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Heterobimetallic Alkyne Complexes in Organic Synthesis: An Asymmetric Variant of the Pauson-Khand Reaction

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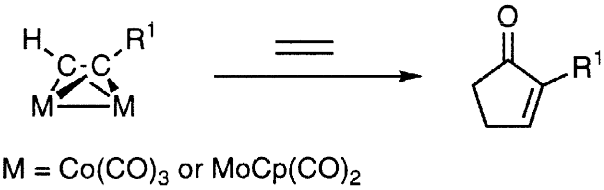
Abstract: The use of heterobimetallic alkyne complexes for the synthesis of cyclopentenones is described. The inherent chirality of the complexes has been used to effect high levels of stereocontrol in transformations giving optically enriched organic end products. © 1998 Elsevier Science Ltd. All rights reserved.

The Pauson-Khand reaction is perhaps one of the most widely used organometallic mediated reactions for the synthesis of cyclopentenones.[1] A number of variations have been reported over the years that modify and enhance the original procedure.[2] In addition, other transition metal systems have been shown to mediate similar cyclisation reactions .[3] In this paper, we show that heterobimetallic alkyne complexes can be used to facilitate cyclopentenone formation (Scheme 1). The mixed metal complexes are formed from the reaction of a dicobalt hexacarbonyl alkyne complex with the cyclopentadienylmolybdenum tricarbonyl anion.[4] The desired complexes are isolated in good yield, are stable to chromatography on silica gel, and can be stored for extended periods. Although complexes of this type have been known for some time, surprisingly they have not been utilised in reactions to form organic products.



M = $Co(CO)_3$ or $MoCp(CO)_2$

Scheme 1

We have found that the desired complexes are easily formed by modification of the literature routes.[4] Molybdenum hexacarbonyl was added to a solution of sodium cyclopentadienyl anion in THF. The mixture was refluxed overnight, then a solution of the *bis*-cobalt alkyne complex in THF added and the mixture heated for a further two hours. Standard aqueous work-up provided the mixed metal complex in good yield after purification by silica gel chromatography (Scheme 2). The complexes are red crystalline solids or liquids and can be easily handled in air for extended periods.

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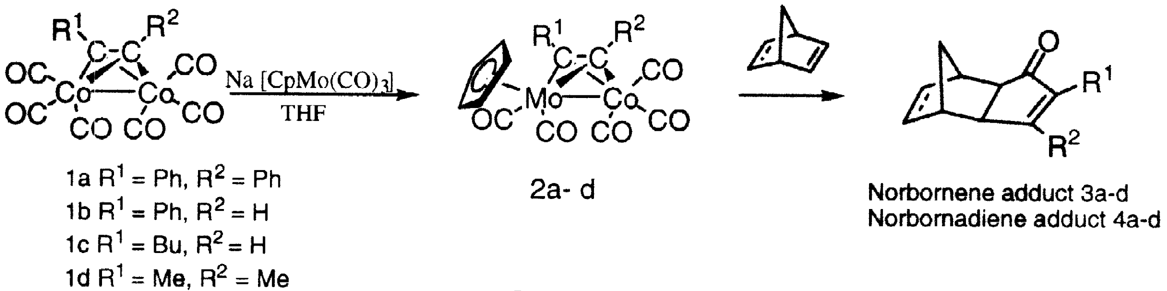


Scheme 2

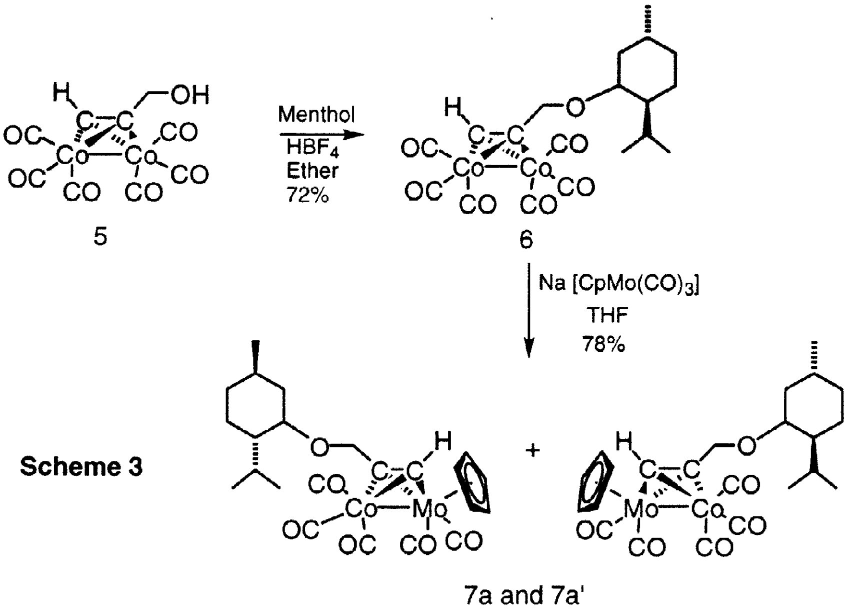
Table 1. Formation of Co/Mo Alkyne Complexes and Cyclopentenones

Complex	Yield	Alkene	Cyclopentenone	Yield from Complex 2	Yield from Complex 1
2a	65	Norbornene	3a	32%	(65%)[5a]
2b	58		3b	69%	(58%)[5b]
2c	61		3c	72%	61%
2d	66		3d	52%	0
		Norbornadiene	4a	60%	(28%)[1a]
			4b	84%	(45%)[1a]
			4c	97%	(53%)[5c]
			4d	90%	82%

Conditions: Cyclopentenone formation was facilitated by heating a mixture of 5 equivalents of the alkene and the mixed metal alkyne complex in toluene to 70°C. The reaction was monitored by TLC for disappearance of starting material. Yields in brackets refer to literature yields for reaction of the *bis*-cobalt alkyne complexes under similar reaction conditions.

