Palladium-Catalyzed Asymmetric Allylic Substitution Reactions Using New Chiral Phosphinite−Oxazoline Ligands Derived from D-Glucosamine

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Novel 2-alkyl- or 2-aryl-4,5-(4,6-*O*-benzylidene-3-*O*-(diphenylphosphino)-1,2-dideoxy-α-D-glucopyrano)-[2,1-*d*]-2-oxazolines (**5a**−**f**) have been prepared from D-glucosamine hydrochloride. They work effectively as chiral ligands and provide a high level of enantiomeric excess in palladium-catalyzed allylic alkylation and amination reactions. The allylic alkylation of 1,3-diphenyl-3-acetoxyprop-1-ene with dimethyl malonate proceeds smoothly in the presence of 0.25 mol % $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ and the chiral ligand **5a** having the smallest substituent on oxazoline at 0 °C within 6 h to furnish the highest enantiomeric excess (96% ee). The ligand **5a** is also effective for the Pd-catalyzed amination of ethyl 1,3-diphenylprop-2-enyl carbonate, leading to the corresponding allylic amine in 94% ee. The full scope and limitations using ligands **5a**−**f** in the allylic substitution reactions are described.

Introduction

Palladium-catalyzed allylic substitution reactions are known as an efficient synthetic tool for the construction of carbon−carbon and carbon−heteroatom bonds.[1] Various C_2- and C_1-symmetric bidentate chiral ligands have been applied to palladium-catalyzed allylic substitution reactions to provide high enantioselectivities.[1b] The chiral phosphine−oxazoline ligands were first developed by Pfaltz,[2] Helmchen,[3] and Williams[4] as effective non-C_2-symmetric ligands for these reactions. Other types of oxazoline ligands which have not only the central chirality but also the planar[5] or axial[6] chirality on the backbone of ligands have emerged for the past few years.

Recently, the carbohydrates such as D-glucose,[7] α,α-trehalose,[8] and D-glucosamine[7b,9] have attracted a great deal of interest in the synthesis of chiral ligands for the following reasons: (1) They exist widely in nature, and thus they are commercially available at a reasonable price. (2) These carbohydrates have many chiral centers and many hydroxy groups in their skeletons, and therefore the regio- and stereoselective introduction of functionality might be possible. Recently, a phosphine−oxazoline ligand having a sugar backbone has been reported by Kunz[9] as illustrated in Figure 1. In this ligand a phosphorus atom is attached to the aromatic ring in the 2-position of oxazoline. In most phosphine−oxazoline ligands a phosphorus atom is introduced to the alkyl chain[3a,10] or aromatic ring[2−4] in the 2-position of oxazoline. To prepare a chiral P−N ligand, an amino-sugar D-glucosamine having a nitrogen atom in its structure is suitable for the starting material. We have prepared new chiral ligands **5a**−**f** from the commercially available D-glucosamine (Figure 1). These ligands have

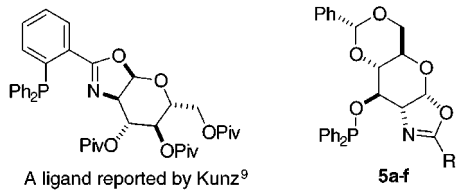

Figure 1.

(1) (a) Tsuji, J. *Palladium Reagents and Catalysis, Innovations in Organic Synthesis*; Wiley: New York, 1995. (b) Trost, B. M.; Van Vranken, D. L. *Chem. Rev.* **1996**, *96*, 395. (c) Johannsen, M.; Jørgensen, K. A. *Chem. Rev.* **1998**, *98*, 1689. (d) Hayashi, T. *J. Organomet. Chem.* **1999**, *576*, 195. (e) Helmchen, G. *J. Organomet. Chem.* **1999**, *576*, 203.

(2) (a) Von Matt, P.; Pfaltz, A. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 566. (b) Prétôt, R.; Pfaltz, A. *Angew. Chem., Int. Ed.* **1998**, *37*, 323.

(3) (a) Sprinz, J.; Helmchen, G. *Tetrahedron Lett.* **1993**, *34*, 1769. (b) Steinhagen, H.; Reggelin, M.; Helmchen, G. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2108.

(4) (a) Dawson, G. J.; Frost, C. G.; Williams, J. M. J. *Tetrahedron Lett.* **1993**, *34*, 3149. (b) Williams, J. M. J. *Synlett* **1993**, 509. (c) Bower, J. F.; Jumnah, R.; Williams, A. C.; Williams, J. M. J. *J. Chem. Soc., Perkin Trans. 1* **1997**, 1411.

(5) (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. (c) Sammakia, T.; Latham, H. A.; Schaad, D. R. *J. Org. Chem.* **1995**, *60*, 10. (d) Sammakia, T.; Latham, H. A. *J. Org. Chem.* **1996**, *61*, 1629. (e) Stangeland, E. L.; Sammakia, T. *Tetrahedron* **1997**, *53*, 16503. (f) Richards, C. J.; Damalidis, T.; Hibbs, D. E.; Hursthouse, M. B. *Synlett* **1995**, 74. (g) Richards, C. J.; Mulvaney, A. W. *Tetrahedron: Asymmetry* **1996**, *7*, 1419. (h) Park, J.; Lee, S.; Ahn, K. H.; Cho, C.-W. *Tetrahedron Lett.* **1995**, *36*, 7263. (i) Ahn, K. H.; Cho, C.-W.; Baek, H.-H.; Park, J.; Lee, S. *J. Org. Chem.* **1996**, *61*, 4937. (j) Zhang, W.; Adachi, Y.; Hirao, T.; Ikeda, I. *Tetrahedron: Asymmetry* **1996**, *7*, 451. (k) Zhang, W.; Hirao, T.; Ikeda, I. *Tetrahedron Lett.* **1996**, *37*, 4545. (l) Kudis, S.; Helmchen, G. *Angew. Chem., Int. Ed.* **1998**, *37*, 3047.

(6) (a) Imai, Y.; Zhang, W.; Kida, T.; Nakatsuji, Y.; Ikeda, I. *Tetrahedron Lett.* **1998**, *39*, 4343. (b) Ogasawara, M.; Yoshida, K.; Kamei, H.; Kato, K.; Uozumi, Y.; Hayashi, T. *Tetrahedron: Asymmetry* **1998**, *9*, 1779.

(7) (a) Nomura, N.; Mermet-Bouvier, Y. C.; RajanBabu, T. V. *Synlett* **1996**, 745. (b) RajanBabu, T. V.; Ayers, T. A.; Halliday, G. A.; You, K. K.; Calabrese, J. C. *J. Org. Chem.* **1997**, *62*, 6012. (c) Barbaro, P.; Currao, A.; Herrmann, J.; Nesper, R.; Pregosin, P. S.; Salzmann, R. *Organometallics* **1996**, *15*, 1879. (d) Albinati, A.; Pregosin, P. S.; Wick, K. *Organometallics* **1996**, *15*, 2419. (e) Boog-Wick, K.; Pregosin, P. S.; Trabesinger, G. *Organometallics* **1998**, *17*, 3254. (f) Boog-Wick, K.; Pregosin, P. S.; Wörle, M.; Albinati, A. *Helv. Chim. Acta* **1998**, *81*, 1622. (g) Selke, R.; Ohff, M.; Riepe, A. *Tetrahedron* **1996**, *52*, 15079.

(8) (a) Brown, J. M.; Cook, S. J.; Kent, A. G. *Tetrahedron* **1986**, *42*, 5097. (b) Brown, J. M.; Cook, S. J.; Kahn, R. *Tetrahedron* **1986**, *42*, 5105. (c) Gilbertson, S. R.; Chang, C.-W. T. *J. Org. Chem.* **1995**, *60*, 6226. (d) Yonehara, K.; Hashizume, T.; Ohe, K.; Uemura, S. *Bull. Chem. Soc. Jpn.* **1998**, *71*, 1967. (e) Yonehara, K.; Hashizume, T.; Mori, K.; Ohe, K.; Uemura, S. *J. Org. Chem.* **1999**, *64*, 5593.

