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Photo-Oxidation of Aldehydes with Molecular Oxygen in the Presence of Catalytic Bromine or Hydrobromic Acid

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Aldehydes were found to be oxidized with molecular oxygen to the corresponding carboxylic acid in the presence of catalytic hydrobromic acid or bromine under photo-irradiation.

Key words aldehyde; bromine; hydrobromic acid; molecular oxygen; photo-oxidation

The notion of green chemistry is becoming well established, and the development of environmentally benign processes is the goal of various research projects.[1] The method using molecular oxygen is one way consistent with this notion due to its high atomic effect or E-factor as an oxidant. With this background in mind, we have been engaged in aerobic photo-oxidation of alcohols and a methyl group at the aromatic nucleus with several bromo sources.[2—8] In the course of our further study for expanding application of this reaction, aldehydes were found to be oxidized to the corresponding carboxylic acids in the presence of catalytic lithium bromide.[9] Although lithium bromide is undoubtedly an inexpensive and safe reagent, it is not necessarily easy to handle due to its hygroscopic property and the promoting effect of lithium bromide is presumed to be lower than that of other bromo sources, bromine or hydrobromic acid, by our previous experiments.[3—7] Herein, we report in detail our study on the generality and limitation of this aerobic photo-oxidation of aldehydes to the carboxylic acids[10—22] in the presence of a catalytic bromine or hydrobromic acid, which are inexpensive, safe and easily separable from the reaction mixture by extraction.

Results and Discussion

Table 1 shows the results of a study of reaction conditions conducted with **1** as test substrate and catalytic bromine as promoter under irradiation with a 400 W high-pressure mercury lamp externally in an oxygen atmosphere. Since passing through water, a test tube and a cooling jacket, which are made of Pyrex glass, and air is necessary for light to effect this reaction, we believe an effective wavelength of the light is 365 nm, which is an emission line of the strongest and longest wave length in an ultraviolet region irradiated from a high-pressure mercury lamp. Among the solvents examined,[23] acetonitrile was found to afford the corresponding carboxylic acid **2** most efficiently against the result with lithium bromide.[5,6] Although the best result from our tests was obtained when using 0.07 eq of bromine for 5 h, **2** was obtained in good yield when using 0.07 eq of bromine for 1 h or 0.0175 eq of bromine for 5 h (entries 5, 8, 11). Since dull red of bromine was thought to inhibit transmission of light, the yield of **2** decreased when using 0.35 eq of bromine (entry 14). That no oxidation proceeded without irradiation of UV or use of bromine shows the necessity of both for this reaction (entries 6, 10). Since **2** was not detected when conducting the reaction in an argon atmosphere, molecular oxygen is thought to be the terminal oxidant (entry 7).

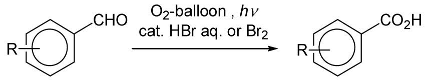
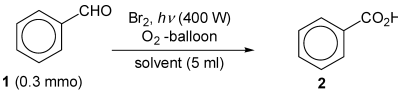


Chart 1

Table 2 shows the generality of this oxidation reaction using a variety of aldehydes. Aromatic aldehydes, **1**, **3** and **5**, afforded the corresponding benzoic acids in high yields (entries 1—3). On the other hand, **7** gave 45% of **8** and 28% of anhydride of **8**, and **9** gave 31% of **10** and several by-products, which were oxidized at the aromatic methyl group, were detected. Aliphatic aldehydes, **11** and **13**, also afforded the corresponding carboxylic acid in good yield in the presence of 0.14 eq of bromine[24]; however, **15** was found to be less reactive than other aldehydes examined, and the starting material seemed to be remained when the reaction stopped (entries 6—8).[25]

As mentioned above, bromine was found to be more effective than lithium bromide since the amount of bromine required for carrying out this reaction smoothly is much smaller than that of lithium bromide.[5,6] On the other hand, it is difficult to say that bromine is a good reagent because of its intractable and toxic properties. Compared with this, hydrobromic acid (48% aqueous solution of hydrogen bromide)

Table 1. Study of Reaction Conditions of Aerobic Photo-Oxidation with Br_2



Entry	Br_2 (eq)	Time (h)	Solvent	Yield of **2** (%)[a]
1	0.07	5	EtOAc	72
2	0.07	5	Acetone	73
3	0.07	5	*i*Pr_2O	66
4	0.07	5	Hexane	63
5	0.07	5	MeCN	100
6	0.07	5	MeCN	0[b]
7	0.07	5	MeCN	0[c]
8	0.07	1	MeCN	92
9	0.07	3	MeCN	98
10	—	5	MeCN	42
11	0.0175	5	MeCN	77
12	0.035	5	MeCN	78
13	0.14	5	MeCN	99
14	0.35	5	MeCN	73

a) All yields are for pure, isolated products. *b*) The reaction was carried out in the dark. *c*) The reaction was carried out in an Ar atmosphere.

