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A New Methodology for Synthesis of a Chiral Phosphinocarboxylic Acid through Michael Cyclization−Aldol Tandem Reaction of Chiral α,*β*,*χ*,*ψ*-Unsaturated Bisphosphine Oxide and Application in Palladium-Catalyzed Asymmetric Allylic Alkylation

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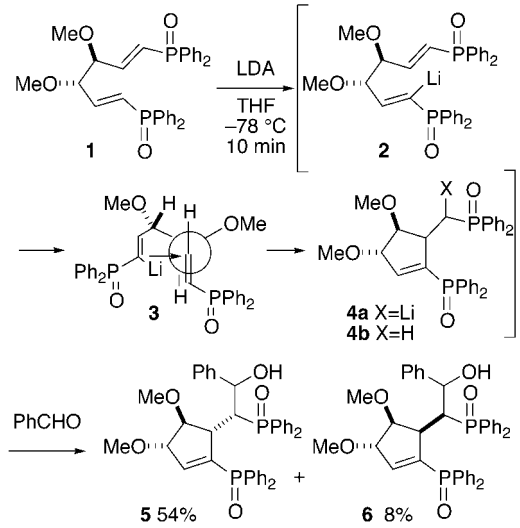
Received March 15, 2002

Abstract: Upon successive treatment with lithium diisopropylamide and then benzaldehyde, a chiral α,*β*,*ψ*,*ω*-unsaturated bisphosphine oxide underwent Michael cyclization−aldol tandem reaction to afford the corresponding endo-α,*β*-unsaturated cyclic bisphosphine oxides. Sequential stereoselective reduction and Horner−Wadsworth−Emmons olefination gave the corresponding monophosphine oxide. Oxidative conversion of an olefin moiety into a carboxyl group and subsequent deoxygenation of an oxide gave the corresponding chiral phosphinocarboxylic acid, which was successfully applied as a chiral and functionalized monophosphine ligand in a palladium-catalyzed asymmetric allylic alkylation.

Introduction

Allylic substitution reactions rank among the most intensively studied catalytic transformations. Since the reports by Tsuji[1] and Trost,[2] this area has seen fast developments in catalyst structure and ligand design for asymmetric version.[3] In our program aimed at development of an efficient and versatile catalytic asymmetric reaction,[4,5] we have been involved in a conjugate addition−intramolecular Michael tandem cyclization reaction of achiral α,*β*,*ψ*,*ω*-unsaturated bisphosphonates that were potential synthetic precursors of bisphosphine ligands.[6] More recently the methodology has been successfully extended to selective lithiation[7]-intramolecular Michael tandem cyclization of chiral C_2 symmetric α,*β*,*ψ*,*ω*-unsaturated bisphosphine oxide **1** and subsequent conversion to a chiral diphosphine, which was applied as a chiral ligand in a catalytic asymmetric hydrogenation of dehydroamino acid derivatives.[8] Because lithiated phosphine oxide **4a**, the intermediate of the tandem cyclization reaction, might be potentially applicable as a carbonucleophile, we designed a synthesis of a chiral monophosphine bearing both a phosphino- and an additional functional group such as a carboxyl.[9] We describe herein the successful synthesis of a chiral phosphinocarboxylic acid **12** and its application in a palladium-catalyzed asymmetric allylic alkylation of 1,3-diphenyl-2-propenyl acetate **13** with malonate.

SCHEME 1. Selective Cyclization-Aldol Tandem Reaction



Results and Discussion

Michael−Aldol Tandem Reaction. In our previous work C_2 symmetric chiral bisphosphine oxide **1**[10] has been treated with LDA in THF at −78 °C to give **2** and subsequent cyclization through **3** gave **4b** in 60% isolated yield, which was a protonation product of lithiated phosphine oxide **4a**.[8] In this study, **4a** and its diastereomer were treated with benzaldehyde to give a cyclized alcohol **5** and its diastereoisomer **6** in 54% and 8% isolated yields, respectively (Scheme 1). The stereochemistry of the newly created asymmetric center on a cyclopentene ring of **5** and **6** was assigned by NMR−NOESY analysis. The major product **5** corresponds to a benzaldehyde-aldol product derived from **4a**. It is noteworthy that the aldol reaction of **4a** and its diastereomer proceeded in a high degree of stereoselectivity to afford

