New Hybrid Ligands with a *trans*-1,2-Diaminocyclohexane Backbone: Competing Chelation Modes in Palladium-Catalyzed Enantioselective Allylic Alkylation

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Three new hybrid ligands with *trans*-1,2-diaminocyclohexane backbone have been synthesized from (1*R*,2*R*)-2-aminocyclohexylcarbamic acid *tert*-butyl ester (**4**), which is prepared through an indirect monoprotection of the diamine. The ligands are (1*R*,2*R*)-*N*-{2-[2-(dimethylamino)benzoyl]amino}-cyclohexyl-2-(diphenylphosphanyl)benzamide and its di-*n*-butylamino- and diphenylamino-derivatives (**3a**−**c**), which belong to formal *P*,*N*-type chelates with possible wide bite angles in the metal chelation. To evaluate the new hybrid ligands against well-known *P*,*N*- and *P*,*P*-chelates (**1** and **2**), they were employed in the palladium-catalyzed allylic alkylations between two standard racemic allylic acetates, 2-acetoxy-1,3-diphenyl-2-propene (**14a**) and 2-acetoxy-1,3-dimethyl-2-propene (**14b**), and dimethyl malonate under different reaction conditions. The catalytic system with the new ligands showed good reactivity toward both the substrates with moderate enantioselectivities (up to 78% ee toward **14a** and 80% ee toward **14b**). Of particular note, dramatic changes in the sense and in the degree of the enantioselectivity were observed depending on the ligands and reaction conditions, which suggested a different chelation mode was competing with the supposed *P*,*N*-chelation mode. An X-ray crystal structure of a chelated palladium complex [Pd(**3c**)(η^3-PhCHCHCHPh)]PF_6 was obtained, which showed a *P*,*O*-chelation mode in which a carboxamide oxygen acted as the *O*-ligand. This is the first example of the enantioselective palladium-catalyzed allylic alkylation in which a *P*,*O*-chelated complex of a carboxamide group participated as the ligand group.

Introduction

The enantioselective palladium-catalyzed allylic alkylation is a useful asymmetric C−C bond forming reaction. To achieve high enantioselectivity in the catalytic reaction, a variety of chiral ligands have been studied.[1] By choosing proper chiral ligands, now we can transform certain types of racemic substrates into chiral ones with excellent enantioselectivities. However, the search for new chiral ligands is still demanded to extend a rather narrower scope of substrates useful in the catalytic reaction. In the course of our study to develop new *P*,*N*-chelates,[2] we were interested in those *P*,*N*-chelates that would exhibit wide bite angles in the metal chelation. *P*,*N*-Chelates such as **1** and analogues have been demonstrated to be useful in several transition metal-catalyzed asymmetric reactions.[3] Ligands **1** show bite angles of around 95° in their chelated (π-allyl)Pd complexes. *P*,*N*-Chelates with larger bite angles than those of ligands **1** may exhibit interesting catalytic behavior. Examples of such ligands are limited,[4] although several flexible *P*,*N*-chelates are known.[5] To endow a *P*,*N*-chelate with a large bite angle in the metal chelation, we decided to synthesize a *P*,*N*-hybrid analogue of Trost's *P*,*P*-chelate **2**. 1,2-Diaminocyclohexane-based *P*,*P*-chelate **2** and its analogues show large bite angles in the palladium chelation, and they have been successfully employed in

(1) For recent reviews, see: (a) Frost, C. G.; Howarth, J.; Williams, J. M. J. *Tetrahedron: Asymmetry*, **1992**, *3*, 1089. (b) Hayashi, T. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH: New York, 1993; Vol. 1, p 325. (c) Trost, B. M.; Van Vranken, D. L. *Chem. Rev.* **1996**, *96*, 395.

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(3) Pd-catalyzed allylic substitutions: (a) von Matt, P.; Pfaltz, A. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 566. (b) Dawson, G. J.; Frost, C. G.; Williams, J. M. J.; Coote, S. J. *Tetrahedron Lett.* **1993**, *34*, 3149. (c) Sprinz, J.; Helmchen, G. *Tetrahedron Lett.* **1993**, *34*, 1769. For reviews, see: (d) Pfaltz, A. *Acta Chem. Scand. B*, **1996**, *50*, 189. (e) Williams, J. M. J. *Synlett*, **1996**, 705. (f) Kudis, S.; Sennhenn, P.; Steinhagen, H.; Helmchen, G. *Pure Appl. Chem.* **1997**, *69*, 513. Heck reactions: (g) Loiseleur, O.; Meier, P.; Pfaltz, A. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 200. (h) Loiseleur, O.; Hayashi, M.; Schmees, N.; Pfaltz, A. *Synthesis*, **1997**, 1338. Ru-catalyzed transfer hydrogenation of ketones: (i) Langer, T.; Helmchen, G. *Tetrahedron Lett.* **1996**, *37*, 1381. (j) Sammakia, T.; Stangeland, E. L. *J. Org. Chem.* **1997**, *62*, 6104. Ir-catalyzed hydrogenation of olefins and imines: (k) Lightfoot, A.; Schnider, P.; Pfaltz, A. *Angew. Chem., Int. Ed.* **1998**, *37*, 2897. (l) Schnider, P.; Koch, G.; Prétôt, R.; Wang, G.; Bohnen, F. M.; Krüger, C.; Pfaltz, A. *Chem. Eur. J.* **1997**, *3*, 887. Rh-catalyzed hydrosilylation of ketones: (m) Newman, L. M.; Williams, J. M. J.; McCague, R.; Potter, G. A. *Tetrahedron: Asymmetry* **1996**, *7*, 1597. (n) Langer, T.; Janssen, J.; Helmchen, G. *Tetrahedron: Asymmetry*, **1996**, *7*, 1599. (o) Sudo, A.; Yoshida, H.; Saigo, K. *Tetrahedron: Asymmetry* **1997**, *8*, 3205. Ir-catalyzed hydrosilylation of ketones: (p) Nishibayashi, Y.; Segawa, K.; Takada, H.; Ohe, K.; Uemura, S. *Chem. Commun.* **1996**, 847. (q) Nishibayashi, Y.; Segawa, K.; Ohe, K.; Uemura, S. *Organometallics* **1995**, *14*, 5486.

(4) (a) Hu, X.; Chen, H.; Zhang, X. *Angew. Chem., Int. Ed.* **1999**, *38*, 3518. (b) A *P*,*N*-ligand having 1,2-diaminocyclohexane skeleton has been appeared in a literature but with little information on its preparation and ligand behavior. See: Trost, B. M.; Hachiya, I. *J. Am. Chem. Soc.* **1998**, *120*, 1104. (c) Gilbertson, S. R.; Xie, D. *Angew. Chem., Int. Ed.* **1999**, *38*, 2750. The ligands in this paper are rigid *P*,*N*-chelates; however, the metal bite angle is not known.

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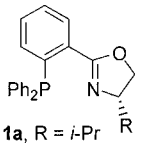
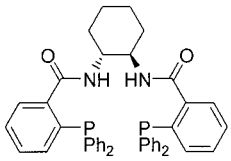
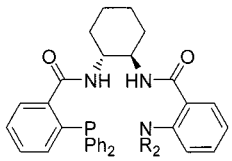
various enantioselective allylic alkylations.[6,7] New *P,N*-chelates **3** may be readily obtained by replacing one of the two *P*-ligands in **2** with an *N*-ligand. The new ligand system is expected to show catalytic activity and enantioselectivity different from those of *P,P*-chelate **2**, possibly owing to the *trans influence*[8] observable by *P,N*-chelates. Herein, we report the synthesis of ligands **3** which belong to formal *P,N*-type ligands and their application to the Pd-catalyzed allylic alkylations.



