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The First Intramolecular Pauson–Khand Reaction in Water Using Aqueous Colloidal Cobalt Nanoparticles as Catalysts

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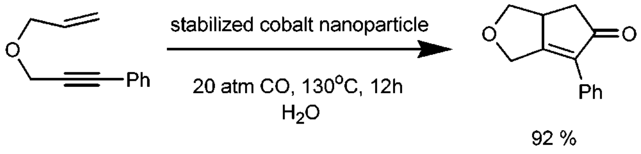
ABSTRACT



The first intramolecular Pauson–Khand reaction in water was successfully carried out by using aqueous colloidal cobalt nanoparticles as catalysts.

Extensive research on new and effective catalytic Pauson−Khand reactions has continued to find ever more efficient methods for the preparation of cyclopentenone compounds.[1] Several excellent homogeneous catalysts have been developed for the reactions. Nevertheless, one serious problem in homogeneous catalysis is separation of the reaction products from the catalyst. To solve this problem, we recently developed[2] novel heterogeneous Pauson−Khand catalysts based on metallic cobalt supported on either mesoporous silicas or charcoal.

Although heterogenized catalysts can solve the separation problem, they still require an organic solvent as a reaction medium. Recently, the possibility of the substitution of conventional organic solvents by the supercritical fluids CO_2 or ethylene was demonstrated by Jeong and co-workers.[3] However, reaction conditions have not yet seen much improvement and are still quite harsh, requiring a long reaction time. Recently, as a consequence of the increasing demand for efficient, safe, and environmentally friendly processes, the application of homogeneous catalysts in aqueous solution and on liquid supports has attracted tremendous attention for many catalytic reactions.[4] These aqueous catalytic systems can offer a great opportunity for practicing green chemistry. However, no catalytic systems that enable the use of water as a solvent in the Pauson−Khand reaction have been developed yet. Furthermore, it has

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been expected[5] that low-valent cobalt organometallics would be unstable and become oxidized in the presence of water. In these circumstances, the development of aqueous colloidal cobalt nanoparticles[6] has attracted our attention. We envision that the use of aqueous colloidal cobalt nanoparticles should provide an opportunity to study the Pauson−Khand reaction in an aqueous solution. Herein we report the first catalytic intramolecular Pauson−Khand reaction by aqueous colloidal cobalt nanoparticles in an aqueous solution. This catalytic system exhibited excellent catalytic performance for intramolecular Pauson−Khand reactions and can be recycled.

Aqueous colloidal cobalt nanoparticles were prepared by reducing an aqueous solution of cobalt acetate containing sodium dodecyl sulfate (SDS) surfactant.[6b,7] The aqueous colloidal cobalt nanoparticles are stable for a limited time (2−3 days) in air, quite stable in the absence oxygen, and easy to handle. The intramolecular Pauson−Khand reaction of an enyne has been investigated as a test reaction[8] (Scheme 1).

Scheme 1

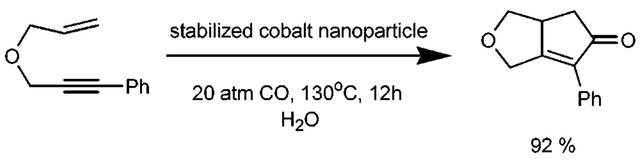


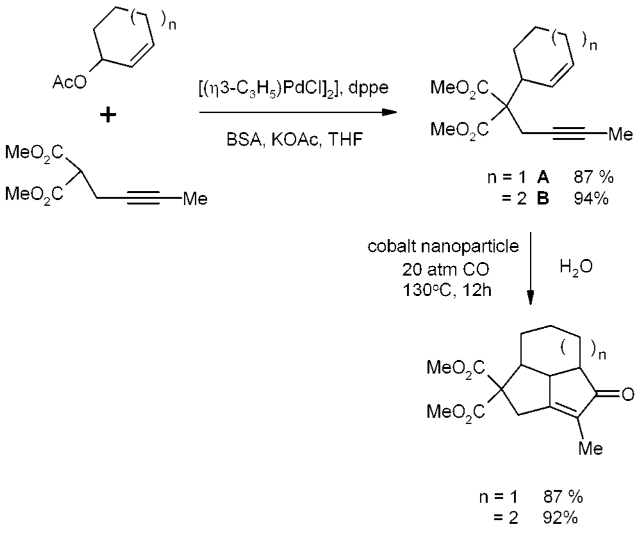
Table 1 summarizes the results of reactions using cobalt nanoparticles, cobalt on charcoal, or $Co_2(CO)_8$.[2] To optimize the reaction conditions, the pressure of CO and the reaction temperature were screened. As Table 1 shows, the optimum reaction conditions were 20 atm of CO at 130 °C. Under the optimum condition, the yield of the reaction was 92%. In contrast, the yields for $Co_2(CO)_8$ and cobalt on charcoal were 8% and 24%, respectively. We envision that the stabilizing SDS surfactant micelles act as nanoreactors to induce better solubilization of organic reactants and ultimately allow the reactants to interact more intimately with the cobalt nanoparticles. The nonpolar alkyl chains remain in a nonpolar environment and the hydrocarbon chains can dissolve the organic substrates. Thus, there was no requirement to employ water-soluble substrates. The solubilized CO molecules might react with the outer surface of cobalt nanoparticles to generate in situ cobalt carbonyl species, which can act as catalysts for the carbonylative cycloaddition. The situation seems to be quite close to that of the Lewis acid surfactant combined catalysts (LASC) in water.[9]

