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Preparation and reaction of desymmetrised cobalt alkyne complexes

David R. Carbery,[a] William J. Kerr,[a,*] David M. Lindsay,[a] James S. Scott [a] and Stephen P. Watson [b]

[a] *Department of Pure and Applied Chemistry, University of Strathclyde, Glasgow G1 1XL, UK*
[b] *Glaxo Wellcome Medicines Research Centre, Gunnels Wood Road, Stevenage, Hertfordshire SG1 2NY, UK*

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Abstract

Prochiral alkyne hexacarbonyl dicobalt complexes are desymmetrised directly with brucine *N*-oxide in the presence of a phosphine or phosphite ligand to produce the corresponding phosphorus-containing pentacarbonyl complex with appreciable enantiomeric excess. In Pauson–Khand reactions, it is found that the enantiomeric integrity of the desymmetrised complex is conserved in the cyclopentenone product. Moreover, the major enantiomer obtained in these reactions is opposite to that from a direct brucine *N*-oxide promoted Pauson–Khand reaction, allowing the preparation of either enantiomeric cyclopentenone in enriched form from a single source of chirality.

Keywords: amine *N*-oxides; asymmetric synthesis; cobalt and compounds; desymmetrisation; Pauson–Khand reactions.

In the preceding paper,[1] we have described the further development of our initial discovery[2] that chiral amine *N*-oxides can induce asymmetry in the Pauson–Khand (P–K) reaction. In this work, we showed that a chiral amine *N*-oxide could effect selective decarbonylation of one cobalt vertex of the dicobalt alkyne cluster, leading, in the presence of alkene, to enantiomerically enriched cyclopentenones of up to 78% ee. Herein, we wish to report the application of this selective decarbonylation concept to the preparation of chiral phosphinated cobalt alkyne complexes and show how this class of desymmetrised dicobalt species has, subsequently, been used in the P–K reaction to, again, provide access to optically enriched cyclopentenones.

The replacement of carbon monoxide by phosphorus-based ligands in alkynehexacarbonyldicobalt complexes is well documented.[3] Dissociation of a carbon monoxide ligand from the hexacarbonyl complex generates a vacant co-ordination site on one of the cobalt atoms which, in turn, may be occupied by the phosphorus ligand. This initial CO dissociation is also proposed as the first step of the P–K mechanism[4] and, paralleling the traditional methods for carrying out the P–K reaction, early reports of the preparation of phosphorus-substituted complexes also relied on thermal conditions to effect dissociation

* Corresponding author. Fax: +44-(0)141-548-4246; e-mail: cbas69@strath.ac.uk (W. J. Kerr)

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of CO.[3] Since most of the improvements to the P–K methodology rely on accelerating this first step, they have also found use in the preparation of these substituted complexes. Thus, both Anderson's photochemical promotion[5] and the use of amine *N*-oxides within our own laboratory[6] have been shown to promote the formation of pentacarbonyl(phosphine) complexes in good yield under mild conditions. Other methods of promotion, as yet untried in the corresponding P–K processes, have also been reported, e.g. electron transfer catalysis.[7]

In terms of structure, the pseudo-tetrahedral dicobalt–alkyne cluster, in simplest terms, may be considered analogous to an sp^3 carbon atom as shown in Fig. 1; the four atoms around carbon are bonded to describe the vertices of a tetrahedron, with the carbon atom itself as the centroid. It follows, therefore, that in dicobalt complexes of unsymmetrical alkynes, the two tricarbonylcobalt vertices are prochiral and so substitution of a CO ligand generates a pair of enantiomers (Fig. 1). On this basis, we envisioned that our chiral amine *N*-oxide methodology, for inducing asymmetry in the P–K reaction, could serve as a method for preparing these substituted complexes in enantiomerically enriched form. Selective decarbonylation of one of the two cobalt units by the chiral *N*-oxide, followed by trapping of the co-ordinatively unsaturated intermediate by a phosphinated ligand (as opposed to an alkene as employed in the P–K reaction) would allow access to these chiral desymmetrised complexes.

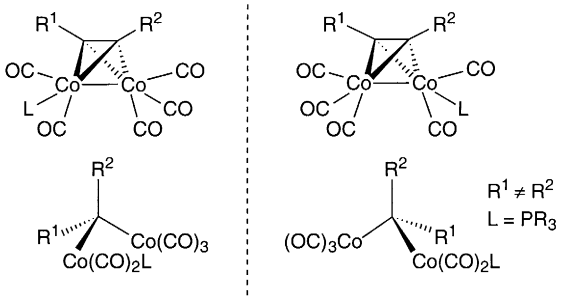


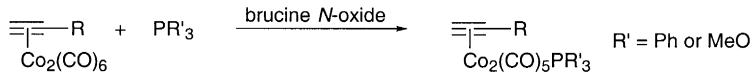
Fig. 1.

