# Asymmetric Synthesis. An Asymmetric Homogeneous Hydrogenation Catalyst Which Breeds Its Own Chirality

**M. D. Fryzuk and B. Bosnich***

*Contribution from The Lash Miller Chemical Laboratories, The Chemistry Department, University of Toronto, Toronto, Ontario, Canada. M5S 1A1.* *Received February 14, 1978*

**Abstract:** The chiral ligand (*R*)-1,2-bis(diphenylphosphino)propane, (*R*)-prophos, has been prepared from (*S*)-lactic acid. The soluble rhodium(I) complex of this ligand acts as an efficient asymmetric hydrogenation catalyst for the production of amino acids. The optical yields appear to be insensitive to the nature of the substituents of the substrates; all are reduced to the "natural" hand of the amino acid in 90 ● 3% optical yield. Moreover, the catalyst is capable of breeding its own chirality so that large quantities of (*R*)-prophos can be produced from the catalytic reduction of a simple olefinic substrate by the (*R*)-prophos catalyst itself.

The modified versions of Wilkinson's catalyst incorporating chiral phosphine ligands have produced some spectacularly high optical yields for asymmetric hydrogenation. In general, chiral catalysts containing unidentate phosphines[1] or flexible bidentate diphosphines[2] give modest optical yields probably because of the lack of rigidity[3] in these systems. Consistently, chiral rhodium catalysts incorporating bidentate diphosphines which form rigid chelate rings[4-6] have given high optical yields for the reduction of (*Z*)-α-acylaminoacrylic acids, the substrates which are hydrogenated to *N*-acyl amino acids.

We recently showed that the rhodium(I) catalyst incorporating the ligand *chiraphos* [2,3-bis(diphenylphosphino)-butane] gave exceptional optical yields in the production of amino acids.[6] The central point of this work was that the presence of chiral phosphorus centers was not an exclusive prerequisite for high optical yields and that effective diastereotopic discrimination[6] could be achieved by fixing the chirality of the chiraphos-rhodium chelate ring by groups at chiral centers in the chelate ring backbone. This paper describes a test for this assertion. We report the results obtained using a new diphosphine ligand, (*R*)-prophos [(*R*)-1,2-bis-(diphenylphosphino)propane] which has only a single methyl group at a chiral center to constrain the chirality of the chelate ring. As a practical proposition, this new system is nearly an ideal catalyst for producing optically active amino acids from (*Z*)-α-acylaminoacrylic acids, since the optical yields appear to be insensitive to the nature of the substituents. Moreover, the catalyst is capable of breeding its own chirality and is therefore self-reproducing.

## Results

**Stereochemical Considerations.** Figure 1 shows the structures of (*S,S*)-chiraphos and (*R*)-prophos as well as the conformations which are adopted when each forms a chelate ring. These chelate rings are puckered and chiral and are fixed in one conformation by the requirement that the methyl groups be equatorially disposed. This puckering also fixes the phenyl-group orientations on the phosphorus atoms so that they occupy quasi-axial and quasi-equatorial dispositions (Figure 1). It is our assumption that the principle source of discrimination between the (coordinated) prochiral olefin faces of the substrate and the catalyst molecule is the chiral array of phenyl groups on the phosphorus atoms. It follows, therefore, that, irrespective of how the chirality of the chelate ring is fixed, the same or similar chiral interaction between the coordinated diphosphine ligand and a given substrate will occur. The catalyst derived from (*S,S*)-chiraphos reduces (*Z*)-α-acylaminoacrylic acids to the corresponding (*R*)-*N*-acyl amino acids. Therefore (*R*)-prophos which fixes the opposite chirality of the chelate ring should give the (enantiomeric) (*S*)-*N*-acyl amino acids and in about the same optical purity. Small differences in the orientations of the phenyl groups may occur for the two chelate ring systems depending on the "flatness" of puckering of one ring relative to the other. We expect, however, that these effects will not lead to greatly different optical yields for comparable substrates.

