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Oxidative Photo-Decarboxylation in the Presence of Mesoporous Silicas

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FSM-16, a mesoporous silica, was found to catalyze oxidative photo-decarboxylation of α-hydroxy carboxylic acid, phenyl acetic acid derivatives and *N*-acyl-protected α-amino acids to afford the corresponding carbonyl compounds. Furthermore, FSM-16 proved to be re-usable by re-calcination at 450 °C after the reaction.

Key words α-amino acid; α-hydroxycarboxylic acid; mesoporous silica; phenylacetic acid derivative; photo-decarboxylation

Recently, the importance of environmentally friendly processes has been recognized over all fields of industry and, needless to say, in the field of synthetic organic chemistry as well.[1)] Easy work-up is an important factor for achieving an environmentally benign process and the use of heterogeneous catalysts is advantageous. Among them, growing attention has been paid to porous solids, due to their potential utility as new heterogeneous catalysts and providing selectivity arising from the shape and size of pores. Mesoporous silicas, one of porous crystals, possess uniform meso pores, of which pore sizes are 2—50 nm, and narrow pore-distribution and high surface area against the amorphous mesoporous materials, such as silica gel or alumina.[2)] In the course of our study on the utility of mesoporous silicas in organic synthesis,[3,4)] we, at first, found that benzilic acid (**1**) was oxidatively decarboxylated under irradiation of UV to give benzophenone (**2**) in the presence of FSM-16,[5,6)] which is one of typical mesoporous silicas such as MCM-41[7)] and HMS[8)] (Chart 1).[9)]

The photo-reactivity of microporous silicas[2)] which contain transition metals also has been studied by many groups[10)]; however, little is known about that of the silica itself.[11—14)] Similar to mesoporous silicas, there is only one report on the photo-reactivity of the silica itself,[15)] and there are no reports about an application of metal-free mesoporous silicas as photo-catalyst to synthetic organic chemistry so far.[16)] This is the driving force of our continued studies on the generality of this reaction, and we have found α-hydroxycarboxylic acids, phenyl acetic acid derivatives,[9)] and *N*-acyl-protected α-amino acids[17)] afforded the corresponding carbonyl compounds through an oxidative decarboxylation reaction in the presence of FSM-16, under photo-irradiation. Although thermal[18—25)] and photolytic[26,27)] oxidative decarboxylation reactions of phenyl acetic acid derivatives have been reported by several groups, they require heavy metals, which are of environmentally high impact, as promoters to carry out the reactions. Against this, our method is considered to be environmentally benign due to both heavy-metal-free conditions and easy work-up. Herein, we report our detailed study on the scope, limitation and mechanism of this oxidative photo-decarboxylation.

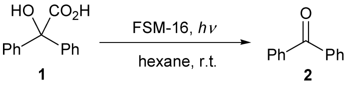


Chart 1

Results and Discuusion

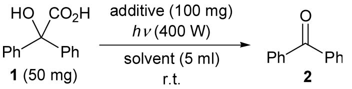
Mesoporous silicas, FSM-16,[5,6)] MCM-41[7)] and HMS,[8)] were prepared according to the previous papers. Table 1 shows the ratios of the framework of mesoporous silicas, which were analyzed by ^{29}Si-NMR spectra, and the pore sizes of the silicas, which were measured by volumetric N_2-gas adsorption method.

Table 2 shows the results of a study of reaction conditions conducted with benzilic acid (**1**, 50 mg, 0.219 mmol) as a test substrate in the presence of additives (100 mg) under external

Table 1. The Ratio of the Framework and the Pore Size of the Silicas

Silica	Q^2	Q^3	Q^4	Pore size (nm)
HMS	4	27	69	2.4
MCM-41	8	9	83	2.9
FSM-16	2	28	70	2.8

Table 2. Study of Reaction Conditions for Oxidative Photo-Deacrboxylation of α-Hydroxycarboxylic Acid



