Stereochemical and mechanistic features of asymmetric Pauson–Khand processes

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Received (in Cambridge, UK) 9th August 2000, Accepted 19th October 2000
First published as an Advance Article on the web 30th November 2000

The absolute stereochemical configurations of a series of optically pure alkyne–$Co_2(CO)_5PPh_3$ complexes and their corresponding cyclopentenones, derived from Pauson–Khand reaction with norbornene, have been established; an X-ray crystal structure of an optically pure cyclopentenone has facilitated this study. In turn, this has led to the unambiguous determination of the site of decarbonylation and alkene complexation when such monophosphine complexes are utilised in asymmetric Pauson–Khand processes.

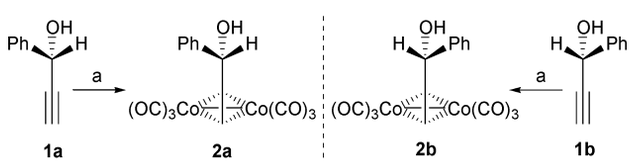
Introduction

The Pauson–Khand (P–K) reaction[1] is a powerful method for the regioselective construction of cyclopentenones from alkynes, *via* their hexacarbonyldicobalt complexes, and alkenes. Indeed, many developments of this annulation methodology have now been reported[2] and foremost amongst these advances has been the use of amine *N*-oxides[3] as reaction promoters. Use of these additives allow transformations to proceed in generally high yields under relatively mild reaction conditions. Consequently, this has widely increased the synthetic utility of the P–K process[1] and, in turn, catalytic[4] and asymmetric[1a–c,5] variants of the reaction have also now been developed.

Until recently, the asymmetric methodology developed for the intermolecular P–K reaction had either utilised diastereomerically pure alkyne–$Co_2(CO)_5PR_3$ complexes,[6] chiral auxiliaries,[7] or a combination of both.[8] On the other hand, in the first direct enantioselective variant of this reaction, ongoing work in our laboratory has focused on the use of chiral amine *N*-oxides to promote and induce asymmetry in the P–K annulation.[9] In particular, we have shown that the use of brucine *N*-oxide (BNO) delivers appreciable levels of enantioselectivity in cyclopentenone formation directly from prochiral alkyne–$Co_2(CO)_6$ complexes.[10] Moreover, the use of BNO in the formation of enantiomerically enriched, chiral alkyne–$Co_2(CO)_5PR_3$ complexes, and the employment of these pentacarbonyl species in subsequent P–K processes, has allowed us to form cyclopentenones enriched in the opposite enantiomer;[11] *i.e.* using these protocols, each cyclopentenone enantiomer may be selectively synthesised using a single source of chirality (BNO). Therefore, it is clear from this work, as well as our previous studies,[6a,b] that chiral $Co_2(CO)_5PR_3$–alkyne complexes have considerable potential for use in asymmetric organic synthesis.† Furthermore, it was envisaged that the reactivity of such configurationally stable, optically enriched species could provide a more detailed insight into the enantioselection observed within our asymmetric P–K processes. In this paper we now detail our observations in this area and, additionally, for the first time show how the absolute stereochemistry at the newly created cyclopentenone stereogenic centres, from our enantioselective P–K processes, have been established.

Results and discussion

In order to initiate our studies, we decided to utilise an alkyne with an asymmetric centre of known configuration on the side chain. Commercially available (*R*)-(−)-**1a** and (*S*)-(+)-1-phenylprop-2-yn-1-ol **1b** were selected as suitable substrates and converted to their corresponding enantiomeric complexes **2a** and **2b** in good yield under mild conditions (Scheme 1).



Scheme 1 *Reagents and conditions*: (a) $Co_2(CO)_8$, petrol, rt; 72% for **2a**, 76% for **2b**.

With the enantiomerically pure compounds **2a/b** in hand, we then planned to investigate the use of amine *N*-oxides in the formation of the corresponding monophosphine complexes. In this respect it had previously been shown that, using a $Co_2(CO)_6$ complex generated from racemic alkyne, formation of the equivalent $Co_2(CO)_5PPh_3$ species under thermal conditions had resulted in complexes which were diastereomeric.[12a] Indeed, this work by Nicholas and co-workers, which had established the relative configurations of the two diastereomeric complexes **3** and **4** by an X-ray structural determination (of the first chromatographically eluting isomer **3**),‡ enabled us to rapidly and confidently determine the stereochemical outcome of our subsequent *N*-oxide promoted studies.

† Other workers have also prepared, and in some instances used, phosphorus containing alkyne–$Co_2(CO)_5$ complexes which possess some degree of stereogenicity.[6c,d,8a,12]

‡ In the major diastereomer produced under thermal conditions (as shown in Scheme 2 for **3a** and **3b**), with the propargylic hydroxy group aligned towards the C_2Co_2 cluster, the PPh_3 ligand occupied the *apical* (axial and *trans* to the Co–Co bond) Co co-ordination site oriented "away" from the bulky phenyl group at the propargylic centre.

