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Studies on Hydrogenolysis. LIV.[1] Catalytic Hydrogenolysis of Optically Active 2-Methyl-2-phenylaziridine[*1]

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In order to obtain further information about the catalytic hydrogenolysis of benzyl-type compounds, the hydrogenolysis of optically active 2-methyl-2-phenylaziridine (I) over several group VIII transition metal catalysts was investigated in ethanol under ordinary pressure and at room temperature. 2-Phenylpropylamine (II) was obtained as the main product over all the catalysts. The configuration of II was inverted over the palladium catalyst. However, the hydrogenolysis over the platinum catalyst occurred with a significant retention of the configuration. Further, in the case of Raney nickel and Raney cobalt catalysts, the configurations of II were retained with the low stereoselectivities, and a small amount of 2-phenyl-2-propylamine (III) was also produced in addition to II. These results are attributable to the free-energy difference at the transition states to form π-benzyl intermediates, which depends on the affinity of these metals for the nitrogen lone-pair, the catalyst hindrance, and other factors. The S_N2-type reaction is favored over the palladium catalyst. On the other hand, the S_Ni-type reaction is favored over platinum, Raney nickel, and Raney cobalt catalysts, where the radical-cleavage reaction will participate in addition to the S_Ni-type reaction over the latter two catalysts. The differences in behavior between styrene imines and styrene oxides on the catalyst surface were also discussed.

The catalytic hydrogenolysis of benzyl-type compounds is an important method for investigating the mechanism of heterogenous catalysis. For several decades, much attention has been paid to the stereochemical courses of this reaction.[1–18] Some of the factors which affect the courses of the reaction are the structure of the compound,[1–9] the catalyst,[1–3,5,8–15] the additive,[13,16,17] and the medium.[16–18] Mitsui and his co-workers[1–3] suggested that the stereoselectivity of this reaction could be ascribed to the free-energy difference at the transition states to form π-benzyl intermediates. However, the corresponding stereoselectivity of benzylamine derivatives has been studied in detail by only Mitsui and Sato.[5] In this paper, we will describe the stereoselectivity of the catalytic hydrogenolysis of optically active 2-methyl-2-phenylaziridine, which has reactive carbon-nitrogen bonds. Moreover, the differences in behavior between styrene imines and styrene oxides on the catalyst surface are studied.

The hydrogenolysis of 2-methyl-2-phenylaziridine (I) in ethanol was carried out under ordinary pressure and at room temperature. The reaction mixtures were analyzed quantitatively by gas

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[1] Part LIII: S. Mitsui, S. Imaizumi and Y. Esashi, This Bulletin, to be published.

[*1] This work has previously been reported in a preliminary form: S. Mitsui and Y. Sugi, *Tetrahedron Letters*, **1969**, 1287.

[2] S. Mitsui and S. Imaizumi, *Nippon Kagaku Zasshi (J. Chem. Soc. Japan, Pure Chem. Sect.)*, **77**, 1516 (1956); This Bulletin, **34**, 774 (1961), **36**, 855 (1963).

[3] S. Mitsui, M. Fujimoto, Y. Nagahisa and T. Sukegawa, *Chem. & Ind. (London)*, **1969**, 241.

[4] S. Imaizumi, *Nippon Kagaku Zasshi (J. Chem. Soc. Japan, Pure Chem. Sect.)*, **77**, 1511 (1956); **81**, 627, 631, 633 (1960); **82**, 245 (1961).

[5] S. Mitsui and E. Sato, *ibid.*, **86**, 416 (1965).

[6] W. A. Bonner, *J. Am. Chem. Soc.*, **74**, 1034, 5086 (1952).

[7] W. A. Bonner, J. A. Zderic and G. A. Caseletto, *ibid.*, **74**, 5089 (1952).

[8] E. W. Garbisch, Jr., L. Schreader and J. J. Frankel, *ibid.*, **89**, 4233 (1967).

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[10] S. Mitsui, Y. Senda and K. Konno, *Chem. & Ind. (London)*, **1963**, 1354.

[11] S. Mitsui, K. Iijima and T. Masuko, *Nippon Kagaku Zasshi (J. Chem. Soc. Japan, Pure Chem. Sect.)*, **84**, 833 (1963).

