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Selective aerobic oxidation of amines to imines by TiO_2 photocatalysis in water†

Ning Li, Xianjun Lang, Wanhong Ma, Hongwei Ji, Chuncheng Chen* and Jincai Zhao

Selective oxidation of benzylic amines to imines with atmospheric O_2 is achieved in water on TiO_2 under UV irradiation. The afforded imine could be easily separated and TiO_2 can be recycled by filtration. To scale up, gram-scale imine products can be obtained.

The selective photocatalytic oxidation of organic compounds has received increased attention, since it could endow room temperature synthesis with O_2 under renewable solar light irradiation.[1] In particular, the selective oxidation of amines to imines, which represents one of the most important functional-group transformations, has been attracting special interest from the catalysis research community.[2] We recently reported the photocatalytic selective aerobic oxidation of benzylamines to imines on TiO_2 in CH_3CN.[3,4] Since then, different genres of photocatalysts such as g-C_3N_4,[5] Nb_2O_5,[6] Au/TiO_2,[7] Ru containing MOF,[8] Ru and Rh complexes[9,10] have been developed to implement this reaction. In these aforementioned photocatalytic systems, organic solvents were always employed as the reaction media.

Water is a more economic and environmentally viable solvent for the organic reaction. Moreover, some organic reactions in water could exhibit special reactivity or selectivity due to the unique physicochemical properties of water. However, not only for amines, literature reports about the selective oxidation of organic compounds in water with O_2 by TiO_2 photocatalysis have been quite sporadic so far. This is in part because of the formation of active oxygen species such as $^{\bullet}OH$ and $O_2^{\bullet -}/HO_2^{\bullet}$ radicals derived from the oxidation of H_2O by h_{vb}^+ and the reduction of O_2 by e_{cb}^- under aqueous conditions, which could induce the overoxidation of organic compounds, even ultimately to CO_2 and H_2O.[11] Thus, to access high selectivity in water, one of the primary tasks is to avoid the overoxidation of the targeted products.

Despite the scarcity, there were encouraging results of photocatalytic synthesis in water that are worth highlighting. Selective aerobic oxidation of benzyl alcohols to benzaldehydes was reported on a home-made rutile TiO_2 (with selectivities of 45–74%)[12] or WO_3/TiO_2 (with selectivities of 41–62%)[13] at 50% conversion of benzyl alcohols under UV irradiation in water. In both cases, the weak adsorption ability of products on the surface of TiO_2 is the key to ensuring high selectivity, bestowing guidance in designing selective photocatalytic aerobic oxidations in water.[14] However, the higher selectivity is at the cost of lower activity of these specially designed TiO_2 photocatalysts.[12,13] It is a more challenging task to achieve high selectivity in water without influencing the high activity of photocatalysts. Thus, we intend to utilize the instinct physicochemical properties between amines (miscible) and imines (non-miscible) in water to avoid overoxidation of the formed products to achieve high selectivity, whilst the most active TiO_2 could be directly selected as a photocatalyst to ensure high efficiency.

Herein, we report our recent findings on the selective oxidation of amines to imines in water with atmospheric O_2 on commercial benchmark Degussa P25 TiO_2 exposed to >300 nm UV irradiation. The oxidation reaction could be run at a much higher rate than that in CH_3CN, suggesting the prompting factor of water for the oxidation process. More intriguingly, we found that TiO_2 could be aggregated along with the accumulation of imines (Fig. S1, ESI†). Hence, by Büchner filtration, imines could be easily separated without tedious work-ups; TiO_2 could be facilely recycled without centrifugation. The reaction was scaled up to a gram-scale imine synthesis, which is one of the best reported results for the selective oxidation by photocatalysis in water.

The time plot for the oxidation of benzylamine to imine in water with 1 atm of air on Degussa P25 TiO_2 is shown in Fig. 1. After >300 nm UV irradiation for 1 h, 32% of benzylamine was converted, and 87% of them was found to be transformed to imine with a selectivity comparable to that in CH_3CN.[3] This is a quite satisfactory result considering the fact that complete degradation of organic compounds into CO_2 and H_2O usually occurs under aqueous conditions on TiO_2 photocatalysts. In addition, the high selectivity at the early stage indicates that the oxidation of amines to products other than desirable intermediates (aldehyde, see below) and overoxidation of the intermediates are not significant in water. After a prolonged irradiation time of 9 h, the selectivity decreased to some extent comparable to photocatalytic oxidation of amine in CH_3CN as studied earlier.[3,4] The selectivity for imine was 63% at benzylamine

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Key Laboratory of Photochemistry, Beijing National Laboratory for Molecular Sciences, Institute of Chemistry, Chinese Academy of Sciences, Beijing 100190, China. E-mail: ccchen@iccas.ac.cn

† Electronic supplementary information (ESI) available: Experimental details and Fig. S1–S4. See DOI: 10.1039/c3cc41407h

