Bimetallic Palladium–Platinum-on-Carbon-Catalyzed H–D Exchange Reaction: Synergistic Effect on Multiple Deuterium Incorporation

Tomohiro Maegawa,[a,1] Nobuhiro Ito,[b] Keiji Oono,[b] Yasunari Monguchi,[a] Hironao Sajiki*[a]

[a] Laboratory of Organic Chemistry, Department of Organic and Medicinal Chemistry, Gifu Pharmaceutical University, Gifu 502-8585, Japan

[b] Chemical Products Research Laboratories, Wako Pure Chemical Industries, Ltd., Matoba, Kawagoe 350-1101, Japan
Fax +81(58)2375979; E-mail: sajiki@gifu-pu.ac.jp

Received 12 February 2009; revised 8 May 2009

Abstract: We prepared several activated carbon-supported bimetallic Pd–Pt catalysts (Pd–Pt/C) by using various reducing reagents, and examined their catalytic activities for the deuteration of alkyl-substituted aromatic compounds. Multiple deuterations catalyzed by Pt–Pd/C proceeded in D_2O at 180 °C under a H_2 atmosphere, and a synergistic effect was observed in relation to the incorporation of deuterium at sterically hindered positions on aromatic rings.

Key words: heterogeneous catalysis, palladium, platinum, H–D exchange, synergy, bimetallic

The development of a variety of applications of deuterium-labeled compounds in a number of scientific fields, such as quantitative analyses using mass spectrometry, mechanistic and metabolic studies, and material science,[2] has led to interest in the development of efficient and convenient methods for synthesizing such compounds. Although deuterium-labeled compounds can be obtained either by multistep syntheses starting from deuterium-labeled small-molecule synthons or by post-synthetic H–D exchange reactions of target compounds, the latter approach is more cost- and time-efficient than the former. Although a number of post-synthetic H–D exchange methods have been reported that involve the use of transition-metal catalysts,[3] supercritical conditions,[4] microwave irradiation,[3q–s,5] or other methods,[6] the vast majority of these requires harsh conditions, expensive reagents (such as D_2 gas), and special (pressure-, acid-, or base-resistant) equipment, and are therefore inefficient.[3–6]

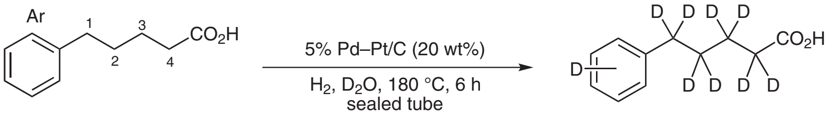
We have developed several novel deuteration methods based on heterogeneously catalyzed H–D exchange reactions of various organic compounds in D_2O under an atmosphere of H_2 in the presence of platinum group catalysts such as palladium-on-carbon (Pd/C),[7] platinum-on-carbon (Pt/C),[7g,1] rhodium-on-carbon,[8] or ruthenium-on-carbon.[9] These methods are simple, efficient, cost-effective, and can be applied in the deuteration of a wide variety of substrates. In our ongoing study of such H–D exchange reactions, we identified a marked synergistic effect when mixtures of Pd/C and Pt/C catalysts were used.[10] Here, we report a method for the preparation of bimetallic platinum–palladium-on-carbon catalysts by using various reducing agents, and we also report the occurrence of synergistic effects in H–D exchange reactions catalyzed by these bimetallic catalysts.

