Aerobic Photooxidative Cleavage of Vicinal Diols to Carboxylic Acids Using 2-Chloroanthraquinone

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Received: 14.05.2012; Accepted after revision: 07.06.2012

Abstract: We developed the aerobic photooxidative cleavage of vicinal diols to carboxylic acids using 2-chloroanthraquinone in the presence of photoirradiation with a high-pressure mercury lamp. This is the first metal-free reaction using molecular oxygen as the terminal oxidant.

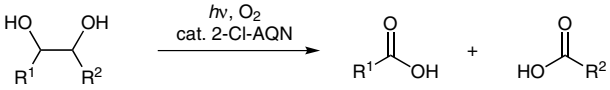
Key words: photooxidation, aerobic, anthraquinone, vicinal diol, carboxylic acid

Oxidative cleavage of vicinal diols is a key reaction in determining the carbohydrate structure, which transforms various polyhydroxylated substances to carbonyl compounds. Furthermore, oxidative cleavage can split the carbon–carbon double bond in combination with dihydroxylation of olefins, which complements ozonolysis or Lemieux–Johnson reaction.

Oxidative cleavage of vicinal diols to aldehyde has been studied extensively, and generally proceeds with lead tetraacetate and periodic acid.[1] On the other hand, oxidative cleavage of vicinal diols to carboxylic acid has been also extensively studied, and anodic oxidation was reported.[2] Furthermore, a transition-metal-catalyzed oxidative cleavage of vicinal diols was reported, which combined a metal catalyst (Mn, Ru, Ni, W, Mo, and V) and a stoichiometric oxidant ($NaIO_4$, $KHSO_5$, H_2O_2, NaOCl, $NaBO_3$, H_5IO_6, and *t*-BuOOH).[3] In addition, two metal-free reactions using stoichiometric amounts of oxidants were reported.[4] Recently, a catalytic metal-free reaction was reported, which proceeds in the presence of 4-iodobenzoic acid, but it requires a stoichiometric amount of Oxone.[5] These reactions typically involve the use of heavy metals or non-atom-economical stoichiometric oxidants. Consequently, they generate large amounts of waste and are not environmentally benign.

Due to the increasing demand for a more environmentally benign synthesis, molecular oxygen has received much attention as the ultimate oxidant because it is photosynthesized by plants, produces little waste, is inexpensive, and has greater atom efficiency than that of other oxidants.[6] The catalytic oxidative cleavage of vicinal diols to carboxylic acid using molecular oxygen as terminal oxidant has been reported. However, these reactions must use metal catalysts (Co, Ru),[7] and to the best of our knowledge, there is no metal-free catalytic oxidative cleavage of vicinal diols to carboxylic acid using molecular oxygen as the terminal oxidant.

Recently, we have developed several catalytic photooxidation methods using molecular oxygen as the terminal oxidant.[8] In the course of our study on this photooxidation protocol, we have found that methyl aromatics were effectively oxidized to the corresponding benzoic acids by photooxidation with molecular oxygen as the terminal oxidant in the presence of 2-chloroanthraquinone.[8b] Therefore, we reasoned that, with this photooxidation protocol, vicinal diols are oxidatively cleaved to the corresponding carboxylic acids with molecular oxygen as the terminal oxidant under metal-free conditions. We report herein the first example of an aerobic, oxidative cleavage of vicinal diols under metal-free conditions (Scheme 1).



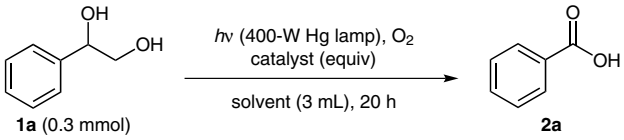
Scheme 1 Oxidative cleavage of vicinal diols

To explore this approach, we selected 1-phenyl-1,2-ethanediol (**1a**) as the test substrate for optimizing the reaction conditions (Table 1). Although we examined the reaction conditions with various photosensitizers, the yields of **2a** were unsatisfactory, except for anthracene and anthraquinone (AQN) derivatives (Table 1, entries 1–8). Further study of the solvent and the amounts of catalyst revealed that using 2-chloroanthraquinone (0.1 equiv) in EtOAc for 20 hours were the best conditions (Table 1, entry 2). Note that this reaction also proceeded in air atmosphere (Table 1, entry 18). Addition of H_2O, K_2CO_3, and PTSA had little effect on this reaction (Table 1, entries 19–21). A lower yield of **2a** was observed when fluorescent or xenon lamps were used instead of an Hg lamp (Table 1, entries 22 and 23). The fact that **2a** was not obtained or was obtained only in low yield without 2-Cl-AQN, irradiation or molecular oxygen shows the necessity of these ingredients for this reaction (Table 1, entries 24–26).