(9) Gläser, B.; Kunz, H. *Synlett* **1998**, 53.

(10) Gilbertson, S. R.; Chang, C.-W. T. *J. Org. Chem.* **1998**, *63*, 8424.

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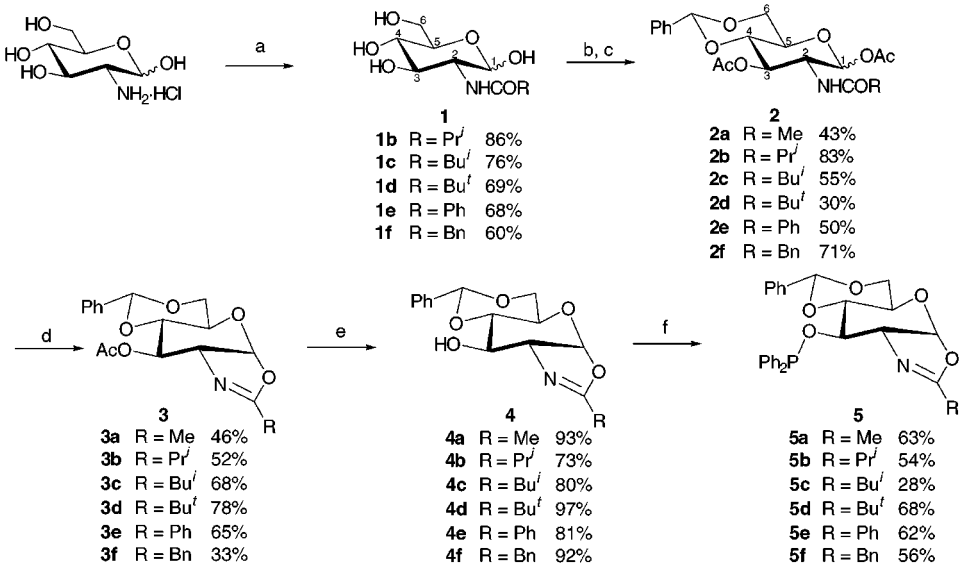
Scheme 1[a]



[a] Reagents and conditions: (a) $(RCO)_2O$, NaOMe/MeOH, rt, 1 d, or RCOCl, $NaHCO_3$(aq), rt, 1 d; (b) PhCHO, $ZnCl_2$, rt, 6 h; (c) Ac_2O, pyridine, rt, 1 d; (d) $SnCl_4$, CH_2Cl_2, rt, 2 h; (e) K_2CO_3, MeOH, rt, 1 h; (e) Ph_2PCl, catalytic 4-(dimethylamino)pyridine, Et_3N−THF, −40 °C, 15 min.

an alkyl or aryl group at the 2-position of oxazoline and a phosphorus atom attached to a sugar backbone through the phosphinite linkage. Since the substituent at the 2-position in our ligand is variable, some kind of steric effect is expected in the asymmetric induction. In this paper, we report the synthesis of such novel phosphinite−oxazoline chiral ligands from D-glucosamine hydrochloride (2-amino-2-deoxy-D-glucopyranoside hydrochloride), which has been less frequently used as a source of chiral ligands, and their application to the palladium-catalyzed allylic substitution of allylic acetates and an allylic carbonate.[11]

Results and Discussion

Synthesis of Phosphinite−Oxazoline Ligands from D-Glucosamine Hydrochloride. The sequence of ligand synthesis is illustrated in Scheme 1. The acylation of the D-glucosamine hydrochloride suspended in NaOMe/MeOH[12] with $(Pr^iCO)_2O$, $(Bu^iCO)_2O$, and $(Bu^tCO)_2O$ afforded the amides **1b**, **1c**, and **1d**, respectively. *N*-Acyl-D-glucosamines **1e** and **1f** were also prepared from the D-glucosamine hydrochloride and PhCOCl or $PhCH_2COCl$ in aqueous $NaHCO_3$, respectively. Then, the protection of hydroxy groups of the 4,6-positions and 1,3-positions of the acylated D-glucosamines **1** with PhCHO[13] and Ac_2O, respectively, gave the protected *N*-acyl-D-glucosamines **2** as a mixture of α- and β-anomers. They were converted to the corresponding oxazolines **3** in the presence of anhydrous $SnCl_4$ without affecting the benzylidene acetal.[14,15] Deacetylation of **3** with K_2CO_3 in MeOH gave the hydroxy compounds **4**, which were treated with Ph_2PCl and a catalytic amount of 4-(dimethylamino)pyridine in THF−Et_3N at −40 °C to give the desired phosphinite−oxazoline ligands **5**.

Asymmetric Allylic Alkylation. We investigated the palladium-catalyzed allylic substitution of 1,3-diphenyl-3-acetoxyprop-1-ene (**6**) and ethyl 1,3-diphenylprop-2-enyl carbonate (**7**) as test substrates with dimethyl malonate using the chiral phosphinite−oxazoline ligands **5a**−**f** (eq 1), the results being summarized in Table 1. The reaction

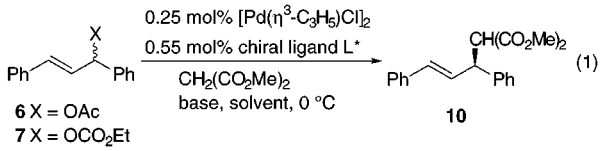


Table 1. Palladium-Catalyzed Asymmetric Allylic Alkylation of 6 and 7 Using Chiral Ligands 5a−f[a]

entry	substrate	L*	solvent	time (h)	% yield[b]	% ee[c]
1	**6**	**5a**	toluene	6	81	96 (*S*)
2	**6**	**5b**	toluene	6	99	90 (*S*)
3	**6**	**5c**	toluene	6	82	95 (*S*)
4	**6**	**5d**	toluene	6	91	83 (*S*)
5	**6**	**5e**	toluene	6	74	94 (*S*)
6	**6**	**5f**	toluene	18	88	78 (*S*)
7	**7**	**5a**	toluene	6	84	95 (*S*)
8[d]	**6**	**5a**	toluene/THF[e] (1:1)	0.5	98	93 (*S*)

[a] Reactions were carried out under Ar using **6** or **7** (1.0 mmol), dimethyl malonate (3.0 mmol), BSA [bis(trimethylsilyl)acetamide] (3.0 mmol), KOAc (0.05 mmol), solvent (2 mL), $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (0.25 mol %), and L* (0.55 mol %). [b] Isolated yield. [c] The values were measured by HPLC, and the absolute configuration was determined by optical rotation.[3a] [d] Carried out at rt with tetrabutylammonium fluoride (3 mmol) as a base instead of BSA and KOAc. [e] Solvent (6 mL).

was carried out in toluene unless otherwise noted using a catalyst generated in situ by mixing 0.25 mol % $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ with 0.55 mol % chiral ligand. The ligands **5a**−**f** were effective in the allylic alkylation of the acetate **6** with the malonate in the presence of *N*,*O*-bis(trimethyl-

(11) The preliminary results were partly reported: Yonehara, K.; Hashizume, T.; Mori, K.; Ohe, K.; Uemura, S. *Chem. Commun.* **1999**, 415.

(12) Inoue, Y.; Onodera, K.; Kitaoka, S.; Hirano, S. *J. Am. Chem. Soc.* **1956**, *78*, 4722.

(13) Roth, W.; Pigman, W. *J. Am. Chem. Soc.* **1960**, *82*, 4608.

(14) Srivastava, V. K. *Carbohydr. Res.* **1982**, *103*, 286.

