butane [**10a'**:0.367 g (22%); ^{1}H NMR δ 7.23 (s, 5 H, aromatic), 2.85 (s, 2 H, CH_2), 2.07 (s, 1 H, OH), 1.85 (m, 6 H, cyclobutyl)] and 1-[2-(1-hydroxycyclobutyl)benzyl]-1-hydroxycyclobutane (**11a'**): 0.59 g (64%); ^{1}H NMR δ 7.18 (s, 4 H, aromatic), 4.65 (s, 2 H, OH), 3.00 (s, 2 H, CH_2), 2.2 (m, 12 H, 2 cyclobutyls); mp 117 °C. Anal. Calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.67. Found: C, 76.91; H, 8.70. With **1r**, hydrolysis of the reaction mixture gave 0.64 g of material that was shown to be a complex mixture by gas chromatography and TLC. NMR, IR, and mass spectra showed the absence of any normal alcohol **10** or diol **11**.

2,4-Dimethylbenzyl Chloride and 2,5-Dimethylbenzyl Chloride. To a solution of 2,4-dimethyl- or 2,5-dimethylbenzyl alcohol (5 g, 0.037 mol) in 10 mL of $CHCl_3$ was added slowly a solution of 3.17 mL of $SOCl_2$ in 5 mL of $CHCl_3$. The mixture was refluxed for 3 h and cooled. Excess $SOCl_2$ and the solvent were removed under vacuum at room temperature over 2 h. Distillation under vacuum gave 2.4-dimethylbenzyl chloride [4.86 g (85%); bp 108 °C (17 mm)] or 2,5-dimethylbenzyl chloride: 4.5 g (79%); bp 98 °C (13 mm). IR spectra showed no OH peak at 3500 cm^{-1}.

Reaction of (2,4-Dimethylbenzyl)magnesium Chloride (7b') or (2,5-Dimethylbenzyl)magnesium Chloride (7c') with Cyclobutanone (1q). To a solution of the Grignard reagent from 2,4-dimethyl- or 2,5-dimethylbenzyl chloride (0.007 mol) was added **1q** (0.014 mol) in 5 mL of diethyl ether at 0 °C over 5 min. The mixture was stirred 1 h at 0 °C, hydrolyzed, and worked up. From **7b'** was obtained 2.1 g of crude material. Column chromatography with acetone-$CHCl_3$ (6:94 v/v) gave 1-(2,4-dimethylbenzyl)-1-hydroxycyclobutane [**10b'**: 0.081 g (6%); ^{1}H NMR δ 7.05 (m, 3 H, aromatic), 2.88 (s, 2 H, CH_2), 2.3 (d, 6H, $2CH_3$), 2.05 (m, 6 H, cyclobutyl), 1.83 (s, 1 H, OH)] and 1-[2-(1-hydroxycyclobutyl)-4,6-dimethylbenzyl]-1-hydroxycyclobutane (**11b'**): 0.465 g (26%); ^{1}H NMR δ 6.92 (s, 2 H, aromatic), 4.72 (s, 2 H, OH), 3.07 (s, 2 H, CH_2), 2.45 and 2 (m, 12 H, cyclobutyl), 2.32 (s, 3 H, CH_3), 2.25 (s, 3 H, CH_3). Anal. Calcd for $C_{17}H_{24}O_2$: C, 78.42; H, 9.29. Found: C, 77.94; H, 9.23.

From **7c'**, 1.45 g of crude material was obtained. Column chromatography with acetone-$CHCl_3$ (4:96 v/v) gave 1-(2,5-dimethylbenzyl)-1-hydroxycyclobutane (**10c'**): 0.8 g (44%); ^{1}H NMR δ 7 (m, 3 H, aromatic), 2.87 (s, 2 H, CH_2), 2.32 (s, 3 H, CH_3), 2.28 (s, 3H, CH_3), 2 (m, 6 H, cyclobutyl), 1.9 (s, 1 H, OH). GLC showed only one peak.

Reaction of (2,5-Dimethylbenzyl)magnesium Chloride (7c') with Acetaldehyde (12). To a solution of Grignard reagent (0.007 mol) prepared as above was added acetaldehyde (0.014 mol) in 5 mL of diethyl ether at 0 °C over 5 min. The mixture was stirred 1 h at 0 °C, hydrolyzed, and worked up to give 1.06 g of crude product. Column chromatography with acetone-$CHCl_3$ (4:96 v/v) gave 1-(2,5-dimethylphenyl)-2-propanol [**10**: 0.05 g (4%); ^{1}H NMR δ 7.07 (s, 3 H, aromatic), 3.95 (m, 1 H, CH), 2.67 (d, 2 H, CH_2), 2 (s, 1 H, OH), 2.4 (s, 6 H, $2CH_3$), 1.2 (d, 3 H, CCH_3)] and 1-[2-(1-hydroxyethyl)-3,6-dimethylphenyl]-2-propanol (**11**): 0.596 g (41%); ^{1}H NMR δ 7.15 (m, 2 H, aromatic), 5.1 (m, 1 H, $C_6H_5CHCH_3$), 3.95 (m, 1 H, $CCHCH_3$), 3.35 (s, 2 H, OH), 2.77 (m, 2 H, CH_2), 2.27 (s, 6 H, $2C_6H_5CH_3$), 1.45 (q, 3 H, CCH_3), 1.25 (q, 3 H, CCH_3); IR 3150 cm^{-1} (OH). Anal. Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 74.44; H, 9.77.

