Cobalt−Phosphite-Catalyzed Asymmetric Pauson−Khand Reaction

Shana J. Sturla and Stephen L. Buchwald*

Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139

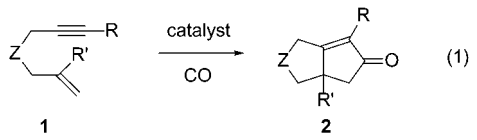
sbuchwal@mit.edu

Received August 16, 2001

A complex formed from dicobalt octacarbonyl and a chiral aryl bisphosphite served as a catalyst for the intramolecular asymmetric Pauson−Khand reaction. Bicyclic cyclopentenones were obtained in up to 75% enantiomeric excess. For a terminal 1,6-enyne, the incremental enantiomeric excess was found to increase from 4 to 26% over the course of the reaction. The scope of this process was examined for a variety of 1,6- and 1,7-enynes, and a moderate degree of enantioselectivity was maintained only in the case of aryl-substituted 1,6-enynes.

Introduction

A general method for the catalytic asymmetric preparation of bicyclic cyclopentenones would be synthetically valuable. The Pauson−Khand (PK) reaction is a powerful technique for the construction of such structural units (eq 1).[1] The first example of a catalytic asymmetric



1 **2** (1)

version of this reaction relied on a chiral Ti *ansa*-metallocene complex.[2] Subsequent reports include catalysts derived from binaphthyl phosphines and iridium,[3] cobalt,[4] or rhodium precatalysts.[5] In general, simple 1,6-enynes (**1**, R = alkyl or aryl, R′ = H) with an ether, amine, or diester linker [**1**, Z = O, RN, $(RO_2C)_2C$] are excellent substrates for the titanium and iridium catalysts; cyclopentenones can be obtained in up to 97% ee.

There remains, however, a continued need for more general systems that demonstrate enhanced catalytic activity. In many of the reported procedures, for instance, small changes in substrate structures or reaction conditions result in a large change in yield, enantiomeric excess, or both. For example, introduction of a methyl group on the olefin (R′ = Me, eq 1) results in generally lower enantioselectivity. In the case of the titanium catalyst,[2] this substitution results in a decrease of enantiomeric excess from 89% to 72% and, for the cobalt catalyst,[4] a decrease from 91% to 63% ee. The methyl substitution also results in a decrease in yield of the cobalt-catalyzed reaction from 53% to 31%. There are few examples of 1,7-enynes as substrates in the asymmetric PK reaction; moderate yields (70−77%) and enantioselectivities (47−55%) are realized using the titanium catalyst.[2,6] Furthermore, there is only one preliminary report of a catalytic asymmetric intermolecular PK reaction and it involves the use of norbornene, a highly activated alkene, to obtain the corresponding cyclopentenone in 32% yield and 93% ee.[3]

Although the classical PK reaction is performed using a stoichiometric quantity of $Co_2(CO)_8$, recent reports have demonstrated that this complex can be used in catalytic amounts.[7] The first efficient example was reported by Jeong and co-workers in 1994.[7b] The cyclocarbonylation of enynes could be effected catalytically with $Co_2(CO)_8$ and triphenyl phosphite at moderate carbon monoxide pressure (30 psig). The generation of an asymmetric variant of this reaction utilizing a chiral phosphite, to our knowledge, has never been disclosed.

Chiral phosphites are increasingly used in asymmetric transition-metal-catalyzed processes. Examples include rhodium- and iridium-catalyzed hydrogenation,[8−10] nickel-

* Corresponding author. Fax: 617-253-3297.

