Efficient Preparation of Optically Active (*S*)-(−)-3-Methyl-γ-butyrolactone by Catalytic Asymmetric Hydrogenation Using Chiral *N*-Substituted Pyrrolidinebisphosphine Rhodium Complexes[1)]

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(*S*)-(−)-2-Methyl succinamic acid, which is a good precursor of (*S*)-(−)-3-methyl-γ-butyrolactone, can be prepared by homogeneous asymmetric hydrogenation of 2-methylene succinamic acid catalyzed by (2*S*,4*S*)-*N*-substituted-4-(diphenylphosphino)-2-[(diphenylphosphino)-methyl]pyrrolidine–rhodium complexes. Various *N*-substituted pyrrolidine-bisphosphines were synthesized to find the optimum ligand for this purpose and to compare the effects of the *N*-substituents.

Keywords *N*-substituted pyrrolidinebisphosphines ligand; asymmetric hydrogenation; rhodium-bisphosphine complex; (*S*)-(−)-3-methyl-γ-butyrolactone; (*S*)-(−)-2-methylsuccinamic acid

(*S*)-(−)-3-Methyl-γ-butyrolactone (**1**) is an important chiral building block for the synthesis of vitamin E, vitamin K, vitamin D_2 and dilichol.[2−5)] Though many attempts[6−9)] at asymmetric synthesis of optically active **1** have been made, highly optically active **1** has not been obtained. In order to establish a practical preparation of optically active **1**, we designed a synthetic pathway containing catalytic asymmetric hydrogenation as the key step (Chart 1).

Our study of the catalytic asymmetric hydrogenation step began with syntheses of various *N*-substituted pyrrolidinebisphosphine ligands (*N*-substituted PPMs). (2*S*,4*S*)-*N*-(*tert*-Butoxycarbonyl)-4-(diphenylphosphino)-2-[(diphenylphosphino)methyl]pyrrolidine, named BPPM, has already been found to be effective as a ligand for rhodium-catalyzed asymmetric hydrogenation of ketopantolactone, dehydroamino acid, itaconic acid, *etc.*[10−14)] When we achieved asymmetric hydrogenation of itaconic acid, *N*-substituted PPMs were also synthesized except *N*-carbamoyl PPMs.[15)] Recently, we found that MCCPM, one of the *N*-carbamoyl CPMs, was an especially efficient ligand in asymmetric hydrogenation of aminoketones rather than BCPM, which is one of the *N*-alkoxycarbonyl CPMs.[16)] So we prepared various PPM analogues, including *N*-carbamoyl PPMs (Chart 2).

BPPM was treated with trifluoroacetic acid (TFA) to give PPM in 94% yield and this was converted into various *N*-substituted PPMs. The abbreviations of the products, yields from PPM, melting points, and $[\alpha]_D$ values are listed in Table I.

As shown in Chart 1, the hydrogenation substrate, 2-methylenesuccinamic acid (**3**), was obtained by hydrolysis of itaconic anhydride (**2**) with 28% ammonium hydroxide. The asymmetric hydrogenation of **3** was carried out in the presence of 1—0.1 mol% of a cationic rhodium complex ($[Rh(COD)\cdot Ligand]^+ClO_4^-$) and an equimolar amount of triethylamine at room temperature for 20 h in methanol ([subst.] = 0.33 M) under an initial hydrogen pressure of 1—30 atm. These results are summarized in Table II and show that *N*-carbamoyl PPMs gave moderately better optical yields. Moreover, even at lower hydrogen pressure, *N*-carbamoyl PPM–rhodium complexes were very effective, resulting in nearly 80%ee. The steric or electronic effects of the *N*-substituent are considered to play an important role in forming the chirality of the complex and so these results suggest that the *N*-carbamoyl PPM–rhodium complex forms a favorable chiral array of the phenyl rings on the phosphines. On the other hand, the hydrogenation did not proceed at all when the BCPM which has a dicyclohexylphosphino group was used.