Registry No. **1a**, 67-64-1; **1b**, 78-93-3; **1c**, 96-22-0; **1d**, 563-80-4; **1e**, 75-97-8; **1f**, 565-80-0; **1g**, 815-24-7; **1h**, 5009-27-8; **1i**, 98-86-2; **1j**, 93-55-0; **1k**, 495-40-9; **1l**, 119-61-9; **1m**, 451-40-1; **1n**, 103-79-7; **1o**, 102-04-5; **1o** trimethylsilyl enol ether, 79990-96-8; **1p**, 108-94-1; **1q**, 1191-95-3; **1r**, 421-50-1; **3b**, 79990-97-9; **3c**, 79990-98-0; **3d**, 79990-99-1; **3e**, 79991-00-7; **3f**, 79991-01-8; **3g**, 79991-02-9; **3h**, 79991-03-0; **3i**, 79991-04-1; **3j**, 79991-05-2; **3k**, 79991-06-3; **3l**, 79991-07-4; **3m**, 79991-08-5; **3n**, 79991-09-6; **3o**, 79991-10-9; **3o** trimethylsilyl ether, 79991-11-0; **3p**, 80010-04-4; **4a**, 76767-85-6; **4b**, 79991-12-1; **4c**, 79991-13-2; **4d**, 79991-14-3; **4n**, 79991-15-4; **4p**, 79991-16-5; **4q**, 79991-17-6; **4r**, 79991-18-7; **5**, 90-12-0; **10**, 27645-00-7; **10a'**, 73013-83-9; **10b'**, 79991-19-8; **10c'**, 79991-20-1; **11**, 79991-21-2; **11a'**, 79991-22-3; **11b'**, 79991-23-4; **12**, 75-07-0; benzyl chloride, 100-44-7; 2,4-dimethylbenzyl chloride, 824-55-5; 2,5-dimethylbenzyl chloride, 824-45-3; [(1-naphthyl)methyl]chloride, 86-52-2.

Supplementary Material Available: Tables III and IV listing eluants and ^{1}H NMR spectral data for alcohols **3** and **4** (2 pages). Ordering information is given on any current masthead page.

Chiral 1,2-Diphosphine Ligands. Synthesis and Application to Rhodium-Catalyzed Asymmetric Hydrogenations[1]

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New chiral 1,2-diphosphine ligands, (*R*)-1,2-bis(diphenylphosphino)-3-(benzyloxy)propane and (*R*)-1,2-bis(diphenylphosphino)-3-*tert*-butoxypropane, have been prepared from D-mannitol. The rhodium(I) cationic complexes of these ligands are efficient asymmetric homogeneous hydrogenation catalysts for dehydro amino acids, giving (*S*)-amino acids in high optical yield (80–90%).

Since the discovery of tris(triphenylphosphine)rhodium chloride as a homogeneous hydrogenation catalyst for various olefins,[2] a large number of chiral phosphine ligands have been synthesized and used for rhodium-catalyzed asymmetric hydrogenations of various prochiral olefinic substrates.[3] It has generally been observed that the rhodium complexes of chiral chelating phosphine ligands give high enantiomeric excesses in the hydrogenation of prochiral olefinic substrates as compared to monodentate phosphine ligands. Of the bidentate phosphine ligands, 1,2-diphosphines which form five-membered conformationally rigid complexes are able to exert high chiral preferance in asymmetric hydrogenations. A number of chiral 1,2-diphosphines such as DIPAMP,[4] Chiraphos,[5] Prophos,[6] Phellanphos,[7] Phenphos,[8] Cycphos,[9] etc. have

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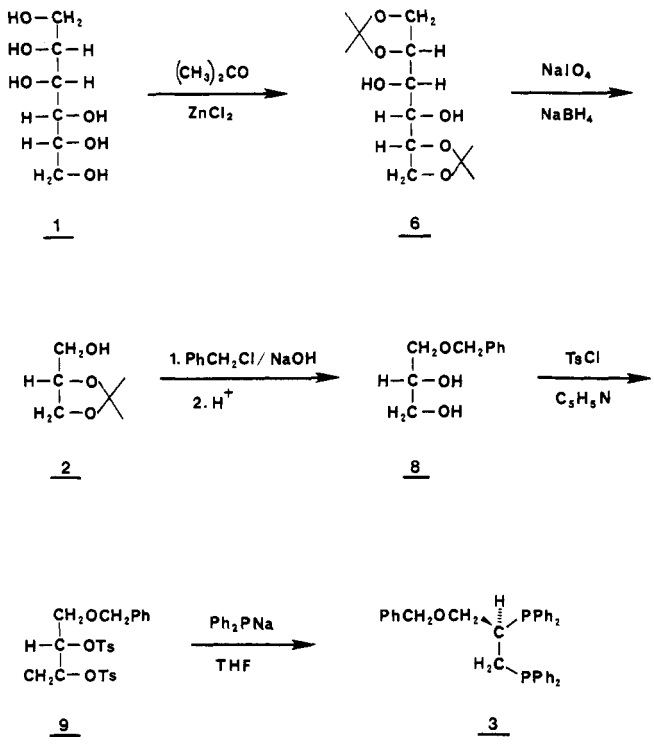
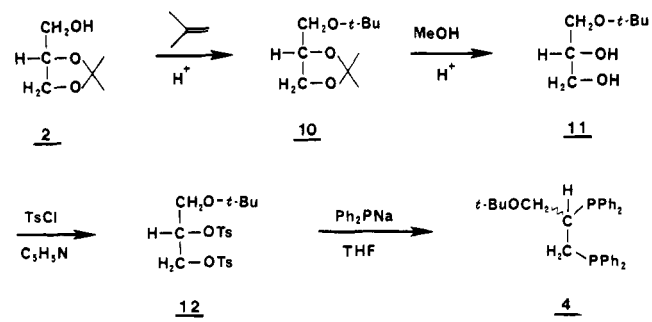
0022-3263/82/1947-0468$01.25/0

Scheme I



Scheme II



been reported. However, the synthesis of many of these ligands involves tedious isolation and purification steps resulting in low overall synthetic yields.

D-Mannitol (1) was investigated as a potential starting material for the synthesis of chiral 1,2-diphosphines because it is an inexpensive readily available material. 1,2-*O*-Isopropylidene-D-glycerol (2) can easily be prepared from D-mannitol in high yield. Starting from 1,2-*O*-isopropylidene-D-glycerol, (*R*)-1,2-bis(diphenylphosphino)-3-(benzyloxy)propane (3), and (*R*)-1,2-bis(diphenylphosphino)-3-*tert*-butoxypropane (4) have been synthesized. Treatment of phosphine 4 with trifluoroacetic acid gave (*R*)-1,2-bis(diphenylphosphino)propan-3-ol (5). The syntheses, spectral characterizations, and the optical yields obtained by using the rhodium complexes of these ligands, 3–5, are reported.

