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Chemoselective hydrogenation using molecular sieves-supported Pd catalysts: Pd/MS3A and Pd/MS5A

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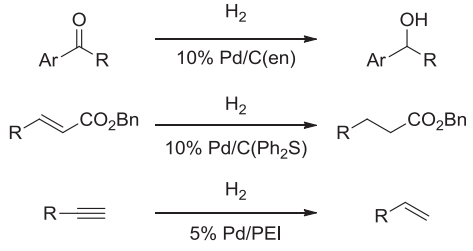
ABSTRACT

Palladium catalysts embedded on molecular sieves (MS3A and MS5A) were prepared by the adsorption of $Pd(OAc)_2$ onto molecular sieves with its in situ reduction to Pd^0 by MeOH as a reducing agent and solvent. 0.5% Pd/MS3A and 0.5% Pd/MS5A catalyzed the hydrogenation of alkynes, alkenes, and azides with a variety of coexisting reducible functionalities, such as nitro group, intact. It is noteworthy that terminal alkenes of styrene derivatives possessing electron-donating functionalities on the benzene nucleus were never hydrogenated under 0.5% Pd/MS5A-catalyzed conditions, while internal alkenes of 1-propenylbenzene derivatives were readily reduced to the corresponding alkanes.

1. Introduction

Transition metal-catalyzed hydrogenation methods have been applied to a number of chemical transformations of various functional groups.[1] Development of chemoselective hydrogenation, selective hydrogenation of a particular reducible functionality within a molecule having coexisting multiple reducible functionalities, is one of the most important topics in organic chemistry to expand the possible synthetic routes especially for the construction of complex molecules, such as natural products, pharmaceuticals, functional materials, and so on.

During our study on the chemoselective hydrogenation, the addition of some specific catalytic poisons, such as nitrogen-[2] and sulfur-containing compounds,[3] which decrease the catalyst activity, to the Pd/C-catalyzed hydrogenation reaction was found to moderately reduce the catalyst activity of Pd/C to control the chemoselectivity among several reducible functionalities. On the basis of these findings, we developed amine- or sulfur-bound heterogeneous palladium catalysts for chemoselective hydrogenation, Pd/C-ethylenediamine [Pd/C(en)],[4] Pd/C-diphenyl sulfide [$Pd/C(Ph_2S)$],[5] and Pd/polyethyleneimine complexes (Pd/PEI)[6] (Scheme 1). Furthermore, immobilization of zero-valent Pd metal on a silk fibroin was achieved by its simple soaking in a MeOH solution of $Pd(OAc)_2$. The Pd/Fib catalyzed the chemoselective hydrogenation of only alkynes, alkenes, and azides to the corresponding alkanes and amines, respectively, in the presence of several other reducible functional groups, such as aromatic halides and ketones[7] (Scheme 2). Chemoselectivities of Pd/PEI and Pd/Fib are considered to be derived from the character of the catalyst support.



Scheme 1. Chemoselective hydrogenation using amine- or sulfur-bound palladium catalysts.

A chemoselective hydrogenation of cinnamaldehyde to the corresponding primary alcohol maintaining the alkene moiety has been achieved by the use of a ruthenium catalyst supported on a Y-type zeolite (Ru/Y).[8] Furthermore, Lee and co-workers reported

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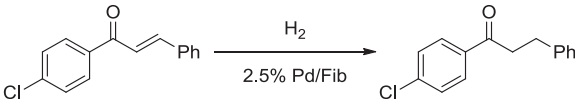


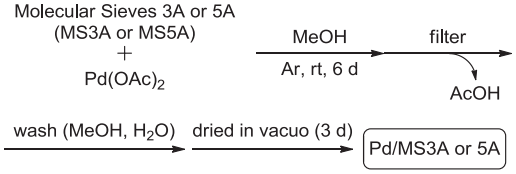
Scheme 2. Pd/Fib-catalyzed hydrogenation.

a selective hydrogenation of benzyl ethers in the presence of trisubstituted alkenes within the molecule using palladium on zeolite MCM-48 (Pd@MCM-48) as a catalyst.[9] Chemoselectivities of these catalysts resulted from the properties of the zeolites, such as surface area, pore size, polarity of the inside cavity, and so on.

Because a variety of zeolites possessing different properties are commercially available, the character or activity of palladium catalysts immobilized on each zeolite are thought to vary with the properties of the zeolite. We recently reported the preparation of a heterogeneous palladium catalyst supported on molecular sieves 3A (MS3A) and its application to the chemoselective hydrogenation of alkyne, alkene, and azide derivatives in the presence of a nitro group as a preliminary communication.[10] This paper demonstrates the details of the Pd/MS3A-catalyzed chemoselective hydrogenation and the novel and unique selectivity of a newly developed molecular sieves 5A (MS5A)-supported palladium (Pd/MS5A) catalyst.

2. Results and discussion

0.5% Pd/MS complexes were simply prepared by the adsorption of $Pd(OAc)_2$ on molecular sieves and its in situ reduction to Pd^0 using MeOH as a reductant in a one-pot manner. Molecular sieves 3A and 5A were individually stirred in a MeOH solution of $Pd(OAc)_2$ at room temperature for 6 days until the rust-colored supernatant solution turned clear. During this period, Pd^{II} was adsorbed on the MS and reduced to Pd^0 by MeOH.[11] The resulting gray powder was then collected by filtration, thoroughly washed with MeOH and H_2O, and dried under vacuum to give the Pd/MS catalysts (Scheme 3).[7] The quantity of the adsorbed Pd metal on molecular sieves of each catalyst was determined to be nearly 0.5 wt % by X-ray fluorescence (XRF) analysis, and it was indicated that more than 90% of the adsorbed Pd species existed as Pd^0 by the X-ray absorption near edge structure (XANES) analysis of both Pd/MS catalysts. The STEM analysis indicated that the Pd particle size of 0.5% Pd/MS3A was smaller than 10 nm[10] and that of 0.5% Pd/MS5A was approximately 15 nm (Fig. 1). The Pd metal surface area of 0.5% Pd/MS5A was found to be 30 m^2/g-Pd by a surface area analysis using the CO adsorption method, and was virtually the same as that for Pd/MS3A (22 m^2/g-Pd).[10]



Scheme 3. Preparation of Pd/MS3A and Pd/MS5A.

