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Vanadium-catalyzed selective aerobic alcohol oxidation in ionic liquid $[bmim]PF_6$

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Abstract—A selective aerobic oxidation of alcohols into the corresponding aldehydes or ketones was developed by using two-component system $VO(acac)_2$/DABCO in the ionic liquid $[bmim]PF_6$, and the catalysts can be recycled and reused for three runs without any significant loss of catalytic activity.

The catalytic conversion of alcohols to the corresponding aldehydes or ketones is a fundamental transformation in both laboratory and industrial synthetic chemistry.[1] From economic and environmental perspectives, the development of new catalytic oxidation systems with molecular oxygen as terminal oxidant is particularly attractive. The use of molecular oxygen as the primary oxidant has several benefits including low-cost, safety, abundance, and water as the sole final byproduct. Accordingly, many transition metals (mainly copper,[2] palladium,[3] ruthenium,[4] and vanadium[5]) have been used as catalysts for aerobic alcohol oxidation. However, many of these catalytic systems are performed in aromatic, or halogenated hydrocarbon solvents.

On the other hand, much attention has been directed toward the reduction or replacement of volatile organic compounds (VOCs) from the reaction media in the Green Chemistry focus area.[6] A variety of environmentally benign media, such as water,[7] ionic liquids,[8] fluorous solvents,[9] and supercritical fluids,[10] have been promoted as replacements to VOCs. Ionic liquids, composed entirely of ions with low viscosities and melting points typically below 100 °C, have been recognized as promising green solvents due to their unique properties, including low volatility, high polarity, good stability over a wide temperature range, and capacity to dissolve various organic, inorganic, organometallic compounds. Furthermore, the proper choice of cation and anion for an ionic liquid can allow for fine-tuning of their miscibility with water and organic solvents to simplify separation processes by liquid–liquid extraction, with either aqueous or conventional organic solvents. Thus, ionic liquids have not only been extensively studied in the last few years as media for organic synthesis and catalysis,[11] but the use of ionic liquids to immobilize and recycle homogeneous catalysts has been one of the most fruitful areas of ionic liquids research to date. Moreover, many ionic liquids have become commercially available.[12] Notwithstanding the advantages of ionic liquids as reaction media for oxidative processes, their potential in transition-metal catalyzed oxidation has yet to be widely recognized.[13]

In continuation of our interest in exploring green oxidation of alcohols in ionic liquids,[14] we herein report a vanadium-catalyzed selective aerobic oxidation of benzylic and allylic alcohols to aldehydes or ketones with an ionic liquid as the solvent. Furthermore, we demonstrate that the catalytic system can be readily recycled and reused for three runs, without any significant loss of catalytic activity.

The initial investigation started with aerobic oxidation of 4-methoxybenzyl alcohol. In the presence of 5 mol % $VO(acac)_2$ and 10 mol % Et_3N under 1 atm oxygen in the ionic liquid $[bmim]BF_4$ (1-butyl-3-methylimidazolium tetrafluoroborate) at 80 °C, 4-methoxybenzaldehyde was obtained in 37% conversion and 24% isolated yield after 6 h of stirring (Scheme 1). Furthermore, no overoxidized product (4-methoxybenzoic acid) was observed by ^1H NMR of the crude reaction mixture.

Keywords: Aerobic alcohol oxidation; Ionic liquids; $[bmim]PF_6$.

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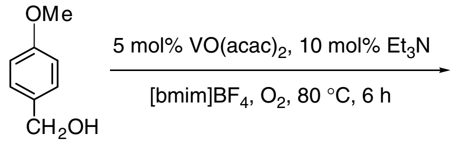


Scheme 1.

Further efforts were then focused on optimizing the reaction conditions, and these results are summarized in Table 1. At first, four imidazolium-type ionic liquids, $[bmim]BF_4$, $[bmim]PF_6$ (1-butyl-3-methylimidazolium hexafluorophosphate), $[bm_2im]BF_4$ (1-butyl-2,3-dimethylimidazolium tetrafluoroborate), and [hmim]OTf (1-hexyl-3-methylimidazolium trifluoromethansulfonate), one pyridinium-type ionic liquid $[bmpy]PF_6$ (1-butyl-4-methylpyridinium hexafluorophosphate), and one pyr-

