Proc. Indian Acad. Sci. (Chem. Sci.), Vol. 106, No. 4, August 1994, pp. 847–855.

Chiral rhodium carboxylates as asymmetric hydrogenation catalysts

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MS received 4 December 1993; revised 7 April 1994

Abstract. The comparative catalytic activities of a few chiral rhodium carboxylato complexes in combination with chiral and achiral phosphines are described. In the hydrogenation of α–acetamidocinnamic acid and its methyl ester, differences are observed in turnover numbers and enantioselectivities. Diastereomeric interactions between chiral carboxylato and chiral phosphine moieties resulting in different rates are clearly seen. Arrhenius plots of (+) and (−) DIOP [DIOP = 2, 3 isopropylidene 2, 3 dihydroxy–1,4 *bis* (diphenylphosphino) butane] with rhodium (−) mandalato complex give markedly different activation energies.

Keywords. Asymmetric; hydrogenation; rhodium; catalysts; carboxylates.

1. Introduction

A few reports on the use of rhodium carboxylate complexes as catalysts in hydrogenation and transfer-hydrogenation reactions have appeared (Rempel *et al* 1973; Pruchnik *et al* 1985; Marcec 1986; Brunner *et al* 1989; Marcec *et al* 1991; Gladiali *et al* 1992). Although these complexes themselves are capable of acting as precatalysts, without the addition of nitrogen or phosphorous ligands degradation of the complexes leading to metal formation occurs (Wilkinson *et al* 1970). Very brief mentions on the use of chiral rhodium carboxylato-complexes in asymmetric hydrogenation reactions can also be found in the literature (James *et al* 1986; Chan and Landis 1989). In these reactions only poor (< 15%) enantiomeric excesses are obtained. This paper describes a comparative evaluation of the efficiencies of different chiral rhodium carboxylates as pre-catalysts. Since the stability of the catalytic systems is dependent on the presence of a phosphorous ligand, diastereomeric interactions are expected if both the carboxylato group and the phosphine ligand are chiral. If such diastereomers are involved as catalytic intermediates difference in the overall rates and enantioselectivities would be observed for different diastereomers. In the present work these catalytic systems have been studied in some detail.

2. Results and discussion

2.1 *Synthesis and characterisations*

The designations of the rhodium carboxylates derived from different chiral acids are given in table 1. Syntheses and X–ray structures of 1, 2b, 3a and 4 have been reported

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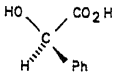
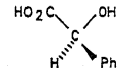
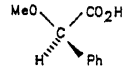
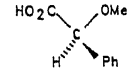
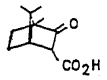
Table 1. Designations of the rhodium carboxylates derived from the different chiral acids.

RCO_2H	$[Rh_2(RCO_2)_4]$
CH_3CO_2H	1
R(-) 	2a
S(+) 	2b
R(−) 	3a
S(+) 	3b
(1S,4R)(−) 	4
(1R,3S)(+) 	5
(+) 	6[a]

[a] Mixture of exo and endo

in the literature (Cotton *et al* 1970, 1971, 1986; Marcec *et al* 1992). Among the reported general procedures (see § 3), fusion of the free carboxylic acids with rhodium acetate has been found to be the most convenient synthetic method for 4 and 5. This however fails for 6 due to the high volatility of camphor carboxylic acid. Thus, for the synthesis of 6 $RhCl_3 . 3H_2O$ was directly reacted with camphor carboxylic acid (see § 3).

The carboxylates 4–6 have been converted to their triphenyl phosphine adducts and the resultant species, 7–9 respectively, have been characterised on the basis of spectroscopy and analytical data (see § 3). The X–ray structures of a large number of rhodium carboxylate adducts of the general formula $[Rh_2(RCO_2)_4L_2]$ are known (Felthouse 1982, Boyer and Robinson 1983, 1985). These structures are best described as two edge-sharing octahedra centred around the two rhodium atoms. Similar co-ordination geometries may be proposed for the complexes 7 and 8 with two *trans*-triphenylphosphines. The infrared spectrum of 8 is indicative of at least one free carboxylic acid group.

The IR stretching frequency for the keto group in 9 is approximately $16\,cm^{-1}$ lower than that for the free ligand. Similarly, the C^{13} NMR signal for the keto group shows a 5 ppm down-field shift in comparison with the free ligand. This indicates substantial interaction between oxygen atom of the keto group and the rhodium centre. We have so far not been able to obtain crystals of 9 suitable for X–ray measurements.

