Dual Catalysis

Aqueous Catalytic Pauson–Khand-Type Reactions of Enynes with Formaldehyde: Transfer Carbonylation Involving an Aqueous Decarbonylation and a Micellar Carbonylation**

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Homogeneous catalysis by transition metal complexes has provided numerous excellent tools for synthetic organic chemists.[1] In most methods, the use of a single catalyst results in a unique type of transformation. Reports have recently also appeared on the use of a combination of different catalytic processes in one phase to catalyze one overall transformation.[2] In terms of synthetic organic chemistry, these methods permit convenient, one-pot catalytic transformations. We have already reported some catalytic transfer carbonylation reactions that involve two cooperative catalytic processes, the decarbonylation of aldehydes accompanied by the carbonylation of other organic substrates.[3] These carbonylation reactions do not involve the direct use of carbon monoxide.[4] Our goal was to develop a novel dual-catalysis system, in which each process proceeds simultaneously in a different reaction field. Such a system, to our knowledge, has not been successfully developed to date.

To investigate this strategy, we chose a microscopically biphasic system in an aqueous medium: a micellar phase surrounded by an aqueous phase. The solubility properties of formaldehyde with respect to organic substrates stimulated us to explore a system that consisted of the decarbonylation of formaldehyde in the aqueous phase and carbonylation of an organic substrate in the micelle. We herein describe this approach for an aqueous catalytic Pauson–Khand-type reaction of enynes in the presence of formaldehyde as the source of carbon monoxide (Scheme 1).[5,6]

We first examined the reaction of enyne **1** with formaldehyde in water. The reaction of **1** with formaldehyde in the presence of SDS, a popular surfactant that is well-known for forming micelles, and a catalytic amount of $[RhCl(cod)]_2$/dppp in water at 100 °C afforded the desired carbonylated product **2** in 57 % yield (Table 1, entry 1). Under conditions

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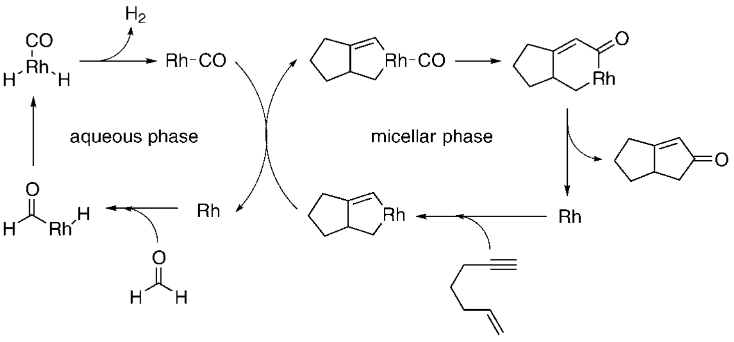
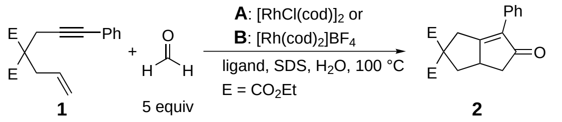


Scheme 1. Working hypothesis for aqueous transfer carbonylation.

reported previously,[3a] **2** was obtained in 53 % yield along with unconverted **1** (14 %) from a reaction for 24 h at 130 °C with 10 equivalents of paraformaldehyde in xylene. The use of water as the solvent clearly resulted in an increase in reactivity, which is consistent with micelle formation in the reaction system. As is frequently observed for organic reactions in aqueous micellar systems, the encapsulation of reactants by a surfactant would lead to a higher effective concentration of reactants, thus resulting in acceleration of the reaction.[7] The use of excess formaldehyde (20 equiv) improved the yield of **2** to 82 % (Table 1, entry 2), probably because of an increased amount of formaldehyde incorporated in the micelle.

