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

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Homogeneous catalysis using the transition metals 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.   Recently, some reports have appeared on the use of a proper combination of several different catalytic processes in one reaction field to achieve one catalysis.[2]   In terms of synthetic organic chemistry, these methods permit the convenient, one-pot catalytic transformations.   We also have already reported on some catalytic transfercarbonylation reactions that involved two cooperative catalytic processes, the decarbonylation of aldehydes and the carbonylation of other organic substrates.[3]   These represent carbonylation reactions that 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 different reaction fields.   Such a system, to our knowledge, has not been successfully developed to date.

For this strategy, we chose a microscopically biphasic system in aqueous media: a micellar phase surrounded by an aqueous phase.   The solubility properties of formaldehyde vis-à-vis organic substrates stimulated us to explore a system, consisting 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 using formaldehyde as the source of carbon monoxide (Scheme 1).[5,6]
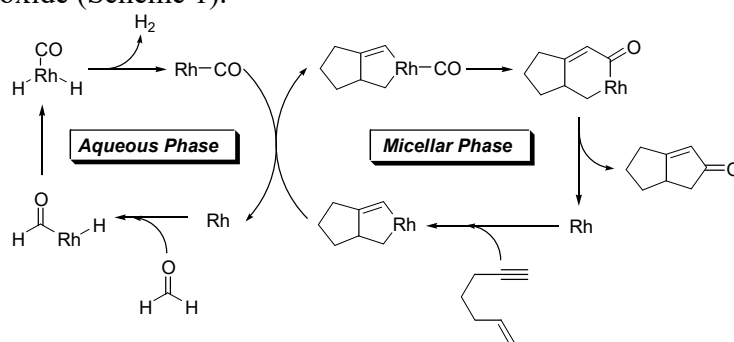

Scheme 1. Working Hypothesis for Aqueous Transfercarbonylation

We first examined the reaction of enyne **1** with formaldehyde in water.   Using SDS, a popular surfactant which is well-known to form micelles, the reaction of **1** and formaldehyde in the presence of

a catalytic amount of [RhCl(cod)]$_2$/dppp in water at 100 °C afforded the desired carbonylated product **2** in 57% isolated yield (Table 1, entry 1). Taking into account the fact that 53% of **2** was obtained along with 14% of unreacted **1** for a reaction using 10 equiv of paraformaldehyde for 24 h at 130 °C under the conditions reported previously, the use of water as a reaction media clearly resulted in an increase in reactivity. This is consistent with micelle formation in the reaction system. Thus, as is frequently observed for organic reactions in aqueous micellar systems, the encapsulation of reactants by a surfactant would lead to a higher concentration of reactants, resulting in an acceleration in the reaction.[7] Use of an excess of formaldehyde (20 equiv) improved the yield of **2** to 82% (entry 2), probably because of the increased amount of formaldehyde incorporated into the micelle.

Table 1: Catalytic Pauson-Khand-Type reaction of enyne **1** using formaldehyde in aqueous media.[a]
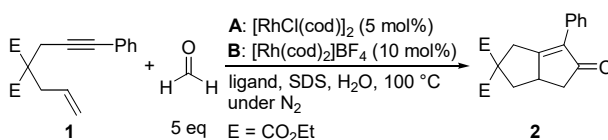
entry	catalyst	ligand	SDS	time	yield of **2**[b]
1	**A**	dppp (10 mol%)	5.0eq	7h	57%
2[c]		dppp (10 mol%)		10h	82% (17%)
3		TPPTS (30 mol%)		6h	0% (82%)
4		dppp (10 mol%) / TPPTS (10 mol%)		5h	87%
5	**B**	dppp (20 mol%)		10h	44% (43%)
6		TPPTS (30 mol%)		6h	0% (65%)
7		dppp (10 mol%) / TPPTS (10 mol%)		7h	65%
8	**A**	dppp (10 mol%) / TPPTS (10 mol%)	none	10h	37% (47%)
9			0.1eq	10h	59% (9%)
10			0.5eq	10h	75% (4%)
11			1.0eq	10h	88%
12			2.0eq	5h	96%
13 [d]			2.0eq	6h	97%

[a] Conditions: **1** (0.25 mmol), 37% formalin (0.1 mL, 1.25 mmol), and H$_2$O (1.9 mL) at 100 °C under N$_2$. [b] Values in parentheses are the yields of **1** recovered. Otherwise, **1** was completely consumed. [c] 20 equiv of formaldehyde was used. [d] Paraformaldehyde (5 equiv) are used instead of formalin. Abbreviations: dppp = 1,3-bis(diphenylphosphino)propane; TPPTS = triphenylphosphine-3,3',3"-trisulfonic acid trisodium salt; SDS = sodium dodecylsulfate.

When TPPTS, a water-soluble phosphine,[8] was used as a ligand instead of dppp, **1** was recovered in 82% with no detectable formation of **2** (Table 1, entry 3). The use of both dppp and

TPPTS as a ligand resulted in a dramatic increase in the yield of **1** (87%) (entry 4). Although reactions using a more hydrophilic rhodium complex, [Rh(cod)$_2$]BF$_4$, as a catalyst, also showed the same tendency as was found for [RhCl(cod)]$_2$, the yields of **1** were lower (entries 5-7). The amount of SDS present also had an effect on the yield of **1** (entries 8-12), and **1** was obtained in nearly quantitative yield when 2.0 equiv of SDS was used (entry 12). Paraformaldehyde, a synthetic equivalent of formaldehyde, also could be utilized as a source of carbon monoxide in this aqueous system (entry 13).