Table 1. Pauson−Khand Reaction with Stabilized Cobalt Nanoparticle in Water[a]

entry	catalyst	*T* (°C)	*P* (atm)	yield (%)[b]
1	cobalt stabilized	130	10	45
2	cobalt stabilized	130	20	92
3	cobalt stabilized	110	20	10
4	recovered from 2	130	20	95
5	recovered from 4	130	20	91
6	recovered from 5	130	20	96
7	recovered from 6	130	20	95
8[c]	$Co_2(CO)_8$	130	20	8
9[d]	Co/C	130	20	24

[a] Reaction conditions: substrate(0.58 mmol), cobalt nanoparticle (23 mg), 130 °C, 20 atm CO, and 12 h. [b] Isolated yield. [c] Using 50 mol % $Co_2(CO)_8$. [d] Using 0.2 g Co/C (13 wt % Co).

Scheme 2



Heterogeneous catalysts often suffer extensive leaching of active metal species during reactions and eventually lose their catalytic activity. Most organic substances are insoluble in water, and many reactive substrates and catalysts are decomposed or deactivated by water. Thus, recovery and reusability of the catalytic system were tested by carrying out consecutive cycles (entries 4−7 in Table 1), with the same catalyst in aqueous solution, carefully separated from

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(7) Cobalt acetate tetrahydrate (1.0 g, 4.0 mmol) and sodium dodecyl sulfate (SDS) (10.0 g) were dissolved in degassed water at room temperature. An aqueous solution of $NaBH_4$ (0.4 g, 10 mmol) in 10 mL of water was added dropwise to the mixture. The color of the solution changed immediately from pink to black, indicating the formation of colloidal particles. The resulting solution was used directly in the PK reaction.

(8) Cobalt nanoparticles (23 mg, the amount of calculated Co) in 5 mL of water and the enyne shown in Scheme 1 (0.10 g, 0.58 mmol) were put in a high-pressure reactor. The reactor was pressurized with 20 atm of CO at room temperature and was heated at 130 °C for 12 h. After the reactor was cooled to room temperature and the excess CO was released, the reaction mixture was transferred into a separatory funnel. The product was extracted with diethyl ether (15 mL × 5). The ethereal solution was dried over anhydrous $MgSO_4$, concentrated, and chromatographed on a silica gel column, eluting with hexane and diethyl ether (v/v, 2:1). Removal of the solvent gave the product in 92% yield (0.11 g). When the catalyst was recycled, excess diethyl ether was added to the reaction mixture after the reaction. The resulting solution was stirred, and the upper layer was pipetted. Removal of the solvent gave the product. The remained aqueous solution was reused for the further catalytic reaction.

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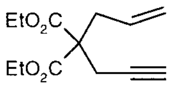
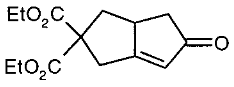
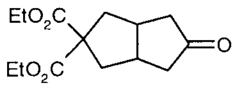
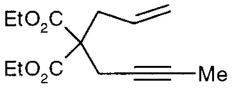
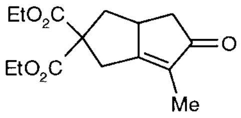
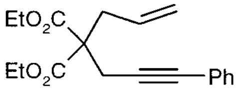
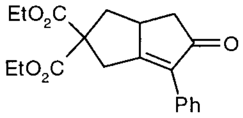
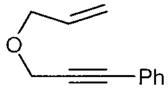
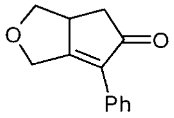
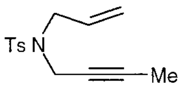
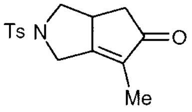
Table 2. Pauson−Khand Reaction with Various Substrates in Water[a]

entry	substrate	product	pressure(atm)	yield(%)[b]
1		 	5 20	5 95(3/1)
2			20	96
3			20	90
4			20	92
5			20	88

