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Oxidative Transformation of Arylmethyl Bromides and Alcohols with a Combination of Mesoporous Silica FSM-16 and Alkali Iodides under Photoirradiation

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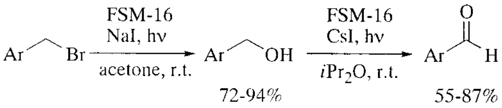
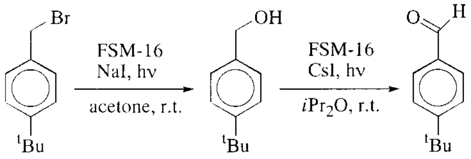
ABSTRACT



A mesoporous silica FSM-16 was found to be a selective and recyclable promoter for the oxidative dehalogenation of arylmethyl bromides to provide the corresponding alcohols and for the oxidation of arylmethyl alcohols to provide the corresponding aldehydes with a combination of alkali iodides and solvents under photoirradiation conditions.

In our studies on the utilization of mesoporous silicas in organic synthesis,[1] we have found that α-hydroxycarboxylic acids, phenyl acetic acid derivatives,[2] and N-protected α-amino acids[3] afforded the carbonyl compounds through an oxidative decarboxylation reaction in the presence of a mesoporous silica, FSM-16,[4] under photoirradiation. Furthermore, arylmethyl bromides, which have no carboxyl group, were found to give the corresponding aromatic carboxylic acids in one step with FSM-16 under photoirradiation.[5] In the course of investigation of this reaction, we found FSM-16 to show new promoting effects in the presence of alkali iodides: exclusive transformation of 4-*tert*-butylbenzyl bromide (**1**) to 4-*tert*-butylbenzyl alcohol (**2**) in the presence of NaI in acetone[6] and oxidation of **2** to 4-*tert*-butylbenzaldehyde (**3**) in the presence of CsI in iPr$_2$O were observed under photoirradiation (Scheme 1).

Scheme 1



1 **2** **3**

Although the transformation of arylmethyl halides to the corresponding alcohols and the oxidation of arylmethyl alcohols to the corresponding aldehydes had been developed by many workers over many years,[7] these methods are sometimes problematic because drastic conditions or environmentally detrimental heavy metals are required.

On the other hand, our reaction is thought to be useful and complementary to other methods,[8] since it is mild and

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(1) Itoh, A.; Kodama, T.; Maeda, S.; Masaki, Y. *Tetrahedron Lett.* **1998**, *39*, 9461. Itoh, A.; Kodama, T.; Masaki, Y. *Synlett* **1999**, 357.

(2) Itoh, A.; Kodama, T.; Inagaki, S.; Masaki, Y. *Org. Lett.* **2000**, *2*, 331.

(3) Itoh, A.; Kodama, T.; Inagaki, S.; Masaki, Y. *Chem. Lett.* **2000**, 542.

(4) Inagaki, S.; Koiwai, A.; Suzuki, N.; Fukushima, Y.; Kuroda, K. *Bull. Chem. Soc. Jpn.* **1996**, *69*, 1449. Inagaki, S.; Fukushima, Y.; Kuroda, K. *J. Chem. Soc., Chem. Commun.* **1993**, 680.

(5) Itoh, A.; Kodama, T.; Inagaki, S.; Masaki, Y. *Org. Lett.* **2000**, *2*, 2455.

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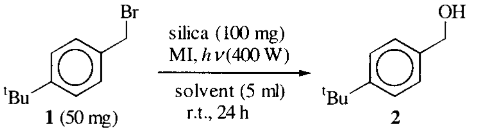
does not require the use of environmentally detrimental reagents. We now report our study on the generality of these oxidative transformations with FSM-16 in the presence of alkali iodides under photoirradiation.

