



Novel oxidation of toluenes catalyzed by reusable vanadyl(IV) sulfate under mild conditions with molecular oxygen

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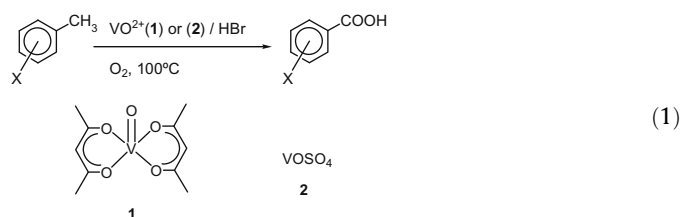
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ABSTRACT

Efficient oxidation system using reusable vanadyl(IV) sulfate catalyst was established. Toluenes were easily oxidized under molecular oxygen (0.1 MPa) at 100 °C catalyzed by vanadyl(IV) sulfate to afford the corresponding benzoic acids in excellent yields. The recovered catalyst could be reused without loss of activity.

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Benzoic acids are synthesized by the oxidation of the corresponding toluenes,^{1,2} and used as important raw materials for various chemicals. For example, huge amount of terephthalic acid from *p*-xylene is provided for fiber and plastic production. Among many methods for the oxidation of toluenes, oxidation using nitric acid or heavy metal peroxides as oxidant is unavoidable toxic waste formation. Because of these problems, oxidation with molecular oxygen (autoxidation) is preferable as a more environmentally friendly method. For the autoxidation in the presence of Co²⁺ catalysts and using *hν*, a lot of preparative methods had been reported.^{3–8} Also, few V₂O₅-catalyzed oxidation of toluenes was also shown.¹ However, V₂O₅ oxidation requires severe reaction conditions (high temperature). Therefore, with our strategy for environmentally friendly aerobic oxidation using commercially available and inexpensive vanadium compounds, we herein wish to report an oxidation of toluenes catalyzed by reusable vanadyl(IV) sulfate (**2**) under mild conditions with molecular oxygen.^{9,10}



A variety of solvents were tested for the oxidation of 4-*tert*-butyltoluene as a model, using vanadyl(IV) acetylacetonate (**1**) catalyst under oxygen atmosphere (0.1 MPa) (Eq. 1 and Table 1). Only acetic acid slightly brought about the oxidation to afford 4-*tert*-butylbenzoic acid (entry 7). In non-acidic solvents, the oxidation was not performed at all, and unchanged 4-*tert*-butyltoluene was recovered

Table 1
Solvent effect on the autoxidation of 4-*tert*-butyltoluene

Entry	Solvent	Catalyst	Temp (°C)	Yield (%)
1	AcOEt	1	80	0
2	AcOMe	1	70	0
3	CH ₃ CN	1	80	0
4	DMF	1	100	0
5	DMSO	1	100	0
6	<i>t</i> -BuOH	1	80	0
7	AcOH	1	100	21
8	AcOH	2	100	22

Reaction conditions: 4-*tert*-butyltoluene (297 mg, 2 mmol), **1** (27 mg, 0.1 mmol) or **2** (22 mg, 0.1 mmol), NaBr (21 mg, 0.2 mmol), O₂ (0.1 MPa), 20 h.

(entries 1–6). It was suggested that VO(IV) catalyst only works under acidic condition in this oxidation. However, under acidic condition, catalyst **1** easily decomposed and gave acetylacetone. Vanadyl(IV) sulfate (**2**), which is fairly stable and does not decompose in acidic solution, shows almost the same reactivity toward the present oxidation, compared with catalyst **1** (entry 8).

Next, the control reactions for the effects of acid and bromide anion were performed (Table 2). Surprisingly, addition of 1 mL of aq H₂SO₄ (1 mol/L) and 1 mmol of NaBr provided 4-*tert*-butylbenzoic acid in 76% yield (entry 1). This result clearly exhibited that addition of acids is essential for the present oxidation, and it was encouraged by us to check the concentrations and amounts of sulfuric acid (entries 1–6 and 10). More than 2 mol/L of concentration and less than 1 mL amount of sulfuric acid were effective for this reaction. Also, suitable amount of NaBr was more than 1 mmol. High temperature (110 °C, close to boiling point) was not suitable for the oxidation and gave 4-*tert*-butylbenzoic acid in unsatisfactory yield, due to low solubility of oxygen gas (entry 11). The necessity of vanadyl(IV) catalyst was confirmed in entry 12. Finally, we successfully found that additive HBr remarkably worked as both acid and bromide anion source to obtain the product in almost quantitative yield (entry 13).

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Table 2
Effects of acid, NaBr, and reaction temperature^a

Entry	Sulfuric acid		NaBr (mmol)	Yield (%)
	(mol/L)	(mL)		
1	1	1	1	76
2	2	1	1	94
3	3	1	1	94
4	4	1	1	93
5	2	0.5	1	93
6	2	2	1	85
7	2	1	0.5	68
8	2	1	1.5	95
9	2	1	2	94
10	0 ^b	1	1	16
11	2 ^c	1	1	58
12	2 ^d	1	1	0
13	3 ^e	0.75	–	98

^a Reaction conditions: 4-*tert*-butyltoluene (1.48 g, 10 mmol), **2** (65 mg, 0.3 mmol), AcOH (10 mL), O₂ (0.1 MPa), 100 °C, 20 h.

^b Water was used instead of sulfuric acid.

^c 110 °C.

^d Without catalyst.

^e Aq HBr was used instead of sulfuric acid.