Results and Discussion

Synthesis of the Chiral 1,2-Diphosphines. D-Mannitol (1) was converted to 1,2:5,6-di-*O*-isopropylidene-D-mannitol (6) by its reaction with acetone in the presence of zinc chloride[10] (Scheme I). Cleavage of the glycol 6 with sodium metaperiodate followed by reduction with sodium borohydride[11] afforded, 1,2-*O*-isopropylidene-D-glycerol (2). Reaction of 2 with benzyl chloride in the presence of a base afforded 1-*O*-benzyl-2,3-*O*-isopropylidene-D-glycerol (7). Without isolation, 7 was subjected to acidic hydrolysis. The product, 1-*O*-benzyl-D-glycerol (8) was isolated and purified by distillation.[12] Treatment of 8 with *p*-toluenesulfonyl chloride in dry pyridine afforded (*S*)-1-*O*-benzyl-2,3-di-*O*-*p*-toluenesulfonyl glycerol (9) in 90–98% yield. Nucleophilic displacement of the *p*-toluenesulfonate groups of 9 with diphenylphosphide anion and purification of the resulting crude product by recrystallization from absolute ethanol gave pure (*R*)-1,2-bis(diphenylphosphino)-3-(benzyloxy)-propane (3) in 40–50% yield.

Hydrogenolysis of 3 to obtain the phosphine alcohol 5 under a variety of conditions such as with a catalytic amount of palladium on charcoal, palladium black, or Raney nickel did not give the expected product in useful amounts. Debenzylation was also attempted with sodium/ethanol and sodium/potassium alloy. However, a clean debenzylated product could not be obtained.

A chiral 1,2-diphosphine with a reactive functionality was desired, and since the cleavage of the benzylether of 3 was not successful, protecting groups other than benzyl ether were investigated. Isobutylene is known to add to alcohols under acidic conditions to form *tert*-butyl ethers.[13] The *tert*-butyl ethers are generally alkali resistant but are cleaved easily on treatment with anhydrous trifluoroacetic acid at 0–25 °C. Hence, alcohol 2 was protected as the *tert*-butyl ether, and the following reactions were carried out (Scheme II).

The acid-catalyzed addition of isobutylene to alcohol 2 at room temperature gave 1-*O*-*tert*-butyl-2,3-*O*-isopropylideneglycerol (10). Acid-catalyzed hydrolysis of 10 in methanol afforded 1-*O*-*tert*-butylglycerol (11). Treatment of 11 with *p*-toluenesulfonyl chloride yielded the ditosylate 12. Nucleophilic displacement of the tosylate groups by sodium diphenylphosphide gave the diphosphine 4, which was purified by complexing with nickel. However, it was found that neither the ditosylate 12 nor the diphosphine 4 was optically active.

It is well estabilished that the optically active center does not isomerize, either during the acid-catalyzed hydrolysis of the isopropylidene group[14] or during *p*-toluenesulfonylation of the hydroxy group.[15] Hence it is very likely that the isopropylidene-D-glycerol 2 isomerized during the acid-catalyzed reaction with isobutylene.

Since 1,2-*O*-isopropylidene-D-glycerol (2) was found to be very susceptible to acid-catalyzed isomerization, it was extremely important to protect the hydroxyl group of 2 under neutral or basic conditions. Hence the alcoholic function of 2 was first protected as the benzoate under neutral conditions and then later was replaced with a *tert*-butyl group prior to the phosphination reaction. The reactions summarized in Scheme III were carried out.

1,2-*O*-Isopropylidene-D-glycerol (2) was converted to 1-benzoyl-2,3-*O*-isopropylidene-D-glycerol (13) by the reaction of 2 with benzoyl chloride in pyridine. Hydrolysis of 13 with aqueous acetic acid afforded 1-benzoyl-L-glycerol

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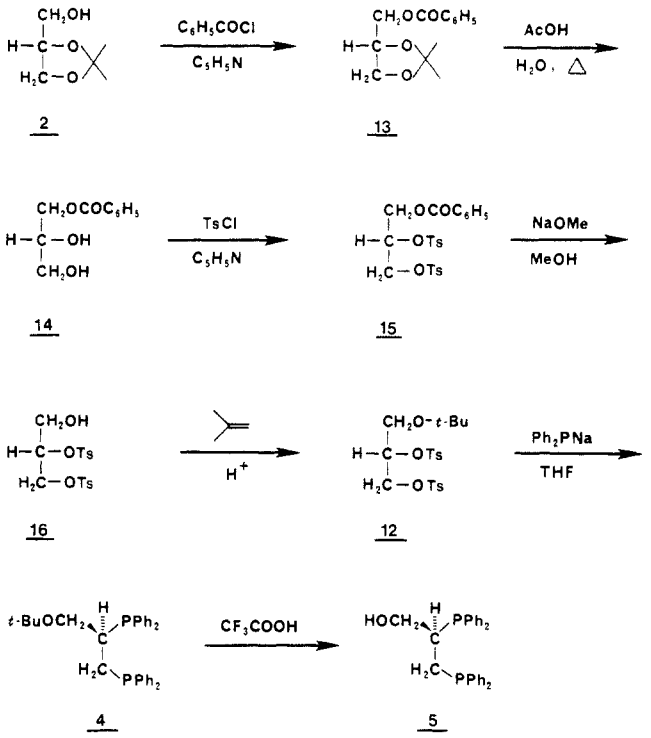
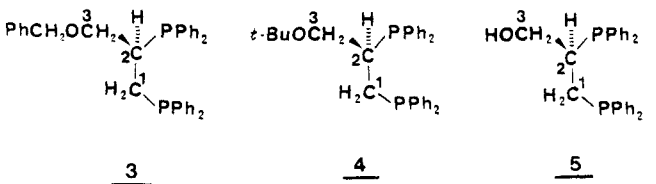
Scheme III



(14). Treatment of 14 with 2.5 equiv of *p*-toluenesulfonyl chloride in pyridine gave 1-benzoyl-2,3-di-*O*-*p*-toluenesulfonyl-L-glycerol (15).

