more easily (+0.32 V compared to +0.55 V) and rapidly oxidized than the corresponding aquo complex. The band which causes the blue color is at shorter wavelength for the ammine (585 nm compared to 605 nm). Incomplete studies of a series of blue ruthenium chloride complexes suggest that there is a good correlation between the basicity of the terminal ligands and the wavelength of the maximum of this band. The nature of this transition is not known, but this correlation suggests that it may involve the d electrons which are of π symmetry in octahedral complexes. In the dimeric complexes these electrons are very likely to be involved in metal–metal bonding.

With both the ammine and aquo complexes, oxidation beyond the ruthenium(III) state apparently results in disruption of the coordination sphere. The most striking difference in the two complexes occurs in the reaction leading to their formation. When HCl is added to $Ru(H_2O)_6^{2+}$ no hydrogen is evolved. However, after a few hours a ruthenium mirror is deposited on the walls of the reaction vessel. Apparently this reaction proceeds by a disproportionation, while hydrogen ion is the oxidizing agent in producing $Ru_2Cl_3(NH_3)_6^{2+}$ from hexaammineruthenium(II).

Acknowledgments. The authors express their thanks to the U. S. Atomic Energy Commission for financial support which made this study possible. We also thank Dr. T. J. Meyer for suggesting that the blue chloroammines may be related to the aquo complexes which we were studying.

Asymmetric Catalytic Reduction with Transition Metal Complexes. I. A Catalytic System of Rhodium(I) with (−)-2,3-*O*-Isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane, a New Chiral Diphosphine

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Abstract: The catalytic system (−)-(diop)–Rh(I) (diop = 2,3-*O*-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane (**7**)) is described and is used for an extensive study of the hydrogenation of various precursors of alanine, phenylalanine, tyrosine, Dopa, and leucine. Optical yields in the range of 70–80% are obtained in the reduction of β-substituted α-acetamidoacrylic acids. The presence of a carboxyl group is found not to be absolutely necessary for good optical yield. The favorable effect of the enamide function on the catalytic process is deduced from comparisons of the rates of hydrogenation of atropic and acetamidocinnamic acids, from the optical yields obtained in the reduction of different precursors of phenylalanine, and from the high optical yield (78%) obtained in the hydrogenation of the enamide **12**, a compound having no carboxyl groups.

The use of asymmetric catalytic systems for the preparation of optically active compounds is a promising method, enabling one to avoid the manipulation of large quantities of optically active material (as resolving agents or chiral reactants). Several reports of asymmetric heterogeneous catalysis have appeared in the literature.[1,2] The best optical yield, about 50%, was obtained in the reduction of ethyl acetoacetate using Raney Nickel modified by (+)-2-metyltartaric acid; the results, however, are difficult to reproduce.[2]

A more rational approach to the problem of asymmetric synthesis consists in the use of transition-metal complexes as homogeneous catalysts, for steric and electronic effects can be introduced by modification of the ligands in the complex. Our requirements for a catalyst system applicable to a wide range of substrates and having a fairly well-known mechanism lead us to investigate the homogeneous catalytic reduction of olefins using rhodium complexes with phosphines as ligands.[3–5] Wilkinson has extensively studied this system, using the catalyst precursor $[P(C_6H_5)_3]_3RhCl$, and has proposed[3] a mechanism involving the catalytic species **1** (L = $P(C_6H_5)_3$). Internal hydrogen transfer onto the olefinic double bond gives rise to the alkane. The transfer is stereospecific (cis addition) but is a stepwise mechanism passing through an alkyl–rhodium complex.[6,7]

One can make the observation that the rhodium atom is asymmetric in **1**, **1a** and **1b** being enantiomers. In the general case where ligands around the rhodium atom are achiral, there is necessarily hydrogen transfer

(1) E. I. Klabunovski and E. S. Levitina, *Russ. Chem. Rev.*, **39**, 1035 (1970).

