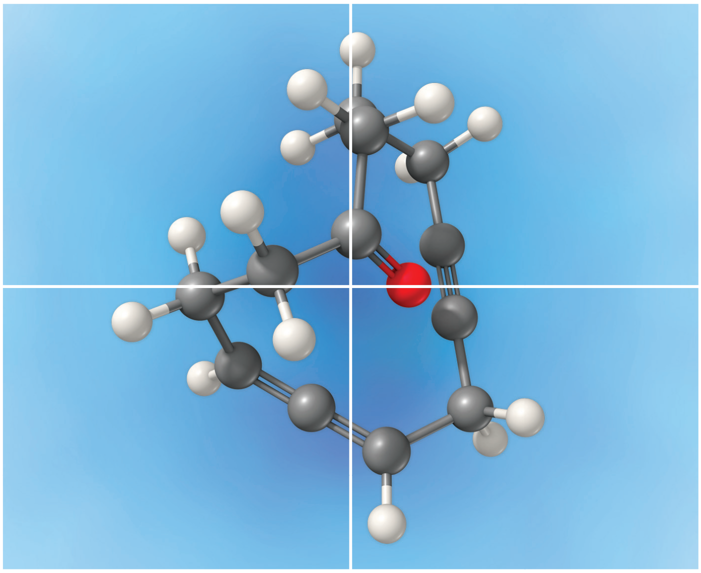
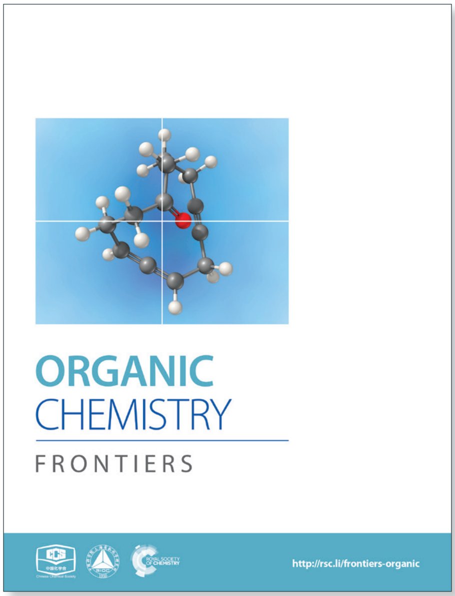
ORGANIC CHEMISTRY
FRONTIERS



Accepted Manuscript



ORGANIC CHEMISTRY

FRONTIERS

http://rsc.li/frontiers-organic

Journal Name

RSCPublishing

ARTICLE

Photoinduced HBr-Catalyzed C-Si Bond Cleavage of Benzylsilanes and Subsequent Oxidation into Benzoic Acids with Air as Terminal Oxidant

Cite this: DOI: 10.1039/x0xx00000x

Received 00th January 2012,
Accepted 00th January 2012

DOI: 10.1039/x0xx00000x

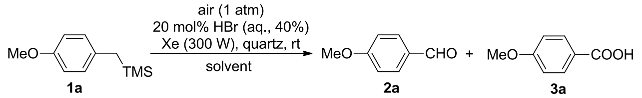
www.rsc.org/

Jing Sun,[a,b,e] Yu Wang,[c,e] Liqiong Han,[a] Dawen Xu,[a] Yiyong Chen,[a] Xinhua Peng[b] and Hao Guo*[a,d]

A photoinduced highly efficient C-Si bond cleavage reaction of benzylsilanes under the catalysis of HBr was developed. The *in situ* generated benzyl radical intermediates were aerobically oxidized into benzoic acids highly chemoselectively. In this transformation, HBr not only acted as the single electron transfer mediator for the initial C-Si bond cleavage, but also efficiently catalyzed the oxidation of benzaldehyde intermediates into benzoic acids.

