Stereoselective Catalytic Hydrogenation of α-Hydroxy Ketoximes

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Two isomers(*E* and *Z*) of benzoin oxime and 2-hydroxy-1-phenyl-1-propanone oxime were catalytically hydrogenated by using palladium on charcoal and erythro amino alcohols were obtained in about 80% diastereomeric excess. The syn-anti isomerization of these oximes in the presence of palladium on charcoal was also studied in connection with the stereoselectivity of the catalytic hydrogenation of the oximes.

The stereochemistry of catalytic hydrogenation of oximes of α-keto amides[1] and Schiff bases prepared from α-keto esters with optically active amines[2] have been studied. The steric course of the catalytic hydrogenation reaction was explained by the chelation mechanism assuming that the substrate forms a five-membered chelated structure with the catalyst and subsequent hydrogenation reaction takes place from the less bulky side of the chelated substrate. This mechanism was supported by various hydrogenolytic catalytic asymmetric transamination[2-4] and also by the infrared absorption spectrum of ethyl 2-hydroxyimino-3-oxo-3-phenylpropionate on palladium metal, which was measured by using the high-sensitivity reflection method.

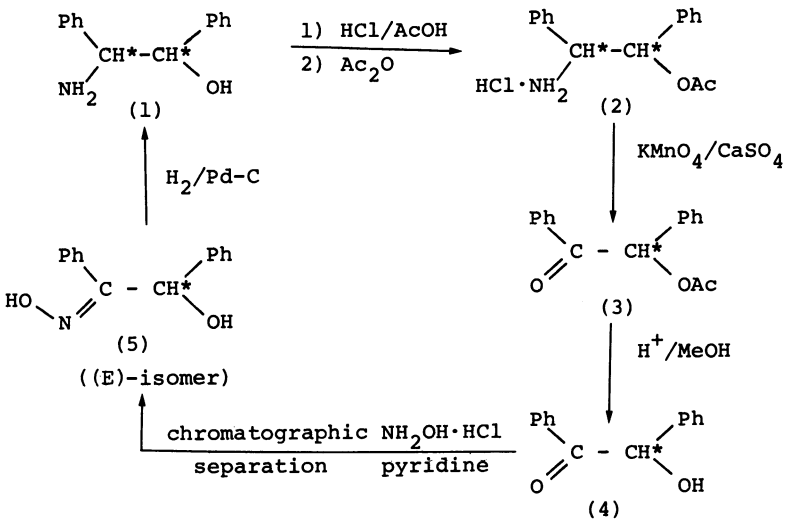
The substrates, which have been used in the previous studies of the chelation mechanism, contain an asymmetric center out of the chelated ring when they form a chelated structure with the catalyst. If the substrate contains an asymmetric center in the five-membered chelated ring, a relatively high asymmetric yield might be obtained by the catalytic hydrogenation. In order to examine the consideration, the catalytic hydrogenation of oximes, whose asymmetric center is in the five-membered chelated ring, was performed.

It was reported that the catalytic hydrogenation of racemic (*E*)-benzoin oxime afforded *erythro*-2-amino-1,2-diphenylethanol (*erythro*-ADE) dominantly.[6] However, the exact ratio of the diastereomer has not been clarified yet. In the present study, a cyclic reaction pathway as shown in Scheme 1 was designed and the catalytic hydrogenation of optically and racemic benzoin oxime was carried out. If the stereoselectivity of the catalytic hydrogenation is sufficiently high, optically active *erythro*-ADE could be synthesized again from optically active *erythro*-ADE used as a starting material. In addition, in order to examine the substituent effect, hydrogenation of (±)-2-hydroxy-1-phenyl-1-propanone oxime (HPPO) was also performed.

Oxime of α-keto amide has (*E*)- and (*Z*)-isomers, and only the (*E*)-isomer could form a five-membered chelated structure with the catalyst. However, the *E*—*Z* isomeric ratio of the substrate used in the catalytic hydrogenation has not been clarified yet, and the steric course of the hydrogenation of (*E*)-oximes might be different from that of (*Z*)-oximes. In order to clarify the stereochemistry of the hydrogenation of oximes, both (*E*)- and (*Z*)-isomers were isolated and each of the oximes was catalytically hydrogenated. The syn-anti isomerization of the oximes in the presence of palladium on charcoal was also studied in connection with the stereoselectivity of the catalytic hydrogenation of the oximes.

