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Direct oxidation of C(sp²)-C(sp³) bond from benzyltrimethylsilanes to phenols

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A novel pathway for direct conversion of benzylsilanes to phenols by oxidation with $Na_2S_2O_8$ and oxygen is efficiently developed under mild and neutral conditions. The reaction shows good functional group tolerance to afford phenols in moderate yields. The possible mechanism is proposed based on the isotopic labeling trials.

The development of novel methods for the preparation of phenols draw interest of organic chemists because of great importance of these compounds in natural products,¹ pharmaceuticals,² and polymers.³ Phenols are traditionally prepared by displacement of other functional groups, such as aryl halides,⁴ sulphonic acids,⁵ nitrogen derivatives.⁶ Although some of the above methods have been applied in industry, high temperature and strong base are ineluctable. Consequently the drawbacks of the harsh reaction conditions were overcome by virtue of metal-based catalytic systems, such as Pd,⁷ Cu⁸ and others⁹. However, preparation of phenols under metal-free conditions was more charming and practical meaning, which was generally realized through C-C / C-Si bond insertion reaction by oxygen atom of peroxyacids or peroxides. Among which there are three common routes as shown in scheme 1. The cumene hydroperoxide route namely hock process.¹⁰ was the general phenol production technology mostly, which is based on oxidation of cumene to cumene hydroperoxide and then rearrangement in acidic medium to

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phenol (Scheme 1a). Benzaldehyde derivatives as precursors which can be transformed to phenols by Dakin oxidation or

(a) Hock process



(b) Baeyer-Villiger or Dakin oxidation

 $\begin{array}{c} 0 \\ \hline \\ H \\ \hline H \\ \hline \\ H$

(c) Tamao-Fleming oxidation

R





Scheme 1. Preparation of phenols via oxygen atom insertion

Baeyer-Villiger (BV) oxidation,¹¹ the mechanism involves nucleophilic attack on carbonyl carbon by peroxide ion and aryl migrates onto the peroxygen, following hydrolysis produced the expected phenol (Scheme 1b). Similarly, this trick can also be applied in arylsilanes namely Tamao–Fleming oxidation,¹² in which the aryl group undergoes 1, 2-migration from the silicon to the oxygen atom,¹³ or C-Si bond is activated by virtue of metal-catalyzed reaction and then oxidized to insert oxygen atom (Scheme 1c).¹⁴

Despite the above advances, room still exists for developing new protocol for the synthesis of phenols under benign conditions and with wider substrate scope. Herein, we present an unprecedented formation of phenol through $C(sp^2)-C(sp^3)$

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bond cleavage using $Na_2S_2O_8$ and oxygen as oxidants under mild and neutral conditions (Scheme 1d).

Table 1. Optimization of reaction conditions^a

Si								
		Oxidant, 55 °C			ОН			
-		Solvent	lvent					
1 1a								
Entry	Oxidant	Solvent	Gas	Time (h)	Yield ^b (%)			
1	$Na_2S_2O_8$	CH₃CN	Air	12	36			
2	$(NH_4)_2S_2O_8$	CH₃CN	Air	24	20			
3 ^c	TBHQ	CH₃CN	Air	24	0			
4	Oxone	CH₃CN	Air	24	Trace			
5	BPO	CH₃CN	Air	24	0			
6	<i>m</i> -CPBA	CH₃CN	Air	24	Trace			
7	$Na_2S_2O_8$	CH₃CN	O ₂	9	57			
8	$Na_2S_2O_8$	CH ₃ CN/H ₂ O(10:1)	O ₂	18	Trace			
9	$Na_2S_2O_8$	DMF	O2	18	N.R			
10	$Na_2S_2O_8$	CH₃OH	O2	18	Trace			
11	$Na_2S_2O_8$	Dioxane	O2	18	N.R			
12	$Na_2S_2O_8$	Toluene,	O ₂	18	N.R			
^a Reaction conditions: substrate (0.2 mmol), Oxidant (1.5 equiv. 0.26 mmol),								

Solvent, stirred at 55 $^{\circ}$ C. ^b Isolated yields. ^cTBHQ = *tert*-Butyl hydroperoxide, stored in decane. Oxone = Potassium monopersulfate triple salt; BPO = benzoyl peroxide; *m*-CPBA = 3-Chloroperoxybenzoic acid.

