3.16 (t, J = 8.27, 1 H, H-3), 3.97 (dq, J = 6.44 and 8.27, 1 H, H-2), 5.21 (d, J = 18.17, 1 H, (Z)-CH_2=C-), 5.23 (d, J = 10.60, 1 H, (E)-CH_2=C-), 6.12 (ddd, J = 8.27, 10.60, and 18.17, 1 H, -CH=C), 7.18-7.34 (m, 5 H, aryl-H); IR (neat) 3400, 3050, 2950, 1640, 1600, 1490, 1410, 1110, 990, 920, 760, 700; HRMS calcd for $C_{11}H_{14}O$ ([M^+]) 162.1044, found 162.1040. Anal. Calcd for $C_{11}H_{14}O$: C, 81.44; H, 8.70. Found: C, 81.47; H, 8.74.

1,2-Diphenylbut-3-en-1-ol:[28] colorless oil (anti >95%); R_f = 0.10 (hexane:EtOAc = 7:1); ^{1}H NMR syn isomer 2.73 (d, J = 2.57, 1 H, OH), 3.88 (d, J = 5.15, 1 H, H-2), 4.56-4.65 (m, 1 H, H-1), 5.00-5.15 (m, 2 H, CH_2=C-), 5.82 (ddd, J = 5.15, 10.30, and 17.04, 1 H, -CH=C), 6.93-7.24 (m, 10 H, aryl-H), anti isomer 2.73 (d, J = 2.57, 1 H, OH), 3.46 (dd, J = 7.69 and 8.84, 1 H, H-2), 4.68 (dd, J = 2.57 and 7.69, 1 H, H-1), 5.01 (ddd, J = 0.76, 1.52, and 17.04, 1 H, (E)-CH_2=C-), 5.12 (ddd, J = 0.76, 1.52, and 10.30, 1 H, (Z)-CH_2=C-), 6.15 (ddd, J = 8.84, 10.30, and 17.04, 1 H, -CH=C), 6.99-7.21 (m, 10 H, aryl-H); IR (neat) 3400, 3050, 1630, 1600, 1490, 1410, 1110, 990, 910, 760, 700; MS (rel intens) 224 (0.3, M^+), 206 (1, [$M - H_2O$]$^+$), 118 (18), 117 (10, [PhCHCH=CH_2]$^+$), 115 (5), 107 (18, $PhCHOH^+$), 105 (5, $PhCO^+$), 91 (15, $C_7H_7^+$), 79 (11, [Ph + 2H]$^+$), 77 (8, Ph^+). Anal. Calcd for $C_{16}H_{16}O$: C, 85.68; H, 7.19. Found: C, 85.71; H, 7.29.

1-Cyclohexyl-2-phenylbut-3-en-1-ol:[28] colorless oil (anti >95%); R_f = 0.39 (hexane:EtOAc = 7:1); GC (column temp 195) t_R = 51.2 (anti), 54.1 (syn); ^{1}H NMR anti isomer 1.08-1.37, 1.59-1.85 (m, 12 H, cyclo-CH, cyclo-CH_2, OH), 3.44 (dd, J = 7.20 and 9.08, 1 H, H-2), 3.53 (m, 1 H, H-1), 5.16 (dd, J = 1.52 and 17.04, 1 H, (Z)-CH_2=C-), 5.20 (dd, J = 1.52 and 10.22, 1 H, (E)-CH_2=C-), 6.14 (ddd, J = 9.09, 10.22, and 17.04, 1 H, -CH=C), 7.15-7.34 (m, 5 H, aryl-H); IR (neat) 3450, 3050, 2900, 1640, 1600, 1500, 1450, 1390, 1130, 990, 920, 760, 700; MS (rel intens) m/e 230 (0.6, M^+), 212 (1, [$M - H_2O$]$^+$), 118 (24), 117 (8, [PhCHCH=CH_2]$^+$), 115 (5), 95 (11), 91 (4, $C_7H_7^+$), 77 (2, Ph^+), 67 (3), 55 (5). Anal. Calcd for $C_{16}H_{22}O$: C, 83.43; H, 9.63. Found: C, 83.48, H, 9.74.

1-Cyclohexyl-4-phenylbut-3-en-1-ol: colorless oil; R_f = 0.30 (hexane:EtOAc = 7:1); ^{1}H NMR 0.89-1.89 (m, 12 H, cyclo-CH_2, cyclo-CH, OH), 2.25 (dd, J = 4.01 and 7.76, 1 H, H-2), 2.39-2.47 (m, 1 H, H-2), 3.39-3.47 (m, 1 H, H-1), 6.22 (ddd, J = 6.44, 7.76, and 15.90, 1 H, H-3), 6.45 (d, J = 15.91, 1 H, H-4), 7.15-7.36 (m, 5 H, aryl-H); IR (neat) 3400, 3050, 2900, 1600, 1500, 1450, 1040, 960, 740, 690; MS (rel intens) m/e 130 (3), 129 (3), 118 (24), 117 (11, [PhCH=CHCH$_2$]$^+$), 115 (5), 95 (13), 91 (6, $C_7H_7^+$), 67 (4), 55 (5). Anal. Calcd for $C_{16}H_{22}O$: C, 83.43; H, 9.63. Found: C, 83.40; H, 9.70.

3-(4-Methoxyphenyl)pent-4-en-2-ol: white solid mp 57 °C (syn:anti = 8:92); R_f = 0.20 (hexane:EtOAc = 6:1); GC (column temp 180) t_R = 24.1 (syn), 26.6 (anti); ^{1}H NMR syn isomer 1.21 (d, J = 6.06, 3 H, H-1), 2.16 (br, 1 H, OH), 3.18 (t, J = 8.33, 1 H, H-3), 3.76 (s, 3 H, OCH_3), 3.91 (dq, J = 6.06 and 8.33, 1 H, H-2), 5.05-5.12 (m, 2 H, CH_2=C-), 6.00 (ddd, J = 8.33, 9.84, and 17.42, 1 H, -CH=C), 6.85 (m, 2 H, aryl-H), 7.10 (m, 2 H, aryl-H), anti isomer 1.05 (d, J = 6.06, 3 H, H-1), 2.16 (br, 1 H, OH), 3.11 (t, J = 8.33, 1 H, H-3), 3.75 (s, 3 H, OCH_3), 3.91 (dq, J = 6.06 and 8.33, 1 H, H-2), 5.16 (d, J = 16.66, 1 H, (Z)-CH_2=C-), 5.19 (d, J = 10.60, 1 H, (E)-CH_2=C-), 6.08 (ddd, J = 8.71, 10.60, and 16.66, 1 H, -CH=C), 6.84 (d, J = 8.71, 2 H, aryl-H), 7.10 (d, J = 8.71, 1 H, aryl-H); IR (KBr) 3440, 3060, 2960, 2830, 1670, 1600, 1500, 1470, 1300, 1240, 1180, 1030, 1000, 910, 810; MS (rel intens) m/e 192 (4, M^+), 174 (2, [$M - H_2O$]$^+$), 149 (14), 148 (100), 147 (95, [CH_2=CH - C_6H_4OMe]$^+$), 133 (17), 117 (13), 115 (15), 103 (9), 91 (14, $C_7H_7^+$), 78 (5), 77 (7, Ph^+). Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.91; H, 8.53.

3-(4-Cyanophenyl)pent-4-en-2-ol: colorless oil (syn:anti = 1:9); R_f = 0.59 (hexane:EtOAc = 1:1); ^{1}H NMR syn isomer 1.22 (d, J = 6.44, 3 H, H-1), 2.79 (br, 1 H, OH), 3.34 (dd, J = 6.44 and 8.33, 1 H, H-3), 4.03 (quintet, J = 6.44, 1 H, H-2), 5.15-5.28 (m, 2 H, CH_2=C-), 5.93-6.30 (m, 1 H, -CH=C), 7.40 (d, J = 8.33, 2 H, aryl-H), 7.63 (d, J = 8.33, 2 H, aryl-H), anti isomer 1.09 (d, J = 6.44, 3 H, H-1), 2.79 (br, 1 H, OH), 3.30 (dd, J = 6.44 and 8.71, 1 H, H-3), 4.03 (quintet, J = 6.44, 1 H, H-2), 5.18 (d, J = 17.04, 1 H, (Z)-CH_2=C-), 5.25 (d, J = 10.23, 1 H, (E)-CH_2=C-), 6.09 (ddd, J = 8.71, 10.23, and 17.04, 1 H, -CH=C), 7.37 (d, J = 8.33, 2 H, aryl-H), 7.60 (d, J = 8.33, 2 H, aryl-H); IR (neat) 3450, 2980, 2230, 1640, 1570, 1450, 1210, 1150, 1080, 920, 830; MS (rel intens) m/e 146 (37), 145 (10), 144 (27), 143 (100), 142 (81), 117 (18), 116 (26), 115 (18). Anal. Calcd for $C_{12}H_{13}NO$: C, 76.98; H, 7.00; N, 7.48. Found: C, 76.95; H, 7.03; N, 7.37.

