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Aerobic photo-oxidation in the presence of catalytic allylbromide

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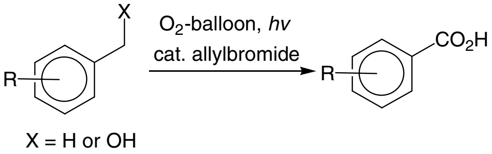
Abstract—Alkyl groups at aromatic nucleus and alcohols were found to be photo-oxidized to the corresponding carboxylic acid in the presence of catalytic allylbromide.

The notion of green chemistry is becoming well established in organic chemistry, and the development of environmentally benign processes is the goal of various research projects.[1] Oxidation is the foundation of synthetic chemistry, and recent methodology using molecular oxygen is one way consistent with this notion due to its high atomic effect or *E*-factor as an oxidant.[2,3] With this background in mind, we have been engaged in aerobic photo-oxidation of alcohols and a methyl group at the aromatic nucleus in the presence of organic or inorganic bromo sources.[4,5] We believe that the bromo radical, formed by continuous aerobic photo-oxidation of the bromo anion, promotes these reactions. Regarding the organic bromo source, we have already reported a method with *N*-bromosuccinimide;[4] however, in this reaction, generation of succinimide is unavoidable and additional post-treatment is necessary to remove it. This is the driving force of our further studies on this oxidation with a new non-metal organic bromo source, which releases the bromo anion easily, and the organic group residue does not remain in the reaction mixture, and we have found that allylbromide is suitable for this purpose. Thus, we now report our detailed study on the generality of aerobic oxidation of alcohols and an aromatic methyl group in the presence of a catalytic amount of allylbromide (Scheme 1).

Table 1 shows the results of our study of reaction conditions for the aerobic oxidation conducted with 4-*tert*-butyltoluene (**1**, 0.3 mmol) as test substrate in the presence of allylbromide in typical solvents equipped with an oxygen balloon under irradiation by a 500 W xenone lamp.[6] Among the solvents and the amount of allylbromide examined, ethyl acetate and 0.3 equiv of allylbromide were found to be suitable for the reaction. Furthermore, the residue arising from the allyl group could not be detected by NMR.



Scheme 1.

Table 2 shows the results of our study on the scope and limitation of this oxidation conducted with several substrates under the reaction conditions mentioned above. Regarding oxidation of the aromatic alkyl group, an electron-donating group at the aromatic nucleus accelerates the reaction, and afforded the corresponding carboxylic acids in high yield; however, electron-withdrawing groups retarded the reaction, and yields of the products were zero to moderate (entries 1–7). 2-Methylnaphthalene afforded a trace amount of 2-naphthoic acid, and cleavage of the carbon–carbon bond was observed when using propyl benzene (**17**) as the substrate, and afforded **4** in 51% yield (entries 8 and 9). Benzyl alcohols show similar reactivity to aromatic methyl group mentioned above, and an electron-donating group at the aromatic nucleus was found to accelerate the reaction and an electron-withdrawing group retarded the reaction (entries 10–13). On the other hand, dodecanol (**23**), an aliphatic alcohol, unfortunately, was intact under this condition, and the starting material was recovered quantitatively (entry 14).

Keywords: Aerobic photo-oxidation; Alcohols; Allylbromide; Alkyl groups at aromatic nucleus; Carboxylic acids.

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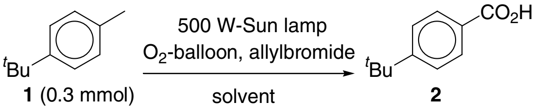
Table 1. Study of reaction conditions of aerobic photo-oxidation



1 (0.3 mmol) **2**

Entry	Equivalent	Solvent	Time (h)	Yield[a] (%)
1	0.1	EtOAc	10	38
2	0.2	EtOAc	10	81
3	0.3	EtOAc	10	90
4	0.5	EtOAc	10	88
5	0.3	EtOAc	7	66
6	0.3	MeCN	10	41
7	0.3	Acetone	10	0
8	0.3	MeOH	10	0
9	0.3	Hexane	10	Trace

[a] All yields are for pure, isolated products.