(1) Brummond, K. M.; Kent, J. L. *Tetrahedron* **2000**, *56*, 3263−3283.
(2) (a) Hicks, F. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **1996**, *118*, 11688−11689. (b) Hicks, F. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 7026−7033.
(3) Shibata, T.; Takagi, K. *J. Am. Chem. Soc.* **2000**, *122*, 9852−9853.
(4) (a) Hiroi, K.; Watanabe, T.; Kawagishi, R., Abe, I *Tetrahedron Lett.* **2000**, *41*, 891−895. (b) Hiroi, K.; Watanabe, T.; Kawagishi, R.; Abe, I. *Tetrahedron: Asymmetry* **2000**, *11*, 797−808.
(5) Jeong, N.; Sung, B. K.; Choi, Y. K. *J. Am. Chem. Soc.* **2000**, *122*, 6771−6772.
(6) Sturla, S. J.; Buchwald, S. L. *J. Org. Chem.* **1999**, *64*, 5547−5550.
(7) For cobalt-catalyzed reactions, see: (a) Rautenstrauch, V.; Mégard, P.; Conesa, J.; Küster, W. *Angew. Chem., Int. Ed.* **1990**, *29*, 1413−1416. (b) Jeong, N.; Hwang, S. H.; Lee, Y.; Chung, Y. K. *J. Am. Chem. Soc.* **1994**, *116*, 3159−3160. (c) Lee, B. Y.; Chung, Y. K.; Jeong, M.; Lee, Y.; Hwang, S. H. *J. Am. Chem. Soc.* **1994**, *116*, 8793−8794. (d) Lee, N. Y.; Chung, Y. K. *Tetrahedron Lett.* **1996**, *37*, 3145−3148. (e) Pagenkopf, B. L.; Livinghouse, T. *J. Am. Chem. Soc.* **1996**, *118*, 2285−2286. (f) Jeong, N.; Hwang, S. H.; Lee, Y. W.; Lim, J. S. *J. Am. Chem. Soc.* **1997**, *119*, 10549−10550. (g) Sugihara, T.; Yamaguchi, M. *J. Am. Chem. Soc.* **1998**, *120*, 10782−10783. (h) Sugihara, T.; Yamaguchi, M. *Synlett* **1998**, 1384−1386. (i) Belanger, D. B.; O'Mahony, D. J. R.; Livinghouse, T. *Tetrahedron Lett.* **1998**, *39*, 7637−7640. (j) Belanger, D. B.; Livinghouse, T. *Tetrahedron Lett.* **1998**, *39*, 7641−7644. (k) Krafft, M. E.; Bonaga, L. V. R.; Hirosawa, C. *Tetrahedron Lett.* **1999**, *40*, 9171−9175. (l) Kim, J. W.; Chung, Y. K. *Synthesis* **1998**, 142−144. (m) Hayashi, M.; Hashimoto, Y.; Yamamoto, Y.; Usuki, J.; Saigo, K. *Angew. Chem., Int. Ed.* **2000**, *39*, 631−633. (n) Kim, S.-W.; Son, S. U.; Lee, S. I.; Hyeon, T.; Chung, Y. K. *J. Am. Chem. Soc.* **2000**, *122*, 1550−1551. (o) Son, S. U.; Lee, S. I.; Chung, Y. K. *Angew. Chem., Int. Ed.* **2000**, *39*, 4158−4160. (p) Jeong, N.; Hwang, S. H. *Angew. Chem., Int. Ed.* **2000**, *39*, 636−638. (q) Comely, A. C.; Gibson, S. E.; Stevenazzi, A.; Hales, N. J. *Tetrahedron Lett.* **2001**, *42*, 1183−1185. (r) Sugihara, T.; Yamaguchi, M. Nishizawa, M. *Chem. Eur. J.* **2001**, *7*, 1589−1595. (s) Krafft, M. E.; Boñaga, L. V. R. *Synlett* **2000**, 959−962. (t) Krafft, M. E.; Boñaga, L. V. R.; Hirosawa, C. *J. Org. Chem.* **2001**, *66*, 3004−3020. (u) Son, S. U.; Lee, S. I.; Chung, Y. K.; Kim, S.-W.; Hyeon, T. *Org. Lett.* **2002**, *4*, 277−279.
(8) Reetz, M. T.; Neugebauer, T. *Angew. Chem., Int. Ed.* **1999**, *38*, 179−181.
(9) Chen, W.; Xiao, J. *Tetrahedron Lett.* **2001**, *42*, 2897−2899.
(10) Pàmies, O.; Net, G.; Ruiz, A.; Claver, C. *Eur. J. Inorg. Chem.* **2000**, 1287−1294.

10.1021/jo016038r CCC: $22.00
Published on Web 04/25/2002

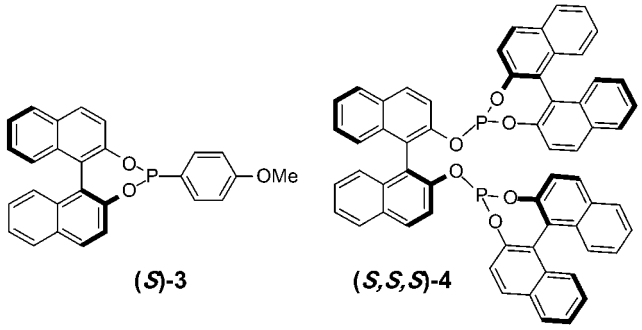


Figure 1. Chiral biaryl phosphites.

catalyzed olefin hydrocyanation, [11] rhodium- and platinum-catalyzed hydroformylation,[12−15] and rhodium-catalyzed hydrosilylation of ketones.[16] In 1991, Pringle reported the preparation of two binaphthyl-derived chiral aryl phosphites (Figure 1) and their application to a nickel-catalyzed hydrocyanation reaction.[17] Nitrile products were obtained in up to 70% chemical yields and with up to 38% ee. While the enantioselectivity was low, it surpassed those obtained using analogous phosphine systems. Furthermore, reactions employing the bisphosphite **4** proceeded with higher enantioselectivities than with the monophosphite **3**, indicating the benefit of chelation. Chan has recently used bisphosphite **4** as a ligand for the $Cu(OTf)_2$-catalyzed enantioselective conjugate addition of diethylzinc to enones, which produces products with up to 90% ee.[18]

Results and Discussion

In initial experiments aimed at preparing enantiomerically enriched bicyclic cyclopentenones using chiral phosphite−cobalt complexes, we investigated the combination of Pringle's ligands **3** and **4** with the catalytic conditions developed by Livinghouse.[7i] Thus, reaction of enyne **1a** with $Co_2(CO)_8$ and **3** or **4** in DME under 3.1 atm of carbon monoxide at 120 °C provided the corresponding bicyclic cyclopentenone **2a**. In the reaction using monophosphite **3**, the product was obtained in 9% ee (54% yield), while the reaction with bisphosphite **4** afforded **2a** in 60% ee (Table 1, entry 1).

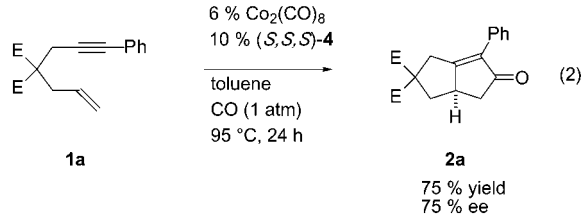


Table 1. Effect of Reaction Conditions on the Formation of 2b[a]

entry	mol % **4**	temp (°C)	solvent	P_{CO} (atm)	% yield[b]	% ee[c]
1	10	120	DME	3.1	89	60
2	10	60	DME	3.1	<10	0
3	10	120	DME	2.0	84	64
4	7	90	DCE[d]	1.0	70	61
5	10	95	DME	1.0	35	73
6	10	95	DME	3.2	82	57
7	10	120	DME	3.2	91	59
8	10	95	toluene	1.0	71	76
9	10	95	toluene	3.2	67	53
10	10	120	toluene	3.2	92	57
11	5	95	toluene	1.0	78	59
12	15	95	toluene	1.0	<10	77
13	21	95	toluene	1.0	<10	81

[a] All reactions were carried out using 6 mol % $Co_2(CO)_8$ for approximately 24 h. [b] Yield based on GC analysis relative to dodecane as an internal standard for a single experiment. Results reported in eq 2 are averaged from several runs, and the yield refers to isolated material. [c] Measured by chiral HPLC. [d] Dichloroethylene.

