}$ = 3056, 2966, 1596, 1498, 1443, 909, 734, 695 cm^{-1}; elemental analysis calcd (%) for $C_{76}H_{66}Cl_2Co_2N_2Pd_2$: C 64.79, H 4.72, N 1.98; found C 64.81, H 4.60, N 2.07.

Synthesis of proline adduct (*S*,S_p)-31: A solution of (S_p)-**28** (0.020 g, 0.014 mmol) in acetone (2 mL) was added to a solution of $NaHCO_3$ (0.003 g, 0.04 mmol) and (*S*)-proline (0.003 g, 0.03 mmol) in water (1 mL). During the addition a copious amount of precipitate was formed. The reaction was then vigorously stirred for 16 h at RT and then diluted with CH_2Cl_2 (5 mL). The phases were separated and the aqueous phase was washed with further portions of CH_2Cl_2 (2×2 mL). The organic phases were combined, dried over $MgSO_4$, filtered and the solvent was removed in vacuo yielding the product as an orange solid (0.020 g, 90%). M.p. 206–208°C; $[\alpha]_D^{21} = -37$ (c = 1.1 mg mL^{-1} in CH_2Cl_2); ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 7.52–7.46 (m, 8H, Ar-*H*), 7.28–7.20 (m, 12H, Ar-*H*), 5.52–5.44 (m, 1H, N*H*), 4.36 (s, 2H, Cp-*H*), 4.25 (s, 1H, Cp-*H*), 3.56 (q, J = 7.9 Hz, 1H, NHC*H*), 3.19–3.01 (m, 2H, NHC*H*H and CpCH*H*N), 3.01–2.94 (m, 1H, NHC*H*H), 2.92–2.84 (m, 1H, NCH_2), 2.79 (d, J = 14.5 Hz, 1H, CpC*H*HN), 2.35–2.21 (m, 2H, CH_2), 2.14–2.04 (m, 1H, C*H*H), 1.82–1.61 (m, 4H, CH_2), 1.44–1.33 (m, 1H, CH*H*), 1.24–1.16 ppm (m, 2H, CH_2); ^{13}C NMR: not obtained due to poor solubility in $CDCl_3$ and [D$_6$]DMSO; IR (neat): $\tilde{\nu}$ = 3444, 2925, 2855, 1733, 1623, 1590, 1497, 1459, 1378, 1259, 1170, 1070, 1023, 926, 782, 745, 702 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{43}H_{42}CoN_2O_2Pd$: 783.1623 [*M*+H]$^+$; found: 783.1615.

Synthesis of proline adduct (*R*,S_p)-32: Prepared in the same way as (*S*,S_p)-**31** from (S_p)-**28** (0.020 g, 0.014 mmol) and (*R*)-proline (0.003 mg, 0.03 mmol) to give the product as an orange solid (0.011 g, 50%). M.p. 206–208°C; $[\alpha]_D^{23} = +72$ (c = 0.5 mg mL^{-1} in CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.69 (d, J = 6.4 Hz, 8H, Ar-*H*), 7.29–7.26 (m, 12H, Ar-*H*), 4.45 (t, J = 2.3 Hz, 1H, Cp-*H*), 4.33 (d, J = 2.6 Hz, 1H, Cp-*H*), 4.20 (d, J =

2.5 Hz, 1H, Cp-*H*), 3.44 (dt, J=11.5, 7.6 Hz, 1H, NHC*H*), 3.34 (ddt, J=13.5, 9.1, 4.9 Hz, 2H, 2×NHC*H*H), 3.13–2.91 (m, 4H, CH_2), 2.71–2.61 (m, 1H, C*H*H), 2.47–2.35 (m, 1H, C*H*H), 2.18–2.10 (m, 1H, C*H*H), 2.05–1.95 (m, 2H, CH_2.), 1.94–1.89 (m, 2H, CH_2), 1.88–1.79 (m, 1H, C*H*H), 1.78–1.72 (m, 1H, C*H*H), 1.64 (br s, 1H, N*H*), 1.51–1.38 ppm (m, 1H, C*H*H); ^{13}C NMR (126 MHz, $CDCl_3$): δ=180.32, 136.76, 128.87, 128.26, 126.09, 104.56, 97.53, 84.31, 83.78, 79.33, 73.73, 66.13, 59.97, 59.65, 59.13, 52.98, 29.60, 25.44, 22.06, 21.95 ppm; IR (neat): $\tilde{\nu}$=3444, 2925, 2855, 1733, 1623, 1590, 1497, 1459, 1378, 1259, 1170, 1070, 1023, 926, 782, 745, 702 cm^{-1}; HRMS (ESI): m/z calcd for $C_{43}H_{42}CoN_2O_2Pd$: 783.1623 $[M+H]^+$; found: 783.1614.

