Rhodium Catalyzed Hydrogenation of Quinolines and Isoquinolines under Water-Gas Shift Conditions

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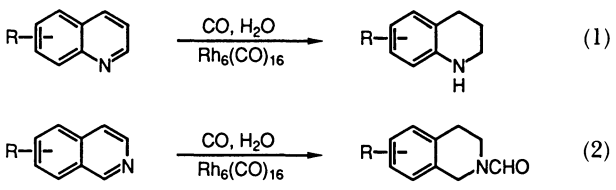
Wide variety of quinolines and isoquinolines can be hydrogenated selectively in the nitrogen-containing ring by means of carbon monoxide and water in the presence of catalytic amount of rhodium carbonyl cluster. These reactions provide a useful method for the preparation of 1,2,3,4-tetrahydroquinolines and 1,2,3,4-tetrahydroisoquinolines which are key intermediates for the synthesis of isoquinoline alkaloids and other biologically active nitrogen compounds.

Polynuclear nitrogen heteroaromatic compounds, such as quinolines and isoquinolines are much contained in coal, oil shale, and tar sands.[1] Selective hydrogenation of these nitrogen heteroaromatics provides potential means for utilization of these natural resources, and various synthetic key intermediates can be obtained. 1,2,3,4-Tetrahydroquinoline derivatives are synthetic intermediates for drugs,[2] agrochemicals,[3] and dyes,[4] while 1,2,3,4-tetrahydroisoquinoline derivatives are useful precursors of isoquinoline alkaloids.[5] Water-gas shift reactions are of importance in view of energy problem because hydrogen can be generated from water and carbon monoxide, which is readily available from low-grade carbonaceous materials such as coal, oil shale, tar sands, and lignite.[6] The metal hydride species which are formed as intermediates of water-gas shift reactions, can be used directly as reducing agents. Therefore, the reduction of various substrates such as nitroarenes, carbonyl compounds, and α,β-unsaturated ketones and nitriles have been studied under water-gas shift conditions.[7]

We have found that hydrogenation of wide variety of quinolines and isoquinolines can be performed selectively under water-gas shift conditions as depicted by Eqs. 1 and 2.[8] The results are different from those obtained from the catalytic hydrogenations of nitrogen aromatics under molecular hydrogen.[9,10] Reduction of nitrogen heteroaromatics using carbon monoxide and water has been studied. Laine[11] reported that the reduction of pyridine to piperidine was catalyzed by rhodium complex. Fish and Kaezs reported that $Fe(CO)_5$[12,13] and $Mn_2(CO)_8(PBu_3)_2$[12] catalyzed the hydrogenation reaction in the presence of base such as KOH. As compared with these reports, we describe the full details of our reactions, which can be utilized for the selective hydrogenation of various types of substituted quinolines and isoquinolines.



Results and Discussion

Hydrogenation of Quinolines. Quinolines are hydrogenated selectively in the nitrogen containing ring to give 1,2,3,4-tetrahydroquinolines under water-gas shift conditions. The catalytic activity of various metal carbonyls was examined with respect to the reaction of quinoline (**1**). The representative results are shown in Table 1. Rhodium carbonyl cluster $Rh_6(CO)_{16}$ gave the best results. The exclusive product detected during the reaction was 1,2,3,4-tetrahydroquinoline (**2**), and neither 5,6,7,8-tetrahydroquinoline nor decahydroquinoline were obtained. Rhodium clusters such as $Rh_4(CO)_{12}$ and $[Rh(COD)Cl]_2$ and ruthenium clusters such as $Ru_3(CO)_{12}$ gave good results. Other metal carbonyls such as $W(CO)_6$ and $Fe(CO)_5$ did not produce the hydrogenated product under the present conditions. Although $Fe(CO)_5$ has been reported to be an active catalyst for the hydrogenation of quinoline in the presence of KOH,[13] the catalytic activity was not