(2) Y. Izumi, M. Imaida, F. Fukowa, and S. Akabori, *Bull. Chem. Soc. Jap.*, **36**, 155 (1963); Y. Izumi, S. Tatsumi, N. Imaida, Y. Fukuda, and S. Akabori, *ibid.*, **39**, 361 (1966).

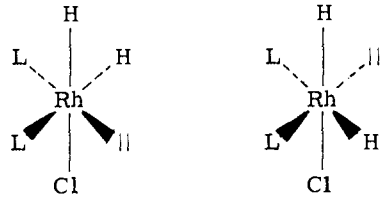
(3) J. A. Osborn, F. J. Jardine, J. F. Young, and G. Wilkinson, *J. Chem. Soc.*, 1711 (1966); S. Montelatici, A. van der Ent, J. A. Osborn, and G. Wilkinson, *J. Chem. Soc. A*, 1954 (1968).

(4) R. Stern, Y. Chevallier, and L. Sajus, *C. R. Acad. Sci., Ser. C*, **264**, 1970 (1967).

(5) J. E. Lyons, L. E. Rennick, and J. L. Burneister, *Ind. Eng. Chem., Prod. Res. Dev.*, **9**, 2 (1970).

(6) J. F. Biellmann and M. J. Jung, *J. Amer. Chem. Soc.*, **90**, 1673 (1968).

(7) A. S. Hussey and Y. Takeuchi, *ibid.*, **91**, 672 (1969); *J. Org. Chem.*, **35**, 643 (1970).



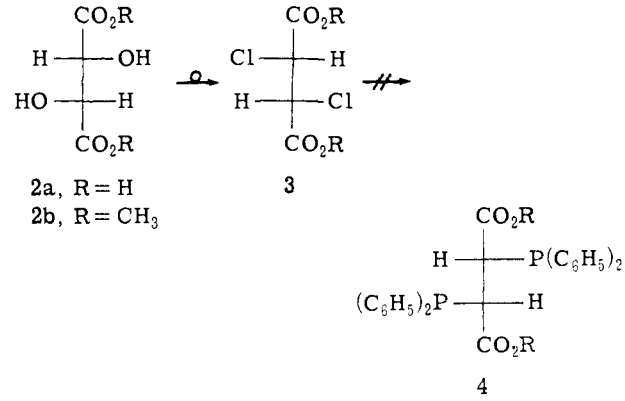
1a 1b

onto a prochiral olefin and since it was out of the question to resolve complexes like **1**, we chose to introduce an external element of asymmetry into the complex, a simple method being to use chiral ligands L.

Several reports of reactions involving chiral phosphines with asymmetric phosphorus atoms have appeared in the literature.[8,9] An optical yield of 28% was obtained in the reduction of atropic acid.[8] Investigations with phosphines whose chirality is due to asymmetric centers in groups bonded to the phosphorus atom have also been published. The best result (optical yield 61%) has recently been the subject of a communication by Morrison[10] and concerns the reduction of α-methylcinnamic acid using a Rh(I)–(diphenylneomenthylphosphine) catalyst system. Modest optical yields have also been obtained in reduction[11] using optically active aminophosphines easily obtainable from asymmetric amines. In a preliminary communication,[12] we demonstrated the usefulness of (chiral diphosphine)-Rh(I) systems. Here, we wish to report detailed results and the generalization of the method. A high degree of stereoselectivity in asymmetric catalysis requires catalysts which exhibit the following properties. (1) The ligand conformations must have maximum rigidity. (2) In order to avoid epimerization equilibria, ligands must stay firmly bonded to the metal.[13] Owing to their chelation power, diphosphines fulfill both these conditions. In addition, we wanted to avoid the possibility of geometric isomerism about the rhodium and thus chose a diphosphine having two equivalent phosphorus atoms. An easily accessible natural product, L(+)-tartaric acid **2a**,[14] was chosen as the starting material.