Results and Discussion

Hydrogenation of Substrates. Substrates, (*E*)- and (*Z*)-benzoin oxime and (*E*)- and (*Z*)-HPPO, were hydrogenated by using palladium on charcoal in several solvents and at various temperatures. The diastereomeric ratio of amino alcohol was determined by gas chromatographic analysis, which are summarized in Tables 1 and 2.



Scheme 1.

Table 1. Catalytic hydrogenation of (*E*)-oximes of *R*(—)-benzoin and racemic 2-hydroxy-1-phenyl-1-propanone

substrate	Solvent	Temp/°C	Yield/%	Erythro: Threo	O.P./%[a]	Configuration[b]
(*E*)-Benzoin oxime	MeOH	20	79	93 : 7	95	*S*
	EtOH	0	78	96 : 4		*S*
	EtOH	20	71	93 : 7		*S*
	EtOH	40	75	93 : 7		*S*
	2-PrOH	20	80	92 : 8		*S*
	DMF	20	69	94 : 6		*S*
(*E*)-2-Hydroxy-1-phenyl-1-propanone oxime	MeOH	20	89	91 : 9		—[c]
	EtOH	20	68	92 : 8		—
	EtOH	40	81	90 : 10		—
	EtOH	60	73	85 : 15		—
	AcOEt	20	69	94 : 6		—

a) Optical purity. b) Configuration of newly formed asymmetric moiety. c) Racemic oxime was used.

Table 2. Catalytic hydrogenation of (*Z*)-oximes of racemic benzoin and racemic 2-hydroxy-1-phenyl-1-propanone

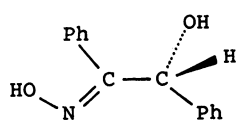
Substrate	Solvent	Temp/°C	Yield[a]/%	Erythro: Threo
(*Z*)-Benzoin oxime	MeOH	20	68	88:12
	EtOH	20	71	89:11
	AcOEt	20	55	86:14
(*Z*)-2-Hydroxy-1-phenyl-1-propanone oxime	MeOH	20	59	91:9
	EtOH	20	64	93:7
	EtOH	40	75	91:9
	EtOH	60	46	85:15
	AcOEt	20	80	93:7

a) Determined by isolation.

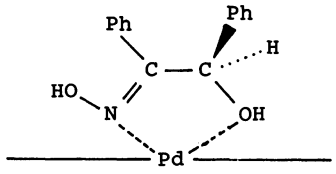
In the hydrogenation of (*E*)-oximes of both benzoin and HPPO, erythro amino alcohols were obtained in about 80% diastereomeric excess in every solvent and at every temperature employed. Similar results were obtained in the hydrogenation of the corresponding (*Z*)-oximes.

In the case of (*E*)-benzoin oxime, the conformation of the substrate in solution could be shown in Structure 1 considering the steric repulsion between the phenyl groups of the molecule. If the hydrogenation of the (*E*)-benzoin oxime proceeds from the less bulky side of the substrate in Structure 1, *threo*-ADE would be produced, which is inconsistent with the experimental results. On the other hand, if the (*E*)-benzoin oxime forms a five-membered chelated structure with the palladium metal first as shown in structure 2, and then hydrogenation proceeds from the less bulky side of the substrate as expected by the chelation mechanism, *erythro*-ADE would be formed dominantly. In the hydrogenation of (*E*)-HPPO, the formation of erythro amino alcohol could also be explained by the chelation mechanism.

The (*E*)-oxime could also form a five-membered intramolecular hydrogen bonding between the nitrogen and the hydroxyl group at α-position. If the hydrogenation reaction proceeds from the less bulky side of the intramolecularly hydrogen bonded substrate, erythro amino alcohol could also be produced. However, examination of the molecular structure by the use of a molecular model indicates that the distance between the nitrogen and the hydroxyl group at the α-position of the (*E*)-benzoin oxime seems to be too long for the formation of rigid intramolecular hydrogen bonding. Therefore, the contribution of the hydrogen bonded steric course for the hydrogenation of (*E*)-oxime would not be so important.



Structure 1.



