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Diastereoselective synthesis of half-sandwich chiral-at-metal cobaltacycles by oxidative cyclisation†

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Reaction of chiral ester linked diynes with chlorotris(triphenylphosphine)cobalt(i) and sodium cyclopentadienide gave (η^5 -cyclopentadienyl)(triphenylphosphine) cobaltacyclopentadiene complexes as single chiral-at-metal diastereoisomers, including a non-racemic example synthesised in three steps from (*S*)-3-butyn-2-ol.

The variability in the structure of chiral organometallic complexes provides novel opportunities for the synthesis of non-racemic ligands, catalysts and materials. Ideally such complexes are air-stable, configurationally-stable, and readily generated as single enantiomers. Chiral organometallics result from the attachment of a metal to a carbon based stereogenic centre (Fig. 1, A).¹ Alternatively, differential di-substitution of metallocenes such as ferrocene (B) gives rise to planar chirality, these and other sandwich complexes having been exploited extensively in chiral ligand syntheses.² Pseudo tetrahedral half-sandwich complexes containing three different additional ligands, with either an η^5 -cyclopentadienyl (C) or an η^6 -arene ligand, contain a stereogenic metal atom.³ Although such complexes have not been utilised as building blocks for ligand synthesis, this metal-focused chirality has been exploited extensively in stoichiometric asymmetric synthesis (notably M = Re, Fe, Mo),⁴ and more recently in catalysis.⁵

Methods for the generation of enantiomerically pure chiral-at-metal half-sandwich complexes began with resolution⁶ and have been extended to diastereoselective protocols mediated either by a chiral η^5 or η^6 π -ligand, or by an introduced mono or bidentate

chiral ligand.³ Known examples of η^5 -cyclopentadienyl cobalt(III) complexes of type C have been generated by the latter procedure following ligand substitution with both neutral and anionic chiral ligands.⁷ In this Communication we report on an alternative oxidative cyclisation protocol for the highly diastereoselective and modular synthesis of cobalt-based chiral half-sandwich complexes, and on the extension of this methodology to the asymmetric synthesis of an air and configurationally stable chiral-at-cobalt complex.

Cobaltacyclopentadiene **1** is readily prepared from the reaction of chlorotris(triphenylphosphine)cobalt(i) and sodium cyclopentadienide with two equivalents of diphenylacetylene.⁸ The same reaction on a diyne containing a stereogenic centre within an acetylene tether will result in a chiral-at-metal cobaltacycle **2** (Scheme 1). Provided the reaction is diastereoselective, and the product configurationally stable, this will provide an accessible route to novel chiral organometallic building blocks.

Non-terminal linked diynes were prepared in two steps by an esterification and Sonogashira cross-coupling sequence; starting either from propargylic alcohols **3** and introduction of $\text{Ar}^2\text{C}\equiv\text{C}-$ onto **4**, or from **5** and introduction of Ar^1 onto **6** (Scheme 2). Diynes **7** were chosen for this study because of the simplicity and modularity of these procedures, and also because they are known to react with (η^5 -cyclopentadienyl)cobaltbisdicarbonyl to give planar chiral (η^5 -cyclopentadienyl)(η^5 -cyclopentadienyl)cobalt metallocenes in moderate diastereoselectivity.⁹

Reaction of **7a** (R = Me, $\text{Ar}^1 = \text{Ar}^2 = \text{Ph}$) with chlorotris(triphenylphosphine)cobalt(i) and sodium cyclopentadienide in THF heated at reflux for 30 minutes resulted in a new air-stable organometallic **8a** isolated in 44% yield following column chromatography (Scheme 3, Table 1, Method A – entry 1). As the reaction likely proceeds *via* the *in situ* formation of (η^5 -cyclopentadienyl)cobaltbis(triphenylphosphine), pre-formation and isolation of this complex¹⁰ was followed by addition of

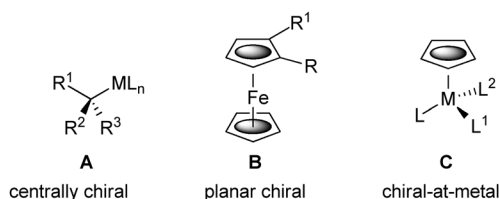
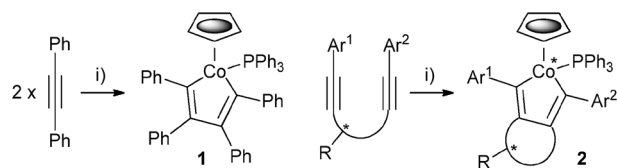


Fig. 1 Representative chiral organometallic complexes.

