Iridium-Catalyzed Asymmetric Hydrosilylation of Imines Using Chiral Oxazolinyl-Phosphine Ligands

Izuru Takei,† Yoshiaki Nishibayashi,† Yasuyoshi Arikawa,‡ Sakae Uemura,*,‡ and Masanobu Hidai*,†

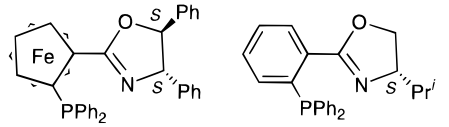
Department of Chemistry and Biotechnology, Graduate School of Engineering, The University of Tokyo, Hongo, Tokyo 113-8656, Japan, and Department of Energy and Hydrocarbon Chemistry, Graduate School of Engineering, Kyoto University, Sakyo-ku, Kyoto 606-8501, Japan

Received December 10, 1998

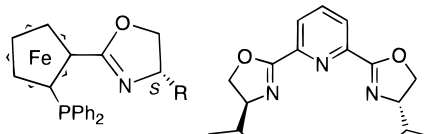
Summary: Chiral oxazolinylphosphines are effective ligands for the Ir(I)-catalyzed asymmetric hydrosilylation of imines to afford the corresponding sec-amines with high enantioselectivities (up to 89% ee) after hydrolysis in almost quantitative yields. The structure of an Ir(I)−oxazolinylferrocenylphosphine complex was determined by X-ray analysis.

Introduction

Catalytic enantioselective hydrosilylation of ketones and imines provides an attractive and useful method for the synthesis of chiral alcohols and amines,[1,2] although the efficient asymmetric hydrogenation and transfer hydrogenation of ketones[1] and imines[3,4] have been realized. We have recently found that [2-(4,5-diphenyl-4,5-dihydro-1,3-oxazolin-2-yl)ferrocenyl]diphenylphosphine (**1a**) [abbreviated as DIPOF] is a quite effective chiral ligand for the Rh(I)- and Ir(I)-catalyzed asymmetric hydrosilylation of a variety of simple ketones without functional groups (up to 96% ee).[5] Interestingly, chiral alcohols with the opposite configuration are obtained from the corresponding ketones when the metal is changed from Rh(I) to Ir(I).[5] In sharp contrast, studies on enantioselective hydrosilylation of prochiral imines are limited.[6] A few examples involving catalysis by the Rh(I)−DIOP system (DIOP = 2,3-*O*-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane) have been reported; however, only moderate enantioselectivities (up to 66% ee) were achieved.[6] Recently, Buchwald and co-workers have found the highly enantioselective titanocene-catalyzed hydrosilylation of imines.[7] On the other hand, we previously reported the Ru(II)-catalyzed asymmetric hydrosilylation of an imine using an oxazolinylferrocenylphosphine **1b** as the ligand.[8] In an extension of this chemistry, the highly enantioselective Ir-catalyzed hydrosilylation of imines using oxazolinylphosphines **1b**−**1e** has now been developed.

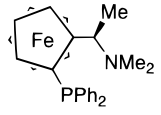


(*S*)-DIPOF (**1a**) **1e**



R = Ph (**1b**)
R = Pr^i (**1c**)
R = Bu^t (**1d**)

1f



1g

† The University of Tokyo.
‡ Kyoto University.

(1) For reviews, see: (a) *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH: New York, 1993. (b) Brunner, H.; Zettimeier, W. *Handbook of Enantioselective Catalysis with Transition Metal Compounds;* VCH: Weinheim, 1993. (c) Noyori, R. *Asymmetric Catalysis in Organic Synthesis*; John Wiley & Sons: New York, 1994.

