Facile Aerobic Photooxidation of Alcohols in the Presence of Catalytic Lithium Bromide

Akichika Itoh,* Shouei Hashimoto, Yukio Masaki

Gifu Pharmaceutical University, Mitahora-higashi, Gifu 502-8585, Japan E-mail: itoha@gifu-pu.ac.jp Received 1 July 2005

Key words: photooxidation, alcohols, lithium bromide, aerobic, carboxylic acid

Oxidation reactions are the foundation of synthetic chemistry, and have been the subject of study by many researchers. However, these reactions substantially involved the use of large quantities of heavy metals and complex organic compounds, which generate large amounts of waste, and were not at all environmentally benign.¹ In the course of our study of photooxidation, we have found that 4-tert-butyl toluene was oxidized directly to 4-tert-butyl benzoic acid in the presence of catalytic lithium bromide in an oxygen atmosphere under irradiation by a high-pressure mercury lamp.² This is the first report on the generality of aerobic photooxidation reactions in synthetic organic chemistry with alkali metal halides,³ and we believe this new type of reaction to be of great interest. We further observed through experiments to expand the applications of this reaction that an oxidation reaction also proceeds using the aliphatic alcohol 1-dodecanol (1) as the test substrate, affording 1-dodecanoic acid (2, Scheme 1). In this letter we report in detail on our investigation of the generality of this reaction.⁴



Scheme 1

Table 1 shows the results of a study of reaction conditions conducted with **1** as test substrate under the conditions of 6-hour external irradiation by a 400 W high-pressure mercury lamp⁵ in an oxygen atmosphere.⁶ Among the al-kali metal halides and solvents examined, only LiBr and ethyl acetate were found to most efficiently afford the corresponding carboxylic acid **2**. We were surprised to find, however, reduction in the yield of **2** regardless of increases or decreases in the amount of LiBr used, and

SYNLETT 2005, No. 17, pp 2639–2640 Advanced online publication: 05.10.2005 DOI: 10.1055/s-2005-918914; Art ID: U20605ST © Georg Thieme Verlag Stuttgart · New York obtained the best results from our tests when using 0.3 equivalents of LiBr. The observation that no oxidation proceeded without either irradiation of UV or the addition of LiBr shows the necessity of both for this reaction. Furthermore, from the fact that yields of the target substance were reduced substantially when conducting the reaction under the flow of argon, we can assume that the actual oxidant in this reaction is molecular oxygen.

Table 1 Study of Reaction Conditions of Aerobic Photooxidation

∕∕ ₁₀ 1 (50 n	MX OH O ng) solve	, hν (400 W) ₂ (balloon) ent (5 mL), 6 h	→ → 10 0H 2	
Entry	MX	Equiv	Solvent	Yield of 2 (%) ^a
1	LiBr	0.1	EtOAc	66
2	LiBr	0.2	EtOAc	76
3	LiBr	0.3	EtOAc	82
4	LiBr	0.4	EtOAc	63
5	LiBr	0.5	EtOAc	7 ^b
6	LiBr	1.0	EtOAc	Trace
7	LiBr	0.3	Acetone	0
8	LiBr	0.3	MeCN	0
9	LiBr	0.3	THF	Trace
10	LiBr	0.3	Benzene	12
11	LiBr	0.3	H_2O	0
12	LiCl	0.3	EtOAc	0
13	NaBr	0.3	EtOAc	0
14	KBr	0.3	EtOAc	0

^a All yields are for pure, isolated products.

^b A total yield of 86% of dodecanyl dodecanoate was obtained.

Table 2 shows the generality of this oxidation reaction using a variety of alcohols.⁷ Both benzyl and aliphatic alcohols, in general, afford the corresponding carboxylic acids in good yields, although there is a difference in reaction times (entries 1–5). Aliphatic secondary alcohols, in general, were less reactive than primary alcohols. For example, only 20% of 4-*tert*-butylcyclohexanone (**12**) was obtained and 59% of starting material was recovered

Abstract: Alcohols were found to be oxidized to the corresponding carboxylic acids in the presence of catalytic lithium bromide under photoirradiation.

