

## ASYMMETRIC SYNTHESIS BY CHIRAL RUTHENIUM COMPLEXES

### IX \*. THE ROLE OF ISOMERIZATION IN THE ASYMMETRIC HYDROGENATION OF PHENYLBUTENES CATALYZED BY $H_4Ru_4(CO)_8[(-)-DIOP]_2$

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#### Summary

Phenylbutenes have been hydrogenated in the presence of  $H_4Ru_4(CO)_8[(-)-DIOP]_2$  to give 2-phenylbutane with a maximum optical purity of 8.5%. Olefin isomerization is shown to lower the optical purity of the hydrogenation product. Factors affecting the steric course of the catalytic reaction are discussed.

#### Introduction

The asymmetric hydrogenation of carbon-carbon double bonds in the presence of chiral catalysts gives products having a relatively high optical purity (o.p.) when an appropriate arrangement of functional groups is present in the substrate, as in  $\alpha$ -acylaminoacrylic acid derivatives, various  $\alpha,\beta$ -unsaturated acids, and enol esters [1-5]. Simple olefins (with the exception of a rhodium catalyzed reaction [6]) give rather low optical purities [7-10]. (*E*)- $\alpha$ -Methylcinnamic acid, for instance, is hydrogenated in the presence of  $H_4Ru_4(CO)_8[(-)-DIOP]_2$  to give the corresponding saturated derivative with 58% o.p., while hydrogenation of 2-phenylbut-1-ene gives only a 5% o.p. [11].

The high values of the o.p. obtained from functionalized substrates have been attributed to the chelation of the substrate to the metal through the two reactive centers, which probably increases the rigidity of the intermediate [1,12-14]. The poor results usually obtained in asymmetric hydrogenation of olefins could, how-

\* For part VIII see ref. 31.

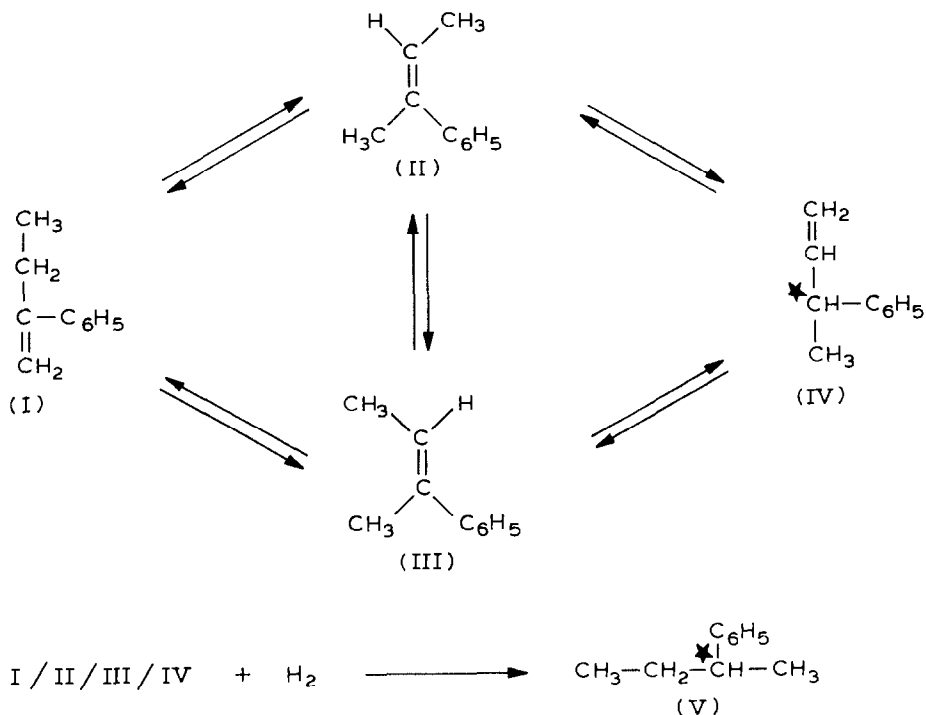
ever, be attributed not only to the low rigidity of the catalytic intermediate but also to the concurrent isomerization of the substrate promoted by ruthenium based catalysts. It has in fact been shown that use of tertiary phosphine- or phosphite-substituted  $H_4Ru_4(CO)_{12}$  derivatives results in considerable isomerization [15–19]. The presence of all possible isomers formed by double bond isomerization, each giving rise to a hydrogenation product having a different configuration and optical purity might explain the poor results.