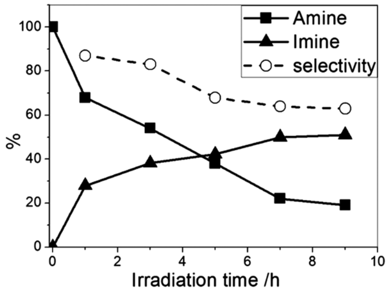


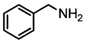
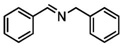
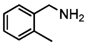
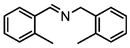
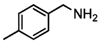
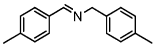
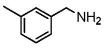
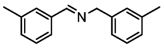
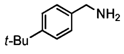
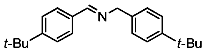
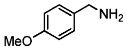
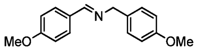
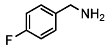
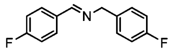
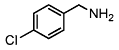
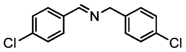
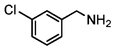
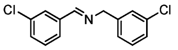
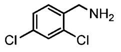
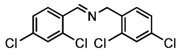
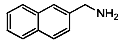
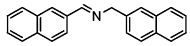
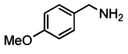
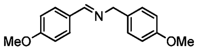
Fig. 1 Conversion of amine (–■–), yield of imine (–▲–) and selectivity (–○–) against irradiation time for the photocatalytic aerobic oxidation of benzylamine on TiO_2. Reaction conditions: benzylamine (0.1 mmol), H_2O (2 mL), TiO_2 (Degussa P25, 10 mg), Hg lamp (100 W), >300 nm, air (1 atm).

conversion of 83%. The decrease in selectivity with irradiation time is understandable as the free radical intermediates, which are famous in the aqueous photocatalytic system, might attack the formed imines to destroy them to some extent.

Motivated by this result, we expanded the scope of the substrates for the oxidation of amines to imines in water by TiO_2 photocatalysis with 1 atm of air as the terminal oxidant. Table 1 summarizes the photocatalytic oxidation of the benzylamines to the corresponding imines at two different conversions corresponding to reaction times of 1 and 9 h, respectively. The selectively oxidative coupling reactions proceeded smoothly in water for all the benzylamine derivatives, and formation of the desired imine products was in moderate to high selectivities (entries 1–10): 56–94% at low conversions under irradiation for 1 h; 52–83% at high conversions (after 9 h). Methyl substituted benzylamines at *o*-, *m*-, *p*-positions of the phenyl ring (Table 1, entries 2–4) could all be transformed to corresponding imines with slight differences in conversions and selectivity. Bulky groups such as *t*-butyl at the *p*-position of the phenyl ring did not decrease the reaction rate (entry 5). It was found that electronic effects associated with electron donating substituents (CH_3– and CH_3O–) and electron withdrawing substituents (F– and Cl–) on the phenyl ring had little effect on the reaction rate and product selectivity of the oxidation reaction. For example, not much difference in the conversions of the *para*-substituted benzylamines was observed, and similar selectivity for the imines was also obtained (entries 1, 3, 5–8), indicating that the photocatalytic selective oxidation of amines to imines in water is not sensitive to substituents and has high functional-group tolerance. It is noteworthy that the oxidative coupling of halo-substituted benzylamines was found to be with good selectivity (entries 7–10), as the halo-substituted positions along with the imine functionality are useful for further transformations. The amine substrate with a bulky aromatic ring such as naphenyl could also be subjected to the photocatalytic oxidation conditions with excellent selectivity of 94% at 31% conversion and moderate selectivity of 55% at 86% conversion (entry 11).

The imine product could be easily precipitated from water as a white solid in the photocatalytic aerobic oxidation of 2,4-dichlorobenzylamine with a high selectivity of 76% at 82% conversion (entry 10) which is comparable with the result in CH_3CN. Thus it was selected as the substrate to investigate the role of water in the photocatalytic coupling of amines. Fig. 2 illustrates a detailed comparison between different reaction rates in water and CH_3CN. The reaction in water proceeded significantly faster than that in the organic solvent, particularly at the beginning of the irradiation.

Table 1 Selective aerobic oxidation of benzylic amines to imines in water photocatalyzed by TiO_2

Entry	Substrate	Product	Conv.[a] (%)	Select.[a] (%)	Conv.[b] (%)	Select.[b] (%)
1			32	87	81	63
2			22	85	81	55
3			37	80	82	61
4			22	72	65	63
5			35	94	85	83
6			35	79	73	67
7			24	90	70	66
8			25	79	72	65
9			33	56	59	52
10			40	94	82	76
11			31	94	86	55
12[c]			—	—	—	51[d]

Reaction conditions: amine (0.1 mmol), H_2O (2 mL), TiO_2 (Degussa P25, 10 mg), Hg lamp (100 W), >300 nm, air (1 atm). Conversions and selectivities were determined by GC analysis using bromobenzene as internal standard. [a] 1 h. [b] 9 h. [c] Amine (5 mmol), H_2O (0.15 L), TiO_2 (Degussa P25, 0.5 g), 15 h, for a more detailed experimental procedure see ESI. [d] Isolated yield by filtration.