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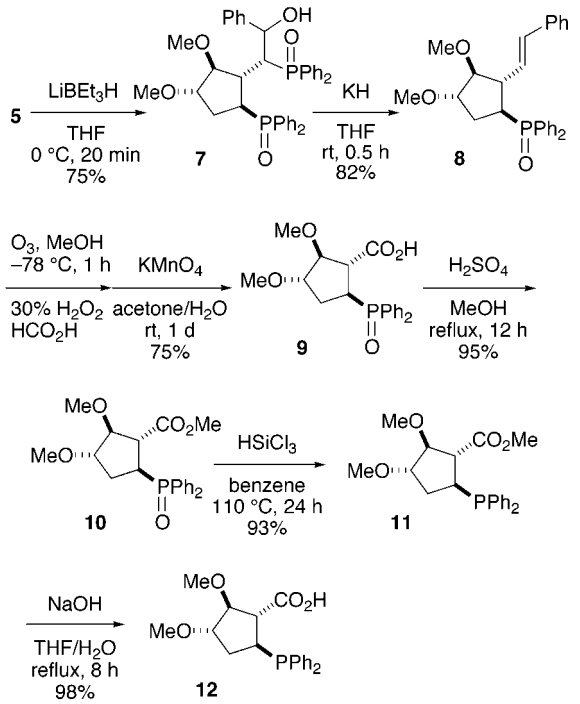
(9) Tandem cyclization has been one of recent topics. (a) Wang, L.-C.: Luis, A. L.; Agapiou, K.; Jang, H. Y.; Krische, M. J. *J. Am. Chem. Soc.* **2002**, *124*, 2404. (b) Frank, S. A.; Mergott, D. J.; Roush, W. R. *J. Am. Chem. Soc.* **2002**, *124*, 2404, and references therein.
(10) Prepared from dimethyl ether of diethyl L-tartrate through DIBALH reduction followed by Horner−Wadsworth−Emmons olefination with methylene(phosphonate)phosphine oxide in 48% overall yield.

10.1021/jo025725v CCC: $22.00
Published on Web 07/11/2002

SCHEME 2. Synthesis of Phosphinocarboxylic Acid 12



only two diastereomers **5** and **6**. The compounds **5** and **6** were obtained as a single stereoisomer, respectively. The relative configuration at the aldol reaction sites of **5** is related to that giving *E*-double bond by olefination through Horner−Wadsworth−Emmons syn-elimination.

Synthesis of Phosphine Ligands. Treatment of **5** with Super-Hydride in THF at 0 °C for 20 min underwent highly stereoselective 1,4-reduction to afford thermodynamically stable *trans*-**7** in 75% yield (Scheme 2). The corresponding cis-product was not detected. Subsequent Horner−Wadsworth−Emmons reaction with potassium hydride in THF gave a monophosphine oxide **8** in 82% yield. The stereochemistry of an olefin moiety was unequivocally assigned to be purely *E* by NMR analysis, indicating the fixed relative configuration of the aldol reaction sites. The ozonolysis of an olefin moiety of **8** and following potassium permanganate oxidation gave a carboxylic acid **9** in 75% yield. The phosphine oxide moiety of **9** failed to be directly converted to the requisite phosphinocarboxylic acid **12**. Therefore the carboxylic acid of **9** was once converted under acid-catalyzed esterification conditions to its methyl ester **10** in 95% yield and was then subjected to reduction with trichlorosilane[11] in benzene at 110 °C for 24 h readily giving the phosphine **11** in 93% yield. Then hydrolysis of **11** with sodium hydroxide in aqueous THF afforded the requisite chiral phosphinocarboxylic acid **12** in nearly quantitative yield.