 DOI: 10.1039/b006523o

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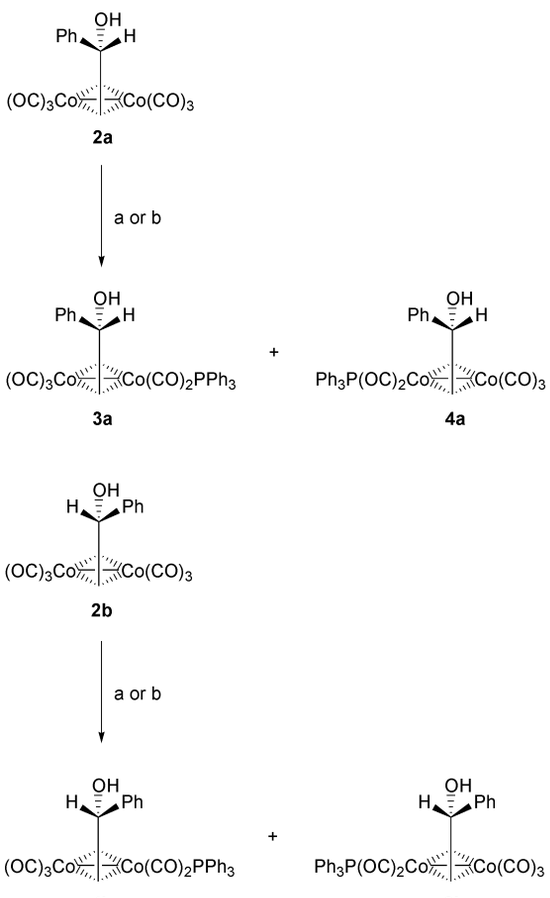
In due course, individually employing the enantiomerically pure hexacarbonyl compounds **2a** and **2b** under achiral *N*-oxide mediated reaction conditions, with anhydrous *N*-methylmorpholine *N*-oxide (NMO) at low temperature (−60 °C), showed no diastereoselectivity in the formation of complexes **3a**, **4a** and **3b**, **4b**. This indicated that, at this temperature, there is no preferred site of phosphine co-ordination. In turn, use of a chiral *N*-oxide (BNO), somewhat surprisingly, gave a similar result with no significant stereoselection being observed in the case of complex **2b**. On the other hand, with complex **2a**, a 70 : 30 ratio of diastereomers **3a** : **4a** was consistently obtained (Scheme 2).



Scheme 2 *Reagents and conditions*: (a) NMO, PPh_3, THF, −60 °C; 98% (51 : 49 **3a** : **4a**) from complex **2a**; 95% (50 : 50 **3b** : **4b**) from complex **2b**; (b) BNO, PPh_3, THF, −59 °C; 66% (70 : 30 **3a** : **4a**) from complex **2a**; 77% (49 : 51 **3b** : **4b**) from complex **2b**.

Whilst, at this stage, it is not possible to formulate a definitive explanation for these observations, the origin of the stereoselectivity in the case of complex **2a** is believed to be due to a matching interaction of the chiral *N*-oxide with the propargylic§ stereocentre, in combination with the Co_2C_2 complex core. It then follows that the lack of selectivity observed in the case of complex **2b** is, in contrast, due to a mismatching of the selectivities arising from the interactions of the *N*-oxide and propargylic stereocentres.

Despite the lower than anticipated selectivities observed in the phosphination reactions, diastereomeric mixtures of complexes **3a**, **4a** and **3b**, **4b** had been readily prepared. Moreover, since optically pure alkynes had been used, simple flash column chromatography enabled us to assess each stereoisomeric complex as a single enantiomer. Furthermore, as the absolute configuration at the propargylic carbon was known, this allowed us to assign the absolute configuration of all four chiral complexes **3a**–**4b**. Optical rotation measurements and

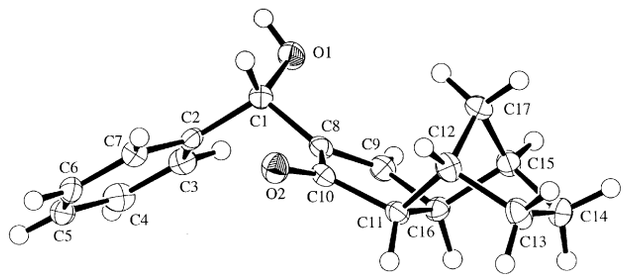
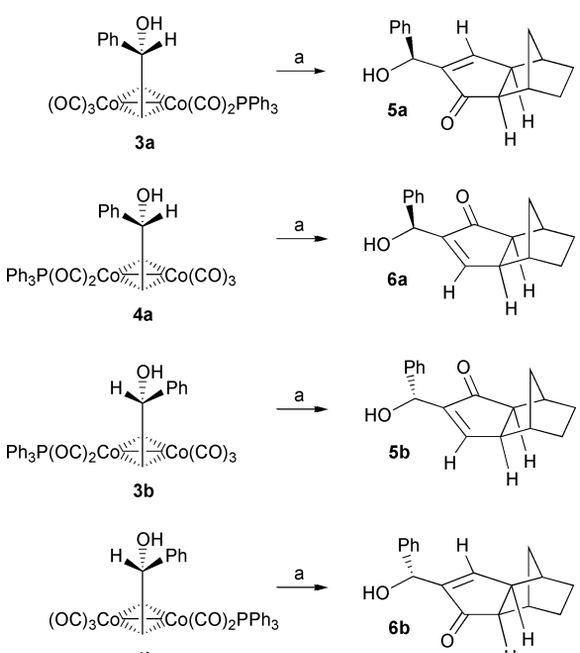


Fig. 1 X-Ray crystallographic representation of the single enantiomer, (3a*R*,4*R*,7*S*,7a*R*,1′*S*)-(−)-3a,4,5,6,7,7a-hexahydro-2-(1′-hydroxy-1′-phenylmethyl)-4,7-methano-1*H*-inden-1-one **5a**.

chromatographic behaviour confirmed that, as expected, the pairs of chiral complexes **3a**, **3b** and **4a**, **4b** were enantiomeric, with ^{1}H NMR and FTIR data corresponding to that previously reported for the corresponding racemic complexes.[12a]

Having gained access to stereopure samples of each complex **3a**–**4b**, we then envisaged that investigation of their corresponding P–K cyclisations, mediated by an achiral *N*-oxide, may offer some insight into the mechanistic behaviour of these preparatively important monophosphine species.[6,8a,11] In due course it was found that, using norbornene¶ with anhydrous NMO at room temperature, each complex was converted into a single cyclopentenone stereoisomer (Scheme 3). Once again, optical



