

# Synthesis of Benzoic Acids by Aerobic Photooxidation with Hydrobromic Acid

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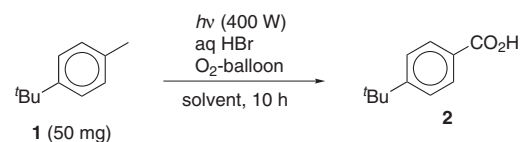
**Abstract:** A methyl group at an aromatic nucleus is oxidized directly to the corresponding carboxylic acid in the presence of molecular oxygen and catalytic hydrobromic acid under photoirradiation.

**Key words:** aerobic, benzoic acid, hydrobromic acid, methyl group, photooxidation

Oxidation, especially introduction of oxygen-containing functional groups to hydrocarbon, is a fundamental and most important reaction in the synthesis of a large number of chemicals from fossil fuel. However, most of them involve the use of large quantities of heavy metals which results in the discharge of considerable amounts of contaminants, and are not at all environmentally benign.<sup>1</sup> With this background in mind, we discovered in the course of our study of photooxidation that 4-*tert*-butyltoluene (**1**) is oxidized directly to 4-*tert*-butyl benzoic acid (**2**) in ethyl acetate in an oxygen atmosphere in the presence of LiBr.<sup>2</sup> The mechanism of this reaction has not yet been determined; however, we believe that HBr is formed in situ from a bromo radical, which is formed under irradiation from LiBr, and a hydrogen radical, which is abstracted from the benzylic position. If addition of hydrobromic acid, which is an inexpensive and easily handled reagent as an aqueous solution of HBr, is enough to effect the oxidation, this reaction is expected to be a useful and convenient oxidation method in view of the use of molecular oxygen as the terminal oxidant and the non-requirement of environmentally detrimental heavy metals and halogenated solvents.<sup>3</sup> In this letter we report in detail our investigation of the generality of this aerobic photooxidation of a methyl group at the aromatic nucleus with hydrobromic acid.

Table 1 shows our initial study of the reaction conditions of the aerobic photooxidation, which was carried out using 4-*tert*-butyltoluene (**1**, 50 mg, 0.269 mmol) as a test substrate with hydrobromic acid in various solvents. We do not know the reason, however, ethyl acetate was found to be the most suitable solvent for this reaction among the typical solvents examined. Since the yield of **2** was almost quantitative when more than 0.2 equivalents of hydrobromic acid with reference to **1** were used, we usually used this amount of hydrobromic acid for the subsequent experiments. That no oxidation proceeded without either ir-

**Table 1** Study of Reaction Conditions of Aerobic Photooxidation



Entry	aq HBr (equiv)	Solvent	Yield of <b>2</b> (%) <sup>a</sup>
1	0.14	Hexane	49
2	0.14	Acetone	51
3	0.14	MeCN	51
4	0.14	<i>i</i> -Pr <sub>2</sub> O	0
5	0.14	EtOAc	93
6	0.10	EtOAc	65
7	0.20	EtOAc	98
8	0.30	EtOAc	96
9	0.40	EtOAc	91
10	0.50	EtOAc	100

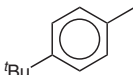
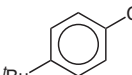
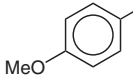
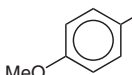
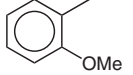
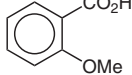
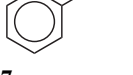
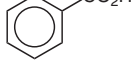
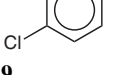
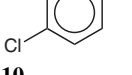
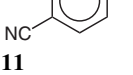
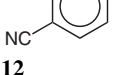
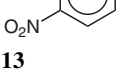
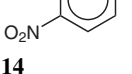

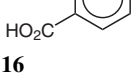
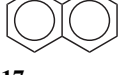



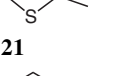
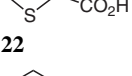
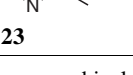
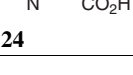
<sup>a</sup> All yields are for pure and isolated products.

radiation of UV or the addition of hydrobromic acid shows the necessity of both for this reaction.

Table 2 shows the results for the oxidation of several substrates under the reaction conditions outlined above. Although an electron-donating group, such as a *tert*-butyl group or a methoxy group at an aromatic nucleus, in general, enhanced the reaction rate, an electron-withdrawing group, such as a cyano or a chloro group, retarded the reaction rate, and gave the corresponding benzoic acid in modest yield (entries 1–6). Especially when 4-nitrotoluene (**13**) was used, no product **14** was obtained after ten hours; however, a 87% yield of **14** was obtained after 36 hours (entry 7). *p*-Xylene (**15**) a polymethylbenzene, was oxidized to terephthalic acid (**16**) in 52% yield in the presence of 0.4 equivalents of HBr. 1-Methylnaphthalene and 2-methylnaphthalene (**17** and **19**) afforded the naphthoic acids **18** and **20**, respectively in high yields. Furthermore, 2-methylthiophene (**21**), a heterocyclic compound, afforded the corresponding carboxylic acid **22** in modest yield. However, a trace amount of **24** was detected when 2-picolone (**23**) was used as the substrate.