The transformation was also catalyzed with a complex formed from the "mixed" diastereomer (*S*,*R*,*S*)-**4** in which the central portion of the ligand is derived from (*R*)-BINOL and the terminal portions are derived from (*S*)-BINOL. In this case, cyclopentenone **2a** was obtained in 87% yield and 13% ee. The dramatic decrease in enantioselectivity may be due to a mismatched situation between the backbone and terminal biaryl moieties.[19] On the basis of ^{31}P NMR,[20] however, (*S*,*R*,*S*)-**4** (δ 145.4) was never cleanly obtained; it was contaminated by (*S*,*S*,*S*)-**4** (δ 144.7) and species indicated by four minor ^{31}P resonances at δ 145.9, 145.7, 144.3, and 144.2. The dramatic decrease of enantioselectivity for the reaction with (*S*,*R*,*S*)-**4** may therefore be caused by the formation of a mixture of diastereomeric catalysts in which the terminal and central portions of the ligand have been transposed.[21] Additionally, the existence of multiple catalytic species may contribute to the diminished enantiomeric excess. Nonetheless, we were pleased that asymmetry could be induced in the PK reaction from the readily available, symmetric chiral aryl bisphosphite (*S*,*S*,*S*)-**4** and proceeded to optimize reaction conditions using this ligand.

We investigated the influence of solvent, temperature, carbon monoxide pressure, and ligand−metal ratios on the efficiency and enantioselectivity of the cobalt−phosphite-catalyzed transformation of **1a** to **2a** (eq 2). Some of these results are summarized in Table 1, and the optimized conditions are represented in eq 2. By using toluene instead of DME (entry 8 vs entry 5), moderate levels of enantioselectivity were realized while the degree of conversion to product was increased. While the enantioselectivity of the reaction improved with higher ligand−metal ratios (entries 12 and 13), the yield deteriorated significantly.

To maintain a high degree of enantioselectivity in this process, it was important to precomplex the phosphite

(11) Yan, M.; Xu, Q.-Y.; Chan, A. S. C. *Tetrahedron: Asymmetry* **2000**, *11*, 845−849.
(12) Kadyrov, R.; Heller, D.; Selke, R. *Tetrahedron: Asymmetry* **1998**, *9*, 329−340.
(13) Buisman, G. J. H.; Veen, L. A. v. d.; Klootwijk, A.; Lange, W. G. J. d.; Kamer, P. C. J.; Leeuwen, P. W. N. M. v.; Vogt, D. *Organometallics* **1997**, *16*, 2929−2939 and references therein.
(14) Moasser, B.; Gladfelter, W. L. *Inorg. Chim. Acta* **1996**, *242*, 125−136.
(15) Cserépi-Szucs, S.; Huttner, G.; Zsolnai, L.; Szölosy, A.; Hegedüs, C.; Bakos, J. *Inorg. Chim. Acta* **1999**, *296*, 222−230.
(16) Sakaki, J.-i.; Schweizer, W. B.; Seebach, D. *Helv. Chim. Acta* **1993**, *76*, 2654−2665.
(17) Baker, M. J.; Pringle, P. G. *J. Chem. Soc., Chem. Commun.* **1991**, 1292−1293.
(18) (a) Yan, M.; Yang, L.-W.; Wong, K.-Y.; Chan, A. S. C. *Chem. Commun.* **1999**, 11−12. (b) Yan, M.; Chan, A. S. C. *Tetrahedron Lett.* **1999**, *40*, 6645−6648.
(19) Masamune, S.; Choy, W.; Peterson, J. S.; Sita, L. R. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 1−30.
(20) ^{31}P NMR, 120 MHz, $CDCl_3$
(21) Cserépi-Szucs and co-workers have applied (*S*,*S*,*S*)-**4** and (*S*,*R*,*S*)-**4** to the platinum-catalyzed hydroformylation of styrene and observed the highest ee (65%) in the case of the "mixed" ligand (*S*,*R*,*S*)-**4**. The hydroformylation was carried out at 23 °C, but the trend was still evident in experiments carried out at 60 °C. See ref 15.

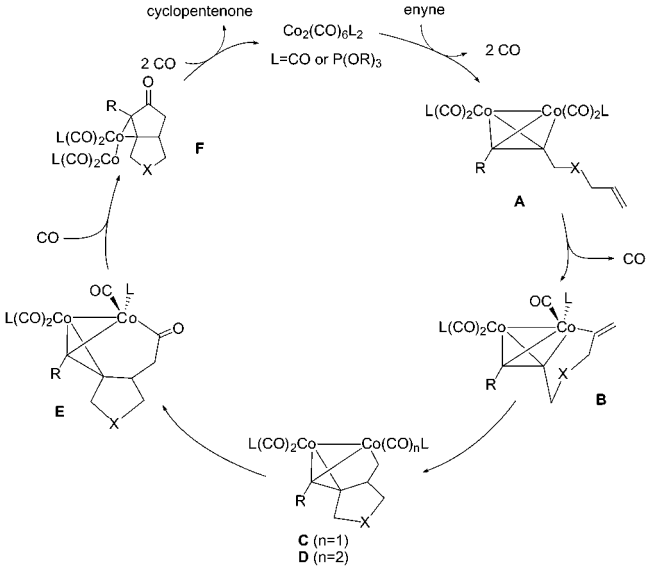
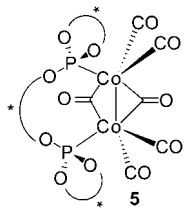


Figure 2. Suggested pathway of the catalytic PK reaction.