The high efficiency of this carbonylation system, especially the effect of the added TPPTS, cannot be rationalized only by high concentrations due to the formation of micelles. A plausible explanation for the dependence of the catalysis on the addition of TPPTS is as follows: for the reaction using the additional TPPTS, the decarbonylation proceeds mainly in the aqueous phase,[9] and the actual carbonylation takes place in the micelle. Clearly, most of formaldehyde exists in the aqueous phase because of its high water-solubility, while the enyne is incorporated into the micelle because of its hydrophobicity. In addition, the presence of TPPTS along with dppp would lead to the formation of two different types of complexes; a water-soluble complex associated with TPPTS (hydrophilic), and a complex that is not associated with TPPTS (hydrophobic). [10] These situations would permit the dual catalytic cycles to each function more efficiently in each phase and hence lead to a more efficient overall catalysis. Furthermore, the circumstance under which no reactants, including highly reactive species generated in each process, interfere with each other would permit the catalysis to function more smoothly and with a higher degree of selectivity.

Table 2. Aqueous Catalytic Pauson-Khand-Type Reactions of Various Enynes with Formalin[a]

entry	enyne	HCHO[b]	time	product[c]	
1		5eq	5h		96% (R = Ph)
2		5eq	8h		84% (R = Bu)
3		10eq	5h		89% (R = Me)
4[d]		100eq	2h		87% (R = Ph)
5		20eq	5h		81% (R = Bu)
6		10eq	4h		94%
7[e]		10eq	5h		94% (1.8/1)[f]
8		10eq	2h		96% (R = Ph)
9		5eq	6h		89% (R = Bu)
10		5eq	12h		67%
11		20eq	6h		91% (2.4/1)[f]
12		5eq	2h		82%
13		5eq	4h		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) and H$_2$O (1.9 mL) at 100 °C under N$_2$. [b] 37% formalin was used. [c] Isolated yield. [d] The reaction was carried out using 2.0 mL of 37% formalin as a solvent and 5.0 eq of SDS at 80 °C. [e] The enyne was used as a *E/Z* mixture (85/15). [f] Diastereomeric ratios were determined by GC. [g] Single stereoisomer.

The present system is applicable to the carbonylation of various enynes in excellent yields. Some selected results are shown in Table 2. The replacement of the phenyl group in **1** by butyl or methyl groups also resulted in the formation of the carbonylated products in excellent yields (entries 2 and 3). Reactions of enynes containing tethered heteroatoms such as oxygen and nitrogen also

afforded the corresponding bicyclic cyclopentenones (entries 4-10, 12 and 13). Enynes containing 1,1- and 1,2-disubstituted alkene portions were also carbonylated smoothly (entries 6 and 7). 1,7-Enynes also were applicable for these conditions and were converted to cyclohexane-fused cyclopentenones (entries 10, 12, and 13). For substrates where two groups are positioned on contiguous carbons of a ring system, the cyclocarbonylation proceeded efficiently, resulting in the formation of tricyclic cyclopentenones (entries 11-13).

In summary, we report on the development of an aqueous catalytic Pauson–Khand-type reaction of enynes using formaldehyde as a water-soluble source of carbon monoxide. In the present system, the decarbonylation and the carbonylation processes would take place independently in different phases, namely aqueous and micellar phases, resulting in a more efficient catalytic carbonylation reaction. The use of formalin, a low-cost feedstock, as a source of carbon monoxide affords 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 to elucidate the mechanism of the dual catalysis, especially the morphology of aggregation of all the reagents and the location of two processes, are currently underway. Moreover, applications to other carbonylation reactions will be appeared in future reports.

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[9]   Even for the reaction using the additional TPPTS, the decarbonylation does not appear to proceed exclusively in the aqueous phase, because a hydrophobic combination of [RhCl(cod)]$_2$ with only

dppp catalyzed the carbonylation reaction (Table 1, entries 1 and 2).

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Abstract
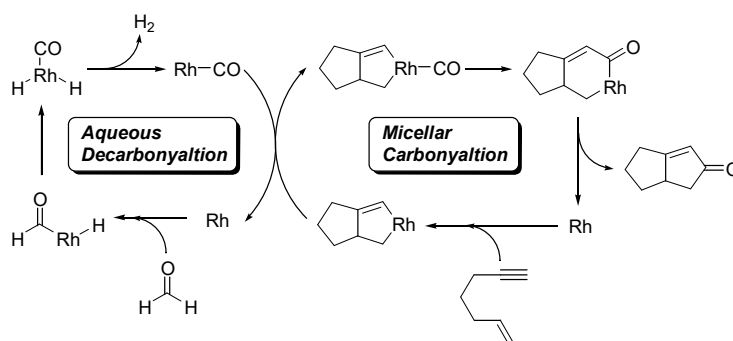
The aqueous Pauson–Khand-type reaction of enynes with formalin was developed using a rhodium catalyst. The use of a water-soluble phosphine ligand in conjunction with a hydrophobic phosphine ligand makes the dual-catalysis system, which would involve the decarbonylation of formaldehyde in the aqueous phase and the carbonylation of enynes in the micellar phase, more efficient.