Treatment of the dichloro ester **3** (Scheme I) by a method similar to that used by Issleib and Thomas[15] for phosphine esters did not lead to any stereospecificity in the substitution, whatever the nucleophile used [$HP(C_6H_5)_2$, $(C_6H_5)_2P^-$], the diphosphine **4** being isolated optically inactive in the form of phosphine oxide. We then turned our attention to the diphosphines **7** and **8** which would form a seven-membered ring of chelation with a rhodium atom. We may draw attention to the important difference between the diphosphine **7** and its open-chain analog **8**, namely, the greater rigidity of **7**, due to the transconfiguration of the dioxolan ring

Scheme I



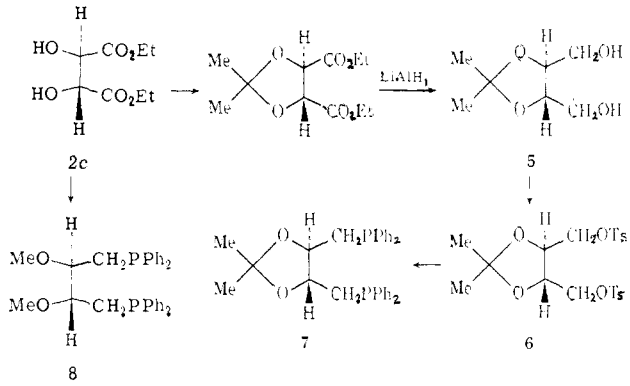
2a, R = H
2b, R = CH_3

3

4

with respect to the seven-membered chelating ring. The levorotatory enantiomer of **7** was prepared from (−)-tartaric ester **2c** as outlined in Scheme II. Tosylates

Scheme II



2c 5 6 7 8

are used as conveniently as halides in the reaction with sodium diphenylphosphide. The diphosphine **7** ((−)-diop) is a solid, mp 88–89°, $[\alpha]^{22}D$ −12.3° (*c* 4.57, C_6H_6), which is easily purified by crystallization and is quite stable toward air oxidation. The dimethoxyphosphine **8** was obtained by similar methods, but does not crystallize and is difficult to purify. All experiments described in this paper were performed with a catalytic rhodium system incorporating (−)-diop as the ligand.

Preparation of the Catalyst. The optically active Rh(I) complex was prepared *in situ* by the following displacement reaction, similar to that used in the case of monophosphines.[3,16a] Few studies have been carried

$$[RhCl(cyclooctene)_2]_2 + 2(-)\text{-diop} + 2S \longrightarrow 2RhCl[(-)\text{-diop}]S + 4\ \text{cyclooctene}$$

9, S = benzene (solvent)

out on Wilkinson-type catalysts incorporating diphosphine.[16b] In our laboratories we found that **9**, under a hydrogen atmosphere, forms an efficient homogeneous catalyst for the reduction of many unsaturated sub-

(8) W. S. Knowles and M. J. Sabacky, *Chem. Commun.*, 1445 (1968); W. S. Knowles, M. J. Sabacky, and B. D. Vineyard, *Ann. N. Y. Acad. Sci.*, **172**, 232 (1970).

(9) L. Horner, H. Siegel, and H. Buthe, *Angew. Chem. Int. Ed. Engl.*, 7, 941 (1968).

(10) J. D. Morrison, R. E. Burnett, A. M. Agniar, C. J. Morrow, and C. Phillips, *J. Amer. Chem. Soc.*, **93**, 1301 (1971).

(11) T. P. Dang and H. B. Kagan, unpublished results.

(12) T. P. Dang and H. B. Kagan, *Chem. Commun.*, 481 (1971); patents pending.

(13) H. Brunner, *Angew. Chem., Int. Ed. Engl.*, 10, 249 (1971).

(14) D(−)-Tartaric acid is also commercially available. As shown in this paper, (−)-diop prepared from L(+)-tartaric acid gives rise to the unnatural *R* or D amino acids, whereas (+)-diop prepared from D(−)-tartaric acid gives the natural *S* or L series.

(15) K. Issleib and G. Thomas, *Chem. Ber.*, **93**, 803 (1960).

