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ASYMMETRIC REDUCTION OF KETONES VIA HYDROSILYLATION CATALYZED BY A RHODIUM(I) COMPLEX WITH CHIRAL PHOSPHINE LIGANDS. II. ON THE MECHANISM OF THE INDUCTION OF ASYMMETRY

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Effective asymmetric reduction of ketones has been achieved via catalytic hydrosilylation using various hydrosilanes in the presence of a rhodium(I) complex with optically active phosphine ligands. The mechanism of the induction of asymmetry is proposed in view of the stereochemical course of the reaction.

Asymmetric reduction of unsaturated compounds by the hydrogenation using homogeneous catalysts currently gathers much interest,[1] and recently, Scorrano and coworkers[2] reported the asymmetric hydrogenation of ketones by the use of a cationic rhodium(I) catalyst with a chiral phosphine ligand even though in a low optical yield. Asymmetric reduction of ketones via hydrosilylation was also achieved using a platinum complex,[3] a rhodium complex[4] and a cationic rhodium complex[5] with chiral phosphine ligands as a catalyst with better optical yields.

Although discussion has been made on the mechanisms of asymmetric induction in the homogeneous asymmetric hydrogenation[1] and hydroformylation,[10] clear explanations are as yet unestablished. This may be partly due to the failure of separating a steric effect or an electronic effect from the many controlling factors in the asymmetric induction. In our systems, however, only a steric effect plays a key role in the induction of asymmetry, and an electronic one can be excluded. Now, we describe in this communication the effective asymmetric reduction of simple ketones via hydrosilylation and propose the mechanism of the induction of asymmetry, which may be the first reasonable stereochemical interpretation on the asymmetric reductions catalyzed by homogeneous transition metal complex.

The results of the asymmetric reduction of ketones using various hydrosilanes are summarized in Table 1. As is seen from Table 1, both the configuration and the

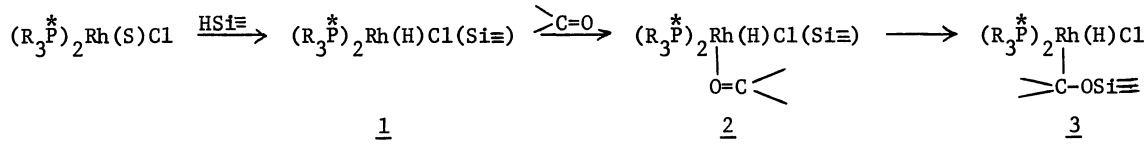
optical yield of the resulting alcohols depend on the structure of hydrosilanes employed. For example, i-propyl phenyl ketone was reduced to (+)-(R)-2-methyl-1-phenyl-1-propanol in 56% optical yield with the use of (-)-(S)-benzylmethylphenylphosphine as a chiral ligand and dimethylphenylsilane as a reducing agent, while (-)-(S)-2-methyl-1-phenyl-1-propanol was obtained in 23% optical yield using the same chiral phosphine and diethylsilane.

Table 1 Asymmetric Reduction of Prochiral Ketones via Hydrosilylation Catalyzed by $[(PhCH_2)MePhP]_2Rh(S)Cl$ [S=Solvent]

	Ketone	Hydrosilane	Silyl ether[a,g] $[\alpha]_D^{21-28}$	Yield (%)	Alcohol[a] $[\alpha]_D^{21-28}$	Configuration	Optical Yield[c] (%)
	Ligand = (-)-(S)-$(PhCH_2)MePhP$			(Optical purity[i] 62%)			
1	$PhCOCH_3$	$PhMe_2SiH$	+ 20.8[d]	92	+ 14.32[e]	R	44
2	$PhCOC_2H_5$	$PhMe_2SiH$	+ 22.6	96	+ 8.74	R	50
3	$PhCOC_3H_7$-i	$PhMe_2SiH$	+ 24.5	95	+ 16.68[f]	R	56
4	$PhCOC_2H_5$	Et_2SiH_2	- 5.10	98	- 2.90	S	17
5	$PhCOC_3H_7$-i	Et_2SiH_2	- 6.33	98	- 6.73[f]	S	23
6	n-$BuCOCH_3$	Et_2SiH_2	+ 3.20[d]	93	+ 2.24	S[h]	30
7	t-$BuCOCH_3$	Et_2SiH_2	+ 3.96	95	+ 1.61	S	39
	Ligand = (+)-(R)-$(PhCH_2)MePhP$			(Optical purity[i] 77%)			
8	$PhCOCH_3$	Et_2SiH_2	+ 5.10	97	+ 6.44[e]	R	16
9	$PhCOC_2H_5$	Ph_2SiH_2	+ 18.5	98	+ 9.04	R	42
10	PhCOBu-t	$EtMe_2SiH$	+ 14.23	97	+ 15.63[f]	R	56
11	PhCOBu-t	$PhMe_2SiH$	- 20.68	92	- 14.91[f]	S	54