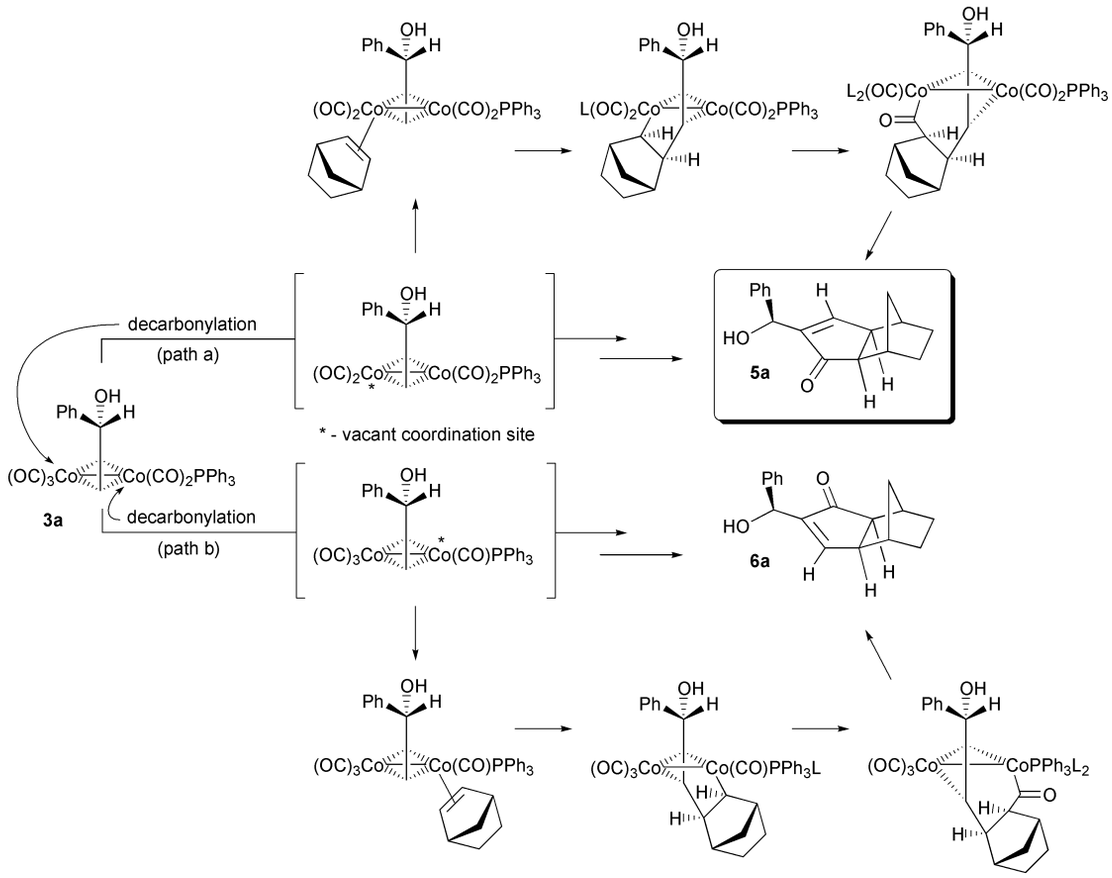
Scheme 3 *Reagents and conditions*: (a) norbornene, NMO, DCM, rt; 77% for **5a**, 40% for **6a**, 69% for **5b**, 58% for **6b**.

rotation measurements and chromatographic elution confirmed that the cyclopentenone pairs **5a**, **5b** and **6a**, **6b** were enantiomeric. Furthermore, to fully establish the stereochemical outcome of the P–K processes, crystals of **5a** were grown by slow evaporation from a petrol–ether solution and the resulting X-ray structure was determined; the X-ray representation, with the stereochemistry of the two new cyclopentenone stereogenic centres explicitly shown, is depicted in Fig. 1. Subsequently, this crystallographic study allowed the assignment of the complete absolute configuration not only of **5a**, but also of the other three cyclopentenone stereoisomers **5b**, **6a**, **6b** (Scheme 3).

With the absolute configurations of all four $Co_2(CO)_5PPh_3$ complexes and the corresponding cyclopentenones resulting from their subsequent P–K reactions established, it was now

§ The IUPAC name for propargyl is prop-2-ynyl.

¶ The IUPAC name for norbornene is bicyclo[2.2.1]hept-2-ene.

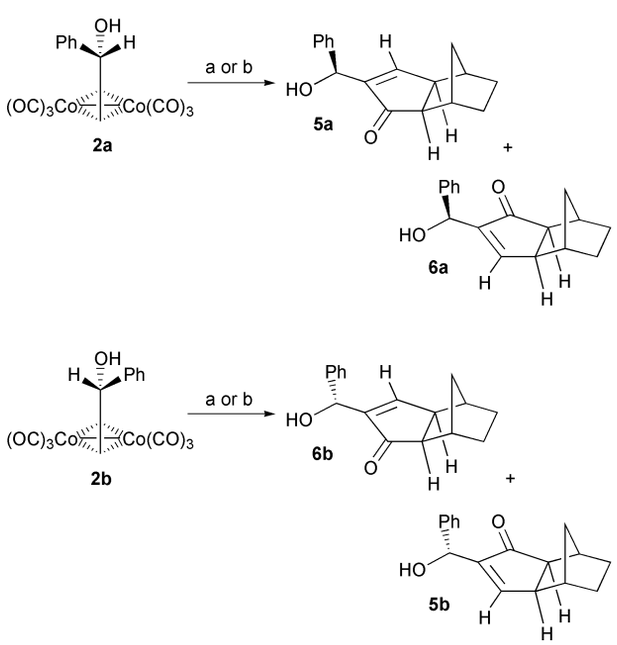


Scheme 4

possible to unambiguously demonstrate for the first time that, with such monophosphine complexes, it is the $Co(CO)_3$ vertex, as opposed to the $Co(CO)_2PPh_3$ unit, at which decarbonylation, alkene co-ordination, and subsequent reaction takes place.[6a] This is demonstrated explicitly for the case of complex **3a** in Scheme 4, whereby the only observed cyclopentenone product **5a** is produced as a result of exclusive reaction *via* path a. More specifically, following complexation of the *exo*-face of norbornene to the vacant coordination site, insertion of the complexed alkene into the last hindered carbon–cobalt bond, CO insertion, and reductive elimination leads to cyclopentenone **5a**; L refers to solvent or an alternative stabilising (2-electron) ligand. Reaction at the alternative cobalt vertex, and proceeding by the analogous mechanistic process, would deliver product **6a**.‖