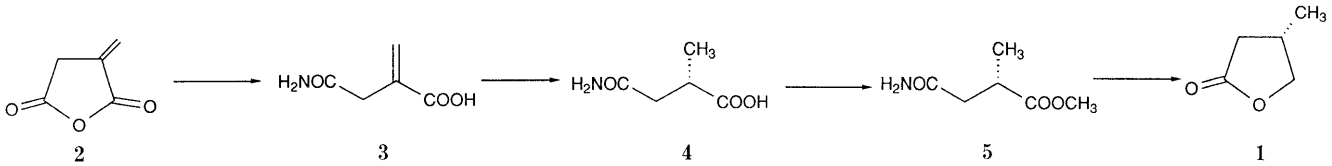
Recrystallization of the hydrogenation product (nearly 80%ee, entry 9 or 13) from methanol gave optically pure (*S*)-(−)-2-methylsuccinamic acid (**4**) in 62% yield from **3**. Then, **4** was esterified with dry hydrogen chloride in methanol to give (*S*)-(−)-2-methylsuccinamic acid methyl ester (**5**) in 90% yield. Reduction of **5** with $NaBH_4$–methanol in tetrahydrofuran (THF) followed by treatment with concentrated hydrochloric acid gave (*S*)-(−)-3-methyl-γ-butyrolactone (**1**) in 50% yield. The overall yield from **3** was 26.8%.

Higher enantioselectivity and catalytic activity may be required in the asymmetric hydrogenation step, but by using *N*-carbamoyl PPMs under atmospheric hydrogenation pressure, the optical yield of the hydrogenation product could be increased to 75—77%ee.

Thus optically active **4** could be obtained by a single recrystallization of the hydrogenation proudct, and we could complete the practical synthesis of (*S*)-(−)-3-methyl-γ-butyrolactone.

Experimental

All melting points were determined with a micro-melting point apparatus (Yanagimoto) and are uncorrected. Optical rotations were measured on a JASCO DIP-140 digital polarimeter. Infrared (IR) spectra were measured on a JASCO A-202 IR spectrophotometer. Proton nuclear magnetic resonance (^{1}H-NMR) spectra were recorded on a JEOL JNM-



2 3 4 5 1

Chart 1

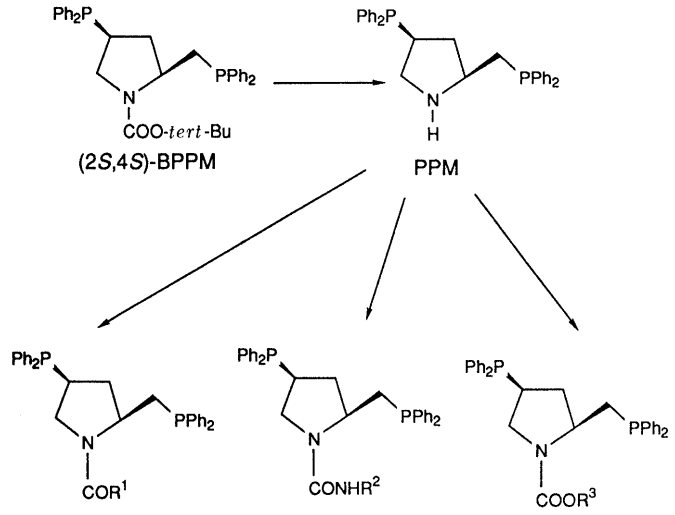


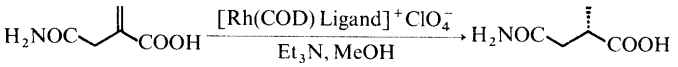
Chart 2. Synthesis of *N*-Substituted PPMs

TABLE I. *N*-Substituted PPMs

R in Chart 2		Abbreviation	Yield %	mp/°C[a]	$[\alpha]_D^{22}$/°[b]
R^1	H	FPPM	65.0	123	−36.4
	CH_3	APPM	70.0	—	−13.8
	Ph	BZPPM	91.2	162	−78.3
	$C(CH_3)_3$	PVPPM	75.0	151	−4.3
R^2	CH_3	MCPPM	94.9	—	−10.5
	Ph	PCPPM	76.2	182	−16.5
	$C(CH_3)_3$	BCPPM	73.1	122	−20.2
R^3	CH_3	MPPM	91.0	—	−38.2
	Ph	PPPM	98.6	—	−44.6

a) —, amorphous. *b*) $[\alpha]_D$, $c=0.5$ in benzene.

