



Effect of solvent and hydrogen during selective hydrogenation

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Abstract—Described is the solvent effect for the chemoselective hydrogenation of alkenes having a benzyloxy group (Bn-O-) using a hydrogenation system employing atomic hydrogen permeating through a Pd sheet electrode. © 2001 Elsevier Science Ltd. All rights reserved.

1. Introduction

The hydrogenation of alkenes having a benzyloxy group without hydrogenolysis is quite difficult under conventional conditions. In order to achieve the selective hydrogenation¹ without hydrogenolysis,² the hydrogenation system³ employing atomic hydrogen permeating through a Pd sheet electrode has been devised.⁴ Although this system was able to achieve selective reduction in benzene as the solvent, hydrogenolysis took place in MeOH.⁵ This result implies that solvent influences surface condition of the Pd sheet, which is used as a catalyst. Therefore, the effect of the aprotic solvent was investigated for twodifferent types of alkenes as substrates including the benzyl ether or benzyl ester site.

2. Experimental

The hydrogenation system is shown in Fig. 1. The substrate was circulated using a roller pump at the rate of 2.4 cm³ min⁻¹ in solvent (reaction concentration of 7.0 mM) at room temperature. During the reaction, atomic hydrogen was provided by the electrolysis of water (galvanostatic electrolysis, 10 mA cm⁻²) in another cell. For comparison, the reaction time was standardized at 4 h (21 F mol⁻¹). After the reaction, the reactant was simply concentrated, and then the residue was weighed and analyzed by ¹H NMR without purification. The ratio and structure of products were deter-

mined by comparison with the ¹H NMR data of authentic samples that were synthesized by an alternative method.

In benzene, the benzyl ester **1**⁶ was hydrogenated for 4 h using the hydrogenation system to give the selective hydrogenation product **2**⁷ in 45% yield (Table 1). After 19 h, the benzyl ester **1** completely disappeared and product **2** was produced in quantitative yield. Although product **2** was subjected to reduction under the same conditions for 24 h, the hydrogenolysis products **3**⁸ and **4**⁹ and any by-product were not detected at all. A

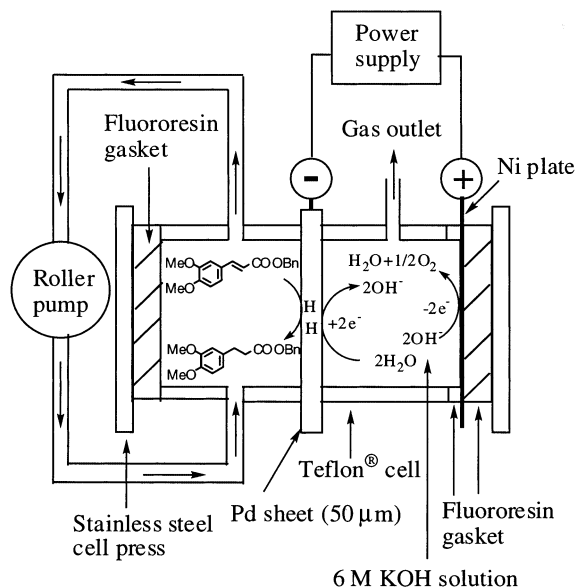
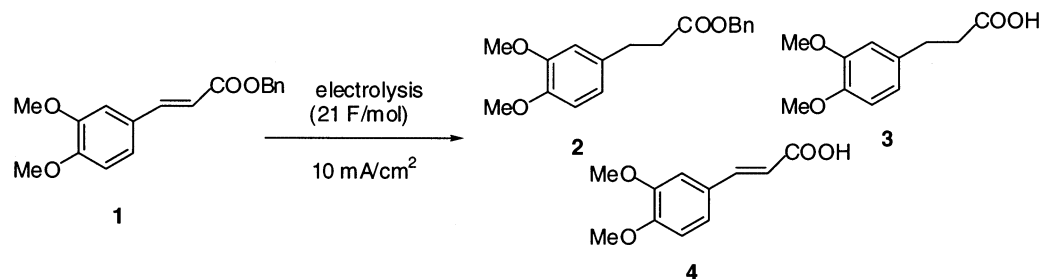


Figure 1.

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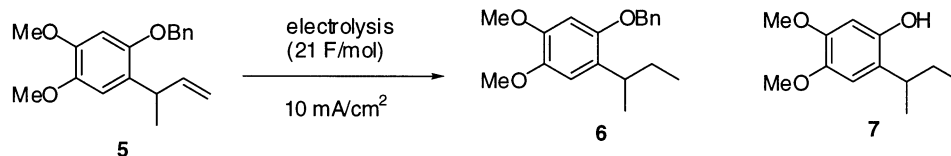
Table 1.