As an extension of our development of an effective multideuteration method,[7–10] we planned to prepare a Pd–Pt bimetallic catalysts that should promote efficient H–D exchange reactions through a synergistic effect. Pd/C is usually prepared by the absorption of a palladium(II) salt from solution into activated carbon, and subsequent reduction by using an appropriate reducing agent. We chose dihydrogen, hydrazine, formaldehyde, and sodium borohydride as reducing agents for the preparation of Pd–Pt bimetallic catalysts on the basis of known procedures for the preparation of Pd/C catalysts.[11] Each catalyst showed a different catalytic activity toward the H–D exchange reaction of 5-phenylpentanoic acid (Table 1). Pd/C was efficient in catalyzing H–D exchange on the alkyl chain (>94%), whereas the amount of deuteration of the aromatic ring was moderate (entry 5). On the other hand, the use of Pt/C alone led to high incorporation of deuterium on the aromatic ring (80%), but a little incorporation on the alkyl chain, except in the benzylic position (C1) (entry 6). Deuteration using bimetallic Pd–Pt/C catalysts, prepared by various protocols, proceeded simultaneously on both the alkyl chain and the aromatic ring with a high efficiency (entries 1–4). Among the bimetallic catalysts, the one prepared by reduction with sodium borohydride [5% Pt–Pd/C($NaBH_4$)] showed a better catalytic activity toward multiple deuteration (entry 4), and the efficiency of deuteration of the aromatic ring (91%) was obviously higher than that of corresponding reaction catalyzed by Pt/C alone (entry 6).[12] A mixture of Pd/C and Pt/C also gave an equivalent level of deuteration of the aromatic ring to 5% Pt–Pd/C($NaBH_4$), but a somewhat lower level of deuteration at the C4 position (entry 7). The mechanism of these synergistic effects is unclear, but we speculate that alloying of the palladium and platinum metals may affect their catalytic activity.[13]

We next examined the use of Pd–Pt/C($NaBH_4$) for the deuteration of hexylbenzene (Table 2). The incorporation of deuterium by the 5% Pd–Pt/C($NaBH_4$)-catalyzed reaction proceeded efficiently to give highly deuterated hexylbenzene-d_{18} in 85% isolated yield (entry 1); this reaction also proceeded efficiently with a mixture of 5% Pd/C and 5% Pt/C catalysts (entry 2), whereas the use of 10% Pd/C alone gave disappointing deuteration efficiencies, espe-

SYNTHESIS 2009, No. 16, pp 2674–2678
Advanced online publication: 10.07.2009
DOI: 10.1055/s-0029-1216895; Art ID: F04009SS

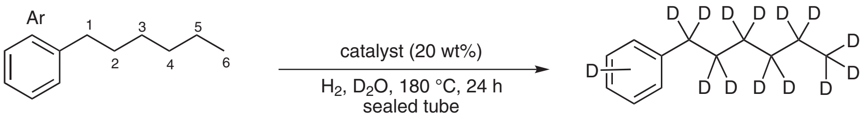
Table 1 5% Pd–Pt/Carbon-Catalyzed Deuteration of 5-Phenylpentanoic Acid



Entry	Reducing Agent	Catalyst	D content (%)				Yield (%)
			Ar	C1	C2 + C3	C4	
1	H_2	5% Pd–Pt/C	75	97	96	97	85
2	NH_2NH_2	5% Pd–Pt/C	78	97	95	94	95
3	HCHO	5% Pd–Pt/C	64	97	94	76	91
4	$NaBH_4$	5% Pd–Pt/C	91	96	94	88	84
5	–	10% Pd/C[a]	68	96	94	95	83
6	–	5% Pt/C	80	96	47	25	quant
7	–	5% Pd/C + 5% Pt/C	87	96	97	77	92

[a] 10 wt% of 10% Pd/C was used as the catalyst.

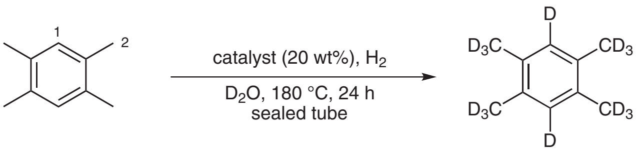
Table 2 5% Pd–Pt/C($NaBH_4$)-Catalyzed Deuteration of Hexylbenzene



Entry	Catalyst	D content (%)					Yield
		Ar	C1	C2	C3–C5	C6	(%)
1	5% Pd–Pt/C($NaBH_4$)	97	97	93	89	86	85
2	5% Pd/C + 5% Pt/C	94	96	94	89	83	97
3	10% Pd/C[a]	35	94	94	61	42	98

[a] 10 wt% of 10% Pd/C was used as the catalyst.

