

ASYMMETRIC SYNTHESIS BY CHIRAL RUTHENIUM COMPLEXES

II *. ENANTIOSELECTIVE HYDROGENATION OF α,β -UNSATURATED CARBOXYLIC ACIDS CATALYZED BY RUTHENIUM COMPLEXES CONTAINING THE LIGAND (–)-DIOP

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Summary

Cluster rutheniumcarbonyl hydrides complexes containing (–)-DIOP as asymmetric ligand are efficient catalysts for asymmetric reduction of α,β -unsaturated acids at 90–120°C under hydrogen pressure. Optical yields up to 68% have been achieved. The course of the reaction has been investigated by IR spectroscopy using a high pressure cell.

Introduction

In recent years there has been much work done on asymmetric hydrogenation catalyzed by transition metal complexes [1]. The most important aspect of this catalytic process consists, of course, in providing an efficient route to a number of chiral biologically valuable compounds starting from achiral substrates [2]. Most of these asymmetric hydrogenations have been accomplished using chiral

* For Part I see ref. 5.

phosphine-rhodium complexes: very high optical yields (up to 95.7%) were reached by their use in the reduction of α -acylaminoacrylic acids [3]. Various cobalt complexes have also been employed in the asymmetric reduction of functional groups, but the asymmetric bias is customarily lower than with rhodium catalysts [1].

Surprisingly, only few examples of asymmetric hydrogenation with chiral ruthenium complexes have been reported [1,4,5,6] in spite of the well-documented catalytic hydrogenating activity displayed by ruthenium derivatives [7]. Moreover, these catalysts should be attractive from an economic viewpoint, provided that the asymmetric inductions are in the same range as those achieved with rhodium catalysts. Recently we reported the asymmetric catalytic reduction of ketones and ketoximes using $\text{H}_4\text{Ru}_4(\text{CO})_8[(-)\text{-DIOP}]_2$ [5]: the rather severe reaction conditions required for effecting the catalytic process led to optical yields not exceeding 15%. In the present paper we report the results obtained in the asymmetric hydrogenation of α,β -unsaturated mono- and dicarboxylic acids using cluster ruthenium carbonyl complexes containing $(-)\text{-DIOP}$ [8] as an optically-active ligand.

Results

The hydrogenation experiments were carried out using $\text{H}_4\text{Ru}_4(\text{CO})_8[(-)\text{-DIOP}]_2$ (A) and $\text{Ru}_6(\text{CO})_{18}[(-)\text{-DIOP}]_3$ (B) as catalytic precursors. The catalytic complex A was prepared in 90% yield from $\text{H}_4\text{Ru}_4(\text{CO})_{12}$ and $(-)\text{-DIOP}$ by a published procedure [9] and purified by crystallization from methanol/methylene chloride; the elemental analysis and molecular weight were consistent with the formulation $\text{H}_4\text{Ru}_4(\text{CO})_8[(-)\text{-DIOP}]_2$. The tetrahedral arrangement of the four ruthenium atoms suggested by NMR and IR spectra was confirmed by X-ray studies [10].

The complex B was obtained in almost quantitative yield from the reaction between $\text{Ru}_3(\text{CO})_{12}$ and the asymmetric diphosphine under the conditions used for the preparation of $\text{Ru}_3(\text{CO})_9\text{L}_3$ complexes ($\text{L} = \text{PPh}_3$ and PBu_3) [11]: during this reaction three moles of carbon monoxide were evolved per mole of $\text{Ru}_3(\text{CO})_{12}$ used. Characterization of complex B was performed by elemental analysis, molecular weight determination and IR spectroscopy.

Both complexes are quite stable in the air, both in the solid state and in solution.

Standard hydrogenation experiments were carried out with both catalytic precursors at 90–120°C and 130 atm of hydrogen: normally 20–40 h reaction times were required to achieve conversions of $\geq 80\%$. The reduction of the olefinic double bond of the α,β -unsaturated monocarboxylic acids proceeded with complete selectivity, whereas $\sim 90\%$ selectivities were found in the reduction of dicarboxylic acids *. Occasional formation of ethyl esters was observed during reductions carried out in toluene/ethanol.