Solvent	Time (h)	2 (%)	3 (%)	4 (%)	1 (%)
Benzene	4	45	0	0	55
	19	100	0	0	0
Acetone	4	29	0	0	71
	20	0	100	0	0
Petroleum ether	4	0	0	0	100
1,4-Dioxane	4	67	0	0	33
	15	21	70	0	9
Isopropyl ether	4	12	0	0	88
	35	0	100	0	0
Toluene	4	43	0	0	57
	20	10	84	0	6
Ethyl acetate	4	78	0	0	22
	15	0	100	0	0
Dichloromethane	4	11	0	0	89
	50	0	100	0	0
Methanol	4	0	100	0	0

methanol solution⁵ gave the product **3** after 4 h in quantitative yield. Because the solubility of **1** was quite low in petroleum ether, the reaction did not take place at all. Toluene has a similar reactivity with benzene and lower toxicity, therefore, toluene was utilized as the reaction solvent instead of benzene. Accordingly, selective hydrogenation was expected in toluene, however, the product **3** was produced before completing the hydrogenation. In other solvents,¹⁰ though the selective hydrogenation took place within about 4 h from the

start, the product **3** was generated due to the succeeding reaction after 4 h.

Results of the benzyl ether **5**¹¹ reaction as a substrate are summarized in Table 2. In benzene, a high hydrogenation selectivity was observed to afford the product **6**⁴ in quantitative yield. For confirming the clear distinction between the hydrogenation and the hydrogenolysis, **6** was subjected to hydrogenation by the hydrogenation system for 24 h. As a result, no

Table 2.

Solvent	Time (h)	6 (%)	7 (%)	5 (%)
Benzene	4	50	0	50
	30	100	0	0
Acetone	4	20	0	80
	30	0	100	0
Petroleum ether	4	17	0	83
	35	99	1	0
1,4-Dioxane	4	67	Trace	33
Isopropyl ether	4	47	24	29
Toluene	4	48	8	44
Ethyl acetate	4	50	8	42
Dichloromethane	4	22	66	11
Methanol	4	0	100	0

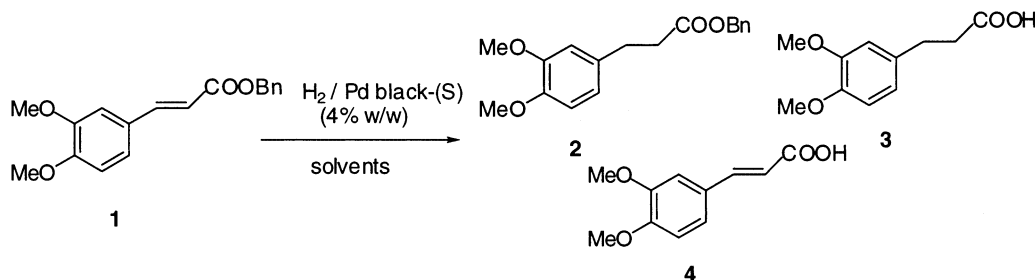
corresponding hydrogenolysis compound **7**¹² and any by-product were obtained.

The hydrogen source of this hydrogenation system is 'atomic hydrogen' which is produced by the electrolysis of water. Pd black that was deposited on the Pd sheet surface, viz. Pd black-(S),¹³ was produced by the hydrogen reduction using the 'atomic hydrogen' being provided from the hydrogenation system. Therefore, it is

suggested that the atomic hydrogen and/or the condition of the Pd black-(S) surface causes the selectivity of the hydrogenation, in addition to the solvent effect.

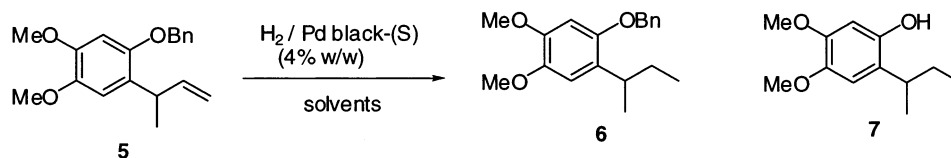
In order to confirm the effect of atomic hydrogen, substrates **1** and **5** were hydrogenated¹⁴ under the hydrogen gas using the Pd black-(S) as a catalyst. As shown in Table 3, several different results were obtained upon comparison with the corresponding result when using the developed hydrogenation system.

Table 3.



Solvent	Time (h)	2 (%)	3 (%)	4 (%)	1 (%)
Benzene	4	100	0	0	0
	8	100	0	0	0
	24	100	0	0	0
Acetone	4	45	55	0	0
Petroleum ether	4	40	0	0	60
	8	36	12	3	49
1,4-Dioxane	4	7	40	20	33
Isopropyl ether	4	33	67	0	0
Toluene	4	78	18	0	4
Ethyl acetate	4	8	92	0	0
Dichloromethane	4	0	100	0	0
1,2-Dimethoxyethane	4	76	24	0	0
Methanol	1	0	100	0	0

Table 4.



