Catalytic Aerobic Photooxidative Cleavage of Carbon–Carbon Triple Bonds Using Carbon Tetrabromide

Tomoaki Yamaguchi, Tomoya Nobuta, Yasuhisa Kudo, Shin-ichi Hirashima, Norihiro Tada, Tsuyoshi Miura, Akichika Itoh*

Gifu Pharmaceutical University, 1-25-4 Daigaku-nishi, Gifu 501-1196, Japan
Fax +81(58)2308108; E-mail: itoha@gifu-pu.ac.jp

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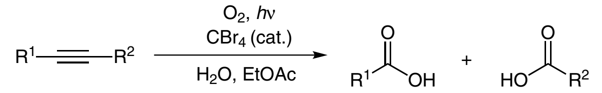
Abstract: We developed the aerobic photooxidative cleavage of carbon–carbon triple bonds to carboxylic acids in the presence of catalytic amounts of carbon tetrabromide under photoirradiation with a high-pressure mercury lamp.

Key words: photooxidation, aerobic, carbon tetrabromide, carbon–carbon triple bond, carboxylic acid

The oxidative cleavage of a carbon–carbon triple bond to the corresponding carboxylic acid is an important transformation of functional groups in organic synthesis.[1] In general, ozonolysis has been used for this purpose; however, ozone is toxic and requires the use of special equipment to generate it. Thus, many oxidative cleavage reactions using heavy-metal catalysts such as ruthenium, osmium, iron, and indium in combination with stoichiometric amounts of oxygen donors such as TBHP, oxone, H_2O_2, and $NaIO_4$ have been reported to date.[2] In addition, few metal-free reactions have been reported. Electron-deficient acetylene can be cleaved using H_2O_2 in the presence of MeONa.[3] Furthermore, stoichiometric amounts of hypervalent iodine reagent $C_6F_5I(OCOCF_3)_2$ have been used for this reaction.[4] Recently, Ochiai's group reported the catalytic oxidative cleavage of carbon–carbon triple bonds using catalytic amounts of iodomesitylene and MCPBA as the terminal oxidant.[5]

Owing to the increasing demand for 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 exhibits higher atom efficiency than other oxidants.[6] However, autoxidation of carbon–carbon triple bonds is slow even under high temperature and gives the corresponding carboxylic acids in low yield.[7] Recently, Jiang's group reported the palladium-catalyzed cleavage of carbon–carbon triple bonds to the corresponding esters using molecular oxygen as the terminal oxidant.[8] To the best of our knowledge, there is no catalytic oxidative cleavage reaction of carbon–carbon triple bonds under metal-free conditions using molecular oxygen as the terminal oxidant.

We have been studying the aerobic photooxidation of various substrates[9] and have already reported the oxidative cleavage of carbon–carbon double bonds with catalytic amounts of a bromine source under photoirradiation.[10] In the course of further studying this reaction, we found that the oxidative cleavage of the carbon–carbon triple bonds occurred in the presence of catalytic amounts of carbon tetrabromide (CBr_4) and water under aerobic photoirradiation conditions (Scheme 1). We report herein a detailed study of this photooxidative cleavage of alkynes.



Scheme 1 Aerobic oxidative cleavage of alkynes

To explore this approach, we selected phenylacetylene (**1a**) as the test substrate to optimize the reaction conditions (Table 1). First, we screened the bromine sources and solvents in the presence of molecular oxygen under photoirradiation from a 400 W mercury lamp (Table 1, entries 1–19). Benzoic acid (**2a**) was produced most efficiently albeit in moderate yields when using CBr_4 as catalyst and ethyl acetate as solvent (Table 1, entry 1). Next, the addition of trifluoroacetic acid (TFA) and potassium carbonate (K_2CO_3) was examined, and the yield increased to 81% with the addition of K_2CO_3 (Table 1, entries 20 and 21). Interestingly, addition of water (150 μL) afforded the same yield of **2a** (Table 1, entry 23). No **2a** was obtained when a fluorescent lamp was used instead of a Hg lamp (Table 1, entry 25). The fact that **2a** was not obtained without CBr_4, photoirradiation, or molecular oxygen shows how critical these ingredients are for this reaction (Table 1, entries 26–28).

