

Catalytic activity of dodecacarbonyltetracobalt in aqueous media: a “greening” of the Pauson–Khand reaction

Llorente V. R. Boñaga, James A. Wright and Marie E. Krafft*

Department of Chemistry and Biochemistry, The Florida State University, Tallahassee, FL 32306-4390, USA. E-mail: mek@chem.fsu.edu; Fax: +1 850-644-7409

Received (in Corvallis, OR, USA) 11th March 2004, Accepted 23rd April 2004

First published as an Advance Article on the web 24th June 2004

The unprecedented reactivity of $\text{Co}_4(\text{CO})_{12}$ with enynes under aqueous conditions, representing the development of a *mild and simple aqueous-phase cobalt-catalyzed PK reaction protocol*, is described herein.

Dodecacarbonyltetracobalt, $\text{Co}_4(\text{CO})_{12}$,¹ is not as widely used in organometallic reactions as dicobaltoctacarbonyl, $\text{Co}_2(\text{CO})_8$ ² and $\text{Co}_3(\text{CO})_9(\mu^3\text{-CH})$.³ While $\text{Co}_2(\text{CO})_8$ has been extensively applied in the Pauson–Khand reaction (PKR),^{4,5} it was not until recently that we discovered the activity of $\text{Co}_4(\text{CO})_{12}$ under mild PKR conditions.⁶ This was an important finding because the deterrence of $\text{Co}_4(\text{CO})_{12}$ formation had been the basis of all previous efforts toward an effective catalysis of the PKR using $\text{Co}_2(\text{CO})_8$.⁶ In follow-up work, we also found that, depending on the nature of the enyne, $\text{Co}_4(\text{CO})_{12}$ can effect a reductive PK reaction and reductive cyclization.⁷ These results led us further to probe the reactivity of $\text{Co}_4(\text{CO})_{12}$ in aqueous media,⁸ since success toward this end would be significant, in particular, as the “greening” of the Pauson–Khand reaction becomes increasingly relevant.⁹

Significant development in realizing catalysis in the Pauson–Khand reaction and related PK-type reactions has been seen only in the past few years.¹⁰ Early attempts involved supercritical fluids, such as CO_2 and ethylene, in $\text{Co}_2(\text{CO})_8$ -catalyzed PKR, albeit these reactions required highly pressurized conditions.¹¹ Relative to our focus, in a water–sodium dodecyl sulfate (SDS) medium, colloidal cobalt nanoparticles were found to be a recoverable and reusable mediator for PK reactions, although a loading of 67 mol% (130 °C, 20 atm CO) was necessary.¹² Rhodium catalyzed PK-type reactions have been reported using formaldehyde as the CO source under aqueous conditions,¹³ and using aromatic and aliphatic aldehydes (1.5 equiv to 20 equiv) in organic solvents.¹⁴ We disclose herein the unprecedented reactivity of $\text{Co}_4(\text{CO})_{12}$ with enynes under aqueous conditions, and the development of a *mild and simple aqueous-phase cobalt-catalyzed PK reaction protocol*.¹⁵

Stoichiometric amounts of $\text{Co}_4(\text{CO})_{12}$ were used in our initial studies under aqueous conditions (Table 1). We were delighted to

find that typical substrates that would undergo the PKR furnished bicyclooctenones in good yields, in the presence of CTAB (entries 2–5).¹⁵ However, an enyne bearing a terminal alkyne moiety provided a bicyclooctanone, instead of the expected bicyclooctenone (entry 1). In fact, substrates of this type have been observed to easily undergo reductive PKR with $\text{Co}_4(\text{CO})_{12}$ in isopropanol,⁷ or colloidal nanoparticles in aqueous media.¹²

Encouraged by these results, we proceeded to investigate the use of catalytic amounts of $\text{Co}_4(\text{CO})_{12}$ in water, and in the presence of surfactants or detergents. Cyclization of enyne **5** in water alone using only 10% of $\text{Co}_4(\text{CO})_{12}$, under a blanket of carbon monoxide, was found to be inefficient, providing only a modest yield of the cycloadduct **6** (35%) and unreacted **5**. Similar low efficiencies were observed in cyclizations conducted in the presence of 0.2 equiv of triphenylphosphane-3,3',3''-trisulfonic acid trisodium salt, tetrabutylammonium bromide, Fisher detergent, or Triton® X-100 reduced form. Fortunately, cyclization efficiency was greatly improved by using Triton® X-100 (0.5 equiv) with 20 mol% of catalyst giving rise to 80% of enone **6**. For comparison, cyclocarbonylation of **5** using 20 mol% of $\text{Co}_2(\text{CO})_8$ in the presence of 0.5 equiv of Triton® X-100 provided only 69% yield of **6**.

