"solvent-intervention" process.[45] Hence the inability of our C-H linkage to hydrogen bond mitigates against solvent participation. But whether or not solvent intervenes, it is clear that the sharp $O^-/H/C$ angle of 106° in the norbornyl system (and by inference also at the active sites of enzymes) need not preclude rapid reaction.

The 106° $O^-/H/C$ angle represents, of course, a ground-state value. Bending and stretching distortions of the C-H bond change this angle for the transition state and contribute substantially to the activation energy for the elimination. We are currently investigating by theoretical methods the relative timing of C-H bending and stretching as the proton transfers from one heavy atom to another.

Conclusion

Proton-transfer rates between B and HA depend on the B/H/A angle and the B/HA distance. Ideally one would like to construct a three-dimensional map having reactivity, angularity, and distance as its axes. Each point on the map would represent a rate constant from a rigid molecule in which B and HA are fixed in a particular ground-state geometry. We have synthesized three such systems, and the data on them are easily summarized: The indane compound with a B/H/A angle of 82° and B/HA distance of 2.9 Å manifests no detectable intramolecular proton transfer; on the other hand, the norbornyl compounds with a B/H/A angle of 106° and B/H distance of 2.2 Å are capable of effective intramolecular transfer. A paltry harvest one might think! Yet there are important aspects to our initial results that should be emphasized in conclusion. (a) One suspects that distance is the critical geometric factor here because the indan and norbornyl systems, although behaving differently, both have severely bent B/H/A angles. Reducing the distance from 2.9 Å (greater than the van der Waals distance) to 2.2 Å (less than the van der Waals distance) probably accounts for much of the reactivity difference. If this is true, then "long distance catalysis" appears unlikely in organic molecules and at the active sites of enzymes. (b) Little doubt now exists that intramolecular proton transfers can take place via severely bent ground-state geometries. Assumptions of linearity in intermolecular transfers[21-24] are therefore suspect. More likely, there exists a "reaction window"[46] encompassing a range of trajectories; each trajectory, we believe, is associated with a particular degree of proton transfer at the transition state. Ramifications of this "multidirectional transition-state theory" are discussed elsewhere.[47] (c) The work herein, along with that published previously,[4] represents our initial effort at an approach that merits further exploitation in the future. The main difficulty lies in synthesizing sets of compounds with subtle variations in the spatial relationships among intramolecular functionalities supported on rigid frameworks. As the synthetic problems are overcome, chemistry will be rewarded with an understanding of reactivity in solution far more detailed than now available.[48]

Acknowledgment. This work was supported by the National Science Foundation and the National Institutes of Health.

Registry No. 1, 86045-81-0; **2**, 58029-23-5; **3**, 75364-33-9; 4-hydroxyindanone, 40731-98-4; 4-benzyloxyindanone, 86045-82-1; 4-benzyloxyindanone tosylhydrozone, 86045-83-2; 7-benzyloxyindene, 86045-84-3; 4-benzyloxyindan-2-ol, 86045-85-4; 4-benzyloxy-2-hydroxyindan tosylate, 86045-86-5; *exo*-5-hydroxybicyclo[2.2.1]heptan-2-one, 58029-22-4; *exo*-5-hydroxy-2-(ethylenedioxy)bicyclo[2.2.1]heptane, 67594-60-9; 2-(ethylenedioxy)bicyclo[2.2.1]heptan-5-one, 67594-61-0; *endo*-5-hydroxy-2-(ethylenedioxy)bicyclo[2.2.1]heptane, 86116-71-4; *endo*-2-hydroxy-*exo*-6-(tosyloxymethyl)bicyclo[2.2.1]heptane, 86045-87-6; 2-iodoindane, 24329-96-2; 2-iodo-4-benzyloxyindane, 86045-88-7; *endo*-5-methoxybicyclo[2.2.1]heptan-2-one, 85164-48-3; *endo*-5-deuteroxy-*exo*-3-deuterobicyclo[2.2.1]heptan-2-one, 86045-89-8; *endo*-5-deuteroxy-3,3-dideuterobicyclo[2.2.1]heptan-2-one, 86045-90-1.

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(48) **Note Added in Proof**: Recent unpublished data indicate that not only is distance important but also the *residence time* within the reaction window plays a critical role.

Catalytic Alkyl Group Exchange Reaction of Primary and Secondary Amines

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Abstract: It has been shown that primary and secondary amines undergo alkyl group exchange reactions upon treatment with palladium catalyst as depicted in the following equation: $R^1R^2CHNHR^3 + R^4R^5NH \xrightarrow{Pd} R^1R^2CHNR^4R^5 + R^3NH_2$. The reaction is operationally simple and highly efficient and hence provides a convenient method for synthesis of unsymmetrical amines. The application of the reaction for the preparation of various substituted amines and heterocyclic compounds such as hexahydropyrimidine **12**, tetrahydropyrimidine **13**, imidazolidine **14**, and imidazoles **15** and **16** is described. The preparation of polyamines such as $H_2N(CH_2)_mNH(CH_2)_nNH_2$ (**10**) and $H_2N(CH_2)_lNH(CH_2)_mNH(CH_2)_nNH_2$ (l-n, = 2,3; **11**) is readily performed by the palladium-catalyzed reactions of azetidine (**6**) and aziridine (**7**) via azetine (**9**) and azirine intermediates. The mechanism of the palladium-catalyzed reaction has been extensively studied on the carbonylation, racemization, and deuterium-exchange reaction of (*S*)-(−)-α-phenylethylamine (**17**). Insertion of palladium into the N-H bond of an amine followed by β-elimination of PdH species gives imine complex intermediate **33**, which is in rapid equilibrium with enamine complex **34**. Addition of a second amine to **33** gives aminal **35**, which subsequently undergoes reductive cleavage to form the product amine. The results of the reaction of **17** with (*S*)-(+)-*sec*-butylamine (**23**) and the reductive cleavage of *N*-phenylbenzamidine (**31**) support the mechanism.

On many methods available for preparation of unsymmetrical secondary and tertiary amines, Hoffmann alkylation,[1] reductive alkylation of carbonyl compounds,[2] and their improved methods[3] are central methods. Recently, catalytic alkylation and allylation of amines by the activation of alcohols[4] and their derivatives[5] have been explored. In relation to the study of the metabolism of

† On leave from Ube Industries Ltd.

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(2) Emerson, W. S. *Org. React.* **1948**, *4*, 147.

0002-7863/83/1505-5002$01.50/0

Scheme I

$$R^1CH_2NHR^2 \xrightarrow{Pd} [R^1CH{=}NR^2] \xrightarrow{R^1CH_2NHR^2}$$

1

$$\left[\begin{array}{l} R^1CHNHR^2 \\ | \\ R^1CH_2NR^2 \end{array}\right] \xrightarrow{PdH_2} R^1CH_2NCH_2R^1 + R^2NH_2$$

R^2

2

amines,[6] we have studied the activation of amines with metals and metal complexes and found the palladium-catalyzed alkyl group exchange reaction of primary and secondary amines as shown in eq 1.[7,8] The reaction is operationally simple and applicable to

$$R^1R^2CHNHR^3 + R^4R^5NH \xrightarrow{Pd} R^1R^2CHNR^4R^5 + R^3NH_2 \quad (1)$$

the preparation of various nitrogen compounds such as unsymmetrical amines, polyamines, and heterocyclic amines.

It is often observed that primary amines undergo condensation as a side reaction in the alkylation of amines with alcohols and in the catalytic hydrogenation of nitriles. Consequently, much effort has been devoted to retard such side reactions,[9] and inversely the condensation of primary amines has been utilized for the preparation of symmetrical amines.[9d,10] However, the activation of amines with metals and metal complex catalysts and its application to the preparation of various nitrogen compounds have never been studied systematically. We describe full details of the catalytic alkyl group exchange reactions of primary and secondary amines with respect to scope, synthetic applications, and mechanism. The reaction involves general, fundamental key steps. The activation of amines with N–H bonds by means of metals and metal complex catalysts gives imine hydride complexes (eq 2).

$$RCH_2NHR^1 \xrightarrow{Pd} \underset{\displaystyle PdH_2}{RCH{=}NH} \quad (2)$$

$$\underset{\displaystyle PdH^-}{RCH_2\overset{R^1}{\overset{|}{N}}R^2 \xrightarrow{Pd} RCH{=}\overset{+}{N}R^1R^2} \quad (3)$$

This is in contrast to the activation of amines with no N–H bond, which results in the formation of iminium ion complexes (eq 3).[11]

Table I. Palladium-Catalyzed Reaction of Primary and Secondary Amines

R^1NHR^2		temp,	time,	product yield[a] of $R^1{}_2NR^2$,	conv,[b]
R^1	R^2	°C	h	%	%
$C_6H_5CH_2$	H	80	5	45	90
$CH_2{=}CHCH_2$	H	25	5	95[c]	95
cyclopropyl carbinyl	H	120	20	95[d]	20
furfuryl	H	140	10	65[e]	22
cyclohexyl	H	130	20	30[f]	22
$C_6H_5CH_2$	CH_3	120	20	85	28
CH_3	C_6H_5	120	20	98[g]	7
CH_3CH_2	C_6H_5	150	48	98	5
C_4H_9	CH_3	160	5	85[h]	95
$(CH_2)_4$		80	10	65[i,j]	7
$(CH_2)_4$		150	5	97[j]	85
$(CH_2)_4$		200	10	56[k]	88
$(CH_2)_5$		200	10	96[l]	80

[a] Yields based on reacted amines. [b] Conversions based on reacted amine, which are easily improved by prolonged reaction time or higher temperature. [c] $C_2H_5CH{=}NCH_2CH{=}CH_2$. [d] *N*-Butylidenecyclopropylcarbinylamine. [e] Another product, *N*-furfurylidenefurylamine (31%). [f] *N*-Phenylcyclohexylamine (25%). [g] Another product, aniline (98%). [h] Another product, tributylamine (8%). [i] 4-Pyrrolidinobutylamine (**3**). [j] Another product, pyrrolidino-2Δ^1-pyrroline (4, 24%). [k] 1,4-Dipyrrolidinobutane (**5**). [l] 1,5-Dipiperidinopentane.