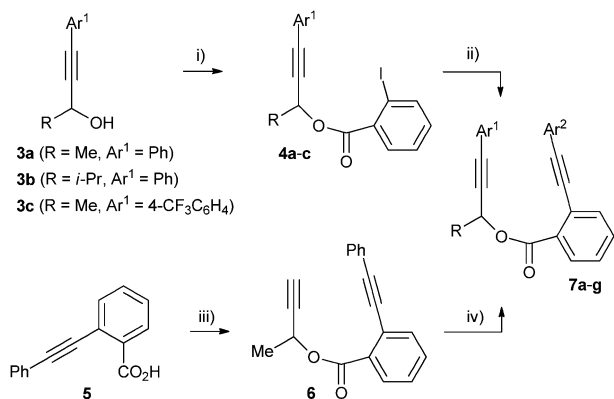
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† Electronic supplementary information (ESI) available: Experimental procedures and characterisation data for **4c**, **6**, (*S*)-**6**, (*S*)-**7a**, **7c–g**, (*S*)-**8a**, **8b–g** and **11a**, **c** and **d**. CCDC 889207 (**8a**) and 889208 (**8c**). For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c2cc34837c

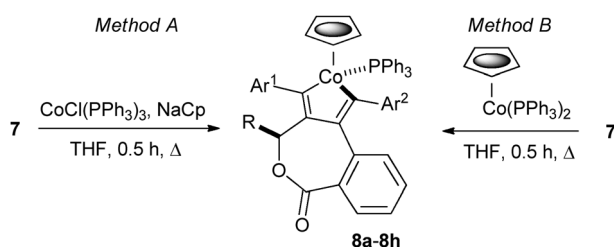


Scheme 1 Known (**1**) and proposed (**2**) products of oxidative cyclisation. Reagents and conditions: (i) NaCp, $\text{CoCl}(\text{PPh}_3)_3$, Δ .





Scheme 2 Diyne syntheses. *Reagents and conditions:* (i) 2-iodobenzoic acid (1.1 eq.), DCC (1.1 eq.), DMAP (0.2 eq.), CH₂Cl₂, RT, 48 h 92–99%. (ii) Ar²CCH (1.1 eq.), PdCl₂(PPh₃)₂ (0.03 eq.), CuI (0.1 eq.), NEt₃, 60 °C, 24 h, 93–99%. (iii) 3-butyne-2-ol (1 eq.), DCC (1.1 eq.), DMAP (0.2 eq.), CH₂Cl₂, RT, 48 h, 94%. (iv) Ar¹I (1.1 eq.), PdCl₂(PPh₃)₂ (0.03 eq.), CuI (0.1 eq.), NEt₃, 60 °C, 24 h, 99%.



Scheme 3 Diastereoselective synthesis of half-sandwich complexes **8**.

Table 1 Diastereoselective synthesis of half-sandwich complexes **8**

| Entry/ diyne | R | Ar ¹ | Ar ² | Method | Product/ yield ^a (%) |
|-----------------|--------------|---|---|--------|------------------------------------|
| 1 7a | Me | Ph | Ph | A | 8a 44 |
| 2 7a | Me | Ph | Ph | B | 8a 75 |
| 3 7b | <i>i</i> -Pr | Ph | Ph | A | 8b 55 |
| 4 7b | <i>i</i> -Pr | Ph | Ph | B | 8b 79 |
| 5 7c | Me | 4-CF ₃ C ₆ H ₄ | Ph | A | 8c 78 |
| 6 7d | Me | Ph | 4-CF ₃ C ₆ H ₄ | A | 8d 72 |
| 7 7e | Me | Ph | 3-C ₃ H ₄ N | B | 8e 89 |
| 8 7f | Me | 2-BrC ₆ H ₄ | Ph | A | 8f 73 |
| 9 7g | Me | 2-Cl-5-C ₃ H ₃ N | Ph | B | 8g 78 |

^a Isolated by column chromatography.

