Practical Cobalt Carbonyl Catalysis in the Thermal Pauson−Khand Reaction: Efficiency Enhancement Using Lewis Bases

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In this report we have shown that the commercially available $Co_2(CO)_8$ and $Co_4(CO)_{12}$, and enyne−$Co_2(CO)_6$ complexes, are sufficiently effective in catalyzing the Pauson−Khand reaction under one atmosphere of CO pressure. It was further demonstrated that the efficiencies of these cyclization protocols could be enhanced by the presence of cyclohexylamine. These procedures have also rendered more practical and highly convenient alternatives for the catalytic Pauson−Khand reaction. Most importantly, we have dispelled the common belief that $Co_4(CO)_{12}$ is inactive in the Pauson−Khand reaction under one atmosphere of carbon monoxide. Of mechanistic importance is that these studies have also shown that the probable formation of $Co_4(CO)_{12}$ is not necessarily a dead end pathway in the $Co_2(CO)_8$-catalyzed Pauson−Khand reaction. It is also of interest that substoichiometric amounts of $Co_2(CO)_8$, in DME and in the presence of cyclohexylamine, are sufficient for the cyclocarbonylation of enynes under a nitrogen atmosphere. Our findings have provided more practical protocols for the Pauson−Khand reaction using catalytic amounts of cobalt carbonyl complexes and a better understanding of the influence of Lewis bases on their efficiency. These reports on the activity of $Co_4(CO)_{12}$ are anticipated to develop into a convenient and practical alternative for $Co_2(CO)_8$ catalysis.

Introduction

The application of transition metal complexes in organic transformations has rendered a powerful means for the expeditious construction of complex cyclic structures from simple and readily available starting materials, in particular, when catalysis is realized in these reactions.[1] The Pauson−Khand reaction, the [2 + 2 + 1] cyclization of an alkene, an alkyne, and CO to furnish a cyclopentenone framework, is no exception to this.[2] When it was first reported by Pauson and co-workers, it involved reaction of alkenes with dicobalthexacarbonyl-complexed alkynes, which were preformed and isolated from the reaction of alkynes with a stoichiometric amount of $Co_2(CO)_8$.[2a] However, as the synthetic potential of this reaction and the limitation of its stoichiometric version were recognized, catalysis in this reaction has become the focus of research among numerous workers in this field. Thus, protocols involving catalytic use of $Co_2(CO)_8$[3] and other alternative sources of cobalt carbonyls, such as $Co_4(CO)_{12}$,[4] $Co_3(CO)_9(\mu^3\text{-CH})$,[5] $Co_4(CO)_{11}P(OPh)_3$,[6] Co(acac)$_2$/$NaBH_4$,[7] (indenyl)Co(cod),[8] $CoBr_2$/Zn/*t*-BuOH,[9] and alkyne−$Co_2(CO)_6$ complex/Et_3SiH[10] have emerged (Scheme 1). Carbonyl complexes of Ti, Ru, Rh, and Ir have likewise been reported to catalyze the analogous structural transformation of enynes.[11] Most recently, catalysis in this reaction has also been successful under heterogeneous conditions. Cobalt carbonyl complexes on polymer support,[12] and metallic cobalt on either mesoporous silica,[13] charcoal, graphite, or mesoporous carbon,[14] have been developed as heterogeneous catalytic systems. Interest-

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(1) (a) Jacobsen, E. N.; Pfaltz, A.; Yamamoto, H., Eds. *Comprehensive Asymmetric Catalysis*; Springer-Verlag: Berlin, 1999; Vols. 1 and 2. (b) Beller, M.; Bolm, C., Eds. *Transition Metals in Organic Synthesis*; Wiley-VCH: Weinhem, 1998; Vols. 1 and 2. (c) Fruhauf, H.-W. *Chem. Rev.* **1997**, *97*, 523. (d) Ojima, I.; Tzamarioudaki, M.; Li, Z.; Donovan, R. J. *Chem. Rev.* **1996**, *96*, 635.

(2) (a) Khand, I. U.; Knox, G. R.; Pauson, P. L.; Watts, W. E.; Foreman, M. I. *J. Chem. Soc., Perkin Trans. 1* **1973**, 977. (b) Pauson, P. L. *Tetrahedron* **1985**, *41*, 5855. (c) Pauson, P. L. In *Organometallics in Organic Synthesis, Aspects of A Modern Interdisciplinary Field*; de Meijere, A.; tom Dieck, H., Eds.; Springer-Verlag: Berlin, 1988; p 233. (d) Schore, N. E. *Chem. Rev.* **1988**, *88*, 1081. (e) Schore, N. E. *Org. React.* **1991**, *40*, 1. (f) Schore, N. E. In *Comprehensive Organic Synthesis*; Trost, B. M.; Fleming, I., Eds.; Pergamon Press Ltd.: Oxford, 1991; Vol. 5, p 1037. (g) Schore, N. E. In *Comprehensive Organometallic Chemistry II*; Abel, E. W.; Stone, F. A.; Wilkinson, G., Eds.; Elsevier: New York, 1995; Vol. 12, p 703. (h) Geis, O.; Schmalz, H. G. *Angew. Chem., Int. Ed.* **1998**, *37*, 911. (i) Ingate, S. T.; Marco-Contelles, J. *Org. Prep. Proced. Int.* **1998**, *30*, 123. (j) Jeong, N. In *Transition Metals in Organic Synthesis*; Beller, M.; Bolm, C., Eds.; Wiley-VCH: Weinhem, 1998; Vol. 1, p 560. (k) Chung, Y. K. *Coordination Chem. Rev.* **1999**, *188*, 297. (l) Buchwald, S. L.; Hicks, F. A. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N.; Pfaltz, A.; Yamamoto, H., Eds.; Springer-Verlag: Berlin, 1999; Vol II, p 491. (m) Brummond, K M.; Kent, J. L. *Tetrahedron* **2000**, *56*, 3263.

(3) (a) Pagenkopf, B. L.; Livinghouse, T. *J. Am. Chem. Soc.* **1996**, *118*, 2285. (b) Belanger, D. B.; O'Mahony, D. J. R.; Livinghouse, T. *Tetrahedron Lett.* **1998**, *39*, 7637. (c) Krafft, M. E.; Boñaga, L. V. R.; Hirosawa, C. *Tetrahedron Lett.* **1999**, *40*, 9171. (d) Sugihara, T.; Yamaguchi, M. *Synlett* **1998**, 1384. (e) Jeong, N.; Hwang, S. H.; Lee, Y.; Chung, Y. K. *J. Am. Chem. Soc.* **1994**, *116*, 3159. (f) Hayashi, M.; Hashimoto, Y.; Yamamoto, Y.; Usuki, J.; Saigo, K. *Angew. Chem., Int. Ed.* **2000**, *39*, 631. (g) Hiroi, K.; Watanabe, T.; Kawagishi, R.; Abe, I. *Tetrahedron Lett.* **2000**, *41*, 891. (h) Jeong, N.; Hwang, S. H.; Lee, Y. W.; Lim, J. S. *J. Am. Chem. Soc.* **1997**, *119*, 10549. (i) Rautenstrauch, V.; Megard, P.; Conesa, J.; Kuster, W. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 1413. (j) Ford, J. G.; Kerr, W. J.; Kirk, G. G.; Lindsay, D. M.; Middlemiss, D. *Synlett* **2000**, 1415.

(4) (a) Kim, J. W.; Chung, Y. K. *Synthesis* **1998**, 142. (b) Krafft, M. E.; Boñaga, L. V. R. *Angew. Chem., Int. Ed.* **2000**, *39*, 3676.

(5) Sugihara, T.; Yamaguchi, M. *J. Am. Chem. Soc.* **1998**, *120*, 10782.

(6) Jeong, N.; Hwang, S. H. *Angew. Chem., Int. Ed.* **2000**, *39*, 636.

(7) Lee, N. Y.; Chung, Y. K. *Tetrahedron Lett.* **1996**, *37*, 3145.

(8) Lee, B. Y.; Chung, Y. K.; Jeong, N.; Lee, Y.; Hwang, S. H. *J. Am. Chem. Soc.* **1994**, *116*, 8793.

(9) Rajesh, T.; Periasamy, M. *Tetrahedron Lett.* **1998**, *39*, 117.

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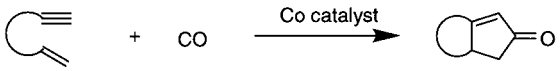
Scheme 1. Cobalt Carbonyl Catalysis in the Pauson−Khand Reaction



Co catalyst: $Co_2(CO)_8$ - with or without additive (phosphite, phosphine, cyclohexylamine, phosphane sulfide, DME, water), $Co_4(CO)_{12}$, $Co_4(CO)_{11}P(OPh)_3$, $Co_3(CO)_9(\mu^3\text{-CH})$, (indenyl)Co(COD), $Co(acac)_2$-$NaBH_4$

ingly, among these multitude of protocols available for the Pauson−Khand cyclization, $Co_2(CO)_8$ continues to be the metal complex of choice for the reaction.

Employment of high operating temperature and CO pressure,[3d,e,h,i] ultraviolet light,[3a] high-intensity ultrasound,[3j] supercritical fluids (as solvents),[3g,6] and additives[3b−f] have been found to enhance $Co_2(CO)_8$ catalysis. Additives that have been shown to be beneficial and effective in the catalytic and stoichiometric Pauson−Khand reactions are typically Lewis bases, which presumably serve as promoters or co-ligands for the cobalt catalyst. Soft Lewis bases, such as phosphines,[3g,15] phosphites,[3e] phosphine oxides,[15] sulfides,[16] and phosphane sulfides[3f] are known. Hard Lewis bases, such as amines,[3c,18] water,[3d] sulfoxides,[17] and ethers[3d] are likewise documented. Under these reaction conditions, an improvement in the yield and rate of the reaction were generally observed, although their mode of action remains speculative at this point.

Cyclohexylamine as an additive in the Pauson−Khand reaction was introduced by Sugihara wherein a significant increase in the efficiency and rate of stoichiometric thermal cycloadditions was observed.[18] It was proposed by the authors that the labilizing ability of the amine, a "hard" ligand, induced a more facile decarbonylation of the alkyne−$Co_2(CO)_6$ complex. Coordination of the reactive alkene onto the metal is consequently facilitated, thereby speeding up the cycloaddition process. Other amines, (α-methylbenzylamine, *N*,*N*,*N*′,*N*′-tetramethylethylenediamine) or alternatively, amides (*N*,*N*-dimethylformamide) have also been used by Periasamy to induce the stoichiometric Pauson−Khand reaction of in situ generated alkyne−$Co_2(CO)_6$ complexes at room temperature.[9] These latter methods for the promotion of cycloadditions were inferior to the thermal counterpart[19] and other known promoters for the Pauson−Khand reaction at ambient temperature, e.g., amine *N*-oxides. Cyclohexylamine was also shown by Livinghouse to improve the yields of thermal Pauson−Khand reactions with an alkyne−$Co_2(CO)_6$/Et_3SiH system as a catalyst precursor under a CO atmosphere.[10]

This paper presents a full account of our studies on the catalytic Pauson−Khand reaction under mild conditions and the effect of Lewis bases in the catalysis of the reaction. This has led to the development of highly practical and convenient catalytic protocols (one atmosphere of CO and mild temperatures) in the Pauson−Khand reaction using cobalt carbonyl complexes, such as $Co_2(CO)_8$, enyne−$Co_2(CO)_6$ complexes, and $Co_4(CO)_{12}$. It further describes the observed efficiency enhancement in these reactions brought about by use of cyclohexylamine, a hard Lewis base, as an additive. Last, it also accounts our observation that efficient cyclizations could be achieved using substoichiometric amounts of $Co_2(CO)_8$ under a nitrogen atmosphere, interestingly, only in the presence of an amine.

Results and Discussion

A. Octacarbonyldicobalt Catalysis. Although the utility of less than an equivalent of $Co_2(CO)_8$ for the Pauson−Khand reaction was first shown by Pauson,[2a] efficient catalysis in the reaction was only achieved later by Rautenstrauch.[3i] In their synthesis of a dihydrojasmonate precursor, a high turnnover number (>220) was realized albeit under high temperature and CO pressure (150 °C, 310−360 bar total pressure). As a consequence, catalytic protocols involving $Co_2(CO)_8$ and other alternative sources of cobalt carbonyls that have evolved were all performed under similarly rigorous conditions (80−150 °C, 3−40 atm CO). It was only in 1996 that the very first practical procedure was reported, where high-intensity visible light was used by Livinghouse to promote efficient cyclizations under much milder conditions (50−55 °C, 1 atm CO).[3a] Noting that temperatures of at least 50 °C were necessary to achieve useful reaction rates, it was later reported from the same laboratories that heat alone was sufficient to promote $Co_2(CO)_8$ catalysis, although at a narrow thermal window (60−70 °C).[3b] It is noteworthy that highly pure $Co_2(CO)_8$ was necessary in this protocol (and in other $Co_2(CO)_8$-catalyzed procedures) to achieve the best efficiency albeit its purification can be difficult and impractical.[3a,d,6] This complex is commercially dispensed with 1−5% hexane as stabilizer and is rigorously purified by either recrystallization or reduced-pressure sublimation at room temperature. When highly pure and hexane-free, however, $Co_2(CO)_8$ is moderately air-sensitive and pyrophoric.[6,20] We investigated the catalytic Pauson−Khand reaction under the Livinghouse conditions, but using the commercially available $Co_2(CO)_8$ and in the presence of an additive, e.g., cyclohexylamine.[21]

Optimization of Reaction Conditions. Initial studies showed that the cyclization of an enyne could be

(10) Belanger, D. B.; Livinghouse, T. *Tetrahedron Lett.* **1998**, *39*, 7641.

(11) Ti: (a) Hicks, F. A.; Kablaoui, N. M.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 5881. (b) Hicks, F. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 7026. Ru: (c) Kondo, T.; Suzuki, N.; Okada, T.; Mitsudo, T. *J. Am. Chem. Soc.* **1997**, *119*, 6187. (d) Morimoto, T.; Chatani, N.; Fukumoto, Y.; Murai, S. *J. Org. Chem.* **1997**, *62*, 3762. Rh (e) Koga, Y.; Kobayashi, T.; Narasaka, K. *Chem Lett.* **1998**, 249. (f) Jeong, N.; Lee, S.; Sung, B. S. *Organometallics* **1998**, *17*, 3642. (g) Jeong, N.; Sung, B. K.; Choi, K. Y. *J. Am. Chem. Soc.* **2000**, *122*, 6771. Ir: (h) Shikata, T.; Takagi, K. *J. Am. Chem. Soc.* **2000**, *122*, 9852.

(12) Comely, A. C.; Gibson, S. E.; Hales, N. J. *Chem. Commun.* **2000**, 305.

(13) Kim, S.-W.; Son, S. U.; Lee, S. I.; Hyeon, T.; Chung, Y. K. *J. Am. Chem. Soc.* **2000**, *122*, 1550.

(14) Son, S. U.; Lee, S. I.; Chung, Y. K. *Angew. Chem., Int. Ed.* **2000**, *39*, 4158.

(15) Billington, D. C.; Helps, I. M.; Pauson, P. L.; Thomson, W.; Willison, D. *J. Organomet. Chem.* **1988**, *354*, 233.

(16) Sugihara, T.; Yamada, M.; Yamaguchi, M.; Nishizawa, M. *Synlett* **1999**, 771.

(17) Chung, Y. K.; Lee, B. Y.; Jeong, N.; Hudecek, M.; Pauson, P. L. *Organometallics* **1993**, *12*, 220.

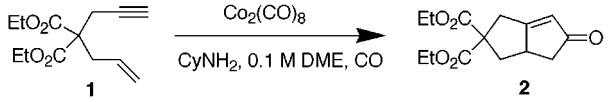
(18) Sugihara, T.; Yamada, M.; Ban, H.; Yamaguchi, M.; Kaneko, C. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2801.

(19) Rajesh, T.; Periasamy, M. *Tetrahedron Lett.* **1999**, *40*, 817.

(20) Kemmitt, R. D. W.; Russell, D. R. In *Comprehensive Organometallic Chemistry*; Abel, E. W.; Stone, F. A.; Wilkinson, G., Eds.; Pergamon Press Ltd.: Oxford, 1982; Vol. 5, p 1.