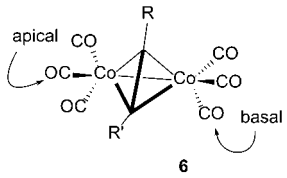
and cobalt before addition of the enyne such that initial unselective cyclization by $Co_2(CO)_8$ is minimized. In the general protocol, a toluene solution of $Co_2(CO)_8$ was added to a slurry of the partially soluble phosphite **4** in toluene. After stirring for 20 min, liberation of carbon monoxide was observed and a homogeneous brown solution was produced. The enyne, followed by carbon monoxide, was then introduced. At this point, the ^{31}P NMR spectrum[20] of the cobalt−phosphite complex contained a single broad peak at δ 174; the free phosphite (*S*,*S*,*S*)-**4** displays a sharp singlet at δ 145.[22] From these data, and by analogy with a related rhodium carbonyl−phosphite complex, it is proposed that a species such as **5** is formed.[14] Upon addition of an enyne to **5** at room temperature, no spectral change (NMR) was evident.



5

As illustrated in Figure 2, the general pathway proposed for the stoichiometric process by Magnus can be modified to describe either the $Co_2(CO)_8$-catalyzed process (L = CO) or the reaction catalyzed by **5** (L_2 = **4**).[23] Density functional theory level calculations have provided information regarding the structures and energetics of various intermediates and transition states proposed for the intermolecular reaction.[24,25] The first step has been experimentally demonstrated to involve the formation of a dicobalt−alkyne complex, **A**, with extrusion of carbon monoxide. It has been proposed that the π-acidic phosphite ligand facilitates the loss of carbon monoxide from complexes such as **A**.[7b] Olefin insertion into the cobalt−carbon bond in the subsequently formed dicobalt−olefin complex **B** generates metallacycle **C** and, in the intramolecular process, a stereogenic center. Remaining steps in the pathway include carbon monoxide binding (**D**), alkyl migration (**E**), reductive elimination (**F**), and decomplexation to yield the free cyclopentenone.

In the cobalt−phosphite-catalyzed reaction, we propose that a cobalt−phosphite−alkyne complex is initially formed, as is supported by ESI MS data. Addition of excess diphenyl acetylene to the cobalt−phosphite complex, **5**, followed by heating at 95 °C for 10 h and concentration under vacuum, provided a brown solid that was purified by flash chromatography (1:4 Et_2O/hexanes). The MS data shows M^+ 1238.2337, corresponding to M^+ calculated for $C_{75}H_{46}Co_2O_7P_2$ (cobalt−phosphite−alkyne complex with loss of three carbon monoxide ligands). There are also small MS peaks corresponding to the proposed complex with loss of one and two carbon monoxide ligands. While monophosphites such as trimethyl phosphite are proposed to replace up to four carbon monoxide ligands on a general cobalt−alkyne complex represented by **6**, to the best of our knowledge,



6

there are no reports of structurally characterized cobalt−bisphosphite−alkyne complexes in the literature.[26] On the other hand, cobalt−ligand−alkyne complexes have been extensively characterized for phosphine ligands. Monophosphines such as triphenylphosphine usually displace one molecule of carbon monoxide from the apical position.[26a,27] In the case of chelating ligands, there exists the potential for each phosphine to bind in either an apical or basal position and to span both cobalt atoms (bridging) or bind to only one. Indeed, structures representing all of the possible combinations (except apical−basal bridged) have been characterized, and the geometry attained in the complex generally depends on the bite angle of the ligand.[26a,28] The crystal structure of (3,3-dimethylbutyne[(*R*)-BINAP]$Co_2(CO)_4$ reveals a basal-bridged species with apical Co−CO bonds [1.767(2)−1.768(2) Å] that are shorter than the basal Co−CO bonds

(22) While IR can be a valuable technique to derive structural information regarding complexes such as **5** and **7**, routine room-temperature IR examination of such species provided little insight. Complex **5** displayed a broad and complex pattern in the carbonyl region where *at least* four major stretches were observed: 2029, 2001, 1987, and 1799 cm^{-1} (KBr). Structural characterization of cobalt carbonyl complexes has been a historically difficult problem and is further complicated by the typically fluxional behavior of such compounds, both in solution and in the solid state. For example, $Co_2(CO)_8$ has three solution structures and entire studies have been dedicated to their characterization by IR. For seminal contributions, see: (a) Bor, G.; Noack, K. *J. Organomet. Chem.* **1974**, *64*, 367−372. (b) Bor, G.; Dietter, U. K.; Noack, K. *J. Chem. Soc., Chem. Commun.* **1976**, 914−916. (c) Sweany, R. L.; Brown, T. L. *Inorg. Chem.* **1977**, *16*, 415−421.

(23) Magnus, P.; Priciple, L. M. *Tetrahedron Lett.* **1985**, *26*, 4851−4854.

(24) Bruin, T. J. M. d.; Milet, A.; Robert, F.; Gimbert, Y.; Greene, A. E. *J. Am. Chem. Soc.* **2001**, *123*, 7184−7185.