To explore the scope of this aqueous catalytic protocol, the cyclization efficiency of various enynes was examined under the catalytic protocol (Table 2, condition I), and compared to the stoichiometric variants (conditions II and III).¹⁵ Results indicated that PK reactions conducted using the former protocol proceeded more efficiently than the latter two. Enynes that would undergo PK reactions conducted in organic solvents^{4,5} also cyclized smoothly under condition I. An enyne with heavily-substituted unsaturated groups underwent cyclization providing an adduct with a tetra-substituted angular center (entry 4). Further, substrates bearing groups prone to hydrolysis, such as the acetal (entry 6), amide (entry 7) and ester groups (entry 8) are stable under aqueous, catalytic conditions. It is noteworthy that no cycloadduct was obtained from the reactions of enynes **17** and **19** in a water–CTAB medium under condition II. We also observed in our earlier work that cyclizations in organic solvents under anhydrous conditions, of substrates bearing alkynes substituted with electron-withdrawing groups, occur in low to modest yields.¹⁶ The thermally-promoted PKR of **17** (toluene, 70 °C, 3 days) gave a 15% yield of **18**, and the NMO-promoted variant (CH_2Cl_2 , rt) provided a modest 59% yield.¹⁶ Hydrogenolysis of the heteroatom group in the propargylic position did not occur under these conditions although it has been observed as a side reaction in PK reactions in organic solvents (entries 9, 10).¹⁷ In fact, it was recently reported that substrates bearing propargylic heteroatoms undergo substantial hydrogenolysis (~50%) under $\text{Co}_4(\text{CO})_{12}$ -mediated PKR in DME with only 20 equiv of water.¹⁸ Cyclizations of 1,7-enynes **19** and **23** proceeded smoothly under the aqueous protocol (entries 8 and 11). Reaction of **23** furnished the PKR adduct in higher yield (entry 11) than with the NMO-promoted method (66%).¹⁶ A substrate devoid of substitution on the tether, and thus lacking Thorpe–Ingold assistance in the cyclization, cleanly underwent PKR under these conditions (entry 12). It should be noted that, under our catalytic or stoichiometric conditions, the reactions of terminal alkynes led to the formation of saturated ketones. PK and PK-type reactions in water or organic solvents which use aldehydes as a CO source have only been successful with internal alkynes as well.^{12–14}

Table 1 PK reactions using stoichiometric $\text{Co}_4(\text{CO})_{12}$ in water–CTAB media^{a,15}

Entry	Substrate	Enone	Yield (%)
1			0 ^{b,c}
2	3	4	82
3	5	6	81
4	7	8	78
5			57

^a Water (0.05 M), 1 equiv $\text{Co}_4(\text{CO})_{12}$, 0.6 equiv CTAB, 70 °C, nitrogen, with a small amount of Celite, *ca.* 18 h. CTAB = cetyltrimethyl ammonium bromide. ^b Using 2 equiv of $\text{Co}_4(\text{CO})_{12}$ and 1 equiv of CTAB, 66% of the bicyclooctanone was isolated. ^c In the absence of CTAB, and in the presence of 1 equiv of $\text{Co}_4(\text{CO})_{12}$, 21% bicyclooctanone and 5% unreacted **1** were isolated.

Table 2 Cobalt-mediated PK reactions under aqueous conditions

(1)

Entry	Substrate	PKR adduct	Yield (%) Reaction conditions ^a		
			I	II	III
1	3	4	79	82	83
2	5	6	80	81	85
3	7	8	85	78	88
4	11	12	86	60	—
5	13	14	78	—	78
6	15	16	82	—	40
7	17	X = NH n = 1 18	73	0	—
8	19	X = O n = 2 20	80	0	—
9	9	Z = NTs Y = nPr 10	84	57	—
10	21	Z = O Y = Ph 22	70	36	74
11	23	24	76	73	65
12	25	26	68	—	—

^a **I:** water, 20 mol% Co₄(CO)₁₂, 0.5 equiv of Triton X-100, 70 °C, CO atm in a resealable tube. **II:** water, 1 equiv Co₄(CO)₁₂, 0.6 equiv CTAB, 70 °C, nitrogen atm. **III:** water, 1 equiv Co₂(CO)₈, 0.6 equiv CTAB, 70 °C, nitrogen atm. Reactions were complete in ca. 6 h.