0.5% Pd/MS3A (**A**) and 0.5% Pd/MS5A (**B**) were found to possess a similar catalyst activity for the hydrogenation under H_2 atmosphere at room temperature (Table 1), although **B** showed a slightly lower activity compared to **A** and the Pd/MS5A-catalyzed reactions generally required longer periods to achieve the same results. These catalysts achieved unique chemoselective hydrogenations: alkyne, alkene, and azide functionalities were completely hydrogenated (Table 1, entries 1–16), while benzyl esters (entries 3–6), benzyl ethers (entries 7 and 8), aromatic chlorides (entries 5 and 6), nitriles (entries 13, 14, 17, and 18), and aromatic ketones (entries 15–18) were never reduced.

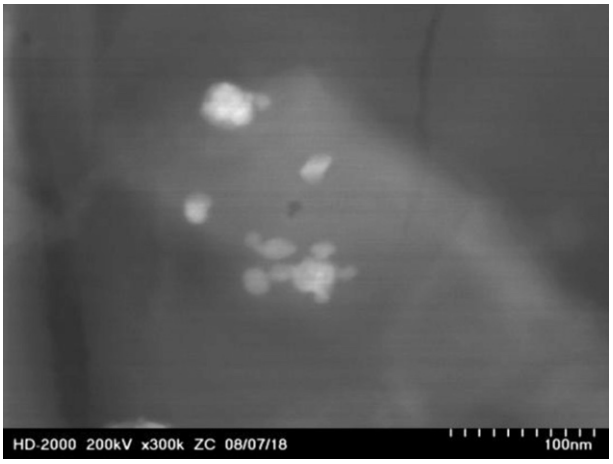
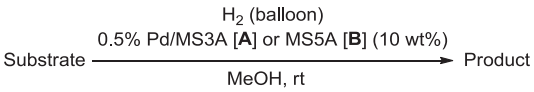


Fig. 1. STEM image of 0.5% Pd/MS5A.

Table 1
Hydrogenation of various functionalities using 0.5% Pd/MS3A (**A**) and 0.5% Pd/MS5A (**B**)



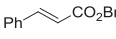
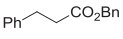
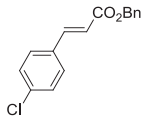
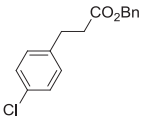
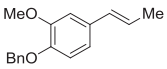
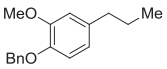
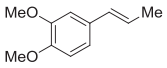
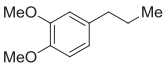
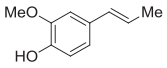
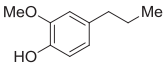
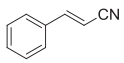
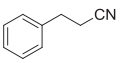
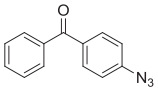
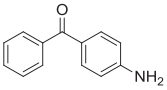
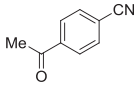
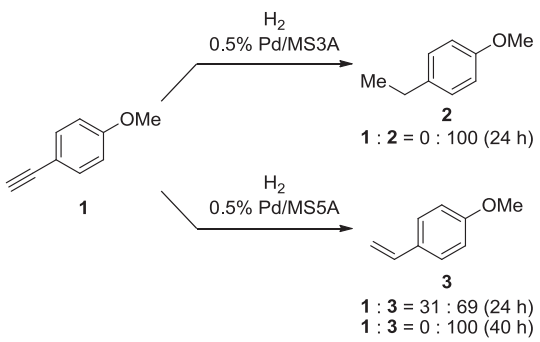
Entry	Substrate	Pd/MS	Product	Time (h)	Yield[a] (%)
1		**A**		24	98
2		**B**		24	97
3		**A**		4	99
4		**B**		8	100
5		**A**		4	95
6		**B**		6	96
7		**A**		3	98
8		**B**		5	98
9		**A**		19	92
10		**B**		22	94
11		**A**		20	98
12		**B**		20	97
13		**A**		9	96
14		**B**		24	95
15		**A**		5	95
16		**B**		12	97

Table 1 (*continued*)

Entry	Substrate	Pd/MS	Product	Time (h)	Yield[a] (%)
17		**A**	No reaction	24	95[b]
18		**B**		24	92[b]

[a] Isolated yield.
[b] Yield of the recovered starting material.

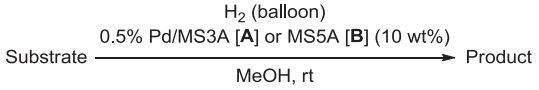
In the case of the hydrogenation of 4-ethynylanisole (**1**), a mono-substituted alkyne, the complete hydrogenation of the alkyne to the corresponding alkane (**2**) could be achieved under 0.5% Pd/MS3A-catalyzed conditions, while the fully hydrogenated 4-ethylanisole (**2**) was never obtained by the use of 0.5% Pd/MS5A as a catalyst (Scheme 4). It is noteworthy that the totally-selective semi-hydrogenation to 4-vinylanisole (**3**) was caused by 0.5% Pd/MS5A because of the low catalyst activity based on its properties, such as the larger pore size of the support and larger Pd cluster sizes (lower superficial area). The catalyst activities of 0.5% Pd/MS3A and 0.5% Pd/MS5A for the hydrogenation of mono-substituted alkynes and alkenes were then circumstantially investigated (Table 2).