Alkyl Group Exchange Reaction of Primary and Secondary Amines

Treatment of primary amines with metal and metal complex catalysts in the presence or absence of solvents at the appropriate temperature gave secondary amines and ammonia. The catalytic activity of metals and metal complexes was examined in the reaction of α-phenylethylamine and hexylamine. Palladium black prepared by the modified Willstätter's method gave the best results among the catalysts examined. The metal catalysts such as palladium, ruthenium, and rhodium, which were prepared by the reduction of the corresponding chlorides with potassium,[12] gave poor results. Palladium complexes such as $PdCl_2$, $Pd(OAc)_2$, and $PdCl_2(PPh_3)_2$ were readily reduced to give palladium black under the reaction conditions. Other metal complexes such as $RuCl_2(PPh_3)_2$, $Ru_3(CO)_{12}$, $RuCl_3$, $RhCl(PPh_3)_3$, $Rh_6(CO)_{16}$, $RhCl_3$, and Raney nickel (see Experimental Section) gave relatively high conversion of the amines, but the yields were low. Primary amines that have an active α-hydrogen underwent the exchange reaction to give secondary amines and/or Schiff bases in high yields under mild conditions. Allylamine was converted into *N*-propylideneallylamine (95%) even at 25 °C. Alkylamines require reaction temperatures higher than 150 °C. The representative results of the palladium-catalyzed exchange reaction of primary amines are summarized in Table I. According to the conventional reaction

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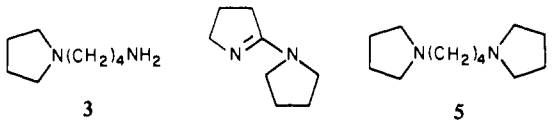
Table II. Palladium-Catalyzed Alkyl-Exchange Reactions of Amines (eq 1)

amines						product yield,[a] %		
$R^1CH_2NHR^2$		R^3NHR^4		temp,	time,			conv,[b]
R^1	R^2	R^3	R^4	°C	h	$R^1CH_2NR^3R^4$	$R^1CH{=}NR^3$	%
C_6H_5	CH_3	C_6H_{13}	H	120	10	55	30	37
C_6H_5	CH_3	C_6H_{11}	H	120	10	10	90	40
C_6H_5	CH_3	C_6H_5	H	120	20	48	52	40
C_6H_5	CH_3	$H_2N(CH_2)_2$	H	120	10	95		24[c]
$CH_2{=}CH$	H	$(CH_2)_2NH_2$	H	25	15	80[d]		61
$CH_2{=}CH$	H	$(CH_2)_3NH_2$	H	25	15	95[e]		95
C_6H_5	CH_3	$(CH_2)_3NH_2$	H	120	15	22[f]		90
C_6H_5	CH_2	$(CH_2)_4NH_2$	H	120	15	70		51
C_6H_5	CH_3	$(CH_2)_6NH_2$[g]	H	120	15	20[h]		90
H	C_6H_5	C_6H_{13}	H	120	40	98		5
C_3H_7	CH_3	C_6H_{13}	H	160	7	75		45
C_6H_5	CH_3	$CH_3(CH_2)_3$	CH_3	120	10	80		55
C_6H_5	CH_3	$(CH_2)_5$		130	10	97		90
C_6H_5	CH_3	$(CH_2)_4$		130	10	75		75
C_3H_7	CH_3	$(CH_2)_5$		160	5	98		85

[a] Yield based on reacted amines. [b] Conversions are easily improved by prolonged reaction time and/or high temperature. [c] At 180 °C, the conversion was 80%. [d] 2-Ethylimidazolidine. [e] 2-Ethylhexahydropyrimidine. [f] 2-Phenyl-3,4,5,6-tetrahydropyrimidine (68%). [g] The ratio of the diamine to *N*-methylbenzylamine was 1:2. [h] $PhCH_2NH(CH_2)_6N{=}CHPh$ (70%).

scheme,[9,13] the reaction can be illustrated by Scheme I. The addition of the starting amine to the imine intermediate **1** gives aminal **2**, which undergoes either reductive cleavage or elimination of R^2NH followed by transfer hydrogenation (R^2 = H) to give a secondary amine and ammonia.

Secondary amines undergo the alkyl group exchange reaction to give tertiary amines with two identical substituents. Treatment of *N*-methylbenzylamine afforded *N*-methyldibenzylamine in 85% yield in addition to methylamine. *N*-Methylaniline was also converted to *N*,*N*-dimethylaniline along with aniline. The liberation of methylamine and aniline can be rationalized in terms of the reductive cleavage of the C–N bond of aminal **2**. This is clearly demonstrated by the exclusive formation of 4-pyrrolidinobutylamine (**3**, 98%) upon treatment of pyrrolidine with pal-



3 4 5

ladium at 150 °C. Noticeable is that the products from the reaction of pyrrolidine depends upon the reaction temperature.[8] The palladium-catalyzed reaction of pyrrolidine at 80 °C gave pyrrolidino-2Δ^1-pyrroline **4**, (65%) and **3** (24%), while at 200 °C 1,5-dipyrrolidinobutane (**5**) was obtained in 56% yield.

With assumption of the formation of tertiary amines in Scheme I, an amine-exchange reaction can be performed, if another amine (R^3R^4NH) is added at the stage of the addition of the imine **1** (eq 4). Indeed, the reaction of secondary amines with secondary

$$[R^1CH{=}NR^2] \xrightarrow{R^3R^4NH} \left[\begin{matrix} R^1CHNHR^2 \\ | \\ NR^3R^4 \end{matrix}\right] \xrightarrow[-R^2NH_2]{PdH_2} R^1CH_2NR^3R^4 \quad (4)$$

1

amines gives unsymmetrical tertiary amines. Thus, the reaction of *N*-methylbenzylamine with *N*-methylbutylamine gave *N*-butyl-*N*-methylbenzylamine (95%), and that of *N*-methylpropylamine with pyrrolidine gave *N*-propylpyrrolidine (98%) along with methylamine:

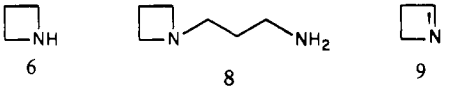
$$MeNHCH_2Ph + MeNHBu \xrightarrow{Pd} BuMeNCH_2Ph + MeNH_2$$

Apparently, for selective alkylation of secondary amines by means of the exchange reaction, *N*-methylalkylamines should be utilized rather than alkylamines, because the liberation of methylamine with lower molecular weight induces the reaction to proceed selectively. Typical results of the alkyl-exchange reaction are summarized in Table II.

Applications of the Exchange Reaction

Variation of the exchange reaction can open new processes for the synthesis of diamines, polyamines, and heterocyclic amines. 1,*n*-Diamines that have more than four methylenes can be readily converted into the corresponding triamines. For example, 1,8-octanediamine, which is available from butadiene,[14] can be readily converted into *N*-(8-aminooctyl)-1,8-octanediamine (73%), whose guanidine derivative is a highly active fungiside for *Fusarium nivale*.[15] As shown in Table II, *N*-benyl-1,*n*-diamines, which are precursors of polyamines,[16] were readily prepared by the exchange reaction of *N*-methylbenzylamine with 1,*n*-diamines (n = 2–4). The similar reaction of 1,6-hexamethylenediamine gave *N*-benzyl-1,6-hexanediamine (20%) and *N*-benzyl-*N'*-benzylidene-1,6-hexanediamine (70%), but the latter imine was hydrolyzed to give the former *N*-benzyl-1,6-diamine. Consequently, *N*-benzyl-1,*n*-diamines are generally prepared catalytically upon treatment of *N*-methylbenzylamine with 1,*n*-diamines.

Primary and secondary amines with the 1,3-propanediamine structure do not undergo the exchange reaction but undergo specific bond cleavage reactions.[11] It has been suggested that palladium inserts into the carbon–nitrogen bond of an amine, giving a five-membered chelating complex, which undergoes β-elimination of PdH species to form allylamine.[11] To overcome this difficulty we chose azetidine[17] (**6**) as an alternative source



6 8 9

of the 3-aminopropyl group. The reaction of **6** with palladium catalyst gave *N*-(3-aminopropyl)azetidine (**8**) quantitatively. Apparently, a highly reactive azetine intermediate is generated in situ by dehydrogenation. It is quite recent that azetine (**9**) was prepared by the elimination reaction of *N*-chloroazetidine.[18]

Polyamines with $-N(CH_2)_3N-$ and/or $-N(CH_2)_2N-$ units[19]

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Table III. Palladium-Catalyzed Reaction of Azetidine (6) with $H_2N(CH_2)_3NH_2$

$H_2N(CH_2)_3NH$/6[a]	temp, °C	conv of 6, %[a]	yield, %[a] 8	yield, %[a] 10[3,3]
0	140	88	99	0
1	140	52	69	31
3	170	86	1	84

[a] Determine by GLC analysis using internal standards.

Table IV. Triamines (10) from the Palladium-Catalyzed Reactions of $H_2N(CH_2)_nNH_2$ with Azetidine (6) and Aziridine (7)

cyclic amine	*n* in $H_2N(CH_2)_nNH_2$	conv of cyclic amine, %	yield of triamine 10, %
7	2	99	81
6	2	100	70
7	3	67	84
6	3	100	73

[a] Mixture of diamine (10 mmol), cyclic amine (6 or 7, 3 mmol), and palladium black (20 mg) was reacted at 120 °C for 12 h under argon. [b] Identified by IR, NMR, and mass spectral data. [c] GLC yield based upon reacted cyclic amine using an internal standard.

are highly interesting compounds because of their potential ability as metal ion[20] and anion receptor molecules[21] and biologically active substance.[22] The treatment of **6** with palladium catalyst in the presence of an amine gives various *N*-(3-aminopropyl)amines highly efficiently. Thus, the treatment of **6** with 1,3-propanediamine gave *N*-(3-aminopropyl)-1,3-propanediamine (*m* = 3, *n* = 3, **10**[3,3]). As shown in Table III, for the selective preparation of triamine **10**[3,3], more than 3 equiv of 1,3-propanediamine is required as an acceptor of the azetine intermediate. According to eq 5 triamines **10** can be generally prepared by the exchange reaction as shown in Table IV.

$$\underbrace{(CH_2)_m}NH + H_2N(CH_2)_nNH_2 \xrightarrow{Pd} H_2N(CH_2)_mNH(CH_2)_nNH_2 \quad (5)$$

6, *m* = 3
7, *m* = 2

10

(19) Polyamines: (a) Alkylation with dihalides: Barefield, E. K.; Wagner, F.; Heringer, A. W.; Dahl, A. R. *Inorg. Synth.* **1976**, *16*, 220. (b) Conjugate addition to acrylonitrile followed by reduction: Buhleier, E.; Wehner, W.; Vögtle, F. *Synthesis* **1978**, 155. Adams, T. C.; Combs, D. W. Doyle Davis, Jr.; Hauser, F. M. *J. Org. Chem.* **1981**, *46*, 4582. (c) Tosylated amines: Wälchi-Schaer, E.; Eugster, C. H. *Helv. Chim. Acta* **1978**, *61*, 928. Kramer, U.; Gugisberg, A.; Hesse, M.; Schmid, H. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 200. (d) *N*-Acylated amines: Humora, M.; Quick, J. *J. Org. Chem.* **1979**, *44*, 1166. Poindexter, G. S. *Synthesis* **1981**, 541. (e) *N*-Benzylamine: ref 16. (f) Reduction of hexahydropyrimidine: Chantrapromma, K.; McManis, J. S.; Ganem, B. *Tetrahedron Lett.* **1980**, *21*, 2475. (g) Reductive cleavage of cyclic amidine: Yamamoto, H.; Maruoka, K. *J. Am. Chem. Soc.* **1981**, *103*, 4186. (h) Recent preparation of macrocyclic polyamines: Martin, A. E.; Bulkowski, J. E. *J. Org. Chem.* **1982**, *47*, 415 and references therein. Smith, W. L.; Ekstrand, J. D.; Raymond, K. N. *J. Am. Chem. Soc.* **1978**, *100*, 3539. Atkins, T. J.; Richman, J. E.; Oettle, W. F. *Org. Synth.* **1978**, *58*, 86. Erhardt, J. M.; Grover, E. R.; Wuest, J. D. *J. Am. Chem. Soc.* **1980**, *102*, 6365. Christensen, J. T.; Eatough, D. J.; Izatt, R. M. *Chem. Rev.* **1974**, *74*, 351.

(20) Busch, D. H. *Acc. Chem. Res.* **1978**, *11*, 392. Coughlin, P. K.; Lippard, S. J. *J. Am. Chem. Soc.* **1981**, *103*, 3228. Dancey, K. P.; Henrick, K.; Judd, P. M.; Owston, P. G.; Peters, R.; Tasker, P. A. *Ibid.* **1981**, *103*, 4952. Barefield, E. K.; Chueng, D.; Van Derver, D. G. *J. Chem. Soc., Chem. Commun.* **1981**, 302. Schibler, W.; Kaden, T. A. *Ibid.* **1981**, 603. Gainsford, G. J.; Jackson, W. G.; Sargeson, A. M. *Ibid.* **1981**, 875. Melhado, L. L.; Gutsche, C. D. *J. Am. Chem. Soc.* **1978**, *100*, 1850.

(21) Anion receptor molecules: Hosseini, M. W.; Lehn, J. M. *J. Am. Chem. Soc.* **1982**, *104*, 3525. Kimura, E.; Sakonaka, A.; Yatsunami, T.; Kodama, M.; *Ibid.* **1982**, *104*, 3182.