**Catalytic Precursor.** The chiral diphosphine ligand was prepared from (*S*)-lactic acid by the route outlined in Figure 2. Two aspects are notable: first, the ditosylate derivative is easily crystallized to optical purity even if the starting lactic acid is only 80% optically pure; second, the diphosphine is readily separated from its reaction mixture as the crystalline nickel complex. The pure diphosphine was displaced from its nickel complex with cyanide and a single crystallization from ethanol gave optically pure (*R*)-prophos as small, air-stable colorless prisms. The overall yield, based on (*S*)-lactic acid, is about 30%. There appears to be little loss of configurational integrity due to neighboring-group participation, although some elimination may occur during the lithium diphenylphosphide reaction.

The catalytic precursor, [Rh((*R*)-prophos) (NBD)]$ClO_4$ (NBD = norbornadiene) was prepared by the following displacement reaction

$$[Rh(NBD)_2]ClO_4 + (R)\text{-prophos} \rightarrow [Rh((R)\text{-prophos})\ (NBD)]ClO_4 + NBD$$

This orange-red complex retains its catalytic activity indefinately if stored under nitrogen at 0 °C.

An absolute crystal structure of [Rh((*R*)-prophos)-NBD]$ClO_4$·0.5$CH_2Cl_2$ has been determined.[7] The structure is the one predicted; the chelate ring is λ, the methyl group is equatorially disposed, and the absolute configuration of the diphosphine is *R*. We assume that this conformational structure will essentially be retained in solution.

**Hydrogenation.** We have investigated the asymmetric hydrogenation of (*Z*)-*N*-acylaminoacrylic acids at 25 °C and at atmospheric pressure using the (*R*)-prophos catalyst so as to compare the results obtained with those we observed with the (*S,S*)-chiraphos catalyst[6] and also because these substrates are precursors for the production of amino acids. All of the *N*-acylaminoacrylic acids were prepared by procedures which give the *Z* isomer exclusively.[8]

When [Rh((*R*)-prophos)NBD]$ClO_4$·0.5$CH_2Cl_2$ is suspended in either purified tetrahydrofuran or 95% ethanol and placed under 1 atm of hydrogen, the orange-red complex dissolves to give a yellow solution which is catalytically active[9] for the reduction of (*Z*)-*N*-acylaminoacrylic acids. The hydrogenations were performed with a catalyst to substrate ratio of 1:250 for which the reactions proceeded rapidly and to completion. At the end of the hydrogenation, the catalyst was removed by the addition of ion-exchange resin ($H^+$ form), and the rotation of the resultant solution was determined at four

0002-7863/78/1500-5491$01.00/0 

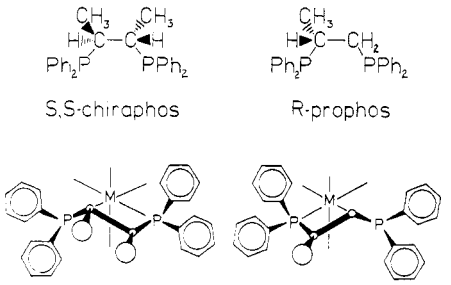



**Figure 1.** The two diphosphine ligands and their respective conformational structures when complexed to a metal.

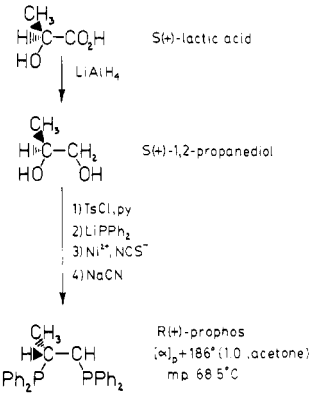



**Figure 2.** An outline of the method of preparation of (*R*)-prophos.

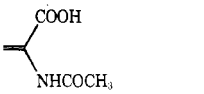
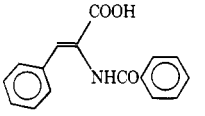
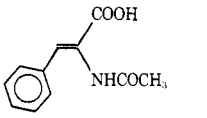
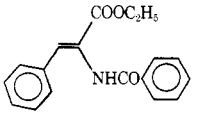
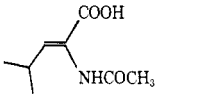
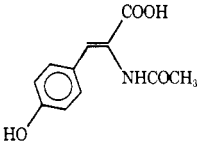
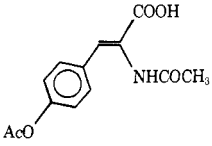
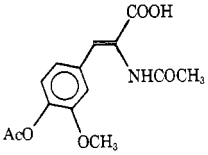
wavelengths and compared to that of an identically made-up solution of the pure, independently prepared *N*-acyl amino acid. The product of hydrogenation was then isolated, as crystals, by removing the solvent under reduced pressure. The recovery was greater than 95% in all cases, and the rotation was checked again and the identity of the product was confirmed by NMR. The rotations obtained by the two methods were the same within 1% and, in all cases, the hydrogenation was quantitative within the detectability by the NMR method.