Acknowledgment. This work was supported by Grant-in-Aid for Scientific Research No. 02640407 from the Ministry of Education, Science and Culture, Japan.

Chiral Phosphine Ligands Modified by Crown Ethers: An Application to Palladium-Catalyzed Asymmetric Allylation of β-Diketones

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Abstract: Chiral ferrocenylphosphine ligands modified by monoaza or diaza crown ethers of varying ring sizes and linker chain lengths (**8a-e**, **9**) were synthesized. The reaction of the phosphine ligand modified by monoaza-18-crown-6 (**8b**) and the di-μ-chlorobis(π-allyl)dipalladium(II) complex in $CDCl_3$ produced the π-allylpalladium(II) complex chelated by the two phosphorus atoms of **8b**, leaving the crown ether moiety free. The ^{1}H{^{1}H} nuclear Overhauser effect study of the π-allylpalladium(II) complex suggests that the aza crown ether moiety of chiral ligand **8b** is located at the proper position to interact with an incoming nucleophile. The palladium catalyst which was prepared in situ by mixing the crown ether-modified chiral ligands and $Pd_2(dba)_3$·$CHCl_3$ was examined for stereoselectivity and catalytic activity in the asymmetric allylation of unsymmetrically substituted β-diketones under solid-liquid, two-phase reaction conditions using potassium fluoride as an insoluble base in mesitylene. The ligands bearing monoaza-18-crown-6 or 1,10-diaza-18-crown-6 with an appropriate length of linker chain (**8b** and **8d**, respectively) significantly accelerated the allylation and showed fairly high enantioselectivity (up to 75% ee). It is proposed that a ternary complex involving a crown ether, a potassium cation, and an enolate anion attacks a π-allylpalladium(II) intermediate.

Asymmetric synthesis employing a chiral metal catalyst is a subject of considerable interest, since a small amount of chiral material can produce a large amount of chiral product.[1] Among the many examples of catalytic asymmetric reactions, palladium-catalyzed asymmetric allylation or allylic alkylation, which involves a (π-allyl)palladium(II) intermediate, has been one of the most studied, and several successful results achieving enantioselectivity of over 80% ee have been reported.[2-9] In general,

(1) For reviews, see: (a) Ojima, I.; Clos, N.; Bastos, C. *Tetrahedron* **1989**, *45*, 6901. (b) Noyori, R.; Kitamura, M. In *Modern Synthetic Methods*; Scheffold, R., Ed.; Springer-Verlag: Berlin, 1989; Vol. 5, p 115. (c) Brunner, H. *Synthesis* **1988**, 645.

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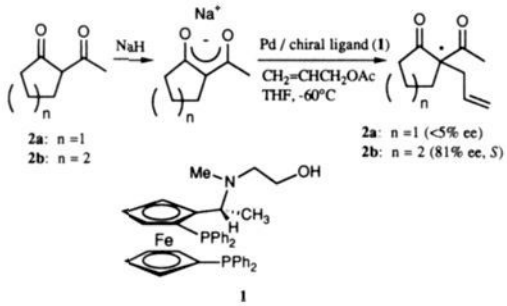
Figure 1. Nucleophilic attack of a soft carbon nucleophile on a π-allylpalladium(II) intermediate.

Scheme I



the selectivity, however, has not been satisfactory. Studies on the stereochemistry of the palladium-catalyzed allylic alkylation reaction have revealed that stabilized carbon nucleophiles such as acetylacetonate attack the π-allyl carbon from the side opposite to the palladium atom.[10-12] Accordingly, it is apparent that a chiral ligand on palladium is far from the attacking nucleophile and has only a limited effect on the asymmetric allylation reaction where *the new asymmetric center is created on the nucleophile* (Figure 1).[13,14] Hayashi et al. designed ferrocenylphosphine ligand **1**, which possesses a hydroxyl group at the end of the pendant

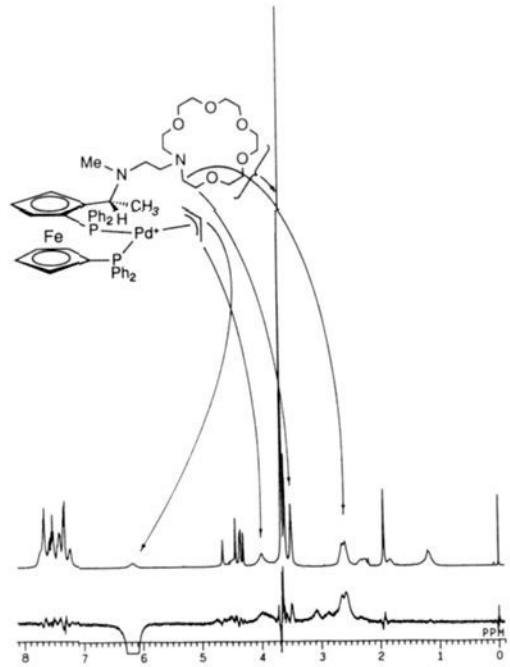


Figure 2. $^1H\{^1H\}$ NOEs of the π-allylpalladium(II) complex bearing crown ether-modified ligand **8b** in $CDCl_3$. (a) ^1H NMR spectrum (400 MHz) at ambient temperature. (b) NOE difference spectrum obtained upon saturation of the internal π-allyl proton (δ 6.16).

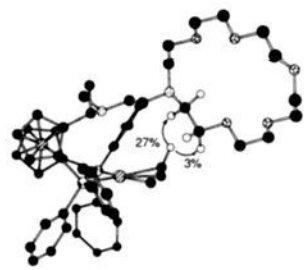


Figure 3. Molecular model of the π-allylpalladium(II) complex bearing crown ether-modified ligand **8b**. Arrows show $^1H\{^1H\}$ NOEs observed.

chain, and used it in the asymmetric allylation of β-diketones, giving enantioselectivities of over 80% ee (Scheme I).[15-18] The high selectivity was explained by hydrogen bonding between the hydroxyl group and the attacking enolate anion.

This article reports the synthesis of new ferrocenylphosphine ligands modified by crown ethers[19] and their applications in the palladium-catalyzed asymmetric allylation of β-diketones. Cram et al. have reported a highly enantioselective Michael reaction of methyl 1-oxo-2-indancarboxylate with methyl vinyl ketone by

(3) (a) Hiroi, K.; Kitayama, R.; Sato, S. *J. Chem. Soc., Chem. Commun.* **1984**, 303. (b) Hiroi, K.; Makino, K. *Chem. Lett.* **1986**, 617. (c) Inomata, K.; Yamamoto, T.; Kotake, I. *Chem. Lett.* **1981**, 1357.

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(7) Togni, A. *Tetrahedron: Asymmetry* **1991**, *2*, 683.

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(13) The first example of this type of asymmetric reaction was reported by Kagan et al. Optical yields were quite low (up to 10% ee), however. See: Fiaud, J.-C.; Hibon De Gournay, A.; Larcheveque, M.; Kagan, H. B. *J. Organomet. Chem.* **1978**, *154*, 175.

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(15) Hayashi, T.; Kanehira, K.; Hagihara, T.; Kumada, M. *J. Org. Chem.* **1988**, *53*, 113.

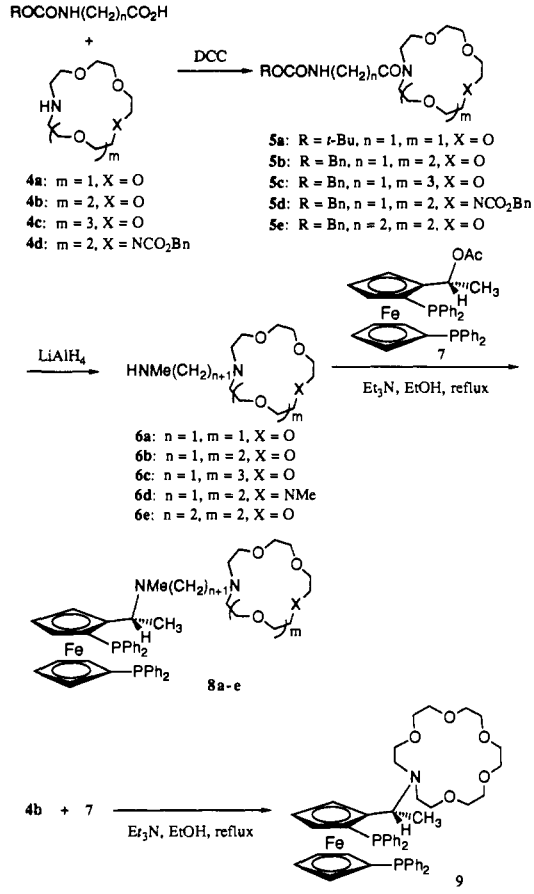
(16) For an application of chiral ligand **1** to asymmetric allylation of methyl α-isocyanocarboxylates, see: Ito, Y.; Sawamura, M.; Matsuoka, M.; Matsumoto, Y.; Hayashi, T. *Tetrahedron Lett.* **1987**, *28*, 4849.