(15) Kiso, M.; Anderson, L. *Carbohydr. Res.* **1985**, *136*, 309. When $FeCl_3$, used in this reference, was employed instead of $SnCl_4$, the benzylidene group was deprotected before the formation of the oxazoline ring.

silyl)acetamide (BSA)[16] (entries 1−6). The best result (96% ee) was achieved using the ligand **5a** having the smallest alkyl group (R) on the oxazoline (entry 1). The chiral ligands **5c** and **5e** also gave good enantioselectivities, 95% and 94% ee, respectively (entries 3 and 5). The ligands **5d** and **5f** having bulky substituents gave lower ee's (83% and 78%) (entries 4 and 6). The sterically less demanding substituents such as Me and Bu^i on the oxazoline are most effective in this reaction. The reaction of the carbonate **7** instead of **6** gave almost the same enantioselectivity (95% ee) in the presence of the ligand **5a** (entry 7). Tetrabutylammonium fluoride instead of BSA can promote the reaction,[17] albeit with slightly lower selectivity (entry 8).[18]

It is known to be more difficult to control the enantioselective substitution of cyclic and 1,3-dimethylallylic systems.[19] Although the highest enantioselectivity in such systems has been reported by Trost[21] and Osborn,[22] the development of enantioselective catalysts for this class of substrates remains challenging. We applied the chiral ligands **5a**−**f** to the palladium-catalyzed allylic alkylation of 3-acetoxycyclohexene (**8**) (eq 2). The reaction proceeded

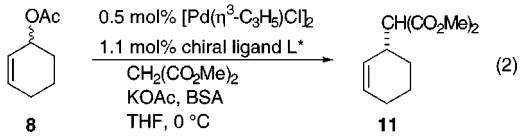


Table 2. Palladium-Catalyzed Asymmetric Allylic Alkylation of 8 Using Chiral Ligands[a]

entry	L*	time	% yield[b]	% ee[c]
1	**5a**	7 h	88	74 (*R*)
2	**5b**	1 d	85	70 (*R*)
3	**5c**	1 d	62	68 (*R*)
4	**5f**	4 d	47	72 (*R*)

[a] Reactions were carried out under Ar using **8** (1.0 mmol), dimethyl malonate (3.0 mmol), BSA [bis(trimethylsilyl)acetamide] (3.0 mmol), KOAc (0.05 mmol), THF (2 mL), [Pd(η^3-C_3H_5)Cl]$_2$ (0.5 mol %), and L* (1.1 mol %). [b] Isolated yield. [c] The values were measured by ^{1}H NMR with Eu(hfc)$_3$, and the absolute configuration was determined by optical rotation.[20]

in THF at 0 °C using 0.5 mol % [Pd(η^3-C_3H_5)Cl]$_2$ and 1.1 mol % chiral ligand. Typical results are shown in Table 2. The chiral ligand **5a** gave the highest enantiomeric excess (74% ee). Other chiral ligands, **5b**, **5c**, and **5f**, gave almost the same enantioselectivity (68−72% ee). In the case of **5f**, the reaction was not complete even after 4 days. The chiral ligands **5d** and **5e** were also examined, but the reactions were sluggish. These results show that our ligand structure having no additional chiral auxiliaries can effectively control the enantioselectivity in

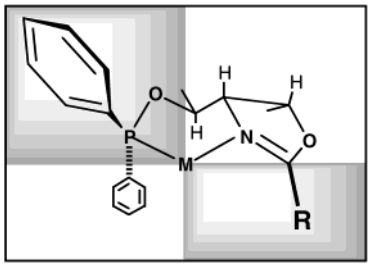


Figure 2. Schematic structure of the metal complex of the phosphinite−oxazoline ligand.

cyclic substrates. Next, the alkylation of 4-acetoxypent-2-ene (**9**) was investigated (eq 3). The results are listed

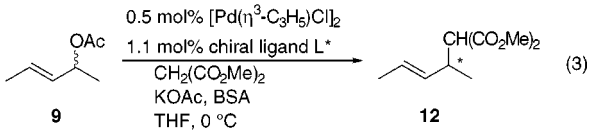


Table 3. Palladium-Catalyzed Asymmetric Allylic Alkylation of 9 Using Chiral Ligands[a]

entry	L*	time (h)	% yield[b]	% ee[c]
1	**5a**	12	69	57
2	**5d**	24	21	57
3	**5f**	12	84	48

[a] Reactions were carried out under Ar using **9** (1.0 mmol), dimethyl malonate (3.0 mmol), BSA [bis(trimethylsilyl)acetamide] (3.0 mmol), KOAc (0.05 mmol), THF (2 mL), [Pd(η^3-C_3H_5)Cl]$_2$ (0.5 mol %), and L* (1.1 mol %). [b] Isolated yield. [c] The values were measured by ^{1}H NMR with Eu(hfc)$_3$.

in Table 3. Among the ligands examined, **5a** afforded moderate selectivity (57% ee). The enantioselectivity obtained here does not exceed the reported value in the same substrate using previously developed phosphine−oxazoline ligands.[2a,9]

To explain the stereoselectivity obtained, a schematic structure of the coordination center is shown in Figure 2. The second quadrant is most sterically occupied by the phenyl group, and the fourth quadrant is the second most sterically occupied by the substituent on the oxazoline ring. The extent of the steric hindrance in these quadrants has an influence on the enantioselectivity. We suppose that a nucleophilic attack occurs predominantly at the allyl terminus trans to the Pd−P bond in a π-allylpalladium intermediate.[3b,23] Since the alkylated product (*S*)-**10** was obtained as a major enantiomer in the reaction of **6** and **7** with the malonate, the reaction probably proceeds through intermediate **A** rather than intermediate **B** in the equilibrium as shown in Figure 3.[24] The steric repulsion in the intermediate **A** between a phenyl moiety on the phosphorus atom and a phenyl group of the π-allyl moiety seems to be smaller than that in **B**. Therefore, the major contribution of the intermedi-

(16) Trost, B. M.; Murphy, D. J. *Organometallics* **1985**, *4*, 1143.
(17) Clark, J. H. *Chem. Rev.* **1980**, *80*, 429.
(18) This reaction did not proceed at 0 °C.
(19) It was reported that the original chiral diphenylphosphinooxazolines (refs 2−4) gave almost racemic products in allylic substitution of 3-acetoxycyclohexene. The reasonable enantioselectivity in the reaction was achieved by employing chiral diarylphosphinooxazoline with a stereogenic phosphorus center[20] or with a planar chirality.[5l]
(20) Sennhenn, P.; Gabler, B.; Helmchen, G. *Tetrahedron Lett.* **1994**, *35*, 8595.
(21) (a) Trost, B. M.; Breit, B.; Peukert, S.; Zambrano, J.; Ziller, J. W. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2386. (b) Trost, B. M.; Krueger, A. C.; Bunt, R. C.; Zambrano, J. *J. Am. Chem. Soc.* **1996**, *118*, 6520. (c) Trost, B. M.; Bunt, R. C. *J. Am. Chem. Soc.* **1994**, *116*, 4089.
(22) 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.
(23) The phosphorus atom is known as a better π-acceptor than the nitrogen atom in a π-allylpalladium complex bearing a P−N bidentate ligand. For examples, see: (a) Åkermark, B.; Krakenberger, B.; Hansson, S.; Vitagliano, A. *Organometallics* **1987**, *6*, 620. (b) Blöchl P. E.; Togni, A. *Organometallics* **1996**, *15*, 4125. (c) Peña-Cabrera, E.; Norrby, P.-O.; Sjögren, M.; Vitagliano, A.; De Felice, V.; Oslob, J.; Ishii, S.; O'Neill, D.; Åkermark, B.; Helquist, P. *J. Am. Chem. Soc.* **1996**, *118*, 4299.
(24) The equilibrium between **A** and **B** should include not only π−σ−π-allyl rotation but also the ligand rotation through the dissociation of the coordinated nitrogen; for an example, see: Gogoll, A.; Örnebro, J.; Grennberg, H.; Bäckvall, J.-E. *J. Am. Chem. Soc.* **1994**, *116*, 3631.

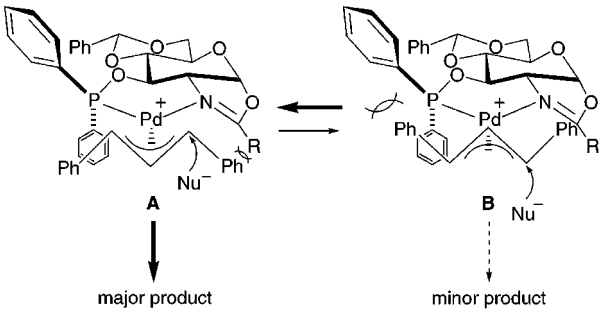


Figure 3. A plausible reaction course in the reaction of **6** and **7**.

ate **A** might be established in the equilibrium. In the intermediate **A**, however, there is an unfavorable interaction between R on the oxazoline ring and another phenyl group of the π-allyl moiety. The larger the R group on the oxazoline ring, the less favorable is intermediate **A**. Thereby, the ratio of two diastereomeric intermediates, **A** to **B**, is decreased to give a lower enantioselectivity.