Table 2 shows the results of scope and limitations of the oxidative cleavage of alkynes under the above-mentioned reaction conditions.[11] Generally, the corresponding carboxylic acids are obtained in good to high yields regardless of the electron-donating or electron-withdrawing group on the benzene ring (Table 2, entries 1–7). In addition, the ethynyl group is more easily oxidized to carboxylic acid than the methyl group, and 4-methylbenzoic acid was obtained in 52% yield (Table 2, entry 3). Furthermore, internal alkynes **1h**, **1i**, and **1j** were also oxidized to **2a** in moderate to good yields (Table 2, entries 8–10). Unfortunately, no 2-picolinic acid was obtained (Table 2, en-

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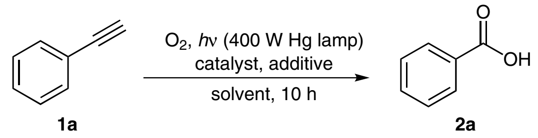
Table 1 Study of Reaction Conditions[a]



Entry	Catalyst (equiv)	Additive	Solvent	Yield (%)[b]
1	CBr_4 (0.1)	–	EtOAc	62
2	NBS (0.1)	–	EtOAc	23
3	Br_2 (0.1)	–	EtOAc	27
4	48% aq HBr (0.1)	–	EtOAc	23
5	LiBr (0.1)	–	EtOAc	35
6	NaBr (0.1)	–	EtOAc	1
7	KBr (0.1)	–	EtOAc	1
8	$MgBr_2·OEt_2$ (0.1)	–	EtOAc	23
9	$AlBr_3$ (0.1)	–	EtOAc	32
10	$SmBr_3$ (0.1)	–	EtOAc	27
11	CBr_4 (0.1)	–	hexane	38
12	CBr_4 (0.1)	–	*i*-Pr_2O	15
13	CBr_4 (0.1)	–	benzene	52
14	CBr_4 (0.1)	–	CH_2Cl_2	10
15	CBr_4 (0.1)	–	acetone	20
16	CBr_4 (0.1)	–	MeCN	34
17	CBr_4 (0.1)	–	AcOH	33
18	CBr_4 (0.1)	–	MeOH	32
19	CBr_4 (0.1)	–	H_2O	8
20	CBr_4 (0.1)	TFA (0.5 equiv)	EtOAc	59
21	CBr_4 (0.1)	K_2CO_3 (0.5 equiv)	EtOAc	81
22	CBr_4 (0.1)	H_2O (50 μL)	EtOAc	59
23	CBr_4 (0.1)	H_2O (150 μL)	EtOAc	81 (86)
24	CBr_4 (0.05)	H_2O (150 μL)	EtOAc	79
25[c]	CBr_4 (0.1)	H_2O (150 μL)	EtOAc	0
26	–	H_2O (150 μL)	EtOAc	0
27[d]	CBr_4 (0.1)	H_2O (150 μL)	EtOAc	0
28[e]	CBr_4 (0.1)	H_2O (150 μL)	EtOAc	0

[a] A solution of phenylacetylene (**1a**, 0.3 mmol), catalyst, and additive in dry solvent (5 mL) purged with an O_2 balloon was stirred and irradiated externally with a 400 W high-pressure mercury lamp for 10 h.

[b] ^{1}H NMR yields. Number in parentheses is isolated yield.

[c] The reaction was carried out using fluorescent lamp.

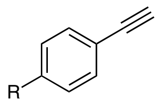
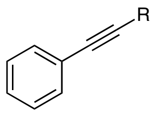
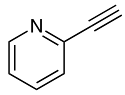
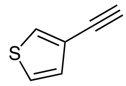
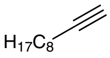
[d] The reaction was carried out in the dark.