Table 3 5% Pd–Pt/C($NaBH_4$)-Catalyzed Deuteration of 1,2,4,5-Tetramethylbenzene



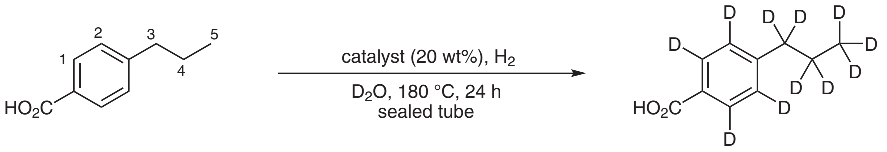
Entry	Catalyst	D content (%)		Yield
		C1	C2	(%)
1	5% Pd–Pt/C($NaBH_4$)	94	95	quant
2	5% Pd/C + 5% Pt/C	75	96	76
3	10% Pd/C[a]	13	97	96
4	5% Pt/C	75	93	92

[a] 10 wt% of 10% Pd/C was used as the catalyst.

cially at the aromatic ring and the C3–C6 positions (entry 3).

In a study on the deuteration of several organic compounds, we found that H–D exchange reactions at sterically hindered positions, such as the aromatic positions *ortho* to carbon substituents, were highly inefficient when Pd/C or Pt/C was used as a sole catalyst. The use of a mixture of 5% Pd/C and 5% Pt/C as the catalyst provided effective incorporation of deuterium at such positions. We therefore used the bimetallic 5% Pd–Pt/C($NaBH_4$) catalyst for the deuteration of 1,2,4,5-tetramethylbenzene (durene), in which the aromatic hydrogens at the 3- and 6-positions (C1 positions in Table 3) are highly hindered by the neighboring methyl groups. Deuteration catalyzed solely by 5% Pt/C, an effective catalyst for deuteration of aromatic nuclei,[7g,l,10] resulted in moderately efficient deuteration (75%) at the aromatic C1 positions (entry 4), whereas the average deuteration efficiency at the C1 positions was only 13% when 10% Pd/C was used (entry 3). Deuteration with a mixed catalyst of 5% Pd/C and 5% Pt/C gave a result similar to that of the reaction catalyzed solely by 5% Pt/C, and no synergistic effect was observed in this particular case (entry 2). On the other hand, the use of the bimetallic 5% Pd–Pt/C($NaBH_4$) catalyst showed a

Table 4 5% Pd–Pt/C($NaBH_4$) Catalyzed Deuteration of 4-Propylbenzoic Acid



Entry	Catalyst	D content (%)					Yield
		C1	**C2**	**C3**	**C4**	**C5**	(%)
1	5% Pd–Pt/C($NaBH_4$)	74	83	96	96	93	98
2	5% Pd/C + 5% Pt/C	94	92	96	96	95	92
3	10% Pd/C[a]	3	4	96	93	92	64
4	5% Pt/C	62	17	15	12	11	84

[a] 10 wt% of 10% Pd/C was used as the catalyst.

notable synergistic effect, and produced an excellent deuteration efficiency (95%), even at the C1 positions (entry 1).

Next, we attempted the deuteration of 4-propylbenzoic acid. The deuteration efficiencies at the positions on the aromatic ring *ortho* to the the alkyl substituent (C2) and to the carboxylic acid (C1) were equally poor when Pd/C or Pt/C was used alone (Table 4, entries 3 and 4, respectively). A significant enhancement in deuterium incorporation at the C1 and C2 positions was achieved by using 5% Pd–Pt/C($NaBH_4$) (entry 1), whereas a mixture of 5% Pd/C and 5% Pt/C gave an even better deuteration efficiency (C1: 94%, C2: 92%; entry 2). It is therefore obvious that quantitative and multiple deuteration might be achieved by complementary use of the bimetallic 5% Pd–Pt/C($NaBH_4$) catalyst or a mixture of 5% Pd/C and 5% Pt/C catalysts, depending on the substrate.