(21) After our initial report (ref 3c), commercially available $Co_2(CO)_8$ was also found to be sufficiently reactive in the catalytic Pauson−Khand reaction using phosphane sulfide as an additive under one atmosphere of CO; see ref 3f.

Table 1. Optimization Studies for $Co_2(CO)_8$ Catalysis under One Atmosphere of CO



1 2

entry[a]	$Co_2(CO)_8$ (mol %)	$CyNH_2$ (mol %)	temp (°C)	time (h)	% yield
1	5	0	65	2	60
2	10	0	65	15	80
3	10	10	65	5	87
4	10	20	65	2.5	84
5	10	20	65	4.5	81
6	10	20	65	4	84
7	10	20	65	4	84
8	5	10	70	5	89
9	10	5	70	15	77

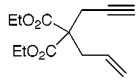
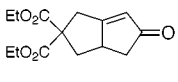
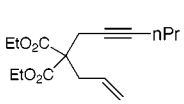
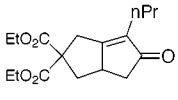
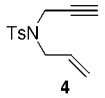
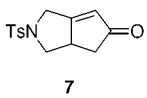
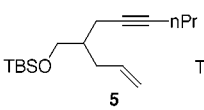
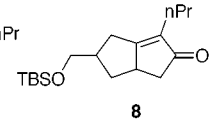
[a] Entry 4: anhydrous DME from Aldrich (sure seal bottle under nitrogen), entries 5−7: $Co_2(CO)_8$ used each came from a different bottle.

achieved in DME using 5−10 mol % of commercially available $Co_2(CO)_8$ at 65−70 °C under an atmospheric pressure of CO, either with or without cyclohexylamine (Table 1). In contrast to most $Co_2(CO)_8$-catalyzed protocols,[3a,b,d,e] we found that the catalytic reaction proceeded to completion with unpurified commercially available $Co_2(CO)_8$,[21] provided carefully base-washed glassware was used. Essentially identical results were obtained when three different bottles of $Co_2(CO)_8$ were employed without purification (entries 5−7). These bottles were stored in a laboratory freezer and had been warmed to room temperature and then exposed to air for material transfer. Thus, we found that good commercial samples of $Co_2(CO)_8$ that have been properly stored (not necessarily in a drybox) were sufficiently reactive for the catalytic process. None of the manipulations were carried out inside a glovebox. It was also observed that inadvertent introduction of air into the system from frequent checking of the reaction by TLC resulted in incomplete consumption of the starting material. Similar results were also obtained from using a fresh bottle of anhydrous DME from Aldrich (sure seal bottle under nitrogen) (entry 4 vs 5−7). Further evaluation of the catalytic reaction in different solvents showed lower yields of cyclized products in THF or toluene than in DME (Table 2). Among the enynes surveyed only enyne **1** gave the same yields in DME and toluene (entries 1−3); a lower yield was observed in THF (entry 4). A 1:1 mixture of DME and toluene gave an intermediate yield and reaction time (entry 6).

Scope and Limitations. The reactions summarized in Table 3 were each carried out in the presence and absence of cyclohexylamine to evaluate the scope and limitations of this protocol. In the examples shown, the use of cyclohexylamine provided an enhancement in the yields in most cases, although this does not appear to be predictable (cf. Table 1). However, a delicate balance of the amine and $Co_2(CO)_8$ is essential to the efficiency of this method. Examination of the results shows that an apparent limitation of the reaction conditions for the catalytic Pauson−Khand reactions under one atmosphere of CO is that enynes bearing internal alkynes and lacking significant Thorpe-Ingold assistance (entries 16, 17, and 18−20) or are sterically encumbered (entries 13 and 14) do not undergo efficient cyclization using 10 mol % catalyst loadings and require higher quantities of catalyst (30−60 mol %). It is speculated that under one atmosphere of CO, there exists a competition between CO and the alkene for coordination onto the newly generated vacant site on the cobalt metal. CO coordination is more favored when (a) steric interactions on the alkene or alkyne inhibit binding, or (b) a significant conformational mobility in the alkene tether slows down the rate of alkene binding. Subsequently, the catalyst decomposes over a prolonged reaction time.

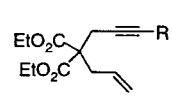
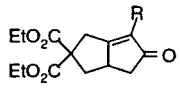
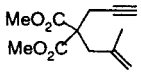
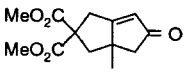
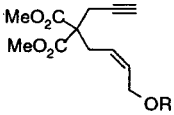
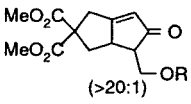
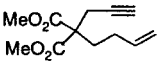
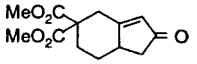
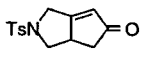
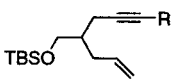
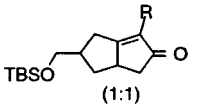
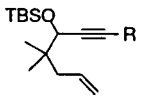
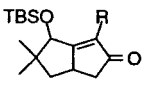
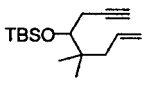
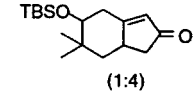
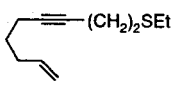
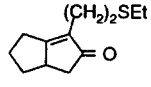
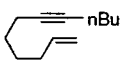
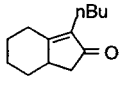
B. Dicobalthexacarbonyl-Complexed Enynes as Catalyst Precursors. Recognizing the difficulty and

Table 2. Solvent Effect on $Co_2(CO)_8$ Catalysis under One Atmosphere of CO[a]

Entry	Substrate	Product	solvent	% Yield (time, h) with $CyNH_2$	% Yield (time, h) without $CyNH_2$
1			DME	89 (22)	
2			DME	84 (2.5)	
3			toluene	94 (2.5)[b]	81 (2.5)[b]
4	1	2	THF	62 (3)	62 (3)
5			toluene	65 (13.5)	66 (5)
6			DME : toluene (1:1)	88 (8)[c]	8, 63 RSM (5)[c]
	3	6			
7			toluene	58 (21)[c]	58 (21)[c]
	4	7			
8			toluene	15, 39 RSM (22)[c]	9, 51 RSM (22)[c]
9			DME : toluene (1:1)	12, 87 RSM (10)	11, 36 RSM (10)
	5	8			

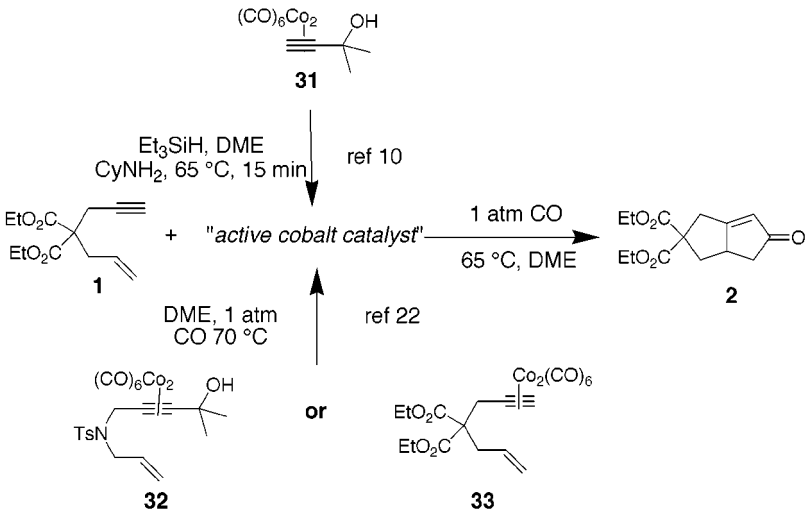
[a] All reactions were carried out using a substrate concentration of 0.1 M in toluene with 10 mol % of $Co_2(CO)_8$ and 0 or 20 mol % of cyclohexylamine under a CO atmosphere at 65 °C, unless stated otherwise. [b] 65−70 °C. [c] 0.2 M substrate concentration, 70 °C. RSM = Recovered Starting Material.

Table 3. Thermally Promoted $Co_2(CO)_8$-Catalyzed Pauson−Khand Reactions[a]

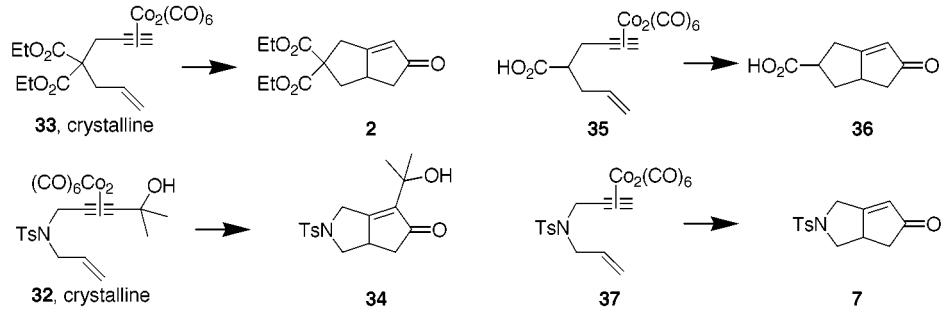
Entry	Substrate	Product (diastereomeric ratio)	% Yield (time, h) mol% $Co_2(CO)_8$: mol% $CyNH_2$ 5:20	10:0	10:20	30:0	30:60
1	 **1** R = H	 **2**	67 (5)[b] **94** (2.5)[c]	80(15)	84(2.5)	–	–
2	**3** R = *n*-Pr	**6**	5 (16) 59 RSM	56 (11.5)	**90** (11.5)	–	–
3	 **9**	 **20**	81 (14.5)[b] 44 (14.5)	**96** (15)	68(15)	–	–
4	 **10** R = TBS	 (>20:1) **21**	**80** (14.5)	74 (15.5)	68 (15.5)	–	–
5	**11** R = Ac	**22**	11 (16.5) 66 RSM	**78** (15.5)	76 (15.5)	–	–
6	 **12**	 **23**	27 (14.5) 51 RSM	**85** (15.5)	**85** (15.5)	–	–
7	 **4**	 **7**	62 (13.5)	63 (10.5)	**89** (14)	–	–
8	 **13** R = H	 (1:1) **24**	**89** (16)	40 (16) 12RSM	85 (16)	–	–
9	**5** R = *n*-Pr	**8**	8 (15) 86 RSM	–	46 (15) 52 RSM	54(15.5)	**95** (15.5)
10					86 (14)[d] 12 RSM		
11					50 (15)[e] 22 RSM		
12	**14** R= H (1:1)	**25**	24 (16.5)	71 (3.5)	**83** (3.5)	–	–
13	**15** R= Me (1:3)	**26**	–	39 (16)[f]	22 (13)[g] 36 RSM	38 (13)	**61** (16.5)
14	**16** R= TMS	**27**	–	NR	NR	NR	NR
15	 **17**	 (1:4) **28**	72 (12)	74 (3.5)	**96** (3.5)	–	–
16			–	55 (6)	16 (6)	**84** (15.5)	80 (15.5)
17	**18**	**29**		7 RSM	66 RSM 57 (13.5)[h] 36 RSM		
18	 **19**	 **30**	–	–	–	31 (17) 21 RSM	19 (17) 42 RSM
19						65(16)[i] 29 RSM	21 (16)[i] 62 RSM
20						64 (16)[j] 15 RSM	40 (16)[j] 28 RSM

[a] All reactions were carried out using a substrate concentration of 0.2 M in DME with varying amounts of $Co_2(CO)_8$ and $CyNH_2$ under a CO atmosphere at 70 °C. [b] 5 mol % $Co_2(CO)_8$. [c] 5 mol % $Co_2(CO)_8$ and 10 mol % $CyNH_2$. [d] 10 mol % $Co_2(CO)_8$ and 40 mol % $CyNH_2$. [e] 10 mol % $Co_2(CO)_8$ and 50 mol % $CyNH_2$. [f] 15 mol % $Co_2(CO)_8$ only. [g] Complex formed during a 2 h period. [h] 10 mol % $Co_2(CO)_8$ and 40 mol % $CyNH_2$. [i] 60 mol % $Co_2(CO)_8$ and 0 or 120 mol % $CyNH_2$. [j] Stoichiometric amounts of $Co_2(CO)_8$ and 0 or 2 equiv of $CyNH_2$, RSM = recovered starting material, NR = no reaction.

Scheme 2. Dicobalthexacarbonyl-Complexed Alkyne and Enyne as Catalyst Precursors



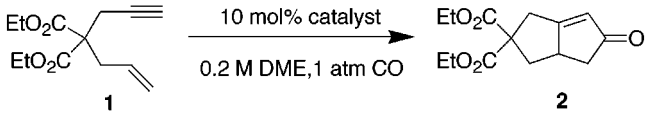
Scheme 3. Survey of Catalyst Precursors



impracticability of $Co_2(CO)_8$ purification, which was believed to be necessary for an efficient Pauson−Khand reaction catalysis under an atmospheric pressure of CO, an alternative reaction procedure was also provided by Livinghouse.[10] This protocol involved the use of a shelf-stable alkyne−$Co_2(CO)_6$ complex, which serves as a convenient surrogate for the labile $Co_2(CO)_8$. The active catalyst was presumably generated in situ from the reduction of the premade and purified initial alkyne−$Co_2(CO)_6$ complex with Et_3SiH (Scheme 2). Since the feasibility of efficient catalytic cycles under mild laboratory conditions using the alkyne−$Co_2(CO)_6$ complex−Et_3SiH system and $Co_2(CO)_8$ itself had been demonstrated, it seemed possible that a suitably substituted enyne−$Co_2(CO)_6$ complex might exhibit the same reactivity. Under a CO atmosphere, the Pauson−Khand reaction of a dicobalthexacarbonyl-complexed enyne could likewise generate the appropriate catalyst, thereby making the reduction step unnecessary (Scheme 2). This section describes the preparation and utility of new catalyst precursors (enyne−$Co_2(CO)_6$ complexes), which obviate the need for the additional reduction step.[22]

Design of Catalyst Precursors. Several requirements were envisioned in the design of a suitable catalyst precursor. First, the enyne complex needed to be sufficiently reactive to undergo cycloaddition and liberate the catalyst at a reasonable rate upon heating. Complexes of enynes bearing terminal alkynes or having Thorpe-Ingold assistance generally cyclize at a sufficient rate. Second, the cycloaddition product from the catalyst precursor must differ in polarity from the desired product to eliminate any separation problems after the reaction. Finally, the catalyst precursor must be shelf-stable, preferably crystalline, and easy to purify. Although it may not always be practical, a catalytic amount of the dicobalthexacarbonyl complex of the actual substrate of interest could also be used.

Table 4. Evaluation of Catalyst Precursors

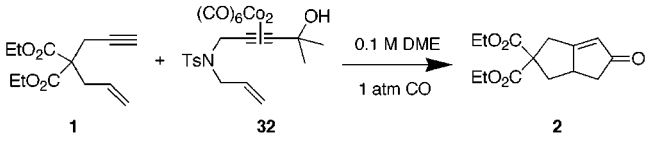


entry	catalyst	temp (°C)	time (h)	% yield
1	$Co_2(CO)_8$	65	15	80
2	**32**	70	2	78
3	**33**	70	5	79[a]
4	**35**	70	1	75
5	**37**	70	1	92

[a] Percent yield calculation based on expected product from the catalyst plus the substrate.