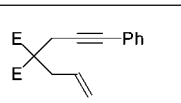
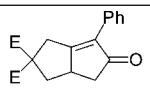
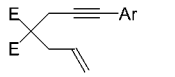
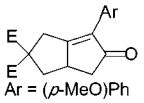
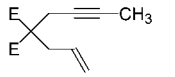
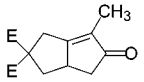
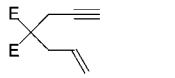
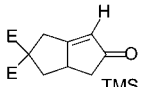
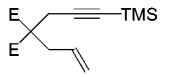
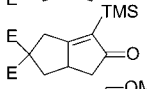
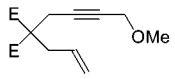
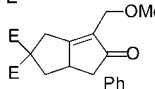
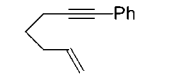
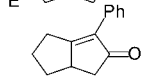
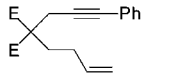
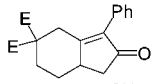
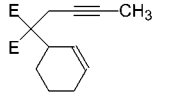
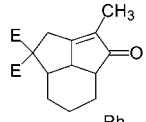
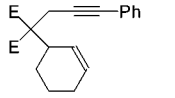
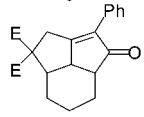
(25) Yamanaka, M.; Nakamura, E. *J. Am. Chem. Soc.* **2001**, *123*, 1703−1708.

(26) For studies involving cobalt−phosphite−alkyne complexes, see: (a) Chia, L. S.; Cullen, W. R.; Franklin, M.; Manning, A. R. *Inorg. Chem.* **1975**, *14*, 2521−2526. (b) Billington, D. C.; Helps, I. M.; Pauson, P. L.; Thomson, W.; Willison, D. *J. Organometallic Chem.* **1988**, *354*, 243−248. (c) Park, H.-J.; Lee, B. Y.; Kang, Y. K.; Chung, Y. K. *Organometallics* **1995**, *14*, 3104−3107. (d) Carbery, D. R.; Derr, W. J.; Lindsay, D. M.; Scott, J. S.; Watson, S. P. *Tetrahedron Lett.* **2000**, *41*, 3235−3239.

(27) Bonnet, J. J.; Mathieu, R. *Inorg. Chem.* **1978**, *17*, 1973−1977.

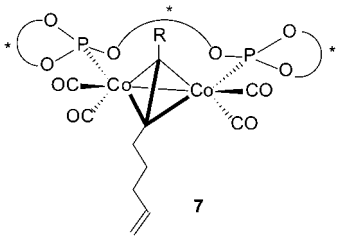
(28) Derdau, V.; Laschat, S.; Dix, I.; Jones, P. G. *Organometallics* **1999**, *18*, 3859−3864.

Table 2. Scope of the Asymmetric Cobalt−Phosphite-Catalyzed Pauson−Khand Reaction

entry	enyne[a] (**1**)	cyclopentenone[a] (**2**)	yield %	ee
a			75	75
b		 Ar = (*p*-MeO)Ph	82	64
c			97	7
d			87	22[b]
e			20	2
f			80	14
g			16[c]	11
h[d]			38	10
i			50	4
j			no reaction	

[a] E = CO_2Et. [b] Incremental ee increases from 4 to 26% over the course of the reaction. [c] Yield based on GC analysis. [d] Reaction carried out at 120 °C.

[1.788(2)−1.795(2) Å].[28] An analogous structure, represented by **7**, may be formed in the case of bisphosphite



7

4. Such a complex would correspond to intermediate **A** in the catalytic sequence (Figure 2). While it is unclear if the olefin displaces a carbon monoxide from an apical or basal position, by comparison of data from previous work,[2b] cyclization with the (*S*,*S*,*S*)-phosphite provides the (*R*)-cyclopentenone (eq 2).

The scope of the asymmetric catalyst was examined by subjecting a variety of enynes to the general reaction protocol. While the aryl-substituted [3.3.0] bicycle **2b** could also be formed having a reasonable enantiomeric excess, other changes in the enyne structure resulted in a sharp deterioration of enantioselectivity (Table 2).

Products of the cyclization of methyl (**2c** and **2i**), terminal (**2d**), and trimethylsilyl-substituted (**2e**) alkynes were obtained with very low enantiomeric excess. In the case of the terminal alkyne, the enantiomeric excess

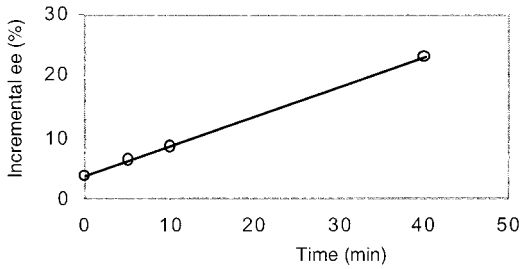
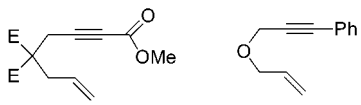


Figure 3. Incremental ee vs time for the formation of **2d**.

changed over the course of the reaction. By collecting data at various time points, we found that the incremental enantiomeric excess increased from 4% to 26% (Figure 3).[29] The incremental enantiomeric excess is the instantaneous enantioselectivity of a reaction at a given time point and is distinguished from the cumulative enantiomeric excess, which represents an integral property that is directly measurable.[30] The initial data point is obtained by quenching the reaction immediately after introducing carbon monoxide. The observations are most simply explained by the initial presence of residual free $Co_2(CO)_8$. Over time, this material is completely ligated by the phosphite or subject to decomposition, and the reaction progresses with a higher degree of selectivity.[31]

We queried whether the cobalt−phosphite catalyst may be effective for the asymmetric cyclization of a potentially chelating substrate such as **1f**. Cyclopentenone **2f**, however, was formed in only 14% ee. In the absence of geminal disubstitution on the alkyne−olefin linker, the reaction proceeded with poor efficiency and enantioselectivity, even with the activating phenyl substituent on the alkyne (entry g). The [4.3.0] bicyclic cyclopentenone **2h**, formed from an arylalkyne precursor, was obtained in 10% ee. Cyclizations of enynes containing a substituted olefin and either an aryl or methyl alkyne were also attempted. In the case of the methyl alkyne (**1i**), the cyclization proceeded, but with essentially no enantioselectivity (**2i**). While data suggested that the [4.3.0]cyclopentenone **2j** may be generated with reasonable enantiomeric excess (because of the arylalkyne precursor), enyne **1j** was unreactive. Finally, use of enynes **1k** or **1l** as substrates resulted in decomposition of the enyne.