In conclusion, we have developed a novel 5% Pd–Pt/C($NaBH_4$) catalyst for efficient multiple deuteration reactions, and we observed a significant synergy in H–D exchange reactions of sterically-hindered aromatic hydrogens that is related to the bimetallic nature of the catalyst. The 5% Pd–Pt/C($NaBH_4$) and a mixture of 5% Pd/C and 5% Pt/C offer can serve as efficient and complementary catalysts for the polydeuteration of substrates with hindered aromatic positions.

The ^1H, ^2H, and ^{13}C NMR spectra were recorded on a JEOL AL-400 or EX-400 spectrometer (^1H: 400 MHz; ^2H: 61 MHz; ^{13}C: 100 MHz). The chemical shifts δ are given in ppm referred to TMS or residual ^1H peaks of the deuterated solvent. The deuterium contents were determined by using an internal standard (4-methoxybenzoic acid). The mass spectra and high-resolution mass spectra were recorded on a JEOL JMS-SX 102A spectrometer. Inductively coupled plasma-atomic emission spectrometry (ICP-AES) analyses were performed on an SPS 3100 [Seiko Instruments Inc. (Chiba, Japan)]. All reagents were obtained from commercial sources and used without further purification. The deuteration efficiency was calculated by the comparison of the integration for the deuterated product and that of an internal standard in the ^1H NMR, and confirmed from the isotope distribution in the MS. (The deuterated product consists of mixture of compounds with different degrees of deuteration that appear as a distribution on the MS chart.)

Preparation of 5% Pd–Pt on Carbon

Each catalyst was prepared by using H_2, NH_2NH_2, $NaBH_4$, and HCHO in turn as reducing agents.

Pretreatment of the Activated Carbon[11a]

The activated carbon (Norit SX-3) was pretreated with 10% aq HNO_3 to remove residual metals. A sample of Norit SX-3 (3.0 g) was suspended in 10% aq HNO_3 (30 mL) and heated at 60 °C for 3 h then filtered and washed with ion-exchanged H_2O until the filtrate was neutral. The resulting activated carbon was dried initially under atmospheric conditions and then at reduced pressure at r.t. to 100 °C.

Reduction with H_2[11b]

A soln of $PdCl_2$ (44 mg) in hot 5.5 M aq HCl (0.5 mL) was poured into a soln of NaOAc (750 mg) in H_2O (5 mL). H_2PtCl_6 (52.5 mg) and pretreated Norit SX-3 (500 mg) were added, and the soln was stirred at r.t. under H_2 (3 atm) for 2 h. The catalyst was collected by filtration, washed with H_2O until the filtrate was neutral then dried, initially under atmospheric conditions and finally at reduced pressure at r.t.

ICP-AES: Pd, 4.1%; Pt, 2.7%.

Reduction with NH_2NH_2[11c]

Pretreated Norit SX-3 (250 mg) was added to a soln of $PdCl_2$ (20.9 mg) and H_2PtCl_6 (26.3 mg) in H_2O (5 mL), and the suspension was stirred at 50 °C for 4 h, then cooled to r.t. The resulting suspension was adjusted to a pH of 10–12 with sat. aq Na_2CO_3, and NH_2NH_2 (0.5 mL) was added dropwise. The mixture was warmed at 50 °C for 2 h to complete the reduction, and then filtered. The residue was washed with H_2O until the filtrate was neutral then dried, initially under atmospheric conditions and finally at reduced pressure at r.t.

ICP-AES: Pd, 4.1%; Pt, 2.8%.