Table 2 shows the scope and limitations of the oxidative cleavage of vicinal diols under the optimized conditions.[9] Generally, the corresponding carboxylic acids were obtained in high yields regardless of the electron-donating or electron-withdrawing group on the benzene ring (Table 2, entries 1–6). On the other hand, the 2-naphthyl derivative

SYNLETT 2012, 23, 2059–2062
Advanced online publication: 26.07.2012
DOI: 10.1055/s-0032-1316585; Art ID: ST-2012-U0418-L

Table 1 Study of Reaction Conditions



1a (0.3 mmol) **2a**

Entry	Catalyst (equiv)	Solvent	Yield (%)[a]
1	1-Cl-AQN (0.1)	EtOAc	40
2	2-Cl-AQN (0.1)	EtOAc	82
3	2-*t*-Bu-AQN (0.1)	EtOAc	82
4	2-Br-AQN (0.1)	EtOAc	75
5	AQN-2-CO_2H (0.1)	EtOAc	74
6	anthracene (0.1)	EtOAc	65
7	rose bengal (0.1)	EtOAc	0
8	methylene blue (0.1)	EtOAc	0
9	2-Cl-AQN (0.1)	MeCN	68
10	2-Cl-AQN (0.1)	acetone	61
11	2-Cl-AQN (0.1)	hexane	74
12	2-Cl-AQN (0.1)	cyclohexane	70
13	2-Cl-AQN (0.1)	H_2O	6
14	2-Cl-AQN (0.1)	AcOH	68
15	2-Cl-AQN (0.1)	*i*-Pr_2O	63
16	2-Cl-AQN (0.05)	EtOAc	65
17	2-Cl-AQN (0.2)	EtOAc	68
18[b]	2-Cl-AQN (0.1)	EtOAc	60
19[c]	2-Cl-AQN (0.1)	EtOAc	78
20[d]	2-Cl-AQN (0.1)	EtOAc	84
21[e]	2-Cl-AQN (0.1)	EtOAc	80
22[f]	2-Cl-AQN (0.1)	EtOAc	59
23[g]	2-Cl-AQN (0.1)	EtOAc	74
24	–	EtOAc	21
25[h]	2-Cl-AQN (0.1)	EtOAc	0
26[i]	2-Cl-AQN (0.1)	EtOAc	1

[a] ^{1}H NMR yields.
[b] Reaction was conducted under air.
[c] Reaction was conducted in the presence of H_2O (50 μL).
[d] Reaction was conducted in the presence of K_2CO_3 (0.5 equiv).
[e] Reaction was conducted in the presence of PTSA (0.5 equiv).
[f] Reaction was conducted using a fluorescent lamp.
[g] Reaction was conducted using a Xe lamp.
[h] Reaction was conducted in the dark.
[i] Reaction was conducted under Ar.

was a poor substrate and resulted in low yield with many minor byproducts (Table 2, entry 7). Aliphatic vicinal diols were also converted into the corresponding carboxylic acids in moderate to good yields (Table 2, entries 9–11). Cyclic vicinal diol yielded the corresponding dicarboxylic acid (Table 2, entry 12). In these aliphatic substrates, further prolonging of reaction time resulted in lower yields. Moreover, tetrasubstituted vicinal diol was converted into the corresponding ketone in good yield (Table 2, entry 8).

We studied the time course of the oxidative cleavage of **1a** to clarify the reaction mechanism (Figure 1). It was revealed that 2-hydroxyacetophenone (**3a**) and phenylglyoxal (**4a**) were detected in the ^{1}H NMR spectra.