(16) (a) If $[Rh(ethylene)_2Cl]_2$ is used in the place of $[Rh(cyclooctene)_2Cl]$, the same results are obtained. When diop is added to a benzene solution of $[Rh(ethylene)_2Cl]_2$ under argon, an evolution of gas is noticed and can be measured; it corresponds to the theoretical amount of displaced ethylene. For this reason the diphosphine–rhodium complex generated in benzene is formulated as indicated and not as $[Rh(cyclooctene)_2diop]^+Cl^-$. Nevertheless, whatever the starting diphosphine–rhodium complex may be, the catalytic species in polar solvent and under hydrogen could be of a cationic type, as suggested by Knowles, *et al.*[17] (b) Y. Chevallier, Docteur-Ingénieur Thesis, Paris, 1970, reprint available from Technip editor (Paris).

(17) W. S. Knowles, M. J. Sabacky, and B. D. Vineyard, *Chem. Commun.*, 10 (1972).

strates. Results of some semiquantitative comparisons with the classical Wilkinson catalyst ($Rh[P(C_6H_5)_3]_3Cl$) are set out in Table I.

Table I. Catalytic Hydrogenation of α-Acetamidocinnamic Acid (**10**)[a]

Phosphine	Ratio P/Rh	Rate,[b] ml of H_2/min	Half-time of hydrogenation, min
7	2.2[c]	3.7	20
7	4.4[d]	0	
$P(C_6H_5)_3$	3[e]	0.42[g]	172
$P(C_6H_5)_3$	2[f]	0.43[g]	176

[a] [Rh] = 3 m*M*; ratio [**10**]/Rh = 100; solvent = C_6H_6–EtOH (1:2), 20 ml; P_{H_2} = 1.1 atm; room temperature. [b] Maximum observed rate. [c] Ratio **7**/Rh = 1.1. [d] Ratio **7**/Rh = 2.2. [e] Catalyst = $RhCl[P(C_6H_5)_3]_3$. [f] Catalytic system = $[RhCl(cyclooctene)_2]_2 + P(C_6H_5)_3$. [g] The maximum rate is obtained at about one-third hydrogenation.

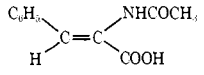
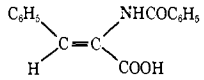
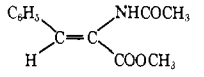
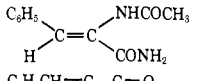
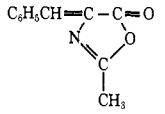
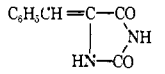
venting simultaneous coordination of the olefin and hydrogen.

The optical induction in the catalytic reduction was first studied using atropic acid, $C_6H_5(COOH)C{=}CH_2$, as the substrate. The highest optical yield (64%) was observed[12] when some triethylamine was added to the medium. The reduction of various types of unsaturated acids and derivatives is under active investigation and will be the subject of a forthcoming publication. Here we report only the reduction of α-*N*-acylaminoacrylic acids and their derivatives leading to the important class of α-amino acids.

Asymmetric Reduction of α-*N*-Acylaminoacrylic Acids

In order to determine the best class of compounds for the study, an investigation into the reduction of several precursors of phenylalanine, using our catalyst, was carried out. Results are reported in Table II. Under atmospheric pressure and at room temperature, 2-methyl-4-benzal-5-oxazolone and benzalhydantoin were

Table II. Catalytic Hydrogenation of Some Precursors of Phenylalanine[a]