Structure 2.

According to the chelation mechanism, the stereoselectivity in the hydrogenation of (*E*)-HPPO is assumed to be smaller than that of (*E*)-benzoin oxime. However, the stereoselectivity in the hydrogenation of (*E*)-HPPO was almost the same as that in (*E*)-benzoin oxime. This might be explained by the adsorption of phenyl groups of benzoin oxime on the catalyst, and other conformation of chelated ring structure could be possible other than the prefered conformation.

On the other hand, the (*Z*)-oxime could not form the five-membered chelated structure, but could form a six-membered intramolecular hydrogen bonding. The distance between the hydroxyl group attached to nitrogen and the hydroxyl group at α-position seems to be adequate to form a rigid intramolecular hydrogen bonding by using a molecular model. If the substrate forms the six-membered intramolecular hydrogen bonding first, and then hydrogenation reaction takes place from the less bulky side of the substrate, erythro amino alcohol would be obtained. This consideration

is consistent with the experimental results. The results obtained in the hydrogenation of the (*Z*)-oxime are similar to those of the corresponding (*E*)-oxime. Considering the conformation of the substrate by using molecular model, the steric bulkiness around the diastereomeric face of the (*E*)-oxime forming the five-membered chelated structure with the catalyst is almost the same as that of the corresponding (*Z*)-oxime forming the six-membered intramolecular hydrogen bonding. This observation suggest that both (*E*)- and (*Z*)-oximes could be hydrogenated in chelated form and in intramolecular hydrogen bonded form, respectively.

Effect of Isomerization of Benzoin Oxime on the Hydrogenation. Isomerization of benzoin oxime in the presence of palladium on charcoal was observed and the time-courses of the isomerization were shown in Fig. 1. The isomerization of a few derivatives of benzoin oxime was also examined. Benzoin acetate oxime, in which the hydroxyl group of the benzoin oxime is protected by an acetyl group, isomerized in the presence of palladium on charcoal. However, *N,O*-diacetylbenzoin oxime, in which the hydroxyimino group of benzoin acetate oxime is protected by an acetyl group, did not isomerize under these conditions. These results indicate that the hydrogen atom of the hydroxyimino group of benzoin oxime might play an important role in the isomerization in the presence of palladium on charcoal. Therefore, benzoin oxime might isomerize *via* a nitroso compound and the hydrogenation of the compound to ADE might proceed as shown in Fig. 2. In order to confirm the possible

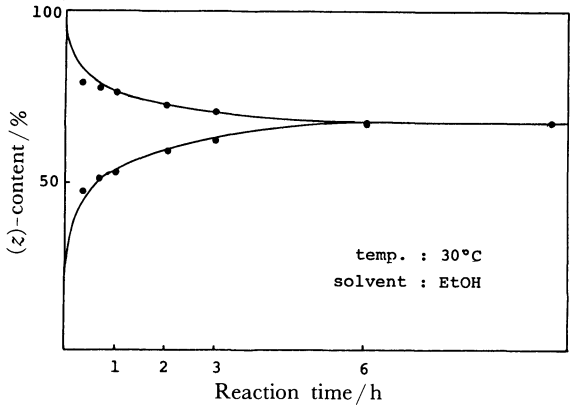


Fig. 1. Isomerization of benzoin oxime in the presence of palladium on charcoal.

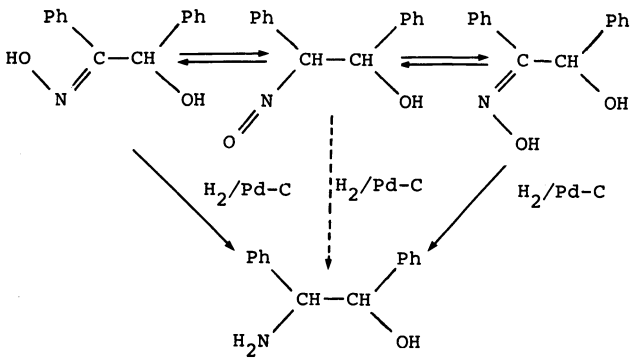


Fig. 2. Mechanism of isomerization of benzoin oxime.