The results are shown in Table I. It is remarkable that, with the prophos catalyst, all of the substrates give products in 90 ± 3% optical purity, and, unlike the chiraphos catalyst,[6] are not very sensitive to the two solvents used. In addition, the turnover numbers are four to five times greater for the prophos catalyst than those for the same substrates when chiraphos is used under the same conditions. The fastest is the production of *N*-acetylalanine with a turnover number of about 600 $h^{-1}$ and the slowest is for the production of *N*-acetyltyrosine for which the turnover number is approximately 50 $h^{-1}$. These numbers appear to be governed by both steric and electronic factors. Finally, as predicted, all of the *N*-acyl amino acids obtained with the (*R*)-prophos catalyst have the "natural" *S* configuration.

**Catalytic Breeder.** Since the prophos catalyst gives such high optical yields which appear to be insensitive to the substituents on the substrates, it seemed to us profitable to introduce a new degree of sophistication to the catalyst. It would be of some interest if the catalyst were capable of breeding its own chirality so that, as it were, the chirality of the catalyst would perpetuate itself. We have achieved this in the following way.

The cheap, readily available compound, ethyl pyruvate, is converted to its enol acetate in acetic anhydride in the presence of an acid catalyst. This enol acetate is rapidly hydrogenated by the (*R*)-prophos catalyst to (*S*)-ethyl *O*-acetyllactate in 81% optical purity. The same hydrogenation using the (*S,S*)-chiraphos catalyst gives, predictably, the enantiomer, (*R*)-ethyl *O*-acetyllactate in 84% optical purity. These products of hydrogenation are readily reduced ($LiAlH_4$) to the corresponding chiral propanediols which, in turn, can be converted to the crystalline ditosylates. Although the ditosylates are only about 80% optically pure, a single crystallization from methylene chloride/cyclohexane gives the optically pure enantiomeric ditosylates in a remarkable 70% recovery based on the optically impure materials. These (*R*)- and (*S*)-ditosylates then give the (*S*)- and (*R*)-prophos ligands, respectively, which can be used in further hydrogenations. It will be noted that (*S,S*)-chiraphos gives (*S*)-prophos which will give (*R*)-amino acids and, once the (*S*)-prophos is generated, it provides a source for breeding more (*S*)-prophos. The amino acid and breeder cycles are presented in Figure 3 for the (*R*)-prophos catalyst. Thus, in principle, infinite amounts of chiral prophos can be produced by using very small amounts of either (*R*)-prophos or (*S,S*)-chiraphos.

**Table I.** Optical Yields (%)

| amino acid | substrate | solvent THF | solvent 95% ETOH |
|---|---|---|---|
| Ala |  | 87 | 90 |
| Phe |  | 93 | 91 |
| |  | 91 | 90 |
| |  | 88 | 87 |
| Leu |  | 87 | 87 |
| Tyr |  | 92 | 89 |
| |  | 89 | 89 |
| DOPA |  | 89 | 87 |

[a] All the acylated amino acids produced by (*R*)-prophos have the *S* configuration.

