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Aerobic photo-oxidative cleavage of the C–C double bonds of styrenes

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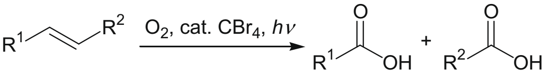
ABSTRACT

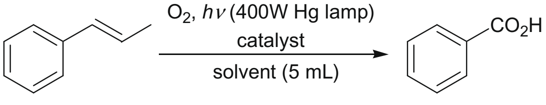
Carbon tetrabromide enables us to carry out oxidative cleavage of the C–C double bonds of styrenes under aerobic photo-irradiation conditions. Oxidative cleavage of the various β-substituted styrenes produced benzoic acid in good yields. Since this reaction is found to be applicable to the α- or β-substituted styrenes, which showed very low reactivity under our previous cleavage reaction condition with FSM-16 and I_2, this reaction can be used complementarily.

Oxidative cleavage of a carbon–carbon double bond to the corresponding carbonyl compounds is an important method in organic syntheses, especially in syntheses of natural products and biologically active compounds. Ozonolysis, in general, has been used for this purpose; however, ozone is explosive and a special equipment is necessary to carry out this method.[1] Since another oxidative cleavage with heavy metals such as RuO_4 and OsO_4 requires the expensive or toxic heavy metals, such as RuO_4 and OsO_4, and a number of stoichiometric oxygen donors to produce the corresponding carboxylic acids or aldehydes,[2] development of a safe and metal-free method is desirable for these synthetic transformations. With this concern, we have studied the aerobic photo-oxidation,[3] and have already reported oxidative cleavage of the double bonds of styrenes with FSM-16, a mesoporous silica, and I_2 under photo-irradiation; however, this method was rather unsatisfactory when α- or β-substituted styrenes were used as substrates.[4] In the course of our further study of this reaction with other catalysts, we also found that oxidative cleavage of the C–C double bonds of styrenes occurred in the presence of cat. carbon tetrabromide (CBr_4) under aerobic photo-irradiation conditions (Eq. 1). We report herein a detailed study of this single-step photo-oxidative cleavage of alkenes.



(1)

Table 1
Study of reaction conditions for aerobic photo-oxidative cleavage of β-methylstyrene (**1**)



1 (0.3 mmol)

2

Entry	Catalyst	Amount (equiv)	Solvent	Time (h)	Yield of **2**[a] (%)
1	CBr_4	0.3	MeOH	10	41
2	CBr_4	0.3	CH_2Cl_2	10	55
3	CBr_4	0.3	*i*Pr_2O	10	58
4	CBr_4	0.3	Acetone	10	61
5	CBr_4	0.3	MeCN	10	63
6	CBr_4	0.3	Hexane	10	79
7	CBr_4	0.3	EtOAc	10	81
8	CBr_4	0.1	EtOAc	10	66
9	CBr_4	0.2	EtOAc	10	73
10	CBr_4	0.4	EtOAc	10	78
11	CBr_4	0.3	EtOAc	10	64[b]
12	CBr_4	0.3	EtOAc	10	0[c,f]
13	CBr_4	0.3	EtOAc	10	0[d,f]
14	CBr_4	0.3	EtOAc	10	0[e,f,g]
15	CBr_4	0.3	EtOAc	7	79
16	CBr_4	0.3	EtOAc	15	85
17	aq HBr	0.3	EtOAc	10	70
18	$MgBr_2{\cdot}OEt_2$	0.3	EtOAc	10	62
19	Br_2	0.3	EtOAc	10	60
20	LiBr	0.3	EtOAc	10	57
21	NBS	0.3	EtOAc	10	49

[a] All yields are for pure, isolated products.
[b] The reaction was carried out under irradiation of 500 W Xenon lamp.
[c] The reaction was carried out under irradiation of fluorescent lamp.
[d] The reaction was carried out in the dark.
[e] The reaction was carried out under Ar atmosphere.
[f] Starting material was recovered: 51% (entry 12), 63% (entry 13) and 35% (entry 14).
[g] (1,2-Dibromo-propyl)-benzene (5%) was obtained.

