Synergistic effect of vanadium–phosphorus promoted oxidation of benzylic alcohols with molecular oxygen in water†

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The synergistic effect of vanadium–phosphorus in aqueous solution is crucial to ensure high efficiency for oxidation of benzylic alcohols with molecular oxygen in water catalyzed by $VOPO_4$/TEMPO (2,2,6,6-tetramethylpiperidyl-1-oxy).

Oxidation of alcohols to their corresponding aldehydes is one of the fundamental transformations in organic chemistry,[1] and green methods have attracted much attention for the development of sustainable chemistry in recent years.[2] Water is abundant and environmentally benign, and catalytic oxidation of alcohols with molecular oxygen in aqueous media is extremely attractive.[2a,3] However, metal catalysts often show low activity because of the occupation of coordination sites by water (*e.g.* formation of $[M(H_2O)_n]^{m+}$).[4] Several successful types of catalytic systems have been reported, especially using precious metals (*e.g.* Pt,[5a–d] Pd,[5e,5f] Au[5g–i]), or employing halogen as a key component.[6] Alkaline environments (*e.g.* with NaOH or K_2CO_3) were indispensable for some catalytic systems.[5f–i,7] However, the quest for green and economical oxidation systems in water remains a great challenge.

Recently we developed an inexpensive system consisting of vanadyl sulfate and sodium nitrite for the catalytic oxidation of benzylic alcohols, but it was still easily deactivated by excess water.[8] Herein, we report the development of vanadium-mediated oxidation of alcohols in water with molecular oxygen, and describe our finding that the synergistic effect of vanadium–phosphorus in aqueous solution is crucial to ensure high efficiency.

V–P–O catalysts have been intensely studied for vapor-phase oxidation of *n*-butane to maleic anhydride.[9] In contrast, application of these catalysts for liquid-phase oxidation in water is relatively rare. Vanadate has long been recognized as an analogue of phosphate with respect to electronic and structural properties in aqueous solution.[10] These results inspired us to explore $VOPO_4$-catalyzed oxidation of alcohols in water.

First, we selected veratryl alcohol as a probe molecule. Initial investigations were performed with molecular oxygen using 5 mol% $VOPO_4$ at 80 °C. However, only 17.6% conversion was obtained after 4 h, roughly agreeing with the previous report.[11] In many biological oxidations, chains of redox couples are often involved for electron transfer from substrates to oxygen under mild conditions.[12] It is known that oxoammonium salts (*e.g.* $TEMPO^+$) are effective for the oxidation of alcohols and can be generated from the 2,2,6,6-tetramethylpiperidyl-1-oxy (TEMPO) radical by oxidation with a stoichiometric oxidant (*e.g.* hypochlorite).[13] We propose here that if TEMPO can be oxidized by high-valence vanadium in water, the catalytic activity should be enhanced. The following results clearly indicate that the combination of TEMPO and $VOPO_4$ leads to a substantial increase in activity compared with $VOPO_4$ alone. Veratryl alcohol was oxidized to veratraldehyde almost quantitatively (yield 96%) within 4 h in water, while TEMPO itself was inactive (Fig. 1, experiments 1 and 2). Indeed the presence of both vanadium species and nitroxyl radical was indispensable for this catalytic system. Moreover, the oxidation could be performed even at room temperature, giving 95.2% conversion within 48 h.

