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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(1) 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-atmetal half-sandwich complexes began with resolution⁶ and have been extended to diastereoselective protocols mediated either by a chiral η^5 or $\eta^6 \pi$ -ligand, or by an introduced mono or bidentate



Fig. 1 Representative chiral organometallic complexes.

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(1) 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 $Ar^{2}C \equiv C$ - 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)cobaltdicarbonyl to give planar chiral (η^{5} -cyclopentadienone)(η^{5} -cyclopentadienyl)cobalt metallocenes in moderate diastereoselectivity.⁹

Reaction of **7a** ($\mathbf{R} = \mathbf{Me}$, $\mathbf{Ar}^1 = \mathbf{Ar}^2 = \mathbf{Ph}$) with chlorotris(triphenylphosphine)cobalt(1) 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



Scheme 1 Known (1) and proposed (2) products of oxidative cyclisation. *Reagents and conditions:* (i) NaCp, CoCl(PPh₃)₃, *Δ*.

School of Chemistry, University of East Anglia, Norwich Research Park, Norwich, NR4 7TJ, UK. E-mail: Chris.Richards@uea.ac.uk; Fax: +44 (0)1603 592003; Tel: +44 (0)1603 592003 † 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 2 Diyne syntheses. *Reagents and conditions*: (i) 2-iodobenzoic acid (1.1 eq.), DCC (1.1 eq.), DMAP (0.2 eq.), CH_2Cl_2 , RT, 48 h 92–99%. (ii) Ar²CCH (1.1 eq.), $PdCl_2(PPh_3)_2$ (0.03 eq.), CuI (0.1 eq.), NEt₃, 60 °C, 24 h, 93–99%. (iii) 3-butyn-2-ol (1 eq.), DCC (1.1 eq.), DMAP (0.2 eq.), CH_2Cl_2 , RT, 48 h, 94%. (iv) Ar¹I (1.1 eq.), $PdCl_2(PPh_3)_2$ (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 7 a	Me	Ph	Ph	А	8a 44			
2 7a	Me	Ph	Ph	В	8a 75			
3 7b	<i>i</i> -Pr	Ph	Ph	А	8b 55			
4 7b	<i>i</i> -Pr	Ph	Ph	В	8b 79			
5 7c	Me	$4-CF_3C_6H_4$	Ph	А	8c 78			
6 7d	Me	Ph	$4-CF_3C_6H_4$	А	8d 72			
7 7 e	Me	Ph	$3-C_5H_4N$	В	8e 89			
8 7f	Me	2-BrC ₆ H ₄	Ph	А	8f 73			
9 7g	Me	2 -Cl- 5 -C $_5$ H $_3$ N	Ph	В	8g 78			
^{<i>a</i>} 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 η^5 -cyclopentadienyl piano-stool complexes **C** is a consequence of facile ligand dissociation.³ For example, epimerisation of the related isoelectronic chiral-at-metal complex (η^5 -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 (η^5 -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 halfsandwich 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	$4\text{-}CF_3C_6H_4$	11d 65
^{<i>a</i>} Isolated by	colum	n chromatogra	iphy.	

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 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 $(\eta^5$ -cyclopentadienyl) $(\eta^4$ -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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