TABLE II. Asymmetric Hydrogenation of 2-Methylenesuccinamic Acid[a]



3 4

Entry	Ligand	[Subst.]/[Rh]	Convn. %[b]	Atm/h	ee%[c]
1	FPPM	100	100	30/20	64
2		100	13	5/20	43
3	APPM	100	100	30/20	61
4	BZPPM	100	100	30/20	63
5	PVPPM	100	100	30/20	48
6	MCPPM	1000	82	30/20	59
7		100	100	30/20	65
8		100	100	5/20	70
9		100	100	1/40	75
10	PCPPM	1000	80	30/20	62
11		100	100	30/20	66
12		100	100	5/20	71
13		100	100	1/40	77
14	BCPPM	100	100	30/20	64
15	MPPM	100	100	30/20	66
16	PPPM	100	100	30/20	59
17	BPPM	1000	22	30/20	53
18		100	100	30/20	60
19		100	5	5/20	—
20	BCPM	1000	Trace	30/20	—

a) All hydrogenations were carried out with [subst.] = 0.33 M in methanol at room temperature. *b*) Determined by ^{1}H-NMR analysis. *c*) %ee was calculated on the basis of maximum optical rotation of pure (*S*)-2-methylsuccinamic acid, $[\alpha]_D$ −17.7° ($c=2.0$, methanol), and all configurations are *S*-form.

FX90Q(90 MHz)FT NMR spectrometer using tetramethylsilane (TMS) as an internal standard and ^{31}P-NMR spectra were taken on a JEOL JNM-GX500 spectrometer (^{31}P, 202.35 MHz); the abbreviations of signal patterns are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. Thin layer chromatography (TLC) was performed on silica gel (Kiesel $60F_{254}$ on aluminum sheet. Merck). Column chromatography was carried out on silica gel (Kiesel gel 60,70—230 mesh, Merck).

(2*S*,4*S*)-4-(Diphenylphosphino)-2-[(diphenylphosphino)methyl]pyrrolidine; PPM Trifluoroacetic acid (50 ml) was added under nitrogen to 11.04 g (20.0 mmol) of BPPM. The mixture was stirred at 0 °C for 1 h and then evaporated under reduced pressure. The residue was dissolved in 100 ml of dichloromethane and then washed with 100 ml of water, 100 ml of 2 N sodium hydroxide and 100 ml of saturated aqueous NaCl. The organic layer was dried over $MgSO_4$ and evaporated under reduced pressure to give 8.51 g of PPM (94.0%), mp 79—81 °C, $[\alpha]_D^{22}$ −15.1° ($c=1.0$, benzene). IR ν_{max}^{KBr} cm^{-1}: 2900 (NH). ^{1}H-NMR δ ($CDCl_3$): 1.13—3.27 (9H, m, $NHCH_2CHCH_2CHCH_2$-), 7.32 (20H, s, Ar-H).