Carbon-silicon bond is ubiquitous in organic chemicals.[1] Its formation reactions have a rich history.[2] Meanwhile, highly efficient and selective cleavage of C-Si bond and its subsequent functionalization have also received much attention.[3] Besides the numerous achievements in thermal reactions, photochemical methods which provide an alternative way for C-Si bond cleavage and functionalization remain underdeveloped. Only few research works have been reported in this field.[4-8] Compared to breaking of the C-Si bond, a more challenging issue in photodesilylation is to control its following transformation, especially for aerobic oxidation. For example, Otsuji and Mizuno[4e] reported a 9,10-dicyanoanthracene (DCA)-sensitized photooxidation of benzylsilanes, affording a mixture of aromatic aldehydes and carboxylic acids in poor chemoselectivities. Albini[5a] reported a TiO_2-catalyzed photoreaction of benzylsilicons, which also yielded a mixture of alcohol, aldehyde, and acid as well as other byproducts. Although the selectivities in such cases are not satisfactory to be applied in synthetic organic chemistry, it provides an alternative but to be improved approach in this field. Two key steps are involved in this reaction: C-Si bond cleavage via photoinduced single electron transfer process and oxidation of the *in situ* formed benzyl radicals. Thus, improvements of both C-Si bond cleavage efficiency and subsequent oxidation selectivity may lead to a new synthetically useful method for this transformation. Herein, we wish to report our recent observation on the photoinduced HBr-catalyzed C-Si bond cleavage of benzylsilanes and subsequent oxidation, affording only benzoic acid derivatives in good to excellent yields.

Table 1. Optimization of reaction conditions.[a]

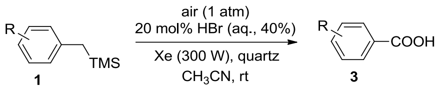


Entry	Solvent	Time (h)	Isolated yield (%)	
			2a	**3a**
1[b]	Benzene	12	38	25
2	Benzene	11	15	65
3	CH_2Cl_2	4.5	37	26
4	CH_3OH	10.5	15	7
5	DMSO	4	45	12
6	CH_3NO_2	11	14	22
7	DMF	25	8	24
8	THF	24	0	17
9	CH_3CN	3.5	0	91
10[c]	CH_3CN	11	0	86
11[d]	CH_3CN	21	66	16

[a] A solution of **1a** (0.2 mmol) and 20 mol% HBr (aq., 40%) in the tested solvent (10 mL) in a quartz reaction tube was irradiated by 300 W Xe lamp at rt in the open air. [b] The reaction was carried out without HBr. [c] Pyrex reaction tube was used. [d] Hg lamp (500 W) was used.

At the beginning of our study, (4-methoxybenzyl)trimethylsilane **1a** was chosen as the model substrate to explore the feasibility of the reaction. Without catalyst, the photoreaction of **1a** in benzene irradiated by Xe lamp at rt yielded a mixture of 4-methoxybenzaldehyde **2a** and 4-methoxybenzoic acid **3a** in a total yield of 63% (**2a**:**3a** = 38:25) (entry 1, Table 1). To improve the yield and selectivity, 20 mol% of HBr (aq., 40%) was applied, the total yield rose up to 80%, however, the chemoselectivity is still poor (entry 2, Table 1). Then, solvent effect was studied carefully. When CH_2Cl_2, CH_3OH, or DMSO was used as the solvent, **2a** was formed as the major product (entries 3-5, Table 1). While for reactions in CH_3NO_2 or DMF, **3a** was generated as the major product (entries 6 and 7, Table 1). In THF, the reaction gave the sole product of **3a** but in a very low isolated yield (entry 8, Table 1). Fortunately, when the reaction was conducted in CH_3CN, **3a** was afforded as the only product in excellent yield with excellent selectivity (entry 9, Table 1). Then pyrex tube was used instead of quartz tube, longer reaction time and lower yield were observed (entry 10, Table 1). Finally, Hg lamp (500 W) was used instead of Xe

Table 2. Photooxidation of **1a-p** under Conditions A.[a,b]