Entry	Additive	Solvent	Time (h)	Recovery of **1** (%)	Yield of **2** (%)[a)]
1	FSM-16	—	5	47	34
2	FSM-16	Acetone	5	35	49
3	FSM-16	MeCN	5	32	50
4	FSM-16	MeOH	5	18	36[b)]
5	FSM-16	H_2O	5	56	12[c)]
6	FSM-16	Toluene	5	21	65
7	FSM-16	Hexane	5	<1	88
8	FSM-16	Hexane	4	11	80
9	FSM-16	Hexane	3	19	63
10	FSM-16	Hexane	5	18	75[d)]
11	FSM-16	Hexane	5	73	<1[e)]
12	FSM-16	Hexane	5	10	79[f)]
13	—	Hexane	24	78	9
14	MCM-41	Hexane	5	25	55
15	HMS	Hexane	5	44	35
16	H-Y	Hexane	5	66	20
17	Na-Y	Hexane	5	56	20
18	H-ZSM-5	Hexane	5	30	66
19	SiO_2	Hexane	5	54	23
20	Al_2O_3	Hexane	5	67	10

a) All yields are for pure, isolated products. *b*) 17% of 1,1-diphenylethyleneglycol was obtained. *c*) 11% of benzopinacol was obtained. *d*) The reaction was carried out with 50 mg of FSM-16. *e*) The reaction was carried out in the dark. *f*) The reaction was carried out under irradiation of 100 W lamp.

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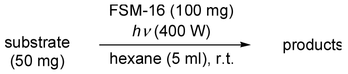
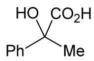
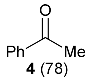
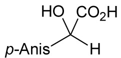
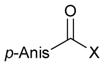
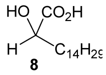
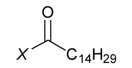
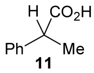
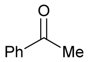
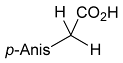
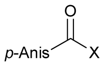
irradiation by a 100 W or 400 W high-pressure mercury lamp in an aerobic atmosphere. The temperature of the final stage of this reaction was about 50 °C. We do not have any direct evidence; however, we believe an effective wavelength of the light is 365 nm, which is an emission line of the strongest and longest wave length in an ultraviolet region irradiated from a high-pressure mercury lamp, since passing through water, a test tube and a cooling jacket, which are made of Pyrex glass, and air are necessary for the light to effect this reaction. Among the solvents examined, hexane was found to afford the best results (entries 1—7).[29] Lowering of the yields was observed when the reaction was carried out in shorter time or with a smaller amount of FSM-16 (entries 8—10). Without irradiation, benzophenone (**2**) was scarcely obtained even in the presence of FSM-16, while the reaction proceeded smoothly under irradiation even with a 100 W lamp (entries 11, 12). Without additives, only a trace amount of the product **2** was obtained even after longer reaction time (24 h), and 78% of the starting benzilic acid (**1**) was recovered (entry 13). MCM-41 and HMS, which are other mesoporous silicas, and H-Y, Na-Y and H-ZSM-5, which are typical microporous zeolites, showed photo-reactivity to some extent; however, they were not so effective as FSM-16 (entries 14—18). Silica gel and alumina, which are amorphous porous materials, afforded **2** in only low yields (entries 19, 20).

Table 3 shows the results for oxidative photo-decarboxylation of several substrates. Other α-hydroxycarboxylic acids (**3**, **5**, **8**) also afforded the corresponding products in the same manner as **1**. Acetophenone (**4**) was obtained in 78% yield as a sole product when atrolactic acid (**3**) was used as a substrate (entry 1). 4-Methoxymandelic acid (**5**) and 2-hydroxypalmitic acid (**8**), which are secondary α-hydroxy carboxylic acids, gave a mixture of the corresponding aldehyde and carboxylic acid (entries 2, 3). Surprisingly, 2-phenylpropionic acid (**11**) and 4-methoxyphenylacetic acid (**12**), which possess no hydroxyl group at the α-position, also afforded acetophenone (**4**: 47%), and a mixture of the corresponding degraded aldehyde (**6**: 30%) and carboxylic acid (**7**: 44%), respectively (entries 4, 5). On the other hand, palmitic acid (**13**), which is a simple carboxylic acid, was unfortunately intact under the conditions, and only the starting material was recovered quantitatively even after 48 h (entry 6).