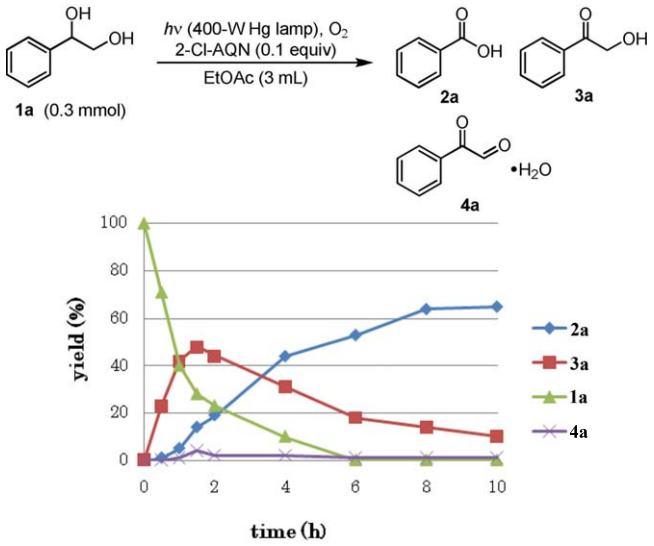
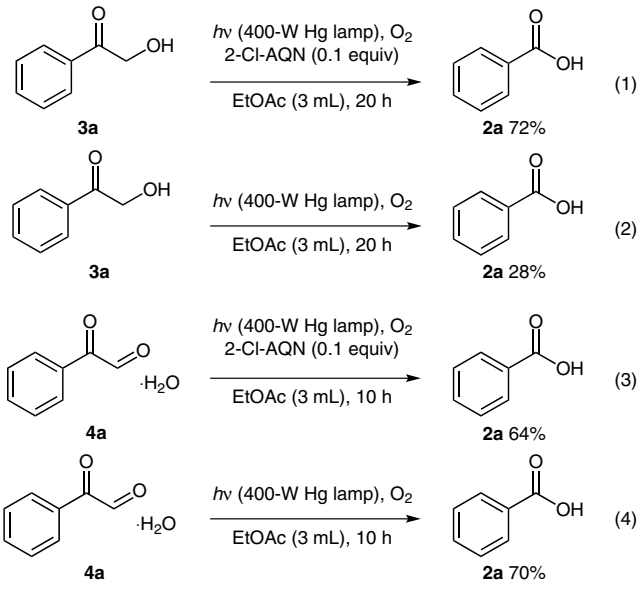


Figure 1 Time course



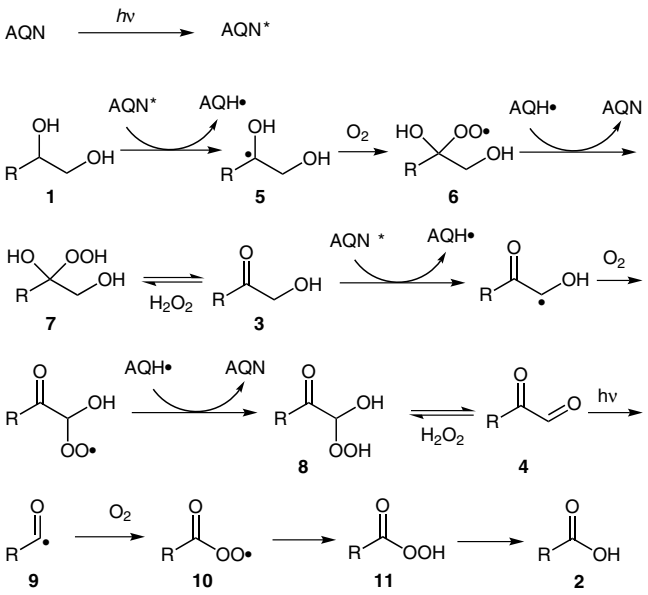
Scheme 2 Study of reaction mechanism

When **3a** was used as substrate under the optimal conditions, benzoic acid (**2a**) was obtained in high yields (Scheme 2, equation 1). On the other hand, **3a** afforded **2a**

in low yield in the absence of 2-chloroanthraquinone (Scheme 2, equation 2). These results suggest that **3a** is the intermediate in this reaction, and anthraquinone is required for the oxidation of **3a**. Furthermore, when phenylglyoxal (**4a**), a plausible reaction intermediate, was used as the substrate under the standard conditions, benzoic acid (**2a**) was obtained in good yields (Scheme 2, equation 3). On the other hand, **4a** afforded higher yields of benzoic acid (**2a**) in the absence of 2-chloroanthraquinone (Scheme 2, equation 4).