(17) High enantioselectivities have been achieved in the palladium-catalyzed allylic alkylations where new asymmetric centers are created in allylic substrates by the use of hydroxylated ferrocenylphosphines. See ref 4.

(18) Hayashi et al. have devised chiral phosphine ligands bearing chiral polar functional groups and demonstrated them to be fairly effective for this type of asymmetric induction in improving the enantioselectivity (up to 52%) in the asymmetric allylation of 2-acetylcyclohexanone (**2b**). See: Hayashi, T.; Kanehira, K.; Tsuchiya, H.; Kumada, M. *J. Chem. Soc., Chem. Commun.* **1982**, 1162.

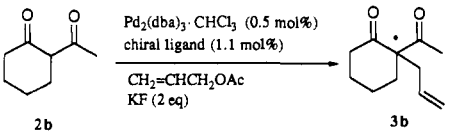
(19) For crown ether/phosphine hybrid ligands, see: (a) Hyde, E. M.; Shaw, B. L.; Shepherd, I. *J. Chem. Soc., Dalton Trans.* **1978**, 1696. (b) Okano, T.; Iwahara, M.; Suzuki, T.; Konishi, H.; Kiji, J. *Chem. Lett.* **1986**, 1467. (c) McLain, S. J. *J. Am. Chem. Soc.* **1983**, *105*, 6355. (d) Powell, J.; Gregg, M. R.; Kuksis, A.; May, C. J.; Smith, S. J. *Organometallics* **1989**, *8*, 2918 and references cited therein. (e) Boyce, B. A.; Carroy, A.; Lehn, J.-M.; Parker, D. *J. Chem. Soc., Chem. Commun.* **1984**, 1546. (f) Balch, A. L.; Rowley, S. P. *J. Am. Chem. Soc.* **1990**, *112*, 6139.

Scheme II



means of a catalytic amount of a chiral crown ether and potassium *tert*-butoxide.[20] The high selectivity (up to 99% ee) is consistent with the formation of a ternary complex involving the crown ether, potassium cation, and enolate anion of the active methine compound, in which the crown ether sterically fits with the enolate anion. On the basis of this result, we expect that the crown ether tethered to a chiral ferrocenylphosphine moiety at an appropriate distance will interact with the enolate anion of the β-diketone, attacking the π-allyl carbon through the formation of a ternary complex, leading to effective enantiofacial selection. The aim of this study is not only to improve the stereoselectivity, which has so far been attained, but also to give insight into a concept of *secondary ligand–substrate interaction*. This concept, originally proposed by Hayashi, has been developed by the authors and Hayashi and has successfully been applied to the gold-catalyzed asymmetric aldol reaction of isocyanoacetate,[21,22] where the terminal amino group of the chiral ligand abstracts an active hydrogen of the gold-coordinated isocyanoacetate to form the ammonium enolate of isocyanoacetate, resulting in a two-point

Scheme III



binding of the enolate, a phenomenon involved in some enzymic reactions.

Results and Discussion

Synthesis of Crown Ether-Modified Ligands. The chiral ferrocenylphosphine ligands modified by aza crown ethers of varying ring sizes and linker chain lengths were synthesized as outlined in Scheme II. The aza crown ethers are employed because the linker chains can be easily introduced onto the nitrogen atoms. Aminoacylation of aza crown ethers **4a–d** by N-protected amino acids followed by reduction of the resultant carbonyl groups with lithium aluminum hydride produced N-alkylated aza crown ethers **6a–e**, which were coupled with optically active ferrocenylethyl acetate **7**.[23] The crown ether-modified ligand which lacks the aminoalkyl linker chain (**9**) was also prepared by a similar reaction. The substitution reaction at the ferrocenylmethyl position has been established to proceed with retention of configuration.[23] All phosphine ligands thus obtained are air-stable, orange-colored oils, soluble in almost all organic solvents, but not in neutral water.

Structure of π-Allylpalladium(II) Complexes. The π-allylpalladium(II) complex is a key intermediate in the palladium-catalyzed allylation.[24] For the structural elucidation of the key intermediate, the π-allylpalladium(II) complex of crown-modified ligand **8b** was prepared by the reaction of **8b** and 1 equiv of the di-μ-chlorobis(π-allyl)dipalladium(II) complex in $CDCl_3$ (6×10^{-2} M) at room temperature. The π-allyl structure chelated by two phosphorus atoms was deduced by ^1H and ^{31}P NMR spectroscopy, and no evidence of the coordination of the crown ether to palladium was obtained. NOE experiments were carried out to investigate in more detail the structure of the complex in solution, especially the relative position of the crown ether moiety. Saturation of the internal π-allyl proton gave rise to a large NOE enhancement at the crown methylene protons α to the pivotal nitrogen atom (27% as a total of NOEs of the four α-protons), together with a small NOE (3%) at the β-methylene protons on the aza crown ether (Figure 2). These NOE enhancements indicated that the α-methylene is located in close proximity above the π-allyl plane. Figure 3 shows the molecular model of the complex created by the Chem 3D molecular modeling program on the basis of X-ray crystal structures of the π-allylpalladium complex of hydroxylated ferrocenylphosphine **1**[4d] and N-alkylated aza crown ethers complexed with potassium cation.[25] These NOEs and the molecular model suggest that the aza crown ether moiety is located at the proper position to interact with incoming nucleophiles. Such a conformation may be induced by weak electrostatic interaction between the palladium atom and the pivotal nitrogen atom.

Asymmetric Allylation of 2-Acetylcyclohexanone (2b). (a) Reaction Conditions. We first tested our crown ether-modified ligands in the asymmetric allylation of pregenerated sodium enolate of 2-acetylcyclohexanone (**2b**) in THF according to Hayashi's procedure,[15] but the enantioselectivities were not improved as compared with BPPFA (**10**). Expecting the enolate to interact with the metal cation which had been complexed with the aza crown ether moiety, we examined various reaction conditions. The

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Table I. Solvent Effect in the Asymmetric Allylation of **2b** Catalyzed by the Palladium Complex of **8b** (Scheme III)[a]

solvent	conversion,[b] % (yield of **3b**,[c] %)	ee, % of **3b** (config.),[d] $[\alpha]^{20}_D$[e]
mesitylene	100 (92)	60 (*R*), −152°
toluene	90 (80)	52 (*R*), −131°
THF	90 (80)	41 (*R*), −105°
CH_3CN	42 (38)	28 (*R*), −71.5°
CH_2Cl_2	81 (68)	21 (*R*), −53.5°
MeOH	0 (0)	

[a] The reaction was carried out at −25 °C for 40 h. **2b**/allyl acetate/KF/$Pd_2(dba)_3$·$CHCl_3$/**8b** = 1/1.5/2/0.005/0.011. [**2b**] = 0.43 M. [b] Determined by GLC analysis of crude product. [c] Isolated yield by MPLC. [d] Enantiomeric excess and configuration were determined by optical rotation of **3b**. The maximum rotation has been reported to be $[\alpha]^{20}_D$ + 257 ± 7° ($CHCl_3$) for (*S*)-**3b** in ref 15. [e] *c* = 1.0–3.0 in $CHCl_3$.