This mechanistic rationale is consistent with the notion that the PPh_3 ligand increases the Co–CO bond order, presumably *via* σ-donation from the phosphine ligand to the cobalt centre and a subsequent increase in π-backbonding with the carbonyl ligands. This hypothesis is supported by a characteristic decrease in wavenumber (30 to 50 cm^{-1}) of FTIR bands in the metal carbonyl stretching region indicating a shift from C≅O to C=O character of the $Co_2(CO)_5PPh_3$ complexes relative to their $Co_2(CO)_6$ analogues. In turn, these factors strengthen the Co–CO bonding at the $Co(CO)_2PPh_3$ vertex, deactivating this site towards decarbonylation. It should also be noted that the markedly more sluggish nature of these alkyne–$Co_2(CO)_5PPh_3$ complexes in P–K reactions, relative to their $Co_2(CO)_6$ counterparts, suggests that there is also some increase in Co–CO bond order at the $Co(CO)_3$ vertex, presumably through transfer of electron density through the Co–Co orbital overlap.

With our increased mechanistic understanding and the absolute configurations of the cyclopentenones established, our attention was then turned to the corresponding *N*-oxide promoted P–K reactions of the parent $Co_2(CO)_6$ complexes. Under both achiral (NMO) and chiral (BNO) *N*-oxide mediated conditions with norbornene at low temperature, we have found that identical levels of diastereoselection (≈30 : 70 dr) were observed in cyclopentenone formation (Scheme 5). In each case, it appears that the propargylic stereocentre is the



Scheme 5 *Reagents and conditions*: (a) norbornene, NMO, acetone, −60 °C; 83% (28 : 72 **5a** : **6a**) from complex **2a**; 79% (29 : 71 **5b** : **6b**) from complex **2b**; (b) norbornene, BNO, acetone, −58 °C; 49% (30 : 70 **5a** : **6a**) from complex **2a**; 61% (31 : 69 **5b** : **6b**) from complex **2b**.

‖ Following the submission of this paper, elegant studies by Castro *et al.* have appeared in the literature and have also shown how decarbonylation and reaction at the $Co(CO)_3$ vertex of alternative monophosphine complexes has been elucidated and, in turn, how the absolute configuration of a series of P–K adducts has been determined; see ref. 13.

controlling feature in these reactions. Furthermore, based on the absolute configurations which have been established as part of this programme, it is clear that it is the $Co(CO)_3$ vertex aligned "away" from the bulky Ph substituent which is being preferentially decarbonylated in each case. Therefore, from these results it is clear that no chiral match/mismatch situation between the propargylic stereocentre and the chiral *N*-oxide is observed in the direct P–K processes.

Through the determination of the absolute stereochemistry of optically pure alkyne–$Co_2(CO)_5PPh_3$ complexes and of the cyclopentenones derived from their corresponding P–K reactions, these studies have now explicitly demonstrated that decarbonylation and alkene complexation occurs exclusively at the $Co(CO)_3$ vertex in monophosphinated alkyne complexes when employed in P–K annulations. With our enhanced understanding of the mechanistic and stereochemical features of the processes described here, work is currently underway in our laboratories to improve the attainable levels of enantioselection in the powerful and direct asymmetric variant of the Pauson–Khand cyclisation.

Experimental

General

Infrared spectra were obtained using a Nicolet Impact 400D FTIR spectrometer and NMR spectra were recorded on a 250 MHz Bruker WM250 or a 400 MHz Bruker WM400 machine referenced to $CDCl_3$. All NMR coupling constants are quoted in hertz and represent ^1H–^1H interactions unless otherwise stated. High resolution mass spectra were recorded on a JEOL instruments JMS-AX505HA mass spectrometer system. Elemental analysis was carried out using a Carlo Erba 1106 CHN analyser. UV spectra were recorded on a Philips PU 8720 UV/VIS Scanning Spectrophotometer. Melting points were obtained on an electrothermal melting point apparatus using open capillaries and are uncorrected. Optical rotation measurements were carried out using a Perkin-Elmer 341 Polarimeter. Chromatographic separations were performed on silica gel (230–400 mesh) using flash technique. Thin layer chromatography was carried out using Camlab silica plates coated with UV_{254}, a fluorescent indicator, and analysed using a Mineralight UVGL-25 lamp or developed using potassium permanganate or MOLY (ammonium molybdate reagent) dip. HPLC was carried out using a CHIRACEL-OD-H (normal phase) chiral column with sample loading of 1 mg ml^{-1} unless otherwise stated. A Waters 501 HPLC pump and a Waters 484 tuneable absorbance detector (at 230 nm) were used with data processed using a Waters 746 data mobile. All reactions were carried out under a nitrogen atmosphere with dry, freshly distilled solvents. Petrol refers to petroleum ether (bp 30–40 °C) which was distilled prior to use. Tetrahydrofuran and ether were distilled from sodium–benzophenone and DCM was distilled from calcium hydride. Norbornene was sublimed under vacuum (1 mmHg) and triphenylphosphine was recrystallised from methanol. Anhydrous *N*-methylmorpholine *N*-oxide was prepared by double recrystallisation of *N*-methylmorpholine *N*-oxide from acetone and heating of the resultant crystals under vacuum for 2 hours (90 °C, 7 mmHg). The resultant white crystalline solid was stored at −20 °C under a nitrogen atmosphere. All cobalt complexes were stored under nitrogen at −20 °C.