We therefore thought it of interest to investigate the hydrogenation of carbon–carbon double bonds with molecular hydrogen in the presence of  $H_4Ru_4(CO)_8[(-)-DIOP]_2$  in order to find out whether this reaction is accompanied by isomerization of the substrate and, if so, how this isomerization affects the extent and type of asymmetric induction.

## Results

2-Phenylbut-1-ene (I) and related isomers were hydrogenated in the presence of  $H_4Ru_4(CO)_8[(-)-DIOP]_2$  under 100 atm of hydrogen. Table 1 shows the results obtained at 80°C starting from I, or from (*Z*)-2-phenylbut-2-ene (II) or (*E*)-2-phenylbut-2-ene (III) which could be derived from I by isomerization (Scheme 1). The rate of hydrogenation of I under these conditions is rather low, and so the composition and changes in the optical purity of the product could easily be followed.

Isomerization of I to II and III takes place at the same time as the hydrogenation



SCHEME 1

TABLE 1  
 ASYMMETRIC HYDROGENATION OF 2-PHENYLBUTENES: CRUDE COMPOSITION AT VARIOUS CONVERSION DEGREES  
 (Substrate 10 g, catalytic precursor  $H_4Ru_4(CO)_8[(-)-DIOP]_2$ , substrate/catalytic precursor (molar ratio) 822,  $p(H_2)$  100 atm at 20°C,  $T$  80°C)

Substrate	Reaction time (h)	Conv. (%)	(Mol. frac.) <sup>a</sup> (%)			2-Phenylbutane		Conf. <sup>b</sup>	O.p. (%)
			2-Phenyl-but-1-ene	(E)-2-Phenyl-but-2-ene	(Z)-2-Phenyl-but-2-ene	(Mol. frac.) <sup>a</sup> (%)	(%)		
2-Phenylbut-1-ene	5.0	7.4	92.6	2.8	0.4	4.2	-	-	
	10.0	32.6	67.4	17.0	0.6	15.0	(S)	1.9	
	22.5	51.2	48.8	17.5	0.9	32.8	(S)	1.4	
(Z)-2-Phenylbut-2-ene	314.0	99.2	0.8	15.6	1.2	82.4	(S)	0.8	
	5.0	5.7	0.3	2.4	94.3	3.0	-	-	
(E)-2-Phenylbut-2-ene	140.0	93.6	0.7	18.6	6.4	74.3	(S)	0.5	
	5.0	0.3	0.0	99.7	0.3	0.0	-	-	
	300.0	1.3	0.0	98.7	0.0	1.3	-	-	

<sup>a</sup> Mol. frac. = molar fraction. <sup>b</sup> Determined taking for (+)-(S)-2-phenylbutane  $d_4^{25}$  0.858 [20] and  $[\alpha]_D^{25}$  +29.3 [21] (see Experimental).

TABLE 2

ASYMMETRIC HYDROGENATION OF (*R,S*)-3-PHENYLBUT-1-ENE(Substrate 3 g, catalytic precursor  $H_4Ru_4(CO)_8[(-)-DIOP]_2$ , substrate/catalytic precursor (molar ratio) 822,  $p(H_2)$  100 atm at 20°C,  $T$  80°C)

Reaction time (h)	Conv. (%)	3-Phenylbut-1-ene			( <i>E</i> )-2-Phenylbut-2-ene	2-Phenylbutane		
		(Mol.frac.) <sup>a</sup> (%)	Conf. <sup>b</sup>	O.p. <sup>b</sup> (%)	(Mol.frac.) <sup>a</sup> (%)	(Mol.frac.) <sup>a</sup> (%)	Conf. <sup>c</sup>	O.p. <sup>c</sup> (%)
5	20.6	79.4	—	—	0.6	20.0	—	—
23	74.9	25.1	( <i>R</i> )	4.1	3.9	71.0	( <i>S</i> )	0.2

<sup>a</sup> Mol. frac. = molar fraction. <sup>b</sup> Determined taking for (*-*)-(*R*)-3-phenylbut-1-ene  $d_4^{25}$  0.8792 [22] and  $[\alpha]_{D_{max}}^{25}$  -6.84 [22] (see Experimental). <sup>c</sup> Determined taking for (+)-(*S*)-2-phenylbutane  $d_4^{25}$  0.858 [20] and  $[\alpha]_{D_{max}}^{25}$  29.3 [21] (see Experimental).

to give 2-phenylbutane (V). The concentration of III increases as the reaction proceeds, and rapidly reaches a value of 15–17% then remains practically constant; the concentration of II is, on the other hand, low throughout the whole reaction. The optical purity of V is low, and falls as the reaction proceeds. Under the same conditions III is neither hydrogenated nor isomerized to any significant extent, while II is hydrogenated to give a product of extremely low optical purity. The remaining isomerization product of I, 3-phenylbut-1-ene (IV), is rapidly hydrogenated to V, which shows a very low, although detectable, optical purity (Table 2).