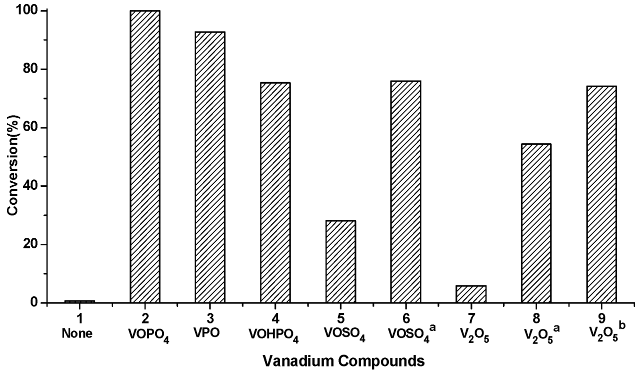

Fig. 1 Oxidation of veratryl alcohol catalyzed by TEMPO and various vanadium compounds. Reaction conditions: 2.5 mmol veratryl alcohol, 0.125 mmol [V] , 0.125 mmol TEMPO, 5 ml H_2O, 0.4 MPa O_2, 80 °C, 4 h. Selectivity for veratraldehyde >99% in all experiments. [a] Addition of 0.125 mmol KH_2PO_4. [b] Addition of 0.125 mmol H_3PO_4.

Further studies revealed the initial valence of vanadium didn't affect the conversion significantly. High conversion was also obtained using VPO (vanadium phosphorus oxide) and $VOHPO_4$ respectively (Fig. 1, experiments 3 and 4). Long induction time was observed when $VOHPO_4$ was used. This may be related to oxidation of V^{IV} to V^{V} by molecular oxygen at the initial stage. In contrast, only 28.1% conversion of veratryl alcohol was obtained when $VOSO_4$ was used (Fig. 1, experiment 5). V_2O_5 was reported to be effective for catalytic oxidation of alcohols using toluene as a solvent,[14] but in our studies it showed rather lower activity in water than $VOPO_4$ (Fig. 1,

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Table 1 Oxidation of alcohols catalyzed by $VOPO_4$–TEMPO[a]

Entry	Substrate	Product	Time (h)	Conversion (%)	Selectivity (%)
1	Veratryl alcohol	Veratraldehyde	4	>99	98.7
2	Benzyl alcohol	Benzaldehyde	4	72.4	93.1
3	4-$MeC_6H_4CH_2OH$	4-MeC_6H_4CHO	6	83.6	96.1
4	2-$MeC_6H_4CH_2OH$	2-MeC_6H_4CHO	7	65.1	92.3
5	3-$MeOC_6H_4CH_2OH$	3-$MeOC_6H_4CHO$	6	63.1	>99
6	4-$MeOC_6H_4CH_2OH$	4-$MeOC_6H_4CHO$	4	93.2	95.7
7	3-$ClC_6H_4CH_2OH$	3-ClC_6H_4CHO	12	62.4	96.6
8	2-$ClC_6H_4CH_2OH$	2-ClC_6H_4CHO	10	69.4	93.2
9	1-Phenylethanol	Acetophenone	6	38.5	89.0
10	Cyclohexanol	Cyclohexanone	10	11.7	>99
11	Isopropanol	Acetone	7	43.6	>99
12	2-Butanol	2-Butanone	10	22.5	>99
13[b]	Veratryl alcohol + thioanisole	Veratraldehyde + thioanisole	4	>99	>99

[a] Reaction conditions: 2.5 mmol alcohol, 0.125 mmol $VOPO_4$, 0.125 mmol TEMPO, 5 ml H_2O, 0.4 MPa O_2, 80 °C. [b] 1.25 mmol veratryl alcohol and 1.25 mmol thioanisole.

experiments 2 and 7). It was interesting that the conversions were greatly enhanced when KH_2PO_4 or H_3PO_4 ($V/P = 1$) was added to the V_2O_5-catalyzed system (Fig. 1, experiments 7, 8 and 9). In contrast, when H_2SO_4 was added instead of H_3PO_4, only moderate conversion (29.4%) was obtained for the V_2O_5–TEMPO–H_2SO_4 system. For $VOSO_4$, the conversion was also raised to 75.9% within 4 h of when KH_2PO_4 was added (Fig. 1, experiments 5 and 6). Obviously, the presence of phosphorus species was crucial to the catalytic activity.

