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## COMMUNICATION

## 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 ( $\eta^5$ -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).<sup>1</sup> 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.<sup>2</sup> Pseudo tetrahedral half-sandwich complexes containing three different additional ligands, with either an  $\eta^5$ -cyclopentadienyl (C) or an  $\eta^6$ -arene ligand, contain a stereogenic metal atom.<sup>3</sup> 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),<sup>4</sup> and more recently in catalysis.<sup>5</sup>

Methods for the generation of enantiomerically pure chiral-at-metal half-sandwich complexes began with resolution<sup>6</sup> and have been extended to diastereoselective protocols mediated either by a chiral  $\eta^5$  or  $\eta^6$   $\pi$ -ligand, or by an introduced mono or bidentate

chiral ligand.<sup>3</sup> Known examples of  $\eta^5$ -cyclopentadienyl cobalt(III) complexes of type C have been generated by the latter procedure following ligand substitution with both neutral and anionic chiral ligands.<sup>7</sup> 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.<sup>8</sup> 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  $\text{Ar}^1$  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 ( $\eta^5$ -cyclopentadienyl)cobalt dicarbonyl to give planar chiral ( $\eta^5$ -cyclopentadienone)( $\eta^5$ -cyclopentadienyl)cobalt metallocenes in moderate diastereoselectivity.<sup>9</sup>

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 ( $\eta^5$ -cyclopentadienyl)cobaltbis(triphenylphosphine), pre-formation and isolation of this complex<sup>10</sup> was followed by addition of

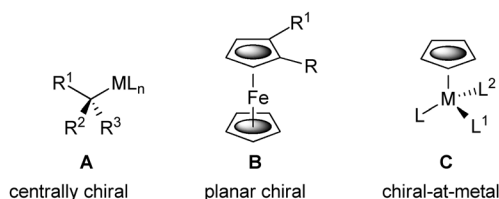
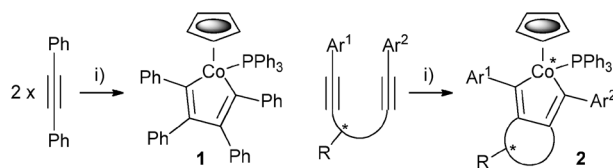


Fig. 1 Representative chiral organometallic complexes.

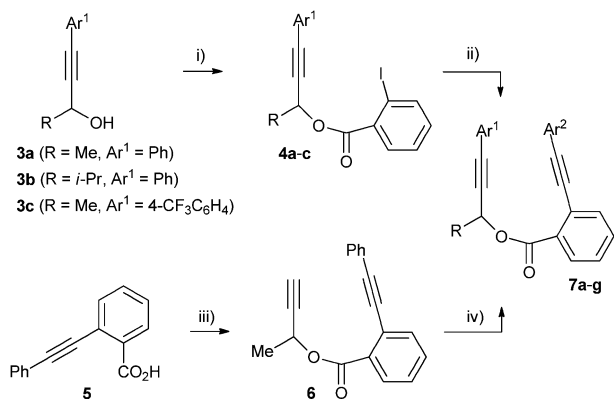
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† Electronic supplementary information (ESI) available: Experimental procedures and characterisation data for **4c**, **6**, (*S*)-**6**, (*S*)-**7a**, **7c–g**, (*S*)-**8a**, **8b–g** and **11a**, **c** and **d**. CCDC 889207 (**8a**) and 889208 (**8c**).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

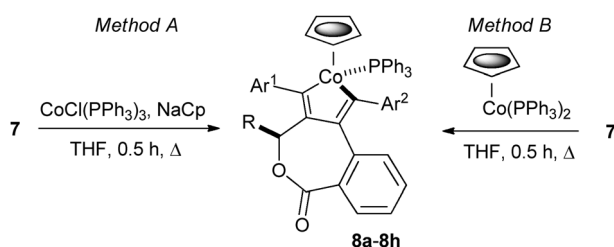


Scheme 1 Known (**1**) and proposed (**2**) products of oxidative cyclisation. Reagents and conditions: (i) NaCp,  $\text{CoCl}(\text{PPh}_3)_3$ ,  $\Delta$ .