Table 1 shows the results of the transformation of 4-*tert*-butylbenzyl bromide (**1**, 50 mg) in the presence of silica (100 mg) and alkali iodide in several solvents using 400-W high-pressure mercury lamps under an aerobic atmosphere at room temperature.[9] Among the solvents used, acetone was found to be suitable for the reaction to afford **2** in 94% yield with FSM-16 (entries 1−7).[10] In the dark, only the starting material was recovered even in the presence of FSM-16 (entry 8). Under N_2, 12% of **2** was obtained, and also only 10% of **2** was obtained even in the presence of 1 mol of H_2O (entries 9 and 10). These results show that the oxygen in air is crucial for this reaction. Among alkali iodides examined, NaI was found to be superior to other iodides to afford **2** in high yield (entries 7, 11−13). Furthermore, more than 1 mole equiv of NaI was required to complete the reaction in 24 h, and a large amount of the starting material was recovered when 0.5 equiv of NaI was used (entries 7, 14, 15). The reason for the difference in the effect between NaI and other iodides is not yet clear, but the solubility in acetone, the size, and the dissociation energy of alkali iodides[11] are assumed to play an important role in this reaction. Other mesoporous silicas, MCM-41,[12] HMS,[13] and 10%Ti−HMS,[14] were found to give **2** in yields somewhat lower than that obtained with FSM-16 (entries 16−18). Only 22% yield of **2** was obtained without FSM-16 under photoirradiation (entry 19).

Table 1. Study of Reaction Conditions for Transformation of Arylmethyl Bromides to Alcohols with FSM-16



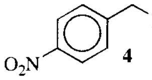
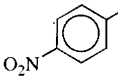
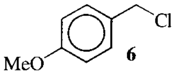
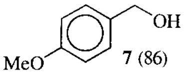
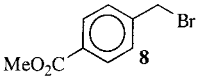
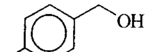
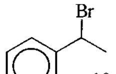
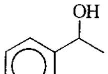
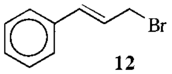
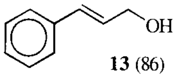
entry	solvent	silica	MI (equiv)	recovery of **1** (%)[a]	yield of **2** (%)
1	hexane	FMS-16	NaI (1.2)	3	30[b]
2	toluene	FMS-16	NaI (1.2)	38	27[c]
3	MeCN	FMS-16	NaI (1.2)	65	18[d]
4	AcOEt	FMS-16	NaI (1.2)	52	15[e]
5	Et_2O	FMS-16	NaI (1.2)	92	5
6	CH_2Cl_2	FMS-16	NaI (1.2)	87	0
7	acetone	FMS-16	NaI (1.2)	trace	94
8	acetone	FMS-16	NaI (1.2)	quant	0[f]
9	acetone	FMS-16	NaI (1.2)	90	12[g]
10	acetone	FMS-16	NaI (1.2)	86	10[h,i]
11	acetone	FMS-16	LiI (1.2)	26	72
12	acetone	FMS-16	KI (1.2)	3	78
13	acetone	FMS-16	CsI (1.2)	8	71
14	acetone	FMS-16	NaI (0.5)	23	61[j]
15	acetone	FMS-16	NaI (2.0)	trace	91
16	acetone	MCM-41	NaI (1.2)	17	67
17	acetone	HMS	NaI (1.2)	2	79
18	acetone	10% Ti-HMS	NaI (1.2)	11	77
19	acetone		NaI (1.2)	35	22

[a] The yield included a small amount of unidentified products, which were inseparable from **1**. [b] Also, 52% of **3** was obtained. [c] Also, 36% of **3** was obtained. [d] Also, 14% of **3** was obtained. [e] Also, 15% of **3** was obtained. [f] The reaction was carried out in the dark. [g] The reaction was carried out under N_2 atmosphere. [h] The reaction was carried out in the presence of 1 equiv of H_2O under N_2. [i] Also, 2% of **3** was obtained. [j] Also, 8% of **3** was obtained.