(2*S*,4*S*)-4-(Diphenylphosphino)-2-[(diphenylphosphino)methyl]-*N*-formylpyrrolidine; FPPM PPM (1.81 g, 4.0 mmol) was added to 0.44 ml (4.8 mmol) of ice-cooled acetic anhydride and 0.2 ml (4.8 mmol) of formic acid. The mixture was stirred under nitrogen at 0—10 °C for 3 h, then evaporated under reduced pressure. The residue was dissolved in 20 ml of ethyl acetate and neutralized with 2 N sodium hydroxide and then washed with 10 ml of saturated aqueous NaCl. The organic layer was evaporated under reduced pressure. The residue was purified on a column (40 g) of silica gel (benzene : ethyl acetate = 9 : 1) to give 1.15 g of FPPM(65.0%), mp 122—123 °C, $[\alpha]_D^{22}$ −36.4° ($c=0.5$, benzene). IR ν_{max}^{KBr} cm^{-1}: 1620 (C=O). ^{1}H-NMR δ ($CDCl_3$): 1.80—2.55 (4H, m, CCH_2C, CH_2P), 2.60—3.45 and 3.50—4.60 (4H, m, $CHCH_2NCH$), 7.20—7.85 (20H, m, Ar-H), 8.15 (1H, d, CHO). *Anal.* Calcd for $C_{30}H_{29}NOP_2$: C, 74.83; H, 6.07; N, 2.91. Found: C, 74.97; H, 6.22; N, 2.88.

The preparation procedure for *N*-substituted PPMs was as described that for APPM. The reagents were used as follows; 0.57 ml of benzyl chloride for BZPPM, 0.59 ml pivaloyl chloride for PVPPM, 0.28 ml of methyl isocyanate for MCPPM, 0.54 ml of *tert*-butyl isocyanate for BCPPM, 0.37 ml of methyl chloroformate for MPPM, 0.61 ml of phenyl chloroformate for PPPM.

(2*S*,4*S*)-*N*-Acetyl-4-(diphenylphosphino)-2-[(diphenylphosphino)-methyl]pyrrolidine; APPM Acetyl chloride (0.35 ml, 4.8 mmol) was added under nitrogen to a mixture of 1.81 g (4.0 mmol) of PPM, 40 ml of dichloromethane and 0.65 ml (4.8 mmol) of triethylamine. The reaction was carried out at 0—5 °C for 2 h, then the reaction mixture was washed with water and dried over $MgSO_4$. The organic layer was evaporated under reduced pressure. The residue was purified on a column (20 g) of silica gel (benzene: ethyl acetate = 2 : 1).

Yield 70.1%, amorphous, $[\alpha]_D^{22}$ −13.8° ($c=0.5$, benzene). IR ν_{max}^{KBr} cm^{-1}: 1650 (C=O). ^{1}H-NMR δ ($CDCl_3$): 1.85 (3H, s, CH_3), 1.80—2.55 (4H, m, CCH_2C, CH_2P), 2.60—3.40 and 3.55—4.40 (4H, m, $CHCH_2$-NCH), 7.15—7.80 (20H, m, Ar-H). *Anal.* Calcd for $C_{31}H_{31}NOP_2$: C, 75.14: H, 6.31; N, 2.83. Found: C, 75.05; H, 6.16; N, 2.67.

(2*S*,4*S*)-*N*-Benzoyl-4-(diphenylphosphino)-2-[(diphenylphosphino)-methyl]pyrrolidine; BZPPM Yield 91.2%, mp 162 °C, $[\alpha]_D^{22}$ −78.3° ($c=0.5$, benzene). IR ν_{max}^{KBr} cm^{-1}: 1650 (C=O). ^{1}H-NMR δ ($CDCl_3$): 1.80—2.55 (4H, m, CCH_2C, CH_2P), 2.60—3.45 and 3.50—4.60 (4H, m, $CHCH_2NCH$), 7.20—7.85 (25H, m, Ar-H). *Anal.* Calcd for $C_{36}H_{33}NOP_2$: C, 77.54; H, 5.97; N, 2.51. Found: C, 77.62; H, 6.02; N, 2.59.

