Intermediates in the Asymmetric Hydrogenation of Unsaturated Carboxylic Acid Derivatives

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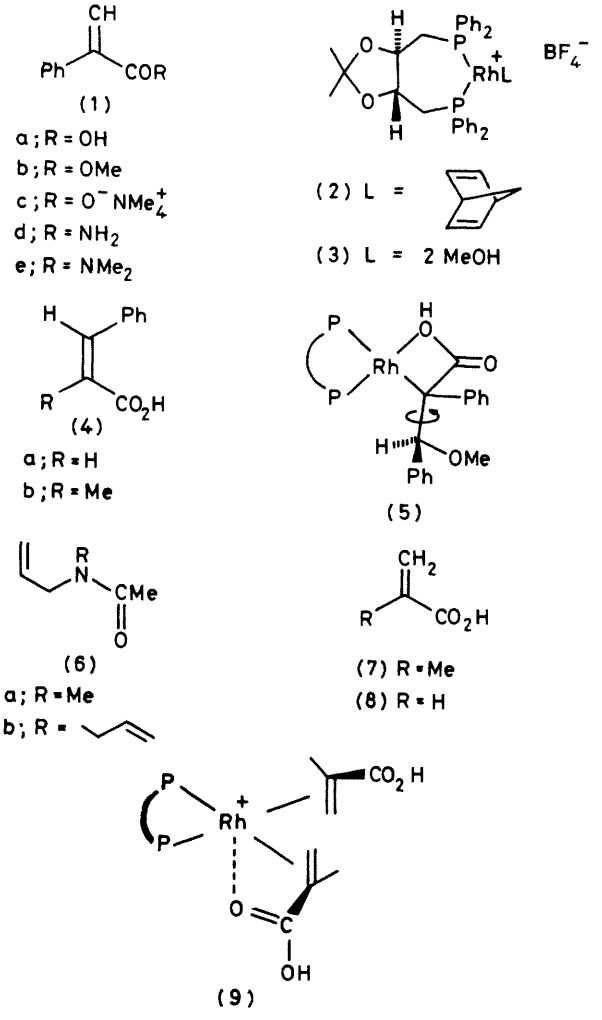
Summary Unsaturated carboxylic acids form several types of rhodium biphosphine complex which may affect the course of asymmetric hydrogenation reactions.

MANY rhodium biphosphine complexes are efficient catalysts for the asymmetric hydrogenation of dehydroamino acids, although other reactants tend to be reduced in

inferior optical yield.[1] Previous work has demonstrated strong bidentate binding of the substrate with selectivity in the former case[2] and we now report experiments which define the structure of rhodium complexes with $\alpha\beta$-unsaturated acids.



Addition of an excess of atropic acid (**1a**) to the complex (**3**) formed by hydrogenation of (**2**) in methanol gives rise to an ill-defined ^{31}P n.m.r. spectrum in which two broadened eight-line multiplets may be observed at 235 K. This is produced by the two possible diastereomeric olefin carboxylate complexes, since it is not formed by the methyl ester (**1b**), whereas tetramethylammonium atropate (**1c**) gives a similar spectrum albeit sharp at ambient temperature, and the spectrum derived from (**1a**) is sharp below 280 K in the presence of triethylamine (Table). Similar species are formed by *cis*-cinnamic acid (**4a**) and (**3**) and by (*Z*)-α-phenylcinnamic acid (**4b**) and (**3**), with sharp spectra observed at room temperature in the presence of triethylamine.[3] Little complexation occurs with *trans*-cinnamic acid, and (*E*)-α-phenylcinnamic acid is catalytically isomerised by (**3**) to the (*Z*)-isomer and its complex at 280 K in the presence of triethylamine, possibly *via* an addition–elimination mechanism, as in (**5**). Our results (Table), and those derived previously, demonstrate that carboxylate anion formation is necessary for effective asymmetric hydrogenation, although there is not a close relationship between the diastereomer ratio observed by n.m.r. spectroscopy and the enantiomer ratio on reduction. Clearly the *trans*-cinnamate structure engenders an unfavourable intracomplex Ph–Ph interaction.

Atropamide (**1d**) and *NN*-dimethylatropamide (**1e**) both form strong complexes on admixture with (**3**) which appear very similar to the carboxylate complexes. These amides are reduced in inferior optical yield, however, and both the enantiomer excess and n.m.r.-derived diastereomer ratio are altered by added triethylamine. The strong binding and powerful Lewis basicity of unsaturated amides is demonstrated by the close similarity of bidentate species formed by allylamides (**6a**) and (**6b**) with (**3**) notwithstanding the fact that diallyl ether acts as a chelating diolefin in its rhodium complexes.[4]

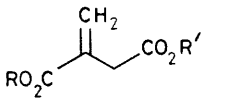
Methacrylic acid (**7**) and acrylic acid (**8**) behave similarly to (**1a**) if triethylamine is present, the latter forming a single complex with high stereoselectivity. In the absence of base an entirely different type of species is formed.[5] Complexation is slow, and careful determination of the stoicheiometry in the case of (**7**) demonstrates it to be 2:1, similar to bis(olefin)rhodium acetylacetonates.[6] A possible structure consistent with the lowered P–P and Rh–P coupling constants is (**9**). Such species may be dominant under hydrogenation conditions employing a large excess of substrate in the absence of base.

