that systems like the one reported here provide in some sense better "resolution". In addition, they allow direct measurement of their precursor equilibria and study of the competition between intramolecular and outer-sphere paths (eq 5). Both in intra- and intermolecular electron transfer across bridging ligands, the presence of the second metal ion, which acts as the sink for the electron, smooths out differences and gives similar rate laws, products, etc. In our system this leveling-off effect is missing. As a result systems differing only, e.g., by one electron, or by one functional group not participating directly in the reaction (e.g., methyl and phenyl groups in pyruvic and phenylglyoxylic acids, respectively), may show not merely a difference in rate and activation parameters, but a more dramatic difference in the rate law itself, the products obtained, the salient features of the mechanism, etc.

Comparing now pyruvic to phenylglyoxylic acid we observe that in the first intramolecular electron transfer is unambiguously distinguished from but is in competition with an outer-sphere path (eq 5). With phenylglyoxylic acid the outer-sphere path does not compete effectively anymore. The presence of the electron attracting phenyl ring presumably makes the metal-to-ligand transfer more effective. Related to this enhanced effectiveness is also the fact that only one phenylglyoxylic acid ligand is enough to attract the electron away from vanadous, whereas one pyruvato ligand cannot do the job. Substitution of one water molecule by one pyruvate ion in the coordination sphere of V(II) may increase the reducing ability of this ion and thus render the transfer of the electron to a second pyruvato ligand possible.

In reactions 3 and 2a the transfer of the electron causes labilization of the metal ion center, which facilitates the release (and subsequent dimerization) of the free radical. In this respect our system is the opposite to Taube's classical system $Cr^{II} \rightarrow Cr^{III}$, and it is perhaps relevant that in the reduction of pyruvic acid by chromous ion we did not observe[2] a free-radical path similar to the one observed with vanadous.

Acknowledgments. The authors wish to thank Mrs. E. Kissa-Meintany for laboratory assistance and the Secretary of the Chemistry Department, Mrs. K. Kaplany-Aravany, for secretarial assistance.

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The Mechanism of Asymmetric Homogeneous Hydrogenation. Rhodium(I) Complexes of Dehydroamino Acids Containing Asymmetric Ligands Related to Bis(1,2-diphenylphosphino)ethane[1]

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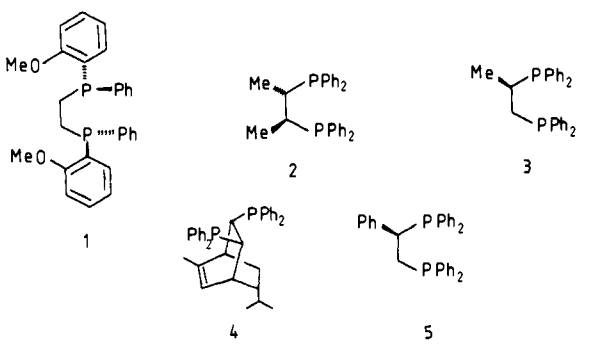
Received February 9, 1979

Abstract: The course of hydrogenation of dehydroamino acids by cationic rhodium complexes derived from bis(1,2-diphenylphosphino)ethane has been studied by phosphorus and carbon NMR. The parent complex reacts with hydrogen (1 atm) in methanol to form norbornane and the corresponding biphosphine rhodium solvate. Addition of (*Z*)-α-benzamidocinnamic acid causes displacement of solvent and formation of the corresponding 1:1 enamide complex. Comparable complexes, which may exist in diastereoisomeric forms, are obtained from chiral bis(1,2-diphenylphosphino)ethane derivatives. The ^{13}C NMR spectra of isotopically enriched enamide complexes demonstrate that the olefin and amide carbonyl groups bind to the metal, but that the carboxylate does not. (*E*)-Dehydroamino acids do not bind strongly to rhodium and isomerize readily with formation of the corresponding (*Z*)-enamide complex, but stable complexes are formed in the presence of triethylamine.

Introduction

Hydrogenation of prochiral olefins may generate a new asymmetric center. It was thus quickly recognized that complexes analogous to $(Ph_3P)_3RhCl$ had potential in asymmetric synthesis, and both chiral solvents[2] and a variety of asymmetric phosphines were employed in earlier work.[3-7] The use of chelating biphosphines proved to be very fruitful, especially in the asymmetric reduction of (*Z*)-dehydroamino acids.[8] While it would be inappropriate to give a comprehensive review here,[9] we note that the most effective catalysts are cationic complexes of chiral biphosphines (**1–5**) related to bis(1,2-diphenylphos-



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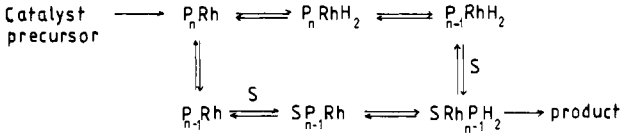
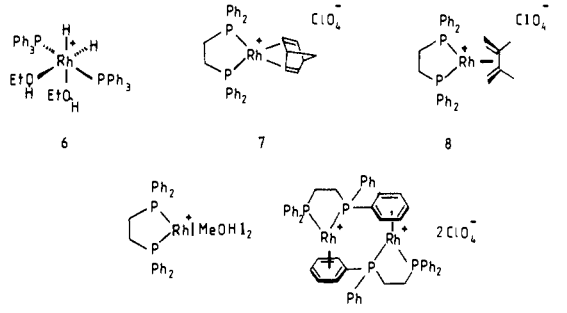
Scheme I. Illustration of "Unsaturate" (Heavy Arrows) and "Hydride" (Light Arrows) Hydrogenation Routes



phino)ethane.[10-14] (*E*)-Dehydroamino acids are reduced with much poorer chemical and optical efficiency[10,15] and isomerize in the presence of hydrogenation catalysts.[16]

Rhodium-catalyzed homogeneous hydrogenation of an olefin may involve sequential addition of hydrogen and olefin to the metal followed by a cis-ligand migration of hydride, or the reverse order of addition. These have come to be known as the "hydride" and "unsaturate" routes, respectively (Scheme I). More complex mechanisms involving monohydride intermediates have been postulated in other cases,[17] but it was generally assumed that asymmetric hydrogenation by cationic chelating phosphine complexes followed the "hydride" route like $(PPh_3)_3RhCl$.[18] This presumption was based in part on the isolation[19] of dihydride complexes such as **6** by hydrogenation of the corresponding bicyclo[2.2.1]heptadiene complex in ethanol, thus demonstrating the stability of a cis-dihydride trans-phosphine arrangement. The fact that this geometry cannot be attained by chelating phosphines was conveniently overlooked, as was further evidence[20] from Schrock and Osborn to the effect that conjugated dienes hydrogenated by a different mechanism from monoolefins when catalyzed by **7**. In this last case the likely intermediate is a diene-rhodium biphosphine complex (**8**) whose characteristic color is observed throughout the reaction.



6 7 8

9 10

Definite evidence in favor of the unsaturate route in catalysis of hydrogenation by rhodium chelate complexes was obtained by Halpern[21] and co-workers, who demonstrated that hydrogenation of **7** in methanol gave rise to a complex containing coordinated phosphines and solvent (**9**) but no hydrogen. This solution deposited **10** on standing, which was characterized by X-ray structure determination. Similar observations were made by Slack and Baird[22] using a variety of chelating biphosphines, all of which formed solvent adducts rather than hydride complexes on hydrogenation in polar solvents.