General procedure (A) for formation of hexacarbonylalkynedicobalt complexes

All apparatus was oven dried and cooled under nitrogen before use. Octacarbonyldicobalt was weighed into a 50 ml Schlenk flask under nitrogen and dissolved in petrol. The resulting solution was stirred for 5 min at room temperature and then a solution of the alkyne in petrol was added dropwise, causing rapid evolution of carbon monoxide. The reaction flask was purged with nitrogen and stirred at room temperature. When TLC indicated that no alkyne remained, the reaction was worked up by filtration through a pad of silica under vacuum. Purification was carried out using flash column chromatography on silica eluting with petrol, to remove any unreacted octacarbonyldicobalt (yellow band, R_f 0.6 (petrol)), followed by a petrol–ether solvent system to elute the complex (red band). Once isolated, the complex was dried under high vacuum (<1 mmHg) to remove any traces of solvent and then placed under nitrogen at −20 °C.

(*S*)-(+)-Hexacarbonyl-1κ^3*C*,2κ^3*C*-{μ-[α-(η^2:η^2-ethynyl)phenylmethanol]}dicobalt(*Co–Co*) 2a. (*R*)-(−)-1-Phenylprop-2-yn-1-ol **1a** (0.527 g, 4.0 mmol) in petrol (25 ml) was reacted with octacarbonyldicobalt (1.40 g, 4.09 mmol, 1.0 equiv.) for 1 hour according to the general procedure A. Chromatographic purification using petrol–ether (10:1; R_f 0.5) gave 1.198 g (72%) of complex **2a** as red crystals; mp 34–35 °C (petrol) (Found: C, 43.07; H, 1.63%. $C_{15}H_8Co_2O_7$ requires C, 43.07; H, 1.93%); $[\alpha]_D^{20}$ +309 (*c* 0.077, DCM); λ_{max} 210.5, 348.9 (ε/dm^3 mol^{-1} cm^{-1} 46400, 5200); ν_{max}(DCM)/cm^{-1} 2095, 2057, 2028 (s, Co–CO); δ_H (250 MHz, $CDCl_3$) 7.48–7.45 (2H, m, *o*-Ar-CH), 7.39–7.28 (3H, m, *m*,*p*-Ar-CH), 6.08 (1H, s, alkyne-CH), 5.91 (1H, d, *J* 3.5, C*H*OH), 2.35 (1H, d, *J* 3.5, CHO*H*); δ_C (62.9 MHz, $CDCl_3$) 199.0 (br, Co-CO), 144.3 (*i*-Ar-C), 128.7 (*m*-Ar-CH), 128.2 (*p*-Ar-CH), 125.5 (*o*-Ar-CH), 101.3 (alkyne-C), 74.2 (alkyne-CH), 72.1 (*C*HOH); *m*/*z* (EI) 420 (M^+ + 3H), 390 (M^+ − CO), 362 (M^+ − 2CO), 334 (M^+ − 3CO), 306 (M^+ − 4CO), 278 (M^+ − 5CO), 250 (M^+ − 6CO) [Found (M^+ + 3H) 420.9148. $C_{15}H_{11}Co_2O_7$ requires 420.9169].

(*R*)-(+)-Hexacarbonyl-1κ^3*C*,2κ^3*C*-{μ-[α-(η^2:η^2-ethynyl)phenylmethanol]}dicobalt(*Co–Co*) 2b. (*S*)-(+)-1-Phenylprop-2-yn-1-ol **1b** (0.500 g, 3.79 mmol) in petrol (25 ml) was reacted with octacarbonyldicobalt (1.32 g, 3.86 mmol, 1.0 equiv.) for 1.5 hours according to the general procedure A. Chromatographic purification using petrol–ether (10:1; R_f 0.5) gave 1.208 g (76%) of complex **2b** as red crystals; mp 33–34 °C (petrol) (Found: C, 43.13; H, 1.99%. $C_{15}H_8Co_2O_7$ requires C, 43.07; H, 1.93%); $[\alpha]_D^{20}$ −311 (*c* 0.065, DCM); spectroscopic and mass spectral data as for enantiomer **2a**.

General procedure (B) for formation of monosubstituted phosphine pentacarbonylalkynedicobalt complexes

All apparatus was oven dried and cooled under nitrogen before use. Dicobalthexacarbonylalkyne complex was weighed into a test-tube or round-bottomed flask and dissolved in the required solvent. The reaction was placed under an atmosphere of nitrogen, transferred to a cryostatically controlled cooling bath and allowed to equilibrate to the required temperature (1 hour). The phosphine was added as a solid and then the amine *N*-oxide was added as a solid. The reaction mixture was placed under nitrogen and allowed to stir with the course of reactions being monitored by TLC. When no starting complex remained, or no change was observed with time, then the reaction was worked up by filtration through a pad of silica under vacuum. Removal of solvent *in vacuo* typically gave red oils which were purified by flash column chromatography on silica with petrol–ether eluant.

Pentacarbonyl-1κ^3*C*,2κ^2*C*-{μ-[α-(η^2:η^2-ethynyl)phenylmethanol]}(triphenylphosphine)-2κ*P*-dicobalt(*Co–Co*) 3a and 4a.[12a] (*a*) Complex **2a** (110.8 mg, 0.265 mmol) in THF (7 ml) at −60 °C was reacted with triphenylphosphine (108.1 mg, 0.412 mmol, 1.6 equiv.) and anhydrous *N*-methylmorpholine *N*-oxide (33.5 mg, 0.286 mmol, 1.1 equiv.) for 96 hours according to the general procedure B. Following workup, HPLC analysis of the mixture indicated a 51:49 mixture of **3a** and **4a**. Chromatographic purification using petrol–ether (10:1) gave 169.9 mg (98%) of a mixture of **3a** (R_f 0.4) and **4a** (R_f 0.2). (*b*) Complex

2a (115.8 mg, 0.277 mmol) in THF (5 ml) at −59 °C was reacted with triphenylphosphine (78.6 mg, 0.300 mmol, 1.1 equiv.) and brucine *N*-oxide (125.2 mg, 0.305 mmol, 1.1 equiv.) for 19 hours according to the general procedure B. Following workup, HPLC analysis of the mixture indicated a 70 : 30 mixture of **3a** and **4a**. Chromatographic purification using petrol–ether (10 : 1) gave 8.38 mg (46%) of **3a** (R_f 0.4) followed by 36.6 mg (20%) of **4a** (R_f 0.2).