7a and heating in THF as before to give **8a** in 75% yield (Method B – entry 2).

Examination of both crude and column isolated **8a** by ¹H NMR spectroscopy revealed four sets of signals in a 11 : 1.5 : 1 : 1 ratio. Following recrystallisation of **8a** the same ratio of signals was observed when the spectrum was recorded within minutes of dissolving the crystals in CDCl₃ at room temperature (20 °C). No change in this ratio was observed over time. The multiplicity of signals in the ¹H NMR pointed to the possibility that these may, in part, result from rapid epimerisation of the metal-based stereogenic centre.¹¹ Stereochemical lability in η⁵-cyclopentadienyl piano-stool complexes **C** is a consequence of facile ligand dissociation.³ For example, epimerisation of the related isoelectronic chiral-at-metal complex (η⁵-cyclopentadienyl)FeCH₃(CO)PPh₂R* (half-life 70 min at 70 °C) proceeds

by phosphine dissociation and formation of a planar 16-electron intermediate.¹² Addition of 1.5 eq. of tri(*p*-tolyl)phosphine to **8a** in CDCl₃ at room temperature and recording the ¹H NMR spectrum after 1 h revealed the presence of only **8a**/tri(*p*-tolyl)phosphine and no new ligand substitution complex. An X-ray structure analysis of **8a** confirmed the anticipated cobaltacycle half-sandwich structure, and revealed the relative configuration as S_{Co}*, S_C* (Fig. 2).¹³

That facile phosphine substitution is not occurring with **8a** reveals that the S_{Co}*, S_C* configuration is maintained in solution and that a single chiral-at-metal diastereoisomer results from oxidative cyclisation *via* an intermediate planar¹⁴ 16 electron (η⁵-cyclopentadienyl)cobaltacyclopentadiene. Coordination of triphenylphosphine opposite the methyl group dictates the configuration of the metal-based chirality.

The solution isomerism is ascribed to the two other elements of chirality present in **8a**. Three-atom linked biphenyls **9** interconvert rapidly between atropisomers¹⁵ containing either an equatorial or axial R substituent, the lowest energy arrangement being dependent upon the identity of X, Y and R (Scheme 4).¹⁶ The X-ray structure of **8a** reveals an axial methyl group and an R_a* configuration with the cobaltacyclopentadiene moiety replacing the bottom phenyl group of **9**. The propeller-like arrangement of the phenyl rings of a metal-coordinated triphenylphosphine complex **10** result in *M* and *P*-configurations which give rise to diastereoisomers with chiral-at-metal half-sandwich complexes.¹⁷ Although the barrier to intramolecular interconversion is usually low, occurring by a two ring-flip

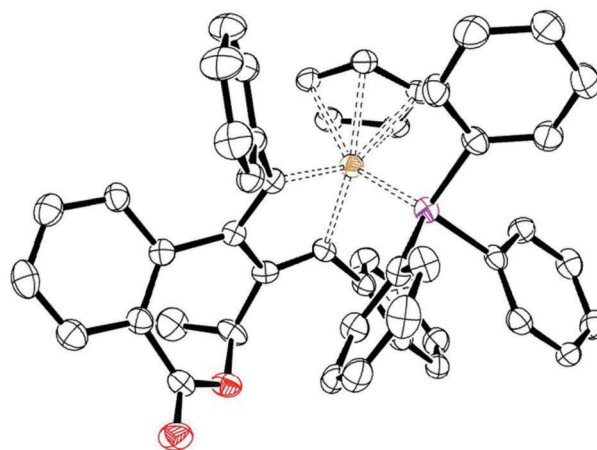
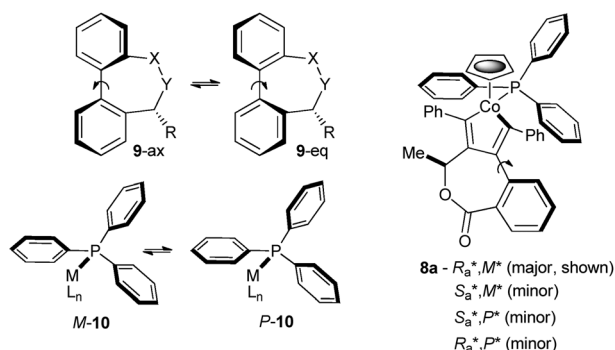
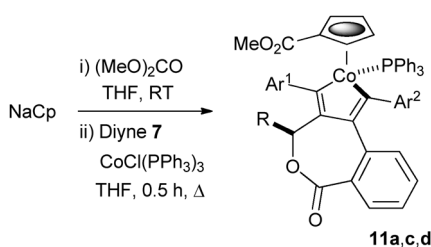


Fig. 2 X-ray crystal structure of S_{Co}*, S_C* **8a**.