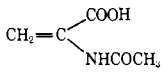
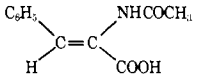
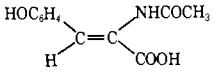
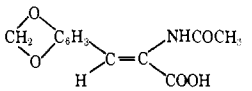
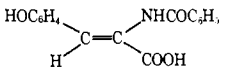
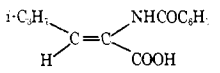
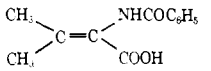
Substrate	Substrate/Rh	Isolated product; chemical yield, %	[α]D, deg	Optical yield, %[e]
	540[b]	*N*-Acetyl-(*R*)-phenylalanine; 95	−37.75 (EtOH)	72
	30[c]	*N*-Acetyl-(*R*)-phenylalanine; 96	−36.8 (EtOH)	70
	30	*N*-Acetyl-(*R*)-phenylalanine; 80	−37.5 (EtOH)	72
	100[d]	*N*-Acetyl-(*R*)-phenylalanine; 86	−36.5 (EtOH)	70
	200	*N*-Benzoyl-(*R*)-phenylalanine; 96	−12.78 (0.4 *N* NaOH)	64
	150	*N*-Acetyl-(*R*)-phenylalanine methyl ester; 90	−11.79 (MeOH)	55
	75	*N*-Acetyl-(*R*)-phenylalaninamide; 72	−19.0 (MeOH)	71
		No hydrogenation		
		No hydrogenation		

[a] [Rh] = 2–5 m*M*; solvent = EtOH–C_6H_6 (2:1); P_{H_2} = 1.1 atm; room temperature unless otherwise stated. [b] [Rh] = 1 m*M*; EtOH–C_6H_6 (4:1). [c] In presence of Et_3N; ratio Et_3N/Rh = 3. [d] At 50°. [e] Optical yields are calculated with respect to the following values for the optically pure compounds: *N*-acetyl-(*R*)-phenylalanine, $[\alpha]^{26}D$ −51.8 (*c* 1, EtOH) (F. Knoop and J. G. Blanco, *Z. Phys. Chem.*, **146**, 272 (1925); V. du Vigneaud and O. J. Irish, *J. Biol. Chem.*, **122**, 360 (1938)); *N*-acetyl-(*S*)-phenylalanine methyl ester, $[\alpha]^{25}D$ +21.4 (*c* 1.9, MeOH) (B. Zerner, R. P. M. Bond, and M. L. Bender, *J. Amer. Chem. Soc.*, **86**, 3674 (1964)); *N*-benzoyl-(*R*)-phenylalanine, $[\alpha]^{24.5}D$ −19.8° (*c* 8.8, 0.4 *N* NaOH) (W. A. Schuller and C. Niemann, *ibid.*, **73**, 1644 (1951)); *N*-acetyl-(*R*)-phenylalaninamide, $[\alpha]^{28}D$ −26.5° (*c* 1, MeOH) (M. L. Bender, G. E. Clement, F. J. Kezdy, and H. D'A. Heck, *ibid.*, **86**, 3681 (1964)).

Our standard conditions were a 3 m*M* solution of catalyst at room temperature under atmospheric pressure. Our catalyst system proved to be much more efficient than the Wilkinson catalyst for the hydrogenation of α-acetamidocinnamic acid. Using a diphosphine to Rh ratio of greater than 2 no catalytic activity was observed, probably due to the formation of the complex $[Rh(-)\text{-diop}_2]^+Cl^-$. $[Rh(diphos)_2]^+Cl^-$ (diphos = bis(diphenylphosphino)ethane) shows no catalytic activity for the hydrogenation of ethylenic compounds.[16b] In these complexes the two diphosphine molecules are strongly bound to the rhodium, prenot reduced. However, the catalyst was not poisoned and was still active for the hydrogenation of other substrates such as α-acetamidocinnamic acid. Other precursors of phenylalanine studied were α-acyl derivatives of cinnamic acid or their esters. These compounds were prepared from aldehydes and acylated glycines *via* the azlactone derivatives using the Erlenmeyer synthesis. Hydrogenation of α-benzamidocinnamic acid gave a lower optical yield than α-acetamidocinnamic acid **10**.