Besides veratryl alcohol, oxidation of other alcohols was also catalyzed by $VOPO_4$/TEMPO (Table 1). Though most benzylic alcohols are only partly soluble in water, they could be oxidized to their corresponding aldehydes with moderate or good conversions (Table 1,entries 1–8). The selectivity for aldehydes remained high compared with Pt-based catalysts.[5a–d] In contrast with the examples performed in an alkaline environment,[5f–i,7] acidic conditions were preferable for this catalytic system. The aliphatic secondary alcohols could also be converted to the ketones, but they were more difficult to oxidize than benzylic alcohols (Table 1, entries 10–12). For example, 44% conversion of isopropyl alcohol could be obtained within 7 h despite its good solubility in water. More interestingly, thioanisole remained intact and had no negative effect on the catalytic systems when a mixture of thioanisole and veratryl alcohol was subjected to oxidation (Table 1, entry 13). Because thioanisole is smoothly oxidized to sulfoxide in some vanadium–peroxide systems,[15] this system should be very useful in organic synthesis in the presence of both alcohol and sulfide functions. This catalytic system shows much better water tolerance than our previous system,[8] and employs neither precious metals nor extra bases.[5,7]

At this point, one question arose: how are the catalytic activities affected by phosphorus species in aqueous solution? Though the forms of vanadium species in aqueous solution vary with pH,[16] the acidity is not the only explanation. The pH values for $VOSO_4$ and $VOHPO_4$ in water are close (ESI, p. 7†), but the conversion of veratryl alcohol was more than 2 times higher when $VOHPO_4$ was used compared with $VOSO_4$ (Fig. 1, experiments 4 and 5). We thus employed ^{51}V and ^{31}P NMR spectroscopy to investigate the form of vanadium and phosphorus in the catalytic system. ^{51}V NMR spectra of the aqueous solutions after reaction (except line d) are shown in Fig. 2. For lines c and d, the signals (−598, −589 and −534 ppm) were assigned to the PV_{14} species $[H_xPV_{14}O_{42}]^{(9-x)-}$ ($x = 4$ or 5), and the resonance occurring at −548 ppm was assigned to VO_2^+.[16,17] Similar ^{51}V NMR signals were also observed at different reaction times (ESI, pp. 5 and 6). The change in the spectra was notable in V_2O_5-catalyzed experiments (lines a and b). Without phosphorus species, vanadium existed in the form of $[H_2V_{10}O_{28}]^{4-}$ (line a)[18] and showed low activity (Fig. 1, experiment 7). When H_3PO_4 was added, the peaks varied dramatically, and they were similar to those in the $VOPO_4$-catalyzed experiment (lines b and c). This should account for the enhanced activity (Fig. 1, experiments 7 and 9). ^{31}P NMR chemical shifts were about 0.75 ppm in the aqueous solutions (ESI, p. 6), which roughly agreed with those of PV_{14} and P species (H_3PO_4 and $H_2PO_4^-$).[16,17] These results suggested that some phosphates act as an inorganic ligand for the vanadium species.[10] The similar properties and interaction of vanadium and phosphorus species in aqueous solutions are thus essential to ensure high activity for this system.

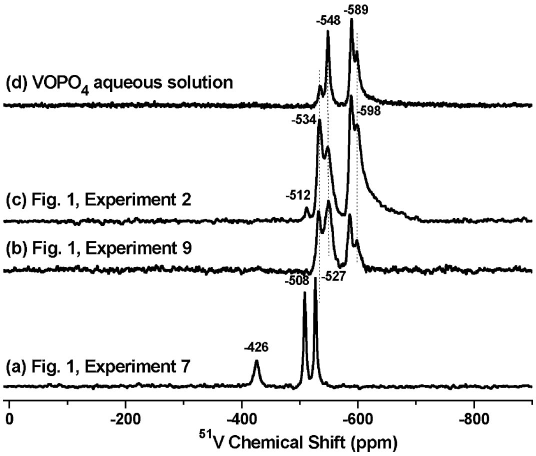


Fig. 2 ^{51}V NMR spectra for various aqueous solutions.