Solvent	Time (h)	6 (%)	7 (%)	5 (%)
Benzene	4	100	0	0
	8	100	0	0
	24	100	0	0
Acetone	4	100	0	0
	8	17	83	0
Petroleum ether	4	<100	Trace	0
	8	83	17	0
1,4-Dioxane	4	51	35	14
Isopropyl ether	4	76	24	0
Toluene	4	<100	0	Trace
	8	100	0	0
	24	100	0	0
Ethyl acetate	4	17	83	0
Dichloromethane	4	33	12	55
1,2-Dimethoxyethane	4	89	11	0
Methanol	1	0	100	0

In benzene, the reaction time was improved and, needless to say, a high selectivity was observed. It was remarkable that the petroleum ether and the 1,4-dioxane solution conditions gave product **4** that was produced by the reaction dominated by the hydrogenolysis. In fact, the benzyl ester **1** was not converted into product **4** by the hydrogenation system, thus, it was implied that hydrogen source influences the reaction selectivity.

On the other hand, the results for the benzyl ether **5** are summarized in Table 4. As a noteworthy point, in

toluene, the benzyl ether **5** was converted into product **6** in almost 100% yield within 4 h and after 24 h, **6** was still stable under this condition without hydrogenolysis. This result indicates that practical application including mass production is possible. In other solvents, the results were almost same using the hydrogenation system.

The Pd black-(S) exhibited selective hydrogenation activity for various substrates in 100% yields¹⁵ (Table 5). In all the substrates, no hydrogenolysis products and by-products were detected.¹⁶ In order to confirm

Table 5.

Substrate		Pd black-(S) (4% w/w) benzene, rt		Product	+	SM
Entry	Substrate	Product	Time (h)	Yield (%)	SM (%)	
1			4	100	0	
			24	100	0	
2			4	0	100	
			24	51	49	
			48	100	0	
3			4	63	37	
			24	100	0	
4			4	24	76	
			24	100	0	
5			4	78	22	
			24	100	0	
6			4	100	0	
			24	100	0	
7			4	66	34	
			24	100	0	
8			4	100	0	
			24	100	0	
9			4	69	31	
			24	100	0	

the clear distinction between the hydrogenation and the hydrogenolysis, every reactant was maintained under reducing conditions for a sufficient time after the hydrogenation was completed. As a result, neither the corresponding hydrogenolysis product nor any by-products were obtained in all cases. A methanol solution⁵ immediately gave the corresponding hydrogenolysis product in quantitative yield.

In conclusion, it is implied that a complex interaction involving the substrate, solvent, surface of the catalyst and hydrogen source affect the hydrogenation selectivity. The mechanism of selectivity including the surface conditions of the catalyst is currently under investigation.