hydrogenation pathway, the hydrogenation of (*E*)-benzoin oxime was carried out in CD_3OD by using palladium on charcoal. If the hydrogenation of (*E*)-benzoin oxime proceeds *via* the nitroso compound, deuterium should be combined to the asymmetric carbon attached to the amino group of ADE. ^1H NMR spectrum of ADE, which was obtained by hydrogenation of (*E*)-benzoin oxime in CD_3OD, indicates that the integrated value of proton on the asymmetric carbon attached to amino group was almost equal to that on the asymmetric carbon attached to hydroxyl group. The mass spectrum of TFA derivative of ADE obtained by hydrogenation of (*E*)-benzoin oxime in CD_3OD was almost equal to that of TFA derivatives of both *erythro*- and *threo*-ADE (Table 3). These results indicate that the hydrogenation reaction does not proceed *via* the nitroso compound but through hydrogenation of the carbon–nitrogen double bond of the substrate oxime.

TABLE 3. FRAGMENT PEAK OF MASS SPECTRA OF *N,O*-BIS (TFA)-ADE AND RELATIVE INTENSITY

N,O-Bis(TFA) derivatives	Fragment peak	Relative intensity/%
erythro-ADE	78	8.8
	107	13.1
	202[a)]	100
	203[b)]	13.3
threo-ADE	78	9.3
	107	14.1
	202[a)]	100
	203[b)]	12.4
ADE obtained by the hydrogenation of (*E*)-benzoin oxime in CD_3OD	78	8.1
	107	13.0
	202[a)]	100
	203[b)]	17.6

a) $Ph\text{-}CH{=}NH^+\text{-}CO\text{-}CF_3$. b) $Ph\text{-}CH{=}O^+\text{-}CO\text{-}CF_3$.

The influence of the syn-anti isomerization of the oximes during the hydrogenaiton was examined. In the hydrogenation of (*E*)-benzoin oxime, if it is assumed that the rate of hydrogenation reaction of the (*Z*)-oxime is much larger than that of the (*E*)-oxime, the (*E*)-oxime would isomerize to the (*Z*)-isomer first, and then the newly formed (*Z*)-isomer would be hydrogenated to form ADE. If this is the case, ADE would be obtained in rather low chemical yield in a short reaction time in the hydrogenation of (*E*)-benzoin oxime, because of the low concentration of the (*Z*)-oxime. In order to estimate the rate of hydrogenation of (*E*)- and (*Z*)-benzoin oxime, the time-courses of the chemical yield of ADE were measured. The results are shown in Fig. 3. The chemical yield of ADE obtained by hydrogenation of the (*E*)-oxime was 15% at the reaction time of 30 min, while the chemical yield of ADE obtained from the (*Z*)-oxime was 18% at the same reaction time. These results suggest that the rate of hydrogenation of the (*E*)-oxime is similar to that of the (*Z*)-oxime.

Considering the overall results, it could be concluded that (*E*)-benzoin oxime is hydrogenated mainly after forming a five-membered chelated structure with the

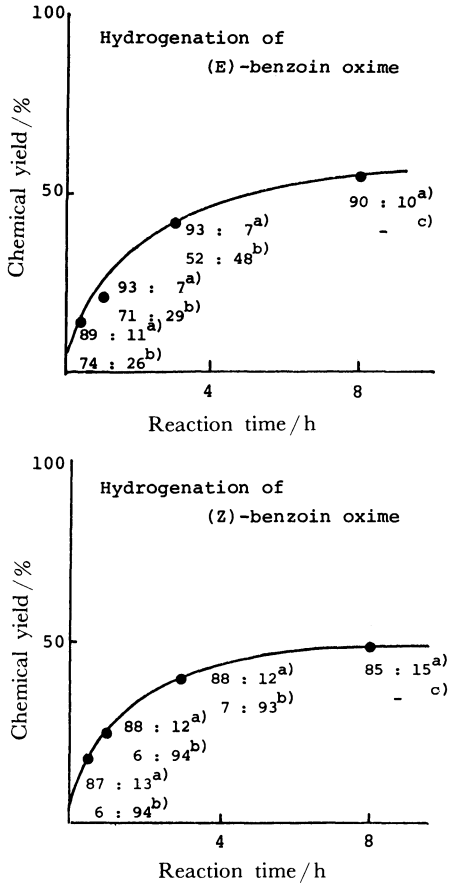


Fig. 3. Time-course of chemical yield of ADE in hydrogenation of benzoin oxime.
a) Diastereomeric ratio, erythro: threo, b) *E*-*Z* isomeric ratio, *E*:*Z*. c) *Syn-anti* isomeric ratio could not be determined.

catalyst (chelation mechanism) and (*Z*)-benzoin oxime is hydrogenated mainly after forming a intramolecular six-membered hydrogen bonding (intramolecular hydrogen bonding mechanism).

