Catalytic Hydrogenation of Styrene Oxide with Cationic Rhodium Complexes

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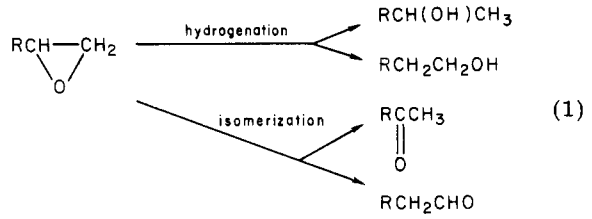
Catalytic hydrogenation of styrene oxide with cationic rhodium complexes was investigated to develop its selective conversion into the specific alcohol. β-Phenylethyl alcohol and phenylacetaldehyde were rather selectively produced without either α-phenylethyl alcohol or acetophenone through a selective antinormal fission of the epoxide ring. The catalytic activity and selectivity were found to depend strongly on the ligand, the activity for the formation of alcohol decreasing in the order, $PEt_3 > PMe_3 \sim PPh_3 \gg$ diphos. The highest yield, achieved by the PEt_3 complex, reached as high as 82% after 8 h of reaction. A possible mechanism was proposed to explain the selective formation of β-phenylethyl alcohol and the role of water as a cocatalyst in the catalytic hydrogenation.

The catalytic activities of metal complexes have been studied extensively because of their high selectivities as well as activities.[1] The rhodium complex[2] is one of the most interesting metal complexes which show the high activities for the hydrogenation of unsaturated compounds. Among rhodium complexes, neutral complexes such as the Wilkinson complex showed no activity for carbonyl compounds under mild conditions, although effectively catalyzing the hydrogenation of alkenes. In contrast, the cationic rhodium complexes were reported to show catalytic activity for the hydrogenation of unsaturated carbon–oxygen bonds in carbonyl groups[3a] as well as olefinic bonds,[3b] although they were rather unstable against some substrates.[3a] The present authors reported briefly in a previous letter[4] that cationic rhodium complexes hydrogenated styrene oxide to the corresponding alcohols, whereas the Wilkinson complex failed to do so. The hydrogenation of asymmetric epoxides has been studied extensively by using metal catalysts,[5] because the selective cleavage of the three-membered ring which is described in eq 1 is one of the most interesting features of the ca-



(1)

talysis. However, the homogeneous catalysis of ring opening has been scarcely investigated except with pentacyanocobaltate[6] and cobalt tetracarbonyl,[7] although the acidic cleavage of the substrate has been studied by many researchers.[8]

Table I. Hydrogenation of Styrene Oxide with $[Rh(NBD)(PR_3)_n]ClO_4$[a]

		yield, %		
$(PR_3)_n$	% conv	$PhCH_2$-CH_2OH	$PhCH_2$-CHO	oligo
$(PEt_3)_2$	90	68	trace	22
$(PMe_3)_3$	43	20	trace	23
$(PPh_3)_2$	100	39	10	51
diphos	100	<1	34	65

[a] Rh, 0.1 mmol; styrene oxide, 10 mmol; 1% aqueous diglyme, 50 mL; P_{H_2}, 1 atm; 30 °C; 6 h.

In the present paper, the catalytic activities of the cationic rhodium complexes carrying some phosphorus ligands were investigated in terms of the influence of the ligand structures on the rate and the selectivity in the hydrogenation of styrene oxide. Very careful procedures for the catalytic process resulted in excellent reproducibility of the high hydrogenation activity of the triethylphosphine complex and overcame its instability.