## Discussion

The striking feature of the results presented in Table I is the insensitivity of the optical yields to substituents. Thus, neither changes at the amine function, changing the acid to an ester, nor the nature of the β-vinyl substituent significantly affects the optical yields. These results are somewhat different from those observed for the chiraphos catalyst[6] for which the yields

were higher in some cases and the variations in optical yield among the present set of substrates were greater. It is difficult to identify precisely what different structural features obtain for the two catalysts, except to note that the flatness of the chelate ring may be different in the two cases[10] and the absence of a methyl group in prophos as compared to chiraphos may cause a difference in the rotameric conformations of the phenyl groups. However, we believe that the consistency of the results in Table I is the more interesting feature, for it suggests that there is a single structural feature of the substrates which has a determining influence on the optical yield. A common feature of all the substrates is the presence of an *N*-acylamino function, and it may well be, as has been suggested,[5] that the carbonyl of the amido group coordinates to the rhodium atom to form a relatively rigid $\pi$-olefin-*O*-carbonylrhodium chelate ring. Such rigidity generally enhances optical yields,[3,11] but it is not obvious why this chelation should allow prophos to give more consistent results than chiraphos.

Although, as yet, the precise origins of the diastereotopic discrimination of the two catalysts are unknown, our original premise for designing these two simple ligands has been substantiated by the present results. Moreover, the fact that prophos gives such constant optical yields for the amino acid precursors and the fact that either hand of the catalyst can be bred by the catalyst itself makes the prophos complex an almost ideal catalyst for the production of optically active amino acids.

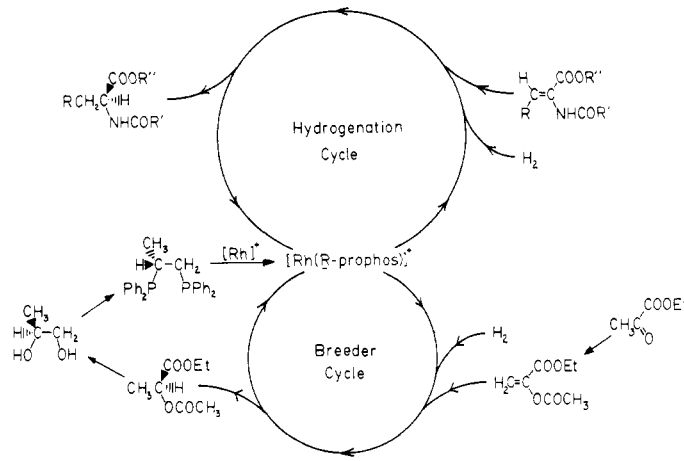



**Figure 3.** The catalytic hydrogenation and breeder cycles for (*R*)-prophos. An identical but enantiomeric cycle obtains for (*S*)-prophos once it has been produced catalytically from the (*S,S*)-chiraphos catalyst.

## Experimental Section

All solvents used for hydrogenation were purified and deoxygenated before use. An example of a hydrogenation is given later in this section. The methods for the preparation of the amino acid precursors and the rotations of the purified *N*-acyl amino acids have been given previously.[6] All melting points are uncorrected. For optically active liquids, the observed rotations, $\alpha$, are quoted for a 10-cm cell. All other rotations, written $[\alpha]$ are specific rotations.

**(*S*)-(+)-1,2-Propanediol.** (*S*)-(+)-Lactic acid (Sigma) (33.4 g, 0.37 mol) in dry tetrahydrofuran (200 mL) was added dropwise to a stirred suspension of lithium aluminum hydride (32.1 g, 0.85 mol) in dry tetrahydrofuran (500 mL) at 0 °C over a period of 2 h. The mixture was allowed to warm to 25 °C and then was refluxed for 2 h. The resulting mixture was cooled and carefully quenched by the dropwise addition of water (32 mL) and then with 4 N NaOH (32 mL), and finally with water (96 mL). The now white precipitate was coagulated by refluxing the mixture for 0.5 h. It was filtered and was washed with tetrahydrofuran. The alumina cake was slurried and washed four times with hot tetrahydrofuran (450 mL). The combined filtrates were evaporated at 40 °C under reduced pressure and the residue was distilled using a vacuum jacketed Vigreux column to give 23.9 g (85%) of the pure (*S*)-(+)-1,2-propanediol as a colorless liquid: bp 78.5 °C, 10 mm (lit.[12] 94–96 °C, 14 mm); $\alpha^{25}_D$ +17.48° (neat) [lit.[12] $[\alpha]^{25}_D$ +15.84° (neat)].