As can be seen from Table 3, the substituent at the α-position of acids is thought to play an important role in this reaction because usual aliphatic carboxylic acids were intact under the reaction conditions. Accordingly, a study of the substituent at the α-position is important to clarify the mechanism and to apply this reaction to organic synthesis. Thus, we next studied photo-decarboxylation of α-amino acids, which possess an amino group at the α-position. At first, glycine (**14**) and alanine (**15**) were examined for this photo-decarboxylation reaction. A suspension of **14** or **15** (50 mg) and FSM-16 (100 mg) in dry hexane (7 ml) was irradiated at room temperature in Pylex glassware with a 400-W high-pressure mercury lamp externally for 60 h; however, the starting materials were recovered in both cases. Similarly with *N*-benzylglycine (**16**), only the starting material was recovered. On the other hand, *N*-benzoylglycine (**17a**) afforded *N*-formylbenzamide (**18a**) in 45% yield after 60 h irradiation. These results suggest that the basicity of the nitrogen atom inhibits the reaction, and it is thought to be necessary to mask the lone pair with protecting groups in order for the reaction to proceed (Chart 2).

Table 3. Oxidative Photo-Deacrboxylation of Several Substrates with FSM-16



Entry	Substrate	Time (h)	Products (% yield)[a]
1	 **3**	12	 **4** (78)
2	 **5**	12	 **6**: X=H (63) **7**: X=OH (20)
3	 **8**	15	 **9** : X=H (37) **10**: X=OH (30)
4	 **11**	60	 **4** (47)
5	 **12**	36	 **6**: X=H (30) **7**: X=OH (44)
6	*n*-$C_{15}H_{31}CO_2H$ **13**	48	No reaction

a) All yields are for pure, isolated products.

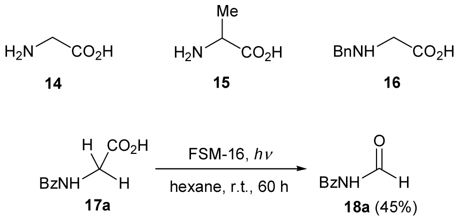
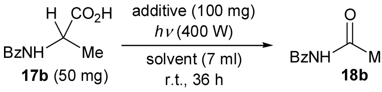


Chart 2

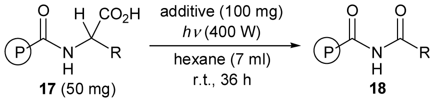
Table 4. Study of Reaction Conditions for Oxidative Photo-Deacrboxylation of *N*-Protected Amino Acid



Entry	Additive	Solvent	Recovery of **17b** (%)	Yield of **18b** (%)[a]
1	FSM-16	Et_2O	44	39
2	FSM-16	Toluene	43	23
3	FSM-16	Acetone	20	51
4	FSM-16	MeCN	17	50
5	FSM-16	Hexane	0	70
6	FSM-16	Hexane	Quant.	0[b]
7	FSM-8	Hexane	62	3
8	FSM-12	Hexane	4	76
9	—	Hexane	Quant.	0

a) All yields are for pure, isolated products. *b*) The reaction was carried out in the dark.

Table 5. Oxidative Photo-Deacrboxylation of *N*-Protected Several Amino Acids with FSM-16



Entry	Substrate			Time (h)	Product	Yield (%)[a]
	Ⓟ	R				
1	Ph	H	**17a**	60	**18a**	45
2	Ph	Me	**17b**	36	**18b**	70
3	Ph	*i*-Bu	**17c**	48	**18c**	54
4	Ph	Ph	**17d**	36	**18d**	74
5	BnO	Me	**17e**	36	**18e**	51
6	BnO	H	**17f**	60	**18f**	66
7	Bn	H	**17g**	60	**18g**	55
8	*t*-BuO	Me	**17h**	36	**18h**	45

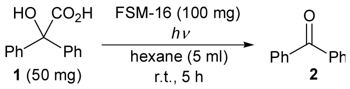
a) All yields are for pure, isolated products.