The investigation was carried out on the reaction of (4methoxybenzyl)trimethylsilane 1 with Na₂S₂O₈ in MeCN at 55 °C, a temperature that $S_2 O_8^{2-}$ could be converted to SO_4^{--} under atmosphere, which was initially assumed to hydroxylate on the phenyl ring. However, 4-methoxyphenol was obtained instead in 36% yield (Table 1, entry 1). Such a result reveals the direct oxidative cleavage of C(sp²)-C(sp³) bond to provide an easy access to phenols that encourages us to further explore the reaction. Other oxidants exhibited little efficiency such as (NH₄)₂S₂O₈, H₂O₂, Oxone and *m*-CPBA, BPO only oxidize 1 to 4methoxybenzaldehyde (Table 1, entries 2 - 6). It is noteworthy oxygen can accelerate the reaction and produce phenol in 57% yield (Table 1, entry 7). Various solvents such as CH₃CN/H₂O, DMF, MeOH, dioxane and toluene were screened (Table 1, entries 8 - 12) and the results showed that MeCN was most suitable for this reaction owing to the fact that MeCN might act as a nucleophile in assisting the C-Si bond cleavage.¹⁵

With the optimized conditions in hand, we applied this strategy to investigate the scope under synergistic effect of $Na_2S_2O_8$ and oxygen. Use of benzylsilanes bearing an electrondonating group on *para-* or *ortho-* benzene ring afforded the corresponding products in moderate yields. Alkoxyl groups showed more effective on this reaction (Entries 1, 2, 5 - 9), whereas *iso-*propyl and *tert-*butyl led to decreased yields (Entries 3 - 4), Benzylsilane bearing electron-neutron group was inactive (Entry 10) and mostly recovered. Electronwithdrawing groups such as Cl and Br also could be tolerated in case of methoxyl group located in *para-* or *ortho-* position of benzene ring (Entries 13-14). Interestingly trimethylsilyl on benzene ring was not tolerated but to give eliminated product. It was noteworthy substituents located on benzyl position didn't restrain the formation of phenol, in contrast which accelerated this

Table 2. Synthesis of phenols from benzylsilanes^a

			Si			
$R_3 \downarrow R_2$				Na ₂ S ₂ O ₈ , 55 °C, O ₂	\sim	ОН
				CH₃CN	$R_3 \frac{11}{11}$	
	Entry	R_1	R ₂	R ₃	Time (h)	Yield ^b (%)
	1	н	н	4-CH₃O	9	57 (1a)
	2	н	н	2-CH ₃ O	9	64 (2a)
	3 ^c	н	н	4-(CH ₃) ₂ CH	20	33 (3a)
	4 ^{<i>c</i>}	н	н	4-(CH ₃) ₃ C	20	46 (4a)
	5	н	н	2-CH ₃ CH ₂ O	12	71 (5a)
	6	н	н	2-(CH ₃) ₂ CHO	9	56 (6a)
	7	н	н	2-CH ₃ (CH ₂) ₂ O	12	70 (7a)
	8	н	н	2-CH ₂ =CHCH ₂ O	18	45 (8a)
	9	н	н	2-PhO	18	70 (9a)
	10	н	н	н	24	0
	11	н	н	2-CH₃O, 5- ^t Bu	12	63 (10a)
	12 ^{<i>d</i>}	н	н	2-CH₃O, 3,5-di- ^t Bu	18	65 (11a)
	13	н	н	2-CH₃O, 5-Cl	12	54 (12a)
	14	н	н	4-CH₃O, 3-Br	9	68 (13a)
	15 ^{<i>d</i>}	н	CH₃	2-CH ₃ O, 5-(CH ₃) ₃ Si	10	72 (2 a)
	16	н	CH₃	4-CH ₃ O	4	62 (1a)
	17	н	ⁿ Bu	2-CH ₃ O	4	77 (2 a)
	18	н	Ph	4-CH ₃ O	4	73 (1a)
	19	н	4-Cl-Ph	2-CH ₃ O	12	71 (1a)
	20	Ph	4-CH₃O-Ph	4-CH₃O	3	65 (1a)