1a, R = *i*-Pr
1b, R = *t*-Bu
1c, R = Ph



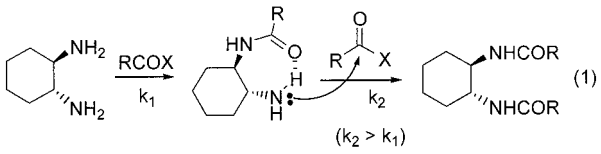
2



3a, R = Me
3b, R = *n*-Bu
3c, R = Ph

Results and Discussion

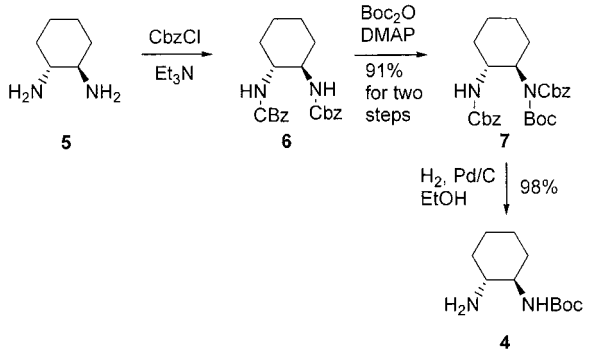
Synthesis of Ligands 3. To synthesize hybrid ligands **3**, monoacylation of 1,2-diaminocyclohexane is required. Treatment of 1,2-diaminocyclohexane with an equimolar amount of a carboxylic acid chloride such as benzoyl chloride produced the corresponding diacylated product predominantly. Attempt at the monoprotection with carbobenzyloxychloride (CbzCl) also gave the corresponding bis(carbobenzyloxycarbamate) as the major product. These results reassure that the corresponding monoacylated intermediates are much more reactive than the parent diamine. This increased reactivity has been ascribed to a general base catalysis through intramolecular hydrogen bonding by the acylamino group (eq 1).[9]



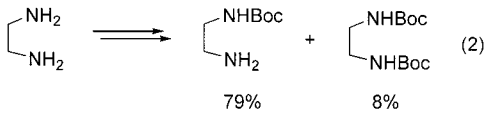
(1)

To synthesize a monoprotected derivative such as **4**, we have devised an indirect approach, as depicted in Scheme 1. 1,2-Diaminocyclohexane was first subjected to diprotection with CbzCl to give compound **6** and then from which monoprotection with di-*tert*-butyl dicarbonate (Boc_2O) was studied. Gratifyingly, in this case monoprotected product **7** was obtained in good yields. Interestingly, use of 2 mol equiv of Boc_2O gave a higher yield than the case of an equimolar reaction. Hydrogenolysis of both Cbz-groups of **7** afforded the desired compound **4** in overall 89% yield for three steps. This indirect method can be used for other 1,2-diamines such as 1,2-ethylenediamine, for which 79% mono- and 8% diprotected products can be isolated after column chromatography, using an equimolar amount of Boc_2O in this case (eq 2).[10]

Scheme 1



5 **6** **7** **4**



(2)

As the *N*-component of ligands **3**, three 2-carboxyaniline derivatives were chosen: *N,N*-dimethyl-, *N,N*-di-*n*-butyl-, and *N,N*-diphenylanilines. *N,N*-Dialkylanilines **8a** and **8b** can be synthesized from 2-carboxyaniline through a reductive amination.[11] In the case of dibutylaniline **8b**, the conversion was low (25% yield, along with a comparable amount of mono-*N*-butyl analogue), possibly due to steric hindrance. Other reductive amination methods using $NaBH_4$ or $NaBH_4-H_2SO_4$[12] gave little or moderate yields of the monoalkylated product only. Diphenylaniline **8c** can be readily synthesized from 2-bromobenzoic acid via a copper-mediated substitution reaction with diphenylamine.[13] 2-Diphenylphosphanylbenzoic acid **9** can be prepared in good yield from methyl

(5) For chiral *P,N*-chelates with flexible metal bite angles, see: (a) ref 2d. (b) Zhang, W.; Yoneda, Y.; Kida, T.; Nakatsuji, Y.; Ikeda, I. *Tetrahedron: Asymmetry* **1998**, *9*, 3371. (c) Imai, Y.; Zhang, W.; Kida, T.; Nakatsuji, Y.; Ikeda, I.; *Tetrahedron Lett.* **1998**, *39*, 4343. (d) Ogasawara, M.; Yoshida, K.; Kamei, H.; Kato, K.; Uozumi, Y.; Hayashi, T. *Tetrahedron: Asymmetry* **1998**, *9*, 1779. (e) Vyskočil, Š.; Smrčina, M.; Hanuš, V.; Polášek, M.; Kočovský, *J. Org. Chem.* **1998**, *63*, 7738.

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(7) For other chiral *P,P*-chelates with relatively large bite angles that have been used in the Pd-catalyzed allylic alkylation, see: (a) Dierkes, P.; Ramdeehul, S.; Barloy, L.; De Cian, A.; Fischer, J.; Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Osborn, J. A. *Angew. Chem., Int. Ed.* **1998**, *37*, 3116. (b) Saitoh, A.; Misawa, M.; Morimoto, T. *Tetrahedron: Asymmetry* **1999**, *10*, 1025. (s) Lee, S.-g.; Lim, C. W.; Song, C. E.; Kim, K. M.; Jun, C. H. *J. Org. Chem.* **1999**, *64*, 4445. The ligands in this paper belong to formal *P,P*-chelates but they seem to act as *P,N*-chelates.

(8) For a review, see: Appleton, T. G.; Clark, H. C.; Manzer, L. E.; *Coord. Chem. Rev.* **1973**, *10*, 335.

(9) Xu, D.; Prasad, K.; Repic, O.; Blacklock, T. *Tetrahedron Lett.* **1995**, *36*, 7357.

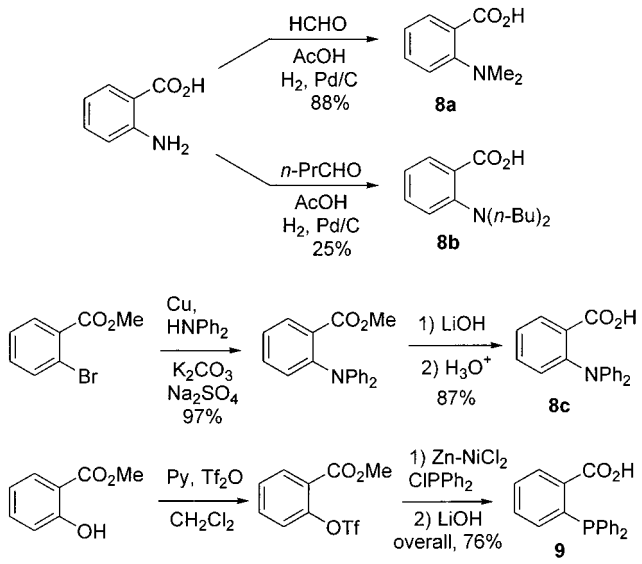
(10) For other approaches to the monoacylation of diamines, see: (a) Stahl, G. L.; Walter, R.; Smith, C. W. *J. Org. Chem.* **1978**, *43*, 2286. (b) ref 9. (c) Wang, T.; Zhang, Z.; Meanwell, N. A. *Tetrahedron Lett.* **1999**, *40*, 6745 and references therein.