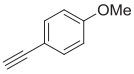
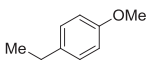
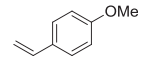
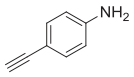
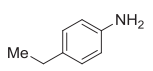
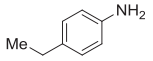
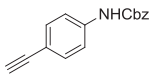
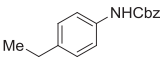
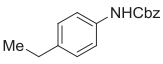
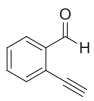
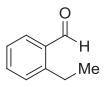
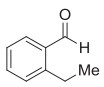
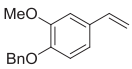
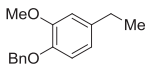
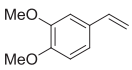
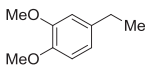
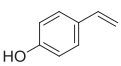
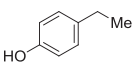
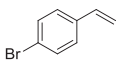
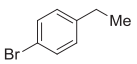
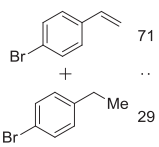
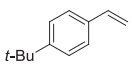
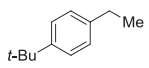
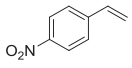
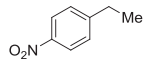


Scheme 4. Hydrogenation of 4-ethynylanisole in MeOH using Pd/MS3A and Pd/MS5A.

Alkyne moieties of ethynylbenzene derivatives (mono-substituted alkynes) bearing a variety of substituents, except for 4-ethynylanisole (Scheme 4; Table 2, entries 1 and 2), were smoothly hydrogenated by either catalyst (entries 3–8) with *N*-Cbz (entries 5 and 6) and aromatic aldehyde (entries 7 and 8) functionalities intact. When the mono-substituted styrene derivatives were used as a substrate, the substituent on the aromatic nucleus significantly affected the reactivity toward the hydrogenation of the alkene moiety (entries 9–22). The comparatively electron-sufficient styrenes possessing two alkoxy groups or a hydroxy group on the aromatic ring were never hydrogenated under 0.5% Pd/MS5A-catalyzed conditions (entries 10, 12, and 14), while 0.5% Pd/MS3A smoothly catalyzed the alkene hydrogenation (entries 9, 11, and 13). The alkene moiety underwent hydrogenation even using 0.5% Pd/MS5A in accordance with the reduction of the electron density on the aromatic ring of the styrene derivatives. The 0.5% Pd/MS5A-catalyzed hydrogenation of 4-bromostyrene afforded a 71:29 mixture of 4-bromostyrene and 4-bromoethylbenzene within 24 h (entry 16), and 4-*tert*-butylstyrene (entries 17 and 18) and 4-nitrostyrene (entries 19 and 20) were easily hydrogenated to the corresponding 4-*tert*-butylethylbenzene and 4-nitroethylbenzene without any problems in nearly quantitative yields. On the other hand, highly electron-sufficient styrene bearing both methoxy and hydroxy groups on the aromatic nucleus was never hydrogenated even by the use of 0.5% Pd/MS3A as a catalyst (entries 21 and 22). As shown in entries 7–12 in Table 1, the internal (di-substituted)

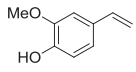
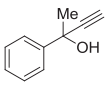
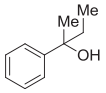
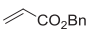
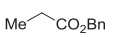
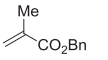
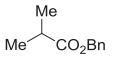
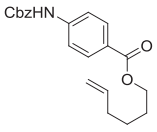
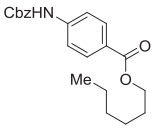
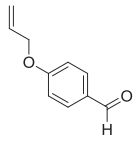
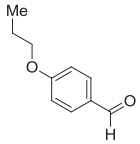
Table 2
0.5% Pd/MS-catalyzed hydrogenation of terminal alkynes and alkenes



Entry	Substrate	Pd/MS	Product	Time (h)	Yield[a] (%)
1		**A**		24	83
2		**B**		40	95
3		**A**		3	90
4		**B**		5	94
5		**A**		3	97
6		**B**		9	95
7		**A**		2	93
8		**B**		5	92
9		**A**		7	98
10		**B**	No reaction	24	97[b]
11		**A**		18	99
12		**B**	No reaction	24	94[b]
13		**A**		24	93
14		**B**	No reaction	24	95[b]
15		**A**		24	72
16		**B**	 71 : 29	24	—
17		**A**		5	94
18		**B**		7	92
19		**A**		3	94
20		**B**		4	92

(*continued on next page*)

Table 2 (*continued*)

Entry	Substrate	Pd/MS	Product	Time (h)	Yield[a] (%)
21		**A**	No reaction	24	98[b]
22		**B**		24	95[b]
23		**A**		4	95
24		**B**		5	96
25		**A**		3	91
26		**B**		5	88
27		**A**		5	90
28		**B**		5	92
29		**A**		3	94
30		**B**		5	98
31		**A**		2	98
32		**B**		3	92

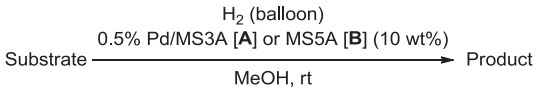
[a] Isolated yield.
[b] Yield of the recovered starting material.

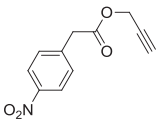
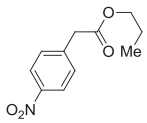
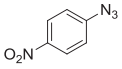
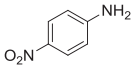
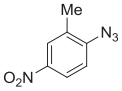
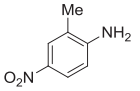
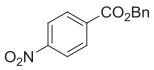
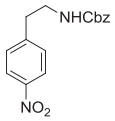
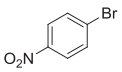
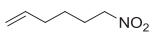
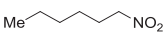
alkenes of 1-propenylbenzene derivatives were completely hydrogenated to the corresponding alkanes by the use of either 0.5% Pd/MS3A or 0.5% Pd/MS5A. Although 4-benzyloxy-3-methoxy-1-propenylbenzene (Table 1, entries 7 and 8) and 3,4-dimethoxy-1-propenylbenzene (Table 1, entries 9 and 10) are structurally very similar to 4-benzyloxy-3-methoxystyrene (Table 2, entries 9 and 10) and 3,4-dimethoxystyrene (Table 2, entries 11 and 12), respectively, the hydrogenation of both mono-substituted alkenes was selectively and totally suppressed under 0.5% Pd/MS5A-catalyzed conditions. It is quite interesting that the 0.5% Pd/MS5A does not catalyze the hydrogenation of only mono-substituted alkenes, but di-substituted alkenes, in spite of the good similarity of the chemical structure of both alkenes, while mono-substituted alkenes are generally much more easily reduced compared with the corresponding di-substituted ones. The difference in the catalyst activity between these MS-supported catalysts may arise from their subtle differences in properties such as cavity size of the MS and Pd particle size.