(22) Macrocyclic spermidine and spermine alkaloids: (a) Smith, T. A. *Phytochemistry* **1975**, *14*, 865. Tabor, H.; Tabor, C. W. *Adv. Enzymol.* **1972**, *32*. Hesse, M.; Schmid, H. *Int. Rev. Sci. Org., Chem. Ser. Two* **1976**, *9*, 265. (b) Yamamoto, H.; Maruoka, *J. Am. Chem. Soc.* **1981**, *103*, 6133. Mcmanis, J. S.; Ganem, B. *J. Org. Chem.* **1980**, *45*, 2041. Wasserman, H. H.; Matsuyama, H. *J. Am. Chem. Soc.* **1981**, *103*, 461. Atkins, J. F.; Lewis, J. B.; Anderson, C. W.; Gesterland, R. F. *J. Biol. Chem.* **1975**, *250*, 5688.

Table V. Tetraamines 11 from Palladium-Catalyzed Reaction of $H_2N(CH_2)_nNH(CH_2)_nNH_2$ with Azetidine (6) and Aziridine (7)[a]

cyclic amine	*n* in triamine 10	conv of cyclic amine, %	yield of tetraamine (11), %
7	2	78	65
6	2	100	62
7	3	74	65
6	3	100	75

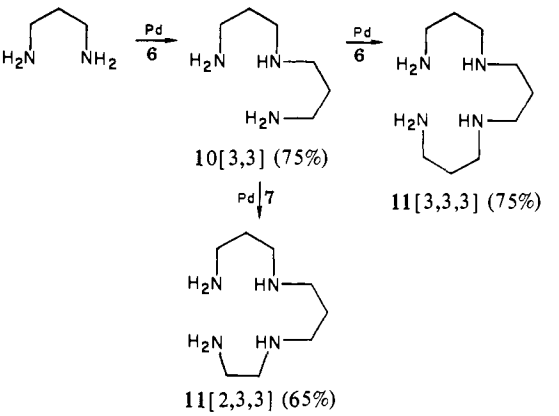
[a] A mixture of triamine (10, 10 mmol), cyclic amine (6 or 7, 3 mmol), and palladium black (20 mg) was reacted at 120 °C for 12 h under argon. [b] Identified by IR, NMR, and mass spectral data. [c] GLC yield based upon the reacted cyclic amine using an internal standard.

This method is extended to the preparation of tetraamines (**11**) according to eq 6. The results are summarized in Table V.

$$\underbrace{(CH_2)_m}NH + H_2N(CH_2)_nNH(CH_2)_nNH_2 \xrightarrow{Pd} H_2N(CH_2)_mNH(CH_2)_nNH(CH_2)_nNH_2 \quad (6)$$

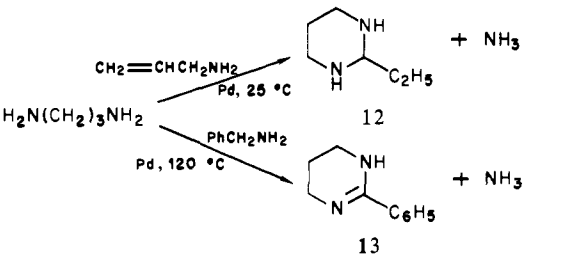
11

N,*N*′-Bis(3-aminopropyl)-1,3-propanediamine (**11**[3,3,3]) was



obtained in 75% yield upon treatment of **6** with palladium in the presence of triamine **10**[3,3]. Fortunately, the formation of tris(3-aminopropyl)amine was less than 4%. Apparently, 1, *n*-diamines (*n* = 2, 3) are less reactive toward palladium in comparison with azetidine because of the stabilization due to the bidentate chelation. Further, nucleophile attack of the primary amino group of **10**[3,3] to the azetine intermediate is favored over that of the more basic secondary amino group. These important characteristics may be due to the steric effect at the stage of the addition of **10**[3,3] across the carbon–nitrogen double bond of the azetine complex. Naturally, aziridine (**7**) also becomes a good precursor of the $-CH_2CH_2NH_2$ group via azirine intermediate. Thus, treatment of **7** in triamine **10**[3,3] gave tetraamine **11**[3,3,2] selectively.

Variation of the exchange reaction can open new processes for the synthesis of heterocyclic compounds. The treatment of 1,3-propanediamine with allylamine at 25 °C gave 2-ethylhexahydropyrimidine (**12**, 95%), which is a highly efficient hydrogen



donor for a selective transfer hydrogenation reaction.[23] Similarly,

(23) Murahashi, S.-I.; Yano, T.; Hino, K. *Tetrahedron Lett.* **1975**, 4235.

Table VI. Deuterium Distribution of the Palladium-Catalyzed Reactions of (S)-(−)-17-α-d_1 and DL-17-N-d_2[a]

substrate	cat.	temp, °C	time h	conv %	racemization, %	deuterium content (%)[b] 17 CH	17 CH_3	18 CH	18 CH_3	19 CH	19 CCH_3	19 $=CCH_3$
(S)-(−)-17-α-d_1[c]	Pd	100	7	92	93	35	27	28	20	57	31	13
(S)-(−)-17-α-d_1[c]	$Pd(OAc)_2$	100	13	76	85	42	10	10	9	58	33	22
DL-17-N-d_2	Pd	150	2	54		40	30	29	30			

[a] The reaction was carried out with 5 mol % of catalyst under argon. [b] Deuterium contents were determined by ^1H NMR spectra on the basis of the protons on phenyl group. [c] $[\alpha]^{29}_D$ −41.12° [c, 1.56, benzene].

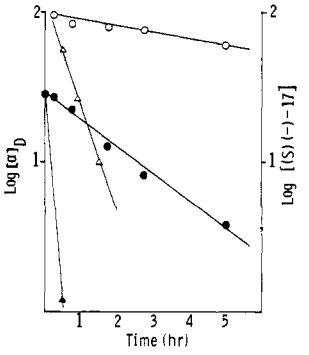
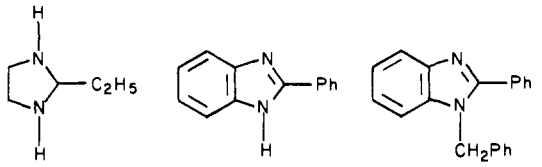


Figure 1. Variation of the optical activities at 50 (●) and 100 °C (▲), and the conversions at 50 (○) and 100 °C (△) for the palladium-catalyzed reaction of (S)-(−)-α-phenylethylamine (**17**).

the treatment of N-methylbenzylamine with 1,3-propanediamine at 120 °C afforded 2-phenyltetrahydropyrimidine (**13**) in 68% yield. The imidazole rings, which are closely related to the enzyme cofactor,[24] can be readily contracted. Thus, 2-ethylimidazolidine (**14**) was prepared from allylamine and 1,2-diaminoethane in 68%

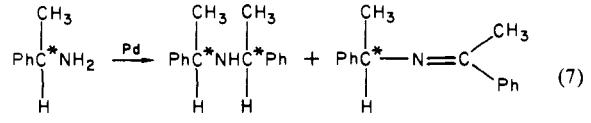


14 **15** **16**

yield. The reaction of N-methylbenzylamine with o-phenylenediamine gave 2-phenylbenzimidazole (**15**, 37%) and 1-benzyl-2-phenylbenzimidazole (**16**, 25%).

Mechanisms for the Exchange Reaction

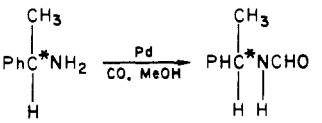
Treatment of optically pure (S)-(−)-α-phenylethylamine (**17**)



17 **18** **19** (7)

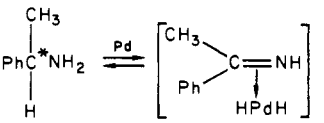
with palladium catalyst at 100 °C gave a mixture of (S,S)-, (S,R)-, and (R,R)-α,α′-dimethyldibenzylamine (**18**, 77%) and N-(methylbenzylidene)-α-methylbenzylamine (**19**, 20%). The optical purities of **18** and **19** were 1.7% and 6.6%, respectively, and the ratio of [S,S + R,R]/S,R isomers of **18** was 4. The time dependence of the palladium-catalyzed reaction of (S)-(−)-**17** has been monitored with respect to the conversion and the loss of its optical activity. As shown in Figure 1, (S)-(−)-**17** undergoes first-order racemization. The rates of racemization at 50 and 100 °C are $k = 5.6 \times 10^{-5}$ and $k = 7.6 \times 10^{-4}$ s^{-1}, respectively, and E_a is 12.5 kcal/mol. On the other hand, the rates of conversion at 50 and 100 °C are $k = 1.6 \times 10^{-5}$ and $k = 2.1 \times 10^{-4}$ s^{-1}, respectively, and E_a is 12.3 kcal/mol. Racemization of (S)-(−)-**17** proceeds about 3.5 times faster than its conversion. These results clearly indicate that a rapid equilibrium is present between the starting amine and its planar imine intermediate.

There are two possible pathways to give the imine intermediate: palladium undergoes insertion into either the N–H bond or the C–H bond on the α-carbon before β-elimination of PdH species.[25] The carbonylation[26] of (S)-(−)-α-phenylethylamine (**17**) with palladium catalyst in methanol under CO (70 atm) at 150 °C gave optically pure (S)-(−)-α-N-phenylethylformamide (**20**). The



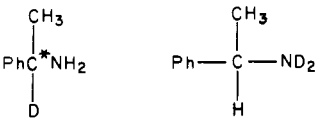
17 **20** (8)

recovered starting amine retained its optical activity. When a similar reaction of (S)-(−)-**17** was carried out in the absence of CO, amine **18** (25%) and imine **19** (17%) were obtained (52% conversion). Optically active **20** may arise either from insertion of CO into the palladium–nitrogen bond of the RNHPdH derived from insertion of palladium into the N–H bond or from nucleophilic attack by the amine **17** on CO adsorbed on the palladium.[27] The isolated metal complexes that have a R^1R^2N–metal bond are limited to those in which R^1 and R^2 have no β-hydrogen.[28]



17 **21**

The deuterium distribution in the palladium-catalyzed reaction of (S)-(−)-α-phenylethylamine-α-d_1 (17-α-d_1)[29] was examined.



17-α-d_1 17-N-d_2

The deuterium contents of **18** and **19** were determined by the analysis of the NMR spectra, and the results are summarized in Table VI. The loss of total deuterium contents is due to the facile proton exchange on the ND_2 group. Similar deuterium distribution

(24) Fife, T. H.; Pellino, A. M. *J. Am. Chem. Soc.* **1980**, *102*, 3062 and references therein.

(25) Diamond, S. E.; Mares, F. *J. Organomet. Chem.* **1977**, *142*, C55. Tang, R.; Diamond, S. E.; Neary, N.; Mares, F. *J. Chem. Soc., Chem. Commun.* **1978**, 562. Kuehne, M. E.; Hall, T. C. *J. Org. Chem.* **1976**, *41*, 2742.

(26) Naota, K., unpublished results. For carbonylation see: Tsuji, J.; Iwamoto, N. *J. Chem. Soc., Chem. Commun.* **1966**, 380. Hegedus, L. S.; Allen, G. F.; Olsen, D. J. *J. Am. Chem. Soc.* **1980**, *102*, 3583.

(27) (a) James, D. E.; Stille, J. K. *J. Am. Chem. Soc.* **1976**, *98*, 1806, 1810. Cowell, A.; Stille, J. K. *Ibid.* **1980**, *102*, 4193. (b) Daroda, R. J.; Blackborow, J. R.; Wilkinson, G. *J. Chem. Soc., Chem. Commun.* **1980**, 1101.