The optical yield of the hydrogenation of the latter, **10**, did not change significantly when triethylamine was

Table III. Hydrogenation of Dehydro *N*-Acylamino Acids

Substrate	Substrate/Rh	Product; yield, %	[α]D of the product, deg	Optical yield, %
	150	*N*-Acetyl-(*R*)-alanine; 96	+46.8 (H_2O)	73
	540	*N*-Acetyl-(*R*)-phenylalanine; 95	−37.7 (EtOH)	72
	100	*N*-Acetyl-(*R*)-tyrosine; 92	−38.9 (H_2O)	80
	50	*N*-Acetyl-3,4-methylenedioxy-(*R*)-phenylalanine; 97	−42.2 (EtOH)	79
	80	*N*-Benzoyl-(*R*)-tyrosine; 95	−12.2 (NaOH 0.3*N*)	62
	75	*N*-Benzoyl-(*R*)-leucine; 98	−2.37 (EtOH)	22
		No hydrogenation		

[a] [Rh] = 3 m*M*; P = 1.1 atm; room temperature. [b] Optical yields are calculated with respect to the following values for the optically pure compounds: *N*-acetyl-(*R*)-alanine, [α]D +66.5° (*c* 2, H_2O) (S. M. Birbaum, L. Levintow, R. B. Kingsley, and J. P. Greenstein, *J. Biol. Chem.*, **194**, 455 (1952)); *N*-acetyl-(*R*)-tyrosine, [α]D +48.3° (H_2O) (J. P. Greenstein and M. Winitz, "Chemistry of the Amino Acid," Wiley, New York, N. Y., 1961, p 2365); *N*-acetyl-3,4-methylenedioxy-(*R*)-phenylalanine, $[\alpha]^{18}D$ −53.4° (*c* 1.8, EtOH) (S. Yamada, T. Fujii, and T. Shiori, *Chem. Pharm. Bull.*, **10**, 680 (1962); *N*-benzoyl-(*R*)-tyrosine, $[\alpha]^{20}D$ −19.6° (*c* 8, 0.4 *N* NaOH) (E. Fischer, *Ber.*, **32**, 3638 (1899)); *N*-benzoylleucine, $[\alpha]^{20}D$ −10.8° (*c* 2.5, EtOH) (P. Karrer, *Helv. Chim. Acta*, **13**, 50 (1930)).

added to the system. Hydrogenation of α-acetamidocinnamic amide gives practically the same optical yield as with the acid **10**. Although the hydrogenation of methyl α-acetamidocinnamate gave *N*-acetyl-(*R*)-phenylalanine methyl ester of lower optical purity than that of the acid **10**, the optical yield was still quite high.

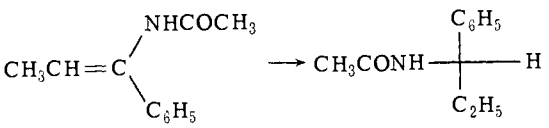
These phenomena differ from those reported previously[5,12] for the hydrogenation of other ethylenic acids, where the absence of triethylamine or esterification led to a drastic reduction in the optical purity of the products. Hydrogenation of **10** using ratios of **10**/Rh of 30 and 540 gave rise to *N*-acetylphenylalanine having the same optical purity, showing that the relative concentration of the catalyst has no influence on the stereoselectivity of the asymmetric reduction. A very slight temperature dependence for the hydrogenation may be deduced from the experiment carried out at 50°.

Our results show that the most advantageous optical yields of amino acids can be obtained using β-substituted α-acetamidoacrylic acids. However, in some cases, due to their more facile availability, studies were carried out on α-benzamidoacrylic acids. Results are reported in Table III.

Dehydro-*N*-benzoylvaline was not reduced under our standard conditions, this observation being consistent with the fact that no examples of the reduction of tetrasubstituted ethylenic compounds with the Wilkinson catalyst have been reported in the literature. All the α-acetamidoacrylic acids were hydrogenated with optical yields higher than 70%.

Several points of interest arise from this study. Amino acids of high optical purity may be conveniently obtained by this method since the optical purity of the N-acylated amino acids is often easily increased by crystallization. For example, the crude *N*-acetylphenylalanine of optical purity 72% provided after one recrystallization from ether an optical purity of 88% (chemical yield 66% with respect to the unsaturated precursor *N*-acetyl-α-aminocinnamic acid). It may be noted that the optical yield (79%) obtained in the asymmetric synthesis of 3,4-methylenedioxy-*N*-acetylphenylalanine is of special interest for the preparation of optically active Dopa.