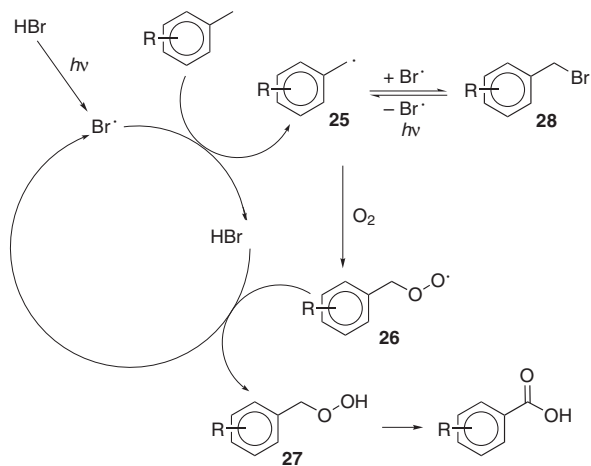
We believe that the benzyl radical species **25** is generated by abstraction of a hydrogen radical with a bromo radical,

**Table 2** Aerobic Photooxidation for Aromatic Methyl Groups

substrate (0.3 mmol)	$h\nu$ (400 W), O <sub>2</sub> -balloon aq HBr EtOAc (5 mL), 10 h	product	
Entry	Substrate	aq HBr (equiv)	Product (%) <sup>a</sup>
1	 <b>1</b>	0.2	 <b>2</b> (98)
2	 <b>3</b>	0.2	 <b>4</b> (87)
3	 <b>5</b>	0.5	 <b>6</b> (92)
4	 <b>7</b>	0.2	 <b>8</b> (46) <sup>b</sup>
5	 <b>9</b>	0.2	 <b>10</b> (50) <sup>b</sup>
6	 <b>11</b>	0.2	 <b>12</b> (53) <sup>c</sup>
7	 <b>13</b>	0.2	 <b>14</b> (87) <sup>d</sup>
8	 <b>15</b>	0.4	 <b>16</b> (52) <sup>e</sup>
9	 <b>17</b>	0.2	 <b>18</b> (76)
10	 <b>19</b>	0.2	 <b>20</b> (92)
11	 <b>21</b>	0.2	 <b>22</b> (46)
12	 <b>23</b>	0.2	 <b>24</b> (trace)

<sup>a</sup> All yields are for pure and isolated products.<sup>b</sup> Starting material, which could not be recovered because of its volatility, remained after the reaction.<sup>c</sup> Unidentified by-products were generated.<sup>d</sup> The reaction was carried out for 36 h.<sup>e</sup> Compound **16** (39%) was obtained when HBr (0.2 equiv) was used.

that was from HBr under irradiation. The radical species traps molecular oxygen to afford the peroxyradical **26**, which gives hydroperoxide **27** and regenerates the bromo radical. However, **25** is presumed to be quenched by the bromo radical easily to afford benzyl bromide **28**,<sup>4</sup> which is cleaved to **25** and the bromo radical again under photoirradiation, since discontinuance of irradiation prevents progress of the reaction (Scheme 1).



**Scheme 1** Possible path of the aerobic photooxidation of methyl group at aromatic nucleus

In conclusion, we have found a useful method for the synthesis of benzoic acids with hydrobromic acid, which uses safe and inexpensive reagents under aerobic UV irradiation. This novel method is thought to be facile and convenient in view of the use of inexpensive hydrobromic acid.

Further study of application of this photooxidation to other organic compounds is now in progress in our laboratory.

All reactions were carried out under an oxygen atmosphere. All of the products are known compounds and were identified by comparing their <sup>1</sup>H NMR spectra (400 MHz on a JEOL AL-400 spectrometer) with those of the authentic samples.

#### Oxidation of **1**; Typical Procedure

A solution (5 mL) of the substrate (0.3 mmol) and hydrobromic acid in anhyd EtOAc was stirred in a test tube fitted with an O<sub>2</sub> balloon (1 atm), and was irradiated externally at r.t. with a 400 W high-pressure mercury lamp for the indicated time. The reaction mixture was concentrated under reduced pressure, and a 10% aq NaOH solution was added. The aqueous solution was washed with Et<sub>2</sub>O, and was then acidified with 2 N aq HCl solution, which was then extracted with Et<sub>2</sub>O. The organic layer was washed with brine, dried over MgSO<sub>4</sub>, and concentrated under reduced pressure. The product was found to be pure and therefore, no further purification was required.

#### References

- (1) *Comprehensive Organic Transformations: A Guide to Functional Group Preparations*; Larock, R. C., Ed.; Wiley-VCH: New York, **1999**.
- (2) Itoh, A.; Hashimoto, S.; Kodama, T.; Masaki, Y. *Synlett* **2005**, 2107.
- (3) Photooxidation of alkylbenzene in the presence of hydrobromic acid under oxygen has been previously reported; however, the corresponding carboxylic acids were obtained in very low yields, see: Nakada, M.; Fukushi, S.; Hirota, M. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 944.
- (4) A trace amount of 4-*tert*-butylbenzyl bromide was detected in the reaction mixture when **1** was used as a substrate.