A Novel Amphiphilic Chiral Ligand Derived from D-Glucosamine. Application to Palladium-Catalyzed Asymmetric Allylic Substitution Reaction in an Aqueous or an Organic Medium, Allowing for Catalyst Recycling

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A novel amphiphilic phosphinite−oxazoline chiral compound, 2-methyl-4,5-[4,6-*O*-benzylidene-3-*O*-bis{4-((diethylamino)methyl)phenyl}phosphino-1,2-dideoxy-α-D-glucopyranosyl]-[2,1-*d*]-2-oxazoline (**1**), has been prepared from natural D-glucosamine hydrochloride. The newly prepared complex, [Pd(2-methyl-4,5-[4,6-*O*-benzylidene-3-*O*-bis{(4-((diethylmethylammonium)methyl)phenyl)}phosphino-1,2-dideoxy-α-D-glucopyranosyl]-[2,1-*d*]-2-oxazoline)(η^3-C_3H_5)]$^{3+}$·3BF_4^- (**3**), is soluble in water and an efficient catalyst for asymmetric allylic substitution reaction in water or an aqueous/organic biphasic medium (up to 85% ee). This catalytic system offers an easy separation of the aqueous catalyst phase from the product phase and allows recycling of the catalyst phase. In addition, compound **1** also works as an effective ligand for the palladium-catalyzed reaction under conventional homogeneous conditions in an organic medium, in which the catalyst (Pd−**1** complex) can be recovered by simple acid/base extraction and reused in the second reaction.

Introduction

Homogeneous chiral catalysts are extensively used in both organic syntheses and several industrial chemical processes, mainly because of their high activity and selectivity.[1] Recently, concerns over hazardous waste generated during catalytic reactions and separation of products from catalyst increasingly led to the development of systems that employ water as solvent.[2] The benefits gained by using aqueous catalytic systems include easier product separation, decreased cost, increased safety, and more efficient catalyst recycling. In these catalytic systems, organometallic complexes are usually soluble in water through the use of chiral hydrophilic ligands incorporating the charged or polar substituents, providing fair to good enantioselectivity in the hydrogenation[3] and hydroformylation[4] of alkenes, the hydrogenolysis of epoxides,[5] and the oxidation of alkenes.[6] Recently, we reported the highly enantioselective hydrogenation of alkenes in water, an aqueous/organic medium, or an aqueous miceller medium using novel water-soluble cationic rhodium(I) complexes bearing hydrophilic ligands derived from α,α- and *β*,*β*-trehaloses.[7a,b] We also reported that the ligand derived from D-glucosamine was very effective for enantioselective palladium-catalyzed allylic substitution reaction in an organic medium (up to 96% ee).[8] These results encouraged us to turn our attention to asymmetric allylic substitution reactions in an aqueous medium.

To our knowledge, scarce attention has been paid to asymmetric palladium-catalyzed reaction[9] in an aqueous medium,[10] except for highly enantioselective allylic alky-

(1) For recent overviews, see: (a) Noyori, R. *Asymmetric Catalysis in Organic Synthesis*; John Wiley: New York, 1994. (b) Ojima I. *Asymmetric Synthesis*; Verlag: New York, 1993.

(2) (a) Cornils, B.; Herrmann, W. A. *Aqueous-Phase Organometallic Catalysis*; Wiley-VCH: New York, 1998. (b) Cornils, B.; Herrmann, W. A. *Applied Homogeneous Catalysis with Organometallic Compounds*; VCH: New York, 1996. (c) Hanson, B. E. *Coord. Chem. Rev.* **1999**, *185*−*186*, 795. (d) Joó, F.; Kathó, Á. *J. Mol. Catal., A* **1997**, *116*, 3. (e) Papadogianakis, G.; Sheldon, R. A. *New J. Chem.* **1996**, *20*, 175. (f) Cornils, B. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1575. (g) Beller, M.; Cornils, B.; Frohning, C. D.; Kohlpaintner, C. W. *J. Mol. Catal., A* **1995**, *104*, 17. (h) Herrmann, W. A.; Kohlpaintner, C. W. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1524.