When TPPTS, a water-soluble phosphane,[8] was used as a ligand instead of dppp, **1** was recovered in 82 % yield with no detectable formation of **2** (Table 1, entry 3). The use of both dppp and TPPTS as ligands resulted in a dramatic increase in the yield of **2** (87 %; Table 1, entry 4). Although reactions in which the more hydrophilic rhodium complex $[Rh(cod)_2]BF_4$ was used as the catalyst showed a similar trend as was found for $[RhCl(cod)]_2$, the yields of **2** were lower (Table 1, entries 5–7). The amount of SDS present also had an effect on the yield of **2** (Table 1, entries 8–12), which was obtained in nearly quantitative yield when 2 equivalents of SDS were used (Table 1, entry 12). Paraformaldehyde, a synthetic equivalent of formaldehyde, could also be utilized as a source of carbon monoxide in this aqueous system (Table 1, entry 13).

Table 1: Catalytic Pauson–Khand-type reaction of enyne **1** in the presence of formaldehyde in an aqueous medium.[a]



1 **2**

Entry	Cat.	Ligand (mol %)	SDS [equiv]	*t* [h]	Yield[b] [%]
1	**A**	dppp (10)	5.0	7	57
2[c]	**A**	dppp (10)	5.0	10	82 (17)
3	**A**	TPPTS (30)	5.0	6	0 (82)
4	**A**	dppp/TPPTS (10:10)	5.0	5	87
5	**B**	dppp (20)	5.0	10	44 (43)
6	**B**	TPPTS (30)	5.0	6	0 (65)
7	**B**	dppp/TPPTS (10:10)	5.0	7	65
8	**A**	dppp/TPPTS (10:10)	none	10	37 (47)
9	**A**	dppp/TPPTS (10:10)	0.1	10	59 (9)
10	**A**	dppp/TPPTS (10:10)	0.5	10	75 (4)
11	**A**	dppp/TPPTS (10:10)	1.0	10	88
12	**A**	dppp/TPPTS (10:10)	2.0	5	96
13[d]	**A**	dppp/TPPTS (10:10)	2.0	6	97

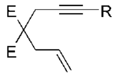
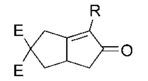
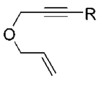
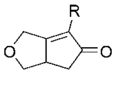
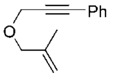
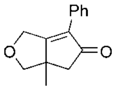
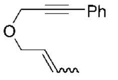
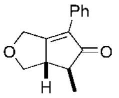
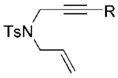
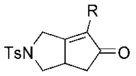
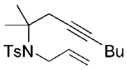
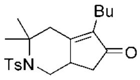
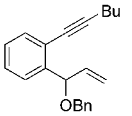
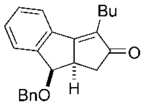
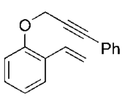
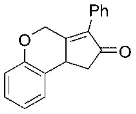
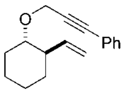
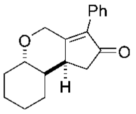
[a] Conditions: **1** (0.25 mmol), formaldehyde (37%; 0.1 mL, 1.25 mmol), H_2O (1.9 mL), catalyst **A** (5 mol %) or **B** (10 mol %), 100 °C, N_2. [b] Yields of **2**. Values in parentheses are the yields of recovered **1**; in other cases, **1** was completely consumed. [c] Formaldehyde: 20 equiv. [d] Paraformaldehyde (5 equiv) was used instead of formaldehyde. cod = cyclooctadiene; dppp = 1,3-bis(diphenylphosphanyl)propane; SDS = sodium dodecylsulfate; TPPTS = triphenylphosphane-3,3′,3″-trisulfonic acid trisodium salt.

The high efficiency of this carbonylation system can not be rationalized simply by the high effective concentrations involved as a result of micelle formation. A plausible explanation for the dependence of the catalysis on the addition of TPPTS is that the decarbonylation occurs mainly in the aqueous phase when additional TPPTS is present,[9] and the actual carbonylation step takes place in the micelle. Evidently most of the formaldehyde exists in the aqueous phase because of its high solubility in water, whereas the enyne is incorporated into the micelle because of its hydrophobicity. The presence of both TPPTS and dppp would lead to the formation of two different types of rhodium(I) complexes: a water-soluble complex associated with TPPTS (hydrophilic), and a complex that is not associated with TPPTS (hydrophobic).[10] These factors would permit the dual catalytic cycles to each function more efficiently in the appropriate phase and thus lead to more efficient overall catalysis. Moreover, no reactants, including highly reactive species generated in each process, should be able to interfere with one another, thus permitting the catalysis to function more smoothly and with a higher degree of selectivity.