The optical yields achieved in our experiments are listed in Tables 1, 2 and 3. Up to 68% enantiomeric excess (e.e.) was reached for unsaturated monocarboxylic acids and 10% e.e. for unsaturated dicarboxylic acids.

* The identities of the by-products are under investigation.

TABLE 1

ASYMMETRIC HYDROGENATION OF α,β -UNSATURATED CARBOXYLIC ACIDS IN THE PRESENCE OF $H_4Ru_4(CO)_8[(-)-DIOP]_2$ TO GIVE SATURATED CARBOXYLIC ACIDS (Substrate 20 mmole; catalyst 0.1 g; solvent toluene (10 ml)/ethanol (10 ml); $p(H_2)$ 130 atm at 25°C; reaction temperature 100°C)

Substrate	α_D^{25} (neat)	Predominant configuration	Asymmetric induction	
			%	Ref.
$\begin{array}{c} \text{H} \quad \text{COOH} \\ \diagdown \quad / \\ \text{C}=\text{C} \\ / \quad \diagdown \\ \text{CH}_3 \quad \text{CH}_3 \end{array}$	+5.72	(S)	31.0	12
$\begin{array}{c} \text{Ph} \quad \text{COOH} \\ \diagdown \quad / \\ \text{C}=\text{C} \\ / \quad \diagdown \\ \text{CH}_3 \quad \text{H} \end{array}$	-14.10	(R)	25.0	13
$\begin{array}{c} \text{Ph} \quad \text{COOH} \\ \diagdown \quad / \\ \text{C}=\text{C} \\ / \quad \diagdown \\ \text{H} \quad \text{CH}_3 \end{array}$	+11.98	(S)	58.0	14
	+6.46 ^a	(S)	31.2 ^a	14
$\begin{array}{c} \text{HOOC} \quad \text{COOH} \\ \diagdown \quad / \\ \text{C}=\text{C} \\ / \quad \diagdown \\ \text{H} \quad \text{CH}_3 \end{array}$	-0.19 ^b	(S)	1.1	15
$\begin{array}{c} \text{HOOC} \quad \text{CH}_3 \\ \diagdown \quad / \\ \text{C}=\text{C} \\ / \quad \diagdown \\ \text{H} \quad \text{COOH} \end{array}$	-1.38 ^c	(S)	8.1	15
	-1.70 ^d	(S)	10.0 ^d	15
$\begin{array}{c} \text{CH}_2=\text{C} \quad \text{CH}_2\text{COOH} \\ \diagdown \quad / \\ \text{COOH} \end{array}$	0.00			

^a Benzene was used as solvent (20 ml). ^b Optical rotation in absolute ethanol at 20°C (c 5.0). ^c Optical rotation in absolute ethanol at 20°C (c 10.7). ^d Reaction carried out in the presence of triethylamine (5 mmol); optical rotation in absolute ethanol at 20°C (c 8.74).

Asymmetric hydrogenation of (*E*)-ethyl α -methylcinnamate with complex A under standard conditions afforded the saturated ester with 12.2% e.e. Since the same (S) configuration and a lower optical purity were found with respect to the corresponding acid, asymmetric hydrogenation of esters was not investigated further.

Substrates without carboxylic groups were hydrogenated with lower asymmetric induction even at lower temperature: with both catalytic systems α -ethylstyrene gave (+)(S)-2-phenylbutane with 4–5% optical purity at 60°C.

Fair enhancements of enantiomeric excess were observed in reductions of α,β -unsaturated acids in the presence of triethylamine (Table 1 and 2).

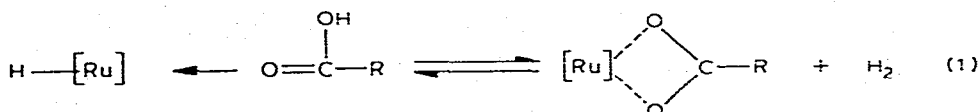
The influence of the hydrogen pressure on the extent of the asymmetric induction was studied in the case of catalytic hydrogenation of (*E*)- α -methylcinnamic acid with complex A. From the results, summarized in Table 3, it appears that a definite increase in optical yields occurred on lowering the hydrogen pressure.

catalytic process carried out at this temperature.