(3) (a) Shin, S.; RajanBabu, T. V. *Org. Lett.* **1999**, *1*, 1229. (b) Holz, J.; Heller, D.; Stürmer, R.; Börner, A. *Tetrahedron Lett.* **1999**, *40*, 7059. (c) Lensink, C.; Rijnberg, E.; de Vries, J. G. *J. Mol. Catal., A* **1997**, *116*, 199. (d) Selke, R.; Ohff, M.; Riepe, A. *Tetrahedron* **1996**, *52*, 15079. (e) Ding, H.; Hanson, B. E.; Bakos, J. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1645. (f) Kumar, A.; Oehme, G.; Roque, J. P.; Schwarze, M.; Selke, R. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2197. (g) Jones, A.; Roberts, D. L.; Davis, M. E. *Nature* **1994**, *370*, 449. (h) Wan, K.-t.; Davis, M. E. *Tetrahedron: Asymmetry* **1993**, *4*, 2461. (i) Wan, K.-t.; Davis, M. E. *J. Chem. Soc., Chem. Commun.* **1993**, 1262. (j) Lensink, C.; de Vries, J. G. *Tetrahedron: Asymmetry* **1992**, *3*, 235. (k) Bakos, J.; Orosz, A.; Heil, B.; Laghmari, M.; Lhoste, P.; Sinou, D. *J. Chem. Soc., Chem. Commun.* **1991**, 1684. (l) Sinou, D.; Safi, M.; Claver, M.; Masdeu, A. *J. Mol. Catal.* **1991**, *68*, L9. (m) Amrani, Y.; Lecomte, L.; Sinou, D.; Bakos, J.; Tóth, I.; Hell, B. *Organometallics* **1989**, *8*, 542. (n) Lecomte, L.; Sinou, D. *J. Mol. Catal.* **1989**, *52*, L21. (o) Lecomte, L.; Sinou, D.; Bakos, J.; Tóth, I.; Heil, B. *J. Organomet. Chem.* **1989**, *370*, 277. (p) Alario, F.; Amrani, Y.; Colleuille, Y.; Dang, T. P.; Jenck, J.; Morel, D.; Sinou, D. *J. Chem. Soc., Chem. Commun.* **1986**, 202. (q) Amrani, Y.; Sinou, D. *J. Mol. Catal.* **1986**, *36*, 319. (r) Benhazma, R.; Amrani, Y.; Sinou, D. *J. Organomet. Chem.* **1985**, *288*, C37. (s) Amrani, Y.; Sinou, D. *J. Mol. Catal.* **1984**, *24*, 231.

(4) Eckl, R. W.; Priermeier, T.; Herrmann, W. A. *J. Organomet. Chem.* **1997**, *532*, 243.

(5) Bakos, J.; Orosz, Á.; Cserépi, S.; Tóth, I.; Sinou, D. *J. Mol. Catal., A* **1997**, *116*, 85.

(6) (a) Hamed, O.; Henry, P. M. *Organometallics* **1998**, *17*, 5184. (b) El-Qisairi, A.; Hamed, O.; Henry, P. M. *J. Org. Chem.* **1998**, *63*, 2790.

(7) (a) Yonehara, K.; Ohe, K.; Uemura, S. *J. Org. Chem.* **1999**, *64*, 9381. (b) Yonehara, K.; Hashizume, T.; Mori, K.; Ohe, K.; Uemura, S. *J. Org. Chem.* **1999**, *64*, 5593. (c) Recently, RajanBabu and a co-worker have independently reported the synthesis of water-soluble chiral Rh complex from α,α-trehalose: see ref 3a.

(8) (a) Yonehara, K.; Hashizume, T.; Mori, K.; Ohe, K.; Uemura, S. *J. Org. Chem.* **1999**, *64*, 9374. (b) Yonehara, K.; Hashizume, T.; Mori, K.; Ohe, K.; Uemura, S. *Chem. Commun.* **1999**, 415. (c) A series of phosphinite−oxazoline compounds derived from D-glucosamine also worked as effective chiral ligands for the palladium-catalyzed asymmetric intermolecular arylation of alkenes. See: Yonehara, K.; Mori, K.; Hashizume, T.; Chung, K.-G.; Ohe, K.; Uemura, S. *J. Organomet. Chem.*, in press.

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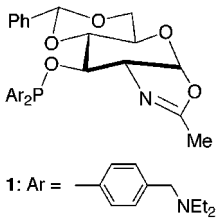


Figure 1. Phosphinite−oxazoline chiral ligands derived from D-glucosamine hydrochloride.

lation in an aqueous medium using heterogeneous resin-supported MOP−palladium catalysts reported by Uozumi and Hayashi.[11] In this paper we report the synthesis of a new *amphiphilic* chiral ligand, **1** (Figure 1), incorporating the diethylaminomethyl group at the 4-position of the phenyl ring on the phosphorus atom and its application to palladium-catalyzed asymmetric allylic substitution in aqueous or organic media, allowing for catalyst recycling. The amino group can be expected to serve as an ionizable inducer by quarternization.[12] Thus, the catalyst involving the ligand having such a quarternized functional group is soluble in water, which facilitates the catalyst recycling as well as the separation of the catalyst from water-immiscible organic products. Furthermore, the pH-controlled quarternization of amino groups and cancellation of quarternization enable the catalyst to transport between an aqueous phase and an organic phase.[13] This catalyst transport between two phases is also applicable to the catalyst recycling for palladium-catalyzed allylic substitution in the conventional organic medium as shown in Figure 2.