Since the benzoate group is unstable to nucleophiles, it was necessary to replace it before treatment with sodium diphenylphosphide. Treatment of the ester with 1 equiv of 1 N sodium hydroxide did not give a cleanly hydrolyzed product. However, the hydrolysis could be carried out by using a catalytic amount of sodium methoxide in methanol at 0 °C, the byproduct being methyl benzoate. The crude 1,2-di-*O*-*p*-toluenesulfonyl-L-glycerol (16) was not purified but was allowed to react directly with isobutylene in the presence of a catalytic amount of sulfuric acid in dry methylene chloride to yield 1-*O*-*tert*-butyl-2,3-di-*O*-*p*-toluenesulfonyl-D-glycerol (12). Ditosylate 12 was purified by recrystallization from absolute ethanol. Displacement of the tosylate with sodium diphenylphosphide afforded crude diphosphine 4. Since 4 could not be purified by simple recrystallization, the crude product was converted to the nickel complex which was filtered and washed thoroughly to remove most of the impurities. Decomposition of the nickel complex with sodium cyanide liberated phosphine 4, which was further purified by repeated recrystallization from absolute ethanol to yield the optically pure (*R*)-1,2-bis(diphenylphosphino)-3-*tert*-butoxypropane. Treatment of the diphosphine 4 with trifluoroacetic acid at room temperature for 18 h afforded (*R*)-1,2-bis(diphenylphosphino)propan-3-ol (5).

Spectral Characterization of the Phosphines 3–5. The 60-MHz proton NMR spectrum of (*R*)-1,2-bis(diphenylphosphino)-3-(benzyloxy)propane (3) showed the



aromatic protons as a multiplet at 7.3 ppm while the

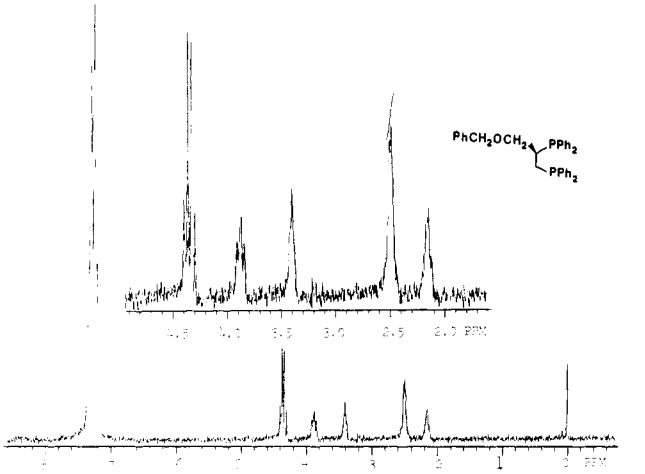


Figure 1. Proton NMR spectrum of 3 (360 MHz).

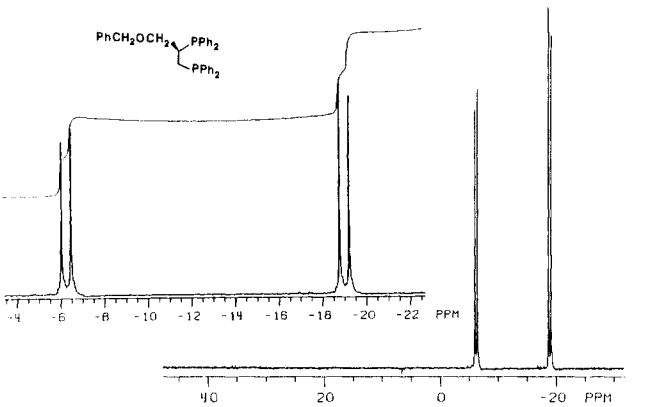


Figure 2. ^{31}P NMR spectrum of 3 (proton decoupled).

benzylic protons appeared as a sharp singlet at 4.35 ppm. The phosphorous coupling, which generally extends across several bonds, couples to all the methylene and methine protons on C_1, C_2, and C_3. This, in addition to the proton–proton coupling, makes the spectrum very complex. The absorption due to these protons appear as broad humps in 2–4-ppm region.

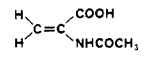
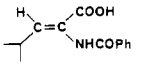
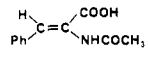
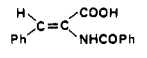
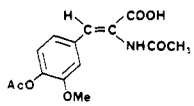
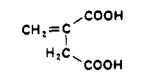
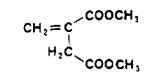
The ^1H NMR spectra of 3 at 360 MHz, however, gave a resolved spectrum (Figure 1). The methine proton at C_2 absorbs at 2.15 ppm, while the CH_2 protons on C_1 absorbs at 2.5 ppm. Both appear as complex multiplets. The two diastereotopic protons on C_3 absorb at 3.4 and 3.9 ppm. The benzylic protons which appear as a strong singlet at 60 MHz appear as two doublets at 4.32 and 4.4 ppm; the asymmetric center at C_1 probably causes both to appear as complex multiplets.

The ^{31}P spectrum (proton decoupled) is simple, and each phosphorous atom appears as doublets at -6 and -19 ppm, respectively (Figure 2). The proton-decoupled spectrum of the rhodium cationic complex of 3 (Figure 3) shows each phosphorous as doublets of of doublets, due to coupling of rhodium and phosphorous. The ^{31}P spectra of 4 and 5 are very similar to that of 3.

Asymmetric Hydrogenations. The rhodium cationic complexes were prepared from the corresponding phosphines 3–5. By use of these complexes as the catalyst precursors, asymmetric hydrogenation of various substrates was studied. In the two instances where methanol was used as the solvent, the enantiomeric excess obtained was slightly lower than that obtained in ethanol.

Conversions were obtained by ^1H NMR and in most cases were quantitative. The optical purities were obtained by measuring the rotation of the product and comparing

Table I. Optical Yields Obtained with Ligands and Comparison with those of Prophos[a]

substrate	product	ligand optical yield, % (config) 3[b]	4[c]	(R)-Prophos
	*N*-acetylalanine	91 (*S*)	92 (*S*)	90 (*S*)
	*N*-benzoylleucine	78 (*S*), 74 (*S*)[c]	88 (*S*)	
	*N*-acetylphenylalanine	87 (*S*)	86 (*S*)	90 (*S*)
	*N*-benzoylphenylalanine	92 (*S*)[d]		91 (*S*)
	*p*-acetoxy-*m*-methoxy-*N*-acetylphenylalanine	91 (*S*)		87 (*S*)
	α-methylsuccinic acid	27 (*R*), 29 (*R*)[d]		
	dimethyl α-methylsuccinate	50 (*R*)		

[a] All hydrogenations were carried out at 1 atm of hydrogen pressure and ambient temperature. [b] Solvent was absolute ethanol unless otherwise mentioned. [c] Solvent 95% ethanol. [d] Solvent methanol.