Experimental

All the melting point are uncorrected. The specific rotation were measured with a JASCO DIP-181 Digital Polarimeter. NMR spectra were obtained with a Hitachi R-24A spectrometer and the chemical shifts were given in δ values (ppm) from tetramethylsilane (TMS). Mass spectra were obtained with a Hitachi RMU-6M mass spectrometer. All the gas chromatographic analyses were carried out with a Hitachi 163 gas chromatograph. 5% Palladium on charcoal was purchased from Nippon Engelhald.

(−)-erythro-2-Amino-1,2-diphenylethyl Acetate Hydrochloride (2). (−)-*erythro*-ADE (**1**) (5.41 g, 0.025 mol) was suspended in 500 ml of AcOH. Hydrogen chloride gas was bubbled into the suspension for 9 h at 80 °C and the resulting clear solution was cooled to room temperature. Then Ac_2O was added to the mixture under stirring and the mixture was stirred for additional 5 h and concentrated *in vacuo*. The crude product obtained was recrystallized from MeOH–Ether, yield 4.74 g (64%), mp 168—169 °C, $[\alpha]_D^{11}$ −89.8° (*c* 1, MeOH), ^{1}H NMR (DMSO-d_6): δ=2.13 (s, 3H), 4.62 (d, 1H), 6.28 (d, 1H), 7.24 (m, 10H), 9.02 (s, br, 3H). Found: C, 65.92; H, 6.14; N, 4.75%. Calcd for $C_{16}H_{18}NO_2Cl$: C, 65.86; H, 6.21; N, 4.75%.

R(−)-Benzoin Acetate (3). To a suspension of $KMnO_4$ (5.02 g, 0.032 mol) and $CaSO_4 \cdot 2H_2O$ (3.75 g, 0.022 mol) in 50 ml of water and 50 ml of *t*-butyl alcohol was added (−)-*erythro*-2-amino-1,2-diphenylethyl acetate hydrochloride (**2**) (4.87 g, 0.017 mol) and the suspension was heated for 2 h at 60 °C. The reaction mixture was filtered and the residue was washed with ethyl acetate. The combined solution was washed with water and dried over magnesium sulfate and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel using benzene–ethyl acetate (100:1 v/v) as an eluent. The solid obtained was recrystallized from hexane, yield 1.61 g (37.3%), mp 80.5—82 °C, $[\alpha]_D^{18}$ −214.3° (*c* 1, chloroform) (lit,[7]) $[\alpha]_D^{14}$ −217.7°), ^{1}H NMR ($CDCl_3$): δ=2.15 (s, 3H), 6.81 (s, 1H), 7.66 (m, 10H). Found: C, 75.86; H, 5.64%. Calcd for $C_{16}H_{14}O_3$: C, 75.57; H, 5.54%.

R(−)-Benzoin (4). A solution of *R*(−)-benzoin acetate (**3**) (800 mg, 3.15×10^{-3} mol) in 30 ml of abs. methanol was refluxed for 2 h in the presence of a catalytic amount of concd. sulfuric acid. To the reaction mixture was added 100 ml of ethyl acetate, and organic layer was washed with saturated $NaHCO_3$ and water and dried over magnesium sulfate, and was concentrated *in vacuo*. The residue was purified by column chromatography on silica gel using benzene–ethyl acetate (20:1 v/v) as an eluent. The solid obtained was recrystallized from ethanol, yield 498 mg (75%), mp 130—131 °C (lit,[8]) 132—133 °C), $[\alpha]_D^{22}$ −111.6° (*c* 1, acetone), (lit,[8]) $[\alpha]_D^{25}$ −118.3°), ^{1}H NMR ($CDCl_3$): δ=4.51 (d, 1H), 5.92 (d, 1H), 7.66 (m, 10H). Found: C, 79.21; H, 5.68%. Calcd for $C_{14}H_{12}O_2$: C, 79.22; H, 5.69%.