Asymmetric Allylic Alkylation. Development of a new chiral phosphine ligand for a metal catalyst has attracted considerable interest in the past 30 years. Several kinds of chiral phosphines have made significant contributions to the development of palladium-catalyzed asymmetric allylic substitution,[12,13] which constitutes one

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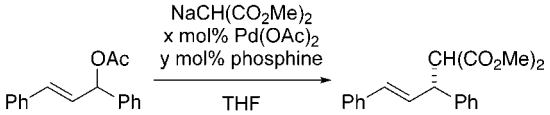
TABLE 1. Asymmetric Allylic Alkylation Using 11 and 12



entry	*x* (mol %)	*y* (mol %)	phosphine	temp	time (h)	yield (%)	ee (%)
1	1	2	**11**	rt	24	0	0
2	1	2	**12**	rt	20	46	91
3	1	2	**12**	reflux	2	97	60
4	3	6	**12**	rt	24	77	93

of the most useful and fundamental carbon−carbon bond forming reactions. Among them, chiral phosphinocarboxylic acids developed by Minami[14] and Helmchen[15] have been reported to be moderately effective in palladium-catalyzed allylic alkylation. In our study we examined our new phosphinocarboxylic acid **12** and its ester **11** in the palladium-catalyzed allylic alkylation of 1,3-diphenyl-2-propenyl acetate **13** with dimethyl malonate.

A palladium complex catalyst was generated in situ by mixing a chiral ligand **11** or **12** with palladium acetate. The reaction of **13** with sodium dimethyl malonate was carried out at room temperature in THF using 1 mol % of palladium acetate and 2 mol % of an ester ligand **11**. However, the alkylation product **14** was not obtained and **13** was recovered unchanged (Table 1, Entry 1). Fortunately, (*R*)-**14** was obtained in 46% yield and 91% ee by using phosphinocarboxylic acid **12** instead of **11** (Entry 2). Improvement of the chemical yield was possible by enforcing the reaction conditions under reflux for 2 h, giving **14** in 97% yield but in unsatisfactory enantioselectivity of 60% (Entry 3). Finally we found that the reaction was catalyzed by 3 mol % of palladium acetate and 6 mol % of **12** at room temperature for 24 h giving **14** in 93% ee and 77% yield (Entry 4). All these observations suggest that the phosphinocarboxylic acid **12** forms a O,P-chelate coordination to palladium rather than only one point coordination by a phosphorus atom.

In summary, the new methodology was proved to be effective for the synthesis of chiral monophosphines through Michael−aldol tandem reaction of chiral α,β,ψ,ω-unsaturated bisphosphine oxide as a key step. Successful

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application of the phosphinocarboxylic acid in a palladium-catalyzed asymmetric allylic alkylation is the clear evidence of the usefulness of the methodology.

Experimental Section[16]

2-(Diphenylphosphoryl)-2-[(1*R*,4*S*,5*S*)-2-(diphenylphosphoryl)-4,5-dimethoxy-2-cyclopenten-1-yl]-1-phenylethanol (5) and 2-(Diphenylphosphoryl)-2-[(1*S*,4*S*,5*S*)-2-(diphenylphosphoryl)-4,5-dimethoxy-2-cyclopenten-1-yl]-1-phenylethanol (6). A solution of bisphosphine oxide **1**[8] (2.71 g, 5 mmol) in THF (75 mL) was added dropwise over a period of 5 min to a solution of LDA (10 mmol) in THF (175 mL) at −78 °C. The mixture was stirred for 10 min at −78 °C. Benzaldehyde (1.55 mL, 15 mmol) was added, and then the mixture was stirred for 20 min at −78 °C. The mixture was added with MeOH (5 mL) and satd NH_4Cl (100 mL) and then was extracted with EtOAc. The extract was washed with satd NaCl and dried over Na_2SO_4. Concentration and recrystallization (EtOAc) gave **5** (1.75 g, 54%) as colorless needles of mp 227−228 °C and $[\alpha]^{25}_D$ −52.2 (*c* 1.00, $CHCl_3$) and **6** (259 mg, 8%) as colorless needles of mp 234−235 °C and $[\alpha]^{25}_D$ +33.5 (*c* 1.00, $CHCl_3$).