Results and Discussion

1. NMR Studies of the Course of Hydrogenation. Exposure of a solution of complex **7** in methanol to hydrogen at room temperature led to a rapid color change from orange to light yellow and at that stage the ^{31}P NMR spectrum showed only the methanol complex (**9**), described by Halpern and coworkers,[21] as a rhodium-coupled signal at 81.3 ppm, $J_{P\text{-}Rh}$ = 209 Hz. Transfer of excess α-benzamidocinnamic acid in methanol under argon at −80 °C to this solution led to a deep red coloration. The NMR spectrum now showed a single species (**11**) with inequivalent phosphines (δ_1 72.9, δ_2 61.0 ppm, $J_{P_1\text{-}Rh}$ = 163, $J_{P_2\text{-}Rh}$ = 158, $J_{P_1\text{-}P_2}$ = 38 Hz). Further exposure to hydrogen at room temperature led to the re-formation of the methanol complex **9**. Under some conditions a second species (δ 77.8 ppm, $J_{P\text{-}Rh}$ = 206 Hz) is produced at this stage. Similar behavior was noted when (*Z*)-methyl α-benzamidocinnamate was used in place of the acid.

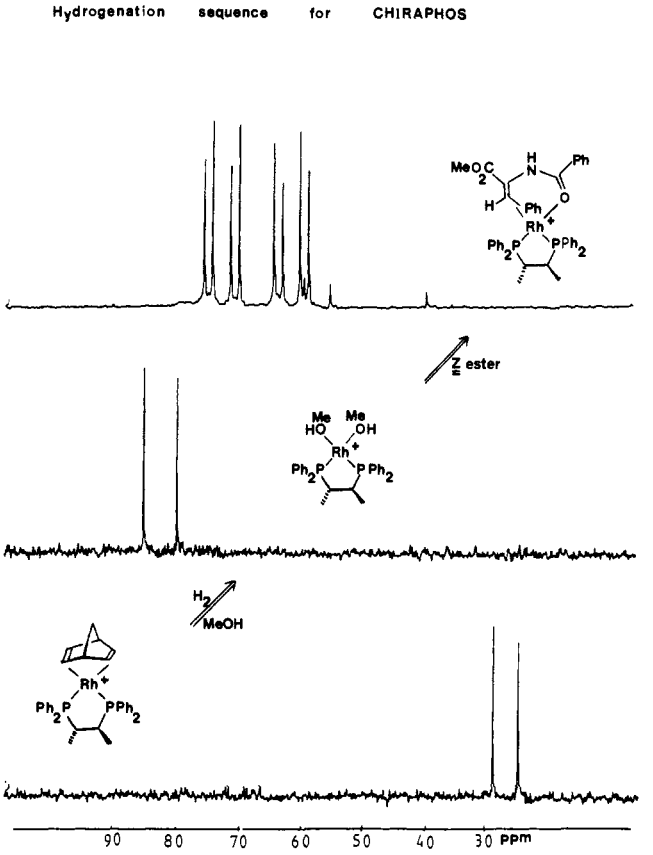
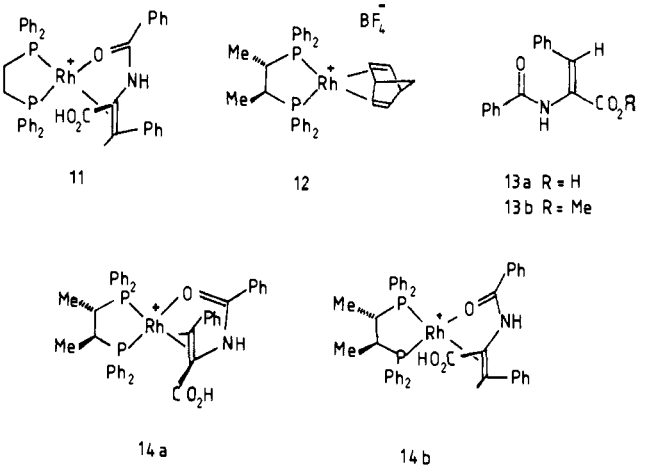


Figure 1. Stable intermediates in enamide hydrogenation by (*S,S*)-*trans*-bis(2,3-diphenylphosphinobutane)rhodium complexes.



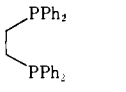
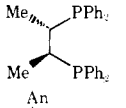
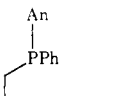
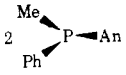
11 12 13a R = H 13b R = Me

14a 14b

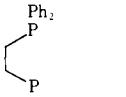
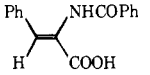
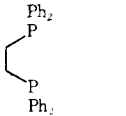
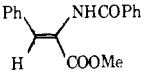
Complex **12** gives the highest optical yields reported to date in hydrogenation of *N*-acyldehydroamino acids, the enantiomer excess being up to 99%.[11] When **12** was hydrogenated in methanol and an excess of **13** (R = H) added subsequently, a similar sequence of spectra was observed to those described above (Figure 1). An important difference in this case is that there are two diastereomeric enamide complexes (**14a** and **14b**) and the absence of a second set of resonances in the ^{31}P NMR spectrum implies that binding is stereospecific within experimental error (>97%). The preferred diastereomer is most probably **14a**, which has the same configuration as the final product of catalytic hydrogenation. The spectrum of the complex derived from **13** (R = Me) is quite similar (Table I).

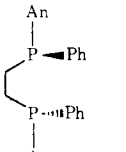
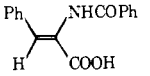
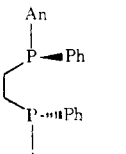
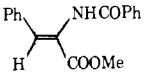
Table I. NMR Spectra of Enamide Complexes

A. ^{31}P NMR

ligand	PhCH=C(CO$_2$R)NHCOR′ R	R′	P_1	P_2	J_{RhP_1}	J_{RhP_2}	$J_{P_1P_2}$	diastereomer ratio
	H	Ph	72.2	60.5	162	158	39	
	Me	Ph	72.9	60.9	162	157	40	
	H	Me	72.7	58.8	163	159	39	
	H[a]	Ph[a]	74.4	56.8	179	176	40	
	H	Ph	73.9	62.7	160	154	52	>97:3
	Me	Ph	74.2	63.6	159	153	52	>97:3
	H	Ph	70.8	49.5	161	154	39	
			69.6	60.0	156	158	38	92:8 (301 K)
	Me	Ph	71.2	49.9	162	151	40	
			69.1	59.9	156	160	36	91:9 (304 K)
	Me	Me	71.7	48.3	162	150	40	
			69.6	58.1	157	160	38	93:7 (303 K)
	H[a]	Ph[a]	70.1	55.0	183	172	39	minor diastereomer (~20%) partly obscured at room temperature
	Me	Ph	28.3	12.0	144	160	49	>97:3 (278 K)

B. ^{13}C NMR

ligand	substrate	labeling site	temp, K	(free ligand)	(bound)	J_{RhC}	J_{CP_1}	J_{CP_2}
		1′(amide)	305	169.8	182.7		1.5	6.0
		1(carboxyl)	305	168.4	169.8			3.0
			213		170.2			3.6
			178		170.4			3.0
		3(olefin)	303	136.5	93.3	11.0		
		1′(amide)	303	169.9	182.9		1.7	6.0
		1(carboxyl)	305	167.2	168.9			3.5
			178		169.2			3.7
		3(olefin)	305	136.4	92.6	11.0		
			241		91.7	11.0		
			191		88.6	11.0		

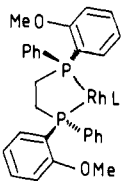
ligand	substrate	labeling site	temp, K	diastereomer	(free ligand)	(bound)	J_{CRh}	J_{CP_1}	J_{CP_2}
		1′(amide)	305	major	169.8	181.0		2.5	7.0
				minor		182.0		2.4	7.0
		1(carboxyl)	304	major	168.4	171.2			4.5
				minor		170.6			4.5
			241	major		171.7			4.5
		3(olefin)	304	major	136.5	82.9	14.7		
				minor		82.3	13.4		
			241	major		81.1	14.6		
			213	major		80.1	14.6		
		1′(amide)	304	major	169.9	181.4		2.5	8.0
				minor		182.5		2.2	7.0
		1(carboxyl)	304	major	167.2	170.5			4.9
				minor		169.7			4.9
			241	major		170.7			4.9
		3(olefin)	304	major	136.4	81.6	14.6		
				minor		81.2	14.6		
			241	major		79.9	15.9		
			213	major		78.9	15.9		

[a] *E* isomer. An = *o*-anisyl.