(2) For recent examples of asymmetric hydrosilylation: (a) Nishiyama, H.; Kondo, M.; Nakamura, T.; Itoh, K. *Organometallics* **1991**, *10*, 500. (b) Nishibayashi, Y.; Singh, J. D.; Segawa, K.; Fukuzawa, S.; Uemura, S. *J. Chem. Soc., Chem. Commun.* **1994**, 1375. (c) Sawamura, M.; Kuwano, R.; Ito, Y. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 111. (d) Hayashi, T.; Hayashi, C.; Uozumi, Y. *Tetrahedron: Asymmetry* **1995**, *6*, 2503. (e) Nishibayashi, Y.; Singh, J. D.; Segawa, K.; Fukuzawa, S.; Ohe, K.; Uemura, S. *Organometallics* **1996**, *15*, 370. (f) Newman, L. M.; Williams, J. M. J.; McCague, R.; Potter, G. A. *Tetrahedron: Asymmetry* **1996**, *7*, 1597. (g) Langer, T.; Janssen, J.; Helmchen, G. *Tetrahedron: Asymmetry* **1996,** *7*, 1599. (h) Herrmann, W. A.; Goossen, L. J.; Kücher, C.; Artus, G. R. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 2805. (i) Nishibayashi, Y.; Singh, J. D.; Arikawa, Y.; Uemura, S.; Hidai, M. *J. Organomet. Chem.* **1997**, *531*, 13. (j) Lee, S.; Lim, C. W.; Song, C. E.; Kim, I. O. *Tetrahedron: Asymmetry* **1997**, *8*, 4027. (k) Haag, D.; Runsink, J.; Scharf, H.-D. *Organometallics* **1998**, *17*, 398.

(3) Recent examples of asymmetric hydrogenation of imines: (a) Willoughby, C. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **1994**, *116*, 8952. (b) Willoughby, C. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **1994**, *116*, 11703. (c) Tani, K.; Onouchi, J.; Yamagata, T.; Kataoka, Y. *Chem. Lett.* **1995**, 955. (d) Schnider, P.; Koch, G.; Pretot, R.; Wang, G.; Bohnen, F. R.; Krüger, C.; Pfaltz, A. *Chem. Eur. J.* **1997**, *3*, 887. (e) Zhu, G.; Zhang, X. *Tetrahedron: Asymmetry* **1998**, *9*, 2415. (f) Satoh, K.; Inenaga, M.; Kanai, K. *Tetrahedron: Asymmetry* **1998**, *9*, 2657. (g) Morimoto, T.; Suzuki, N.; Achiwa, K. *Tetrahedron: Asymmetry* **1998**, *9*, 183.

(4) Asymmetric transfer hydrogenation of imines: Uematsu, N.; Fujii, A.; Hashiguchi, S.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1996**, *118*, 4916−4917.

(5) (a) Nishibayashi, Y.; Segawa, K.; Ohe, K.; Uemura, S. *Organometallics* **1995**, *14*, 5486. (b) Nishibayashi, Y.; Segawa, K.; Takada, H.; Ohe, K.; Uemura, S. *Chem. Commun.* **1996**, 847.

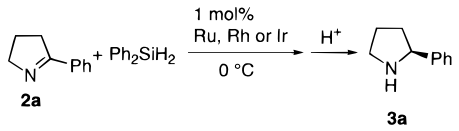
(6) (a) Kagan, H. B.; Langlois, N.; Dang, T.-P. *J. Organomet. Chem.* **1975**, *90*, 353. (b) Becker, R.; Brunner, H.; Mahboobi, S.; Wiegrebe, W. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 995.

(7) (a) Verdaguer, X.; Lange, U. E. W.; Reding, M. T.; Buchwald, S. L. *J. Am. Chem. Soc.* **1996**, *118*, 6784. (b) Verdaguer, X.; Lange, U. E. W.; Buchwald, S. L. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 1103. (c) Reding, M. T.; Buchwald, S. L. *J. Org. Chem.* **1998**, *63*, 6344.

(8) Nishibayashi, Y.; Takei, I.; Uemura, S.; Hidai, M. *Organometallics* **1998**, *17*, 3420.

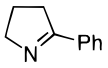
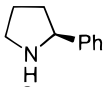
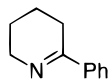
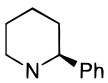
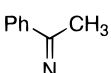
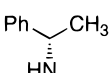
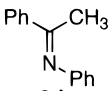
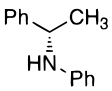
10.1021/om981005w CCC: $18.00
Publication on Web 04/20/1999

Scheme 1



Ru = [$RuCl_2(PPh_3)$(**1b**)]; Rh or Ir = $[M(COD)Cl]_2$ (M = Rh or Ir) + a chiral ligand