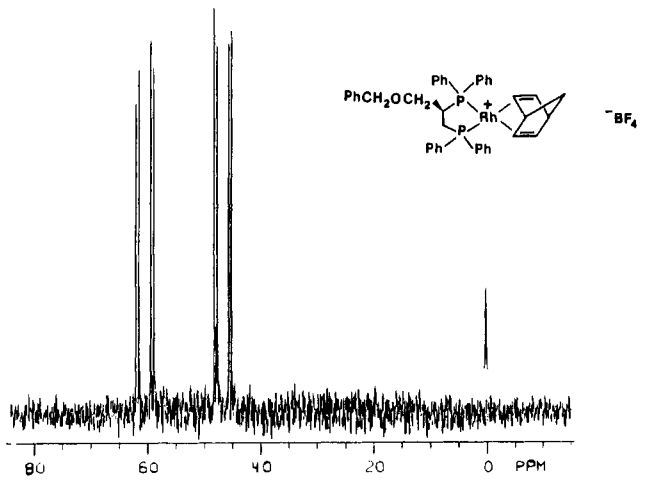


Figure 3. ^{31}P NMR spectrum of the rhodium complex of ligand **3**.

it with that of the pure enantiomer. In order to obtain reproducible results by polarimetry, it was extremely important to remove the chiral catalyst completely. The use of a cation-exchange resin to remove the rhodium complex has been reported,[2,3,8] but this method was not very efficient. In most examples removal of the solvent followed by aqueous extraction of the product was used to separate it from the catalyst.

As in the case of (*R*)-Prophos, ligand **3** also gave predominantly the *S* isomer in the hydrogenation of dehydro amino acid derivatives (Table I). The optical yields obtained were generally high (80–90%). Although itaconic acid gave only a 27% optical yield, a reasonable optical yield was obtained with dimethyl itacontate (50%). Atropic acid could not be hydrogenated under standard reaction conditions.

The cationic rhodium complex of **4** was also an efficient catalytic precursor, giving predominantly the *S* isomer in the hydrogenation of dehydro amino acid derivatives (Table I). The optical yield obtained in these hydrogenations was very similar to that of the complex derived from **3**, except in the case of the leucine derivative, which gave a slightly higher optical yield, viz., 88% ee (compared to 78% ee obtained with the catalytic precursor obtained from **3**).

The cationic rhodium complex of **5** was found not to be an efficient catalytic percursor for the hydrogenation of dehydro amino acid derivatives. α-*N*-Acetamidoacrylic acid could not be hydrogenated by using this complex. (*Z*)-α-*N*-Acetylcinnamic acid hydrogenated poorly (about 20% conversion in 48 h). Since the conversion was very low, the optical yield could not be determined accurately.

Experimental Section

All reactions were routinely performed under an inert atmosphere of nitrogen or argon. Reactions involving phosphines were carried out by using either Schlenk techniques, a glovebag, or a drybox. ^1H NMR spectra were determined on a Varian EM360, JEOL FX-100, or Nicolet NT-360 spectrometers. ^{13}C NMR spectra were obtained on a JEOL FX-100 spectrometer. ^{31}P NMR spectra were obtained on a Nicolet NT-150 instrument. Infrared spectra were obtained either on a Perkin-Elmer 267 or on a Beckman Acculab 3 spectrometer as neat samples or as potassium bromide pellets. Elemental analyses were performed by Micro-Tech Laboratories. Optical rotations were measured on a Perkin-Elmer Model 241 polarimeter. Melting points are uncorrected.

1-*O*-Benzyl-D-glycerol was prepared in three steps from D-mannitol.[12] Diphenylphosphine was synthesized by following a literature procedure.[16]

1,2-Di-*O*-*p*-toluenesulfonylglycerol 3-*O*-Benzyl Ether (9). To a solution of 37.4 g (0.206 mol) of the monobenzyl ether of D-glycerol (**12**) in 100 mL of dry pyridine cooled in an ice bath was added 90.0 g (0.472 mol) of recrystallized *p*-toluenesulfonyl chloride dissolved in 150 mL of dry pyridine. The solution was left in a refrigerator for 144 h. Water (10 mL) was added, and the mixture was stirred for 10 min. The solution was then poured into 600 mL of cold water with stirring. The precipitated **13** was

(16) Morrison, J. D.; Masler, W. F. *J. Org. Chem.* **1974**, *39*, 270.

dissolved in chloroform, and the water was extracted with three 100-mL portions of chloroform. The combined chloroform solution was washed with 4 N hydrochloric acid until the wash water was acidic to litmus. The chloroform layer was then washed successively with water, 5% sodium bicarbonate solution, and finally with water. The chloroform solution was dried over anhydrous sodium sulfate. The solvent was then removed under reduced pressure, and the residue was dried overnight. The crude **9** thus obtained was recrystallized from absolute ethanol to yield 92 g (0.19 mol, 91%) of pure **9**: mp 61–62 °C $[\alpha]_D$ +1.4° ($CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.7–7.5 (4 H, m), 7.2 (9 H, m), 4.7–4.4 (1 H, m), 4.3 (2 H, s), 4.15 (2 H, d), 2.35 (6 H, s); ^{13}C NMR ($CDCl_3$) δ 144.87, 144.77, 135.95, 132.68, 131.78, 131.73, 129.62, 129.52, 129.28, 127.97, 127.48, 127.14, 76.80, 72.91, 67.41, 21.35. Anal. Calcd for $C_{24}H_{26}O_7S_2$: C, 58.54; H, 5.70; S, 13.02. Found: C, 58.68; H, 5.37; S, 13.07.

