CHEMISTRY
A European Journal

A Journal of
ChemPubSoc Europe

Accepted Article

Title: Stereoselective and Stereospecific Reactions of Cobalt Sandwich Complexes. Application to the Synthesis of a New Class of Single Enantiomer Bulky Planar Chiral P-N and P-P Ligands.

Authors: Christopher John Richards, Ross Arthurs, Peter Horton, and Simon Coles

To be cited as: *Chem. Eur. J.* 10.1002/chem.201705113

Link to VoR: http://dx.doi.org/10.1002/chem.201705113

Supported by
ACES

WILEY-VCH

10.1002/chem.201705113

WILEY-VCH

Stereoselective and Stereospecific Reactions of Cobalt Sandwich Complexes. Application to the Synthesis of a New Class of Single Enantiomer Bulky Planar Chiral P-N and P-P Ligands.

Ross A. Arthurs,[a] Peter N. Horton,[b] Simon J. Coles[b] and Christopher J. Richards*[a]

Dedication ((optional))

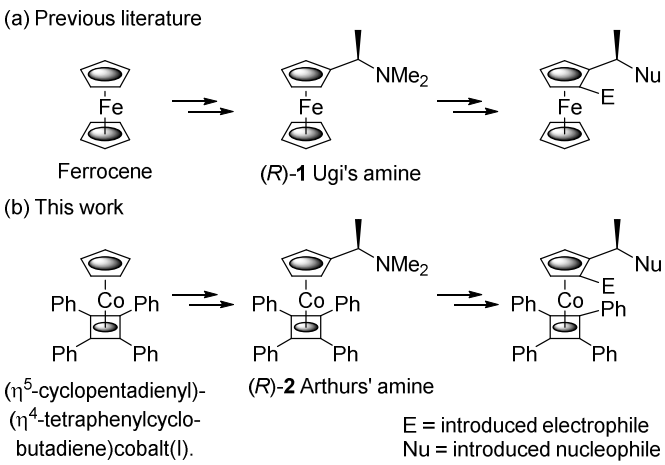
Abstract: Starting from (η^5-acetylcyclopentadienyl)(η^4-tetraphenylcyclobutadiene)cobalt(I), highly enantioselective (99% ee) (*S*)-CBS catalysed ketone reduction followed by stereospecific alcohol-azide exchange, azide reduction and dimethyllation gave (*R*)-(η^5-α-*N*,*N*-dimethylaminoethylcyclopentadienyl)(η^4-tetraphenylcyclobutadiene) cobalt(I) (Arthurs' amine). This underwent highly diastereoselective cyclopalladation to give di-μ-acetate-bis-(*R*)-[(η^5-(S_p)-2-(α-*N*,*N*-dimethylaminoethyl)cyclopentadienyl, 1-*C*, *N*)(η^4-tetraphenylcyclobutadiene)cobalt(I)]dipalladium, and highly diastereo-selective lithiation to give (*R*)-(η^5-(S_p)-1-(α-*N*,*N*-dimethylaminoethyl)-2-(diphenylphosphino)cyclopentadienyl)(η^4-tetraphenylcyclobutadiene)cobalt(I) (PPCA) following the addition as electrophile of chlorodiphenylphosphine. This PN-ligand was converted into (*R*)-(η^5-(S_p)-1-(α-dicyclohexylphosphinoethyl)-2-(diphenylphosphino)cyclopentadienyl)(η^4-tetraphenylcyclobutadiene)cobalt(I), a PP-ligand (Rossiphos), by stereospecific amine-phosphine exchange using $HPCy_2$. These air-stable P-N and P-P complexes are the first examples of a new class of bulky planar chiral ligands for application in asymmetric catalysis.

Introduction

Chiral non-racemic organometallic complexes are employed extensively in several areas of investigation that include asymmetric synthesis,[1] materials chemistry,[2] supramolecular chemistry,[3] and the discovery of metal-based bioactive compounds.[4] This is especially the case if the complexes are air-stable, are based on inexpensive earth-abundant metals, and are available readily in enantiopure form. Ferrocene complexes generally meet these criteria, not least because differentially disubstituted derivatives display planar chirality. Several methods have been devised to synthesise planar chiral ferrocene derivatives,[5] the most significant of these being the use of Ugi's amine **1**. This undergoes highly diastereoselective lithiation, such that subsequent addition of an electrophile generates a product as predominantly a single diastereoisomer (Scheme 1).[6,7] In addition, the dimethylamino group may be replaced readily by a nucleophile in a stereospecific substitution reaction,[6] and notable applications of this chemistry include the synthesis of bisphosphine ligands that are commercially available and applied widely in asymmetric catalysis.[8]

Another class of organometallic complexes that broadly meet the above criteria are derived from (η^5-cyclopentadienyl)(η^4-tetraphenylcyclobutadiene)cobalt(I).[9] Planar chiral derivatives of this parent sandwich complex have been applied successfully in asymmetric catalysis,[10] and in these cases the size of the η^4-tetraphenylcyclobutadiene moiety is a key factor leading to high enantioselectivity. However, methodology to generate planar chiral derivatives remains very limited,[11] and amine **2**, a complex from which a wide variety of derivatives could potentially be synthesised, has to the best of our knowledge not been reported.

In this paper we describe accessible methodology for the asymmetric synthesis of **2**, and the use of this complex as a key building block to synthesise (η^5-cyclopentadienyl)(η^4-tetraphenylcyclobutadiene)cobalt(I) complexes displaying both planar and central chirality. This methodology demonstrates that highly diastereoselective metallation and stereospecific substitution are also applicable to these cobalt sandwich complexes, providing access to a new class of air-stable chiral organometallics. This is illustrated with the synthesis of new bulky bidentate ligands for application in asymmetric catalysis.



Scheme 1. Known and new methods for the asymmetric synthesis of air-stable sandwich complexes displaying both central and planar chirality.

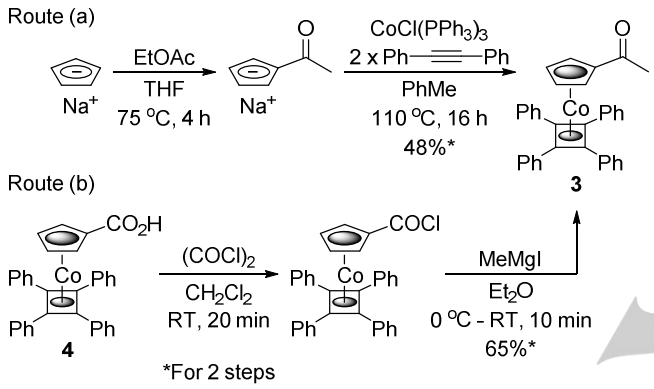
[a] Dr R. A. Arthurs, Dr C. J. Richards
School of Chemistry
University of East Anglia
Norwich Research Park, Norwich, NR4 7TJ, U.K.
E-mail: Chris.Richards@uea.ac.uk

[b] Dr. P. N. Horton, Prof. S. J. Coles
EPSRC National Crystallography Service, School of Chemistry,
University of Southampton,
Highfield, Southampton, SO17 1BJ, U.K.

Supporting information for this article is given via a link at the end of the document.

Results and Discussion

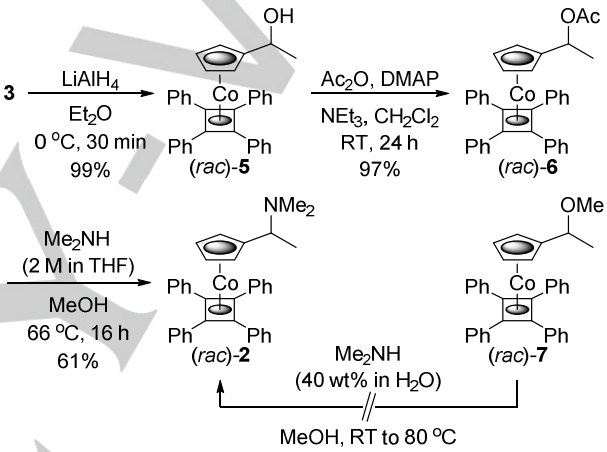
The complex (η^5-cyclopentadienyl)(η^4-tetraphenylcyclobutadiene)cobalt(I) is readily synthesised in one step from commercially available starting materials.[12] This is in contrast to pentaphenylferrocene which requires a non-trivial multistep synthesis,[13] and this difference is a key factor in our choosing the former as the basis for generating bulky complexes and ligands displaying planar chirality for use in asymmetric catalysis. A disadvantage, however, of the cobalt over the iron-based chemistry is that (η^5-cyclopentadienyl)(η^4-tetraphenylcyclobutadiene)cobalt(I) cannot be directly functionalised by Friedel-Crafts acylation,[14] and lithiation as a means of monofunctioalisation only proceeds to a limited extent.[11c]



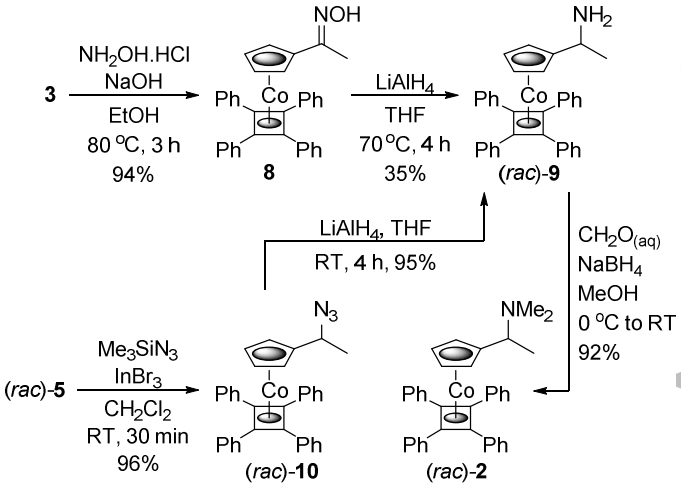
Scheme 2. Routes to the synthesis of ketone **3**.