Table 4 shows the results of our study of reaction conditions conducted with *N*-benzoylalanine (**17b**) as a test substrate. At first, the reactivity of **17b** in several organic solvents was examined, and hexane proved to be a better solvent than other typical ones (entries 1—5). The results that without irradiation or FSM-16, only the starting material was recovered (entries 6, 9) show the necessity of both irradiation and FSM-16 for this reaction. Furthermore, the pore size of the silica seems to be important for this reaction. *N*-Benzoylalanine (**17b**) was irradiated for 36 h in the presence of FSM-8 (D<1.5 nm; D, pore diameter) and FSM-12 (D=2.0 nm). Although a large amount of the starting **17b** was recovered with FSM-8, 76% of *N*-acetylbenzamide (**18b**) was obtained in the presence of FSM-12 (entries 7, 8). These results show that FSM-16 (D=2.7 nm) is superior for the substrates of similar or larger size than that of **17b** to other FSMs of small pore size, and that the reaction field is actually inside the pores of FSMs, because the composition and the chemical properties of FSMs are basically the same.

Table 5 shows the results for the photo-decarboxylation with several *N*-acyl-protected α-amino acids. *N*-Benzoyl- (**17a**), *N*-benzyloxycarbonyl- (**17f**), and *N*-phenylacetylglycine (**17g**) took a longer time to complete the reaction (entries 1, 6, 7). On the other hand, conversion of *N*-benzoyl- (**17b**), *N*-benzyloxycarbonyl- (**17e**), and *N*-*tert*-butoxycarbonylalanine (**17h**) to the corresponding imides completed in relatively short time (entries 2, 5, 8). *N*-Benzoylleucine (**17c**) afforded the product **18c** in a moderate yield (entry 3). The best yield in our study was attained by the reaction with *N*-benzoylphenylglycine (**17d**) (entry 4). From these results, the suitable protective group for each α-amino acid seems to be different. Although the substrate **17a** is smaller than **17b**, **17c** and **17d**, the yield was lower than that of the others (entries 1—4). Furthermore **17f** and **17g**, which are thought to be more bulky than **17a**, afforded **18f** and **18g** respectively in higher yields than **17a** did. These results suggest that not only the shape of the substrates, but also the electronic effect of the substituents participate in the direction of this reaction.

Furthermore, the promoter FSM-16 was found to be recyclable and useful as a photocatalyst. Thus, the recovered FSM-16, which was re-calcined at 450 °C for 4 h after the photo-reaction of **1**, showed high activity in the reaction, providing 81% yield of **2** even after being re-used 5 times (Table 6).

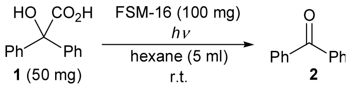
Table 6. Re-use of FSM-16



Cycle of FSM-16	1st	2nd	3rd	4th	5th
Yield of **2** (%)[a]	87	91	86	86	81

a) All yields are for pure, isolated products.

Table 7. Effect of Oxygen



Time (h)	Yield of **2** (%)[a]		
	Under N_2	Under O_2	Under air
3	5	61	69
5	7	73	88

a) All yields are for pure, isolated products.

Reaction Mechanism In our study with α-hydroxycarboxylic acids, the real oxidant is assumed to be the oxygen in air. Table 7 shows the results of a study of the effect of oxygen. Only a small amount of product **2** was obtained under N_2, while under O_2 the yield of **2** was comparable to that under air. Since no acceleration of this reaction was observed under O_2, a high concentration of oxygen was not required; however, oxygen proved to be an important factor for this reaction.

Among the typical solvents examined, the order of solubility of oxygen is hexane>toluene>acetone>acetnitrile.[29)] Although the yield of **2** correlated to the order, the yields of **18b** did not correlate to the order except hexane of the highest solubility of oxygen (Tables 2, 4). The reason is not clear; however, concentration effect due to hydrophobicity of hexane is assumed to accelerate the photo-reaction in the pores of FSM-16s.

