Wacker Oxidation in an Aqueous Phase through the Reverse Phase-Transfer Catalysis of a Self-Assembled Nanocage

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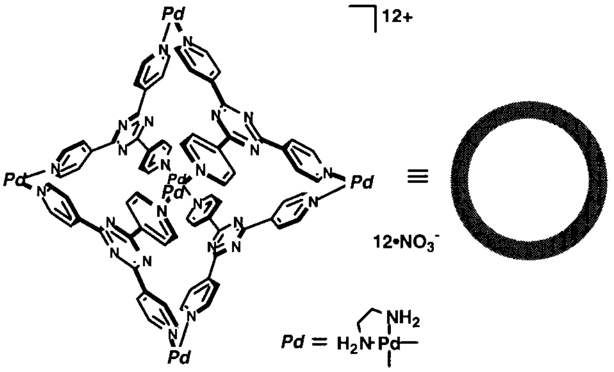
Self-assembled nanocage **1** was found to promote the aerobic, aqueous oxidation of styrene and its derivatives with the aid of (en)Pd$(NO_3)_2$. Obviously, the reaction was promoted by a double catalysis system: i.e., cage **1** acted as a reverse phase-transfer catalyst, whereas (en)Pd^{2+} as an oxidation catalyst.

Chemical transformation in aqueous media is a current trend in synthetic chemistry in view of developing clean technology.[1,2] One of the most promising approaches to water-based reactions is to develop reverse phase-transfer catalysts[3] which bring organic substrates into aqueous phase, let them react with aqueous reagents, and take out products from the aqueous phase. Recently reported coordination nanocage **1** is expected to be a good and unique candidate for the reverse phase-transfer catalyst because of its good solubility in water and high binding ability toward large and neutral organic molecules.[4] Although chemical transformations within self-assembled cages were reported recently,[5] their phase transfer catalysis has not been explored. Only a few previous reports dealt with reverse phase-transfer catalyst, wherein cyclodextrins were employed as catalysts.[3]



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In expectation of developing such a functional coordination system, we studied the catalysis by cage **1** of Wacker oxidation of olefins which is a typical Pd(II)-promoted catalytic reaction. Thus, when styrene (0.05 mmol) was suspended in D_2O (1 mL) solution of **1** (0.005 mmol), styrene was partly transferred into the aqueous phase forming **1**·(styrene)$_n$ clathrate complex (n = ca. 3) as monitored by ^{1}H NMR (Figure 1a).[6] The signals of styrene were highly upfield shifted due to the enclathration in the cavity. To this mixture, (en)Pd$(NO_3)_2$ (**2**, 0.005 mmol, 10 mol%) was added as an aqueous reagent to promote the reaction efficiently. Since Pd(II)-pyridine bond is reversible, addition of other metal components will cause unfavorable metal exchange in the cage framework. Notably, however, cage **1** remains intact upon the addition of the same metal component, (en)Pd$(NO_3)_2$. After the solution was heated at 80 °C for 24 h, the aqueous phase was again monitored by ^{1}H NMR. The signals of styrene disappeared and a new set of signals appeared at δ 6.6-7.3 and δ 1.7 ppm (Figure 1b). The product, after being extracted with $CDCl_3$, was identified as acetophenone and the yield was determined by NMR to be 82% (Table 1, run 1).

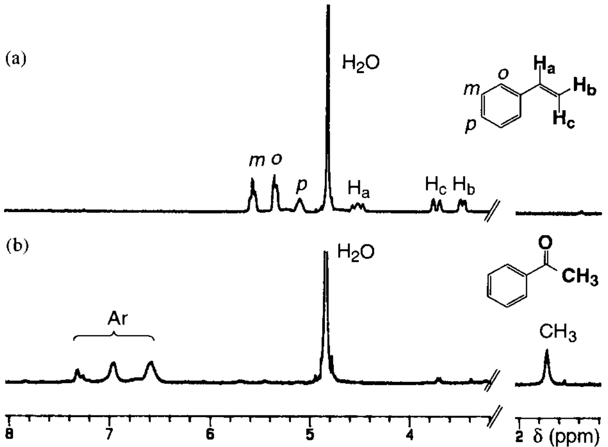
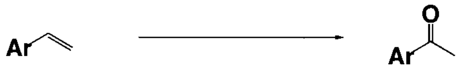


Figure 1. ^{1}H NMR monitoring of the D_2O phase in the aerobic oxidation of styrene catalyzed by **1** and (en)Pd$(NO_3)_2$. (a) Only styrene was treated with the D_2O solution of **1**. (b) (en)Pd$(NO_3)_2$ was added and the D_2O phase was monitored after 24 h at 80 °C.

Table 1. Aerobic oxidation of styrene and its derivatives catalyzed by **1** and **2**



Run	Ar	**1** / mol%	**2** / mol%	Yield of ketones /%[b]
1	phenyl	10	10	82
2	phenyl	-	10	4
3[a]	phenyl	10	10	3
4	phenyl	10	-	4
5	*p*-methoxyphenyl	10	10	53
6	*p*-tolyl	10	10	64
7	*p*-nitrophenyl	10	10	13
8	2-naphthyl	10	10	12

[a]1,3,5-Trimethoxybenzene (1 equiv to styrene) was added. [b]Determined by ^{1}H NMR.