(*R*)-1,2-Bis(diphenylphosphino)-3-(benzyloxy)propane (3). To 25 mL of liquid ammonia cooled in a methanol–dry ice bath was added 0.575 g (25.0 mmol) of sodium, and the solution was stirred for 10 min. To the sodium in liquid ammonia solution was added 4.6 g (25 mmol) of diphenylphosphine dissolved in 20 mL of dry tetrahydrofuran dropwise over about 10 min. Once the addition was over, the dry ice bath was removed, and the ammonia was allowed to evaporate. When the solution attained room temperature, 5.40 g (11.02 mmol) of **9** dissolved in 30 mL of dry tetrahydrofuran was added dropwise. Once the addition was over, the reaction mixture was stirred at room temperature overnight and then at 40–45 °C (bath temperature) for 4 h. The yellow reaction mixture was then centrifuged, and the clear yellow liquid thus obtained was concentrated in vacuo, dried overnight, and recrystallized from absolute ethanol to yield 2.4 g (4.6 mmol, 42%) of **3**: mp 88–88.5 °C; $[\alpha]^{20}_D$ +71.7° (*c* 1.4, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.1 (m, Ar H), 4.35 (s, $C_6H_5CH_2$), 3.9 (m, 1 H), 3.4 (m, 1 H), 2.5 (m, 2 H), 2.15 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 138.82, 138.28, 138.23, 137.84, 137.63, 136.73, 136.68, 136.05, 135.46, 133.6, 133.54, 133.2, 132.86, 132.76, 132.15, 131.45, 128.72, 128.68, 128.63, 128.43, 128.26, 128.14, 128.07, 127.95, 127.88, 127.73, 127.32, 127.20, 127.05, 126.88, 126.71, 72.65 (s), 69.35 (t), 34.77 (q), 27.86 (t). Anal. Calcd for $C_{34}H_{32}OP_2$: C, 78.75; H, 6.66; P, 11.95. Found: C, 78.62; H, 6.19; P, 12.12. ^{31}P NMR (reference H_3PO_4)-6.26 (d, J = 26.5 Hz), −18.99 (d, J = 26.5 Hz) ppm.

1-*O*-*tert*-Butyl-2,3-*O*-isopropylideneglycerol (10). To a pressure bottle containing 100 mL of liquid isobutylene and 0.5 mL of concentrated sulfuric acid at −78 °C was added 17.4 g (132 mmol) of 1,2-*O*-isopropylideneglycerol (**2**) in 100 mL of dichloromethane. The reaction mixture was allowed to warm to room temperature gradually and was stirred overnight. The excess isobutylene was removed under a stream of nitrogen, and the solution was neutralized with sodium bicarbonate solution. The organic layer was separated, washed with water, dried (Na_2SO_4), and concentrated to yield **10** as a colorless oil: ^1H NMR ($CDCl_3$) δ 4.3–3.4 (m, 5 H), 1.48 (s, 3 H), 1.4 (s, 3 H), 1.3 (s, 9 H).

1-*O*-*tert*-Butylglycerol (11). To a solution of **10** in 250 mL of dry methanol was added 0.8 g of *p*-toluenesulfonic acid, and the mixture was stirred at room temperature for 18 h. The solution was neutralized with potassium carbonate solution, the excess methanol was removed on a rotary evaporator, and the residue was distilled under reduced pressure to yield 11 g (76 mmol, 58% from **2**) of **11** as a colorless oil: bp 76–78 °C (0.025 mmHg); ^1H NMR ($CDCl_3$) δ 3.6–3.2 (m, 5 H), 3.05 (s, 2 H, OH), 1.15 (s, 9 H, $C(CH_3)_3$); ^{13}C NMR (D_2O, external Me_4Si) δ 76.36 (s), 73.56 (d), 65.62 (t, 2 C), 29.71 (q).

3-Benzoyl-1,2-*O*-isopropylidene-L-glycerol (13). This compound was prepared by a literature procedure:[11] $[\alpha]_D$ +14.4° (neat) [lit.[11] + 14.6° (neat)]; ^1H NMR ($CDCl_3$) δ 7.8 (m, 2 H), 7.2 (m, 3 H), 4.25–3.6 (m, 5 H), 1.4 (s, 3 H), 1.3 (s, 3 H).

1-Benzoyl-L-glycerol (14). This compound was prepared by a literature procedure.[17] $[\alpha]^{25}_D$ −15°C (*c* 10, pyridine) [lit.[17] $[\alpha]_D$ −15.3° (*c* 10, pyridine)]; ^1H NMR ($CDCl_3$) δ 8 (m, 2 H), 7.5 (m, 3 H), 4.6 (br s, 2 H, OH), 4.4 (m, 2 H), 4.2 (m, 1 H), 3.8 (m, 2 H).

1-Benzoyl-2,3-di-*O*-*p*-toluenesulfonyl-L-glycerol (15). To a solution of 35.5 g (181 mmol) of **14** in 250 mL of dry pyridine at 0 °C was added 83.0 g (433 mmol) of *p*-toluenesulfonyl chloride. The mixture was stirred at 0 °C for 15 min and then stored in a refrigerator for 144 h. After the reaction mixture was cooled to 0 °C, 10 mL of water was added, and the mixture was stirred for 10 min and poured into excess water. The aqueous solution was separated from the gummy product and extracted with chloroform. The gummy residue was dissolved in chloroform, and the combined chloroform solution was washed with 3 N hydrochloric acid, water, 5% sodium bicarbonate solution, and water. The chloroform solution was dried (Na_2SO_4) and concentrated under reduced pressure to yield a solid which on recrystallization from absolute ethanol gave 65.5 g (130 mmol, 72.0%) of **15**: mp 107–108 °C; $[\alpha]^{20}_D$ −22.70° (*c* 5.92, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 8–7 (m, 13 H), 4.9 (m, 1 H), 4.45 (d, 2 H, J = 6 Hz), 4.35 (d, 2 H, J = 6 Hz), 2.42 (s, 3 H), 2.38 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 165.162, 145.136, 133.108, 132.466, 131.649, 129.430, 128.671, 128.087, 127.678, 75.306, 66.899, 61.994, 21.591.

