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# Synthesis, Reaction, and Recycle of Fluorous Palladium Catalysts for an Asymmetric Allylic Alkylation without Using Fluorous Solvents

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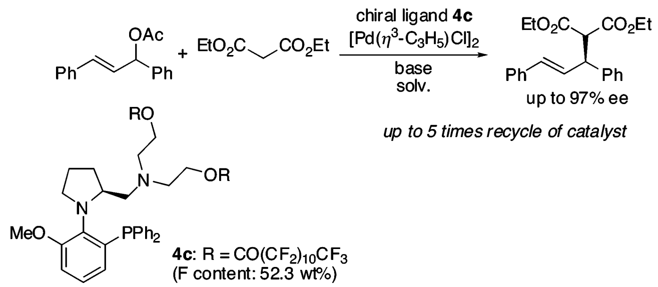

Chiral fluorous aminophosphine **4c** bearing two fluorous ponytails was prepared from (*S*)-prolinol and applied to palladium-catalyzed asymmetric allylic alkylation of 1,3-diphenyl-2-propenyl acetate (**7**) with a dialkyl malonate-BSA-LiOAc system with high enantioselectivities (up to 97% ee). Results indicated that the chiral fluorous palladium catalyst from ligand **4c** was easily separated from the reaction mixture by simple solid/liquid separation and could be reused up to five times.

## Introduction

Palladium-catalyzed allylic alkylation is a widely employed process in organic synthesis,[1] and the development of efficient enantioselective catalysis for this reaction is eagerly awaited.[2] It has been found that chiral 2-(phosphinoaryl)oxazoline can induce high enantiomeric excesses in this reaction.[3] Following this pioneering study, aminophosphines have been used as ligands for this reaction; in particular pyrrolidinyl-containing aminophosphines were found to be efficient chiral sources.[4] Previously, we reported the preparation of chiral aminophosphine **1**,[5] diaminophosphine **2**,[6] and their derivatives and investigated the effect of the terminal groups of side chain on the ligand in palladium-catalyzed asymmetric allylic alkylation (AAA reaction).

Because of the broad range of applications belonging to this class of ligands and the high enantioselectivities obtained, many efforts have been devoted to its immobilization on supports in order to recover and recycle

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[1] (a) Tsuji, J.; Minami, I. *Acc. Chem. Res.* **1987**, *20*, 140. (b) Trost, B. M.; Verhoeven, T. R. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon: Oxford, 1982; Vol. 8, p 799. (c) Trost, B. M. *Acc. Chem. Res.* **1980**, *13*, 385. (d) Heck, R. F. In *Palladium Reagents in Organic Syntheses*; Academic Press: Orlando, 1985.

[2] (a) Trost, B. M. *Chem. Pharm. Bull.* **2002**, *50*, 1 (b) Trost, B. M.; Lee, C. In *Catalytic Asymmetric Synthesis*, 2nd ed; Ojima, I., Ed.; VCH Publishers: New York, 2000; p 893. (c) Helmchen, G. *J. Organomet. Chem.* **1999**, *576*, 203. (d) Pfaltz, A.; Lautens, M. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: Tokyo, 1999; Vol. 2, p 833 and references therein.

[3] (a) Dawson, J. G.; Frost, C. G.; Williams, J. M. J.; Coote, S. J. *Tetrahedron Lett.* **1993**, *34*, 3149. (b) Von Matt, P.; Pfaltz, A. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 566. (c) Sprinz J.; Helmchen, G. *Tetrahedron Lett.* **1993**, *34*, 1769.

[4] (a) Kondo, K.; Kazuta, K.; Fujita, H.; Sakamoto, Y.; Murakami, Y. *Tetrahedron* **2002**, *58*, 5209. (b) Farrell, A.; Goddard, R.; Guiry, P. J. *J. Org. Chem.* **2002**, *67*, 4209. (c) Mino, T.; Tanaka, Y.; Sakamoto, M.; Fujita, T. *Tetrahedron: Asymmetry* **2001**, *12*, 2435. (d) Mino, T.; Tanaka, Y.; Akita, K.; Anada, K.; Sakamoto, M.; Fujita, T. *Tetrahedron: Asymmetry* **2001**, *12*, 1677. (e) Mino, T.; Tanaka, Y.; Sakamoto, M.; Fujita, T. *Heterocycles* **2000**, *53*, 1485. (f) Okuyama, Y.; Nakano, H.; Hongo, H. *Tetrahedron: Asymmetry* **2000**, *11*, 1193. (g) Suzuki, Y.; Abe, I.; Hiroi, K. *Heterocycles* **1999**, *50*, 89. (h) Hiroi, K.; Suzuki, Y.; Abe, I. *Tetrahedron: Asymmetry* **1999**, *10*, 1173. (i) Cahill, J. P.; Cunneen, D.; Guiry, P. J. *Tetrahedron: Asymmetry* **1999**, *10*, 4157. (j) Hattori, T.; Komuro, Y.; Hashizaka, N.; Takahashi, H.; Miyano, S. *Enantiomer* **1997**, *2*, 203.