5: ^{1}H NMR: 3.13 (3H, s, OMe), 3.19 (1H, brs, CH), 3.45 (3H, s, OMe), 4.07 (1H, brs, CH), 4.35 (1H, m), 4.48 (1H, brs, OH), 4.70 (1H, brs, CH), 5.24 (1H, m), 5.60 (1H, d, *J* = 11.2 Hz, CH), 6.89−8.11 (25H, m, Ph). ^{13}C NMR: 48.5 (d, *J* = 68.3 Hz), 50.4 (d, *J* = 9.3 Hz), 56.8, 57.6, 74.1 (d, *J* = 4.1 Hz), 89.8 (dd, *J* = 5.2, 7.2 Hz), 90.2 (d, *J* = 15.5 Hz), 126.6, 126.7, 127.6 (d, *J* = 12.4 Hz), 127.7, 128.1 (d, *J* = 12.4 Hz), 128.3 (d, *J* = 12.4 Hz), 128.7 (d, *J* = 12.4 Hz), 129.2, 130.4, 130.6 (d, *J* = 9.3 Hz), 130.7, 131.1 (d, *J* = 9.3 Hz), 131.5 (d, *J* = 9.3 Hz), 131.97 (d, *J* = 2.1 Hz), 132.03 (d, *J* = 2.1 Hz), 132.9 (d, *J* = 9.3 Hz), 134.0 (d, *J* = 90.0 Hz), 135.6 (d, *J* = 99.3 Hz), 140.1 (d, *J* = 96.2 Hz), 142.0 (d, *J* = 6.2 Hz), 144.4 (d, *J* = 9.3 Hz). ^{31}P NMR: 25.7, 33.6. IR (Nujol): 3200, 1590, 1180 cm^{-1}. FABMS *m*/*z*: 649 (M + H$^+$). HRMS Calcd for $C_{39}H_{39}O_5P_2$: 649.2273. Found: 649.2283.

6: ^{1}H NMR: 3.14 and 3.36 (each 3H, s, OMe), 3.51 (1H, m), 3.61 (1H, brs, CH), 3.92 (1H, d, *J* = 7.0 Hz, CH), 4.46 (1H, d, *J* = 10.7 Hz, CH), 5.23 (1H, d, *J* = 8.5 Hz, CH), 5.41 (1H, d, *J* = 11.3 Hz, CH), 6.64−8.44 (25H, m, Ph). ^{13}C NMR: 46.0 (d, *J* = 67.2 Hz), 47.4 (d, *J* = 6.2 Hz), 56.3, 57.2, 71.5, 85.0 (dd, *J* = 3.1, 8.3 Hz), 88.9 (d, *J* = 15.5 Hz), 125.1, 126.6, 127.3 (d, *J* = 12.4 Hz), 127.6, 128.3 (d, *J* = 12.4 Hz), 128.6 (d, *J* = 12.4 Hz), 128.7 (d, *J* = 12.4 Hz), 129.5, 130.7, 130.9 (d, *J* = 9.3 Hz), 131.3, 131.5 (d, *J* = 9.3 Hz), 131.6 (d, *J* = 9.3 Hz), 131.79 (d, *J* = 90.0 Hz), 131.84 (d, *J* = 9.3 Hz), 134.5 (d, *J* = 99.3 Hz), 135.7 (d, *J* = 96.2 Hz), 140.7 (d, *J* = 96.2 Hz), 141.0 (d, *J* = 12.4 Hz), 144.5 (d, *J* = 11.4 Hz). ^{31}P NMR: 26.5, 34.8. IR (Nujol): 3300, 1600, 1170 cm^{-1}. FABMS *m*/*z*: 649 (M + H$^+$). HRMS Calcd for $C_{39}H_{39}O_5P_2$: 649.2273. Found: 649.2264.