**(*S*)-(−)-1,2-Propanediol Di-*p*-toluenesulfonate.** To an ice-cold solution of freshly recrystallized (from hexane) *p*-toluenesulfonyl chloride (134 g, 0.7 mol) in dry pyridine (135 mL) was added (*S*)-(+)-1,2-propanediol (23.6 g, 0.31 mol) in dry pyridine (30 mL) over a period of 0.5 h. The solution soon set to a solid mass and was allowed to stir at 25 °C for 18 h. Small portions of ice-water were added to the mixture and after each addition the contents were vigorously shaken. After a time, a solid formed. The product was poured into ice (600 mL) and concentrated HCl (12 M, 130 mL) and stirred for 1 h. The solid was collected and washed thoroughly with water. It was then dissolved in methylene chloride (400 mL) and the solution was first extracted with 0.5 N HCl (2 × 100 mL) and then with water (150 mL). The organic layer was separated and dried ($MgSO_4$) and the solvent was then removed under reduced pressure. On cooling, the resultant oil solidified. The solid was taken up in a minimum volume of methylene chloride, and cyclohexane was added to the cloud point at 40 °C. On standing at 25 °C, the solution began to deposit crystals. More cyclohexane was added after about 3 h at 25 °C, and the mixture was then held at 5 °C for 12 h. The white feathery crystals of the pure ditosylate were collected, washed with cyclohexane, and dried over $CaCl_2$ in vacuo. The yield was 114 g (95%): mp 62 °C; $[\alpha]^{25}_D$ −20.3° (1.15 in $CHCl_3$). Anal. Calcd for $C_{17}H_{20}O_6S_2$: C, 53.1; H, 5.2; S, 16.7. Found: C, 53.3; H, 5.1; S, 16.8.

**(*R*)-(+)-1,2-Bis(diphenylphosphino)propane [(*R*)-Prophos].** A solution of lithium diphenylphosphide (0.47 mol) was generated from lithium strips (6.52 g, 0.94 mol) and recrystallized triphenylphosphine (123 g, 0.47 mol) in dry tetrahydrofuran (300 mL), and the phenyl lithium was destroyed with *tert*-butyl chloride (43.7 g, 0.47 mol). The details of these reactions are given elsewhere.[6] The resulting deep orange-red solution was cooled to −4 °C, and a solution of (*S*)-(−)-1,2-propanediol di-*p*-toluenesulfonate (51.9 g, 0.134 mol) in dry tetrahydrofuran (75 mL) was added over a period of 45 min to the stirred phosphide solution. The cooling bath was then removed, and after the solution had reached room temperature it was stirred for a further 45 min. Deoxygenated water (250 mL) was then added, and most of the tetrahydrofuran was removed under reduced pressure. The resulting oily aqueous residue was extracted with ether (250 mL) under nitrogen. This initial ether extract was washed with water (100 mL). The aqueous reaction mixture was extracted two more times with ether (150 mL). The three ether extracts were combined and filtered (under $N_2$) into a vigorously stirred solution of $Ni(ClO_4)_2 \cdot 6H_2O$ (29.1 g, 0.08 mol) in absolute ethanol (250 mL). A yellow precipitate formed from a red supernatant liquor. The mixture was stirred as a saturated hot ethanolic solution of NaNCS (29 g) was added over a period of 30 min. A deep green-black solution formed together with a golden-brown precipitate. The solution was stirred for 12 h, and the solid was collected and washed thoroughly with ethanol and then with ether. The combined filtrates were set aside to give more of the diphosphine complex. The ultimate yield of the complex ranged from 45 to 55 g.

The nickel complex (22 g) was suspended in absolute ethanol (165 mL) under nitrogen, and to the stirred suspension at 25 °C was added dropwise NaCN (11 g) in water (55 mL) over a period of 15 min. The mixture first turned deep red and as more cyanide was added the color turned to a clear orange as an oil deposited. Water (400 mL) was then added, and the resultant mixture was extracted with ether (3 × 250 mL). The combined ether extracts were washed with water (5 × 200 mL) and then were clarified with brine (2 × 200 mL) and dried over $Na_2SO_4$. The ether was removed under reduced pressure, and the resulting oil was taken up in absolute ethanol at 50 °C under $N_2$. The solution was allowed to slowly cool to 25 °C and then was held at 5 °C for 24 h. The diphosphine (10 g) was collected and then was recrystallized from absolute ethanol (100 mL) to give 7.5 g of pure (*R*)-prophos as small colorless prisms. Further crystallization did not change the rotation: mp 68.5 °C (sealed tube under $N_2$); $[\alpha]^{26}_D$ +186.0° (1.0, acetone). Anal. Calcd for $C_{27}H_{26}P_2$: C, 78.6; H, 6.4; P, 15.0. Found: C, 78.9; H, 6.4; P, 14.8.

