Facile Aerobic Photooxidation of Alcohols in the Presence of Catalytic *N*-Bromosuccinimide

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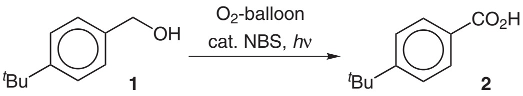
Abstract: Alcohols were found to be oxidized to the corresponding carboxylic acid in the presence of catalytic *N*-bromosuccinimide in an oxygen atmosphere.

Key words: aerobic, alcohols, *N*-bromosuccinimide, carboxylic acid, photooxidation

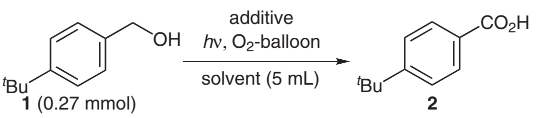
N-Bromosuccinimide (NBS) is a convenient and widely used reagent not only for bromination but also for oxidation of a variety of organic compounds.[1] Although oxidation of alcohols to aldehydes or ketones with NBS has been reported by several research groups,[2] to our knowledge, direct oxidation of alcohols to carboxylic acids has not been studied previously. On the other hand, with the notion of Green Chemistry in mind, we searched for directions for the use of molecular oxygen, which is considered to be an infinite resource because it is photosynthesized by plants and is an effective oxidant of larger atom efficiency than that of other oxidants. In the course of our study of photooxidation, we have found that 4-*tert*-butyltoluene was oxidized directly to 4-*tert*-butylbenzoic acid in the presence of catalytic *N*-bromosuccinimide in an oxygen atmosphere under irradiation by a high-pressure mercury lamp.[3] We further observed through experiments to expand applications of this reaction that an oxidation reaction also proceeds using the aliphatic alcohol 4-*tert*-butylbenzyl alcohol (**1**) as the test substrate, affording 4-*tert*-butylbenzoic acid (**2**) (Scheme 1).[4] In this paper, we report in detail our investigation of the generality of this reaction.



Scheme 1 Aerobic photooxidation of 4-*tert*-butylbenzyl alcohol

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[5] in an oxygen atmosphere at ambient temperature. Among the solvents examined, ethyl acetate and acetonitrile were found to most efficiently afford the corresponding carboxylic acid **2** (entries 1–4).[6] We also found the yields of **2** were almost the same when the reactions were carried out in the presence of more than 0.1 equivalent of NBS. That yields of **2** were reduced substantially when conducting the reaction in the dark or in an argon atmosphere shows the necessity of both photoirradiation, not heating, and molecular oxygen for this reaction (entries 11–13). Furthermore, *N*-chlorosuccinimide (NCS) and *N*-iodosuccinimide (NIS) were examined as another addi-

Table 1 Conditions Studied for the Photooxidation of 4-*tert*-Butylbenzyl Alcohol (**1**)



Entry	Solvent	Additive (equiv)	Time (h)	Yield (%)[a]
1	EtOAc	NBS (1.0)	10	95
2	acetone	NBS (1.0)	10	81
3	CH_2Cl_2	NBS (1.0)	10	80
4	MeCN	NBS (1.0)	10	95
5	MeCN	NBS (0.5)	10	95
6	MeCN	NBS (0.2)	10	97
7	MeCN	NBS (0.1)	4	80
8	MeCN	NBS (0.1)	2	98
9	MeCN	NBS (0.1)	1	99
10	MeCN	NBS (0.05)	10	84
11	MeCN	NBS (0.1)	1	trace[b]
12	MeCN	NBS (0.1)	1	trace[c]
13	MeCN	NBS (0.1)	1	trace[d]
14	MeCN	NCS (0.1)	1	29
15	MeCN	NIS (0.1)	1	6
16	MeCN	–	1	trace

[a] All yields are for pure, isolated products.
[b] The reaction was carried out in the dark.
[c] The reaction was carried out under argon.
[d] The reaction was carried out at 60 °C in the dark.