We present in Scheme 2 what we assume is a plausible path of this oxidation, which is postulated by considering the necessity of a catalytic amount of allylbromide and of molecular oxygen in this reaction. The radical species **24** is thought to be generated by abstraction of a hydrogen radical with a bromo radical, formed by continuous aerobic photo-oxidation of the bromo anion from allylbromide (Scheme 2, Eqs. 1–3). Then, bromine was formed by aerobic photo-oxidation of hydrogen bromide, which is generated in Eq. 3, and bromo radical was generated under photo-irradiation condition (Eqs. 4 and 5). Hydroperoxide **26** was afforded through peroxiradical **25**, which was generated by the reaction of **24** with molecular oxygen (Eqs. 6 and 7). Aldehyde **27** was given by dehydration from **26**, and the re-generated bromo radical abstracted the hydrogen radical from **27**

Table 2. Aerobic photo-oxidation of alkyl group at aromatic nucleus in the presence of allylbromide

$$\text{substrate} \xrightarrow[\text{EtOAc, 10 h}]{\substack{h\nu\text{ (500 W-Sun lamp), O}_2\text{-balloon} \\ \text{allylbromide (0.3 equiv.)}}} \text{product}$$

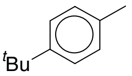
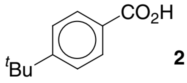
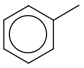
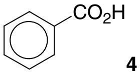
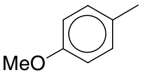
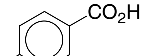
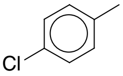
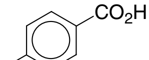
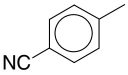
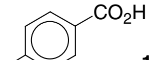
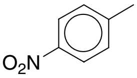
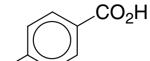
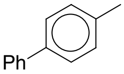
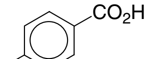
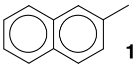
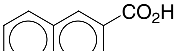
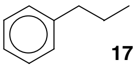
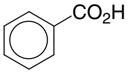
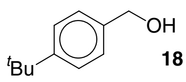
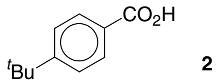
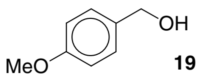
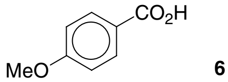
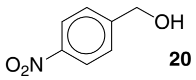
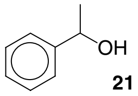
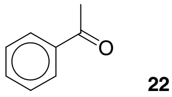
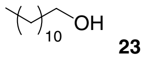
Entry	Substrate	Product	Yield[a] (%)
1	 **1**	 **2**	90
2	 **3**	 **4**	72
3	 **5**	 **6**	79
4	 **7**	 **8**	80[b]
5	 **9**	 **10**	57[b]
6	 **11**	 **12**	0[b,c]
7	 **13**	 **14**	50
8	 **15**	 **16**	Trace[d]
9	 **17**	 **4**	51

Table 2 (*continued*)

Entry	Substrate	Product	Yield[a] (%)
10	 **18**	 **2**	83
11	 **19**	 **6**	75
12	 **20**	—	0[e]
13	 **21**	 **22**	47
14	 **23**	—	0

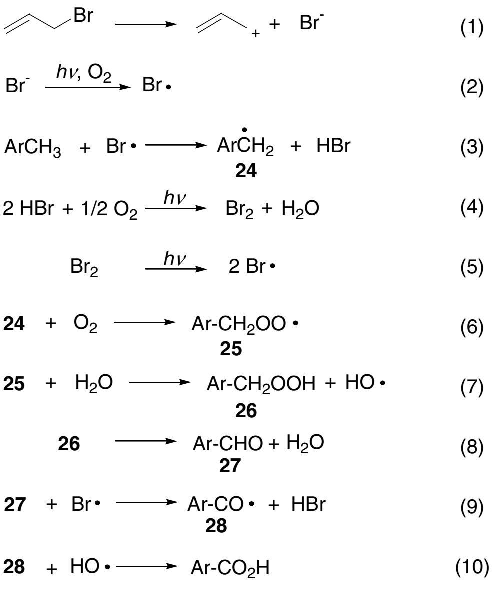
[a] All yields are for pure, isolated products.

[b] The reaction was carried out for 24 h.

[c] A total of 59% of **11** was recovered.

[d] The reaction was carried out for 48 h.

[e] A total of 9% of 4-nitrobenzaldehyde was obtained.



$$CH_2{=}CHCH_2Br \longrightarrow CH_2{=}CHCH_2^{+} + Br^{-} \quad (1)$$

$$Br^{-} \xrightarrow{h\nu,\ O_2} Br\bullet \quad (2)$$

$$ArCH_3 + Br\bullet \longrightarrow Ar\dot{C}H_2\ (\mathbf{24}) + HBr \quad (3)$$

$$2\,HBr + 1/2\,O_2 \xrightarrow{h\nu} Br_2 + H_2O \quad (4)$$

$$Br_2 \xrightarrow{h\nu} 2\,Br\bullet \quad (5)$$

$$\mathbf{24} + O_2 \longrightarrow Ar\text{-}CH_2OO\bullet\ (\mathbf{25}) \quad (6)$$

$$\mathbf{25} + H_2O \longrightarrow Ar\text{-}CH_2OOH\ (\mathbf{26}) + HO\bullet \quad (7)$$

$$\mathbf{26} \longrightarrow Ar\text{-}CHO\ (\mathbf{27}) + H_2O \quad (8)$$

$$\mathbf{27} + Br\bullet \longrightarrow Ar\text{-}CO\bullet\ (\mathbf{28}) + HBr \quad (9)$$

$$\mathbf{28} + HO\bullet \longrightarrow Ar\text{-}CO_2H \quad (10)$$

Scheme 2. Plausible path for aerobic oxidation of methyl group at aromatic nucleus.