Results

Catalytic Activities of Cationic Complexes Derived from the Precursor $[Rh(NBD)(PR_3)_{2or3}]^+ClO_4^-$. Conversions and product distributions in the hydrogenation of styrene oxide (reaction time 6 h) with various cationic rhodium complexes derived from catalyst precursors, $[Rh(NBD)(PR_3)_n]^+ClO_4^-$, are listed in Table I. The reactions were fairly fast. The complexes used except for the PMe_3 derivative allowed 100% conversion of the epoxide within 6 h. The low activity of the PMe_3 complex may be due to steric hindrance of tricoordination. The variable selectivities of the products which depended on the phosphorus ligands are to be noted. PEt_3 and PMe_3 complexes gave high selectivities for β-phenylethyl alcohol. The PPh_3 complex afforded mainly β-phenylethyl alcohol and oligomers with minor production of phenylacetaldehyde. In contrast, the diphos complex was a poor hydrogenation catalyst and gave, preferentially, phenylacetaldehyde and oligomers (vide infra). The selective formation of β-phenylethyl alcohol and phenylacetaldehyde without either α-phenylethyl alcohol or acetophenone implies that the antinormal cleavage of the inner carbon–oxygen bond was accelerated selectively by the catalyst.

Variations in catalyst activities are related schematically to the type of phosphorus ligands used in Figure 1. The

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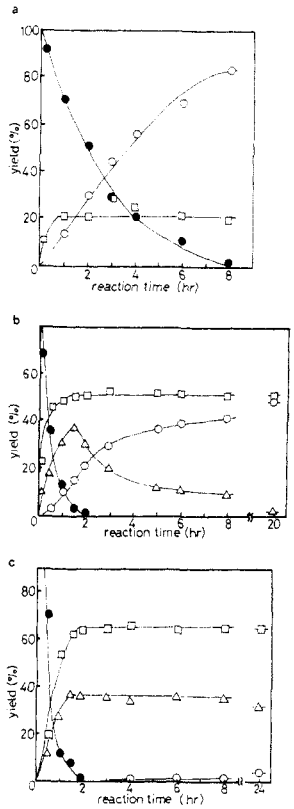


Figure 1. Hydrogenation of styrene oxide with cationic rhodium complexes: (a) $[Rh(NBD)(PEt_3)_2]^+ClO_4^-$, (b) $[Rh(NBD)(PPh_3)_2]^+ClO_4^-$, (c) $[Rh(NBD)(diphos)]^+ClO_4^-$. For the reaction conditions, see Table I. Symbols: ●, styrene oxide; ○, β-phenylethyl alcohol; △, phenylacetaldehyde; □, oligomers.

Table II. Hydrogenation of Phenylacetaldehyde with $[Rh(NBD)(PR_3)_n]ClO_4^-$ [a]

$(PR_3)_n$	% conv	yield,[b] %	$(PR_3)_n$	% conv	yield,[b] %
$(PEt_3)_2$	77.5	68	$(PPh_3)_2$	36.0	39
$(PMe_3)_3$	32.2	20	diphos	<1	<1

[a] Rh, 0.1 mmol; substrate, 10 mmol; 1% aqueous diglyme, 50 mL; P_{H_2}, 1 atm; 30 °C; 5 h. [b] Yield of alcohol from styrene oxide in 6 h.

PEt_3 complex catalyzed hydrogenation proceeded with a monotonic decrease in styrene oxide concentration and an increase in β-phenylethyl alcohol concentration. The formation of phenylacetaldehyde was negligible throughout the reaction. The PEt_3 complex gave the highest yield of β-phenylethyl alcohol: 82% after 8 h of reaction. The PMe_3 complex showed similar profiles.

The PPh_3 complex showed a contrasting profile. In the early stage of the reaction, phenylacetaldehyde and oligomers were produced, corresponding to the major consumption of the substrate. The phenylacetaldehyde concentration reached its maximum value after about 2 h and then decreased in the later course of the reaction, giving β-phenylethyl alcohol. The consecutive hydrogenation of the aldehyde with the diphos complex was remarkably slow, although the formation of the aldehyde and the oligomers was extremely fast. The oligomers were unaffected during the hydrogenation of the aldehyde.

