Supporting Information

Direct Use of Allylic Alcohols for Platinum-Catalyzed Monoallylation of Amines

Masaru Utsunomiya, Yoshiki Miyamoto, Junji Ipposhi, Takashi Ohshima,* and Kazushi Mashima*

Department of Chemistry, Graduate School of Engineering Science, Osaka University, Toyonaka, Osaka 560-8531, Japan

General: Nuclear magnetic resonance (^1H NMR and ^{13}C NMR) spectra were measured on a Varian MERCURY300-C/H spectrometer operating at 300 MHz (^1H NMR) and 75 MHz (^{13}C NMR) in 5 mm NMR tubes. All ^1H NMR chemical shifts were reported in ppm relative to internal references of TMS at δ 0.00. All ^{13}C NMR chemical shifts were reported in ppm relative to carbon resonance in chloroform- d_1 at δ 77.00. Low and high resolution mass spectra (EI, FAB) were measured on JEOL JMS-700. ESI mass spectra were measured on JEOL JMS-700 coupled with an electrospray ionization probe (MS-ESIP15). IR spectra were recorded on Jasco FT/IR-230 spectrometer and Jasco FT/IR-410 spectrometer. Elemental analyses were conducted by Perkin-Elmer 2400II. Melting points were measured using Yanaco micro melting point apparatus. All reactions were performed under an argon atmosphere with dry dioxane, which was distilled from benzophenone-ketyl under argon atmosphere. All other reagents were purchased at highest commercial quality and used without further purification.

Bite-Angle Shown in Table 1

(1) Bite-angle of Pd complexes (P–Pd–P)

- For DPEphos and Xantphos, see: John, A. M.; Utsunomiya, M.; Incarvito, C. D.; Hartwig, J. F. *J. Am. Chem. Soc.* **2006**, *128*, 1828.
- For DPPE, DPPP, and DPPF, see: Oestreich, M. *Eur. J. Org. Chem.* **2005**, 783.
- For BINAP, see: Amatore, C.; Broecker, G.; Jutand, A.; Khalil, F. *J. Am. Chem. Soc.* **1997**, *119*, 5176.

(2) Bite-angle of (DPEPhos)Pt(π -allyl)Cl and of (Xantphos)Pt(π -allyl)Cl complexes optimized with B3LYP function

- Starting from the structure of (Xantphos)Pd(π -allyl)Cl complex obtained by X-ray crystallographic analysis (John, A. M.; Utsunomiya, M.; Incarvito, C. D.; Hartwig, J. F. *J. Am. Chem. Soc.* **2006**, *128*, 1828), Pd element was replaced by Pt element to make initial structure of (Xantphos)Pt(π -allyl)Cl complex. Then, this initial structure was optimized by B3LYP hybrid density functional methods using a 6-31G** basis set with Gaussian 03 (Figure SI-1).
- Initial structure of (DPEPhos)Pt(π -allyl)Cl complex was made by removal of dimethylmethane unit from the optimized structure of (Xantphos)Pt(π -allyl)Cl complex. Then, in the same way, structural optimization was performed (Figure SI-2).

Figure SI-1

Figure SI-2

Effects of Metal Source

Table SI-1. Screening of Metal Source with DPEphos ligand on Direct Amination of Allyl Alcohol^a

$\text{1a} + \text{3a} \xrightarrow[\text{dioxane, reflux, 4 h}]{\text{metal source (1.0 mol\% metal), DPEphos (2.0 mol\%)}} \text{4aa}$

entry	metal source	yield (%) ^b
1	Pt(cod)Cl ₂	91
2	Pt(cod)Br ₂	64
3	[Pt(ethylene)Cl ₂] ₂	7
4	Pt(PhCN)Cl ₂	28
5	Pt(acac) ₂	51
6	Pt(cod)(OTf) ₂	64
7	Pt(PPh ₃) ₄	89
8	Pd(OAc) ₂	2
9	Pd(OCOCF ₃) ₂	6
10	[Pd(allyl)Cl] ₂	3
11	Pd ₂ dba ₃	11
12	Ni(OAc) ₂	0
13	Ni(cod) ₂	0

^a 1.0 mmol scale, dioxane (0.5 mL). ^b Determined by GC analysis.