(11) Green, P. N.; Young, J. R. A.; Doherty, J. (Ward, Blenkinsop and Co. Ltd.) GB-A 1547919, 1979. [*Chem. Abstr.* **1979**, *92*, 23535].

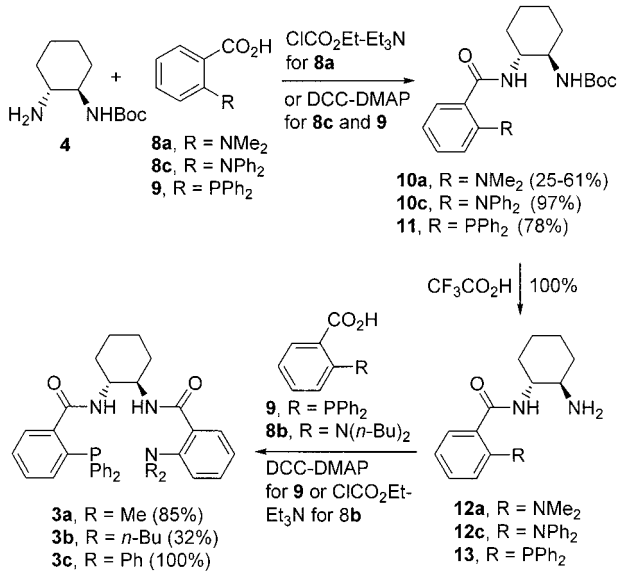
(12) Vyskočil, Š.; Jaracz, S.; Smrčina, M.; Štícha, M.; Hanuš, V.; Polášek, M.; Kočovský, *J. Org. Chem.* **1998**, *63*, 7727.

(13) Gilman, H.; McCracken, R. *Organic Syntheses*; Wiley: New York, 1941; Collect. Vol. I, p 544.

Scheme 2



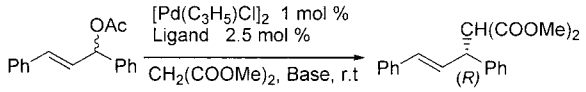
Scheme 3



2-hydroxybenzoate according to the literature procedure (Scheme 2).[14]

For the synthesis of *P*,*N*-hybrid ligands **3**, two standard coupling reactions, a mixed anhydride and dicyclohexylcarbodiimide−4-(dimethylamino)pyridine (DCC−DMAP) methods, were used to introduce the *N*- and *P*-ligand. In the case of acid **8a**, the amide formation with amine **4** can be done by the mixed anhydride method, giving **10a** in variable yields (25−61%) depending on reaction conditions (Scheme 3). In the cases of acids **8c** and **9**, however, the coupling reaction can be done in high yields using DCC−DMAP method, producing the corresponding amide products **10c** and **11** in 97% and 78% yields, respectively. Deprotection of the Boc group of amides **10** and **11** with CF_3CO_2H gave amines **12** and **13** in quantitative yields in all cases. Finally, the subsequent coupling of amines **12a** and **12c** with acid **9** by DCC−DMAP method produced desired ligands **3a** and **3c** in 85% and quantitative yields, respectively. Similarly, the coupling reaction between amine **13** and acid **8b** by the mixed anhydride method gave **3b** in 32% yield. In this case, reversal of the coupling sequence, that is, *N*-ligand formation followed by *P*-ligand coupling, resulted in a poor yield.

Table 1. Pd-Catalyzed Enantioselective Allylic Alkylation of Acetate 14a Using Ligands 3 and 11



entry	ligand	time, h	base	solvent	yield, %[a]	ee (%)[b]
1	**3a**	72	BSA, KOAc	CH_2Cl_2	33	47
2	**3b**	8	BSA, KOAc	CH_2Cl_2	>91	65 (*S*)
3	**3c**	6	BSA, KOAc	CH_2Cl_2	97	69 (*S*)
4	**3a**	24	NaH	THF	89	61
5	**3b**	24	NaH	THF	67	50
6	**3c**	8	NaH	THF	96	57
7	**3a**	24	Cs_2CO_3	CH_2Cl_2	73	78
8	**3b**	24	Cs_2CO_3	CH_2Cl_2	17	54
9	**3c**	24	Cs_2CO_3	CH_2Cl_2	25	25 (*S*)
10	**3a**	48	Cs_2CO_3	CH_3CN	92	17
11	**3a**	48	Cs_2CO_3	$Cl(CH_2)_2Cl$	20	36
12	**11**	19	BSA, KOAc	CH_2Cl_2	97	47 (*S*)

[a] Isolated yield. [b] Determined by HPLC (Chiralcel OD column).

Asymmetric Pd-Catalyzed Allylic Alkylations with Ligands 3. To evaluate new hybrid ligands **3** against the established *P*,*N*-chelates **1** and *P*,*P*-chelate **2**, we studied the palladium-catalyzed asymmetric allylic alkylation with the ligands. Two typical racemic allylic substrates, 2-acetoxy-1,3-diphenyl-2-propene (**14a**) and 2-acetoxy-1,3-dimethyl-2-propene (**14b**), and a standard nucleophile, dimethyl malonate, were chosen. In the case of allyl acetate **14a**, generally excellent enantioselectivities are observed in the catalytic reaction with *P*,*N*-chelates **1** and analogous ligands, whereas in the case of allyl acetate **14b** generally poor to moderate enantioselectivities are observed with the same ligands.[3a] An opposite situation is observed with *P*,*P*-chelate **2** toward the two substrates: over 90% ee has been achieved in the case of allyl acetate **14b**, whereas little reaction proceeded in the case of **14a**.[6b] Therefore, examination of the catalytic reaction with ligands **3** toward the two substrates would characterize their ligand properties.

Table 1 summarizes the enantioselectivities observed with the new catalytic system toward allyl acetate **14a** under several reaction conditions. Depending on the ligands and reaction conditions, dramatic changes in the enantioselectivity were observed. Notably, the catalytic system showed good reactivity toward the substrate, producing the substitution product in up to 97% yield. As mentioned previously, the catalytic system of *P*,*P*-chelate **2** is ineffective toward substrate **14a**. The observed reactivity in our case may be ascribed to the trans influence resulting from a *P*,*N*-chelation mode. Surprisingly, the three ligands **3a**−**c** exhibited different sense of enantioselection under the same reaction conditions. The catalytic reaction with ligand **3a** gave the product of (*R*)-configuration in 47% ee under the condition of *N*,*O*-bis(trimethylsilyl)acetamide (BSA)−KOAc/CH_2Cl_2,[15] whereas those with ligands **3b** and **3c** gave the (*S*)-isomer in 65% and 68% ee, respectively. The sense of enantioselectivity was also dependent on the reaction conditions. Under the condition of NaH/THF, only the (*R*)-isomer was observed in all cases; however, under the other two

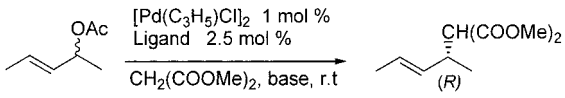
(14) Ager, D. J.; East, M. B.; Eisenstadt, A.; Laneman, S. A. *Chem. Commun.* **1997**, 2359.