Hydrogenation Reactivity of Phenylacetaldehyde. Catalytic activities of cationic rhodium complexes for hydrogenation of phenylacetaldehyde are listed in Table II. The catalytic activities decreased in the order of PEt_3 > PPh_3 ~ PMe_3 ≫ diphos complexes. The observed rates with PPh_3 and diphos complexes were comparable to those for β-phenylethyl alcohol from styrene oxide under the same conditions. PEt_3 and PMe_3 complexes showed a larger rate of conversion for phenylacetaldehyde than for styrene oxide into alcohol. Thus, phenylacetaldehyde may be an intermediate in the hydrogenation reaction of styrene oxide. Although Osborn et al. reported the severe deactivation of the complex catalyst at an early stage in the hydrogenation of aldehydes,[3a] the total catalytic turnover number of the PEt_3 complex was greater than 77.5 with this aldehyde.

Table III. Hydrogenation of Styrene Oxide with $[Rh(NBD)(PEt_3)_2]^+ClO_4^-$ [a]

P_{H_2}, atm	% conv	yield, % I	yield, % II	yield, % III
0	75		34.2	40.8
0.25	76.1	27.5	10.6	33.8
0.5	77.3	44.3	3.3	29.7
3.0	90.0	68.0	trace	22.0
1.0[b]	0			

[a] Rh^+, 0.1 mmol; styrene oxide, 10 mmol; 1% aqueous diglyme, 50 mL; 30 °C; 6 h. I = $PhCH_2CH_2OH$, II = $PhCH_2CHO$, and III = oligomer. [b] 0.2 mmol of NEt_3.

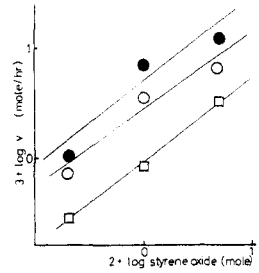


Figure 2. *Effect of the concentration of styrene oxide on the* catalytic activity of PEt_3 complex. For the reaction conditions, see Table I. Symbols: ●, conversion; ○, β-phenylethyl alcohol; □, oligomers.

Activity of the PEt_3 Complex under Various Reaction Conditions. The catalytic activity of the PEt_3 complex, which showed the largest activity for the formation of β-phenylethyl alcohol, was investigated under various reaction conditions.

The effects of the pressure of hydrogen during the reaction are listed in Table III. Under a nitrogen atmosphere the hydrido complex showed no hydrogenation activity, phenylacetaldehyde and oligomers being produced exclusively. The rate of formation of β-phenylethyl alcohol increased with the increase of hydrogen pressure in an approximately first-order manner. The formation of phenylacetaldehyde decreased remarkably with the increasing hydrogen pressure, becoming almost negligible at 1 atm.

The catalytic activities under variable substrate concentrations are illustrated in Figure 2. Conversions and yields of products increased with the increasing substrate concentration in a nearly first-order manner.

The addition of excess NEt_3 (0.2 mmol) to the complex, where the monohydride species II is expected to be dominant according to reaction 2,[3b] hindered the hydrogenation

$$\underset{\text{I}}{[RhH_2L_nS_x]^+} + NEt_3 \rightarrow \underset{\text{II}}{RhHL_nS_y} + H^+ NEt_3 \quad (2)$$

as well as the isomerization reaction, indicating that the dihydrido species I is catalytically active for the hydrogenation and isomerization of styrene oxide.

Effects of Counteranions on the Catalytic Activities. Cationic rhodium complexes are accompanied by

Table IV. Hydrogenation of Styrene Oxide with $[Rh(NBD)(PR_3)_2]^+A^-$ [a]

PR_3	A^-	% conv	yield, % I	II	III
PEt_3	ClO_4^-	90	68		22
	BPh_4^-	trace			trace
PPh_3	ClO_4^-	100	39	10	51
	BPh_4^-	trace			trace

[a] Rh^+, 0.1 mmol; styrene oxide, 10 mmol; 1% aqueous diglyme, 50 mL; P_{H_2}, 1 atm; 30 °C; 6 h. I = $PhCH_2CH_2OH$, II = $PhCH_2CHO$, and III = oligomer.