Reduced with HCHO[11b]

A suspension of pretreated Norit SX-3 (250 mg) in H_2O (3.5 mL) was heated to 80 °C and solns of $PdCl_2$ (20.9 mg) in dil HCl (0.08 mL of concd HCl and 0.12 mL of H_2O) and H_2PtCl_6 (26.3 mg) in H_2O (0.25 mL) were added. A 37% aq soln of HCHO (0.1 mL) was added to the suspension, followed by the addition of 30% aq NaOH to give a slightly alkaline suspension that was stirred at 80 °C for 5 min. The resulting catalyst was collected on a filter and washed with

H_2O until the filtrate was neutral, then dried, initially under atmospheric conditions and then at reduced pressure at r.t.

ICP-AES: Pd, 3.9%; Pt 2.7%.

Reduced with $NaBH_4$[11d,e]

Pretreated Norit SX-3 (250 mg) was added to a soln of K_2PdCl_4 and K_2PtCl_4 in H_2O (4 mL), and the mixture was stirred at r.t. for 2 h. A soln of $NaBH_4$ (137 mg) in H_2O (1.5 mL) was added to the suspension and the mixture was vigorously stirred at r.t. for 12 h. The catalyst was collected by filtration and washed with H_2O until the filtrate was neutral then dried, initially under atmospheric conditions and finally at reduced pressure at r.t.

ICP-AES: Pd, 3.6%; Pt, 3.5%.

Reduction of Aromatic Compounds: General Procedure

A mixture of the substrate (0.5 mmol) and 5% Pd–Pt/C (20 wt% of the substrate) in D_2O (2 mL) was stirred at 180 °C in a sealed tube under H_2 for 6–24 h. After cooling, the catalyst was removed by using a membrane filter (Millipore Millex-LG, 0.45 mm) then washed with Et_2O (2 × 10 mL). The combined filtrates were washed with H_2O (2 × 30 mL) and brine (30 mL), dried ($MgSO_4$), and concentrated under reduced pressure to give the deuterated product.

[^{2}H]-Phenylbutanoic Acid (Table 1, Entry 4)

Isotope distribution by EI-MS: d_{10}, 4%; d_{11}, 12%; d_{12}, 22%; d_{13}, 21%; d_{14}, 3%.

^{1}H NMR (CD_3OD, 4-$MeOC_6H_4CO_2H$ internal standard): δ = 7.15–7.05 (m, 0.38 H), 2.49 (s, 0.07 H), 2.20–2.18 (m, 0.22 H), 1.58–1.50 (m, 0.24 H).

^{2}H NMR (CH_3OH): δ = 7.26 (br s), 7.18 (br s), 2.55 (br s), 2.24 (br s), 1.56 (br s).

[^{2}H]-Hexylbenzene (Table 2, Entry 1)

Isotope distribution (EI-MS): d_{11}, 12%; d_{12}, 28%; d_{13}, 39%; d_{14}, 10%; d_{15}, 7%.

^{1}H NMR (CD_3OD, 4-$MeOC_6H_4CO_2H$ internal standard): δ = 7.14–7.04 (m, 0.16 H), 2.46 (br s, 0.06 H), 1.56–1.45 (m, 0.14 H), 1.20–1.16 (m, 0.65 H), 0.80–0.74 (m, 0.41 H).

^{2}H NMR (CH_3OH): δ = 7.25 (br s), 7.17 (br s), 2.52 (br s), 1.62–1.52 (m), 1.22–1.09 (m), 0.81 (br s).

[^{2}H]-1,2,4,5-Tetramethylbenzene (Table 3, Entry 1)

Isotope distribution (EI-MS): d_{10}, 3%; d_{11}, 10%; d_{12}, 25%; d_{13}, 47%; d_{14}, 55%; d_{15}, 6%.

^{1}H NMR (CD_3OD, 4-$MeOC_6H_4CO_2H$ internal standard): δ = 6.73 (s, 0.13 H), 2.02–2.01 (m, 0.57 H).

^{2}H NMR (CH_3OH): δ = 6.85 (br s), 2.09 (br s).