3a: (1*S*,2*R*,3*S*) red crystals $[\alpha]_D^{20}$ +32 (*c* 0.040, DCM); λ_{max} 210.9, 376.9 (ε/dm^3 mol^{-1} cm^{-1} 68800, 10600); ν_{max}(DCM)/cm^{-1} 2064, 2014, 2002, 1964 (s, Co–CO); δ_H (250 MHz, $CDCl_3$) 7.68–7.38 (15H, m, P-Ar-CH), 7.22–7.08 (3H, m, *m*,*p*-Ar-CH), 6.98–6.87 (2H, m, *o*-Ar-CH), 5.14 (1H, d, $J_{P\text{-}H}$ 2.7, alkyne-CH), 4.84 (1H, d, *J* 5.6, C*H*OH), 2.07 (1H, d, *J* 5.6, CHO*H*); HPLC (1% EtOH–heptane; Flow 1.0 ml min^{-1}), RT 9.2 min. **4a**: (1*R*,2*S*,3*S*) beige crystals $[\alpha]_D^{20}$ +333 (*c* 0.042, DCM); λ_{max} 210.6, 376.8 (ε/dm^3 mol^{-1} cm^{-1} 73200, 10000); ν_{max}(DCM)/cm^{-1} 2064, 2011, 2002, 1969 (s, Co–CO); δ_H (250 MHz, $CDCl_3$) 7.58–7.45 (15H, m, P-Ar-CH), 7.25–7.15 (5H, m, Ar-CH), 5.39 (1H, d, $J_{P\text{-}H}$ 4.8, alkyne-CH), 5.08 (1H, d, *J* 3.5, C*H*OH), 1.63 (1H, d, *J* 3.5, CHO*H*); HPLC (1% EtOH–heptane; Flow 1.0 ml min^{-1}), RT 25.6 min.

Pentacarbonyl-1κ^3*C*,2κ^2*C*-{μ-[(η^2 : η^2-ethynyl)phenylmethanol]}(triphenylphosphine)-2κ*P*-dicobalt(*Co–Co*) 3b and 4b.[12a] (*a*) Complex **2b** (105.6 mg, 0.253 mmol) in THF (7 ml) at −60 °C was reacted with triphenylphosphine (77.0 mg, 0.294 mmol, 1.2 equiv.) and anhydrous *N*-methylmorpholine *N*-oxide (32.0 mg, 0.274 mmol, 1.1 equiv.) for 96 hours according to the general procedure B. Following workup, HPLC analysis of the mixture indicated a 50 : 50 mixture of **3b** and **4b**. Chromatographic purification using petrol–ether (10 : 1) gave 156.0 mg (95%) of a mixture of **3b** (R_f 0.4) and **4b** (R_f 0.2).

(*b*) Complex **2b** (128.2 mg, 0.307 mmol) in THF (5 ml) at −59 °C was reacted with triphenylphosphine (87.7 mg, 0.335 mmol, 1.1 equiv.) and brucine *N*-oxide (141.2 mg, 0.344 mmol, 1.1 equiv.) for 19 hours according to the general procedure B. Following workup, HPLC analysis of the mixture indicated a 49 : 51 mixture of **3b** and **4b**. Chromatographic purification using petrol–ether (10 : 1) gave 74.0 mg (37%) of **3b** (R_f 0.4) followed by 79.4 mg (40%) of **4b** (R_f 0.2).

3b: (1*R*,2*S*,3*R*) red crystals $[\alpha]_D^{20}$ −36 (*c* 0.028, DCM); spectroscopic data as for enantiomer **3a**; HPLC (1% EtOH–heptane; Flow 1.0 ml min^{-1}), RT 13.0 min. **4b**: (1*S*,2*R*,3*R*) red crystals $[\alpha]_D^{20}$ −359 (*c* 0.044, DCM); spectroscopic data as for enantiomer **4a**; HPLC (1% EtOH–heptane; Flow 1.0 ml min^{-1}), RT 18.0 min.

General procedure (C) for Pauson–Khand (P–K) reactions

All apparatus was oven dried and cooled under nitrogen before use. The dicobalt complex was weighed into a test-tube or round-bottomed flask and dissolved in the required solvent. The reaction was placed under an atmosphere of nitrogen, transferred to a cryostatically cooling bath and allowed to equilibrate to the required temperature (1 hour). The alkene was added and then the *N*-oxide was added as a solid. The reaction mixture was placed under nitrogen and allowed to stir with the course of reaction being monitored by TLC. When no starting complex remained (the reaction becomes purple or green), or no change was observed with time, then the reaction was worked up by addition of dilute hydrochloric acid. The reaction was then extracted with DCM, dried over magnesium sulfate, filtered, and the solvent was removed *in vacuo*. Purification was achieved by flash column chromatography on silica with petrol–ether eluant.