[12] S. Mitsui and K. Iijima, *ibid.*, **84**, 682 (1964).

[13] S. Mitsui and S. Imaizumi, *ibid.*, **86**, 219 (1965).

[14] S. Mitsui, Y. Kudo and M. Kobayashi, *Tetrahedron*, **25**, 1921 (1969).

[15] J. H. Brewster and W. E. Braden, Jr., *Chem. & Ind. (London)*, **1964**, 1759.

[16] K. Iijima and S. Mitsui, *Nippon Kagaku Zasshi (J. Chem. Soc. Japan, Pure Chem. Sect.)*, **85**, 687 (1964).

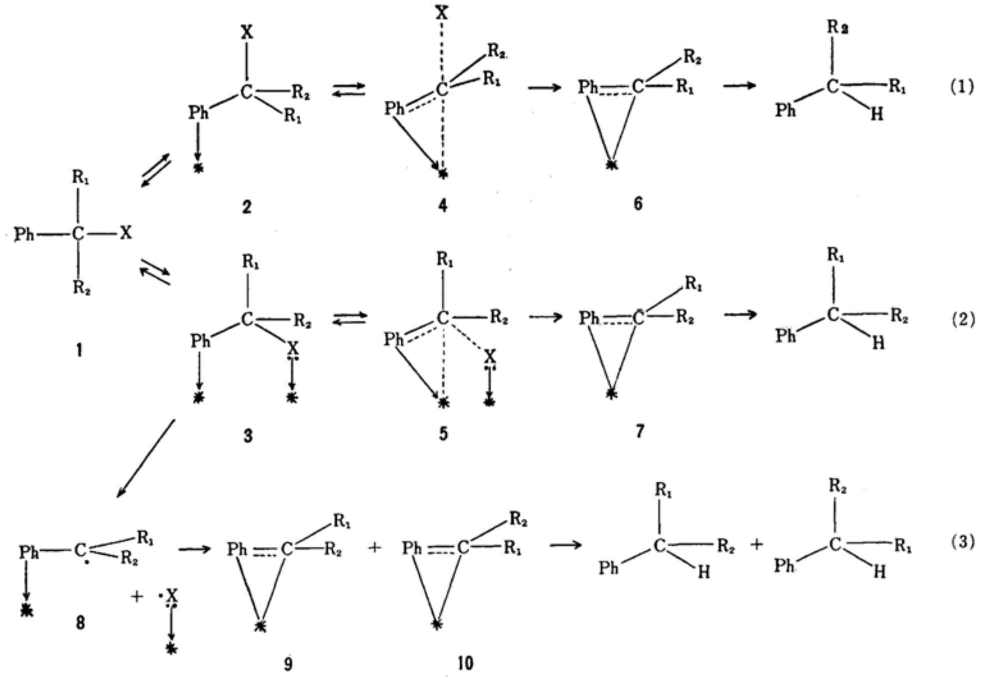
[17] S. Mitsui and Y. Sugi, *Tetrahedron Letters*, **1969**, 1291.

[18] R. A. Grimm and W. A. Bonner, *J. Org. Chem.*, **32**, 3470 (1967).

chromatography. The results are summarized in Table 1. 2-Phenylpropylamine (II) was the main product over all the catalysts, but the following compounds were also obtained: 2-Phenyl-2-propylamine (III) over Raney nickel and Raney cobalt catalysts, 2-phenylpropane and 2-cyclohexylpropylamine over the platinum catalysts, and 2-phenylpropene over the Raney cobalt catalyst.

(+)-I has the S configuration, as will be described in the Experimental section. (−)-II also has the S configuration.[19,20] Therefore, when (+)-II is obtained from (+)-I, the reaction occurs with a retention of the configuration. On the basis of these relationships, the stereochemical consequences of the hydrogenolysis of I are found to be listed as in Table 1. The maintained optical activities and the configurations of II varied with the catalysts. The hydrogenolysis proceeded with a predominant inversion of the configuration over the palladium catalysts; the maintained optical activities were 50—70%. The configurations of II were retained significantly over platinum catalysts, but the maintained optical activity with platinum oxide was higher than that with platinum black. Further, the hydrogenolysis occurred with a predominant retention of the configuration over Raney nickel and Raney cobalt catalysts, but the maintained optical activities were only 10—20%. Since II was racemized only slowly under these conditions, the above results may be considered to exhibit the stereoselectivities of the hydrogenolysis of I.