R(−)-(E)-Benzoin Oxime (5). To a solution of *R*(−)-benzoin (**4**) (473 mg, 2.23×10^{-3} mol) in 5 ml of pyridine was added a solution of hydroxylamine hydrochloride (468 mg, 6.73×10^{-3} mol) in 5 ml of pyridine under cooling in an ice bath. The reaction mixture was stirred for 90 min at room temperature and then concentrated *in vacuo*. The residue was extracted with ethyl acetate and the extract was washed with 10% citric acid and water and dried over magnesium sulfate, and was concentrated *in vacuo*. The residue was purified by column chromatography on silica gel using benzene–ethyl acetate (5:1 v/v) as an eluent. The solid obtained was recrystallized from benzene, yield 295 mg (58%), mp 156—158 °C (lit,[7]) 163—164 °C), $[\alpha]_D^{20}$ −2.9° (*c* 0.5, chloroform) (lit,[7]) $[\alpha]_D^{24}$ −3.2°). Found: C, 73.97; H, 5.75; N, 6.19%. Calcd for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.76; N, 6.16%.

(±)-(Z)-Benzoin Oxime. (±)-(*Z*)-Benzoin oxime was isolated by column chromatography of (±)-benzoin oxime as in the same way as *R*(−)-(*E*)-benzoin oxime. Yield from benzoin was 47%, mp 102.5—103.5 °C (lit,[9] 99 °C). Found: C, 73.88; H, 5.75; N, 6.15%. Calcd for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.76; N, 6.16%.

(±)-2-Hydroxy-1-phenyl-1-propanone. To a solution of PhMgBr, prepared from bromobenzene (10.36 g, 0.066 mol) and magnesium (1.60 g, 0.066 atom), in 40 ml of ether was added a solution of lactonitrile (2.13 g, 0.03 mol) in 10 ml of ether and the mixture was refluxed for 90 min. Then 10 ml of water and 30 ml of 10% sulfuric acid was added to the mixture. The ether layer was washed with saturated $NaHCO_3$ and water and dried over magnesium sulfate, and was concentrated *in vacuo*. The residue was purified by column chromatography on silica gel using benzene–ethyl acetate (25:1 v/v) as an eluent, yield 2.35 g (57%), bp 72 °C/3 mmHg (lit,[10] 125—126 °C/14 mmHg), ^{1}H NMR ($CDCl_3$): δ=1.40 (d, 3H), 3.88 (s, 1H), 5.08 (q, 1H), 7.60 (m, 5H). Found: C, 72.62; H, 6.94%. Calcd for $C_9H_{10}O_2$: C, 71.98; H, 6.71%.

(±)-(E)-2-Hydroxy-1-phenyl-1-propanone Oxime and (±)-(Z)-2-Hydroxy-1-phenyl-1-propanone Oxime. To a solution of (±)-2-hydroxy-1-phenyl-1-propanone (1.967 g, 0.013 mol) in 20 ml of pyridine was added a solution of hydroxylamine hydrochloride (2.711 g, 0.039 mol) in 20 ml of

pyridine under cooling. The reaction mixture was stirred for an additional 2 h at room temperature and concentrated *in vacuo*. The residue was extracted with ethyl acetate and the extract was washed with 10% citric acid and water and dried over magnesium sulfate, and was concentrated *in vacuo*. The oily product obtained was purified by silica-gel column chromatography. Elution was carried out with benzene–ethyl acetate (10:1 v/v) to separate (*E*)-isomer and (*Z*)-isomer. (*E*)-Isomer was purified by thin-layer chromatography using benzene–ethyl acetate (1:1 v/v) as a developing solvent, yield 1058 mg (49.3%), oil, ^{1}H NMR (DMSO-d_6): δ=1.51 (d, 3H), 3.62 (s, 1H), 4.80 (q, 1H), 5.30 (s, 1H), 7.56 (s, 5H). Found: C, 64.60; H, 6.75; N, 8.05%. Calcd for $C_9H_{11}NO_2$: C, 65.43; H, 6.71; N, 8.47%. (*Z*)-Isomer was recrystallized from benzene, yield 441 mg (20.6%), mp 130—131 °C, ^{1}H NMR (DMSO-d_6): δ, 1.32 (d, 3H), 2.50 (s, 1H), 5.00 (s, 1H), 5.28 (q, 1H), 7.92 (m, 5H). Found: C, 65.43; H, 6.71; N, 8.44%. Calcd for $C_9H_{11}NO_2$: C, 65.43; H, 6.71; N, 8.47%.