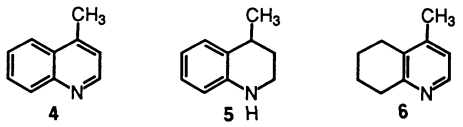
Table 1. Catalytic Activity of Various Metal Complexes for the Hydrogenation of **1**[a]

Entry	Catalyst	Amount/mol%	Convn.[b]/%	Yield[b]/%
1	$Rh_6(CO)_{16}$	0.81	100	97
2	$Rh_4(CO)_{12}$	1.2	80	75
3	$[Rh(COD)Cl]_2$	2.4	65	62
4	$Ru_3(CO)_{12}$	1.6	70	65
5	$W(CO)_6$	3.3	0	0
6	$Fe(CO)_5$	3.3	0	0

a) A mixture of quinoline (2.31 mmol), water (0.5 ml), and catalyst in 2-methoxyethanol (2 ml) was heated at 150 °C for 12 h under the pressure of CO (56 kg cm^{-2}). b) Determined by GLC analysis.

observed under the present conditions. The addition of bases enhances the catalytic activity of transition metal carbonyls under water-gas shift conditions.[14] The key point of the present reaction is that quinolines behave as bases to enhance the hydrogenation and are also reduced regioselectively in the nitrogen-containing ring. Most of the solvents examined such as, 2-methoxyethanol, toluene, dioxane, and dimethylformamide gave good results; however, chloroform retarded the reaction. Without a solvent **2** was obtained in low yields.

The representative results of the hydrogenation of quinolines under water-gas shift conditions are summarized in Table 2. In general, 1,2,3,4-tetrahydroquinolines are obtained selectively under the present reaction conditions. Substituted quinolines have been recovered under the conditions using $Fe(CO)_5$ catalyst.[13] It is noteworthy that 4-methylquinoline (**4**) can be converted into 4-methyl-1,2,3,4-tetrahydroquinoline (**5**) selectively (Entry 3) under the present water-gas shift conditions. In the nickel catalyzed hydrogenation of methyl substituted quinolines with molecular hydrogen, substituent on the benzene ring leads to exclusive formation of 1,2,3,4-tetrahydroquinolines, while substituent loading of the pyridine ring favors the formation of 5,6,7,8-tetrahydro compounds.[15] Typically, tetrahydroquinoline **5** was obtained selectively in 91% yield under the present reaction conditions. However, catalytic hydrogenation of **4** afforded a mixture of **5** and 4-methyl-5,6,7,8-tetrahydroquinoline (**6**) in 33% and 66% yields, respectively. The $Rh_6(CO)_{16}$ catalyzed hydrogenation of **4** under hydrogen (10 kg cm^{-2}) also gave **6** exclusively



(50% conversion). Moreover, the hydrogenation of 2,4-dimethylquinoline (**10**) under the present conditions gave 2,4-dimethyl-1,2,3,4-tetrahydroquinoline (**11**) exclusively in 89% yield (Entry 6), while the hydrogenation of **10** with nickel catalyst under molecular hydrogen gave **11** only in 20% yield along with 80% of 5,6,7,8-tetrahydroquinoline.[15] The cis/trans ratio of

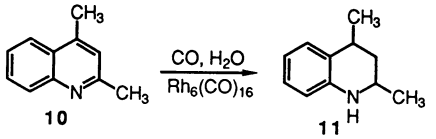
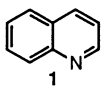
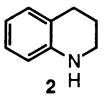
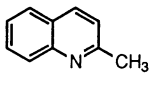
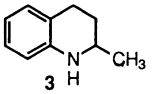
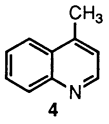
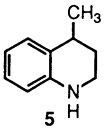
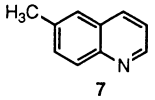
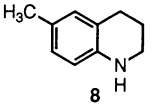
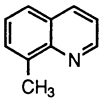
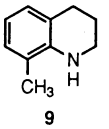
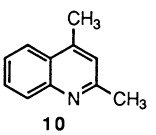
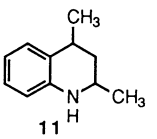
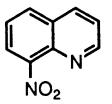
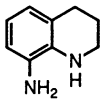
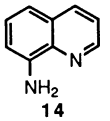
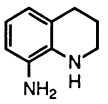
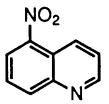
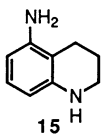
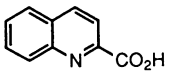
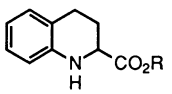
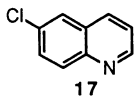
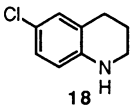
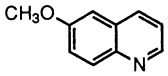
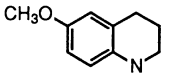