1k **1l**

(29) The incremental enantiomeric excess was calculated on the basis of the following data and equations: t = 0 min, 75% starting material (sm), 7% product (pdt) in 2% ee; t = 5 min, 62% sm, 33% pdt in 6% ee; t = 10 min, 57% sm, 35% pdt in 7% ee; t = 40 min, 7% sm, 76% pdt in 13% ee; t = 798 min, 1% sm, 90% pdt in 14% ee; (i) ee = $(R - S)/(R + S)$ [where R = mol fraction (R)-isomer and S = mol fraction (S)-isomer]; (ii) ee(inc) = d(ee)/dt = [d($R - S$)/dt]/[d($R + S$)/dt]; (iii) ee = $N_{A0}X_A$ [where N_{AO} = initial fraction of substrate (A) and X_A = fraction of A consumed in the reaction]; (iv) ee = $R - S/N_{A0}X_A$; (v) $R - S$ = (ee)$N_{A0}X_A$; (vi) $R + S = N_{A0}X_A$; and (vii) ee(inc) = $[X_A\text{ee}' + \text{ee}X']/X'$.

(30) Levenspiel, O. *Chemical Reaction Engineering*; Wiley: New York, 1999.

(31) At high temperatures, $Co_2(CO)_8$ exists in equilibrium with $Co_4(CO)_{12}$; conversion to the corresponding (toluene)$Co_4(CO)_9$ complex has also been proposed. Furthermore, cobalt carbonyl compounds are subject to thermal decomposition to metallic cobalt and free CO. Bor, G.; Dietler, U. K. *J. Organomet. Chem.* **1980**, *191*, 295−302.

Conclusions

It has been known for several years that the PK reaction can be catalyzed by a cobalt−phosphite complex.[7b] While the efficacy of chiral phosphites in a variety of metal-catalyzed transformations is clear, to our knowledge there have been no reports of a chiral cobalt−phosphite catalyst for the PK reaction. We have found that a complex formed from $Co_2(CO)_8$ and chiral aryl bisphosphite **4** can efficiently cyclocarbonylate aryl-substituted 1,6-enynes to cyclopentenones in up to 75% ee. However, the scope of this process is, unfortunately, quite limited.

Experimental Section

General Considerations. Chiral HPLC analyses were carried out by using Chiracel columns and monitoring the chromatogram at 254 nm, under the conditions described. Chiral GC analyses were carried out using Chiraldex columns with an FID. Anhydrous DMF, DCE, and DME were purchased from Aldrich. Resealable Schlenk tubes were purchased from Kontes. Toluene was purified by passing it through a dry alumina column under argon.[32] Carbon monoxide was scientific grade (minimum purity 99.997%) from MG Industries. Melting points were determined with a Mel-Temp II from Laboratory Devices and are uncorrected. Dicobalt octacarbonyl was purchased from Strem Chemicals, Inc., stored at 0 °C in an argon-filled glovebox, and used without further purification. The phosphite **4** was prepared as previously described.[17]

2-Allyl-2-(4-methoxybut-2-ynyl)malonic Acid Diethyl Ester (1f). The title compound was prepared by the method of Padwa et al. from diethyl allyl malonate (2.0 mL, 10.1 mmol).[33] Purification by flash chromatography (1:9 Et_2O/hexanes) afforded 2.58 g (91% yield) of a colorless oil. ^{1}H NMR (500 MHz, C_6D_6): δ 5.72 (m, 1H), 5.16 (m, 1H), 5.01 (m, 1H), 3.95 (q, J = 7.0 Hz, 4H), 3.83 (t, J = 2.1 Hz, 2H), 3.15 (s, 2H), 3.10 (m, 5H), 0.89 (t, J = 7.0 Hz, 6H). ^{13}C NMR (125 MHz, C_6D_6): δ 169.7, 132.4, 119.7, 81.5, 80.0, 61.5, 59.8, 57.1, 56.9, 37.1, 23.4, 14.0. IR (neat): 2984, 1733. Anal. Calcd for $C_{15}H_{22}O_5$: C, 63.80; H, 7.86. Found: C, 64.18; H, 7.89.

2-(But-3-enyl)-2-(3-phenylprop-2-ynyl)malonic Acid Diethyl Ester (1h). Diethyl(phenylpropargyl)malonate[2b] (1.8 g, 6.9 mmol) was added to a slurry of NaH (0.3 g, 12.5 mmol) in DMF (8 mL) at 0 °C. The reaction mixture was warmed to 25 °C and stirred for 1 h. The mixture was cooled to 0 °C, 1-bromo-3-butene was added, and the mixture was allowed to warm to 25 °C. After 12 h, the reaction mixture was cautiously quenched with saturated aqueous NH_4Cl and extracted into Et_2O. The Et_2O solution was rinsed with brine, dried with Na_2SO_4, filtered, and concentrated. Purification by flash chromatography afforded 1.55 g (69% yield) of a colorless oil. ^{1}H NMR (300 MHz, C_6D_6): δ 7.42 (m, 2H), 6.94 (m, 3H), 5.73 (m, 1H), 5.03 (dd, J = 16.9, 1.8 Hz, 1H), 4.90 (dd, J = 10.1, 1.8 Hz, 1H), 3.96 (qd, J = 7.2, 1.8 Hz, 4H), 3.30 (s, 2H), 2.56 (m, 2H), 2.13 (m, 2H), 0.89 (t, J = 7.2 Hz, 6 H). ^{13}C NMR (125 MHz, C_6D_6): δ 170.2, 137.7, 132.0, 128.5, 128.1, 123.8, 115.3, 85.1, 84.1, 61.4, 57.4, 32.1, 28.9, 24.3, 14.0. IR (neat): 2984, 1729. Anal. Calcd for $C_{20}H_{24}O_4$: C, 73.13; H, 7.37. Found: C, 73.24; H, 7.42.