**[Rh((*R*)-prophos)(NBD)]$ClO_4 \cdot 0.5CH_2Cl_2$.** Freshly recrystallized $[Rh(NBD)_2]ClO_4$[6] (0.388 g, 1.00 mmol) and (*R*)-prophos (0.437 g, 1.106 mmol) were dissolved together in a mixture of methylene chloride (4 mL) and purified tetrahydrofuran (4 mL) under $N_2$. To this orange-red solution was added hexane (4 mL) dropwise. The solution was allowed to stand at 25 °C for 5 h and then at 5 °C for 12 h. The product was quickly filtered and washed with a minimum

volume of ice-cold tetrahydrofuran and then with hexane. The orange-red blocks (0.63 g) of the pure catalytic precursor were dried under a stream of dry $N_2$. The $0.5CH_2Cl_2$ of crystallization was confirmed by NMR. Anal. Calcd for $[Rh(C_{27}H_{26}P_2)(C_7H_8)]ClO_4 \cdot 0.5CH_2Cl_2$: C, 55.3; H, 4.7; P, 8.3; Cl, 9.5. Found: C, 55.4; H, 4.9; P, 8.3; Cl, 9.5.

**Ethyl α-Acetoxyacrylate.**[13] Ethyl pyruvate (58 g, 0.5 mol), acetic anhydride (102 g), and *p*-toluenesulfonic acid (0.5 g) were refluxed together under $N_2$ for 20 h. Fractional distillation under reduced pressure gave 40 to 50 g of the required enol acetate. This material tends to polymerize upon standing even at 5 °C under $N_2$. It was redistilled before use.

The literature[14] value of the specific rotation of (*S*)-(−)-ethyl *O*-acetyllactate is less than that of the optically pure material. The optically pure material was prepared as follows.

**(*S*)-(−)-Ethyl *O*-Acetyllactate.** Optically pure (*S*)-(+)-lactic acid (Sigma) (16.6 g, 0.18 mol) was dissolved in absolute ethanol (165 mL) and hexane (105 mL) together with concentrated sulfuric acid (0.2 mL). The mixture was refluxed for 30 h, and the distillate was continuously passed through a Soxhlet extractor containing $MgSO_4$. The acid was neutralized with solid $NaHCO_3$ (0.65 g), and then the solvents were carefully removed under reduced pressure. Distillation of the residue through a Vigreux column gave (*S*)-(−)-ethyl lactate (11.2 g): bp 47-48 °C at 10 mm; $\alpha^{25}_D$ −11.3° (neat).

(*S*)-(−)-Ethyl lactate (10.85 g, 0.092 mol) was dissolved in cold, dry pyridine (40 mL), and then acetic anhydride (10.6 g, 0.1 mol) was rapidly added to the cold reaction. The solution was allowed to stir at 25 °C for 12 h. The clear solution was poured into a mixture of crushed ice (~500 mL) and hydrochloric acid (35 mL, 12 N) with stirring. When the ice had melted, the mixture was extracted with ether (3 × 250 mL), and the combined ether extracts were first washed with hydrochloric acid (2 × 150 mL, 0.1 N), then with water (2 × 150 mL), and finally with brine (2 × 150 mL). The ether was dried ($MgSO_4$) and was removed under reduced pressure. The residue was fractionally distilled under reduced pressure to yield optically pure (*S*)-(−)-ethyl *O*-acetyllactate (12.3 g): bp 76 °C at 10 mm; $\alpha^{25}_D$ −53.26° (neat) [lit.[14] $[\alpha]_D$ −44.6° (neat)]; $[\alpha]^{25}_D$ −50.3° (0.99, $CHCl_3$) [lit.[14] $[\alpha]^{22}_D$ −47.6° (0.90, $CHCl_3$)].