It has previously been proposed that the catalytic hydrogenolysis of benzyl-type compounds proceeds *via* paths (1) and (2) unless the substituent X has a very strong affinity for the catalyst.[1-3] The configuration of the product is determined by the free-energy difference at the transition states **4** and **5** to form the π-benzyl intermediates **6** and **7**, respectively. When X is an electron-withdrawing group and has a relatively weak affinity for the catalyst, the stereoelectronic effect is operative, so path (1) becomes more probable than path (2). Consequently, the hydrogenolysis proceeds with a predominant inversion of the configuration. However, when X is not so bulky and has a relatively strong affinity for the catalyst, the strong chemisorption of X makes it so prone to the hydrogenolysis as to overcome the unfavorable stereoelectronic situation. Therefore, the free-energy level of the transition state **5** becomes lower than that of **4**, and the configuration of the product is retained predominantly. Further, when X has a very strong affinity for the catalyst, path (3) as well as path (2) participates in this reaction. The benzyl carbon-X bond cleaves into two radicals **8** and ·X, on the catalyst because of the strong chemisorption of X and the phenyl group. Consequently, the racemic product is obtained. In summary, the catalytic hydrogenolysis of benzyl-type compounds occurs competitively *via* paths (1), (2), and (3), and the configuration of the product is determined at the moment of forming π-benzyl intermediates.



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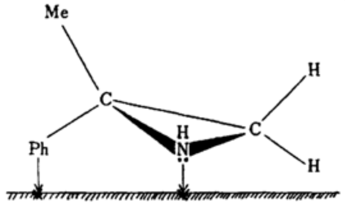
[19] P. A. Levene, L. A. Mikeska and K. Passoth, *J. Biol. Chem.*, **88**, 27 (1930).

[20] E. L. Eliel and J. P. Freeman, *J. Am. Chem. Soc.*, **74**, 923 (1952).

The mechanism of the hydrogenolysis of I will now be discussed on the basis of the above considerations.

In spite of the low reactivity of benzylamine derivatives, not only 2-phenylaziridines, as reported in this paper, but also 2-alkylaziridines undergo catalytic hydrogenolysis even under ordinary pressure and at room temperature.[21] These high reactivities is attributable to the high strain of the aziridine ring.



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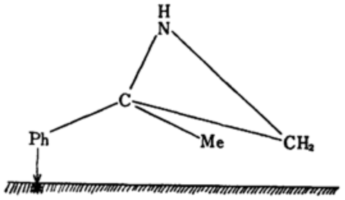

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Because of the tetrahedral character of the nitrogen of aziridine, I will favorably be adsorbed edgewise on the catalyst as **11**, which corresponds to **3**. Since palladium has not such a strong affinity for the nitrogen lone-pair, the benzyl carbon in **11** does not bear a sufficiently large positive charge and can not approach so closely to the catalyst as that in **12**, which corresponds to **2**. Moreover, the stereoelectronic requirement at the transition state to form the π-benzyl intermediate is fulfilled *via* the latter state. Therefore, the hydrogenolysis *via* **12** is more probable than that *via* **11**, and the configuration of II will predominantly be inverted over the palladium catalyst. Mitsui and Sato,[5] however, estimated that the hydrogenolysis of ethyl 2-amino-2-phenylpropionate (IV) over a palladium catalyst occurred with a predominant retention of the configuration on the basis of the assumption of the configuration of IV by Cram and his co-workers.[22] This estimation has been confirmed to be correct, for Mizuno and his coworkers[23] reported that (+)-IV has the S configuration. These differences in I and IV suggest the following considerations. The benzyl carbon of I in **11** can not approach so closely to the catalyst as that in **12**, as has been mentioned above, whereas the benzyl carbon of IV can approach to the catalyst at two states, those corresponding to **2** and **3**. Therefore, path (2) is more probable than path (1) in the hydrogenolysis of IV over the palladium catalyst in contrast with that of I.