Table 1. Asymmetric Hydrosilylation of Imines

run	metal	imine	reaction time/h	amine	yield[a] (%)	ee[b] (%)	config.
1	Ru[c]	 **2a**	40	 **3a**	60	88	*S*
2	Ru[c,d]		40		82	70	*S*
3	Ir[e]		20		>95	85	*S*
4	Rh[e]		20		75	34	*S*
5	Ru[c]	 **2b**	50	 **3b**	10	25	*S*
6	Ir[e]		100		18	7	*S*
7	Ru[c]	 **2c**	90	 **3c**	51	73	*S*
8	Ir[e]		60		56	89	*S*
9	Ir[e,f]		48		24	16	*S*
10	Rh[e]		48		23	<5	*S*
11	Ir[e]	 **2d**	60	 **3d**	25	23	*S*

[a] GLC yield. [b] Determined by GLC of the corresponding trifluoroacetamides on a cyclodextrin phase (Chiraldex GT-A, 30 m). [c] The reaction of diphenylsilane (2.0 mmol) and imine (1.0 mmol) was carried out in the presence of [$RuCl_2(PPh_3)$(**1b**)] (0.01 mmol) in toluene (10 mL) at 0 °C. [d] At room temperature. [e] The reaction of diphenylsilane (2.0 mmol) and imine (1.0 mmol) was carried out in the presence of $[M(COD)Cl]_2$ (M = Rh or Ir) (0.005 mmol) and **1b** (0.01 mmol) in Et_2O (5 mL) at 0 °C. [f] **1e** was used in place of **1b**.

Results and Discussion

In a previous communication,[8] we reported the asymmetric hydrosilylation of imine **2a** with diphenylsilane in the presence of [$RuCl_2(PPh_3)$(**1b**)], in which the corresponding chiral amine **3a** was obtained in 60% yield with 88% ee (*S*) (Scheme 1). We have now employed other cyclic and acyclic imines to obtain the corresponding chiral amines. All the reactions described here were clean, and byproducts were not observed. Typical results are shown in Table 1. Unfortunately, in the case of a cyclic imine **2b** with a six-membered ring, the hydrosilylation did not proceed smoothly, and the chiral amine **3b** was obtained only in 10% GLC yield with 25% ee (Table 1; run 5). On the other hand, the reaction of an *N*-methyl acyclic imine **2c** with diphenylsilane proceeded smoothly at 0 °C for 90 h to afford the corresponding *N*-methylamine **3c** in 51% GLC yield with 73% ee (*S*) (Table 1; run 7).

As an extension of our study on the asymmetric hydrosilylation of imines, we have now investigated the reaction of **2a** by using Rh and Ir complexes with oxazolinylphosphines **1** (Scheme 1). Typical results are shown in Table 2. Compared with the iridium−**1b** system, the rhodium−**1b** system showed low catalytic activity with low enantioselectivity (Table 2; run 3). The iridium-catalyzed hydrosilylation of **2a** proceeded very smoothly at 0 °C to give the amine **3a** in >95% GLC yield with 85% enantiomeric excess (ee) (Table 2; run 1). At −10 °C, the enantioselectivity was slightly improved, up to 88% ee (Table 2; run 2). Oxazolinylferrocenylphosphine **1c** was also found to be effective for the asymmetric hydrosilylation of imine **2a**, but not as effective as **1b** in terms of catalytic activity (Table 2; runs 1 and 4). The use of oxazolinylferrocenylphosphine **1d** with a bulky *tert*-butyl group on the oxazoline ring inhibited the reaction completely (Table 2; run 5). DIPOF **1a** was also employed as a chiral ligand for the Ir and Rh system, because **1a** was effective for the asymmetric hydrosilylation of ketones. Unexpectedly, the Ir- and Rh-catalyzed asymmetric hydrosilylation of imines using **1a** did not work effectively (Table 2; runs 6 and 7). Interestingly, oxazolinylphenylphosphine **1e**, which does not have planar chirality due to ferrocene, showed almost the same enantioselectivity as oxazolinylferrocenylphosphine **1c** with the same substituent on the oxazoline ring (Table 2; runs 4 and 8). When α-naphthylphenylsilane was used in place of diphenylsilane, the reaction proceeded more slowly to give **3a** with lower enantioselectivity (Table 2; run 9). It may be noted that the absolute configuration of product **3a** prepared by this hydrosilylation of **2a** was the same in both the Rh(I) and Ir(I) cases, which is in contrast to the hydrosilylation of ketones (*vide supra*). This result suggests that the mechanism of the hydrosilylation of imines is different from that of ketones. To the best of our knowledge, this is the first example of an Ir-catalyzed highly enantioselective hydrosilylation of imines. On the other hand, DIOP,[9] *ip*-pybox [2,6-bis-(4′-isopropyloxazolin-2′-yl)pyridine][2a] (**1f**), and PPFA [*N*,*N*-dimethyl-1-[2-(diphenylphosphino)ferrocenyl]ethylamine][10] (**1g**) did not work effectively.