On the other hand, structurally different types of mono-substituted alkynes and alkenes, which are not conjugated with arene nuclei, smoothly underwent hydrogenation to the corresponding alkanes as the usual Pd-catalyzed hydrogenation with either 0.5% Pd/MS3A or 0.5% Pd/MS5A (entries 23–32), leaving benzyl ester (entries 25–28) and *N*-Cbz (entries 29 and 30), and aromatic aldehyde (entries 31 and 32) moieties untouched.

During the investigation, we also found that 0.5% Pd/MS3A- and 0.5% Pd/MS5A-catalyzed hydrogenation never affected aromatic nitro groups (Table 2, entries 19 and 20). The aromatic nitro groups are very susceptible to the hydrogenation and are easily reduced to the corresponding amines.[1b] Therefore, it is extremely hard to achieve the chemoselective hydrogenation of unsaturated multiple bonds, such as alkynes, alkenes, and azides, in the presence of nitro groups. Such a background led us to explore the applicability of 0.5% Pd/MS3A and 0.5% Pd/MS5A for the chemoselective hydrogenation of unsaturated multiple bonds within the nitro-containing compounds (Table 3). As a result, alkyne, alkene, and azide functionalities were selectively hydrogenated with nitro groups intact (entries 1–6, 13, and 14). The aliphatic nitro functions were also tolerant as were aromatic nitro groups under the conditions (entries 13 and 14). Aryl bromide (entries 11 and 12) as well as benzyl ester (entries 7 and 8) and *N*-Cbz (entries 9 and 10) moieties were also not reactive, and the nitro-containing compounds were quantitatively recovered even after 24 h (entries 7–12).

Table 3
Chemoselective hydrogenation in the presence of a nitro group

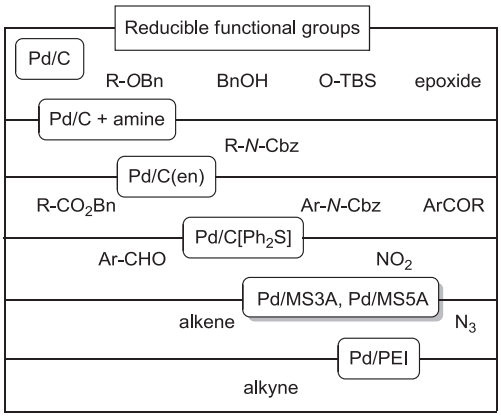


Entry	Substrate	Pd/MS	Product	Time (h)	Yield[a] (%)
1		**A**		24	95
2		**B**		24	94
3		**A**		24	98
4		**B**		24	98
5		**A**		24	90
6		**B**		24	93
7		**A**	No reaction	24	98[b]
8		**B**		24	96[b]
9		**A**	No reaction	24	94[b]
10		**B**		24	94[b]
11		**A**	No reaction	24	96[b]
12		**B**		24	95[b]
13		**A**		7	88
14		**B**		7	90

[a] Isolated yield.
[b] Yield of the recovered starting material.

3. Conclusion

Molecular sieves-supported Pd catalysts, 0.5% Pd/MS3A and 0.5% Pd/MS5A, were easily prepared by immersing the supports in a MeOH solution of $Pd(OAc)_2$. Use of either 0.5% Pd/MS3A or 0.5% Pd/MS5A made it possible to selectively reduce alkynes, alkenes, and azides in the presence of a variety of reducible functionalities including nitro groups (Scheme 5). When 0.5% Pd/MS5A was used as the catalyst for the hydrogenation of styrene derivatives bearing



Scheme 5. Pd catalysts for the chemoselective hydrogenation. Each catalyst can reduce the functionalities under the bar.

electron-donating substituents on the aromatic ring, the terminal alkene moiety was never hydrogenated to the corresponding alkane, although the internal alkene of 1-propenylbenzene derivatives underwent smooth hydrogenation. The present chemoselectivity indicates a unique catalyst activity of 0.5% Pd/MS5A, which has never been reported in the literature. Although the phenomena are not rationally explained, they are apparently derived from the properties of 0.5% Pd/MS5A, such as pore size of the supports. Therefore, the use of zeolite as a catalyst support has a great possibility for creating unknown and novel catalyst activities.

4. Experimental

4.1. General experimental

All reagents and solvents were obtained from commercial sources and used without further purification. Analytical thin-layer chromatography (TLC) was carried out on pre-coated Silica Gel 60 F_{254} plates (Merck, Art 5715) and visualized with UV light and/or stained (phosphomolybdic acid in EtOH or *p*-anisaldehyde in EtOH/H_2SO_4/AcOH). The ^{1}H NMR and ^{13}C NMR spectra were recorded by a JEOL EX-400 (400 MHz for ^{1}H NMR; 100 MHz for ^{13}C NMR). $CDCl_3$ was used as the solvent for NMR measurement. Chemical shifts (δ) are expressed in part per million and internally referenced (0.00 ppm for tetramethylsilane/$CDCl_3$ for ^{1}H NMR and 77.0 ppm for $CDCl_3$ for ^{13}C NMR). The mass spectra (EI and FAB) were taken by a JEOL JMS-SX102A instrument at the Mass Spectrometry Laboratory of the Gifu Pharmaceutical University. XANES experiments were performed at the BL14B2 in the SPring-8 with the approval of the Japan Synchrotron Radiation Research Institute (JASRI) (proposal no. 2008 A1896). All products are known compounds. The ^{1}H NMR spectra of the products were identical with those of the corresponding authentic samples from commercial sources or those in the literature.