[5] (a) Tanaka, Y.; Mino, T.; Akita, K.; Sakamoto, M.; Fujita, T. *J. Org. Chem.* **2004**, *69*, 6679. (b) Mino, T.; Tanaka, Y.; Akita, K.; Sakamoto, M.; Fujita, T. *Heterocycles* **2003**, *60*, 9.

[6] Mino, T.; Saito, A.; Tanaka, Y.; Hasegawa, S.; Sato, Y.; Sakamoto, M.; Fujita, T. *J. Org. Chem.* **2005**, *70*, 1937.

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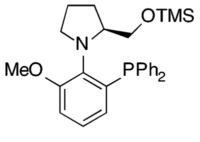
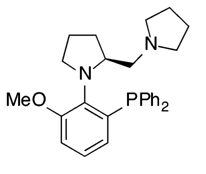
the catalyst. Over the past decade, many new catalysts with affinities for fluorous solvents have been synthesized[7] since the pioneering studies of Vogt[8] and the work of Horváth[9] were reported. This protocol exploits the thermomorphic nature of fluorous solvents, which form a monophasic solution with an organic solvent when heated. After the reaction, the catalyst, possessing fluorous ligands, can be separated from the products by means of an organo/fluorous liquid/liquid biphasic work-up and reused. The high fluorine content of the catalyst would make its partition high enough to be recovered by this fluorous phase separation technique.



**1**



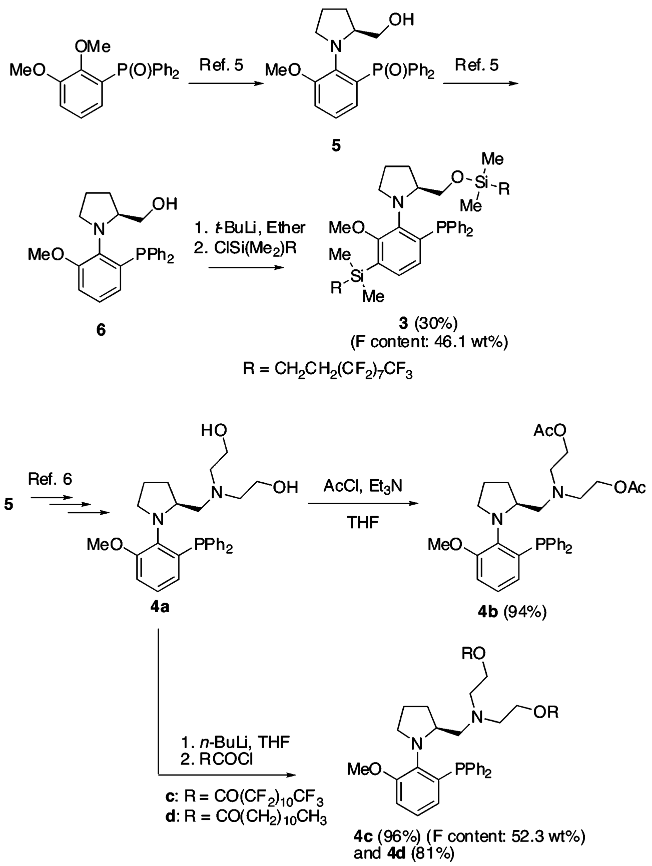
**2**

Recently a protocol for fluorous catalysts that does not use fluorous solvents has also been reported in which ordinary organic solvents are employed exclusively as a medium for reactions using fluorous catalysts.[10] This protocol exploits the temperature-dependent miscibilities of a fluorous catalyst with an organic solvent, but the catalyst precipitates when the solution is cooled and can be recovered by simple solid/liquid separation. There are also a few reports on asymmetric reactions by fluorous catalysts using this protocol.[11] Here, we report the synthesis of chiral fluorous aminophosphines **3** and **4c** bearing two fluorous ponytails, their use as chiral ligands in palladium-catalyzed asymmetric allylic alkylation, and the recovery of the chiral fluorous palladium catalyst in the case of one prepared from **4c** by this solid/liquid protocol.

## Results and Discussion

**Synthesis of Chiral Aminophosphine Ligands 3 and 4.** The chiral aminophosphine ligands **3** and **4** were readily prepared from commercially available, optically pure (*S*)-prolinol (Scheme 1). A nucleophilic aromatic substitution ($S_NAr$) reaction of a diphenyl(2,3-dimethoxyphenyl)phosphine oxide with bislithiated (*S*)-prolinol gave the corresponding aminophosphine oxide **5** and the corresponding aminophosphine **6**.[5] This aminophosphine **6** was converted into the desired chiral aminophosphine **3** using 2 equiv of *t*-BuLi and the corresponding fluorous silyl chloride. The calculated fluorine content of **3** was 46.1%. On the other hand, aminophosphine oxide **5** was converted into the desired chiral aminophosphine **4a**.[6] Bisacetylated ligand **4b** was easily prepared from **4a** using acetyl chloride with triethylamine. Under perfluorododecanoic chloride-triethylamine method, fluorous aminophosphine **4c** bearing two fluorous ponytails could not obtained. However the desired phosphine **4c** was prepared with perfluorododecanoic chloride[12] using bislithiated derivatives of **4a** obtained from **4a** and 2 equiv of *n*-BuLi in 96% yield. The calculated fluorine content of **4c** was 52.3%. Similar aminophosphine **4d** bearing two nonfluorous type ponytails was also prepared in 81% yield.