2-(Diphenylphosphoryl)-2-[(1*S*,2*S*,3*S*,5*S*)-5-(diphenylphosphoryl)-2,3-dimethoxycyclopentyl]-1-phenylethanol (7). To a solution of **5** (5.26 g, 8.11 mmol) in THF (312 mL) was added Super-Hydride (1.0 M, 24.8 mL) in THF at 0 °C. The mixture was stirred at 0 °C for 20 min, quenched with MeOH (4 mL) and satd NH_4Cl (260 mL), and then extracted with EtOAc. The organic layer was washed with brine and then dried over Na_2SO_4. Concentration and chromatography (EtOAc/MeOH = 100/1) gave **7** (3.97 g, 75%) as colorless plates of mp 196−197 °C (DME) and $[\alpha]^{25}_D$ −25.5 (*c* 1.00, $CHCl_3$). ^{1}H NMR: 1.50−1.68 (2H, m), 2.45 (1H, m), 3.175 and 3.184 (each 3H, s, OMe), 3.22−3.33 (2H, m), 3.89 (1H, m), 3.95 (1H, brs, OH), 4.37 (1H, dd, *J* = 4.3, 7.9 Hz, CH), 5.19 (1H, m), 7.13−8.04 (25H, m, Ph). ^{13}C NMR: 30.7, 35.2 (d, *J* = 74.5 Hz), 43.9, 47.7 (d, *J* = 67.2 Hz), 56.4, 57.1, 74.3, 84.4 (d, *J* = 7.2 Hz), 86.3 (dd, *J* = 3.1, 9.3 Hz), 127.1(d, *J* = 4.1 Hz), 128.06 (d, *J* = 11.4 Hz), 128.08, 128.2 (d, *J* = 11.4 Hz), 128.3 (d, *J* = 11.4 Hz), 128.7 (d, *J* = 11.4 Hz), 130.9, 131.3 (d, *J* = 9.3 Hz), 131.5 (d, *J* = 9.3 Hz), 131.7 (d, *J* = 9.3 Hz), 131.8 (d, *J* = 9.3 Hz), 130.4 (d, *J* = 96.2 Hz), 132.7 (d, *J* = 96.2 Hz), 134.1 (d, *J* = 96.2 Hz), 135.3 (d, *J* = 96.2 Hz), 142.3 (d, *J* = 7.2 Hz). ^{31}P NMR: 34.4, 36.2. IR (Nujol): 3200, 1190 cm^{-1}. FABMS *m*/*z*: 651 (M+H$^+$). HRMS Calcd for $C_{39}H_{41}O_5P_2$: 651.2429. Found: 651.2432.

{(1*S*,2*S*,3*S*,4*S*)-3,4-Dimethoxy-2-[2-phenylethenyl]cyclopentyl}diphenylphosphine Oxide (8). A solution of **7** (567 mg, 0.87 mmol) in THF (4 mL) was added to a suspension of KH (100 mg, 0.87 mmol) in THF (4 mL) at −78 °C. The mixture was allowed to warm to room temperature over 0.5 h. The mixture was quenched with satd NH_4Cl (3 mL) and extracted with benzene. The organic layer was washed with brine and then dried over Na_2SO_4. Concentration and chromatography (EtOAc/MeOH = 100/1) gave **8** (307 mg, 82%) as a colorless solid of mp 178−179 °C and $[\alpha]^{25}_D$ +83.0 (*c* 1.00, $CHCl_3$). ^{1}H NMR: 1.84 (1H, m), 2.30 (1H, dddd, *J* = 6.4, 9.5, 11.9, 13.7 Hz, CH_2), 2.85 (1H, dq, *J* = 1.8, 9.5 Hz, CH), 3.08 (1H, ddd, *J* = 5.8, 8.9, 15.3 Hz, CH), 3.35 and 3.37 (each 3H, s, OMe), 3.58 (1H, dd, *J* = 4.0, 5.8 Hz, CH), 3.80 (1H, m), 5.79 (1H, dd, *J* = 8.9, 15.6 Hz, CH), 5.86 (1H, d, *J* = 15.6 Hz, CH), 6.96−7.84 (15H, m, Ph). ^{13}C NMR: 29.6, 39.6 (d, *J* = 75.5 Hz), 47.2, 56.8, 57.8, 84.4 (d, *J* = 8.3 Hz), 91.3 (d, *J* = 8.3 Hz), 126.0, 127.0, 128.0, 128.2 (d, *J* = 11.4 Hz), 128.6 (d, *J* = 11.4 Hz), 130.6, 130.7, 130.8, 131.2 (d, *J* = 9.3 Hz), 131.3 (d, *J* = 9.3 Hz), 131.5, 132.0 (d, *J* = 96.2 Hz), 133.0 (d, *J* = 96.2 Hz), 136.8. ^{31}P NMR: 31.5. IR (Nujol): 1600, 1180 cm^{-1}. FABMS *m*/*z*: 433 (M+H$^+$). HRMS Calcd for $C_{27}H_{30}O_3P$: 433.1933. Found: 433.1941. Anal. Calcd for $C_{27}H_{29}O_3P$: C, 74.96; H, 6.76. Found: C, 74.78; H, 6.75.