Lastly, the issue of a CO-free catalytic PKR procedure was briefly addressed.^{12–14} We observed a slight decrease in the yield of cycloadducts from reactions conducted under an argon atmosphere. For example, PK cyclization of enynes **5** and **7** using 20 mol% of Co₄(CO)₁₂ furnished 70% and 59% yields of cyclopentenones **6** and **8**, respectively (cf. Table 2, entries 2 and 3, condition I). Nevertheless, these results show the potential of the aqueous protocol in the absence of CO, and warrant further studies.

In summary, we have illustrated the reactivity of Co₄(CO)₁₂ towards enynes in a water–CTAB medium, and more importantly, its catalytic activity in the PKR in a water–Triton® X-100 medium. These conditions have led to the first examples of a mild and simple cobalt-catalyzed aqueous protocol for the thermal PK reaction of enynes bearing internal alkynes. The water–Triton® X-100 medium using Co₄(CO)₁₂ has rendered the catalytic, aqueous thermal PKR one which proceeds with high efficiency, exceeding that of the aqueous reactions using stoichiometric amounts of Co₄(CO)₁₂ and Co₂(CO)₈. Enyne substrates that possess groups prone to undergo hydrolysis were shown to be stable under these conditions.¹⁹

This work was generously supported by the National Science Foundation and the MDS Research Foundation.

Notes and references

1 General review on tetranuclear clusters contains many references to Co₄(CO)₁₂: (a) P. Chini and B. T. Heaton, *Top. Curr. Chem.*, 1977, **71**, 3; (b) see also: R. D. W. Kemmitt and D. R. Russell, in *Comprehensive Organometallic Chemistry*, Vol 5, eds. E. W. Abel, F. A. Stone and G. Wilkinson, Pergamon, Oxford, 1982, p. 7. Co₄(CO)₁₂ is less prone to air oxidation than Co₂(CO)₈.