**SCHEME 1. Preparation of Aminophosphine Ligand 4**



**Palladium-Catalyzed Asymmetric Allylic Alkylation.** The chiral diaminophosphines **1**−**4** were applied as chiral ligands in the palladium-catalyzed AAA reaction of 1,3-diphenyl-2-propenyl acetate (**7**) with dimethyl malonate (**8a**). This reaction was performed in the presence of 2 mol % of $[\mathrm{Pd}(\eta^3\text{-}\mathrm{C_3H_5})\mathrm{Cl}]_2$, 4 mol % of aminophosphine, and a mixture of *N*,*O*-bis(trimethylsilyl)acetamide (BSA) and 2 mol % of lithium acetate[13] (Table 1).

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(7) (a) Horváth, I. T. *Acc. Chem. Res.* **1998**, *31*, 641. (b) de Wolf, E.; van Koten, G.; Deelman, B.-J. *Chem. Soc. Rev.* **1999**, *28*, 37. (c) Cavazzini, M.; Montanari, F.; Pozzi, G.; Quici, S. *J. Fluorine Chem.* **1999**, *94*, 183. (d) Hope, E. G.; Stuart, A. M. *J. Fluorine Chem.* **1999**, *100*, 75. (e) Yoshida, J.; Itami, K. *Chem. Rev.* **2002**, *102*, 3693. (f) Dobbs, A. P.; Kimberly, M. R. *J. Fluorine Chem.* **2002**, *118*, 3. (g) Gladysz, J. A.; Curran, D. P. *Tetrahedron* **2002**, *58*, 3823 and the following articles in this special issue entitled "Fluorous Chemistry". (h) Gladysz, J.; Curran, D.; Horváth, I. In *The Handbook of Fluorous Chemistry*; Wiley-VCH Publishers: Weinheim, 2004.

(8) (a) Keim, W.; Vogt, M.; Wasserscheid, P.; Driessen-Hölscher, B. *J. Mol. Catal. A: Chem.* **1999**, *139*, 171. (b) Vogt, M. Ph.D. Thesis, University of Aachen, 1991.

(9) Horváth, I. T.; Rabái, J. *Science* **1994**, *266*, 72.

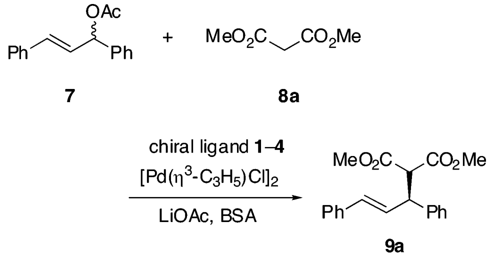
(10) (a) Wende, M.; Gladysz, J. A. *J. Am. Chem. Soc.* **2003**, *125*, 5861. (b) Rocaboy, C.; Gladysz, J. A. *New J. Chem.* **2003**, *27*, 39. (c) Rocaboy, C.; Gladysz, J. A. *Org. Lett.* **2002**, *4*, 1993. (d) Ishihara, K.; Hasegawa, A.; Yamamoto, H. *Synlett* **2002**, 1299. (e) Xiang, J.; Orita, A.; Otera, J. *Adv. Synth. Catal.* **2002**, *344*, 84. (f) Wende, M.; Meier, R.; Gladysz, J. A. *J. Am. Chem. Soc.* **2001**, *123*, 11490. (g) Ishihara, K.; Kondo, S.; Yamamoto, H. *Synlett* **2001**, 1371.

(11) Bayardon, J.; Sinou, D. *J. Org. Chem.* **2004**, *69*, 3121.

(12) George, M.; Snyder, S. L.; Terech, P.; Glinka, C. J.; Weiss, R. G. *J. Am. Chem. Soc.* **2003**, *125*, 10275.

(13) (a) Mino, T.; Shiotsuki, M.; Yamamoto, N.; Suenaga, T.; Sakamoto, M.; Fujita, T.; Yamashita, M. *J. Org. Chem.* **2001**, *66*, 1795. (b) Mino, T.; Imiya, W.; Yamashita, M. *Synlett* **1997**, 583.

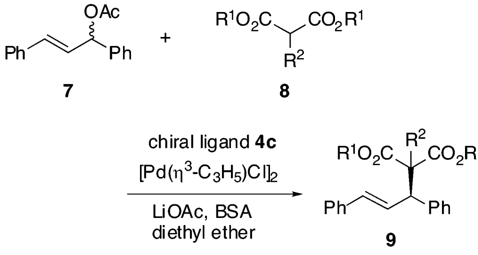
**TABLE 1. Palladium Catalyzed Asymmetric Allylic Alkylation Using 1−4**[a]