(1*R*,2*S*,3*S*,5*S*)-5-(Diphenylphosphoryl)-2,3-dimethoxycyclopentanecarboxylic Acid (9). Ozone was passed through a solution of **8** (130 mg, 0.30 mmol) in dry MeOH (1.5 mL) at −78 °C for 2 h. Argon gas was passed through the mixture. The mixture was concentrated at 0 °C and was added to a mixture of formic acid (90%, 1 mL) and hydrogen peroxide (30%, 0.5 mL). The mixture was stirred at 40 °C for 1 h and at 70 °C for 1 h and then concentrated. To the solution of the residue in acetone (8 mL) was added dropwise a solution of $KMnO_4$ (100 mg) in water (4 mL) at room temperature. After the mixture was stirred for 1 day, concentrated HCl was added to the mixture until a clear solution was obtained. The mixture was extracted with $CHCl_3$. The organic layer was washed with water and then dried over Na_2SO_4. Concentration and recrystallization (Et_2O) gave **9** (84 mg, 75%) as a white powder of mp 163−164 °C and $[\alpha]^{20}_D$ +54.6 (*c* 1.0, $CHCl_3$). ^{1}H NMR: 1.92−2.02 (2H, m), 3.12 (1H, ddd, *J* = 4.0, 9.5, 16.5 Hz, CH), 3.28 and 3.31 (each 3H, s, OMe), 3.46 (1H, q, *J* = 9.5 Hz, CH), 3.58 (1H, m), 4.21 (1H, m), 7.43−7.84 (10H, m, Ph). ^{13}C NMR: 30.8, 37.0 (d, *J* = 74.5 Hz), 50.3, 56.6, 56.7, 84.5 (d, *J* = 7.2 Hz), 88.4 (d, *J* = 7.2 Hz), 128.2 (d, *J* = 11.4 Hz), 128.4 (d, *J* = 11.4 Hz), 131.4 (d, *J* = 9.3 Hz), 131.6 (d, *J* = 9.3 Hz), 132.18 (d, *J* = 83.8 Hz), 132.24, 178.9. ^{31}P NMR: 39.7. IR (Nujol): 1720, 1150 cm^{-1}. FABMS *m*/*z*: 375 (M + H$^+$). HRMS Calcd for $C_{20}H_{24}O_5P$: 375.1361. Found: 375.1352.