As this work required initially an expedient synthesis of ketone **3**, from which to investigate the asymmetric synthesis of amine **2**, the first approach revisited the literature procedure for the synthesis of **3** involving *in situ* generation of sodium acetylcyclopentadienylide followed by complexation [Scheme 2 – Route (a)].[15] By changing methyl acetate for ethyl acetate the previously reported yield of 26% was improved to a more reasonable 48%. As an alternative procedure, readily synthesised carboxylic acid **4**[12b] was converted into its corresponding acid chloride followed by addition of one equivalent of methylmagnesium iodide [Scheme 2 – Route (b)]. This gave ketone **3** in 65% yield without competitive formation of the tertiary alcohol resulting from the further reaction of **3** with the Grignard reagent.

We chose first to identify an efficient route for the synthesis of racemic **2** as the basis of a subsequent asymmetric synthesis. The first reported asymmetric synthesis of Ugi's amine **1** (it having been obtained previously as a single enantiomer by resolution[6]) involved asymmetric reduction of acetylferrocene, acetylation of the resulting secondary alcohol, and substitution with dimethylamine.[16] Thus in the same vein ketone **3** was reduced to (*rac*)-**5** essentially quantitatively using lithium aluminium hydride (Scheme 3). Use instead of sodium borohydride in ethanol gave (*rac*)-**5** in a yield of only 48%, together with a number of byproducts, following prolonged heating at 70 °C.[17] Acetylation of (*rac*)-**5** was also essentially quantitative, but subsequent reaction of the product (*rac*)-**6** with aqueous dimethylamine in methanol (the conditions used for the synthesis of **1**), gave only a low yield of the new amine (*rac*)-**2**. The major by-product was identified as methyl ether (*rac*)-**7**, and following isolation, this was shown not to convert to the amine under the reaction conditions. Varying the solvent, temperature and the source of dimethylamine (either a commercial MeOH or THF solution) revealed that a protic solvent is required for this reaction to take place, but the solubility of the acetate (*rac*)-**6** in alcohols is poor.[17] The best result was obtained by the use of a THF solution of dimethylamine in methanol at 66 °C which led to amine (*rac*)-**2** in a yield of 61%. Under these conditions however the ether *rac*-**7** is still formed in significant quantities.



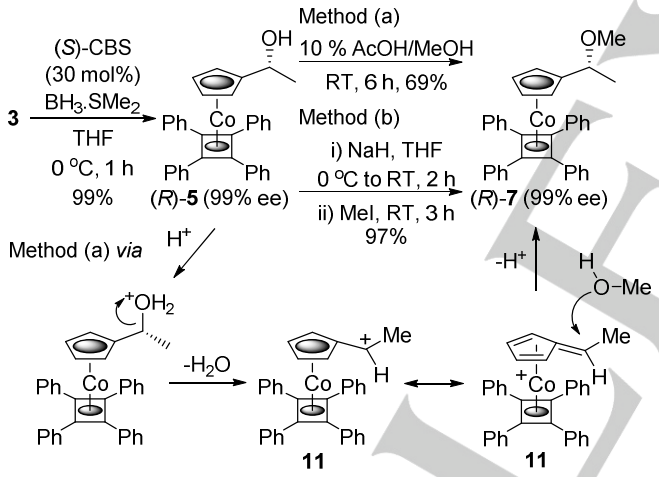
Scheme 3. Preliminary investigations into the synthesis of racemic Arthurs' amine **2**.



Scheme 4. Further investigations into the synthesis of racemic Arthurs' amine **2**.

As the direct nucleophilic introduction of the dimethylamino moiety was less than satisfactory, we sought to generate amine **2** by an alternative route. This first involved the introduction of nitrogen by formation of oxime **8** (Scheme 4), a compound isolated as a mixture of *E* and *Z* isomers. Recrystallisation gave predominantly the *E* isomer, as determined by X-ray crystallography,[17] and an examination of the material isolated from the mother liquor by ^{1}H NMR spectroscopy ($CDCl_3$) revealed a half-life for *Z* to *E* isomerisation of approximately 22 h at room temperature.[17] Reduction to primary amine (*rac*)-**9** was low yielding (due to the formation of unidentified side products), but the availability of this compound enabled tertiary amine (*rac*)-**2** to be generated readily from a reductive amination with formaldehyde.

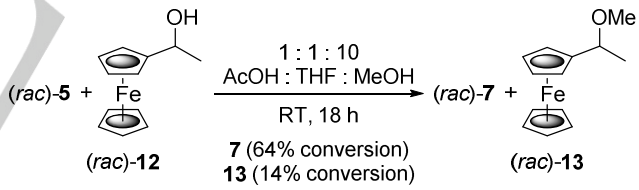
In seeking a higher yielding route to (*rac*)-**9** we carried out the reaction of alcohol (*rac*)-**5** with trimethylsilyl azide. On heating in water/DMF (1 : 1) at 80 °C for 48 hours this resulted in a 66% yield of azide (*rac*)-**10**,[17] and this yield was improved to 96% by use of indium tribromide as catalyst and stirring the reactants at room temperature in dichloromethane for just 30 minutes.[18] Thus using the optimum reaction conditions the amine (*rac*)-**2** was generated in an overall yield of 83% from ketone **3** using a route applicable to the asymmetric synthesis of **2**.



Scheme 5. Asymmetric reduction and stereospecific methanolysis.

The basis of this approach was the expectation that substitution reactions occurring at an α-stereogenic centre would proceed stereospecifically with retention of configuration. This is well established where one of the substituents of a carbon-based stereogenic centre is ferrocene,[19] or another organometallic structure[20] that imparts configurational stability on the carbenium ion resulting from loss of a nucleofuge. As the CBS-oxazaborolidine catalyst[21] has been applied successfully to the asymmetric reduction of acetylferrocene (98% ee),[22] this was applied at 30 mol% loading in conjunction with borane dimethylsulfide to ketone **3** resulting in an essentially quantitative yield of (*R*)-**5** in 99% ee, as determined by chiral HPLC (Scheme 5). Use of 5 mol% of the catalyst resulted in a reduction of the ee to 49%. The absolute configuration was assigned initially by comparison to literature precedent,[21,22] and was later confirmed by X-ray crystallography (*vide infra*). As an initial investigation into the stereochemical integrity of α-substitution (*R*)-**5** was stirred with 10% acetic acid in methanol which resulted in formation of methyl ether (*R*)-**7** [Method (a)], the absolute configuration of which was confirmed following independent synthesis by oxygen methylation [Method (b)]. Both samples of (*R*)-**7** were obtained in 99% ee as determined by chiral HPLC revealing that methanolysis under acidic conditions proceeds with complete overall retention of configuration *via* an intermediate carbenium ion **11**, the latter being configurationally stable under these reaction conditions. This was also the case when (*R*)-**5** was heated at 60 °C with 10% acetic acid in methanol to give (*R*)-**7** in 99% yield and 99% ee.[17]

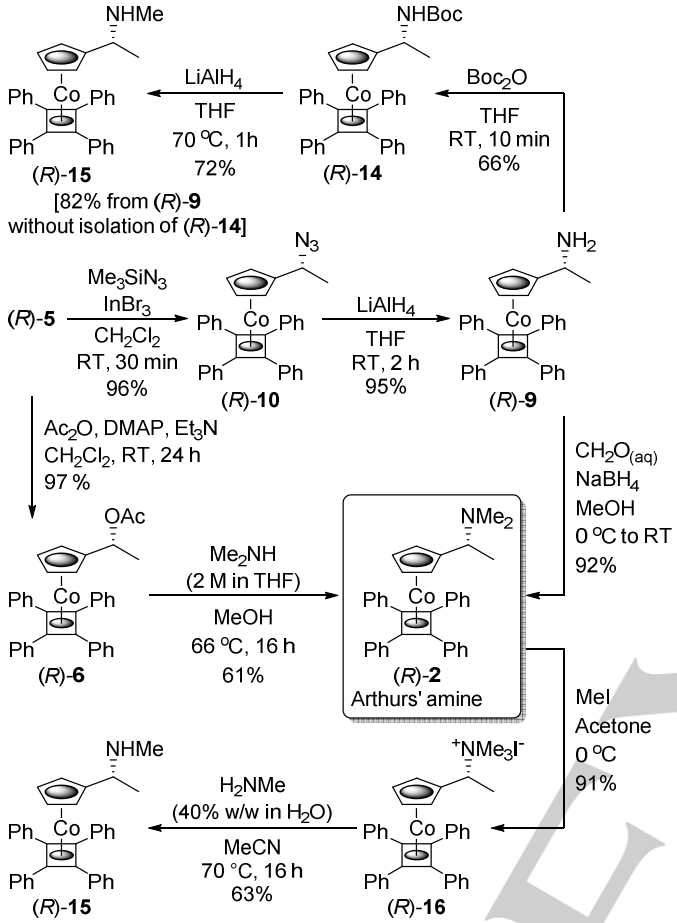
To investigate further the facility of α-substitution *via* carbenium ion **11**, a competition experiment was performed between (*rac*)-**5** and (*rac*)-**12** in 10% acetic acid in methanol, to which was also added THF to ensure complete dissolution (Scheme 6). After 18 h ^{1}H NMR spectroscopy revealed a 64% conversion of (*rac*)-**5** to the corresponding methyl ether compared to a 14% conversion for (*rac*)-**12**. Assuming that the percentage conversion is indicative of the relative stability of the corresponding α–carbenium ion (formed via rate-limiting loss of water), this outcome is in agreement with a previous study comparing a diarylferrocenylmethylium ion to a related cationic species containing (η^5-cyclopentadienyl)(η^4-cyclobutadiene)-cobalt(I). This revealed the cyclobutadienecobalt moiety of the latter as better able to stabilse the positive charge.[23]