One-Step Synthesis of Antifungal Drug Naftifine Hydrochloride (4bs•HCl)

In the presence of 1 mol% of the catalyst, the substitution reaction of *trans*-cinnamyl alcohol (**1b**) (3.14 g, 23.4 mmol) with *N*-methyl-1-naphthylamine (**3s**) (3.90 mL, 23.9 mmol, 1.02 equiv) was completed in 12 h, and the crude mixture was treated with 1 M HCl in EtOH (30 mL). After concentration under reduced pressure, the resulting solid was purified by recrystallization from EtOH/Et₂O to provide pure naftifine hydrochloride (**4bs•HCl**) (6.29 g, 83% yield) as a white fine crystal. (m.p. = 174-176 °C, Lit. m.p. = 173-175 °C; Berney, D; Schuh, K. *Helv. Chim. Acta* **1978**, *61*, 1262.).

Scheme SI-1.

In the precedent manuscripts, naftifine (**4bs**) was synthesized from cinnamaldehyde and 1-naphthylamine through (i) imine formation, (ii) reduction of imine, and *N*-methylation (Loibner, H.; Pruckner, A.; Stütz, A. *Tetrahedron Lett.* **1984**, *25*, 2535. Stütz, A.; Georgopoulos, A.; Granitzer, W.; Petranyi, G.; Berney, D. *J. Med. Chem.* **1986**, *29*, 112.) and one-pot oxidation–imine-formation–reduction reaction of *trans*-cinnamyl alcohol and *N*-methyl-1-naphthylamine using much excess amount of MnO₂ and polymer-supported cyanoborohydride reagents (Kanno, H.; Taylor, R. J. K. *Tetrahedron Lett.* **2002**, *43*, 7337.).

General Procedure for Direct Amination of Allyl Alcohols Catalyzed by Pt–DPEphos Complex (Table 2, entry 2)

A schlenk flask was charged with Pt(cod)Cl₂ (15 mg, 0.040 mmol, 1.0 mol%) and DPEphos (43 mg, 0.080 mmol, 2 mol%) followed by the addition of 1,4-dioxane (5.0 mL) under an argon atmosphere. Aniline (**3a**, 0.547 mL, 6.0 mmol, 1.5 equiv) was added to the mixture, and after heating (oil bath temp. 110 °C), allyl alcohol (**1a**, 0.272 mL, 4.0 mmol) was gradually added. After being refluxed for 6 h, the reaction mixture was concentrated under reduced pressure and the resulting residue was purified by silica gel column chromatography (hexane/EtOAc = 30/1) to afford monoallylation product **4aa** (458 mg, 86% yield) and diallylation product **5aa** (44 mg, 6% yield).

ppm (t1)

200

150

100

50

0

0

1000

2000

3000

4000

ppm (f1)

5.0

0.0

ppm (f1)

200

150

100

50

0

ppm (f1)

200

150

100

50

0

ppm (t1)

5.0

0.0

0

500 ω

1000

ppm (t1)

200

150

100

50

0

ppm (f1)

5.0

0.0

ppm (f1)

200

150

100

50

0

ppm (f1)

5.0

0.0

ppm (f1)

200

150

100

50

0

ppm (f1)

5.0

0.0

ppm (f1)

200

150

100

50

0

ppm (f1)

5.0

0.0

ppm (f1)

5.0

0.0

ppm (f1)

5.0

0.0

ppm (f1)

10.0

5.0

0.0

ppm (f1)

150

100

50

0

ppm (f1)

5.0

0.0

ppm (f1)

200

150

100

50

0

ppm (f1)

5.0

0.0

ppm (f1)

5.0

0.0

ppm (f1)

5.0

0.0

ppm (f1)

ppm (f1)

5.0

0.0

ppm (f1)

200

150

100

50

0

4bs

ppm (f1)

10.0

5.0

0.0

465

ppm (f1)

150

100

50

0

ppm (τ₁)

10.0

5.0

0.0