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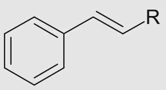
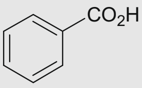
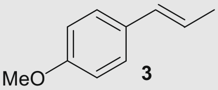
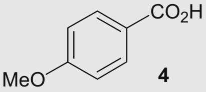
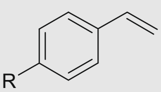
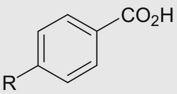
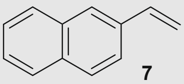
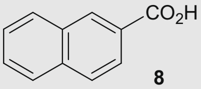
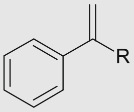
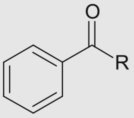
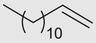
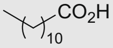
Table 2
Aerobic photo-oxidative cleavage of C–C double bonds

$$\underset{\text{(0.3 mmol)}}{\text{substrate}} \xrightarrow[\text{EtOAc (5 mL), 10h}]{O_2,\ h\nu\ \text{(400W Hg lamp)},\ CBr_4\ \text{(0.3 equiv.)}} \text{product}$$

Entry	Substrate		Product	Yield[a] (%)
1		R = Me: **1a**	 **2**	81
2		R = Ph: **1b**		71[b]
3		R = CH_2OH: **1c**		77
4		R = NO_2: **1d**		71
5		R = COMe: **1e**		88
6		R = COPh: **1f**		82[b]
7	 **3**		 **4**	82
8		R = ^{t}Bu: **5a**	 **6a**	62
9		R = OMe: **5b**	**4**	56
10		R = Cl: **5c**	**6c**	60
11		R = NO_2: **5d**	**6d**	16[c]
12	 **7**		 **8**	18
13		R = Me: **9**	 **10**	38[d]
14		R = Ph: **11**	**12**	48[d]
15	 **13**		 **14**	32[e]

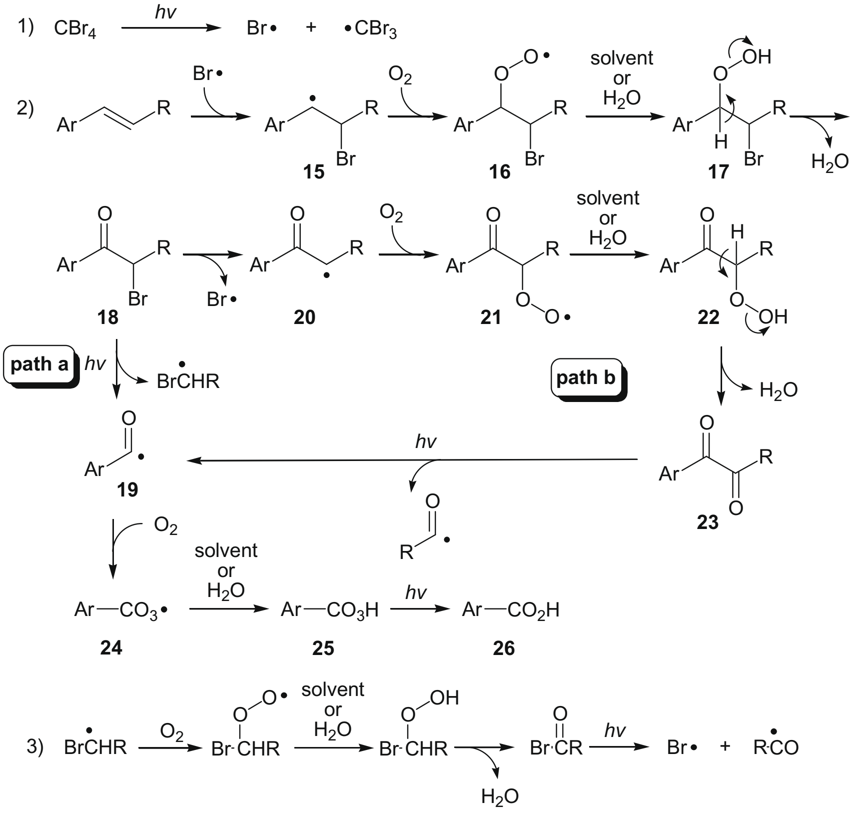
[a] All yields are for pure, isolated products.

[b] The yield was calculated as 2 equiv of benzoic acid.

[c] 4-Nitrophenacyl bromide was also obtained in 20% yield.

[d] The reaction was carried out with 0.1 equiv of aq HBr.

[e] The reaction was carried out with 0.6 equiv of CBr_4 in hexane for 24 h.