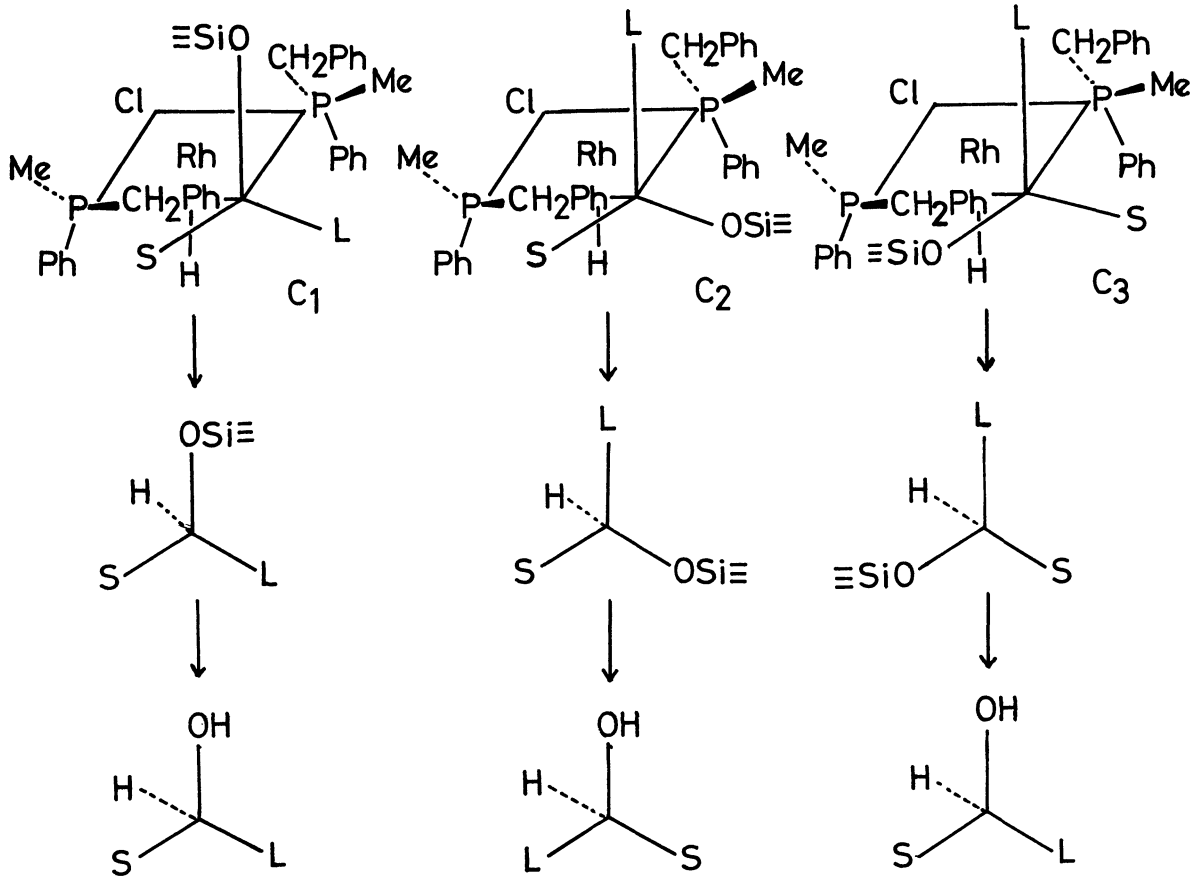
a All optical rotations are for the neat liquid unless otherwise noted. b Yield of a silyl ether (glpc analysis). The hydrolysis was accomplished in almost quantitative yield. c Optical yield is calculated from the specific rotation of the pure enantiomer which is reported in the literature, [U. Nagai, T. Shishido, R. Chiba, and H. Mitsuhashi, Tetrahedron, 21, 1701 (1965); R. MacLeod, F. J. Welch, and H. S. Mosher, J. Amer. Chem. Soc., 82, 876 (1960); W. M. Foley, F. J. Welch, E. M. LaComb, and H. S. Mosher, ibid., 2779 (1959).] and calibrated for the optical purity of the chiral phosphine employed. d Specific rotation in benzene. e Specific rotation in dichloromethane. f Specific rotation in ether. g The nmr spectra and elemental analyses of the silyl ethers were consistent with the assigned structures. h We had assigned an erroneous configuration to (+)-hexan-2-ol in a previous paper.[4] i The optical purity was determined by quaternization using n-propyl bromide.[11]

