New Synthetic Method of Imides through Oxidative Photodecarboxylation Reaction of *N*-Protected α-Amino Acids with FSM-16

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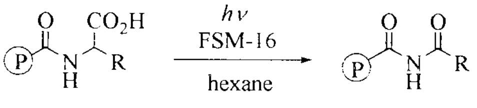
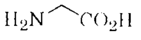
FSM-16, a mesoporous silica, was found to promote the oxidative photodecarboxylation of *N*-acyl-protected α-amino acids in hexane to afford the corresponding imides.

Imides have not only been used as the starting materials for preparation of N-containing heterocycles,[1] but also have been focussed on from the view point of biological activity.[2] In general the preparation of imides involves acylation of amides with anhydrides,[3] acyl chlorides,[2,4] or ketene,[5] and, more recently, with α,α,α-trichloromethyl carbonyl compounds[6] and enol esters;[7] however, these methods involve some problems, such as low yield or high environmental impact of the solvents used or waste produced. On the other hand, we have been engaged in applications of mesoporous zeolites, which have pores large enough to incorporate usual molecules of low molecular weight,[8] to organic synthesis,[9] and found that α-hydroxy carboxylic acids afforded the corresponding carbonyl compounds through oxidative photodecarboxylation reaction in the presence of FSM-16,[10] a mesoporous silica.[11] The mechanism of this reaction has not been elucidated yet; however, 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. In the course of our investigation, we have found that *N*-protected α-amino acids with acyl groups afforded the corresponding imides (Scheme 1). Now we report a new synthetic method of imides through oxidative photodecarboxylation reaction.

Scheme 1.



At first, glycine (**1**) and alanine (**2**) were examined for this photodecarboxylation reaction. A suspension of **1** or **2** (50 mg) and FSM-16 (100 mg) in dry hexane (7 mL) was irradiated at room temperature in a pylex glass wear 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 (**3**), only the starting material was recovered. On the other hand, *N*-benzoylglycine (**4a**) afforded *N*-formylbenzamide (**5a**) in 45% yield after 60 h irradiation.[12] 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.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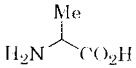
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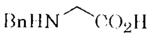
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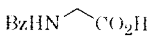
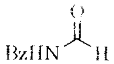
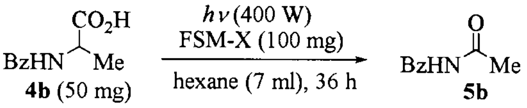

4a


5a

Furthermore, the pore size of the silica seems to be important for this reaction. Table 1 shows the results of a study of the pore size effect of FSMs. *N*-benzoylalanine (**4b**) was irradiated for 36 h in the presence of FSM-8 ($D < 1.5$ nm; D, pore diameter), FSM-12 ($D = 2.0$ nm), and FSM-16 ($D = 2.7$ nm). Although a large amount of the starting **4b** was recovered with FSM-8 (entry 1), 76 and 70% of *N*-acetylbenzamide (**5b**) were obtained in the presence of FSM-12 and FSM-16 respectively (entries 2 and 3). These results show that FSM-16 is superior for the substrates of similar or larger size than that of **4b** 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.

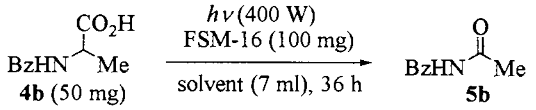
Table 1. Pore size effect of FSM-X



Entry	FSM-X	Pore size /nm	Recovery of **4b**/%	Product **5b**/%
1	FSM- 8	<1.5	62	3
2	FSM-12	2.0	4	76
3	FSM-16	2.7	0	70

The solvents are also thought to play an important role in this reaction. The reactivity of **4b** in several organic solvents was examined, and hexane proved to be a better solvent than other typical ones (Table 2). In our previous paper on the oxidative photodecarboxylation of α-hydroxycarboxylic acids, the real oxidant assumed to be the oxygen in air.[11] The solvents in Table 2 are arranged in the order of the solubility of oxygen.[13] Although hexane of the highest solubility of oxygen among the typical organic solvents examined afforded **5b** in highest yield, the yields of **5b** generally does not correlate to the order.

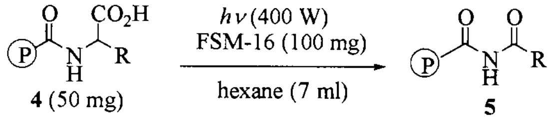
Table 2. Solvent effect



Entry	Solvent	Recovery of **4b**/%	Product **5b**/%
1	hexane	0	70
2	diethyl ether	44	39
3	toluene	43	23
4	acetone	20	51
5	acetonitrile	17	50

Table 3 shows the results for the reaction with several α-amino acids which are protected with a variety of acyl groups. The results that without FSM-16 or irradiation, only the starting material was recovered (entries 1 and 2) show the necessity of both FSM-16 and irradiation for this reaction. *N*-Benzoyl- (**4a**), *N*-benzyloxycarbonyl- (**4f**), and *N*-phenylacetylglycine (**4g**) took a longer time to complete the reaction (entries 4, 8, and 9), on the other hand, conversions of *N*-benzoyl- (**4b**), *N*-benzyloxycarbonyl- (**4e**), and *N*-*tert*-butoxycarbonylalalanine (**4h**) to the corresponding imides completed in relatively short time (entries 3, 7, and 10). *N*-Benzoylleucine (**4c**) afforded the product **5c** in a moderate yield (entry 5). The best yield in our study was attained by the reaction with *N*-benzoylphenylglycine (**4d**) (entry 6). From these results, the suitable protective group for each α-amino acid seems to be different. Although the substrate **4a** is smaller than **4b**, **4c** and **4d**, the yield was lower than that of the others (entries 3-6). Furthermore **4f** and **4g**, which are thought to be more bulky than **4a**, afforded **5f** and **5g** respectively in higher yields than **4a** 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.

Table 3. Oxidative photodecarboxylation of N-protected several amino acids with FSM-16



Entry	Ⓟ	R	Substrate	*t*/h	Product	Yield/%
1	Ph	Me	**4b**	36	**5b**	0 [a]
2	Ph	Me	**4b**	36	**5b**	0 [b]
3	Ph	Me	**4b**	36	**5b**	70
4	Ph	H	**4a**	60	**5a**	45
5	Ph	iBu	**4c**	48	**5c**	54
6	Ph	Ph	**4d**	36	**5d**	74
7	BnO	Me	**4e**	36	**5e**	51
8	BnO	H	**4f**	60	**5f**	66
9	Bn	H	**4g**	60	**5g**	55
10	^{t}BuO	Me	**4h**	36	**5h**	45

[a] The reaction was carried out without FSM-16. [b] The reaction was carried out in the dark.

In conclusion, this new synthetic method of imides is thought to be more environmentally friendly than previous methods, because easily available α-amino acids are used as the starting materials, and organic solvents of high environmental impact, such as halogenated solvents or benzene, are not used. Furthermore, the reaction is operationally simple from the view point of the convenience of the work-up in which FSM-16 can be removed only by filtration of the reaction mixture.

References and Notes

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12 A typical procedure follows: A suspension of *N*-protected amino acid (**4**, 50 mg) and FSM-16 (100 mg) in dry hexane (7 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 **5** was obtained after purification by preparative TLC.

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