The asymmetric center of the ligand is remote from the site of enamide coordination in this case, and hence stereoselectivity must be a consequence of induced chirality in the diphenylphosphino groups.[23] The structurally related ligand **1** (dipamp) is chiral at phosphorus and likewise gives high optical yields in the hydrogenation of enamides, although the minor amino acid enantiomer is always formed to some extent. In preliminary experiments we discovered that the cyclooctadiene complex **15a** was not appreciably hydrogenated under 1 atm of hydrogen and decomposed under forcing conditions. The corresponding bicyclo[2.2.1]heptadiene complex (**15b**) could not be prepared by conventional methods since disproportionation occurred readily. A successful synthesis of **17** was accomplished by reacting the ligand with an excess of bis(norbornadiene)rhodium tetrafluoroborate. Hydrogenation of the resulting solution led to precipitation of metallic rhodium, and filtration under argon gave a solution containing the methanol complex (**17**), usually contaminated with a small amount of **16.** Reaction with an excess of enamide **13** (R = H) gives clean conversion into the complex **18,** whose ^{31}P NMR spectrum demonstrated the presence of two diastereomers in ratio 91:9, both having similar Rh–P and P–P coupling con-

stants. A third unidentified species is formed on prolonged standing but is never present to the extent of more than 5% at the total signal. There is some overlap of the low-field resonances of the two diastereomers but they are fortuitously quite separate in the corresponding complex of the methyl ester **13** (R = Me). The diastereomer ratio is very similar for acid and ester but in both cases is quite sensitive to temperature since the minor species represents no more than 3% of the total complexed material at 274 K but 12% at 312 K (Figure 2). Over this temperature range all the lines in the spectrum were sharp, showing that intra- and intermolecular exchange processes are rather slow. The results are consistent with C_2 local symmetry in the coordinated biphosphine; otherwise more complicated spectra would be anticipated.

At low temperatures the spectrum of **17** in methanol is broad



15a L = 

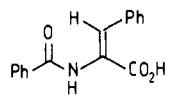
15b L = 

16 L = (1)

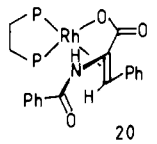
17 L = 2 MeOH

and complex, and more than one species is present. Addition of a slight deficiency of **13** (R = Me) and monitoring of the ^{31}P NMR spectrum at 220 K demonstrate that complexation is very slow at that temperature. At 235 K it occurs at an appreciable rate ($t_{1/2} \sim 2$ h) but the initially formed enamide complex contains 35% of the minor diastereomer. This proportion decreases with time and on warming to room temperature and recooling the normal ratio is restored. This demonstrates that the kinetic stereoselectivity of the enamide binding step is low, and possibly suggests that olefin coordination plays a minor role in its rate-determining step.

(*E*)-Dehydroamino acids behave quite differently when reacted with the methanol complexes. There is some initial complexation of **19** based on the broad ^{31}P NMR spectra obtained on adding the acid to **17** but rapid isomerization[16] to the (*Z*)-enamide complex ($t_{1/2} \sim 500$ s) occurs at room temperature. A rather slower but similar reaction occurs with the bis(diphenylphosphino)ethane analogue ($t_{1/2} = 3000$ s), although slow dissolution of complex **9** under the reaction conditions may well be responsible for the difference in rate. In the presence of excess triethylamine, however, **19** forms a



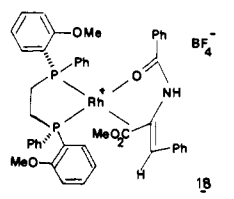
19



20

strong complex on reaction with **9** which is stable to isomerization over several days. The similarity of this species to other rhodium carboxylate complexes derived from **19**[24] (δ_{P_1} 74.4, δ_{P_2} 56.9 ppm, $J_{RhP_1} = 179$, $J_{RhP_2} = 176$, $J_{RhP_1} = 40$ Hz) suggests that it has structure **20.** A comparable complex, also stable to isomerization, is derived from dipamp (δ_{P_1} 70.1, δ_{P_2} 55.0 ppm, $J_{RhP_1} = 183$, $J_{RhP_2} = 172$, $J_{P_1P_2} = 39$ Hz) at room temperature. On cooling the sample to 260 K, two further species, with similar coupling constants, are observed, possibly reflecting conformational isomers of the ligand. Carboxylate complexes of this type may be involved in the hydrogenation of (*E*)-enamides, which is slow and optically inefficient.

Similar experiments were carried out with the monodentate asymmetric ligand (*R*)-(*o*-methoxyphenyl)phenylmethylphosphine.[7,25] The bicyclo[2.2.1]heptadiene complex of this ligand (**21**) hydrogenates readily, the only observed product being the methanol complex **22,** which has no affinity for hydrogen at normal pressure.[25] The latter complex reacts with



18

and minor diastereomer

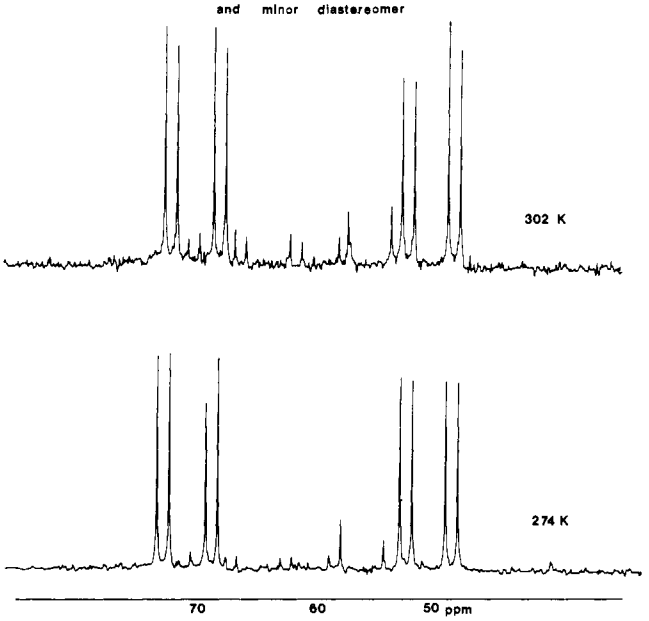
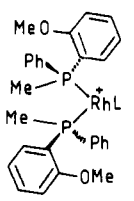
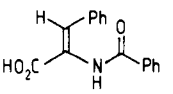


Figure 2. Temperature dependence of the diastereomer ratio in the enamide complex **18.**