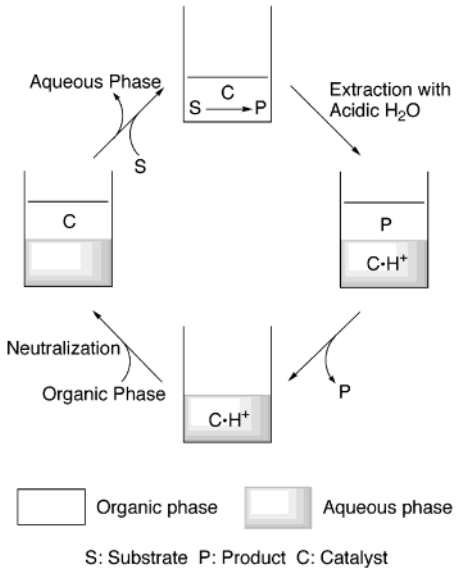


Figure 2. Catalyst recycling by pH-controlled extraction.

Results and Discussion

Syntheses of Phosphinite−Oxazoline Ligand 1 and Water-Soluble Palladium Complex 3. The preparative methods for 2-methyl-4,5-[4,6-*O*-benzylidene-3-*O*-bis{4-((diethylamino)methyl)phenyl}phosphino-1,2-dideoxy-α-D-glucopyranosyl]-[2,1-*d*]-2-oxazoline (**1**) and [Pd(2-methyl-4,5-[4,6-*O*-benzylidene-3-*O*-bis{4-((diethylmethylammonium)methyl)phenyl}phosphino-1,2-dideoxy-α-D-glucopyranosyl]-[2,1-*d*]-2-oxazoline)(η^3-C_3H_5)]$^{3+}$·3BF_4^- (**3**) are shown in Scheme 1. Initially, treatment of 2-methyl-4,5-(4,6-*O*-benzylidene-1,2-dideoxy-α-D-glucopyranosyl)-[2,1-*d*]-2-oxazoline (**2**), prepared from D-glucosamine hydrochloride in five steps,[8a,b] with bis[4-((diethylamino)methyl)phenyl]phosphinous diethylamide[13a] and 1*H*-tetrazole in degassed dry tetrahydrofuran (THF) gave the new chiral phosphinite−oxazoline **1** in 57% yield. Next, a palladium complex, [Pd(**1**)(η^3-C_3H_5)]$^+$·BF_4^-, was prepared in situ by the reaction of [Pd(cod)(η^3-C_3H_5)]$^+$·BF_4^- [14] with the ligand **1** in degassed acetone under Ar. The treatment of the solution with Me_3OBF_4[12h,k] followed by the addition of degassed dry Et_2O afforded a cationic palladium complex, **3**, in 88% yield in which two amino groups were quarternized. As can be expected, the complex **3** is soluble in water (ca. 1.47 g/100 mL at 20 °C). It is also soluble in polar organic solvents such as MeOH, MeCN, and acetone, but insoluble in hexane, toluene, and Et_2O.

Palladium-Catalyzed Asymmetric Allylic Substitution Reaction in an Aqueous Medium. First, asymmetric allylic substitution reaction of 1,3-diphenyl-3-acetoxyprop-1-ene in an MeCN/H_2O biphasic medium with various nucleophiles was examined using the catalyst **3**. The catalyst **3** was soluble in MeCN as well as in an aqueous phase. However, after the reaction, all of the catalyst in MeCN could be transferred into an aqueous phase by addition of Et_2O in which the complex **3** is insoluble, thereby being separated from the product phase. These results are summarized in Table 1. The

(9) (a) Tsuji, J. *Palladium Reagents and Catalysis, Innovations in Organic Synthesis*; Wiley: New York, 1995. (b) Helmchen, G. *J. Organomet. Chem*. **1999**, *576*, 203. (c) Hayashi, T. *J. Organomet. Chem*. **1999**, *576*, 195. (d) Trost, B. M.; Van Vranken, D. L. *Chem. Rev*. **1996**, *96*, 395. (e) Dawson, G. J.; Frost, C. G.; Williams, J. M. J. *Tetrahedron Lett*. **1993**, *34*, 3149. (f) Sprinz, J.; Helmchen, G. *Tetrahedron Lett*. **1993**, *34*, 1769. (g) Matt, P.; Pfaltz, A. *Angew. Chem., Int. Ed. Engl*. **1993**, *32*, 566.