It is noteworthy that the reductions of the same substrates using two different catalytic precursors (A and B) give products with the same predominant configuration and comparable optical purity (Table 1 and 2). This suggests that the complexes A and B under the conditions used may give rise to the same catalytic intermediate(s).

The asymmetric inductions obtained with different unsaturated acids (Table 1 and 2), and with (*E*)-ethyl α -methylcinnamate and α -ethylstyrene suggest the following comments; (i) a free carboxylate group is required for the production of substantial asymmetric bias, at least in the case of unsaturated monocarboxylic acids. This is in agreement with the findings of other authors [16], who proposed a mechanism involving bifunctional substrate coordination through both the carboxylate anion and the olefinic bond; (ii) the lower optical yields obtained with α,β -unsaturated dicarboxylic acids compared with the other substrates can be tentatively attributed to a different bifunctional coordination to the metal in these cases involving both carboxylate groups, which will be specially favoured when these groups are in *cis* positions. In such a hypothetical intermediate catalytic complex the olefinic bond may be only weakly coordinated to the metal and thus be subject to poor steric control. The lack of optical activity in the reduction product from itaconic acid (Table 1) is consistent with such a hypothesis.

The stereoselectivity of the reaction is strongly dependent upon the hydrogen pressure (Table 3). This may be tentatively rationalized by assuming the existence of equilibria, the position of which depend upon the hydrogen pressure, between hydridoruthenium complexes with different catalytic activity and/or between two types of carboxylate complexes, as shown in the following scheme, which exhibit different conformational homogeneity (eq. 1).



For a deeper insight into the course of the catalytic process the reduction of tiglic acid with complex A was investigated by means of a IR high pressure cell [17]. Fig. 1 shows the IR spectra recorded under the most representative reaction conditions. At room temperature and 70 atm of hydrogen no appreciable interaction between the catalyst and the substrate occurs (pattern a). Under conditions associated with a reasonable reaction rate (100°C, $p(\text{H}_2)$ 80 atm) the IR spectrum shows marked variations (pattern b); the considerable decrease of the band of the tiglic acid ($\nu(\text{C}=\text{O})$ 1690 cm^{-1} ; $\nu(\text{C}=\text{C})$ 1674 cm^{-1}) is associated with the appearance of the band of the 2-methylbutanoic acid ($\nu(\text{C}=\text{O})$ 1710 cm^{-1}). In addition two bands observed at 1765 and 1590 cm^{-1} may be attributed to a possible intermediate catalytic complex between the metal and the substrate: the absorption at lower frequency can be ascribed to a $\nu(\text{C}=\text{O})$ of an acyl group coordinated to the metal [18] or to a ruthenium carboxylate complex formed during the catalytic process [19]. It is interesting to note that the carbonyl bands of the catalytic precursor A show negligible variation under hydrogen pressure at 100°C both in the presence and in the absence of the substrate.

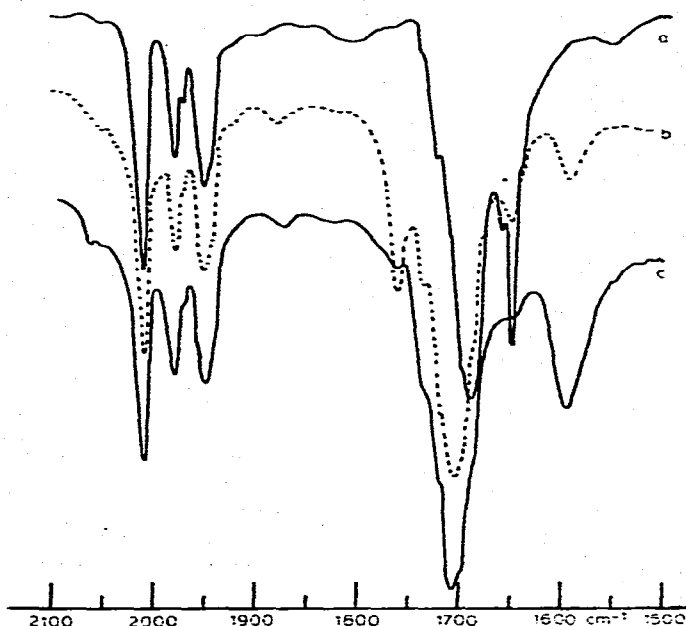
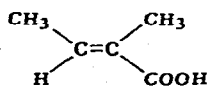


Fig. 1. Infrared spectra of the system $\text{H}_4\text{Ru}_4(\text{CO})_8[(-)\text{-DIOP}]_2 +$



(a) $T\ 20^\circ\text{C}; p(\text{H}_2)$

70 atm; (b) $T\ 100^\circ\text{C}; p(\text{H}_2)$ 80 atm; (c) $T\ 20^\circ\text{C}; p(\text{H}_2)$ 70 atm.