21, L = 

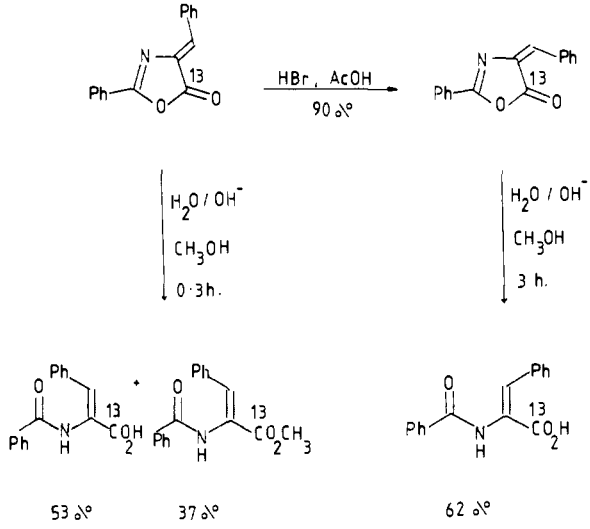
22, L = 2 MeOH

23, L = 

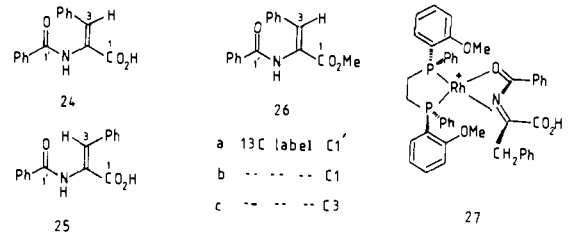
the (*Z*)-dehydroamino acid ester **13** (R = Me) to form an enamide complex of the type previously described, with one significant difference. There is an exchange process which broadens the spectrum of the complex **23** very considerably at room temperature, although the conventional eight-line spectrum is obtained below 260 K. The mechanism of this line-broadening process is assumed, although not proved here, to be intermolecular exchange of free and bound enamides which equivalences the phosphines without destroying the phosphorus-rhodium coupling. The marked difference in lability of the chelate complexes **18** and the bisphosphine complex **23** toward intermolecular exchange may reflect the greater tendency of the more flexible complex to undergo associative reactions. Although the nonchelate complex **23** is formed with high stereoselectivity, the reported optical yield in related hydrogenation catalyzed by complexes of this ligand is 58% compared with 96% in the case of **1.** It seems to be a general feature of asymmetric hydrogenation that rigid chelate complexes are more efficient than flexible species, perhaps demonstrating a more rigorous adherence to a single mechanistic pathway.

2. Complexes of Carbon-13 Enriched Enamides. In order to clarify the precise mode of binding in these complexes, carbon-13 enriched analogues of **13** have been prepared with the label residing at C_1, C_1', or C_3, respectively (Scheme II). The first was prepared conventionally from carbonyl-labeled benzoyl chloride[26] and glycine followed by azlactone synthesis

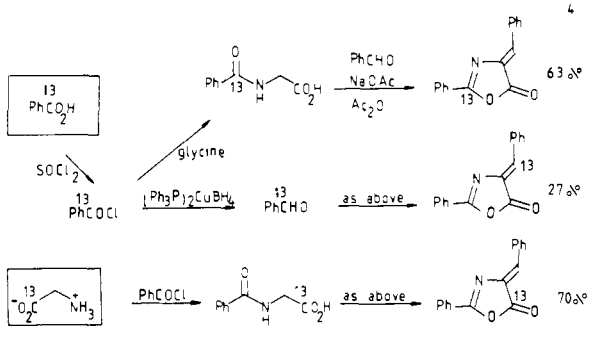
Scheme II. Synthetic Routes to Carbon-13 Enriched Enamides



with benzaldehyde.[27] Part of the (*Z*)-azlactone so produced was solvolyzed in methanol giving a mixture of acid **24a** and its methyl ester. The remainder was isomerized to the (*E*)-azlactone with HBr in acetic acid followed by a similar procedure giving the acid **25a.** The carbonyl-labeled isotopomer



24b was prepared from carboxyl-labeled glycine, as above. Synthesis of the olefin-labeled enamide proved to be more difficult and to obtain carbonyl-enriched benzaldehyde in a state of sufficient purity it was necessary to modify literature[28] methods. Reduction of acid chlorides to aldehydes[29] may be carried out efficiently by employing a suspension of copper(I) borohydride triphenylphosphine complex and excess triphenylphosphine in acetone. In order to facilitate the separation of the labeled product we carried out the reaction in the involatile solvent tetraglyme and distilled benzaldehyde out of the reaction mixture at intervals. Acceptably pure material was thus obtained which was converted into the (*Z*)-azlactone as before and hence to both isomers of dehydroamino acid.



Initial experiments were carried out with C_1- and C_1'-labeled *Z* acid and ester and both carbon and phosphorus NMR spectra of their complexes with rhodium bis(diphenylphosphino)ethane recorded. Taking the acid **24a** enriched at the carbonyl carbon first, the effect of coordination is strong since the ^{13}C carbonyl resonance shifts 12.9 ppm to lower field. The signal is split by coupling and examination of the ^{31}P NMR spectrum of the sample demonstrates that this comprises a 6-Hz coupling to the high-field phosphine, which is trans to the bound olefin, and 1.5 Hz to the low-field phosphine, which is trans to the amide. There is no detectable coupling to the rhodium nucleus, suggesting that the amide is bound in similar manner to acetylacetonates, where rhodium-carbon spin-spin coupling is not observed.[30] The carboxyl-labeled enamide **24b** shows only slight perturbation of the ^{13}C chemical shift on binding, yet there is a 3.5-Hz coupling in the high-field phosphine corroborated by the ^{31}P NMR spectrum. In contrast the olefin-labeled enamide **24c** shows a normal upfield complexation chemical shift and a rhodium-carbon coupling of 12 Hz, although in this case there is no through coupling to the phosphorus nuclei. Corresponding experiments with the *Z* methyl esters **26a–c** show similar complexation shifts and coupling so that the ester and acid are bound in rhodium in the same manner (Table I).

A related set of experiments was carried out using the asymmetric ligand dipamp in the place of bis(diphenylphosphino)ethane. This provided an opportunity to determine the stoichiometry of complexation since all the species involved are highly soluble. In a sample containing a 25 mol % excess of **24c** over **17** prepared in situ, both free and bound species may be observed in the carbon magnetic resonance spectrum, in the ratio 1:5. Although the estimate of relative proportions neglects differences in ^{13}C relaxation time between the two species, it clearly indicates 1:1:1 enamide:rhodium:phosphine complexation. Furthermore, the major and minor diastereomers of the enamide occur in the same proportion irrespective of changes in the substrate:complex ratio and therefore have the same stoichiometry. The major and minor diastereomers of enamide complex are distinguishable by carbon magnetic resonance in all three series **24a–c** (Table IC) and complexes derived from **26** show very similar spectra. Taken together, this evidence demonstrates that the diastereomers are structurally similar and related by binding of opposite prochiral faces of the olefin to rhodium.

The availability of labeled *E* acid **25c** permits an examination of the mechanism of isomerization in the presence of cationic rhodium complexes.[16] After addition of a threefold excess of **25c** to a CD_3OD solution approximately 0.04 M in complex **17,** the ^{13}C NMR spectrum was monitored at intervals. Initially no complexed species were observed, even at 275 K. On keeping the sample at 284 K, a signal at 53.6 ppm due to the (*Z*)-enamide complex was observed which reached a limiting intensity after about 90 min at 284 K. At this stage no trace of **24c** was observed, but the signal due to this subsequently increased in intensity, 85% isomerization having occurred after 1 week at room temperature. There is no deuterium incorporation at C_3 of either of the limiting species, ruling out the possibility of a coordinated imine intermediate (**27**) in the isomerization process, since amide N-H exchanges very rapidly with protic deuterated solvents.[31] Isomerization must occur within the coordination sphere and, since enamide/enamide exchange at rhodium is fast on a *chemical* time scale, it slows down appreciably when **17** is completely converted into **18,** which suppresses still further the weak binding of the *E* acid.

