October 2006 Notes Chem. Pharm. Bull. 54(10) 1457—1458 (2006) 1457

Facile Aerobic Photo-Oxidation of Aldehydes in the Presence of Catalytic Lithium Bromide

Shin-ichi HIRASHIMA and Akichika ITOH*

Gifu Pharmaceutical University; Mitahora-higashi, Gifu 502–8585, Japan.

Received May 25, 2006; accepted July 18, 2006

Aldehydes were found to be oxidized to the corresponding carboxylic acid in the presence of catalytic lithium bromide under photo-irradiation.

Key words aerobic photo-oxidation; aldehyde; carboxylic acid; catalytic lithium bromide

Oxidation reactions are the foundation of synthetic chemistry; however, most of the oxidants, which have been investigated so far, involve heavy metals and complex organic compounds and go against the notion of Green Chemistry.[1] On the other hand, molecular oxygen, which is photosynthesized by plants, is considered to be an infinite resource and is an effective oxidant of larger atom efficiency than that of other oxidants, and has recently received much attention. In the course of our study of photo-oxidation with molecular oxygen, we have found that a methyl group at an aromatic nucleus and alcohols were oxidized directly to the corresponding carboxylic acid, respectively, in the presence of catalytic lithium bromide under irradiation by a high-pressure mercury lamp.[2,3] We further observed through experiments to expand application of this reaction that an oxidation reaction also proceeds using 4-*tert*-butylbenzaldehyde (**1**) as the test substrate, affording 4-*tert*-butylbenzoic acid (**2**) (Chart 1). In this letter we report in detail our investigation of the generality of this reaction.[4—6]

Results and Discussion

Table 1 shows the results of a study of reaction conditions conducted with **1** as test substrate under the conditions of external irradiation by a 400 W high-pressure mercury lamp in an oxygen atmosphere. We do not have any direct evidence; however, 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, since passing through water, a test tube and a cooling jacket, which are made from Pyrex glass, and air is necessary for the light to effect this reaction. Among the alkali metal halides[7] and solvents examined, lithium bromide[8] and ethyl acetate were found to afford the corresponding carboxylic acid **2** most efficiently, and typical alkali metal halides other than lithium bromide were found to be little reactive for this oxidation in similar to the previous reaction we examined.[2,3] Although the best result from our tests was obtained when using 0.4 eq of lithium bromide, the difference in the yield when using 0.2 or 0.3 eq of lithium bromide was hardly discernible (entries 1, 2, 4). Since bubbling of O$_2$ through the reaction mixture was found to be not effective, all of the reactions were carried out under O$_2$-balloon (entry 5). Although addition of H$_2$O did not affect the yield of **2**, we exclusively used anhydrous solvents for this study since the solvents are purer than other grade of general solvents (entry 6). That no oxidation proceeded without irradiation of UV and that the decrease in chemical yield of **2** without lithium bromide even after 24-h irradiation show the necessity of both for this reaction (entries 7, 8). Furthermore, from the fact that the target substance was not detected when conducting the reaction in an argon atmosphere, we can assume that the actual oxidant in this reaction is molecular oxygen (entry 9).

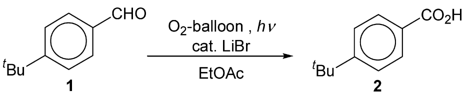
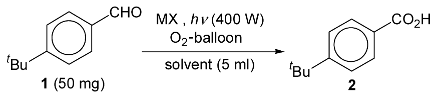


Chart 1

Table 2 shows the generality of this oxidation reaction using a variety of aldehydes. Aromatic aldehydes, in general, afford the corresponding benzoic acids in good yields (entries 1—4). Aliphatic aldehydes, in general, were less reactive than aromatic aldehydes, and afforded the corresponding carboxylic acids in high to modest yield (entries 5—7) under the conditions of 5-h external irradiation by 400 W high-pressure mercury lamp. Although we also carried out the re-

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



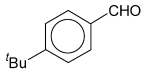
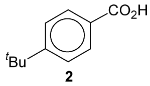
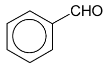
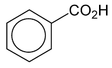
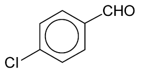
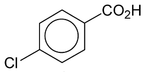
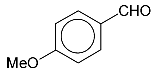
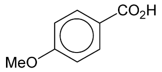
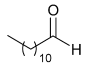
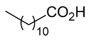
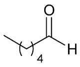
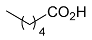
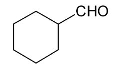
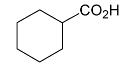
Entry	MX	(eq)	Time (h)	Solvent	Yield of **2** (%)[a]
1	LiBr	0.2	5	EtOAc	88
2	LiBr	0.3	5	EtOAc	91
3	LiBr	0.4	3	EtOAc	72
4	LiBr	0.4	5	EtOAc	93
5	LiBr	0.4	5	EtOAc	94[b]
6	LiBr	0.4	5	EtOAc	92[c]
7	LiBr	0.4	5	EtOAc	0[d]
8	—	—	24	EtOAc	54
9	LiBr	0.4	5	EtOAc	0[e]
10	LiBr	0.4	10	EtOAc	83
11	LiBr	0.5	5	EtOAc	89
12	LiBr	1.0	5	EtOAc	62
13	LiBr	0.4	5	acetone	59
14	LiBr	0.4	5	hexane	79
15	LiBr	0.4	5	MeCN	57
16	LiCl	0.4	5	EtOAc	68
17	NaBr	0.4	5	EtOAc	60
18	KBr	0.4	5	EtOAc	64

a) All yields are for pure, isolated products. *b*) The reaction was carried out under the bubbling of O$_2$. *c*) The reaction was carried out in the presence of 1 eq of H$_2$O. *d*) The reaction was carried out in the dark. *e*) The reaction was carried out in an Ar atmosphere.