In the reaction of 3-acetoxycyclohexene (**8**), the resulting cyclic allyl ligand has anti,anti-configuration as in intermediates **C** and **D** shown in Figure 4. Different from

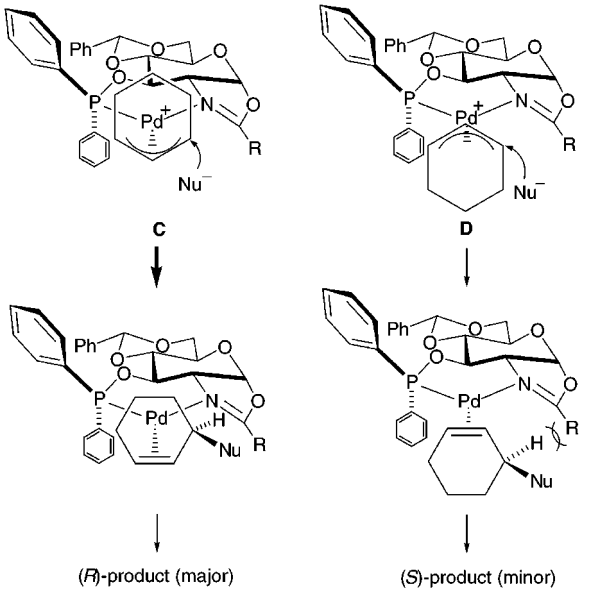


Figure 4. A plausible reaction course in the reaction of **8**.

the diphenyl-substituted case of **6** and **7**, this anti,anti-configuration lacks the steric interaction from both the phenyl ring on the P atom and the R group on the oxazoline ring in both intermediates. In fact, the observed enantioselectivities of the product are in the range of 68−74% ee irrespective of the nature of R as shown in Table 2. The *R* configuration of the major enantiomeric product shows that the product can arise by reaction at the allylic carbon trans to the P atom in the intermediate **C**, which is also postulated in the case of the acyclic substrate. The intermediates **C** and **D** might be produced by the oxidative addition (ionization step) via four diastereomeric olefin−palladium complexes, respectively.[25] Although no

(25) Two of the four diastereomeric complexes lead to complex **C**, and the others to complex **D**. Trost *et al.* suggested the importance of such ionization steps for the enantioselection in the allylic substitution of cyclic substrates; see: Trost, B. M.; Van Vranken, D. L.; Bingel, C. *J. Am. Chem. Soc.* **1992**, *114*, 9327.

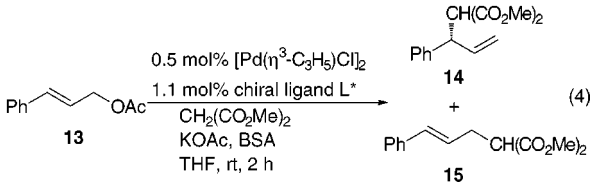
Table 4. Palladium-Catalyzed Asymmetric Allylic Alkylation of 13 Using Chiral Ligands[a]

entry	L*	% yield[b]	**14**:**15**[c,d]	% ee[e]
1	**5a**	74	25:75	75 (*S*)
2	**5d**	85	11:89	90 (*S*)

[a] Reactions were carried out under Ar using **13** (1.0 mmol), dimethyl malonate (3.0 mmol), BSA [bis(trimethylsilyl)acetamide] (3.0 mmol), KOAc (0.05 mmol), THF (2 mL), $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (0.5 mol %), and L* (1.1 mol %). [b] Isolated yield of **14** and **15**. [c] The ratios were determined by ^{1}H NMR. [d] For ^{1}H NMR data, see ref 27. [e] The values and absolute configuration were determined by HPLC.[28i]

experimental details on the ratio of intermediates **C** and **D** and the reactivity of **C** and **D** were obtained, its ratio and the formation of the olefin−palladium complex via the nucleophilic attack followed by the rotation of the cyclohexenyl[26] group might be crucial in enantiodifferentiation.

Next, we examined the regio- and stereoselective allylic alkylation of cinnamyl acetate (**13**) with dimethyl malonate in the presence of the palladium catalyst and chiral ligands, the products being a mixture of regioisomers of **14** and **15** (eq 4). There are several reports[28] on the regio-



and stereoselective reaction of this substrate using a variety of catalysts, but the regioselectivity for **14** is quite low using a Pd catalyst and P,N-bidentate ligands[27,29] except a recent report by Pfaltz and a co-worker.[2b] They claimed that both the electronegative substituents at the coordinating P atom and the steric interaction which affects the ratio of π-allylpalladium intermediates are important to obtain the product in high regioselectivity (**14**:**15** = 76:24).[2b] In our phosphinite−oxazoline ligands the P atom seems more electropositive than that of phosphine−oxazoline ligands. We performed the reaction in THF at room temperature using 0.5 mol % $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ and 1.1 mol % chiral ligands. As shown in Table 4, unfortunately, the regioselectivity for **14** was not high in our case. Thus, the chiral ligand **5a** which was expected to give the highest branch:normal ratio gave products **14** with 75% ee and **15** in a ratio of 25:75. The

(26) The hydrogen atom on the sp^3 carbon center formed by nucleophilic attack should sterically interact with the R group in clockwise rotational motion of the cyclohexenyl group from intermediate **B**. There is no such interaction in the counterclockwise motion via intermediate **C**. The importance of the rotational motion has been suggested by Brown,[27] Osborn,[22] and Helmchen.[5l]

(27) Brown, J. M.; Hulmes, D. I.; Guiry, P. J. *Tetrahedron* **1994**, *50*, 4493.

(28) [Mo]: (a) Trost, B. M.; Lautens, M. *Tetrahedron* **1987**, *43*, 4817. (b) Trost, B. M.; Hachiya, I. *J. Am. Chem. Soc.* **1998**, *120*, 1104. (c) Glorius, F.; Pfaltz, A. *Org. Lett.* **1999**, *1*, 141. [Ru]: (d) Kondo, T.; Ono, H.; Satake, N.; Mitsudo, T.; Watanabe, Y. *Organometallics* **1995**, *14*, 1945. [Pd]: Reference 2b. (e) Hayashi, T.; Kawatsura, M.; Uozumi, Y. *J. Am. Chem. Soc.* **1998**, *120*, 1681. [W]: (f) Lehmann, J.; Lloyd-Jones, G. C. *Tetrahedron* **1995**, *51*, 8863. (g) Lloyd-Jones, G. C.; Pfaltz, A. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 462. [Ir]: (h) Takeuchi, R.; Kashio, M. *J. Am. Chem. Soc.* **1998**, *120*, 8647. (i) Janssen, J. P.; Helmchen, G. *Tetrahedron Lett.* **1997**, *38*, 8025. (j) Bartels, B.; Helmchen, G. *Chem. Commun.* **1999**, 741.

(29) Vyskočil, Š.; Smrčina, M.; Hanuš, V.; Polášek, M.; Kočovský, P. *J. Org. Chem.* **1998**, *63*, 7738.

chiral ligand **5d** which has a bulky substituent gave a lower ratio of **14** to **15** (11:89), but with a higher level of enantioselectivity in **14** (90% ee). The plausible intermediates in the alkylation of **13** are illustrated in Figure 5. The predominant formation of the linear product **15** might suggest that intermediate **F** is most favored. The absolute configuration of the branched product **14** was (*S*), which appeared to stem from an intermediate $\mathbf{E^1}$. As in the case of 3-acetoxycyclohexene, the hydrogen atom on the sp^3 carbon of an alkene−Pd complex formed by nucleophilic attack on the intermediate $\mathbf{E^2}$ followed by the clockwise rotation of cinnamyl group should sterically interact with the R group of the oxazoline ring, while there is no such interaction in the alkene−Pd complex obtained from the intermediate $\mathbf{E^1}$ with the counterclockwise rotation. Thus, the (*S*) product becomes predominant.