Methyl (1*R*,2*S*,3*S*,5*S*)-5-(Diphenylphosphoryl)-2,3-dimethoxycyclopentanecarboxylate (10). A solution of **9** (225 mg, 0.6 mmol) and concentrated H_2SO_4 (0.03 mL) in methanol (7.2 mL) was heated under reflux for 12 h and was then treated with aq Na_2CO_3. The mixture was extracted with $CHCl_3$. The organic layer was washed with brine and then dried over Na_2SO_4. Concentration and chromatography (EtOAc/MeOH = 100/1) gave **10** (222 mg, 95%) as a white solid of mp 88−90 °C and $[\alpha]^{20}_D$ +13.3 (*c* 1.02, $CHCl_3$). ^{1}H NMR: 1.87 (1H, m), 2.29 (1H, m), 3.15 (1H, ddd, *J* = 5.8, 9.5, 15.3 Hz, CH), 3.25, 3.31, and 3.35 (each 3H, s, OMe), 3.45 (1H, dq, *J* = 1.5, 9.5 Hz, CH), 3.77 (1H, m), 3.91 (1H, dd, *J* = 4.3, 5.8 Hz, CH), 7.41−7.85 (10H, m, Ph). ^{13}C NMR: 29.4, 36.8 (d, *J* = 75.5 Hz), 47.8, 51.9, 56.9, 57.5, 84.4 (d, *J* = 7.2 Hz), 89.6 (d, *J* = 7.2 Hz), 128.3 (d, *J* = 11.4 Hz), 128.7 (d, *J* = 11.4 Hz), 130.8 (d, *J* = 8.3 Hz), 131.2 (d, *J* = 8.3 Hz), 131.7, 131.8 (d, *J* = 2.1 Hz), 132.3 (d, *J* = 71.4 Hz), 173.8. ^{31}P NMR: 31.6. IR (Nujol): 1735, 1190 cm^{-1}. FABMS *m*/*z*: 389

(16) ^{1}H, ^{13}C, and ^{31}P NMR spectra were taken at 500, 126, and 202 MHz in $CDC1_3$. Chemical shift values are expressed in ppm relative to internal tetramethylsilane and external 85% H_3PO_4 for ^{31}P. Abbreviations are as follows: s, singlet; d, doublet; t, triplet; m, multiplet. Purification was carried out using silica gel column chromatography unless otherwise noted. TLC analyses were performed on Merck silica gel 60 F254. Column chromatography was carried out with silica gel, Fuji Silysia BW820. All reactions were carried out under an argon atmosphere unless otherwise stated.

($M + H^+$). Anal. Calcd for $C_{21}H_{25}O_5P$: C, 64.94; H, 6.49. Found: C, 64.67; H, 6.42.

Methyl (1*R*,2*S*,3*S*,5*S*)-5-(Diphenylphosphino)-2,3-dimethoxycyclopentanecarboxylate (11). Trichlorosilane (2.0 mL, 20 mmol) was added to a stirred mixture of **10** (400 mg, 1.03 mmol) and triethylamine (2.8 mL, 20 mmol) in dry benzene (40 mL) under an argon atmosphere at 0 °C in a sealed tube. The mixture was stirred at 110 °C for 24 h. The mixture was added to 30% aq NaOH (90 mL) at 0 °C and stirred at 60 °C for 0.5 h. The mixture was extracted with benzene. The organic layer was washed with brine and then dried over Na_2SO_4. Concentration and chromatography (EtOAc) gave **11** (356 mg, 93%) as a white solid of mp 59−61 °C and $[\alpha]^{25}_D$ +26.9 (*c* 1.10, $CHCl_3$). ^{1}H NMR: 1.81−2.01 (2H, m), 2.68 (1H, ddd, *J* = 6.4, 9.2, 11.9 Hz, CH), 3.26 (1H, m), 3.28, 3.31 and 3.35 (each 3H, s, OMe), 3.69 (1H, m), 3.92 (1H, dd, *J* = 4.3, 6.4 Hz, CH), 7.30−7.53 (10H, m, Ph). ^{13}C NMR: 33.4 (d, *J* = 15.5 Hz), 34.4 (d, *J* = 10.3 Hz), 51.7, 52.7 (d, *J* = 20.7 Hz), 57.0, 57.8, 85.0 (d, *J* = 6.2 Hz), 90.0 (d, *J* = 6.2 Hz), 128.2 (d, *J* = 8.3 Hz), 128.4 (d, *J* = 8.3 Hz), 129.0 (d, *J* = 23.8 Hz), 133.2 (d, *J* = 20.7 Hz), 133.9 (d, *J* = 20.7 Hz), 136.2 (d, *J* = 13.4 Hz), 136.7 (d, *J* = 13.4 Hz), 174.2 (d, *J* = 3.1 Hz). ^{31}P NMR: −3.55. IR (Nujol): 1730 cm^{-1}. FABMS *m*/*z*: 373 ($M + H^+$). HRMS Calcd for $C_{21}H_{26}O_4P$: 373.1569. Found: 373.1571. Anal. Calcd for $C_{21}H_{25}O_4P \cdot {}^1/_4H_2O$: C, 66.92; H, 6.82. Found: C, 66.87; H, 6.77.