Table 1. Optimization of the reaction conditions for oxidizing 4-methoxybenzyl alcohol to 4-methoxybenzaldehyde[a]

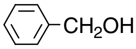
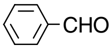
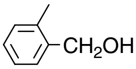
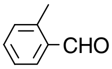
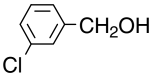
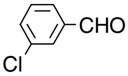
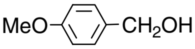
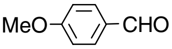
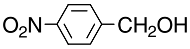
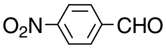
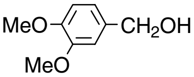
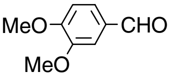
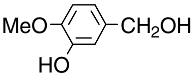
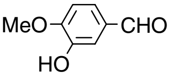
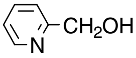
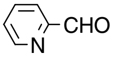
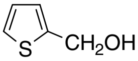
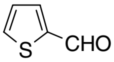
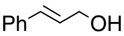
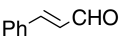
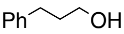
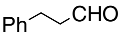
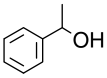
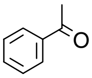
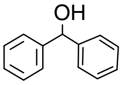
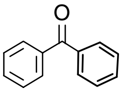
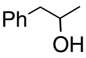
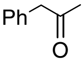
Entry	Ionic liquid	Additive	Convn./sel.[b] (%)	Yield[c] (%)
1	$[bmim]BF_4$	Et_3N	37/>99	24
2	$[bm_2im]BF_4$	Et_3N	31/>99	20
3	[hmim]OTf	Et_3N	52/>99	43
4	$[bmpy]PF_6$	Et_3N	59/>99	51
5	$[bmpyr]NTf_2$	Et_3N	62/>99	49
6	$[bmim]PF_6$	Et_3N	64/>99	58
7	$[bmim]PF_6$	Pyridine	28/>99	17
8	$[bmim]PF_6$	DMAP	51/>99	40
9	$[bmim]PF_6$	DBU	90/45	—
10	$[bmim]PF_6$	DABCO	98/>99	91

[a] Employing 2 mmol 4-methoxybenzyl alcohol, 5 mol % $VO(acac)_2$, 10 mol % additive, 1 atm O_2, and 0.5 g ionic liquid at 80 °C for 6 h.

[b] Conversion and selectivity are determined by ^1H NMR analysis of the crude product mixture.

[c] Isolated yield by flash chromatography.

Table 2. Aerobic oxidation of alcohols in $[bmim]PF_6$[a]

Entry	Alcohols	Time (h)	Products	Convn.[b]/yield[c] (%)
1		6		99/96
2		6		98/90
3		12		100/95
4		6		98/91
5		12 6[d]		22/— 96/85
6		12		96/94
7		12		94/82
8		6[d]		99/91
9		12		100/87
10		9		98/86
11		24[d]		14/—
12		12 6[d]		35/29 94/90
13		6[d]		100/87
14		24[d]		<5/—

[a] Employing 2 mmol alcohol, 5 mol % $VO(acac)_2$, 10 mol % DABCO, and 0.5 g $[bmim]PF_6$ at 80 °C for the appropriate time.

[b] Conversion is determined by ^1H NMR analysis of the crude product mixture.

[c] Isolated yield by flash chromatography.

[d] The reaction was carried out at 100 °C.

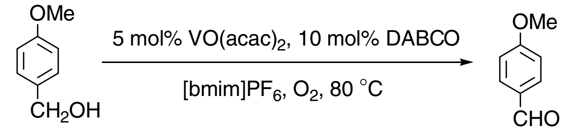
rolidinium-type ionic liquid [bmpyr]NTf_2 (1-butyl-1-methylpyrrolidinium bis(trifluoromethylsulfonyl)imide) were tested with $VO(acac)_2$ as the catalyst and Et_3N as the additive. It is clear that all the ionic liquids gave comparable conversions and isolated yields. In addition, hydrophobic ionic liquids gave better conversion, and [bmim]PF_6 showed to be optimal (Table 1, entries 1–6). Next, select additives including, pyridine, DMAP (4-*N*,*N*-dimethylaminopyridine), DBU (1,8-diazabicyclo-[5.4.0]undec-7-ene), and DABCO (1,4-diazabicyclo-[2.2.2]octane) were screened to improve this transformation. While DBU was found to decrease the selectivity significantly,[15] the others gave excellent selectivity toward the aldehyde (Table 1, entries 6–10). DABCO proves to be the best with 98% conversion and 91% isolated yield.