[a] Reaction conditions: substrate (0.58 mmol), cobalt nanoparticle (23 mg, the amount of caculated Co), 130 °C, 20 atm CO, and 12 h. [b] Isolated yield.

the organic phase at the end of each run. The conversion yields were quite high even at the fourth run. The relative invariance of the conversion yields means that the catalyst system is quite stable during the recycling. The catalytic system can be recycled at least four times without loss of performance and without producing any waste.

Various substrates have been successfully used in the aqueous colloidal cobalt nanoparticles catalyzed Pauson−Khand reaction. Table 2 summarizes representative examples of the reactions. When a terminal enyne (entry 1 in Table 2) was used as a substrate, the corresponding enone and the reduced ketone were obtained in the ratio 3:1 with a 95% overall yield. This catalytic reaction was quite effective with substituted enynes. The heteroatom tethered substrates (entries 4 and 5 in Table 2) were tested to generate the corresponding products in high yields.

Reaction of *endo*-cyclic enynes[10] produced the corresponding tricyclic enone compounds in high yields (Scheme 2). Aqueous colloidal cobalt nanoparticles are quite effective for intramolecular Pauson−Khand reaction.

In conclusion, we have demonstrated that aqueous colloidal cobalt nanoparticles are quite effective catalysts for many intramolecular Pauson−Khand reactions in water. The cobalt nanoparticles can be reused several times without any apparent loss of activity. Aqueous colloidal cobalt nanoparticles are easily available and can be applied to various types of catalytic reactions in water. Thus, their use as catalysts in aqueous media will contribute to progress in chemical processes.

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[10] **Procedure of Synthesis of Substrate and Characterization Data of New Compounds.** Substrate **A** in Scheme 2 [$(\eta^3\text{-}C_3H_5PdCl)_2$] (3 mg, 8.2×10^{-3} mmol), dppe (7 mg, 0.017 mmol), and 5 mL of THF was put in a 50 mL Schlenk flask. After the solution was stirred for 10 min, 3-acetoxycyclohexene (0.23 g, 1.6 mmol), dimethyl 2-butynylmalonate (0.36 g, 1.9 mmol), *N*,*O*-bis(trimethylsilyl)acetamide (0.2 mL), and KOAc (a trace amount) were added to the solution. After the resulting solution was stirred for 18 h, low-boiling chemicals were removed by rotary evaporator. The high-boiling residue was chromatographed on a silica gel column, eluting with hexane and diethyl ether (v/v, 10:1). Removal of the solvent gave the product in 87% yield (0.38 g). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.73 (s, 2 H), 3.74 (s, 3 H), 3.70 (s, 3 H), 3.10 (m, 1 H), 2.78 (s, 2 H), 1.95 (m, 2 H), 1.82 (m, 2 H), 1.74 (s, 3 H), 1.55 (m 1 H), 1.33 (q, 11.0 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ 1705, 170.2, 128.6, 127.6, 78.6, 73.7, 60.5, 52.3, 52.0, 38.6, 24.7, 24.1, 22.8, 22.2, 3.38 ppm, HRMS (M^+) calcd 264.1356, obsd 264.1364. Substrate **B** in Scheme 2. The same procedure as the synthesis above was applied; yield 94%. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.80 (m, 1 H), 5.70 (dd, 4.7, 11.0 Hz, 1 H), 3.73 (s, 6 H), 3.16 (dd, 3.8, 10.0 Hz, 1 H), 2.77 (q, 2.6 Hz, 2 H), 2.15 (m, 2 H), 1.86 (m, 1 H), 1.83 (dt, 4.1, 13.0 Hz, 1 H), 1.74 (t, 2.6 Hz, 3 H), 1.68 (m, 2 H), 1.24 (m, 1 H), 1.20 (m, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ 170.2, 132.6, 131.4, 78.2, 73.6, 60.5, 52.0, 42.6, 31.4, 29.3, 27.6, 25.7, 23.5, 3.13 ppm. HRMS (M^+) calcd 278.1518, obsd 278.1517