(10) Nonasymmetric allylic substitution reaction catalyzed by palladium−tris(sodium-*m*-sulfonatophenyl)phosphine in an aqueous medium has also been reported: (a) Genêt, J. P.; Savignac, M. *J. Organomet. Chem*. **1999**, *576*, 305. (b) dos Santos, S.; Tong, Y.; Quignard, F.; Choplin, A.; Sinou, D.; Dutasta, J. P. *Organometallics* **1998**, *17*, 78. (c) Sigismondi, S.; Sinou, D. *J. Mol. Catal., A* **1997**, *116*, 289. (d) Lemaire-Audoire, S.; Savignac, M.; Pourcelot, G.; Genêt, J. P.; Bernard, J.-M. *J. Mol. Catal., A* **1997**, *116*, 247. (e) Blart, E.; Genêt, J. P.; Safi, M.; Savignac, M.; Sinou, D. *Tetrahedron* **1994**, *50*, 505. (f) Genêt, J. P.; Blart, E.; Savignac, M.; Lemeune, S.; Lemaire-Audoire, S.; Paris, J.-M.; Bernard, J.-M. *Tetrahedron* **1994**, *50*, 497. (g) Genêt, J. P.; Blart, E.; Savignac, M. *Synlett* **1992**, 715. (h) Safi, M.; Sinou, D. *Tetrahedron Lett*. **1991**, *32*, 2025.

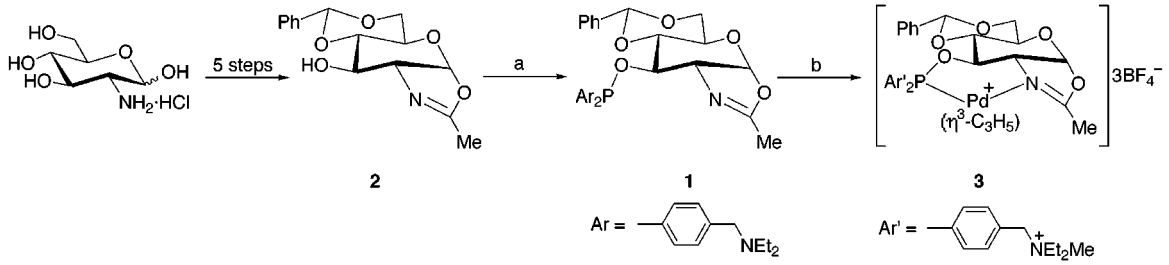
(11) Uozumi, Y.; Danjo, H.; Hayashi, T. *Tetrahedron Lett*. **1998**, *39*, 8303.

(12) For the quaternization of the amino group to gain solubility in water, see: (a) Tóth, I.; Guo, I.; Hanson, B. E. *J. Mol. Catal., A* **1997**, *116*, 217. (b) Mohr, B.; Lynn, D. M.; Grubbs, R. H. *Organometallics* **1996**, *15*, 4317. (c) Bitterer, F.; Kucken, S.; Stelzer, O. *Chem. Ber*. **1995**, *128*, 275. (d) Tóth, I.; Hanson, B. E. *Organometallics* **1993**, *12*, 1506. (e) Tóth, I.; Hanson, B. E.; Davis, M. E. *J. Organomet. Chem*. **1990**, *396*, 363. (f) Tóth, I.; Hanson, B. E.; Davis, M. E. *Tetrahedron: Asymmetry* **1990**, *1*, 913. (g) Tóth, I.; Hanson, B. E. *Tetrahedron: Asymmetry* **1990**, *1*, 895. (h) Tóth, I.; Hanson, B. E.; Davis, M. E. *Catal. Lett*. **1990**, *5*, 183. (i) Peiffer, G.; Chhan, S.; Bendayan, A.; Waegell, B.; Zahra, J.-P. *J. Mol. Catal*. **1990**, *59*, 1. (j) Nagel, U.; Kinzel, E. *Chem. Ber*. **1986**, *119*, 1731. (k) Smith, R. T.; Ungar, R. K.; Sanderson, L. J.; Baird, M. C. *Organometallics* **1983**, *2*, 1138.

(13) (a) Buhling, A.; Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Elgersma, J. W.; Goubitz, K.; Fraanje, J. *Organometallics* **1997**, *16*, 3027. (b) Buhling, A.; Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Elgersma, J. W. *J. Mol. Catal., A* **1997**, *116*, 297. (c) Buhling, A.; Elgersma, J. W.; Nkrumah, S.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. *J. Chem. Soc., Dalton Trans*. **1996**, 2143. (d) Buhling, A.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. *J. Mol. Catal*. **1995**, *98*, 69. (e) Bayón, J. C.; Rael, J.; Claver, C.; Polo, A.; Ruiz, A. *J. Chem. Soc., Chem. Commun*. **1989**, 1056. (f) Kurtev, K.; Ribola, D.; Jones, R. A.; Cole-Hamilton, D. J.; Wilkinson, G. *J. Chem. Soc., Dalton Trans*. **1980**, 55.