Itaconic acid (**10a**) and its derivatives afford the possibility of competitive or co-operative binding by α and β carboxylates. It is of interest that high optical yields in asymmetric hydrogenation have been observed for this

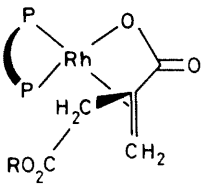
TABLE. Typical ^{31}P n.m.r. spectra of complexes in MeOH[a]

Substrate	Conditions	Complex type	δ_1	δ_2	$J_{Rh-P(1)}$	$J_{Rh-P(2)}$	J_{P-P}	Diastereomer[b] ratio[c]	% E.e. in hydrogenation
(**1c**)	300 K	Carboxylate: (**3**)	35·3	13·1	173	173	50	3:2	67 (*S*)
			37·6	10·7	177	171	50		
(**1e**)	230 K	Amide: (**3**)	40·0	9·7	175	162	53	1:1	34 (*S*)[d]
			36·0	14·1	172	169	53		
(**7**)	260 K	2:1 Carboxylic	30·8	29·7	141	137	39	>5:1	—
		acid: (**3**)	31·4	17·6	140	134	41		
(**10d**)	230 K	Carboxylate: (**12**)	76·5	50·9	175	175	38	4:1	
			76·9	51·6	173	173	38		
(**10d**)	300 K	1:1 Carboxylic	69·7	52·4	150	153	22	4:1	53 (*R*) [55 (*R*)[f]]
		acid: (**12**)	68·0	52·2	148	152	21		

[a] Chemical shifts recorded in p.p.m. downfield from H_3PO_4. [b] Typically 0·03 M [Rh^+] with a 6-fold excess of substrate. [c] Eu(hfc)$_3$, CCl_4 determination on derived dimethylamides. [d] NEt_3 present, 14 (*R*) in its absence. [e] Major species first. [f] Ref. 7.



(10) a, R, R′ = H
b, R = Me, R′ = H
c, R = R′ = Me
d, R = H, R′ = Me



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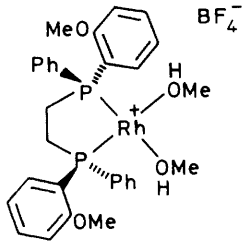

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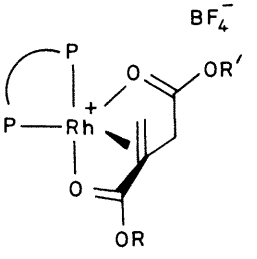

(13)

substrate with both 5-[7] and 7-ring rhodium biphosphine chelates [8] The ^{31}P n m r spectrum of species formed by complexation of (**3**) with (**10a**) or its α-methyl ester (**10b**) is exchange-broadened at all temperatures in the presence or absence of base The dimethyl ester (**10c**) does not bind to rhodium but the β-methyl ester (**10d**) gives a sharp spectrum below 278 K in the presence of triethylamine, similar to the 1,1 bidentate olefin carboxylate complexes described above Thus, only the α-carboxylate group is strongly bound, as in (**11**) With the 5-ring chelate complex (**12**) derived from (*RR*)-bis(*o*-methoxyphenylphenylphosphino)ethane,[9] related 1 : 1 complexes are formed from (**10a**) and (**10d**) in the presence of base, but with higher stereoselectivity, and (**10c**) forms a complex of similar structure but much lower stability (Table) An insoluble precipitate is formed from (**10b**) and (**12**) under basic conditions In the absence of triethylamine a different kind of 1 : 1 complex is formed by (**10a**)—(**10d**) which is very lightly coloured, has a greatly reduced P–P coupling constant, and is consistent with the terdentate structure (**13**) but not with selective β-complexation, as implied earlier [7] A bidentate complex is fleetingly formed from (**10a**) or (**10b**) at low temperatures

These latter results highlight potential differences between 5- and 7-ring chelate biphosphine rhodium complexes The former are highly effective in the reduction of enamides and other substrates which are potentially terdentate, but rather ineffective in other cases [9] The latter are less efficient with enamides but tolerant of potentially bidentate substrates Thus the chelate angle PRhP,[10] and phosphine basicity[11] may play a critical role in asymmetric catalysis

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[2] J M Brown and P A Chaloner, *J Chem Soc, Chem Commun*, 1979, **613**, and earlier references
[3] C F Koelsch and P R Johnson, *J Am Chem Soc*, 1943, **65**, 565, L A Singer and N P Kong, *ibid*, 1966, **88**, 5213 We thank Dr D Sinou for a sample of (**5**)
[4] R Grigg, B Kongkathip and T J King *J Chem Soc, Dalton Trans*, 1978, 333
[5] A rhodium complex of itaconic acid with an asymmetric biphosphine derived from (*S*)-proline shows a very similar spectrum and appears to be a 2 1 complex rather than bidentate 1 1 as claimed I Ojima and T Kogure, *Chem Lett*, 1978, 1145, 1979, 641, K Achiwa, Y Ogha, and Y Iitaka, *ibid*, 1979 865
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[8] K Achiwa, *Chem Lett*, 1978, 561
[9] B D Vineyard, W S Knowles, M J Sabacky, G L Bachman, and D J Weinkauff, *J Am Chem Soc*, 1977, **99**, 6262, and references therein, D Parker, unpublished work
[10] Typically 82° for 5-ring chelates and 96° for 7-ring chelates (A S C Chan, J J Pluth, and J Halpern, *Inorg Chim Acta*, 1979, **37**, L477, V Gramlich and G Consiglio, *Helv Chim Acta*, 1979, **62**, 1016)
[11] J E Huheey and S O Grim, *Inorg Nucl Chem Lett*, 1974, **10**, 973