Table V. Oligomer Produced in Hydrogenation of Styrene Oxide with $[Rh(NBD)(PR_3)_n]^+ClO_4^-$ [a]

$(PR_3)_n$	mol wt	$(PR_3)_n$	mol wt
$(PEt_3)_2$	207	$(PPh_3)_2$	325
$(PMe_3)_3$	208	diphos	~194

[a] Rh, 0.1 mmol; substrate/[Rh] ratio is 100; 1% aqueous diglyme, 50 mL; P_{H_2}, 1 atm; 30 °C; 8 h.

counteranions[3c] which may interact weakly with the metal ion. The catalytic activities of PEt_3 and PPh_3 complexes with ClO_4^- and BPh_4^- anions, respectively, are compared in Table IV. The lack of activity of BPh_4^- complexes for hydrogenation, isomerization, and oligomerization must be noted.

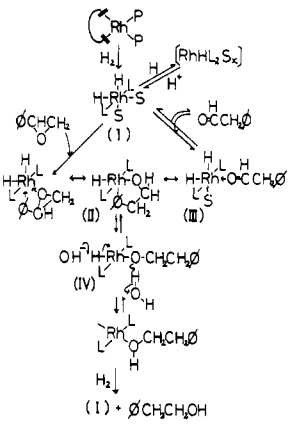
Oligomeric Byproducts in the Hydrogenation of Styrene Oxide. As shown in Table I, oligomers of styrene oxide were significant products of each catalyst used, especially if the diphos complex was used. In the case of the PEt_3 complex, more than ten different oligomers were detected by TLC. Their average molecular weight was 207 (Table V), suggesting that dimers are a major component. One of the identified dimers was 2,5-diphenyl-1,4-dioxane. With other complexes, the average molecular weights were 200–300. Trimers as well as dimers may be produced.

Interaction of Styrene Oxide with the Cationic Complex. The hydrogenation rate of styrene oxide catalyzed by the PEt_3 complex under atmospheric hydrogen at room temperature is comparable to those of acetone by the PMe_2Ph complex[3a] and by the PEt_3 complex.[9] The similar properties of the catalyst may play important roles in the hydrogenation of an epoxide, as well as ketones, being different from that for olefin.

Discussion of the high catalytic activity of the complex for these substrates is of value in comparison with the activity of the Wilkinson catalyst, which shows the highest activity for olefin but no activity for styrene oxide. The epoxide may have some extent of π unsaturation in its ring structure; however, it should be too small to coordinate the metal ion through π-electron donation. Thus, the cationic nature of the catalyst is reasonably presumed to play a key role for its coordination to the epoxide oxygen as postulated for hydrogenation of ketones.[3a]

In addition to the oxygen coordination, the phenyl group may interact with the metal ion in a manner similar to that assumed in the π-arene complexes, although the extent of interaction may be much weaker. Such coordination assists the selective cleavage of the epoxide ring as well as the activation of the substrate. The negligible reactivity of 1,2-epoxybutane for the hydrogenation into butanol with the same catalyst (0.65% conversion by 100 h of reaction) and the retarding effect of tetraphenylborate anion may support the above interaction.[10]

Scheme I [a]



[a] L = phosphorus ligand; ϕ = phenyl group.

Tentative Reaction Scheme. Hydrogenation of styrene oxide effected by the cationic complex may be tentatively described by Scheme I, which is essentially according to the scheme proposed for ketone hydrogenations by Osborn et al.[3a] The active catalyst for isomerization as well as the hydrogenation is probably the dihydrido complex as was also assumed for the hydrogenation of acetone and olefins.[3a,b] Styrene oxide reacts with the dihydrido complex I to give an alkoxy complex II, in which the substrate phenyl moiety may coordinate to rhodium, leading to the selective formation of β-phenylethyl alcohol and phenylacetaldehyde. The intermediate II produces intermediate IV through proton transfer assisted by water. The intermediate IV yields β-phenylethyl alcohol by the addition of a hydrogen molecule, which revives the dihydrido complex too. The fact that hydrogenation of styrene oxide did not proceed without water suggests the importance of the proton-transfer step. At the same time, the intermediate II may isomerize to the intermediate III through the β-elimination of hydrogen, the latter intermediate providing phenylacetaldehyde, an isomerization product. The addition of hydrogen to produce the alcohol may be the essential step for the high selectivety of hydrogenation, as suggested by the reaction being first order in hydrogen. As shown in Tables I and III, β-phenylethyl alcohol was produced much faster in the hydrogenation reaction than phenylacetaldehyde was in the absence of hydrogen. A major portion of the alcohol may be produced directly from styrene oxide without passing through the aldehyde (I → II → IV in Scheme I).