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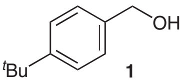
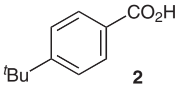
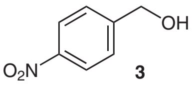
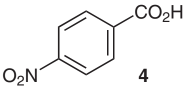
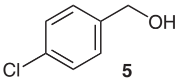
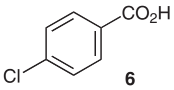
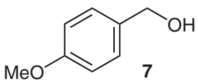
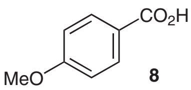
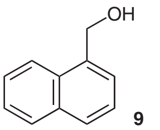
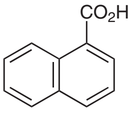
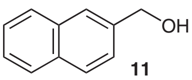
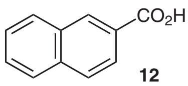
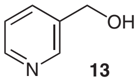
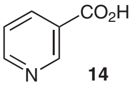
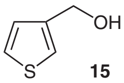
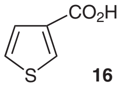
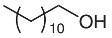
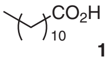
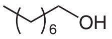
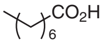
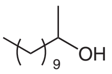
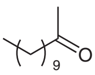
tive; however, the target product was obtained only in low yield (entries 14 and 15).

Table 2 shows the generality of this oxidation reaction using a variety of alcohols (1 mmol) in the presence of NBS (0.1 equiv). The corresponding benzoic acid was obtained in good yield regardless of an electron-donating or electron-withdrawing group at the aromatic nucleus when using benzyl alcohols (entries 1–4). 1- and 2-Naphthalenemethanol (**9** and **11**) also afforded the corresponding naphthoic acids **10** and **12** in high yield (entries 5 and 6). Among the heterocyclic substrates examined, 3-pyridinemethanol (**13**) was found to afford **14** in high yield; however, 3-thiophenemethanol (**15**) gave a complex mixture and the corresponding carboxylic acid **16** was obtained only in 15% yield. Aliphatic primary and secondary alcohols, in general, afforded the corresponding carboxylic acids in moderate yields (entries 9–11).

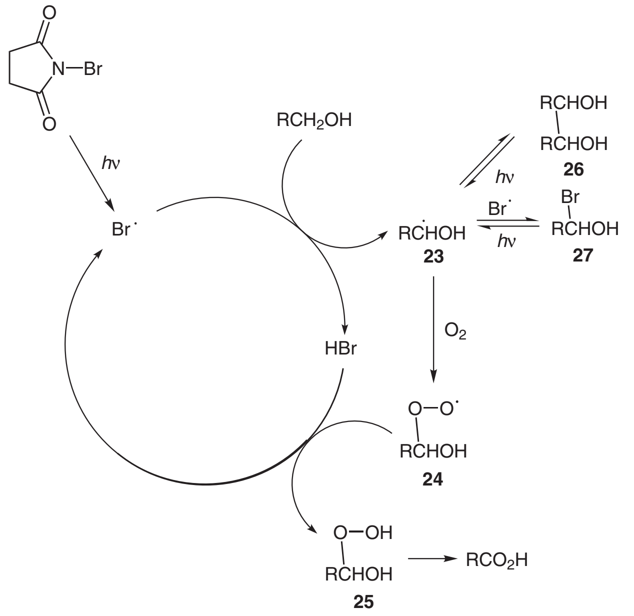
We present in Scheme 2 what we believe is a path of this oxidation, postulated by considering both the necessity of a catalytic amount of NBS and of molecular oxygen in this reaction. We believe that the radical species **23** is generated by abstraction of a hydrogen radical with a bromo radical, formed under irradiation from NBS. The radical species traps molecular oxygen to afford peroxy radical species **24**, which subsequently transforms to a carboxylic acid via hydroperoxide **25**. Although we do not have any evidence, **23** is assumed to be quenched through dimerization or with a bromo radical to afford **26** or **27**, which are