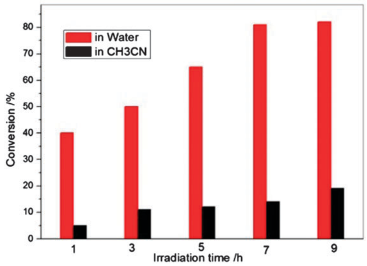
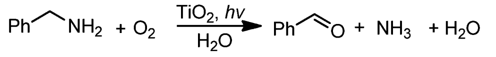
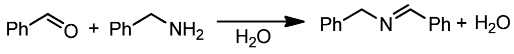


Fig. 2 Comparison of the photocatalytic aerobic oxidation rates of 2,4-dichlorobenzylic amine when the reaction is carried out in water and in CH_3CN. Reaction conditions: amine (0.1 mmol), solvent (2 mL), TiO_2 (Degussa P25, 10 mg), Hg lamp (100 W), air (1 atm).

After 1 h of irradiation, 40% of amine was converted in water, whereas the conversion was less than 5% of amine for the reaction in CH_3CN; after 9 h, 82% of amine was converted in water, whereas only 20% of amine was converted in CH_3CN, indicating that the oxidation of amine is significantly accelerated by water. Adding a reasonable amount of water,[15] using an acidic catalyst[2e,16] or employing water as a solvent[17] has been observed to facilitate the aerobic oxidation of amines to imines in the thermally catalytic systems.



(1)



(2)

According to our previous results in CH_3CN,[3,4] the aerobic oxidation of benzylamine to imine on TiO_2 in water under UV irradiation should follow a two-step process: benzaldehyde is first generated by the oxygenation of benzylamine with O_2 (eqn (1)); nucleophilic addition of the formed benzaldehyde by benzylamine affords the final imine (eqn (2)). This pathway should hold true in aqueous systems. In the first step, photocatalytic oxidation of amine is a series of electron transfer and proton transfer processes (dehydrogenation of the amine and the reduction of oxidant O_2). The presence of water would greatly accelerate these proton concerted electron transfer reactions by providing more protons and by forming hydrogen bonds on the surface of TiO_2. For example, we recently discovered that the loading of protons on the surface of TiO_2 could accelerate the aerobic oxidation of alcohols under >300 nm UV irradiation, because the protons could aid in the decomposition of peroxide intermediates.[18] Accordingly, the prompting effect of water on the oxidation of amines might arise from the protonic properties of water. In fact, the positive effects of adding proton sources such as organic acid (CF_3COOH)[19] and H_2O[20] were all reported in the heterogeneous photocatalytic systems. Intuitively, employing water as the solvent could have a detrimental effect shifting the equilibrium backward in eqn (2). In addition, the protonation of the amino groups would hinder the nucleophilic reaction. However, based on the pK_b of benzylamine (4.66), only 2% of the amino groups are protonated. It is possible for the nucleophilic reaction to occur.

Another issue hindering photocatalysis in practical application is the recyclability of TiO_2. We observed that the photocatalyst could aggregate along with the formation of imine to allow for easy separation of both the product and the photocatalyst (Fig. S1, ESI†). Because the newly formed C=N bonds have less polarity than the $-NH_2$ groups in the substrates, the imine products exhibit much less solvability in water, which offers a unique opportunity to easily separate the product, preventing further destruction of the products in the photocatalytic systems.

With 4-methoxylbenzylamine as the substrate, we scaled up the current aerobic oxidation protocol by TiO_2 photocatalysis by using 0.69 g benzylamine in 150 mL water with 0.5 g TiO_2. After separation of the reacted suspensions by simple Büchner filtration, the substrate and product distribution in the filtrate and the solid was carefully analysed using GC. The unreacted amine was the dominant organic species in the filtrate, whereas the imine was enriched in the solid (Fig. S2 and S3, ESI†). The GC analysis also confirmed that the aldehyde is the essential intermediate for the imine formation. In another experiment, we filtered out the solid every 5 h of irradiation. After separating the products using 30 mL acetonitrile, TiO_2 was put back into the filtrate for the further conversion of the unreacted amine. Three such runs afforded 0.32 g (51% isolated yield) of imine (see ESI† for details). Both the GC and NMR revealed that the isolated product is imine with purity higher than 95% (Fig. S4, ESI†).

In summary, water can be used as the ideal medium for scalable synthesis of imines with good selectivities by TiO_2 photocatalysis. Besides providing a more environment friendly and economic solvent alternative, the photocatalytic selective oxidation of amine occurs much more rapidly in water than that in CH_3CN. Our work also presents an excellent example that the immiscibility of the products with water can be used to avoid overoxidation of the products and to realize the easy separation of the product and the recycling of the photocatalyst.

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