In order to investigate the possibility of the addition of hydrogen from the top of π-benzyl intermediates, the hydrogenolysis of I was carried out with occluded hydrogen in palladium under a helium atmosphere. Similar results were obtained under both hydrogen and helium atmospheres. Kowaka[24] reported that the occluded hydrogen in palladium is more reactive than molecular or physically-adsorbed hydrogen in the catalytic hydrogenation of ethylene. From these evidences, the hydrogenolysis of I may be said to occur by means of chemisorbed hydrogen from the bottom of the adsorbed molecule on the catalyst surface. These considerations are supported also by the hydrogenolysis of 1-phenylcyclohexane-1,2-diol derivatives[3] and the hydrogenation of 1-phenylcyclohexene derivatives.[25]

The hydrogenolysis of styrene oxide derivatives over the palladium catalysts occurred predominantly with an inversion of the configuration similar to that of I, because of the small affinity of palladium for the oxygen.[13]

Several workers have reported the anchor effect of the nitrogen lone-pair for the platinum catalyst.[26-28] Platinum is less sensitive to the catalyst hindrance than palladium and nickel.[25] Therefore, path (2) is more probable than path (1) in the hydrogenolysis of I over the platinum catalysts, and the configuration of II will be retained predominantly. The maintained optical activity with platinum oxide was higher than that with platinum black, which was prepared by the hydrogen reduction of platinum oxide and by washing with water. This is the effect of alkaline substances contained in platinum oxide.[17] The hydrogenolysis of styrene oxide derivatives over platinum catalysts, however, occurs with an inversion of the configuration.[13] This difference may be ascribed to the differences in the electronegativity and in the affinity for platinum between nitrogen and oxygen.

Nickel and cobalt have stronger affinities for the nitrogen lone-pair than platinum and palladium.

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21) S. Mitsui, Y. Sugi and M. Nagata, unpublished work.

22) D. J. Cram, L. K. Gaston and H. Jäger, *J. Am. Chem. Soc.*, **83**, 2183 (1961).

23) H. Mizuno, S. Terashima, K. Achiwa and S. Yamada, *Chem. Pharm. Bull.* (*Tokyo*), **25**, 1747 (1967).

24) M. Kowaka, *Shokubai* (*Catalyst*), **2**, 197 (1960).

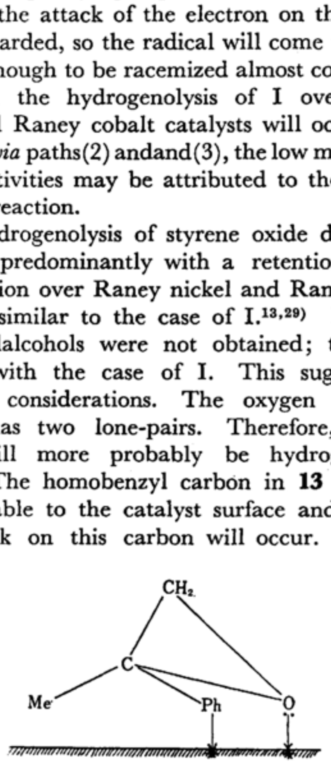
25) S. Mitsui, Y. Nagahisa, K. Tomomura and M. Shionoya, *ibid.*, **10**, Preprint for the 23th Symposium on Catalysis, Chem. Soc. Japan, 75 P. (1968).

26) H. Kugita and E. L. May, *J. Org. Chem.*, **26**, 1954 (1961).

27) H. O. House, H. C. Müller, C. G. Pitt and P. P. Wickham, *ibid.*, **28**, 2407 (1963).

28) C. P. Rader, G. W. Wichs, Jr., R. L. Young, Jr., and H. S. Aaron, *ibid.*, **29**, 2252 (1964).

Therefore, the hydrogenolysis occurs *via* **11.** Both benzyl and homobenzyl carbons approach closely to the catalyst and bear positive charges because of the strong chemisorption of the phenyl group and the nitrogen. Therefore, hydrogen will attack nucleophilically not only the benzyl but also the homobenzyl carbons; consequently, II and a small amount of III will be obtained.[*2] However, some of I will cleave to the radical because of the high strain of aziridine and the strong chemisorption of the phenyl group and the nitrogen. In this case, the attack of the electron on the radical will be retarded, so the radical will come to have a life long enough to be racemized almost completely. Therefore, the hydrogenolysis of I over Raney nickel and Raney cobalt catalysts will occur competitively *via* paths(2) andand(3), the low maintained optical activities may be attributed to the radical-cleavage reaction.