Entry	1	R	Time (h)	3	Isolated yield (%)
1	**1a**	*p*-OMe	3.5	**3a**	91
2	**1b**	*m*-OMe	7.5	**3b**	46
3	**1c**	*o*-OMe	4.5	**3c**	50
4	**1d**	*p*-Bu^t	3	**3d**	66
5	**1e**	*p*-Ph	24	**3e**	83
6	**1f**	H	5	**3f**	74
7	**1g**	*p*-Cl	5.5	**3g**	70
8	**1h**	*p*-F	9	**3h**	82
9	**1i**	*p*-P(O)(Ph)$_2$	17	**3i**	62
10	**1j**	*p*-Ac	10	**3j**	81
11	**1k**	*p*-COOMe	9	**3k**	86
12	**1l**	*p*-COOEt	8.5	**3l**	90
13	**1m**	*p*-C(O)N(Pr^i)$_2$	18.5	**3m**	81
14	**1n**	*p*-CF$_3$	3	**3n**	80
15	**1o**	*m*-CF$_3$	8	**3o**	74
16	**1p**	*o*-CF$_3$	7	**3p**	77

[a] A solution of **1** (0.2 mmol) and 20 mol% HBr (aq., 40%) in CH_3CN (10 mL) in a quartz reaction tube was irradiated by 300 W Xe lamp at rt in the open air. [b] No aldehydes were formed, determined for the crude reaction mixture by 400 MHz ^1H NMR analysis.

lamp (300 W), however, **3a** was formed as the minor product (entry 11, Table 1). Thus, we applied Conditions A (20 mol% HBr (aq., 40%), CH_3CN, Xe lamp (300 W), quartz, air (1 atm), and rt) for the photooxidation of benzylsilanes.

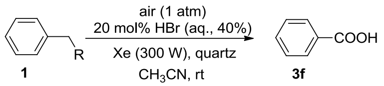
With the optimized conditions in hands, we further investigated the scope of this reaction. A series of benzyltrimethylsilanes were subjected to the standard reaction conditions. The results are summarized in Table 2. It was observed that both electron-donating and -withdrawing groups could be installed to the phenyl ring of the benzyltrimethylsilanes affording corresponding benzoic acids as the only product in good to excellent yields. When methoxy group was introduced to the phenyl ring of the substrates, the relative position showed some influence. (3-Methoxybenzyl)-trimethylsiane **1b** and (2-methoxybenzyl)trimethylsiane **1c** gave much lower yields of the desired products than that of **1a** (entries 1-3, Table 2), which might be due to lower efficiency of the transformation of aldehyde intermediate (*vide infra*) into benzoic acid. While for trifluoromethyl substituted reactants **1n-p**, similar yields were generated (entries 14-16, Table 2).

A scrutiny on the reactivity of different silyl groups was then conducted (Table 3). In all tested cases, **3f** was formed in good isolated yields as the only observed product, indicating that the substituents on silicon atom showed no obvious influence on neither the yield nor the selectivity.

Then allylictrimethylsilanes **4** and aliphatictrimethylsilanes **5** were applied under Conditions A. In both cases, only benzoic acid **3f** was formed (Scheme 1).

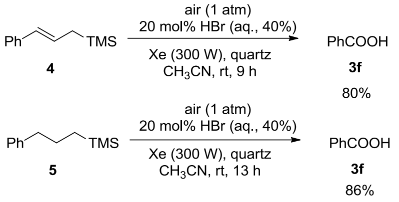
Notably, this reaction could easily proceed in a high yield in gram scale (Scheme 2).

Table 3. Photooxidation of **1f** and **1q-t** under Conditions A.[a,b]

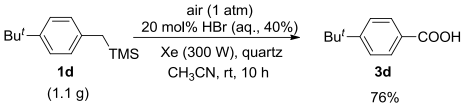


Entry	1	R	Time (h)	Isolated yield (%)
1	**1f**	SiMe$_3$	5	74
2	**1q**	SiEt$_3$	3.5	83
3	**1r**	SiBu^{t}Me$_2$	3	70
4	**1s**	SiPhMe$_2$	4.5	82
5	**1t**	SiPh$_2$Me	8	60

[a] A solution of **1** (0.2 mmol) and 20 mol% HBr (aq., 40%) in CH_3CN (10 mL) in a quartz reaction tube was irradiated by 300 W Xe lamp at rt in the open air. [b] No aldehydes were formed, determined for the crude reaction mixture by 400 MHz ^1H NMR analysis.