3. Binding Modes of Enamides to Rhodium. Binding of enamides to rhodium via the olefin and amide carbonyl residues has been inferred from asymmetric hydrogenation data,[32] and directly observed in the solid state[33] by Halpern and coworkers. Their preliminary structure for the methyl ester of **11** demonstrates π bonding by the olefin and σ bonding by amide carbonyl in a square-planar complex. Taken together, the ^{31}P and ^{13}C NMR spectra described here show clearly that this structure is maintained in solution. The deep orange to scarlet colors of the complexes and expected values[34] of $J_{P\text{-}P}$ and $J_{P\text{-}Rh}$ indicate square planarity (Table I). In both **11** and **18** there is long-range ^{13}C-^{31}P coupling between the high-field

phosphine and the amide carbon and a rather weaker coupling from that phosphine to the carboxyl carbon (Figure 3). Long-range intracomplex ^{13}C-^{31}P couplings have previously been observed and are frequently larger for trans- than for cis-disposed ligands.[35] The only ^{103}Rh–^{13}C coupling observed is to the olefinic carbon and its value[36] is within the normal range for olefin–rhodium π complexes. Changes in chemical shift on coordination are more informative and consistent with a solution structure in which the olefin is orthogonal to the coordination plane but the amide residue is rotated so that the metal–oxygen bond has a pronounced σ-donor component. This accords with the solid-state structure of **11**,[33] with the lack of ^{103}Rh–^{13}C coupling to the amide carbon, likewise observed in acetylacetonates,[36] and with the fact that a strain-free molecular model can be constructed with a $RhOC_1$ angle of 120°. Examination of this model in relation to crystal structures of chiral biphosphine rhodium diolefin complexes[37,38] shows that interactions of the carboxyl group with an equatorial *P*-phenyl ring are minimized in the preferred diastereomer of **14** or **18**. The inferior complexation of (*E*)-dehydroamino acids follows from this model, since simultaneous coordination by olefin and amide places the β-phenyl group in close proximity to the *P*-phenyl rings. Nonbonded interactions are alleviated in carboxylate complex **20**.

4. Relationship between These Studies and the Mechanism of Asymmetric Hydrogenation. Complex **17** is the only detectable species formed on hydrogenation of the corresponding bicyclo[2.2.1]heptadiene complex (0.04 M), and **18** is then the only detectable species formed on addition of dehydroamino acid **13** (0.2 M), implying that its formation constant is >500 M^{-1}. Extrapolation of the equilibration rate to room temperature suggests that in the presence of a high concentration of substrate it will occur more rapidly than hydrogenation. Catalytic hydrogenation is normally conducted with a ca. 100-fold excess of substrate over catalyst, the latter being present at low concentration, typically 10^{-3} M. This implies that enamide complex **18** will be the sole rhodium-containing species present at steady-rate equilibrium and either the addition of hydrogen or cis-ligand migration must be the rate-determining step.

If the stereoselectivity of enamide binding were the sole criterion for determining the optical yield in hydrogenation, then rate constants for reaction of the diastereomeric enamide complexes would have to be identical. It is clear that this is not the case, since the optical yields observed by Knowles and coworkers in hydrogenation of **13** are higher than the diastereoselectivity we observe in binding.[48] This implies that $k_a \sim 3k_b$, the more stable enamide complex hydrogenating three times faster than the minor diastereomer. It is of some interest that hydrogenation of **13** is reported to be pressure dependent,[10] and at 27 atm the optical yield is reduced to 78%, the enantiomer ratio of 89:11 corresponding closely with a diastereomer ratio of 91:9 which we observe by ^{31}P NMR in **18**.[39] This may mean that at very high pressures the displacement of methanol by enamide becomes rate determining.

Optical yields for the hydrogenation of dehydroamino acids are consistently higher than those observed for other substrates. The present work clarifies the role of the amide group and also the relative steric effects of *E* and *Z* β-phenyl groups. The carboxylate group does not participate in (*Z*)-enamide binding, although Knowles and co-workers[10] have clearly demonstrated that it is important in determining both the rate and selectivity of the catalytic reaction, possibly by an electrostatic interaction with a cationic rhodium hydride. Hence the overall selectivity involved in asymmetric hydrogenation may be higher than the thermodynamic selectivity, observed in the diastereomeric ratio of bound enamide complexes.[48]

Experimental Section

General Methods and Materials. Melting points were determined on a Reichert Köfler block and are uncorrected. ^1H NMR spectra were recorded on a Perkin-Elmer R32 spectrometer relative to tetramethylsilane as internal standard. Phosphorus and carbon NMR spectra were recorded on a Bruker WH90 spectrometer. Phosphorus chemical shifts are quoted relative to external 85% phosphoric acid and carbon chemical shifts relative to external tetramethylsilane. Optical rotations were measured with a Perkin-Elmer 141 polarimeter. Microanalyses were performed by Dr. F. B. Strauss, Oxford. Reagent-grade solvents were purified according to standard procedures before use. All manipulations involving organometallic species were carried out in Schlenck apparatus under an atmosphere of dry argon and solvents were thoroughly degassed before use according to standard vacuum line techniques.

(*Z*)-α-Benzamidocinnamic Acid and (*Z*)-Methyl α-Benzamidocinnamate-*1*-^{13}C (24b and 26b). To a solution of glycine-*1*-^{13}C (91 atom %) (750 mg, 10 mmol) and sodium hydroxide (500 mg, 12.5 mmol) in water (6 mL) were added in turn portions of benzoyl chloride (1.28 ml, 11 mmol) and a solution of sodium hydroxide (800 mg, 20 mmol, in 2 mL of water) over 0.5 h at such a rate that the solution remained alkaline. The mixture was stirred for a further 0.5 h and then poured into concentrated hydrochloric acid (2 mL). The white precipitate was filtered, washed with cold water, and dried under high vacuum (2.45 g). This was then boiled in CCl_4 (25 mL) for 10 min. The remaining white solid was collected, dried, and recrystallized (boiling water) to give hippuric acid-*1*-^{13}C (1.43 g, 80%), mp 189–190 °C (lit.[40] 191–192 °C). A suspension of hippuric acid-*1*-^{13}C (1.407 g, 7.85 mmol), freshly fused sodium acetate (0.95 g, 14.4 mmol), and benzaldehyde (1.6 mL, 16 mmol) in acetic anhydride (8 mL) was heated at a temperature carefully maintained between 85 and 95 °C for 1 h. Ethanol (10 mL) and water (10 mL) were added cautiously to the warm solution causing the precipitation of a yellow solid. The slurry was poured into water (50 mL), and the solid collected by filtration, washed with water and hexane, and dried under vacuum to give (*Z*)-2-phenyl-4-benzylidene-5(4*H*)-oxazolone-*5*-^{13}C (1.65 g, 85%): mp 167–170 °C (lit.[41] 166–167 °C); ^1H NMR ($CDCl_3$) δ 7.2 ppm (olefinic C–H, $^3J_{CH}$ = 5.2 Hz); ^{13}C NMR ($CDCl_3$) δ 167.6 ppm. The labeled (*Z*)-azlactone (1.5 g, 6.02 mmol) was added to a mixture of methanol (30 mL) and sodium hydroxide solution (1 M, 15 mL) and stirred until completely dissolved. Methanol was then removed under reduced pressure and the solution extracted with ether (3 × 25 mL). The ether extract was dried (Na_2SO_4) and concentrated to give a white solid which was recrystallized from aqueous methanol to give (*Z*)-methyl α-benzamidocinnamate-*1*-^{13}C (550 mg, 32%): mp 139–140 °C (lit.[42] 142–143 °C); ^1H NMR ($CDCl_3$) δ 3.8 ppm (COO*Me*, $^3J_{CH}$ = 3.8 Hz); ^{13}C NMR (CD_3OD) δ 167.2 ppm. Concentrated hydrochloric acid was added to the aqueous layer until the pH value was 2. The white precipitate was collected, washed with water, and dried under high vacuum to give (*Z*)-α-benzamidocinnamic acid-*1*-^{13}C (854 mg, 53%): mp 226–230 °C dec (lit.[41] 223–226 °C); ^{13}C NMR (CD_3OD) δ 168.4 ppm.