^{*a*} Reaction conditions: substrate (0.2 mmol), Na₂S₂O₈ (1.5 equiv, 0.3 mmol), CH₃CN (2.0 mL), stirred at 55 $^{\circ}$ C. ^{*b*} Isolated yields. ^{*c*} Na₂S₂O₈ (3.0 equiv. 0.6 mmol), at 65 $^{\circ}$ C. ^{*d*} Na₂S₂O₈ (3.0 equiv. 0.6 mmol)

reaction probably due to the stabilization of radical intermediates (Entries 15-19, see mechanism discussion). When the benzyl group was substituted with two groups, the 4-methoxyphenol also was obtained with 65% yield (Entry 20).

To reveal the source of phenolic oxygen, we performed the oxidative cleavage reaction of **19** in the presence of H_2O^{18} which gave ¹⁸O-unlabelled 2-methoxyphenol **2a** and 4-chlorobenzaldehyde (eq.1). Subsequently, we have performed the reaction in the presence of ¹⁸O₂ gas which afforded ¹⁸O-labelled 2-methoxyphenol **2a** based upon GCMS analysis (eq.2). These experimental results indicate that the phenolic oxygen might originate from O₂.



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On the basis of all the results mentioned above, a possible reaction pathway was proposed as depicted in Scheme 2. Initially, SO_4^- is generated through hemolytic cleavage of $S_2O_8^{2^-}$ under heating.¹⁶ Benzylsilane **1** is oxidized to intermediate A stabilized by β -silicon effect¹⁷ by SO_4^- via the single electron transfer (SET) which was then transformed to benzyl radical **B** after desilyl process. Coupling of **B** and SO_4^- generates monosulfate anion **C**, which is oxidized to **D**. Following adsorption of O_2 on **D** lead to formation of a three - component combination radical **E**, electron transfer rearrangement causes cleavage of $C(sp^2)$ - $C(sp^3)$ bond and affords peroxyl radical **F**, which abstracts a hydrogen atom and produce phenol **1a**, meanwhile two neutral fragments SO_3 and formaldehyde are released.



Scheme 2. The proposed reaction pathway

Further to confirm the truth of mechanism and find unity of this reaction, benzylsilane **21** was synthesized for the purpose of intramolecular reaction. Interestingly, besides a few phenolic aldehyde **21a** was detected, diphenol **21b** as major product was obtained. Thus **21b** should be formed through a tandem hydroxylation reaction which involved oxidative hydroxylation of benzylsilane **21** and following similar Baeyer-Villiger oxidation of aldehyde **21a**.



In summary, we have developed a novel synthetic approach to phenols by direct oxidation of benzyltrimethylsilanes using Na₂S₂O₈ and oxygen as the oxidant. This method was found to be potential useful for the preparation of diphenols from designed benzyltrimethylsilanes in combination with Baeyer-Villiger reaction.

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Notes and references

‡ Footnotes relating to the main text should appear here. These might include comments relevant to but not central to the matter under discussion, limited experimental and spectral data, and crystallographic data.