Asymmetric Allylic Amination. Finally, we carried out the palladium-catalyzed allylic amination of the carbonate **7** (eq 5). Typical results are shown in Table 5.

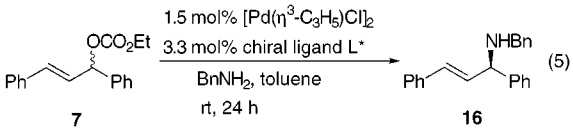


Table 5. Palladium-Catalyzed Asymmetric Allylic Amination of 7 Using Chiral Ligands 5a−f[a]

entry	L*	% yield	% ee[b]
1	**5a**	78	94 (*R*)
2	**5b**	57	87 (*R*)
3	**5c**	72	95 (*R*)
4	**5d**	48	69 (*R*)
5	**5e**	86	86 (*R*)
6	**5f**	47	87 (*R*)

[a] Reactions were carried out under Ar using **7** (0.33 mmol), benzylamine (1.0 mmol), toluene (2 mL), $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (1.5 mol %), and L* (3.3 mol %). [b] The value was measured by HPLC,[34] and the absolute configuration was determined by optical rotation.[30]

When benzylamine was used as a nucleophile, the highest enantiomeric excess (95% ee) was observed using the chiral ligand **5c** (R = Bu^i). Almost the same level of enantioselectivity (94% ee) was observed using the chiral ligand **5a**. The absolute stereochemistry is consistent with the case of a carbon nucleophile. The absolute configuration of the amination product **16** lends support to the mechanism of this allylic substitution via the intermediate **A** (see Figure 3).

Conclusion

We were successful in the preparation of the novel chiral phosphinite−oxazoline ligands **5a**−**f** from a natural D-glucosamine hydrochloride. These were effective ligands for the palladium-catalyzed enantioselective allylic alkylation and amination reactions. In previously reported phosphine−oxazoline ligands, a phosphorus atom is bound to an alkyl chain or an aromatic ring in the 2-position of oxazoline. In our ligands, the substituents at the 2-position are variable, and the steric effect of the substituents is remarkable. Although the enantioselectivities reported here are almost comparable to the level of ee achieved by original chiral phosphine−oxazoline ligands, it is noted that our ligands without further modification furnish good selectivity in the cyclic substrate. The rigidity of an oxazoline moiety in our ligands presumably influences the enantiodifferential course of reactions. Further application of the ligands **5a**−**f** and other ligands without benzylidene protection to other asymmetric catalytic reactions will be reported in due course.

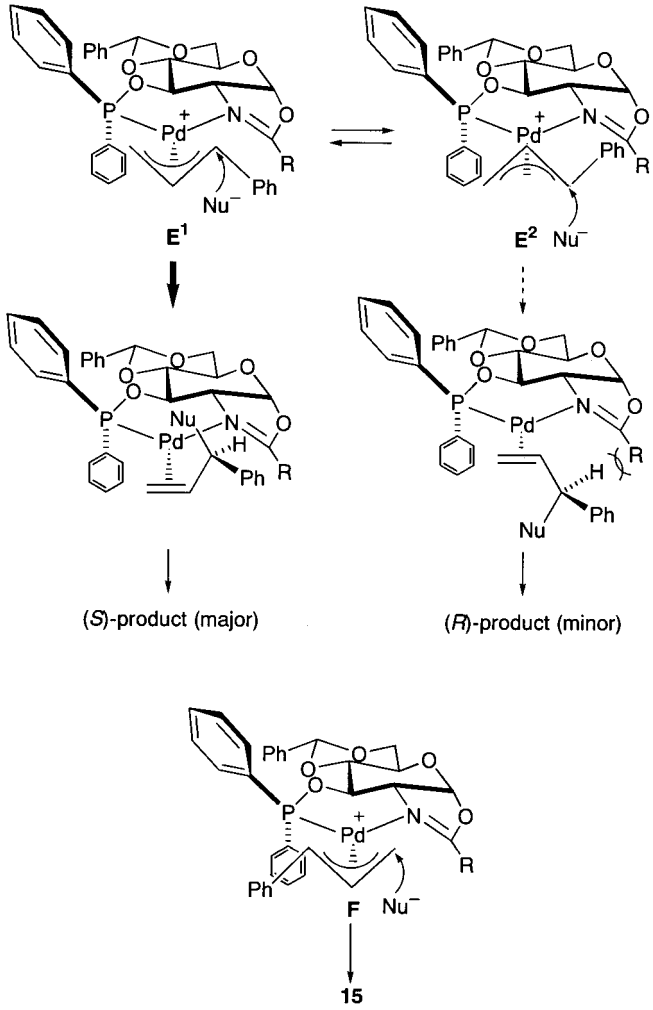


Figure 5. A plausible reaction course in the reaction of **13**.

Experimental Section

General Procedures. Tetrahydrofuran (THF) and diethyl ether were distilled from sodium benzophenone ketyl under argon. Dichloromethane, *N*,*N*-dimethylformamide (DMF), and triethylamine were distilled from calcium hydride. The NMR spectra were measured for solutions in $CDCl_3$ with Me_4Si as an internal standard (^1H and ^{13}C) or with $P(OMe)_3$ as an external standard (^{31}P). Melting points are uncorrected. Elemental analyses were performed at the Microanalytical Center of Kyoto University. *N*-Acetyl-D-glucosamine (**1a**) is commercially available. *N*-Isopropyl-D-glucosamine (**1b**), *N*-isovaleryl-D-glucosamine (**1c**), *N*-trimethylacetyl-D-glucosamine (**1d**), *N*-benzoyl-D-glucosamine (**1e**), and *N*-phenylacetyl-D-glucosamine (**1f**) were prepared by N-acylation of commercial D-glucosamine hydrochloride with acid anhydride or acid chloride according to literature procedures.[12] 1,3-Diphenyl-3-acetoxyprop-1-ene (**6**),[30] ethyl 1,3-diphenylprop-2-enyl carbonate (**7**),[30] and 4-acetoxypent-2-ene (**9**)[31] were prepared accord-

(30) Hayashi, T.; Yamamoto, A.; Ito, Y.; Nishioka, E.; Miura, H.; Yanagi, K. *J. Am. Chem. Soc.* **1989**, *111*, 6301.

(31) Von Matt, P.; Loiseleur, O.; Koch, G.; Pfaltz, A.; Lefeber, C.; Feucht, T.; Helmchen, G. *Tetrahedron*: *Asymmetry* **1994**, *5*, 573.

ing to literature procedures. 3-Acetoxycyclohexene (**8**) was prepared by the reduction of 2-cyclohexen-1-one with $NaBH_4$ and $CeCl_3 \cdot 7H_2O$ in MeOH[32] and acetylation with Ac_2O. The spectral data of alkylated products **10**,[33] **11**,[33] **12**,[33] **14**,[27] and **15**[27] and aminated product **16**[30] are reported in previous papers.