**Scheme 2** Diyne syntheses. *Reagents and conditions:* (i) 2-iodobenzoic acid (1.1 eq.), DCC (1.1 eq.), DMAP (0.2 eq.), CH<sub>2</sub>Cl<sub>2</sub>, RT, 48 h 92–99%. (ii) Ar<sup>2</sup>CCH (1.1 eq.), PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub> (0.03 eq.), CuI (0.1 eq.), NEt<sub>3</sub>, 60 °C, 24 h, 93–99%. (iii) 3-butyne-2-ol (1 eq.), DCC (1.1 eq.), DMAP (0.2 eq.), CH<sub>2</sub>Cl<sub>2</sub>, RT, 48 h, 94%. (iv) Ar<sup>1</sup>I (1.1 eq.), PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub> (0.03 eq.), CuI (0.1 eq.), NEt<sub>3</sub>, 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 <sup>1</sup>	Ar <sup>2</sup>	Method	Product/ yield <sup>a</sup> (%)
1 <b>7a</b>	Me	Ph	Ph	A	<b>8a</b> 44
2 <b>7a</b>	Me	Ph	Ph	B	<b>8a</b> 75
3 <b>7b</b>	<i>i</i> -Pr	Ph	Ph	A	<b>8b</b> 55
4 <b>7b</b>	<i>i</i> -Pr	Ph	Ph	B	<b>8b</b> 79
5 <b>7c</b>	Me	4-CF <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	Ph	A	<b>8c</b> 78
6 <b>7d</b>	Me	Ph	4-CF <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	A	<b>8d</b> 72
7 <b>7e</b>	Me	Ph	3-C <sub>3</sub> H <sub>4</sub> N	B	<b>8e</b> 89
8 <b>7f</b>	Me	2-BrC <sub>6</sub> H <sub>4</sub>	Ph	A	<b>8f</b> 73
9 <b>7g</b>	Me	2-Cl-5-C <sub>3</sub> H <sub>3</sub> N	Ph	B	<b>8g</b> 78

<sup>a</sup> Isolated by column chromatography.

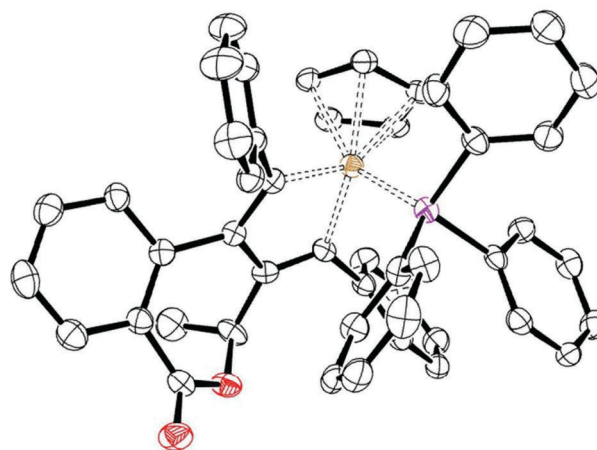
**7a** and heating in THF as before to give **8a** in 75% yield (Method B – entry 2).

Examination of both crude and column isolated **8a** by <sup>1</sup>H 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 CDCl<sub>3</sub> at room temperature (20 °C). No change in this ratio was observed over time. The multiplicity of signals in the <sup>1</sup>H NMR pointed to the possibility that these may, in part, result from rapid epimerisation of the metal-based stereogenic centre.<sup>11</sup> Stereochemical lability in η<sup>5</sup>-cyclopentadienyl piano-stool complexes **C** is a consequence of facile ligand dissociation.<sup>3</sup> For example, epimerisation of the related isoelectronic chiral-at-metal complex (η<sup>5</sup>-cyclopentadienyl)FeCH<sub>3</sub>(CO)PPh<sub>2</sub>R\* (half-life 70 min at 70 °C) proceeds