(15) Trost, B. M.; Murphy, D. J. *Organometallics* **1985**, *4*, 1143.

conditions, both isomers were obtained, with a large fluctuation in the enantioselectivity. These results indicate that different chelation modes may operate depending on the ligands. Trost and co-workers noted that *P,O*-chelation could possibly compete with *P,P*-chelation in the case of ligand **2**.[16] In our case, it seems that there is more significant competition between *O*-ligation and *N*-ligation in the metal chelation. When partially acylated compound **11** that has no amine nitrogen was used as the ligand, the catalytic reaction also gave the substitution product of (*S*)-isomer with 47% ee and 97% yield (Table 1, entry 12). In this case, it is likely that the carboxamide oxygen participates as the ligand in the catalytic reaction. A similar *P,O*-chelation mode may be expected in the case of ligands **3**.

To get additional insight on the binding mode, we carried out an X-ray crystallography on a key reaction intermediate, a (π-allyl)Pd complex composed of ligand **3c**. The crystal structure unambiguously shows that ligand **3c** chelates the (π-allyl)Pd in the *P,O*-chelation mode (Figure 1, Supporting Information).[17] During our study, Lloyd-Jones and co-workers reported an X-ray crystal structure of a *P,O*-chelated (π-allyl)Pd complex that contains *P,P*-chelate **2**. The *P,O*-complexation mode was also observed in solution.[18] In the case of ligand **3c**, a carboxamide oxygen, instead of the diphenylamino nitrogen, coordinates the (π-allyl)palladium in the solid state, making a six-membered ring structure with bite angle of 89.2°. The diphenylallyl moiety has a *syn,syn*-conformation and adopts an *endo* form with respect to the cyclohexane moiety, as similarly observed in the case of palladium complexes of *P,N*-ligand **1**.[19] The length of the Pd−C bond that is *trans* to *P* is 2.20 Å, and that of the Pd−C bond which is *trans* to *O* is 2.07. If the reaction proceeds via the *P,O*-chelated complex, the malonate nucleophile would attack at the carbon that is *trans* to *P*,[19a,20] producing (*R*)-isomer. However, the opposite isomer was observed as the major product, which suggested that other factors were involved in the course of stereodifferentiation. Among plausible factors, relative reactivity of the *P,O*- and *P,N*-chelated complexes should be considered. In addition, intramolecular hydrogen bonding between the amidic proton and the nearby amine nitrogen may also influence the chelation mode. ^{1}H NMR study on the **3c**·(π-allyl)Pd complex showed a small downfield shift ($\Delta\delta$ = 0.02 ppm) of the amidic proton near the *P*-ligand. The shift was not changed at different concentrations, which suggests that it is caused by the *P,O*-chelation, not by intermolecular ligand association.[21] Although a *P,O*-chelated complex is apparently involved in the catalytic reactions, its relative stability and reactivity compared to other chelation modes including *P,N*-mode have to be assessed for further interpretation of the stereochemical results.[22]

Table 2. Pd-Catalyzed Enantioselective Allylic Alkylation of Acetate 14b Using Ligands



entry	ligand	time (day)	base	solvent	yield[a]	ee (%)[b]
1	**3a**	3	BSA, KOAc	CH_2Cl_2	67	59
2	**3b**	2	BSA, KOAc	CH_2Cl_2	24	80
3	**3a**	1	NaH	THF	41	61
4	**3b**	1	NaH	THF	17	43
5	**3c**	10 h	NaH	THF	40	61
6	**3a**	3	Cs_2CO_3	CH_2Cl_2	79	46
7	**3b**	6	Cs_2CO_3	CH_2Cl_2	4	−
8	**3a**	3	Cs_2CO_3	CH_3CN	−	−

[a] Isolated yield. [b] Determined by NMR using Eu[(+)-hfc]3 in $CDCl_3$. The relative configuration was assigned based on the optical rotation of literature.

In contrast to the case of 1,3-diphenylallyl acetate, in the case of 1,3-dimethylallyl acetate all the three ligands exhibited the same sense of enantioselection under several reaction conditions studied. Table 2 summarizes the results. The observed enantioselectivities are in the range of 43−80% ee, which are significantly lower than those observed with *P,N*-chelate **2**.[3a] The sense of enantioselection and low enantioselectivities observed may also be attributed to competition of the *P,O*-chelation mode, in which less efficient chiral environment is expected: In this mode, only one of the two chiral centers of the cyclohexanediamine moiety is likely to exert significant chiral influence over the allylic carbons because the other is remote from the reaction sites.

Conclusions

We have synthesized new hybrid ligands via a monoprotected 1,2-cyclohexanediamine, which is prepared

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(17) Crystal data for [Pd(**3c**)(η^3-PhCHCHCHPh)]PF_6 (from ethanol/ether): $C_{59}H_{53}F_6N_3O_2P_2Pd$, M = 1118.38, monoclinic, space group $P2_1$, a = 9.5367(6) Å, b = 22.1025(14) Å, c = 15.4026(10) Å, α = 90°, β = 91.7720(10)°, γ = 90°, V = 3245.1(4) Å^3, Z = 2, T = 213(2) K, D_c = 1.145 mg/cm^3, μ = 0.390 mm^{-1}, F(000) = 1148, crystal size = 0.30 × 0.30 × 0.08 mm, Siemens SMART CCCD diffractometer, Mo−Kα radiation, 13374 reflections collected, 9417 independent reflections, R1 = 0.1229, wR2 = 0.2968 [$I > 2\sigma(I)$], R1 = 0.1730, wR2 = 0.3336 (all data), GOF = 1.201. For structural data, see the Supporting Information.

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(21) $\Delta\delta = \delta$ (ligand−Pd complex) − δ (free ligand) = 6.52 ppm − 6.50 ppm. Determined at 0.015−0.04 M solution in $CDCl_3$ at 25 °C. We have also studied the coordination mode in solution by IR spectroscopy, which showed small changes in amidic $\nu_{C=O}$ depending on the species: (i) free ligand **3c** in THF, 1660.1 cm^{-1}; (ii) [Pd(**3c**)(η^3-PhCHCHCHPh)]PF_6 in THF prepared by mixing ligand **3c**, [Pd(η^3-PhCHCHCHPh)Cl]$_2$, and $AgPF_6$ in a molar ratio of 1:0.5:1, 1662.4 cm^{-1} (in this case, a shoulder peak at 1650.6 cm^{-1} was separately observed); (iii) [Pd(**3c**)(η^3-PhCHCHCHPh)]PF_6 and NaH (1.2 mol equiv) in THF, 1658.5 cm^{-1}. Other bands except amide II band around 1530 cm^{-1} showed little changes. Although these experiments suggest that amidic *N*-coordination may intervene under the condition of NaH in THF, as suggested by a reviewer, a further systematic study with a simple monocarboxamide ligand is necessary to address such competing coordination modes in solution.

(22) For example, steric hindrance in the vicinity of the ligating nitrogen atom seems to be more significant in the case of ligand **3c** than the case of ligand **3a**; hence, the *P,N*-chelation mode is disfavored in the case of ligand **3c** compared to the case of ligand **3a**. However, if we invoke the steric-strain reactivity argument, that is, more strained (π-allyl)Pd complexes are more reactive than less strained ones, due to their tendency to release steric strain,[20c] we may also explain the observed enantioselectivity with ligand **3c** by the *P,N*-chelation mode.

through a selective monoprotection route. The new ligands belong to formal *P*,*N*-type chelates with possible wide bite angles in the metal chelation. The hybrid ligands were employed in the palladium-catalyzed allylic alkylation between two standard allylic acetates and a malonate nucleophile under several reaction conditions. The ligands behaved differently from the well-known *P*,*P*-chelates and *P*,*N*-chelates in the sense and in the degree of enantioselectivity. The results are explained by the competing chelation mode between *P*,*O*- and *P*,*N*-chelation. An X-ray crystal structure of a (π-allyl)Pd complex is obtained, which unambiguously shows the *P*,*O*-chelation mode in which a carboxamide oxygen act as the *O*-ligand. A further mechanistic study is underway along with the development of a new ligand system that may suppress the competing *O*-ligation mode.