4.2. Preparation of 0.5% Pd/MS catalysts

To the solution of $Pd(OAc)_2$ (52.7 mg, 0.235 mmol, 0.5 wt % vs MS) in MeOH (50 mL) were added the molecular sieves (powder) (5.00 g) with stirring until the color of the supernatant of the suspension turned clear (6 days). The suspension was then filtered and the obtained solid was washed successively with MeOH (10 mL×3) and H_2O (10 mL×3) and dried under vacuum for 3 days to give the 0.5% Pd/MS catalyst as a gray powder.

4.3. Typical procedure for the chemoselective hydrogenation

The mixture of the substrate (0.250 mmol), 0.5% Pd/MS3A or 0.5% Pd/MS5A (10 wt % of the substrate) and MeOH (1 mL) was stirred under H_2 atmosphere (balloon) at room temperature. After a given period, the reaction mixture was filtered through a membrane filter (Millipore, Millex®-LH, 0.45 mm), and the filtrate was concentrated in vacuo to produce the corresponding reduced product.

4.3.1. Bibenzyl (Table 1, entries 1 and 2).[12] Yields 44.8 mg (98%) (entry 1) and 44.2 mg (97%) (entry 2). ^{1}H NMR δ 7.31–7.28 (m, 4H), 7.22–7.18 (m, 6H), 2.94 (s, 4H); ^{13}C NMR δ 141.8, 128.4, 128.3, 125.9, 37.9; MS (EI) *m*/*z* 182 (M^+, 39%), 165 (4%), 152 (1%), 115 (1%), 104 (4%), 91 (100%), 65 (25%), 51 (4%).

4.3.2. Benzyl 3-phenylpropionate (Table 1, entries 3 and 4).[10] Yields 59.6 mg (99%) (entry 3) and 59.9 mg (100%) (entry 4). ^{1}H NMR δ 7.17–7.37 (m, 10H), 5.11 (s, 2H), 2.97 (t, *J*=7.8 Hz, 2H), 2.68 (t, *J*=7.8 Hz, 2H); ^{13}C NMR δ 172.7, 140.4, 135.9, 128.5, 128.5, 128.3, 128.2, 126.2, 66.2, 35.9, 30.9; MS (EI) *m*/*z* 240 (M^+, 4%), 180 (48%), 149 (23%), 107 (79%), 91 (100%), 65 (11%), 51 (5%).

4.3.3. Benzyl 3-(4-chlorophenyl)propanoate (Table 1, entries 5 and 6).[13] Yields 65.0 mg (95%) (entry 5) and 65.9 mg (96%) (entry 6). ^{1}H NMR δ 7.37–7.22 (m, 7H), 7.11 (d, *J*=8.2 Hz, 2H), 5.10 (s, 2H), 2.94 (t, *J*=7.6 Hz, 2H), 2.66 (t, *J*=7.6 Hz, 2H); ^{13}C NMR δ 172.9, 139.3, 136.2, 132.5, 130.2, 129.1, 128.8, 128.7, 66.8, 36.2, 30.7; MS (EI) *m*/*z* 214 (M^+, 20%), 183 (36%), 167 (1%), 141 (46%), 125 (11%), 113 (1%), 103 (14%), 91 (100%), 77 (19%), 51 (4%).

4.3.4. 1-Benzyloxy-2-methoxy-4-propylbenzene (Table 1, entries 7 and 8).[10] Yields 62.7 (98%) (entry 7) and 63.0 mg (98%) (entry 8). ^{1}H NMR δ 7.27–7.44 (m, 5H), 6.79 (d, *J*=8.2 Hz, 1H), 6.72 (s, 1H), 6.64 (d, *J*=8.2 Hz, 1H), 5.11 (s, 2H), 3.87 (s, 3H), 2.51 (t, *J*=7.3 Hz, 2H), 1.56–1.66 (m, 2H), 0.93 (t, *J*=7.3 Hz, 3H); ^{13}C NMR δ 149.5, 146.2, 137.5, 136.1, 128.4, 127.7, 127.2, 120.2, 114.2, 112.4, 71.2, 55.9, 37.7, 24.6, 13.8; MS (EI) *m*/*z* 256 (M^+, 40%), 165 (47%), 137 (6%), 91 (100%), 77 (8%), 65 (11%), 43 (10%).

4.3.5. 1,2-Dimethoxy-4-propylbenzene (Table 1, entries 9 and 10).[14] Yields 41.5 mg (92%) (entry 9) and 42.3 mg (94%) (entry 10). ^{1}H NMR δ 6.79 (m, 1H), 6.72 (m, 2H), 3.86 (s, 3H), 3.88 (s, 3H), 2.53 (t, *J*=7.8 Hz), 1.64 (m, 2H), 0.94 (t, *J*=7.3 Hz, 3H); ^{13}C NMR δ 148.8, 147.1, 135.4, 120.2, 111.9, 111.2, 55.9, 55.8, 37.7, 24.8, 13.8; MS (EI) *m*/*z* 180 (M^+, 39%), 165 (2%), 151 (100%), 135 (3%), 121 (2%), 107 (9%), 91 (9%), 77 (11%), 65 (7%), 51 (3%).

4.3.6. 2-Methoxy-4-propylphenol (Table 1, entries 11 and 12).[15] Yields 40.6 mg (98%) (entry 11) and 40.2 mg (97%) (entry 12). ^{1}H NMR δ 6.83 (m, 1H), 6.67 (m, 2H), 5.52 (s, 1H), 3.86 (s, 3H), 2.57 (t, *J*=7.6 Hz, 2H), 1.61 (m, 2H), 0.92 (m, 3H); ^{13}C NMR δ 146.5, 143.8, 134.9, 121.2, 114.3, 111.3, 56.1, 38.0, 25.1, 14.0; MS (EI) *m*/*z* 166 (M^+, 45%), 137 (100%), 122 (14%), 105 (3%), 94 (10%), 77 (10%), 65 (6%), 51 (5%).