To demonstrate the generality of using enyne complexes in initiating the catalytic cycle, the enyne−$Co_2(CO)_6$ complexes depicted in Scheme 3 were chosen as representative catalyst precursors. Comparative Pauson−Khand reactions of enyne **1** using these enyne−$Co_2(CO)_6$ complexes are listed in Table 4, which show the effectiveness of these catalyst precursors in initiating the cycloaddition. While catalyst precursor **33** demonstrates the use of the substrate itself as the catalyst precursor, enyne complex **32** typifies a precatalyst which generates a cycloadduct (enone **34**) that is polar enough to be readily separated from the desired cyclization products. Enone **36**, formed from precatalyst **35**, can be either washed out with base or removed by filtration of the reaction mixture through a short plug of silica gel

Table 5. Optimization Studies for Thermal Cycloadditions Catalyzed by an Enyne−$Co_2(CO)_6$ Complex[a]



1 32 2

entry	catalyst precursor (mol %)	$CyNH_2$ (mol %)	temp (°C)	time (h)	% yield 1	% yield 2
1	5	10	65	7	73	25
2	10	0	65	6.5	15	63
3	10	20	65	6	9	78
4	10	0	70	4.5	−	70
5	10	20	70	4	−	82

[a] Entries 3−5: 0.2 M substrate concentration.

necessary to remove the cobalt residues. In the same manner, enone **7** from precursor **37**, can be removed via an acid wash or filtration through a silica gel plug.

Optimization of Reaction Conditions. Table 5 shows the results from reactions designed to determine the best conditions for the Pauson−Khand reaction using enyne−$Co_2(CO)_6$ complex **32** as precatalyst. We have chosen complex **32** as our precatalyst for the reaction since it is crystalline and stable to be conveniently stored in a laboratory freezer. The yield enhancement brought about by the presence of cyclohexylamine in the $Co_2(CO)_8$-catalyzed reactions prompted us to use the amine in these cyclizations. Complete reactions were only achieved at 70 °C (entries 4 and 5). A lower temperature resulted only in incomplete conversion, even with varying amounts of the precatalyst and cyclohexylamine (entries 1−3). As previously demonstrated, cyclohexylamine is important for this reaction (entry 2 vs 3 and entry 4 vs 5).

Generality of the Procedure. The examples in Table 6 illustrate the generality of using catalyst precursor **32** for initiating the intramolecular Pauson−Khand reaction. As was previously observed, some of the cycloadditions proceeded in higher yields in the presence of cyclohexylamine. The reasons for this yield enhancement is not entirely clear, and the outcome does not appear to be predictable with these examples. While the amine may serve in several capacities during the reaction manifold, it may be a catalyst carrier, which increases the longevity of the intermediate complexes. Likewise, it may also regenerate and/or preserve the active cobalt species.

C. Dodecacarbonyltetracobalt Catalysis. Extant knowledge on $Co_2(CO)_8$-catalyzed Pauson−Khand reactions reveals that under mild conditions, $Co_4(CO)_{12}$ formation deters catalysis and is in fact considered as a dead end pathway in this reaction.[2j,3i,23] $Co_4(CO)_{12}$, which is presumably generated from dimerization of "$Co_2(CO)_n$" upon release of the cyclopentenone product is believed to be inactive under these conditions. Thermal decomposition of $Co_2(CO)_8$ in hexane, heptane, and toluene to provide $Co_4(CO)_{12}$ is well-documented.[24] This cobalt cluster was also isolated by Pauson from the thermal cyclizations of (acetylene)$Co_2(CO)_6$ complexes with strained alkenes in isooctane under a nitrogen atmosphere.[2a] Isolation of (arene)$Co_4(CO)_9$ complexes under thermal Pauson−Khand reaction conditions in aromatic solvents also indicated the possible generation of this cluster under these cyclization conditions.[25] In effect, development of methods involving $Co_2(CO)_8$ catalysis has been based on preserving the catalytic cobalt species and preventing the formation of inactive cobalt species, such as $Co_4(CO)_{12}$.

Reactions demonstrating effective $Co_4(CO)_{12}$ catalysis in the Pauson−Khand reaction were only achieved at high temperature and pressure (10 atm CO, 150 °C)[4a] or in a supercritical fluid as a solvent (5 atm CO, 110 atm supercritical ethylene, 85 °C).[6] It has been believed that under these conditions, $Co_4(CO)_{12}$ is disproportionated into $Co_2(CO)_8$ and is also prevented from forming.[4a] The analogous methylidenyne nonacarbonyl cluster, $Co_3(CO)_9(\mu^3\text{-CH})$,[5] and the phosphine-substituted cobalt cluster, $Co_4(CO)_{11}P(OPh)_3$,[6] have been disclosed to serve as catalyst precursors for these cyclizations. Unfortunately, these air stable clusters are not readily available unlike the parent cluster, $Co_4(CO)_{12}$, and the reported protocols employing them involve elevated temperatures and pressures.[5,6]

In an attempt to understand the efficiency enhancement provided by cyclohexylamine (vide supra) we conducted Pauson−Khand cyclization studies employing the $Co_4(CO)_{12}$ cluster under our reaction conditions. We postulated that cyclohexylamine preserves the active catalyst and induces catalyst formation via disproportionation of $Co_4(CO)_{12}$, which may possibly be formed during catalytic reactions using $Co_2(CO)_8$. In fact, a well-established equilibrium between $Co_2(CO)_8$ and $Co_4(CO)_{12}$ is known.[24]

Preliminary Studies. We began our investigations with the thermal cyclizations of enyne **3** using stoichiometric quantities of $Co_4(CO)_{12}$ in DME at 70 °C under a nitrogen atmosphere (Table 7). A good yield of the cyclopentenone was obtained from the cyclization of **3**, only when it was carried out in the presence of the amine (entry 1 vs 2). Although the reactions were incomplete, cyclizations using catalytic amounts of $Co_4(CO)_{12}$ were still achieved in fair yields at 60 and 70 °C even under a nitrogen atmosphere (entries 3 and 4). Incidentally, cyclizations under an atmosphere of CO provided a better yield (entry 6) and allowed a lower catalyst loading to achieve complete reaction (entries 6 and 7), more so at a higher temperature, i.e., 70 °C (entry 8). These results demonstrated that catalytic amounts of $Co_4(CO)_{12}$ could be used in conjunction with cyclohexylamine to catalyze thermal Pauson−Khand reactions under practical reaction conditions. Under these reaction conditions, no cyclizations were evident when $Mo(CO)_6$ and $W(CO)_6$ were used as the metal carbonyls.

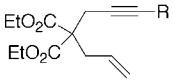
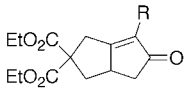
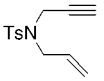
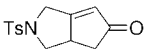
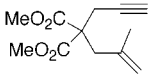
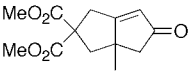
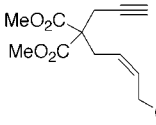
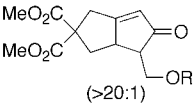
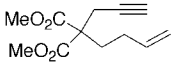
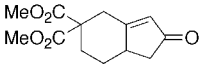
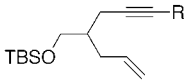
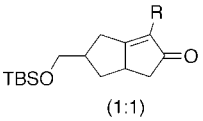
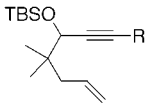
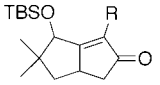
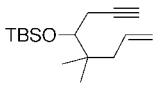
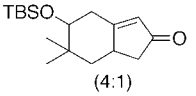
Comparison of the Cobalt Carbonyl-$CyNH_2$ Catalytic Systems. An attempt was made to compare the catalytic efficiencies of the two cobalt carbonyl-$CyNH_2$ systems in DME (Table 8). However, it should be noted that $Co_2(CO)_8$ and $Co_4(CO)_{12}$, and their corresponding cyclohexylamine systems have been observed to behave variably under our test solvents (vide infra). Nevertheless, results consistently indicate that, in DME, an optimal molar ratio of cobalt carbonyl complex to cyclohexylamine is 1:6 for $Co_4(CO)_{12}$ and 1:3 for $Co_2(CO)_8$

(22) Krafft, M. E.; Hirosawa, C.; Boñaga, L. V. R. *Tetrahedron Lett.* **1999**, *40*, 9177.

(23) Magnus, P.; Principe, L. M.; Slater. M. J. *J. Org. Chem.* **1987**, *52*, 1483.

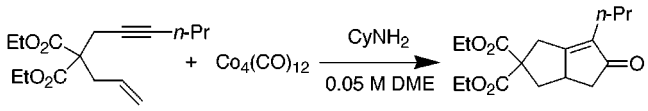
(24) (a) Ungvary, F.; Marko, L. *Inorg. Chim. Acta* **1970**, *4*, 324. (b) Ungvary, F.; Marko, L. *J. Organomet. Chem.* **1974**, *71*, 283. (c) Bor, G.; Dietler, U. K.; Pino, P.; Poe, A. *J. Organomet. Chem.* **1978**, *154*, 301. (d) Bor, G.; Dietler, U. K. *J. Organomet. Chem.* **1980**, *191*, 295. (e) Mirbach, M. F.; Saus, A.; Krings, A. M.; Mirbach, M. J. *J. Organomet. Chem.* **1981**, *205*, 229.

Table 6. Pauson–Khand Reaction Using an Enyne–$Co_2(CO)_6$ Complex as a Catalyst Precursor[a]

Entry	Substrate		Product	% Yield (time, h)
1		**1** R = H	 **2**	78 (2)
2		**3** R = *n*-Pr	**6**	67 (9)[b]
3		**4**	 **7**	94 (8)[b]
4		**9**	 **20**	84 (16)
5		**10** R = TBS	 **21**	94 (6)[b]
6		**11** R = Ac	**22** (>20:1)	93 (16)[b]
7		**12**	 **23**	81 (20)[b]
8		**13** R = H	 **24**	81 (16)[b]
9		**5** R = *n*-Pr	**8** (1:1)	72 (16)[c]
10		**14** R = H (1:1)	 **25**	83 (16)
11		**15** R = Me (3:1)	**26**	61 (6)
12		**16** R = TMS	**27**	NR
13		**17**	 **28** (4:1)	75 (5)

[a] All reactions were carried out using a substrate concentration of 0.2 M in DME with 10 mol % of complex **32** under a CO atmosphere at 70 °C, unless stated otherwise. [b] 20 mol % $CyNH_2$ was used. [c] 40 mol % $CyNH_2$ was used.

Table 7. Preliminary Results on the $Co_4(CO)_{12}$-Catalyzed Pauson–Khand Reaction



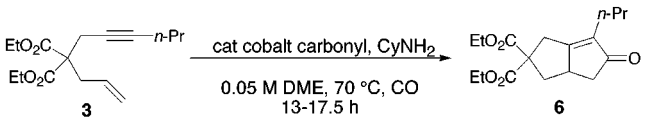
3 **6**

entry	$Co_4(CO)_{12}$ (mol %)	$CyNH_2$ (mol %)	temp (°C)	reaction atmosphere	% yield **3**	% yield **6**
1	100	0	70	N_2	–	7
2	100	300	70	N_2	–	81
3	15	0	60	N_2	–	14
4	15	95	60	N_2	8	60
5	15	100	70	N_2	14	58
6	15	0	60	CO	–	69
7	15	100	60	CO	–	91
8	5	30	70	CO	–	94
9	2.5	15	70	CO	20	58

(Table 3 and Table 11, entries 4–7). Interestingly, a molar ratio of 1:3 (alkyne–$Co_2(CO)_6$ or $Co_2(CO)_8$ complex/additive) has been also used with cyclohexylamine,[18] thiophene,[3b] α-methylbenzylamine,[9] *N*,*N*,*N*′,*N*′-tetramethylethylenediamine,[9] *N*,*N*-dimethylformamide,[9] and *n*-butylphosphane sulfide,[3f] although these reactions were carried out under different reaction conditions.

Scope of the $Co_4(CO)_{12}$-$CyNH_2$ Protocol. We then verified the generality of these observations in a series of catalytic cyclizations of a variety of substrates employing the $Co_4(CO)_{12}$–$CyNH_2$ system (Table 9). As was

Table 8. Comparison of Cobalt Carbonyl-$CyNH_2$ Catalytic Systems in DME

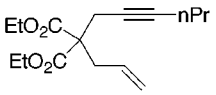
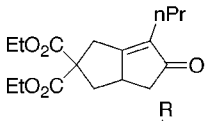
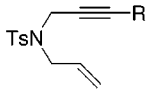
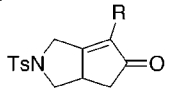
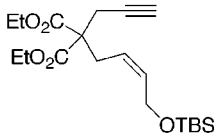
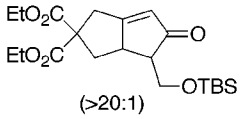
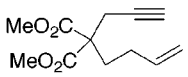
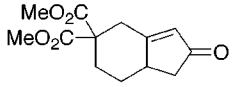
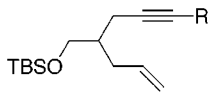
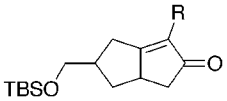
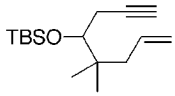
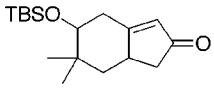
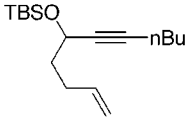
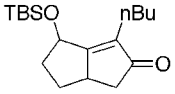
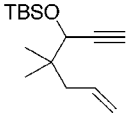
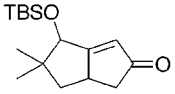


3 **6**

entry	cobalt carbonyl/$CyNH_2$ (mol %:mol %)	% yield $Co_4(CO)_{12}$ **3**	% yield $Co_4(CO)_{12}$ **6**	% yield $Co_2(CO)_8$ **3**	% yield $Co_2(CO)_8$ **6**
1	5:0	–	23	9	41
6	5:15	–	74	52	28
3	5:30	–	94	82	4
4	10:0	–	59	–	82
5	10:60	–	92	46	55

observed with the $Co_2(CO)_8$–$CyNH_2$ catalytic system,[3c] good to excellent yields were obtained from enynes having significant Thorpe–Ingold properties (entries 1–3, 5, 8), although a lower yield was obtained from an enyne bearing a disubstituted olefin (entry 4). With the present catalyst system complete cyclization of enyne **5** was achieved using only a 10/60 ratio of $Co_4(CO)_{12}$/$CyNH_2$ whereas, with the $Co_2(CO)_8$–$CyNH_2$ system, a 30/60 ratio of $Co_2(CO)_8$/$CyNH_2$ was necessary (cf. Table 3, entries 9–11). Similarly, enynes bearing internal alkynes and lacking significant Thorpe–Ingold assistance (entry 9), or which are sterically hindered (entry 10) needed a higher catalyst loading (30 mol %) for complete reactions, albeit still in modest yields. In our efforts to improve the

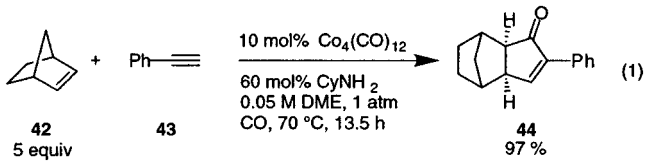
Table 9. $Co_4(CO)_{12}$−$CyNH_2$ as Catalyst System for a Practical Thermal Pauson−Khand Reaction[a]

Entry	Substrate		Product[16] (diastereomeric ratio, dr)	% Yield
1		**3** **6**		92, 94[b]
2		**4** R= H **7**		88[b]
3		**38** R= *n*-Pr **40**		81
4		**10** **21**	 (>20:1)	64
5		**12** **23**		92, 70[c], 89[d], 55[e]
6		**13** R= H **24**	 (1:1)	85, 70[d], 65[e]
7		**5** R= *n*-Pr **8**		91
8		**17** **28**	 (4:1)	80
9		**39** **41**	 (1:1)	56[f], 61[c]
10		**14** **25**	 (1:1)	44[f], 30[c]

[a] Reactions were carried out at substrate concentrations of 0.05 M in DME using 10 mol % $Co_4(CO)_{12}$ and 60 mol % $CyNH_2$ under a CO atmosphere at 70 °C. Reactions were typically done in 13−18 h. [b] 5 mol % $Co_4(CO)_{12}$, 30 mol % $CyNH_2$. [c] With pyridine. [d] In 1,2- DCE. [e] In octane. [f] 30 mol % $Co_4(CO)_{12}$, 60 mol % $CyNH_2$. TBS= *tert*-butyldimethylsilyl.

cyclizations depicted in entries 9 and 10, pyridine was substituted for cyclohexylamine,[26,27] but essentially identical results were obtained. Pyridine is one of the Lewis bases known to induce disporportionation of $Co_2(CO)_8$ and $Co_4(CO)_{12}$.[26,28] In contrast, cyclization of enyne **12** with pyridine as the additive was found to be inferior to cyclohexylamine (entry 5). An intermolecular version of the new $Co_4(CO)_{12}$/$CyNH_2$-catalyzed cyclization was also demonstrated by the reaction of phenylacetylene and the reactive alkene norbornene to give the cycloadduct in 97% yield (eq 1).