Assignment of Structure of Two Oximes ((±)-(E)-2-Hydroxy-1-phenyl-1-propanone Oxime and (±)-(Z)-2-Hydroxy-1-phenyl-1-propanone Oxime). Of the two isomers of benzoin oxime, the (*E*)-isomer is known to be colored blue by spraying a 0.5% $CuCl_2$ solution on thin layer chromatography.[9] In the case of 2-hydroxy-1-phenyl-1-propanone oxime, one isomer was colored blue and other isomer was not colored on thin-layer chromatography, therefore the structure of the former isomer was determined as the (*E*)-isomer.

Catalytic Hydrogenation of R(−)-(E)-Benzoin Oxime (5). *R*(−)-(*E*)-Benzoin oxime 5 (20 mg, 8.8×10^{-5} mol) was hydrogenated by using 5% palladium on charcoal (10 mg) in a solvent (2 ml) (methanol, ethanol, 2-propanol and *N,N*-dimethylformamide) at a temperature (0, 20, and 40 °C) at atmospheric pressure. After hydrogenation, the solvent was removed *in vacuo*. The ratio of each diastereomers was determined by gas chromatography of the trifluoroacetyl derivative of the hydrogenated product and the chemical yield was determined by isolation.

Hydrogenations of (±)-(*Z*)-benzoin oxime, (±)-(*E*)-2-hydroxy-1-phenyl-1-propanone oxime and (±)-(*Z*)-2-hydroxy-1-phenyl-1-propanone oxime were carried out in the same way as described above. The results are summarized in Table 1 and 2.

Trifluoroacetylation of Hydrogenated Product. To a suspension of 2 mg of the hydrogenated product in 0.4 ml of ethyl acetate was added 0.2 ml of trifluoroacetic anhydride and the mixture was heated in a screw capped vial for 2 h at 80 °C. The solvent was evaporated *in vacuo* and the residue was extracted with ethyl acetate. The extract was washed with 10% citric acid, saturated $NaHCO_3$ and water and dried over magnesium sulfate, and was concentrated *in vacuo*. The residue was dissolved in ethyl acetate and the solution was injected into a gas chromatograph to determine the ratio of the diastereomers of amino alcohol. A stainless steel column (2 m×3 mm I.D.) filled with Chromosorb W AW DMCS coated with 5% SE-52 was used for determination of diastereomeric ratio of ADE obtained by the hydrogenation of (*E*)- and (*Z*)-benzoin oxime. Column temperature was raised from 100 °C to 180 °C at a rate of 1 °C per minute. The retention times of *erythro*- and *threo*-isomers were 52.6 and 56.2 min, respectively. A glass capillary column (25 m×0.3 mm I.D.) coated with a chiral stationary phase (Chirasil-Val) was used for determination of diastereomeric ratio of 1-amino-1-phenyl-2-propanol obtained by the hydrogenation of (*E*)- and (*Z*)-2-hydroxy-1-phenyl-1-propanone oxime. Column temperature was raised from 100 °C to 180 °C at a rate of 3 °C per minute. The retention times of (1*S*,2*S*)-, (1*R*,2*R*)-, (1*S*,2*R*)- and (1*R*,2*S*)-isomers were 13.12, 13.87, 14.79, and 15.28 min, respectively. The same glass capillary column was used for determination of optical purity of ADE obtained by the hydrogenation of *R*(−)-(*E*)-benzoin oxime. Column temperature was raised from 80 °C to 180 °C at a rate of 0.5 °C per minute. The retention times of (1*S*,2*R*)-, (1*R*,2*S*)-, (1*S*,2*S*)- and (1*R*,2*R*)-isomers were 65.86, 66.16, 66.86 and 67.55 minute, respectively.