to give radical species **28** (Eqs. 8 and 9).[7] The carboxylic acid was formed by reaction with hydroxy radical, generated in Eq. 7 (Eq. 10).[8] The final structure arising from the allyl cation, which is shown in Eq. 1, is not clear yet; we believe the product could not be detected in the reaction mixture due to its low boiling point.[9]

In conclusion, we have found a facile oxidation of an alkyl group at the aromatic nucleus and alcohols in the presence of a catalytic amount of allylbromide under irradiation of a xenon lamp. This method is more useful than that using *N*-bromosuccinimide from the viewpoint of easy post-treatment and the use of inexpensive reagent.

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2. For recent examples of oxidation of alcohols to the corresponding carboxylic acids with molecular oxygen, see: (a) Figiel, P. J.; Sobczak, J. M.; Ziolkowski, J. J. *Chem. Commun.* **2004**, 244–245; (b) Ebitani, K.; Ji, H.-B.; Mizugaki, T.; Kaneda, K. *J. Mol. Catal. A: Chem.* **2004**, *212*, 161–170; (c) Baucherel, X.; Gonsalvi, L.; Arends, I. W. C. E.; Ellwood, S.; Sheldon, R. A. *Adv. Synth. Catal.* **2004**, *346*, 286–296; (d) Matsumura, Y.; Yamamoto, Y.; Moriyama, N.; Furukubo, S.; Iwasaki, F.; Onomura, O. *Tetrahedron Lett.* **2004**, *45*, 8221–8224; (e) Uozumi, Y.; Nakao, R. *Angew. Chem., Int. Ed.* **2003**, *42*, 194–197; (f) Ji, H.; Mizugaki, T.; Ebitani, K.; Kaneda, K. *Tetrahedron Lett.* **2002**, *43*, 7179–7183; (g) Bjorsvik, H.-R.; Liguori, L.; Merinero, J. A. V. *J. Org. Chem.* **2002**, *67*, 7493–7500; (h) Cicco, S. R.; Latronico, M.; Mastrorilli, P.; Suranna, G. P.; Nobile, C. F. *J. Mol. Catal. A: Chem.* **2001**, *165*, 135–140; (i) Jenzer, G.; Schneider, M. S.; Wandeler, R.; Mallat, T.; Baiker, A. *J. Catal.* **2001**, *199*, 141–148; (j) Ishii, Y.; Sakaguchi, S.; Iwahama, T. *Adv. Synth. Catal* **2001**, *343*, 393–427, and references cited therein.
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6. When using primary alcohol as the substrate, a typical procedure follows: a solution (5 mL) of the substrate (0.3 mmol) and allyl bromide (0.3 equiv) in dry EtOAc in a pyrex glass test tube fitted with an O_2-balloon was stirred and irradiated at rt with a 500 W xenon lamp externally for the indicated time. The reaction mixture was concentrated under reduced pressure, and 10% NaOH aq solution was added. The aqueous solution was washed with Et_2O, and then acidified with 6% HCl aq solution, which was extracted with Et_2O. The organic layer was washed with brine and dried over Na_2SO_4, and concentrated under reduced pressure. The product was pure without further purification. When using secondary alcohol as the substrate, a typical procedure follows: a solution (5 mL) of the substrate (0.3 mmol) and allylbromide (0.3 equiv) in dry EtOAc was stirred and irradiated at rt with a 500 W xenon lamp externally for the indicated time. The reaction mixture was concentrated under reduced pressure, and 10% NaOH aq solution was added. The aqueous solution was washed with Et_2O and the organic layer was concentrated, and the residue was purified by preparative TLC.
7. Minisci, F.; Porta, O.; Recupero, F.; Punta, C.; Gambarotti, C.; Pierini, M.; Galimberti, L. *Synlett* **2004**, 2203–2205.
8. Aldehydes can be oxidized to the corresponding carboxylic acids under the same conditions. 4-*tert*-Butylbenzoic acid (78%) was obtained when using 4-*tert*-butylbenzaldehyde as a substrate.
9. Although we tried to detect the by-product arising from bromo source by using cinnamyl bromide instead of allyl bromide, only benzoic acid, which possesses no allyl residue, was obtained.