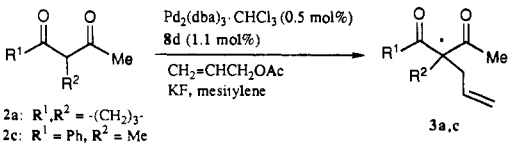
Table II. Asymmetric Allylation of **2b** Catalyzed by Palladium Complexes of Various Chiral Ligands (Scheme III)[a]

entry	chiral ligand	conversion,[b] % (yield of **3b**,[c] %)	ee, % of **3b** (config),[d] $[\alpha]^{20}_D$[e]
1	(*R*)-BINAP	15 (12)	<10[i]
2	(*S*,*S*)-DIOP	5 (3)	<10[i]
3	(*R*)-(*S*)-BPPFA (**10**)	78 (67)	32 (*R*), −82.1°
4	**10** (+18-crown-6)[g]	83 (75)	28 (*R*), −72.1°
5	**10** (+18-crown-6)[h]	94 (83)	29 (*R*), −73.8°
6	**11**	63 (54)	6 (*R*), −16.1°
7	**12**	65 (57)	22 (*R*), −56.6°
8	**8a**	30 (21)	49 (*R*), −125°
9	**8b**	100 (92)	60 (*R*), −152°
10[f]	**8b**	100 (91)	68 (*R*), −170°
11	**8c**	59 (50)	49 (*R*), −123°
12	**8d**	97 (90)	72 (*R*), −184°
13[f]	**8d**	100 (92)	75 (*R*), −190°
14	**8e**	40 (34)	53 (*R*), −134°
15	**9**	16 (14)	9 (*R*), −22.7°
16	**1**	66 (57)	60 (*S*), +152°

[a] The reaction was carried out in mesitylene for 40 h unless otherwise noted. **2b**/allyl acetate/KF/$Pd_2(dba)_3$·$CHCl_3$/ligand = 1/1.5/2/0.005/0.011. [**2b**] = 0.43 M. [b] Determined by GLC analysis of crude product. [c] Isolated yield by MPLC. [d] Enantiomeric excess and configuration were determined by optical rotation of **3b**. The maximum rotation has been reported to be $[\alpha]^{20}_D$ + 257 ± 7° ($CHCl_3$) for (*S*)-**3b** in ref 15. [e] *c* = 1.0–3.0 in $CHCl_3$. [f] Reaction was carried out at −40 °C for 150 h. [**2b**] = 0.77 M. [g] 1 mol % of 18-crown-6 was used as an additive. [h] 10 mol % of 18-crown-6 was used as an additive. [i] Determined by ^1H NMR analysis using the chiral shift reagent Eu(dcm)$_3$.

use of strong bases such as potassium *tert*-butoxide and potassium hydride caused a drastic decrease in the enantioselectivity. Solid–liquid, two-phase reaction conditions using potassium fluoride as an insoluble base were found to be most suitable for the enantioselective allylation of **2b** (Scheme III).[26] It has been reported that a catalytic amount of 18-crown-6 can activate potassium fluoride in the solid–liquid, two-phase conditions, such that the "naked" fluoride anion promotes the nucleophilic substitution and elimination reactions.[27] Since the potassium fluoride complexed with the tethered aza crown ether can act as a stronger base, the solid–liquid, two-phase conditions may suppress the formation of the potassium enolate which has not been complexed with the aza crown ether. The reaction of **2b** with allyl acetate in the presence of 1 mol % of palladium catalyst generated in situ by mixing $Pd_2(dba)_3$·$CHCl_3$ and **8b**, the chiral ligand bearing the monoaza-18-crown-6 moiety, was carried out at −25 °C for 40 h in various solvents, as shown in Table I. Both higher enantioselectivity and reactivity were found in less polar solvents such

Table III. Asymmetric Allylation of β-Diketones (**2a**,**c**) Catalyzed by the Palladium Complex of **8d**[a]



2a: R^1,R^2 = -$(CH_2)_3$-
2c: R^1 = Ph, R^2 = Me

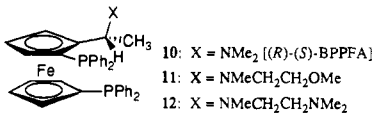
3a,c

β-diketone, **2**	temp, °C	yield of **3**,[b] %	ee of **3**, % ($[\alpha]^{20}_D$)[c]
2a	−50	90 (**3a**)	65[d] (−149°)
2c	−37	93 (**3c**)	72[e] (−10.5°)

[a] The reaction was carried out in mesitylene for 150 h. Conversion to **3** was 100%. **2**/allyl acetate/KF/$Pd_2(dba)_3$·$CHCl_3$/**8d** = 1/1.5/2/0.005/0.011. [**2**] = 0.77 M. [b] Isolated yield by MPLC. [c] Measured in $CHCl_3$. *c* = 1.61 for **3a**. *c* = 3.47 for **3c**. [d] Determined by ^1H NMR analysis of **3a** using the chiral shift reagent Eu(dcm)$_3$. [e] Determined by optical rotation of **3**. The maximum rotation was calculated to be $[\alpha]^{20}_D$ −14.5° ($CHCl_3$) from the reported rotation of **3c** of 60% ee (ref 15).

as mesitylene and toluene, in which electrostatic interactions between the aza crown ether and the potassium enolate generated in situ should be enhanced.

(b) Reaction with Various Chiral Ligands (Table II). Table II summarizes the results of the allylation of **2b** under KF/mesitylene two-phase conditions using various chiral ligands. The rate of conversion to allylated product **3b** and its optical purity were compared in the reaction at −25 °C for 40 h. Palladium catalysts with either (*R*)-BINAP[28] or (*S*,*S*)-DIOP,[29] which have been successfully used for many catalytic asymmetric reactions, showed low catalytic activity, resulting in the formation of an almost racemic product **3b** (entries 1 and 2). Rather high reactivity was observed for the ferrocenylphosphine ligand BPPFA (**10**), which has a dimethylamino group at the ferrocenylmethyl position, but the enantioselectivity was still low (32% ee, *R*, entry 3). A slight acceleration of the reaction was observed when 18-crown-6 was added to the allylation reaction which was catalyzed by the palladium complex of BPPFA (**10**), but the enantioselectivity was not improved (entries 4 and 5). Both modified ferrocenylphosphine ligands bearing a methoxy group and a dimethylamino group at the end of the pendant chain (**11** and **12**) were not effective (entries 6 and 7).



10: X = NMe_2 [(*R*)-(*S*)-BPPFA]
11: X = $NMeCH_2CH_2OMe$
12: X = $NMeCH_2CH_2NMe_2$

Ligands **8a**–**c** have monoaza crown ethers of varying ring sizes tethered with the same length of linker chain. As expected from the complementarity between the hole size of a crown ether and the ionic radius of a guest cation, the ligand **8b** with a monoaza-18-crown-6 moiety significantly accelerated the allylation with increased enantioselectivity (60% ee, entry 9), while the monoaza-15-crown-5 and monoaza-21-crown-7 moieties of **8a** and **8c**, respectively, retarded the reaction, giving the allylation product in low yields with an enantioselectivity of 49% (entries 8 and 11). The high efficiency of **8b** allowed the reaction to be performed at lower temperatures. Thus, the reaction at −40 °C was complete within 150 h, improving the enantioselectivity to 68% (entry 10), which was further improved by modifying the crown ether moiety of **8b** to 1,10-diaza-18-crown-6. The palladium complex of the modified ligand **8d** showed almost the same catalytic activity as that of **8b** and gave a selectivity of 72% ee at −25 °C and 75% ee at −40 °C (entries 12 and 13). It should be noted that the chiral sense of enantioselection by the use of crown-modified chiral

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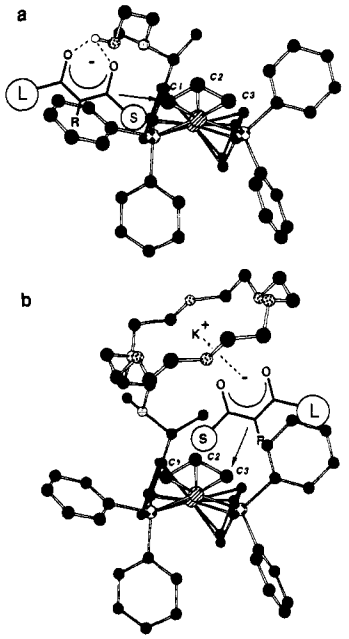

Figure 4. Nucleophilic attack of an enolate of the β-diketone on the π-allylpalladium(II) intermediate bearing hydroxylated ferrocenylphosphine ligand **1** (a) and crown ether-modified ligand **8b** (b).

ligands is opposite to that of hydroxylated ligand **1** (60% ee, *S*, entry 16).

The importance of the length of linker chain in derivatives of **8** is clearly shown by entries 14 and 15. Although the stereoselectivity with **8e**, which has a longer chain by one methylene unit than **8b**, was comparable to that with **8b**, the reaction-acceleration effect by the tethered crown ether was no longer observed. Ligand **9**, which has no linker chain, gave an almost racemic product in very low yields. Since the potassium cation-binding abilities of ligands **8b**, **8e**, and **9** do not seem to differ significantly, the difference of reaction acceleration may possibly be ascribed to the stabilization of the transition state of carbon–carbon bond formation.[30]

Asymmetric Allylation of Other β-Diketones (Table III). The efficiency of the crown ether-modified ligands over hydroxylated ligand **1** was evident in the reaction of 2-acetylcyclopentanone (**2a**). The allylation of **2a** was catalyzed at −50 °C by the palladium complex with **8e**, which was the most effective crown ether-modified ligand in the reaction of 2-acetylcyclohexanone (**2b**), to give **3a** in 65% ee. This finding is to be noted, since the use of **1** as the chiral ligand in the allylation of **2a** gave almost racemic **3a**.[15] This result may suggest that the secondary interaction between a chiral ligand and 2-acetylcyclohexanone (**2a**) is more effectively operative with the palladium complex of **8e** than with the palladium complex of **1**, leading to the higher degree of enantiofacial differentiation of **2a**. Ligand **8e** was also effective in the reaction of acyclic β-diketone **2c**, which was allylated in 72% ee at −37 °C, and the sense of enantioselection was opposite to that reported by Hayashi using the hydroxylated ligand **1**,[15] which gave the (+) isomer of **3c** in 60% ee at −60 °C.