| entry | ligand | solvent | temp (°C) | time (h) | yield (%)[b] | ee (%) (*S*)[c] |
|---|---|---|---|---|---|---|
| 1[d] | **1** | PhMe | −10 | 24 | 97 | 95 |
| 2[e] | **2** | diethyl ether | −10 | 24 | 99 | 95 |
| 3 | **3** | PhMe | 20 | 24 | 64 | 86 |
| 4[d] | **4a** | diethyl ether | −10 | 24 | 98 | 95 |
| 5[d] | **4b** | diethyl ether | −10 | 24 | 77 | 95 |
| 6 | **4b** | diethyl ether | 0 | 24 | 95 | 94 |
| 7 | **4c** | diethyl ether | 0 | 48 | 64 | 94 |
| 8 | **4d** | diethyl ether | 0 | 24 | 96 | 94 |
| 9 | **4c** | diethyl ether | −20 | 48 | 5 | 94 |
| 10 | **4c** | diethyl ether | −10 | 48 | 11 | 94 |
| 11 | **4c** | diethyl ether | 10 | 48 | 93 | 93 |
| 12 | **4c** | diethyl ether | 20 | 24 | 94 | 92 |
| 13 | **4c** | diethyl ether | 30 | 5 | 96 | 90 |
| 14 | **4c** | $PhCF_3$ | −10 | 48 | 36 | 95 |
| 15 | **4c** | hexane | 50 | 1 | 99 | 84 |

[a] The reactions were carried out at 0.5 mmol scale in various solvents (2 mL) at various temperature swith 3.0 equiv of **8a** and BSA, in the presence of LiOAc (2 mol %), ligand **1**−**4** (4 mol %), and $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (2 mol %). [b] Isolated yields. [c] Determined by HPLC analysis using a chiral column (Chiralcel OD-H). [d] See ref 5. [e] See ref 6.

**TABLE 2. Palladium-Catalyzed Asymmetric Allylic Alkylation Using 4c**[a]



**a** : $R^1$ = Me, $R^2$ = H; **b** : $R^1$ = Et, $R^2$ = H
**c** : $R^1$ = Et, $R^2$ = Me

| entry | malonate | temp (°C) | time (h) | yield (%)[b] | ee (%)[c] | config[c] |
|---|---|---|---|---|---|---|
| 1 | **8a** | 30 | 5 | 96 | 90 | *S* |
| 2 | **8b** | 30 | 6.5 | 98 | 91 | *S* |
| 3 | **8c** | 30 | 5 | 93 | 81 | *R* |
| 4[d] | **8b** | 10 | 24 | 93 | 95 | *S* |
| 5[d] | **8b** | 0 | 48 | 93 | 97 | *S* |
| 6[e] | **8b** | 30 | 5 | 95 | 93 | *S* |

[a] The reactions were carried out at 0.5 mmol scale in diethyl ether (2 mL) at various temperature with 3.0 equiv of **8** and BSA, in the presence of LiOAc (2 mol %), ligand **4c** (4 mol %), and $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (2 mol %). [b] Isolated yields. [c] Determined by chiral HPLC analysis. [d] This reaction was carried out using 10 mol % catalyst. [e] This reaction was carried out under 0.5 M of solution.

We attempted this palladium-catalyzed AAA reaction using fluorous aminophosphine **3** bearing two fluorous ponytails in toluene at room temperature. The reaction proceeded smoothly, but the enantioselectivity of **9a** was lower than in the case of using similar silylated ligand **1**[5] (entry 1 vs 3). When the reaction was carried out using ligand **4a** at −10 °C in diethyl ether, (*S*)-**9a** was obtained in a good chemical yield with good enantioselectivity (95% ee) similar to the case of **2** (entry 2 vs 4).[6] The conversion was slightly lower when using bisacetylated ligand **4b** instead of **4a** (entry 4 vs entry 5). When the reaction was conducted using **4b** at 0 °C, it was almost finished within 24 h with good enantioselectivity (entry 5 vs entry 6). Next, we attempted palladium-catalyzed AAA reaction using **4c** as the ligand. Although the enantioselectivity of **9a** was approximately 94% ee, the conversion was slower than in the case of **4b** (entry 6 vs 7). On the other hand, nonfluorous aminophosphine **4d** bearing hydrocarbon ponytails acted as a good ligand in this reaction (entry 8). We examined the effect of reaction temperature on the palladium-catalyzed AAA reaction (entries 7 and 9−13). In the case of increasing the reaction temperature, the reaction became faster. In the case of 30 °C, the reaction was almost finished within 5 h in good enantioselectivity (90% ee). When α,α,α-trifluorotoluene was used as the solvent at −10 °C, low conversion was observed (entry 10 vs 14). Although the conversion increased, the enantioselectivity fell to 84% ee using a low-polar solvent, such as *n*-hexane, at 50 °C (entry 15).

In addition, we examined the AAA reactions of various dialkyl malonates using **4c** as the ligand. As Table 2 shows, the reaction using diethyl malonate (**8b**) as a nucleophile provided a similar level of chemical yield and enantioselectivity (entry 1 vs 2). When diethyl methylmalonate (**8c**) was used, however, higher conversion was observed, though the enantioselectivity was only moderate (entry 3). Decreasing the reaction temperature slowed the conversion. When the reaction was performed at 0 °C using 10 mol % of chiral catalyst, it was almost finished within 48 h in high enantioselectivity (97% ee) (entry 5). Changing the concentration in the reaction from 0.25 to 0.5 M increased both the conversion and enantioselectivity in comparison with entry 2 (entry 6).