1,2-Di-*O*-*p*-toluenesulfonyl-L-glycerol (16). To a slurry of 20 g (40 mmol) of the ester **15** in 250 mL of dry methanol, cooled in an ice bath, was added 250 mg (10.87 mmol) of sodium under a nitrogen atmosphere. The mixture was stirred at 0 °C for 3 h, during which time the solution became homogeneous, indicating the completion of hydrolysis. The solution was neutralized by use of an ion-exchange resin (Dowex 50 W-X8, H^+ form), the resin was filtered, the solvent was removed on a rotary evaporator, and the product was dried in vacuo. It was redissolved in 200 mL of chloroform, washed with water, dried (Na_2SO_4), and concentrated to yield 14.0 g (35 mmol, 88%) of **16** as a viscous oil: ^1H NMR ($CDCl_3$) δ 7.8 (m, 4 H), 7.4 (m, 4 H), 4.7 (m, 1 H), 4.2 (d, 2 H, J = 5 Hz), 3.75 (t, 2 H, J = 6 Hz), 2.7 (t, 1 H, OH), 2.5 (s, 6 H). $[\alpha]^{20}_D$ −18.53° (*c* 6.6, $CHCl_3$).

1-*O*-*tert*-Butyl-2,3-di-*O*-*p*-toluenesulfonylglycerol (12) from 11. To a solution of 9.0 g (60.8 mmol) of alcohol **11** in 150 mL of dry pyridine at 0 °C was added 28.0 g (147 mmol) of recrystallized *p*-toluenesulfonyl chloride. The mixture was stirred at 0 °C for 15 min and stored in a refrigerator for 144 h. The solution was then cooled in an ice bath, 10 mL of water was added, and the mixture was stirred for 10 min. The reaction mixture was poured into excess water and extracted with chloroform. The chloroform solution was washed successively with cold 3 N hydrochloric acid, water, sodium bicarbonate solution, and water. The chloroform solution was dried (Na_2SO_4), and the solvent was removed on a rotary evaporator. The residue obtained was dried in vacuo. Recrystallization from absolute ethanol afforded 22 g (48 mmol, 79%) of racemic **12** as white crystals: mp 69–70 °C; ^1H NMR ($CDCl_3$) δ 7.8 (m, 4 H), 7.3 (m, 4 H), 4.5 (m, 1 H), 4.15 (d, 2 H), 3.35 (d, 2 H), 2.45 (s, 6 H), 1.1 (s, 9 H); ^{13}C NMR (Me_2SO-d_6) δ 21.050 (q), 26.713 (q), 59.467 (t), 68.109 (t), 73.013 (s), 78.093 (d), 129.647, 129.881, 131.516, 132.683, 144.652, 144.886. Anal. Calcd for $C_{21}H_{28}O_7S_2$: C, 55.24; H, 6.18; S, 14.04. Found: C, 55.01; H, 6.11; S, 13.88.

1-*O*-*tert*-Butyl-2,3-di-*O*-*p*-toluenesulfonyl-D-glycerol (12) from 16. To a solution of 13.8 g (34.5 mmol) of **16** in 100 mL of dry methylene chloride in a pressure bottle was added 100 mL of liquid isobutylene at −78 °C. Concentrated sulfuric acid (0.2 mL) was added to the above reaction mixture, the contents were stirred, and the mixture was then allowed to warm to room temperature and stirred for 16 h. The pressure was gradually released, and the solution was neutralized with sodium bicarbonate solution. The organic layer was separated, washed with water, and dried (Na_2SO_4), the solvent was removed on a rotary evaporator, and the crude product was dried under reduced pressure. Recrystallization from absolute ethanol afforded white crystals of **12**: 11 g (24 mmol, 70%); mp 70–71 °C; $[\alpha]^{20}_D$ +3.44° (*c* 5.9, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.8 (m, 4 H), 7.3 (m, 4 H), 4.5 (m, 1 H), 4.15 (d, 2 H), 3.35 (d, 2 H), 2.45 (s, 6 H), 1.1 (s, 9 H).

(*R*)-1,2-Bis(diphenylphosphino)-3-*tert*-butoxypropane (4). To 100 mL of liquid ammonia was added 1.31 g (57.0 mmol) of sodium, and the mixture was stirred for 10 min. To the resulting dark blue solution of sodium in liquid ammonia was added 10.6 g (57.0 mmol) of diphenylphosphine dissolved in 50 mL of dry THF dropwise over a period of 45 min. By the time all the diphenylphosphine was added, the color of the solution had become orange. Excess ammonia was allowed to evaporate from the clear orange solution under a stream of argon. When the solution attained room temperature, a solution of 13.0 g (28.5 mmol) of **12** ($[\alpha]^{20}_D$ +3.44°) in 50 mL of dry THF was added

(17) Baer, E.; Cushing, I. B.; Fischer, H. O. L. *Can. J. Res., Sect. B* **1942**, *21*, 119.

dropwise over a period of 30 min. The mixture was allowed to stir at room temperature for 18 h. The precipitated sodium *p*-toluenesulfonate was removed by centrifugation. The clear THF solution was concentrated under reduced pressure to give the impure phosphine.

The crude phosphine was redissolved in 50 mL of absolute ethanol under an argon atmosphere, a solution of 7 g of nickel chloride hexahydrate in 25 mL of absolute ethanol was added to it, and the contents were stirred for 15 min. This was followed by addition of a solution of 7 g of potassium thiocyanate in 25 mL of 90% aqueous ethanol. The complex, $[Ni(SCN)\text{-}(PH_3)_2]$-SCN, that separated as a yellow powder after the mixture was stirred over a period of 18 h was filtered and washed thoroughly with absolute ethanol and ether.

For freeing of the phosphine from the nickel complex, the complex was suspended in 50 mL of dichloromethane, and a solution of 18 g of sodium cyanide in 50 mL of water was added. The mixture was stirred vigorously for 1 h. During this time all the nickel complex was dissolved, and the dark red color of the organic layer changed to pale yellow. The organic layer was separated, washed with water, and concentrated under reduced pressure to yield a light yellow phosphine. Recrystallization of this slightly impure phosphine from absolute ethanol gave 2.0 g (4.1 mmol, 14%) of white needlelike crystals of (*R*)-1,2-bis(diphenylphosphino)-3-*tert*-butoxypropane (**4**): mp 77–78 °C; $[\alpha]^{20}_D$ +91° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.1 (m, 20 H), 3.85 (m, 1 H), 3.35 (m, 1 H), 2.45 (m, 1 H), 2.1 (m, 1 H), 1.1 (s, 9 H); ^{31}P NMR ($CDCl_3$, reference 85% H_3PO_4) −5.412 (d, J = 25 Hz), −19.077 (d, J = 25 Hz) ppm; ^{13}C NMR ($CDCl_3$) δ 139.38, 138.86, 138.54, 137.95, 137.37, 136.70, 136.11, 134.04, 133.93, 133.25, 133.14, 132.32, 131.62, 128.70, 128.38, 128.17, 128.09, 127.94, 127.82, 127.70, 72.74 (s), 60.97 (t, J = 10 and 11 Hz), 34.72 (t, J = 13.9 and 13.2 Hz), 27.897 (t, J = 16 Hz), 27.488 (s). Anal. Calcd for $C_{31}H_{34}OP_2$: C, 76.84; H, 7.07; P, 12.78. Found: C, 77.38; H, 7.06; P, 12.79.