(28) R. is $SiMe_3$; Cetinkaya, B; Lappert, M. F.; Torroni, S. *J. Chem. Soc., Chem. Commun.* **1979**, 843. R is aryl: Beck, W.; Bauder, M. *Chem. Ber.* **1970**, *103*, 583. Alcock, N. W.; O'Sullivan, R. D.; Parkins, A. W.

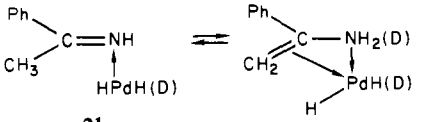
(29) Guthrie, R. D.; Jaeger, D. A.; Meister, W.; Cram, D. J. *J. Am. Chem. Soc.* **1971**, *93*, 5137.

Table VII. Relative Rate of Palladium-Catalyzed Reaction of Primary Amines with Benzylamine[a]

amine	pK_B	rel rate
n-$C_6H_{11}NH_2$	2.3[b]	1.9
p-$CH_3C_6H_4NH_2$	8.9[c]	1.2
p-$ClC_6H_4NH_2$	10[c]	1.1
p-$O_2NC_6H_4NH_2$	13[c]	1.0

[a] A mixture of two amines (20 mmol) and benzylamine (37 mmol) was allowed to react in the presence of palladium catalyst (1.9 mmol). [b] Rieux, A.; Rumean, M.; Tremillon *B. Bull. Soc. Chim. Fr.* **1964**, 1053. [c] Fall, A. F. *J. Am. Chem. Soc.* **1930**, *52*, 5115.

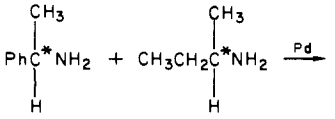
was also observed in the palladium-catalyzed reaction of **17**-*N*-d_2. The deuterium distribution to the methyl group shows the intermediacy of enamine complex **22** and its isomerization to **21**.



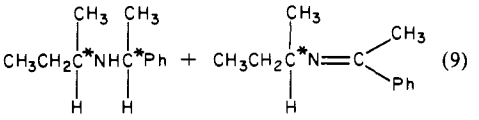
21 **22**

It is known that the enamine intermediate undergoes isomerization to the imine in the hydrogenation of enamines.[30] We have demonstrated that deuterium exchange on the α- and β-C–H bonds takes place readily in the palladium-catalyzed reaction of tertiary amines via isomerization between iminium ion and enamine complexes.[31]

The addition of a free amine to the imine intermediate was confirmed by the following facts. When amine **17** was allowed to react with excess (*S*)-(−)-*sec*-butylamine (**23**) in the presence of palladium catalyst at 100 °C, *N*-*sec*-butyl-α-phenylethylamine (**24**) and *N*-(methylbenzylidene)-*sec*-butylamine (**25**) were ob-



(*S*)-(−)-**17** (*S*)-(+)-**23**



(*S,S*/*S,R*)-**24** (*S*)-(−)-**25** (9)

tained in 38% and 51% yields, respectively. **24** consisted of *S,S* and *S,R* isomers in the ratio 53:47. The latter imine, **25**, showed $[\alpha]^{27}_D$ +53.8°, which corresponded to 93% optical purity, indicating that the *sec*-butyl group in **25** retained its optical activity. It was reported that an amine underwent addition across the carbon–nitrogen bond of the α-methylbenzylamine–palladium complex.[32]

It is noteworthy that more basic amines add to the imine intermediate more easily. The relative rates of the additions of an amine to a benzylimine complex have been determined by the competitive catalytic reaction of benzylamine with two amines as shown in Table VII. The rate of the exchange reaction is dependent on the pK_b values of the amines.

The role of palladium after the formation of imine complex **22** was examined concerning to the palladium-catalyzed reaction of *N*-methylbenzylamine. Since there is no report concerning the addition of a secondary amine to a Schiff base,[33] the reaction of

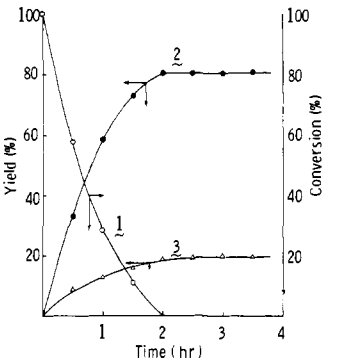
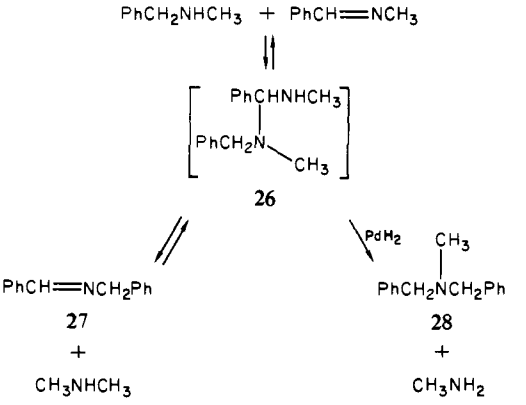


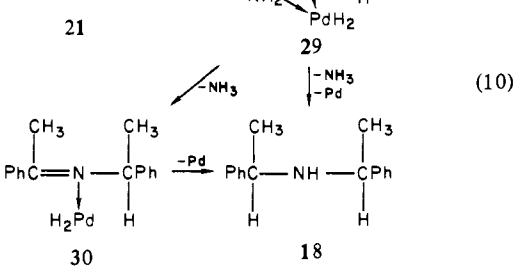
Figure 2. Product yields from the palladium-catalyzed reaction of α-phenethylamine (**17**) at 100 °C: (○) conversions of **17**; (●) yields of α,α-dimethyldibenzylamine (**18**); (△) yields of *N*-(methylbenzylidene)-α-methylbenzylamine.

Scheme II



N-methylbenzylamine with *N*-benzylidenemethylamine was examined in the presence and absence of palladium catalyst under the conditions employed for the exchange reaction. In the latter reaction no *N*-methyldibenzylamine (**28**) could be detected, and *N*-benzylidenebenzylamine (**27**) was obtained exclusively. As shown in Scheme II, reversible addition–elimination via aminal intermediate **26** is operative. By contrast, in the presence of palladium catalyst, **27** and **28** were obtained in the ratio 60:40, indicating that palladium species plays an important role in the reductive cleavage of the C–N bond of the aminal **26**.

The decomposition of aminal intermediates is a process both of biological significance and of importance in a number of synthetic transformations.[36] The last problem to be solved is whether amine **18** is derived from the reductive cleavage of the aminal intermediate **29** or the elimination of ammonia to give **30** followed by hydrogenation as shown in eq 10. The palladium-



21 **29** **30** **18** (10)

(30) Paukstelis, J. V. "Enamines"; Cook, A. G., Ed.; Marcel Dekker: New York, 1969; p 169.
(31) Murahashi, S.-I.; Watanabe, T. *J. Am. Chem. Soc.* **1979**, *101*, 7429.
(32) Chenard, J. Y.; Commereuc, D.; Chauvin, Y. *J. Organomet. Chem.* **1971**, *33*, C69.
(33) Layer, R. W. *Chem. Rev.* **1963**, *63*, 489.
(34) (a) Yoshida, T.; Harada, K. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 3706. (b) Overberger, C. G.; Marullo, N. P.; Hiskey, R. G. *J. Am. Chem. Soc.* **1961**, *83*, 1374.
(35) Fischer, H.; De Candis, F. X.; Ogden, S. D.; Jencks, W. P. *J. Am. Chem. Soc.* **1980**, *102*, 1340. Hoggs, J. L.; Jencks, D. A.; Jencks, W. P. *Ibid.* **1977**, *99*, 4772. Abott, E. H.; Martell, A. E. *Ibid.* **1971**, *93*, 5852.
(36) Barrows, T. H.; Farina, P. R.; Chrzarowski, R. L.; Benkovic, P. A.; Benkovic, S. J. *J. Am. Chem. Soc.* **1976**, *98*, 3678. Moad, G.; Benkovic, S. J. *Ibid.* **1978**, *100*, 5495.

Table VIII. Palladium-Catalyzed Reaction of α-Phenylethylamine (17) with *N*-(Methylbenzylidene)-α-methylbenzylamine (19)[a,b]

configuration of 17	configuration of 19	recovered 17		recovered 19		product 18		
		conv, %	ee, %	conv, %	ee, %	yield, %	(±)/meso	ee, %
S	*S*	83	0	42	15	23	2.0	32
(±)	*S*		0	32	10	30	2.5	29
S	(±)		0	34	24	33	2.6	30
S	*S*[c]	86	0	49	11	40	3.1	25

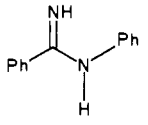
[a] All reactions were carried out under argon in the presence of 5 mol % of palladium catalyst at 100 °C for 15 h. [b] Yields and conversions were determined by GLC analyses using the conditions employed for the palladium-catalyzed reaction of 17. [c] Schiff base 19 was added after 15 min.

catalyzed reaction of **17** was monitored precisely. The representative data used to define reaction conditions are summarized in Figure 2 for the conversion of **17** to a mixture of **18** and **19** (eq 7). The palladium-catalyzed reaction of **17** with **23** results in a similar figure. These results clearly show that amine **18** is formed not from the consecutive reaction via **19** but from the concurrent reaction of **29** together with **19**.

The following stereochemical result also supports the reductive cleavage of aminal intermediate **29**. The palladium-catalyzed reaction of (*S*)-(−)-**17** at 50 °C gave **18** (17% yield) and **19** (24% yield), and their optical purities were 46% and 10%, respectively. Since it is known that the catalytic hydrogenation of (*S*)-**19** gives (*S*,*S*)-**18** selectively,[34] the higher optical purity of **18** obtained in comparison with **19** indicates that **18** is not derived simply from the hydrogenation of imine **19**.

Generally, transamination between an amine and an imine takes place readily via the aminal intermediates.[35] An attempt to detect the palladium-catalyzed transfer hydrogenation of (*S*)-(−)-**19** with (*S*)-(−)-**17** was in vain since transamination and/or racemization of (*S*)-(−)-**17** was fast. However, the following result indicates that the formation of asymmetric aminal followed by reductive cleavage seems to be operative rather than asymmetric transfer hydrogenation. The product amine **18** showed 30% ee by use of (*S*)-**19** and even (±)-**19**, although (*S*)-(−)-**17** undergoes rapid racemization under the reaction condition.

Reduction of amidines gives aminals that undergo further reduction to give amines and iminium ion.[36] As a model, palladium-catalyzed hydrogenolysis of *N*-phenylbenzamidine (**31**) with



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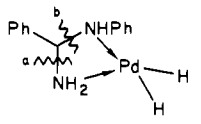
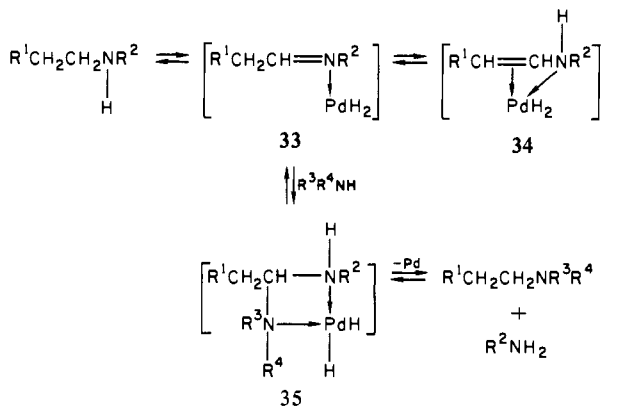


32

molecular hydrogen was carried out. Treatment of **31** with palladium under hydrogen (32 atm) at 120 °C gave toluene (74%), aniline (78%), benzylamine (4%), and *N*-benzylaniline (3%). The control experiment showed that toluene and aniline were the second-order products of hydrogenolysis of the aminal intermediate. Thus, hydrogenation of *N*-benzylideneaniline at 50 °C for 1 h under hydrogen (1 atm) afforded *N*-benzylaniline quantitatively, and continuous hydrogenation resulted in the decrease of *N*-benzylaniline in proportion to the increase of aniline and toluene. Therefore, the aminal intermediate **32** undergoes bond cleavage between carbon and NH_2 group (cleavage a) predominantly rather than between carbon and NHPh group (cleavage b). The formation of benzylamine supports the intermediacy of aminal **32** and its reductive cleavage. Noteworthy is that the bond cleavage between carbon and the primary amino group proceeds 24 times faster than that between carbon and the secondary amino group. This is consistent with the general results obtained in the amine-exchange reactions; that is, the extrusion of ammonia takes place predominantly, giving secondary and tertiary amines.