Table 2. Influence of Chiral Ligands on Iridium- and Rhodium-Catalyzed Asymmetric Hydrosilylation of 2a[a]

run	metal	chiral ligand	reaction time/h	amine (*S*) yield[b] (%)	amine (*S*) ee[c] (%)
1	Ir	**1b**	20	>95	85
2[d]	Ir	**1b**	60	>95	88
3	Rh	**1b**	20	75	34
4	Ir	**1c**	50	78	88
5	Ir	**1d**	50	trace	
6	Ir	**1a**	30	>95	71
7	Rh	**1a**	30	17	32
8	Ir	**1e**	40	>95	86
9[e]	Ir	**1b**	60	<5	26

[a] All the reactions of diphenylsilane (2.0 mmol) and **2a** (1.0 mmol) were carried out in the presence of $[M(COD)Cl]_2$ (M = Ir or Rh) (0.005 mmol) and chiral ligand (0.013 mmol) in Et_2O (5 mL) at 0 °C. [b] GLC yield. [c] Determined by GLC of the corresponding trifluoroacetamides on a cyclodextrin phase (Chiraldex GT-A, 30 m). [d] At −10 °C. [e] α-Naphthylphenylsilane was used in place of diphenylsilane.

Hydrosilylation of other imines with diphenylsilane was investigated in the presence of a catalytic amount of $[Ir(COD)Cl]_2$ and **1b**. Typical results are shown in Table 1. Unfortunately, in the case of a cyclic imine **2b** with a six-membered ring, the hydrosilylation did not proceed smoothly (Table 1; run 6). On the other hand,

(9) Takei, I.; Nishibayashi, Y.; Hidai, M. Unpublished results.
(10) Hayashi, T.; Mise, T.; Fukushima, M.; Kagotani, M.; Nagashima, N.; Hamada, Y.; Matsumoto, A.; Kawakami, S.; Konishi, M.; Yamamoto, K.; Kumada, M. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 1138.

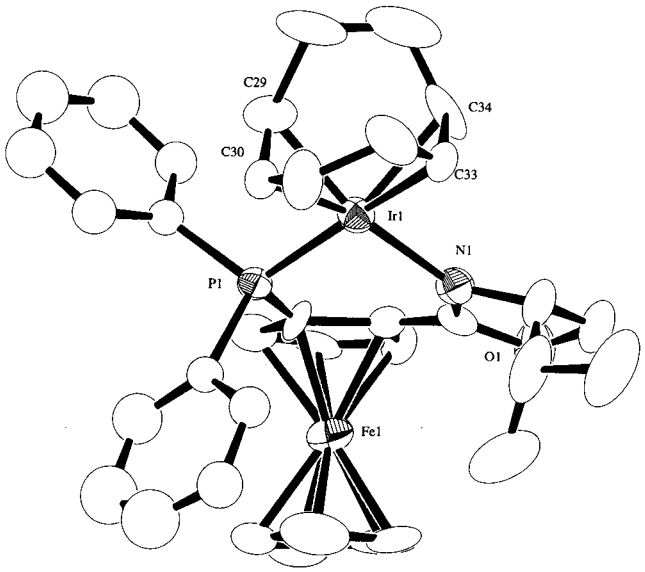


Figure 1. ORTEP drawing of [Ir(**1c**)(COD)]BF_4 (**4**). The hydrogen atoms and BF_4 are omitted for clarity. Selected distances (Å) and angle (deg): Ir(1)−P(1), 2.280(7); Ir(1)−N(1), 2.12(2); P(1)−Ir(1)−N(1), 90.9(6).

the reaction of an *N*-methyl acyclic imine **2c** proceeded smoothly to afford the corresponding *N*-methylamine **3c** in 56% yield with 89% ee (*S*) (Table 1; run 8). However, employment of **1e** in place of **1b** did not work effectively, in contrast to the reaction of **2a** (Table 1; run 9). In the case of an *N*-phenyl acyclic imine **2d**, an *N*-phenylamine **3d** was obtained only in 25% yield with 23% ee (Table 1; run 11).