Synthesis of chloro[(η^5-(S_p)-*N*,*N*-dimethylaminomethylcyclopentadienyl,1-*C*,3′-*N*)(η^4-tetraphenylcyclobutadiene)cobalt]2-(diphenylphosphino)-phenylferrocene-palladium (37): 2-(Diphenylphosphino)phenylferrocene (0.007 g, 0.016 mmol) was added to a solution of (S_p)-**11** (0.010 g, 0.015 mmol) in CH_2Cl_2 (1 mL) and the solution was stirred for 16 h. The solvent was removed in vacuo and the product was purified by column chromatography (SiO_2, 49:1 CH_2Cl_2/MeOH) to give the product (S_p)-**35** as a red/orange solid (0.015 g, 88%). Crystals suitable for X-ray crystallography were obtained by slow diffusion of hexane into a CH_2Cl_2 solution (~50:1 hexane/CH_2Cl_2). M.p. 171 °C; $[\alpha]_D^{21}$ = +26 (c=0.5 mg mL^{-1} in CH_2Cl_2); ^{1}H NMR (500 MHz, CDCl3): δ=7.90–7.80 (m, 2H, Ar-H), 7.48–7.10 (m, 28H, Ar-*H*), 7.00 (t, J=7.6 Hz, 1H, Ar-*H*), 6.90 (t, J=6.8 Hz, 2H, Ar-*H*), 6.76 (dd, J=11.1, 7.5 Hz, 1H, Ar-*H*), 4.48 (br s, 1H, Cp-*H*), 4.36 (br s, 1H, Cp-*H*), 4.12 (s, 1H, Cp-*H*), 4.07 (s, 1H, Cp-*H*), 4.00 (s, 1H, Cp-*H*), 3.93 (s, 5H, Cp-*H*), 3.84 (s, 1H, Cp-*H*), 3.22 (s, 1H, Cp-*H*), 3.03 (d, J=14.1 Hz, 1H, C*H*HNMe$_2$), 2.92 (dd, J=14.0, 2.5 Hz, 1H, CH*H*NMe$_2$), 2.65 (s, 3H, CH_3), 2.38 ppm (d, J=2.4 Hz, 3H, CH_3); ^{13}C NMR (126 MHz, $CDCl_3$): δ=136.66, 135.99, 132.84, 130.20, 129.42, 129.06, 128.05, 127.99, 127.95, 127.91, 127.52, 127.44, 125.89, 120.35, 80.82, 77.60, 77.29, 77.03, 76.78, 76.24, 73.82, 69.68, 61.90, 52.06 ppm; ^{31}P NMR (202 MHz, $CDCl_3$): δ=32.22 ppm; IR (neat): $\tilde{\nu}$=3056, 2923, 1732, 1596, 1497, 1436, 1194, 911, 732, 695, 559 cm^{-1}; elemental analysis calcd (%) for $C_{64}H_{54}ClCoFeNPPd$: C 68.34, H 4.85, N 1.25; found C 66.35, H 5.05, N 1.46.

General procedure for transcyclopalladation: A mixture of (S_p)-**14** (0.030 g, 0.02 mmol) and either **33** (0.019 g, 0.04 mmol) or **34** (0.020 g, 0.04 mmol) were heated in toluene (0.5 mL) under nitrogen for 24 h. After being cooled the solvent was evaporated in vacuo and the residue was re-dissolved in 2:1 acetone/water and sodium acetylacetonate (0.005 g, 0.04 mmol) was added to it. After being stirred at room temperature for 16 h the mixture was diluted with CH_2Cl_2, washed with water, dried ($MgSO_4$), filtered and the solvent was removed in vacuo. The *ee* and absolute configuration of **35** and **36** were determined by HPLC (Chiracel OD-H, 99.7:0.3 *n*-hexane/IPA, 0.8 mL min^{-1}).

General procedure for catalysis: The required amount of imidate stock solution was added to a flask charged with catalyst. If silver salts and/or proton sponge was used this was subsequently added. The solution was protected from light then heated to the desired temperature for the allotted time. On completion, the solution was passed through a short pad of Celite and the solvent was removed in vacuo. Purification by flash chromatography, eluting with 24:1 hexanes/EtOAc, yielded the product amide 2,2,2-trifluoro-*N*-(4-methoxyphenyl-*N*-(1-propylallyl)acetamide (**43**) as a pale yellow oil. Chiral HPLC analysis was used to determine enantiomeric excess after cleavage of the trifluoroacetate group[5a] (Chiracel OD-H, 99.8:0.2 *n*-hexane/IPA, 0.8 mL min^{-1}). In the same manner amides **44a–d** were isolated as colourless oils and chiral HPLC analysis was used to determine the enantiomeric excess (Chiracel OD-H, 99.5:0.5 *n*-hexane/IPA, 0.8 mL min^{-1}).[5b,d]

CCDC-931363 ((S,S_p)-**12**), 931364 (**15**) and 931365 ((S_p)-**37**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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