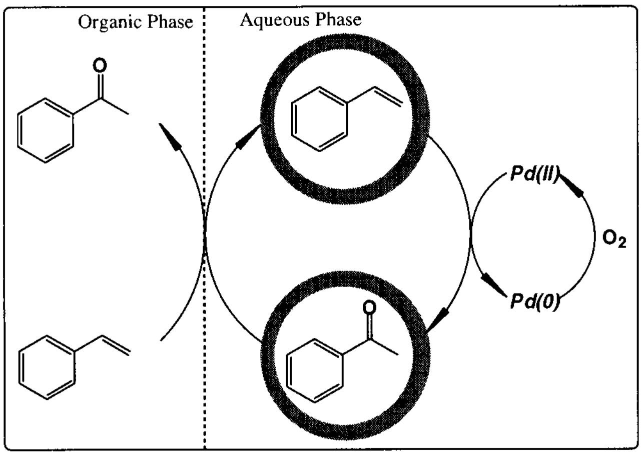


Figure 2. Schematic presentation of the reverse phase-transfer catalysis of **1** for the Wacker oxidation of styrene.

Control experiments revealed that this reaction proceeded in the aqueous phase. Under the same conditions, no reaction took place in the absence of cage **1** (Table 1, run 2). Even in the presence of cage **1**, the reaction was suppressed by the addition of an "inhibitor", 1,3,5-trimethoxybenzene (1 equiv to styrene), which has much higher affinity to the cage than styrene (run 3). Small amount of (en)Pd$(NO_3)_2$ (10 mol%) was essential because the catalytic activity of Pd(II)-linked cage **1** itself for the oxidation of styrene was inferior (conversion: 4%), unfortunately (run 4).

Obviously and interestingly, the reaction was promoted by a unique double catalysis system: i.e., cage **1** acted as a reverse phase-transfer catalyst, whereas (en) Pd^{2+} as an oxidation catalyst. Concerning the reverse phase-transfer catalysis of **1**, the catalytic cycle should involve the following steps. First, a substrate (styrene), which itself forms organic phase, is enclathrated by cage **1** and transferred into the aqueous phase. (ii) Then, styrene in the cage is oxidized to acetophenone by the action of Pd(II) reagent. (iii) Finally, acetophenone (less hydrophobic) is replaced by unreacted styrene (more hydrophobic). The decreased hydrophobicity of the substance should promote smooth product-substrate replacement (Figure 2).

The Pd(II)-promoted Wacker oxidation in the aqueous phase featured a remarkable aspect: the oxidation smoothly proceeded without employing any reoxidant of Pd(0) species. Since the catalytic reaction was completely suppressed with a degassed solvent under argon atmosphere, the Pd(0) species involved in the catalytic cycle must be reoxidized to Pd(II) by air. The aerobic reoxidation might be promoted by a trace amount of metal contamination in the Pd(II) reagent. The reaction efficiency was unaffected by the addition of $Cu(NO_3)_2$ (10 mol%).

Due to the strong binding ability of **1** toward electron-rich aromatic compounds, the reaction was particularly efficient for electron-rich substrates. For example, *p*-methoxystyrene and *p*-methylstyrene, which are strongly bound by **1**, were converted to acetophenone and its derivatives in good yields (Table 1, runs 5 and 6). In contrast, the oxidation of *p*-nitrostyrene, which is poorly bound by **1**, was hardly observed (run 7). The reaction was also sensitive to the size of the substrate: 2-vinylnaphthalene seems less effectively bound by **1** and the yield was low (run 8).

References and Notes

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6 A titration experiment also showed the 1:3 host-guest stoichiometry. The ^{1}H NMR spectrum of **1**·(styrene)$_3$ complex prepared stoichiometrically (270 MHz, D_2O, TMS as an external standard): for the host, δ 2.99 (s, 24H; CH_2), 8.64 (d, J = 6.7 Hz, 24H; PyH_a), 9.25 (d, J = 6.7 Hz, 24H; PyH_b); for the guest, 3.35 (d, J = 11 Hz, 3H; C*H*), 3.63 (d, J = 17 Hz, 3H; C*H*), 4.34 (dd, J = 11, 17 Hz, 3H; C*H*), 4.97 (t, J = 8 Hz, 3H; Ar*H*(*p*-)), 5.27 (d, J = 8 Hz, 6H; Ar*H*(*o*-)), 5.50 (t, J = 8 Hz, 6H; Ar*H*(*m*-)). Chemical shifts shown in Figure 1a are somewhat down-field shifted due to the complexation with slightly larger amount (> 3.0 equiv) of styrene. ^{13}C NMR (67.5 MHz, D_2O, TMS as an external standard) δ 47.35 (CH), 112.48 (CH), 124.88 (CH), 125.93 (CH), 126.57 (CH), 127.58 (CH), 135.05 (CH), 135.99 (Cq), 145.71 (Cq), 152.83 (CH), 169.54 (Cq).