Experimental Section

The complexes of the catalyst precursors $[Rh(NBD)(PR_3)_2]^+A^-$ (NBD = norbornadiene, PR_3 = tertiary phosphine, A^- = ClO_4^- or BPh_4^-) were prepared under a nitrogen atmosphere according to the methods described in the literature.[3c] Because the catalyst precursors were very unstable with oxygen and moisture, they were dried under vacuum and stored under pure, dry nitrogen in a sealed tube. The commercial reagents NBD, triphenylphosphine (PPh_3), $NaClO_4$, triethylphosphine (PEt_3), $RhCl_3 \cdot 3H_2O$ (Wako Junyaku Co.), trimethylphosphine (PMe_3), diphenylphosphinoethane (diphos, Strem Chemical Inc.), and $NaBPh_4$ (Wako Junyaku Co.) were used without further purification. The complex was examined by elemental analysis and IR and NMR spectra.[3c] Styrene oxide (Wako Junyaku Co., GR grade) was used without further purification. Diglyme (Wako Junyaku Co.) as a reaction solvent was dried by being refluxed with sodium,

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(10) Schrock, R. R.; Osborn, J. A. *Inorg. Chem.* **1970**, *9*, 2339. Brooks, P. R. *J. Organomet. Chem.* **1972**, *43*, 415.

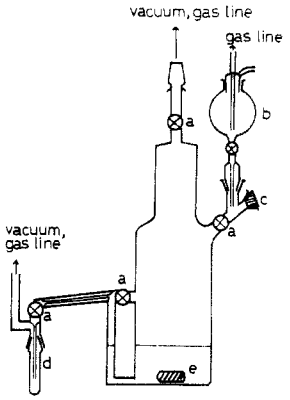

Figure 3. Reactor equipment: a, greaseless valve made of Teflon; b, solvent reservoir; c, silicon rubber stopper; d, sampling vessel; e, spinner.

distilled, and stored in a sealed, glass tube.

The reaction was carried out in a glass reactor equipped with greaseless valves. After the complex of catalyst precursor (0.1 mmol) was dissolved in 1% aqueous diglyme (50 mL) under a nitrogen atmosphere, nitrogen was replaced with hydrogen, the solution being aged for 5 min strictly (essential for reproducibility) under atmospheric pressure of hydrogen, to yield the active hydrido complex. *The PEt_3 complex in its solid form should never be exposed to dry hydrogen. It occasionally reacted explosively.* The epoxide (10 mmol) was injected with a syringe through a silicon rubber stopper to start the reaction. The reaction was followed by gas chromatographic analysis [column: polyethylene glycol (20 M), 2 m] of a small portion of the reaction mixture (ca. 0.2 mL) which was sampled by use of the equipment (Figure 3) at appropriate intervals without any contact of the reaction system with air.

After the hydrogenation reaction, oligomers were separated from the reaction mixture by the evaporation of solvent and other products under vacuum ($<1 \times 10^{-4}$ torr) at 30 °C. Oligomers were separated by TLC and by the Kugelrohr method. TLC analyses showed that oligomers consisted of more than ten species. The average molecular weights of oligomers were measured by means of a vapor-pressure osmometer (Hitachi 115). 2,5-Diphenyl-1,4-dioxane was separated in crystalline form by use of the Kugelrohor method with ca. 20% of oligomers when the PEt_3 complex was used: mass spectru, m/e (M^+) 240; mp 170 °C; ^1H NMR ($CDCl_3$) δ 3.63 (q, 2 H), 4.08 (q, 2 H), 4.70 (q, 2 H), 7.35 (m, 10 H), $J_{\alpha-\beta}$ = 12 Hz, $J_{\beta-\gamma}$ = 10 Hz, $J_{\alpha-\gamma}$ = 3 Hz.