Experimental Section

General. Column chromatography was carried out on Merck silica gel 60, 230−400 mesh ASTM. All reactions were monitored by TLC Merck 60 F_{254} precoated silica gel plate. Melting points were uncorrected. Specific rotations ($[\alpha]_D$) are reported in degrees per decimeter at room temperature, and the concentration (*c*) is given in grams per 100 mL in the specific solvent. HRMS and Elemental analyses were performed at the Inter-University Center of National Science Research Facilities in Seoul National University. Solvent such as CH_2Cl_2, THF, or DMF was purified according to standard procedures before use.

(1*R*,2*R*)-[1,2-Bis(benzyloxycarbonylamino)cyclohexyl]-carbamic Acid *tert*-Butyl Ester (7). To a mixture of (1*R*,2*R*)-1,2-diaminocyclohexane (1.92 g, 16.8 mmol) and benzyloxycarbonyl chloride (5.76 mL, 40.4 mmol) in CH_2Cl_2 (30 mL) at 0 °C was added triethylamine (7.0 mL, 50.4 mmol) dropwise under argon atmosphere. The reaction mixture was stirred for 15 min at the same temperature, and it was allowed to warm to room temperature and stirred for an additional 2 h. Then, the reaction mixture was diluted with CH_2Cl_2 and washed with brine. The organic phase was dried and concentrated to give Cbz-protected compound **6** as a white solid, which was subjected to the next step without further purification.

To a solution of **6** in THF (50 mL) was added *N*,*N*-dimethyl-4-aminopyridine (411 mg, 3.36 mmol) followed by di-*tert*-butyl dicarbonate (7.34 g, 33.6 mmol), and the mixture was stirred at room temperature for 1 day. Extractive workup with EtOAc and purification by column chromatography (hexane:EtOAc, 19:1 → 9:1) afforded **7** (7.38 g, 91%) as a colorless oil. R_f = 0.45 (hexane:EtOAc, 4:1); mp 155−158 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.12−1.37 (m, 4H), 1.38 (s, 9H), 1.66−1.84 (m, 2H), 2.00−2.16 (m, 2H), 3.87−3.97 (m, 1H), 4.06−4.15 (m, 1H), 4.82 (d, J = 8.9 Hz, 1H), 4.99−5.18 (m, 4H), 7.25−7.36 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.1, 137.1, 135.8, 128.9, 128.8, 128.7, 128.3, 83.5, 69.0, 66.7, 61.1, 52.2, 34.5, 30.3, 28.2, 26.1, 25.1.

(1*R*,2*R*)-2-Aminocyclohexylcarbamic Acid *tert*-Butyl Ester (4). A solution of **7** (2.30 g, 4.77 mmol) in ethanol (30 mL) was subjected to hydrogenolysis in the presence of 10 wt % Pd/C (500 mg) under hydrogen atmosphere (about 1 atm) at room temperature for 2 h. The reaction mixture was filtered through Celite, and the filtrate was concentrated to give **4** (1.16 g, 98%) as a white solid. A small portion of **4** was recrystallized from CH_2Cl_2−hexane to give an analytically pure sample as a white crystal: mp 114−115 °C; ^{1}H NMR (300 MHz, CD_3OD) δ 1.15−1.39 (m, 4H), 1.45 (s, 9H), 1.65−1.72 (m, 2H), 1.85−1.94 (m, 2H), 2.36−2.42 (m, 1H), 3.06−3.09 (m, 1H); ^{13}C NMR (75 MHz, CD_3OD) δ 157.4, 78.9, 57.1, 54.4, 33.9, 32.6, 27.9, 25.3, 25.1.

2-Dimethylaminobenzoic Acid (8a). To a stainless steel reactor with a magnetic stirring bar were added anthranilic acid (2.1 g, 15 mmol), 37% formaldehyde (6.7 mL, 90 mmol), acetic acid (1.7 mL, 30 mmol), and 10 wt % Pd/C (200 mg) sequentially. The reactor was sealed and charged with hydrogen gas at 100 psi, and it was heated to 100 °C for 1 day with gentle stirring. After being cooled to room temperature, the reaction mixture was filtered through Celite and concentrated. The residue was diluted with CH_2Cl_2 and poured into saturated aqueous $NaHCO_3$ solution. Extractive workup and purification by column chromatography (CH_2Cl_2:MeOH, 9:1) afforded **8a** (2.19 g, 88%) as a white solid: R_f = 0.6 (CH_2Cl_2:MeOH, 8:2); mp 63−65 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.81 (s, 6H), 7.39−7.47 (m, 2H), 7.56−7.59 (m, 1H), 8.27 (dd, J = 1.6, 7.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.0, 152.0, 134.5, 132.5, 128.2, 125.4, 122.2, 46.1.

2-Di-*n*-butylaminobenzoic Acid (8b). This compound was obtained similarly as above through reductive amination of anthranilic acid (1.37 g, 10 mmol) with *n*-butyraldehyde (9 mL, 100 mmol) in 25% yield (613 mg) as a green solid: R_f = 0.3 (EtOAc:hexane, 6:4); mp 46−47.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.82 (t, J = 6.9 Hz, 6H), 1.22−1.32 (m, 6H), 1.50−1.55 (m, 2H), 3.0 (br d, J = 24.5 Hz, 4H), 7.33−7.41 (m, 2H), 7.54−7.60 (m, 1H), 8.29 (dd, J = 1.6, 7.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.5, 148.9, 134.3, 132.3, 128.3, 128.1, 122.8, 57.7, 29.1, 20.9, 14.3.

2-Diphenylaminobenzoic Acid (8c). To a stirred solution of diphenylamine (372 mg, 2.2 mmol), K_2CO_3 (304 mg, 2.2 mmol), Na_2SO_4 (312 mg, 2.2 mmol), and copper powder (13 mg, 0.2 mmol) in nitrobenzene (3 mL) at room temperature was added methyl 2-bromobenzoate (430 mg, 2 mmol) under argon atmosphere, and the resulting mixture was heated to 220 °C for 1 day. After being cooled to room temperature, nitrobenzene was removed by vacuum distillation. The residue was diluted with EtOAc and poured into a saturated aqueous NH_4Cl solution. Extractive workup and purification by column chromatography (hexane:EtOAc, 9:1) afforded methyl 2-diphenylaminobenzoate (587 mg, 97%) as a yellow solid: R_f = 0.45 (hexane:EtOAc, 9:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.4 (s, 3H), 6.93−7.09 (m, 6H), 7.15−7.24 (m, 6H), 7.40−7.45 (m, 1H), 7.68 (dd, J = 1.5, 7.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.3, 148.2, 147.0, 133.1, 131.7, 129.5, 129.4, 124.7, 124.0, 123.3, 122.7, 52.2.