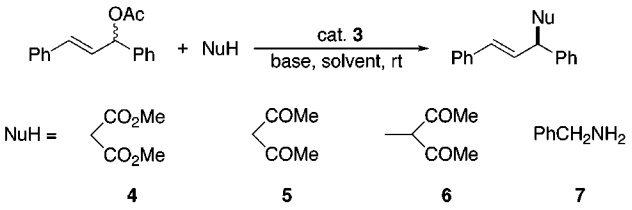
(14) White, D. A. *Inorg. Synth*. **1972**, *13*, 61.

Scheme 1[a]



[a] Reagents and conditions: (a) bis[4-((diethylamino)methyl)phenyl]phosphinous diethylamide, 1*H*-tetrazole, THF, rt, 30 min, 57%; (b) (i) $[Pd(cod)(\eta^3\text{-}C_3H_5)]^+ \cdot BF_4^-$, acetone, rt, 30 min; (ii) Me_3OBF_4, rt, 30 min, 88% (two steps).

Table 1. Asymmetric Allylic Substitution of 1,3-Diphenyl-3-acetoxyprop-1-ene Using 3 in an Aqueous Medium[a]



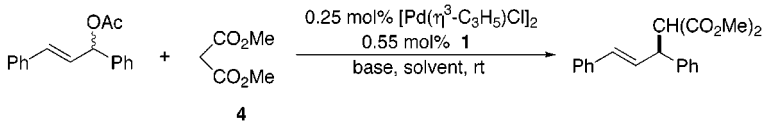
entry	NuH	base	solvent	cat. (mol%)	time (h)	yield (%)[b]	ee (%)[c,d]
1	**4**	BSA + cat. KOAc	MeCN	1	1	95	92 (*S*)
2	**4**	K_2CO_3	MeCN/H_2O = 4/1	5	48	0	–
3	**5**	K_2CO_3	MeCN/H_2O = 4/1	5	3	85	83 (*S*)
4	**6**	K_2CO_3	MeCN/H_2O = 4/1	5	12	66	77 (*R*)
5	**6**	K_2CO_3	toluene/H_2O = 1/1	5	24	51	80 (*R*)
6	**7**	K_2CO_3	MeCN/H_2O = 4/1	4	5	80	84 (*R*) (77)[e]
7	**7**	K_2CO_3	H_2O	4	18	73	85 (*R*) (60)[e]

[a] Reactions were carried out under Ar using 1,3-diphenyl-3-acetoxyprop-1-ene (0.80 mmol), NuH (1.6 mmol), base (3.6 mmol), solvent (3.0 mL), and catalyst **4** (1−5 mol %). [b] Isolated yield. [c] The ee (%) values were determined by HPLC. [d] The absolute configuration was determined by its optical rotation.[9f,15−17] [e] The enantiomeric excess obtained from the second use of the aqueous solution containing the catalyst.

reaction with dimethyl malonate (**4**) using *N*,*O*-bis(trimethylsilyl)acetamide (BSA) proceeded smoothly in MeCN to give high enantioselectivity (92% ee) (entry 1), while this reaction did not take place in an MeCN/H_2O = 4/1 biphasic system in the presence of K_2CO_3 (entry 2). However, the reaction with acetylacetone (**5**) in place of dimethyl malonate gave the corresponding product in good yield (85%) with 83% ee under the biphasic conditions (entry 3). The lack of reactivity of dimethyl malonate (pK_a = 13.3) compared to acetylacetone (pK_a = 8.94) is probably due to its higher pK_a; the formation of the enol form disfavors the presence of water.[10c] The reaction with 3-methyl-2,4-pentanedione (**6**) also proceeded to give the corresponding product with 77% ee (entry 4). In a toluene/H_2O biphasic medium in which the catalyst was dissolved only in the aqueous phase, the product was also obtained with 80% ee, although the yield decreased (entry 5). When benzylamine (**7**) was used as a nucleophile, the reaction was complete within 5 h and high enantioselectivity (84% ee) was obtained. After the reaction, the aqueous phase containing the catalyst was easily separated by phase separation as mentioned above and reused for the same allylic amination to give 77% ee (entry 6). The reaction proceeded even in H_2O to give the product with 85% ee, but the reaction was slower compared to that in the biphasic system. In this case, after the extraction of the product using hexane, the aqueous phase containing the catalyst was also reused for the same reaction to give 60% ee (entry 7).