General Procedure for the Conversion of Enynes to Cyclopentenones. In a dry scintillation vial in an argon-filled glovebox, a solution of $Co_2(CO)_8$ (10 mg, 0.03 mmol) in toluene (2 mL) was added to a slurry of phosphite **4** (46 mg, 0.05 mmol) in toluene (2 mL). Residual $Co_2(CO)_8$ was rinsed into the mixture with additional toluene (1 mL). After 20 min of stirring, the enyne was added to the homogeneous solution. The reaction mixture was then transferred to a resealable Schlenk tube. The flask was sealed, removed from the glovebox, and attached to a CO source in line with a vacuum pump and a pressure gauge. The headspace of the flask was evacuated and refilled with CO at least three times and then filled with CO (1 atm) and sealed. The flask was heated for 24 h. **CAUTION:** *It is important to take appropriate safety precautions when using carbon monoxide, particularly at elevated pressure. All operations should be carried out in an efficient fume hood behind a blast shield*. The reaction mixture was allowed to cool to 25 °C and the CO was carefully released in the hood. The crude reaction mixture was diluted with ether, filtered through a plug of silica, concentrated, and purified by flash chromatography.

5-Oxo-6-phenyl-3,3a,4,5-tetrahydro-1*H*-pentalene-2,2-dicarboxylic Acid Diethyl Ester (2a). Reaction of **1a**[34] (140 mg, 0.48 mmol) using the general reaction conditions afforded 108 mg (71% yield) of a colorless oil. The enantiomeric excess was determined to be 76% by chiral HPLC (OD column; 0.5 mL/min; 90:10 hexanes/IPA; major peak, 25.0 min; minor peak, 23.0 min). The ^{1}H NMR of the product matched the published spectrum.[34]

6-(4-Methoxyphenyl)-5-oxo-3,3a,4,5-tetrahydro-1*H*-pentalene-2,2-dicarboxylic Acid Diethyl Ester (2b). Reaction of **1b**[2b] (140 mg, 0.47 mmol) using the general reaction conditions afforded 125 mg (82% yield) of a colorless oil. The enantiomeric excess was determined to be 64% by the previously described method[2b] [reduction of the ketone and derivitization with (*S*)-(−)-MTPA; ^{19}F NMR (470 MHz, C_6D_6) major isomer, δ −71.4 ppm; minor isomer, δ −71.9]. The ^{1}H NMR of the product matched the published spectrum.[2b]

6-Methyl-5-oxo-3,3a,4,5-tetrahydro-1*H*-pentalene-2,2-dicarboxylic Acid Diethyl Ester (2c). Reaction of **1c**[35] (105 mg, 0.42 mmol) using the general reaction conditions afforded 114 mg (97% yield) of a colorless oil. The enantiomeric excess was determined to be 7% by chiral GC (G-TA column; 2.0 mL/min; 150 °C isothermal; major peak, 21.2 min; minor peak, 20.6 min). The ^{1}H NMR of the product matched the published spectrum.[36]

5-Oxo-3,3a,4,5-tetrahydro-1*H*-pentalene-2,2-dicarboxylic Acid Diethyl Ester (2d). Reaction of **1d**[7e] (141 mg, 0.56 mmol) using the general reaction conditions afforded 137 mg (87% yield) of a colorless oil. The enantiomeric excess was determined to be 22% by chiral GC (B-PH column; 1.0 mL/min; 150 °C isothermal; major peak, 61.0 min; minor peak, 58.9 min). The ^{1}H NMR of the product matched the published spectrum.[7e]

5-Oxo-6-trimethylsilyl-3,3a,4,5-tetrahydro-1*H*-pentalene-2,2-dicarboxylic Acid Diethyl Ester (2e). Reaction of **1e**[37,38] (160 mg, 0.57 mmol) under the general reaction conditions, using $Co_2(CO)_8$ (13 mg, 0.038 mmol), phosphite **4** (20 mg, 0.044 mmol), and CO (32 psig), afforded 35 mg (20% yield) of a colorless oil. The enantiomeric excess was determined to be 2% by chiral GC (B-PH column; 1.0 mL/min; 150 °C isothermal; major peak, 38.0 min; minor peak, 36.7 min). The ^{1}H NMR of the product matched the published spectrum.[37]

6-Methoxy-5-oxo-3,3a,4,5-tetrahydro-1*H*-pentalene-2,2-dicarboxylic Acid Diethyl Ester (2f). Reaction of **1f** (137 mg, 0.49 mmol) using the general reaction conditions afforded 122 mg (80% yield) of a colorless oil. The enantiomeric excess was determined to be 14% by chiral HPLC (OD column; 0.5 mL/min; 95:5 hexanes/IPA; major peak, 23.4 min; minor peak, 25.1 min). ^{1}H NMR (500 MHz, C_6D_6): δ 4.08 (d, J = 13.5 Hz, 1H), 4.01 (d, J = 13.5 Hz, 1H), 3.91 (m, 4H), 3.54 (d, J = 19.0 Hz, 1H), 3.38 (d, J = 19.0 Hz, 1H), 3.03 (s, 3H), 2.62 (m, 2H), 2.22 (dd, J = 17.5, 6.0 Hz, 1H), 1.68 (dd, J = 17.5, 3.0 Hz, 1H), 1.46 (m, 1H), 0.89 (t, J = 7.0 Hz, 3H), 0.87 (t, J = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, C_6D_6): δ 205.9, 179.1, 171.5, 170.8,