- (a) Z. Mao, W. Sun, L. Fu, H. Luo, D. Lai and L. Zhou, Molecules., 2014, **19**, 5088; (b) T. Bunyapaiboonsri, S. Yoiprommarat, P. Srikitikulchai, K. Srichomthong and S. Lumyong, J. Nat. Prod. 2010, **73**, 55; (d) Synthetic and Natural Phenols, ed. J. H. P. Tyman, Elsevier, New York, 1996.
- (a) P. Chaudhuri, B. Ganguly, S. Bhattacharya, J. Org. Chem., 2007, 72, 1912; (b) A. Kamal, V. Srinivasulu, M. Sathish, Y. Tangella, V. L. Nayak, M. P. Narasimha. Rao, N. Shankaraiah, and N. Nagesh, Asian. J. Org. Chem., 2014, 3, 68.
- 3 (a) M. R. Bassett, T. Morishita, H. F. Wilson, A. S. Barnard, M. J. S. Spencer, *J. Phys. Chem. C*, 2016, **120**, 6762; (b) A. P. Katsoulidis, M. G. Kanatzidis, *Chem. Mater.*, 2011. **23**, 1818; (c) W. Liu, A. L. Cholli, J. Kumar, S. Tripathy, L. Samuelson, *Macromolecules.*, 2001, **34**, 3522.
- 4 (a) V. E. Meharg and I. Allen, J. Am. Chem. Soc., 1932, 54, 2920; (b) N. R. Shreve and C. J. Marsel, Ind. Eng. Chem., 1946. 38, 254; (c) J. F. Bunnett and R. E. Zahler, Chem. Rev., 1951. 49, 273; (d) A. P. Krapcho and D. Waterhouse, Synth. Commun., 1998. 28, 3415.
- 5 (a) S. Oae, N. Furukawa, M. Kise and M. Kawanishi, Bull. Chem. Soc. Jpn., 1966, **39**, 1212; (b) L. R. Buzbee, J. Org. Chem., 1966, **31**, 3289.
- 6 (a) H. Rapoport, T. P. King and J. B. Lavigne, J. Am. Chem. Soc., 1951. 73, 2718; (b) E. S. Lewis and J. M. Insole, J. Am. Chem. Soc., 1964, 86, 32; (c) T. Cohen, A. G. Dietz and J. R. Miser, J. Org. Chem., 1977. 42, 2053; (d) J. P. Mayer, J. M. Cassady and D. E. Nichols, Heterocycles., 1990. 31, 1035.
- 7 (a) Y. Wang, C. Zhou and R. Wang, *Green Chem.*, 2015, 17, 3910; (b) G-L. Song, Z. Zhang, Y-X. Da and X-C. Wang, *Tetrahedron.*, 2015, 71, 8823; (c) Y. Xiao, Y. Xu, H-S. Cheon, J. Chae, J. Org. Chem., 2013, 78, 5804; (d) F. Ke, X. Chen, Z. Li, H. Xiang and X. Zhou, *RSC Adv.*, 2013, 3, 22837; (d) K. G. Thakur and G. Sekar, *Chem. Commun.*, 2011, 47, 6692; (e) A. Mehmood and N. E. Leadbeater, *Catal. Commun.*, 2010, 12, 64; (f) A. Tlili, N. Xia, F. Monnier and M. Taillefer, *Angew. Chem., Int. Ed.*, 2009, 48, 8725; (g) S. Maurer, W. Liu, X. Zhang, Y. Jiang and D. Ma, *Synlett*, 2010, 2010, 976.
- 8 (a) C. L. Fleming, T. D. Nalder, E. H. Doeven, C. J. Barrow, F. M. Pfeffer and T. D. Ashton, *Dyes and Pigments.*, 2016, **126**, 118; (b) C. W. Cheung and S. L. Buchwald, *J. Org. Chem.*, 2014, **79**, 5351; (c) T. Schulz, C. Torborg, B. Schäffner, J. Huang, A. Zapf, R. Kadyrov, A. Börner and M. Beller, *Angew. Chem.*, *Int. Ed.*, 2009, **48**, 918; (e) A. G. Sergeev, T. Schulz, C. Torborg, A. Spannenberg, H. Neumann and M. Beller, *Angew. Chem.*, *Int. Ed.*, 2009, **48**, 7595; (a) K. W. Anderson, T. Ikawa, R. E. Tundel and S. L. Buchwald, *J. Am. Chem. Soc.*, 2006, **128**, 10694.
- 9 (a) Y. Yang, Y. Lin and Y. Rao, Org. lett., 2012, 14, 2874; (b) V.
 S. Thirunavukkarasu, S. I. Kozhushkov and L. Ackermann, Chem Commun., 2014, 50, 29; (c) V. S. Thirunavukkarasu and L. Ackermann, Org let., 2012, 14, 6206; (d) R. Bal, M. Tada, T.
 Sasaki and Y. Iwasawa, Angew. Chem. Int. Ed., 2006, 45, 448; (e) L. Ackermann, Acc. Chem. Res., 2014, 47, 281; (f) R. E.
 Maleczka, F. Shi, D, Holmes and M. R. Smith, J. Am. Chem. Soc., 2003, 125, 7792.
- 10 H. Hock and S. Lang, Ber Dtsch Chem Ges.. 1944, 77, 257.
- (a) B. Saikia and P. Borah, N. ChandraáBarua, Green Chem., 2015, **17**, 4533; (b) B. Saikia and P. Borah, RSC Adv., 2015, **128**, 105583; (c) S. Chen, M. S. Hossain and F. W. FossJr, Org. Lett., 2012, **14**. 2806; (d) S. Chen and F. W. FossJr, Org. Lett., 2012, **14**, 5150; (e) R. Bernini, A. Coratti, G. Provenzano, G.