**Temperature-Dependent Solubility of Fluorous Palladium Catalyst.** The solubility of the palladium complex prepared from $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ and ligand **4c** was measured over the temperature range of −20 to 30 °C in diethyl ether and of 0 °C to nearly the boiling point in hexane. Indeed, the palladium complex was strongly thermomorphic, as indicated in Figure 1. Between −20 and 30 °C, its solubility in diethyl ether increased ca. 15-fold (1.14, 1.86, 3.20, 4.28, 8.40, and 16.66 mM at −20, −10, 0, 10, 20, and 30 °C). Furthermore between 0 and 69 °C in hexane, its solubility increased ca. 200-fold (0.027, 0.25, 0.38, 1.85, and 5.38 mM at 0, 10, 30, 50, and 69 °C). The solubility increased to an even higher ca. 600-fold from 0 °C in hexane to 30 °C in diethyl ether.[14]

**Recycling of Fluorous Palladium Catalyst.** Next, we attempted to recycle the fluorous palladium catalyst by simple solid/liquid separation after a palladium-catalyzed AAA reaction in organic solvent (Table 3). After 10 mol % of the palladium complex was prepared in situ from $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ and ligand **4c**, the reaction mixture was warmed to 30 °C and became almost homogeneous. The reaction with dimethyl malonate as a nucleophile

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(14) The solubility of a palladium complex prepared from $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ and ligand **4b** was 45.3 mM in hexane at 30 °C.

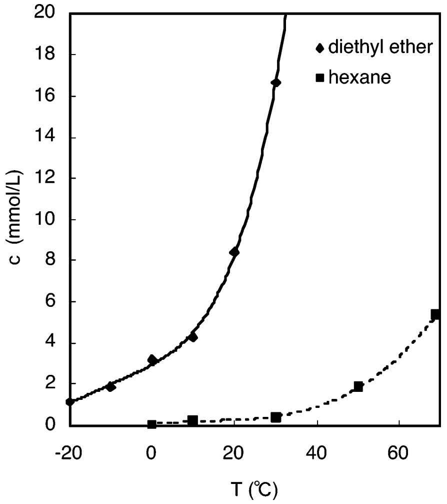


**FIGURE 1.** Solubility of fluorous palladium complex from $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ and **4c** as a function of temperature.

**TABLE 3. Recycle of Fluorous Palladium Catalyst in Asymmetric Allylic Alkylation Using 4c**[a]

| entry | malonate | cycle | time (h) | conv (%)[b] | ee (%) (*S*)[c] |
|---|---|---|---|---|---|
| 1 | **8a** | 1 | 3 | >99 | 90 |
| 2 | | 2 | 3 | >99 | 90 |
| 3 | | 3 | 3 | 98 | 89 |
| 4 | | 4 | 3 | 90 | 89 |
| 5 | | 5 | 3 | 36 | 87 |
| 6 | **8b** | 1 | 4.5 | >99 | 92 |
| 7 | | 2 | 4.5 | 97 | 92 |
| 8 | | 3 | 4.5 | 95 | 92 |
| 9 | | 4 | 4.5 | 99 | 92 |
| 10 | | 5 | 4.5 | 97 | 91 |
| 11 | | 6 | 4.5 | 98 | 90 |
| 12[d] | | 1 | 4.5 | >99 | 92 |
| 13[d] | | 2 | 4.5 | 21 | 89 |

[a] The reactions were carried out at 0.5 mmol scale in diethyl ether (2 mL) at 30 °C with 3.0 equiv of **8** and BSA, in the presence of LiOAc (5 mol %), ligand **4c** (10 mol %), and $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (5 mol %). [b] Determined by $^1H$ NMR. [c] Determined by chiral HPLC analysis. [d] This reaction was carried out using **4b** instead of **4c**.

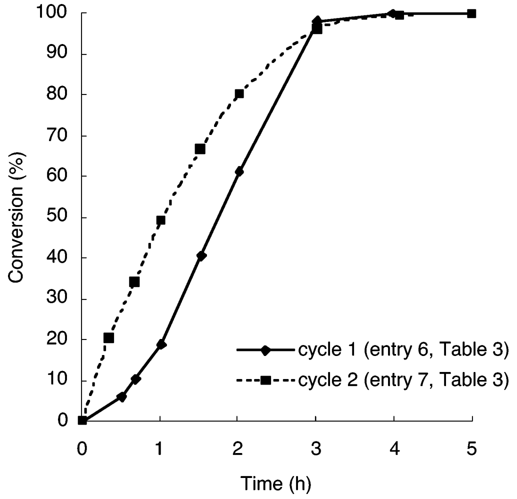


**FIGURE 2.** Conversion as a function of time for asymmetric allylic alkylation using fluorous palladium catalyst.

**TABLE 4. Solubility of Fluorous Palladium Catalysts**

| entry | catalysts | hexane at 0 °C (mg/mL) | diethyl ether at 30 °C (mg/mL) | HRMS (FAB-MS) |
|---|---|---|---|---|
| 1 | $Pd(\eta^3\text{-}C_3H_5)Cl$-**4c** | 0.05 | 30.9 | 1817.0947 $[M - Cl]^+$ |
| 2 | recovered catalyst | 0.05 | 6.5 | 1935.1149 |