Scheme 1. Photooxidation of **4** and **5** under Conditions A.

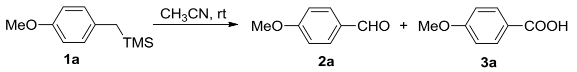


Scheme 2. Gram-scale synthesis of **3d**.

To gain insight into the reaction mechanism, a series of control experiments were carried out (Table 4). The results showed that (i) under Conditions A, this reaction proceeded smoothly to afford only **3a** in excellent yield (entry 1, Table 4); (ii) photoirridiation was required for the conversion (entry 2, Table 4); (iii) oxygen in air could be the terminal oxidant for the oxidation step (entry 3, Table 4); (iv) if the reaction under Conditions A was quenched after 15 minutes, the formation of **2a** was observed (entry 4, Table 4), indicating the intermediacy of **2a** in the whole process; (v) if the photoirradiation was removed after 15 minutes, the reaction stopped sharply, since similar recovered yield of **1a** and isolated yields of **2a** and **3a** were observed (entry 5, Table 4); (vi) notably, without catalyst, this photooxidation could occur to form a mixture of **2a** and **3a** in a poor chemoselectivity (entry 6, Table 4), which meant that HBr not only improved the efficiency of the C-Si bond cleavage, but also catalyzed the transformation of benzaldehyde intermediates into benzoic acids.

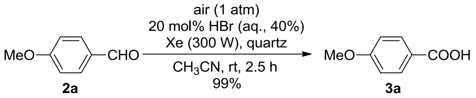
To further confirm the intermediacy of aldehyde, **2a** was applied under Conditions A. As expected, after full conversion of aldehyde, acid **3a** was afforded in almost quantitative isolated yield (Scheme 3).

Table 4. Photooxidation of **1a** under different conditions.[a]



Entry	20 mol% HBr (aq., 40%)	Air (1atm)	hν	Time (h)	Isolated yield (%)		
					1a	**2a**	**3a**
1	+	+	+	3.5	0	0	91%
2	+	+	-	3.5	87%	0	0
3	+	-	+	3.5	0	0	0
4	+	+	+	0.25	18%	45%	17%
5	+	+	+[b]	0.25[c] (3.5)[d]	16%	47%	20%
6	-	+	+	5	0	33%	52%

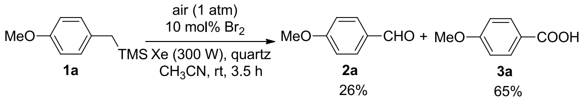
[a] A solution of **1a** (0.2 mmol) in CH_3CN (10 mL) in a quartz reaction tube was irradiated by 300 W Xe lamp at rt. [b] The photoirradition was stopped after 15 minutes. [c] Reaction time under photoirradiation. [d] Total reaction time.



Scheme 3. The conversion of **2a** to **3a** under Conditions A.

Next, the following test reactions were carried out. A 0.1 M solution of HBr in CH_3CN was irradiated by 300 W Xe lamp at rt in the open air. After 30 minutes, it was tested with starch iodide paper which turned blue quickly, revealing the *in situ* formation of Br_2. Then 10 mol% of Br_2 was applied instead of HBr (aq., 40%). After reacted for 3.5 hours under Conditions A, 26% of **2a** together with 65% of **3a** were afforded (Scheme 4), which showed that Br_2 could also catalyze this photooxidation but with lower efficiency.