To a stirred solution of methyl 2-diphenylaminobenzoate (570 mg, 1.87 mmol) in THF−water (1:1, 8 mL) was added lithium hydroxide hydrate (1.6 g, 37.4 mmol), and then the resulting mixture was heated to 70 °C for 1 day. After being cooled to room temperature, the reaction mixture was diluted with EtOAc and poured into a 10% aqueous citric acid solution. Extractive workup with EtOAc and purification by column chromatography (hexane:EtOAc, 9:1) afforded **8c** (470 mg, 87%) as a light green solid. R_f = 0.3 (hexane:EtOAc, 9:1); mp 187−188°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.80−6.99 (m, 6H), 7.08−7.20 (m, 6H), 7.39−7.45 (m, 1H), 7.85 (dd, J = 1.2, 7.7 Hz, 1H), 8.2−10.4 (br, 1H, observable on magnifying); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0, 148.3, 148.2, 134.4, 132.9, 130.5, 129.8, 128.3, 125.7, 123.6, 123.4.

Methyl 2-Trifluoromethanesulfonyloxybenzoate.[14] Pyridine (0.32 mL, 4.17 mmol) was added to a stirred solution of methyl salicylate (530 mg, 3.48 mmol) in CH_2Cl_2 (12 mL) at room temperature. After being stirred for 20 min, the reaction mixture was treated slowly with trifluoromethanesulfonic anhydride (0.72 mL, 4.52 mmol) at 0 °C, and then the resulting mixture was allowed to warm to room temperature over 1 h. After being diluted with water, the reaction mixture was subjected to a standard workup, followed by column chromatography (hexane:EtOAc, 9:1), to afford the product in 95% yield (943 mg) as a colorless oil. R_f = 0.35 (hexane:EtOAc, 9:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.99 (s, 3H), 7.33 (d, J = 8.2 Hz, 1H), 7.47−7.7.53 (m, 1H), 7.62−7.68 (m, 1H), 8.11 (dd, J = 1.8, 7.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.8, 149.0, 134.9, 133.4, 129.1, 125.8, 125.1, 123.4, 121.5, 117.3, 113.0, 53.3.

2-Diphenylphosphanylbenzoic Acid (9).[14] To a stirred solution of methyl 2-trifluoromethanesulfonyloxybenzoate (1.14 g, 4.0 mmol) and [1,2-bis(diphenylphosphino)ethane]dichloronickel(II) (116 mg, 0.20 mmol) in DMF (15 mL) was added chlorodiphenylphosphine (0.72 mL, 4.0 mmol) under argon atmosphere. To this mixture was added zinc dust (418 mg,

6.4 mmol) at 5−10°C, and then the resulting mixture was heated to 100−110 °C for 17 h. After being cooled to room temperature, the reaction mixture was diluted with ether and sequentially washed with 5% aqueous $Na_2S_2O_3$ solution, 10% citric acid solution, and saturated $NaHCO_3$ solution. The organic layer was dried, filtered, and concentrated. The residue was purified by column chromatography (hexane:EtOAc, 9:1) to afford methyl 2-diphenylphosphanylbenzoate (975 mg, 76%) as a white solid: $R_f = 0.30$ (hexane:EtOAc, 9:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.75 (s, 3H), 6.93−6.96 (m, 1H), 7.25−7.41 (m, 1H), 8.05−8.07 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.6, 141.1, 140.7, 138.4, 138.2, 134.8, 134.7, 134.4, 134.2, 132.4, 131.1, 129.1, 129.0, 128.9, 128.6, 52.5.

To a stirred solution of methyl 2-diphenylphosphanylbenzoate (1.45 g, 4.53 mmol) in THF−water (1:1, 16 mL) at room temperature was added lithium hydroxide hydrate (4.0 g, 90 mmol), and the resulting mixture was heated to 70 °C for 12 h. After being cooled to room temperature, the reaction mixture was diluted with EtOAc and poured into 10% citric acid solution. Extractive workup with EtOAc and purification by column chromatography (CH_2Cl_2:MeOH, 9:1) afforded **9** (1.6 g, 100%) as a white solid: $R_f = 0.1$ (hexane:EtOAc, 8:2); mp 165−167 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.96−6.99 (m, 1H), 7.25−7.43 (m, 12H), 8.15−8.17 (m 1H), 11.0−11.8 (br, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.1, 142.6, 142.3, 138.2, 138.0, 134.7, 134.6, 134.3, 133.1, 132.9, 132.2, 129.1, 128.9, 128.8, 128.6.

(1*R*,2*R*)-2-[*N*-(2-Dimethylamino)benzoylamino]cyclohexylcarbamic Acid *tert*-Butyl Ester (10a). To a stirred solution of 2-dimethylaminobenzoic acid **8a** (18 mg, 0.11 mmol) and triethylamine (0.018 mL, 0.143 mmol) in THF (0.5 mL) at −25 °C was added ethyl chloroformate (0.012 mL, 0.143 mmol) slowly under argon atmosphere. After being stirred for 30 min, the reaction mixture was treated with monoprotected amine **4** (21.4 mg, 0.10 mmol), and it was allowed to warm to room temperature over 12 h. The reaction mixture was diluted with EtOAc and poured into a saturated NH_4Cl solution. Extractive workup with EtOAc and purification by column chromatography (hexane:EtOAc, 9:1) afforded **10a** (22.2 mg, 61%) as a white solid: $R_f = 0.2$ (hexane:EtOAc, 8:2); mp 135−136 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.26 (s, 9H), 1.20−1.38 (m, 4H), 1.64−1.75 (m, 2H), 2.03−2.15 (m, 2H), 2.71 (s, 6H), 3.36−3.40 (m, 1H), 3.90−3.94 (m, 1H), 5.06 (d, $J = 8.1$ Hz, 1H), 7.11−7.18 (m, 2H), 7.35−7.41 (m, 1H), 8.05 (dd, $J = 1.6$, 7.6 Hz, 1H), 9.57 (d, $J = 8.4$ Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.6, 152.7, 147.5, 132.2, 131.7, 127.8, 124.2, 119.8, 79.3, 56.0, 52.5, 45.5, 33.7, 33.1, 28.6, 25.3, 25.2; HRMS (FAB)-calcd for $C_{20}H_{31}N_3O_3$ $(M + H)^+$ 362.2444, found 362.2443.

(1*R*,2*R*)-2-[*N*-(2-Diphenylamino)benzoylamino]cyclohexylcarbamic Acid *tert*-Butyl Ester (10c). To a stirred solution of 2-diphenylaminobenzoic acid **8c** (32 mg, 0.11 mmol) in CH_2Cl_2 (1.0 mL) were added dicyclohexylcarbodiimide (DCC, 23 mg, 0.11 mmol), monoprotected amine **4** (21.4 mg, 0.10 mmol), and DMAP (1.2 mg, 0.01 mmol) at 0 °C. The resulting mixture was allowed to warm to room temperature over 2 h, and it was diluted with CH_2Cl_2 and poured into saturated NH_4Cl solution. Extractive workup with CH_2Cl_2 and purification by column chromatography (hexane:EtOAc, 8:2) afforded **10c** (47 mg, 97%) as a white solid: $R_f = 0.2$ (hexane:EtOAc, 8:2); mp 73−74 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.62−0.73 (m, 1H), 1.08−1.25 (m, 3H), 1.33 (s, 9H), 1.31−1.63 (m, 3H), 1.94−1.98 (m, 1H), 3.20−3.25 (m, 1H), 3.49−3.54 (m, 1H), 4.72 (d, $J = 8.5$ Hz, 1H), 6.88−7.06 (m, 7H), 7.16−7.26 (m, 6H), 7.33−7.39 (m, 1H), 7.75 (d, $J = 7.6$ Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.0, 156.3, 147.7, 144.7, 133.1, 131.7, 130.4, 129.4, 129.1, 125.1, 122.7, 122.5, 79.1, 54.2, 33.9, 32.6, 31.8, 28.2, 24.8, 24.4; HRMS (FAB) calcd for $C_{30}H_{35}N_3O_3$ $(M + H)^+$ 486.2757, found 486.2676.