occurred successfully in diethyl ether as the solvent at 30 °C for 3 h. In accordance with the progress of the reaction's first cycle, there was a slight precipitation of the catalyst. After the reaction mixture was cooled to 0 °C and diethyl ether was almost removed by argon flowing, the product was extracted with cold hexane, and the supernatant was removed via a syringe several times until the product could not be detected by TLC. The alkylated product **9a** was obtained in good yields with good enantioselectivity (entry 1), and the recovered catalyst was employed for four further cycles without deterioration of the enantioselectivity (entries 2−5). Using the same protocol, the reaction was conducted with diethyl malonate (**8b**) as a nucleophile, and it was found that the fluorous palladium catalyst could be successfully reused five times without any detectable loss in catalytic activity and enantioselectivity (entries 6−11). There was a slight precipitation of the reused fluorous palladium catalyst at 30 °C in diethyl ether, although it did not become homogeneous in some cases. Figure S1 shows pictures of a reaction sequence (see Supporting Information). We also attempted to recycle the nonfluorous catalyst prepared from **4b** instead of **4c** as a ligand (entries 12 and 13). The conversion of cycle 2 was remarkably decreased to 21% (entry 13), because the catalyst became dark brown gum by adding hexane and slightly solved to hexane.

The reaction rate was monitored for the first used palladium catalyst prepared in situ from $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ and ligand **4c** and the reused palladium catalyst in the second cycle as summarized in Figure 2. The first cycle appeared to show an induction period, whereas the second one did not; moreover, the second cycle was faster than the first one.

We also investigated the solubility of a recovered palladium catalyst after the first cycle of a palladium-catalyzed AAA reaction with diethyl malonate under the same condition as entry 6 in Table 3, measured at 0 °C in hexane and at 30 °C in diethyl ether (Table 4). Although the solubility in hexane did not change, it is clear that the catalyst's solubility in diethyl ether decreased. We also examined this recovered palladium catalyst using high-resolution FAB-MS. The HRMS of a palladium catalyst prepared from $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ and ligand **4c** exhibited one peak at *m/z* 1817.0947, corresponding to the cationic palladium complex (calcd for $C_{55}H_{38}N_2O_5F_{46}P^{106}Pd^+$ ($[M - Cl]^+$): 1817.0819). On the other hand, the HRMS of the recovered palladium catalyst indicated a new species at *m/z* 1935.1149 with the disappearance of the species at *m/z* 1817.0947. We propose that this species could be the cationic palladium enolate complex with ligand **4c** and diethyl malonate (calcd for $C_{59}H_{44}N_2O_9F_{46}P^{106}Pd^+$: 1935.1085) (Figure 3). The FAB-MS spectra of the palladium complexes are shown in Figure S2 (see Supporting Information). Previously, Muzart reported on an ESI-MS analysis of a

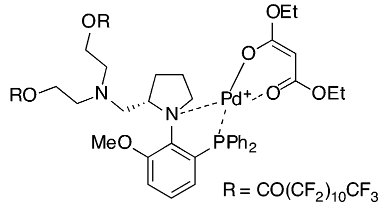
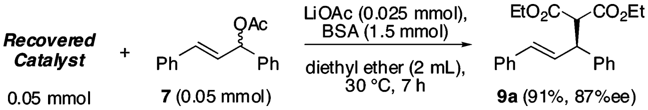


**FIGURE 3.** Proposed structure of the cationic palladium enolate complex on FAB-MS analysis.

**SCHEME 2. Stoichiometric Asymmetric Allylic Alkylation of Recovered Fluorous Palladium Catalysts**



similar palladium enolate complex with acetylacetone.[15] This palladium enolate complex was generated by complexation with excess diethyl malonate and precipitation according to the progress of the reaction during the first cycle (entry 6, Table 3).

The palladium-catalyzed AAA reaction of 1,3-diphenyl-2-propenyl acetate (**7**) using the recovered palladium enolate complex as a palladium source without addition of diethyl malonate as a nucleophile was carried out under the stoichiometric condition (Scheme 2). This reaction was almost complete within 7 h, the corresponding product was obtained with good enantioselectivity, and the recovered enolate palladium complex was active for the palladium-catalyzed AAA reaction. Therefore the induction period did not appear in the second cycle of this reaction (Figure 2).

## Conclusion

We have successfully obtained chiral fluorous aminophosphine **4c** from (*S*)-prolinol and demonstrated that palladium-catalyzed asymmetric allylic alkylation of 1,3-diphenyl-2-propenyl acetate (**7**) with malonates occurred with good enantiomeric excesses. Chiral fluorous palladium catalysts were easily separated from the reaction mixture by simple solid/liquid separation and could be reused up to five times. Further studies on the technique's application to other asymmetric reactions are underway.