Based on the above data and literature precedents,[9-13] a possible mechanism was proposed as shown in Scheme 5. Bromine was formed by aerobic photooxidation of hydrogen bromide (Eq. 1)[9] and further converted into bromine radical under continuous photoirradiation (Eq. 2).[6a,9,10] It is known that bromine radical is a good oxidant (E^o = 2.0 V vs NHE in H_2O)[6b,11] for the oxidation of benzylsilane derivatives.[6a,6b] Thus, in the next step, single electron transfer (SET) from **1** to bromine radical resulted in a pair of radical ions $ArCH_2SiR_3^{\oplus\bullet}$ **4** and $Br^{\ominus}$ (Eq. 3).[6a,6b] Here, HBr was a key factor to improve the oxidizing ability of the whole system, since stronger acidity of the reaction mixture would lead to a higher E^o value of the $Br^{\bullet}/Br^{\ominus}$ couple, due to better solvation for $Br^{\ominus}$ via hydrogen bonds.[6b] This might be the reason why Br_2 could catalyze this photooxidation but with lower efficiency than that of HBr (Scheme 4). The radical cation **4** underwent fast desilylation probably via a nucleophile-assisted cleavage of the C-Si bond by the solvent of acetonitrile[4d,4e,12] to form benzyl radical **5** (Eq. 4).[4d,4e,5a,12,13] Considering that this photooxidation could occur without catalyst under continuous photoirradiation (entry 6, Table 4), the transformation from **1** into **5** might also be promoted by light. It is known that **5** could be aerobically oxidized into aldehyde **2** easily (Eq. 5).[4d,4e,10] Finally, **2** was further oxidized into **3** under Conditions A (Scheme 3) (Eq. 6).[14]



Scheme 4. Br_2-catalyzed photooxidation of **1a**.

$$4\,HBr + O_2 \xrightarrow{h\nu} 2\,Br_2 + 2\,H_2O \tag{1}$$

$$Br_2 \xrightarrow{h\nu} 2\,Br\cdot \tag{2}$$

$$\underset{\mathbf{1}}{ArCH_2SiR_3} + Br\cdot \xrightarrow[SET]{HBr} \underset{\mathbf{4}}{ArCH_2SiR_3^{\oplus\bullet}} + Br^{\ominus} \tag{3}$$

$$\underset{\mathbf{4}}{ArCH_2SiR_3^{\oplus\bullet}} \xrightarrow{CH_3CN} \underset{\mathbf{5}}{ArCH_2^{\bullet}} + SiR_3^{\oplus} \tag{4}$$

$$\underset{\mathbf{5}}{ArCH_2^{\bullet}} \xrightarrow{O_2} \longrightarrow \underset{\mathbf{2}}{ArCHO} \tag{5}$$

$$\underset{\mathbf{2}}{ArCHO} \xrightarrow{\text{Conditions A}} \underset{\mathbf{3}}{ArCOOH} \tag{6}$$

Scheme 5. Plausible mechanism

Conclusions

In summary, we have developed a photoinduced HBr-catalyzed highly efficient C-Si bond cleavage reaction of benzylsilanes. The resulting benzyl radical intermediates were highly chemoselectively oxidized into benzoic acids using air as the terminal oxidant. A possible reaction pathway was proposed based on a series of control experiments. Notably, HBr not only acts as the single electron transfer mediator for the initial C-Si bond cleavage, but also efficiently catalyzes the transformation of benzaldehyde intermediates into benzoic acids. Further investigations in this field are in progress in our laboratory.

Acknowledgements

We greatly acknowledge the financial support from Shanghai Rising-Star Program (14QA1400500), National Basic Research Program of China (973 Program, 2012CB720300), National Nature Science Foundation of China (21102016 and 21274023), and Shanghai Scientific and Technological Innovation Project (13520711500).

Notes and references

[a] Department of Chemistry, Fudan University, 220 Handan Road, Shanghai, 200433, P. R. China. Tel: +86-21-55664361, Fax: +86-21-55664361, E-mail: Hao_Guo@fudan.edu.cn .

[b] School of Chemical Engineering, Nanjing University of Science and Technology, Nanjing, 210094, P. R. China.

[c] Department of Head and Neck Surgery, Fudan University Shanghai Cancer Center; Department of Oncology, Shanghai Medical College, Fudan University, Shanghai, P. R. China.

[d] Key Laboratory of Organofluorine Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences.

[e] They contributed equally.