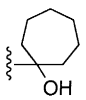
Consequently, a range of cobalt alkyne complexes were treated with brucine *N*-oxide (BNO) in the presence of triphenylphosphine or trimethylphosphite at low temperature. The results from this study are shown in Table 1 and constitute *the first direct access to these novel enantiomerically enriched complexes*.[8]

The desymmetrised complexes are generally formed in moderate to good yield and, furthermore, with enantioselectivities which mirror those from the corresponding P–K processes. For example, the optimum substrate, in terms of e.r., in our asymmetric P–K studies[1] was the complex of dimethylpropargyl alcohol. This is also the case in these desymmetrisations, where monosubstituted complexes with triphenylphosphine and trimethylphosphite are accessed with enantiomeric ratios of 84:16 and 80:20, respectively (Entries 1 and 2). Indeed, the overall trends in, and levels of, enantioselection with relation to substrate are strikingly similar to those found with our direct asymmetric P–K methodology; substituted propargylic alcohols perform best (Entries 1–7) and propargyl alcohol itself (Entry 8) shows effectively no enantioselectivity. This close correlation of enantioselectivity with substrate in these two individual transformations points to a similar mechanism for the asymmetric processes: selective decarbonylation (or activation) of the starting complex to afford a chiral co-ordinatively unsaturated (or activated) intermediate complex, which is then trapped by either an alkene or, in this case, a phosphorus ligand.

During the course of these studies, we also discovered that recrystallisation of the phosphinated complexes provided a less usual method of enantiomeric enrichment. For example, a sample of the pentacarbonyl triphenylphosphine complex of dimethylpropargyl alcohol (80:20 e.r.) was crystallised from the minimum amount of petrol at −20°C. Although the crystals which were subsequently collected

Table 1
Desymmetrisation of cobalt alkyne complexes using brucine *N*-oxide



Entry	R	PR'$_3$	Solvent	Temp. (°C)	Reaction Time (h)	Yield (%)	Enantiomeric Ratio (e.r.)[a]
1		PPh_3	THF/DCM	-65	168	48	84:16
2		$P(OMe)_3$	THF/DCM	-60	144	81	80:20
3		PPh_3	THF	-60	288	49	62:38
4		$P(OMe)_3$	THF	-50	384	36	73:27
5		PPh_3	THF	-49	140	67	69:31
6		PPh_3	THF	-48	144	54	69:31
7		PPh_3	THF	-50	528	89	72:28
8		PPh_3	THF/DCM	-60	18	35	52:48

[a]Enantiomeric ratios were determined by chiral HPLC analysis and are presented as the 1st eluting : 2nd eluting enantiomers.

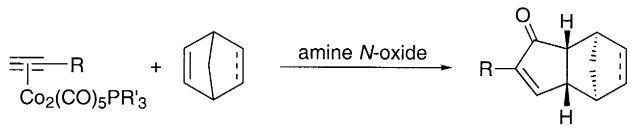
showed a decrease in e.r. (to 68:32), analysis of the mother liquor showed an e.r. of 95:5.[9] For crystalline Co–alkyne complexes, this then represents a method for obtaining highly enantio-enriched samples.

With several desymmetrised complexes now in hand, attention was turned to their utilisation in the P–K reaction. Under conditions previously developed for reaction of our diastereomerically pure chiral phosphine complexes,[10] the desymmetrised compounds were converted, in the presence of either norbornene or norbornadiene, to the corresponding cyclopentenones in good to excellent yield and with appreciable levels of enantiomeric excess (Table 2).

As can be seen from Table 2, at the outset the use of Ph_3P as the ligand led to appreciable loss of optical enrichment in the cyclopentenone product (e.g. Entry 1). However, by careful optimisation of the reaction conditions these losses could be kept to a minimum (e.g. Entry 2). Moreover, running the reactions below room temperature with the powerful promoter BNO (which should show no chiral discrimination at these temperatures), enantiomeric ratios of 87:13 and 89:11 were obtained with norbornene and norbornadiene, respectively (Entries 4 and 5). Additionally, the use of $(MeO)_3P$ as the ligand allowed the transformations to proceed at room temperature with the less powerful promoter *N*-methylmorpholine *N*-oxide and with a negligible loss of stereochemical integrity (Entries 6 and 7).

Returning to Table 2, and more specifically the cyclopentenone derived from dimethylpropargyl alcohol complex, it can be seen that the major stereoisomer obtained from the desymmetrised complex is the first eluting enantiomer by HPLC (e.g. Entry 4). Notably, this is in contrast to that obtained from the