We have therefore shown that efficient cycloadditions of enynes could be attained using catalytic amounts of $Co_4(CO)_{12}$, with cyclohexylamine enhancing the efficiency. These findings further exemplified the utility of additives, such as amines, in improving the catalytic efficiency of



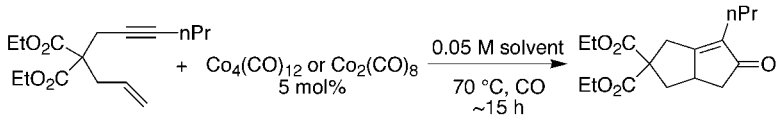
42 5 equiv **43** **44** 97 % (1)

cobalt carbonyls in Pauson−Khand reactions. In the early studies on the thermal decomposition of $Co_2(CO)_8$ (in toluene) it was shown by Ungvary and Marko that coordinatively unsaturated $Co_2(CO)_6$ fragments are necessary for the formation of $Co_4(CO)_{12}$.[24a] Hence, an atmosphere of CO or the presence of coordinating ligands, such as cyclohexylamine would be expected to inhibit the formation of these fragments and consequently, the dimerization to the tetranuclear cluster. On the contrary, it had been suggested that only at high pressures of CO atmosphere would formation of the dinuclear cobalt carbonyl be effectively favored from $Co_4(CO)_{12}$.[3l]

Catalysis by $Co_4(CO)_{12}$ without an Additive. Cyclizations of enyne **3** using $Co_4(CO)_{12}$, in the absence of additives, in solvents commonly used in Pauson−Khand reactions were examined to elucidate the efficiency of the

(25) (a) Khand, I. U.; Knox, G. R.; Pauson, P. L.; Watts, W. E. *J. Chem. Soc. Chem. Commun.* **1971**, 36. (b) Khand, I. U.; Knox, G. R.; Pauson, P. L.; Watts, W. E. *J. Chem. Soc., Perkin Trans. 1* **1973**, 975.
(26) Wender, I.; Sternberg, H. W.; Orchin, M. *J. Am. Chem. Soc.* **1952**, *74*, 1216.
(27) Krafft, M. E.; Boñaga, L. V. R. *Synlett* **2000**, 959.
(28) Manuel, T. A. *Adv. Organomet. Chem.* **1965**, *3*, 181.

Table 10. $Co_4(CO)_{12}$ and $Co_2(CO)_8$ Catalyses in Different Solvents



3 **6**

		$Co_4(CO)_{12}$			$Co_2(CO)_8$		
		% yield		turnover	% yield		turnover
entry	solvent	**3**	**6**	number[a]	**3**	**6**	number[a]
1	dimethyl sulfoxide (DMSO)	93	–	0	94	–	0
2	acetonitrile	61	35	6.9	76	9	1.7
3	dichloromethane (CH_2Cl_2)	47	–	0			
4	1,2-dichloroethane (DCE)	–	68	**14.3**	29	26	5.0
5					–	37[b]	3.7
6					–	50[c]	2.4
7	tetrahydrofuran (THF)	–	21	4.4			
8	1,2-dimethoxyethane (DME)	–	23	4.4	9	41	**7.8**
9			59[b]	6.0	–	82[b]	8.3
10	toluene	86	9	1.9			
11	*n*-hexane	24	37	6.2			
12	*n*-heptane	30	41	8.7			
13	isooctane	–	59	**12.5**	31	19	3.3
14		–	61[b]	6.5	–	57[c]	2.6

[a] Mol product/mol catalyst. [b] 10 mol %. [c] 20 mol %.

cycloaddition in the presence of different solvents (Table 10). Although we intended to confirm its lack of reactivity under our reaction conditions, we discovered otherwise that $Co_4(CO)_{12}$ catalyzes the cycloaddition in a number of solvents under normal laboratory conditions. The highest catalytic efficiency was observed in either 1,2-DCE and isooctane. Interestingly, Pauson and co-workers isolated $Co_4(CO)_{12}$ from stoichiometric Pauson–Khand reactions in isooctane as the solvent.[2a] For comparison, cyclization efficiencies in either 1,2-DCE and DME under the reaction conditions described in Table 9 are comparable (cf. Table 9, entries 5 and 6). However, under these catalytic conditions, no cyclization was evident in DMSO presumably due to the formation of inactive DMSO–cobalt complexes. A rate-decelerating effect of DMSO was also evident in the amine oxide-promoted stoichiometric Pauson–Khand reaction presumably due to the strong coordinating ability of DMSO as ligand.[29] In effect, DMSO possibly formed complexes with $Co_4(CO)_{12}$ or its degradation products, which were inert toward catalysis in the Pauson–Khand reaction. In contrast, DMSO has been used as an additive to promote Pauson–Khand reactions implying that DMSO is beneficial to enyne–$Co_2(CO)_6$ complexes, which renders them more reactive for alkene coordination, but is detrimental to $Co_2(CO)_8$ and $Co_4(CO)_{12}$ complexes. $Co_2(CO)_8$ exhibited highest catalytic activity in DME, which is typically used as the solvent in cobalt-catalyzed Pauson–Khand reactions.[3a–c,e,8,10,22] A subsequent increase in yield was noted for cyclizations in DME when higher amounts of $Co_2(CO)_8$ were used (entries 8 vs 9), although less notably in 1,2-DCE (entries 4–6) and isooctane (entries 13 and 14). As was already reported by Chung, $Co_4(CO)_{12}$ did not exhibit any catalytic activity in CH_2Cl_2 under one atmosphere pressure of CO and optimal catalysis was only achieved at 150 °C and 10 atm pressure of CO.[4a]

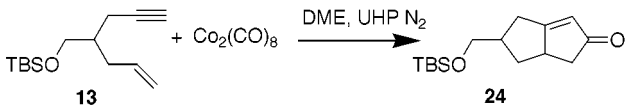
The observed reactivity of $Co_4(CO)_{12}$ at 70 °C and one atmosphere of CO pressure, in a number of solvents, suggested that, under our conditions, it probably underwent disproportionation into $Co_2(CO)_8$ or a similar catalytically active cobalt species. It was reported that under one atmosphere of CO, at 53 °C a hexane solution of $Co_4(CO)_{12}$ would be converted to a solution in which 50% of the cobalt content is present as $Co_2(CO)_8$ ($t_{1/2}$ = 160 days).[24c] Although the generation of $Co_4(CO)_{12}$ under the $Co_2(CO)_8$-catalyzed conditions has been only assumed, we have discounted the assumption that $Co_4(CO)_{12}$ is inactive toward the Pauson–Khand cyclizations under mild conditions, such as normal pressure of CO atmosphere and lower temperature. Thus, $Co_4(CO)_{12}$ can now serve as an alternative for $Co_2(CO)_8$, which is more prone to air oxidation, and possibly $Co_3(CO)_9(\mu^3\text{-CH})$[5] and $Co_4(CO)_{11}P(OPh)_3$,[6] that both require further preparation. Upon exposure to air, $Co_4(CO)_{12}$ is known to be oxidized to a purple Co(II) species, but this proceeds at an appreciably slower rate than $Co_2(CO)_8$.[20,30] Optimal catalysis of the methylidene tricobalt nonacarbonyl cluster was achieved in toluene only at 120 °C under 7 atm of CO.[5] It is of interest that use of $Co_4(CO)_{12}$ was not reported in these studies. It is also noteworthy that commercially available $Co_4(CO)_{12}$ was used without purification and was found to be catalytically efficient.

D. Pauson–Khand Reactions using Substoichiometric Amounts of $Co_2(CO)_8$ under a Nitrogen Atmosphere. The alternative procedures described above for the cobalt-catalyzed Pauson–Khand cycloadditions[3c,4b,22] demonstrate that efficient cyclizations under an atmosphere of carbon monoxide could also be achieved using catalytic quantities of different cobalt carbonyl complexes. We further observed during these studies that, in DME and in the presence of cyclohexylamine, 1,6- and 1,7-enynes could be practically converted to bicyclic cyclopentenones using only 35–50% of $Co_2(CO)_8$ under an atmosphere of nitrogen. To allow for regeneration of the active catalyst, Pauson–Khand reactions employing less than an equivalent of $Co_2(CO)_8$ are typically carried out under an atmosphere of carbon monoxide. An exception is in an account by Schore where a nitrogen

(29) Krafft, M. E.; Scott, I. L.; Romero, R. H.; Feibelmann, S.; Van Pelt, C. E. *J. Am. Chem. Soc.* **1993**, *115*, 7199.

(30) King, R, B, In *Organometallic Syntheses*; Eisch, J. J.; King, R. B., Eds.; Academic Press: New York, 1965; Vol. 1, p 103.

Table 11. Optimization Studies for the Amine-assisted Substoichiometric Thermal Pauson−Khand Reaction under a Nitrogen Atmosphere



13 24

entry	reaction concn (M)	$Co_2(CO)_8$ (mol %)	$CyNH_2$ (mol %)	temp (°C)	time (h)	% yield
1[a]	0.20	10	20	70	15	37
2[b]	0.20	10	20	70	15	40
3	0.20	10	20	70	15	36
4	0.05	30	0	70	15	21
5	0.05	30	60	70	15	39
6	0.05	30	90	70	15	72
7	0.05	30	150	70	16	61
8	0.01	30	90	70	15.5	38
9	0.10	30	90	70	15.5	40
10	0.20	35	105	70	16	25
11	0.05	35	105	50	13.5	67
12	0.05	30	90	60	15.5	86
13	0.05	35	105	60	13	58
14[c]	0.05	30	90	70	1	60
15[d]	0.05	30	90	70	2	19
16	0.05	35	35	60	16	78

[a] Ultrahigh purity (UHP) Ar atmosphere. [b] N_2 atmosphere. [c] DCE. [d] Toluene.

atmosphere was found to be more beneficial than carbon monoxide in the thermal cyclization of norbornadiene with several alkynes using less than stoichiometric amounts of $Co_2(CO)_8$.[31]

Optimization Studies. We made several observations during our optimization studies summarized in Table 11: (1) Essentially the same efficiency was observed in reactions carried out under an argon atmosphere compared to nitrogen. (2) High dilution, a narrow temperature range (50−60 °C) and an optimal 3:1 molar ratio of amine relative to $Co_2(CO)_8$ were expedient for achieving good yields of cyclized products. A narrow temperature range (60−70 °C) was also observed by Livinghouse, in his report on the catalytic thermal cyclizations under an atmospheric pressure of CO.[3b] An optimal 3:1 ratio of cyclohexylamine relative to enyne−$Co_2(CO)_6$ complex was reported by Sugihara[18] and Periasamy.[9] The same ratio was also used by Livinghouse when using cyclohexylamine as an additive although a 6:1 ratio was employed for reactions using thiophene.[10] (3) Reactions carried out in 1,2-dichloroethane or toluene gave inferior yields than those in DME. 1,2-Dichloroethane was the solvent used in the first report on the thermal stoichiometric cyclizations with cyclohexylamine as an additive under an Ar atmosphere.[18] DME is typically used as a solvent in cobalt-catalyzed Pauson−Khand reactions.[3a−c,e,8,10,22] However, when catalytic cyclizations were conducted in toluene, DME was observed to be a better additive than cyclohexylamine.[3d] (4) A large excess of the cyclohexylamine was observed to be detrimental to the efficiency of the reaction.

Generality of the Observation. The scope of using substoichiometric amounts (35−50%) of $Co_2(CO)_8$ under a nitrogen atmosphere to promote the Pauson−Khand cycloaddition is demonstrated in Table 12. These results show that the presence of cyclohexylamine, three molar equivalents relative to $Co_2(CO)_8$, is crucial to the efficiency of the present cyclization procedure. In all cases, the starting enynes were completely consumed to give the corresponding bicyclic cyclopentenones in good yields. In some cases we found it advantageous to use 50 mol % of $Co_2(CO)_8$.

Comparison of Common Additives for the Pauson−Khand Reaction. Compared to other known additives for the cycloaddition (vide supra) cyclohexylamine was determined to be the most efficacious in our present studies (Table 13). During the course of these studies, *n*-butyl methyl sulfide was reported to be the best suited additive for substrates bearing a propargylic heteroatom.[16] Addition of 3 mol equiv of this sulfide to the cyclization of enyne **4** yielded only 51% of the cyclized product **7**. Lower yields were likewise observed from cyclizations of substrates **10** and **13** (60% yields). We further examined pyridine and 1,10-phenanthroline[26] and found that these aromatic *N*-containing Lewis bases were inferior to cyclohexylamine. While the monodentate pyridine behaved much better than the bidentate 1,10-phenanthroline, it provided variable results in the cyclizations of representative substrates in comparison to cyclohexylamine (Table 12, entries 2, 4, 6, 7). Addition of 70 mol % of 1,10-phenanthroline into the reaction of enyne **3** gave only 16% of **6** along with 67% of recovered **3**.

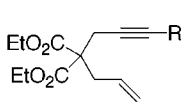
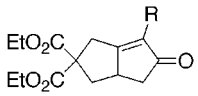
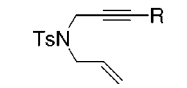
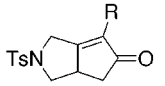
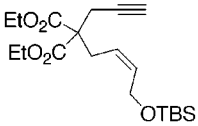
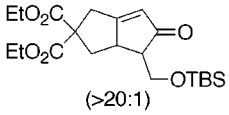
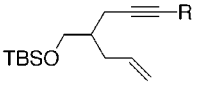
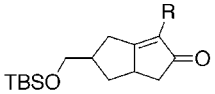
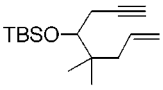
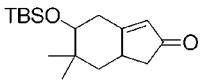
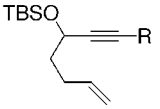
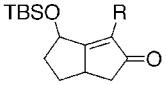
Mechanistic Studies. In reactions conducted under substoichiometric conditions, we propose that the amine preserves the active catalytic species and enhances the longevity of the intermediate catalytic complexes. It may also prevent the deleterious effects of nonviable cobalt residues formed during the reaction. With regard to the source of CO for incorporation into the enyne moieties, we speculate that an iterative disproportionation of cobalt residues brought about by the amine resulted in regeneration of dicobalt clusters bearing five to six CO ligands. Alternatively, CO molecules from the initial ligand exchange reaction of $Co_2(CO)_8$ with either the alkyne or cyclohexylamine possibly remained in solution and were further utilized in the reformation of the active catalyst.

We further designed a series of experiments to probe the fate of the two CO molecules liberated from the initial alkyne−$Co_2(CO)_6$ formation (based on the accepted mechanism for the Pauson−Khand reaction) and its effect on reaction efficiency. These molecules could either be mixed with the nitrogen atmosphere or remained dissolved in the solvent. Dissolved CO molecules could then possibly bind to any coordinatively unsaturated cobalt species in the reaction residues or intermediates. $Co_2(CO)_8$ and enyne−$Co_2(CO)_6$ complexes **32** and **33** were employed as sources of cobalt carbonyls to mediate the cyclization of enyne **1**; these results are summarized in Table 14. We have recently shown the utility of enyne−$Co_2(CO)_6$ complexes as catalyst precursors in Pauson−Khand reactions under a CO atmosphere.[22] With catalyst precursors **32** and **33**, the only source of CO molecules is clearly the enyne−$Co_2(CO)_6$ complex, and not dissolved CO, as is possible with $Co_2(CO)_8$. Under similar reaction conditions, cyclizations using $Co_2(CO)_8$ showed better efficiency than reactions promoted by these catalyst presursors (entries 2 vs 3 and 5). These results suggest that, under these conditions, the CO molecules remained dissolved in the reaction system and further enhanced the efficacy of the reaction.