[e] The reaction was carried out under argon.

try 11). On the other hand, 3-ethynylthiophene was converted into 3-thiophenecarboxylic acid albeit in low yield (Table 2, entry 12). Aliphatic alkyne was also converted into the corresponding carboxylic acid in modest yield (Table 2, entry 13).

Table 2 Scope and Limitations[a]

$$\underset{\mathbf{1}}{\text{substrate}} \xrightarrow[\text{EtOAc}]{\text{O}_2,\ h\nu\ \text{(400 W Hg lamp)}\quad \text{CBr}_4\ \text{(0.1 equiv), H}_2\text{O (150 mL)}} \underset{\mathbf{2}}{\text{product}}$$

Entry	Substrate		Time (h)	Yield (%)[b]
1		**1b** R = OMe	20	78
2[c]		**1c** R = *t*-Bu	10	71
3[c]		**1d** R = Me	5	52
4		**1e** R = Ph	40	62
5		**1a** R = H	10	86
6		**1f** R = F	20	90
7		**1g** R = NO_2	40	97
8		**1h** R = Ph	40	56[d]
9		**1i** R = Me	20	83[e]
10		**1j** R = CO_2Et	20	75[f]
11		**1k**	20	0
12		**1l**	20	16
13		**1m**	40	34

[a] A solution of substrate (**1a**, 0.3 mmol), CBr_4 (0.1 equiv), and H_2O (150 μL) in dry EtOAc (5 mL) purged with an O_2 balloon was stirred and irradiated externally with a 400 W high-pressure mercury lamp.

[b] Isolated yields.

[c] The reaction was carried out with CBr_4 (0.05 equiv).

[d] Benzoic acid (0.34 mmol) was obtained.

[e] Benzoic acid (0.25 mmol) was obtained.

[f] Benzoic acid (0.225 mmol) was obtained.

We studied the time course of the oxidative cleavage of **1a** to clarify the reaction mechanism in the presence or absence of water (Figure 1 and Figure 2). ^{1}H NMR spectroscopy was used to detect 2,2-dibromoacetophenone (**3a**) and phenylglyoxylic acid (**4a**) under both conditions. Unfortunately, in the absence of water, only benzoic acid (**2a**) was obtained, and the other products could not be determined by ^{1}H NMR spectroscopy and GC–MS within ten hours (Figure 2). Next, **3a** was used as a substrate under the optimal conditions to give **2a** and ethyl benzoate (**5a**) regardless of the presence or absence of CBr_4 (Scheme 2, eq. 1). Furthermore, **4a** afforded **2a** and **5a** in the presence of CBr_4 in 80% and 19% yield, respectively (Scheme 2, eq. 2). These results suggest that **3a** and **4a** are reaction intermediates.

Scheme 3 shows a plausible path for the oxidative cleavage of alkynes, which is postulated by considering the de-

