STEREOCHEMISTRY AND MECHANISM OF HOMOGENEOUS HYDROGENATION OF SUBSTITUTED 2-CYCLOHEXENOLS WITH TRIS(TRIPHENYLPHOSPHINE)CHLORORHODIUM

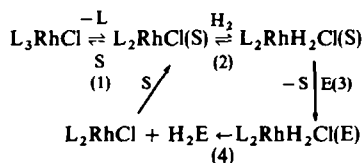Y. Senda*, T. Iwasaki and S. Mitsui

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Abstract—Substituted 2-cyclohexenols were hydrogenated with tris(triphenylphosphine)chlororhodium in benzene or benzene:ethanol. Isomer distribution of the resulting cyclohexanols showed that the thermodynamically more stable of the two possible products was preferably obtained. In addition to the saturated products, 3-substituted cyclohexenols gave appreciable amounts of saturated ketones, derived by double bond migration, while no ketone was obtained from 2-substituted cyclohexenols. Results suggest that the rate and product determining step of the reaction is the intramolecular transfer of the second hydrogen in the σ-alkylrhodium species.

It has been shown by Wilkinson *et al.* that tris(triphenylphosphine)chlororhodium, $RhCl(PPh_3)_3$, is an efficient catalyst for the hydrogenation of alkenes and alkynes. They have proposed a mechanism involving: (1) dissociation of one ligand, (2) insertion of rhodium into the hydrogen–hydrogen bond, (3) coordination of alkene with the resulting *cis*-dihydridorhodium species and (4) simultaneous transfer of the bound hydrogens to the alkene. Kinetic studies have shown that the rate and product determining step of this reaction is the coordination of olefins with the dihydridorhodium species.[1]

SCHEME 1

$$L_3RhCl \overset{-L}{\underset{\underset{(1)}{S}}{\rightleftharpoons}} L_2RhCl(S) \overset{H_2}{\underset{(2)}{\rightleftharpoons}} L_2RhH_2Cl(S)$$

$$S \diagup \qquad -S \Big| E(3)$$

$$L_2RhCl + H_2E \leftarrow L_2RhH_2Cl(E)$$
$$(4)$$

L: triphenylphosphine
S: solvent
E: olefin

Hussey and Takeuchi have presented evidence that the transfer of bound hydrogen from rhodium to the alkene linkage is stepwise, and formation of the alkene catalyst complex and alkylrhodium intermediate are reversible.[2]

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Scheme 2

$$L_3RhCl \underset{S}{\overset{-L}{\rightleftharpoons}} L_2RhCl(S) \overset{H_2}{\rightleftharpoons} L_2RhH_2Cl(S) \underset{-S}{\overset{E}{\rightleftharpoons}} L_2RhH_2Cl(E)$$

$$L_2RhCl + H_2E \longleftarrow L_2RhHCl(HE)$$

L: triphenylphosphine
S: solvent
E: olefin

Stereochemical investigation of the heterogeneous hydrogenation of substituted 2-cyclohexenols was studied by Mitsui et al.[3] When a platinum catalyst was used, cis products were always favored. The rate and product determining step of this reaction is considered to be the formation of the half-hydrogenated intermediate.[4] In the hydrogenation using a Pd/C catalyst, the rate and product determining step of which is the transfer of the second hydrogen to the half-hydrogenated intermediate,[5] 2-cyclohexenols gave the thermodynamically more stable of the two possible products. The isomeric ratios of the products of the Raney Ni hydrogenation suggested that the hydrogen seems to attack preferentially from the same side as the hydroxyl group, that is, a directive effect[6] of the hydroxyl group on the isomer distribution was observed. They confirmed the rate and product determining step of the reaction to be the adsorption of the substrates on the catalyst.[3] The results of the Rh/C hydrogenation suggested that its stereospecificity lies between Ni and Pt.[7]

In order to compare the stereochemistry of the homogeneous hydrogenation with that of the heterogeneous hydrogenation and to examine whether or not we can find the effect of the hydroxyl group on the isomeric ratio, several substituted 2-cyclohexenols were hydrogenated with RhCl(PPh$_3$)$_3$.

Van Bekkum et al. reported that in the hydrogenation of cyclohexene over RhCl-(PPh$_3$)$_3$, the addition of oxygen markedly increased the hydrogenation rate.[8] Augustine and Van Peppen found that when a benzene solution of RhCl(PPh$_3$)$_3$ was stirred in air, oxidized material precipitated.[9] Thus we vigorously excluded air from the reaction system.