2.2 *Homogeneity of the catalytic systems*

The ability of 1 to act as a hydrogenation catalyst for olefins in the presence of triphenylphosphine and a non-complexing acid such as HBF_4 was first reported by Wilkinson and co-workers in 1970. It was pointed out that at 50°C, in the absence of phosphine, decomposition of the complex to metal occurred. For the present work it was therefore necessary to identify the optimum ligand concentration under which homogeneity of the catalytic system was maintained.

The ligand to metal ratio that leads to a stable homogeneous systems is dependent on the substrate and the ligand employed. The effects of two phosphorous ligands, PPh_3 and (+) DIOP and two substrates, cyclohexene and α–acetamidocinnamic acid have been studied in detail.

With 1 as the precatalyst and cyclohexene as the substrate a high ligand to metal molar ratio is needed to maintain the homogeneity of the system. For PPh_3 and (+) DIOP these ratios are $\geqslant 12$ and $\geqslant 1$ respectively. However, with α–acetamido cinnamic acid as the substrate a much lower ligand to metal molar ratio ($\geqslant 2$ for PPh_3, $\geqslant 0{\cdot}5$ for (+) DIOP) is adequate for ensuring that metal formation does not take place. For α–acetamidocinnamic acid, catalytic activity ceases altogether with a 1 to (+) DIOP molar ratio of four.

It is well known that in the hydrogenation of α–acetamidocinnamic acid by other rhodium phosphine complexes, coordination by the acetamido group along with the olefinic double bond takes place. It is reasonable to assume that the enhanced coordinating ability of α-acetamidocinnamic acid in comparison with that of cyclohexene ensures that even with less phosphine the catalytic system remains homogeneous.

2.3 *Ligands and solvents*

All phosphorous ligands when combined with rhodium carboxylates do *not* generate catalytically active systems. Thus in the hydrogenation of α-acetamidocinnamic acid no conversion is achieved with combinations of 1 and BINAP (2,2-*bis*(diphenylphosphino)-1,1-binaphthyl), PROPHOS (1,2-*bis*(diphenylphosphino) propane), DPPM (*bis*(diphenylphosphino)-methane), DPPE (1,2-*bis*(diphenylphosphino) ethane) or DPPH (1,6–*bis*(diphenylphosphino)hexane). With DPPP (1,3-*bis*(diphenylphosphino)propane) noticably lower conversion ($\leqslant$ 1/4th) than that with (+) DIOP or PPh_3 is obtained. No conversion is obtained with other monodentate phosphines also such as tricyclohexyl phosphine or tri-*n*-butyl phosphine.

The activities of the catalytic systems are influenced to some extent by the solvent employed (table 2). Thus with methyl α-acetamidocinnamate or 2-acetamidoacrylic acid as the substrate, 1 in combination with (+) DIOP fails to show any catalytic activity in THF (THF = tetrahydrofuran). For α-acetamidocinnamic acid much reduced activity is observed in this solvent. In contrast, with the same catalytic system high activity is observed in methanol. This is true for all the three substrates.

Change of solvent has no apparent effect on the (−) or (+) mandalato complex plus (+) DIOP-based catalytic systems. With these complexes, both in methanol and in THF, high conversions are achieved for α-acetamidocinnamic acid and its methyl ester.

Table 2. Catalytic conversions in different solvents.[a]

Substrate	Solvent	Conversion (%)
1 as the catalyst		
α-Acetamidocinnamic acid	Methanol	100
α-Acetamidocinnamic acid	Tetrahydrofuran	20
Methyl α-acetamidocinnamate	Methanol	100
Methyl α-acetamidocinnamate	Tetrahydrofuran	0
2-Acetamidoacrylic acid	Methanol	100
2-Acetamidoacrylic acid	Tetrahydrofuran	0
2a as the catalyst[b]		
α-Acetamidocinnamic acid	Methanol	100
α-Acetamidocinnamic acid	Tetrahydrofuran	100
Methyl α-acetamidocinnamate	Methanol	100
Methyl α-acetamidocinnamate	Tetrahydrofuran	100

[a] All reactions carried out at 27°C with a catalyst (0·0125 mmol): substrate and (+) DIOP (0·025 mmol) molar ratio of 1:100:2 in 20 ml solvent over a period of 16 h.

[b] Similar results with (2b) as the catalyst.

2.4 *Comparative activities and enantioselectivities*

Data on the hydrogenation of two prochiral substrates with different catalysts is listed in table 3. The following points should be noted. First, for both the substrates catalysts 1, 2a and 2b are more active than catalysts 3–6 (experiments (i)–(iii), (vi)–(xiii) and (xv)–(ixx)). Second, with PPh_3 and chiral carboxylato complexes, low but measurable enantioselectivities are obtained (experiments (iv), (v) and (xiv)). Third, in experiments with (+) DIOP, the turnover numbers and especially the enantiomeric excesses obtained by complexes containing the enantiomers of a given carboxylato group are noticably different. This is true for both the mandalato (experiments (ii), (iii), (xii) and (xiii)) and the methoxy mandalato (experiments (vi), (vii), (xv) and (xvi)) complexes.