Table 2 shows the results for transformation of several arylmethyl halides to the corresponding alcohols. Neither an electron-withdrawing nor -donating group such as 4-nitro (**4**) and 4-methoxy group (**6**) as an aromatic substituent exerted

Table 2. Transformation of Arylmethyl Bromides to Alcohols with FSM-16/NaI/*hν*

$$\text{substrate} \xrightarrow[\text{acetone (5 ml), r.t.}]{\text{FSM-16 (100 mg), NaI (1.2 eq.)}\ h\nu(400\ \text{W})} \text{product}$$

entry	halomethylarenes	*t* (h)	products (% yield)
1	 **4**	24	 **5** (87)
2	 **6**	24	 **7** (86)
3	 **8**	24	 **9** (93)
4	 **10**	36	 **11** (72)
5	 **12**	24	 **13** (86)
6	$C_{16}H_{33}Br$ **14**	48	no reaction

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(6) Photolysis of benzyl halides has been reported by several groups: Alvaro, M.; Corma, A.; Garcia, H.; Miranda, M. A.; Primo, J. *J. Chem. Soc., Chem. Commun*. **1993**, 1041. Fukuzumi, S.; Hironaka, K.; Tanaka, T. *J. Am. Chem. Soc.* **1983**, *105*, 4722. Gardini, G. P.; Charlton, J. L.; Bargon, J. *Tetrahedron Lett*. **1982**, *23*, 987. Appleton, D. C.; Brocklehurst, B.; McKenna, J.; McKenna, J. M.; Thackeray, S.; Walley, A. R. *J. Chem. Soc., Perkin Trans. 2* **1980**, 87. Katritzky, A. R.; Cook, M. J.; Brown, S. B.; Cruz, R.; Millet, G. H.; Anani, A. *J. Chem. Soc., Perkin Trans. 1* **1979**, 2493. Katritzky, A. R.; Brown, S. B. *Synthesis* **1978**, 619. Appleton, D. C.; Brocklehurst, B.; McKenna, J.; McKenna, J. M.; Smith, M. J.; Taylor, P. S.; Thackeray, S.; Walley, A. R. *J. Chem. Soc., Chem. Commun.* **1977**, 108.

(7) *Comprehensive Organic Transformations: A Guide to Functional Group Preparations*; Larock, R. C. Ed.; Wiley-VCH: New York, 1989.

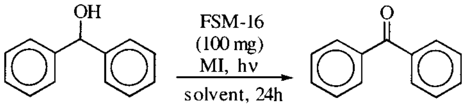
(8) We have already discovered that arylmethyl alcohols and allylic alcohols provided the corresponding aldehydes or ketones with iodine under photoirradiation conditions; however, the method using CsI instead of iodine is more facile since CsI is easier to handle than iodine: Itoh, A.; Kodama, T.; Masaki, Y. *Chem. Lett.*, in press.

(9) **Typical Procedure.** In a Pyrex tube, a suspension of 4-*tert*-butylbenzyl bromide (**1**, 50 mg), silica (100 mg), and NaI (39.6 mg, 1.2 equiv) in dry acetone (5 mL) was stirred and irradiated externally at room temperature with a 400-W high-pressure mercury lamp under an aerobic atmosphere for 24 h. FSM-16 was then filtered off and washed with ethyl acetate, and the filtrate was washed with aqueous sodium thiosulfate solution and brine. The organic layer was dried over magnesium sulfate and concentrated under reduced pressure. Pure 4-*tert*-butylbenzyl alcohol (**2**) (33.9 mg, 94%) was obtained after purification by preparative TLC.

any negative influence on the reaction (entries 1 and 2). The base-sensitive ester moiety of methyl 4-(bromomethyl)-benzoate (**8**) remained intact under the reaction conditions, and the corresponding alcohol **9** was obtained in high yield (entry 3).[15] α-Methylbenzyl bromide (**10**), a secondary bromide, also afforded α-methylbenzyl alcohol (**11**) in the same manner as **1** (entry 4). Furthermore, cinnamyl bromide (**12**), which possesses a double bond conjugated with the aromatic nucleus, afforded cinnamyl alcohol (**13**) in high yield (entry 5). *n*-Hexadecyl bromide (**14**), a simple alkyl halide, was intact even after 48 h under the same reaction conditions (entry 6).