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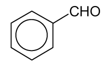
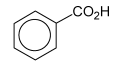
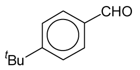
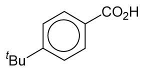
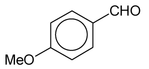
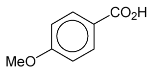
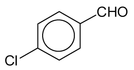
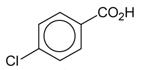
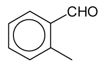
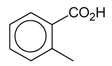
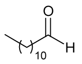
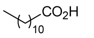
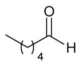
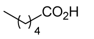
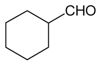
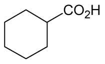
Table 2. Aerobic Photo-Oxidation with Br_2

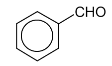
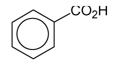
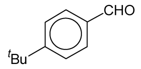
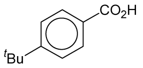
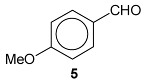
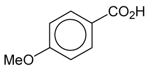
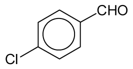
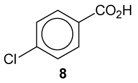
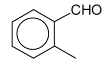
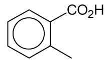
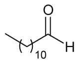
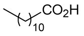
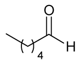
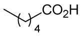
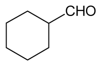
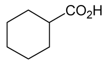
$$\text{substrate (0.3 mmol)} \xrightarrow[\text{MeCN (5 ml), 5 h}]{\text{Br}_2,\ h\nu\ (400\ \text{W}),\ \text{O}_2\text{-balloon}} \text{product}$$

Entry	Substrate	Br_2 (eq)	Product	Yield (%)[a]
1	 **1**	0.07	 **2**	(100)
2	 **3**	0.07	 **4**	(94)
3	 **5**	0.07	 **6**	(97)
4	 **7**	0.07	 **8**	(45)[b]
5	 **9**	0.07	 **10**	(31)
6	 **11**	0.14	 **12**	(88)
7	 **13**	0.14	 **14**	(71)
8	 **15**	0.14	 **16**	(47)

[a] All yields are for pure, isolated products. [b] 28% of 4-chlorobenzoic anhydride was also obtained.

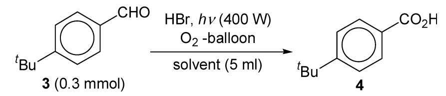
Table 4. Aerobic Photo-Oxidation with HBr aq.

$$\text{substrate (0.3 mmol)} \xrightarrow[\text{MeCN (5 ml), 5 h}]{\text{HBr},\ h\nu\ (400\ \text{W}),\ \text{O}_2\text{-balloon}} \text{product}$$

Entry	Substrate	HBr (eq)	Product	Yield (%)[a]
1	 **1**	0.2	 **2**	(90)
2	 **3**	0.2	 **4**	(100)
3	 **5**	0.2	 **6**	(100)
4	 **7**	0.2	 **8**	(100)
5	 **9**	0.2	 **10**	(22)[b]
6	 **11**	0.1	 **12**	(71)
7	 **13**	0.1	 **14**	(37)
8	 **15**	0.1	 **16**	(45)

[a] All yields are for pure, isolated products. [b] 20% of 3-hydroxy-1(3*H*)-isobenzofuranone was also obtained.

Table 3. Study of Reaction Conditions of Aerobic Photo-Oxidation with HBr aq.



3 (0.3 mmol) **4**

Entry	HBr (eq)	Time (h)	Solvent	Yield of **2** (%)[a]
1	0.2	5	EtOAc	67
2	0.2	5	Acetone	64
3	0.2	5	Hexane	69
4	0.2	5	MeCN	100
5	0.2	5	MeCN	0[b]
6	0.2	5	MeCN	0[c]
7	0.2	3	MeCN	74
8	—	5	MeCN	72
9	0.1	5	MeCN	95
10	0.3	5	MeCN	100

[a] All yields are for pure, isolated products. [b] The reaction was carried out in the dark. [c] The reaction was carried out in an Ar atmosphere.

$$\text{HBr} \longrightarrow \text{H}^+ + \text{Br}^- \xrightarrow{h\nu,\ \text{O}_2} \text{HOO}\bullet + \text{Br}\bullet \qquad (1)$$

$$\text{Br}_2 \xrightarrow{h\nu,\ \text{O}_2} 2\ \text{Br}\ \bullet \qquad (1)'$$

$$\text{R-CHO} + \text{Br}\bullet \longrightarrow \underset{\mathbf{17}}{\text{R-}\overset{\bullet}{\text{C}}\text{O}} + \text{HBr} \qquad (2)$$

$$2\ \text{HBr} + 1/2\ \text{O}_2 \xrightarrow{h\nu} \text{Br}_2 + \text{H}_2\text{O} \qquad (3)$$

$$\mathbf{17} + \text{Br}_2 \longrightarrow \underset{\mathbf{18}}{\text{R-COBr}} + \text{Br}\bullet \qquad (4)$$

$$\mathbf{18} + \text{H}_2\text{O} \longrightarrow \text{R-CO}_2\text{H} + \text{HBr} \qquad (5)$$