(3a*R*,4*R*,7*S*,7a*R*,1′*S*)-(−)-3a,4,5,6,7,7a-Hexahydro-2-(1′-hydroxy-1′-phenylmethyl)-4,7-methano-1*H*-inden-1-one 5a. Complex **3a** (405.6 mg, 0.622 mmol) in DCM (10 ml) at room temperature was reacted with norbornene (137.5 mg, 1.463 mmol, 2.4 equiv.) and anhydrous *N*-methylmorpholine *N*-oxide (432.8 mg, 3.699 mmol, 5.9 equiv.) for 14 hours according to the general procedure C. Chromatographic purification using petrol–ether (1 : 1; R_f 0.4) gave 121.4 mg (77%) of cyclopentenone **5a** as colourless crystals; mp 92–93 °C (petrol–ether) (Found: C, 80.22; H, 7.15%. $C_{17}H_{18}O_2$ requires C, 80.29; H, 7.13%); $[\alpha]_D^{20}$ −45.4 (*c* 1.67, DCM); λ_{max} 206.2, 228.2 (ε/dm^3 mol^{-1} cm^{-1} 18800, 11000); ν_{max}(DCM)/cm^{-1} 3687, 3597, 3510 (w, O-H), 3062 (w, C=CH + Aromatic C-H), 2961, 2930, 2914, 2875 (s, aliphatic C-H), 1692 (s, C=O), 1624, 1605 (s, C=C); δ_H (400 MHz, $CDCl_3$) 7.39–7.33 (4H, m, *o*,*m*-Ar-CH), 7.30–7.26 (1H, m, *p*-Ar-CH), 7.07 (1H, dd, *J* 2.6, 1.0, 3-CH), 5.54 (1H, s, 1′-CH), 3.47 (1H, s br, OH), 2.62–2.57 (1H, m, 3a-CH), 2.42 (1H, d, *J* 3.8, 7-CH), 2.22 (1H, d, *J* 5.0, 7a-CH), 2.17 (1H, d, *J* 4.1, 4-CH), 1.71–1.54 (2H, m, 5-CH_{eq} + 6-CH_{eq}), 1.33–1.23 (2H, m, 5-CH_{ax} + 6-CH_{ax}), 1.05 (1H, dt, *J* 10.6, 1.7, 8-CH), 0.96 (1H, dt, *J* 10.6, 1.3, 8-CH); δ_C (100 MHz, $CDCl_3$) 211.2 (1-C), 160.4 (3-CH), 150.8 (*i*-Ar-C), 141.7 (2-C), 128.7 (*m*-Ar-C), 128.0 (*p*-Ar-C), 126.5 (*o*-Ar-C), 70.2 (1′-CH), 54.9 (7a-CH), 48.6 (3a-CH), 39.3 (7-CH), 38.2 (4-CH), 31.4 (8-CH_2), 29.3 (5-CH_2), 28.5 (6-CH_2); *m*/*z* (EI) [Found (M^+) 254.1309. $C_{17}H_{18}O_2$ requires 254.1307]; HPLC (1% EtOH–heptane; Flow 0.5 ml min^{-1}), RT 65.9 min. A colourless crystal of cyclopentenone **5a** was grown by slow evaporation from a petrol–ether solution and was cut to 0.55 × 0.40 × 0.30 mm and mounted on a Rigaku AFC7S diffractometer at 123 K.

Crystal structure determination of cyclopentenone 5a. *Crystal data*. $C_{17}H_{18}O_2$, $M = 254.33$, orthorhombic, $a = 9.538(2)$, $b = 16.348(4)$, $c = 8.395(2)$ Å, $U = 1308.9(4)$ Å^3, $T = 123$ K, space group $P2_12_12_1$, $Z = 4$, μ(Mo-Kα) = 0.083 mm^{-1}, 3925 reflections measured, 3008 unique ($R_{int} = 0.0317$). Final refinement to convergence[14] on *F* gave $R = 0.0363$ for 2550 observed reflections with $I > 2\sigma(I)$ and $Rw = 0.0448$ for all reflections. All non-hydrogen atoms were treated anisotropically and all hydrogen atoms isotropically. Although Friedel pairs were collected for all reflections the dataset was not sensitive to the absolute configuration and this is therefore based on the known geometry at C1′. CCDC reference number 188/277.

See http://www.rsc.org/suppdata/p1/b0/b006523o/ for crystallographic files in .cif format.

(3a*S*,4*S*,7*R*,7a*S*,1′*S*)-(+)-3a,4,5,6,7,7a-Hexahydro-2-(1′-hydroxy-1′-phenylmethyl)-4,7-methano-1*H*-inden-1-one 6a. Complex **4a** (24.5 mg, 0.038 mmol) in DCM (5 ml) at room temperature was reacted with norbornene (9.7 mg, 0.103 mmol, 2.7 equiv.) and anhydrous *N*-methylmorpholine *N*-oxide (38.3 mg, 0.327 mmol, 8.7 equiv.) for 12 hours according to the general procedure C. Chromatographic purification using petrol–ether (1 : 1, R_f 0.2) gave 3.8 mg (40%) of cyclopentenone **6a** as a colourless gum (Found: C, 80.22; H, 7.15%. $C_{17}H_{18}O_2$ requires C, 80.29; H, 7.13%); $[\alpha]_D^{20}$ +96.0 (*c* 0.70, DCM); λ_{max} 210.3, 226.0 (ε/dm^3 mol^{-1} cm^{-1} 17200, 9000); ν_{max}(DCM)/cm^{-1} 3593, 3503 (w br, O-H), 3063, 3032 (w, C=CH + Aromatic C-H), 2963, 2931, 2913, 2875 (s, aliphatic C-H), 1693 (s, C=O), 1626, 1604 (s, C=C); δ_H (250 MHz, $CDCl_3$) 7.38–7.26 (5H, m, Ar-CH), 7.08 (1H, t, *J* 1.2, 3-CH), 5.55 (1H, s, 1′-CH), 3.52 (1H, s br, OH), 2.64–2.58 (1H, m, 3a-CH), 2.43–2.38 (1H, m, 7-CH), 2.26 (1H, d, *J* 5.1, 7a-CH), 2.17 (1H, d, *J* 2.9, 4-CH), 1.73–1.51 (2H, m, 5-CH_{eq} + 6-CH_{eq}), 1.34–1.21 (2H, m, 5-CH_{ax} + 6-CH_{ax}), 1.05–0.96 (2H, m, 8-CH_2); δ_C (100 MHz, $CDCl_3$) 211.2 (1-C), 160.5 (3-CH), 150.8 (*i*-Ar-C), 141.6 (2-C), 128.7 (*m*-Ar-C), 128.0 (*p*-Ar-C), 126.6 (*o*-Ar-C), 70.1 (1′-CH), 54.9 (7a-CH), 48.6 (3a-CH), 39.2 (7-CH), 38.2 (4-CH), 31.4 (8-CH_2), 29.3 (5-CH_2), 28.5 (6-CH_2); *m*/*z* (EI) [Found (M^+) 254.1319. $C_{17}H_{18}O_2$ requires 254.1307]; HPLC (1% EtOH–heptane; Flow 0.5 ml min^{-1}), RT 69.8 min.