Palladium Catalyst Recycling by pH-Controlled Extraction. After the reaction was performed using the complex bearing the ligand **1** in an organic medium, the catalyst could be extracted into an acidic aqueous phase as an ammonium salt, allowing the simple separation of the product, and re-extracted into fresh organic solvent after neutralization of the aqueous phase. Table 2 shows the results of the catalyst recycling in asymmetric allylic alkylation. First, the reaction was carried out in toluene using a catalyst generated in situ by mixing 0.25 mol % $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ with 0.55 mol % ligand **1** in the presence of BSA at room temperature. After the reaction, 0.48 M aqueous HBF_4 was added to the mixture to quarternize two amino groups, and the quarternized catalyst was extracted into an aqueous phase. An organic phase containing the product (85% yield, 93% ee) was separated, and then fresh toluene was added. The acidic solution was neutralized with saturated aqueous $NaHCO_3$ under rapid stirring until the aqueous phase became colorless. The separated toluene layer containing the catalyst was placed in the reaction vessel, and again the reaction was carried out under the same conditions. However, the second use of the catalyst unfortunately was frustrated in the conversion of the substrate (5% yield, 86% ee) (entry 1). Next, the reaction was carried out in tetrahydrofuran (THF) in place of toluene. After the first reaction was complete, 0.48 M aqueous HBF_4 was added and the product (95% yield, 91% ee) was extracted with hexane. After fresh CH_2Cl_2 was added to an acidic aqueous solution, it was neutralized under rapid stirring with saturated aqueous $NaHCO_3$, and then the organic layer including the catalyst was separated. Evaporation of organic solvent from the recovered CH_2-

Table 2. Results of the Recycling Experiments[a]



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			time (h)		yield (%)[b]		ee (%)[c] (*S*)[d]	
entry	base	solvent	1st	2nd	1st	2nd	1st	2nd
1	BSA + cat. KOAc	toluene	1	36	85	5	93	86
2	BSA + cat. KOAc	THF	1	12	95	79	91	92
3	NaH	THF	2	12	97	90	89	89

[a] Reactions were carried out under Ar using 1,3-diphenyl-3-acetoxyprop-1-ene (1.0 mmol), dimethyl malonate (2.0 mmol), base (2.0 mmol), solvent (3.5 mL), $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (2.5×10^{-3} mmol), and ligand (5.5×10^{-3} mmol). Recycling conditions are as follows: (1) Extraction of the catalyst with 0.48 M aqueous HBF_4. (2) Neutralization of an aqueous phase with $HaHCO_3$ and re-extraction of the catalyst with an organic solvent. [b] Isolated yield. [c] Determined by HPLC. [d] Determined by its optical rotation.[9f]

Cl_2 solution gave the yellow residue,[15] which was dissolved in degassed dry THF and used again under the same conditions. This procedure substantially improved the product yield to 79% without a decrease of enantioselectivity (92% ee) in the second reaction (entry 2). Moreover, the use of NaH instead of BSA and KOAc did not cause the unfavorable decrease of the chemical yield as well as selectivity in the second reaction (entry 3).

Summary

Starting from natural D-glucosamine, the amphiphilic phosphinite−oxazoline **1** bearing a diethylaminomethyl group on the phenyl ring of the phosphinite moiety and the water-soluble cationic palladium complex **3** were newly prepared. Complex **3** worked effectively as a catalyst and provided good enantiomeric excess in allylic alkylation and amination in water or an aqueous/organic biphasic medium (up to 85% ee). The product could be easily separated from the water-soluble catalyst by simple phase separation. To the best of our knowledge, these are the first examples of palladium-catalyzed asymmetric allylic substitution reaction in an aqueous medium using a homogeneous catalyst. In addition, it was demonstrated that the palladium complex bearing the ligand **1** was an effective catalyst for allylic substitution reaction in an organic medium, and it could be reused in the second reaction by pH-controlled phase separation without a decrease of both yield and enantioselectivity.

Experimental Section

General Procedures. Tetrahydrofuran (THF) and diethyl ether were distilled from sodium benzophenone ketyl under argon. Analytical thin-layer chromatographies (TLC) were performed with silica gel 60 Merck F-254 plates or aluminum oxide 60 Merck F-254. Column chromatographies were performed with Merck silica gel 60 or ICN Alumina Akt I (neutral). The NMR spectra were measured for solutions in $CDCl_3$ or d_6-acetone with Me_4Si as an internal standard (^1H and ^{13}C) or with $P(OMe)_3$ as an external standard (^{31}P). The following abbreviations are used: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. IR spectra were recorded with an FT-IR spectrometer. Optical rotations were recorded at 589 nm. Enantiomeric ratios were determined by HPLC with a Daicel Chiralcel AD or OJ column (4.6 × 250 mm) at 40 °C. Melting points are uncorrected. Elemental analyses were performed at the Microanalytical Center of Kyoto University. Compound **2** was prepared according to the reported procedure.[8a,b]