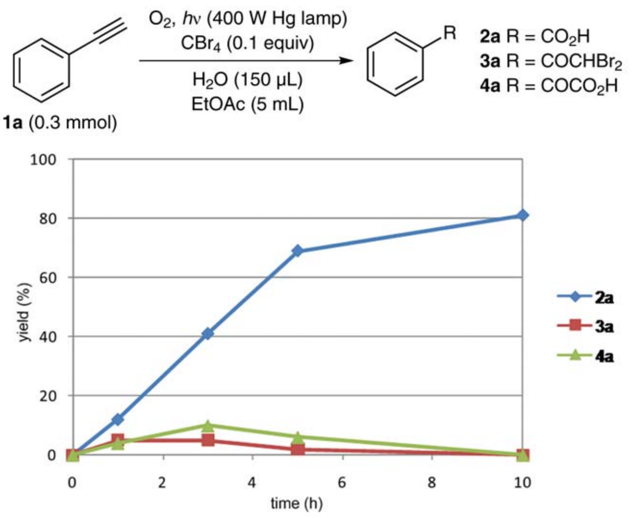


Figure 1 Time course of oxidative cleavage of alkyne in the presence of H_2O

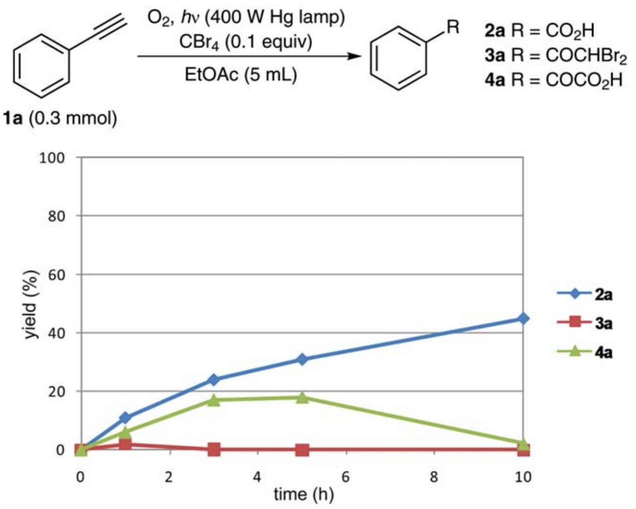


Figure 2 Time course of oxidative cleavage of alkyne in the absence of H_2O

tected intermediates and by the necessity of continuous irradiation, a bromine source, and molecular oxygen for this reaction. The bromo radical, generated by the homolysis of CBr_4 during photoirradiation, was added to **1** to afford vinyl radical **6**, which traps the molecular oxygen to provide dibromoketone **3** via bromination of bromoenol **8** with the bromine or hypobromous acid. Because dibromoketone **3a** was oxidized to carboxylic acid in the absence of CBr_4 (Scheme 2, eq. 1), dibromoketone **3** was probably converted into 1,2-dicarbonyl compound **12** via the homolytic cleavage of the C–Br bond to **9** and the subsequent oxidation (path A). In the case of terminal alkyne, 1,2-dicarbonyl compound **12** was oxidized to glyoxylic acid **4**. Compound **4** was homolytically cleaved to acyl radical **15**[12] via the Norrish type I reaction by photoirradiation and oxidized to carboxylic acid via percarboxylic acid **16**. On the other hand, in the case of internal alkyne, 1,2-diketone **12** was homolytically cleaved to acyl radical **15** via the Norrish type I reaction. Under these conditions, the direct formation of acyl radical **15** from **3** is also possible via the Norrish type I reaction (path B). Furthermore, abstraction of hydrogen of **3** by bromine radical to **17** is not also ruled out (path C).

In conclusion, we developed the aerobic photooxidative cleavage of carbon–carbon triple bonds to carboxylic acids using catalytic amounts of carbon tetrabromide in the presence of water under photoirradiation from a high-pressure mercury lamp. Furthermore, detailed mechanistic studies, which include the role of additive water, are ongoing in our laboratory.