Mechanism of Asymmetric Induction. The increase of both reaction rate and enantioselectivity by the aza crown ether tethered to chiral ferrocenylphosphine may suggest the formation of a ternary complex involving the crown ether, potassium cation, and enolate anion. A similar *secondary ligand–substrate interaction* has been proposed for the asymmetric allylation using the hydroxylated ligand **1**,[15] in which hydrogen bonding between the hydroxyl group and the enolate anion may be involved. The opposite sense of enantioselection may originate from the regiochemical difference between the π-allyl carbon atoms in the nucleophilic attack of enolate. Figure 4a,b illustrates the nucleophilic attack of enolate on the π-allylpalladium intermediates bearing **1** and **8b**, respectively. Our hypothesis is as follows: (1) The hydrogen bonding between the hydroxyl group of **1** and enolate anion causes the preferential attack of the enolate on π-allyl carbon atom C1, as shown in Figure 4a. On the other hand, the sterically bulky crown ether moiety blocks the approach of enolate to C1, providing a chiral pocket around π-allyl carbon C3 (Figure 4b). (2) The π-allyl carbons are attacked by the enolate, in which the larger substituent L and smaller one S are directed outside and inside, respectively.

Conclusion

We illustrated that the crown ether-modified chiral ferrocenylphosphine ligands with the appropriate ring size of crown ethers and length of linker chains are effective for the palladium-catalyzed asymmetric allylation of β-diketones under carefully controlled reaction conditions. The palladium catalysts bearing crown ether-modified ligands may be regarded as artificial enzyme-like catalysts, in that the catalysts activate an electrophile (allyl acetate or π-allyl cation) and a nucleophile (potassium enolate) simultaneously. Stereoselectivity was achieved as a result of the multiple recognition of stereodifferentiating transition states involving coordinative, electrostatic, and steric interactions.

Experimental Section

General. Optical rotations were measured with a Perkin-Elmer 243 polarimeter. ^{1}H NMR spectra were obtained with a Varian VXR-200 (200 MHz) or JEOL JNM-GX-400 (400 MHz) spectrometer. ^{13}C{^{1}H} (50 MHz) and ^{31}P{^{1}H} (81 MHz) NMR spectra were obtained with a Varian VXR-200 spectrometer. Preparative medium-pressure liquid chromatography (MPLC) was performed with a silica gel prepacked C.I.G. (Kusano) column.

Materials. Aza crown ethers **4a–c** were prepared by Okahara's method as described in the literature.[30] Di-μ-chlorobis(π-allyl)dipalladium(II)[32] and $Pd_2(dba)_3$·$CHCl_3$[33] were prepared as described. The preparation of optically active ferrocenylphosphines **1**, **7**, **10**,[23] **11**,[15] and **12**[23] has been reported. (*R*)-BINAP and (*S*,*S*)-DIOP were commercially available and used without further purification. Chiral shift reagent Eu(dcm)$_3$ was prepared as described.[34]

***N*-(Benzyloxycarbonyl)-1,10-diaza-18-crown-6 (4d).** To a solution of 1,10-diaza-18-crown-6 (Merck, Kryptofix 22) (0.983 g, 3.75 mmol) and triethylamine (1.53 g, 15.1 mmol) in 7.5 mL of dry benzene was slowly added 0.638 g (3.74 mmol) of benzyloxycarbonyl chloride in 3.7 mL of benzene at 30 °C. After the addition was complete (1.5 h), the mixture was stirred for an additional 1 h at the same temperature. The mixture was diluted to a volume of 50 mL and then washed three times with 5% sodium hydroxide solution to remove unreacted 1,10-diaza-18-crown-6, which was recovered in 54% yield by the evaporation of most of the water from combined aqueous extracts followed by extraction with dichloromethane. The organic phase was dried over sodium sulfate and evaporated. Chromatography on silica gel (ethyl acetate/trimethylamine) gave 0.481 g (24%) of *N*,*N*′-bis(benzyloxycarbonyl)-1,10-diaza-18-crown-6 and 0.270 g (18%) of **4d**: ^{1}H NMR ($CDCl_3$/TMS, 200 MHz) δ 2.81 (q, *J* = 5.7 Hz, 4 H), 3.5–3.7 (m, 24 H), 5.12 (s, 2 H), 7.2–7.4 (m, 5 H).

***N*-[[*N*-(Benzyloxycarbonyl)amino]acetyl]-1-aza-18-crown-6 (5b). Typical Procedure for the Aminoacylaction of Aza Crown Ethers.** To a solution of 6.66 g (31.8 mmol) of *N*-(benzyloxycarbonyl)glycine (Z-Gly) and 7.20 g (34.9 mmol) of 1,3-dicyclohexylcarbodiimide (DCC) in 60 mL of dry dichloromethane was added 8.44 g (32.1 mmol) of 1-aza-18-crown-6 (**4b**) in 50 mL of dichloromethane at 2 °C. The reaction mixture was stirred at 2 °C for 30 min and then at room temperature for overnight. The mixture was filtered, washed with ethyl acetate, and evaporated. Ethyl acetate (50 mL) was added, and the mixture was allowed to stand at −20 °C for 1 h. After a precipitate was filtered off, chromatography on silica gel (from hexane/ethyl acetate (1:2) to ethyl

(30) (a) Hamilton et al. demonstrated the stabilization of the transition state in the intramolecular Diels–Alder reaction by "complexation control" with artificial receptors bearing two binding sites tethered to each other at an appropriate distance. See: Hirst, S. C.; Hamilton, A. D. *J. Am. Chem. Soc.* **1991**, *113*, 382. (b) A similar bisubstrate reaction template had been reported by Kelly et al. See: Kelly, T. R.; Zhao, C.; Bridger, G. J. *J. Am. Chem. Soc.* **1989**, *111*, 3744.

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(34) McCreary, M. D.; Lewis, D. W.; Wernick, D. L.; Whitesides, G. M. *J. Am. Chem. Soc.* **1974**, *96*, 1038.

acetate/acetone (3:1)) gave 10.47 g (72%) of **5b**: ^{1}H NMR ($CDCl_3$/TMS, 200 MHz) δ 3.5–3.8 (m, 24 H), 4.13 (d, J = 4.3 Hz, 2 H), 5.12 (s, 2 H), 5.8 (broad t, 1 H), 7.3–7.4 (m, 5 H).

***N*-[[*N*-(*tert*-Butoxycarbonyl)amino]acetyl]-1-aza-15-crown-5 (5a)** was prepared from 3.68 g (21.0 mmol) of *N*-(*tert*-butoxycarbonyl)glycine, 4.33 g (21.0 mmol) of DCC, and 4.57 g (20.8 mmol) of **4a** and used without chromatographic purification: ^{1}H NMR ($CDCl_3$/TMS, 200 MHz) δ 1.45 (s, 9 H), 3.46 (t, J = 6.6 Hz, 2 H), 3.55–3.75 (m, 12 H), 3.80 (t, J = 6.6 Hz, 2 H), 4.02 (d, J = 4.2 Hz, 2 H), 5.5 (broad, 1 H).

***N*-[[*N*-(Benzyloxycarbonyl)amino]acetyl]-1-aza-21-crown-7 (5c)** was prepared from 1.92 g (9.18 mmol) of Z-Gly, 2.08 g (10.1 mmol) of DCC, and 2.82 g (9.18 mmol) of **4c** in 70% yield: ^{1}H NMR ($CDCl_3$/TMS, 200 MHz) δ 3.4–3.9 (m, 28 H), 4.13 (d, J = 4.2 Hz, 2 H), 5.12 (s, 2 H), 5.93 (broad, 1 H), 7.3–7.4 (m, 5 H).

***N*-(Benzyloxycarbonyl)-*N'*-[[*N*-(benzyloxycarbonyl)amino]acetyl]-1,10-diaza-18-crown-6 (5d)** was prepared from 0.157 g (0.751 mmol) of Z-Gly, 0.155 g (0.751 mmol) of DCC, and 0.271 g (0.682 mmol) of **4d** in 84% yield: ^{1}H NMR ($CDCl_3$/TMS, 200 MHz) δ 3.5–3.7 (m, 24 H), 4.07 (d, J = 4.2 Hz, 2 H), 5.12 (s, 4 H), 5.77 (broad, 1 H), 7.3–7.4 (m, 10 H).