We already suggested the intermediacy of the organorhodium complex (3), the most stable conformation of which is likely to determine the selectivities, in a previous paper which dealt with stereoselective reductions of terpene ketones by the hydrosilane-rhodium(I) complex combinations.[6]



1 2 3

Therefore, we believe that the intermediate organorhodium complex also plays a key role in the asymmetric induction of the present cases. It is reasonable to assume the square-pyramidal structure of the complex 3 on account of the established structures of a silylhydrido complex[7] and dihydrido complex[8] derived from tris(triphenylphosphine)chlororhodium.[7]



Scheme 1

The configuration of the carbon moiety in the most stable conformation of the complex 3 may depend upon the relative bulkiness of the substituents of ketones, those of the chiral phosphine and the silyloxy groups. For example, when the silyloxy group is bulkier than either of the substituents of the ketones, i.e., ≡SiO> L> S, the thermodynamical consideration leads to the conclusion that the silyloxy group should occupy the quasi-apical position which is the least hindered site and lies between methyl and benzyl group of the chiral phosphines. It follows then that the substituent, L, lies between methyl and phenyl group and the substituent, S, lies between benzyl and phenyl group. The conformation which satisfies these requirements is depicted as C_1 in the Scheme 1 in which the (-)-(S)-benzylmethylphenylphosphine is employed as a ligand.

In a similar manner, when the order of bulkiness is L> ≡SiO > S, the most stable conformation is C_2 and when that is L> S> ≡SiO, the most stable conformation is C_3. As is immediately seen from the Scheme 1, the alcohol derived from C_1 has the same configuration as that derived from C_3, whereas the alcohol derived from C_2 has an opposite configuration when the priority sequence[9] of the substituents of the carbon is identical in each case.

According to the proposed mechanism, the relationship between the configuration of the chiral phosphine and that of the resulting alcohol should fall into six different cases shown in Table 2 on account of both bulkiness and priority sequence.[9]

Table 2

Case	Bulkiness	Configurational Relationship[a]	Conformation of the Complex 3
	Priority Sequence[9] L>S		
A	≡SiO> L > S	opposite	C_1
B	L> ≡SiO > S	same	C_2
C	L > S > ≡SiO	opposite	C_3
	Priority Sequence[9] L<S		
A'	≡SiO > L > S	same	C_1
B'	L> ≡SiO > S	opposite	C_2
C'	L > S> ≡SiO	same	C_3

a Relationship between the configuration of the chiral phosphine and that of the resulting alcohols .

We found that configurations, i.e., R and S, of the resulting alcohols are consistently predicted on the basis of the mechanism just mentioned above, when the bulkiness of the silyloxy groups is estimated as follows; t-Bu$\rangle$ $PhMe_2SiO\rangle$ Ph$\rangle$ $EtMe_2SiO\sim Ph_2HSiO\sim Et_2HSiO\rangle$ i-Pr$\rangle$ Et$\rangle$ Me, n-Bu$\rangle$ $Et_2HSiO\rangle$ Me. The correlations between experimental results and the prospects are shown in Table 3. It should be noted that the mechanism of asymmetric induction in the homogeneous catalytic system is clearly explained for the first time only on the basis of a stereochemical point of view like usual organic asymmetric reactions.

Table 3

	Substituents			Corresponding Case	Configurational Relationship (observed)
	L	S	≡SiO		
1	Ph	Me	$PhMe_2SiO$	A	opposite
2	Ph	Et	$PhMe_2SiO$	A	opposite
3	Ph	i-Pr	$PhMe_2SiO$	A	opposite
4	Ph	Et	Et_2HSiO	B	same
5	Ph	i-Pr	Et_2HSiO	B	same
6	n-Bu	Me	Et_2HSiO	B	same
7	t-Bu	Me	Et_2HSiO	B	same
8	Ph	Me	Et_2HSiO	B	same
9	Ph	Et	Ph_2HSiO	B	same
10	t-Bu	Ph	$EtMe_2SiO$	C'	same
11	t-Bu	Ph	$PhMe_2SiO$	B'	opposite

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