General Procedure for the Synthesis of 2-Alkyl- or -Aryl-4,5-(4,6-*O*-benzylidene-1,2-dideoxy-α-D-glucopyrano)-[2,1-*d*]-2-oxazoline (4). To a solution of **3a** (0.552 g, 1.65 mmol) in MeOH (30 mL) and $CHCl_3$ (10 mL) was added K_2CO_3 (140 mg, 1 mmol), and the mixture was stirred for 1 h. After the solvent was removed under reduced pressure, the residue was subjected to column chromatography on SiO_2 with $CHCl_3$/acetone (v/v, 1:3) as an eluent to give 2-methyl-4,5-(4,6-*O*-benzylidene-1,2-dideoxy-α-D-glucopyrano)-[2,1-*d*]-2-oxazoline (**4a**) (0.441 g, 1.51 mmol, 93%) as a white solid: mp 168.1−169.0 °C; $[\alpha]^{20}_D = +29.2°$ ($c = 0.25$, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.91 (d, $J = 2.9$ Hz, 3H), 3.59−3.76 (m, 4H), 3.94 (dt, $J = 2.9$, 6.5 Hz, 1H), 4.37 (dd, $J = 3.1$, 9.0 Hz, 1H), 5.59 (s, 1H), 5.97 (d, $J = 6.5$ Hz, 1H), 7.30−7.49 (m, 5H) ppm; ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 13.9, 63.9, 68.3, 68.8, 73.9, 78.5, 101.7, 103.6, 126.2, 128.0, 129.0, 137.7, 166.5 ppm; IR (KBr) 1654 cm^{-1}; HRMS (FAB) calcd for $C_{15}H_{18}NO_5$ ($M + H^+$) 292.1185, found 292.1192. Anal. Calcd for $C_{15}H_{17}NO_5$: C, 61.85; H, 5.88; N, 4.81; O, 27.46. Found: C, 61.23; H, 5.92; N, 4.82; O, 27.08.

2-Isopropyl-4,5-(4,6-*O*-benzylidene-1,2-dideoxy-α-D-glucopyrano)-[2,1-*d*]-2-oxazoline (4b): 73% yield, a white solid; mp 173.0−173.9 °C; $[\alpha]^{20}_D = +97.8°$ ($c = 0.25$, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.11 (d, $J = 7.0$ Hz, 3H), 1.13 (d, $J = 7.0$ Hz, 3H), 2.59 (sept, $J = 7.0$ Hz, 1H), 3.61−3.76 (m, 4H), 3.96 (dd, $J = 5.1$, 7.7 Hz, 1H), 4.38 (dd, $J = 4.2$, 10.3 Hz, 1H), 5.59 (s, 1H), 5.96 (d, $J = 7.7$ Hz, 1H), 7.33−7.50 (m, 5H) ppm; ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 19.0, 19.2, 28.4, 63.0, 68.4, 68.7, 74.0, 78.8, 101.6, 103.2, 126.2, 128.1, 129.0, 137.1, 173.2 ppm; IR (KBr) 1653 cm^{-1}; HRMS (FAB) calcd for $C_{17}H_{22}NO_5$ ($M + H^+$) 320.1498, found 320.1499. Anal. Calcd for $C_{17}H_{21}NO_5$: C, 63.94; H, 6.63; N, 4.39; O, 25.05. Found: C, 63.43; H, 6.60; N, 4.41; O, 25.43.

2-Isobutyl-4,5-(4,6-*O*-benzylidene-1,2-dideoxy-α-D-glucopyrano)-[2,1-*d*]-2-oxazoline (4c): 80% yield, a white solid; mp 138.0−139.5 °C; $[\alpha]^{20}_D = +101.3°$ ($c = 0.25$, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.86 (d, $J = 6.9$ Hz, 3H), 0.88 (d, $J = 7.1$ Hz, 3H), 2.00 (m, 1 H), 2.16 (d, $J = 7.4$ Hz, 2H), 3.56−3.77 (m, 2H), 3.94 (dd, $J = 5.5$, 7.7 Hz, 1H), 4.38 (dd, $J = 3.6$, 9.6 Hz, 1H), 5.59 (s, 1H), 5.96 (d, $J = 7.7$ Hz, 1H), 7.33−7.50 (m, 5H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.1, 22.2, 26.0, 37.1, 64.0, 68.5, 68.8, 74.2, 78.6, 101.8, 103.5, 126.3, 128.2, 129.1, 137.2, 168.8 ppm; IR (KBr) 1654 cm^{-1}; HRMS (FAB) calcd for $C_{18}H_{24}NO_5$ ($M + H^+$) 334.1654, found 334.1654. Anal. Calcd for $C_{18}H_{23}NO_5$: C, 64.85; H, 6.95; N, 4.20; O, 24.00. Found: C, 64.43; H, 7.05; N, 4.24; O, 24.00.

2-*tert*-Butyl-4,5-(4,6-*O*-benzylidene-1,2-dideoxy-α-D-glucopyrano)-[2,1-*d*]-2-oxazoline (4d): 97% yield, a white solid; mp 138.0−139.0 °C; $[\alpha]^{20}_D = +75.1°$ ($c = 0.25$, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.23 (s, 9H), 3.61−3.77 (m, 4H), 3.95 (dd, $J = 5.2$, 7.7 Hz, 1H), 4.39 (dd, $J = 4.1$, 10.4 Hz, 1H), 5.59 (s, 1H), 5.94 (d, $J = 7.7$ Hz, 1H), 7.35−7.51 (m, 5H) ppm; ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 27.3, 33.6, 63.3, 68.5, 69.1, 74.1, 79.2, 101.6, 103.0, 126.2, 128.1, 129.0, 137.0, 174.9 ppm; IR (KBr) 1647 cm^{-1}; HRMS (FAB) calcd for $C_{18}H_{24}NO_5$ ($M + H^+$) 334.1654, found 334.1649. Anal. Calcd for $C_{18}H_{23}NO_5$: C, 64.85; H, 6.95; N, 4.20; O, 24.00. Found: C, 64.24; H, 6.89; N, 3.84; O, 24.05.

2-Phenyl-4,5-(4,6-*O*-benzylidene-1,2-dideoxy-α-D-glucopyrano)-[2,1-*d*]-2-oxazoline (4e). This compound was recrystallized from $CHCl_3$ and hexane: 81% yield, a white solid; mp 228.0−229.0 °C; $[\alpha]^{20}_D = +141.7°$ ($c = 0.25$, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.70−3.84 (m, 3H), 3.96 (dd, $J = 5.5$, 8.4 Hz, 1H), 4.24 (dd, $J = 5.5$, 7.7 Hz, 1H), 4.43 (m, 1H), 5.63 (s, 1H), 6.17 (d, $J = 7.7$ Hz, 1H), 7.14−7.97 (m, 10H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 63.7, 68.5, 69.0, 74.3, 79.0, 102.1, 103.6, 126.4, 128.3, 128.4, 128.5, 129.3, 132.3, 137.1, 164.5 ppm; IR (KBr) 1637 cm^{-1}. Anal. Calcd for $C_{20}H_{19}NO_5$: C, 67.98; H, 5.42; N, 3.96. Found: C, 67.70; H, 5.43; N, 4.08.

2-Benzyl-4,5-(4,6-*O*-benzylidene-1,2-dideoxy-α-D-glucopyrano)-[2,1-*d*]-2-oxazoline (4f): 92% yield, a white solid; mp 156.0−157.0 °C; $[\alpha]^{20}_D = +114.3°$ ($c = 0.25$, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.44−3.72 (m, 6H), 3.95 (dd, $J = 5.9$, 7.3 Hz, 1H), 4.34 (dd, $J = 2.8$, 9.5 Hz, 1H), 5.58 (s, 1H), 5.93 (d, $J = 7.3$ Hz, 1H), 7.23−7.43 (m, 10H) ppm; ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 35.0, 64.0, 68.3, 68.5, 74.2, 78.4, 101.7, 104.0, 126.1, 127.1, 128.1, 128.6, 128.9, 129.0, 134.1, 136.9, 167.8 ppm; IR (KBr) 1648 cm^{-1}. Anal. Calcd for $C_{21}H_{21}NO_5$: C, 68.65; H, 5.76; N, 3.81; O, 21.77. Found: C, 68.37; H, 5.71; N, 3.78; O, 21.77.