***N*-[3-[*N*-(Benzyloxycarbonyl)amino]propanoyl]-1-aza-18-crown-6 (5e)** was prepared from 0.49 g (2.2 mmol) of Z-β-alanine, 0.46 g (2.2 mmol) of DCC, and 0.53 g (2.0 mmol) of **4b** in 92% yield: ^{1}H NMR ($CDCl_3$/TMS, 200 MHz) δ 2.60 (t, J = 5.5 Hz, 2 H), 3.52 (dt, J = 6.1 Hz, 5.5 Hz, 2 H), 3.55–3.75 (m, 24 H), 5.09 (s, 2 H), 5.64 (broad, 1 H), 7.26–7.38 (m, 5 H).

***N*-[2-(*N*-Methylamino)ethyl]-1-aza-18-crown-6 (6b). Typical Procedure for the Reduction of 5.** A solution of 10.47 g (23.0 mmol) of **5b** in 50 mL of dry THF was added dropwise to a suspension of 2.64 g (69.6 mmol) of lithium aluminum hydride in 40 mL of dry THF at 0 °C. After the addition was complete, the mixture was stirred at room temperature for 1 h, refluxed for 2 h, and cooled by an ice–water bath. Aluminum complexes were decomposed by the successive addition of 2.6 mL of water, 2.6 mL of 15% sodium hydroxide, and 5.2 mL of water. The resulting salts were removed by suction and washed with hot ethyl acetate. A filtrate and the washings were concentrated under reduced pressure. Distillation of a residue (160 °C/0.2 mmHg) gave 6.34 g (86%) of **6b**: ^{1}H NMR ($CDCl_3$/TMS, 200 MHz) δ 2.43 (s, 3 H), 2.63 (s, 4 H), 2.73 (t, J = 5.7 Hz, 4 H), 3.60 (t, J = 5.7 Hz, 4 H), 3.55–3.80 (m, 16 H).

***N*-[2-(*N*-Methylamino)ethyl]-1-aza-15-crown-5 (6a)** was obtained from crude **5a** in 35% yield based on the amount of **4a** used: bp 125 °C/0.3 mmHg; ^{1}H NMR ($CDCl_3$/TMS, 200 MHz) δ 2.42 (s, 3 H), 2.62 (dd, J = 9.6 Hz, 3.4 Hz, 4 H), 2.73 (t, J = 6.0 Hz, 4 H), 3.60 (t, J = 5.7 Hz, 4 H), 3.55–3.72 (m, 16 H).

***N*-[2-(*N*-Methylamino)ethyl]-1-aza-21-crown-7 (6c)** was prepared from 3.02 g (6.42 mmol) of **5c** in 42% yield: ^{1}H NMR ($CDCl_3$/TMS, 200 MHz) δ 2.44 (d, J = 3.8 Hz, 3 H), 2.6–2.8 (m, 4 H), 2.75 (t, J = 5.7 Hz, 4 H), 3.57 (t, J = 5.7 Hz, 4 H), 3.5–3.8 (m, 24 H).

***N*-[2-(*N*-Methylamino)ethyl]-*N'*-methyl-1,10-dlaza-18-crown-6 (6d)** was prepared from 0.337 g (0.573 mmol) of **5d** and isolated by bulb-to-bulb distillation (150–200 °C/1 mmHg) in quantitative yield (contaminated with 2% of benzyl alcohol): ^{1}H NMR ($CDCl_3$/TMS, 200 MHz) δ 2.32 (s, 3 H), 2.44 (s, 3 H), 2.6–2.7 (m, 4 H), 2.69 (t, J = 5.7 Hz, 4 H), 2.75 (t, J = 5.7 Hz, 4 H), 3.58 (t, J = 5.7 Hz, 4 H), 3.62 (t, J = 5.7 Hz, 4 H), 3.62 (s, 8 H).

***N*-[3-(*N*-Methylamino)propyl]-1-aza-18-crown-6 (6e)** was prepared from 0.852 g (1.82 mmol) of **5e** in 57% yield: bp 150–200 °C (bulb-to-bulb distillation); ^{1}H NMR ($CDCl_3$/TMS, 200 MHz) δ 1.6–1.8 (m, 2 H), 2.47 (s, 3 H), 2.5–2.8 (m, 2 H), 2.58 (t, J = 7.0 Hz, 2 H), 2.74 (t, J = 5.7 Hz, 4 H), 3.61 (t, J = 5.7 Hz, 4 H), 3.55–3.75 (m, 16 H).

Preparation of Crown Ether-Modified Ferrocenylphosphine Ligands 8 and 9. The procedure for the preparation of **8b** is typical. A solution of 1.03 g (1.60 mmol) of **7**, 1.58 g (4.92 mmol) of **6b**, and 0.45 mL (3.2 mmol) of triethylamine in 5 mL of dry ethanol was refluxed for 20 h. After the ethanol was evaporated under reduced pressure, the residue was diluted with 40 mL of water, extracted with four 30-mL portions of benzene, and washed with 20 mL of water. Addition of 10 g of sodium hydroxide to the combined aqueous phases, extraction with six 20-mL portions of dichloromethane, evaporation, and bulb-to-bulb distillation permitted the recovery of 0.98 g (62%) of **6b**. The combined organic phases were evaporated, and chromatography on silica gel (hexane/ethyl acetate/triethylamine) gave 1.00 g (69%) of **8b**: $[\alpha]^{25}_D$ −240° (*c* 0.76, $CHCl_3$); ^{1}H NMR ($CDCl_3$/TMS, 200 MHz) δ 1.13 (d, J = 6.7 Hz, 3 H), 1.64 (s, 3 H), 1.7–2.0 (m, 2 H), 2.15–2.52 (m, 2 H), 2.58 (t, J = 5.9 Hz, 4 H), 3.47 (t, J = 5.9 Hz, 4 H), 3.4–3.73 (m, 2 H), 3.55–3.73 (m, 16 H), 3.9–4.0 (m, 1 H), 4.0–4.1 (m, 2 H), 4.2–4.3 (m, 1 H), 4.34 (s, 2 H), 7.0–7.55 (m, 20 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$/TMS, 50 MHz) δ 8.88, 34.32, 52.26, 53.90, 54.29, 57.56 (d, J_{C-P} = 7.3 Hz), 69.83, 70.39, 70.76, 71.40 (d, J_{C-P} = 2.4 Hz), 72.63, 72.78 (d, J_{C-P} = 19.3 Hz), 73.00 (d, J_{C-P} = 2.2 Hz), 74.09 (d, J_{C-P} = 1.4 Hz), 74.17, 75.15, 75.56, 75.95, 76.09, 76.58, 76.78, 77.20, 97.87 (d, J_{C-P} = 23.3 Hz), 127.04, 127.22, 127.35, 127.78, 127.95, 128.02, 128.10, 128.15, 128.24, 128.56, 128.79, 132.26 (d, J_{C-P} = 18.0 Hz), 133.04 (d, J_{C-P} = 18.9 Hz), 133.68 (d, J_{C-P} = 19.9 Hz), 135.28 (d, J_{C-P} = 10.9 Hz), 138.50 (d, J_{C-P} = 10.0 Hz), 139.40 (d, J_{C-P} = 10.0 Hz), 141.04 (d, J_{C-P} = 8.0 Hz); $^{31}P\{^1H\}$ NMR ($CDCl_3/H_3PO_4$, 81 MHz) −23.12, −16.72. Anal. Calcd for $C_{51}H_{62}N_2O_5P_2Fe$: C, 68.00; H, 6.94; N, 3.11. Found: C, 67.73; H, 7.16; N, 2.96.