Acknowledgements

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5. Other protic solvents, for example EtOH and *t*PrOH, gave similar results with MeOH.
6. Compound **1**: ¹H NMR (270 MHz, CDCl₃): δ 3.90 (3H, s), 3.91 (3H, s), 5.25 (2H, s), 6.36 (1H, d, *J*=15.8 Hz), 6.86 (1H, d, *J*=8.5 Hz), 7.04 (1H, d, *J*=2.0 Hz), 7.10 (1H, dd, *J*=8.5, 2.0 Hz), 7.31–7.44 (5H, complex), 7.67 (1H, d, *J*=15.8 Hz); ¹³C NMR (67.8 MHz, CDCl₃): δ 55.83 (q), 55.93 (q), 66.22 (t), 109.54 (d), 110.98 (d), 115.51 (d), 122.67 (d), 127.30 (s), 128.19 (d), 128.24 (d), 128.56 (d), 136.13 (s), 145.05 (d), 149.17 (s), 151.14 (s), 166.98 (s); HREIMS: found *m/z* 298.1201 (M⁺); calcd for C₁₈H₁₈O₄ 298.1205.
7. Compound **2**: ¹H NMR (270 MHz, CDCl₃): δ 2.67 (2H, t, *J*=7.2 Hz), 2.92 (2H, t, *J*=7.2 Hz), 3.83 (3H, s), 3.85 (3H, s), 5.11 (2H, s), 6.70–6.79 (3H, complex), 7.28–7.39 (5H, complex); ¹³C NMR (67.8 MHz, CDCl₃): δ 30.56 (t), 36.12 (t), 55.76 (q), 55.88 (q), 66.23 (t), 111.28 (d), 111.63 (d), 120.10 (d), 128.15 (d), 128.19 (d), 128.51 (d), 133.01 (s), 135.90 (s), 147.48 (s), 148.87 (s), 172.73 (s); HREIMS: found *m/z* 300.1367 (M⁺); calcd for C₁₈H₂₀O₄ 300.1362.
8. Compound **3**: ¹H NMR (270 MHz, CDCl₃): δ 2.67 (2H, t, *J*=7.6 Hz), 2.91 (2H, t, *J*=7.6 Hz), 3.86 (3H, s), 3.87 (3H, s), 6.73–6.82 (3H, complex); ¹³C NMR (67.8 MHz, CDCl₃): δ 30.24 (t), 35.79 (t), 55.81 (q), 55.91 (q), 111.35 (d), 111.66 (d), 120.08 (d), 132.76 (s), 147.58 (s), 148.92 (s), 178.54 (s); HREIMS: found *m/z* 210.0896 (M⁺); calcd for C₁₁H₁₄O₄ 210.0892.
9. Compound **4**: ¹H NMR (270 MHz, CDCl₃): δ 3.93 (6H, s), 6.33 (1H, d, *J*=15.8 Hz), 6.88 (1H, d, *J*=8.2 Hz), 7.08 (1H, d, *J*=1.7 Hz), 7.14 (1H, dd, *J*=8.2, 1.7 Hz), 7.73 (1H, d, *J*=15.8 Hz); ¹³C NMR (67.8 MHz, CDCl₃): δ 55.85 (q), 55.94 (q), 109.68 (d), 110.97 (d), 114.95 (d), 123.07 (d), 127.01 (s), 146.82 (d), 149.19 (s), 151.43 (s), 172.44 (s); HREIMS: found *m/z* 208.0730 (M⁺); calcd for C₁₁H₁₂O₄ 208.0736.
10. When 1,4-dioxane was used as the reaction solvent, there was a trace of **3** formed in several cases.
11. Compound **5**: ¹H NMR (270 MHz, CDCl₃): δ 1.30 (3H, d, *J*=7.0 Hz), 3.83 (6H, s), 3.90–4.00 (1H, m), 5.00–5.08 (2H, complex), 5.04 (2H, s), 5.96–6.09 (1H, m), 6.58 (1H, s), 6.71 (1H, s), 7.32–7.46 (5H, complex); ¹³C NMR (67.8 MHz, CDCl₃): δ 19.59 (q), 35.20 (d), 56.12 (q), 56.56 (q), 71.80 (t), 99.84 (d), 111.58 (d), 112.82 (t), 126.33 (s), 127.33 (d), 127.82 (d), 128.50 (d), 137.46 (s), 142.94 (d), 143.48 (s), 147.58 (s), 149.79 (s); HREIMS: found *m/z* 298.1573 (M⁺); calcd for C₁₉H₂₂O₃ 298.1569.
12. Compound **7**: ¹H NMR (270 MHz, CDCl₃): δ 0.87 (3H, t, *J*=7.5 Hz), 1.22 (3H, d, *J*=6.6 Hz), 1.60 (2H, quin, *J*=7.5 Hz), 2.84 (1H, qt, *J*=7.5, 6.6 Hz), 3.81 (3H, s), 3.83 (3H, s), 4.52 (1H, br. s, -OH), 6.41 (1H, s), 6.66 (1H, s); ¹³C NMR (67.8 MHz, CDCl₃): δ 12.17 (q), 20.75 (q), 30.12 (t), 33.82 (d), 55.92 (q), 56.76 (q), 100.86 (d), 110.94 (d), 123.89 (d), 143.29 (s), 146.73 (s), 147.52 (s); HREIMS: found *m/z* 210.1254 (M⁺); calcd for C₁₂H₁₈O₃ 210.1256.
13. For the palladinization, 6 M KOH solution was put in the compartment having a Ni sheet anode and a Pd cathode for the production of active hydrogen. A 1 M HCl solution containing 28.0 mM PdCl₂ was introduced into the other compartment for the deposition of Pd black. The palladinization was carried out by hydrogen reduction using atomic hydrogen, which was produced by galvanostatic electrolysis at 10 mA cm⁻², followed by passage through the Pd sheet electrode. During the palladinization, the PdCl₂ solution was circulated at a flow rate of 2.4 cm³ min⁻¹ using a roller pump (Furue Science, RP-NE). For the hydrogenation reaction, the Pd black, which was deposited on the Pd sheet, was washed with degassed distilled water and then dried with Ar gas.
14. The reaction was conducted under the same condition used for the hydrogenation system except for the hydrogen source.
15. The structures of the substrates and the reaction products were determined based on the various spectral data (IR, Mass, ¹H NMR, ¹³C NMR).
16. All reactants were simply filtered and concentrated, then the generation rate and construction of the reaction products were confirmed by measuring the ¹H NMR without any treatment, for example, isolating or purifying the residue. Moreover, a further experiment was carried out for all the reactions, and the reproducibility was confirmed.