(*Z*)-α-Benzamidocinnamic Acid and (*Z*)-Methyl α-Benzamidocinnamate-*1'*-^{13}C (24a and 26a). Benzoic acid-*1*-^{13}C was prepared in 77% yield from phenylmagnesium bromide and barium carbonate (90.5 atom %) according to the published procedure.[43] A solution of the labeled acid (1.6 g, 13.1 mmol) and thionyl chloride (2.6 mL) in benzene (13 mL) was heated under reflux for 3 h, when benzene and unreacted thionyl chloride were removed by distillation.[26] The complete removal of thionyl chloride was ensured by addition of further benzene (10 mL) and a second distillation. The crude benzoyl chloride thus obtained was treated with glycine as described above to give after recrystallization hippuric acid-*1'*-^{13}C (1.48 g, 63% from benzoic acid), mp 194–196 °C. Azlactone synthesis[27] followed by methanolysis as above yielded (*Z*)-α-benzamidocinnamic acid-*1'*-^{13}C [mp 220–230° (20%); ^{13}C NMR (CD_3OD) δ 169.8 ppm] and (*Z*)-methyl α-benzamidocinnamate-*1'*-^{13}C [mp 145–146 °C (51%); ^{13}C NMR (CD_3OD) δ 169.9 ppm].

(*Z*)-α-Benzamidocinnamic Acid and (*Z*)-Methyl α-Benzamidocinnamate-*3*-^{13}C (24c and 26c). Benzoic acid-*1*-^{13}C (2 g, 16.4 mmol) was converted to benzoyl chloride as described above. It was then added to a slurry of triphenylphosphine (8.6 g, 32.8 mmol) and bis(triphenylphosphine)copper borohydride in tetraglyme (5 mL, dried by distillation from sodium) and the mixture stirred at room temperature for 3.5 h. The apparatus was then connected to vacuum and benzaldehyde (1.65 g) distilled out (40 °C, 0.15 mm). The ^1H NMR showed that this was contaminated with benzene and tetraglyme but it was used without further purification. Azlactone synthesis as de-

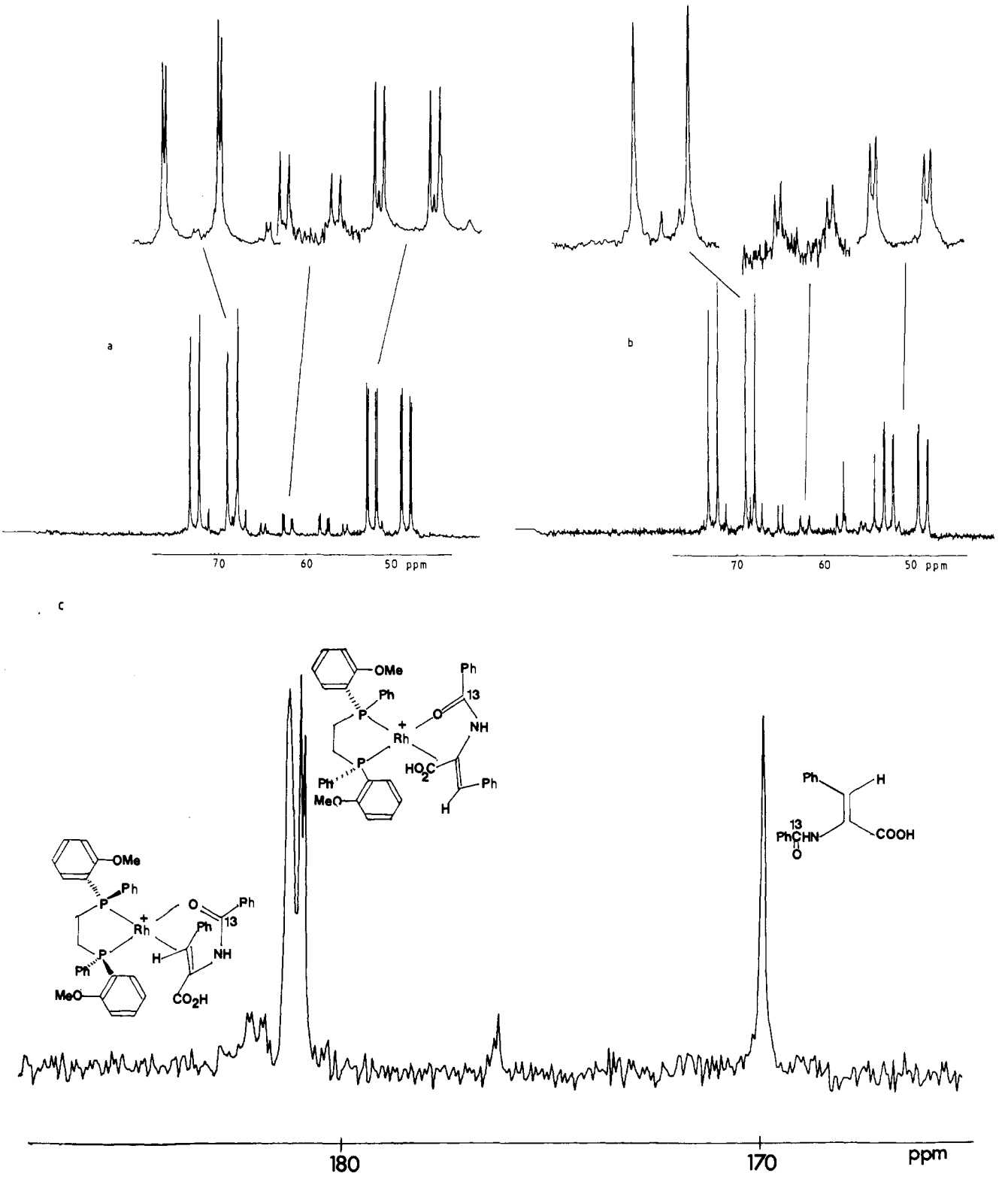


Figure 3. NMR spectra of carbon-13 enriched complexes of DIPAMP: (a) ^{31}P NMR spectrum (from ligand **24a**); (b) ^{31}P NMR spectrum (from ligand **24b**); (c) ^{13}C NMR spectrum (from ligand **24a**).

scribed above (1.3 g of hippuric acid) yielded (*Z*)-2-phenyl-4-benzylidene-5(4*H*)-oxazolone-6-^{13}C (1.12 g, 28% from benzoic acid (mp 165–167 °C)): ^1H NMR ($CDCl_3$) δ 7.2 (6-H, $^1J_{C-H}$ = 160 Hz); ^{13}C NMR ($CDCl_3$) δ 131.54 ppm. Methanolysis of the azlactone (0.5 g, 2 mmol) as described above yielded (*Z*)-α-benzamidocinnamic acid-3-^{13}C [mp 225–230 °C (51%); ^{13}C NMR (CD_3OD) δ 136.55 ppm] and (*Z*)-methyl α-benzamidocinnamate [mp 142–144 °C (25%); ^1H NMR ($CDCl_3$) δ 7.56 ppm ($^1J_{C-H}$ = 157 Hz); ^{13}C NMR (CD_3OD) δ 136.4 ppm].