Imines would be formed when hydrogen is removed from the aminal complex **29** to produce free aminal intermediates which undergo elimination of amines. Indeed if a suitable hydrogen acceptor is present in the substrate, imines are formed by intramolecular transfer hydrogenation. Thus, the palladium-catalyzed reaction of allylamine gives *N*-propylideneallylamine (95% yield), while that of cyclopropylcarbinylamine gives *N*-butylidenecyclopropylcarbinylamine (95% yield).

Scheme III



In conclusion, the palladium-catalyzed alkyl group exchange reaction can be rationalized by Scheme III. The initial step may be the insertion of palladium into the N–H bond of an amine. β-Elimination of PdH species gives a key intermediate of imine complex **33**, which undergoes rapid equilibrium with enamine complex **34**. Addition of a free amine to imine complex **33** gives aminal **35**, which undergoes reductive cleavage to give the product amine. The activation of amines with N–H bonds gives the key intermediate of imine hydride complexes (eq 2), which is in contrast to the formation of iminium ion complexes from tertiary amines (eq 3).[11,31]

The present reaction may be a simulation of the oxidative deamination of mitcontrial monoamine oxidase with metal complexes. Two one-electron transfers from an amine to the flavin are considered to proceed to give iminium ion.[6]

Experimental Section

General Procedures. NMR spectra were run as CCl_4 and $CDCl_3$ solutions on a JNM-MH 60- or 100-MHZ spectrometer: chemical shifts were reported in parts per million downfield from Me_4Si. IR spectra were taken in a NaCl cell on Hitachi 215 spectrometer. Analytical GLC evaluations of product mixtures were performed on a JEOL JGC-20KFP gas chromatograph equipped with a FID detector, while preparative GLC was performed on a JEOL 20K. Optical rotations were measured by using a JASCO-DIP-4 spectrometer. Mass spectra were obtained on a Hitachi RMS-4 mass spectrometer at 80 eV.

Palladium Catalyst. Willstätter's method[37] was modified. Palladium chloride (7.0 g, 40 mmol) was dissolved in distilled water (100 mL) with stirring and filtered off. To a 300-mL three-necked flask fitted with a mechanical stirrer thermometer, and dropping funnel was placed the palladium chloride solution, and this was cooled to −10 °C. An aqueous solution of HCHO (33%, 50 mL) that was precooled to 0 °C was added in one portion. A solution of KOH (50 g in 50 mL of distilled water) was added dropwise from the dropping funnel with vigorous stirring at 0–3 °C. The reaction mixture was stirred for additional 5 min and heated at 60 °C for 25 min. After decantation, palladium black was

(37) Willstätter, R.; Waedschmidt-Leitz, E. *Chem. Ber.* **1921**, *54*, 113.

transferred into a 300-mL beaker and washed by decantation with ether (100 mL) and then with distilled water several times in order to remove Cl^- completely. Further, palladium black was washed by decantation with distilled methanol (100 mL) and with ether (100 mL). The slightly moist palladium was dried in a desiccator over P_2O_5 under argon atmosphere at reduced pressure for 48 h. Palladium black was subdivided into several brown sample tubes under Ar. The sealed tubes were stored at 0 °C.

General Procedure for Alkyl Group Exchange Reaction. A mixture of a 1–10-g scale of amine and palladium black (5 mol %) in a flask equipped with a magnetic stirring bar and a reflux condenser fitted with an argon inlet was reacted with stirring. When the reaction requires high temperature, it was carried out in an autoclave or a sealed tube equipped with a magnetic stirring bar. After the reaction, the mixture was filtered off and distilled. The GLC analysis of the distillate using an internal standard gave the conversion of the starting amine and the yields of products. A solvent was not used unless otherwise noted. For large-scale preparation, Pd/C and other supported catalysts can be conveniently used as well as palladium black.

Catalytic Activity of Various Metals and Metal Complexes. A mixture of (±)-α-phenylethylamine (**17**, 3.0 mmol) and a catalyst (5.0 mol %) was heated with stirring in a sealed glass tube at 150 °C for 3 h. The conversion of the starting amine and the yields of α,α′-dimethyldibenzylamine (**18**) and N-(methylbenzylidene)-α-methylbenzylamine (**19**) were determined by GLC (10% CW-20M, 200 °C) using an internal standard (tetradecane). The results with various catalysts are as follows: Pd black, conversion 85%, (yields of **18** and **19** are 42% and 39%, respectively), $Pd(OAc)_2$, 73% (32%, 36%), $Pd(PPh_3)_4$, 43% (~1%, 16%); R–Ni, 80% (52%, 25%); $Ni(OAc)_2$, 53% (~1%, ~1%); $RuH_2(PPh_3)_4$, 45% (~1%, ~1%); $RuCl_2(PPh_3)_3$, 53% (~1%, 1%); $RuCl_3{\cdot}3H_2O$, 64% (2%, 20%); $Ru_3(CO)_{12}$, 51% (5%, 9%); $RhCl(PPh_3)_3$, 41% (~1%, 4%); $RhCl_3{\cdot}3H_2O$, 49% (~1%, 4%); $Rh_6(CO)_{16}$, 44% (~1%, 5%). The reaction of hexylamine at 160 °C for 8 h showed the similar results, giving dihexylamine and trihexylamine. The reactions of (±)-**17** (0.37 mmol) with the metal catalysts that were prepared by the reduction of the corresponding metal chlorides (0.15 mmol) with potassium[12] was carried out in THF at 150 °C (13 h) under argon. The conversions of **17** (and the yields of **18** and **19**) were as follows: Pd, 23% (17%, 35%), Ru, 27% (15%, 67%), Rh, 28% (11%, 25%), Ni, 29% (1%, 3%).

Products. Except when particularly described, the structures of the products were established by comparison of their spectral data with those of the authentic samples. Schiff bases[38] were generally prepared by the condensation of the corresponding amines with aldehydes in ethanol at 25–75 °C with or without $ZnCl_2$ catalyst. Secondary amines were prepared by hydrogenation of the resulting Schiff base over palladium catalyst.

***N*-Methyldibenzylamine**: bp 108–109 °C (3 mmHg); mass spectrum, *m/e* 211 (M^+); ^1H NMR ($CDCl_3$) δ 2.17 (s, 3 H, CH_3), 3.50 (s, 4 H, CH_2Ph), 7.12~7.38 (m, 10 H, Ph). Anal. ($C_{15}H_{17}N$) C, H, N.

Difurfurylamine: bp 80–95 °C (3 mmHg); mass spectrum, *m/e* 177 (M^+); IR (neat) 3350 cm^{-1} (NH); ^1H NMR (CCl_4) δ 1.35 (s, 1 H, NH), 3.24 (s, 4 H, CH_2), 6.15–6.35, 7.25–7.35 (m, 6 H, olefin H). Anal. ($C_{10}H_9NO_2$) C, H, N.

***N*-Furfurylidenefurylamine**: mass spectrum, *m/e* 175 (M^+); ^1H NMR (CCl_4) δ 4.72 (s, 2 H, CH_2), 6.20–6.80 (m, 2 H), 7.25–7.48 (m, 6 H, olefin H), 8.18 (s, 1 H, N=CH). Anal. ($C_{10}H_7NO_2$) C, H, N. Difurfurylamine was prepared by hydrogenation of *N*-furylfurylidenefurylamine over palladium (72%), bp 90 °C (5 mmHg).

***N*-Butylidenecyclopropylcarbinylamine**: ^1H NMR ($CDCl_3$) δ 0.08–0.70 (m, 4 H, cyclopropyl H), 0.95 (t, *J* = 6.5 Hz, 3 H, CH_3), 1.55 (tq, *J* = 6.5 Hz, 2 H, CH_2Me), 2.03–2.67 (m, 2 H, N=CCH_2), 3.59 (d, *J* = 6.5 Hz, 2 H, NCH_2), 8.47 (t, *J* = 5.0 Hz, 1 H, cyclopropyl H); IR (neat) 3080, 3010, 1670 cm^{-1}.

4-Pyrrolidinobutylamine (3): bp 65–80 °C (5 mmHg); mass spectrum, *m/e* 142 (M^+); ^1H NMR (CCl_4) δ 1.40–1.90 (m, 8 H, ring H), 2.00–2.72 (m, 8 H, CH_2); IR (neat) 3350 cm^{-1} (NH). Anal. ($C_8H_{18}N_2$) C, H, N. The authentic sample[39] (95%) was prepared by Na-*t*-BuOH reduction of 1-pyrrolidinebutyronitrile (bp 115 °C (8 mmHg)), obtained from 4-chlorobutyronitrile and pyrrolidine in acetone (100 °C, 20 h) in an autoclave (78% yield).

Pyrrolidine-2Δ′-pyrroline (4): mass spectrum *m/e* 138 (M^+); ^1H NMR ($CDCl_3$) δ 1.65–2.20 (m, 6 H, Ch_2), 2.32–2.65 (m, 2 H, CH_2), 3.20–4.02 (m, 6 H, CH_2). The authentic sample was prepared from the reaction of butyrolactam methyl ether with pyrrolidine.[40]

1,4-Dipyrrolidinobutane (5): mass spectrum *m/e* 196 (M^+). Anal. ($C_{12}H_{24}N_2$) C, H, N. The authentic sample was prepared from the reaction of 1,4-dibromobutane with pyrrolidine lithium amide.

1,5-Dipiperidinopentane: mass spectrum, *m/e* 238 (M^+), ^1H NMR ($CDCl_3$) δ 1.25–1.65 (m, 18 H, CH_2), 2.10–2.40 (m, 12 H, CH_2). Anal. ($C_{15}H_{30}N_2$) C, H, N.

***N*-(8-Aminooctyl)-1,8-octanediamine**: A mixture of 1,5-octanediamine (0.574 g, 4 mmol) and palladium black (0.30 g, 0.28 mmol) was reacted with stirring in a sealed tube at 180 °C for 12 h under argon. To the reaction mixture 5 mL of ether was added. Filtration followed by removal of ether and unreacted 1,8-octanediamine (51% recovered, 120 °C (4 mmHg)) and Kugelrohr distillation (180 °C (4 mmHg)) gave the white solid *N*-(8-aminooctyl)-1,8-octanediamine (0.195 g, 73%): mp 89–90 °C; mass spectrum, *m/e* (relative intensity) 271(M^+, 10), 240 (8), 186 (7), 158 (3), 144 (64), 136 (13) 112 (19), 84 (22), 70 (22), 56 (38), 42 (62), 31 (100); ^1H NMR ($CDCl_3$) δ 1.32 (br s, 29 H), 2.46–2.77 (br m, 8 H); IR (Nujol) 3272 (NH), 3162, 1589, 1128 (CN), 891 cm^{-1}. Anal. ($C_{16}H_{37}N_3$) N.

***N*-Benzylethylenediamine**: mp (picrate) 223–224 °C; mass spectrum *m/e* (M^+; 150 °C); ^1H NMR ($CDCl_3$) δ 1.50 (s, 3 H, NH), 2.60–2.80 (m, 4 H, CH_2), 3.75 (s, 2 H, CH_2). Anal. (picrate, $C_{21}H_{20}N_8O_{14}$) C, H, N.