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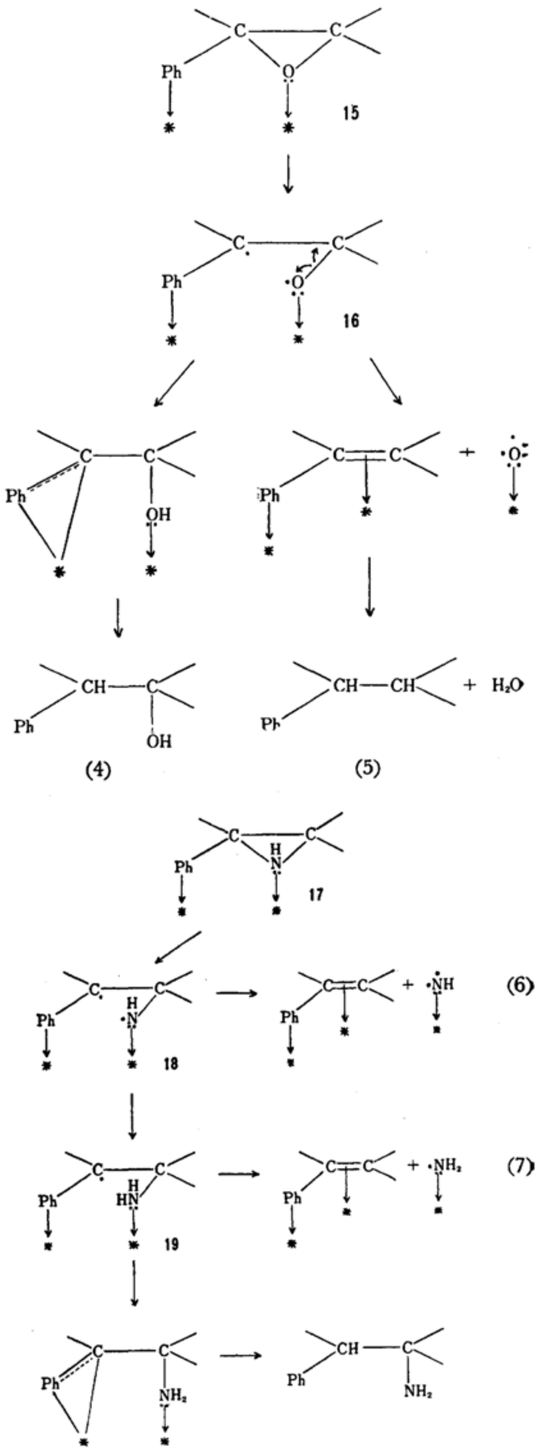

The hydrogenolysis of styrene oxide derivatives occurred predominantly with a retention of the configuration over Raney nickel and Raney cobalt catalysts, similar to the case of I.[13,29] However, α-phenetylalcohols were not obtained; this is in contrast with the case of I. This suggests the following considerations. The oxygen atom in oxirane has two lone-pairs. Therefore, styrene oxides will more probably be hydrogenolysed *via* **13**. The homobenzyl carbon in **13** is not so approachable to the catalyst surface and scarcely any attack on this carbon will occur. Further, styrene oxide derivatives gave the corresponding hydrocarbons in addition to β-phenetylalcohols in the hydrogenolysis over Raney nickel and Raney cobalt catalysts.[29] Mitsui and his co-workers[29] confirmed these hydrocarbons to be formed *via* olefins and proposed a possible mechanism. Because oxygen has a strong affinity for nickel, the styrene oxide derivative **15** cleaves to the radical **16** in addition to nucleophilic reactions *via* paths (1) and (2). This radical follows competitively paths (4) and (5), and the alcohol and the hydrocarbon are formed respectively. However, I, gave little hydrocarbon with the Raney nickel catalyst. This suggests that nickel can not stabilize $\cdot\dot{N}H$ and/or $\cdot\ddot{N}H_2$, which are formed according to paths (6) and (7), respectively. On the other hand, 2-phenyl pro-

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[*2] It suggests also an importance of the distances between the carbon and the catalyst surface that the less-substituted carbon-nitrogen bond cleaved selectively in the hydrogenolysis of 2-alkyl- and 2,2-dialkylaziridines over the Raney nickel catalyst.[21]

29) S. Mitsui, S. Imaizumi, M. Hisashige, M. Fujimoto, T. Sukegawa, M. Yokozawa and K. Okamura, unpublished work.