(*E*)-**α-Benzamidocinnamic Acid-1-^{13}C (25b).** Gaseous hydrogen bromide was bubbled for 1 h through a slurry of (*Z*)-2-phenyl-4-benzylidene-5(4*H*)-oxazolone-5-^{13}C (2.0 g, 8.03 mmol) in glacial acetic acid (100 mL) with vigorous stirring. This was then poured into water (200 mL) and the yellow precipitate collected, washed with water, and dried under vacuum. This crude (*E*)-2-phenyl-4-benzylidene-5(4*H*)-oxazolone-5-^{13}C (1.75 g, 87%), mp 135–136 °C (lit.[62] 148–149 °C), contained a small amount (~5%) of the *Z* isomer (^1H NMR) but was used without further purification. ^{13}C NMR ($CDCl_3$): δ 164.33 ppm. A solution of the crude azlactone (1.75 g, 7 mmol) in methanol (50 mL) and sodium hydroxide solution (0.5 M, 34 mL) was

stirred at room temperature for 3 h. The methanol was then removed under reduced pressure and any ester was removed by extraction with ether (2 × 30 mL). The aqueous layer was then acidified with concentrated hydrochloric acid and the white precipitate collected, washed with water, dried, and twice recrystallized (methanol/ether/hexane) to give (*E*)-α-benzamidocinnamic acid-*1*-^{13}C (1.03 g, 48% from the (*Z*)-azlactone): mp 199–200 °C (lit.[44] 198–199 °C); ^{13}C NMR (CD_3OD) δ 168.4 ppm.

(*E*)-α-Benzamidocinnamic Acids-*1'*-^{13}C (25a) and -*3*-^{13}C (25c). The other isotopomers of (*E*)-α-benzamidocinnamic acid were prepared as described above from the corresponding (*Z*)-azlactones. (*E*)-2-Phenyl-4-benzylidene-5(4*H*)-oxazolone-*2*-^{13}C was isolated in 90% yield, mp 140–146 °C, and converted to (*E*)-α-benzamidocinnamic acid-*1'*-^{13}C (56% overall yield): mp 195–200 °C; ^{13}C NMR (CD_3OD) δ 168.64 ppm. (*E*)-2-Phenyl-4-benzylidene-5(4*H*)-oxazolone-*6*-^{13}C was isolated in 80% yield [mp 140–145 °C; ^{13}C NMR ($CDCl_3$) δ 139.9 ppm] and converted to (*E*)-α-benzamidocinnamic acid-*3*-^{13}C (42% overall yield): mp 199–200 °C; ^1H NMR (CD_3OD) δ 6.6 ppm (C_3H, $^1J_{C-H}$ = 158 Hz); ^{13}C NMR (CD_3OD) δ 125.92 ppm.

Bicyclo[2.2.1]heptadiene - 1,2 - bis(diphenylphosphino)ethanerhodium(I) Perchlorate (7). This was prepared from bicyclo[2.2.1]heptadienerhodium acetylacetonate according to the published procedure[45] in 91% yield.

Bicyclo[2.2.1]heptadiene - 2(*S*),3(*S*)-2,3-bis(diphenylphosphino)butanerhodium(I) Tetrafluoroborate (12). This was prepared in 86% yield by the same method as that described for the perchlorate salt, tetrafluoroboric acid (40% in water) replacing perchloric acid: ^{31}P NMR (CH_3OH) δ 58.4 ppm, J_{Rh-P} = 154 Hz.

Bicyclo[2.2.1]heptadiene-(*R*,*R*)-1,2-bis(*o*-methoxyphenylphenylphosphino)ethanerhodium(I) Tetrafluoroborate (15b). Bis(bicyclo[2.2.1]heptadiene)rhodium(I) tetrafluoroborate[45] (10 mg, 26.7 mol) and (*R*,*R*)-1,2-bis(*o*-methoxyphenylphenylphosphino)ethane (4.5 mg, 10 mol) were dissolved in methanol (1 mL). The ^{31}P NMR spectrum showed signals at δ 50.2 ppm, J_{Rh-P} = 159 Hz, due to **15b** and δ 56.4 ppm, J_{Rh-P} = 137 Hz, due to bis(bis(*o*-methoxyphenyl)-phenylphosphino)rhodium(I) tetrafluoroborate (**16**).

Bicyclo[2.2.1]heptadiene Bis((*R*)-*o*-methoxyphenylmethylphenylphosphino)rhodium(I) Tetrafluoroborate (Prepared by Mr. P. N. Nicholson). A mixture of di-μ-chloro-bis(bicyclo[2.2.1]heptadiene)dirhodium (100 mg, 0.22 mmol) in dichloromethane (4 mL) and sodium tetrafluoroborate (0.076 g, 0.7 mmol) in water (2 mL) was stirred vigorously while (*R*)-*o*-methoxyphenylmethylphenylphosphine (0.5 g, 2.17 mmol) was added. After 5 min at room temperature the dichloromethane layer was removed, washed with water (2 × 2 mL), and evaporated to half its volume under reduced pressure. The resulting solution was added dropwise to freshly distilled diethyl ether (20 mL) with vigorous stirring. The fine precipitate thus formed was filtered and dried in vacuo, giving the cationic complex as an orange powder: mp 105–114 °C dec; $[\alpha]^{593}_D$ −83.0° (methanol, 1%); ^{31}P NMR (CH_3OH) δ 9.81, J_{Rh-P} = 156 Hz. Anal. ($C_{35}H_{38}BF_4O_2P_2Rh$) C, H, F, P (racemic complex, ±0.3%).

1,2-Bis(diphenylphosphino)ethanerhodium(I) Methanol and Enamide Complexes. Sample preparations are given. Unlabeled enamide complexes with enamide/rhodium ratios 5/1 and 1/1 were prepared in methanol. All ^{13}C-labeled enamide complexes were prepared using an enamide/rhodium ratio of 1.2/1 and CD_3OD as solvent.

Methanol Adduct. A suspension of bicyclo[2.2.1]heptadiene-1,2-bis(diphenylphosphino)ethanerhodium(I) perchlorate (10 mg, 14.4 mol) in methanol (1.2 mL) in an 8-mm NMR tube was thoroughly degassed by three freeze–thaw cycles. The tube was attached to the vacuum line by a septum-capped adapter and was narrowed slightly before use to facilitate sealing. The tube was then evacuated and hydrogen was admitted. The tube was then agitated at room temperature under a positive pressure of hydrogen until the characteristic orange color of the olefin complex was discharged to give a pale yellow solution containing suspended solid (~5 min). The hydrogen was then removed by three further freeze–thaw cycles and the tube finally sealed under argon. The ^{31}P NMR spectrum was obtained with the 8-mm tube placed in a 10-mm tube with D_2O as the external lock signal in the annular space. This procedure was followed for all spectra recorded at room temperature; CD_3OD was used as external lock for low-temperature work. ^{31}P NMR (CH_3OH): δ 81.4 ppm, J_{Rh-P} = 206 Hz.

1,2-Bis(diphenylphosphino)ethanerhodium(I) Adduct of (*Z*)-α-Benzamidocinnamic Acid (15). The methanol complex was prepared as above from **7** (30 mg, 43.1 μmol) in methanol (0.7 mL). (*Z*)-α-Benzamidocinnamic acid (40 mg, 150 μmol) in methanol (0.5 mL) was carefully degassed by three freeze–thaw cycles in a Schlenck tube. The solution was then transferred under argon through a narrow steel tube directly into the NMR tube. On allowing to warm to room temperature and mixing the solutions the pale yellow color of the solvent adduct was replaced by a deep red-orange color. The solution was once more degassed by three freeze–thaw cycles before the tube was sealed under argon: ^{31}P NMR (CH_3OH) δ 72.22 (dd, P_1, J_{Rh-P} = 163 Hz), 60.48 ppm (dd, P_2, J_{Rh-P} = 158, $J_{P_1P_2}$ = 39 Hz).