***N*-Benzyl-1,3-propanediamine**: mp (picrate) 155–156 °C; ^1H NMR ($CDCl_3$) δ 1.58 (tt, *J* = 6.3 Hz, 2 H, CCH_2C), 1.85 (s, 3 H, NH), 2.65 (t, *J* = 6.3 Hz, 2 H, CH_2), 2.72 (t, *J* = 6.3 Hz, 2 H, CH_2N), 3.72 (s, 2 H, CH_2Ph), 7.23 (s, 5 H, Ph). Anal. (picrate, $C_{22}H_{22}N_8O_{14}$) C, H, N.

***N*-Benzyl-1,4-butanediamine**: mp (picrate) 196–198 °C; ^1H NMR ($CDCl_3$) δ 1.38 (s, 3 H, NH), 1.33–1.67 (m, 4 H, CH_2), 2.50–2.84 (m, 4 H, CH_2) 3.77 (s, 2 H, CH_2), 7.32 (s, 5 H, Ph). Anal. (picrate, $C_{23}H_{24}N_8O_{14}$) C, H, N.

***N*-Benzyl-1,6-hexanediamine**: ^1H NMR ($CDCl_3$) δ 1.17–1.63 (m, 8 H, CH_2), 1.63 (s, 3 H, NH), 2.42–2.72 (m, 4 H, CH_2), 3.70 (s, 2 H, CH_2), 7.20 (s, 5 H, Ph).

***N*-Benzyl-*N*′-benzylidene-1,6-hexanediamine**: ^1H NMR ($CDCl_3$) δ 1.20 (s, 1 H, NH), 1.17–1.58 (m, 8 H, CH_2), 3.33–3.67 (m, 2 H, CH_2), 3.67 (s, 2 H, CH_2), 7.00–7.67 (m, 10 H, Ph), 8.08 (s, 1 H, N=CH). Anal. ($C_{20}H_{26}N_2$) C, H, N.

General Procedure for Synthesis of Triamines 10[*n*,*m*]. *N*-(3-Aminopropyl)-1,3-propanediamine (**10**[3,3]) is described as a typical example. A mixture of azetidine (**6**, 0.171 g, 3 mmol), 1,3-propanediamine (0.74 g, 10 mmol), and palladium black (20 mg, 0.19 mmol) was reacted with stirring in a sealed tube at 120 °C for 12 h under argon. To the reaction mixture, ether (5 mL) was added, and the solution was filtered off. The ether solution was analyzed by GLC (5% silicone SE 30, column temperature 60≃220 °C) by using biphenyl as an internal standard. After removal of ether and unreacted amines, Kugelrohr distillation (90 °C (4 mmHg)) gave **10**[3,3] (10.3 g, 73%): mass spectrum, *m/e* (relative intensity) 131 (8, M^+), 113 (10), 86 (26), 83 (39), 44 (100); ^1H NMR ($CDCl_3$) δ 1.20 (s, 5 H, NH), 1.30–1.73 (m, 4 H, $NCCH_2CN$), 2.65 (t, *J* = 6.5 Hz, 4 H CH_2NH), 2.75 (t, *J* = 5 Hz, 4 H, H_2NCH_2C); IR (neat) 3231 (NH), 2908, 1595, 1465, 1368, 1122 (CN) cm^{-1}.

***N*-(2-Aminoethyl)ethylenediamine (10[2,2])**: bp (Kugelrohr) 100–105 °C (30 mmHg); mass spectrum *m/e* (relative intensity) 103 (8, M^+), 85 (13), 72 (85), 55 (54), 28 (100); ^1H NMR ($CDCl_3$) δ 1.40 (s, 5 H), 2.51–2.88 (m, 8 H); IR (neat) 3269 (NH), 2935, 1598, 1462, 1373, 1122 (CN) cm^{-1}.

***N*-(2-Aminoethyl)-1,3-propanediamine (10[2,3])**: bp (Kugelrohr) 95–100 °C (4 mmHg); mass spectrum, *m/e* (relative intensity) 117 (32, M^+), 86 (100), 69 (42), 55 (94); ^1H NMR ($CDCl_3$) δ 1.18 (s, 5 H), 1.45–1.78 (m, 2 H), 2.50–2.92 (m, 8 H); IR (neat) 3268 (NH), 2924, 1593, 1460, 1303, 1115 (CN) cm^{-1}.

General Procedure for Synthesis of Tetraamines 11[l,m,n]. A typical example is the preparation of *N*,*N*′-bis(3-aminopropyl)-1,3-propanediamine (**11**[3,3,3]). A mixture of azetidine (**6**, 0.460 g, 8.06 mmol), *N*-(3-aminopropyl)-1,3-propanediamine (**10**[3,3], 2.94 g, 22.4 mmol), and palladium black (30 mg, 0.028 mmol) was reacted with stirring in a sealed tube at 120 °C for 12 h under argon. Ether (5 mL) was added to the reaction mixture and filtered off. After removal of the solvent and excess **10**[3,3], Kugelrohr distillation gave **11**[3,3,3] in 75% yield; bp 135–140 °C (3 mmHg); NMR ($CDCl_3$) δ 1.50 (q, *J* = 6.8 Hz, 6 H, $NCCH_2CN$), 1.85 (s, 6 H, NH), 2.59 (quint, *J* = 6.8 Hz, NCH_2); IR (neat) 3295 (s, NH), 1590 (m), 1470 (m), 1320 (w) cm^{-1}. The authentic sample was prepared by the reduction of β-cyanoethylamine with $LiAlH_4$ in THF. The content of tris(3-aminopropyl)amine was determined to be less than 4% by GLC and liquid chromatographic analyses. Tris(3-aminopropyl)amine was prepared by Barefield's method;[19a] bp (Kugel-

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rohr) 135–140 °C (1 mmHg); NMR ($CDCl_3$) δ 1.40 (s, 6 H, NH), 1.60 (t, J = 6.8 Hz, 6 H, $NCCH_2C$), 2.63 (t, J = 6.8 Hz, 6 H, $HNCH_2C$), 2.74 (t, J = 6.8 Hz, 6 H, H_2NCH_2C); IR (neat) 3250 (s, NH), 1640 (w), 1460 (m), 1120 (s, CN) cm^{-1}.

***N,N'*-Bis(2-aminoethyl)ethylenediamine (11[2,2,2])**: bp (Kugelrohr) 90–95 °C (4 mmHg); mass spectrum, m/e (relative intensity) 116 (18, M^+), 99 (21), 83 (18), 73 (53), 56 (48), 44 (100); ^1H NMR ($CDCl_3$) δ 1.38 (s, 6 H), 2.52–2.87 (m, 12 H); IR (neat) 3269 (NH), 2933, 2428, 1598, 1455, 1122 (CN), 725 cm^{-1}.

***N*-(2-Aminoethyl)-*N'*-(3-aminopropyl)ethylenediamine (11[2,2,3])**: bp (Kugelrohr) 115–120 °C (4 mmHg); mass spectrum, m/e (relative intensity) 130 (4, $M^+ - CH_2NH_2$), 113 (10), 99 (17), 87 (43), 73 (28), 70 (19), 56 (57), 42 (100); ^1H NMR ($CDCl_3$) (s, 6 H), 1.47–1.82 (m, 2 H), 2.55–2.88 (m, 12 H); IR (neat) 3268 (NH), 2924, 1602, 1472, 1253, 1122 (CN) cm^{-1}.

***N*-(2-Aminoethyl)-*N'*-(3-aminopropyl)-1,3-propanediamine (11[2,3,3])**: bp (Kugelrohr) 125–130 °C (4 mmHg); mass spectrum, m/e (relative intensity) 144 (25, $M^+ - CH_2NH_2$), 127 (18), 101 (7), 87 (12), 84 (23), 73 (13), 58 (100); ^1H NMR ($CDCl_3$) δ 1.28 (s, 6 H), 1.33–1.82 (m, 4 H), 2.48–2.87 (m, 12 H); IR (neat) 3278 (NH), 2935, 1609, 1474, 1122 (CN), 829 cm^{-1}.

***N*-(3-Aminopropyl)azetidine (8).** A mixture of azetidine (0.342 g, 6.0 mmol) prepared according to the Wadsworth method[17a] and palladium black (20 mg) was heated at 140 °C for 2 h in a sealed tube. Distillation of the reaction mixture gave *N*-(3-aminopropyl)azetidine in 88% yield; bp (Kugelrohr) 88–90 °C (30 mmHg); mass spectrum, m/e (relative intensity) 114 (3, M^+), 97 (33), 84 (12), 70 (77), 56 (100), 42 (83); ^1H NMR ($CDCl_3$) δ 1.45 (t, J = 6.9 Hz, 2 H), 1.78 (s, 2 H), 1.89–2.25 (m, 2 H), 2.42 (t, J = 6.9 Hz, 2 H), 2.70 (t, 6.9 Hz, 2 H), 3.13 (t, J = 6.8 Hz, 4 H).

2-Ethylhexahydropyrimidine (12): A mixture of allylamine (2.8 g, 0.05 mol), 1,3-propanediamine (3.7 g, 0.05 mol) and palladium black was treated at 30 °C for 15 h. After usual treatment, distillation (bp 50–60 °C (20 mmHg) gave 5 g of crude **12**. Preparative GLC gave pure sample: mass spectrum, m/e (M^+) 124; ^1H NMR ($CDCl_3$) δ 0.95 (t, J = 7.0 Hz, 3 H, Me), 1.22–1.78 (m, 4 H), 1.47 (s, 2 H, NH), 2.58–3.25 (m, 4 H), 3.42 (t, J = 6.0 Hz, 1 H); IR (neat) 3260 cm^{-1} (NH).

2-Phenyl-1,4,5,6-tetrahydropyridine (13): A mixture of *N*-methylbenzylamine (6.1 g, 0.05 mol), 1,3-propanediamine (3.7 g, 0.05 mol), and palladium black (0.20 g) was reacted at 120 °C for 15 h. The distillate (bp 150 °C (3 mmHg)) (7.8 g) contained 81% of **13** and 19% of *N*-benzyl-1,3-propanediamine. **13**: mass spectrum, m/e 160 (M^+); ^1H NMR ($CDCl_3$) δ 1.78 (tt, 2 H, 5.8 Hz, CH_2), 3.43 (t, J = 5.8, 4 H, CH_2), 5.12 (s, 1 H, NH), 7.17–7.80 (m, 5 H, Ar). Anal. ($C_{10}H_{12}N_2$) C, H, N.

2-Ethylimidazolidine (14). A mixture of ethylenediamine (3.00 g, 0.05 mol), allylamine (2.90 g, 0.05 mol), and palladium black (0.25 g) was stirred at room temperature for 15 h. Filtration of palladium followed by distillation (bp 45–52 °C (45 mmHg)) gave 2-ethylimidazolidine (3.1 g, 68%). Redistillation gave pure sample:[41] ^1H NMR (CCl_4) δ 0.95 (t, J = 7.0 Hz, 3 H, CH_3), 1.27 (s, 2 H, NH), 1.48, (dq, J = 6.5, 7.0 Hz, 2 H, CH_2), 2.75–2.87 (m, 4 H, CH_2N), 3.52 (t, J = 6.5 Hz, 1 H, CH); IR (neat) 3280 cm^{-1} (NH).