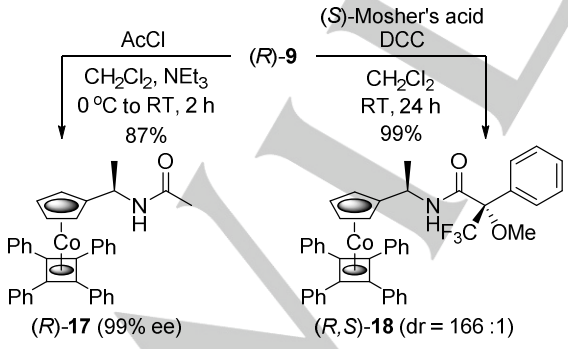
Scheme 6. Competitive methanolysis of alcohols (*rac*)-**5** and (*rac*)-**12**.

This facility for stereospecific α-substitution was extended to the generation of azide (*R*)-**10** (Scheme 7) for which the absolute configuration was confirmed by X-ray crystallography.[17] Following reduction to (*R*)-**9**, subsequent methylation by reductive amination gave the required amine (*R*)-**2**, named here as Arthurs' amine after its originator (RAA). Alternatively, acetylation of (*R*)-**5** followed by reaction of the product (*R*)-**6** with dimethylamine also furnished amine (*R*)-**2** although is slightly lower overall yield (59%, 3 steps from **3**) than obtained *via* the azide route (83%, 4 steps from **3**). In addition, following conversion of the primary amine (*R*)-**9** into Boc derivative (*R*)-**14**, subsequent reduction with lithium aluminium hydride furnished secondary amine (*R*)-**15**, the synthesis of which could be achieved in a higher yield without isolation of intermediate (*R*)-**14**. Alternatively, quarternarisation of (*R*)-**2** with methyl iodide led to the quaternary amine (*R*)-**16** that could in turn be

converted into (*R*)-**15** by a stereospecific substitution reaction with methylamine.



Scheme 7. Asymmetric synthesis of Arthurs' amine (*R*)-**2** and related primary and secondary amines.



Scheme 8. Derivatives of amine (*R*)-**9** used for the determination of enantiomeric excess.

Attempts to determine the enantiomeric excess of azide (*R*)-**10** and amine (*R*)-**9** (and by extension (*R*)-**2** and (*R*)-**15**) by chiral HPLC were unsuccessful, therefore other methods were devised to confirm the stereochemical integrity of these compounds. Following monoacetylation of (*R*)-**9**, the ee of amide (*R*)-**17** was determined as 99% by chiral HPLC analysis. Alternatively, DCC mediated coupling of (*R*)-**9** with (*S*)-Mosher's acid gave amide (*R*,*S*)-**18** for which the ^{19}F NMR spectrum contained almost exclusively a single signal (-68.61 ppm), and only a trace (dr = 166 : 1) of the additional signal observed following the reaction of (*rac*)-**9** with (*S*)-Mosher's acid (-68.88 ppm).[24] Finally, a known NMR method to determine quickly the ee of Ugi's amine **1**[25] was extended to Arthurs' amine **2**. Addition of excess (*S*)-mandelic acid to a $CDCl_3$ solution of the amine, followed by filtration and recording of the ^{1}H NMR spectrum, gave clear differentiation between racemic and enantioenriched amine samples (Figure 1). Under these conditions the dimethylamino group signals for the two diastereoisomers arising from (*rac*)-**1** are separated. In contrast, for amine **2**, separation is greater for the signals arising from the methyl group attached to the stereogenic centre. Irrespective of which of the two methods was used for the synthesis of (*R*)-**2**, the other enantiomer was not detected using this method.

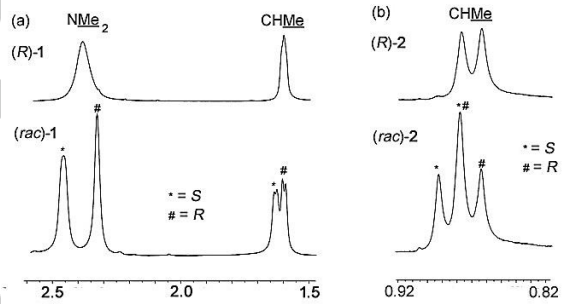


Figure 1 ^{1}H NMR spectra ($CDCl_3$ – ppm scale) of (a) (*R*)-**1**/(*rac*)-**1** and (b) (*R*)-**2**/(*rac*)-**2** following addition of (*S*)-mandelic acid.

Unlike Ugi's amine **1**, which is an oil at room temperature, Arthurs' amine **2** was obtained as a crystalline solid which enabled the X-ray crystal structure to be determined. The unit cell contained both *P* and *M* configured propeller isomers with only the latter represented here (Figure 2). In addition to providing further confirmation of the absolute configuration as *R*, this structure of Arthurs' amine provided a basis for analysing the outcomes of the diastereoselective metallation reactions that we explored next.

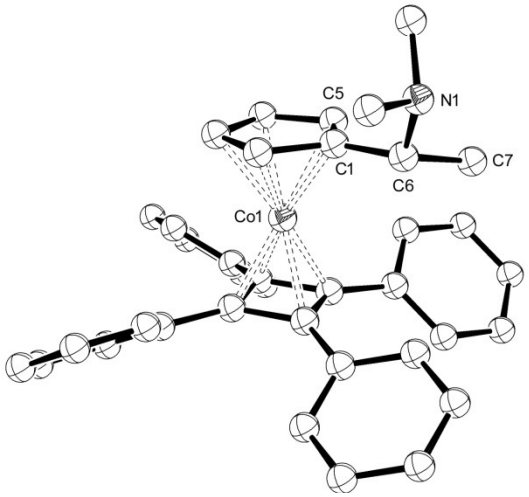
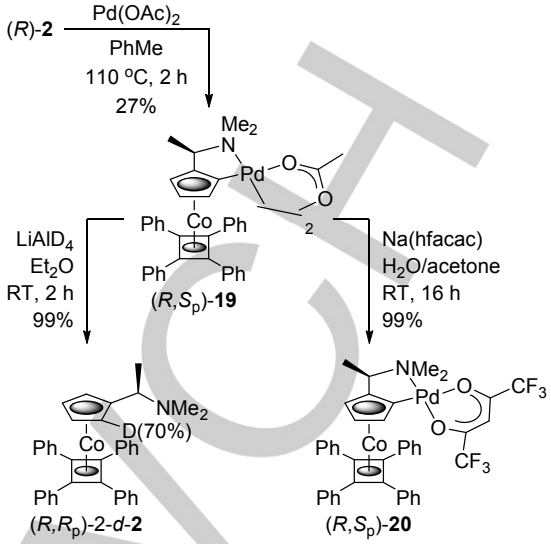


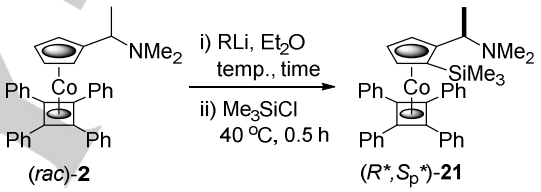
Figure 2. Representation of the X-ray crystal structure of Arthurs' amine (*R*)-**2** (values quoted are for the represented *M* configured structure - hydrogen atoms omitted for clarity). Principal bond lengths [Å] include: C(1)-C(6) = 1.519(4), C(6)-N(1) = 1.470(4), Co(1)-Cp (centre of mass) = 1.6707(14), Co(1)-Cb (centre of mass) = 1.6930(14). Principal torsions [°] include: C(5)-C(1)-C(6)-C(7) = -15.3(4), C(5)-C(1)-C(6)-N(1) = 109.3(3).