(*R*)-1,2-Bis(diphenylphosphino)propan-3-ol (5). A solution of 0.2 g of (*R*)-1,2-bis(diphenylphosphino)-3-*tert*-butoxypropane (**4**) in 25 mL of anhydrous trifluoroacetic acid under an argon atmosphere was stirred at room temperature for 14 h. The trifluoroacetic acid was removed under reduced pressure. The residue was dissolved in 20 mL of dichloromethane and the mixture washed with 5% sodium bicarbonate solution and water. The solvent was removed under reduced pressure and the residue dried to yield 0.16 g of (*R*)-1,2-bis(diphenylphosphino)propan-3-ol (**5**) as a sticky solid: ^1H NMR ($CDCl_3$) showed the absence of $C(CH_3)_3$ protons; ^{13}C NMR ($CDCl_3$) δ 137.90, 137.43, 136.90, 134.98, 134.74, 134.16, 134.04, 133.81, 133.69, 133.28, 132.87, 132.41, 132.11, 131.65, 131.47, 131.01, 130.83, 130.66, 130.48, 129.31, 129.02, 128.61, 128.44, 128.32, 68.61 (dd, J = 15.7, 10.5 Hz), 32.95 (dd, J = 17.8, 12.8 Hz), 28.01 (t, J = 17 Hz).

Rhodium Complex of 3. The catalyst was prepared and used under an inert atmosphere. Extreme care was taken to exclude air from the solvents. To a solution of 42.7 mg (0.0925 mmol) of the dimer of rhodium norbornadiene chloride in 3 mL of methanol was added 105 mg (0.203 mmol) of **3**. The reaction mixture was stirred at room temperature for 2 h. To this was added a solution of 1.95 g of sodium tetrafluoroborate in 18 mL of water. The rhodium complex **3** was precipitated as a yellow cheesey solid. The solid was filtered, washed with water, and dried. This complex was used for the asymmetric hydrogenation of various α-(acylamino)acrylic acid derivatives: ^{31}P NMR (CH_3OD, reference H_3PO_4) 60.22 (dd, J_{Rh-P} = 157 Hz, J_{P-P} = 155 Hz, J_{P-P} = 32 Hz) ppm.

Rhodium Complex of 4. A solution of 12 mg (0.020 mmol) of the phosphine **4** and 4.6 mg (0.010 mmol) of rhodium norbornadiene chloride dimer in 1 mL of methanol was stirred at room temperature for 1 h. The catalyst was precipitated as the cationic complex by the addition of 0.15 g (1.4 mmol) of sodium tetrafluoroborate in 3 mL of water. The precipitated catalyst was filtered, washed with water, and dried.

Rhodium Complex of 5. This complex was also prepared by a procedure analogous to the one used for preparing the rhodium complexes of **3** and **4**.

General Hydrogenation Procedure. Ethanol and methanol were distilled from magnesium ethoxide and methoxide, respectively, and deoxygenated by repeatedly pumping and filling with argon. The substrate (0.3–0.5 g) was weighed into a two-necked flask fitted with a gas inlet and a serum cap. It was degassed by evacuating and filling it with argon several times. The catalytic precursor (the rhodium complex of **4** or **17**) dissolved in 10–15 mL of the solvent was transferred to the flask containing the substrate via a needle stock. The solution was vigorously stirred under 1 atm of hydrogen pressure for a period of 2–24 h. After this period of time the solvent was removed, and the product was separated from the catalyst either by dissolving the product in water and filtering the solution to remove the catalyst (alanine, α-methylsuccinic acid, and L-DOPA derivatives) or by dissolving the product in 0.5 N NaOH solution, filtering the solution to remove the catalyst, acidification of the aqueous filtrate, and extraction with ether. The conversions were determined by using ^1H NMR, and optical purities were determined by checking the rotation on a polarimeter.

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Registry No. **2**, 22323-82-6; **3**, 80106-02-1; **3** Rh complex, 80145-74-0; **4**, 80106-03-2; **4** Rh complex, 80145-72-8; **5**, 80106-04-3; **5** Rh complex, 80145-70-6; **8**, 56552-80-8; **9**, 16495-11-7; (±)-**10**, 80183-00-2; (±)-**11**, 80183-01-3; (±)-**12**, 80106-05-4; D-**12**, 80183-02-4; **13**, 51432-60-1; **14**, 51432-61-2; **15**, 80106-06-5; **16**, 80106-07-6; 2-acetamidoacrylic acid, 5429-56-1; (*Z*)-2-acetamido-4-methyl-2-pentenoic acid, 64896-31-7; (*Z*)-α-acetamidocinnamic acid, 55065-02-6; (*Z*)-α-benzamidocinnamic acid, 26348-47-0; (*Z*)-α-acetamido-*p*-acetoxy-*m*-methoxycinnamic acid, 55739-56-5; α-methylenesuccinic acid, 97-65-4; dimethyl α-methylenesuccinate, 617-52-7; *N*-acetyl-L-alanine, 97-69-8; *N*-benzoyl-L-leucine, 1466-83-7; *N*-acetyl-L-phenylalanine, 2018-61-3; *N*-benzoyl-L-phenylalanine, 2566-22-5; *p*-acetoxy-*m*-methoxy-*N*-acetyl-L-phenylalanine, 31269-52-0; (*R*)-α-methylsuccinic acid, 3641-51-8; dimethyl (*R*)-α-methylsuccinate, 22644-27-5.