Table 3 shows the results of photooxidation of benzhydrol (**15**) to benzophenone (**16**), the second step in Scheme 1, in the presence of FSM-16 and alkali iodide in several solvents using 400-W high-pressure mercury lamps at room temperature under an aerobic atmosphere.[16] Among the solvents examined, *i*Pr$_2$O was found to afford the best results and to give **16** in 87% yield (entries 1−10).[17] Although a stoichiometric amount of CsI was required to give **16** in high yield, an excess amount of CsI retarded the oxidation (entries 11 and 12). On the other hand, the result that, without irradiation, oxygen, FSM-16 or alkali iodide, **16** was not obtained or obtained only in low yield shows the necessity of all of the foregoing factors for this reaction (entries 13−17). NaI and KI were also found to promote this oxidation; however, the yield of **16** was lower than that with CsI (entries 18 and 19). The results with other mesoporous silicas, MCM-41,[12] HMS,[13] and 10% Ti-HMS,[14] showed FSM-16 to be better as a promoter of the oxidation (entries 20−22).

Table 3. Study of Reaction Conditions for Transformation of Arylmethyl Alcohols to Aldehydes with FSM-16



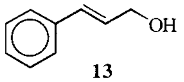
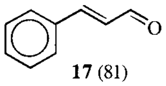
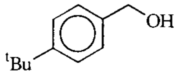
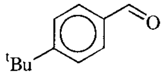
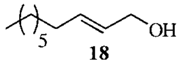
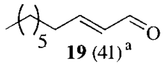
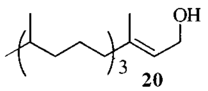
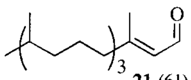
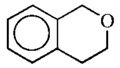
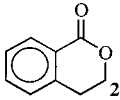
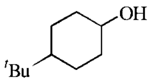
15 (50 mg) **16**

entry	solvent	silica	MI (equiv)	recovery of **15** (%)	yield of **16** (%)
1	Et$_2$O	FMS-16	CsI (1.0)	16	61
2	acetone	FMS-16	CsI (1.0)	97	2
3	hexane	FMS-16	CsI (1.0)	29	68
4	MeOH	FMS-16	CsI (1.0)	88	6
5	THF	FMS-16	CsI (1.0)	91	1
6	DMF	FMS-16	CsI (1.0)	90	0
7	benzene	FMS-16	CsI (1.0)	19	72
8	MeCN	FMS-16	CsI (1.0)	97	0
9	H$_2$O	FMS-16	CsI (1.0)	0	64
10	*i*Pr$_2$O	FMS-16	CsI (1.0)	0	87
11	*i*Pr$_2$O	FMS-16	CsI (0.5)	34	17
12	*i*Pr$_2$O	FMS-16	CsI (2.0)	39	26
13	*i*Pr$_2$O	FMS-16	CsI (1.0)	99	0[a]
14	*i*Pr$_2$O	FMS-16	CsI (1.0)	91	0[b]
15	*i*Pr$_2$O		CsI (1.0)	*c*	14
16	*i*Pr$_2$O	FMS-16		*c*	50
17	*i*Pr$_2$O			*c*	14
18	*i*Pr$_2$O	FMS-16	NaI (1.0)	34	57
19	*i*Pr$_2$O	FMS-16	KI (1.0)	trace	85
20	*i*Pr$_2$O	MCM-41	CsI (1.0)	34	56
21	*i*Pr$_2$O	HMS	CsI (1.0)	8	78
22	*i*Pr$_2$O	10% Ti-HMS	CsI (1.0)	trace	85

[a] The reaction was carried out in the dark. [b] The reaction was carried out under a flow of argon. [c] Not negligible amount of **15** was recovered with inseparable byproducts.

