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Chromium(VI) Oxide-Catalyzed Benzylic Oxidation with Periodic Acid

Shigekazu Yamazaki

Toyama Industrial Technology Center, 150 Futagami, Takaoka,
Toyama 933-0981, Japan

s-yamazk@itc.pref.toyama.jp

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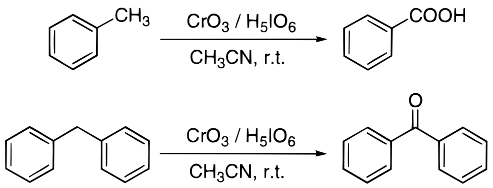
ABSTRACT



CrO_3 has been found to be an efficient catalyst for benzylic oxidation with periodic acid as the terminal oxidant in acetonitrile. Substituted toluenes with an electron-withdrawing group at the 4- or 3-position and diarylmethanes such as diphenylmethane and fluorene were oxidized to the corresponding substituted benzoic acids and ketones in excellent yields. Benzyl ethers such as isochroman and phthalan were converted to 3,4-dihydroisocoumarin and phthalide in quantitative yields.

Oxidations are of fundamental importance to synthetic organic chemistry, and numerous methods are reported in the literature.[1,2] The laboratory-scale liquid-phase benzylic oxidations are generally carried out with a large excess of metal oxidants such as chromium reagents and manganese reagents.[2] Since the metal residues are environmentally undesirable and often provide problems during reaction and workup, development of oxidizing methods requiring only a catalytic amount of metal reagent in combination with appropriate stoichiometric oxidant is a subject of interest. There are reports on the catalytic methods for benzylic oxidation including CrO_3/*t*-BuOOH,[3] heterogeneous chromium catalysts/*t*-BuOOH,[4] $Cr(CO)_6$/*t*-BuOOH,[5] heteropolyoxometalate/O_2,[6] *N*-hydroxyphthalimide/O_2,[7] $CoCl_2$/O_2,[8] cobalt Schiff base complexes/O_2,[9] Mn(salen)/NaOCl,[10] $RuCl_3$/NaOCl,[11] $RuCl_2(PPh_3)_3$/*t*-BuOOH,[12] $Ni(bpy)_2Cl_2$/NaOCl,[13] and CeO_2/$NaBrO_3$.[14] However, these methods have disadvantages and limitations, and new oxidation methods are still desired.

Recently the Merck group reported a novel CrO_3-catalyzed oxidation of primary and secondary alcohols to carboxylic acids and ketones with H_5IO_6 as the terminal oxidant.[15] We

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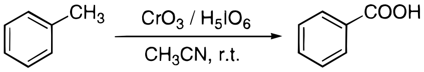
now report that CrO_3/H_5IO_6 acts as an efficient catalytic system for the oxidation of toluenes, alkylbenzenes, and cyclic benzyl ethers to the corresponding benzoic acids, ketones, and lactones.

First, the influence of the amount of catalyst and oxidant on the oxidation of toluene was examined. The results are summarized in Table 1. The reactions were performed by addition of toluene to a stirring solution of H_5IO_6 and CrO_3 in acetonitrile at room temperature. The only isolated product was benzoic acid, and the remainder of the reaction mixture was toluene only. The yields indicated in Table 1 are based on the amount of toluene used. The use of a relatively low amount of catalyst (2–10 mol %) resulted in a low yield of benzoic acid (entries 1–3), and the use of an amount of catalyst larger than 20 mol % gave a high yield of the product (entries 6 and 9). The use of 3.5 equiv of H_5IO_6 maximized the yield of benzoic acid (entries 4–6), and the use of a larger amount of oxidant than 3.5 equiv did not increase the yield of benzoic acid (entries 7 and 8).

Table 1. CrO_3-Catalyzed Oxidation of Toluene with H_5IO_6[a]



entry	CrO_3, mol %	H_5IO_6, equiv	time, h	benzoic acid, %[b]
1	2	3.5	1	33
2	5	3.5	1	49
3	10	3.5	1	67
4	20	2	1	54
5	20	3	1	72
6	20	3.5	1	79
7	20	5	3	76
8	20	8	3	76
9	50	3.5	1	85

[a] Reaction at room temperature in acetonitrile. [b] Isolated yields based on toluene used. The remaining material is essentially toluene.