2-Methyl-4,5-[4,6-*O*-benzylidene-3-*O*-bis{4-((diethylamino)methyl)phenyl}phosphino-1,2-dideoxy-α-D-glucopyranosyl]-[2,1-*d*]-2-oxazoline (1). To a solution of **2** (0.56 g, 1.9 mmol) in 10 mL of degassed dry THF (25 mL) was added bis[4-((diethylamino)methyl)phenyl]phosphinous diethylamide[13a] (1.1 g, 2.5 mmol) followed by the addition of 1*H*-tetrazole (0.20 g, 3.0 mmol) at room temperature, and the mixture was stirred for 30 min. It 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) containing 1% triethylamine as an eluent to give 2-methyl-4,5-[4,6-*O*-benzylidene-3-*O*-bis{(4-((diethylamino)methyl)phenyl}phosphino-1,2-dideoxy-α-D-glucopyranosyl]-[2,1-*d*]-2-oxazoline (**1**) (0.71 g, 1.1 mmol, 57%) as a white solid: mp 103.2−104.0 °C; $[\alpha]^{21}_D = -55.5$ (*c* = 0.25, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.01 (t, *J* = 7.1 Hz, 6H), 1.03 (t, *J* = 7.1 Hz, 6H), 2.04 (d, *J* = 1.1 Hz, 3H), 2.47 (q, *J* = 7.1 Hz, 4H), 2.51 (q, *J* = 7.1 Hz, 4H), 3.50 (s, 2H), 3.52 (s, 2H), 3.59−3.68 (m, 2H), 3.76 (t, *J* = 8.5 Hz, 1H), 4.23−4.40 (m, 3H), 5.35 (s, 1H), 5.97 (d, *J* = 7.5 Hz, 1H), 7.20−7.46 (m, 13H) ppm; ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 11.7, 14.3, 46.7, 57.3, 62.8, 68.6, 69.5 (d, *J* = 5.0 Hz), 79.9 (d, *J* = 3.7 Hz), 82.0 (d, *J* = 19.9 Hz), 101.1, 102.1, 126.0−130.7 (8 carbons), 140.0 (d, *J* = 19.3 Hz), 140.3 (d, *J* = 13.7 Hz), 141.28, 141.32, 164.9 ppm; ^{31}P NMR (161.9 MHz, $CDCl_3$) δ 115.0 ppm; IR (KBr) 1455, 1666, 3443 cm^{-1}. Anal. Calcd for $C_{37}H_{48}N_3O_5P$: C, 68.82; H, 7.49; N, 6.51; P, 4.80. Found: C, 68.61; H, 7.66; N, 6.42; P, 4.91.

[Pd(2-methyl-4,5-[4,6-*O*-benzylidene-3-*O*-bis{(4-((diethylmethylammonium)methyl)phenyl)}phosphino-1,2-dideoxy-α-D-glucopyranosyl]-[2,1-*d*]-2-oxazoline)(η^3-C_3H_5)]$^{3+}$·3BF_4^- (3). $[Pd(cod)(\eta^3\text{-}C_3H_5)]^+ \cdot BF_4^-$ [14] (38 mg, 0.11 mmol) and **1** (75 mg, 0.12 mmol) were dissolved in degassed acetone (0.60 mL), and the mixture was stirred under Ar. After 30 min, Me_3OBF_4 (38 mg, 0.26 mmol) was added to the above solution, and the mixture was stirred for a further 30 min. Degassed dry Et_2O (4.0 mL) was added, and the solution was cooled at 0 °C for 2 h. The supernatant solution was decantated, and a separated yellow syrup was dried under reduced pressure to give the product **3** (105 mg, 9.7×10^{-2} mmol, 88%) as a pale yellow powder: mp 188.0−191.0 °C; ^{31}P NMR (161.9 MHz, d_6-acetone) δ 121.9, 122.4 (1:1 mixture of diastereomers) ppm. Anal. Calcd for $C_{42}H_{59}B_3F_{12}N_3O_5PPd$: C, 46.55; H, 5.49; N, 3.88. Found: C, 46.12; H, 5.42; N, 3.97.