Under the same experimental conditions, the trisubstituted α-acetamidocinnamic acid **10** is hydrogenated 17 times faster than the disubstituted atropic acid **11**. The free carboxylic group in **10** seems not to be crucial for a high optical yield, as the methyl ester or the amide of **10** also gives a good result. The favorable influence of the enamide function on the steric course of the reaction may arise through labile coordination with the metal and, indeed, would appear to be of a general character since the enamide **12**,[18a] although lacking a carboxylic function, was reduced to (*S*)-*N*-acetylamino-1-phenyl-1-propane (**13**)[18b] (optical purity 78%; yield 95%). This result opens a new approach toward the asymmetric synthesis of chiral amines.

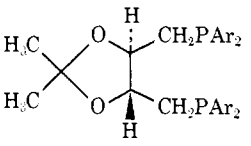


12 13

Investigations into the use of diphosphines structurally similar to diop are now being carried out. For example, the use of the diphosphine **14** in the hydrogenation of α-acetamidocinnamic acid **10** gives *N*-acetyl-(*R*)-phenylalanine with an optical yield of 39%. A report of optical yields of up to 90% being ob-

(18) (a) Y. H. Suen, A. Horeau, and H. B. Kagan, *Bull. Soc. Chim. Fr.*, 1454 (1965); (b) A. La Manna, V. Ghislandi, O. B. Hulbert, and O. M. Scopes, *Farmaco, Ed. Sci.*, **22**, 1037 (1967).

tained with monophosphines having chirality on the phosphorus has recently been published.[17] It would be of interest to ascertain the effect on the asymmetric induction of modification of the substituents on the phosphorus atoms of diop.



14. Ar = 2,5-$(CH_3)_2C_6H_3$

Experimental Section

General. A conventional apparatus for hydrogenation under atmospheric pressure was used. The hydrogenation flask was stoppered by a serum cap allowing addition of liquids by injection with syringes. Optical rotations were measured in a thermostated 1-dm cell with a Perkin-Elmer 141 polarimeter. Nmr spectra were recorded on a Jeolco 60 spectrometer using internal tetramethylsilane as reference.

Chemicals and Solvents. α-Acetamidocinnamic acid (mp 194–195°) and α-acetamidoacrylic acid (mp 194°) were purchased from Fluka and used as received. 2-Methyl-4-benzal-5-oxazolone,[19] α-benzamidocinnamic acid,[20] methyl α-acetamidocinnamate,[21] α-acetamidocinnamic acid,[22] α-acetamido-4-hydroxycinnamic acid,[23] α-acetamido-3,4-methylenedioxycinnamic acid,[24] α-benzamido-4-hydroxycinnamic acid,[25] β-isopropyl-α-benzamidoacrylic acid,[26] enamide **12**[18a] (unknown stereochemistry), β,β-dimethyl-α-acetamidoacrylic acid,[27] and benzalhydantoin[28] were prepared according to the procedures described in the cited literature. Solvents for hydrogenation were prepared as follows: benzene was purified by passing through a basic alumina column, followed by distillation over sodium hydride; absolute ethanol was distilled over sodium diethyl phthalate and was stored under argon; $[RhCl(cyclooctene)_2]_2$ was prepared as previously described;[29,30] dimethyl dichlorosuccinate $(CHClCOOCH_3)_2$ was prepared according to the method of Darzens and Sejourne,[31] mp 62°, $[\alpha]^{32}D$ −71.5° (*c* 7.4, $CHCl_3$).

Reaction of (D)$(CHClCOOCH_3)_2$ with $P(C_6H_5)_2K$. This reaction was carried out in dioxane. An optically inactive product, mp 236°, was obtained in low yield (20–30%) and proved to be the diphosphine dioxide: nmr ($CDCl_3$) τ 7.05 (s, CH_3), 5.22 (d, J_{HOP} = 5.5 Hz, CH).