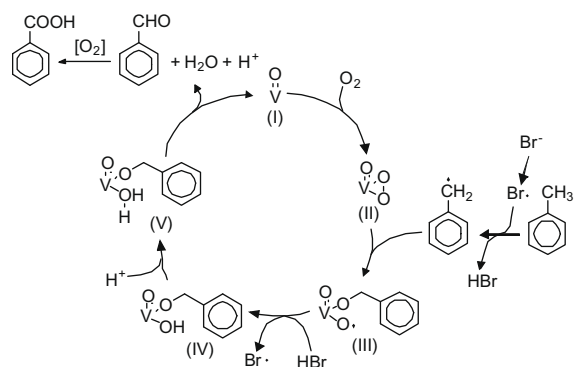
Based on the control experiment given in Table 2, entry 13, the oxidation of various substrates was performed in the presence of catalyst **2** and aq HBr (Table 3).¹¹ The present oxidation was efficiently accomplished for toluenes to provide the corresponding substituted benzoic acids in almost quantitative yields with excellent functional group tolerance from electron-donating to electron-withdrawing groups (entries 1–5 and 7). Also, *p*-xylene was selectively oxidized to terephthalic acid, and *p*-toluic acid was not detected at all (entry 6). This reaction might be a good preparative method for multipoint oxidation.

The role of catalyst (**2**) in this reaction was not clear. However, a plausible reaction path was shown in Scheme 1,^{18,19} based upon the necessity of acid and bromide anion. The bromide radical reacts with toluene to generate benzyl radical. This radical reacts with VO(O₂) complex (II) formed from vanadyl (I) and molecular oxygen to give complex (III). The complex (III) is converted into complex (V) with HBr and proton. By the elimination of the benzaldehyde, water, and proton, vanadyl (I) is regenerated.^{12–14} The obtained benzaldehyde is reoxidized using molecular oxygen with catalyst (**2**) system to form the final benzoic acids.

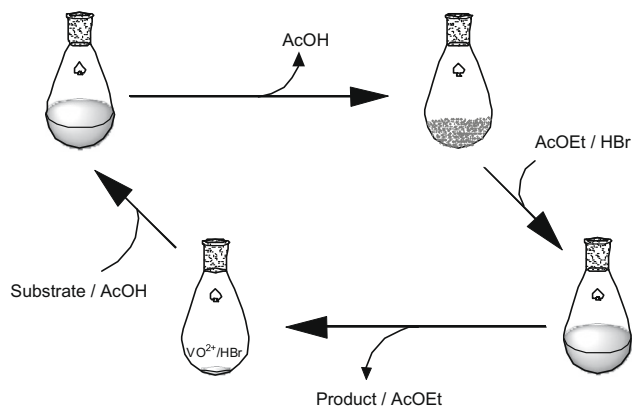
Table 3
Autoxidation of substituted toluenes

Entry	Substrate	Product	Yield (%)
1			98
2			98
3			97
4			96
5			95
6			98
7			97

Reaction conditions: substrate (10 mmol), AcOH (10 mL), **2** (65 mg, 0.3 mmol), aq 3 mol/L HBr (0.75 mL), O₂ (0.1 MPa), 100 °C, 20 h.

**Scheme 1.** A possible reaction path.**Table 4**
Autoxidation in the presence of reused catalyst (**2**)¹⁷

Run	Yield (%)
1	95
2	97
3	94
4	92
5	94

**Scheme 2.** Reuse system of catalyst.

Finally, reusability of catalyst **2** was studied. If aq HBr (3 mol/L, 0.75 mL) is used for the extraction of catalyst, the collected aqueous solution has the same composition as that of the initial VO(IV) solution. Therefore, VO(IV) catalyst could be recovered and reused with no activation. The recovered aqueous solution including catalyst **2** was employed in the next run, and no loss of activity was observed up to five cycles (Table 4).¹⁶ Easy manipulation of recovery and reuse of catalyst **2** in aq HBr were clearly shown in Scheme 2.

In conclusion, useful autoxidation of toluenes to the corresponding benzoic acids catalyzed by VO²⁺ (**2**)/HBr in acetic acid with molecular oxygen under mild conditions (0.1 MPa, 100 °C) was established. The commercially available vanadium catalyst (**2**) was easily recovered and reused repeatedly as aq HBr solution without lowering of activity.

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17. *Recovery and reuse of catalyst for the oxidation of 4-bromotoluene:* 4-Bromotoluene (1.71 g, 10 mmol) and acetic acid (10 mL) were added to the recovered VO^{2+} (**2**)/aq HBr. The mixture was heated to 100 °C for 20 h under O₂ atmosphere (0.1 MPa). After the removal of the solvent from thereaction mixture, AcOEt (100 mL) and aq HBr (3 mol/L, 0.75 mL) were added to the residue. The evaporation of the solvent of organic phase and recrystallization gave 4-bromobenzoic acid in a pure form. The water phase with VO(IV) (**2**) could be reused for next oxidation without any manipulation.
18. A referee pointed out the possibility that vanadium participates in the generation of bromide radical. We cannot deny the opinion. But we think that proper mechanism is similar to the one already reported. Therefore, we selected the mechanism described in Scheme 1.
19. A referee pointed out insufficient novelty and urgency. However, few Letters are reported for the oxidation of toluene-catalyzed vanadyl(IV) compound (many kinds of vanadium-catalyzed oxidation are reported for the other substrates, alcohols, olefines, etc.). Therefore, we believe that the paper is worth publishing as a Letter.