Authentic threo and erythro amino alcohols (ADE and 1-amino-1-phenyl-2-propanol) were derivatized with trifluoroacetic anhydride and the products were analyzed by gas chromatography. In each analysis, only original diastereomer was detected. These results indicate that the epimerization during the derivatization would be very small or none.

Isomerization of Benzoin Oxime in the Presence of Palladium on Charcoal. To a solution of (±)-(*E*)-benzoin oxime (30 mg, 1.32×10^{-4} mol) in 3 ml of ethanol was added 5% palladium on charcoal (30 mg). After stirring for a definite time (20, 40, and 60 min and 2, 3, and 6 h) at 30 °C, 0.1 ml of the mixture was collected and filtered. The filtrate was concentrated *in vacuo* and the residue was dissolved in 0.1 ml of pyridine. To the solution was added 0.1 ml of trimethylsilylating reagent [*N,O*-bis(trimethylsilyl)-1-iminoethanol:*N*-trimethylsilylimidazole:trimethylchlorosilane 1:1:1 v/v/v] and the reaction mixture was stirred for 15 min at room temperature and was injected into a gas chromatograph with a stainless steel column (2 m×3 mm I.D.), which was filled with Chromosorb W AW DMCS coated with 5% SE-52, to determine *E–Z* isomeric ratio. Column temperature was 180 °C. The retention times of (*E*)- and (*Z*)-isomers were 14.68 and 17.94 min, respectively. Isomerization of (±)-(*Z*)-benzoin oxime was carried out in the same way as that of (±)-(*E*)-benzoin oxime.

Hydrogenation of (±)-(E)-Benzoin Oxime (Experiment of the Time-course of Reaction Yield). (±)-(*E*)-Benzoin oxime (20 mg, 8.8×10^{-5} mol) was dissolved in 2 ml of ethanol and to the solution was added 10 mg of palladium on charcoal. After stirring for a definite time (30 min, 60 min, 3 h, and 8 h) at 20 °C under hydrogen atmosphere, 0.2 ml of the mixture was collected and filtered. A solution of 1-naphthylamine (internal standard) (2 mg, 1.4×10^{-5} mol) in 0.2 ml of ethanol was added to the filtrate and concentrated *in vacuo*. The residue was trifluoroacetylated in the same way as written above. The ratio of each diastereomers and reaction yield were determined by gas chromatography of the trifluoroacetyl derivative of the hydrogenated product.

Hydrogenation of (±)-(*Z*)-benzoin oxime and analysis of the hydrogenated product were carried out in the same way as those of (±)-(*E*)-benzoin oxime.

Hydrogenation of (±)-(E)-Benzoin Oxime in CD_3OD. (±)-(*E*)-Benzoin oxime (50 mg, 2.3×10^{-4} mol) was dissolved in 5 ml of CD_3OD and the solution was stirred for 1 h at 20 °C. Then to the solution was added 25 mg of 5% palladium on charcoal and the mixture was stirred for 6 h at 20 °C under hydrogen atmosphere. Catalyst was filtered off and the filtrate was concentrated *in vacuo*.

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References

1) K. Harada and K. Matsumoto, *J. Org. Chem.*, **32**, 1794 (1967).
2) K. Harada and T. Yoshida, *Bull. Chem. Soc. Jpn.*, **43**, 921 (1970).
3) K. Harada and Y. Kataoka, *Chem. Lett.*, **1978**, 791.
4) K. Harada and M. Tamura, *Bull. Chem. Soc. Jpn.*, **52**, 1227 (1979).
5) M. Osawa, A. Hata, K. Harada, and W. Suetaka, *Bull. Chem. Soc. Jpn.*, **49**, 1512 (1976).
6) J. Weijlard, K. Pfister, E. F. Swanezy, C. A. Robinson,

and M. Tishler, *J. Am. Chem. Soc.*, **73**, 1216 (1951).
7) H. Wren, *J. Chem. Soc.*, **1909**, 1583.
8) J. Kenyon and P. L. Patel, *J. Chem. Soc.*, **1965**, 435.
9) M. H. Jakovljevic, I. P. Tadic, and A. Stojilikovic, *J. Chromatogr.*, **12**, 70 (1963).
10) K. U. Auwers, *Ber.*, **50**, 1177 (1917).