Table 2. Hydrogenation of Methyl Substituted Quinolines under Water-Gas Shift Conditions[a]

Entry	Quinoline	Tetrahydroquinoline	Yield[b]/%
1			97
2			95
3			91
4			96
5			90
6			89[c]

a) A mixture of quinoline (2.31 mmol), $Rh_6(CO)_{16}$ (0.0188 mmol), and water (0.5 ml) in 2-methoxyethanol (2 ml) was heated at 150 °C for 24 h under the pressure of CO (56 kg cm^{-2}). b) Isolated yield. c) *cis*-**11**/*trans*-**11**=7/3.

Table 3. Hydrogenation of Substituted Quinolines under Water-Gas Shift Conditions[a)]

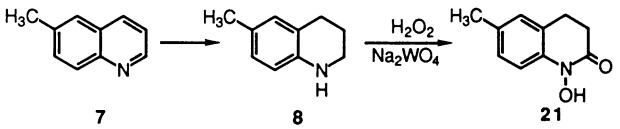
Entry	Quinoline	Tetrahydroquinoline	Yield[b)]/%
1	 **12**	 **13**	81[c)]
2	 **14**	 **13**	84
3		 **15**	85
4		 **16** R = $CH_2CH_2OCH_3$	61
5	 **17**	 **18**	91[d)]
6	 **19**	 **20**	94

a) A mixture of quinoline (2.31 mmol), $Rh_6(CO)_{16}$ (0.0188 mmol), and water (0.5 ml) in 2-methoxyethanol (2 ml) was heated at 150 °C for 24 h under the pressure of CO (56 kg cm^{-2}). b) Isolated yield. c) Reaction time was 48 h. d) Reaction time was 12 h.

11 was determined to be 7/3 on the basis of ^1H and ^{13}C NMR analyses.

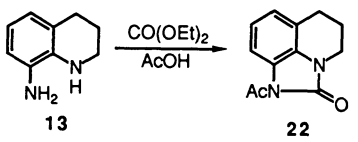
Quinolines bearing other functional groups also undergo the hydrogenation on the pyridine ring to give the corresponding 1,2,3,4-tetrahydroquinolines. These results are summarized in Table 3. 8-Nitroquinoline (**12**) was reduced under the rhodium catalyzed water-gas shift conditions (48 h) to give 8-amino-1,2,3,4-tetrahydroquinoline (**13**) exclusively (Entry 1), while the same reaction of **12** for shorter time (24 h) gave **13** and 8-aminoquinoline (**14**) in 61% and 16% yields, respectively. 8-Aminoquinoline **14** was also converted into **13** highly efficiently (Entry 2). Therefore, the reduction of the nitro group of **12** proceeds faster than that of the pyridine ring. 5-Aminoquinoline was also converted into 5-amino-1,2,3,4-tetrahydroquinoline (**15**) (Entry 3). The reaction of 2-quinolinecarboxylic acid afforded 2-methoxyethyl 1,2,3,4-tetrahydroquinoline-2-carboxylate (**16**) (Entry 4), which was formed by hydrogenation followed by esterification with 2-methoxyethanol. 6-Chloroquinoline (**17**) was converted into 6-chloro-1,2,3,4-tetrahydroquinoline (**18**) selectively without cleavage of carbon–halogen bond (Entry 5). By using this product, various functional groups can be introduced at 6-position of tetrahydroquinolines.