Subsequently, the catalytic system[16] was then applied to various benzylic, allylic, and aliphatic alcohols, as summarized in Table 2. It is clear that all primary benzylic and allylic alcohols were selectively oxidized into the corresponding aldehydes in excellent conversions and yields (Table 2, entries 1–10). In addition, conversion of electron-rich and electron-neutral benzylic alcohols is faster, and more efficient, with over 98% conversions (Table 2, entries 1–4). However, electron-deficient benzylic alcohol was less reactive, and an elevated temperature was needed to reach good conversion (Table 2, entry 5). The two lignin model compounds (Table 2, entries 6 and 7) could be selectively oxidized into the corresponding aldehydes in excellent conversions and yields which is relevant to our special interest in the oxidation of lignin-like structures.[17] It should also be noted that the heteroatom-containing (S, N) substrates 2-pyridine methanol and 2-thiophene methanol, could be smoothly converted into the aldehydes, in excellent yields (Table 2, entries 8 and 9). However, the aliphatic primary alcohol of 3-phenyl-1-propanol was not reactive, and a very low conversion was obtained even at elevated temperature. Reactive secondary alcohols such as 1-phenylethanol and diphenylmethanol could be oxidized to the corresponding ketones in excellent conversions and isolated yields (Table 2, entries 12 and 13). In contrast, no oxidation was observed with 1-phenyl-2-propanol (Table 2, entry 14).

Next, we examined the recyclability of the two-component catalytic system $VO(acac)_2$/DABCO for the aerobic oxidation of 4-methoxylbenzyl alcohol in the ionic liquid [bmim]PF_6. Due to the good solubility of both $VO(acac)_2$ and DABCO in [bmim]PF_6, the catalytic system could be reused directly for a new cycle, after full extraction of the product with *n*-pentane.[18] The results shown in Table 3 demonstrate that this oxidative system was readily recyclable for three runs, with only a slight drop in catalytic activity.

In conclusion, an efficient aerobic oxidation of various alcohols into aldehydes or ketones by using $VO(acac)_2$–DABCO system has been developed in the ionic liquid [bmim]PF_6. Furthermore, the catalytic system shows excellent selectivity toward oxidation of benzylic and allylic alcohols, and is notably not deactivated by heteroatom-containing (S, N) compounds. Most importantly, the newly developed catalytic system could also be recycled and reused for three runs without any significant loss of catalytic activity.

Table 3. Recycling of the catalytic system for the aerobic oxidation of 4-methoxybenzyl alcohol into aldehyde[a,b]



Run	Time (h)	Conversion[c] (%)	Yield[d] (%)
1	6	98	91
2	6	93	87
3	9	97	92

[a] Employing 2 mmol 4-methoxybenzyl alcohol, 5 mol % $VO(acac)_2$, 10 mol % DABCO, and 0.5 g [bmim]PF_6 at 80 °C for the specific time.

[b] Selectivity is over 99% determined by ^1H NMR analysis of the crude product mixture.

[c] Conversion is determined by ^1H NMR analysis of the crude product mixture.

[d] Isolated yield by flash chromatography.

Acknowledgments

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15. The byproducts are 4-methoxybenzoic acid and 4-methoxybenzyl 4-methoxybenzoate.
16. *A general procedure for aerobic oxidation of 4-methoxybenzylic alcohol follows*: To a solution of 4-methoxybenzyl alcohol (276 mg, 2 mmol) in 0.5 g ionic liquid [bmim]PF_6 were added VO(acac)$_2$ (26.5 mg, 5 mol %) and DABCO (22.4 mg, 10 mol %). The reaction mixture was stirred at 80 °C under O_2 (1 atm) for 6 h, and then extracted with *n*-pentane (5×6 mL). The combined *n*-pentane phase was concentrated in vacuo. The residue was subjected to ^{1}H NMR analysis, and then purified by flash chromatography (*n*-pentane/diethyl ether = 8:1) to afford 4-methoxybenzaldehyde (colorless oil, 247 mg, yield 91%).
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18. It has to be noted that both VO(acac)$_2$ and DABCO are insoluble in *n*-pentane and [bmim]PF_6 is immiscible with *n*-pentane.