TABLE 1. THE CATALYTIC HYDROGENOLYSIS OF 2-METHYL-2-PHENYLAZIRIDINE (I)

Exp. No.	Catalyst (g)	Optical purity of I*1	Products			II			
			II	III	HC*6	$[\alpha]_D$	Optical purity*2	Maintained optical activity	Configuration
1	$Pd(OH)_2$ 0.05	R 43.6	100	—	trace	+ 9.28	31	72	Inversion
2	Pd(H)*3 5.0	R 43.6	100	—	trace	+ 6.08	21	47	Inversion
3	Pd(H)*4 5.0	R 43.6	100	—	trace	+ 7.08	24	55	Inversion
4	PtO_2 0.1	R 43.6	88(6*5)	—	6	−10.60	36	83	Retention
5	PtO_2 0.1	R 37.3	92(4*5)	—	4	−10.36	35	95	Retention
6	Pt-black 0.1	R 43.6	89(3*5)	—	8	− 7.65	26	70	Retention
7	Pt-black 0.1	S 91.0	94(3*5)	—	3	+19.60	67	73	Retention
8	Ra-Ni 1(wet)	S 91.0	93	7	trace	+ 6.26	21	23	Retention
9	Ra-Co 4 (alloy)	S 91.0	92	3	5*7	+ 3.76	13	14	Retention

I, 1.33 g; Solvent: Ethanol, 20 m*l*; Under ordinary pressure and at room temperature.
*1 optically pure $[\alpha]^{22}_D$ +33.3° (*c* 9.22, ethanol). *2 optically pure $[\alpha]_D$ +29.5° (ethanol). *3 Under a hydrogen atmosphere. *4 Under a helium atmosphere. *5 2-Cyclohexylpropylamine. *6 2-Phenylpropane. *7 2-Phenylpropene.

pene was obtained from I with the Raney cobalt catalyst. The stabilizing ability of cobalt for $\cdot\underset{\cdot\cdot}{\dot{N}}H$ and/or $\cdot\underset{\cdot\cdot}{N}H_2$ is greater than that of nickel, because cobalt has a stronger affinity for the nitrogen.

In conclusion, the variations in the configuration and in the maintained optical activity of II in the hydrogenolysis of I are attributable to the free-energy difference at the transition states to form π-benzyl intermediates, which depends on the affinity of catalysts for the nitrogen, the catalyst hindrance, and other factors.

Experimental

S(+)- and R(−)-Ethyl 2-Amino-2-phenylpropionates (IV). 2-Amino-2-phenylpropionic acid was prepared according to the procedure of Steiger[30] and was converted into IV.[31] IV was resolved by the fractional recrystallization of its tartrate from ethanol. The resulting salt (mp 175.5—176.0°C, $[\alpha]^{20}_D$ +45.57° (*c* 8.91, water)) afforded S(+)-IV; bp 137—139°C/15 mmHg, α^{18}_D +10.80° (neat), $[\alpha]^{18}_D$ +25.02° (*c* 9.43, ethanol). R(−)-IV: $\alpha^{23.5}_D$ −5.00° (neat) was also obtained from mother liquor. For the rotation of optically pure IV, we adopted the greatest value (α^{24}_D +12.14° (neat))[22] hitherto reported for the ester.

S(+)-2-Amino-2-phenylpropanol (V). The aminoalcohol V was obtained according to the procedure of Tsuboyama[32] for the preparation of isoleucinol. S(+)-IV (38.6 g α^{20}_D +11.01° (neat), 90.2% optically pure) in ether (100 m*l*) was added dropwise with stirring to lithium aluminum hydride (8.0 g) in ether (100 m*l*), and the resulting mixture was heated under reflux for 2 hr. After cooling, water (30 m*l*) was added with vigorously stirring, and the ethereal layer was decanted from the precipitates. The resulting precipitates were dissolved with aqueous sodium hydroxide, and then the aqueous solution was continuously extracted with ether for 24 hr, the combined ethereal solution was dried over anhydrous sodium sulfate. After the evaporation of the ether, the oily residue was distilled under a nitrogen stream to give 23.0 g of S(+)-V; bp 116—118°C/0.4 mmHg, $[\alpha]^{22}_D$ +17.16° (*c* 9.39, benzene).