Oxidation of various substituted toluenes was examined by this catalytic system. The results are summarized in Table 2. The toluenes substituted at the 4-position by electron-withdrawing groups such as nitro, chloro, bromo, and cyano groups were oxidized smoothly to the corresponding benzoic acids in excellent yields (entries 1 and 4–6). 3-Nitrotoluene was also oxidized to the corresponding benzoic acid in excellent yield (entry 2). The partial oxidations of dimethylbenzenes were observed. Oxidation of *p*-xylene gave a mixture of *p*-toluic acid and terephthalic acid in yields of 86% and 6%, respectively (entry 7). *o*-Xylene afforded 61% of *o*-toluic acid and 4% of phthalic acid (entry 8). On the other hand, 2-nitrotoluene, toluene substituted at the 2-position, was oxidized to 2-nitrobenzoic acid in only 31% yield under the same reaction conditions as those for the reaction of 4- or 3-nitrotoluene (entry 3). Oxidation of 4-methylanisol, an electron-rich toluene, gave a low yield of *p*-anisic acid (34%) along with a small amount of benzaldehyde (entry 9).

Table 2. CrO_3-Catalyzed Oxidation of Substituted Toluenes with H_5IO_6[a]

entry	toluenes	convn, %	benzoic acids, %[b]
1	4-NO_2	100	92
2	3-NO_2	100	93
3	2-NO_2	70	31
4	4-Cl	100	89
5	4-Br	100	90
6	4-CN	100	84
7	4-CH_3	95	86[c]
8	2-CH_3	88	61[d]
9	4-OCH_3	68	34[e]

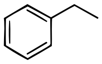
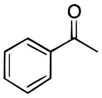
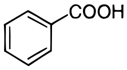
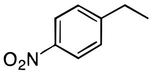
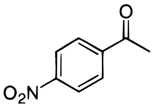
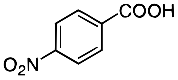
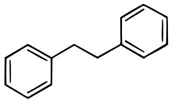
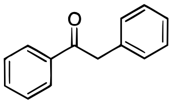
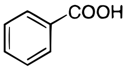
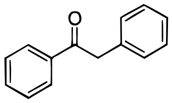
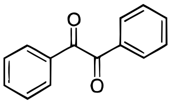
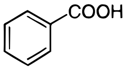
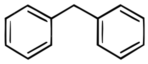
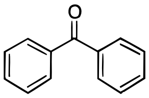
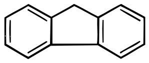
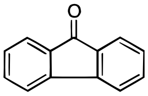
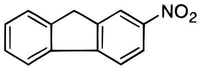
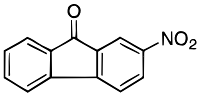
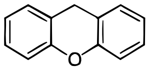
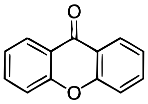
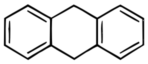
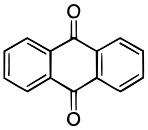
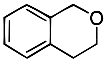
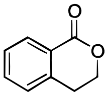
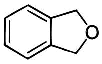
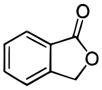
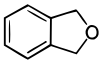
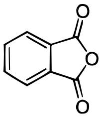
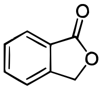
[a] Reaction conditions: at room temperature in acetonitrile for 1 h. Substrate/H_5IO_6/CrO_3 = 1/3.5/0.2. [b] Isolated yields of substituted benzoic acids based on toluenes used. [c] Terephthalic acid was also obtained in 6% yield. [d] Phthalic acid was also obtained in 4% yield. [e] 4-Methoxybenzaldehyde 7%.

The stoichiometric chromium oxidants effectively oxidize toluenes substituted by either electron-withdrawing or -donating groups to the corresponding benzoic acids.[2] However, in general, these reactions require high temperatures and long reaction times. Although the catalytic oxidations of toluenes by heterogeneous chromium catalysts absorbed on insoluble supports were reported,[4a,c] these reactions require high temperatures (reflux of solvent) and long reaction times (20–45 h). The method for toluene oxidation described here proceeds at room temperature and is generally completed within 1 h.

The results of the oxidation of various benzylic compounds were indicated in Table 3. Ethylbenzene was oxidized to acetophenone (49%) and benzoic acid (35%) (entry 1). The oxidation of 4-nitroethylbenzene afforded 4-nitroacetophenone (74%) along with a small amount of 4-nitrobenzoic acid (18%) (entry 2). The oxidation of bibenzyl produced 48% of benzyl phenyl ketone (entry 3). Benzyl phenyl ketone was further oxidized under the same conditions to benzil in 61% yield with a considerable amount of benzoic acid (entry 4). One of the drawbacks of this method is the formation of a considerable amount of benzoic acid as the byproduct in the oxidation of the substrates such as ethylbenzene and bibenzyl. Heterogeneous chromium-catalyzed oxidations[4] have been reported to give higher yields of ketones than those described here in the oxidation of ethylbenzene and bibenzyl without the formation of benzoic acid.