(2*S*,4*S*)-4-(Diphenylphosphino)-2-[(diphenylphosphino)methyl]-*N*-pivaloylpyrrolidine; PVPPM Yield 75.0%, mp 148—151 °C, $[\alpha]_D^{22}$ −4.3° ($c=0.5$, benzene). IR ν_{max}^{KBr} cm^{-1}: 1650 (C=O). ^{1}H-NMR δ ($CDCl_3$): 1.17 (9H, s, $C(CH_3)_3$), 1.80—2.50 (4H, m, CCH_2C, CH_2P), 2.60—3.40 and 3.55—4.40 (4H, m, $CHCH_2NCH$), 7.20—7.80 (20H, m, Ar-H). *Anal.* Calcd for $C_{34}H_{37}NOP_2$: C, 75.96; H, 6.94; N, 2.61. Found: C, 76.02; H, 7.02; N, 2.57.

(2*S*,4*S*)-4-(Diphenylphosphino)-2-[(diphenylphosphino)methyl]-*N*-methylcarbamoylpyrrolidine; MCPPM Yield 94.9%, amorphous, $[\alpha]_D^{22}$ −10.5° ($c=0.5$, benzene). IR ν_{max}^{KBr} cm^{-1}: 3320 (NH), 1680 (C=O). ^{1}H-NMR δ ($CDCl_3$): 1.70—2.40 (4H, m, CCH_2C, CH_2P), 2.50—3.47 and 3.50—3.89 (4H, m, $CHCH_2NCH$), 2.74 (3H, d, CH_3), 2.78 (1H, s, NH), 7.20— 7.82 (20H, m, Ar-H). *Anal.* Calcd for $C_{31}H_{32}N_2OP_2$: C, 72.93; H, 6.32; N, 5.49. Found: C, 73.03; H, 6.35; N, 5.28.

(2*S*,4*S*)-4-(Diphenylphosphino)-2-[(diphenylphosphino)methyl]-*N*-phenylcarbamoylpyrrolidine; PCPPM Yield 76.2%, mp 181—182 °C, $[\alpha]_D^{22}$ −16.5° ($c=0.5$, benzene). IR ν_{max}^{KBr} cm^{-1}: 3250 (NH), 1700 (C=O). ^{1}H-NMR δ ($CDCl_3$): 1.70—2.40 (4H, m, CCH_2C, CH_2P), 2.50—3.47 and

3.50—3.89 (4H, m, $CHCH_2NCH$), 5.80 (1H, s, NH), 7.20—7.82 (20H, m, Ar-H). *Anal.* Calcd for $C_{36}H_{34}N_2OP_2$: C, 75.51; H, 5.98; N, 4.89. Found: C, 75.25; H, 5.80; N, 4.72.

(2*S*,4*S*)-*N*-*tert*-Butylcarbamoyl-4-(diphenylphosphino)-2-[(diphenylphosphino)methyl]pyrrolidine; BCPPM Yield 73.1%, mp 120—122 °C, $[\alpha]_D^{22}$ −20.2° (c=0.5, benzene). IR ν_{max}^{KBr} cm^{-1}: 3450 (NH), 1700 (C=O). ^{1}H-NMR δ ($CDCl_3$): 1.22 (9H, s, $C(CH_3)_3$), 1.70—2.40 (4H, CCH_2C, CH_2P), 2.60—3.40 and 3.55—3.89 (4H, m, $CHCH_2NCH$), 3.40 (1H, s, NH), 7.20—7.70 (20H, m, Ar-H). *Anal.* Calcd for $C_{34}H_{38}N_2OP_2$: C, 73.90; H, 6.93; N, 5.07. Found: C, 74.04; H, 6.93; N, 5.04.

(2*S*,4*S*)-4-(Diphenylphosphino)-2-[(diphenylphosphino)methyl]-*N*-methoxycarbonylpyrrolidine; MPPM Yield 91.0%, amorphous, $[\alpha]_D^{22}$ −38.2° (c=0.5, benzene). IR ν_{max}^{KBr} cm^{-1}: 1700 (C=O). ^{1}H-NMR δ ($CDCl_3$): 1.80—2.50 (4H, m, CCH_2C, CH_2P), 2.60—3.40 and 3.55—4.40 (4H, m, $CHCH_2NCH$), 3.62 (3H, s, CH_3), 7.20—7.70 (20H, m, Ar-H). *Anal.* Calcd for $C_{31}H_{31}NO_2P_2$: C, 72.79; H, 6.11; N, 2.74. Found: C, 72.17; H, 6.17; N, 2.66.

