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CATALYTIC ASYMMETRIC SYNTHESES

II *. HYDROGENATION OF α,β-UNSATURATED KETONES USING CHIRAL RUTHENIUM COMPLEXES

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Summary

α,β-Unsaturated ketones have been hydrogenated in the presence of $HRuCl(TBPC)_2$ (TBPC = (−)-*trans*-1,2-bis(diphenylphosphinomethyl)cyclobutane) to give ketones with a maximum optical purity of 62%. Factors affecting the stereoselectivity of the catalytic reaction are discussed.

Introduction

The use of chiral catalysts in the asymmetric hydrogenation of prochiral enamides to the corresponding amides with high optical yields is one of the most impressive achievements in the field of catalytic selectivity [1]. The preparation of L-(3-(3,4-dihydroxyphenyl)alanine) (L-DOPA) by such a route constitutes an important commercial application of this stereoselective catalysis. However, except in some rhodium-catalysed reactions [2], simple olefins give rather low optical purities [3–5]. The high enantiomeric excess (ee) values obtained from functionalized substrates have been attributed to the chelation of the metal through two active centers, which probably increases the rigidity of the intermediate [1,6,7]. We therefore thought it is of interest to investigate the hydrogenation of α,β-unsaturated ketones by molecular hydrogen in the presence of chiral ruthenium complexes in order to find out whether this would also lead to highly selective asymmetric syntheses. We have reported previously the formation of optically active ketones from the hydrogenation of cycloalkenones using chiral cobalt catalysts [8]. In this paper we describe the asymmetric synthesis of chiral ketones (ee > 60%) by the enantioselective reduction of the double bond in cyclic α,β-unsaturated ketones [9].

* For part I, see ref. 8.

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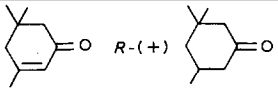
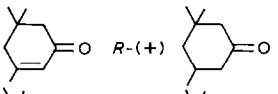
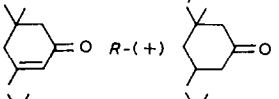
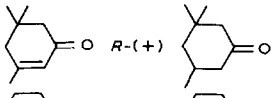
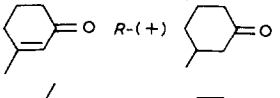
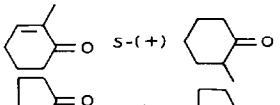
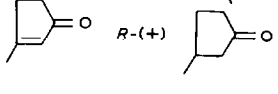
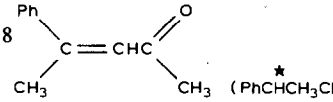
Results

Isophorone (entries 1,2, Table 1) and related substrates were hydrogenated in the presence of $HRuCl(TBPC)_2$ [10] under 40 atm of hydrogen. The rates of hydrogenation of the double bond were rather low but the olefinic bonds in unsaturated ketones were reduced with only a small amount of concurrent carbonyl hydrogenation (the hydrogenation of 3-methyl-2-cyclohexanone was found to be an exception, giving 28% of a *cis–trans* mixture of the fully reduced alcohols). The best asymmetric induction was obtained with the hydrogenation of isophorone at 50 °C (ee 62%). It should be also noted that both 3- and 2-methyl-2-cyclohexenones gave positive results, with similar enantiomeric excesses of 22 and 26%, respectively (entries 5 and 6). The latter results is in contrast with those from our studies on asymmetric hydrogenation using chiral cobalt carbonyl catalysts [8]; in that case, ketones bearing a chiral carbon in the α-position relative to the carbonyl group were found to be racemic.

The influence of the temperature on the extent of the asymmetric induction was studied in the case of catalytic hydrogenation of isophorone with $HRuCl(TBPC)_2$.

TABLE 1

ASYMMETRIC HYDROGENATION OF CYCLOHEXENONES CATALYSED BY $HRuCl(TBPC)_2$ [a]

Entry	Substrate	Product	Yield (%)	Enantiomeric excess (%)	Alcohol (%)	Time (h)	Temperature (°C)
1	 R-(+)		25	40	0	24	80
2	 R-(+)		20	62	0	45	50
3 [b]	 R-(+)		12	60	0	136	50
4 [c]	 R-(+)		25	39	0	24	80
5	 R-(+)		40	22	28	22	80
6	 S-(+)		38	26	6.5	22	80
7	 R-(+)		70	4.5	10	8	80
8		★ (PhCHCH$_3$CH$_2$COCH$_3$)	60	1	0	8	80

[a] 40 atm H_2; substrate/catalyst: 200/1; solvent: benzene. [b] 4 atm H_2. [c] Solvent: Dimethylacetamide (DMA).