The nature of the species generated when dirhodium tetracarboxylates are activated with non-coordinating acids have been investigated by several workers (Taube and Wilson 1975; Drago and Telser 1984). It has been suggested that species such as $Rh_2(RCO_2)_3^+$ and $Rh_2(RCO_2)_2^{2+}$ are generated when $Rh_2(RCO_2)_4$ is treated with non-complexing acids. All the observations listed above indicate the presence of one or more carboxylato groups in the catalytic intermediates.

Different carboxylato complexes will exhibit different turnover efficiencies and enantioselectivities only if at least one carboxylato group remains bound to the rhodium centre after activation with a non-complexing acid. Also, it is only under such conditions that diastereomeric interactions between chiral carboxylato groups and (+) DIOP are expected. Such interactions in the two enantiomeric derivatives of a given carboxylic acid would lead to differences in the overall rate i.e. turnover numbers, as well as enantioselectivities.

Similarly, the diastereomeric interactions expected between 2a and (+) DIOP on the one hand and 2a and (−) DIOP on the other, should result in different overall

Table 3. Comparative catalytic efficiencies[a] and enantioselectivities of complexes 1–6.

Experiment	Catalyst[b]	Turnover number (h^{-1})	Enantiomeric[d] excess (%)
Substrate = α-Acetamidocinnamic acid			
(i)	1	40	55
(ii)	2a	45	60
(iii)	2b	35	20
(iv)[c]	2a	18	< 10
(v)[c]	2b	18	< 10
(vi)	3a	12	20
(vii)	3b	9	60
(viii)	4	2	25
(ix)	5	4	50
(x)	6	2	34
Substrate = Methyl α-acetamidocinnamate			
(xi)	1	41	30
(xii)	2a	43	70
(xiii)	2b	30	25
(xiv)[c]	2a	20	< 15
(xv)	3a	2	57
(xvi)	3b	0·5	41
(xvii)	4	1	15
(xviii)	5	1	50
(xix)	6	1·5	40

[a]All reactions carried out at 27°C with a catalyst (0·0125 mmol) and substrate (1·25 mmol) molar ratio of 1:100 in methanol (20 ml). [b]Excepting (iv), (v) and (xiv), in all experiments (+) DIOP (0·025 mmol) used. [c] PPh_3 (0·05 mmol) used. [d]On the basis of optical rotation values.

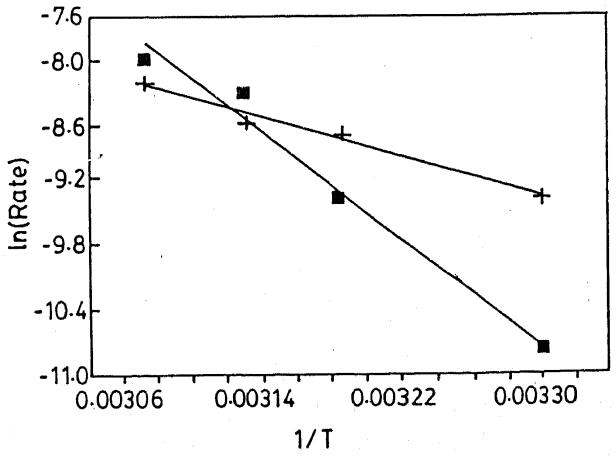


Figure 1. Plot of ln (rate) vs $1/T$ for the hydrogenation of acetamidocinnamic acid with (2a) and (−) DIOP (+) and (2a) and (+) DIOP (■) as the catalysts.

rates. To provide an approximate quantitative estimate, rate measurements for both the systems at different temperatures have been carried out. As can be seen from figure 1, the Arrhenius plots yield markedly different activation energies. Since a complex rate expression is more than likely, the activation energies are only approximate. However, it is worth noting that there is a substantial ($\sim$ 15 kcal) difference between the activation energies. The activation energy of (2a) with (+) DIOP is about 25 kcal while for (2a) with (−) DIOP it is about 10 kcal. Complexes that have an enantiomeric rather than a diastereomeric relationship with each other should exhibit the same overall rate. Although not shown in table 3, this has been observed to be the case. The initial rates of the two catalytic systems, 2a with (−) DIOP and 2a with (+) DIOP are identical within experimental error.