(2*S*,4*S*)-4-(Diphenylphosphino)-2-[(diphenylphosphino)methyl]-*N*-phenoxycarbonylpyrrolidine; PPPM Yield 98.6%, amorphous, $[\alpha]_D^{22}$ −44.6° (c=0.5, benzene). IR ν_{max}^{KBr} cm^{-1}: 1710 (C=O). ^{1}H-NMR δ ($CDCl_3$): 1.80—2.50 (4H, m, CCH_2C, CH_2P), 2.60—3.40 and 3.55—4.40 (4H, m, $CHCH_2NCH$), 7.10—7.80 (25H, m, Ar-H). *Anal.* Calcd for $C_{36}H_{33}NO_2P_2$: C, 75.38; H, 5.80; N, 2.44. Found: C, 75.14; H, 5.94; N, 2.40.

Cationic rhodium complexes of these ligands were prepared in the same manner, as follows.

MCPPM(cyclo-octa-1,5-diene)rhodium Perchlorate: [Rh(COD)-MCPPM]$^+$·ClO_4^- Under a nitrogen atmosphere, acetylacetonato(cyclo-octa-1,5-diene)rhodium (500 mg, 1.6 mmol) was dissolved in THF (6 ml), and 70% perchloric acid (d 1.66, 230 mg) in THF (2 ml) was added. The mixture was stirred for 5 min, then MCPPM (816 mg, 1.6 mmol) was added at room temperature and stirring was continued for 5 min. The color of the solution turned deep red, and degassed dry ether (30 ml) was added all at once to give orange-red crystals of MCPPM–rhodium cationic complex in quantitative yield. $[\alpha]_D^{20}$ +43.8° (c=0.5, MeOH). ^{31}P-NMR δ: 16.4 ppm (dd, J_{Rh-P1}=140.2 Hz, J_{P1-P2}=38.1 Hz), 43.7 ppm (dd, J_{Rh-P2}=145.0 Hz, J_{P1-P2}=38.1 Hz).

BCPPM(cyclo-octa-1,5-diene)rhodium Perchlorate; [Rh(COD)-BCPPM]$^+$·ClO_4^- $[\alpha]_D^{22}$ +37.3° (c=0.5, MeOH). ^{31}P-NMR δ: 14.9 ppm (dd, J_{Rh-P1}=139.2 Hz, J_{P1-P2}=37.2 Hz), 43.5 ppm (dd, J_{Rh-P2}=145.0 Hz, J_{P1-P2}=37.2 Hz).

PCPPM(cyclo-octa-1,5-diene)rhodium Perchlorate; [Rh(COD)-PCPPM]$^+$·ClO_4^- $[\alpha]_D^{20}$ +17.7° (c=0.5, MeOH). ^{31}P-NMR δ:16.4 ppm (dd, J_{Rh-P1}=140.2 Hz, J_{P1-P2}=37.2 Hz), 43.9 ppm (dm, J_{Rh-P2}=145.0 Hz).

FPPM(cyclo-octa-1,5-diene)rhodium Perchlorate; [Rh(COD)FPPM]$^+$·ClO_4^- $[\alpha]_D^{20}$ +48.0° (c=0.5, MeOH). ^{31}P-NMR δ: A; 15.4 ppm (dd, J_{Rh-P1}=141.2 Hz, J_{P1-P2}=36.2 Hz), 45.4 ppm (dd, J_{Rh-P2}=145.0 Hz, J_{P1-P2}=36.2 Hz). B; 16.2 ppm (dd, J_{Rh-P1}=141.2 Hz, J_{P1-P2}=37.2 Hz), 45.2 ppm (dd, J_{Rh-P2}=145.0 Hz, J_{P1-P2}=37.2 Hz).