How do the catalytic redox cycles proceed? The stoichiometric reactions under N_2 atmosphere were investigated (ESI, p. 7). Though alcohols are often used to reduce V^V during synthesis of V–P–O-based catalysts (*e.g.* reflux in neat alcohols),[9] reaction of equivalent amounts of $VOPO_4$ and veratryl alcohol afforded only 1.5% veratraldehyde in 4 h at room temperature in water. In contrast, the conversion of veratryl alcohol was 35.9% when 5 mol% TEMPO was added, and the color of mixture changed from reddish-brown to green. These results indicated that the oxidation of veratryl alcohol with $VOPO_4$ was catalyzed by TEMPO, a process that probably involves V^V/V^{IV} redox cycles. This was further confirmed by electron paramagnetic resonance (EPR) in controlled experiments under N_2 atmosphere (ESI, pp. 8–10). There was no apparent EPR signal for $VOPO_4$ aqueous solution. After adding TEMPO and agitating at room temperature under N_2 atmosphere, a V^{IV} signal appeared (Fig. 3).‡ [19] This result suggested that V^V could be reduced to V^{IV} directly by TEMPO. When veratryl alcohol was added, the EPR signal of V^{IV} was further strengthened, and veratraldehyde could be detected by GC in the mixture. The color of the mixture also gradually changed to dark green. Therefore, such redox cycles are proposed to play a part in the catalytic route (Scheme 1): TEMPO is oxidized to $TEMPO^+$ by V^V, and V^V regenerated from V^{IV} in the presence of O_2; then veratryl alcohol is oxidized by $TEMPO^+$. TEMPO acts as a mediator to bridge veratryl alcohol and vanadium species. The combined redox cycles make the oxidation of veratryl alcohol with O_2 run smoothly under mild conditions. However, the mechanism of this catalytic system at a molecular level remains unknown.

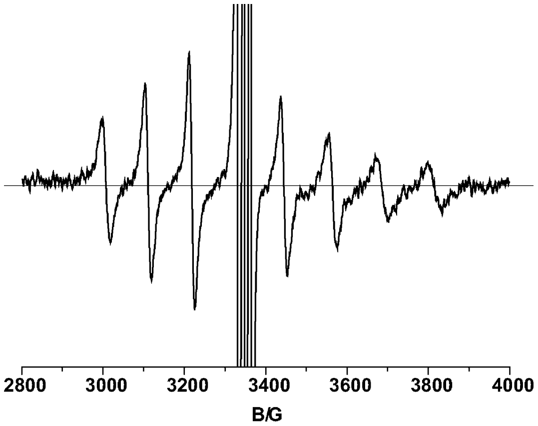
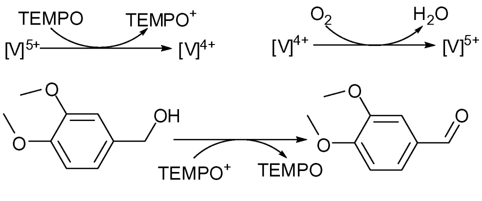


Fig. 3 EPR spectrum of V^{IV} species.



Scheme 1 Proposed redox cycles.

In summary, we have developed $VOPO_4$ in combination with TEMPO for the catalytic oxidation of benzylic alcohols with molecular oxygen using water as a solvent. The presence of phosphorus species was crucial to ensure high efficiency by influencing the form of the vanadium species in water. Based on the findings in this paper, we expect to be able to develop more highly efficient vanadium-based catalytic systems in aqueous media.

Acknowledgements

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Notes and references

‡ The nuclear spin of the V^{IV} is $I = 7/2$, and the EPR lines of mononuclear V^{IV} are split into 8 lines ($2I + 1$). One of the eight lines for V^{IV} overlaps with the strong signal of TEMPO.

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