**Breeder Cycle for (*R*)-Prophos. Hydrogenation of Ethyl α-Acetoxyacrylate.** To a sloping manifold hydrogenation apparatus was attached a 500-mL round-bottom, two-necked flask containing a magnetic stirrer, the catalytic precursor [Rh((*R*)-prophos)(NBD)]$ClO_4 \cdot 0.5CH_2Cl_2$ (0.15 g, 0.21 mmol), and a serum cap attached to one of the necks. The flask was purged of oxygen and filled with hydrogen at normal pressure. Dry, freshly distilled ($LiAlH_4$) and deoxygenated tetrahydrofuran (80 mL) was injected through the serum cap, and the mixture was stirred until all of the complex had dissolved to give a very pale-yellow solution. Freshly distilled ethyl α-acetoxyacrylate (10.7 g, 0.068 mol) was dissolved in dry, deoxygenated tetrahydrofuran (40 mL), and this was injected through the serum cap into the catalytic solution. The solution was stirred as hydrogen was absorbed. About 5–6 h were required to carry the reaction to completion.

When the reaction was complete, the solvent was carefully removed under reduced pressure, and the residue was distilled under reduced pressure to give pure (*S*)-(−)-ethyl *O*-acetyllactate, 9.9 g, 91%. It had an observed rotation of $\alpha^{25}_D$ −43.0° (neat) and was therefore 81% optically pure.

**(*S*)-(+)-1,2-Propanediol.** The above (81% optically pure) (*S*)-(−)-ethyl *O*-acetyllactate (26.4 g, 0.16 mol) in dry tetrahydrofuran (75 mL) was added dropwise to a stirred, cold (−4 °C) suspension of lithium aluminum hydride (10 g, 0.26 mol) in dry tetrahydrofuran (150 mL) over a period of 1 h. The resulting mixture was allowed to warm to 25 °C and then was refluxed for 1 h. The mixture was then cooled in ice and vigorously stirred as the reaction was quenched by the dropwise addition of water (10 mL), then with 4 N NaOH (10 mL), and finally with water (30 mL). The alumina cake was thoroughly extracted with hot tetrahydrofuran as described for the reduction of lactic acid. There was obtained upon distillation 10.8 g (89%) of (*S*)-(+)-propanediol which had an observed rotation of $\alpha^{25}_D$ +14.0° (neat) and was therefore 80% optically pure.

**(*S*)-(−)-1,2-Propanediol Di-*p*-toluenesulfonate.** Using the above (80% optically pure) (*S*)-(−)-1,2-propanediol and employing the same procedure, excluding the recrystallization as described for the optically pure diol, there was obtained a nearly quantitative yield of crystalline *S*-(−)-1,2-propanediol di-*p*-toluenesulfonate which also was 80% optically pure. It was obtained optically pure as follows.

The optically impure (*S*)-(−)-1,2-propanediol di-*p*-toluenesulfonate (10 g) was dissolved in methylene chloride (40 mL), and the solution was carefully diluted with cyclohexane (300 mL) at 40 °C. The solution was allowed to stand at room temperature for 1 h or until crystals began to form. (Crystallization is aided by adding seed crystals of the optically pure material.) The mixture was then put aside at 5 °C for 12 h. More cyclohexane (100 mL) was then added, and the mixture was allowed to stand at 5 °C for a further 12 h. The optically pure (*S*)-(−)-1,2-propanediol di-*p*-toluenesulfonate deposited as white feathery needles, which were collected and washed with cyclohexane. The yield was 7.1 g of optically pure material: $[\alpha]^{25}_D$ −20.3 (1.15 in $CHCl_3$). This material produces (*R*)-prophos.

**Preparation of (*S*)-Prophos.** An identical procedure to that just described for the breeding of (*R*)-prophos was used for the production of (*S*)-prophos, except that ethyl α-acetoxyacrylate was reduced using the catalytic precursor [Rh((*S,S*)-chiraphos)(NBD)]$ClO_4$.[6] The (*R*)-(+)-ethyl *O*-acetyllactate so produced was 84% optically pure [$\alpha^{25}_D$ +44.55° (neat)].