Scheme 1. Plausible path of aerobic photo-oxidative cleavage of C–C double bonds.

Table 1 shows the data for study of catalysts with β-methylstyrene (**1**), which resulted in poor yield under our previous method,[4] and, among our examination, benzoic acid (**2**) was produced most efficiently when using CBr_4 as catalysts and ethyl acetate as solvent (entries 1–7 and 17–21).[5] The optimal result was obtained in the presence of 0.3 equiv of CBr_4 (entries 7–10). That no oxidation proceeded without irradiation of UV and that only additional reaction of bromine to the double bond proceeded without molecular oxygen show the necessity of both for this reaction (entries 13 and 14). The yield of **2** was little affected by extension of the reaction time, and 500 W Xenon lamp or fluorescent lamp was less effective than 400 W high-pressure mercury lamp (entries 11, 12 and 16).

Table 2 shows the results for limitation and scope of this oxidation under the reaction conditions mentioned above. Oxidative cleavage of the various β-substituted styrenes **1** produced benzoic acid (**2**) in good yields (entries 1–7). On the other hand, since non-substituted styrenes, **5** and **7**, were found to be liable to form the polymers or other unidentified by-products under this reaction condition, yield of the corresponding products, **4**, **6** and **8**, was generally modest (entries 8–12). Corresponding acetophenone (**10**) and benzophenone (**12**), which are unstable under this condition, were obtained only in modest yield when using **9** and **11**, α-substituted styrenes, as substrates (entries 13 and 14). Surprisingly, we found that 1-dodecene (**13**), a non-conjugated alkene which was intact under our previous condition with FSM-16 and I_2, afforded the corresponding carboxylic acid **14** in 32% yield.

Scheme 1 shows a plausible path of this oxidation, which is postulated by considering the detectable intermediates, phenacyl bromides **18**, and the necessity of continuous irradiation, bromo source and molecular oxygen in this reaction. Benzyl radical species **15** is generated by addition of bromo radical, formed by heterolysis of CBr_4, to the double bond of styrenes. The resulting radical species **15** traps molecular oxygen to afford **18** via peroxyradical **16** and hydroperoxide **17**. Since **26** (Ar = 4-BrC_6H_4) was obtained in 82% yield when using **18** (Ar = 4-BrC_6H_4, R = H) as substrate without bromo source, we infer that there are two paths to produce acyl radical **19** through cleavage of C–C bond of phenacyl bromides (path a) or 1,2-dicarbonyl compounds (path b) under photo-irradiation, namely Norrish Type I reaction. We think that this reaction mainly proceeds through path a, since only 35% of benzoic acid was produced when using benzil as substrate without CBr_4 under photo-irradiation conditions.

In conclusion, we report a practical method for CBr_4-catalyzed aerobic photo-oxidative cleavage of carbon-carbon double bonds. Since this reaction is found to be applicable to the α- or β-substituted styrenes, which showed very low reactivity under our previous cleavage reaction condition with FSM-16 and I_2, this reaction can be used complementarily. Further studies on the use of bromo-catalyst and additional applications of the photo-oxidation are currently underway in our laboratory.

References and notes

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3. (a) Itoh, A.; Hashimoto, S.; Kodama, T.; Masaki, Y. *Synlett* **2005**, 2107–2109; (b) Itoh, A.; Hashimoto, S.; Masaki, Y. *Synlett* **2005**, 2639–2640; (c) Hirashima, S.; Itoh, A. *Synthesis* **2006**, 1757–1759; (d) Hirashima, S.; Hashimoto, S.; Masaki, Y.; Itoh, A. *Tetrahedron* **2006**, *62*, 7887–7891; (e) Hirashima, S.; Itoh, A. *J. Synth. Org. Chem. Jpn.* **2008**, *66*, 748–756.
4. Itoh, A.; Kodama, T.; Masaki, Y.; Inagaki, S. *Synlett* **2002**, 522–524.
5. *A typical procedure is as follows*: A solution of β-methylstyrene (**1a**, 0.3 mmol) and CBr_4 (0.09 mmol) in dry EtOAc (5 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% NaOH aqueous solution was added. The aqueous solution was washed with Et_2O, and then acidified with 2 N HCl aqueous solution, which was extracted with Et_2O. The organic layer was washed with brine and dried over $MgSO_4$, and concentrated in vacuo. The product obtained is pure without further purification.