Table 2 Aerobic Photooxidation of Various Alcohol Substrates

$$\text{substrate (1 mmol)} \xrightarrow[\text{MeCN (8 mL)}]{h\nu\text{ (400 W-Hg), NBS (0.1 equiv)}} \text{product}$$

Entry	Substrate	Time (h)	Product	Yield (%)[a]
1	 **1**	3	 **2**	74
2	 **3**	10	 **4**	78
3	 **5**	10	 **6**	56
4	 **7**	6	 **8**	77
5	 **9**	10	 **10**	97
6	 **11**	10	 **12**	97
7	 **13**	10	 **14**	90
8	 **15**	10	 **16**	15
9	 **17**	10	 **18**	64
10	 **19**	6	 **20**	57
11	 **21**	3	 **22**	53

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



Scheme 2 Possible paths for the aerobic photooxidation of alcohols

cleaved again to **23** under photoirradiation since the continuous photoirradiation is necessary for the progress of this reaction.

We have only studied the system for this reaction in small scale; however, 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.

All reactions were carried out under O_2. All of the products are known compounds. ^{1}H NMR spectra were recorded on JEOL 400 MHz instruments (EX-400 and AL-400) using solvent peak as a standard. Mass spectrometric data were collected on a JEOL JMS-SX 102A mass spectrometer.

Oxidation of Primary Alcohols; 4-*tert*-Butylbenzoic Acid (2); Typical Procedure

A solution of 4-*tert*-butylbenzyl alcohol (**1**; 164 mg, 1 mmol) and *N*-bromosuccinimide (17.8 mg, 0.1 mmol) in anhyd MeCN (8 mL) was stirred in a test tube fitted with an O_2-balloon (1 atm) and irradiated externally with a 400 W high-pressure mercury lamp for 3 h at r.t.. The mixture was concentrated under reduced pressure, and aq 10% NaOH solution was added. The aqueous solution was washed with Et_2O, and then acidified with aq 2 N HCl, which was extracted with Et_2O. The organic layer was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. The product was obtained pure and needed no further purification; yield: 132 mg (74%) (Table 2).

^{1}H NMR (400 MHz, acetone-d_6): δ = 7.96 (d, J = 8.7 Hz, 2 H, H-2, H-6), 7.54 (d, J = 8.7 Hz, 2 H, H-3, H-5), 1.34 (s, 9 H, t-C_4H_9).

MS: *m*/*z* = 163.

4-Nitrobenzoic Acid (4)

^{1}H NMR (400 MHz, acetone-d_6): δ = 8.36 (d, J = 9.2 Hz, 2 H, H-3, H-5), 8.28 (d, J = 9.2 Hz, 2 H, H-2, H-6).

MS: *m*/*z* = 167.

4-Chlorobenzoic Acid (6)

^{1}H NMR (400 MHz, acetone-d_6): δ = 8.03 (d, J = 8.7 Hz, 2 H, H-2, H-6), 7.55 (d, J = 8.7 Hz, 2 H, H-3, H-5).

MS: *m*/*z* = 139.

4-Anisic Acid (8)

^{1}H NMR (400 MHz, CD_3OD): δ = 7.98 (d, J = 8.7 Hz, 2 H, H-2, H-6), 7.01 (d, J = 8.7 Hz, 2 H, H-3, H-5), 3.87 (s, 3 H, OCH_3).

MS: *m*/*z* = 152.

1-Naphthoic Acid (10)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.07 (d, J = 8.0 Hz, 1 H, H-8), 8.40 (dd, J = 7.3, 1.5 Hz, 1 H, H-2), 8.08 (d, J = 8.0 Hz, 1 H, H-4), 7.91 (dd, J = 8.0, 0.7 Hz, 1 H, H-5), 7.65 (ddd, J = 8.5, 7.0, 1.5 Hz, 1 H, H-7), 7.58 (m, 2 H, H-3, H-6).

