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Direct transformation of benzilic amines to carbonyls using polyacrylamide-bound tungstate under phase-transfer catalysis conditions

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Abstract—A recyclable catalytic system under heterogeneous phase-transfer catalysis conditions was designed by using polyacrylamide-bound tungstate. A convenient method for the oxidative direct transformation of benzilic amines to carbonyls with hydrogen peroxide was then developed.

Solid-phase catalysts offer a number of important advantages over their homogeneous counterparts.[1,2] For example, their separation from reaction products is easy and their subsequent recycling steps have the potential for green chemical processes. Despite these advantages, solid-phase catalysts show low reactivity due to weak affinity between the substrate and catalyst under heterogeneous conditions. Therefore, the creation of efficient reaction systems utilizing solid-phase catalysts is recognized as an important topic in the current organic synthesis.

Recently, the use of an amphiphatic solid-phase catalyst under a phase-transfer condition or an aqueous system is regarded as a potential strategy to form highly reactive catalytic systems.[3,4] Since an amphiphatic-molecular mediated reaction in water often causes difficulties in the removal of surfactants and the clean-up of the used water, the utilization of a recyclable solid-phase type catalyst may take a lot of advantages when isolating product from solution and removing surfactants that cause environmental pollution in many cases.

The chemical transformation of amino groups to carbonyl ones is sometimes utilized in organic synthesis.[5] Some metal oxidizing reagents such as $KMnO_4$,[6] K_2FeO_4,[7] $Pb(OAc)_4$,[8] NiO_2,[9] and $HgO–I_2$[10] have been used to convert amines to carbonyl compounds through imines. However, these processes require stoichiometric or large amounts of poisonous late transition metals. Although multi-step process using a strong base such as *n*-butyllithium or DBU to generate imines from amines and subsequent hydrolysis could provide an alternative, examples of the simple and convenient transformation methods are still limited.[11–13]

In the course of our research on the creation of a new solid-phase catalyst, utilization of poly(*N*-isopropylacrylamide) (PNIPAAm) polymers as a catalyst supported material was found to be useful in the development of recyclable reaction systems and some efficient schemes under organic solvent free conditions were reported.[14–16] This work focuses much attention on the use of PNIPAAm-based catalyst under phase-transfer conditions and provided a novel oxidation system for the direct transformation of benzilic amines to carbonyls.

Previously, we have investigated the self-assembled process between PNIPAAm-based polymer ligands and an inorganic species.[14,15] This process afforded a networked supramolecular complex where the polymers are cross-linked together by the inorganic species. Thus the obtained complex with phosphotungstate (**1**) was insoluble

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Keywords: Phase-transfer catalysis; Oxidation; Supported catalysts; Benzilic amines; Green chemistry.

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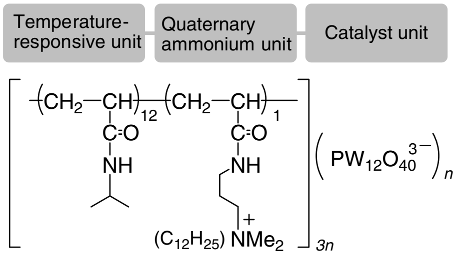
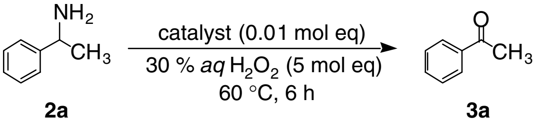


1

Scheme 1. Networked PNIPAAm – $PW_{12}O_{40}^{3-}$ complex (**1**).

Table 1. Direct catalytic transformation of 1-phenethylamine (**2a**) into acetophenone (**3a**) with hydrogen peroxide



Entry	Catalyst[a]	Solvent	Yield[b] (%)
1	**1**	Toluene	92[c]
2	**1** (2nd use)	Toluene	90
3	**1**	CH_3CN[d]	80
4	**1**	*t*-BuOH[d]	81
5	**1**	—	50
6	Na_2WO_4[e]	Toluene	Trace[f]

[a] The oxidation hardly proceeded in the absence of catalyst.

[b] Yield of isolated product.

[c] The oxime was obtained in 25% yield at 0 °C.

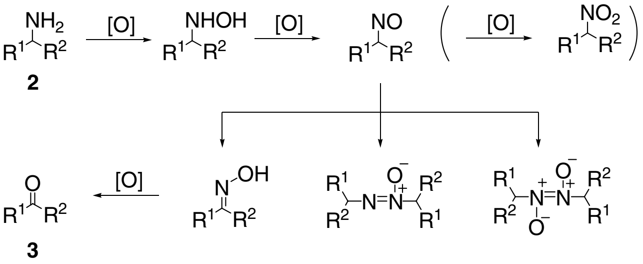
[d] Compound **1** was soluble in MeCN or *tert*-butyl alcohol at 60 °C.

[e] Additive: $[CH_3(n\text{-}{}_8H_{17})_3N]\cdot HSO_4$ and $NH_2CH_2PO_3H$.

[f] The oxime was obtained in 25% yield at 0 °C.

in water and worked as an efficient oxidation catalyst under organic solvent free conditions in water (Scheme 1). In addition, the application of the unique potentiality of poly(*N*-isopropylacrylamide) (PNIPAAm),[17] which undergoes thermally reversible changes between hydrophilic and hydrophobic states, brought valuable catalyst recycling strategies via the thermo-regulated formation of stable emulsion species.[16] To exploit the utility of PNIPAAm-based catalyst in the creation of a new solid-phase catalysis, the potentiality of PNIPAAm-bound phosphotungstate under phase-transfer conditions was explored in the oxidative transformation of benzilic amines to carbonyls with hydrogen peroxide.