(1*R*,2*S*,3*S*,5*S*)-5-(Diphenylphosphino)-2,3-dimethoxycyclopentanecarboxylic acid (12). To a solution of **11** (54 mg, 0.15 mmol) in THF (0.75 mL) was added a solution of NaOH (29 mg, 0.73 mmol) in water (0.75 mL). The mixture was stirred at 50 °C for 12 h. After the mixture was neutralized with 2 N HCl, the mixture was extracted with CH_2Cl_2. The organic layer was washed with water and dried over Na_2SO_4. Concentration and chromatography (benzene/EtOAc = 1/4) gave **12** (51 mg, 98%) as a colorless oil of $[\alpha]^{25}_D$ +25.6 (*c* 0.75, CH_2Cl_2). ^{1}H NMR: 1.80−2.05 (2H, m), 2.69 (1H, ddd, *J* = 5.1, 8.2, 12.8 Hz, CH), 3.29 (1H, m), 3.31 and 3.38 (each 3H, s, OMe), 3.72 (1H, m), 3.94 (1H, dd, *J* = 3.4, 5.1 Hz, CH), 7.26−7.51 (10H, m, Ph). ^{13}C NMR: 32.9 (d, *J* = 12.4 Hz), 34.2 (d, *J* = 12.4 Hz), 53.0 (d, *J* = 18.6 Hz), 57.0, 57.3, 85.4 (d, *J* = 5.2 Hz), 89.5 (d, *J* = 5.2 Hz), 128.29 (d, *J* = 8.3 Hz), 128.35 (d, *J* = 8.3 Hz), 128.9 (d, *J* = 23.8 Hz), 133.4 (d, *J* = 19.7 Hz), 133.7 (d, *J* = 19.7 Hz), 136.7 (d, *J* = 13.4 Hz), 136.8 (d, *J* = 13.4 Hz), 178.8 (d, *J* = 3.1 Hz). ^{31}P NMR: −3.20. IR (neat): 1730 cm^{-1}. FABMS *m*/*z*: 359 ($M + H^+$). HRMS Calcd for $C_{20}H_{24}O_4P$: 359.1412. Found: 359.1400.

Palladium-Catalyzed Asymmetric Allylic Alkylation of 1,3-Diphenyl-2-propenyl Acetate 13 (Table 1. Entry 4). A mixture of **12** (7.8 mg, 0.022 mmol) and $Pd(OAc)_2$ (2.4 mg, 0.011 mmol) in THF (1.1 mL) was stirred at room temperature for 0.5 h. After addition of a solution of **13** (92 mg, 0.36 mmol)[17] in THF (0.7 mL), the mixture was stirred for 0.5 h at room temperature. A solution of sodium dimethyl malonate (0.54 mmol) in THF (1.8 mL) was added to the mixture. The mixture was stirred at room temperature for 24 h and quenched with 2 N HCl and then extracted with AcOEt. The organic layer was washed with water and brine, and then dried over Na_2SO_4. Concentration and chromatography (hexane/AcOEt = 9/1) gave (*R*)-**14** (91 mg, 77%) as a colorless oil of $[\alpha]^{20}_D$ +20.5 (*c* 0.8, $CHCl_3$). The enantiomeric excess was determined to be 93% by HPLC analysis (Daicel Chiralcel AD, hexane/2-propanol = 95/5, 254 nm, 1.0 mL/min: major peak 19.3 min, minor peak 27.1 min). The absolute configuration was determined to be (*R*) by the optical rotation.[18]

Acknowledgment. This research was supported by a Grant-in-Aid for Scientific Research on Priority Areas (A) "Exploitation of Multi-Element Cyclic Molecules" from the Ministry of Education, Culture, Sports, Science and Technology, Japan.

Supporting Information Available: Spectroscopic data (NMR) of the products. This material is available free of charge via the Internet at http://pubs.acs.org/.

JO025725V

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