TABLE 2

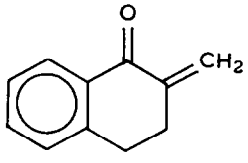
ASYMMETRIC HYDROGENATION OF 2-METHYLENE-1-TETRALONE CATALYSED BY $HRuCl(TBPC)_2$ (A) AND $Ru_2Cl_4(Diop)_3$ (B) [a]

Entry	Catalyst	Solvent	$p(H_2)$	Enantiomeric excess (%)	Time (h)	Yield (%)
1 [b]	B	benzene	30	47	12	90
1	A	benzene	4	23	24	100
3	A	ethanol/ benzene (50/50)	4	16	20	80
4	A	ethanol/ benzene (50/50)	20	19	17	80
5 [c]	A	ethanol/ benzene (50/50)	20	6	3	50
6	A	DMA	20	1.5	15	100

[a] *T* 50 °C; substrate/catalyst: 200/1. [b] *T* 60 °C. [c] $N(Et)_3/Ru = 100$.

From the results, summarized in Table 1, there appears to be a definite increase in optical yield on lowering the temperature (entries 1,2). In contrast the decrease in the hydrogen pressure results in a marked drop in the rate of the reaction, but has little effect on the enantiomeric excess (entry 3, Table 1).

Asymmetric induction also seems to be very sensitive to steric effects, and hydrogenation of a linear olefin gives a very low ee (entry 8, Table 1). Although all the reactions with the cyclohexenones gave positive results, the fact that these unsaturated ketones necessarily have a transoid arrangement of the conjugate double bonds causes difficulty in formulating a general mechanism. Consequently, it is possible that the stereoselectivity observed for the hydrogenation should be regarded as typical, and it was thought appropriate to examine the stereoselectivity of the hydrogen addition to an unsaturated ketone possessing a cisoid arrangement of the conjugate double bonds and for this purpose, 2-methylene-1-tetralone seemed an ideal choice (I).



(I)

The results for the $HRuCl(TBPC)_2$ and $Ru_2Cl_4(Diop)_3$ [11] catalysts are listed in Table 2. Overall, the chemical yields shown in Tables 1 and 2 are in accord with expectation. Thus, it is well-known that a variety of ruthenium-catalysed reactions proceed more rapidly with an alk-1-ene than with internal or cyclic olefines [12]. In accord with this, hydrogenation of 2-methylene-1-tetralone in benzene at 50 °C and 4 atm hydrogen pressure gave a 100% yield of hydrogenated product. A 47% ee was obtained with James' catalyst, while use of $HRuCl(TBPC)_2$ gave 2-methyl-1-tetralone in only 23 ee. Moreover, the presence of $N(Et)_3$ in the benzene solution caused a large decrease in selectivity (Table 2, entry 5), and the use of dimethylacetamide (DMA) as solvent was accompanied by a loss of the optical activity of the

2-methyl-1-tetralone (entry 6) [13]. Such behavior, which was not observed with isophorone (Table 1, entry 4), seems to be related to the cisoid arrangement.

Discussion

A general mechanism, previously suggested by James [11] for the hydrogenation of acrylamide is given in eqs. a, b and c:

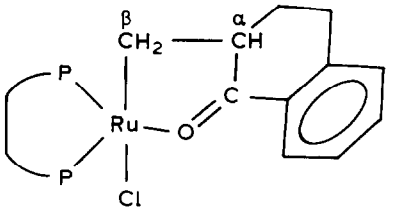
$$HRuCl(TBPC)_2 + \text{olefin} \rightleftarrows RuCl(\text{alkyl})(TBPC) + TBPC \quad (a)$$

$$RuCl(\text{alkyl})(TBPC) + H_2 \rightarrow HRuCl(TBPC) + \text{product} \quad (b)$$

$$HRuCl(TBPC) + TBPC \rightarrow HRuCl(TBPC)_2 \quad (c)$$

The importance of the first equilibrium (a) in the catalytic cycle is confirmed by the fact that the addition of an excess of chiral ligand (TBPC) in the solution inhibits the catalytic reaction. However, in view of the complexity of a catalytic system, attempts to deduce mechanisms from kinetic studies [1,12] of the overall catalytic reaction generally lead to provide incomplete information. The mechanistic features of such a catalytic system can also be elucidated by examining the various catalyst-substrate systems that influence the enantioselectivity of the reaction [7].