APPM(cyclo-octa-1,5-diene)rhodium Perchlorate; [Rh(COD)APPM]$^+$·ClO_4^- $[\alpha]_D^{20}$ +26.5° (c=0.5, MeOH). ^{31}P-NMR δ: A; 16.1 ppm (dd, J_{Rh-P1}=141.1 Hz, J_{P1-P2}=38.1 Hz), 45.4 ppm (dd, J_{Rh-P2}= 145.0 Hz, J_{P1-P2}=37.2 Hz). B; 16.7 ppm (dd, J_{Rh-P1}=142.0 Hz, J_{P1-P2}= 38.1 Hz), 46.2 ppm (dd, J_{Rh-P2}=145.0 Hz, J_{P1-P2}=38.1 Hz.

BZPPM(cyclo-octa-1,5-diene)rhodium Perchlorate; [Rh(COD)-BZPPM]$^+$·ClO_4^- $[\alpha]_D^{20}$ +6.5° (c=0.5, MeOH). ^{31}P-NMR δ: 14.1 ppm (dd, J_{Rh-P1}=140.2 Hz, J_{P1-P2}=36.2 Hz), 45.2 ppm (dd, J_{Rh-P2}=145.9 Hz, J_{P1-P2}=36.2 Hz).

PVPPM(cyclo-octa-1,5-diene)rhodium Perchlorate; [Rh(COD)-PVPPM]$^+$·ClO_4^- $[\alpha]_D^{20}$ +26.0° (c=0.5, MeOH). ^{31}P-NMR δ: 13.7 ppm (dm, J_{Rh-P1}=142.1 Hz), 44.9 ppm (dm, J_{Rh-P2}=145.0 Hz).

MPPM(cyclo-octa-1,5-diene)rhodium Perchlorate; [Rh(COD)-MPPM]$^+$·ClO_4^- $[\alpha]_D^{20}$ +27.6° (c=0.5, MeOH). ^{31}P-NMR δ: A; 16.0 ppm (dd, J_{Rh-P1}=140.7 Hz, J_{P1-P2}=37.2 Hz), 43.7 ppm (dd, J_{Rh-P2}=144.0 Hz, J_{P1-P2}=37.2 Hz). B; 16.2 ppm (dd, J_{Rh-P1}=141.1 Hz, J_{P1-P2}=38.2 Hz), 46.2 ppm (dd, J_{Rh-P2}=145.0 Hz, J_{P1-P2}=38.2 Hz).

PPPM(cyclo-octa-1,5-dienerhodium Perchlorate; [Rh(COD) PPPM]$^+$·ClO_4^- $[\alpha]_D^{20}$ +7.7° (c=0.5, MeOH). ^{31}P-NMR δ: A; 15.2 ppm (dd, J_{Rh-P1}=140.2 Hz, J_{P1-P2}=37.2 Hz), 43.6 ppm (dd, J_{Rh-P2}=145.0 Hz, J_{P1-P2}=37.2 Hz). B; 15.3 ppm (dd, J_{Rh-P1}=140.2 Hz, J_{P1-P2}=37.2 Hz), 44.6 ppm (dd, J_{Rh-P2}=145.0 Hz, J_{P1-P2}=37.2 Hz).

2-Methylenesuccinamic Acid (3) Itaconic anhydride (**2**, 112.1 g, 1.0 mol) was added to an ice-cooled 28% NH_4OH solution (163 g, 1.3 mol). The reaction was carried out at room temperature for 18 h. The reaction mixture was treated with 3 N HCl to give crystals. Recrystallization from ethanol (200 ml) gave 62.0 g of colorless crystals. Yield 48.0%, mp 150—152 °C. IR ν_{max}^{KBr} cm^{-1}: 3360 (OH), 3200 (NH), 1710 (COOH), 1670 (CH_2=C), 1640 ($CONH_2$). ^{1}H-NMR δ (dimethylsulfoxide (DMSO)-d_6): 3.08 (2H, s, CH_2CON), 5.65 and 6.09 (each 1H, each d, =CH_2), 6.83 and 7.31 (each 1H, each br s, NH_2).