(3a*S*,4*S*,7*R*,7a*S*,1′*R*)-(+)-3a,4,5,6,7,7a-Hexahydro-2-(1′-hydroxy-1′-phenylmethyl)-4,7-methano-1*H*-inden-1-one 5b. Complex **3b** (64.1 mg, 0.098 mmol) in DCM (5 ml) at room temperature was reacted with norbornene (17.4 mg, 0.185 mmol, 1.9 equiv.) and anhydrous *N*-methylmorpholine *N*-oxide (63.0 mg, 0.538 mmol, 5.5 equiv.) for 12 hours according to the general procedure C. Chromatographic purification using petrol–ether (1:1, R_f 0.4) gave 17.2 mg (69%) of cyclopentenone **5b** as colourless crystals; mp 87–91 °C (petrol–ether) (Found: C, 79.99; H, 7.17%. $C_{17}H_{18}O_2$ requires C, 80.29; H, 7.13%); $[\alpha]_D^{20}$ +40.2 (*c* 1.67, DCM); spectroscopic and mass spectral data as for enantiomer **5a**; HPLC (1% EtOH–heptane; Flow 1.0 ml min^{-1}), RT 31.4 min.

(3a*R*,4*R*,7*S*,7a*R*,1′*R*)-(−)-3a,4,5,6,7,7a-Hexahydro-2-(1′-hydroxy-1′-phenylmethyl)-4,7-methano-1*H*-inden-1-one 6b. Complex **4b** (24.9 mg, 0.038 mmol) in DCM (5 ml) at room temperature was reacted with norbornene (8.1 mg, 0.086 mmol, 2.3 equiv.) and anhydrous *N*-methylmorpholine *N*-oxide (30.5 mg, 0.261 mmol, 6.8 equiv.) for 12 hours according to the general procedure C. Chromatographic purification using petrol–ether (1:1, R_f 0.2) gave 5.6 mg (58%) of cyclopentenone **6b** as a colourless gum (Found: C, 79.99; H, 7.17%. $C_{17}H_{18}O_2$ requires C, 80.29; H, 7.13%); $[\alpha]_D^{20}$ −96.6 (*c* 0.785, DCM); spectroscopic and mass spectral data as for enantiomer **6a**; HPLC (1% EtOH–heptane; Flow 1.0 ml min^{-1}), RT 51.8 min.

Pauson–Khand reactions of complex 2a

(*a*) Complex **2a** (102.8 mg, 0.246 mmol) in acetone (7 ml) at −60 °C was reacted with norbornene (115.0 mg, 1.223 mmol, 5.0 equiv.) and anhydrous *N*-methylmorpholine *N*-oxide (203.0 mg, 1.735 mmol, 7.0 equiv.) for 96 hours according to the general procedure C. HPLC analysis of the mixture indicated a 28:72 mixture of **5a** and **6a**. Chromatographic purification using petrol–ether (1:1) gave 51.7 mg (83%) of a mixture of cyclopentenones **5a** (R_f 0.4) and **6a** (R_f 0.2).

(*b*) Complex **2a** (92.7 mg, 0.222 mmol) in acetone (5 ml) at −58 °C was reacted with norbornene (30.3 mg, 0.322 mmol, 1.5 equiv.) and brucine *N*-oxide (554.6 mg, 1.353 mmol, 6.1 equiv.) for 68 hours according to the general procedure C. HPLC analysis of the mixture indicated a 30:70 mixture of **5a** and **6a**. Chromatographic purification using petrol–ether (1:1) gave 8.8 mg (16%) of **5a** (R_f 0.4) followed by 18.7 mg (33%) of **6a** (R_f 0.2).

Pauson–Khand reactions of complex 2b

(*a*) Complex **2b** (162.4 mg, 0.388 mmol) in acetone (7 ml) at −60 °C was reacted with norbornene (196.5 mg, 2.090 mmol, 5.4 equiv.) and anhydrous *N*-methylmorpholine *N*-oxide (283.7 mg, 2.425 mmol, 6.3 equiv.) for 96 hours according to the general procedure C. HPLC analysis of the mixture indicated a 29:71 mixture of **5b** and **6b**. Chromatographic purification using petrol–ether (1:1) gave 78.2 mg (79%) of a mixture of **5b** (R_f 0.4) and **6b** (R_f 0.2).

(*b*) Complex **2b** (99.0 mg, 0.237 mmol) in acetone (5 ml) at −58 °C was reacted with norbornene (33.7 mg, 0.359 mmol, 1.5 equiv.) and brucine *N*-oxide (591.1 mg, 1.442 mmol, 6.1 equiv.) for 68 hours according to the general procedure C. HPLC analysis of the mixture indicated a 31:69 mixture of **5b** and **6b**. Chromatographic purification using petrol–ether (1:1) gave 11.1 mg (18%) of **5b** (R_f 0.4) followed by 25.8 mg (43%) of **6b** (R_f 0.2).

Acknowledgements

We gratefully acknowledge financial support from the EPSRC and Glaxo Wellcome for an Industrial CASE Studentship (D. M. L.) and from the Carnegie Trust for the Universities of Scotland for a postgraduate scholarship (J. S. S.).

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