In the absence of the olefinic substrate and dihydrogen, addition of a large excess of PPh_3 to the acid activated methanolic solution of 1 results in the precipitation a species which on the basis of microanalysis and spectroscopic data is formulated as $Rh_2(OAC)_3(PPh_3)_2(MeOH)_3]BF_4$, 10. Complexes of very similar stoichiometries have recently been reported and structurally characterised (Dunbar *et al* 1993). To test if such species are involved as active catalytic intermediates, the ability of 10 to function as a precatalyst has been evaluated. In the absence of PPh_3, under catalytic condition 10 undergoes degradation to finely divided metal. However, with added PPh_3 a catalytically active, stable, homogeneous system is obtained. Keeping the overall metal to PPh_3 ratio the same, the turnover numbers of 10 and 1 based catalytic systems are different. The latter is about twice as active. This indicates that while species like 10 may be involved, other species must also take part in the overall catalytic cycle.

3. Experimental

All reactions and manipulations were carried out under an atmosphere of dry nitrogen unless specified otherwise. Infrared and NMR spectra were recorded on a PE 781 and a Brucker 80 MHz F T instrument. ^{31}P peak positions were measured in ppm from 85% H_3PO_4 as external standard. The ^{31}P NMR experiments were carried out at ambient temperatures. Computer-simulated analysis of the spectrum, as has recently been reported in the literature (Boyer and Robinson 1985) for the *bis* phosphine adducts, was not carried out. A Shimadzu GC 9A and Jasco DIP 140 polarimeter were used for gas chromatographic analysis and optical rotation measurements respectively. A Carlo-Erba 1106 instrument was used for microanalyses. Camphanic acid, camphor carboxylic acid and camphoric acid were purchased from Aldrich. The carboxylates 1, 2 and 3 were prepared according to literature reported procedures (Cotton and Norman 1972; Wilkinson *et al* 1972; Brunner *et al* 1989; McKervey *et al* 1990; Noels *et al* 1990).

3.1 *Catalytic experiments*

In a typical run, 1 (6·0 mg, 0·0125 mmol) was magnetically stirred with 32% HBF_4 (17·0 mg, 0·025 mmol) in methanol (20 ml) at 60°C for 2 h. After cooling the solution to room temperature (+) DIOP (12 mg, 0·0250 mmol) was added to the solution, stirred for 10 min and then α-actamidocinnamic acid (256 mg, 1·25 mmol) was

added. The extent of conversion after the desired time interval (0·5 to 16 h) was measured by taking the solution to dryness and recording the ^1H NMR spectrum of the residue.

For accurate optical rotation measurements α-acetamidocinnamic acid was extracted as the sodium salt and then regenerated. This however rarely gave values significantly different from those obtained for the crude residue. The methyl ester after hydrogenation was purified by thin layer chromatography. In experiments where 2a and 2b in combination with (+) and (−) DIOP were used, the optical rotation values were corrected for the small contribution from the optical isomers of mandelic acid.

3.2 *Synthesis of 4*

A mixture of 1 (25 mg, 0·056 mmol) and (1*S*,4*R*)–(−)– camphanic acid (250 mg, 1·26 mmol) were heated together till the acid melted. The solution was stirred for 10 min and then cooled to room temperature. The dark green solid melt was ground to a powder, extracted with dichloromethane, and repeatedly washed with saturated aqueous sodium bicarbonate solution to remove excess acid. After drying over Na_2SO_4 the green solution was taken to dryness. Dark green crystals were obtained by slow evaporation of a solution of dichloromethane and diethylether, and dried under vacuum. Yield 20 mg (80%).

Analysis, Found:C, 48·50, H, 5·35%, $C_{40}H_{52}O_{16}Rh_2$ Calc.:C, 48·20; H, 5·23%.
IR (KBr, cm^{-1}):$\nu_{(CO)}$ (lactone), 1785 (*vs*); $\nu_{(COO)}$ 1605 (*s*), 1435 (*s*)

3.3 *Synthesis of 5*

A mixture of 1 (50 mg, 0·113 mmol) and (1*R*,3*S*)–(+)–camphoric acid (500 mg, 2·5 mmol) was heated gently till the acid melted. The solution was stirred for 10 min and then cooled to room temperature. The dark blue solid melt was ground to a powder and washed repeatedly with hot water to remove excess acid. The aqueous solution was filtered through celite and then the blue solid along with celite was extracted with diethylether. The blue ether solution was filtered dried over Na_2SO_4 and taken to dryness. On dryness under vacuum a blue solid was obtained. Yield 40 mg (80%).