(1*R*,2*R*)-2-[*N*-(2-Diphenylphosphanyl)benzoylamino]cyclohexylcarbamic Acid *tert*-Butyl Ester (11). 9c was similarly synthesized as above by DCC-mediated coupling of monoprotected amine **4** (42.9 mg, 0.2 mmol) with 2-diphenylphosphanyl benzoic acid **9** (61.3 mg, 0.2 mmol) in 78% yield (78 mg) as a white solid: $R_f = 0.15$ (hexane:EtOAc, 8:2); mp 95−97 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.88−1.01 (m, 1H), 1.11−1.35 (m, 3H), 1.39 (s, 9H), 1.58−1.74 (m, 2H), 1.83−2.01 (m, 2H), 3.25−3.40 (m, 1H), 3.61−3.73 (m, 1H), 4.81 (d, $J = 8.5$ Hz, 1H), 6.42 (d, $J = 7.9$ Hz, 1H), 6.90−6.94 (m, 1H), 7.24−7.33 (m, 12H), 7.55−7.59 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.6, 157.3, 141.7, 141.3, 138.5, 137.7, 137.4, 134.9, 134.7, 134.4, 130.8, 129.2, 129.1, 129.0, 128.0, 80.1, 55.5, 54.7, 33.4, 32.8, 29.1, 25.6, 25.2; HRMS (FAB) calcd for $C_{30}H_{35}N_2O_3P$ $(M + H)^+$ 503.2464, found 503.2448.

(1*R*,2*R*)-*N*-(2-Amino)cyclohexyl-2-(dimethylamino)benzamide (12a). To a stirred solution of **10a** (275 mg, 0.76 mmol) in CH_2Cl_2 (2 mL) at 0 °C was added trifluoroacetic acid (1.2 mL, 15.2 mmol) under argon atmosphere. The reaction mixture was allowed to warm to room temperature for 12 h, and it was diluted with CH_2Cl_2 and poured into saturated $NaHCO_3$ solution. Extractive workup with CH_2Cl_2 and purification by column chromatography (CH_2Cl_2:MeOH, 9:1) afforded **12a** (201 mg, 100%) as a white solid: $R_f = 0.15$ (CH_2Cl_2:MeOH, 9:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.21−1.53 (m, 4H), 1.70−1.79 (m, 2H), 2.02−2.16 (m, 2H), 2.69 (s, 6H), 2.90−2.95 (m, 1H), 3.95−3.98 (m, 1H), 5.88 (br s, 2H), 7.09−7.26 (m, 2H), 7.36−7.42 (m, 1H), 8.00 (dd, $J = 1.3$, 7.8 Hz, 1H), 10.17 (d, $J = 7.9$ Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.2, 152.8, 132.7, 131.8, 127.2, 125.0, 120.6, 56.4, 53.4, 45.7, 32.2, 32.0, 24.8, 24.6.

(1*R*,2*R*)-*N*-(2-Amino)cyclohexyl-2-(diphenylamino)benzamide (12c). Similarly, deprotection of **10c** (640 mg, 1.32 mmol) with trifluoroacetic acid (2.03 mL, 26.4 mmol) gave **12c** in a quantitative yield (518 mg) as a pale yellow solid: $R_f = 0.2$ (CH_2Cl_2:MeOH, 9:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.84−0.96 (m, 1H), 1.11−1.30 (m, 3H), 1.55−1.80 (m, 3H), 1.89 (br s, 1H), 1.23 (br s, 1H), 2.48 (br s, 2H), 3.51−3.62 (m, 1H), 6.94−7.14 (m, 7H), 7.22−7.33 (m, 6H), 7.41−7.47 (m, 1H), 8.03 (dd, $J = 0.9$, 7.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.3, 147.4, 144.4, 132.4, 131.3, 130.3, 129.4, 126.2, 123.8, 122.9, 122.1, 55.6, 55.5, 33.9, 32.0, 24.8 (coincided two peaks).

(1*R*,2*R*)-*N*-(2-Amino)cyclohexyl-2-(diphenylphosphanyl)benzamide (13). Similarly, deprotection of **11** (326 mg, 0.65 mmol) with trifluoroacetic acid (0.5 mL, 6.48 mmol) gave **13** in a quantitative yield (260 mg) as a white solid: $R_f = 0.3$ (CH_2Cl_2:MeOH, 9:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.82−0.95 (m, 1H), 1.07−1.23 (m, 3H), 1.57−1.64 (m, 2H), 1.77−1.92 (m, 2H), 2.29−2.36 (m, 1H), 2.85 (br s, 2H), 3.56−3.68 (m, 1H), 6.09 (br s, 1H), 6.87−6.91 (m, 1H), 7.17−7.34 (m, 12H), 7.59−7.63 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.5, 141.3, 136.9, 134.2, 134.0, 133.9, 133.7, 133.6, 130.2, 129.0, 128.9, 128.8, 128.7, 128.6, 128.2, 56.0, 55.3, 33.9, 32.0, 24.8 (coincided two peaks).

(1*R*,2*R*)-*N*-{2-[2-(Dimethylamino)benzoyl]amino}cyclohexyl-2-(diphenylphosphanyl)benzamide (3a). According to the procedure of the synthesis of **10c**, **3a** was synthesized by DCC-mediated coupling of **12a** (24.7 mg, 0.10 mmol) with 2-diphenylphosphanylbenzoic acid **9** (32 mg, 0.11 mmol) in 85% yield (47 mg) as a white solid: $R_f = 0.2$ (hexane:EtOAc, 8:2); $[\alpha]^{28}_D$ +12.0 (*c* 1.17, $CHCl_3$); mp 90−92 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.99−1.11 (m, 1H), 1.22−1.43 (m, 3H), 1.65−1.77 (m, 2H), 1.87−2.08 (m, 2H), 2.68 (s, 6H), 3.72−3.84 (m, 1H), 3.95−4.05 (m, 1H), 6.84−6.92 (m, 2H), 7.12−7.31 (m, 14H), 7.37−7.44 (m, 1H), 8.07 (dd, $J = 1.7$, 7.8 Hz, 1H), 9.87 (d, $J = 8.4$ Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.2, 167.0, 152.1, 137.8, 137.6, 136.9, 136.5, 133.7, 133.5, 133.2, 131.6, 130.8, 129.5, 128.1, 128.0, 127.8, 127.7, 126.6, 126.6, 126.5, 123.7, 119.4, 55.1, 51.2, 44.8, 31.9, 31.7, 24.5, 24.0; ^{31}P NMR (121 MHz, $CDCl_3$) δ -6.267; HRMS (FAB) calcd for $C_{34}H_{36}N_3O_2P$ $(M + H)^+$ 550.2623, found 550.2615. Anal. Calcd for $C_{34}H_{36}N_3O_2P$: C, 74.30; H, 6.60; N, 7.65. Found: C, 74.06; H, 6.99; N, 7.69.