**Reduction of the (*Z*)-α-Acylaminoacrylic Acids.** The method of hydrogenation of these substrates was the same as that just described for ethyl α-acetoxyacrylate except that, on completion of the hydrogenation, ion-exchange resin ($H^+$ form) was added to remove the catalyst. The subsequent steps are described in detail elsewhere.[6] The resin in exchanging the catalyst releases an equivalent of acid, and with alcohols esterification tends to occur when the alcohol is pumped off. This can be suppressed by using 95% EtOH in the workup.

**Acknowledgments.** This work was supported by the National Research Council of Canada. We thank N. C. Payne for communicating crystallographic information before publication.

## References and Notes

(1) L. Horner, H. Siegel, and H. Büthe, *Angew. Chem., Int. Ed. Engl.*, **7**, 941 (1968); W. S. Knowles and M. J. Sabacky, *Chem. Commun.*, 1445 (1968); W. S. Knowles, M. J. Sabacky, and B. D. Vineyard, *ibid.*, 10 (1972); J. D. Morrison, R. E. Burnett, A. M. Aquiar, C. J. Morrow, and C. Phillips, *J. Am. Chem. Soc.*, **93**, 1301 (1971); W. S. Knowles, M. J. Sabacky, and B. D. Vineyard, *CHEMTECH*, 590 (1972); G. Pracejus and H. Pracejus, *Tetrahedron Lett.*, 3497 (1977); C. Fisher and H. S. Mosher, *Tetrahedron Lett.*, 2487 (1977); W. C. Cullen and E.-S. Yeh, *J. Organomet. Chem.*, **139**, C13 (1977).
(2) H. B. Kagan and T.-P. Dang, *J. Am. Chem. Soc.*, **94**, 6429 (1972); M. Tanaka and I. Ogata, *J. Chem. Soc., Chem. Commun.*, 735 (1975); T.-P. Dang, J. C. Poulin, and H. B. Kagan, *J. Organomet. Chem.*, **91**, 105 (1975); K. Achiwa, *J. Am. Chem. Soc.*, **98**, 8265 (1976); K. Achiwa, *Tetrahedron Lett.*, 3735 (1977); I. Ojima, T. Kogure, and K. Achiwa, *J. Chem. Soc., Chem. Commun.*, 428 (1977); T. Hayashi, M. Tanaka, and I. Ogata, *Tetrahedron Lett.*, 295 (1977).
(3) H. Boucher and B. Bosnich, *J. Am. Chem. Soc.*, **99**, 6253 (1977).
(4) T. Hayashi, T. Mise, S. Mitachi, K. Yamamoto, and M. K. Kumada, *Tetrahedron Lett.*, 1133 (1976); T. Hayashi, T. Mise, and M. Kumada, *ibid.*, 4351 (1976).
(5) B. D. Vineyard, W. S. Knowles, M. J. Sabacky, G. L. Bachman, and D. J. Weinkauff, *J. Am. Chem. Soc.*, **99**, 5946 (1977).
(6) M. D. Fryzuk and B. Bosnich, *J. Am. Chem. Soc.*, **99**, 6262 (1977).
(7) N. C. Payne, personal communication.
(8) Y. S. Rao and R. Filler, *Synthesis*, 749 (1975), and references cited therein.
(9) For kinetic evidence of the nature of the catalytic species, see, J. Halpern, D. P. Riley, A. S. C. Chan, and J. J. Pluth, *J. Am. Chem. Soc.*, **99**, 8055 (1977).
(10) L. J. DeHayes and D. H. Busch, *Inorg. Chem.*, **12**, 1505 (1973).
(11) A. I. Meyers, G. Knaus, K. Kamata, and M. E. Ford, *J. Am. Chem. Soc.*, **98**, 567 (1976).
(12) C. Melchiorre, *Chem. Ind. (London)*, 218 (1976).
(13) J. Monnin, *Helv. Chim. Acta*, **39**, 172 (1956).
(14) S. G. Cohen, J. Crossley, E. Khedouri, R. Zand, and L. H. Lee, *J. Am. Chem. Soc.*, **85**, 1685 (1963).