As is illustrated above, reactions performed in the presence of amine were more efficient than those without the amine (entry 1 vs 2, 4 vs 5). As expected, the absence

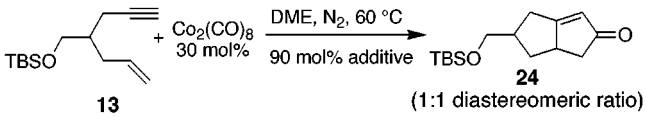
(31) Schore, N. E. *Synth. Commun.* **1979**, *9*, 41.

Table 12. Amine-Assisted Substoichiometric Pauson−Khand Reactions under a Nitrogen Atmosphere[a]

Entry	Substrate		Product (diastereomeric ratio)[b]	% Yield $CyNH_2$	% Yield Pyridine[f]
1		**1** R= H **2**		80	
2		**3** R= *n*-Pr **6**		78	91
3		**4** R= H **7**		66[c]	50
4		**38** R= *n*-Pr **40**		81	60
5		**10** **21**	 (>20:1)	69	
6		**13** R= H **24**	 (1:1)	86[d]	80
7		**5** R= *n*-Pr **8**		87	84
8		**17** **28**	 (4:1)	68	
9				83[e]	
10		**39** R= *n*-Bu **41**	 R= *n*-Bu (1:1) R= Ph (10:1)	65	
11				75[e]	
12		**45** R= Ph **46**		76	

[a] All reactions were carried out using a catalyst concentration of 0.02 M in DME with 35 mol % $Co_2(CO)_8$ and 105 mol % $CyNH_2$ or pyridine under a nitrogen atmosphere at 60 °C. Reactions were typically done in 14−15.5 h except for entry 1 (3 h). [b] Determined by 300 MHz ^1H NMR spectroscopy. [c] 70 mol % $CyNH_2$. [d] 30 mol % $Co_2(CO)_8$, 90 mol % $CyNH_2$. [e] 50 mol % $Co_2(CO)_8$, 150 mol % $CyNH_2$. [f] 140 mol % pyridine.

Table 13. Comparison of Known Additives for the Pauson−Khand Reaction



13 **24** (1:1 diastereomeric ratio)

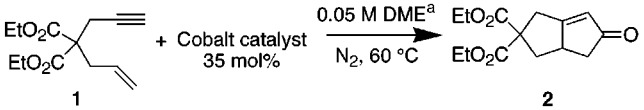
additive	% yield
cyclohexylamine	86
n-butyl methyl sulfide	60
thiophene	27
thioanisole	56
triphenyl phosphite	30

of the additive was compensated for by carrying out the reaction under a CO atmosphere (entry 5 vs 6). Cyclization was further shown to be more effective in DME than in toluene (entry 5 vs 7). For purposes of comparison, reaction of enyne **47** from which **32** was derived using 35% of $Co_2(CO)_8$ and 105% of cyclohexylamine under an atmosphere of nitrogen gave only **34** in 66% yield. Likewise, cyclizations of enyne **1** using precatalyst **32** showed no decomplexed enyne **47** in the product mixture (entries 4, 5, and 7). Furthermore, any unreacted $Co_2(CO)_8$ could react with cyclohexylamine to produce CO molecules that could possibly become another source of CO.

The reactivity of the cobalt species formed from the reaction of $Co_2(CO)_8$ and cyclohexylamine was further investigated (Table 15). Studies on the cyclization of enyne **3** suggested that the cobalt species generated from reaction of $Co_2(CO)_8$ and cyclohexylamine (30 min reaction time) at room temperature (entry 1) and at 60 °C (entry 2) are viable toward the Pauson−Khand reaction providing moderate yields of **6**, along with recovered starting materials. As anticipated, heating $Co_2(CO)_8$ prior to addition of the enyne would be deleterious to the reaction even in the presence of cyclohexylamine (entry 3). It is worth noting that a slight improvement in the reaction efficiency was observed when $Co_2(CO)_8$ was heated with the cyclohexylamine (entry 2 vs 3). A mixture of $Co_2(CO)_8$, cyclohexylamine and enyne also showed incomplete reaction although this reaction condition gave the highest yield of the product (entry 4). These results further confirmed that the optimal procedure involves alkyne complexation and subsequent activation of the enyne−$Co_2(CO)_6$ complex upon addition of cyclohexylamine (entry 5).

We have shown that a substoichiometric amount of $Co_2(CO)_8$ is sufficient to promote the intramolecular Pauson−Khand reaction under nitrogen rather than a carbon monoxide atmosphere. The amine may have acted in a role to facilitate an iterative disproportionation of cobalt residues forming a viable cobalt catalyst for further cycloaddition. Presumably, it also prevented detrimental effects of nonviable cobalt residues on the reaction. Our experiments also suggested that the CO molecules, which evolved from the initial complexation step remained dissolved in the reaction system and were further used in the reaction.

Table 14. Mechanistic Studies: Fate of CO and Its Effect on Reaction Efficiency



1 2

entry	cobalt catalyst	$CyNH_2$ (mol %)	% yield 2	% yield 34
1	$Co_2(CO)_8$	0	52	–
2	$Co_2(CO)_8$	105	80	–
3	**33**	105	54[b]	–
4	**32**	0	22	55
5	**32**	105	68	50
6[c]	**32**	0	83	95
7[d]	**32**	105	49	22

[a] Reactions were performed using a substrate concentration of 0.05 M in DME with 35 mol % of cobalt catalyst and $CyNH_2$ under a N_2 atmosphere at 60 °C. Reactions were typically done in 2−3 h. [b] Percent yield is based on **2** derived from enyne **1** plus enyne−$Co_2(CO)_6$ complex **33**. [c] Under a CO atmosphere. [d] Toluene.

Cobalt catalysts:

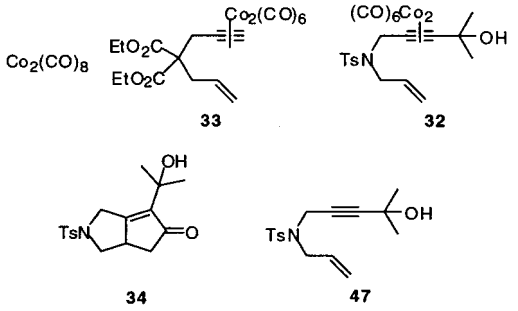
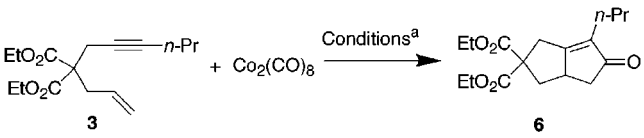


Table 15. Generation of the Active Cobalt Species



3 6

entry	reaction conditions	% yield 3	% yield 6
1	$Co_2(CO)_8$, $CyNH_2$, rt, 30 min; then **3**, 60 °C	23	53
2	$Co_2(CO)_8$, $CyNH_2$, 60 °C, 30 min; then **3**, 60 °C	23	56
3	$Co_2(CO)_8$, 60 °C, 30 min; then $CyNH_2$ and **3**, 60 °C	50	42
4	$Co_2(CO)_8$, $CyNH_2$, **3**, 60 °C	18	71
5	**3**, $Co_2(CO)_8$, rt, 30 min; then $CyNH_2$, 60 °C	0	78

[a] Reactions were carried out using a substrate concentration of 0.05 M in DME with 35 mol % $Co_2(CO)_8$ and 105 mol % $CyNH_2$ under a nitrogen atmosphere at 60 °C.

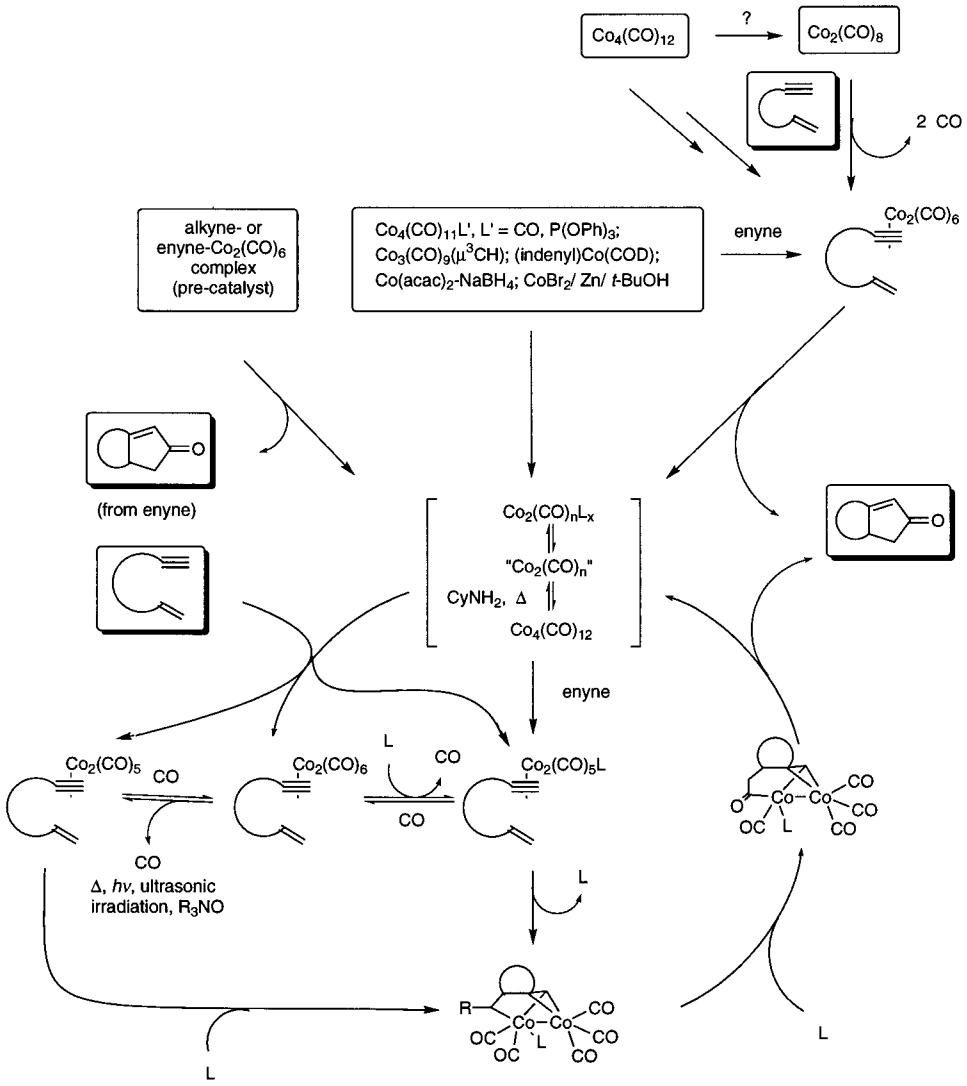
Summary and Conclusions

Methods that have been developed for the catalytic (and stoichiometric) Pauson−Khand reactions are typically based on a combination of one or more of the following premises: (a) in situ generation of the active cobalt carbonyl species, (b) preservation of the active cobalt carbonyl species, (c) preservation of the intermediate complexes, and (d) facilitation of decarbonylation, hence increased alkene complexation rate. Furthermore, catalysis in the Pauson−Khand reaction is best achieved in reactions that are carried out under an atmosphere of carbon monoxide so that regeneration of the active catalyst is possible. The current state of the art in the Pauson−Khand reaction methods is summarized in Scheme 4.

In this report of our studies, we have determined that enyne−$Co_2(CO)_6$ complexes, and the commercially available $Co_2(CO)_8$ and $Co_4(CO)_{12}$ are sufficiently effective in the catalytic Pauson−Khand reaction under one atmosphere of CO pressure. It was further shown that the efficiencies of these cyclization protocols could be enhanced by the presence of cyclohexylamine. These procedures have also rendered more practical and highly convenient alternatives for the catalytic Pauson−Khand reaction. Most importantly, we have dispelled the common belief that $Co_4(CO)_{12}$ is inactive in the Pauson−Khand reaction under one atmosphere of carbon monoxide. Of mechanistic importance is that these studies have also demonstrated that the probable formation of $Co_4(CO)_{12}$ is not necessarily a dead end pathway in the $Co_2(CO)_8$-catalyzed Pauson−Khand reaction. It is also of interest that substoichiometric amounts of $Co_2(CO)_8$, in DME and in the presence of cyclohexylamine, are sufficient for the cyclocarbonylation of enynes under a nitrogen atmosphere.

The protocols developed in our studies have been based primarily on the efficiency enhancement brought about by Lewis bases, which has been most pronounced and general with cyclohexylamine. In these studies we invoked an amine-derived stabilization of reaction intermediates, which originates from its coordination to coordinatively unsaturated cobalt species in the reaction, e.g., reaction intermediates and "$Co_2(CO)_n$". Thus, the amine serves as a catalyst carrier by prolonging its lifetime, consequently improving the reaction efficiency (higher turnover number). It is further noteworthy that, for an unknown reason, molar ratios of 1:2−3 (enyne−$Co_2(CO)_6$ complex or $Co_2(CO)_8$/cyclohexylamine) and 1:6 ($Co_4(CO)_{12}$/cyclohexylamine have been found to be optimal under these reaction conditions. A 1:3 molar ratio has similarly been described in several reports.[9,10,18] A delicate balance of $Co_2(CO)_8$ and cyclohexylamine was apparently essential for the enhancement effect in reactions performed under CO and N_2 atmospheres and a large excess of the amine was observed to be detrimental. We also proposed that with the substoichiometric conditions under a N_2 atmosphere, cyclohexylamine effected an iterative disproportionation of residual cobalt species, "$Co_2(CO)_nL_{8-n}$" (L = CO, cyclohexylamine, or DME) to generate viable cobalt carbonyl species. Disproportionation of residual cobalt species might also be possible in reactions using $Co_2(CO)_8$ and $Co_4(CO)_{12}$ under a CO atmosphere, where regeneration of the active cobalt carbonyl is more facile. By virtue of their Lewis basicity, results suggest that amines facilitate the initial decarbonylation step creating a vacant site on the cobalt center thereby resulting in an increased reaction rate. As a consequence, the reaction proceeds to completion before the catalyst decomposes. The facility of the cobalt cluster $Co_4(CO)_{12}$ as a catalyst precursor suggests that it presumably disproportionated into $Co_2(CO)_8$ or a similar catalytically active cobalt species, which could be accelerated by the presence of the amine. Alternatively, it may have formed an (alkyne)$Co_4(CO)_{10}$ complex upon reaction with the alkyne and may be subsequently transformed to the (alkyne)$Co_2(CO)_6$ complex under the Pauson−

Scheme 4. Summary of Cobalt Catalysis in the Pauson−Khand Reaction



L : Lewis Base = RNH_2, NH_3, NH_4OH, RSR, R_2SO, R_3PS, OR_2, $P(OR)_3$, PAr_3, SiO_2

Khand reaction conditions and undergo cyclization with the alkene and CO.[36]

In conclusion, our findings have provided more practical protocols for the Pauson−Khand reaction using catalytic amounts of cobalt carbonyl complexes. We have provided a more general and coherent overview of the influence of Lewis bases on the efficiency of Pauson−Khand reactions which have recently seen substantial interest. Finally, our findings on the use of $Co_4(CO)_{12}$ are anticipated to develop into a convenient and practical alternative to $Co_2(CO)_8$ catalysis. More detailed studies on the interaction of these complexes with cyclohexylamine in the presence of an alkyne or enyne under the Pauson−Khand reaction conditions are underway.

Experimental Section

Enynes

1:[3a] ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.62 (dddd, J = 17.4, 9.9, 7.4, 7.4 Hz, 1H, C*H*=CH_2), 5.18 (dm, J = 17.1 Hz, 1H, CH=C*H*H), 5.13 (dm, J = 9.9 Hz, 1H, CH=CH*H*), 4.21 (q, J = 7.2 Hz, 4H, 2 CH_2O), 2.79−2.82 (m, 4H, 2 CH_2), 2.01 (t, J = 2.7 Hz, 1H, CC*H*), 1.25 (t, J = 7.2 Hz, 6H, 2 CH_3). MS [CI, *m*/*z* (rel intensity)]: 239.1 (M^+ + 1, 100). Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.27; H, 7.63.