## Experimental Section

**Preparation of Aminophosphine 4a and 4b.** Aminophosphine **4a** and **4b** were prepared according to the literature method.[5,6]

**Preparation of Aminophosphine 3.** To aminophosphine **6** (0.196 g, 0.50 mmol) in diethyl ether (2 mL) was added dropwise *t*-BuLi in hexane (0.71 mL, 1.04 mmol, 1.47 M) at −78 °C. The mixture was stirred at room temperature for 2 h then treated with 1*H*,1*H*,2*H*,2*H*-perfluorodecyl(dimethyl)silyl chloride (0.37 mL, 1.0 mmol). After stirring at room temperature for 24 h, the reaction mixture was diluted with diethyl ether and quenched with saturated aqueous $NH_4Cl$. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (elution with *n*-hexane/EtOAc = 40/1): 0.207 g, 0.15 mmol, 30%; colorless liquid; $[\alpha]^{25}_D$ 15.7 (*c* 1, $CHCl_3$); $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ −0.05 (s, 6H), 0.31 (d, $J$ = 6.5 Hz, 6H), 0.58−0.69 (m, 2H), 0.95−1.07(m, 2H), 1.55−2.14 (m, 8H), 2.60 (bs, 1H), 2.96 (bs, 1H), 3.04 (q, $J$ = 7.4 Hz, 1H), 3.69 (s, 3H), 3.83−3.94 (m, 1H), 4.03 (bs, 1H), 6.65 (dd, $J$ = 3.5 and 7.5 Hz, 1H), 7.03 (d, $J$ = 7.5 Hz, 1H), 7.16−7.37 (m, 10H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ −2.63 to − 2.56 (m), −2.26, 5.40, 5.68, 24.0, 25.1 (t, $J_{CF}$ = 24.2 Hz), 26.1 (t, $J_{CF}$ = 24.0 Hz), 30.3, 54.0, 54.2, 60.6, 61.6, 65.9, 105−120 (m), 128.4−128.5 (m), 128.9, 130.4, 130.8, 132.5, 133.6, 133.9, 134.0, 134.2, 137.5 (d, $J_{CP}$ = 12.4 Hz), 138.0 (d, $J_{CP}$ = 13.0 Hz), 143.2 (d, $J_{CP}$ = 21.2 Hz), 162.8 (d, $J_{CP}$ = 5.3 Hz); $^{31}P$ NMR (121 MHz, $CDCl_3$) $\delta$ −13.6; FAB-MS *m/z* (rel intensity) 1398 ($M^+$ − 1, 40); HRMS (FAB-MS) *m/z* calcd for $C_{48}H_{43}F_{34}NO_2PSi_2$ 1398.2027 ([M − H]$^+$), found 1398.1986.

**Preparation of Aminophosphine 4c.** To aminophosphine **4a** (0.191 g, 0.40 mmol) in THF (2 mL) was added dropwise *n*-BuLi in hexane (0.56 mL, 0.88 mmol, 1.57 M) over 10 min at −78 °C. The mixture was stirred at room temperature for 1 h and then treated with perfluorododecanoic chloride (0.632 g, 1.0 mmol). After stirring at room temperature for 15 min and direct evaporation of the solvent, the residue was purified by short silica gel chromatography (elution with diethyl ether): 0.640 g, 0.38 mmol, 96%; white solid; mp 77−79 °C; $[\alpha]^{25}_D$ 3.9 (*c* 1, $CHCl_3$); $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 1.38−1.52 (m, 1H), 1.60−1.72 (m, 2H), 1.88−2.02 (m, 2H), 2.25 (dd, $J$ = 3.5 and 13.1 Hz, 1H), 2.53−2.85 (m, 6H), 3.52−3.63 (m, 1H), 3.79 (s, 3H), 4.07−4.31 (m, 4H), 6.42 (ddd, $J$ = 1.1, 2.8 and 6.5 Hz, 1H), 6.88 (d, $J$ = 7.8 Hz, 1H), 7.07 (t, $J$ = 7.8 Hz, 1H), 7.22−7.35 (m, 10H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 23.7, 30.7, 52.3, 53.2, 54.9, 59.8, 60.2, 66.5, 108.1 (t, $J_{CF}$ = 33.1 Hz), 115.2 (t, $J_{CF}$ = 33.0 Hz), 119.0 (t, $J_{CF}$ = 33.1 Hz), 104−116 (m), 112.5, 125.1, 126.6, 128.2−128.3 (m), 134.1, 134.2, 134.4, 134.5, 138.4 (d, $J_{CP}$ = 12.4 Hz), 138.9 (d, $J_{CP}$ = 13.8 Hz), 140.0 (d, $J_{CP}$ = 21.2 Hz), 142.3 (d, $J_{CP}$ = 4.2 Hz), 158.2 (d, $J_{CP}$ = 3.5 Hz), 158.3 (t, $J_{CF}$ = 29.5 Hz); $^{31}P$ NMR (121 MHz, $CDCl_3$) $\delta$ −14.9; FAB-MS *m/z* (rel intensity) 1669 ($M^+$ − 1, 17); HRMS (FAB-MS) *m/z* calcd for $C_{52}H_{32}F_{46}N_2O_5P$ 1669.1314 ([M − H]$^+$), found 1669.1312; HRMS (ESI-TOF-MS) *m/z* calcd for $C_{52}H_{34}F_{46}N_2O_5P$ 1671.1471 ([M + H]$^+$), found 1671.1420.