The oxidation of diarylmethanes afforded excellent results. Diphenylmethane was oxidized to benzophenone quantitatively with only a 0.02 M amount of catalyst (entry 5). Fluorene, 2-nitrofluorene, and xanthene were converted to the corresponding ketones in 90%, 100%, and 99% yield, respectively (entries 6–8). 9,10-Dihydronaphthalene was oxidized to the corresponding diketone, 9,10-naphthoquinone, in 92% yield by using a 7 M amount of oxidant (entry 9). Although chromium-catalyzed oxidations of benzylic methylenes by homogeneous[3,5] and heterogeneous[4] systems have been reported, these reactions require a large excess of the oxidant,[3] a high temperature,[4b,c,5] and a long reaction period.[3–5] The oxidation method described here is advanta-

Table 3. CrO_3-Catalyzed Oxidation of Benzylic Methylenes with H_5IO_6[a]

entry	substrate	CrO_3	H_5IO_6	time	conv	product
		mol %	mol equiv	min	%	(%)[b]
1		2	2.5	60	100	 (49)  (35)
2		5	3.0	60	100	 (74)  (18)
3		5	2.5	30	88	 (48)[c]  (16)
4		10	3.5	30	>99	 (61)  (30)
5		2	2.5	60	100	 (99)
6		7	3.5	30	100	 (90)
7		5	3.5	60	100	 (100)
8		5	3.5	30	100	 (99)
9		5	7.0	30	100	 (92)
10		1	2.05	10	100	 (99)
11		1.2	2.01	15	100	 (99)
12		5	5.0	15	100	 (87)  (7)

[a] All the reactions were performed at room temperature in acetonitrile. [b] Isolated yields based on starting materials used. [c] Benzil was also isolated in 6%.

geous to those reactions because the reaction proceeds at room temperature with a small excess of oxidant within a short reaction period.

Cyclic benzyl ethers were also oxidized to the corresponding lactones in excellent yields. Isochroman was oxidized to 3,4-dihydroisocoumarin quantitatively by using 2.05 equiv of oxidant and 1 mol % of catalyst (entry 10). Phthalan was also oxidized to phthalide quantitatively with 1.2 mol % of catalyst and 2.01 equiv of oxidant (entry 11). On the other hand, the oxidation of phthalan using 5 equiv of oxidant and 5 mol % of catalyst afforded 87% of phthalic anhydride with

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7% of phthalide (entry 12). Though there have been a few report on the catalytic oxidation of cyclic benzyl ethers, the present oxidation is superior to those oxidations in the yields of products, lower reaction temperature, and short reaction time.[6,7,16,17]

In summary, CrO_3 has been found to be an efficient catalyst for benzylic oxidation with H_5IO_6 as the terminal oxidant in acetonitrile. Specifically, substituted toluenes with an electron-withdrawing group at the 4- or 3-position, diarylmethanes, and cyclic benzyl ethers were oxidized to the corresponding substituted benzoic acids, ketones, and lactones in good to quantitative yield. The use of easily accessible commercial reagents, the simple operation, the rapid reaction rate at room temperature, and the formation of product in excellent yield make this method more useful than existing procedures.[18]

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(18) A typical procedure is as follows: H_5IO_6 (1.69 g, 7.43 mmol) was dissolved in acetonitrile (25 mL) by vigorous stirring, and then CrO_3 (5.9 mg, 0.059 mmol) was dissolved into the solution. Diphenylmethane (0.500 g, 2.97 mmol) was added to the above solution with stirring. A white precipitate formed immediately with exothermic reaction. After 1 h of stirring, the supernatant liquid of the reaction mixture was decanted to a flask, and the solvent was removed by evaporation. The residues after decantation and evaporation were dissolved in H_2O and CH_2Cl_2, combined, and then extracted with CH_2Cl_2 (10 mL × 2). The organic layer was washed successively with aqueous $NaHSO_3$ and brine and then dried over anhydrous Na_2SO_4. The solvent was distilled off under a reduced pressure. The obtained residue was benzophenone (0.535 g, 99%) which was pure by ^1H NMR and GC analyses.