Table 4. Transformation of Arylmethyl Alcohols to Aldehydes with FSM-16/CsI/*hν*

substrate (50 mg) $\xrightarrow[iPr_2O]{\text{FSM-16 (100 mg)}\ h\nu\text{, CsI (1 equiv.)}}$ **product**

entry	substrate	*t* (h)	product (% yield)
1	 **13**	12	 **17** (81)
2	 **2**	24	 **3** (55)
3	 **18**	24	 **19** (41)[a]
4	 **20**	12	 **21** (61)
5	 **22**	24	 **23** (31)[b]
6	 **24**	48	-[c]

[a] Also, 18% of **18** was recovered. [b] Also, 42% of **22** was recovered. [c] Also, 86% of **24** was recovered.

Other primary arylmethyl alcohols and allylic alcohols exclusively afforded the corresponding aldehydes (Table 4). Cinnamyl alcohol (**13**) was oxidized to cinnamaldehyde (**17**) in high yield (81%) in the presence of FSM-16 and 1 equiv of CsI (entry 1). 4-*tert*-Butylbenzyl alcohol (**2**) was less reactive than **13**; however, **3** was obtained in 55% yield after 24 h (entry 2). Both *trans*-2-decen-1-ol (**18**) and phytol (**20**),

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(10) FSM-16 used in this study was synthesized according to ref 4. The unit cell dimension of this FSM-16 was 4.63 nm. The pore diameter was 2.9 nm, and the specific surface area was 882 m^2/g.

(11) Su, T.-M R.; Riley, S. J. *J. Chem. Phys.* **1979**, *71*, 3194.

(12) Kresge, C. T.; Leonowicz, M. E.: Roth, W. J.; Vartuli, J. C.; Beck, J. S. *Nature* **1992**, *359*, 710.

(13) Tanev, P. T.; Pinnavaia, T. J. *Science* **1995**, *267*, 865.

(14) Zhang, W.; Froba, M.; Wang, J.; Tanev, P. T.; Wong, J.; Pinnavaia, T. J. *J. Am Chem. Soc.* **1996**, *118*, 9164. Tanev, P. T.; Chibwe, M.; Pinnavaia, T. J. *Nature* **1994**, *368*, 321.

(15) Since a commonly used method for the transformation of arylmethyl halides to the corresponding alcohols includes the nucleophilic displacement of halogen by a hydroxide ion in basic aqueous solution, our method is mild and complementary to other methods and is thought to be useful for base-sensitive substrates; see ref 7.

which are allylic alcohols, were found to afford the corresponding aldehydes **19** and **21** in moderate yield (entries 3 and 4). In all the cases mentioned above, the corresponding carboxylic acids could not be detected. Furthermore, isochromanone (**23**) was directly obtained from isochroman (**22**) in 31% yield (entry 5). Unfortunately, 4-*tert*-butylcyclohexyl alcohol (**24**), which is a simple alkanol, remained intact under the conditions, and only the starting material was recovered even after 48 h (entry 6).

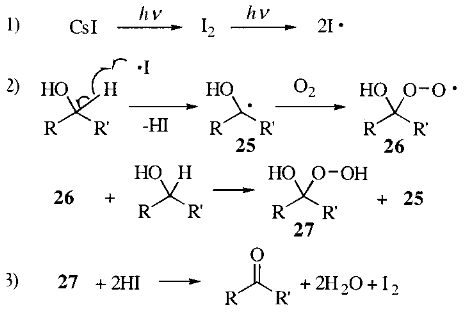
The promoter FSM-16 was found to be a recyclable photocatalyst for both steps. Thus, the recovered FSM-16, which was washed with distilled water to remove alkali iodides and dried at room temperature for 2 h under reduced pressure, showed no loss of activity for the reaction after being used three times (Table 5).