(32) Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H. *Organometallics* **1996**, *15*, 1518−1520.
(33) Padwa, A.; Meske, M.; Ni, Z. *Tetrahedron* **1995**, *51*, 89−106.
(34) Zhang, M.; Buchwald, S. L. *J. Org. Chem.* **1996**, *61*, 4498−4499.
(35) Grossman, R. B.; Buchwald, S. L. *J. Am. Chem. Soc.* **1994**, *116*, 8593−8601.
(36) Grossman, R. B.; Buchwald, S. L. *J. Org. Chem.* **1992**, *57*, 5803−5805.
(37) Kondo, T.; Suzuki, N.; Okada, T.; Mitsudo, T.-a. *J. Am. Chem. Soc.* **1997**, *119*, 6187−6188.
(38) Hay, A. M.; Kerr, W. J.; Kirk, G. G.; Middlemiss, D. *Organometallics* **1995**, *14*, 4986−4988.

134.2, 66.4, 61.7, 61.6, 61.3, 58.5, 43.5, 41.4, 38.9, 34.9, 13.9. IR (neat): 2983, 2935, 1727, 1710, 1673. Anal. Calcd for $C_{16}H_{22}O_6$: C, 61.91; H, 7.15. Found: C, 61.78; H, 7.21.

3-Phenyl-4,5,6,6a-tetrahydro-1*H*-pentalen-2-one (2g). Reaction of **1g**[39] (82 mg, 0.48 mmol) using the general reaction conditions with dodecane as an internal standard indicated a 16% yield of the cyclopentenone by GC. The enantiomeric excess was determined to be 11% by chiral GC (B-PH column; 150 °C isothermal; 1.0 mL/min; major peak, 45.9 min; minor peak, 50.1 min). The ^{1}H NMR of the isolated material matched the published spectrum.[38]

2-Oxo-3-phenyl-1,2,4,6,7,7a-hexahydroindene-5,5-dicarboxylic Acid Diethyl Ester (2h). Reaction of **1h** (145 mg, 0.44 mmol) using the general reaction conditions (at 120 °C) followed by purification by flash chromatography (1:2 EtOAc/hexanes) afforded 60 mg (38% yield) of a white solid, mp 104 °C. The enantiomeric excess was determined to be 10% by chiral HPLC (OD column; 0.5 mL/min; 3% IPA/hexanes; major peak, 58.6 min; minor peak, 52.0 min). ^{1}H NMR (300 MHz, C_6D_6): δ 7.56, (d, J = 8.0 Hz, 2H), 7.22 (t, J = 7.7 Hz, 2H), 7.09 (tt, J = 7.4, 1.4 Hz, 1H), 3.80 (m, 5H), 2.53 (m, 2H), 2.29 (dd, J = 18.6, 6.6 Hz, 1H), 1.97 (m, 1H), 1.72 (m, 2H), 1.57 (m, 1H), 1.29 (qd, J = 13.5, 3.3, 1H), 0.81 (t, J = 7.2 Hz, 3H), 0.64 (t, J = 7.2 Hz, 3H). ^{13}C NMR (125 MHz, C_6D_6): δ 204.0, 171.1, 170.0, 169.7, 139.9, 132.0, 129.6, 128.4, 128.3, 61.6, 61.3, 56.4, 41.4, 38.9, 33.7, 31.1, 30.4, 13.8, 13.6. IR (neat): 2984, 1729, 1702, 1644. Anal. Calcd for $C_{21}H_{24}O_5$: C, 70.75; H, 6.79. Found: C, 70.88; H, 6.79.

3-Methyl-4-oxo-2,4,4a,5,6,7,7a,7b-octahydrocyclopenta-[*cd*]indene-1,1-dicarboxylic Acid Diethyl Ester (2i). Reaction of **1i**[2b] (80 mg, 0.27 mmol) under the general reaction conditions, using $Co_2(CO)_8$ (6 mg, 0.018 mmol) and phosphite **4** (20 mg, 0.022 mmol), afforded 43 mg (50% yield) of a colorless oil. The enantiomeric excess was determined to be 4% by chiral GC (B-PH column; 1.0 mL/min; 150 °C isothermal; major peak, 152.9 min; minor peak, 158.3 min). The ^{1}H NMR of the product matched the published spectrum.[2b]

Acknowledgment. We thank Dr. Utpal K. Singh for the calculations of incremental enantiomeric excess and helpful discussions. We are grateful to Mr. Jeremy M. Baskin for the synthesis of compound **4**. Mass spectrometric analyses were performed by Li Li of the MIT department of chemistry instrumentation facility. We thank Dr. Alex R. Muci for assistance in the preparation of the manuscript. S.J.S. acknowledges the American Chemical Society, Division of Organic Chemistry, for a graduate fellowship sponsored by Pfizer, Inc. We thank the National Institutes of Health (GM46059) for support of this research and the National Science Foundation for instrumentation grants (DBI-9729592, CHE-9808061).

JO016038R

(39) Negishi, E.-i.; Holmes, S. J.; Tour, J. M.; Miller, J. A.; Cederbaum, R. R.; Swanson, D. R.; Takahashi, T. *J. Am. Chem. Soc.* **1989**, *111*, 3336−3346.