Registry No. Styrene oxide, 96-09-3; β-phenylethyl alcohol, 60-12-8; phenylacetaldehyde, 122-78-1; $[Rh(NBD)(PEt_3)_2]^+ClO_4^-$, 65466-19-5; $[Rh(NBD)(PMe_3)_3]^+ClO_4^-$, 76963-03-6; $[Rh(NBD)(PPh_3)_2]^+ClO_4^-$, 32799-31-8; $[Rh(NBD)(diphos)]^+ClO_4^-$, 32799-34-1; $[Rh(NBD)(PEt_3)_2]^+BPh_4^-$, 76986-43-1; $[Rh(NBD)(PPh_3)_2]^+BPh_4^-$, 31666-38-3.

Acyclic Stereoselection. 12. Double Stereodifferentiation with Mutual Kinetic Resolution. A Superior Class of Reagents for Control of Cram's Rule Stereoselection in Synthesis of *erythro*-α-Alkyl-β-hydroxy Carboxylic Acids from Chiral Aldehydes[1,2]

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Chiral α-[(trimethylsilyl)oxy] ketones **7-9** have been prepared and their aldol condensations studied. Compound **8** shows from good to excellent inherent diastereoface selectivity in reactions with achiral aldehydes. Stereoselectivity is related to the size of the alkyl group attached to the aldehyde carbonyl; highest selectivity is observed with diphenylacetaldehyde (>10:1) and pivaldehyde (>19:1). Ketone **8** also shows high diastereoface selectivity in its reactions with chiral, racemic aldehydes **21**, **25**, **29**, and **17**, only one stereoisomeric aldol being obtained in each case. Furthermore, the four aforementioned aldehydes show much higher diastereoface selectivity with ketone **8** than they do with the related ketone **1**. As a result, the reactions of racemic **8** with these chiral, racemic aldehydes show a high degree of "mutual kinetic resolution". In fact, the rate of the (*R*)-enolate plus (*R*)-aldehyde condensation is at least 35 times the rate of the (*R*)-enolate plus (*S*)-aldehyde condensation. It is shown by simple logical argument that such mutual kinetic resolution is expected in reactions between two chiral racemic compounds and that the magnitude of the effect should be proportional to the inherent diastereoselectivity shown by each compound in its reaction with achiral reaction partners. Thus, reagents such as **8** can be used to obtain the benefits of double stereodifferentiation even in the racemic form. As an application of the chemistry developed, (±)-blastmycinone (**47**) has been prepared in four steps from ketone **9** (20% overall yield).

In previous papers in this series, we have introduced ketone **1** as a reagent for the achieving high erythro selectivity[3] in preparation of α-alkyl-β-hydroxy carboxylic acids,[4] aldehydes,[5] and ketones.[6] Although this compound

(1) For part 11 see C. H. Heathcock, C. T. White, J. J. Morrison, and D. VanDerveer, *J. Org. Chem.*, **46**, 1296 (1981).

(2) A portion of this work has been communicated in preliminary form: (a) C. H. Heathcock, C. T. Buse, W. A. Kleschick, M. C. Pirrung, and J. E. Sohn, 2nd International IUPAC Symposium on Organic Synthesis, Jerusalem, Sept 12, 1978. (b) C. H. Heathcock, M. C. Pirrung, C. T. Buse, J. P. Hagen, S. D. Young, and J. E. Sohn, *J. Am. Chem. Soc.*, **101**, 7077 (1979).

(3) It is convenient to have stereochemical nomenclature which is invariant of the nature of the α-alkyl group. We prefer the prefixes erythro and threo and use them in the following sense: when the backbone of the aldol is written in an extended (zig-zag) manner, if the α-alkyl substituent and the β-hydroxy substituent both extend toward the viewer or away from the viewer, this is the erythro diastereomer.

(4) C. H. Heathcock, C. T. Buse, W. A. Kleschick, M. C. Pirrung, J. E. Sohn, and J. Lampe, *J. Org. Chem.*, **45**, 1066 (1980).

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