Furthermore, an attempt was made to detect the intermediates to clarify the reaction pathway by terminating the reaction with **12** at 12 h; however, the possible intermediates, **5** or 4-methoxybenzylalcohol (**19**), were not detected by 400 MHz-NMR analysis (Chart 3, Eq. 1). On the other hand, **19** was allowed to react under the same conditions as for **12**, and found to afford **6** (9%) and **7** (3%), which were similar to results for **12** (Chart 3, Eq. 2). This suggests the final oxidized products were provided by oxidation of a benzylalcohol species as the possible intermediates.

Although the mechanism of this reaction is not clear yet, the active sites produced by dehydration from silanol groups on the wall of FSM-16 during calcination are thought to play an important role in decarboxylation of the substrate. We present in Charts 4 and 5 what we assume is a mechanism of this oxidation, which is postulated by considering all of the results mentioned above. At first, Chart 4 summarizes the generation step of the active sites and initial photoexcitation step of photo-decarboxylation. Non-bonding oxygen hole

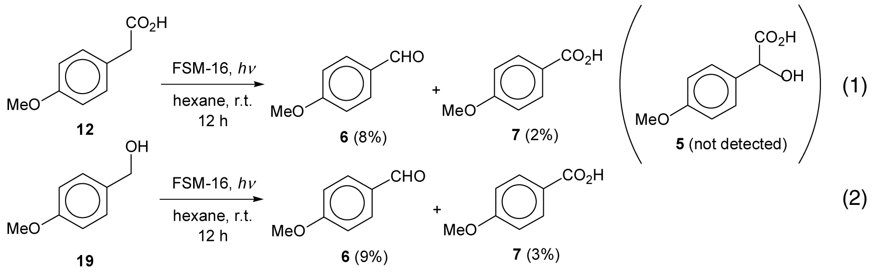


Chart 3

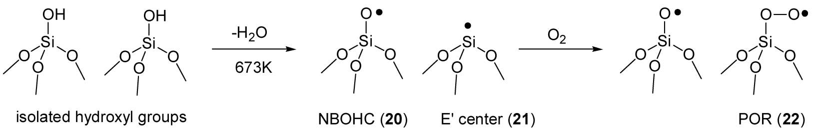


Chart 4

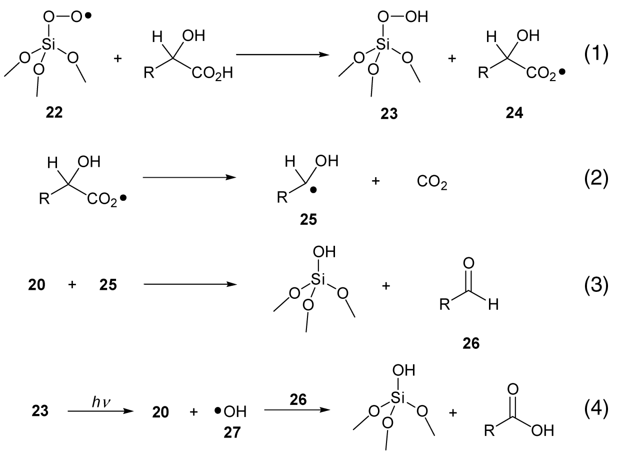


Chart 5

center (NBOHC) (**20**) and E′ center (**21**) are formed by dehydroxylation from the isolated hydroxyl groups of silanols through be calcined at 450 °C.[30] Oxygen is, then, adsorbed on the E′ center, and generates the peroxy radical (POR) (**22**), which we believe to be the active site of this decarboxylation.[31] Chart 5 shows a plausible path of this reaction. The radical species **24** is thought to be generated by abstraction of a hydrogen radical with **22** and decarboxylated to give the radical species **25** (Eqs. 1, 2). Aldehyde **26** was afforded by abstraction of a hydrogen radical with **20** (Eq. 3), and the hydroperoxide **23** was homolytically cleaved under photo-irradiation to **20** and hydroxyl radical **27**, which reacts with **26** to afford the corresponding carboxylic acid (Eq. 4).