3:[32] ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.63 (dddd, J = 17.5, 10.1, 7.4, 7.4 Hz, 1H, C*H*=CH_2), 5.16 (br d, J = 18.1 Hz, 1H, CH=C*H*H), 5.11 (br d, J = 10.1 Hz, 1H, CH=C*H*H), 4.18 (q, J = 7.4 Hz, 4H, 2 OCH_2), 2.78 (d, J = 7.4 Hz, 2H, CH_2CH=C), 2.75 (t, J = 2.7 Hz, 2H, CH_2CC-*n*-Pr), 2.09 (ddt, J = 8.7, 6.7, 2.0 Hz, 2H, CCC$H_2$$CH_2$), 1.47 (ddq, J = 14.1, 6.7, 6.7 Hz, 2H, $CH_2CH_2CH_3$), 1.24 (t, J = 7.4 Hz, 6H, 2 OCH_2CH_3), 0.95 (t, J = 7.4 Hz, 3H, CH_2CH_3).

4:[3a] ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.74 (d, J = 8.2 Hz, 2H, aromatic H), 7.30 (d, J = 8.5 Hz, 2H, aromatic H), 5.73 (dddd, J = 17.2, 10.3, 6.5, 6.5 Hz, 1H, C*H*=CH_2), 5.29 (br d, J = 17.8 Hz, 1H, CH=C*H*H), 5.24 (br d, J = 9.7 Hz, 1H, CH=CH*H*), 4.10 (d, J = 2.5 Hz, 2H, CH_2CCH), 3.83 (d, J = 6.5 Hz, 2H, CH_2CH=CH_2), 2.43 (s, 3H, CH_3), 2.00 (t, J = 2.5 Hz, 1H, CCH).

5: ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.77 (ddt, J = 17.5, 10.1, 7.4 Hz, 1H, C*H*=CH_2), 5.04 (br d, J = 15.4 Hz, 1H, CH=C*H*H),

(32) Zhang, M.; Buchwald, S. L. *J. Org. Chem.* **1996**, *61*, 4498.
(33) Magnus, P.; Exon, C.; Albaugh-Robertson, P. *Tetrahedron* **1985**, *41*, 5861.
(34) Shambayati, S.; Crowe, W. E.; Schreiber, S. L. *Tetrahedron Lett.* **1990**, *31*, 5289.
(35) Schore, N. E.; Croudace, M. C. *J. Org. Chem.* **1981**, *46*, 5436.
(36) (a) Dickson, R. S.; Tailby, G. R. *Aust. J. Chem.* **1970**, *23*, 229. (b) Dickson, R. S.; Fraser, P. J. *Adv. Organomet. Chem.* **1974**, *12*, 323. (c) Cadierno, V.; Gamasa, M. P.; Gimeno, J.; Moreto, J. M.; Ricart, S.; Roig, S.; Molins, E. *Organometallics* **1998**, *17*, 697.

5.00 (br d, J = 8.7 Hz, 1H, CH=CHH), 3.56 (d, J = 6.1 Hz, 2H, CH_2OSi), 2.18−2.22 (m, 2H, CH_2CH=C), 2.10−2.16 (m, 4H, CH_2CCCH_2), 1.66−1.75 (m, 1H, OCH$_2$CH), 1.50 (ddt, J = 14.8, 7.4, 7.4 Hz, 2H, $CH_2CH_2CH_3$), 0.97 (t, J = 7.4 Hz, 3H, CH_2CH_3), 0.89 (s, 9H, $C(CH_3)_3$), 0.04 (s, 6H, $Si(CH_3)_2$). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 136.7, 116.2, 81.2, 78.2, 64.3, 40.2, 34.6, 25.9, 22.5, 20.7, 19.9, 18.3, 13.5, 0.97. IR (thin film, cm^{-1}): 2958, 2938, 2859, 1472, 1258, 1104, 913, 837, 777, 668. Anal. Calcd for $C_{17}H_{32}OSi$: C, 72.79; H, 11.50. Found: C, 72.77; H, 11.61.

9:[3b] ^{1}H NMR ($CDCl_3$, 300 MHz): δ 4.92 (br s, 1H, CH_3C=CHH), 4.85 (br s, 1H, CH_3C=CHH), 3.74 (s, 6H, 2 OCH_3), 2.83−2.85 (m, 4H, CH_2CCH, CH_2C=C), 2.03 (t, J = 2.7 Hz, 1H, CCH), 1.65 (s, 3H, CH_3C=C).

10:[3b] ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.70 (dt, J = 12.1, 6.1 Hz, 1H, C=CHCH$_2$O), 5.19 (dtm, J = 12.7, 8.1 Hz, 1H, CCH$_2$CH=CHCH$_2$O), 4.27 (d, J = 6.0 Hz, 2H, CH_2O), 3.74 (s, 6H, 2 OCH_3), 2.82 (d, J = 8.1 Hz, 2H, CH_2CH=C), 2.79 (d, J = 2.7 Hz, 2H, CH_2CCH), 2.01 (t, J = 2.7 Hz, 1H, CCH), 0.89 (s, 9H, $C(CH_3)_3$), 0.06 (s, 6H, $Si(CH_3)_2$).

11:[3b] ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.73 (dt, J = 13.4, 6.7 Hz, 1H, C=CHCH$_2$O), 5.46 (dtm, J = 13.4, 8.1 Hz, 1H, CCH$_2$CH=CHCH$_2$O), 4.66 (d, J = 6.7 Hz, 2H, CH_2O), 3.75 (s, 6H, 2 OCH_3), 2.89 (d, J = 8.1 Hz, 2H, CH_2CH=C), 2.80 (d, J = 2.7 Hz, 2H, CH_2CCH), 2.06 (s, 3H, C(=O)CH_3), 2.04 (t, J = 2.7 Hz, 1H, CCH).

12:[3a] ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.80 (dddd, J = 16.8, 10.7, 6.7, 6.7 Hz, 1H, CH=CH_2), 5.05 (ddm, J = 17.4, 2.0 Hz, 1H, CH=CHH), 4.99 (ddm, J = 10.1, 2.0 Hz, 1H, CH=CHH), 3.74 (s, 6H, 2 OCH_3), 2.84 (d, J = 2.4 Hz, 2H, CH_2CCH), 2.14−2.19 (m, 2H, CH_2CH=C), 2.01 (t, J = 2.7 Hz, 1H, CCH), 1.93−1.99 (m, 2H, CH_2CH$_2$CH=C).

13: ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.75 (dddd, J = 17.5, 10.1, 7.4, 7.4 Hz, 1H, CH=CH_2), 5.06 (ddm, J = 17.5, 2.0 Hz, 1H, CH=CHH), 5.02 (d, J = 10.1 Hz, 1H, CH=CHH), 3.57 (dddd, J = Hz, 2H, CH_2OSi), 2.25 (dd, J = 6.0, 2.7 Hz, 2H, CH_2CCH), 2.14 (dddd, J = 6.7, 6.7, 1.3, 1.3 Hz, 2H, CH_2CH=CH_2), 1.93 (t, J = 2.7 Hz, 1H, CCH), 1.70−1.82 (m, 1H, OCH$_2$CH), 0.89 (s, 9H, $C(CH_3)_3$), 0.04 (s, 6H, $Si(CH_3)_2$). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 136.4, 116.5, 82.8, 69.2, 64.1, 39.7, 34.5, 25.9, 19.6, 18.3. IR (thin film, cm^{-1}): 3313, 2956, 2930, 2859, 1641, 1472, 1256, 1107, 915, 838, 776, 634. Anal. Calcd for $C_{14}H_{26}OSi$: C, 70.52; H, 10.99. Found: C, 70.30; H, 10.93.

14:[33] ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.81 (ddt, J = 16.8, 10.7, 7.4 Hz, 1H, CH=CH_2), 5.06 (br d, J = 16.8 Hz, 1H, CH=CHH), 5.01 (br d, J = 10.7 Hz, 1H, CH=CHH), 4.01 (d, J = 2.0 Hz, 1H, CHOSi), 2.36 (d, J = 2.0 Hz, 1H, CCH), 2.11 (br dd, J = 7.4, 2.7 Hz, 2H, CH_2CH=C), 0.93 (s, 3H, C(CH_3)CH$_3$), 0.92 (s, 3H, C(CH$_3$)CH_3), 0.90 (s, 9 H, $SiC(CH_3)_3$), 0.15 (s, 3H, $SiCH_3$), 0.09 (s, 3H, $SiCH_3$.

15:[33] ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.81 (ddt, J = 16.8, 9.4, 7.4, Hz, 1H, CH=CH_2), 5.04 (br d, J = 16.8 Hz, 1H, CH=CHH), 5.00 (br d, J = 9.4 Hz, 1H, CH=CHH), 3.98 (app d, J = 2.0 Hz, 1H, CHOSi), 2.08 (br dd, J = 6.0, 6.0 Hz, 2H, CH_2CH=C), 1.83 (d, J = 2.1 Hz, 3H, CCCH_3), 0.90 (s, 9 H, $C(CH_3)_3$), 0.88 (s, 6H, $C(CH_3)_2$, 0.12 (s, 3H, $SiCH_3$), 0.07 (s, 3H, $SiCH_3$).

16:[33] ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.82 (ddt, J = 16.8, 10.7, 7.4 Hz, 1H, CH=CH_2), 5.05 (br d, J = 16.8 Hz, 1H, CH=CHH), 5.00 (br dd, J = 10.7, 2.0 Hz, 1H, CH=CHH), 4.00 (s, 1H, CHOSi), 2.10 (dd, J = 7.4, 3.4 Hz, 2H, CH_2CH=C), 0.91 (s, 6H, C(CH_3)$_2$), 0.90 (s, 9H, $C(CH_3)_3$), 0.15 (s, 9H, $Si(CH_3)_3$), 0.14 (s, 3H, $OSiCH_3$), 0.08 (s, 3H, $OSiCH_3$).

17:[34] ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.82 (dddd, J = 18.1, 10.7, 7.4, 7.4 Hz, 1H, CH=CH_2), 5.04 (br dm, J = 18.1 Hz, 1H, CH=CHH), 4.99 (br dm, J = 10.1 Hz, 1H, CH=CHH), 3.54 (dd, J = 4.7, 4.7 Hz, 1H, CHOSi), 2.51 (ddd, J = 17.5, 4.7, 2.7 Hz, 1H, CHHCCH), 2.20 (ddd, J = 17.5, 5.4, 2.7 Hz, 1H, CHHCCH), 2.08 (ddm, J = 14.1, 7.4 Hz, 1H, CHHCH=C), 2.02 (obscured ddm, J = 14.7, 6.9 Hz, 1H, CHHCH=C), 1.98 (obscured t, J = 2.7 Hz, 1H, CH_2CCH), 0.90 (s, 9H, $SiC(CH_3)_3$), 0.87 (s, 3H, C(CH_3)CH$_3$, 0.86 (s, 3H, $CCH_3(CH_3)$, 0.15 (s, 3H, $SiCH_3CH_3$), 0.08 (s, 3H, $SiCH_3CH_3$).

18:[29] ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.26 (t, 3H, J = 7.1 Hz, CH_2CH_3), 1.57 (tt, 2H, J = 7.1, 7.1 Hz, CH_2CH$_2$CH=C), 2.13 (obscured dtdd, 2H, J = 7.1, 6.6, 1.6, 1.1 Hz, CH_2CH=C), 2.17 (obscured tt, 2H, J = 7.1, 2.2 Hz, CH_2CCC(CH$_2$)$_2$S), 2.44 (tt, 2H, J = 7.1, 2.2 Hz, CCCH_2CH$_2$S), 2.58 (q, 2H, J = 7.1, SCH_2-CH$_3$), 2.66 (t, 2H, J = 7.1 Hz, CCCH_2S), 4.97 (obscured ddt, 1H, J = 9.9, 2.2, 1.1 Hz, CH=CHH), 5.03 (obscured ddt, 1H, J = 17, 2.2, 1.6 Hz, CH=CHH), 5.80 (ddt, 1H, J = 17, 9.9, 6.6 Hz, CH=CH_2). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 14.9, 18.3, 20.5, 26.2, 28.3, 31.4, 33.0, 79.1, 81.3, 115.5, 138.6. IR (neat, cm^{-1}): 1630. MS, *m*/*e* (EI): 153 (M^+ − 29).

19:[35] ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.81 (dddd, J = 16.8, 10.1, 6.1, 6.1 Hz, 1H, CH=CH_2), 5.00 (dddd, J = 17.5, 4.0, 2.0, 2.0 Hz, 1H, CH=CHH), 4.95 (dddd, J = 10.1, 10.1, 2.0, 2.0 Hz, 1H, CH=CHH), 2.11−2.16 (m, 4H, CH_2CCCH_2), 2.03−2.09 (m, 2H, CH_2C=C), 1.23−1.51 (m, 8H), 0.90 (t, J = 7.5 Hz, 3H, CH_3).

38: ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.75 (d, J = 8.3 Hz, 2H, aromatic H), 7.29 (d, J = 8.1 Hz, 2H, aromatic H), 5.75 (dddd, J = 16.6, 10.0, 6.4, 6.4 Hz, 1H, CH=CH_2), 5.27 (dd, J = 17.1, 1.2 Hz, 1H, CH=CHH), 5.22 (dd, J = 10.3, 1.2 Hz, 1H, CH=CHH), 4.06 (d, J = 2.2 Hz, 2H, NCH_2CCH), 3.81 (br d, J = 6.6 Hz, 2H, NCH_2CH=C), 2.42 (s, 3H, $ArCH_3$), 1.89 (ddt, J = 6.8, 6.8, 2.2 Hz, 2H, CH_2CH$_2$CH$_3$), 1.29 (ddt, J = 7.3, 7.3, 7.3 Hz, 2H, $CH_2CH_2CH_3$), 0.82 (t, J = 7.3 Hz, 3H, CH_2CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 143.1, 136.0, 132.0, 129.2, 127.7, 119.4, 86.0, 72.2, 48.7, 36.2, 21.6, 21.3, 20.3, 13.2. IR (thin film, cm^{-1}): 2965, 2934, 2873, 2361, 1599, 1496, 1446, 1348, 1163, 1092, 1058, 992, 931, 901, 815, 757, 667, 580, 545. Anal. Calcd for $C_{16}H_{21}NO_2S$: C, 65.95; H, 7.26; N, 4.81. Found: C, 66.00; H, 7.30, N, 4.86.

39: ^{1}H NMR ($CDCl_3$, 500 MHz): δ 5.83 (ddt, J = 16.8, 10.3, 6.6 Hz, 1H, CH=CH_2), 5.03 (dddd, J = 17.2, 1.8, 1.8, 1.8 Hz, 1H, CH=CHH), 4.96 (ddm, J = 10.3, 1.3 Hz, 1H, CH=CHH), 4.35 (ddt, J = 6.6, 6.6, 1.8 Hz, 1H, CHOSi), 2.19 (obscured ddd, J = 7.0, 7.0, 2.0 Hz, 2H, CH_2CH=C), 2.15−2.18 (m, 2H, $COCCCH_2$), 1.74 (dtd, J = 16.7, 6.8, 6.8 Hz, 1H, CHHCHO), 1.71 (dtd, J = 17.4, 6.8, 6.8 Hz, 1H, CHHCHO), 1.37−1.51 (m, 4H, CH_2CH$_2$CH$_3$), 0.90 (s, 9H, $C(CH_3)_3$), 0.90 (t, J = 7.0 Hz, 3H, CH_3), 0.12 (s, 3H, $SiCH_3$), 0.10 (s, 3H, $SiCH_3$). Anal. Calcd for $C_{17}H_{32}OSi$: C, 72.79; H, 11.50. Found: C, 72.77; H, 11.58.