In the unreacted olefin at the end of the hydrogenation of IV there is an excess (4.1%) of the (*R*) enantiomer. This indicates that the hydrogenation catalyst is able to select between the two stereoisomers, giving rise to differentiation between the isomers in the hydrogenation.

An increase of catalyst concentration (Table 3) leads not only to a higher rate, but also to formation of the hydrogenation product V with a higher optical purity, and to production of smaller amounts of the isomeric olefins.

When the temperature is increased (Table 4) the rate increases, but the optical purity of V formed falls considerably.

TABLE 3

## ASYMMETRIC HYDROGENATION OF 2-PHENYLBUT-1-ENE USING A SUBSTRATE/CATALYTIC PRECURSOR (MOLAR RATIO) 274

(Substrate 10 g, catalytic precursor  $H_4Ru_4(CO)_8[(-)-DIOP]_2$ ,  $p(H_2)$  100 atm at 20°C,  $T$  80°C)

Reaction time (h)	Conv. (%)	(Mol.frac.) <sup>a</sup> (%)			2-Phenylbutane		
		2-Phenylbut-1-ene	( <i>E</i> )-2-Phenylbut-2-ene	( <i>Z</i> )-2-Phenylbut-2-ene	(Mol.frac.) <sup>a</sup> (%)	Conf. <sup>b</sup>	O.p. <sup>b</sup> (%)
2	20.0	80.0	3.8	0.1	16.1	—	—
96	78.4	21.6	4.4	0.0	74.0	( <i>S</i> )	4.5

<sup>a</sup> Mol.frac. = molar fraction. <sup>b</sup> Determined taking for (+)-(*S*)-2-phenylbutane  $d_4^{25}$  0.858 [20] and  $[\alpha]_{D_{max}}^{25}$  +29.3 [21] (see Experimental).

TABLE 4

## ASYMMETRIC HYDROGENATION OF 2-PHENYLBUT-1-ENE AT 120°C

(Substrate 10 g, catalytic precursor  $H_4Ru_4(CO)_8[(-)-DIOP]_2$ , Substrate/catalytic precursor (molar ratio) 822,  $p(H_2)$  100 atm at 20°C)

Reaction time (h)	Conv. (%)	(Mol.frac.) <sup>a</sup> (%)			2-Phenylbutane		
		2-Phenylbut-1-ene	(E)-2-Phenylbut-2-ene	(Z)-2-Phenylbut-2-ene	(Mol.frac.) <sup>a</sup> (%)	Conf. <sup>b</sup>	O.p. <sup>b</sup> (%)
2	94.8	5.2	56.3	7.6	30.9	—	—
25	100	0.0	1.7	0.0	98.3	(S)	0.3

<sup>a</sup> Mol.frac. = molar fraction. <sup>b</sup> Determined taking for (+)-(S)-2-phenylbutane  $d_4^{25}$  0.858 [20] and  $[\alpha]_{D_{max}}^{25}$  +29.3 [21] (see Experimental).

## Discussion

The results show that the hydrogenation of I is accompanied by isomerization. Of the two isomeric internal olefins thus formed, II and III, the first makes a higher contribution to the formation of V.

The decrease in the optical purity of V obtained by hydrogenation of I as the degree of conversion increases may be explained by taking into account (a) the increasing contribution of II to the formation of V as the reaction proceeds, and (b) the low optical purity of V formed from II.

Olefin IV might also, in principle, make a substantial contribution to the formation of V in view of the fact that its rate of hydrogenation is higher than those of the other olefins. However the low concentration of IV [23,24] in the olefin equilibrium mixture, which is consistent with its absence from the reaction products, is a strong indication that it makes only a small contribution to the formation of V.