[^{2}H]-4-Propylbenzoic acid (Table 4, Entry 1)

Isotope distribution (EI-MS): d_7, 3%; d_8, 8%; d_9, 16%; d_{10}, 30%; d_{11}, 39%; d_{12}, 5%.

^{1}H NMR (CD_3OD,4-$MeOC_6H_4CO_2H$ internal standard): δ = 7.92–7.90 (m, 0.46 H), 7.27–7.25 (m, 0.32 H), 2.60 (br s, 0.07 H), 1.60 (m, 0.07 H), 0.95–0.88 (m, 0.18 H).

^{2}H NMR (CH_3OH): δ = 7.94 (br s), 7.29 (br s), 2.58 (br s), 1.58 (br s), 0.86–0.81 (m).

Acknowledgment

This work was partially supported by a Grant-in-Aid for Young Scientists (B) (17790016) and by the Research Foundation of Gifu Pharmaceutical University.

References

(1) Present address: Graduate School of Pharmaceutical Sciences, Osaka University, Suita Osaka, 565-0871, Japan.

(2) (a) Atzrodt, J.; Derdau, V.; Fey, T.; Zimmermann, J. *Angew. Chem. Int. Ed.* **2007**, *46*, 7744. (b) Junk, T.; Catallo, W. J. *Chem. Soc. Rev.* **1997**, *26*, 401.

(3) (a) Brown, W. G.; Garnett, J. L. *J. Am. Chem. Soc.* **1958**, *80*, 5272. (b) Fraser, R. R.; Renaud, R. N. *J. Am. Chem. Soc.* **1966**, *88*, 4365. (c) Garnett, J. L.; Hodges, R. J. *J. Am. Chem. Soc.* **1967**, *89*, 4546. (d) Garnett, J. L.; Long, M. A.; McLaren, A. B.; Peterson, K. B. *J. Chem. Soc., Chem. Commun.* **1973**, 749. (e) Blake, M. R.; Garnett, J. L.; Gregor, I. K.; Hannan, W.; Hoa, K.; Long, M. A. *J. Chem. Soc., Chem. Commun.* **1975**, 930. (f) Hesk, D.; Jones, J. R.; Lockley, W. J. S. *J. Labelled Compd. Radiopharm.* **1990**, *28*, 1427. (g) Hesk, D.; Jones, J. R.; Lockley, W. J. S. *J. Pharm. Sci.* **1991**, *80*, 887. (h) Heys, J. R.; Shu, A. Y. L.; Senderoff, S. G.; Phillips, N. M. *J. Labelled Compd. Radiopharm.* **1993**, *33*, 431. (i) Lukey, C. A.; Long, M. A.; Garnett, J. L. *Aust. J. Chem.* **1995**, *48*, 79. (j) Buncel, E.; Clement, O. *J. Chem. Soc., Perkin Trans. 2* **1995**, 1333.
(k) Van Genderen, M. H. P.; Pfaadt, M.; Moller, C.; Valiyaveettil, S.; Spiess, H. W. *J. Am. Chem. Soc.* **1996**, *118*, 3661. (l) Hardacre, C.; Holbrey, J. D.; McMath, S. E. J. *Chem. Commun.* **2001**, 367. (m) Klei, S. R.; Golden, J. T.; Tilley, T. D.; Bergman, R. G. *J. Am. Chem. Soc.* **2002**, *124*, 2092. (n) Hickey, M. J.; Jones, J. R.; Kingston, L. P.; Lockley, W. J. S.; Mather, A. N.; McAuley, B. M.; Wilkinson, D. J. *Tetrahedron Lett.* **2003**, *44*, 3959.
(o) Matsubara, S.; Yokota, K.; Oshima, K. *Chem. Lett.* **2004**, *33*, 294. (p) Yamamoto, M.; Oshima, K.; Matsubara, S. *Chem. Commun.* **2004**, 1714. (q) Yamamoto, M.; Oshima, K.; Matsubara, S. *Org. Lett.* **2004**, *6*, 5015. (r) Takahashi, M.; Oshima, K.; Matsubara, S. *Chem Lett.* **2005**, *34*, 192. (s) Ishibashi, K.; Takahashi, M.; Yokota, Y.; Oshima, K.; Matsubara, S. *Chem Lett.* **2005**, *34*, 664. (t) Derdau, V.; Atzrodt, J. *Synlett* **2006**, 1918. (u) Yamamoto, M.; Oshima, K.; Matsubara, S. *Heterocycles* **2006**, *67*, 353. (v) Prechtl, M. H. G.; Holscher, M.; Ben-David, Y.; Theyssen, N.; Loschen, R.; Milstein, D.; Leitner, W. *Angew. Chem. Int. Ed.* **2007**, *46*, 2269.