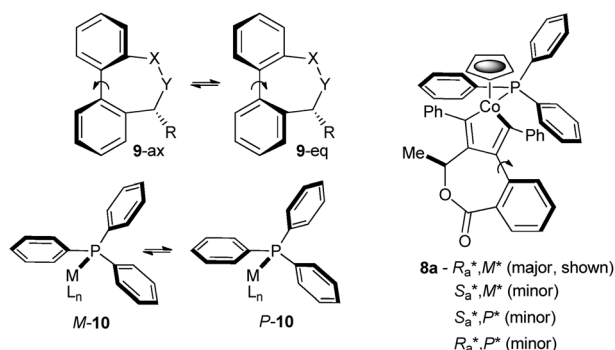
by phosphine dissociation and formation of a planar 16-electron intermediate.<sup>12</sup> Addition of 1.5 eq. of tri(*p*-tolyl)phosphine to **8a** in CDCl<sub>3</sub> at room temperature and recording the <sup>1</sup>H NMR spectrum after 1 h revealed the presence of only **8a**/tri(*p*-tolyl)phosphine 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<sub>Co</sub>\*, S<sub>C</sub>\* (Fig. 2).<sup>13</sup>

That facile phosphine substitution is not occurring with **8a** reveals that the S<sub>Co</sub>\*, S<sub>C</sub>\* configuration is maintained in solution and that a single chiral-at-metal diastereoisomer results from oxidative cyclisation *via* an intermediate planar<sup>14</sup> 16 electron (η<sup>5</sup>-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 atropisomers<sup>15</sup> containing either an equatorial or axial R substituent, the lowest energy arrangement being dependent upon the identity of X, Y and R (Scheme 4).<sup>16</sup> The X-ray structure of **8a** reveals an axial methyl group and an R<sub>a</sub>\* 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.<sup>17</sup> Although the barrier to intramolecular interconversion is usually low, occurring by a two ring-flip

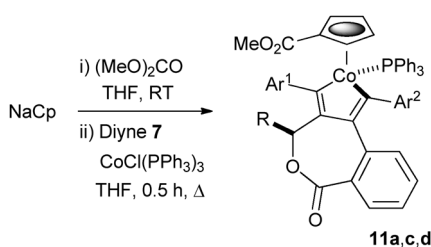


**Fig. 2** X-ray crystal structure of S<sub>Co</sub>\*, S<sub>C</sub>\* **8a**.



**Scheme 4** Isomerism of **9**, **10** and extension to S<sub>Co</sub>\*, S<sub>C</sub>\* **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 <sup>1</sup>	Ar <sup>2</sup>	Product/yield <sup>a</sup> (%)
1 <b>7a</b>	Me	Ph	Ph	<b>11a</b> 64
3 <b>7c</b>	Me	4-CF <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	Ph	<b>11c</b> 49
4 <b>7d</b>	Me	Ph	4-CF <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	<b>11d</b> 65

<sup>a</sup> Isolated by column chromatography.

mechanism,<sup>17a,18</sup> isolable *M* and *P* epimers have been obtained with a bulky chiral bidentate ligand, epimerisation occurring *via* reversible phosphine dissociation.<sup>19</sup> Further examination of the X-ray structure reveals an *M*<sup>\*</sup> configuration,<sup>20</sup> and assuming the maintenance of this *R*<sub>a</sub><sup>\*</sup>, *M*<sup>\*</sup>-structure as the dominant species in solution, isomerisation gives rise to the three minor isomers listed in Scheme 4.<sup>21</sup> 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<sup>†</sup>), and the X-ray structure of **8c** reveals the same configuration for all four elements of chirality (*S*<sub>Co</sub><sup>\*</sup>, *S*<sub>C</sub><sup>\*</sup>, *R*<sub>a</sub><sup>\*</sup>, *M*<sup>\*</sup>).

Ester substituted cyclopentadienyl complexes were readily prepared following *in situ* generation of sodium carbomethoxycyclopentadienide (Scheme 5, Table 2).<sup>22</sup> 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 <sup>1</sup>H NMR of **8a** recorded at 60 °C,<sup>23</sup> 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 (η<sup>5</sup>-cyclopentadienyl)(η<sup>4</sup>-tetraphenylcyclobutadiene)cobalt.<sup>8</sup>

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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