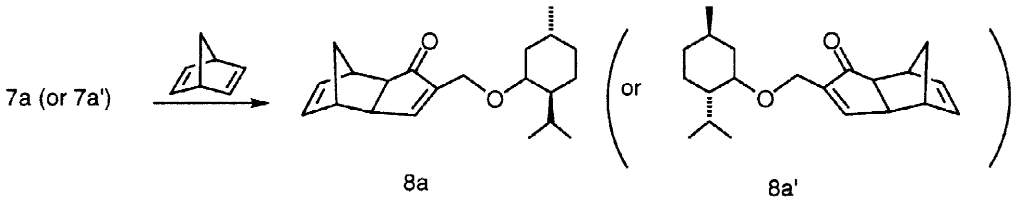
Reaction of the complexes with alkenes was achieved by simply by heating in toluene. Norbornene and norbornadiene were used initially since these are known to be active substrates in the Pauson-Khand reaction. Heating a mixture of the mixed metal alkyne complex with an excess of the alkene gave a clean reaction providing the desired organic products. The yields of cyclopentenone are moderate to excellent, as shown in Table 1, and compare favourably with those obtained from the corresponding *bis*-cobalt alkyne complexes under analogous reaction conditions.[6] Thus, the new mixed metal system has shown promising activity and is a new variant on the Pauson-Khand reaction.

Of more interest is the inherent chirality of the mixed metal alkyne complexes. When unsymmetrical alkynes are employed, the four corners of the metal-alkyne core are differentiated, and the complex is rendered chiral. We reasoned that the electronic differences between the metals might induce chirality in a subsequent cyclisation reaction. The mixed metal complexes of propargyl menthyl ether (7a and 7a') were synthesised as indicated in Scheme 3. The diastereoisomers were separated by chromatography to yield the resolved complexes, and the purity of the products was assessed by ^{1}H and ^{13}C NMR spectroscopy. The chemical shift and coupling of the propargylic protons was substantially different in the two complexes, allowing simple determination of the diastereoisomeric excess.



Scheme 3

Once isolated, separate reaction of the individual, diastereomerically pure complexes with norbornadiene gave the expected cyclopentenones (8a or 8a') in good yield (Scheme 4). ^{13}C NMR spectroscopy showed that different diastereoisomeric cyclopentenones were isolated from each cyclisation reaction.[2g] Thus the diastereomerically pure metal alkyne complexes each gave rise to a distinct organic product, with no sign of the other diastereoisomer in either case. We attribute this to the chirality present in the metal-alkyne core.



Scheme 4

Complex	Yield of Cyclopentenone	diastereomeric excess
7a	61%	100% by ^{13}C NMR
7a'	67%	100% by ^{13}C NMR

Control experiments with the corresponding *bis*-cobalt alkyne complex (6) showed only a slight diastereomeric excess in the cyclopentenone product, presumably arising from the presence of the menthyl group. We therefore assume that in the new mixed metal mediated cyclisation, reaction occurs preferentially around only one of the two possible metal sites. Cyclisation around, for example, the molybdenum, would lead to one diastereoisomeric cyclopentenone being formed, while cyclisation around the cobalt would give the other diastereoisomer. The difference in reactivity of the two metals has induced reaction to occur at one site preferentially, and produced a highly diastereoselective reaction. Thus we have differentiated the metal sites and produced an effective chiral induction in the cyclopentenone forming reaction. This tuning of reactivity of metals in metal-alkyne complexes has been noted previously,[7] by complexation of a phosphine ligand. In our case, however, the mixed metal complexes are thermally more stable than the phosphine substituted complexes, which were prone to racemisation at the higher temperatures required for the classical Pauson-Khand reaction.[8] We have thus produced a viable alternative to the established means of inducing chirality in the Pauson-Khand reaction.

Conclusion: We have illustrated a new variant of the Pauson-Khand. The complexes are easily synthesised and the cyclisation reactions simply carried out by heating. Further experiments with promoters such as *N*-oxides will be reported in due course. In addition, this new technique has great potential as an asymmetric version of the PKR. Work to determine the root of the stereoselection is in progress.

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6 It should be noted that improved yields can be obtained by using promoters such as Dry State Adsorption Conditions or amine *N*-oxides. Use of these with the mixed metal complexes has not been addressed as yet.

7 See 2e,f In addition see: a) Montenegro, E.; Poch, M.; Moyano, A.; Pericàs, M. A.; Rierra, A.; *Tetrahedron Lett.*, **1998**, *39*, 335. b) Tormo, J.; Verdaguer, X.; Moyano, A.; Pericàs, M. A; Rierra, A.; *Tetrahedron*, **1996**, *52*, 14021.

8 It should be noted that by using milder *N*-oxide techniques, the phosphine complexes can be shown to react with little or no racemisation throughout the reaction to provide organic products of high stereochemical integrity. See ref. 2f and 2g.