(4) (a) Junk, T.; Catallo, W. J. *Tetrahedron Lett.* **1996**, *37*, 3445. (b) Junk, T.; Catallo, W. J.; Civils, L. D. *J. Labelled Compd. Radiopharm.* **1997**, *36*, 625. (c) Junk, T.; Catallo, W. J.; Elguero, J. *Tetrahedron Lett.* **1997**, *38*, 6309.

(5) (a) Vaidyanathan, S.; Surber, B. W. *Tetrahedron Lett.* **2005**, *46*, 5195. (b) Hakala, U.; Wahala, K. *J. Org. Chem.* **2007**, *72*, 5817.

(6) (a) Garnett, J. L.; Hodges, R. J. *J. Am. Chem. Soc.* **1967**, *89*, 4645. (b) Garnett, J. L.; Hodges, R. J. *Chem. Commun.* **1967**, 1001. (c) Bean, G. P.; Johnson, A. R.; Katritzky, A. R.; Ridgewell, B. J.; White, A. M. *J. Chem. Soc. B* **1967**, 1219. (d) Long, M. A.; Garnett, J. L.; Vining, R. F. W.; Mole, T. *J. Am. Chem. Soc.* **1972**, *94*, 8632. (e) Werstiuk, N. H.; Kadai, T. *Can. J. Chem.* **1974**, *52*, 2169. (f) Tashiro, M.; Nakayama, K. *J. Chem. Soc., Perkin Trans. 1* **1983**, 2315. (g) Iranzo, G. Y.; Elguero, J. *J. Labelled Compd. Radiopharm.* **1990**, *28*, 967. (h) Okazaki, M.; Uchino, N.; Nozaki, N.; Kubo, K. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 1024.

(7) (a) Sajiki, H.; Hattori, K.; Aoki, F.; Yasunaga, K.; Hirota, K. *Synlett* **2002**, 1149. (b) Sajiki, H.; Aoki, F.; Esaki, H.; Maegawa, T.; Hirota, K. *Org. Lett.* **2004**, *6*, 1485. (c) Sajiki, H.; Kurita, T.; Esaki, H.; Aoki, F.; Maegawa, T.; Hirota, K. *Org. Lett.* **2004**, *6*, 3521. (d) Maegawa, T.; Akashi, A.; Esaki, H.; Aoki, F.; Sajiki, H.; Hirota, K. *Synlett* **2005**, 845. (e) Sajiki, H.; Esaki, H.; Aoki, F.; Maegawa, T.; Hirota, K. *Synlett* **2005**, 1385. (f) Maegawa, T.; Akashi, A.; Esaki, H.; Aoki, F.; Sajiki, H.; Hirota, K. *Synlett* **2005**, 845. (g) Sajiki, H.; Ito, N.; Esaki, H.; Maesawa, T.; Maegawa, T.; Hirota, K. *Tetrahedron Lett.* **2005**, *46*, 6995. (h) Esaki, H.; Aoki, F.; Maegawa, T.; Hirota, K.; Sajiki, H. *Heterocycles* **2005**, *66*, 361. (i) Esaki, H.; Ito, N.; Sakai, S.; Maegawa, T.; Monguchi, Y.; Sajiki, H. *Tetrahedron* **2006**, *62*, 10954. (j) Esaki, H.; Ohtaki, R.; Maegawa, T.; Monguchi, Y.; Sajiki, H. *J. Org. Chem.* **2007**, *72*, 2143. (k) Esaki, H.; Aoki, F.; Umemura, M.; Kato, M.; Maegawa, T.; Monguchi, Y.; Sajiki, H. *Chem. Eur. J.* **2007**, *13*, 4052. (l) Ito, N.; Esaki, H.; Maesawa, T.; Imamiya, E.; Maegawa, T.; Sajiki, H. *Bull. Chem. Soc. Jpn.* **2008**, *81*, 278. (m) Kurita, T.; Hattori, K.; Seki, S.; Mizumoto, T.; Aoki, F.; Yamada, Y.; Ikawa, K.; Maegawa, T.; Monguchi, Y.; Sajiki, H. *Chem. Eur. J.* **2008**, *14*, 664. (n) Kurita, T.; Aoki, F.; Mizumoto, T.; Maejima, T.; Esaki, H.; Maegawa, T.; Monguchi, Y.; Sajiki, H. *Chem. Eur. J.* **2008**, *14*, 3371.