4.3.7. 3-Phenylpropionitrile (Table 1, entries 13 and 14).[10] Yields 31.5 mg (96%) (entry 13) and 31.0 mg (95%) (entry 14). ^{1}H NMR δ 7.22–7.46 (m, 5H), 2.95 (t, *J*=7.3 Hz, 2H), 2.61 (t, *J*=7.3 Hz, 2H); ^{13}C NMR δ 138.0, 128.8, 128.2, 127.2, 119.1, 31.5, 19.3; MS (EI) *m*/*z* 131 (M^+, 27%), 91 (100%), 65 (12%), 51 (8%).

4.3.8. 4-Aminobenzophenone (Table 1, entries 15 and 16).[10] Yields 46.7 mg (95%) (entry 15) and 47.8 mg (97%) (entry 16). ^{1}H NMR δ 7.70–7.73 (m, 4H), 7.43–7.55 (m, 3H), 6.66 (d, *J*=8.2 Hz, 2H), 4.19 (br s, 2H); ^{13}C NMR δ 195.3, 151.0, 138.8, 132.9, 131.4, 129.5, 128.0, 127.3,

113.6; MS (EI) *m*/*z* 197 (M^+, 69%), 120 (100%), 105 (5%), 92 (15%), 77 (10%), 65 (9%).

4.3.9. 4′-Cyanoacetophenone (Table 1, entries 17 and 18). No reaction took place. Starting material was recovered in 95% (34.5 mg) (entry 17) and 92% (33.3 mg) yields (entry 18).

4.3.10. 4-Ethylanisole (Table 2, entry 1).[10] Yield 28.2 mg (83%). ^{1}H NMR δ 7.11 (d, *J*=8.5 Hz, 2H), 6.83 (d, *J*=8.5 Hz, 2H), 3.78 (s, 3H), 2.59 (q, *J*=7.6 Hz, 2H), 1.21 (t, *J*=7.6 Hz, 3H); ^{13}C NMR δ 157.6, 136.4, 128.7, 113.7, 55.2, 28.0, 15.9; MS (EI) *m*/*z* 136 (M^+, 20%), 121 (100%), 91 (10%), 77 (8%).

4.3.11. 4-Methoxystyrene (Table 2, entry 2).[12] Yield 31.8 mg (95%). ^{1}H NMR δ 7.35 (d, *J*=9.0 Hz, 2H), 6.86 (d, *J*=9.0 Hz, 2H), 6.66 (dd, *J*=17.6, 10.9 Hz 1H), 5.62 (dd, *J*=17.6, 0.6 Hz, 1H), 5.12 (dd, *J*=10.9, 0.6 Hz, 1H), 3.81 (s, 3H); ^{13}C NMR δ 159.6, 136.4, 130.7, 127.6, 114.1, 111.8, 55.5; MS (EI) *m*/*z* 134 (M^+, 100%), 119 (56%) 103 (5%), 91 (85%), 65 (46%), 51 (10%).

4.3.12. 4-Ethylaniline (Table 2, entries 3 and 4).[12] Yields 27.2 mg (90%) (entry 3) and 28.5 mg (94%) (entry 4). ^{1}H NMR δ 7.00 (d, *J*=8.2 Hz, 2H), 6.64 (d, *J*=8.2 Hz, 2H), 3.54 (br s, 2H), 2.54 (q, *J*=7.7 Hz, 2H), 1.19 (t, *J*=7.7 Hz, 3H); ^{13}C NMR δ 144.1, 134.4, 128.6, 115.3, 28.0, 15.9; MS (EI) *m*/*z* 121 (M^+, 42%), 106 (100%) 91 (7%), 77 (24%).

4.3.13. Benzyl N-(4-ethylphenyl)carbamate (Table 2, entries 5 and 6).[10] Yields 61.9 mg (97%) (entry 5) and 60.6 mg (95%) (entry 6). ^{1}H NMR δ 7.24–7.40 (m, 7H), 7.12 (d, *J*=8.5 Hz, 2H), 6.67 (br s, 1H), 5.18 (s, 2H), 2.59 (q, *J*=7.6 Hz, 2H), 1.20 (t, *J*=7.6 Hz, 3H); ^{13}C NMR δ 153.4, 139.6, 136.1, 135.3, 128.6, 128.3, 128.3, 118.9, 66.9, 28.2, 15.6; MS (EI) *m*/*z* 255 (M^+, 40%), 211 (15%) 196 (22%), 132 (8%), 91 (100%), 65 (5%).

4.3.14. 2-Ethylbenzaldehyde (Table 2, entries 7 and 8).[16] Yields 31.2 mg (93%) (entry 7) and 30.8 mg (92%) (entry 8). ^{1}H NMR δ 10.30 (s, 1H), 7.83 (dd, *J*=7.5, 1.2 Hz, 1H), 7.52 (td, *J*=7.5, 1.5 Hz, 1H), 7.37 (t, *J*=7.5 Hz, 1H), 7.30 (d, *J*=7.8 Hz, 1H), 3.08 (q, *J*=7.5 Hz, 2H), 1.28 (t, *J*=7.5 Hz, 3H); ^{13}C NMR δ 192.4, 147.0, 133.9, 133.4, 131.7, 130.2, 126.3, 25.7, 16.3; MS (EI) *m*/*z* 133 (M^+, 100%), 115 (22%), 105 (63%), 91 (69%), 77 (42%), 51 (21%).

4.3.15. 4-Benzyloxy-3-methoxyethylbenzene (Table 2, entry 9).[10] Yield 59.1 mg (98%). ^{1}H NMR δ 7.27–7.45 (m, 5H), 6.80 (d, *J*=8.0 Hz, 1H), 6.75 (s, 1H), 6.66 (d, *J*=8.0 Hz, 1H), 5.12 (s, 2H), 3.88 (s, 3H), 2.58 (q, *J*=7.6 Hz, 2H), 1.21 (t, *J*=7.6 Hz); ^{13}C NMR δ 149.6, 146.2, 137.6, 137.5, 128.4, 127.7, 127.2, 119.5, 114.4, 111.9, 71.3, 55.9, 28.4, 15.7; MS (EI) *m*/*z* 242 (M^+, 55%), 151 (44%), 123 (5%), 91 (100%), 77 (6%), 65 (8%).