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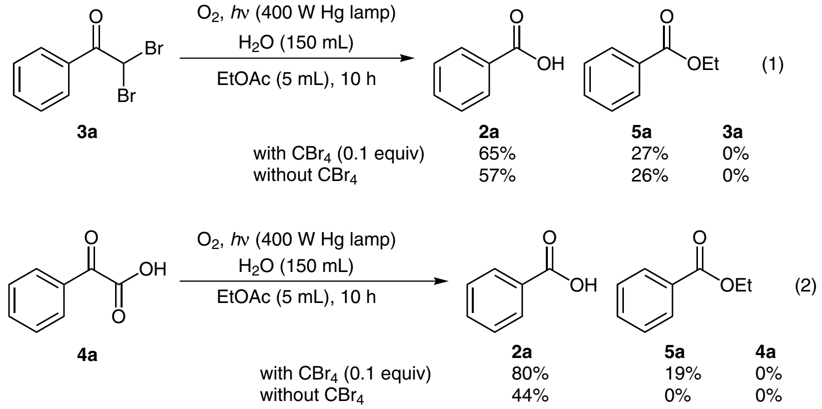
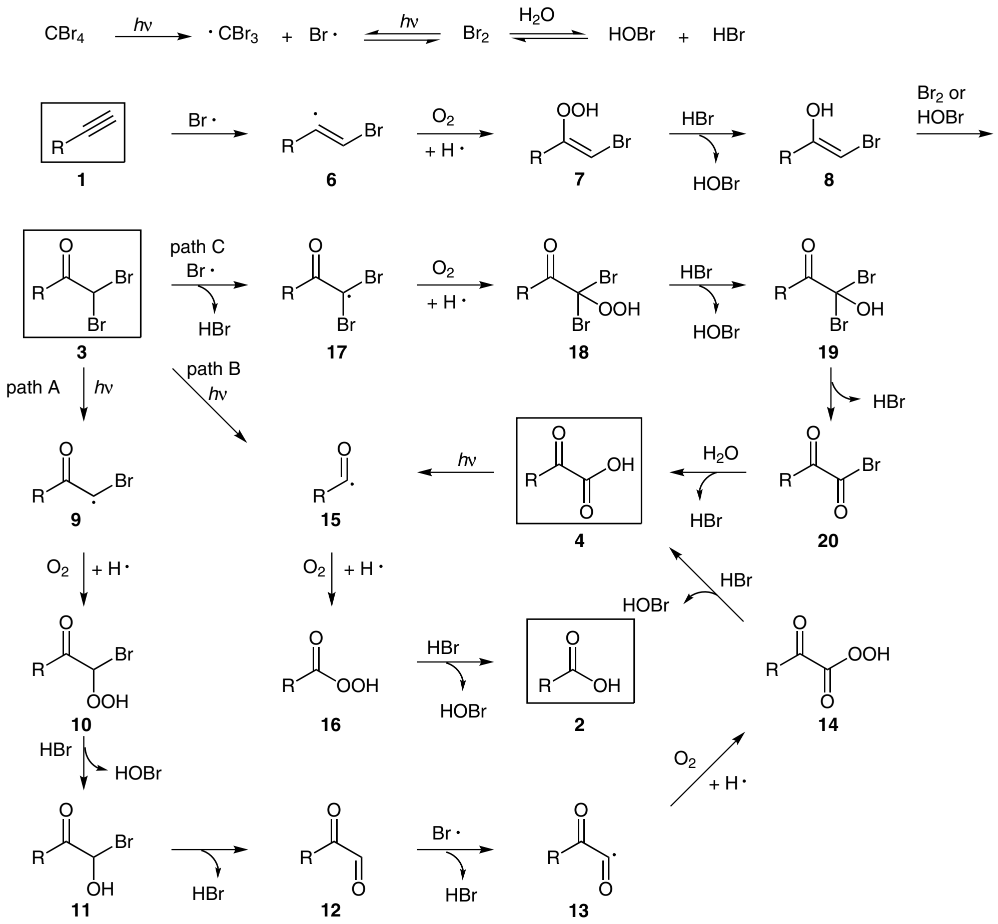


Scheme 2 Study of reaction intermediate



Scheme 3 Plausible reaction mechanism

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(11) **General Procedure**
A solution of phenylacetylene (**1a**, 0.3 mmol), CBr_4 (0.03 mmol), and H_2O (150 μL) 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 10 h. The reaction mixture was concentrated in vacuo, and 10% aq NaOH was added. The aqueous solution was washed with $CHCl_3$, and then acidified with 2 N aq HCl solution, which was extracted with $CHCl_3$. The organic layer was dried over $MgSO_4$, and concentrated in vacuo provided benzoic acid (31.4 mg, 86%).

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