MS: *m*/*z* = 172.

2-Naphthoic Acid (12)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.70 (s, 1 H, H-1), 8.10 (dd, J = 8.7, 1.5 Hz, 1 H, CH), 7.98 (d, J = 7.8 Hz, 1 H, CH), 7.90 (m, 2 H, CH), 7.62 (dd, J = 7.0, 1.3 Hz, 1 H, H-5), 7.58 (dd, J = 7.7, 1.3 Hz, 1 H, H-6), 7.55 (dd, J = 6.8, 1.2 Hz, 1 H, H-7).

MS: *m*/*z* = 172.

Nicotinic Acid (14)

^{1}H NMR (400 MHz, CD_3OD): δ = 9.12 (s, 1 H, H-2), 8.73 (dd, J = 5.0, 1.5 Hz, 1 H, H-6), 8.42 (ddd, J = 6.0, 1.9, 1.9 Hz, 1 H, H-4), 7.57 (ddd, J = 7.2, 5.0, 0.7 Hz, 1 H, H-5).

MS: *m*/*z* = 123.

3-Thiophenecarboxylic Acid (16)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.17 (dd, J = 2.9, 1.5 Hz, 1 H, H-2), 7.50 (dd, J = 5.3, 1.5 Hz, 1 H, H-4), 7.27 (dd, J = 5.3, 2.9 Hz, 1 H, H-5).

MS: *m*/*z* = 128.

Dodecanoic Acid (18)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.32 (t, J = 7.4 Hz, 2 H, CH_2CO_2H), 1.60 (m, 2 H, $CH_2CH_2CO_2H$), 1.23 (m, 16 H, 8 CH_2), 0.86 (t, J = 6.8 Hz, 3 H, CH_3).

MS: *m*/*z* = 200.

Octanoic Acid (20)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.32 (t, J = 7.6 Hz, 2 H, CH_2CO_2H), 1.60 (q, J = 7.4 Hz, 2 H, $CH_2CH_2CO_2H$), 1.40–1.25 (m, 8 H, 4 CH_2), 0.85 (t, J = 7.1 Hz, 3 H, CH_3).

MS: *m*/*z* = 144.

Dodecan-2-one (22)

A solution of dodecan-2-ol (**21**; 186 mg, 1 mmol) and *N*-bromosuccinimide (17.8 mg, 0.1 mmol) in anhyd MeCN (8 mL) was stirred in a test tube fitted with an O_2-balloon (1 atm) and irradiated externally with a 400 W high-pressure mercury lamp at r.t. for 3 h. The mixture was concentrated under reduced pressure, and aq 10% NaOH solution was added. The aqueous solution was extracted with Et_2O, the organic layer concentrated, and the residue was purified by preparative TLC (eluent: hexane–EtOAc, 5:1); yield: 97.4 mg (53%) (Table 2).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.35 (t, J = 7.4 Hz, 2 H, CH_2CO), 2.07 (s, 3 H, CH_3CO), 1.50 (m, 2 H, CH_2CH_2CO), 1.20 (m, 14 H, 7 CH_2), 0.82 (t, J = 6.8 Hz, 3 H, CH_3).

MS: *m*/*z* = 184.

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(4) Aerobic radical oxidation of alcohols to carboxylic acids has been reported, see: Ishii, Y.; Nakayama, K.; Takeno, M.; Sakaguchi, S.; Iwahana, T.; Nishiyama, Y. *J. Org. Chem.* **1995**, *60*, 3934.

(5) We believe the effective wavelength of the light for this reaction to be 365 nm.

(6) Since purification of **2** was difficult due to the residue of the reaction mixture when using EtOAc as solvent, MeCN was exclusively used for subsequent studies.