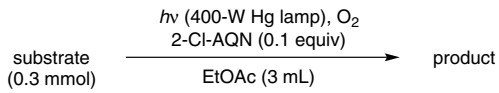
Scheme 3 shows a plausible path for this reaction, which is postulated by considering the requirement of continuous irradiation, a catalytic amount of anthraquinone, and molecular oxygen. Excited anthraquinone abstracts the hydrogen radical at the benzyl position of vicinal diol to produce radical **5**, which traps the molecular oxygen. 2-Hydroxyacetophenone (**3**) is formed via peroxyradical **6** and hydroperoxide **7**, and then it is transformed to hydroperoxide **8** via abstraction of the hydrogen radical by the excited anthraquinone and followed by oxidation. Phenylglyoxal (**4**) is produced by the elimination of hydrogen peroxide. Next, phenylglyoxal produces the acyl radical **9** by Norrish I reaction, which traps the molecular oxygen. Carboxylic acid **2** is formed through the peroxy radical **10** and peracid **11**.

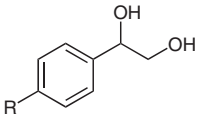
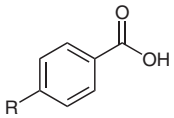
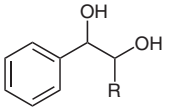
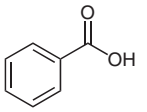
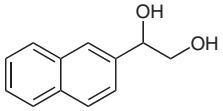
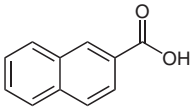
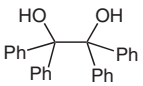
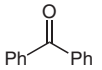
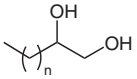
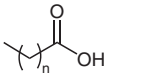
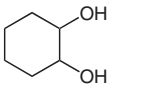
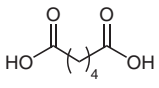
In conclusion, we have developed the aerobic photooxidative cleavage of vicinal diols to carboxylic acids using 2-chloroanthraquinone and photoirradiation from a high-pressure mercury lamp. This method is of interest from the viewpoint of green chemistry because of the use of molecular oxygen and anthraquinones as organocatalysts.



Scheme 3 Plausible path of oxidative cleavage of vicinal diol

Table 2 Scope and Limitations



Entry	Substrate		Time (h)	Product		Yield (%)[a]
1		**1a** R = H	20		**2a**	86
2		**1b** R = Cl	20		**2b**	89
3		**1c** R = *t*-Bu	20		**2c**	80
4		**1d** R = OMe	20		**2d**	82
5		**1e** R = Me	30		**2a**	81
6		**1f** R = Ph	30		**2a**	80[b]
7		**1g**	30		**2g**	30
8		**1h**	30		**2h**	70[c]
9		**1i** n = 7	20		**2i**	75
10		**1j** n = 9	30		**2j**	58[d]
11		**1k** n = 11	30		**2k**	52[d]
12		**1l**	50		**2l**	59[d]

[a] Isolated yields.
[b] Compound **2a** (0.48 mmol) was obtained.
[c] Compound **2h** (0.43 mmol) was obtained.
[d] Substrates were recovered in 10% (entry 10), 8% (entry 11), and 18% (entry 12) yields, respectively.

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(9) **General Procedure**

A solution of 1-phenyl-1,2-ethanediol (**1a**, 0.3 mmol) and 2-chloroanthraquinone (0.03 mmol) in dry EtOAc (3 mL) in a Pyrex test tube, purged with an O_2 balloon, was stirred and irradiated externally with a 400 W high-pressure mercury lamp for 20 h. The reaction mixture was concentrated in vacuo, and 1% aq NaOH was added. The aqueous solution was washed with Et_2O, and then acidified with 2 M aq HCl solution, which was extracted with Et_2O. The organic layer was washed with brine and dried over $MgSO_4$, and concentrated in vacuo. Purification of the crude product by PTLC ($CHCl_3$–MeOH = 9:1) provided benzoic acid (R_f = 0.6, 31.4 mg, 86%).