Olefin IV has a centre of asymmetry at carbon atom 3, and may be formed either as a racemic or as an optically active mixture arising from an enantioface dis-

TABLE 5

## ASYMMETRIC HYDROGENATION OF 2-PHENYLBUT-1-ENE: EFFECT OF CATALYST CONCENTRATION

(Catalytic precursor  $H_4Ru_4(CO)_8[(-)-DIOP]_2$ ,  $p(H_2)$  100 atm at 20°C,  $T$  80°C)

Catalytic precursor (mmol l <sup>-1</sup> )	Substrate/catalytic precursor (Molar ratio)	(Mol.frac.) <sup>a</sup> (%)		Mol isomerized olefins/Mol hydrogenated product	2-Phenylbutane	
		Hydrogenation product	Isomerized olefins		Conf. <sup>b</sup>	O.p. <sup>b</sup> (%)
8.2	822	4.2	3.2	0.76	(S)	0.8
16.4	411	8.3	3.0	0.36	(S)	1.7
24.6	274	16.1	3.9	0.24	(S)	4.5
82.2	82	1.2 <sup>c</sup>	0.0	0.00	(S)	5.6

<sup>a</sup> Mol.frac. = molar fraction. <sup>b</sup> Determined on the product recovered after high conversion of starting olefin ( $\geq 75\%$ ), taking for (+)-(S)-2-phenylbutane  $d_4^{25}$  0.858 [20] and  $[\alpha]_{D_{max}}^{25}$  +29.3 [21]. <sup>c</sup> At this conversion the o.p. of (+)-(S)-2-phenylbutane is 8.5%.

TABLE 6

ASYMMETRIC HYDROGENATION OF 2-PHENYL-3,3-DIMETHYLBUT-1-ENE IN THE PRESENCE OF  $H_4Ru_4(CO)_8L_2$  (L = (-)-DIOP or (+)-DIOP)

(Substrate 4 g, substrate/catalytic precursor (molar ratio) 411,  $p(H_2)$  100 atm at 20°C, reaction time 86 h,  $T$  80°C)

Chiral ligand	Yield (%)	2-Phenyl-3,3-dimethylbutane		
		$\alpha_{D(25)}^{25}$ (neat) (°)	Conf. <sup>a</sup>	O.p. <sup>a</sup> (%)
(-)-DIOP	99.6	-2.177	(R)	9.7
(+)-DIOP	100	+2.109	(S)	9.4

<sup>a</sup> Determined assuming for (+)-(*S*)-2-phenyl-3,3-dimethylbutane  $d_4^{25}$  0.8700 [25] and  $[\alpha]_{D_{max}}^{25} + 25.7$  [21].

criminating isomerization. When fully hydrogenated, IV can contribute to the optical activity of V only if it is itself formed as optically active.

The data for the optical purity of V at various conversion degrees of I (Table 1) point to an unfavorable influence of the olefin isomerization on the optical purity of the hydrogenation product. In keeping with this, reduction of the amount of the isomeric olefins during the hydrogenation (Table 5) leads to increase in the optical purity of V. However even under the best conditions (high catalyst concentration, low olefin conversion (1.5%), and negligible olefin isomerization) the optical yield does not exceed 8.5%. Under the same conditions an olefin similar to I but more heavily substituted, 2-phenyl-3,3-dimethylbut-2-ene, in which double bond migration is impossible, gave a hydrogenation product with about 10% o.p. (Table 6). Catalysts containing ligands of the opposite chirality gave products of opposite configuration but the same optical purity.

We conclude that olefin isomerization does lower the optical purity of the product of the hydrogenation of a prochiral olefin carried out in the presence of chiral catalysts but it is not the main cause of the low optical purity. The rigidity of the catalytic chiral intermediate may well be the most important factor determining the steric course of a catalytic reaction.

## Experimental

Physico-chemical determinations were performed with the following instruments: NMR Perkin-Elmer R32 spectrometer; Perkin-Elmer 241 polarimeter; IR Perkin-Elmer 580B data system. GLC analyses were performed with a Perkin-Elmer Sigma 1 system.

The products were separated by use of a Perkin-Elmer 251 spinning band distillation column and a Perkin-Elmer F21 preparative scale gas-chromatograph.

### Chromatographic analyses of the reaction products

Quantitative analyses of mixtures of 2-phenylbutane, 2-phenylbut-1-ene, 3-phenylbut-1-ene, (*Z*)-2-phenylbut-2-ene and (*E*)-2-phenylbut-2-ene were performed by GLC using 2 m × 1/8 inch columns packed with bis-2-methoxy ethyl adipate (20%) on Chromosorb P 80-100 mesh (80%) and kept at 90°C.