When the reaction was performed on the toluene–aqueous hydrogen peroxide system in the presence of catalyst **1**,[18–20] 1-phenylethylamine (**2a**) was smoothly converted to acetophenone (**3a**) (Table 1, entry 1). In addition the catalyst could be recovered by simple filtration and reused without significant loss of activity (entry 2). The ^{31}P NMR spectrum of recovered **1** was unchanged relative to that of **1** before the reaction and no other species was evident.[15b,20] Alternatively, the reactions were also carried out under homogeneous systems by using polar organic solvent such as MeCN or *tert*-butyl alcohol, but slight lower yields were exerted attributable to the production of undesired side products and excess amounts of organic solvents were required for the extractive workup process (entries 3 and 4).[21] In addition, the reaction under organic solvent free condition was also ineffective and undesired side products were obtained again (entry 5). On the other hand, carbonyl product **3a** was not obtained when the reaction was carried out using sodium tungstate in the presence of surfactants (entry 6). The higher yield of the desired carbonyl product obtained utilizing easily recyclable heterogeneous catalyst **1** under phase-transfer condition is noteworthy and temperature dependent nature which would cause strong affinity for the organic substrate at high temperature might play an important role in the activation.



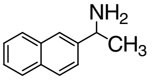
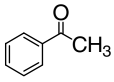
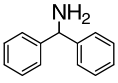
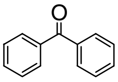
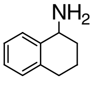
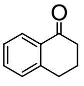
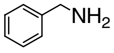
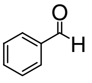
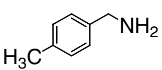
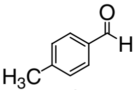
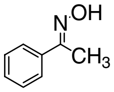
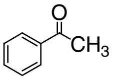
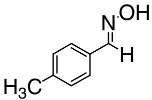
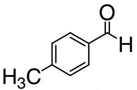
Scheme 2. Possible reaction formation mechanism for **3**.

Scheme 2 depicts a plausible reaction pathway. The oxygenation of primary amines possessing an α-C–H bond generally produces hydroxylamines initially, which is subsequently oxidized to nitroso compounds. The unstable nitroso compounds transform to oxime by tautomerization or to the nitrosodimer by dimerization. Some of the nitroso compounds react with hydroxylamines to form azoxy compounds. Further oxidation of oxime produces carbonyl compounds. In the **1**-catalyzed oxidation of **2a** under phase-transfer condition, carbonyl product **3a** was the only significant product (Table 1, entry 1). On the other hand, loss of the selectivity was observed under the homogeneous condition (entries 3 and 4) or the organic solvent free condition (entry 5), and the mixture of oxime, nitroso dimer, and azoxy compound was mainly obtained when the oxidation was carried out using sodium tungstate (entry 6).

The scope of this oxidation system was studied further with various benzilic amines (**2**).[22] Oxidation proceeded efficiently to give the corresponding carbonyl products (**3**) under phase-transfer systems (Table 2, entries 1–5). In addition, oxidation of oximes also afforded the corresponding carbonyl products (**3**) (Table 2, entries 6 and 7).

We have devised a novel catalytic heterogeneous oxidation system utilizing PNIPAAm-based tungsten catalyst with hydrogen peroxide and demonstrated its efficiency in the oxidative direct transformation of benzilic amines to carbonyls. The reaction driving under the heterogeneous phase-transfer conditions led to an acceleration of the reactivity and ease in catalyst recycling in the oxidation. The results described here will enhance the mul-

Table 2. Oxidation of benzylamines (**2**) and oximes (**4**) catalyzed by **1**[a]

Entry	Substrate	Product	Yield[b] (%)
1	 **2b**	 **3a**	80
2	 **2c**	 **3c**	89
3	 **2d**	 **3d**	93
4	 **2e**	 **3e**	69
5	 **2f**	 **3f**	78
6	 **4a**	 **3a**	91
7	 **4f**	 **3f**	80

[a] Condition: **1** (0.01 mol equiv), 30% aq H_2O_2 (5 mol equiv), toluene, 60 °C, 3–6 h.

[b] Yield of isolated product.

tifunctional utility of our PNIPAAm-based tungsten catalyst and efforts to extend this system to other types of reactions are currently ongoing.

Acknowledgments

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18. Poly(*N*-isopropylacrylamide) (PNIPAAm) based tungsten catalyst (**1**) was synthesized by improvement of previous method.[15b]
19. *A typical experimental procedure for the direct transformation of benzilic amines to carbonyls using* **1** *under phase-transfer condition:* A mixture of **1** (0.32 g, 0.04 mmol), benzilic amine **2** (4 mmol) and 30% aq H_2O_2 (1.9 ml, 20 mmol) in toluene (or $C_6H_5CF_3$, 10 ml) was heated to 60 °C and stirred for 2–3 h. After the reaction mixture had been allowed to cool, water (10 ml) was added. The organic and aqueous phases were removed and the recovered **1** was washed with Et_2O and distilled water, which were then added to the aqueous phase. The recovered **1** was reused for subsequent catalytic experiments. The aqueous phase was extracted two times with

Et_2O (10 ml) and the combined organic extracts were washed with brine. The organic phase was then dried over $MgSO_4$ and concentrated under reduced pressure. The products were purified by column chromatography with silica gel and the isolated yields were determined. All carbonyl products (**3**) were commercially available and corresponded.

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22. When the oxidation was carried out with aliphatic amines, the mixture of carbonyl, oxime, nitroso dimer, and azoxy compound was obtained (Aliphatic amine = $PhCH_2CH_2NH_2$; carbonyl 26%, oxime < 5%, nitroso dimmer 36%, azoxy 19%).