∗ To whom correspondence should be addressed. e-mail: itoha@gifu-pu.ac.jp

Table 2. Aerobic Photo-Oxidation for Various Aldehyde Substrates

$$\underset{(50\,\text{mg})}{\text{Substrate}} \xrightarrow[\text{EtOAc (5 ml), 5 h}]{\text{LiBr (0.4 eq)}, h\nu\,(400\,\text{W}),\ O_2\text{-balloon}} \text{Product}$$

Entry	Substrate	Product (yield %)[a]
1	 **1**	 **2** (93)
2	 **3**	 **4** (89)
3	 **5**	 **6** (95)
4	 **7**	 **8** (97)
5	 **9**	 **10** (85)
6	 **11**	 **12** (62)
7	 **13**	 **14** (45)

a) All yields are for pure, isolated products.

$$\text{LiBr} \longrightarrow \text{Li}^+ + \text{Br}^- \xrightarrow{h\nu,\,O_2} \text{LiOO}\bullet + \text{Br}\bullet \quad (1)$$

$$\text{R-CHO} + \text{Br}\bullet \longrightarrow \underset{\mathbf{15}}{\text{R-}\dot{\text{C}}\text{O}} + \text{HBr} \quad (2)$$

$$2\,\text{HBr} + 1/2\,O_2 \xrightarrow{h\nu} \text{Br}_2 + H_2O \quad (3)$$

$$\mathbf{15} + \text{Br}_2 \longrightarrow \underset{\mathbf{16}}{\text{R-COBr}} + \text{Br}\bullet \quad (4)$$

$$\mathbf{16} + H_2O \longrightarrow \text{R-CO}_2\text{H} + \text{HBr} \quad (5)$$

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

actions with **9** and **13** under bubbling of O_2, increase of the yields of **10** and **14** could not be observed.[9]

Reaction Mechanism We present in Chart 2 what we believe is a path of this oxidation, which is postulated by considering all the necessity of the catalytic amount of lithium bromide, molecular oxygen and continuous photo-irradiation to complete this reaction. We believe that the radical species **15** 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 lithium bromide (Eqs. 1, 2).[10] Bromine, then, was formed by aerobic photo-oxidation of hydrogen bromide, which is generated in equation 2 (Eq. 3). Radical species **15** was transformed to acyl bromide **16**, and the carboxylic acid was formed by reaction with water (Eqs. 4, 5).[11—15]

Conclusion

This new form of oxidation reaction is interesting in keeping with the notion of Green Chemistry due to non-use of heavy metals, waste reduction, use of molecular oxygen, inexpensive acquisition of reagents, and possible solvent recovery.

Experimental

All of 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. 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 LiBr (0.4 eq) in dry ethyl acetate was stirred and irradiated at room temperature with a 400-W high-pressure mercury lamp externally for the indicated time. 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.

References and Notes

1) "Comprehensive Organic Transformations: A Guide to Functional Group Preparations," ed. by Larock R. C., Wiley-VCH, New York, 1999.
2) Itoh A., Hashimoto S., Kodama T., Masaki Y., *Synlett*, **2005**, 2107—2109 (2005).
3) Itoh A., Hashimoto S., Masaki Y., *Synlett*, **2005**, 2639—2640 (2005).
4) Chen H., An T., Fang Y., Yu T., *Indian J. Chem. Sec. B*, **38B**, 805—809 (1999).
5) Kharat A. N., Pendleton P., Badalyan A., Abedini M., Amini M. M., *J. Mol. Catal. A: Chem.*, **175**, 277—283 (2001).
6) Partenheimer W., Grushin V. V., *Adv. Synth. Catal.*, **343**, 102—111 (2001).
7) We have examined only alkali metal halides since they are inexpensive, easy to handle, and more environmentally benign than other metal halides.
8) Among our examined, lithium bromide of at least 1.72 g (20 mmol) is dissolved in 5 ml of ethyl acetate.
9) The yields of **10** and **14** were 80% and 47% respectively.
10) Minisci F., Porta O., Recupero F., Punta C., Gambarotti C., Pierini M., Galimberti L., *Synlett*, **2004**, 2203—2205 (2004).
11) Hamamoto M., Nakayama K., Nishiyama Y., Ishii Y., *J. Org. Chem.*, **58**, 6421—6425 (1993).
12) Mastrorilli P., Nobile F., *Tetrahedron Lett.*, **35**, 4193—4196 (1994).
13) Yamada T., Takai T., Rhode O., Mukaiyama T., *Chem. Lett.*, **1991**, 1—4 (1991).
14) Yamada T., Takai T., Rhode O., Mukaiyama T., *Bull. Chem. Soc. Jpn.*, **64**, 2109—2117 (1991).
15) Takai T., Hata E., Yamada T., Mukaiyama T., *Bull. Chem. Soc. Jpn.*, **64**, 2513—2518 (1991).