Cyclopalladation was investigated first as this is a metallation reaction that has been applied successfully to other substituted derivatives of (η^5-cyclopentadienyl)(η^4-tetraphenylcyclobutadiene)cobalt(I) to achieve both high diastereoselectivity[11b,d,e] and high enantioselectivity.[10d] Heating (*R*)-**2** with palladium acetate in toluene heated at reflux gave a new complex containing three cyclopentadienyl signals (4.14, 4.08 and 4.03 ppm) in the resulting ^{1}H NMR spectrum ($CDCl_3$), and a methyl singlet (1.60 ppm) indicative of a bridging acetate ligand. Furthermore, the dimethylamino moiety gave rise to two diastereotopic methyl singlets, an expected consequence of palladium coordination.[10d] The identity of this new complex as (R,S_p)-**19** was confirmed following its conversion into hexafluoroacetylacetonate (hfacac) monomer (R,S_p)-**20** for which the CD spectrum correlated closely with related S_p configured planar chiral palladacycles.[10d,11e,17] No spectroscopic evidence was observed for the alternative R_p configured complex. The highly selective cyclopalladation of Arthurs' amine **2** is in contrast to the cyclopalladation of Ugi's amine **1** which results the same sense of selectivity, but with a diastereoisomer ratio of just 85 : 15.[26]

The reaction of acetate-bridged dimer (R,S_p)-**19** with lithium aluminium deuteride resulted in replacement of palladium by deuterium[27] to give a significant quantity of (R,R_p)-2-*d*-**2**.[28] The ^{1}H NMR spectrum of the product revealed diminution (70%) of only one of the two diastereotopic α–hydrogen signals enabling assignment of the pro-S_p and pro-R_p hydrogens in **2** (4.58 and 4.67 ppm respectively).



Scheme 9. Cyclopalladation of Arthurs' amine (*R*)-**2**, ligand substitution and deuterium introduction.



Scheme 10. Lithiation followed by silylation of Arthurs' amine **2**.

Table 1. Investigations into the diastereosective lithiation of Arthurs' amine (*rac*)-**2** in Et_2O resulting in (R^*,S_p^*)-**21**.

Entry	Base (equivalents)	Temp.	Time	Yield[a]	d.r.[b]
1	*n*-BuLi (1.5)	RT	2 h	7%	>99:1
2	*n*-BuLi (10)	40 °C	1 h	0%[c]	-
3	*s*-BuLi (10)	RT	2 h	18%	>99:1
4	*s*-BuLi (10)	40 °C	2h	52%	>99:1
5	*s*-BuLi (10)	40 °C	3h	58%[d]	>99:1
6	*s*-BuLi (2)	40 °C	24h	0%[e]	-

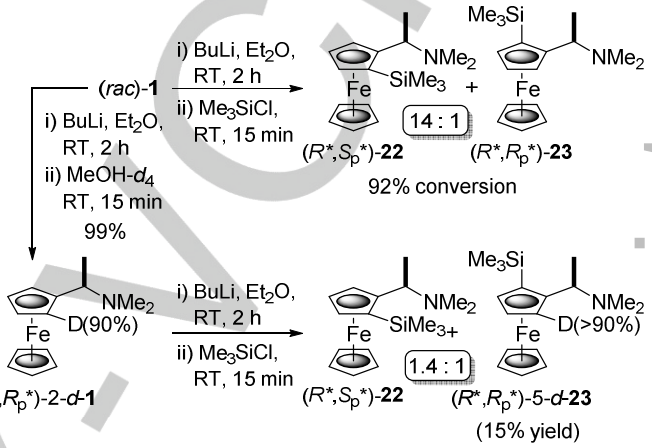
[a] Following isolation by column chromatography. [b] Determined by ^{1}H NMR spectroscopy prior to chromatography. [c] Starting material recovered. [d] Starting with (*R*)-**2** to give (R,S_p)-**21**. [e] Observation of (η^5-vinylcyclopentadienyl)(η^4-tetraphenylcyclobutadiene)cobalt(I) in product mixture.

An investigation into the lithiation of Arthurs' amine initially used the same reaction conditions that have been employed frequently for the diastereoselective lithiation of Ugi's amine **1**. Thus addition of *n*-butyllithium to an ether solution of (*rac*)-**2**, followed by the addition of trimethylsilyl chloride, resulted in

substitution of the cyclopentadienyl ring and formation of what appeared to be a single diastereoisomer, albeit in just 7% yield (Scheme 10, Table 1 – entry 1). The relative configuration of the product **21** was assigned initially as R^*,S_p^*, by analogy with the lithiation diastereoselectivity displayed by Ugi's amine under similar conditions, and the configuration of the new element of planar chirality was later confirmed by chemical correlation and X-ray crystallography (*vide infra*). Increasing the quantity of *n*-butyllithium to ten equivalents with a reaction temperature of 40 °C (*i.e.* the reaction heated at reflux) resulted in no product formation (entry 2), but use of ten equivalents of *s*-butyllithium at room temperature resulted in an 18% yield (entry 3). This increased to 52% on heating at 40 °C for 2 hours (entry 4), and 58% with a three hour reaction time (entry 5), the latter reaction starting with (*R*)-**2** to give (R,S_p)-**21**. In all cases only a single diastereoisomer of the product was observed by ^{1}H NMR spectroscopy. Product **21** was not observed when 2 equivalents of *s*-BuLi were used at a reaction temperature of 40 °C for 24 hours. Instead the ^{1}H NMR spectrum of the unpurified reaction mixture following work-up revealed the presence of a vinyl substituted sandwich complex derived from the starting material by an elimination reaction (entry 6). Thus it appears that the lithiated intermediate is itself not stable for prolonged periods under the conditions required for its formation, and a large excess of *s*-BuLi is required to achieve lithiation relatively quickly. It is of note that the conditions optimised with the use of trimethylsilyl chloride as electrophile (58% yield) resulted in essentially complete conversion to product with the other electrophiles (*vide infra*).

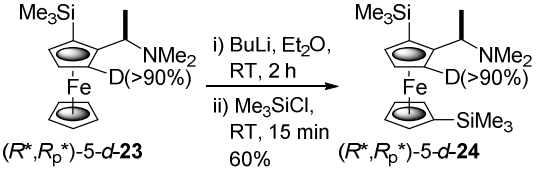
When the minor isomer from a diastereoselective reaction can not be observed there is a degree of doubt as to the selectivity observed as, for example, the ^{1}H NMR signals of the minor diastereoisomer could be coincident with those of the major diastereoisomer. Thus we set out to synthesise the minor diastereoisomer using a deuterium blocking group to disfavour the formation of the major diastereoisomer, a technique we have employed previously to reverse the diastereoselectivity of ferrocenyloxazoline lithiation.[29] First we investigated the application of this technique to Ugi's amine (Scheme 11). Addition at room temperature of *n*-butyllithium to an ether solution of (*rac*)-**1** followed by trapping with trimethylsilyl chloride resulted in a 14 : 1 ratio of diastereoisomers (R^*,S_p^*)-**22** and (R^*,R_p^*)-**23**. Several repetitions of this reaction gave the same selectivity, and it is of note that this ratio is less than the 22 : 1 ratio of isomers reported in the first description of this chemistry.[30]

Adding instead deuterated methanol following lithiation gave predominantly (R^*,R_p^*)-2-*d*-**1** as ^{1}H NMR spectroscopy revealed approximately 90% deuterium incorporation at the 2-position.[31] When this deuterated material was lithiated under the same conditions, followed by the addition of trimethylsilyl chloride, the crude product mixture contained a 1 : 0.72 : 0.53 ratio of starting material to (R^*,S_p^*)-**22** to (R^*,R_p^*)-5-*d*-**23** respectively. The latter silylated product was isolated as a single diastereoisomer by column chromatography, albeit in low yield. Thus following introduction of a deuterium substituent the ratio of the two silylated diastereoisomers changed from 14 : 1 to 1.4 : 1. Taking into account the percentage of (R^*,R_p^*)-2-*d*-**1**, and ignoring the possible presence of (R^*,S_p^*)-2-*d*-**1**, the value of k_H/k_D is approximately 12, *i.e.* less that the primary kinetic isotope effect value of ~20 determined from similar experiments on a ferrocenyloxazoline,[29] and significantly less than the value of >50 observed for some non-diastereoselective lithiation reactions.[32]

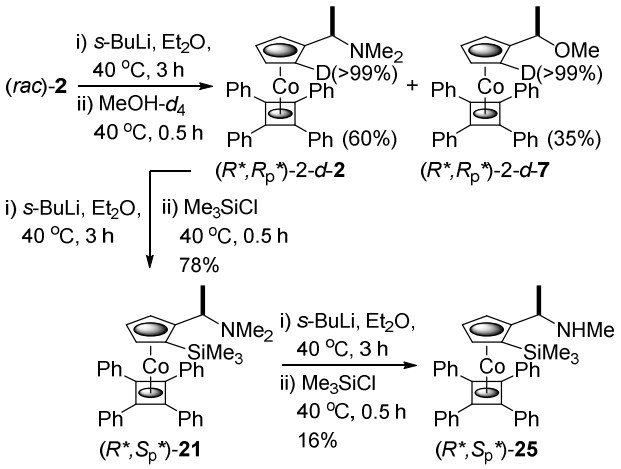


Scheme 11. Use of a deuterium blocking group to lower the lithiation diastereoselectivity of Ugi's amine.