These results indicate that the cluster structure of the complex A is not much affected during the catalytic process. An alternative interpretation is that the intermediate catalytic complex must be present in the reaction medium only in very low concentration.

The two bands at 1765 and 1590 cm^{-1} behave differently when the system is cooled to room temperature (25°C , 70 atm of hydrogen): a sharp decrease in the intensity of the first band takes place, while the second one is little changed (pattern c). The patterns b and c are reproduced also when further substrate is added to the system. The nature of the species associated with these bands are now under investigation.

Experimental

NMR spectra were recorded on a Varian T 60 spectrometer; IR spectra were measured in the specified solvents with a Perkin-Elmer 225 instrument. Infrared spectra under pressure were recorded using a cell having NaCl optics, developed by us, capable of withstanding high pressure (200 atm) and temperature (up to 150°C). The rotatory powers were measured on a Perkin-Elmer 241 polarimeter; GLC analysis were performed on a Perkin-Elmer F30 instrument; molecular weight were determined with a Mechrolab apparatus.

Materials

Tiglic acid (Fluka), citraconic acid (Fluka), mesaconic acid (Ega), α -methylcinnamic acid (Ega) and itaconic acid (Fluka) were purchased.

α -Ethylstyrene was prepared according to the literature [20]. α -Ethylacrylic acid was prepared by Ag_2O oxidation of α -ethylacrolein. β -Methylcinnamic acid was prepared by saponification of the corresponding methyl ester, obtained by a known procedure [21].

(+)(S)-Ethyl-2-methyl-3-phenylpropanoate was prepared by esterification of a sample of the corresponding acid, $\alpha_D^{25} (l = 1) + 6.46$ (o.p. 31.2% [14]). The ester had b.p. $45^\circ\text{C}/0.07$ mmHg, $\alpha_D^{25} (l = 1) + 7.49$.

Preparation of complexes

$\text{H}_4\text{Ru}_4(\text{CO})_8[(-)\text{-DIOP}]_2$ (A). Tetraruthenium dodecacarbonyl tetrahydride (0.43 g), (–)-DIOP (0.65 g), toluene (30 ml) and hydrogen (140 atm) were heated in a 125 ml stainless steel autoclave at 150°C for 5 h. The resulting red solution was evaporated to dryness at room temperature under vacuum and the remaining solid was washed several times with cold methanol (0°C , 30 ml), then dissolved in methanol/methylene chloride (90/10). The solvent was allowed to evaporate at room temperature, to give orange red needles (0.8 g).

Analysis: Found: C, 50.82; H, 4.38; Mol. wt., 1580. $\text{C}_{70}\text{H}_{68}\text{O}_{12}\text{P}_4\text{Ru}_4$ calcd.: C, 51.60; H, 4.21%; mol. wt., 1629.51. The NMR spectrum shows hydride resonance at: (int. TMS, solvent C_6D_6) τ (ppm) 25.1 (m, 2H, Ru–H), 26.2 (m, 2H, Ru–H).

Infrared spectrum in the $2200\text{--}1800\text{ cm}^{-1}$ region: 2007 s, 1978m, 1968w, 1950s, (cyclohexane solution).

$\text{Ru}_6(\text{CO})_{18}[(-)\text{-DIOP}]_3$ (B). In a gas volumetric apparatus dodecacarbonyl triruthenium (0.383 g) and (–)-DIOP (0.5 g) in methanol (30 ml) were heated at reflux (8 h) with evolution of carbon monoxide (43.3 ml at n.t.p.) to give a deep violet product which was crystallized from benzene/pentane (0.7 g).

Analysis: Found: C, 51.7; H, 3.98; mol. wt., 2468. $\text{C}_{111}\text{H}_{96}\text{O}_{24}\text{P}_6\text{Ru}_6$ calcd.: C, 51.15; H, 3.71%; mol. wt., 2606.29.