General Procedure for the Synthesis of Diphenylphosphinite 5. To a solution of **4a** (0.291 g, 1 mmol) and a catalytic amount of 4-(dimethylamino)pyridine (10 mg) in 10 mL of degassed THF/Et_3N (v/v, 2:1) was slowly added chlorodiphenylphosphine (0.2 mL, 1.1 mmol) at −40 °C, and the mixture was stirred at this temperature. After 15 min, the mixture was concentrated to dryness, and the residue was subjected to column chromatography on Al_2O_3 with degassed toluene/CH_2Cl_2 (v/v, 1:2) as an eluent to give 2-methyl-4,5-(4,6-*O*-benzylidene-3-*O*-(diphenylphosphino)-1,2-dideoxy-α-D-glucopyrano)-[2,1-*d*]-2-oxazoline (**5a**) (0.301 g, 0.633 mmol, 63%) as a white solid: mp 169.1−169.6 °C; $[\alpha]^{20}_D = -75.7°$ ($c = 0.25$, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.05 (d, $J = 1.1$ Hz, 3H), 3.61−3.69 (m, 2H), 3.76 (t, $J = 8.5$ Hz, 1H), 4.23−4.32 (m, 2H), 4.36 (dd, $J = 3.3$, 8.5 Hz, 1H), 5.35 (s, 1H), 5.98 (d, $J = 7.4$ Hz, 1H), 7.23−7.53 (m, 15H) ppm; ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 14.3, 62.9, 68.6, 69.4 (d, $J = 5.2$ Hz), 79.6 (d, $J = 3.6$ Hz), 82.3 (d, $J = 20.2$ Hz), 101.2, 102.2, 126.0−136.9 (16 carbons), 141.9 (d, $J = 21.3$ Hz), 142.2 (d, $J = 16.4$ Hz), 165.0 ppm; ^{31}P NMR (161.9 MHz, $CDCl_3$) δ 114.5 ppm; IR (KBr) 1665, 1433 cm^{-1}. Anal. Calcd for $C_{27}H_{26}NO_5P$: C, 68.20; H, 5.51; N, 2.95; P, 6.51. Found: C, 68.12; H, 5.61; N, 2.69; P, 6.69.

2-Isopropyl-4,5-(4,6-*O*-benzylidene-3-*O*-(diphenylphosphino)-1,2-dideoxy-α-D-glucopyrano)-[2,1-*d*]-2-oxazoline (5b): 54% yield, a white solid; mp 169.0−169.5 °C; $[\alpha]^{20}_D = -49.4°$ ($c = 0.25$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.209 (d, $J = 6.8$ Hz, 3H), 1.213 (d, $J = 6.8$ Hz, 3H), 2.63 (sept, $J = 6.8$ Hz, 1H), 3.57 (dt, $J = 4.9$, 9.8 Hz, 1H), 3.64 (t, $J = 9.8$ Hz, 1H), 3.74 (t, $J = 9.8$ Hz, 1H), 4.22−4.43 (m, 2H), 4.37 (dd, $J = 4.9$, 9.8 Hz, 1H), 5.33 (s, 1H), 5.96 (d, $J = 7.3$ Hz, 1H), 7.23−7.58 (m, 15H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.2, 19.3, 28.5, 62.9, 68.6, 69.1 (d, $J = 5.0$ Hz), 79.9 (d, $J = 3.7$ Hz), 82.3 (d, $J = 19.9$ Hz), 101.1, 102.0, 126.0−136.9 (16 carbons), 142.0 (d, $J = 19.9$ Hz), 142.3 (d, $J = 14.3$ Hz), 171.9 ppm; ^{31}P NMR (161.9 MHz, $CDCl_3$) δ 114.8 ppm; IR (KBr) 1658, 1433 cm^{-1}. Anal. Calcd for $C_{29}H_{30}NO_5P$: C, 69.17; H, 6.01; N, 2.78; P, 6.15. Found: C, 69.08; H, 6.08; N, 2.76; P, 6.44.

2-Isobutyl-4,5-(4,6-*O*-benzylidene-3-*O*-(diphenylphosphino)-1,2-dideoxy-α-D-glucopyrano)-[2,1-*d*]-2-oxazoline (5c): 28% yield, a white solid; mp 142.8−143.2 °C; $[\alpha]^{20}_D = -28.1°$ ($c = 0.25$, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.98 (d, $J = 6.7$ Hz, 3H), 0.99 (d, $J = 6.7$ Hz, 3H), 2.08 (sept, $J = 6.7$ Hz, 1H), 2.20−2.23 (m, 2H), 3.59−3.69 (m, 2H), 3.75 (t, $J = 8.6$ Hz, 1H), 4.21−4.31 (m, 2H), 4.35 (dd, $J = 3.6$, 9.3 Hz, 1H), 5.34 (s, 1H), 5.96 (d, $J = 7.3$ Hz, 1H), 7.24−7.53 (m, 15H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.5, 26.1, 37.3, 63.1, 68.6, 69.2 (d, $J = 5.0$ Hz), 79.9 (d, $J = 3.7$ Hz), 82.6 (d, $J = 19.9$ Hz), 101.2, 102.0, 126.0−136.9 (16 carbons), 142.0 (d, $J = 19.9$ Hz), 142.3 (d, $J = 14.3$ Hz), 167.4 ppm; ^{31}P NMR (161.9 MHz, $CDCl_3$) δ 114.7 ppm; IR (KBr) 1658, 1434 cm^{-1}. Anal. Calcd for $C_{30}H_{32}NO_5P$: C, 69.62; H, 6.23; N, 2.71; P, 5.98. Found: C, 69.31; H, 6.23; N, 2.60; P, 5.80.

2-*tert*-Butyl-4,5-(4,6-*O*-benzylidene-3-*O*-(diphenylphosphino)-1,2-dideoxy-α-D-glucopyrano)-[2,1-*d*]-2-oxazoline (5d): 68% yield, a white solid; mp 168.1−169.0 °C; $[\alpha]^{20}_D = -26.5°$ ($c = 0.25$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.24 (s, 9H), 3.57 (dt, $J = 4.7$, 9.8 Hz, 1H), 3.64 (t, $J = 9.8$ Hz, 1H), 3.73 (dd, $J = 8.3$, 9.8 Hz, 1H), 4.20−4.30 (m, 2H), 4.36 (dd, $J = 4.7$, 9.8 Hz, 1H), 5.32 (s, 1H), 5.95 (d, $J = 7.3$ Hz, 1H), 7.24−7.53 (m, 15H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 27.3, 33.5,

(32) Luche, J.-L.; Rodriguez-Hahn, L.; Crabbé, P. *J. Chem. Soc., Chem. Commun.* **1978**, 601.
(33) Kang, J.; Cho, W. O.; Cho, H. G. *Tetrahedron: Asymmetry* **1994**, *5*, 1347.

63.0, 68.7, 69.2 (d, J = 5.6 Hz), 80.0 (d, J = 3.1 Hz), 82.5 (d, J = 20.6 Hz), 101.1, 102.3, 126.0−136.9 (16 carbons), 142.0 (d, J = 19.3 Hz), 142.3 (d, J = 14.9 Hz), 174.0 ppm; ^{31}P NMR (161.9 MHz, $CDCl_3$) δ 115.4 ppm; IR (KBr) 1648, 1434 cm^{-1}. Anal. Calcd for $C_{30}H_{32}NO_5P$: C, 69.62; H, 6.23; N, 2.71; P, 5.98. Found: C, 69.37; H, 6.20; N, 2.73; P, 6.25.

2-Phenyl-4,5-(4,6-*O*-benzylidene-3-*O*-(diphenylphosphino)-1,2-dideoxy-α-D-glucopyrano)-[2,1-*d*]-2-oxazoline (5e): 62% yield, a white solid; mp 176.0−176.6 °C; $[\alpha]^{20}_D$ = +37.6° (c = 0.25, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.65−3.75 (m, 2H), 3.80 (t, J = 8.8 Hz, 1H), 4.39−4.47 (m, 3H), 5.36 (s, 1H), 6.17 (d, J = 7.3 Hz, 1H), 7.27−8.00 (m, 20H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 63.2, 68.6, 69.6 (d, J = 5.5 Hz), 79.8 (d, J = 3.6 Hz), 82.5 (d, J = 22.0 Hz), 101.3, 102.7, 126.0−136.9 (22 carbons), 141.9 (d, J = 18.4 Hz), 142.3 (d, J = 16.5 Hz), 163.7 ppm; ^{31}P NMR (161.9 MHz, $CDCl_3$) δ 115.9 ppm; IR (KBr) 1634, 1434 cm^{-1}. Anal. Calcd for $C_{32}H_{28}NO_5P$: C, 71.50; H, 5.25; N, 2.61; P, 5.76. Found: C, 71.48; H, 5.14; N, 2.41; P, 6.04.