8a was prepared from 1.6 g (2.5 mmol) of **7** and 2.1 g (7.7 mmol) of **6a** in 53% yield: $[\alpha]^{25}_D$ −252° (*c* 0.63, $CHCl_3$); ^{1}H NMR ($CDCl_3$/TMS, 200 MHz) δ 1.13 (d, J = 6.8 Hz, 3 H), 1.64 (s, 3 H), 1.7–2.0 (m, 2 H), 2.15–2.5 (m, 2 H), 2.57 (t, J = 6.1 Hz, 4 H), 3.51 (t, J = 6.1 Hz, 4 H), 3.58–3.8 (m, 12 H), 3.4–3.8 (m, 2 H), 3.85–4.0 (m, 1 H), 4.0–4.1 (m, 2 H), 4.1–4.2 (m, 1 H), 4.3–4.4 (m, 2 H), 7.0–7.6 (m, 20 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$/TMS, 50 MHz) δ 8.76, 11.61, 34.26, 41.38, 46.71, 47.20, 52.10, 54.61, 69.88, 72.02, 70.34, 70.88, 71.35 (d, J_{C-P} = 2.7 Hz), 72.31 (d, J_{C-P} = 2.7 Hz), 72.69, 72.96, 74.09 (d, J_{C-P} = 4.6 Hz), 75.11, 75.52, 75.81, 75.95, 76.50, 76.69, 77.21, 97.75 (d, J_{C-P} = 23.1 Hz), 127.00, 127.16, 127.29, 127.71, 127.89, 127.96, 128.04, 128.09, 128.17, 128.50, 128.71, 132.19 (d, J_{C-P} = 18.1 Hz), 132.95 (d, J_{C-P} = 19.0 Hz), 134.20 (d, J_{C-P} = 19.9 Hz), 135.19 (d, J_{C-P} = 21.6 Hz), 138.39 (d, J_{C-P} = 10.9 Hz), 138.45 (d, J_{C-P} = 9.0 Hz), 139.33 (d, J_{C-P} = 9.9 Hz), 140.90 (d, J_{C-P} = 8.1 Hz); $^{31}P\{^1H\}$ NMR ($CDCl_3/H_3PO_4$, 81 MHz) −23.34, −16.89. Anal. Calcd for $C_{49}H_{58}N_2O_4P_2Fe$: C, 68.69; H, 6.82; N, 3.27. Found: C, 68.16; H, 6.75; N, 3.27.

8c was prepared from 0.641 g (1.00 mmol) of **7** and 0.980 g (2.69 mmol) of **6c** in 40% yield: $[\alpha]^{25}_D$ −232° (*c* 0.54, $CHCl_3$); ^{1}H NMR ($CDCl_3$/TMS, 200 MHz) δ 1.13 (d, J = 6.8 Hz, 3 H), 1.64 (s, 3 H), 1.8–2.0 (m, 2 H), 2.1–2.5 (m, 2 H), 2.58 (t, J = 5.9 Hz, 4 H), 3.44 (t, J = 5.9 Hz, 4 H), 3.4–3.5 (m, 1 H), 3.5–3.8 (m, 21 H), 3.9–4.0 (m, 1 H), 4.0–4.1 (m, 2 H), 4.1–4.2 (m, 1 H), 4.3–4.4 (m, 2 H), 7.0–7.6 (m, 20 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$/TMS, 50 MHz) δ 8.86, 21.68, 34.32, 52.38, 53.58, 54.29, 57.57 (d, J_{C-P} = 7.4 Hz), 69.91, 70.40, 70.70, 70.78, 70.84, 70.93, 71.40 (d, J_{C-P} = 5.4 Hz), 72.66, 72.80, 73.05, 74.14 (d, J_{C-P} = 3.3 Hz), 75.16, 75.57, 75.96, 76.10, 76.58, 76.79, 77.20, 97.88 (d, J_{C-P} = 23.3 Hz), 127.04, 127.22, 127.35, 127.79, 127.96, 128.02, 128.10, 128.16, 128.24, 128.56, 128.80, 132.25 (d, J_{C-P} = 18.0 Hz), 133.03 (d, J_{C-P} = 18.9 Hz), 133.71 (d, J_{C-P} = 19.8 Hz), 135.28 (d, J_{C-P} = 21.7 Hz), 138.48 (d, J_{C-P} = 9.5 Hz), 139.40 (d, J_{C-P} = 10.0 Hz), 141.06 (d, J_{C-P} = 8.2 Hz); $^{31}P\{^1H\}$ NMR ($CDCl_3/H_3PO_4$, 81 MHz) −23.22, −16.84. Anal. Calcd for $C_{53}H_{66}N_2O_6P_2Fe$: C, 67.37; H, 7.04; N, 2.96. Found: C, 66.99; H, 6.96; N, 2.95.

8d was prepared from 0.367 g (0.573 mmol) of **7** and 0.198 g (0.573 mmol) of **6d** in 27% yield: $[\alpha]^{25}_D$ −248° (*c* 0.62, $CHCl_3$); ^{1}H NMR ($CDCl_3$/TMS, 200 MHz) δ 1.13 (d, J = 6.7 Hz, 3 H), 1.64 (s, 3 H), 1.72–2.00 (m, 2 H), 2.10–2.56 (m, 2 H), 2.31 (s, 3 H), 2.59 (t, J = 5.9 Hz, 4 H), 2.69 (t, J = 5.6 Hz, 4 H), 3.46 (t, J = 5.9 Hz, 4 H), 3.5–3.8 (m, 14 H), 3.95 (m, 1 H), 4.05 (m, 2 H), 4.14 (dq, J = 2.6 Hz, 6.7 Hz, 1 H), 4.34 (m, 2 H), 6.97–7.38 (m, 20 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$/TMS, 50 MHz) δ 8.80, 34.28, 43.86, 52.24, 53.76, 54.11, 56.65, 57.55 (d, J_{C-P} = 7.4 Hz), 69.32, 69.84, 70.34, 70.57, 71.35 (d, J_{C-P} = 20.6 Hz), 75.95 (d, J_{C-P} = 7.0 Hz), 76.63 (d, J_{C-P} = 9.8 Hz), 97.82 (d, J_{C-P} = 23.2 Hz), 127.00, 127.18, 127.31, 127.75, 127.92, 127.99, 128.06, 128.12, 128.19, 128.53, 128.76, 132.20 (d, J_{C-P} = 18.1 Hz), 132.98 (d, J_{C-P} = 18.9 Hz), 133.64 (d, J_{C-P} = 19.8 Hz), 135.23 (d, J_{C-P} = 21.6 Hz), 138.42 (d, J_{C-P} = 9.4 Hz), 138.46 (d, J_{C-P} = 9.4 Hz), 139.35 (d, J_{C-P} = 9.9 Hz), 140.99 (d, J_{C-P} = 8.1 Hz); $^{31}P\{^1H\}$ NMR ($CDCl_3/H_3PO_4$, 81 MHz) −23.15, −16.77. Anal. Calcd for $C_{52}H_{65}N_3O_4P_2Fe$: C, 68.34; H, 7.17; N, 4.60. Found: C, 68.34; H, 7.29; N, 4.43.

8e was prepared from 0.190 g (0.296 mmol) of **7** and 0.297 g (0.888 mmol) of **6e** in 62% yield: $[\alpha]^{25}_D$ −218° (*c* 1.01, $CHCl_3$); ^{1}H NMR ($CDCl_3$/TMS, 200 MHz) δ 1.14 (d, J = 6.8 Hz, 3 H), 0.9–1.1 (m, 1 H), 1.64 (s, 3 H), 2.0–2.4 (m, 5 H), 2.56 (t, J = 5.9 Hz, 4 H), 3.45 (m, 1 H), 3.51 (t, J = 5.9 Hz, 4 H), 3.55–3.80 (m, 21 H), 3.90 (m, 1 H), 4.06 (m, 2 H), 4.08–4.20 (m, 1 H), 4.35 (m, 2 H), 7.00–7.17 (m, 5 H), 7.17–7.40 (m, 12 H), 7.40–7.55 (m, 3 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$/TMS, 50 MHz) δ 8.74, 25.18, 33.60, 52.70, 53.79, 53.96, 57.00 (d, J_{C-P} = 7.0 Hz), 69.89, 70.32, 70.19, 70.77, 71.39, 72.51, 72.66, 72.89, 74.08 (d, J_{C-P} = 4.6 Hz), 75.39 (d, J_{C-P} = 20.8 Hz), 75.96 (d, J_{C-P} = 6.9 Hz), 76.65 (d, J_{C-P} = 10.6 Hz), 98.05 (d, J_{C-P} = 23.7 Hz), 126.93, 127.16, 127.28, 127.74, 127.90, 127.97, 128.05, 128.10, 128.16, 128.52, 128.76, 132.05 (d, J_{C-P} = 17.7 Hz), 132.95 (d, J_{C-P} = 18.9 Hz), 133.65 (d, J_{C-P} = 19.9 Hz), 135.29 (d, J_{C-P} = 21.9 Hz), 138.42 (d, J_{C-P} = 9.7 Hz), 138.67 (d, J_{C-P} = 9.1 Hz), 139.39 (d, J_{C-P} = 9.9 Hz), 141.21 (d, J_{C-P} = 8.0 Hz); $^{31}P\{^1H\}$ NMR ($CDCl_3/H_3PO_4$, 81 MHz) −23.00, −16.79. Anal. Calcd for $C_{52}H_{64}N_2O_5P_2Fe$: C, 68.27; H, 7.05; N, 3.06. Found: C, 68.12; H, 7.11; N, 2.80.