45: ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.40−7.42 (m, 2H, aromatic H), 7.30 (app t, J = 2.1 Hz, 3H, aromatic H), 5.86 (ddt, J = 16.9, 10.3, 6.6 Hz, 1H, CH=CH_2), 5.07 (br dd, J = 17.1, 1.7 Hz, 1H, C=CHH), 4.99 (br dd, J = 11.2, 1.2 Hz, 1H, C=CHH), 4.59 (t, J = 6.6 Hz, 1H, CHOSi), 2.27 (dtd, J = 14.7, 7.1, 7.1 Hz, 1H, CHHCH=C), 2.25 (dtd, J = 14.9, 6.8, 6.8 Hz, 1H, CHHCH=C), 1.87 (dtd, J = 13.9, 7.1, 7.1 Hz, 1H, OCHCHH), 1.84 (dtd, J = 14.2, 7.3, 7.3 Hz, 1H, OCHCHH), 0.93 (s, 9H, $C(CH_3)_3$), 0.18 (s, 3H, $SiCH_3$), 1.05 (s, 3H, $SiCH_3$).). ^{13}C NMR ($CDCl_3$, 75 MHz): δ −4.9, −4.4, 18.2, 25.8, 29.5, 37.8, 62.8, 84.3, 90.9, 114.9, 123.1, 128.1, 128.2, 131.5, 138.0.

47: To a solution of *N*-tosyl-*N*-allylpropargylamine (492 mg, 1.97 mmol) in THF (20 mL) at −78 °C was added *sec*-BuLi (2.0 mL, 2.6 mmol, 1.3 M in hexanes). The reaction was then warmed to ambient temperature, and acetone was added (2 mL). After stirring for 30 min, the resulting mixture was quenched with water and extracted with EtOAc. The organic layer was dried over Na_2SO_4 and concentrated in vacuo. Purification by flash chromatography (SiO_2, 50% EtOAc in hexanes) yielded 347 mg of *N*-tosyl-*N*-allyl-4-hydroxy-4-methyl-2-pentynylamine (57% yield) as a colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.74 (d, J = 8.1 Hz, 2H, aromatic H), 7.32 (d, J = 8.1 Hz, 2H, aromatic H), 5.74 (ddt, J = 16.8, 10.1, 6.7 Hz, 1H, CH=CH_2), 5.28 (ddm, J = 17.4, 1.3 Hz, 1H, CH=CHH), 5.24 (ddm, J = 10.4, 1.4 Hz, 1H, CH=CHH), 4.09 (s, 2H, CH_2CCCO), 3.82 (d, J = 6.0 Hz, 2H, CH_2CH=CH_2), 2.42 (s, 3H, CH_3Ar), 1.6 (s, 1H, OH), 1.26 (s, 6H, $C(CH_3)_2O$). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 143.48, 135.98, 131.76, 129.43, 127.70, 119.76, 90.42, 74.28, 64.53, 48.92, 35.87, 30.86, 21.34. IR (neat, cm^{-1}): 3515, 2982, 2930, 1598, 1446, 1348, 1235, 1162, 1093, 949, 890, 855, 816, 760, 665. Anal. Calcd for $C_{16}H_{21}O_3NS$: C, 62.51; H, 6.89. Found: C, 62.42; H, 6.81.

Enyne−$Co_2(CO)_6$ Complexes

Enyne−$Co_2(CO)_6$ Complex 32. To a solution of *N*-tosyl-*N*-allyl-4-hydroxy-4-methyl-2-pentynylamine (159 mg, 0.517 mmol) in a 1:1 mixture of petroleum ether:CH_2Cl_2 (5 mL) was added solid $Co_2(CO)_8$ (220 mg, 0.643 mmol) at room temperature. After stirring for 30 min, the reaction mixture was directly subjected to column chromatography (SiO_2, 50% petroleum ether in Et_2O). Concentration of the eluent at room temperature in vacuo gave 260 mg of **25** (90% yield) as a red-brown solid. ^{1}H NMR and IR spectra of this complex could not be obtained. Anal. Calcd for $C_{22}H_{21}O_9NSCo_2$: C, 44.53; H, 3.57. Found: C, 44.44; H, 3.62.

Enyne−$Co_2(CO)_6$ Complex 33. To a solution of enyne **1** (101 mg, 0.424 mmol) in petroleum ether (4 mL) was added solid $Co_2(CO)_8$ (160 mg, 0.468 mmol), and the mixture was stirred under a nitrogen atmosphere at room temperature for 1 h (or until complex formation was complete by TLC). Filtration through a short pad of Celite (eluent petroleum ether) followed by concentration under reduced pressure at room temperature gave a quantitative yield of enyne−$Co_2(CO)_6$ complex **33**. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.98 (s, 1H, CH_2-CC*H*), 5.68 (dddd, J = 17.5, 10.1, 7.4, 7.4 Hz, 1H, C*H*=CH_2), 5.18 (dm, J = 10.1 Hz, 1H, CH=C*H*H), 5.13 (dm, J = 17.0 Hz, 1H, CH=CH*H*), 4.27 (dq, J = 14.8, 7.4 Hz, 2H, 2 CH_2O), 4.17 (dq, J = 14.1, 7.4 Hz, 2H, 2 CH_2O), 3.62 (2, 2H, CH_2CCH), 2.76 (d, J = 7.4 Hz, 2H, 2 CH_2CH=C), 1.26 (t, J = 7.4 Hz, 6H, 2 CH_3). Enyne−$Co_2(CO)_6$ complexes **35** and **37** were prepared in the same manner as enyne−$Co_2(CO)_6$ complex **33**.

Representative Experimental Procedures for Cycloadditions. A typical procedure from each section is described. Progress of the reactions was monitored by TLC by taking a sample of the reaction mixture using a long capillary tube inserted through the septum with the aid of a needle. For reactions using volatile enyne substrates, e.g., **18**, **19**, and phenylacetylene, the system was not pumped, but rather only purged with the appropriate reaction atmosphere. For reactions yielding volatile products, e.g., **29**, **30**, diethyl ether was used as the eluent for filtration and the organic layer was concentrated in vacuo at room temperature. Additives were typically added as premixed solutions in DME, except for solids, e.g., 1,10-phenanthroline.

Modification and Limitations in the Livinghouse Catalytic Reaction. In a flask equipped with a three-way stopper and a balloon of CO, a mixture of diethyl(2-hexynyl) allylmalonate **3** (121 mg, 0.432 mmol) and $Co_2(CO)_8$ (15 mg, 0.044 mmol, 10 mol %) was pumped briefly and purged three times with CO. DME (1.6 mL) was added, and the resulting solution was stirred at ambient temperature for 30 min. Cyclohexylamine (10 μL, 0.087 mmol, 20 mol %) in DME (0.6 mL) was then added, and the reaction was heated at 70 °C for 11.5 h. Upon completion of the reaction, the mixture was cooled to room temperature, diluted with 3 mL of 10% EtOAc in hexanes and plugged through a pad of silica gel. Subsequent removal of the solvent and purification by flash chromatography (SiO_2, 10% EtOAc in hexanes) afforded 120 mg of bicyclic enone **6** (90% yield) as a colorless oil. For the reaction without the amine, the mixture was also stirred for 30 min at room temperature prior to heating at 70 °C and was worked up in the same manner upon completion.

Dicobalthexacarbonyl-Complexed Enynes as Catalyst Precursors. A 10-mL flask containing a mixture of enyne **1** (51 mg, 0.21 mmol) and catalyst **32** (12 mg, 0.020 mmol, 10 mol %) was equipped with a three-way stopper, a condenser, and a balloon of CO and was pumped briefly and purged three times with CO. DME (1 mL) was added, and the resulting solution was heated at 70 °C and stirred for 2 h. Upon completion of the reaction, the mixture was cooled to room temperature, quenched with water, and extracted with EtOAc. The organic layer was dried over Na_2SO_4 and concentrated in vacuo. Purification by flash chromatography (SiO_2, 33% EtOAc in hexanes) afforded 44 mg of bicyclopentenone **2** (78% yield) as a colorless oil. If appropriate, cyclohexylamine was added prior to heating. Alternatively, the reaction could be worked up by dilution with 10% EtOAc in hexanes and plugged through a pad of silica gel using hexane/EtOAc as the eluent.

Pauson−Khand Reactions Using Substoichiometric Amounts of $Co_2(CO)_8$ under a Nitrogen Atmosphere. In a round-bottom vessel equipped with a balloon of ultrahigh purity (UHP) nitrogen, diethylpropargyl allyl malonate **1** (51 mg, 0.21 mmol), $Co_2(CO)_8$ (26 mg, 0.076 mmol, 38 mol %), and DME (2.3 mL) were added. After stirring for 30 min at ambient temperature, cyclohexylamine (25 μL, 0.22 mmol, 105 mol %) in DME (2 mL) was added, and the reaction was heated at 60 °C for 3 h. Upon completion of the reaction, the mixture was cooled to room temperature, diluted with 3 mL of 10% EtOAc in hexanes, and plugged through a pad of silica gel. Subsequent removal of the solvent and purification by flash chromatography (SiO_2, 20% EtOAc in hexanes) afforded 45 mg of bicyclopentenone **2** (80% yield) as a colorless oil.

Dodecacarbonyltetracobalt Catalysis in the Thermal Pauson−Khand Reaction. In a vessel equipped with a three-way stopper and a balloon of CO, a mixture of enyne **3** (31 mg, 0.11 mmol) and $Co_4(CO)_{12}$ (3 mg, 0.05 mmol, 5 mol %) was pumped briefly and purged three times with CO. DME (1.2 mL) and $CyNH_2$ (3.6 μL, 0.031 mmol, 30 mol %) in DME (1 mL) were added successively, and the resulting deep purple solution was heated at 70 °C for 13 h. Upon completion of the reaction, the brown mixture was cooled to room temperature, diluted with 3 mL of 10% EtOAc in hexanes, and plugged through a pad of silica gel. Subsequent removal of the solvent and purification by flash chromatography (SiO_2, 20% EtOAc in hexanes) afforded 32 mg of bicyclopentenone **6** (94% yield) as a colorless oil. For the reactions using $Co_4(CO)_{12}$ only, the reagents were dissolved in the appropriate solvent, and the mixture was heated to 70 °C.

A similar general procedure was followed for the intermolecular variant. In a flask equipped with a three-way stopper and a balloon of CO, a mixture of phenylacetylene (34 mg, 0.33 mmol), norbornene (157 mg, 1.7 mmol), and $Co_4(CO)_{12}$ (19 mg, 0.03 mmol, 10 mol %) was purged three times with a balloon of CO. DME (5.7 mL) and a solution of $CyNH_2$ (22.8 μL, 0.199 mmol, 60 mol %) in DME (1 mL) were added successively, and the resulting deep purple solution was heated at 70 °C for 13.5 h. The mixture was worked up in the same manner as described above and 72 mg of cyclopentenone **44** (97%) was obtained as a white solid.

Pauson−Khand Reaction Cycloadducts

2:[17,3a,e,12b] ^{1}H NMR ($CDCl_3$, 500 MHz): δ 5.92 (s, 1H, C=CH), 4.25 (q, J = 7.3 Hz, 2H, OCH_2), 4.21 (q, J = 7.3 Hz, 2H, OCH_2), 3.35 (AB, J_{AB} = 19.1 Hz, 1H, C*H*HC=C), 3.25 (AB, J_{AB} = 18.8 Hz, 1H, CH*H*C=C), 3.10 (br m, 1H, CH_2CHCH_2), 2.80 (dd, J = 12.7, 7.6 Hz, 1H, C*H*HC=O), 2.63 (dd, J = 17.8, 6.4 Hz, 1H, $(EtO_2C)_2$CC*H*HCH), 2.13 (dd, J = 17.8, 3.2 Hz, 1H, $(EtO_2C)_2$CCH*H*CH), 1.74 (dd, J = 12.7, 12.7 Hz, 1H, CH*H*C=O), 1.28 (t, J = 7.1 Hz, 3H, OCH_2CH_3), 1.26 (t, J = 7.3 Hz, 3H, OCH_2CH_3). MS [CI, *m*/*z* (rel intensity)]: 267.1 (M^+ + 1, 100).

6:[12a,32] ^{1}H NMR ($CDCl_3$, 300 MHz): δ 4.25 (q, J = 7.4 Hz, 2H, OCH_2), 4.21 (q, J = 7.4 Hz, 2H, OCH_2), 3.22 (br s, 2H, CH_2C=C), 2.96 (br m, 1H, CH_2CHCH_2), 2.79 (dd, J = 12.8, 7.4 Hz, 1H, C*H*HC=O), 2.64 (dd, J = 17.5, 6.0 Hz, 1H, $(EtO_2C)_2$CC*H*HCH), 2.22 (dt, J = 14.8, 7.4 Hz, 1H, C=CC*H*HCH$_2$), 2.07 (obscured dt, J = 14.8, 7.4 Hz, 1H, C=CCH*H*CH$_2$), 2.08 (obscured dd, J = 17.5, 3.4 Hz, 1H, $(EtO)_2$CCH*H*CH), 1.64 (dd, J = 12.8, 12.8 Hz, 1H, CH*H*C=O), 1.48 (dqt, J = 14.7, 7.4, 7.4, 1H, CH_2CHHCH_3), 1.47 (dqt, J = 14.7, 7.4, 7.4, 1H, CH_2CHHCH_3), 1.28 (t, J = 7.4 Hz, 3H, 2 OCH_2CH_3), 1.26 (t, J = 7.4 Hz, 3H, 2 OCH_2CH_3), 0.89 (t, J = 7.4 Hz, 3H, $CH_2CH_2CH_3$). Anal. Calcd for $C_{17}H_{24}O_5$: C, 66.21; H, 7.85. Found: C, 65.39; H, 7.87.

7:[3a,e,5,8] ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.73 (d, J = 8.1 Hz, 2H, aromatic H), 7.35 (d, J = 8.3 Hz, 2H, aromatic H), 5.99 (s, 1H, C=CH), 4.34 (AB, J_{AB} = 16.4 Hz, 1H, NC*H*HC=C), 4.04 (obscured AB, J_{AB} = 16.4 Hz, 1H, NCH*H*C=C), 4.03 (obscured dd, J = 8.8, 8.8 Hz, 1H, NC*H*HCH), 3.15 (br m, 1H, CH_2CHCH_2), 2.63 (obscured dd, J = 11.0, 9.3 Hz, 1H, NCH-*H*CH), 2.59 (obscured dd, J = 18.1, 6.6 Hz, 1H, CH*H*C=O), 2.44 (s, 3H, $ArCH_3$), 2.06 (dd, J = 17.8, 3.7 Hz, 1H, CH*H*C=O).

8 (**major isomer**): ^{1}H NMR ($CDCl_3$, 500 MHz): δ 3.62 (d, J = 6.6 Hz, 2H, CH_2OSi), 2.86−2.92 (br m, 1H, CH_2CHCH_2), 2.68 (ABd, J_{AB} = 18.0, 8.4 Hz, 1H, $CHCHHC{=}C$), 2.62 (dd, J = 18.0, 6.4 Hz, 1H, $CHHC{=}O$), 2.52 (m, 1H, $CHCH_2OSi$), 2.29 (ABd, J_{AB}= 18.0, J = 4.2 Hz, 1H, $CHCHHC{=}C$), 2.22 (dt, J = 14.3, 7.9 Hz, 1H, $C{=}CCHHCH_2$), 1.96−2.13 (m, 2H, $C{=}CCHHCH_2$ and $CHCHHCH$), 1.98 (dd, J = 18.0, 3.1 Hz, 1H, $CHHC{=}O$), 1.47 (ABtq, J = 15.0, 7.5 Hz, 1H, $CHHCH_3$), 1.47 (ABtq, J = 15.0, 7.5 Hz, 1H, $CHHCH_3$), 1.24 (ABd, J_{AB} = 9.0, J = 12.4, 12.4 Hz, 1H, $CHCHHCH$), 0.91 (s, 9H, $C(CH_3)_3$), 0.88 (t, J = 4.5 Hz, 3H, CH_2CH_3), 0.07 (s, 6H, $Si(CH_3)_2$). Anal. Calcd for $C_{18}H_{32}O_2Si{\cdot}0.1H_2O$: C, 69.66; H, 10.39. Found: C, 69.26; H, 10.52.

IR (neat, cm^{-1}): **Minor isomer**; 2958, 2929, 2858, 1710, 1666, 1471, 1360, 1253, 1103, 1005, 836, 779. **Major isomer**; 2958, 2931, 2858, 1711, 1664, 1360, 1253, 1105, 1005, 838, 777. MS [EI, *m*/*z* (rel intensity)]: 175.0 (52), 251.0 (100), 308.0 (M^+).