1,2-Bis(diphenylphosphino)ethanerhodium(I) Adduct of (*Z*)-α-Benzamidocinnamic Acid-*1'*-^{13}C. The CD_3OD complex was prepared as previously described from **7** (20 mg, 28.9 μmol). (*Z*)-α-Benzamidocinnamic acid-*1'*-^{13}C (8.5 mg, 31.8 μmol in CD_3OD) was transferred as before and further degassed and the tube sealed. The solution became red-orange but not all the solvent adduct was solubilized. Both ^{13}C and ^{31}P NMR spectra were obtained on this sample: ^{31}P NMR (CD_3OD) δ 72.2 (ddd, P_1, J_{Rh-P} = 163, J_{P-C} = 1.7 Hz), 60.5 ppm (ddd, P_2, J_{Rh-P} = 158, J_{P-C} = 6, $J_{P_1P_2}$ = 39 Hz); ^{13}C NMR (CD_3OD) δ 182.75 (slightly broadened doublet, bound amide, J_{C-P} = 6.1 Hz; the smaller coupling is not resolved), 169.83 ppm (free amide).

Hydrogenation of (*Z*)-Methyl α-Benzamidocinnamate with Bicyclo[2.2.1]heptadiene-1,2-bis(diphenylphosphino)ethanerhodium(I) Perchlorate. The adduct of (*Z*)-methyl α-benzamidocinnamate and 1,2-bis(diphenylphosphino)ethanerhodium(I) was prepared as described above from the bicyclo[2.2.1]heptadiene complex (40 mg, 57.4 μmol) and the ester (40 mg, 142.3 μmol). The tube containing the adduct was then evacuated and hydrogen readmitted and then agitated at room temperature under a positive pressure of hydrogen until the deep red color was discharged. After removal of the hydrogen and further degassing the tube was sealed: ^{31}P NMR (CH_3OH) δ 81.3 (J_{Rh-P} = 206 Hz), 77.8 ppm (J_{Rh-P} = 204 Hz). The second species predominated in the ratio 2:1.[46]

Bis((*R*)-*o*-methoxyphenylmethylphenylphosphine)rhodium(I) Solvent and Enamide Adducts. The solvent adduct and the (*Z*)-enamide adducts were prepared as described above.

(2*S*,3*S*)-Bis(diphenylphosphino)butanerhodium(I) Solvent and Enamide Adducts. These were prepared from the bicyclo[2.2.1]heptadiene complex by the same procedure as that described for 1,2-bis(diphenylphosphino)ethanerhodium(I) adducts. They were, however, very much more stable.

(*R*,*R*)-1,2-Bis(*o*-methoxyphenylphenylphosphino)ethanerhodium(I) Solvent and Enamide Adducts. Methanol Adduct. Bicyclo[2.2.1]heptadiene-(*R*,*R*) - 1,2 - bis(*o*-methoxyphenylphenylphosphino)ethanerhodium(I) tetrafluoroborate (10 μmol) was prepared in situ as above in methanol (1.2 mL) in a Schlenck tube and thoroughly degassed. Hydrogen was then admitted and the solution agitated vigorously until black, metallic rhodium was deposited. After degassing the solution was filtered through a steel tube blocked with filter paper into an 8-mm NMR tube as before. After further degassing the tube was sealed: ^{31}P NMR (CH_3OH) δ 80.8 ppm, J_{Rh-P} = 209 Hz (methanol adduct). Minor amounts of the corresponding bis(biphosphine) cationic complex (δ 55.4 ppm, J_{Rh-P} = 137 Hz) were normally observed.

(*Z*)-Methyl α-Benzamidocinnamate Adduct. The methanol adduct (33 μmol in 0.8 mL of methanol) was prepared in a Schlenck tube as described above. (*Z*)-Methyl α-benzamidocinnamate (35 mg, 124.5 μmol) in methanol (0.5 mL) in an 8-mm NMR tube was thoroughly degassed. The methanol adduct was then filtered through a steel tube, as before into the NMR tube, the deep red solution once more degassed, and the tube sealed. In some experiments some rhodium metal was inadvertently transferred. After the tube was sealed this could be removed from solution by centrifugation of the tube, inverted, and carefully packed in cotton wool. Clear red solutions were thus obtained: ^{31}P NMR (CH_3OH) δ 71.2 (dd, P_1, major diastereomer, J_{Rh-P} = 162 Hz), 49.9 (dd, P_2, major diastereomer, J_{Rh-P} = 151, $J_{P_1P_2}$ = 40 Hz), 69.1 (dd, P_1, minor diastereomer, J_{Rh-P} = 156 Hz), 59.9 (dd, P_2, minor diastereomer, J_{Rh-P} = 160, $J_{P_1P_2}$ = 36 Hz), 55.4 ppm (d, bis(biphosphine)rhodium(I) tetrafluoroborate, J_{Rh-P} = 137 Hz). The diastereomer ratio was determined by integration and the values quoted in the text represent an average of at least three different experiments.

(*Z*)-Methyl α-Benzamidocinnamate-*1*-^{13}C Adduct (18). This was prepared in CD_3OD as described above from the methanol adduct (49 μmol) and (*Z*)-methyl α-benzamidocinnamate-*1*-^{13}C (16.5 mg, 58.7 μmol) and both its ^{13}C and ^{31}P NMR spectra were recorded: ^{31}P NMR (CD_3OD) δ 71.65 (dd, P_1, major diastereomer, J_{Rh-P} = 162

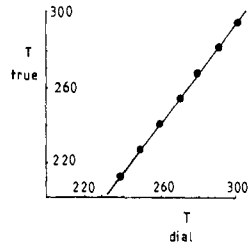


Figure 4.

Hz), 50.5 (ddd, P_2, major diastereomer, $J_{Rh-P} = 150$, $J_{P_1P_2} = 40$, $J_{P_2-C} = 4.9$ Hz), 69.75 (dd, P_1, minor diastereomer, $J_{Rh-P} = 155$ Hz), 60.3 ppm (ddd, P_2, minor diastereomer, $J_{Rh-P} = 160$, $J_{P_1P_2} = 36$, $J_{P_2-C} = 4.9$ Hz); ^{13}C NMR (CD_3OD) δ 180.5 (d, $J_{C-P_2} = 4.9$ Hz, bound ester, major diastereomer), 169.7 (d, $J_{C-P_2} = 4.9$ Hz, bound ester, minor diastereomer), 167.4 ppm (free ester).

Temperature Calibration of the Bruker WH90. Two different methods were used; the graph in Figure 4 illustrates the deviations between the temperature set and that observed. The first involved a thermocouple and a digital thermometer both of which were independently calibrated. This was carried out with a nonspinning sample and the decoupler switched off. The other method[47] involved calibration of the variation of the ^{13}C chemical shifts of ethyl iodide sealed in a capillary tube in a conventional sample. Both methods give similar results. In all variable-temperature experiments at least 5 min was allowed for temperature equilibration before accumulation was commenced.

Acknowledgments. We thank Drs. W. S. Knowles and B. Bosnich for gifts of chemicals, Johnson Matthey for the loan of rhodium salts, and Prochem Ltd. for carbon-13 labeled materials. Fellowships from IBM and the E.P. Abraham Research Fund (to P.A.C.) are gratefully acknowledged.

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