- 2 (a) For the Nicholas reaction: B. J. Teobald, *Tetrahedron*, 2002, **58**, 4133; (b) for conversion of aziridine to β-lactams: M. E. Piotti and H. Alper, *J. Am. Chem. Soc.*, 1996, **118**, 111; (c) for conversion of 1-(1-alkynyl)cyclopropanols to 2-cyclopentenones: N. Iwasawa, T. Matsuo, M. Iwamoto and T. Ikeno, *J. Am. Chem. Soc.*, 1998, **120**, 3903; (d) for 1,4-reduction of unsaturated carbonyl compounds: H.-Y. Lee and M. An, *Tetrahedron Lett.*, 2003, **44**, 2775; (e) for a tandem cycloaddition reaction: A. Oledra, C.-J. Wu, R. J. Madhushaw, S.-L. Wang and R.-S. Liu, *J. Am. Chem. Soc.*, 2003, **125**, 9610.
- 3 For examples, see: (a) T. Sugihara and M. Yamaguchi, *J. Am. Chem. Soc.*, 1998, **120**, 10782; (b) T. Sugihara, M. Yamaguchi and M. Nishizawa, *Chem. Eur. J.*, 2001, **7**, 1589; (c) T. Sugihara, A. Wakabayashi, Y. Nagai, H. Takao, H. Imagawa and M. Nishizawa, *Chem. Commun.*, 2002, 576; (d) T. Sugihara, A. Wakabayashi, H. Takao, H. Imagawa and M. Nishizawa, *Chem. Commun.*, 2001, 2456.
- 4 K. M. Brummond and J. L. Kent, *Tetrahedron*, 2000, **56**, 3263.
- 5 S. E. Gibson and A. Stevenazzi, *Angew. Chem., Int. Ed.*, 2003, **42**, 1800.
- 6 (a) M. E. Krafft and L. V. R. Boñaga, *Angew. Chem., Int. Ed.*, 2000, **39**, 3676 and references cited therein. Co₄(CO)₁₂ was initially used to catalyze the PKR under harsh conditions (150 °C, 10 atm CO), and believed to be detrimental to Co₂(CO)₈ catalysis in the PKR (b) J. W. Kim and Y. K. Chung, *Synthesis*, 1998, 142.
- 7 M. E. Krafft, L. V. R. Boñaga, J. A. Wright and C. Hirose, *J. Org. Chem.*, 2002, **67**, 1233.
- 8 Water, used as an additive, enhanced the rate of PK reactions in toluene. T. Sugihara and M. Yamaguchi, *Synlett*, 1998, 1384.
- 9 (a) U. M. Lindström, *Chem. Rev.*, 2002, **102**, 2751; (b) *Aqueous-Phase Organometallic Catalysis*, eds. B. Cornils and W. A. Herrmann, Wiley-VCH, Weinheim, 1998.
- 10 An early attempt involved cyclizations of (enyne)Co₂(CO)₆ complexes in a mixture of 1,4-dioxane and 2 M aqueous NH₄OH (1 : 3, v/v) at 100 °C. T. Sugihara, M. Yamada, H. Ban, M. Yamaguchi and C. Kaneko, *Angew. Chem., Int. Ed. Engl.*, 1997, **36**, 2801.
- 11 2.5 mol% Co₂(CO)₈, P_{CO₂} = 112 atm (37 °C), P_{CO} = 30 atm, 90 °C, 24 h; (a) N. Jeong, S. H. Hwang, Y. W. Lee and J. S. Lim, *J. Am. Chem. Soc.*, 1997, **119**, 10549. Co₄(CO)₁₁P(OPh)₃, 5 atm CO, 110 atm ethylene, 34 to 85 °C, 24 h (b) N. Jeong and S. H. Hwang, *Angew. Chem., Int. Ed.*, 2000, **39**, 636.
- 12 S. U. Son, S. I. Lee, Y. K. Chung, S. W. Kim and T. Hyeon, *Org. Lett.*, 2002, **4**, 277; W. H. Suh, M. Choi, S. I. Lee and Y. K. Chung, *Synthesis*, 2003, 2169.
- 13 F. Koji, T. Morimoto, K. Tsutsumi and K. Kakiuchi, *Angew. Chem., Int. Ed.*, 2003, **42**, 2409.
- 14 (a) T. Morimoto, K. Fuji, K. Tsutsumi and K. Kakiuchi, *J. Am. Chem. Soc.*, 2002, **124**, 3806; (b) T. Shibata, N. Toshida and K. Kagai, *J. Org. Chem.*, 2002, **67**, 7446; (c) T. Shibata, N. Toshida and K. Takagi, *Org. Lett.*, 2002, **4**, 1619; (d) K. H. Park, S. U. Son and Y. K. Chung, *Chem. Commun.*, 2003, 1898.
- 15 M. E. Krafft, J. A. Wright and L. V. R. Boñaga, *Tetrahedron Lett.*, 2003, **44**, 3417.
- 16 M. E. Krafft, R. H. Romero and I. L. Scott, *J. Org. Chem.*, 1992, **57**, 5277.
- 17 J. Cassayre and A. Z. Zard, *J. Organomet. Chem.*, 2001, **64**, 316(a) J. Cassayre and A. Z. Zard, *J. Am. Chem. Soc.*, 1999, **121**, 6072; (b) L. Pérez-Serrano, J. Blanco-Urgoiti, L. Casarrubios, G. Dominguez and J. Pérez-Castells, *J. Org. Chem.*, 2000, **65**, 3513; (c) T. Sugihara, M. Yamada, M. Yamaguchi and M. Nishizawa, *Synlett*, 1999, 771.
- 18 H.-Y. Lee, M. An and J.-H. Sohn, *Bull. Korean Chem. Soc.*, 2003, **24**, 539.
- 19 General procedure: To a resealable tube containing enyne **5** (80 mg, 0.29 mmol), Co₄(CO)₁₂ (32 mg, 0.057 mmol, 20 mol%) and Triton® X-100 (91 mg, 0.14 mmol, 0.5 equiv) was added water (1.5 mL). Carbon monoxide was then bubbled through the mixture (1–2 min), and the reaction mixture was heated at 70 °C for 18 hours. Upon completion of the reaction (ca. 6 h), the mixture was filtered through a filter paper on a Büchner funnel, extracted with ethyl acetate, dried over MgSO₄, and filtered through a short pad of Celite. Subsequent concentration followed by purification by flash column chromatography provided 70 mg of enone **7** (80% yield). Co₄(CO)₁₂ was purchased from Strem Chemical Co., and used without further purification. Compounds **1**, **2**, **9**, **10**, **25**, **26**: (a) M. E. Krafft, L. V. R. Boñaga and C. Hirose, *J. Org. Chem.*, 2001, **66**, 3004. Compounds **5**, **6**: T. Kondo, N. Suzuki, T. Okada and T. Mitsudo, *J. Am. Chem. Soc.*, 1997, **119**, 6187. Compound **15**: N. Vicart and R. Whitby, *Chem. Commun.*, 1999, 1241; Compounds **3**, **4**, **7**, **8**, **21**, **22**: ref. 7. Compounds **11–14**, **16**, **23**, **24**: ref. 15. Compounds **17–20**: ref. 16.