Photochemical Promotion of the Intramolecular Pauson−Khand Reaction. A New Experimental Protocol for Cobalt-Catalyzed [2 + 2 + 1] Cycloadditions

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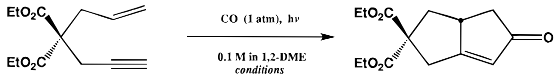
Metal-mediated cocyclization reactions are becoming increasingly popular as tools for selective organic synthesis.[2] Since its disclosure in 1973, the Pauson−Khand reaction, which represents a formal [2 + 2 + 1] cycloaddition involving an alkyne, alkene, and carbon monoxide, has become regarded as one of the most convergent methods for the synthesis of cyclopentenones.[3] A major disincentive to the large-scale use of the classical Pauson−Khand reaction rests in its requirement for stoichiometric quantities of $Co_2(CO)_8$.[4] Very recently, Jeong and collaborators reported that selected 1,6-enynes could be converted to the corresponding cyclopentenones in the presence of CO (at 4−5 atm pressure), 3−5 mol % $Co_2(CO)_8$ and 10−20 mol % $(PhO)_3P$ at 120 °C.[5] Although highly significant as one of a very limited number of successful accounts involving truly catalytic quantities of $Co_2(CO)_8$,[6] the relatively strenuous conditions of the Jeong procedure may discourage its widespread adoption in many laboratory settings. In this communication, we report that *high-intensity visible light effectively promotes catalytic Pauson−Khand reactions at 50−55 °C and 1 atm of CO pressure*. It has previously been disclosed that tertiary amine *N*-oxides and DMSO markedly accelerate stoichiometric Pauson−Khand reactions.[7] These reagents have been proposed to function via the oxidative removal of CO, thereby providing an empty coordination site for alkene complexation. For many years it has been known that various metal carbonyl complexes undergo photoinduced CO dissociation.[8] It is therefore most surprising that this simple expedient has not been reported in connection with facilitating catalytic Pauson−Khand reactions.[9]

Table 1. Comparison of Reaction Conditions for the Photopromoted Pauson−Khand Reaction



1a **1b**

	$Co_2(CO)_8$ mol %	hν Source	Time	Temperature	Yield %
1.	5.0	Q - Beam®	4h	50 - 55 °C	95
2.	0.5	Q - Beam®	12h	50 - 55 °C	30
3.	5.0	Q - Beam®	12h	0 °C *or* 17 °C	N. R.
4.	12.5	Vitalite®	12h	50 °C	64

[a] All yields given in this table correspond to isolated, chromatographically purified product.

Our first attempts at photopromotion using 10 mol % $Co_2(CO)_8$ under 1 atm of CO were not satisfying in that only low levels (<30%) of substrate conversion were realized. We ultimately discovered that the *purity of $Co_2(CO)_8$*[10] and the choice of an appropriate light source[11] were both critically important for successful catalytic reactions. In addition, reaction temperatures in the range of 50 °C were found necessary for reasonable rates of product formation. Among the several light sources examined, the Q-Beam MAX MILLION 10^6 candlepower spotlight distributed by Brinkmann, Inc.,[11,12] proved extraordinary for photoinitiation. A summary of various procedures that were utilized for the carbonylative cyclization of enyne **1a** to the corresponding cyclopentenone **1b** under 1 atm of CO appears in Table 1.[13]

Of the various solvents that were examined, only 1,2-dimethoxyethane (1,2-DME), ethyl acetate, and diglyme permitted efficient conversion of **1a** to **1b** (in 95%, 86%, and 69% *isolated* yields, respectively). Hexane, THF, and CH_3CN were

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(1) Fellow of the Alexander von Humboldt Foundation 1993−1995.

(2) Lautens, M.; Klute, W.; Tam, W. *Chem. Rev.*, in press.

(3) (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) Schore, N. E. *Chem. Rev.* **1988**, *88*, 1081. (d) Shore, N. E. *Org. React. (N.Y.)* **1991**, *41*, 1. (e) Schore, N. E. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon: Oxford, 1991; Vol. 5, p 1037. (f) Schore, N. E. In *Comprehensive Organometallic Chemistry II*; Hegedus, L. S.; Elsevier: Oxford, 1995; Vol. 12, p 703.