 Table 2
 Aerobic Photooxidation for Various Alcohol Substrates

LiBr (0.3 equiv), hv (400 W)

substra (50 m	g) EtOAc (5 m	n nL)	→ product	
Entry	Substrate	t (h)	Product	Yield (%) ^a
1	() ₁₀ ОН	6	С () 10 ОН	82
2	(), ОН	15		75
3	3	2	4	83
4	5	5	6	89
5	7	9	8 0 0	82
6	9 9 0H	24		20 ^b
	24		12	

^a All yields are for pure, isolated products.

^b A total yield of 59% of **11** was recovered.

even after 24 hours reaction time when using 4-*tert*-butyl-cyclohexanol (**11**, entry 6).

The reaction mechanism has not been clearly understood; however, we present here a supposed mechanism (Scheme 2). In Scheme 2 is shown a path of this oxidation, which is postulated by considering both the necessity of the catalytic amount of LiBr and of molecular oxygen in this reaction. The pale yellow coloration of the suspension suggests that bromine is generated in situ from lithium bromide under UV irradiation.⁶ We believe that the radical species **13** is generated by abstraction of a hydrogen radical with a bromo radical, formed under irradiation from bromine. The radical species traps molecular oxygen to afford peroxy radical species **14**, which subsequently transforms to a carboxylic acid via hydroperoxide **15**.

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.

Synlett 2005, No. 17, 2639–2640 © Thieme Stuttgart · New York



Scheme 2 Possible path of the aerobic photooxidation of alcohols

References

- 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) Regarding photooxidation with alkali metal halides, the conversion of CO to CO₂ and H₂ to H₂O in the presence of hydrogen exposed to over 200 nm of ultraviolet light has been previously reported, see: Ryabchuk, V. *Catal. Today* **2000**, *58*, 89.
- (4) (a) For direct oxidations of alcohols to carboxylic acid without photoirradiation, see ref. 1. See also: (b) Zhao, M.; Li, J.; Song, Z.; Desmond, R.; Tschaen, D. M.; Grabowski, E. J. J.; Reider, P. J. *Tetrahedron Lett.* **1998**, *39*, 5323.
 (c) Zhao, M.; Li, J.; Mano, E.; Song, Z.; Tschaen, D. M.; Grabowski, E. J. J.; Reider, P. J. *J. Org. Chem.* **1999**, *64*, 2564. (d) Ji, H.; Mizugaki, T.; Ebitani, K.; Kaneda, K. *Tetrahedron Lett.* **2002**, *43*, 7179. (e) Yasuda, K.; Ley, S. V. J. Chem. Soc., Perkin Trans. 1 **2002**, 1024.
- (5) We believe an effective wavelength of light is 365 nm.
- (6) When using primary alcohol as substrate, a typical procedure follows: a solution (5 mL) of the substrate (50 mg) and LiBr (0.3 equiv) in dry EtOAc was stirred and irradiated at r.t. with a 400 W high-pressure mercury lamp externally for the indicated time. The reaction mixture was concentrated under reduced pressure, and 1% NaOH aq solution was added. The aqueous solution was washed with Et₂O, and then acidified with 2 N HCl aq solution, which was extracted with Et₂O. The organic layer was washed with brine and dried over Na₂SO₄, and concentrated under reduced pressure. The product was pure without further purification. When using secondary alcohol as substrate, a typical procedure follows: a solution (5 mL) of the substrate (50 mg) and LiBr (0.3 equiv) in dry EtOAc was stirred and irradiated at r.t. with a 400 W high-pressure mercury lamp externally for the indicated time. The reaction mixture was concentrated under reduced pressure, and 1% NaOH aq solution was added. The aqueous solution was washed with Et₂O and the organic layer was concentrated, and the residue was purified by preparative TLC. The aqueous layer was then acidified with 2 N HCl aq solution and extracted with Et₂O the same as in the former cases.
- (7) Catalytic bromine oxidized **1** to **2** in 59% yield under similar conditions.