**Preparation of Aminophosphine 4d.** To aminophosphine **4a** (0.289 g, 0.60 mmol) in THF (2 mL) was added dropwise *n*-BuLi in hexane (0.91 mL, 1.32 mmol, 1.45 M) over 10 min at −78 °C. The mixture was stirred for 15 min and then treated with dodecanoic chloride (0.36 mL, 1.50 mmol). After stirring for 15 min at −78 °C, the mixture was directly purified by short silica gel chromatography (elution with *n*-hexane/EtOAc = 8/1): 0.413 g, 0.49 mmol, 81%; white solid; mp 24−25 °C; $[\alpha]^{25}_D$ = 14.7 (*c* 1.0, $CHCl_3$); $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 0.88 (t, $J$ = 6.7 Hz, 6H), 1.21−1.33 (m, 32H), 1.50−1.64 (m, 7H), 1.86−2.12 (m, 2H), 2.22−2.34 (m, 5H), 2.44−2.70 (m, 5H), 2.77 (q, $J$ = 7.7 Hz, 1H), 3.53−3.66 (m, 1H), 3.80 (s, 3H), 3.84−4.03 (m, 4H), 6.40 (ddd, $J$ = 1.3, 2.8 and 7.6 Hz, 1H), 6.87 (d, $J$ = 7.7 Hz, 1H), 7.05 (ddd, $J$ = 0.6, 7.6 and 8.2 Hz, 1H), 7.23−7.34 (m, 10H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 14.1, 22.7, 23.8, 25.0, 29.2, 29.3, 29.4, 29.5, 29.6, 30.8, 31.9, 34.3, 52.2, 53.6, 55.0, 60.0, 60.5, 62.6, 112.4, 125.0, 126.4, 128.1−128.3 (m), 134.1, 134.2, 134.3, 134.4, 138.5 (d, $J_{CP}$ = 12.9 Hz), 139.0 (d, $J_{CP}$ = 14.1 Hz), 140.3 (d, $J_{CP}$ = 21.1 Hz), 142.4 (d, $J_{CP}$ = 4.4 Hz), 158.2 (d, $J_{CP}$ = 3.4 Hz), 173.8; $^{31}P$ NMR (121 MHz, $CDCl_3$) $\delta$ −14.9; FAB-MS *m/z* (rel intensity): 841 ($M^+$ − 1, 5). HRMS (FAB-MS) *m/z* calcd for $C_{52}H_{78}N_2O_5P$ 841.5648 ([M − H]$^+$), found 841.5688.

**General Procedure for the Palladium-Catalyzed Allylic Alkylation.** To a mixture of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (0.004 g, 0.01 mmol), chiral aminophosphine **3** or **4** (0.02 mmol), and lithium acetate (0.001 g, 0.01 mmol) in a solvent (2 mL) were added *N*,*O*-bis(trimethylsilyl)acetamide (BSA) (0.37 mL, 1.5 mmol), racemic allylic ester **7** (0.126 g, 0.5 mmol), and malonate **8** (1.5 mmol) under an argon atmosphere. After being stirred for the corresponding times, the reaction mixture was

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[15] Chevrin, C.; Le Bras, J.; Hénin, F.; Muzart, J. *Organometallics* **2004**, *23*, 4796.

diluted with diethyl ether and quenched with saturated aqueous $NH_4Cl$. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel chromatography.

**General Procedure for Measurement of the Solubility of Fluorous Palladium Catalyst.** A mixture of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (0.037 g, 0.1 mmol) and **4c** (0.334 g, 0.2 mmol) in a solvent (15 mL) was stirred for 30 min at room temperature under an argon atmosphere. The mixture was placed in a thermostated bath and stirred at the corresponding temperature for 30 min. Stirring was discontinued, and the suspension was allowed to settle. After 10 min, 1 mL of the clear solution was removed from supernatant via syringe. The amount of catalyst was measured after evaporation under reduced pressure.

**General Procedure for the Recycle of Fluorous Palladium Catalyst on Palladium-Catalyzed Allylic Alkylation.** To a mixture of racemic allylic ester **7** (0.126 g, 0.5 mmol), $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (0.0093 g, 0.025 mmol), chiral aminophosphine **4c** (0.084 mmol, 0.05 mmol), and lithium acetate (0.0016 g, 0.025 mmol) in a diethyl ether (2 mL) was added *N*,*O*-bis(trimethylsilyl)acetamide (BSA) (0.37 mL, 1.5 mmol) under an argon atmosphere. After the mixture was stirred for 30 min and warmed to 30 °C, malonate **8** (1.5 mmol) was added, and the reaction mixture was stirred for the corresponding times at 30 °C. The diethyl ether was almost removed by argon flowing from the reaction vessel. The residue was diluted with cold hexane (5 mL) at 0 °C, and the supernatant was removed via syringe several times by the simple decantation of the supernatant liquid until the product did not detected by TLC. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The conversion was determined by $^1H$ NMR analysis. The residue was purified by silica gel chromatography. The precipitate was washed cold hexane, and the solvent was removed under reduced pressure. The recovered catalyst was reused in next catalytic allylic alkylation without further addition of palladium source and ligand **4c**.

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**Supporting Information Available:** Figures S1 and S2, NMR spectra of new compounds, and copies of HPLC charts of **9**. This material is available free of charge via the Internet at http://pubs.acs.org.

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