2-Methyl-2-cyclohexenol gave 75% of trans 2-methylcyclohexanol and 2-phenyl-2-cyclohexenol gave 88% of trans 2-phenylcyclohexanol. In these cases no other component other than the saturated products was obtained. On the other hand, hydrogenation of 3-substituted 2-cyclohexenols proceeded to give the cis isomers preferably. 3-Methyl-2-cyclohexenol gave 60% and 3,5,5-trimethyl-2-cyclohexenol gave 63% of the corresponding cis cyclohexanols. In these cases appreciable amounts of 3-substituted cyclohexanones were also obtained. In the case of 3-phenyl-2-cyclohexenol most of which isomerized to 3-phenylcyclohexanone during the reaction, only 7% of the saturated product was obtained. The isomer distribution of the resulting 3-phenylcyclohexanol was 56% of the cis and 44% of the trans isomer. The isomer distribution of the resulting cyclohexanols showed that the thermodynamically more stable products (the trans isomers from 2-substituted and the cis from 3-substituted 2-cyclohexenols) were preferably obtained.

TABLE 1. HOMOGENEOUS HYDROGENATION OF 2-CYCLOHEXENOLS WITH $RhCl(PPh_3)_3$

2-Cyclohexenol	Solvent	Reaction time(hr)	Conversion[a] (%)	Products composition(%) Cyclohexanol	Cyclohexanone	Cyclohexanol (trans)
2-Methyl-	C_6H_6	20	100	100	0	75
	C_6H_6—EtOH	15	100	100	0	76
3-Methyl-	C_6H_6	20	97	89	11	40
	C_6H_6—EtOH	15	78	91	9	40
3,5,5-Trimethyl-	C_6H_6	120	66	95	5	37
	C_6H_6—EtOH	48	29	96	4	37
2-Phenyl-	C_6H_6	120	90	100	0	88
	C_6H_6—EtOH	48	56	100	0	78
3-Phenyl-	C_6H_6	120	37	7	93	44[b]

[a] Nothing was obtained other than cyclohexanols and cyclohexanones, so that conversion means the percentages of the amounts of cyclohexanols and cyclohexanones in the resulting mixture.
[b] The amount of the resulting 3-phenylcyclohexanol was so small that the isomeric ratio was inaccurate.

Table 1 summarizes the isomer distribution of the products when a series of substituted 2-cyclohexenols was hydrogenated.

Wilkinson et al. reported that the addition of polar solvents eg alcohol to the benzene solution normally employed gave a substantial increase in the rate of substrate hydrogenation.[1] In order to ascertain the effects of the co-solvent on the cis/trans ratio of the resulting saturated alcohols, a benzene–ethanol mixture was also employed as solvent. The results show that no appreciable solvent effects on the isomeric ratio were observed (Table 1).

In addition to the hydrogenated products 3-substituted 2-cyclohexenols gave appreciable amounts of saturated ketones which were derived by the migration of the double bond, whereas no ketone was obtained at all from 2-substituted 2-cyclo-hexenols. The isomerization of such allylic alcohols to ketones suggests that the hydrogen transfer from the dihydridorhodium species to the olefin proceeds in stepwise fashion as reported by Hussey and Takeuchi,[2] and the carbon–metal bond forms with the less substituted carbon in the σ-alkylrhodium complex. The stability of the carbon–metal bond is usually in the order; primary > secondary > tertiary.[10]

The sequence of steps which accommodates the formation of the hydrogenated products and the isomerized species is briefly presented in Scheme 3.

SCHEME 3A   3-Substituted 2-cyclohexenol

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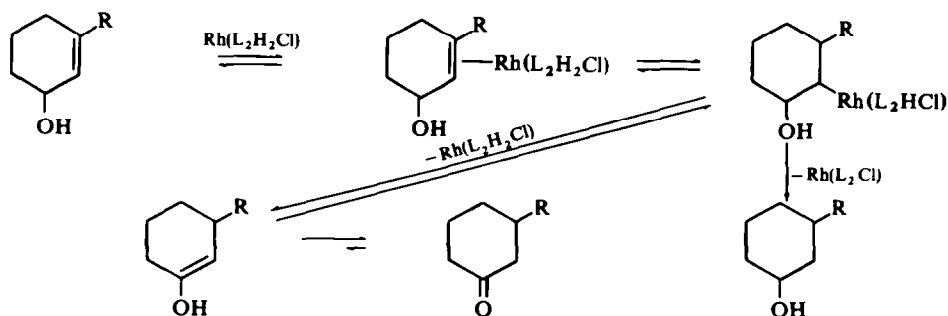
SCHEME 3B 2-Substituted 2-cyclohexenol