Chart 2. Possible Path of the Aerobic Photo-Oxidation of Aldehyde

is superior in the point of easy treatment. Table 3 shows the results of a study of reaction conditions with hydrobromic acid under the irradiation of UV. As shown in Table 1, among the solvents examined, acetonitrile was found to be the most suitable in a similar manner with bromine. Although the best result was obtained when using 0.2 eq of hydrobromic acid[26] for 5 h, **4** was also obtained in high yield even when using 0.1 eq of hydrobromic acid (entries 4, 9). In general, the yield of the product is low without a bromo source as shown in Table 1; however, **3** showed high reactivity under the oxidation condition in the absence of a bromo source, and afforded **4** in 72% yield (entry 8).

Table 4 shows the generality and limitation of this reaction using a variety of aldehydes. In general, aromatic aldehydes afforded the corresponding carboxylic acids in high yield with 0.2 eq of hydrobromic acid; however, **10** was obtained in low yield due to production of 20% of 3-hydroxy-1-(3*H*)-isobenzofuranone, which was oxidized at the aromatic methyl group, when using **9** as substrate. On the other hand, aliphatic aldehydes gave the products in moderate yield with

0.1 eq of hydrobromic acid[27] as well as the case using bromine as shown in Table 2.

Reaction Mechanism Chart 2 shows a plausible path of this oxidation due to the necessity of a catalytic amount of bromine or hydrobromic acid, molecular oxygen and continuous photo-irradiation to complete this reaction. We believe that the radical species **17** is generated by abstraction of a hydrogen radical from an aldehyde with a bromo radical, formed by continuous aerobic photo-oxidation of the bromo anion from hydrogen bromide or bromine (Eqs. 1, 1′ and 2).[28] Bromine, then, was formed by aerobic photo-oxidation of hydrogen bromide, which is generated in Eq. 2 (Eq. 3). Radical species **17** was transformed to acyl bromide **18**, and the carboxylic acid was formed by reaction with water (Eqs. 4 and 5). We do not have any direct evidence for generation of **18**; however, we believe a considerable amount of carboxylic anhydride was formed through **18** (entry 4 in Table 2).

Conclusion

As mentioned above, photo-oxidation with molecular oxygen of aldehydes in the presence of a catalytic amount of bromine, and hydrogen bromide, was studied, and the corresponding carboxylic acid was obtained in moderate to high yield. Especially, hydrobromic acid is inexpensive, safe, and easy to handle due to its non-hygroscopic property, and thus, this new form of oxidation reaction is interesting in keeping with the notion of Green Chemistry.

Experimental

All dry solvents were obtained from Kanto Kagaku Co., Ltd. Other chemicals used were of reagent grade and were obtained from Aldrich Chemical Co., Tokyo Kasei Kogyo Co., Ltd. and Wako Pure Chemical Industries, Ltd. Acetonitrile solution of bromine was previously prepared for easy treatment. HBr was added as 48% hydrobromic acid. All reactions were carried out in a Pyrex test tube equipped with an O_2-balloon, which was set up from the center of 400-W high pressure mercury lamp to the distance of 37.5 mm. All of the products are known compounds and were identified by comparison of their NMR spectra with those of authentic samples.

Typical Procedure A solution (5 ml) of the substrate (50 mg) and Br_2 (0.07 eq) in dry acetonitrile was stirred and irradiated at room temperature with a 400-W high-pressure mercury lamp externally for 5 h. The reaction mixture was concentrated under reduced pressure, and 10% NaOH aqueous solution was added. The aqueous solution was washed with diethyl ether, and then acidified with 2 N HCl aqueous solution, which was extracted with diethyl ether. 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.

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23) We exclusively used anhydrous solvents for this study since the solvents are purer than other grades of general solvents.
24) The corresponding carboxylic acids were obtained in moderate yields when using 0.07 eq of bromine.
25) Since the boiling point of **15** is not so high, remained **15** in the crude product was thought to be evaporated under reduced pressure with a vacuum pump.
26) The equivalent indicates the amount of hydrogen bromide in the hydrobromic acid.
27) Since the reaction mixture was tarry and the product **12** was obtained only in 33% yield when using **11** and 0.2 eq of hydrobromic acid, 0.1 eq of hydrobromic acid was exclusively used for aliphatic aldehydes.
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