Found: C, 71.40; H, 8.72; N, 9.11%. Calcd for $C_9H_{13}NO$: C, 71.49; H, 8.66; N, 9.26%.

S(+)-2-Methyl-2-phenylaziridine (I). The imine I was prepared by the procedure of Brois[33] with slight modifications. A cold mixture of sulfuric acid (16.8 g) and water (50 m*l*) was added, with shaking, to a solution of (+)-V (23.0 g, $[\alpha]^{22}_D$ +17.16° (*c* 9.39, benzene) and water (50 m*l*). The water was removed by heating at 15—20 mmHg and finally at 0.5—1 mmHg below 140°C for 20 hr. A cold solution of 40% sodium hydroxide was added to the solidified product, and then the mixture was slowly heated in an oil bath. The basic material was steam-distilled into a cooled receiver and saturated with sodium hydroxide. The imine product was extracted with ether and dried over sodium hydroxide pellets. The evaporation of the ether and subsequent distillation under a nitrogen stream afforded 16.2 g of S(+)-I; bp 94—95°C/14 mmHg, α^{22}_D +45.60° (neat), $[\alpha]^{22}_D$ +30.04° (*c* 9.22, ethanol).

Found: C, 80.89; H, 8.47; N, 10.19%. Calcd for $C_9H_{11}N$: C, 81.15; H, 8.33; N, 10.52%.

Catalysts. The Raney nickel and Raney cobalt were prepared by the method used for W-4[34] and were stored in ethanol. The palladium hydroxide ($Pd(OH)_2$) was obtained by the method of Takagi *et al.*[35] The palladium hydride (Pd(H)) was prepared as has previously been described.[1] The platinum oxide was purchased from the Wako Junyaku Co., Ltd., Osaka. The platinum black was prepared by the hydrogen reduction of platinum oxide and was washed well with water.

Catalytic Hydrogenolysis. The following general

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30) R. E. Steiger, "Organic Syntheses," Coll. Vol. III, p. 88 (1955).

31) A. McKenzie and J. Hyles, *Ber.*, **65**, 309 (1932).

32) S. Tsuboyama, This Bulletin, **35**, 1004 (1962).

33) S. J. Brois, *J. Org. Chem.*, **27**, 3532 (1963).

34) H. Adkins and A. A. Pavlic, *J. Am. Chem. Soc.*, **69**, 3039 (1947).

35) Y. Takagi, T. Naito and S. Nishimura, This Bulletin, **38**, 2119 (1965).

procedure was used. After a definite amount of catalyst in ethanol had been agitated under a hydrogen atmosphere for 1 hr, 1.33 g (0.01 mol) of I in ethanol was added; the resulting suspension was agitated with hydrogen under ordinary pressure and at room temperature. After the theoretical amount of hydrogen had been absorbed, the catalyst was filtered off, and the mixture was analyzed by gas chromatography (polyethylene glycol 4000 and potassium hydroxide dispersed on firebrick at 150—180°C using helium-carrier gas). After the evaporation of the ethanol, the oily residue was distilled under reduced pressure to give II; 78—82°C/17 mmHg. When the unreacted imine was involved, the oily residue was treated with dilute hydrochloric acid. After standing for several hours, the hydrochloride solution was made basic with aqueous ammonia. The resulting suspension was extracted with ether, and the etheral solution was dried over anhydrous sodium sulfate. The evaporation of ether and subsequent distillation afforded II. Moreover, when the reaction mixture involved substances other than II, II was purified by preparative gas chromatography. The rotation of II was measured in ethanol at *c* 9.0—10.0. For the rotation of optically pure II, we adopted $[\alpha]_D$ 29.5° (ethanol), a value which was calculated from the values given by Levene *et al.*[24] and by Eliel and Freeman.[25]

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