Fabrizi, and D. Tofani, *Tetrahedron.*, 2005, **61**, 1821; (f) M. Renz, and B. Meunier, *Eur. J. Org. Chem.*, 1999, **4**. 737;

- (a) K. Tamao, Proc. Jpn. Acad, Ser. B., 2008, 84, 123; (b) I.
 Fleming, H. Rolf and P. Howard, J. Chem. Soc., Chem. Commun., 1984, 1, 29; (c) G. R. Jones, Y. Landais, Tetrahedron., 1996, 52, 7599.
- 13 (a) E. J. Rayment, N. Summerhill and E. A. Anderson, *J. Org. Chem.*, 2012, **77**, 7052; (b) S. Bracegirdle, E. A. Anderson, *Chem. Commun.*, 2010, **46**, 3454.
- 14 (a) K. Gondo, J. Oyamada, T. Kitamura, Org. Lett., 2015, 17, 4778; (b) E. M. Simmons, J. F. Hartwig, J. Am. Chem. Soc. 2010, 132, 17092.
- (a) J. P. Dinnocenzo, S, Farid, J. L. Goodman, I. R. Gould, S. L. Mattes and W. P. Todd, *J. Am. Chem. Soc.*, 1989, **111**, 8973;
 (b) J. P. Dinnocenzo, S. Farid, J. L. Goodman, I. R. Gould and W. P. Todd, *Mol. Ctyst. Liq. Cryst.*, 1991, **194**, 151; *(c)* K. P. Dockery, J.-P. Dinnocenzo, S. Farid, J. L. Goodman, I. R. Gould and W. P. Todd, *J. Am. Chem. Soc.*, 1997, **119**, 1876.
- (a) C. Liang, H. W. Su, *Ind. Eng. Chem. Res.*, 2009, 48, 5558;
 (b) L. W. Matzek and K. E. Carter, *Chemosphere.*, 2016, 151, 178.
- 17 J. B. Lambert, Tetrahedron, 1990, 46, 2677.

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A novel pathway for direct conversion of benzylsilanes to phenols by oxidation with $Na_2S_2O_8$ and oxygen is efficiently developed under mild and neutral conditions.