Scheme 4 Isomerism of **9**, **10** and extension to S_{Co}*, S_C* **8a**.





Scheme 5 Diastereoselective synthesis of carbomethoxy substituted half-sandwich complexes **11**.

Table 2 Diastereoselective synthesis of carbomethoxy substituted half-sandwich complexes **11**

| Entry/diyne | R | Ar ¹ | Ar ² | Product/yield ^a (%) |
|-------------|----|---|---|--------------------------------|
| 1 7a | Me | Ph | Ph | 11a 64 |
| 3 7c | Me | 4-CF ₃ C ₆ H ₄ | Ph | 11c 49 |
| 4 7d | Me | Ph | 4-CF ₃ C ₆ H ₄ | 11d 65 |

^a Isolated by column chromatography.

mechanism,^{17a,18} isolable *M* and *P* epimers have been obtained with a bulky chiral bidentate ligand, epimerisation occurring *via* reversible phosphine dissociation.¹⁹ Further examination of the X-ray structure reveals an *M*^{*} configuration,²⁰ and assuming the maintenance of this *R*_a^{*}, *M*^{*}-structure as the dominant species in solution, isomerisation gives rise to the three minor isomers listed in Scheme 4.²¹ In contrast, the isopropyl substituted complex **8b**, prepared by both Methods A and B (entries 3 and 4), resulted in only a single observable stereoisomer in solution, a consequence of the greater conformational control imparted by the larger isopropyl group.

A number of other complexes were prepared in good yield (**8c–8g**, entries 5–9), including examples with pyridyl ligand substituents (**8e**, **8g**), and a complex with a 2-bromophenyl substituent (**8f**) with the potential for further functionalisation. Like parent methyl substituted complex **8a**, all of these gave four solution species with one dominant (*e.g.* 11 : 1 : 1 : 1 for **8c** – see ESI[†]), and the X-ray structure of **8c** reveals the same configuration for all four elements of chirality (*S*_{Co}^{*}, *S*_C^{*}, *R*_a^{*}, *M*^{*}).

Ester substituted cyclopentadienyl complexes were readily prepared following *in situ* generation of sodium carbomethoxycyclopentadienide (Scheme 5, Table 2).²² As before, these complexes containing a methyl substituted stereogenic centre derived from **7a**, **7c** and **7d** resulted in up to four solution stereoisomers.

A non-racemic sample of **8a** was synthesised starting with commercially available (*S*)-3-butyn-2-ol. Following ester formation with **5** as outlined in Scheme 2 (96%), followed by Sonogashira coupling with iodobenzene (>99%), (*S*)-**7a** was complexed by Method B to give (*S*)-**8a** in 74% yield. Chiral HPLC analysis gave a single peak in contrast to the two well separated peaks observed for racemic **8a**. These results are consistent with the observation of four solution species of **8a** by NMR spectroscopy at room temperature where interconversion between these species is rapid. Essentially no difference was observed in the ¹H NMR of **8a** recorded at 60 °C,²³ and heating at higher temperatures resulted in decomposition. This is in marked contrast to **1** where heating at reflux in toluene results

in phosphine dissociation and clean formation of (η⁵-cyclopentadienyl)(η⁴-tetraphenylcyclobutadiene)cobalt.⁸

In conclusion, we have demonstrated a short highly diastereoselective modular synthesis of new air-stable cobalt-based chiral-at-metal half-sandwich complexes obtained by oxidative cyclisation. The methodology is applicable to both substituted or unsubstituted cyclopentadienyl ligands and was readily adapted to the synthesis of a configurationally stable single enantiomer. These complexes provide an alternative to chiral metallocene frameworks as the basis of novel ligands, catalysts and materials.

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