9 was prepared from 0.320 g (0.50 mmol) of **7** and 0.395 g (1.5 mmol) of **4b** in 73% yield: $[\alpha]^{25}_D$ −305° (*c* 0.71, $CHCl_3$); ^{1}H NMR ($CDCl_3$/

TMS, 200 MHz) δ 1.24 (d, J = 6.3 Hz, 3 H), 2.50 (t, J = 6.6 Hz, 4 H), 2.82-3.02 (m, 2 H), 3.02-3.20 (m, 2 H), 3.30-3.42 (m, 4 H), 3.42-3.48 (m, 1 H), 3.48-3.56 (m, 4 H), 3.56-3.68 (m, 8 H), 3.68-3.72 (m, 1 H), 3.84-3.90 (m, 1 H), 4.02-4.08 (m, 2 H), 4.16 (dq, J = 3.0 Hz, 6.6 Hz, 1 H), 4.30-4.36 (m, 1 H), 4.36-4.40 (m, 1 H), 7.10-7.35 (m, 18 H), 7.42-7.58 (m, 2 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$/TMS, 50 MHz) δ 10.88, 49.53, 56.39 (d, J_{C-P} = 7.4 Hz), 69.79, 70.18, 70.35, 70.58, 71.46, 72.26, 72.42, 73.77, 75.00, 75.41, 75.51, 75.72, 75.87, 97.38 (d, J_{C-P} = 24.6 Hz), 127.03, 127.23, 127.36, 127.49, 127.65, 127.81, 128.23, 128.54, 132.16 (d, J_{C-P} = 18.3 Hz), 132.63 (d, J_{C-P} = 19.1 Hz), 13.32 (d, J_{C-P} = 20.1 Hz), 134.86 (d, J_{C-P} = 22.0 Hz), 137.77 (d, J_{C-P} = 9.2 Hz), 138.07 (d, J_{C-P} = 9.7 Hz), 138.98 (d, J_{C-P} = 10.1 Hz), 140.32 (d, J_{C-P} = 8.3 Hz); $^{31}P\{^1H\}$ NMR ($CDCl_3/H_3PO_4$, 81 MHz) -25.51, -17.24. Anal. Calcd for $C_{48}H_{55}NO_5P_2Fe$: C, 68.33; H, 6.57; N, 1.66. Found: C, 68.51; H, 6.66; N, 1.62.

Preparation of the π-Allylpalladium(II) Complex of 8b. To a small glass vessel were added 27.4 mg (0.0304 mmol) of **8b** and 5.6 mg (0.0153 mmol) of di-μ-chlorobis(π-allyl)dipalladium(II) and then dissolved in 0.3 mL of $CDCl_3$. The solution was rinsed into an NMR tube (5 φ) with $CDCl_3$, and the total volume was adjusted to 0.7 mL with $CDCl_3$: ^1H NMR ($CDCl_3$/TMS, 400 MHz) δ 1.0-1.4 (broad, 3 H), 1.72-1.88 (m, 1 H), 1.93 (s, 3 H), 2.15-2.39 (m, 2 H), 2.39-2.75 (m, 5 H), 3.50 (t, J = 5.4 Hz, 4 H), 3.55-3.80 (m, 21 H), 3.86-4.17 (broad, 4 H), 4.31 (m, 1 H), 4.35 (m, 1 H), 4.37 (m, 1 H), 4.44 (m, 2 H), 4.40-4.56 (broad, 1 H), 4.65 (m, 1 H), 6.16 (broad, 1 H), 7.15-7.82 (m, 20 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$/TMS, 50 MHz) δ 9.77, 30.85, 34.20, 54.03, 54.32, 58.84, 68.90, 70.13, 70.51, 70.58, 70.71, 71.24 (d, J_{C-P} = 5.7 Hz), 72.99 (d, J_{C-P} = 5.3 Hz), 73.24 (d, J_{C-P} = 6.1 Hz), 73.93 (d, J_{C-P} = 10.1 Hz), 77.21, 77.90, 78.05, 97.43 (d, J_{C-P} = 14.8 Hz), 123.57 (t, J_{C-P} = 5.4 Hz), 127.58 (d, J_{C-P} = 10.2 Hz), 128.09, 128.34, 128.71 (d, J_{C-P} = 10.7 Hz), 129.19 (d, J_{C-P} = 10.3 Hz), 129.61 (d, J_{C-P} = 10.2 Hz), 130.13, 131.48, 131.70, 131.78, 132.26, 132.43, 132.62, 132.85, 133.55, 133.79, 135.59, 135.87, 135.91; $^{31}P\{^1H\}$ NMR ($CDCl_3/H_3PO_4$, 81 MHz) 23.34 (AB q, J_{AB} = 38.7 Hz, Δν = 110 Hz).

$^1H\{^1H\}$ Nuclear Overhauser Effect Experiment. A sample of the π-allylpalladium(II) complex was prepared as above, and the solution was degassed by the freeze-thaw method and sealed. The $^1H\{^1H\}$ NOE experiment was performed at 400 MHz. The decoupler was set to the resonance of internal π-allyl proton (δ 6.16) and turned on for 10 s. This pre-irradiation period was followed by a short (0.05 s) switching time to prevent the occurrence of unwanted decoupling, immediately followed by a 45° acquisition pulse and a 4-s acquisition. Reference spectra were obtained in a similar manner with the decoupler frequency set to irradiate an empty region of the spectrum. Eight transients were acquired with the decoupler on resonance followed by eight reference transients. A total of 512 transients were collected. Percent NOE enhancements were determined by integration of the difference spectra as totals of the enhancements for all equivalent protons.

General Procedure for the Palladium-Catalyzed Asymmetric Allylation. In a small glass vessel, 0.011 mmol of a chiral ligand and 0.005 mmol of $Pd_2(dba)_3 \cdot CHCl_3$ were dissolved in a solvent (1 mL for Table II, entries 8 and 11, and Table III; 2 mL for Table I and Table II, entries 1-7, 9, 10, and 12-16) and stirred for 1 h at room temperature. The solution was added to 2.0 mmol of potassium fluoride (spray-dried) placed in 20-mL Schlenk tube under an argon atmosphere. The suspension was stirred for 30 min before the addition of 1.0 mmol of β-diketone **2**, followed by stirring for 15 min. The mixture was cooled to a given reaction temperature before the addition of 1.5 mmol of allyl acetate and was kept stirring at the temperature for a given reaction time. The reaction was quenched by 6 N hydrochloric acid and extracted with ether. The ether extracts were washed with sodium bicarbonate solution and brine, dried over magnesium sulfate, and evaporated. The residue was analyzed by GLC to determine the conversion. Product **3** was isolated by MPLC (silica gel, hexane/ethyl acetate) and bulb-to-bulb distillation.

Acknowledgment. This work was partially supported by a Grant-in-Aid for scientific Research from the Ministry of Education, Science and Culture, Japan (No. 02855213). M.S. acknowledges support from the Eisai Award in Synthetic Organic Chemistry, Japan.

Solution- and Solid-State Structural Studies of (Halomethyl)zinc Reagents

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Abstract: (Halomethyl)zinc cyclopropanation reagents have been investigated by solution NMR and X-ray crystallographic methods. Treatment of glycol-ether complexes of diethylzinc with chloroiodomethane or diiodomethane quantitatively produced glycol-ether complexes of bis(chloromethyl)zinc and bis(iodomethyl)zinc, respectively. Similarly, treatment of acetone solutions of diethylzinc with either dihalomethane produced the corresponding bis(halomethyl)zinc species. The bis(chloromethyl)zinc complexes displayed characteristic NMR resonances at 2.4-2.7 ppm (^1H) and 29.5-29.8 ppm (^{13}C) for the methylene unit, while the bis(iodomethyl)zinc complexes displayed characteristic resonances at 1.35-1.40 ppm (^1H) and -16.4 to -19.6 ppm (^{13}C). The first X-ray crystallographic analysis of an (iodomethyl)zinc compound, bis(iodomethyl)zinc complex **9**, is also reported. Some key features of the structure include Zn-C bond lengths of 1.92-2.02 Å, C-I bond lengths of 2.13-2.21 Å, and Zn-C-I bond angles of 106.9-116.4°. In addition, bis(iodomethyl)zinc complexes were demonstrated to lose one methylene upon concentrating in vacuo, and the iodomethylzinc iodide complexes were established to exist predominantly as the bis(iodomethyl)zinc/zinc iodide pair in acetone solution.

Introduction

The Simmons-Smith[1] cyclopropanation of olefins is arguably the most important application of organozinc reagents in organic synthesis.[2] Several factors make this reaction synthetically useful, including (1) stereospecificity (strict retention of olefin geometry); (2) broad generality with regard to olefin structure; (3) modest tolerance of other functional groups, including carbonyls; and (4) the syn-directing effect of proximal oxygen functions. The strong directing effect of oxygen substituents was recognized early on[3] and has both preparative[4] and mechanistic[5] significance. This

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