(1*R*,2*R*)-*N*-{2-[2-(Di-*n*-butylamino)benzoyl]amino}cyclohexyl-2-(diphenylphosphanyl)benzamide (3b). To a stirred solution of 2-di-*n*-butylaminobenzoic acid **8b** (27 mg, 0.11 mmol) and triethylamine (0.018 mL, 0.14 mmol) in THF (0.5 mL) at −10 °C was added ethyl chloroformate (0.013 mL, 0.14 mmol) slowly under argon atmosphere. After being stirred for 30 min, phosphino-acid **13** (40 mg, 0.10 mmol) was added to the reaction mixture at 0 °C, and then the resulting mixture was allowed to warm to room temperature over 12 h. The reaction mixture was subjected to a standard extraction with

EtOAc, followed by column chromatography (hexane:EtOAc, 8:2) to afford **3b** in 32% yield (20 mg) as a white solid: R_f = 0.15 (hexane:EtOAc, 8:2); $[\alpha]^{28}_D$ +41.7 (*c* 1.4, $CHCl_3$); mp 80−81 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.78 (t, *J* = 7.3 Hz, 6H), 0.91−1.26 (m, 5H), 1.30−1.39 (m, 7H), 1.60−1.80 (m, 2H), 2.01−2.06 (m, 2H), 2.93 (t, *J* = 7.6 Hz, 4H), 3.67−3.73 (m, 1H), 4.00−4.04 (m, 1H), 6.84−6.89 (m, 1H), 7.14−7.34 (m, 14H), 7.40−7.55 (m, 3H), 8.22 (dd, *J* = 1.7, 8.3 Hz, 1H), 10.70 (d, *J* = 8.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.0, 168.1, 151.1, 139.3, 139.0, 138.8, 138.2, 137.9, 134.8, 134.7, 134.4, 132.4, 131.9, 130.4, 129.4, 129.1, 129.0, 128.9, 128.8, 127.5, 125.5, 124.0, 57.2, 55.5, 52.1, 32.9, 32.7, 29.2, 25.8, 25.0, 21.2, 14.5; ^{31}P NMR (121 MHz, $CDCl_3$) δ -5.822; HRMS (FAB) calcd for $C_{40}H_{48}N_3O_2P$ $(M + H)^+$ 634.3562, found 634.3568. Anal. Calcd for $C_{40}H_{48}N_3O_2P$: C, 75.80; H, 7.63; N, 6.63. Found: C, 74.80; H, 7.87; N, 6.38.

(1*R*,2*R*)-*N*-{2-[2-(Diphenylamino)benzoyl]amino}cyclohexyl-2-(diphenylphosphanyl)benzamide (3c). Similarly as above, **3c** was synthesized by DCC-mediated coupling of **12b** (430 mg, 1.10 mmol) with 2-diphenylphosphanylbenzoic acid **9** (337 mg, 1.20 mmol) in a quantitative yield (673 mg) as a white solid: R_f = 0.5 (hexane:EtOAc, 6:4); $[\alpha]^{28}_D$ −9.3 (*c* 1.3, $CHCl_3$), mp 119−121 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.81−0.95 (m, 2H), 1.05−1.20 (m, 2H), 1.40−1.60 (m, 2H), 1.78−1.87 (m, 2H), 3.60−3.70 (m, 2H), 6.50 (d, *J* = 6.5 Hz, 1H), 6.90−7.45 (m, 28H), 7.75 (d, *J* = 7.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.5, 168.0, 148.2, 145.4, 141.7, 141.4, 138.6, 138.5, 138.4, 137.5, 137.2, 135.0, 134.6, 134.3, 133.7, 132.6, 131.3, 130.7, 130.4, 129.9, 129.3, 129.2, 129.1, 129.0, 128.0, 127.9, 126.3, 123.2, 55.0, 53.9, 32.5, 25.3, 25.1; ^{31}P NMR (121 MHz, $CDCl_3$) δ −6.8886; HRMS (FAB) calcd for $C_{44}H_{40}N_3O_2P$ $(M + H)^+$ 674.2936, found 674.2949. Anal. Calcd for $C_{44}H_{40}N_3O_2P$: C, 78.43; H, 5.98; N, 6.24. Found: C, 78.37; H, 5.98; N, 6.30.

General procedures for the Pd-Catalyzed Allylic Alkylations. Method A: A mixture of $[(\pi\text{-allyl})PdCl]_2$ (3.7 mg, 0.01 mmol) and one of chiral ligands **3** (0.025 mmol) in CH_2Cl_2 (1.7 mL) was stirred at room temperature for 30 min. To this Pd-catalyst were added allylic acetate **14a** or **14b** (1.0 mmol) in CH_2Cl_2 (1.7 mL), followed by dimethyl malonate (0.34 mL, 3.0 mmol), BSA [*N*,*O*-bis(trimethylsilyl)acetamide] (0.74 mL, 3.0 mmol), and KOAc (2.0 mg, 0.02 mmol) sequentially. After the reaction was complete (judging from TLC analysis) or after a certain time elapsed, the reaction mixture was diluted with CH_2Cl_2 and poured into cold saturated aqueous NH_4Cl solution. The organic layer was separated, dried over $MgSO_4$, and concentrated under a reduced pressure. The residue was purified by column chromatography (hexane:EtOAc, 8:1).

Method B: A mixture of $[(\pi\text{-allyl})PdCl]_2$ (3.7 mg, 0.01 mmol) and one of chiral ligands **3** (0.025 mmol) in THF (1.7 mL) was stirred at room temperature for 30 min. To this Pd-catalyst was added allyl acetate **14a** or **14b** (1 mmol) in THF (1.7 mL), followed by a THF (1 mL) solution of dimethyl malonate (0.23 mL, 2.0 mmol) and NaH (60% in mineral oil, 60 mg, 1.5 mmol) at room temperature. The extractive workup and purification procedures were followed as above.

Method C: A mixture of $[(\pi\text{-allyl})PdCl]_2$ (3.7 mg, 0.01 mmol) and one of chiral ligands **3** (0.025 mmol) in CH_2Cl_2 (1.7 mL) was stirred at room temperature for 30 min. To this Pd-catalyst was added the acetate (1 mmol) in CH_2Cl_2 (1.7 mL), followed by dimethyl malonate (0.23 mL, 2.0 mmol) and Cs_2CO_3 (489 mg, 1.5 mmol) sequentially. The extractive workup and purification procedures were followed as above.

Determination of Enantioselectivity of the Substitution Products. In the case of methyl 2-methoxycarbonyl-3,5-diphenyl-4-pentenoate, enantioselectivity was determined by HPLC analysis using a chiral column [Chiralcel OD; 25 cm × 0.46 cm; hexane:*i*-PrOH = 98:2; flow rate = 0.5 mL/min; t_R = 19.60 (*R*-isomer), 20.64 (*S*-isomer) min] or ^{1}H NMR analysis with a chiral shift reagent Eu(hfc)$_3$ (one of the two methyl ester groups that appear at 3.70 ppm was split into two peaks, for example, at 3.97 ppm (*R*-isomer) and 3.93 ppm (*S*-isomer) when 0.8 equiv of the shift reagent was added). Care must be exercised using the HPLC method, since racemic product tends to precipitate from hexane solutions, thus incidentally affording higher ee's than the actual ones. This spontaneous optical enrichment was not observed when the sample was handled in CH_2Cl_2. In the case of methyl 2-methoxycarbonyl-3-methyl-4-hexenoate, enantioselectivity was calculated by comparison of its specific rotation with literature value {$[\alpha]_D$ ±27.9 (*c* 1.1, $CHCl_3$)}.[23] The absolute stereochemistry of the products was assigned based on the optical rotation sign.[5e]

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Supporting Information Available: ^{1}H NMR spectra of all the compounds described in the Experimental Section and X-ray structural information on **3c**·[π-(1,3-diphenylallyl)Pd]-PF_6 (PDF) including an ORTEP plot (Figure 1). This material is available free of charge via the Internet at http://pubs.acs.org.

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