(4) (a) Smit, W. A.; Simonyan, S. O.; Tarasov, V. A.; Mikaelian, G. S.; Gybin, A. S.; Ibragimov, I. I.; Caple, R.; Froen, D.; Kreager, A. *Synthesis* **1989**, 472 and references therein. (b) Krafft, M. E.; Scott, I. L.; Romero, R. H.; Feibelmann, S.; Van Pelt, C. E. *J. Am. Chem. Soc.* **1993**, *115*, 7199. For examples involving the use of a substoichiometric amount of $Co_2(CO)_8$, see: (c) Billington, D. C. *Tetrahedron Lett.* **1983**, *24*, 2905. (d) Magnus, P.; Principe, L. M.; Slater, M. J. *J. Org. Chem.* **1987**, *52*, 1483. (e) Billington, D. C.; Kerr, W. J.; Pauson, P. L.; Farnocchi, C. F. *J. Organomet. Chem.* **1988**, *356*, 213. (f) MacWhorter, S. E.; Sampath, V.; Olmstead, M. M.; Schore, N. E. *J. Org. Chem.* **1988**, *53*, 203. (g) A batch-catalytic protocol with $W(CO)_5THF$ has been reported by Hoye and Suriano: Hoye, T. R.; Suriano, J. A. *J. Am. Chem. Soc.* **1993**, *115*, 1154.

(5) Jeong, N.; Hwang, S. H.; Lee, Y.; Chung, Y. K. *J. Am. Chem. Soc.* **1994**, *116*, 3159.

(6) Rautenstrauch, V.; Megard, P.; Conesa, J.; Kuster, W. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 1413. More recently, the catalytic conversion of enynes into bicyclic cyclopentenones employing the early transition metal complex $Cp_2Ti(PMe_3)_2$ had been reported: Berk, S. C.; Grossman, R. B.; Buchwald, S. L. *J. Am. Chem. Soc.* **1994**, *116*, 8593.

(7) (a) Shambayati, S.; Crowe, W. E.; Schreiber, S. L. *Tetrahedron Lett.* **1990**, *31*, 5289. (b) Jeong, N.; Chung, Y. K.; Lee, B. Y.; Lee, S. H.; Yoo, S.-e. *Synlett* **1991**, 204. (c) Chung, Y. K.; Lee, B. Y.; Jeong, N.; Hudecek, M.; Pauson, P. L. *Organometallics* **1993**, *12*, 220.

(8) For recent applications of organometallic photochemistry in synthesis, see: (a) Rigby, J. H.; Ateeq, H. S.; Charles, N. R.; Cuisiat, S. V.; Ferguson, M. D.; Henshilwood, J. A.; Krueger, A. C.; Ogbu, C. O.; Short, K. M.; Heeg, M. J. *J. Am. Chem. Soc.* **1993**, *115*, 1382. (b) Hegedus, L. S.; de Weck, G.; D'Andrea, S. *J. Am. Chem. Soc.* **1988**, *110*, 2122.

(9) Several instances of photochemically driven *stoichiometric* Pauson−Khand reactions which proceed in low yield have been reported: Brown, S. W.; Pauson, P. L. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1205.

(10) Impure samples of commercial $Co_2(CO)_8$ must be rigorously purified by recrystallization from degassed HPLC grade hexane or room temperature sublimation at 50 mTorr immediately prior to use. For the majority of the cyclizations described herein, a freshly opened sample of $Co_2(CO)_8$ (Strem Chemical Co., Inc.) which was stored in a Vacuum Atmospheres drybox was utilized.

(11) Barton, D. H. R.; Jaczberenyi, J. Cs.; Tang, D. *Tetrahedron Lett.* **1993**, *34*, 3381.

(12) Purchased at K-Mart, Inc., 1126 N. 7th Ave., Bozeman, MT.

(13) Representative procedure: A solution of enyne **1a** (119 mg, 0.5 mmol) and dicobalt octacarbonyl (8.5 mg, 0.025 mmol, 5 mol %) in degassed 1,2-DME (5 mL) was magnetically stirred at room temperature under an atmosphere of CO. After 30 min, the reaction mixture was irradiated with a Q-beam MAX MILLION spotlight. During the course of irradiation, the position of the lamp was adjusted such that the internal reaction temperature was maintained between 50 and 55 °C. After 4 h, irradiation was discontinued and the cooled reaction mixture was diluted with EtOAc (15 mL), washed with brine (2 × 2 mL), dried (Na_2SO_4), filtered, and concentrated in vacuo. The residual material was purified by chromatography on silica gel (30−50% EtOAc/hexane gradient for elution) to afford 127 mg (95%) of enone **1b** as a slightly yellow oil. For preparative scale, longer irradiation times are required. Accordingly, a solution of enyne **1a** (4.77 g, 20.0 mmol) and dicobalt octacarbonyl (274 mg, 0.8 mmol, 4 mol %) in degassed 1,2-DME (200 mL) was magnetically stirred at room temperature under an atmosphere of CO for 30 min. The resulting solution was then irradiated for 16 h at 50−55 °C. The reaction mixture was concentrated in vacuo, and the resulting oil was purified by chromatography on silica gel (10−50% EtOAc/hexane gradient for elution) to afford 4.41 g (83%) of enone **1b** as a yellow oil.