(*S*)-(−)-2-Methylsuccinamic Acid (4) A typical asymmetric hydrogenation was carried out as follows. 2-Methylenesuccinamic acid (**3**, 2.58 g, 20 mmol), methanol (60 ml), triethylamine (2.78 ml, 20 mmol) and[Rh(COD)·MCPPM]$^+$$ClO_4^-$ (102.1 mg, 0.2 mmol) were placed in a autoclave (300 ml). The air was immediately evacuated and replaced with nitrogen to 5 atm. This procedure was repeated 3—4 times and then the autoclave was pressurized with hydrogen to 5 atm. After 20 h, the completion of the hydrogenation was analyzed by ^{1}H-NMR. The reaction solution was treated with Amberlite 120B and then evaporated to give a brown oil. This was taken up in benzene and the solution was evaporated. Further extraction with benzene and evaporation give white crystals of **4**. Recrystallization once from methanol gave optically pure crystals (1.62 g, 12.4 mmol). Yield 62%, mp 72 °C, $[\alpha]_D^{22}$ −17.7° (c=2.0, MeOH). IR ν_{max}^{KBr} cm^{-1}: 3440 (OH), 3220 (NH), 1705 (COOH), 1645 ($CONH_2$). ^{1}H-NMR δ (DMSO): 1.06 (3H, d, CH_3), 1.95—2.40 (2H, m, CH_2CO), 2.42—2.81 (1H, m, CH), 6.79 and 7.31 (each 1H, each br s, NH_2).

(*S*)-(−)-2-Methylsuccinamic Acid Methyl Ester (5) Compound **4** (2.48 g, 18.9 mmol) was dissolved in 45 ml of ice-cooled methanol and then hydrogen chloride gas was bubbled into the solution. The bubbling was continued with stirring at room temperature for 1 h, then the reaction mixture was evaporated to give a colorless oil. The oil was dissolved in 50 ml of chloroform and washed with saturated aqueous NaCl. The organic layer was dried over $MgSO_4$ and evaporated to obtain **5** as a colorless oil (2.30 g, 15.9 mmol). Yield 84%, $[\alpha]_D^{22}$ −4.47° (c=1.0, MeOH). IR ν_{max}^{NaCl} cm^{-1}: 3440 (OH), 3210 (NH), 1735 ($COOCH_3$), 1670 ($CONH_2$). ^{1}H-NMR δ ($CDCl_3$): 1.23 (3H, d, CH_3C), 2.15—2.76 (2H, m, CH_2), 2.65—3.10 (1H, m, $CHCH_3$), 3.70 (3H, s, $COOCH_3$), 5.99 (2H, br s, NH_2).

(*S*)-(−)-3-Methyl-γ-buthyrolactone (1) Compound **5** (1.45 g, 10 mmol), THF (40 ml) and sodium borohydride ($NaBH_4$, 0.76 g, 20 mmol) were mixed and stirred. Methanol (8 ml) was added dropwise to the solution at room temperature and the mixture was stirred for 2 h. Then 10 ml of water was added to quench the reaction. After being stirred for 1 h, the reaction mixture was evaporated to remove the organic solvent and then refluxed with 35%HCl (10 ml) for 1 h. The residue was extracted with benzene, dried over $MgSO_4$ and then evaporated. Distillation of the residue gave **1** as a colorless oil (0.50 g, 5.0 mmol). Yield 50%, bp 95—97 °C (15 mmHg), $[\alpha]_D^{22}$ −25.7° (c=1.0, MeOH), IR ν_{max}^{NaCl} cm^{-1}: 1770 (C=O). ^{1}H-NMR δ ($CDCl_3$): 1.16 (3H, d, CH_3), 2.11 (1H, d, H_E), 2.43—2.85 (2H, m, H_C, H_D), 3.87 (1H, d, H_B), 4.42 (1H, d, H_A).

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