Table 2
P–K reactions of desymmetrised pentacarbonyl phosphine complexes



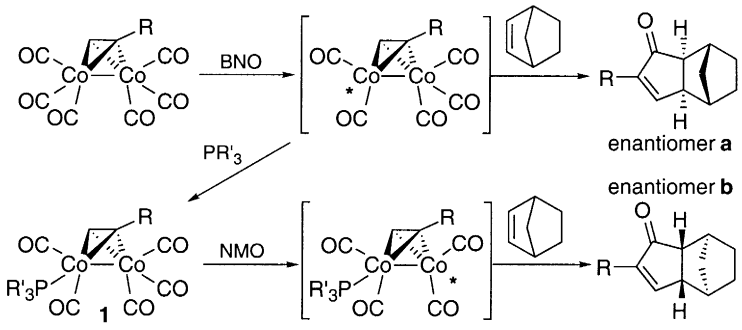
Entry	R	PR'3	Starting Complex e.r.	Amine *N*-oxide	Solvent	Temp. (°C)	Time (h)	Yield (%)	Cyclopentenone e.r.[a]
1[b]		PPh_3	70:30	NMO[d]	DCM	r.t.	14	50	55:45
2[b]		PPh_3	79:21	NMO[d]	DCM	10	38	88	77:23
3[b]		PPh_3	93:7	NMO[d]	acetone	6	6	49	79:21
4[b]		PPh_3	93:7	BNO	acetone	6	4	62	87:13
5[c]		PPh_3	95:5	BNO	acetone	-10	66	86	89:11
6[b]		$P(OMe)_3$	78:22	NMO[d]	acetone	r.t.	16	47	74:26
7[b]		$P(OMe)_3$	65:35	NMO[d]	DCM	r.t.	48	56	35:65

[a]Enantiomeric ratios were determined by chiral HPLC analysis and are presented as the 1st eluting : 2nd eluting enantiomers.
[b]Reaction with norbornene.
[c]Reaction with norbornadiene.
[d]NMO: anhydrous *N*-methylmorpholine *N*-oxide.

direct asymmetric P–K reaction,[1] where the second eluting enantiomer was formed in excess. Therefore, it is important to note that these methodologies, when combined, *afford the opportunity to synthesise either cyclopentenone enantiomer in enriched form from a single source of chirality* (Scheme 1). Thus, treatment of the starting hexacarbonyl complex with brucine *N*-oxide in the presence of norbornene gives enantiomer **a** in enriched form. However, trapping the activated intermediate with a phosphorus ligand allows formation of the desymmetrised complex **1**, in which the two cobalt atoms are sterically and electronically differentiated, with the electron-donating phosphorus ligand strengthening the Co–CO bonds of the cobalt to which it is attached. Subsequent treatment with an achiral *N*-oxide will then preferentially remove a CO from the opposite cobalt leading, in the presence of norbornene, to enantiomer **b** in enriched form.

To conclude, we have demonstrated that our chiral amine *N*-oxide methodology, originally formulated for the asymmetric P–K reaction, is able to deliver, for the first time, enantiomerically enriched desymmetrised cobalt alkyne complexes. In combination with our asymmetric P–K protocols, this allows access to either enantiomeric cyclopentenone in enriched form from a single source of chirality. Work directed at improving this asymmetric methodology and investigating other uses of these desymmetrised complexes is currently underway in our laboratory and will be reported in due course.

Typical experimental procedure: A solution of hexacarbonyl(2-methylbut-3-yn-2-ol)dicobalt (109.6 mg, 0.296 mmol) and trimethylphosphite (52 μl, 0.444 mmol) in dry THF (3.5 ml) and dry CH_2Cl_2 (3.5 ml) was cooled to −60°C in a cryostatically cooled MeOH bath. Brucine *N*-oxide (126.0 mg, 0.307 mmol) was added and the reaction was stirred under N_2 for 6 days. The reaction mixture was then



Scheme 1.

filtered through a pad of silica and the residues were washed with ether. The filtrate was concentrated in vacuo and the residue was purified by flash column chromatography (1:1 petrol:ether) to give 111.3 mg (81% yield) of pentacarbonyl(2-methylbut-3-yn-2-ol)trimethylphosphitedicobalt as a deep red oil. HPLC analysis (Chiracel OD-H column, 0.5% *i*-PrOH/heptane, 1 ml min^{-1}, UV detector at 210 nm, retention times 15.2 min and 16.4 min) indicated an enantiomeric ratio of 80:20 (60% e.e.). IR (hexanes): 3553 (w, OH), 2071 (s), 2020 (s), 2012 (s), 2001 (m), 1979 cm^{-1} (m, Co−C≡O). ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.53 (3H, s, Me), 1.55 (3H, s, Me), 3.09 (1H, s, OH), 3.66 (9H, d, $^3J_{P-H}$=11.7 Hz, OMe), 5.65 ppm (1H, d, $^3J_{P-H}$=3.6 Hz, C≡CH). ^{13}C NMR (63 MHz, $CDCl_3$): δ 201.8, 102.0, 72.4, 69.3, 52.3 (d, $^2J_{P-C}$=3.5 Hz), 33.2, 32.9. HRMS: *m/z* calcd for $C_{13}H_{17}Co_2O_9P$: (M^+) 465.9275. Found: 465.9264. Anal. calcd for $C_{13}H_{17}Co_2O_9P$: C, 33.50; H, 3.68; P, 6.64. Found: C, 33.24; H, 3.64; P, 6.43%.

Acknowledgements

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