To bias further the reaction in favour of (R^*,R_p^*)-5-*d*-**23** requires reaction conditions for the lithiation of non-deuterated Ugi's amine that result in a reduction in the 14 : 1 diastereoselectivity. Several experiments were performed with this aim, and although the selectivity could be reduced significantly, this was always accompanied by a very low reaction yield which precluded further application.[17] This is unfortunate as higher yielding access to what is normally the minor discarded diastereoisomer of a lithiation/electrophile quench sequence with Ugi's amine could potentially provide many additional ligands for testing in asymmetric catalysis.[33] Furthermore, subjecting (R^*,R_p^*)-5-*d*-**23** to the standard conditions for lithiation/trimethylsilyl chloride quench gave predominantly (R^*,R_p^*)-5-*d*-**24** as a result of 1'-lithiation, with both deuterium and the trimethylsilyl group preventing lithiation of the substituted cyclopentadienyl ring (Scheme 12). Non-deuterated (R^*,R_p^*)-**24** is unavailable using existing methodology.



Scheme 12. Use of deuterium and trimethylsilyl blocking groups to favour 1'-lithiation.



Scheme 13. Attempted replacement of the of pro-S_p hydrogen of Arthurs' amine **2**.

Arthurs' amine (*rac*)-**2** was lithiated as before and quenched with deuterated methanol to give deuterated Arthurs' amine for which the ^{1}H NMR signal at 4.67 ppm had vanished, and the signal for the diastereotopic hydrogen at 4.58 ppm was unchanged (Scheme 13). This formation of (*R**,R_p*)-2-*d*-**2** confirmed that lithiation is highly diastereoselective, and also revealed the selectivity for the new element of planar chirality (*i.e.* by comparison to (*R**,R_p*)-2-*d*-**2** previously synthesised by cyclopalladation/deuterium replacement). A second compound was isolated by column chromatography and identified as deuterated (*R**,R_p*)-2-*d*-**7**, the relative configuration of which was confirmed following the quaternization of (*R**,R_p*)-2-*d*-**2** and reaction with methanol.[17] As apart from (*rac*)-**2** no non-deuterated methyl source was used in the reaction or workup, the methyl group of ether (*R**,R_p*)-2-*d*-**7** is presumably derived from the dimethylamino group of the starting material by an as yet unknown mechanism. Application of the same lithiation conditions to (*R**,R_p*)-2-*d*-**2** followed by addition of trimethylsilyl chloride gave *only* (*R**,S_p*)-**21**, with ^{1}H and ^{13}C NMR spectroscopy revealing no indication of the presence of a diastereoisomer in the crude product mixture. Thus even following introduction of a deuterium blocking group, the transition state leading to the alternative diastereoisomer is inaccessible, pointing to a diastereomeric ratio of >99.9 : 0.1 for the lithiation of **2**. When (*R**,S_p*)-**21** was subjected to the same lithiation/silylation sequence, recovered starting material was obtained predominantly, together with a quantity of demethylated amine (*R**,S_p*)-**25** (ratio ~3 :1) In this instance the unavailability of the alternative cyclopentadienyl lithiation reaction allows for an alternative reaction pathway. This is in contrast to the analogous reaction with (*R**,S_p*)-**22** where the cyclopentadienyl ring may be functionalised readily by a lithiation/electrophilic quench sequence.[34]

It has been argued that the lithiation diastereoselectivity observed with **1** is a result of repulsion between the methyl group of the α–stereogenic centre and the iron-cyclopentadienyl group of ferrocene in the transition state leading to the minor product.[6,35] This is represented as TS-**B(i)** in Figure 3, and contrasts with TS-**A(i)** leading to the major diastereoisomer. Subsequent DFT calculations support this basic model,[36] and give values for the difference between the two transition states of between 10 and 13 kJ mol^{-1} depending on the degree on *n*-butyllithium aggregation and solvent (Et_2O) coordination to lithium. In all of the calculated transition states for the formation of the major diastereoisomer the methyl group of the α–stereogenic centre is essentially in the plane of the cyclopentadienyl ring. The X-ray crystal structure of **2** reveals a similar arrangement (torsion angles -15.3(4) and -20.8(4)° for the two structures in the unit cell, see Figure 2) with the methine hydrogen pointing towards the bulk of the sandwich complex. Thus a similar minimum energy conformation in solution requires little change in rotation about the C(Cp)-C(α) bond to access the transition state TS-**A(ii)** leading to the only observed diastereoisomer, in accordance with the principle of least motion.[37] Furthermore, the transition state TS-**B(ii)** that would lead to the minor diastereoisomer contains a more significant repulsion than is the case for TS-**B(i)** due to the larger size of the Co(η^4-C_4Ph_4) moiety. A >99.9:0.1 diastereoselectivity as a result of kinetic control in this way requires an energy difference between the two transition states of >18 kJ mol^{-1} (at 40 °C). The diastereoselectivity of cyclopalladation is presumably the result of a similar transition state discrimination following amine coordination to palladium, and participation of an acetate ligand in a concerted metallation-deprotonation step.[38]

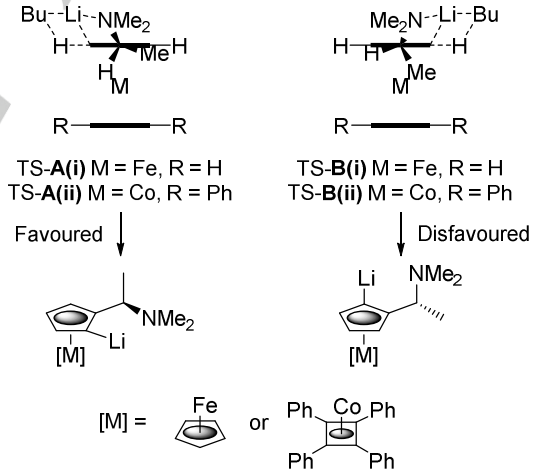
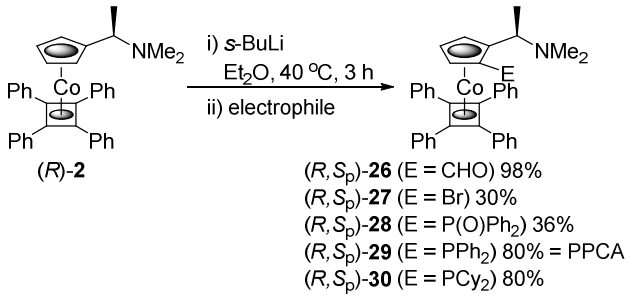


Figure 3. Representation of the diastereomeric transition states for α–lithiation of amines **1** and **2**.

A number of other planar chiral compounds were synthesised from Arthurs' amine (*R*)-**2** by utilisation of the optimised lithiation conditions (Scheme 14). Addition as electrophile of DMF gave an excellent yield of (*R*,S_p)-**26** displaying a single aldehyde proton signal at 9.43 ppm in the ^{1}H NMR spectrum. Utilising 1,2-dibromotetrachloroethane as an electrophile led to (*R*,S_p)-**27**, albeit in a reduced yield due to difficulties separating the product from remaining (*R*)-**2**. Use as

the electrophile of chlorodiphenylphosphine oxide or chlorodiphenylphosphine resulted, respectively, in the formation of phosphineoxide (R,S_p)-**28** and phosphine (R,S_p)-**29**. The latter was readily separated from a small quantity of (R,S_p)-**28** presumably formed on work-up. In addition, the use of chlorodicyclohexylphosphine as an alternative phosphine electrophile yielded (R,S_p)-**30**. All five planar chiral products were formed as single diastereoisomers, and for (R,S_p)-**28,** (R,S_p)-**29** and (R,S_p)-**30** this was confirmed additionally by ^{31}P NMR spectroscopy.



Scheme 14. Synthesis of planar chiral derivatives from (*R*)-**2**.

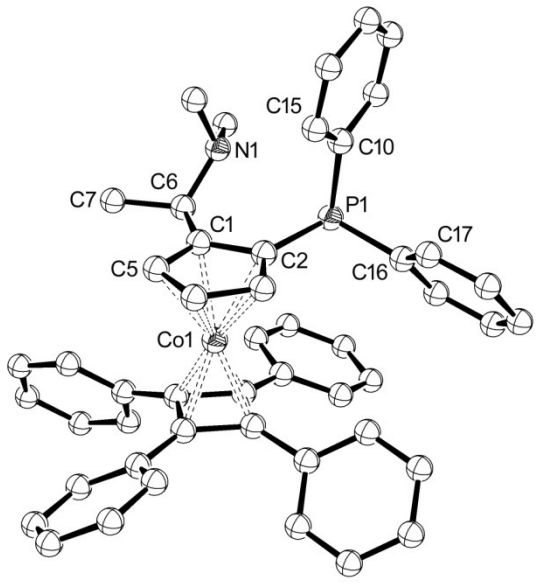


Figure 4. Representation of the X-ray crystal structure of (R,S_p)-PPCA [(R,S_p)-**29**] (hydrogen atoms omitted for clarity). Corresponding values for PPFA in parenthesis.[39] Principal bond lengths [Å] include: C(1)-C(6) = 1.518(4) [1.480] C(6)-N(1) = 1.468(4) [1.468], C(2)-P(1) 1.833(2) [1.803]. Principal torsions [°] include: C(5)-C(1)-C(6)-C(7) = -1.1(4) [-16.32], C(5)-C(1)-C(6)-N(1) = 127.1(3) [112.42], C(1)-C(2)-P(1)-C(10) 91.0(2) [89.0], C(1)-C(2)-P(1)-C(16) -168.9(2) [-166.01], C(2)-P(1)-C(10)-C(15) 17.0(3) [12.90], C(2)-P(1)-C(16)-C(17) -65.5 [-80.12].