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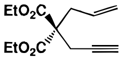
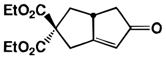
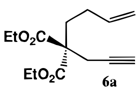
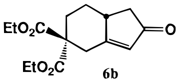
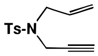
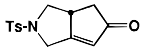
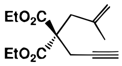
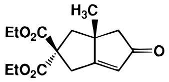
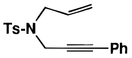
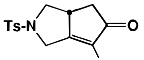
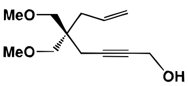
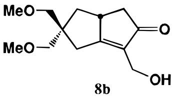
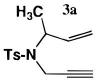
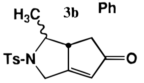
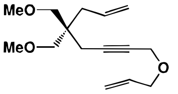
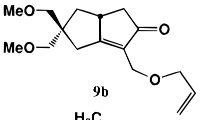
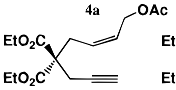
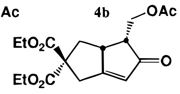
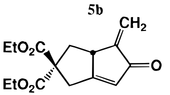
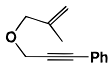
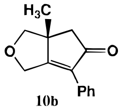
Table 2. Catalytic Pauson−Khand Photocyclizations under 1 atm of CO[a]

Substrate	Product	Yield[b] %	Substrate	Product	Yield %
 **1a**	 **1b**	95[c]	 **6a**	 **6b**	74
 **2a**	 **2b**	81	 **7a**	 **7b**	91
 **3a**	 **3b**	75	 **8a**	 **8b**	80
 **4a**	 **4b**	90[d]	 **9a**	 **9b**	67[f]
 **5a**	 **5b**	67[e]			
	 **5c**	--	 **10a**	 **10b**	N. R.

[a] Unless otherwise note, all reactions were conducted using 5 mol % $Co_2(CO)_8$ and a substrate concentration of 0.1 M in 1,2-DME under irradiation for 12 h at 50−55 °C. [b] All yields given in this table correspond to isolated, chromatographically purified products. [c] Irradiation time = 4 h. [d] Ratio of diastereomers = 1.1:1.0. [e] Reaction performed with 10 mol % $Co_2(CO)_8$. [f] Reaction performed with 12.5 mol % $Co_2(CO)_8$.

all determined to be inferior. In general, carbonylative cyclization of representative enynes (0.1 M in DME) could be effected by simply stirring in the presence of 5 mol % $Co_2(CO)_8$ under 1 atm of CO pressure at 50−55 °C with "Q-beam" irradiation for 12 h.[13] A series of catalytic enyne−CO cocyclizations involving a wide range of substrates is shown in Table 2.

Several of the results presented in Table 2 are worthy of comment. The successful conversion of **6a** to **6b** demonstrates the utility of the new photochemical procedure for the cyclization of 1,7-enynes. The efficient cyclization of **8a** shows the compatiblity of the prescribed reaction conditions with relatively labile hydroxyl moieties. The *selective* cyclization of **5a** to **5b** is most significant. Cyclization of **5a** under Jeong's reaction conditions (120 °C) gives rise to **5b** (58%) admixed with 19% of the elimination product **5c**.[5] Interestingly, carbonylative photocyclization of **9a** furnished **9b** to the complete exclusion of the isomeric 1*H*-cyclopenta[*c*]furan-5-one. The latter result is presumably a manifestation of the Thorpe−Ingold effect.[14]

In conclusion, we have developed an eminently practical photochemically driven Pauson−Khand reaction that proceeds catalytically under mild reaction conditions (50−55 °C) and 1 atm of CO pressure. The influence of achiral and chiral ligands on the course of light-induced carbonylative enyne cyclizations is currently under investigation. The results of these studies will be disclosed in future accounts from these laboratories.

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Supporting Information Available: Listings of ^1H and ^{13}C NMR, DEPT, IR, and HRMS or elemental composition data for all new compounds (11 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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(14) Jung, M. E.; Gervay, J. *J. Am. Chem. Soc.* **1991**, *113*, 224.