Rh(L$_2$H$_2$Cl)

—Rh(L$_2$H$_2$Cl)

Rh(L$_2$HCl)

R

OH

—Rh(L$_2$H$_2$Cl)

R

OH

Rh(L$_2$HCl)

R

OH

−Rh(L$_2$HCl)

−Rh(L$_2$Cl)

−Rh(L$_2$H$_2$Cl)

R

OH

Rh(L$_2$HCl)

R

OH

−Rh(L$_2$Cl)

R

OH
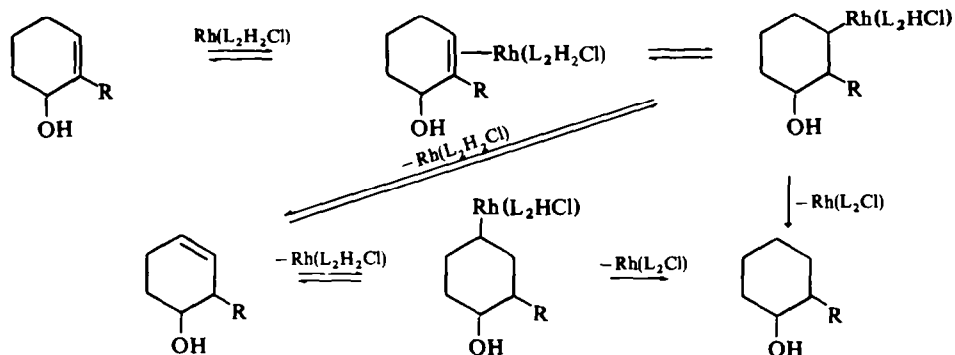
Coordination of the olefin with the cis-dihydridorhodium species was considered on the basis of kinetic studies on the disubstituted olefins to be the rate and product determining step of this reaction.[1] However, the results obtained in the present study and those of the hydrogenation of 1-methyl-4-isopropyl-[2] and 1-methyl-4-t-butyl-cyclohexene[11] in which 70% and 80% of the trans isomers were obtained respectively show that the isomeric distribution of the products from trisubstituted olefins seems to be a reflexion of the relative stability of the two isomeric σ-alkylrhodium intermediates. The intramolecular transfer of the second hydrogen in the σ-alkylrhodium species may be restricted to some extent owing to steric hindrance in the hydrogenation of trisubstituted olefins. As a consequence, the preceding reactants and intermediates should tend to become equilibriated with one another. A consideration of the energy states of the several half-hydrogenated intermediates of substituted cyclohexenols supplies a rationale for these results as in Fig. 1.

OH

R

M

A

OH

R

M

B

OH

M

R

C

OH

M

R

D
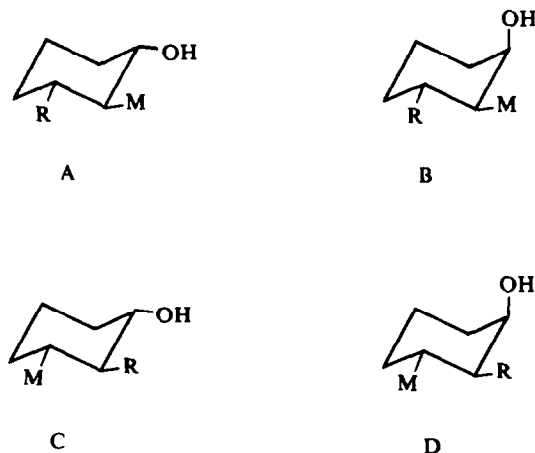
FIG. 1. Conformations of the substituted cyclohexylrhodium intermediates.

Structure A for 3-substituted cyclohexenol and D for a 2-substituted one lead to the *cis* isomers, while the *trans* isomers are obtained from B and C respectively. Of these four isomers B and D are of much higher energy and are less likely, while A and C are of lower energy and more favored. Consequently, the *cis* isomers may be obtained preferably from 3-substituted cyclohexenols and the *trans* from 2-substituted cyclohexenols.

Hussey and Takeuchi performed the deuteration of several substituted cyclohexenes and methylenecyclohexane.[2] They found that the disubstituted olefin yielded exclusively the d_2 product, whereas d_0, d_1, d_3 and d_4 products as well as the d_2 component were obtained from trisubstituted olefins. This result seems to support that intramolecular transfer of the second hydrogen in the σ-alkylrhodium species which is derived from mono or disubstituted olefins occurs fairly easily, whereas in trisubstituted olefins the transfer of the second hydrogen is restricted to some extent.