For comparison, the relationship between enantioselectivities of the hydrosilylation of imines and metal complexes with the same chiral ligand **1b** is shown in Table 1. In the case of the cyclic imine **2a**, both the Ru- and the Ir-system showed almost the same stereoselectivity; however, the Ir-system exhibited slightly higher catalytic activity than the Ru-system (Table 1; runs 1, 3, and 4). On the other hand, the Ir-system was more effective than the Ru-system for the asymmetric hydrosilylation of the acyclic imine **2c** (Table 1; runs 7 and 8).

To obtain some information about the molecular structure of the iridium complex coordinated by an oxazolinylferrocenylphosphine, we tried to isolate the iridium complex containing **1c**. Treatment of **1c** with $[Ir(COD)Cl]_2$ and $AgBF_4$ in acetone at room temperature for 1 h afforded a cationic Ir complex [Ir(**1c**)(COD)]BF_4 (**4**) in 78% yield. Its structure was unambiguously confirmed by X-ray analysis. An ORTEP drawing of **4** is shown in Figure 1 along with selected bond lengths and bond angle. The molecular structure of **4** is very similar to that of [Rh(**1c**)(COD)]BF_4.[11b]

Coordination of **1c** to the iridium atom under the catalytic conditions was supported by the ^1H and $^{31}P\{^1H\}$ NMR spectra of a stoichiometric mixture of $[Ir(COD)Cl]_2$ and 2 equiv of **1c** in $CDCl_3$. The $^{31}P\{^1H\}$ NMR spectrum exhibited a singlet at δ 9.0 ($^{31}P\{^1H\}$ NMR of **4** δ 10.1; and **1c** δ −17.0). In the ^1H NMR spectrum, resonances due to the methyl protons of the oxazolinyl group (δ 0.96 (d, 3H, J = 7.3 Hz), 1.13 (d, 3H, J = 7.3 Hz)) appeared at the same region as those of **4** (δ 0.93 (d, 3H, J = 7.3 Hz), 1.12 (d, 3H, J = 7.3 Hz)), which are completely different from those of free ligand **1c** (δ 0.68 (d, 3H, J = 6.8 Hz), 0.82 (d, 3H, J = 6.8 Hz)).

In conclusion, we have found that the Ir(I)-catalyzed asymmetric hydrosilylation of imines by using chiral oxazolinylferrocenylphosphines as chiral ligands afforded the corresponding *sec*-amines with high enantioselectivities (up to 89% ee) after hydrolysis.

Experimental Section

General Comments. ^1H (270 MHz) and $^{31}P\{^1H\}$ NMR spectra (109 MHz) were recorded on a JEOL JNM-EX-270 spectrometer as solutions in $CDCl_3$. GLC analyses were performed on a Shimadzu GC-14A instrument (25 m HiCap-CBP-10-S25 capillary column) with a flame-ionization detector and nitrogen as carrier gas. Elemental analyses were performed on a Perkin-Elmer 2400 series II CHN analyzer. All reactions were carried out under a dry nitrogen atmosphere. Solvents were dried by the usual methods and distilled before use. Prochiral imines **2a**,[3a,12] **2b**,[3a] **2c**,[7a] and oxazolinylferrocenylphosphines[11] were prepared by the reported methods.

General Procedure for Iridium-Catalyzed Asymmetric Hydrosilylation of Imines. In a 20 mL flask were placed $[Ir(COD)Cl]_2$ (3.3 mg, 0.005 mmol; 1.0 mol %) and a chiral oxazolinylphosphine (0.013 mmol; 1.3 mol %) under N_2. Anhydrous diethyl ether (5 mL) was added, and then the mixture was magnetically stirred at room temperature for 1 h. After addition of an imine (1.0 mmol), the reaction flask was immersed in a thermoregulated bath at 0 °C. Diphenylsilane (2.0 mmol) was then slowly added by syringe. The reaction was allowed to proceed at 0 °C. For workup, methanol (1 mL) was slowly added at 0 °C to the reaction mixture, which was stirred for 0.5 h. After gas evolution ceased, 1 N aqueous HCl (5 mL) was added to the reaction mixture, which was stirred at room temperature for 1 h. The reaction mixture was extracted with water (50 mL), and then 3 N aqueous NaOH (20 mL) was added to the aqueous solution. This solution was extracted with diethyl ether (50 mL × 3), and the diethyl ether solution was dried over anhydrous $MgSO_4$. For the GLC analysis, naphthalene was added as an internal standard. The optical purity was determined by GC analysis of the corresponding trifluoroacetamides on a cyclodextrin phase (Chiraldex GT-A, 30 m). The absolute configuration was determined by an optical rotation.