A Typical Procedure of Allylic Substitution Reaction of 1,3-Diphenyl-3-acetoxyprop-1-ene in an MeCN/H_2O Biphasic Medium. To complex **3** (34.8 mg, 3.2×10^{-2} mmol) in degassed H_2O (0.60 mL) was added a solution of (*E*)-1,3-diphenyl-3-acetoxyprop-1-ene (0.20 g, 0.80 mmol) in degassed MeCN (2.4 mL) followed by the addition of benzylamine (0.18 mL, 1.6 mmol) and K_2CO_3 (0.51 g, 3.6 mmol) in this order,

(15) The recovered catalyst weighed 9.0 mg, which was much more than the total amount of catalyst and ligand loaded in the first catalytic reaction. The increase of the amount of catalyst may be due to the ligand exchange from both simple allyl to 1,3-diphenylallyl and chloride to BF_4 or others.

and the mixture was stirred vigorously under Ar. After the complete conversion was confirmed by TLC monitoring (5 h), Et_2O (3.0 mL) was added, and the mixture was stirred vigorously for 10 min. After the organic phase was separated by decantation, the solvent was evaporated 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 the product (0.19 g, 0.64 mmol, 80%). The separation of the racemic mixture under HPLC conditions is as follows: (*E*)-1-benzylamino-1,3-diphenylprop-2-ene (OJ, 1.0 mL/min, 5% 2-PrOH/hexane, 254 nm), (*S*), $t_1 = 16.3$ min; (*R*), $t_2 = 19.1$ min; (*E*)-methyl 2-methoxycarbonyl-3,5-diphenylpent-4-enoate (AD, 1.0 mL/min, 5% 2-PrOH/hexane, 254 nm); (*S*), $t_1 = 11.1$ min; (*R*), $t_2 = 14.2$ min; (*E*)-3-acetyl-4,6-diphenylhex-5-en-2-one (AD, 1.0 mL/min, 1% 2-PrOH/hexane, 254 nm); (*S*), $t_1 = 25.6$ min; (*R*), $t_2 = 32.3$ min; (*E*)-3-acetyl-3-methyl-4,6-diphenylhex-5-en-2-one (OJ, 1.0 mL/min, 10% 2-PrOH/hexane, 254 nm); (*S*), $t_1 = 11.3$ min; (*R*), $t_2 = 15.4$ min. The absolute configurations were determined by their optical rotation.[9f,16−18]

Palladium Complex Recycling Experiment. The chiral ligand **1** (3.6 mg, 5.5×10^{-3} mmol) and $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (0.91 mg, 2.5×10^{-3} mmol) were dissolved in degassed dry THF (0.50 mL) under Ar, and the solution was stirred at room temperature. After 30 min, (*E*)-1,3-diphenyl-3-acetoxyprop-1-ene (0.25 g, 1.0 mmol) was added, and the mixture was stirred for 30 min. A 0.66 M sodium dimethyl malonate/THF solution (3.0 mL, 2.0 mmol), which was prepared from dimethyl malonate (0.24 mL, 2.0 mmol) and NaH (48 mg, 2.0 mmol) in degassed dry THF (3.0 mL), was added to the above mixture, and the resulting mixture was stirred at this temperature for 2 h. Aqueous HBF_4 (0.48 M) (2.3 mL, 1.1 mmol) was added, then the product was extracted with hexane (3.0 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 the product (*E*)-methyl 2-methoxycarbonyl-3,5-diphenylpent-4-enoate (0.32 g, 0.97 mmol, 97%). The yellow aqueous layer was poured into a flask, and fresh degassed CH_2Cl_2 was added. The acidic solution was neutralized with saturated aqueous $NaHCO_3$ under rapid stirring until the aqueous phase became colorless, and then the organic layer was separated. The aqueous phase was again extracted with CH_2Cl_2 (3.0 mL), and the combined yellow organic phase was concentrated to dryness. The residue, which weighed 9.0 mg, was dissolved in degassed dry THF (0.5 mL), (*E*)-1,3-diphenyl-3-acetoxyprop-1-ene (0.25 g, 1.0 mmol) and then 0.66 M sodium dimethyl malonate solution in THF (3.0 mL, 2.0 mmol) were added, and the mixture was stirred at room temperature. After 12 h, 0.48 M aqueous HBF_4 (2.3 mL, 1.1 mmol) was added, the product was extracted with hexane (3.0 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 the product (*E*)-methyl 2-carbomethoxy-3,5-diphenylpent-4-enoate (0.29 g, 0.90 mmol, 90%). The enantiomeric excess (first use, 89% ee; second use, 89% ee) was determined by HPLC.

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

(17) Hayashi, T.; Yamamoto, A.; Hagihara, T.; Ito, Y. *Tetrahedron Lett.* **1986**, *27*, 191.

(18) The absolute configuration of (*R*)-(*E*)-3-acetyl-3-methyl-4,6-diphenylhex-5-en-2-one assigned in ref 11, where the direction of optical rotation is described as (−), seems to be incorrect. The direction of optical rotation of (*R*)-(*E*)-3-acetyl-3-methyl-4,6-diphenylhex-5-en-2-one is indeed (+) in our measurement.