2-Benzyl-4,5-(4,6-*O*-benzylidene-3-*O*-(diphenylphosphino)-1,2-dideoxy-α-D-glucopyrano)-[2,1-*d*]-2-oxazoline (5f): 56% yield, a white solid; mp 154.6−155.0 °C; $[\alpha]^{20}_D$ = −29.3° (c = 0.25, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.53 (dt, J = 5.0, 9.7 Hz, 1H), 3.61 (t, J = 9.7 Hz, 1H), 3.67 (s, 2H), 3.74 (t, J = 9.7 Hz 1H), 4.24−4.31 (m, 3H), 5.33 (s, 1H), 5.95 (d, J = 7.8 Hz, 1H), 7.22−7.52 (m, 20H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 35.2, 63.0, 68.5, 69.3 (d, J = 5.0 Hz), 79.6 (d, J = 3.7 Hz), 82.3 (d, J = 19.9 Hz), 101.2, 102.5, 126.0−136.9 (22 carbons), 141.9 (d, J = 23.0 Hz), 142.2 (d, J = 18.1 Hz), 166.4 ppm; ^{31}P NMR (161.9 MHz, $CDCl_3$) δ 114.9 ppm; IR (KBr) 1657, 1434 cm^{-1}. Anal. Calcd for $C_{33}H_{30}NO_5P$: C, 71.86; H, 5.48; N, 2.54; P, 5.62. Found: C, 71.74; H, 5.36; N, 2.45; P, 6.01.

Typical Procedure of Allylic Alkylation of 1,3-Diphenyl-3-acetoxyprop-1-ene (6). The chiral ligand **5a** (2.62 mg, 5.5 × 10^{-3} mmol) and [Pd(η^3-C_3H_5)Cl]$_2$ (0.91 mg, 2.5 × 10^{-3} mmol) were dissolved in degassed toluene (0.5 mL) under Ar, and the solution was stirred at room temperature. After 30 min the acetate **6** (0.25 g, 1.0 mmol) in toluene (1.5 mL) was added, and the mixture was stirred for 30 min. *N*,*O*-Bis(trimethylsilyl)acetamide (0.74 mL, 3 mmol), dimethyl malonate (0.35 mL, 3 mmol), and KOAc (5 mg) were added to the above mixture in this order at 0 °C, and the mixture was stirred at this temperature. After 6 h the reaction mixture was added to saturated NH_4Cl(aq) and extracted with Et_2O (10 mL × 3), and the extract was dried over $MgSO_4$. Solvent was removed under reduced pressure, and the residue was subjected to column chromatography on silica gel with hexane/AcOEt (v/v, 5:1) as an eluent to give compound **10** (0.27 g, 0.81 mmol, 81%). The enantiomeric excess was determined by HPLC (Chiralcel AD column, 1.0 mL/min, hexane:2-propanol = 95:5). The absolute configuration was determined by optical rotation.[3a]

Typical Procedure of Allylic Alkylation of 1,3-Diphenyl-3-acetoxyprop-1-ene (6) in the Presence of Tetrabutylammonium Fluoride. The chiral ligand **5a** (2.62 mg, 5.5 × 10^{-3} mmol) and [Pd(η^3-C_3H_5)Cl]$_2$ (0.91 mg, 2.5 × 10^{-3} mmol) were dissolved in degassed toluene (0.5 mL) under Ar, and the solution was stirred at room temperature. After 30 min the acetate **6** (0.25 g, 1.0 mmol) in toluene (1.5 mL) was added to the above solution, and the mixture was stirred for 30 min. Dimethyl malonate (0.35 mL, 3 mmol) and 1 M tetrabutylammonium fluoride in THF (3 mL, 3 mmol) were added at room temperature, and the mixture was stirred for 2 h at this temperature. Purification and determination of ee were the same as those described above.

Allylic Alkylation of 3-Acetoxycyclohexene (8). The chiral ligand **5a** (5.24 mg, 11 × 10^{-3} mmol) and [Pd(η^3-C_3H_5)Cl]$_2$ (1.82 mg, 5.0 × 10^{-3} mmol) were dissolved in degassed THF (0.5 mL) under Ar, and the solution was stirred at room temperature. After 30 min, the acetate **8** (0.14 g, 1.0 mmol) in THF (1.5 mL) was added, and the solution was stirred for 30 min. *N*,*O*-Bis(trimethylsilyl)acetamide (0.74 mL, 3 mmol), dimethyl malonate (0.35 mL, 3 mmol), and KOAc (5 mg) were added in this order at 0 °C, and the stirring was continued at this temperature. After 7 h the reaction mixture was added to saturated NH_4Cl(aq) and extracted with Et_2O three times, and the extract was dried over $MgSO_4$. Solvent was removed under reduced pressure, and the residue was subjected to column chromatography on silica gel with hexane/AcOEt (v/v, 5:1) as an eluent to give compound **11** (0.17 g, 0.88 mmol, 88%). The enantiomeric excess was determined by Eu(hfc)$_3$. The absolute configuration was determined by optical rotation.[20]

Allylic Alkylation of 4-Acetoxypent-2-ene (9). The acetate **9** (0.13 g, 1.0 mmol) was used instead of **8**, and the product was purified by column chromatography on silica gel with hexanes/Et_2O (v/v, 5:1) as an eluent to give compound **12** (0.14 g, 0.69 mmol, 69%). The enantiomeric excess was determined by ^{1}H NMR with Eu(hfc)$_3$.

Typical Procedure of Allylic Alkylation of Cinnamyl Acetate (13). The chiral ligand **5d** (5.70 mg, 11 × 10^{-3} mmol) and [Pd(η^3-C_3H_5)Cl]$_2$ (1.81 mg, 5.0 × 10^{-3} mmol) were dissolved in degassed toluene (0.5 mL) under Ar, and the solution was stirred at room temperature. After 30 min the acetate **13** (0.176 g, 1.0 mmol) in toluene (1.5 mL) was added to the above solution, and the mixture was stirred for 30 min. *N*,*O*-Bis(trimethylsilyl)acetamide (0.74 mL, 3 mmol), dimethyl malonate (0.35 mL, 3 mmol), and KOAc (5 mg) were added to the mixture in this order at room temperature, and the mixture was stirred at this temperature. After 2 h, the reaction mixture was added to saturated NH_4Cl(aq) and extracted with Et_2O (10 mL × 3), and the extract was dried over $MgSO_4$. The crude product (^{1}H NMR, **14**:**15** = 11:89)[27] was purified by column chromatography on silica gel with hexane/AcOEt (v/v, 5:1) as an eluent to afford a mixture of **14** and **15** (0.21 g, 0.85 mmol, 85%). The enantiomeric excess of **14** and the absolute configuration were determined by HPLC (Chiralcel OJ column).[28i]

General Procedure of Allylic Amination of Ethyl 1,3-Diphenylprop-2-enyl Carbonate (7). The chiral ligand **5a** (5.24 mg, 11 × 10^{-3} mmol) and [Pd(η^3-C_3H_5)Cl]$_2$ (1.82 mg, 5.0 × 10^{-3} mmol) were dissolved in degassed toluene (0.5 mL) under Ar, and the solution was stirred at room temperature. After 30 min, the solution of the carbonate **7** (94 mg, 0.33 mmol) and benzylamine ($BnNH_2$) (107 mg, 1.0 mmol) in toluene (1.5 mL) was added to the above solution, and the solution was stirred at room temperature. After 24 h, solvent was removed under reduced pressure, and the residue was subjected to column chromatography on silica gel with hexane/AcOEt (v/v, 5:1) as an eluent to give compound **16** (79 mg, 0.26 mmol, 78%). The enantiomeric excess was determined by HPLC (Chiralcel OJ column, 1.0 mL/min, hexane:2-propanol = 95:5).[34] The absolute configuration was determined by optical rotation.[30]

Supporting Information Available: Spectral and analytical data for new compounds **2a**−**f** and **3a**−**f**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(34) Sudo, A.; Saigo, K. *J. Org. Chem.* **1997,** *62,* 5508.