Analysis Found:C, 47·10; 6·06%, $C_{40}H_{60}O_{16}Rh_2$ Calc.:C, 47·90; H, 5·98%.
IR (KBr, cm^{-1}): $\nu_{(COO)}$, 1695 (*s*); 1580 (*m*); 1400 (*s*).

3.4 *Synthesis of 6*

A mixture of $RhCl_3.3H_2O$ (75 mg, 0·285 mmol) (+)–camphor carboxylic acid (111 mg, 0·57 mmol) in 12 ml of 1:1 H_2O/EtOH was refluxed for 1 hour. The resulting mixture, a green solution containing rhodium metal, was evaporated to dryness. It was then extracted with ether and filtered through celite. The green ether solution was first washed with saturated aqueous sodium bicarbonate solution, then with water, dried over Na_2SO_4 and taken to dryness under vacuum to give a green solid. Yield 15 mg (20%).

3.8 *Synthesis of 10*

To a solution of 1 (12 mg, 0·025 mmol), and 32% HBF_4 (34 mg, 0·05 mmol) in methanol (20 ml), heated at 60°C for 2 h, an excess of PPh_3 (65 mg, 0·25 mmol) was added. On stirring the solution for another 2 h, an orange yellow precipitate of 1 (22 mg, 0·02 mmol) separated out. This was filtered, washed with methanol, diethylether and vacuum dried.

Analysis. Found: C, 49·81; H, 4·20%. $C_{45}H_{51}O_9P_2BF_4Rh_2$ (10) with three molecules of methanol, Calc. C, 49·54; H, 4·67%.
IR (KBr, cm^{-1}): $\nu_{(COO)}$ 1590 (*s*).
^1H NMR ($CDCl_3$): δ 6·7–7·8 (*m*, 30H); 1·9 (*s*, 9H); 3·3 (*s*, 9H).

Acknowledgement

Financial support by ICI India is gratefully acknowledged.

References

Boyer E B and Robinson S D 1983 *Coord. Chem. Rev.* **50** 109
Boyer E B and Robinson S D 1985 *J. Chem. Soc., Dalton Trans.* 629
Brunner H Graf E, Watz K and Laitner W 1989 *Synthesis* 743
Brunner H, Klischanzoff H and Watz K 1989 *Bull. Soc. Chim. Belg* **98** 63
Chan A S C and Landis C R 1989 *J. Catal* **49** 165
Cotton F A, Agaskar P A, Falvello L R and Han S 1986 *J. Am. Chem. Soc.* **108** 1214
Cotton F A, DeBoer B G, LaPrade M D, Pipal J R and Ucko D A 1970 *J. Am. Chem. Soc.* **92** 2926
Cotton F A, DeBoer B G, LaPrade M D, Pipal J R and Ucko D A 1971 *Acta Crystallogr.* **B27** 1664
Cotton F A and Norman J G Jr 1972 *J. Am. Chem. Soc.* **94** 5697
Drago R S and Telser J 1984 *Inorg. Chem.* **23** 1798
Dunbar K R, Crawford C A, Matonic J H, Streib W E, Huffman J C and Christon G 1993 *Inorg. Chem.* **32** 3125
Felthouse T R 1982 *Prog. Inorg. Chem.* **29** 73
Gladiali S, Mestroni G and Zassinovich G 1992 *Chem. Rev.* **92** 1051
James B R, Pruchnik F and Kvintovis P 1986 *Can. J. Chem.* **64** 936
Marcec R 1986 *React. Kinet. Catal. Lett.* **31** 337
Marcec R, Prodic B K, Nigovic B, Raza Z and Sunjic V 1992 *Tetrahedron: Asymmetry* **3** 1
Marcec R, Raza Z and Sunjic V 1991 *J. Mol. Catal.* **69** 25
McKervey M A, Kennedy M, Maguire A R and Roos G H P 1990 *J. Chem. Soc., Chem. Commun* 361
Noels A F, Demonceau A and Hubert A J 1990 *Tetrahedron* **46** 3889
Pruchnik F P 1989 *Pura Appl. Chem.* **1** 795
Pruchnik F P, Pasternak H and Lancman E 1985 *J. Mol. Catal.* **29** 13
Rempel G L, Hui B C Y and Teo W K 1973 *Inorg. Chem.* **12** 757
Taube H and Wilson C R 1975 *Inorg. Chem.* **14** 2276
Wilkinson G, Legzdins P, Mitchell R W, Rempel G L and Ruddick J D 1970 *J. Chem. Soc.* (*A*) 3322
Wilkinson G, Smith M, Rempel P A and Legzdins P 1972 *Inorg. Synth.* **13** 90