20:[5] ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.84 (br d, J = 1.2 Hz, 1H, $C{=}CH$), 3.81 (s, 3H, OCH_3), 3.73 (s, 3H, OCH_3), 3.51 (ABd, J = 18.1, 2.0 Hz, 1H, $CHHC{=}C$), 3.22 (ABd, J = 18.0 Hz, 1H, $CHHC{=}C$), 2.60 (AB, J_{AB} = 13.2 Hz, 1H, $(MeO_2C)_2CHHCCH_3$), 2.39 (s, 2H, $CH_2C{=}O$), 2.23 (AB, J_{AB} = 13.3 Hz, 1H, $(MeO_2C)_2CHHCH_3$), 1.15 (s, 3H, CCH_3).

21:[3b] ^{1}H NMR (C_6D_6, 500 MHz): δ 5.70 (br s, 1H, $C{=}CH$), 3.78 (ABd, J_{AB} = 10.2, J = 6.4 Hz, 1H, $CHHOSi$), 3.66 (ABd, J_{AB} = 10.2, J = 3.0 Hz, 1H, $CHHOSi$), 3.30 (s, 3H, OCH_3), 3.28 (s, 3H, OCH_3), 3.12 (AB, J_{AB} = 19.1 Hz, 1H, $(MeO_2C)_2CCHHC{=}C$), 3.06 (AB, J_{AB} = 19.1 Hz, 1H, $(MeO_2C)_2CCHHC{=}C$), 2.91 (dddm, J = 13.2, 6.6, 6.6 Hz, 1H, $CH_2CHCHC{=}O$), 2.69 (dd, J = 12.6, 7.7 Hz, 1H, $(MeO_2C)_2CCHHCH$), 2.41 (dd, J = 12.8, 12.8 Hz, 1H, $(MeO_2C)_2CCHHCH$), 2.35 (ddd, J = 6.6, 6.6, 3.0 Hz, 1H, $CHCHCH_2O$), 0.87 (s, 9H, $C(CH_3)_3$), 0.00 (s, 3H, $SiCH_3CH_3$), −0.03 (s, 3H, $Si(CH_3)CH_3$).

22:[3b] ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.96 (s, 1H, $C{=}CH$), 4.28 (dd, J = 11.4, 4.7 Hz, 1H, $CHHOAc$), 4.06 (dd, J = 11.4, 8.7 Hz, 1H, $CHHOAc$), 3.81 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3), 3.41 (br AB, J = 19.5 Hz, 1H, $CHHCH{=}C$), 3.27 (obscured broad AB, J = 19.5 Hz, 1H, $CHCH{=}C$), 3.24 (obscured m, 1H, CH_2CHCH), 2.92 (ddd, J = 4.7, 6.7, 8.7 Hz, 1H, $CHCH_2O$), 2.66 (dd, J = 12.8, 7.4 Hz, 1H, $(MeO_2C)_2CHHCH$), 2.04 (s, 3H, $COCH_3$), 1.92 (dd, J = 12.8, 12.8 Hz, 1H, $(MeO_2C)_2CHHCH$).

23:[3a] ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.97 (s, 1H, $C{=}CH$), 3.76 (s, 3H, OCH_3), 3.72 (s, 3H, OCH_3), 3.49 (dd, J = 14.0, 2.3 Hz, 1H, $CHHC{=}C$), 2.68 (obscured m, 1H, CH_2CHCH_2), 2.67 (br d, J = 14.2 Hz, 1H, $CHHC{=}C$), 2.57 (dd, J = 18.7, 6.6 Hz, 1H, $CHHC{=}O$), 2.52 (ddd, J = 14.0, 6.0, 3.2 Hz, $(MeO_2C)_2CCHHCH_2$), 2.17 (dddd, J = 13.6, 6.0, 3.8, 3.4 Hz, 1H, $(MeO_2C)_2CCH_2CHH$), 1.98 (obscured dd, J = 18.5, 2.1 Hz, 1H, $CHH{=}O$), 1.94 (ddd, J = 13.8, 13.8, 3.8 Hz, 1H, $(MeO_2C)_2CHHCH_2$), 1.28 (dddd, J = 13.6, 13.6, 3.6, 3.2 Hz, 1H, $(MeO_2C)_2CCH_2HH$).

24. Inseparable (1:1) mixture of isomers. Anal. Calcd for $C_{15}H_{25}O_2Si$: C, 67.62; H, 9.83. Found: C, 67.6; H, 9.96.

25 (**major isomer**): ^{1}H NMR ($CDCl_3$, 500 MHz): δ 5.93 (d, J = 2.1 Hz, 1H, $C{=}CH$), 4.11 (s, 1H, $CHOSi$), 3.30−3.41 (m, 1H, CH_2CHCH_2), 2.69 (dd, J = 18.1, 6.7 Hz, 1H, $CHHC{=}O$), 2.04 (dd, J = 18.1, 3.4 Hz, 1H, $CHHC{=}O$), 2.01 (dd, J = 12.1, 12.1 Hz, 1H, Me_2CCHH), 1.11 (obscured s, 3H, CCH_3CH_3), 1.08 (obscured dd, J = 12.8, 8.1 Hz, Me_2CCHH), 0.90 (s, 3H, CCH_3CH_3), 0.89 (s, 9H, $C(CH_3)_3$), 0.10 (s, 3H, $SiCH_3CH_3$), 0.04 (s, 3H, $SiCH_3CH_3$).). ^{13}C NMR ($CDCl_3$, 75 MHz): −5.1, −4.9, 18.0, 24.4, 25.6, 29.0, 37.0, 43.7, 43.8. Anal. Calcd for $C_{16}H_{28}O_2Si$: C, 68.52; H, 10.06. Found: C, 68.34; H, 10.11.

25 (**minor isomer**): ^{1}H NMR ($CDCl_3$, 500 MHz): δ 5.98 (t, J = 2.0 Hz, 1H, $C{=}CH$), 4.47 (d, J = 1.5 Hz, 1H, $CHOSi$), 2.94−3.00 (m, 1H, CH_2CHCH_2), 2.67 (dd, J = 17.8, 6.6 Hz, 1H, $CHHC{=}O$), 2.06 (dd, J = 17.8, 3.2 Hz, 1H, $CHHC{=}O$), 2.00 (dd, J = 13.2, 10.0 Hz, 1H, Me_2CCHH), 1.31 (dd, J = 13.2, 8.3 Hz, 1H, Me_2CHH), 1.18 (s, 3H, CCH_3CH_3), 0.93 (s, 9H, $C(CH_3)_3$), 0.85 (s, 3H, CCH_3CH_3), 0.10 (s, 3H, $SiCH_3CH_3$). 0.09 (s, 3H, $SiCH_3CH_3$).

26 (**cis isomer**):[12b,45] ^{1}H NMR ($CDCl_3$, 300 MHz): δ 4.09 (s, 1H, $CHOSi$), 3.22 (br m, 1H, CH_2CHCH_2), 2.72 (dd, J = 18.1, 6.0 Hz, 1H, $CHHC{=}O$), 2.01 (dd, J = 12.8, 10.8 Hz, 1H, Me_2CHH), 1.99 (dd, J = 18.1, 2.7 Hz, 1H, $CHHC{=}O$), 1.75 (d, J = 2.0 Hz, 3H, $C{=}CCH_3$), 1.12 (s, 3H, $C(CH_3)CH_3$), 1.04 (dd, J = 13.4, 7.4 Hz, 1H, Me_2CHH), 0.88 (s, 9H, $SiC(CH_3)_3$), 0.80 (s, 3H, $C(CH_3)CH_3$), 0.10 (s, 3H, $SiCH_3CH_3$), 0.01 (s, 3H, $SiCH_3CH_3$).

28 (**major isomer**): ^{1}H NMR (C_6D_6, 500 MHz): δ 5.67 (s, 1H, $C{=}CH$), 3.04 (dd, J = 11.0, 4.5 Hz, 1H, $CHOSi$), 2.46 (dd, J = 13.4, 5.1, 1H, $CHHC{=}CH$), 2.21 (dd, J = 18.3, 6.6 Hz, 1H, $CHHC{=}O$), 2.10 (dddm, J = 13.0, 6.5, 6.5, 1H, CH_2CHCH_2), 2.05 (t, J = 12.4, 1H, $CHHC{=}CH$), 1.62 (dd, J = 18.3, 2.3, 1H, $CHHC{=}O$), 1.22 (dd, J = 13.2, 5.7, 1H, $(CH_3)_2CCHHCH$), 0.95 (s, 9H, Si*t*Bu), 0.79 (s, 3H, CCH_3CH_3), 0.77 (s, 3H, CCH_3CH_3), 0.41 (t, J = 13.0, 1H, $(CH_3)_2CCHHCH$), −0.01 (s, 3H, $SiCH_3CH_3$), −0.02 (s, 3H, $SiCH_3CH_3$). ($CDCl_3$, 75 MHz): −5.0, −4.1, 17.8, 17.9, 25.7, 28.8, 36.5, 36.9, 37.5, 41.9, 45.2, 77.3, 128.0, 182.0, 209.1. Anal. Calcd for $C_{17}H_{30}O_2Si$: C, 69.33; H, 10.27. Found: C, 69.26; H, 10.28. CH_2CHCH_2

29:[29] ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.07 (dddd, 1H, J = 11.5, 11.5, 11.5, 8.3, 6-H), 1.23 (t, 3H, J = 7.7, 12-H), 1.90−2.20 (m, 5 H), 2.37 (ABt, 1H, J_{AB} = 14.3, J = 7.1, 9-H), 2.45−2.70 (m, 7 H), 2.77 (m, 1H, 7-H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 14.9, 24.5, 25.5, 25.8, 26.0, 30.1, 31.4, 41.9, 44.8, 134.9, 185.9, 210.9.

30:[29] ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.82−2.87 (m, 1H), 2.49−2.57 (m, 2H), 2.09−2.17 (m, 4H), 1.94−2.04 (m, 2H), 1.81−1.89 (m, 2H), 1.48 (m, 1H), 1.21−1.39 (m, 4H), 1.03 (ddd, J = 15.9, 13.2, 3.9 Hz, 1H), 0.88 (t, J = 7.5 Hz, 3H).

34:[221] ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.74 (d, J = 8.3 Hz, 2H, aromatic H), 7.35 (d, J = 8.1 Hz, 2H, aromatic H), 4.36 (AB, J_{AB} = 17.3 Hz, 1H, $NCHHC{=}C$), 4.23 (AB, J_{AB} = 17.1 Hz, 1H, $NCHHC{=}C$), 3.99 (dd, J = 8.5, 8.5 Hz, 1H, $NCHHCH$), 2.99 (br m, 1H, CH_2CHCH_2), 2.60 (obscured dd, J = 18.8, 6.4 Hz, 1H, $CHHC{=}O$), 2.56 (obscured dd, J = 11.2, 9.5 Hz, 1H, $NCHHCH$), 2.44 (s, 3H, $ArCH_3$), 2.07 (dd, J = 18.1, 3.9 Hz, 1H, $CHHC{=}O$), 1.38 (s, 3H, CCH_3CH_3O), 1.35 (s, 3H, CCH_3CH_3O).

40:[3a,3e,5,8] ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.73 (d, J = 8.3 Hz, 2H, aromatic H), 7.34 (d, J = 8.5 Hz, 2H, aromatic H), 4.24 (AB, J_{AB} = 16.0 Hz, 1H, $NCHHC{=}C$), 4.02 (obscured AB, J_{AB} = 16.2 Hz, 1H, $NCHHC{=}C$), 3.99 (obscured dd, J = 8.9, 8.9 Hz, 1H, $NCHHCH$), 3.02 (br m, 1H, CH_2CHCH_2), 2.59 (obscured dd, J = 17.9, 6.4 Hz, 1H, $CHHC{=}O$), 2.56 (obscured dd, J = 11.1, 9.4 Hz, 1H, $NCHHCH$), 2.44 (s, 3H, $ArCH_3$), 2.18 (dt, J = 14.5, 7.2 Hz, 1H, $C{=}CCHHCH_2$), 2.03 (obscured dt, J = 14.5, 7.2 Hz, 1H, $C{=}CCHHCH_2$), 2.02 (obscured dd, J = 17.9, 3.4, 1H, $CHHC{=}O$), 1.41 (dqt, J = 13.8, 7.2, 7.2 Hz, 1H, CH_2CHHCH_3), 1.40 (dqt, J = 13.8, 7.2, 7.2 Hz, 1H, CH_2CHHCH_3), 0.81 (t, J = 7.4 Hz, 3H, $CH_2CH_2CH_3$).

41 (**major isomer**): ^{1}H NMR ($CDCl_3$, 500 MHz): δ 4.80 (dd, J = 3.6, 3.6 Hz, 1H, $CHOSi$), 3.06 (br m, 1H, CH_2CHCH_2), 2.66 (dd, J = 18.1, 6.3 Hz, 1H, $CHHC{=}O$), 2.30 (dddd, J = 13.6, 8.8, 6.8, 2.6 Hz, 1H, $CHOCHH$), 2.15−2.23 (m, 4H), 2.00 (dd, J = 18.1, 2.7 Hz, 1H, $CHHC{=}O$), 1.86 (dddd, J = 13.6, 10.1, 7.9, 4.2 Hz, 1H, $CHOCHH$), 1.37−1.51 (m, 3H), 1.26−36 (m, 3H), 0.99 (dddd, J = 19.6, 10.8, 8.8, 4.4 Hz, 1H, CH_2CHHCH), 0.90 (s, 9H, $C(CH_3)_3$), 0.13 (s, 3H, $SiCH_3CH_3$), 0.11 (s, 3H, $SiCH_3CH_3$). MS [EI, *m*/*z* (rel intensity)]: 75.0 (56), 271.1 (100). Anal. Calcd for $C_{20}H_{28}O_2Si{\cdot}0.5H_2O$: C, 71.17; H, 8.36. Found: C, 71.49; H, 8.37.

44:[5] ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.70 (m, 2H, aromatic H), 7.64 (d, J = 3.0 Hz, 1H, $C{=}CH$), 7.36−7.39 (m, 2H, aromatic H), 7.31−7.34 (m, 1H, aromatic H), 2.71 (dd, J = 3.2, 4.9 Hz, 1H), 2.50 (br d, J = 3.8 Hz, 1H), 2.37 (d, J = 5.3 Hz, 1H), 2.28 (br d, J = 4.3 Hz, 1H), 1.72 (dddd, J = 13.6, 11.9, 4.3, 4.3 Hz, 1H), 1.62 (dddd, J = 13.6, 11.9, 4.3, 4.3 Hz, 1H), 1.38 (dddd, J = 2.3, 3.8, 9.3, 9.3 Hz, 1H), 1.33 (dddd, J = 2.3, 3.8, 9.3, 9.3 Hz, 1H), 1.13 (apparent dt, J = 10.6, 1.7 Hz, 1H), 1.00 (apparent dt, J = 10.6, 1.3 Hz, 1H).

46 (**major isomer**): ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.63 (m, 2H, aromatic H), 7.32−7.40 (m, 3H, aromatic H), 4.82 (br dd, J = 5.5, 5.5 Hz, 1H, $CHOSi$), 3.23 (m, 1H, CH_2CHCH_2), 2.85 (dd, J = 18.1, 6.4 Hz, 1H, $CHHC{=}O$), 2.37 (dddd, J = 13.7, 8.6, 6.6, 2.0 Hz, 1H, $CHOCHH$), 2.28 (m, 1H, CH_2CHHCH), 2.23 (dd, J = 18.1, 2.8 Hz, 1H, $CHHC{=}O$), 1.95 (dddd,

J = 13.6, 10.6, 7.7, 4.3 Hz, CHOCH*H*), 1.07 (dddd, J = 19.6, 12.3, 10.8, 8.8 Hz, 1H, CH_2CHHCH), 0.94 (s, 9H, $C(CH_3)_3$, 0.12 (s, 3H, $SiCH_3CH_3$), 0.10 (s, 3H, $SiCH_3CH_3$). MS [EI, m/z (rel intensity)]: 75.0 (56), 271.1 (100). Anal. Calcd for $C_{20}H_{28}O_2Si \cdot 0.5H_2O$: C, 71.17; H, 8.36. Found: C, 71.49; H, 8.37.

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