Heterogeneous hydrogenation over Pd catalyst of dialkyl substituted cyclohexenes and cyclopentenes gave the thermodynamically more stable of the two possible isomeric products. Since the rate and product determining step of this reaction is considered to be the conversion of the half-hydrogenated states to products, these results show that the relative stability of the half-hydrogenated intermediates controls the product composition.[5] On the other hand, hydrogenation of compounds with an aryl substituent at the olefinic carbon atom gave the thermodynamically less stable products. These results intimate that the alkyl substituted olefins form the half-hydrogenated intermediates in which the carbon–metal bond exists at the less substituted carbon atom, while the olefins with an aryl group at the sp^2 carbon atom form the π-benzylic species in which the carbon–metal bond exists at the carbon atom with an aryl group because this species may be energetically more favored than the alternative.[12]

SCHEME 4 Examples of the hydrogenation of dialkyl and alkylphenyl substituted cyclohexene over palladium charcoal.

Half-hydrogenated
intermediate
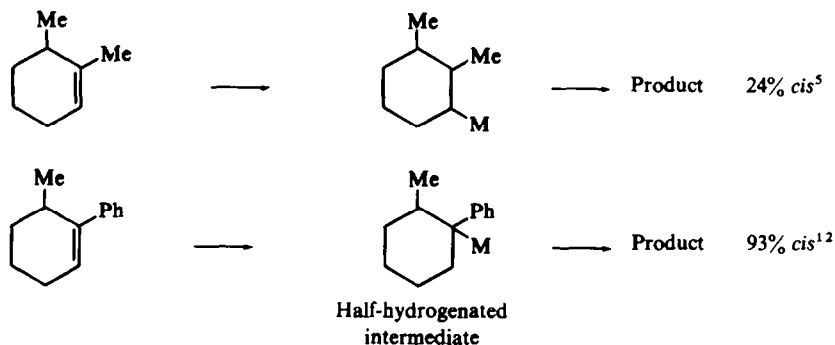
We cannot conclude whether or not a π-benzylic species forms on the other metal catalysts; Ni, Pt or Rh, but presumably this species would form more or less on the transition metal catalysts.

In contrast with heterogeneous hydrogenation, the results presented here indicate 2-cyclohexenols with a phenyl substituent at the olefinic carbon atom may not form such a π-benzylic type intermediate in the homogeneous hydrogenation with $RhCl(PPh_3)_3$.

EXPERIMENTAL

The catalyst was prepared by refluxing rhodium chloride trihydrate and triphenylphosphine in EtOH.[1a] The RhCl(PPh₃)₃ was filtered and washed with EtOH and ether.

3-Phenyl-2-cyclohexenol was prepared by the NaBH₄ reduction of 3-phenyl-2-cyclohexenone, obtained by the reaction of 3-ethoxy-2-cyclohexenone with PhMgBr.[13] 3,5,5-Trimethyl-2-cyclohexenol was prepared by the LAH reduction of commercial isophorone. 3-Methyl-2-cyclohexenol was prepared by the LAH reduction of 3-methyl-2-cyclohexenone, obtained by the condensation of ethyl acetoacetate and paraformaldehyde in the presence of piperidine followed by decarboxylation in hot 20% H₂SO₄.[14] 2-Methyl and 2-phenyl-2-cyclohexenol were prepared by the LAH reduction of corresponding acetates which were obtained by allylic oxidation of the substituted cyclohexenes with Hg(OAc)₂ in AcOH.[15] All cyclohexenols agreed in physical constants with samples earlier prepared.

Hydrogenation. All reactions were carried out at atmospheric pressure and temperature. In a typical experiment 50 mg of RhCl(PPh₃)₃ was added to the reaction flask and the hydrogen system was alternately evacuated and flushed with hydrogen 3 times. With the hydrogen pressure set near 1 atm. 3 ml of C₆H₆ (in the case of mixed solvent, C₆H₆ and EtOH mixture [3:1] was used) was added through the side-arm entry port to the flask. The flask was then stirred for 2 hr at which time 1 mmol of the substrate in 2 ml of the solvent was added through the side-arm entry port. After the reaction was stirred for 15 to 120 hr the resulting mixture was quantitatively analyzed by gas chromatography.

Gas chromatography. Gas chromatographic analyses were performed with Shimadzu 5AP with 8 m PEG on celite column or Hitachi K 53 equipped with 45 m PEG Goley column with flame ionization detector.

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