The asymmetric inductions obtained with two different structural arrangements (transoid vs. cisoid) suggest the following comments; (i) the position of the chiral carbon relative to the carbonyl group in hydrogenated ketones (α vs. β) may be an important factor in the asymmetric induction, but an α relationship does not lead to racemic ketones, as was previously reported for reactions with chiral cobalt catalyst [8]. Consequently the formation of a π-oxapropenyl intermediate [14] is unlikely, and the addition of $HRuCl(TBPC)_2$ to cyclohexenones may lead to an α-ruthenium alkyl intermediate. Such a complex has recently been isolated and characterized [15]; (ii) the very low optical yields obtained in DMA or in the presence of $N(Et)_3$ from 2-methylene-1-tetralone compared with those from the transoid substrates can be tentatively attributed to a different coordination to the metal in this case, involving both carbon–carbon double bond and keto group, which will be especially favoured when these groups are in a cisoid disposition (II) [16]. In the hypothetical intermediate catalytic complex the carbonyl group may be only weakly coordinated to the metal, and thus there may be rapid dissociation in the presence of DMA or $N(Et)_3$. It was previously reported that these ligands coordinated to the ruthenium metal [11,17]; (iii) the stereoselectivity of the reaction depends strongly upon the degree of cyclohexenone substitution, the sterically hindered isophorone giving the best optical yield.



(II)

We conclude that the rigidity of the catalytic chiral intermediates may well be the most important factor affecting the selectivity of this catalytic hydrogenation.

Experimental

The following instruments were used: Varian T60 NMR spectrometer; Unicam SP 1100 IR spectrophotometer; Perkin–Elmer 241 polarimeter. An Intersmat system (column: Carbowax 1540, *l* 18 m, ∅ 0.5 mm) was used for GLC analyses.

The substrates: 3-methyl-2-cyclohexenone, 3-methyl-2-cyclopentenone, isophorone were purchased from Aldrich Chemical Co and 2-methylene-1-tetralone [18] and 2-methyl-2-cyclohexenone [19] were prepared by published procedures. Optical yields are calculated relative to the values for the optically pure compounds: 2-methyl-1-tetralone $|\alpha|_D = +51.2$ (dioxane) [20] and ref. 8.

(*R*)-(−)-TBPC [21] and (−)-Diop [22] were prepared by published procedures, as were $Ru_2Cl_4(Diop)_3$ [11] and $HRuCl(TBPC)_2$ [10]. The reactions were carried out in a 300 ml Engineer autoclave with a magnetic stirrer [8].

References

1 H.B. Kagan, in G. Wilkinson (Ed.), Comprehensive Organometallic Chemistry, Pergamon Press, Oxford, 1982, Vol. 8, p. 463.
2 T. Hayashi, M. Tanaka and I. Oyata, Tetrahedron Lett., (1977) 295.
3 J.D. Morrison, R.E. Burnett, A.M. Agmar, C.J. Morrows and C. Phillips, J. Am. Chem. Soc., 93 (1971) 1301.
4 P. Salvadori, R. Lazzaroni, A. Raffaelli, S. Pucci, S. Bertozzi, D. Pini and G. Fatti, Chim. Ind. (Milan), 63 (1981) 492.
5 G. Sbrana, G. Broca and E. Giannetti, J. Chem. Soc., Dalton Trans., (1976) 1847.
6 J.M. Brown and D. Parker, J. Chem. Soc., Chem. Commun., (1980) 342.
7 J. Halpern, Inorg. Chim. Acta, 50 (1981) 11.
8 P. Le Maux, V. Massonneau and G. Simonneaux, J. Organomet. Chem., 284 (1985) 101.
9 Preliminary communication: V. Massonneau, P. Le Maux and G. Simonneaux, Tetrahedron Lett., (1986) 5497.
10 V. Massonneau, P. Le Maux, R. Dabard, G. Simonneaux, P. Aviron-Violet and T. Phat Dang, Inorg. Chem., in press.
11 B.R. James, R.S. McMillan, R.H. Morris and D.K. Wang, Adv. Chem. Ser., 167 (1978) 122.
12 B.R. James, Homogeneous Hydrogenation, Wiley, New-York, 1972, p. 84.
13 The absence of product racemization was first checked for the hydrogenation of α,β-unsaturated ketones in DMA or in the presence of triethylamine.
14 R.W. Goetz and M. Orchin, J. Am. Chem. Soc., 85 (1963) 2782.
15 S. Gopinathan, K. Joseph and C. Gopinathan, J. Organomet. Chem., 269.
16 M. McPartlin and R. Mason, J. Chem. Soc. (A), (1970) 2206.
17 T. Ihariya, Y. Ishii, H. Kawano, T. Arai, M. Saburi, S. Yoshikawa and S. Akutagawa, J. Chem. Soc., Chem. Commun., (1985) 922.
18 J.L. Gras, Tetrahedron Lett., (1978) 2111.
19 E.W. Warnhoff, D.G. Martin and W.S. Johnson, Org. Synth. IV, (1963) 162.
20 G. Jaouen and A. Meyer, J. Am. Chem. Soc., 97 (1975) 4667.
21 P. Aviron-Violet, Y. Colleuille and J. Varagnat, J. Mol. Catal., 41 (1979) 41.
22 T.P. Dang and H.B. Kagan, J. Chem. Soc. Chem. Commun., (1971) 481.