Phosphine (R,S_p)-**29** is the (η^5-cyclopentadienyl)(η^4-tetraphenylcyclobutadiene)cobalt(I) equivalent to PPFA (R,S_p)-**31** (Figure 5), a chiral bidentate ligand in its own right and a very significant intermediate for the synthesis of several extensively utilised ferrocene-based bis-phosphine ligands. By analogy an acronym suggested for (R,S_p)-**29** is PPCA.[40] The X-ray crystal structure of this new ligand was determined, this further confirming both the relative and absolute configuration as R,S_p (Figure 4). The conformation displayed by the two cyclopentadienyl substituents in the solid state is similar to that displayed by PPFA in the same state,[39] the largest difference being the orientation of the methyl group attached to the stereogenic centre away from the η^4-tetraphenylcyclobutadiene moiety [C(5)-C(1)-C(6)-C(7) = -1.1(4)° compared to the corresponding torsion angle of -16.32° in PPFA].

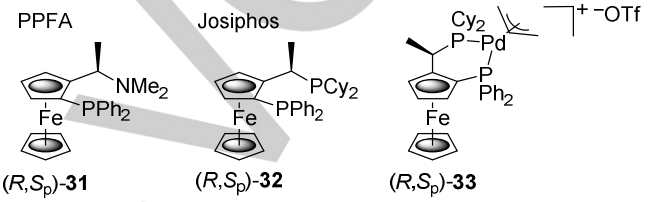
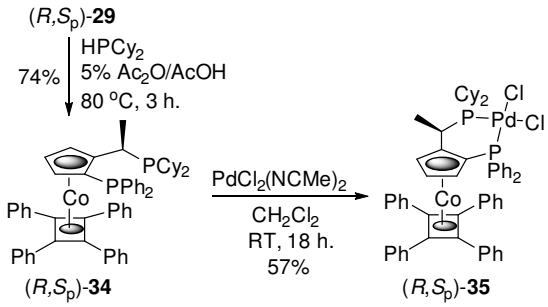


Figure 5. Ferrocene-based PPFA (R,S_p)-**31** and Josiphos (R,S_p)-**32** ligands, and palladium complex (R,S_p)-**33**.

As α-substitution reactions of (η^5-cylopentadienyl)(η^4-tetraphenylcyclobutadiene)cobalt(I) complexes proceed readily, and with retention of configuration [*e.g.* (*R*)-**5** into (*R*)-**10**], it was anticipated that PPCA (R,S_p)-**29** could be used for the synthesis of a related bis-phosphine ligand. Heating (R,S_p)-**29** with dicyclohexylphosphine in acetic acid resulted in clean conversion into a new bisphosphine formed as a single diastereoisomer (Scheme 15), as revealed by the two signals in the resulting ^{31}P NMR spectrum [(MeCN-d_3) at 11.90 (*P*Cy$_2$) and -33.53 (*P*Ph$_2$) ppm]. It was observed that the ^{1}H NMR spectrum of (R,S_p)-**34** in $CDCl_3$ was complex, and varied from sample to sample, an outcome attributed to residual acid present in this solvent.

The identity of the bisphosphine as (R,S_p)-**34** was confirmed by determination of the X-ray crystal structure of (R,S_p)-**35**, obtained by reaction of the ligand with bis(acetonitrile)dichloropalladium(II) (Figure 6). The new bisphosphine ligand, dubbed 'Rossiphos', is similar with respect to the electronic properties of the two coordinating phosphine moieties to the Josiphos ligand (R,S_p)-**32**[8a] (Figure 5) [($CDCl_3$) 15.7 (*P*Cy$_2$) and -25.8 (*P*Ph$_2$) ppm]. However, comparison of the X-ray crystal structure of (R,S_p)-**35** to that of the (η^3-allyl)palladium complex (R,S_p)-**33**,[41b] which itself is representative of other Josiphos transition metal complexes,[41] revealed significant differences in the conformation of the palladium coordinated ligands. Due to the size of the η^4-tetraphenylcyclobutadiene moiety the C(2)-C(1)-P(1)-C(8) torsion angle in (R,S_p)-**35** is -159.4(12)°, compared to the corresponding angle of -107.94° in (R,S_p)-**33**, as a result of the proximity of a phenyl group to the η^5-cyclopentadienyl group of ferrocene. This phenyl group in the ferrocene derivative (R,S_p)-**33** can be regarded as pseudo-axial with respect to the six-

membered chelate ring, with the other phenyl group attached to phosphorus being pseudo-equatorial. In the cobalt complex (R,S_p)-**35** these assignments are reversed due to the significant conformational restriction imposed by the bulky sandwich complex. These differences are highlighted by an overlay of the two X-ray crystal structures (Figure 7). Other manifestations of this restriction include the C(2)-C(6)-P(2)-Pd(1) torsion angle in (R,S_p)-**35** of 30.2(12)° compared to the corresponding torsion angle in (R,S_p)-**33** of 72.46°, and the Co-Pd distance of 4.895(2) Å compared to the Fe-Pd distance of 5.237 Å. In complex (R,S_p)-**35** one side of the palladium-centred square-plane is largely covered by a phenyl group of the η⁴-tetraphenylcyclobutadiene moiety.



Scheme 15. Synthesis of 'Rossiphos' ligand (R,S_p)-**34** and its palladium chloride complex (R,S_p)-**35**.

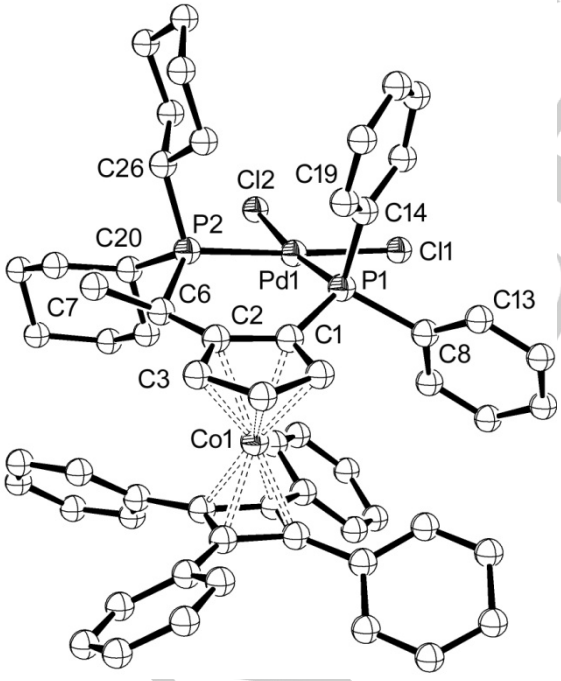


Figure 6. Representation of the X-ray crystal structure of (R,S_p)-**35** (hydrogen atoms and solvent of crystallisation omitted for clarity). Principal bond lengths [Å] include: C(2)-C(6) = 1.552(19), C(6)-P(2) 1.830(14), C(1)-P(1) 1.800(14), P(1)-Pd(1) 2.238(4), P(2)-Pd(1) 2.296(4), Pd(1)-Cl(1) 2.354(4), Pd(1)-Cl(2) 2.364(4). Principal angles [°] include: P(1)-Pd(1)-P(2) 93.76(14), Cl(1)-Pd(1)-Cl(2) 87.38(15). Principal torsions [°] include: C(3)-C(2)-C(6)-C(7) 34.2(17), C(3)-C(2)-C(6)-P(2) 164.3(10), C(2)-C(1)-P(1)-C(14) 92.8(13), C(2)-C(1)-P(1)-C(8) -159.4(12), C(1)-P(1)-C(14)-C(19) 3.8(14), C(1)-P(1)-C(8)-C(13) -89.9(12), C(2)-C(6)-P(2)-C(26) -98.2(11), C(2)-C(6)-P(2)-C(20) 151.1(10), C(2)-C(6)-P(2)-Pd(1) 30.2(12), C(2)-C(1)-P(1)-Pd(1) -26.0(14).

The facility with which ligand (R,S_p)-**34** was formed in a reaction proceeding with complete retention of configuration is significant as it reveals that complexes such as (R,S_p)-**29** [PPCA] have the potential to be precursors to a range of ligands based upon the sandwich complex (η⁵-cyclopentadienyl)(η⁴-tetraphenylcyclobutadiene)cobalt(I). Thus the planar chiral bidentate PN and PP complexes reported herein are the first examples of a new and potentially diverse class of bulky ligands with the potential to be applied in several areas of asymmetric catalysis.

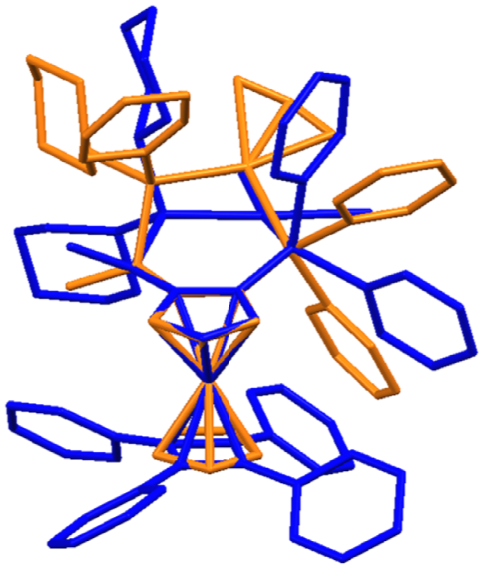


Figure 7. Overlap of the X-ray crystal structures of palladium complexes (R,S_p)-**35** (blue) and (R,S_p)-**33** (orange - counter ion removed).