Infrared spectrum in the $2200\text{--}1800\text{ cm}^{-1}$ region show: 1995s, 1977s, 1965s, 1950(sh) (C_6D_6 solution).

Hydrogenation procedure

The air was evacuated from a 125 ml stainless steel autoclave, containing the substrate and the catalyst, and solvent was introduced by suction. Hydrogen was then introduced up to the desired pressure (see Tables 1–3). The autoclave was then rocked, and heated at the selected temperature.

When desired the autoclave was connected to an IR cell. The reaction in the vessel was continuously followed by slowly passing the solution through the high pressure IR cell and recording the spectra in the $2200\text{--}600\text{ cm}^{-1}$ region.

Degrees of conversion were determined from the crude product by GLC analysis, after esterification of the acids with diazomethane, using 2 m columns packed with Ucon oil LB 550 X (15%) on Chromosorb W (85%).

The solvent was removed under reduced pressure and the product was extracted into a 10% NaOH solution, which was acidified and then extracted with ether. The ether extracts were dried (Na_2SO_4) and fractionated (or evaporated

and recrystallized from benzene in the case of acids solid at room temperature) to obtain the acids, the rotary powers of which were determined (see Tables 1-3).

The hydrogenation products were identified by comparison with authentic samples.

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References

- 1 J.D. Morrison, W.F. Masler and M.K. Neuberger, *Adv. Catal.*, 25 (1976) 81.
- 2 J.W. Scott and D. Valentine, Jr., *Science*, 185 (1974) 943.
- 3 W.S. Knowles, M.J. Sabacky, B.D. Vineyard and D.J. Weinkauff, *J. Amer. Chem. Soc.*, 97 (1975) 2567.
- 4 B.R. James, D.K.W. Wang and R.F. Voight, *Chem. Commun.*, (1975) 574.
- 5 C. Botteghi, M. Bianchi, E. Benedetti and U. Matteoli, *Chimia*, 29 (1975) 257.
- 6 B.R. James, R.S. McMillan and K.J. Reiner, *J. Mol. Catal.*, 1 (1975/76) 439.
- 7 R.E. Harmon, S.K. Gupta and D.J. Brown, *Chem. Rev.*, 73 (1973) 21.
- 8 H.B. Kagan and T.P. Dang, *J. Amer. Chem. Soc.*, 94 (1972) 6429.
- 9 F. Piacenti, M. Bianchi, P. Frediani and E. Benedetti, *Inorg. Chem.*, 10 (1971) 2759.
- 10 V. Gramlich, private communication.
- 11 F. Piacenti, M. Bianchi, E. Benedetti and G. Braca, *Inorg. Chem.*, 7 (1968) 1815.
- 12 L. Lardicci, C. Botteghi and E. Belgodere, *Gazz. Chim. Ital.*, 97 (1967) 610.
- 13 D.J. Cram, *J. Amer. Chem. Soc.*, 74 (1952) 2137.
- 14 D.J. Cram and P. Haberfield, *J. Amer. Chem. Soc.*, 83 (1961) 2363.
- 15 R. Rossi, P. Diversi and G. Ingrosso, *Gazz. Chim. Ital.*, 98 (1968) 1391.
- 16 (a) W.S. Knowles, M.J. Sabacky and B.D. Vineyard, *Ann. N.Y. Acad. Sci.*, 172 (1970) 232; (b) J.D. Morrison, R.E. Burnett, A.M. Aguiar, C.J. Morrow and C. Phillips, *J. Amer. Chem. Soc.*, 93 (1971) 1301.
- 17 M. Bianchi, E. Benedetti and F. Piacenti, *Chim. Ind. (Milan)*, 51 (1969) 613.
- 18 S. Komiya and A. Yamamoto, *Chem. Lett. (Japan)*, (1975) 475.
- 19 G. Sbrana, G. Braca and E. Giannetti, *J. Chem. Soc. Dalton*, (1976) 1847.
- 20 C.G. Overberger and D. Tanner, *J. Amer. Chem. Soc.*, 77 (1955) 369.
- 21 D. Lipkin and I.D. Stewart, *J. Amer. Chem. Soc.*, 61 (1939) 3295.