4.3.16. 4-Benzyloxy-3-methoxystyrene (Table 2, entry 10). No reaction took place. Starting material was recovered in 97% yield (58.3 mg).

4.3.17. 1,2-Dimethoxy-4-ethylbenzene (Table 2, entry 11).[17] Yield 41.1 mg (99%). ^{1}H NMR δ 6.80 (d, *J*=7.8 Hz, 1H), 6.74 (d, *J*=7.8 Hz, 1H), 6.73 (s, 1H), 3.88 (s, 3H), 3.86 (s, 3H), 2.60 (q, *J*=7.4 Hz, 2H), 1.23 (t, *J*=7.4 Hz, 3H); ^{13}C NMR δ 148.7, 146.9, 136.9, 119.4, 111.2, 111.1, 55.9, 55.7, 28.4, 15.8; MS (EI) *m*/*z* 166 (M^+, 76%), 151 (100%), 135 (11%), 123 (6%), 108 (12%), 95 (20%), 77 (24%), 65 (10%), 51 (7%).

4.3.18. 1,2-Dimethoxy-4-styrene (Table 2, entry 12) No reaction took place. Starting material was recovered in 94% yield (38.5 mg).

4.3.19. 4-Ethylphenol (Table 2, entry 13).[12] Yield 28.4 mg (93%) (entry 13). ^{1}H NMR δ 7.06 (d, *J*=7.1 Hz, 2H), 6.78 (d, *J*=7.1 Hz, 2H), 5.57 (s, 1H), 2.59 (q, *J*=6.5 Hz, 2H), 1.21 (t, *J*=6.5 Hz, 3H); ^{13}C NMR (100 MHz) δ 153.2, 136.5, 128.8, 115.1, 27.9, 15.8; ^{13}C NMR δ 153.2, 136.5, 128.8, 115.1, 27.9, 15.8; MS (EI) *m*/*z* 122 (M^+, 32%), 107 (100%), 91 (19%), 77 (45%).

4.3.20. 4-Hydroxystyrene (Table 2, entry 14). No reaction took place. Starting material was recovered in 95% yield (28.6 mg).

4.3.21. 4-Bromoethylbenzene (Table 2, entry 15).[10] Yield 33.2 mg (72%). ^{1}H NMR δ 7.39 (d, *J*=8.4 Hz, 2H), 7.06 (d, *J*=8.4 Hz, 2H), 2.60 (q, *J*=7.6 Hz, 2H), 1.21 (t, *J*=7.6 Hz, 3H); ^{13}C NMR δ 143.1, 131.3, 129.6, 119.2, 28.3, 15.4; MS (EI) *m*/*z* 184 (M^+, 76%), 169 (100%), 105 (84%), 90 (21%), 77 (24%), 63 (12%), 51 (17%).

4.3.22. 1-tert-Butyl-4-ethylbenzene (Table 2, entries 17 and 18).[18] Yields 38.1 mg (94%) (entry 17) and 37.3 mg (92%) (entry 18). ^{1}H NMR δ 7.30 (d, *J*=8.2 Hz, 2H), 7.13 (d, *J*=8.2 Hz, 2H), 2.62 (q, *J*=7.6 Hz, 2H), 1.31 (s, 9H), 1.23 (t, *J*=7.6 Hz, 2H); ^{13}C NMR δ 148.2, 141.0, 127.4, 125.1, 34.4, 31.5, 28.3, 15.6; MS (EI) *m*/*z* 162 (M^+, 26%), 147 (100%), 131 (5%), 119 (29%), 105 (6%), 91 (31%), 79 (14%), 51 (4%).

4.3.23. 4-Ethylnitrobenzene (Table 2, entries 19 and 20).[12] Yields 35.5 mg (94%) (entry 19) and 34.7 mg (92%) (entry 20). ^{1}H NMR δ 8.14 (d, *J*=8.4 Hz, 2H), 7.34 (d, *J*=8.4 Hz, 2H), 2.76 (q, *J*=7.2 Hz, 2H), 1.29 (t, *J*=7.2 Hz, 3H); ^{13}C NMR δ 152.0, 146.3, 128.6, 123.7, 28.9, 15.1; MS (EI) *m*/*z* 122 (M^+, 32%), 107 (100%), 91 (19%), 77 (45%).

4.3.24. 2-Methoxy-4-vinylphenol (Table 2, entries 21 and 22) No reaction took place. Starting material was recovered in 98% (36.8 mg) (entry 21) and 95% (35.7 mg) (entry 22).

4.3.25. 2-Phenyl-2-butanol (Table 2, entries 23 and 24).[19] Yields 35.6 mg (95%) (entry 23) and 36.0 mg (96%) (entry 24). ^{1}H NMR δ 7.44 (t, *J*=7.2 Hz, 2H), 7.34 (dd, *J*=7.7, 7.2 Hz, 2H), 7.24 (t, *J*=7.7 Hz, 1H), 2.06 (m, 2H), 1.55 (s, 3H), 0.81 (t, *J*=7.2 Hz, 3H); ^{13}C NMR δ 147.5, 128.2, 126.6, 125.1, 74.8, 36.6, 29.5, 8.2; MS (EI) *m*/*z* 150 (M^+, 5%), 121 (100%).

4.3.26. Benzyl propionate (Table 2, entries 25 and 26).[12] Yields 37.3 mg (91%) (entry 25) and 36.1 mg (88%) (entry 26). ^{1}H NMR δ 7.30–7.37 (m, 5H), 5.12 (s, 2H), 2.38 (q, *J*=7.6 Hz, 2H), 1.16 (t, *J*=7.6 Hz, 3H); ^{13}C NMR δ 174.3, 136.0, 128.5, 128.1, 50.7, 27.5, 9.0; MS (EI) *m*/*z* 164 (M^+, 55%), 108 (100%), 91 (85%), 79 (12%), 65 (10%), 57 (22%).