Conclusions

Asymmetric synthesis methodology, that has been exploited extensively for the synthesis of a number of widely employed and commercially available ferrocene-based ligands, is applicable to the synthesis of complexes based on substituted cyclopentadienyl derivatives of the sandwich complex (η⁵-cyclopentadienyl)(η⁴-tetraphenylcyclobutadiene)cobalt(I). Specifically, the synthesis of (*R*)-(η⁵-α-*N*,*N*-dimethyl-aminoethylcyclopentadienyl)(η⁴-tetraphenylcyclobutadiene) cobalt(I) (*R*)-**2** (Arthurs' amine), showed that CBS-catalysed methyl ketone reduction is highly enantioselective (99% ee), that substitution reactions at the resulting α-stereogenic centre proceed with complete retention of configuration, and that palladation and lithiation are highly diastereoselective (>99: 1 dr). For the lithiation reaction, the alternative diastereoisomer could not be detected despite attempting to exploit the high value of

k_H/k_D for lithiation following introduction of a deuterium blocking group. In contrast, application of this technique to Ugi's amine, the ferrocene-based analogue, changed the lithiation diastereoselectivity from 14 : 1 to 1.4 : 1. The three key aspects of the chemistry of (η^5-cyclopentadienyl)(η^4-tetraphenylcyclobutadiene)cobalt(I) derivatives demonstrated in this work (enantioselective reduction, stereospecific substitution and diastereoselective lithiation) enabled the synthesis of first in class P-N ligand (R,S_p)-**29** (PPCA) and P-P ligand (R,S_p)-**34** (Rossiphos). Despite the superficial similarity of the new cobalt sandwich complex based ligands to the equivalent ferrocene-based structures, the X-ray crystal structure of the palladium chloride complex (R,S_p)-**35** reveals both a significant conformational difference, and a steric influence on palladium of the η^4-tetraphenylcyclobutadiene moiety. The impact of these features on the effectiveness of the new ligands applied to metal catalysed asymmetric reactions is currently under investigation.

Experimental Section

Preparation of (R)-(η^5-(S_p)-1-(α-*N*,*N*-dimethylaminoethyl)-2-(diphenylphosphino)cyclopentadienyl)(η^4-tetraphenylcyclobutadiene)cobalt(I) (R,S_p)-**29** (PPCA)

(R)-**2** (0.200 g, 0.36 mmol) was added to a flame dried Schlenk tube under an inert atmosphere and dissolved in dry diethyl ether (10 mL). To this was added *sec*-butyllithium (1.4 M in hexanes) (2.59 mL, 3.63 mmol) and the sealed reaction mixture was heated in an oil bath at 40 ℃ with stirring for 3 hours. The reaction was cooled to room temperature, where upon freshly distilled chlorodiphenylphosphine (0.74 mL, 4.00 mmol) was added and the reaction stirred for 30 mins. The reaction was then quenched with saturated sodium hydrogen carbonate and the resulting yellow suspension was dissolved in dichloromethane, separated with water and dried over potassium carbonate. Column chromatography (SiO_2, 20 % EtOAc in hexane) yielded the product as a yellow crystalline solid (0.21 g, 80 %). The sample for X-ray analysis was obtained by evaporation of the column fractions and trituration with hexane:[42] R_f 0.65 (30 % EtOAc in hexane); M.p. 243 - 244 ℃; $[\alpha]_D^{23℃}$ = -436 (c = 0.2, chloroform); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.25-7.21 (12H, m, *m*+*p*-Ph*H*), 7.18-7.15 (8H, m, *o*-Ph*H*), 7.15-7.08 (6H, m, *o*,*m*+*p*-Ph*H*), 7.04 (2H, brt, J = 7.3, *m*-Ph*H*), 6.74 (2H, brt, J = 7.2, *o*-Ph*H*), 4.83 (1H, d, J = 1.4, Cp*H*), 4.75 (1H, t, J = 2.4, Cp*H*), 4.53 (1H, brs, Cp*H*), 3.80 (1H, dq, J = 6.7, 1.7, C*H*), 1.52 (6H, s, N(CH_3)$_2$), 0.51 (3H, d, J = 6.7, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 138.6 (*ipso*-Ph*C*), 136.1 (*ipso*-Ph*C*), 136.0 (d, J = 22.7, *o*-Ph*C*), 135.9 (*ipso*-Ph*C*), 132.3 (d, J = 20.5, *o*-Ph*C*), 129.2 (*o*-Ph*C*), 128.4 (*p*-Ph*C*), 128.1 (d, J = 7.5, *m*-Ph*C*), 128.1 (*m*-Ph*C*), 128.0 (*p*-Ph*C*), 127.3 (d, J = 7.4, *m*-Ph*C*), 126.3 (*p*-Ph*C*), 107.6 (*ipso*-Cp*C*), 89.6 (d, J = 17.4, *ipso*-Cp*C*), 87.2 (d, J = 6.3, Cp*C*), 84.6 (Cp*C*), 81.8 (d, J = 3.7, Cp*C*), 74.5 (Cb*C*), 56.1 (d, J = 4.6, *C*H), 38.7 (N(*C*H_3)$_2$), 7.6 (*C*H_3); ^{31}P NMR (202 MHz, $CDCl_3$) δ = -32.37 (*P*Ph_2). IR (film): $\tilde{\nu}$ = 3055, 2963, 2927, 2853, 2817, 2773, 1600, 1498 cm^{-1}; HRMS (AS) m/z calcd for $C_{49}H_{44}CoNP$: 736.2543 $[M+H]^+$; found 736.2543.

Acknowledgements

The AI-Chem Channel and the EPSRC (EP/N019393/1) are thanked for financial support. We also thank the EPSRC National Mass Spectrometry Centre (University of Wales, Swansea) and Myles Cheesman (UEA) for assistance with and use of the UEA circular dichroism facility.

Keywords: cobalt • diastereoselectivity • enantioselectivity • ligands • sandwich complexes

[1] *New Frontiers in Asymmetric Catalysis* (Eds.: K. Mikami, M. Lautens) Wiley,Hoboken New Jersey **2007**.

[2] *Molecular Organometallic Materials for Optics* (Eds: H. Le Bozec, V. Guerchais) Springer-Verlag, Berlin Heidelberg **2010**.

[3] *Supramolecular Organometallic Chemistry* (Eds.: I. Haiduc, F. T. Edelmann) Wiley-VCH, Weinheim, **2008**.

[4] *Bioorganometallic Chemistry: Applications in Drug Discovery, Biocatalysis, and Imaging* (Eds.: G. Jaouen, M. Salmain) Wiley-VCH, Weinheim, **2015**.

[5] *Chiral Ferrocenes in Asymmetric Catalysis: Synthesis and Applications* (Eds.: L.-X. Dai, X.-L. Hou), Wiley-VCH, Weinheim, **2010**.

[6] D. Marquarding, H. Klusacek, G. Gokel, P. Hoffmann, I. Ugi, *J. Am. Chem. Soc.* **1970**, *92*, 5389.

[7] T. Hayashi, K. Yamamoto, M. Kumada, *Tetrahedron Lett.* **1974**, 4405.

[8] **Josiphos**: (a) A. Togni, C. Breutel, A. Schnyder, F. Spindler, H. Landert, A. Tijani, *J. Am. Chem. Soc.* **1994**, *116*, 4062. **BoPhoz**: (b) N. W. Boaz, S. D. Debenham, E. B. Mackenzie, S. E. Large, *Org. Lett.* **2002**, *4*, 2421. **Walphos**: (c) T. Sturm, W. Weissensteiner, F. Spindler, *Adv. Synth. Cat.* **2003**, *345*, 160. **TriFer**: (d) W. Chen, P. J. McCormack, K. Mohammed, W. Mbafor, S. M. Roberts, J. Whittall, *Angew. Chem. Int. Ed.* **2007**, *46*, 4141. **ChenPhos**: (e) W. Chen, F. Spindler, B. Pugin, U. Nettekoven, *Angew. Chem. Int. Ed.* **2013**, *52*, 8652. Also synthesised using similar approach is **Mandyphos**: (f) L. Schwink, P. Knochel, *Tetrahedron Lett.* **1996**, *37*, 25.

[9] A. Nakamura, N. Hagihara, *Bull. Chem. Soc. Jp.* **1961**, *34*, 452.

[10] Review: (a) H. Nomura, C. J. Richards, *Chem. Asian J.* **2010**, *5*, 1726. See also: (b) H. V. Nguyen, D.C.D. Butler, C. J. Richards, *Org. Lett.* **2006**, *8*, 769. (c) M. Ismail, H. V. Nguyen, G. Ilyashenko, M. Motevalli, C. J. Richards, *Tetrahedron Lett.* **2009**, *50*, 6332. (d) D. J. Cassar, G. Ilyashenko, M. Ismail, J. Woods, D. L. Hughes, C. J. Richards, *Chem. Eur. J.* **2013**, *19*, 17951.