The present system is applicable to the carbonylation of a variety of enynes in excellent yields. Selected results are shown in Table 2. The use of analogues of **1**, in which a butyl or a methyl group replaces the phenyl group, also resulted in the formation of the carbonylated products in excellent yields (Table 2, entries 2 and 3). Reactions of substrates that contain a heteroatom such as oxygen or nitrogen in the tether between the alkene and the alkyne also afforded the corresponding bicyclic cyclopentenones (Table 2, entries 4–10, 12, and 13). Enynes with 1,1- and 1,2-disubstituted alkene portions were carbonylated smoothly (Table 2, entries 6 and 7), as were 1,7-enynes, which were converted into cyclopentenones fused to a six-membered ring (Table 2, entries 10, 12, and 13). When ring systems substituted at adjacent carbon centers with an alkene and an alkyne were used as substrates, the cyclocarbonylation proceeded efficiently and resulted in the formation of tricyclic cyclopentenones (Table 2, entries 11–13).

In summary, we have reported the development of an aqueous catalytic Pauson–Khand-type reaction of enynes in the presence of formaldehyde as a water-soluble source of carbon monoxide. The decarbonylation and the carbonylation processes are thought to take place independently in different phases of the reaction system, namely in the aqueous and micellar phases, respectively, which results in a more efficient catalytic carbonylation reaction. The use of the low-cost

Table 2: Aqueous catalytic Pauson–Khand-type reactions of enynes with formaldehyde.[a]

Entry	Enyne	HCHO[b] [equiv]	*t* [h]	Product[c]	
1		5	5		96% (R = Ph)
2		5	8		84% (R = Bu)
3		10	5		89% (R = Me)
4[d]		100	2		87% (R = Ph)
5		20	5		81% (R = Bu)
6		10	4		94%
7[e]		10	5		94% (1.8:1)[f]
8		10	2		96% (R = Ph)
9		5	6		89% (R = Bu)
10		5	12		67%
11		20	6		91% (2.4:1)[f]
12		5	2		82%
13		5	4		93%[g]

[a] Conditions: enyne (0.25 mmol), $[RhCl(cod)]_2$ (0.0125 mmol), dppp (0.025 mmol), TPPTS (0.025 mmol), SDS (0.50 mmol), H_2O (1.9 mL), 100 °C, N_2. [b] Formaldehyde (37%) was used. [c] Yield of isolated product. [d] The reaction was carried out with formaldehyde (37%; 2.0 mL) as solvent and SDS (5.0 equiv) at 80 °C. [e] The enyne was used as an *E*/*Z* mixture (85:15). [f] Diastereomeric ratio was determined by GC. [g] Obtained as a single stereoisomer.

feedstock formaldehyde as the source of carbon monoxide gives rise to a more convenient Pauson–Khand-type reaction of enynes than the conventional reactions currently in use. This strategy has the potential to become a general protocol that could be used in a wide variety of carbonylation reactions. Further efforts are underway toward the elucidation of the mechanism of the dual catalysis, to improve our understanding of where the two processes occur and of the morphology of aggregation of the reagents. Applications to other carbonylation reactions are also under investigation.

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[9] Even in the reaction in the presence of additional TPPTS, the decarbonylation probably does not proceed exclusively in the aqueous phase, because a hydrophobic combination of $[RhCl(cod)]_2$ and dppp catalyzed the carbonylation reaction in the absence of TPPTS (Table 1, entries 1 and 2).

[10] It has been reported that the use of both TPPTS and PPh_3 distributes the rhodium catalyst between the aqueous and the organic phases in the biphasic (toluene/water) hydroformylation of 1-octene: a) P. Kalck, M. Dessoudeix, S. Schwarz, *J. Mol. Catal. A* **1999**, *143*, 41; b) P. Kalck, M. Dessoudeix, *Coord. Chem. Rev.* **1999**, *190–192*, 1185.