4.3.27. Benzyl isobutylate (Table 2, entries 27 and 28).[10] Yields 40.1 mg (90%) (entry 27) and 40.9 mg (92%) (entry 28). ^{1}H NMR δ 7.29–7.39 (m, 5H), 5.11 (s, 2H), 2.60 (m, 1H), 1.19 (d, *J*=7.1 Hz, 6H); ^{13}C NMR δ 176.9, 136.2, 128.5, 128.1, 127.9, 66.0, 34.0, 18.9; MS (EI) *m*/*z* 178 (M^+, 38%), 108 (27%), 91 (100%), 71 (10%), 43 (11%).

4.3.28. Hexyl 4-(benzyloxycarbonylamino)benzoate (Table 2, entries 29 and 30).[7c] Yields 83.4 mg (94%) (entry 29) and 87.0 mg (98%) (entry 30). ^{1}H NMR δ 7.99 (d, *J*=8.8 Hz, 2H), 7.47–7.34 (m, 7H), 6.86 (br s, 1H), 5.22 (s, 2H), 4.29 (t, *J*=7.0 Hz, 2H), 1.78–1.71 (m, 2H), 1.43–1.32 (m, 6H), 0.90 (t, *J*=7.0 Hz, 3H); ^{13}C NMR δ 166.2, 152.8, 141.9, 135.7, 130.9, 128.7, 128.5, 128.4, 125.4, 117.6, 67.4, 65.0, 31.5, 28.7, 25.7, 22.5, 14.0; MS (EI) *m*/*z* 355 (M^+, 18%), 311 (11%), 163 (44%), 146 (44%), 91 (100%).

4.3.29. 4-Propoxybenzaldehyde (Table 2, entries 31 and 32).[12] Yields 40.1 mg (98%) (entry 31) and 37.8 mg (92%) (entry 32). ^{1}H NMR δ 9.88 (s, 1H), 7.83 (d, *J*=8.8 Hz, 2H), 7.00 (d, *J*=8.8 Hz, 2H), 4.02 (t, *J*=6.6 Hz, 2H), 1.80–1.87 (m, 2H), 1.06 (t, *J*=7.6 Hz, 3H); ^{13}C NMR δ 190.8, 164.2, 132.0, 129.7, 114.7, 69.9, 22.3, 10.7; MS (EI) *m*/*z* 164 (M^+, 30%), 138 (23%), 122 (30%), 121 (100%).

4.3.30. Propyl 3-(4-nitrophenyl)acetate (Table 3, entries 1 and 2).[10] Yields 52.9 mg (95%) (entry 1) and 52.3 mg (94%) (entry 2).

^{1}H NMR δ 8.19 (d, J=8.5 Hz, 2H), 7.47 (d, J=8.5 Hz, 2H), 4.08 (t, J=6.7 Hz, 2H), 3.74 (s, 2H), 1.65 (m, 2H), 0.91 (t, J=7.4 Hz, 3H); ^{13}C NMR δ 173.1, 146.6, 136.4, 128.6, 123.7, 66.7, 43.5, 24.9, 10.8; MS (EI) m/z 223 (M^+, 40%), 164 (15%), 136 (100%), 106 (20%), 78 (50%), 63 (20%), 51 (10%).

4.3.31. 4-Nitroaniline (Table 3, entries 3 and 4).[10] Yields 33.8 mg (98%) (entry 3) and 33.8 mg (98%) (entry 4). ^{1}H NMR δ 8.07 (d, J=9.0 Hz, 2H), 6.63 (d, J=9.0 Hz, 2H), 4.40 (br s, 2H); ^{13}C NMR δ 152.5, 126.3, 116.7, 113.3; MS (EI) m/z 138 (M^+, 100%), 108 (40%), 92 (31%), 80 (12%), 65 (38%).

4.3.32. 4-Nitro-o-toluidine (Table 3, entries 5 and 6).[10] Yields 34.1 mg (90%) (entry 5) and 35.3 mg (93%) (entry 6). ^{1}H NMR δ 7.95–7.99 (m, 2H), 6.62 (d, J=8.8 Hz, 1H), 4.33 (br s, 2H), 2.21 (s, 3H); ^{13}C NMR δ 150.9, 126.6, 124.1, 121.1, 113.1, 17.2; MS (EI) m/z 152 (M^+, 100%), 122 (50%), 106 (30%), 77 (36%), 51 (7%).

4.3.33. Benzyl 4-nitrobenzoate (Table 3, entries 7 and 8). No reaction took place. Starting material was recovered in 98% (62.9 mg) (entry 7) and 96% (61.5 mg) (entry 8) yields.

4.3.34. Benzyl 4-nitrophenethylcarbamate (Table 3, entries 9 and 10). No reaction took place. Starting material was recovered in 94% yield (70.6 mg) (entry 9) and 94% (70.2 mg) (entry 10) yields.

4.3.35. 4-Bromonitrobenzene (Table 3, entries 11 and 12). Starting material was recovered in 96% (48.4 mg) (entry 11) and 95% (47.9 mg) (entry 12) yields.

4.3.36. 1-Nitrohexane (Table 3, entries 13 and 14).[10] Yields 28.9 mg (88%) (entry 13) and 29.5 mg (90%) (entry 14). ^{1}H NMR δ 4.38 (t, J=7.1 Hz, 2H), 2.01 (m, 2H), 1.28–1.43 (m, 6H), 0.90 (t, J=7.0 Hz, 3H); ^{13}C NMR δ 75.7, 30.9, 27.3, 25.8, 22.3, 13.8; Molecular ion peak was not located in the mass spectra (EI and FAB), but the EI mass spectrum was identical with that obtained from the Integrated Spectral Database System of Organic Compounds (the National Institute of Advanced Industrial Science and Technology, Japan).

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