[11] (a) M. Uno, K. Ando, N. Komatsuzaki, T. Tsuda, T. Tanaka, M. Sawada, S. Takahashi, *J. Organomet. Chem.* **1994**, *473*, 303. (b) A. M. Stevens and C. J. Richards, *Organometallics* **1999**, *18*, 1346. (c) R. G. Arrayás, O. G. Mancheño, J. C. Carretero, *Chem. Commun.* **2004**, 1654.(d) R. S. Prasad, C. E. Anderson, C. J. Richards, L. E. Overman, *Organometallics* **2005**, *24*, 77. (e) D. J. Cassar, H. Roghzai, D. Villemin, P. N. Horton, S. J. Coles, C. J. Richards, *Organometallics* **2015**, *34*, 2953.

[12] (a) C. E. Anderson, L. E. Overman, C. J. Richards, M. P. Watson, N. White, *Org. Synth.* **2007**, *84*, 139. (b) H. V. Nguyen, M. R. Yeamine, J. Amin, M. Motevalli, C. J. Richards, *J. Organomet. Chem.* **2008**, *693*, 3668.

[13] (a) S. McVey, P. L. Pauson, *J. Chem. Soc.* **1965**, 4312. (b) D. C. D. Butler, C. J. Richards, *Organometallics* **2002**, *21*, 5433.

[14] M. D. Rausch, R. A. Genetti, *J. Org. Chem.* **1970**, *35*, 3888.

[15] Y. Ortin, K. Ahrenstorf, P O'Donohue, D. Foede, H. Müller-Bunz, P. McArdle, A. R. Manning, M. J. McGlinchey, *J. Organomet. Chem.* **2004**, *689*, 1657.

[16] (a) N. W. Boaz, *Tetrahedron Lett.* **1989**, 30, 2061. See also: (b) Y. Matsumoto, A. Ohno, S.-J. Lu, T. Hayashi, N. Oguni, M. Hayashi, *Tetrehedron: Asymmetry* **1993**, *4*, 1763. (c) M. Woltersdorf, R. Kranich, H.-G. Schmalz, *Tetrahedron* **1997**, *53*, 7219.

[17] Complete details are provided in the supporting information.

[18] P. Vicennati, P. G. Cozzi, *Eur. J. Org. Chem.* **2007**, 2248.

[19] (a) G. Gokel, P. Hoffmann, H. Klusacek, D. Marquarding, E. Ruch, I. Ugi, *Angew. Chem., Int. Ed. Engl.* **1970**, *9*, 64.

[20] (a) Ruthenocene: T. Hayashi, A. Ohno, S. Lu, Y. Matsumoto, E. Fukuyo, K. Yanagi, *J. Am. Chem. Soc.* **1994**, *116*, 4221. (b) Osmocene: M. Goto, Y. Yamazaki, K. Honda, A. Masaki, *Bull. Chem. Soc. Jp.* **1995**, *68*, 1305. (c) Cyrhetrene: C. Bolm, L. Xiao, L. Hintermann, T. Focken, G. Raabe, *Organometallics* **2004**, 23, 2362. (d) (η^4-C_4H_4)Fe(CO)$_3$: A. Pfletschinger, U. Schneider, J. Lex, H.-G. Schmalz, *Eur. J. Org. Chem.* **2007**, 3991. (e) (η^6-C_6H_6)Cr(CO)$_3$:Y. Hayashi, H. Sakai, N. Kaneta, M, Uemura, *J. Organomet. Chem.* **1995**, *503*, 143.

[21] E. J. Corey, R. K. Bakshi, S. Shibata, *J. Am. Chem. Soc.* **1987**, *109*, 5551.

[22] J. Wright, L. Frambes, *J. Organomet. Chem.* **1994**, *476*, 215.

[23] R. Gleiter, H. Schimanke, S. J. Silverio, M. Büchner, G. Huttner, *Organometallics* **1996**, *15*, 5635.

[24] Clear differentiation between the (*R*,*S*) and (*S*,*S*) diastereoisomers was also observed in the ^{1}H NMR spectrum. See supporting information for more details.

[25] N. A. Kataeva, Y. K. Grishin, V. V. Dunina, *Russ. Chem. Bull.* **2001**, *50*, 1323.

[26] (a) V. I. Sokolov, L. L. Troitskaya, O. A. Reutov, *J. Orgamomet. Chem.* **1977**, *133*, C28 (b) T. K. Hollis, L. E. Overman, *Tetrahedron Lett.* **1997**, *38*, 8837.

[27] M. E. Günay, C. J. Richards, *Organometallics* **2009**, *28*, 5833.

[28] In this paper, compounds that differ only by the presence or absence of deuterium have the same number. Position 1 of the substituted cyclopentadienyl ring of amines **1** and **2**, and derivatives thereof, is attached to the α-dimethylaminoethyl substituent.

[29] R. A. Arthurs and C. J. Richards, *Org. Lett.* **2017**, *19*, 702.

[30] The ratio of diastereoisomers was determined following chromatographic separation of (*R*,*S*$_p$)-**21** (57.3%) and (*R*,*R*$_p$)-**22** (2.6%). See reference 6.

[31] The percentage deuterium incorporation at the other position (i.e. of (*R**,*S*$_p$*)-2-*d*-**1**) could not be determined as this signal is obscured by other ferrocenyl signals.

[32] (a) D. Hoppe, M. Paetow. F. Hintze, *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 394. (b) J. Clayden, J. H. Pink, N. Westlund, F. X. Wilson, *Tetrahedron Lett.* **1998**, *39*, 8377.

[33] There are a few examples of ligands derived from (*R*,*S*$_p$)-**22** (or its enantipode) where a $SiMe_3$ group was used as a removal blocking group following the introduction of PPh_2 at the other position adjacent to the α–*N*,*N*-dimethylaminoethyl substituent. See for example: (a) T. Hayashi, T. Mise, M. Fukusima, M. Kagotani, N. Nagashima, Y. Hamada, A. Matsumoto, S. Kawakami, M. Konishi, K. Yamamoto, M. Kumada, *Bull. Chem. Soc. Jp.* **1980**, *53*, 1138. (b) X. Hu, H. Chen, H. Dai, X. Hu, Z. Zheng, *Tetrahedron: Asymmetry* **2003**, *14*, 2073. (c) X.-P. Hu, Z. Zheng, *Org. Lett.* **2004**, *6*, 3585. (d) X.-P. Hu, H.-L. Chen, Z. Zheng, *Adv. Synth. Catal.* **2005**, *347*, 541.

[34] I. R. Butler, W. R. Cullen, S. J. Rettig, *Organometallics* **1986**, *5*, 1320.

[35] I. R. Butler, W. R. Cullen, F. G. Herring, N. R. Jagannathan, *Can. J. Chem.* **1986**, *64*, 667.

[36] A. Skvorcová, R. Šebesta, *Org. Biomol. Chem.* **2014**, *12*, 132.

[37] J. Hine, *Adv. Phys. Org. Chem.* **1977**, *15*, 1.

[38] D. Lapointe, K. Fagnou, *Chem. Lett.* **2010**, *39*, 1118.

[39] F. W. B. Einstein, A. C. Willis, *Acta Cryst.* **1980**, *B36*, 39.

[40] PPFA = (*R*)-*N*,*N*-dimethyl-1-[(*S*)-2-(di*p*henyl*p*hosphino)*f*errocenyl)-ethyl*a*mine. Thus PPCA describes by comparison ligand **29** with F (ferrocenyl) replaced by C (cobalt).

[41] (a) C. Gambs, G. Consiglio, A. Togni, *Helv. Chim. Acta* **2001**, *84*, 3105. (b) A. Togni, C. Breutel, M. C. Soares, N. Zanetti, T. Gerfin, V. Gramlich, F. Spindler, G. Rihs, *Inorg. Chim. Acta* **1994**, *222*, 213.

[42] CCDC 1578881 (**8**), 1578882 (**10**), 1578883 (**32**), 1578884 (**27**) and 1578885 (**2**) contain the supplementary crystallographic data for this paper. These data are provided free of charge by The Cambridge Crystallographic Data Centre.

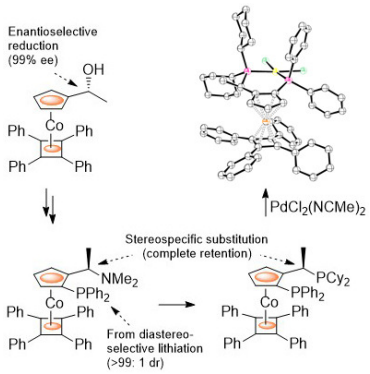
10.1002/chem.201705113

WILEY-VCH

Entry for the Table of Contents

FULL PAPER

Who ate all the pies? A cobalt sandwich complex of π groups and substituents provides a bulky framework for the synthesis of a new class of chiral bidentate ligands. These result from the facility of highly enantioselective ketone reduction, stereospecific α–substitution reactions, and highly diastereoselective metallation (lithiation and palladation) to generate the element of planar chirality.



*Ross A. Arthurs, Peter N. Horton, Simon J. Coles and Christopher J. Richards**

Page No. – Page No.

Stereoselective and Stereospecific Reactions of Cobalt Sandwich Complexes. Application to the Synthesis of a New Class of Single Enantiomer Bulky Planar Chiral P-N and P-P Ligands