Reaction of *N*-Methylbenzylamine with *o*-Phenylenediamine. A mixture of *o*-phenylenediamine (2.0 g, 18 mmol), *N*-methylbenzylamine (5.0 g, 41 mmol), and palladium (0.20 g) was stirred at 120 °C for 15 h under nitrogen. The crystalline material was separated, washed with ether, and dissolved in methanol. Filtration followed by recrystallization gave 2-phenylbenzimidazole (**15**, 1.3 g, 37%): mp 265–267 °C; mass spectrum, m/e (M^+), 194. Anal. ($C_{13}H_{10}N_2$) C, H, N. From the ether solution was obtained 1.2 g of 1-benzyl-2-phenylbenzimidazole (**16**, 25%): mp 131.5–132.5 °C (MeOH); mass spectrum, m/e 284 (M^+); ^1H NMR (CCl_4) δ 5.33 (s, 2 H, CH_2), 6.80–7.70 (m, Ph, 15 H). Anal. ($C_{20}H_{16}N_2$) C, H, N.

(*S*)-(−)-α-Phenylethylamine (17) was prepared according to the Ingersol's method, $[\alpha]^{23}_D$ 40.00 ° [neat] (lit.[42] $[\alpha]^{25}_D$ − 39.7°).

Reaction of (*S*)-(−)-α-Phenylethylamine (17) with Palladium Catalyst. A mixture of (*S*)-(−)-α-phenylethylamine (**17**, 10 mmol; $[\alpha]^{23}_D$ −40.00° [neat]) and palladium black (5 mol %) in a 25-mL round bottomed flask was stirred in 100 °C under argon for 5 h. After cooling, the mixture was filtered off. GLC analysis of the filtrate (10% SE-30, 200 °C) showed that the conversion of **17** was 97%, and the yields of α,α'-dimethylbenzylamine (**18**) and *N*-(methylbenzylidene)-α-methylbenzylamine (**19**) were 77% and 20%, respectively. The products **18** and **19** were separated by means of GLC and identified by comparison of spectral data with those of authentic samples. **(±)-18**: NMR ($CDCl_3$) δ 1.25 (d, J = 7.0 Hz, 6 H), 1.71 (br s, 1 H), 3.52 (q, J = 7.0 Hz, 1 H), 7.24 (s, 10 H); IR (NaCl) 3325, 3060, 3025, 2960, 2925, 2865, 1603, 1495, 1455, 1472, 1208, 1125 cm^{-1}. ***meso*-18**: NMR ($CDCl_3$) δ 1.36 (d, J = 7.0 Hz, 6 H), 1.71 (br s, 1 H), 3.78 (q, J = 7.0 Hz, 1 H), 7.24 (s, 10 H). **(±)-19**: NMR ($CDCl_3$) δ 1.25 (d, J = 7 Hz, 3 H), 2.20 (s, 3 H), 4.76 (q, J = 7 Hz, 1 H), 7.30 (m, 8 H), 7.90 (m, 2 H); IR (NaCl) 3060, 3027, 2973, 2925, 2880, 1635, 1579, 1496, 1448, 1375, 1286, 1270 cm^{-1}. The ratio of racemic to meso isomers was 4. The optical activity of **18** was found to be $[\alpha]^{28}_D$ −3.50° (*c* 0.23, CCl_4), which corresponds to 1.9% ee, calculated on the basis of $[\alpha]^{28}_D$ −188.9° (*c* 2.86, CCl_4). On the other hand **19** showed $[\alpha]^{28}_D$ +6.6° (*c* 0.33, CCl_4), which corresponds to 6.6% ee calculated on the basis of $[\alpha]^{28}_D$ +91.8° (*c* 0.61, CCl_4). The similar reaction of **17** at 50 °C gave **18** and **19** in 17% and 24% yields, respectively, and the ratio of racemic to meso isomers was 3.6. The optical activity of **18** was found to be $[\alpha]^{28}_D$ −91.2° (*c* 0.21, CCl_4), which corresponds to 48% ee calculated on the basis of $[\alpha]^{28}_D$ −188.9° (*c* 2.86, CCl_4). On the other hand, **19** showed $[\alpha]^{28}_D$ +9.5° (*c* 0.35, CCl_4), which corresponded to 10% ee calculated on the basis of $[\alpha]^{23}_D$ +91.8° (*c* 0.61, CCl_4).

Palladium-Catalyzed Racemization of (*S*)-(−)-α-Phenylethylamine (17). A mixture of (*S*)-(−)-α-phenylethylamine (1.06 g, 8.75 mmol) and palladium black (0.05 g, 0.47 mmol) in a 25-mL round-bottom flask was stirred at 50 °C (or 100 °C) under argon. Aliquots of the reaction mixture were collected in the course of the reaction at 15, 45, 105, 165, and 225 min. The conversion of **17** was determined by GLC (10% SE-30, 200 °C), with *n*-tetradecane as internal standard. The optical rotation of **17**, which was purified by preparative GLC, was determined.

Monitoring the Palladium Catalyzed Reaction of (*S*)-(−)-α-Phenylethylamine (17). A mixture of (*S*)-(−)-α-phenylethylamine (**17**) (1.19 g, 9.82 mmol) and palladium black (0.05 g, 0.5 mmol) was reacted with stirring under argon at 100 °C. Aliquots of the reaction mixture were taken at 30, 60, 90, 120, 150, 180, and 240 min and analyzed with GLC (10% SE-30, 200 °C), with tetradecane as internal standard. The results are shown in Figure 2.

(*S*)-(−)-*N*-(Methylbenzylidene)-α-methylbenzylamine (19). A solution of (*S*)-(−)-α-phenylethylamine (2.0 g, 16.5 mmol; $[\alpha]^{24}_D$ −38.4°, which corresponded to 96% optical purity calculated on the basis of $[\alpha]^{23}_D$ −40.0°), freshly distilled acetophenone (2.0 g, 16.6 mmol), and a catalytic amount of *p*-toluenesulfonic acid in benzene (30 mL) was refluxed under nitrogen, while water was continuously removed by means of a Dean–Stark trap. The reaction mixture was cooled with an ice bath, washed with 10 mL of a dilute ice-cold sodium bicarbonate solution and twice with an ice-cold saturated aqueous NaCl solution, and then dried over $MgSO_4$. Benzene was removed at reduced pressure, and Kugelrohr distillation gave a slightly yellow oil (1.9 g, 51%); bp 120 °C (0.2 mmHg); $[\alpha]^{23}_D$ −91.8° (*c* 0.61, CCl_4) (lit.[84a] $[\alpha]^{23}_D$ −98.4° (*c* 5.59, Bz)); ^1H NMR (CCl_4) δ 1.25 (d, J = 7.0 Hz, 3 H), 2.20 (s, 3 H), 4.75 (q, J = 7.0 Hz, 1 H), 7.30 (m, 8 H) 7.90 (m, 2 H). Anal. ($C_{16}H_{17}N$) C, H, N. The control experiment showed that (*S*)-(−)-**19** did not undergo racemization upon treatment with palladium at 100 °C. Thus, the treatment of (*S*)-(−)-**19** ($[\alpha]^{26}_D$ 82.0° (*c* 1.10, EtOH)) with palladium black at 100 °C for 5 h gave imine **19** exclusively. Preparative GLC showed that **19** had $[\alpha]^{26}_D$ 83.0° (*c* 0.52, EtOH), indicating that **19** retained its optical activity.

(*S,S*)-α,α'-Dimethyldibenzylamine [(*S,S*)-18]. This compound was prepared by the hydrogenation of the Shiff base (*S*)-(−)-**19** obtained above by using 10% palladium on charcoal according to Harada's method,[34a] $[\alpha]^{28}_D$ −188.9° (*c* 2.89, CCl_4).

(*S*)-(−)-*N*-Phenylethylformamide (20). Into a glass-covered autoclave (10 mL) were placed palladium black (0.05 g, 0.47 mmol), (*S*)-(−)-**17** (1.045 g, 8.62 mmol), and methanol (2 mL), and this was charged with carbon monoxide (70 kg/cm^2). The autoclave was heated with shaking at 150 °C for 22 h. After cooling, the reaction mixture was collected and filtered off. The Kugelrohr distillation gave (*S*)-(−)-*N*-phenylethylformamide (**20**) in 20% yield. The sample collected by preparative GLC showed the following: $[\alpha]^{28}_D$ −175.1° (*c* 0.86, CCl_4) (lit.[43] $[\alpha]_D$ −178°); ^1H NMR ($CDCl_3$) δ 1.36 (d, J = 7.0 Hz, 3 H), 4.85 (q, J = 7.0 Hz, 1 H), 7.13 (s, 5 H), 7.78 (br s, 1 H); IR (NaCl), 3265, 3050, 2978, 2935, 2875, 1660 (C=O) 1535, 1495, 1452, 1382, 1240 cm^{-1}. When a similar reaction was carried out in the absence of CO at 150 °C for 7 h, amine **17** was converted (52%) to amine **18** and amine **19** in 25% and 17% yields, respectively.

(*S*)-(−)-α-Phenylethylamine-α-d_1 (17-α-d_1). Acetophenone oxime-*O*-d_1, which was prepared from protiooxime and deuterium oxide by Cram's method, (calculated deuterium content was over 99.5%), was reduced on a 54-g scale by sodium and acetic acid-*O*-d_1.[29] (±)-α-Phenylethylamine-α-d_1 was obtained in 49% yield, bp 70–75 °C (10 mmHg). The amine (23 g) was resolved upon treatment with α-tartaric

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acid to give 7.1 g (31%) of (*S*)-(−)-α-phenylethylamine-α-d_1: $[\alpha]^{29}_D$ −41.12° (*c* 156, benzene); ^{1}H NMR ($CDCl_3$) δ 1.38 (s, 3 H), 1.45 (br s, 2 H), 7.30 (s, 5 H). The NMR analysis showed that the methyne proton was deuteriated ca. 100%.

DL-α-**Phenylethylamine-*N*-d_2 (17-*N*-d_2)** was prepared by treating a solution of the protic amine (3.0 g, 2.5 mmol) in dry ether (30 mL) with 1 mL of deuterium oxide (99.8%), until the calculated deuterium content was ca. 100%; ^{1}H ($CDCl_3$) δ 1.32 (d, 3 H, *J* = 7.0 Hz), 4.03 (q, 1 H), 7.25 (s, 5 H).

Competitive Reaction of Primary Amines toward Benzylamines. A mixture of two amines among *p*-methylaniline, *p*-chloroaniline, *p*-nitroaniline, and hexylamine (20 mmol each), benzylamine (4 g, 37 mmol), and palladium catalyst (0.20 g, 1.9 mmol) was allowed to react at 90 °C for 10 h. After filtration of the catalyst, the reaction mixture was subjected to GLC analysis (microwax or SE-30). The products were established by comparison of their spectral data with those of authentic samples. For example, for a mixture of benzylamine (4.0 g), *p*-methylaniline (2.14 g, 0.02 mol), *p*-chloroaniline (2.25 g, 0.02 mol), palladium catalyst (0.20 g) at 90 °C for 10 h, the GLC analysis (SE-30, 160 °C) showed that besides *N*-benzylidenebenzylamine, *N*-benzylidene-*p*-chloroaniline (bp 45 °C (2 mmHg)) and *N*-benzylidene-*p*-methylaniline (bp 130 °C (2 mmHg)) were obtained, and the relative ratio of the latter products was 1.1 ± 0.1 by using an internal standard. The authentic Schiff bases were prepared independently. The other relative product ratios are as follows: $CH_3C_6H_4N{=}CHPh/ClC_6H_4N{=}CHPh$, 1.1 ± 0.1; $C_6H_{11}N{=}CHPh/ClC_6H_4N{=}CPh$, 1.7 ± 0.1; $C_6H_{11}N{=}CHPh/O_2NC_6H_4N{=}CHPh$, 1.9 ± 0.1.

(*S*)-(+)-Butylamine (23). This compound was resolved upon treatment with tartaric acid; $[\alpha]^{28}_D$ +9.36° (*c* 3.75, CCl_4) (lit.[44] $[\alpha]^{20}_D$ +7.80° (neat)).