Preparation of [Ir(1c)(COD)]BF_4 (4). In a 20 mL flask were placed $[Ir(COD)Cl]_2$ (34 mg, 0.05 mmol) and $AgBF_4$ (19 mg, 0.10 mmol) under nitrogen. Anhydrous acetone (2 mL) was added, and the mixture was stirred at room temperature for 0.5 h. The chiral oxazolinylferrocenylphosphine **1c** (48 mg, 0.10 mmol) was then added, and the resulting solution was magnetically stirred at room temperature for 1 h. When diethyl ether (20 mL) was added to the solution, **4** precipitated as an orange solid, which was collected by filtration and dried under vacuum: 68 mg, 78% isolated yield. ^1H NMR

(11) (a) Nishibayashi, Y.; Uemura, S. *Synlett* **1995**, 79. (b) Nishibayashi, Y.; Segawa, K.; Arikawa, Y.; Ohe, K.; Hidai, M.; Uemura, S. *J. Organomet. Chem.* **1997**, *545−546*, 381, and references therein.

(12) Sorgi, K. L.; Maryanoff, C. A.; McComsey, D. F.; Graden, D. W.; Maryanoff, B. E. *J. Am. Chem. Soc.* **1990**, *112*, 3567.

($CDCl_3$): δ 0.93 (d, 3H, $J = 7.3$ Hz), 1.22 (d, 3H, $J = 7.3$ Hz), 1.6−2.5 (m, 9H), 3.25 (m, 2H), 3.77 (s, 5H), 4.22 (m, 2H), 4.60 (m, 1H), 4.71 (m, 1H), 4.94 (m, 1H), 4.99 (m, 1H), 5.19 (m, 1H), 5.22 (m, 1H), 7.0−8.2 (m, 10H). $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ 10.1 (s). Anal. Calcd for $C_{36}H_{40}BF_4FeIrNOP$: C, 49.78; H, 4.64; N, 1.61. Found: C, 49.60; H, 4.96; N, 1.28.

X-ray Structural Determination of [Ir(1c)(COD)]-BF_4 (4) (Figure 1). Crystal data for **4** (an orange crystal, grown by slow diffusion of diethyl ether into an acetone solution of **4** at room temperature) of $C_{36}H_{40}BF_4FeIrNOP$ were collected on a Rigaku AFC7R diffractometer with graphite-monochromated Mo Kα radiation ($\lambda = 0.710\,69$ Å) and a 12 kW rotating anode generator. Crystal data for **4** are as follows: orthorhombic, space group $P2_12_12_1$; $a = 12.986(3)$ Å, $b = 24.004(3)$ Å, $c = 10.957(4)$ Å, $V = 3415(1)$ Å^3, $Z = 4$, $F_{000} = 1720.00$, $D_c = 1.689$ g/cm^3, μ(Mo Kα) = 44.26 cm^{-1}. The final R value was 0.064 ($R_w = 0.056$) for 2126 unique reflections with $I > 3\sigma(I)$. The structure was solved by the Patterson method (DIRDIF92 PATTY). The carbon atoms of phenyl rings were refined isotropically. All other non-hydrogen atoms were refined anisotropically. Hydrogen atom position was geometrically calculated or taken from a difference Fourier map.

Acknowledgment. This work was supported by a Grant-in-Aid for Specially Promoted Research (09102004) from the Ministry of Education, Science, Sports, and Culture, Japan.

Supporting Information Available: Tables of information on data collection, structure solution, and refinement, atom coordinates, anisotropic displacement parameters, and all bond distances and angles of **4**. This material is available free of charge via the Internet at http://pubs.acs.org.

OM981005W