Anal. Calcd for $C_{30}H_{28}O_6P_2$: C, 65.99; H, 5.13. Found: C, 65.68; H, 5.23.

Diethyl 2,3-*O*-Isopropylidene-L-tartrate and 2,3-*O*-Isopropylidene-L-threitol (5). These compounds were prepared by the method of Feit.[32]

1,4-Ditosyl-2,3-*O*-isopropylidene-L-threitol (6). This compound was prepared following the procedure of Carmack and Kelley:[33] mp 92°; $[\alpha]^{32}D$ −12.1° (*c* 4.4, $CHCl_3$) (lit.[22] $[\alpha]^{34}D$ −12.4° (*c* 5, $CHCl_3$).

Reaction of 6 with $P(C_6H_5)_2Na$. $P(C_6H_5)_2Na$ was prepared using a modified method of Issleib and Muller.[34] A solution containing 0.12 mol of $P(C_6H_5)_2Cl$ in 150 ml of dioxane was refluxed under an inert atmosphere with 0.5 mol of sodium for 7 hr with strong mechanical stirring. The yellow reaction mixture was allowed to cool to room temperature, whereupon 100 ml of anhydrous THF was added. Ditosylate **6** (0.045 mol) in 50 ml of THF was added dropwise, and the mixture was stirred for a further 2 hr and filtered. The precipitate was washed with benzene and the filtrate and washings were combined and evaporated to dryness under reduced pressure. The residue was taken up in 60 ml of ethanol and allowed to stand in a refrigerator. After a few hours a solid precipitated from the solution and was filtered, washed with a little ethanol, and dried under vacuum. The crude diphosphine was recrystallized twice from ethanol affording 10.6 g (48%) of pure **7**. Tlc on silica gel using acetone–hexane as eluent was used to ascertain the purity of the product: mp 88–89°; nmr ($CDCl_3$) τ 8.65 (s, $C(CH_3)_2$), 7.61 (d, *J* = 5.5 Hz, CH_2), 6.08 (q, CH), 2.73 (aromatic).

Anal. Calcd for $C_{31}H_{32}O_2P_2$: C, 74.70; H, 6.47; P, 12.43. Found: C, 74.50; H, 6.65; P, 12.46.

Diphosphine 14 was prepared from sodium di(2,5-dimethylphenyl)phosphide and the ditosylate **6** by the same procedure as described above for diop: mp 121–122°; $[\alpha]^{25}D$ −18.9° (*c* 1.6, C_6H_6).

Anal. Calcd for $C_{35}H_{40}O_2P_2$: C, 76.70; H, 7.92; P, 10.14. Found: C, 76.70; H, 7.99; P, 10.14.

Preparation of the Catalytic Solution. To a benzene solution of $[RhCl(cyclooctene)_2]_2$ under argon was added the diphosphine (stored in a capsule). The solution was stirred for 15 min and was introduced into the hydrogenation flask by means of a syringe. Any contact with air was avoided.

The order of addition of reactants into the hydrogenation flask was substrate, hydrogen, ethanol, catalyst solution.

Work-up of the Hydrogenation Product. The solution was evaporated to dryness and one of the following procedures was used to isolate the hydrogenation product. A. For *N*-acetylalanine and *N*-acetyltyrosine, the residue was dissolved in water and separated from the insoluble catalyst by filtration. Evaporation to dryness afforded the product. B. For *N*-acetylphenylalaninamide, *N*-acetylphenylalanine methyl ester, and *N*-acetylamino-1-phenyl-1-propane (**13**), the product was isolated by tlc on silica gel; the eluents were acetone–methanol for *N*-acetylphenylalaninamide and ethyl acetate–hexane for the two other compounds. C. For other *N*-acylamino acids the residue was dissolved in 0.5 *N* NaOH and separated from the insoluble catalyst by filtration. The filtrate was acidified with dilute HCl, extracted with ether, and washed with a little water. The ethereal phase was dried over sodium sulfate and evaporated to dryness.

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