### Materials

Acetophenone, 2-phenylpropanal, 1-phenyl-2,2-dimethylpropan-1-one and 2-phenylbutanoic acid were Fluka AG products. 2-Phenylbut-1-ene ( $\alpha$ -ethylstyrene) was prepared from 2-phenylbutanoic acid according to Overberger and Tanner [26]. The catalytic precursor  $H_4Ru_4(CO)_8[(-)\text{-DIOP}]_2$  was prepared by a known procedure [11]. All solvents were purified and dried by standard procedures. All solvents and reagents were distilled under nitrogen before use.

### (E)- and (Z)-2-Phenylbut-2-ene

These compounds were prepared by a Wittig reaction [27].

A solution of acetophenone (25.2 g, 0.210 mol) in diethyl ether (50 ml) was added slowly, at room temperature with stirring to triphenylethylidenephosphorane prepared from 0.200 mol of triphenylethylphosphonium bromide in diethyl ether (400 ml) and 100 ml of a 2 M solution of butyllithium in n-hexane. After stirring (12 h) at room temperature the mixture was treated with ice-water (500 ml) then the organic layer was separated and dried over  $Na_2SO_4$ . The solvent was evaporated and the residue fractionated through a spinning band column.

(E)-2-Phenylbut-2-ene (6.9 g, 0.052 mol, b.p. 193°C) and (Z)-2-phenylbut-2-ene (3.6 g, 0.027 mol, b.p. 173°C) were thus obtained with 38% yield.

Physical properties and IR spectra were in agreement with those reported by Cram [28], and the NMR data with those reported by Kawata et al. [29].

### (R,S)-3-Phenylbut-1-ene

This olefin was obtained by a published method [30]. A solution of methylene iodide (67 g, 0.250 mol) and 2-phenylpropanal (33.6 g, 0.250 mol) in diethyl ether (200 ml) was added dropwise with stirring to a suspension of magnesium turnings (13.8 g, 0.568 mol) in diethyl ether (75 ml). The mixture was then refluxed for 5 h then cooled and treated with a saturated solution of  $NH_4Cl$  at 0°C. The organic layer was separated and the aqueous phase extracted with diethyl ether. The combined ethereal solutions were dried over  $Na_2SO_4$  and the solvent was evaporated. Fractional distillation of the residue gave (R,S)-3-phenylbut-1-ene (21.4 g, 0.162 mol, 65% yield) having b.p. 104–105°C/100 mmHg. The olefin had NMR data identical to those reported by Kawata et al. [29].

### 2-Phenyl-3,3-dimethylbut-1-ene

A solution of methylolithium (0.200 mol) in n-hexane (100 ml) was added dropwise with stirring to a solution of 1-phenyl-2,2-dimethylpropan-1-one (33.4 g, 0.206 mol) in petroleum ether (200 ml) at -60°C. The mixture was then allowed to warm to room temperature and treated with water. The usual work up gave 2-phenyl-3,3-dimethylbutan-2-ol (32.4 g, 0.182 mol) in 88% yield.

Thionyl chloride (23.0 g, 0.193 mol) was added dropwise at 0°C to a solution of the alcohol in a mixture of pyridine (56 ml) and diethyl ether (100 ml). The mixture was stirred at room temperature for 15 h then treated with ice-water. The usual work up gave the crude olefin, which was purified by distillation over Na. 2-Phenyl-3,3-dimethylbut-1-ene (24.7 g, 0.154 mol) having b.p. 84°C/23 mmHg was isolated in 85% yield. The olefin had physical properties and spectral data identical to those previously reported [25].

### Hydrogenation procedure

As a typical procedure the first experiment in Table 1 is described.

A 125 ml stainless steel autoclave containing the catalytic precursor (0.150 g,  $0.092 \times 10^{-3}$  mol) was evacuated. The substrate (10 g,  $75.6 \times 10^{-3}$  mol) was introduced by suction and hydrogen was then introduced up to 100 atm. The autoclave was rocked and heated at 80°C in a thermostatic oil bath. Conversions at various times were determined by GLC analyses on samples drawn from the autoclave.

The optical activities of intermediate samples and the final product were determined as follows: 3 ml of the reaction solution was distilled under vacuum (0.2 mmHg) to remove the catalyst. The distillate was hydrogenated at 150 atm and 60°C using Ni/Raney (10% wt. of the substrate) as catalyst. After removal of the catalyst, the optical activity of the formed 2-phenylbutane was determined.

Optical rotations, measured with pure liquid, at 32.6, 51.2 and 99.2% conversions were  $\alpha_{D(1)}^{25} + 0.467$ ,  $+0.360$  and  $+0.195^\circ$ , respectively.

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