Electronic Supplementary Information (ESI) available: [General experimental methods, experimental procedures, and the characterization data of compounds]. See DOI: 10.1039/b000000x/

1 For reviews, see: a) H. J. Zhang, D. L. Priebbenow, C. Bolm, *Chem. Soc. Rev.* **2013**, *42*, 8450; b) J. Yoshida, K. Kataoka, R. Horcajada, A. Nagaki, *Chem. Rev.* **2008**, *108*, 2265; c) S. Farkas, *CNS Drug Reviews* **2006**, *12*, 218.

2 For reviews, see: a) J. K. Puri, R. Singh, V. K. Chahal, *Chem. Soc. Rev.* **2011**, *40*, 1791; b) L. W. Xu, L. Li, G. Q. Lai, J. X. Jiang, *Chem. Soc. Rev.* **2011**, *40*, 1777; c) P. C. Bulman Page, S. S. Klair, S. Rosenthal, *Chem. Soc. Rev.* **1990**, *19*, 147.

3 For reviews, see: a) H. F. Sore, W. R. J. D. Galloway, D. R. Spring, *Chem. Soc. Rev.* **2012**, *41*, 1845; b) Y. Nakao, T. Hiyama, *Chem. Soc. Rev.* **2011**, *40*, 4893; c) A. Hosomi, *Acc. Chem. Res.* **1988**, *21*, 200.

4 a) T. Hayamizu, H. Maeda, K. Mizuno, *J. Org. Chem.* **2004**, *69*, 4997; b) T. Hayamizu, H. Maeda, M. Ikeda, K. Mizuno, *Tetrahedron Lett.* **2001**, *42*, 2361; c) T. Hayamizu, M. Ikeda, H. Maeda, K. Mizuno, *Org. Lett.* **2001**, *3*, 1277; d) T. Tamai, K. Mizuno, I. Hashida, Y. Otsuji, *Bull. Chem. Soc. Jpn.* **1993**, *66*, 3747; e) T. Tamai, K. Mizuno, I. Hashida, Y. Otsuji, *Chem. Lett.* **1992**, *21*, 781; f) K. Mizuno, M. Ikeda, Y. Otsuji, *Chem. Lett.* **1988**, 1507; g) E. Hasegawa, M. A. Brumfield, P. S. Mariano, U. C. Yoon, *J. Org. Chem.* **1988**, *53*, 5435.

5 a) L. Cermenati, M. Fagnoni, A. Albini, *Can. J. Chem.* **2003**, *81*, 560; b) L. Cermenati, A. Albini, *J. Adv. Oxid, Technol.* **2002**, *5*, 58.

6 a) E. Baciocchi, M. Crescenzi, T. D. Giacco, *J. Chem .Soc. Perkin Trans. 1* **1991**, 3377-3378; b) E. Baciocchi, M. Crescenzi, *Angew. Chem.* **1990**, *102*, 667; *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 658.

7 S. Montanaro, D. Ravelli, D. Merli, M. Fagnoni, A. Albini, *Org. Lett,* **2012**, *14*, 4218.

8 Y. Miyake, Y. Ashida, K. Nakajima, Y. Nishibayashi, *Chem. Commun.* **2012**, *48*, 6966.

9 S. Hirashima, A. Itoh, *Chem. Pharm. Bull.* **2007**, *55*, 156.

10 T. Sugai, A. Itoh, *Tetrahedron Lett.* **2007**, *48*, 2931.

11 L. Eberson, *Adv. Phys. Org. Chem.* **1982**, *18*, 1 ff.

12 J. P. Dinnocenzo, S. Farid, J. L. Goodman, I. R. Gould, W. P. Todd, S. L. Mattes, *J. Am. Chem. Soc.* **1989**, *111*, 8973.

13 L. Cermenati, M. Mella, A. Albini, *Tetrahedron* **1998**, *54*, 2575.

14 For other bromide-catalyzed aerobic photooxidation of benzaldehydes into benzoic acids, see: S. Hirashima, A. Itoh, *Chem. Pharm. Bull.* **2006**, *54*, 1457.