Although we have not measured metal content in our synthesized FSM-16, it is incontrovertible that the metals, which came from a water glass (sodium silicate made by Tokuyama Siltech Co.), made possible to effect the photo-catalytic activity, since the water glass included metals such as Al (85 ppm), Fe (30 ppm), Ti (30 ppm), Ca (10 ppm) and Mg (7 ppm).[32]

In conclusion, this new method of decarboxylation is thought to be more environmentally benign than previous methods since our method eliminates the use of heavy metals and organic solvents of high environmental impact, such as halogenated solvents or benzene, and the reaction is operationally simple from the viewpoint of the convenience of the work-up in which recyclable FSM-16 can be removed only by filtration of the reaction mixture.

Experimental

General Diethyl ether was freshly distilled from Na metal/benzophenone ketyl. All other dry solvents were obtained from Kanto Kagaku Co., Ltd. Other chemicals used were of reagent grade and were obtained from Aldrich Chemical Co., Tokyo Kasei Kogyo Co., Ltd. and Wako Pure Chemical Industries, Ltd. H-Y, Na-Y and H-ZSM-5 were purchased from TOSOH Co. SiO_2 (230—400 mesh) and Al_2O_3 were purchased from Merck Co. and Nacalai Tesque Inc. respectively. All reactions were carried out in a Pyrex test tube under aerobic conditions, which was set up from the center of a 400-W high pressure mercury lamp to the distance of 37.5 mm. All of the products are known compounds, and were identified by comparison of their NMR spectra with those of authentic samples.

Synthesis of FSM-16 Kanemite was prepared as paste by filtration of a suspension of sodium silicate (50 g) and dist. H_2O (500 ml), which was stirred for 3 h at r.t. Kanemite (as paste) was added to an aqueous solution (1 l) of hexadecyltrimetylammonium chloride (32 g, 0.1 mol), and stirred for 3 h at 70 °C. After adjusting the pH at 8.5 with 2 N dil. HCl, the suspension was further stirred for 3 h at 70 °C. The white precipitate was filtered, washed with dist. H_2O, dried at 60 °C for 12 h, and calcined at 550 °C for 5 h.

Synthesis of MCM-41 Tetraethylorthosilicate (20.8 g, 0.1 mol) was added by pipette to a solution of hexadecyltrimetylammonium bromide (7.3 g, 0.02 mol) and conc. HCl (8.3 ml, 0.1 mol) in H_2O (270 ml), and stirred for 48 h at r.t. The white precipitate was filtered and washed with dist. H_2O. The solid was dried at 120 °C for 12 h, and calcined at 650 °C for 4 h.

Synthesis of HMS A ethanol solution of tetraethylorthosilicate (20.8 g, 0.1 mol) was added to a suspension of dodecylamine (5.0 g, 0.027 mol) in H_2O (38 ml) under vigorous stirring for 1 h, and aged for 18 h at r.t. The white precipitate was washed with ethanol and H_2O, and calcined at 650 °C for 4 h.

Typical Procedure of Photo-Decarboxylation A suspension of substrate (50 mg) and FSM-16 (100 mg) in dry hexane (5 ml) was irradiated at room temperature with a 400-W high-pressure mercury lamp externally for the indicated time. FSM-16 was then filtered off and washed with ethyl acetate, and the filtrate was concentrated under reduced pressure. Pure product was obtained after purification by preparative TLC.

Typical Procedure of Re-use of FSM-16 A suspension of substrate (50 mg) and FSM-16 (100 mg) in dry hexane (5 ml) was irradiated at room temperature with a 400-W high-pressure mercury lamp externally for the indicated time. FSM-16 was then filtered off and washed with ethyl acetate. The used FSM-16 was collected and re-calcined at 450 °C for 4 h by an electric furnace before being re-used.

References and Notes

1) Sheldon R. A., *Chemtech*, **24**, 38—47 (1994).
2) IUPAC recommends classification of pores to micropore ($D<2$ nm; D,

pore diameter) and mesopore (2 nm$<D<$50 nm), see: Everett D. H., *Pure Appl. Chem.*, **31**, 579—638 (1972).

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