Table 5. Recycle of FSM-16

	yield of product (%)		
	1st cycle	2nd cycle	3rd cycle
$\mathbf{1} \xrightarrow[\text{acetone, rt, 24 h}]{\text{FSM-16, NaI, } h\nu} \mathbf{2}$	91	85	86
$\mathbf{15} \xrightarrow[i\text{Pr}_2\text{O, rt, 24 h}]{\text{FSM-16, CsI, } h\nu} \mathbf{16}$	86	86	83

Although the mechanism of this series of transformations, including the solvent effect and which steps are promoted by FSM-16, is not clear, oxygen in air has an important role. It is required for these reactions to proceed smoothly, since the yield of the product for each step was reduced under a flow of nitrogen or argon. In regard to the first step, formation of the alcohol, several intermediates can be considered. In nucleophilic substitution reactions of alkyl bromides or alkyl chlorides, NaI is sometimes used as a promoter that generates the corresponding iodide in situ. 4-*tert*-Butylbenzyl iodide, however, afforded the corresponding alcohols **2** only in 18% yield under the conditions without NaI, although 92% yield of **2** was obtained in the presence of NaI. Furthermore, aldehyde **3**, which is a possible intermediate from **1** under the conditions without NaI,[5] was recovered intact. Since the arylmethyl bromides generally afforded the corresponding aldehyde and carboxylic acid without NaI,[5] the iodide anion must inhibit the oxidation steps from alcohol to aldehyde and/or carboxylic acid. We believe a benzyl radical species, generated from the bromides under photoirradiation,[18] participates in the course of this reaction. In the second step, oxidation of the alcohols, iodine was thought to be generated from CsI in situ as judged by the color of the reaction mixture, which changes from colorless to dark brown. As shown in Scheme 2, an iodo radical, which is generated under the photoirradiation conditions, abstracts the hydrogen atom at the benzylic position of the starting material.[19] The resulting radical species **25** reacts with molecular oxygen to generate the peroxy radical species **26**, which produces **27** and **25** through an autoxidation path. The hydroperoxide **27** is thought to be reduced by hydrogen iodide that is generated in situ, to the corresponding carbonyl product.[20] We have not obtained any direct evidence for the intermediates in this path, and a more detailed study is now in progress in our laboratory.[21]

Scheme 2



In conclusion, this new method for the transformation of arylmethyl bromides to the corresponding aldehydes via arylmethyl alcohols is thought to be convenient in view of the weak acidic conditions, the use of a recyclable solid catalyst, and the non-requirement of environmentally detrimental heavy metals such as MnO_2.

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(16) **Typical Procedure.** In a Pyrex tube, a suspension of benzhydrol (**14**, 50 mg), FSM-16 (100 mg), and CsI (70.5 mg, 1 equiv) in dry $i\mathrm{Pr_2O}$ (5 mL) was stirred and irradiated externally at room temperature with a 400-W high-pressure mercury lamp under an aerobic atmosphere for 24 h. FSM-16 was then filtered off and washed with ethyl ether and distilled water. The filtrate was washed with aqueous sodium thiosulfate solution and brine. The organic layer was dried over sodium sulfate and concentrated under reduced pressure. Pure benzophenone (**15**) (43.1 mg, 87%) was obtained after purification by preparative TLC.

(17) Unfortunately, direct transformation from **1** to **3** under the same condition was not successful: only 15% of **3** and 11% of **2** were obtained with 49% recovery of **1**.

(18) Kerr, J. A. *Chem. Rev.* **1966**, *66*, 465.

(19) Mallory, F. B.; Mallory, C. W. *Org. React.* **1984**, *30*, 1.

(20) We believe that iodine is reproduced in situ, since the dark brown color of the reaction mixture seemed to remain unchanged as such.

(21) Participation of the peroxide species from $i\mathrm{Pr_2O}$, which may be generated by oxygen and photoirradiation, cannot be ruled out since the reaction also proceeded without CsI (entry 16 in Table 3).