Benzoic Acid (2a)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.13 (d, *J* = 7.4 Hz, 2 H), 7.62 (t, *J* = 7.4 Hz, 1 H), 7.48 (t, *J* = 7.4 Hz, 2 H). ^{13}C NMR (100 MHz, acetone-d_6): δ = 172.6, 133.9, 130.3, 129.4, 128.6.

4-Chlorobenzoic Acid (2b)

^{1}H NMR (500 MHz, acetone-d_6): δ = 8.01 (d, *J* = 8.6 Hz, 2 H), 7.53 (d, *J* = 8.6 Hz, 2 H). ^{13}C NMR (100 MHz, acetone-d_6): δ = 166.7, 139.5, 132.1, 130.3, 129.5.

4-*tert*-Butylbenzoic Acid (2c)

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.06 (d, *J* = 8.7 Hz, 2 H), 7.49 (d, *J* = 8.7 Hz, 2 H), 1.35 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 172.6, 157.7, 130.2, 126.7, 125.6, 35.3, 31.2.

4-Methoxybenzoic Acid (2d)

^{1}H NMR (500 MHz, acetone-d_6): δ = 7.96 (d, *J* = 9.2 Hz, 2 H), 7.00 (d, *J* = 9.2 Hz, 2 H), 3.85 (s, 3 H). ^{13}C NMR (100 MHz, acetone-d_6): δ = 167.5, 164.4, 132.5, 123.7, 114.5, 55.8.

2-Naphthoic Acid (2g)

^{1}H NMR (400 MHz, acetone-d_6): δ = 8.66 (s, 1 H), 8.07 (dd, *J* = 8.5, 1.7 Hz, 2 H), 7.99 (dd, *J* = 8.5, 5.6 Hz, 2 H), 7.66–7.57 (m, 2 H). ^{13}C NMR (100 MHz, acetone-d_6): δ = 168.9, 134.9, 134.2, 132.3, 131.3, 129.4, 128.4, 127.9, 127.0, 126.7, 125.5.

Benzophenone (2h)

^{1}H NMR (500 MHz,$CDCl_3$): δ = 7.80 (d, *J* = 8.0 Hz, 4 H), 7.58 (t, *J* = 8.0 Hz, 2 H), 7.48 (t, *J* = 8.0 Hz, 4 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 196.8, 137.8, 132.5, 130.2, 128.4.

Nonanoic Acid (2i)

^{1}H NMR (500 MHz,$CDCl_3$): δ = 2.35 (t, *J* = 7.6 Hz, 2 H), 1.70–1.60 (m, 2 H), 1.39–1.22 (m, 10 H), 0.89 (t, *J* = 6.9 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 181.0, 34.5, 32.2, 29.6, 29.5, 29.5, 25.1, 23.1, 14.5.

Undecanoic Acid (2j)

^{1}H NMR (500 MHz,$CDCl_3$): δ = 2.35 (t, *J* = 7.5 Hz, 2 H), 1.66–1.59 (m, 2 H), 1.35–1.21 (m, 14 H), 0.88 (t, *J* = 6.6 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.8, 32.0, 29.6, 29.5, 29.4, 29.3, 29.2, 29.1, 24.7, 22.7, 14.2.

Tridecanoic Acid (2k)

^{1}H NMR (500 MHz,$CDCl_3$): δ = 2.35 (t, *J* = 7.5 Hz, 2 H), 1.65–1.55 (m, 2 H), 1.34–1.20 (m, 18 H), 0.88 (t, *J* = 6.9 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 179.8, 33.8, 31.6, 29.4, 29.3, 29.2, 29.1, 29.0, 28.8, 24.4, 22.4, 13.8.

Adipic Acid (2l)

^{1}H NMR (500 MHz, DMSO-d_6): δ = 2.22–2.18 (m, 4 H), 1.52–1.47 (m, 4 H). ^{13}C NMR (125 MHz, DMSO-d_6): δ = 174.5, 33.5, 24.2.