Palladium-Catalyzed Reaction of (*S*)-(−)-α-Phenylethylamine (17) with (*S*)-(+)-*sec*-Butylamine (23). In order to know the reaction conditions under which α-phenylethylamine is activated with palladium exclusively, the palladium-catalyzed reactions of **17** and **23** were checked. The conversions of **17** after 5 h were 59% at 50 °C and 100% at 100 °C, while those of **23** after 15 h were 0% at 100 °C, 49% at 160 °C, 79% at 180 °C, and 87% at 200 °C. Therefore, we chose 100 °C for activation of **17** exclusively. A mixture of palladium black (0.099 g, 0.93 mmol), (*S*)-(−)-α-phenylethylamine (**17**, 0.218 g, 1.80 mmol), and (*S*)-(+)-*sec*-butylamine (**23**, 1.05 g, 14.3 mmol) was stirred at 100 °C for 5 h in a sealed tube under argon. The reaction mixture was filtered, and the products were analyzed by GLC. *N*-*sec*-Butyl-α-methylbenzylamine (**24**) and (*S*)-(+)-*N*-(methylbenzylidene)-*sec*-butylamine (**25**) were isolated by preparative GLC and identified by comparison of their spectral data with those of authentic samples. The GLC analysis showed that **24** and **25** were formed in 38% and 51% yields, respectively. The latter product shows $[\alpha]^{27}_D$ +53.8° (*c* 0.63, CCl_4], which corresponds to 93% optical purity calculated on the basis of the $[\alpha]_D$ value of the sample derived from (*S*)-(+)-**24** ($[\alpha]^{26}_D$ +57.6°) and acetophenone. GLC analysis using a capillary column (10% SE-30, 30 m) showed that amine **24** consisted of *S*,*S* and *S*,*R* isomers in the ratio 53:47. (*S*,*S*)-**24**: ^{1}H NMR (CCl_4) δ 0.86 (q, *J* = 7.0 Hz, 3 H), 0.97 (d, *J* = 7.0 Hz, 3 H), 1.29 (d, *J* = 7.0 Hz, 3 H), 1.31 (m, 2 H), 1.80 (br s, 1 H), 2.36 (tq, *J* = 7.0 Hz, *J* = 7.0 Hz, 1 H), 3.83 (q, *J* = 7.0 Hz, 1 H), 7.20 (s, 5 H). (*S*,*R*)-**24**: mass spectrum, *m*/*e* 177, 162, 148. ^{1}H NMR (CCl_4) δ 0.86 (q, *J* = 7.0 Hz, 3 H), 0.97 (d, *J* = 7.0 Hz, 3 H), 1.28 (d, *J* = 7.0 Hz, 3 H), 1.31 (m, 2 H), 1.80 (br s, 1 H), 2.37 (tq, *J* = 7.0 Hz, *J* = 7.0 Hz, 1 H), 3.86 (q, *J* = 7.0 Hz, 1 H), 7.20 (s, 5 H); IR (NaCl) 3330, 3080, 3045, 2975, 2940, 1500, 1460, 1376 cm^{-1}. (*S*)-(+)-**25**: ^{1}H NMR (CCl_4) δ 0.83 (t, *J* = 7.0 Hz, 3 H), 1.11 (d, *J* = 7.0 Hz, 3 H), 1.54 (m, 3 H), 2.18 (s, 3 H), 3.54 (q, *J* = 7.0 Hz, 1 H), 7.24 (m, 3 H), 7.74 (m, 2 H).

***N*-*sec*-Butyl-α-methylbenzylamine (24)** was prepared by the reduction of the Schiff base **25** with $LiAlH_4$ according to Charle's method.[45] The product consists of *S*,*S* and *S*,*R* amines, $[\alpha]^{25}_D$ ±14.8° (*c* 0.12, CCl_4).

(*S*)-(+)-*N*-(Methylbenzylidene)-*sec*-butylamine (25). A solution of 1.03 g (14 mmol) of *sec*-butylamine ($[\alpha]^{28}_D$ +9.36 (*c* 3.15, CCl_4)) and 1.70 g (14.2 mmol) of acetophenone in benzene (15 mL) containing a catalytic amount of *p*-toluenesulfonic acid was refluxed under nitrogen for 34 h, while water was continuously removed by means of a Dean–Stark trap. The reaction mixture was cooled with an ice bath, washed quickly with 5 mL of an ice-cold $NaHCO_3$ solution and twice with an ice-cold saturated aqueous NaCl, and then dried over $MgSO_4$. After removal of benzene at reduced pressure, Kugelrhor distillation under reduced pressure gave a mixture of the product amine and acetophenone. Preparative GLC gave (*S*)-(+)-*N*-(methylbenzylidene)-*sec*-butylamine (**25**): $[\alpha]^{26}_D$ +57.6° (*c* 0.58, CCl_4); ^{1}H NMR (CCl_4), 0.85 (t, *J* = 7 Hz, 3 H), 1.09 (d, *J* = 7 Hz, 3 H), 1.52 (q, *J* = 7 Hz, 2 H), 2.14 (s, 3 H), 3.55 (q, *J* = 7 Hz, 1 H), 7.20 (m, 3 H), 7.70 (m, 2 H).

Reaction of *N*-Benzylidenemethylamine and *N*-Methylbenzylamine. A mixture of *N*-benzylidenemethylamine (1.0 g) and *N*-methylbenzylamine (1.0 g) was stirred at 120 °C for 10 h. Distillation (115 °C (4 mmHg)) gave 1.7 g of the product mixture. Preparative GLC (Apieson L) gave *N*-benzylidenebenzylamine in 73% yield: mass spectrum, *m*/*e* 195 (M^+); ^{1}H NMR ($CDCl_3$) δ 4.68 (s, 2 H, $PhCH_2$), 7.11–7.83 (m, 10 H, Ph), 8.21 (s, 1 H, CH=N). Anal. ($C_{14}H_{13}N$) C, H, N. Next, a mixture of *N*-benzylidenemethylamine (1.0 g), *N*-methylbenzylamine (1.0 g), and palladium (0.10 g) was heated with stirring at 120 °C for 10 h. GLC analysis is showed that the product mixture consisted of *N*-methyldibenzylamine and *N*-benzylidenbenzylamine in the ratio of 60:40.

Hydrogenation of *N*-Phenylbenzamidine (31). Into a 10-mL stainless steel autoclave fitted with a magnetic stirring bar were placed palladium black (4.2 mg, 0.04 mmol), *N*-phenylbenzamidine (**31**, mp 118–119 °C (lit.[46] mp 118–119 °C), 75.3 mg, 0.38 mmol), and THF (1 mL). The autoclave was charged with hydrogen (32 kg/cm^2) and then heated with stirring at 120 °C for 6 h. After cooling, the products were analyzed carefully with GLC (10% Carbowax-20M, 200 °C with tetradecane as internal standard. The conversions of *N*-phenylbenzamide was 83%. The products were toluene (74%), aniline (78%), benzylamine (4%), and *N*-benzylaniline (3%). As a control experiment, the hydrogenolysis of *N*-benzylideneaniline was carried out in THF under hydrogen (1 atm) at 50 °C. The reaction products were monitored. At the early stage *N*-benzylaniline was formed quantitatively, then as *N*-benzylaniline decreased, the amount of aniline and toluene increased. The product yields of *N*-benzylaniline, aniline, and toluene at certain times were as follows: after 0.5 h, *N*-benzylaniline was obtained in 99%; 1 h, *N*-benzylaniline (98%), aniline (2%); 2.5 h, *N*-benzylaniline (93%), aniline (5%), toluene (2%); 3.5 h, *N*-benzylanilin (84%), aniline (21%), toluene (7%); 5.5 h, *N*-benzylaniline (64%), aniline (31%), toluene (21%).

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Registry No. 1 (R′ = 2-furyl; R^2 = furfuryl), 19377-82-3; **1** (R′ = propyl; R^2 = cyclopropylcarbinyl), 86013-59-4; **1** (R′ = C_6H_5; R^2 = CH_3), 622-29-7; **3**, 24715-90-0; **3** (nitrile), 35543-25-0; **4**, 1004-83-7; **5**, 41726-75-4; **6**, 503-29-7; **7**, 151-56-4; **7** (1,2-didehydro), 157-16-4; **8**, 54262-75-8; **9**, 6788-85-8; **10**[2,2], 111-40-0; **10**[2,3], 13531-52-7; **10**[3,3], 56-18-8; **10**[8,8], 39202-36-3; **11**[2,2,2], 112-24-3; **11**[2,2,3], 70209-08-4; **11**[2,3,3], 41240-14-6; **11**[3,3,3], 4605-14-5; **12**, 22385-49-5; **13**, 25099-77-8; **14**, 86013-64-1; **15**, 716-79-0; **16**, 739-88-8; (±)-**17**, 618-36-0; (±)-**17**-α-d_1, 86013-66-3; (*S*)-(−)-**17**, 2627-86-3; (*S*)-(−)-**17**-α-d_1, 86087-18-5; (DL)-**17**-*N*-d_2, 86013-67-4; (±)-**18**, 21003-56-5; *meso*-**18**, 21003-57-6; (*S*,*S*)-**18**, 56210-72-1; (±)-**19**, 40636-56-4; (*S*)-(−)-**19**, 40636-57-5; (*S*)-(−)-**20**, 19145-06-3; (*S*)-(+)-**23**, 513-49-5; (*S*,*S*)-**24**, 86013-68-5; (*S*,*R*)-**24**, 86013-69-6; (*S*)-(+)-**25**, 86013-70-9; **31**, 1527-91-9; Pd, 7440-05-3; $Pd(OAc)_2$, 3375-31-3; $Pd(PPh_3)_4$, 14221-01-3; $Ni(OAc)_2$, 373-02-4; $RuH_2(PPh_3)_4$, 19529-00-1; $RuCl_2(PPh_3)_3$, 15529-49-4; $RuCl_3$, 10049-08-8; $Ru_3(CO)_{12}$, 15243-33-1; $RhCl(PPh_3)_3$, 14694-95-2; $RhCl_3$, 10049-07-7; $Rh_6(CO)_{16}$, 28407-51-4; Ru, 7440-18-8; Rh, 7440-16-6; Ni, 7440-02-0; $PhCH_2NH(CH_2)_2NH_2$, 4152-09-4; $PhCH_2NH(CH_2)_2NH_2$·picrate, 86013-60-7; $PhCH_2NH(CH_2)_3NH_2$, 13910-48-0; $PhCH_2NH(CH_2)_3NH_2$·picrate, 86013-61-8; $PhCH_2NH(CH_2)_4NH_2$, 29867-04-7; $PhCH_2NH(CH_2)_4NH_2$·picrate, 86013-62-9; $H_2N(CH_2)_8NH_2$, 373-44-4; $PhCH_2NH(CH_2)_6NH_2$, 25079-94-1; $H_2N(CH_2)_3NH_2$, 109-76-2; $H_2N(CH_2)_2NH_2$, 107-15-3; hexylamine, 111-26-2; *N*-methyldibenzylamine, 102-05-6; difurfurylamine, 18240-50-1; 4-chlorobutyronitrile, 628-20-6; pyrrolidine, 123-75-1; butyrolactam methyl ether, 5264-35-7; 1,4-dibromobutane, 110-52-1; pyrrolidine·Li, 4439-90-1; 1,5-dipiperidinopentane, 24362-44-5; *N*-benzyl-*N*′-benzylidene-1,6-hexanediamine, 86013-63-0; tris(3-aminopropyl)amine, 4963-47-7; allylamine, 107-11-9; *N*-methylbenzylamine, 103-67-3; *o*-phenylenediamine, 95-54-5; acetophenone, 98-86-2; β-cyanoethylamine, 151-18-8; acetophenone oxime-*O*-d_1, 86013-65-2; *p*-methylaniline, 106-49-0; *p*-chloroaniline, 106-47-8; *p*-nitroaniline, 100-01-6; benzylamine, 100-46-9.

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