(8) Maegawa, T.; Fujiwara, Y.; Inagaki, Y.; Esaki, H.; Monguchi, Y.; Sajiki, H. *Angew. Chem. Int. Ed.* **2008**, *47*, 5394.

(9) Maegawa, T.; Fujiwara, Y.; Inagaki, Y.; Monguchi, Y.; Sajiki, H. *Adv. Synth. Catal.* **2008**, *350*, 2215.

(10) (a) Ito, N.; Watahiki, T.; Maesawa, T.; Maegawa, T.; Sajiki, H. *Adv. Synth. Catal.* **2006**, *348*, 1025. (b) Ito, N.; Watahiki, T.; Maesawa, T.; Maegawa, T.; Sajiki, H. *Synthesis* **2008**, 1467.

(11) (a) Mozingo, R. *Org. Synth. Coll. Vol. III*; John Wiley & Sons: London, **1955**, 685. (b) Alexander, E. R.; Cope, A. C. *J. Am. Chem. Soc.* **1944**, *66*, 886. (c) Arimoto, O.; Katayama, S. JP 7090664, **1999** *Chem. Abstr.* **1995**, *122*, 324895. (d) Scott, R. W. J.; Datye, A. K.; Crooks, R. M. *J. Am. Chem. Soc.* **2003**, *125*, 3708. (e) Crooks, R. M.; Zhao, M.; Sun, L.; Chechik, V.; Yeung, L. K. *Acc. Chem. Res.* **2001**, *34*, 181.

(12) The Pt and Pd contents of 5% Pd–Pt/C($NaBH_4$) were almost equal (Pd, 3.6%; Pt, 3.5% by ICP-AES), whereas 5% Pd–Pt/C(H_2), 5% Pd–Pt/C(NH_2NH_2), and 5% Pd–Pt/C(HCHO) showed higher contents of Pd than of Pd (Pd, 3.9–4.1%; Pt, 2.7–2.8%).

(13) (a) Koutsopoulos, S.; Eriksen, K. M.; Fehrman, R. *J. Catal.* **2006**, *238*, 270. (b) Matsui, T.; Harada, M.; Bnado, K. K.; Toba, M.; Yoshimura, Y. *Appl. Catal., A* **2005**, *290*, 73. (c) Navarro, R. M.; Pawelec, B.; Trejo, J. M.; Mariscal, R.; Fierro, J. L. G. *J. Catal.* **2000**, *189*, 184. (d) Fujikawa, T.; Tsuji, K.; Mizuguchi, H.; Goto, H.; Idei, K.; Usui, K. *Catal. Lett.* **1999**, *63*, 27. (e) Karpiński, Z.; Kościelski, T. *J. Catal.* **1980**, *63*, 313.