The tetrahydroquinolines thus obtained are valuable synthetic intermediates. Tungstate catalyzed oxidation of tetrahydroquinolines with hydrogen peroxide gives the corresponding hydroxamic acids,[16)] which show antibacterial activity[17)] and also are precursors of biologically active compounds, such as 3,4-dihydrocarbostyril compounds. Typically, the treatment of tetrahydroquinoline **8**, which was obtained from **7** in 96% yield, with aqueous 30% hydrogen peroxide in the presence of catalytic amount of Na_2WO_4 gave 1-hydroxy-6-methyl-1,2,3,4-tetrahydroquinolin-2-one (**21**)



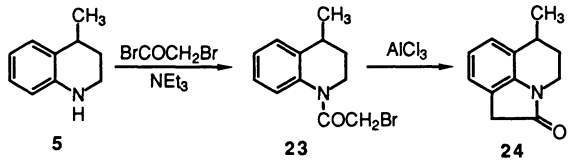
7 **8** **21**

in 82% yield. Amino-1,2,3,4-tetrahydroquinolines are useful precursors of hair coloring compositions[4)] and fungicides.[18)] Treatment of **13** with diethyl carbonate in acetic acid gave 1,2,5,6-tetrahydroimidazoquinolin-2-one **22**.[18)] Furthermore, the reaction of **5** with



13 22

bromoacetyl bromide followed by intramolecular alkylation gives 1,2,5,6-tetrahydropyrroloquinolin-2-one **24**, which has pharmacological activity and has been used as CNS depressant agents.[19]



5 23 24

Next, the reactivity of four 6-substituted quinolines, that is, quinoline (**1**), 6-methylquinoline (**7**), 6-chloroquinoline (**17**), and 6-methoxyquinoline (**19**) was compared. The results are listed in Table 4. Quinolines **1** and **17** were reduced completely within 5 h; however, the conversion of quinolines **7** and **19** were only 30% and 35% after 5 h and 70% and 80% after 10 h, respectively. The rate difference seems to reflect electronic requirement of substituents at the 6-position. Thus, electron withdrawing substituents such as chloro group accelerate the reaction, while electron donating substituents retard the reactivity.

Table 4. Reactivity of Quinolines **1**, **7**, **17**, and **19** for the Hydrogenation[a]

Run time	Convn. of quinolines[b]/%			
	1	**17**	**7**	**19**
5 h	>98	>98	30	35
12 h			70	80
24 h			>98	>98

a) A mixture of quinoline (2.31 mmol), $Rh_6(CO)_{16}$ (0.0188 mmol), and water (0.5 ml) in 2-methoxyethanol (2 ml) was heated at 150 °C under the pressure of CO (56 kg cm^{-2}). b) Determined by 270 MHz ^1H NMR analysis.

Hydrogenation of Isoquinolines. Isoquinolines were converted into *N*-formyl-1,2,3,4-tetrahydroisoquinolines under the same conditions. Typically, the reaction of isoquinoline gave *N*-formyl-1,2,3,4-tetrahydroisoquinoline (**25**) in 69% isolated yield. When the same reaction was carried out for shorter reaction time, a mixture of **25** and 1,2,3,4-tetrahydroisoquinoline (**26**) was obtained, indicating that initial formation of **26** and subsequent *N*-formylation. The *N*-formylation of tetrahydroisoquinoline **26** may be due to higher basicity of nitrogen of **26** in comparison with **2**. Indeed, **25** was obtained from **26** in 76% yield under the same conditions. The representative results of the hydrogenation of isoquinolines are summarized in Table 5. It is noteworthy that benzyloxy group torelates the reaction, although benzyloxy group is readily removed by reductive cleavage under usual hydrogenation conditions. Thus, 6-benzyloxy-7-methoxyisoquinoline was converted into the corresponding *N*-formyl-6-benzyloxy-7-methoxy-1,2,3,4-tetrahydroisoquinoline (**27**) (Entry 2).

N-Formyltetrahydroisoquinolines thus obtained can be readily converted into *N*-methyltetrahydroisoquinolines upon treating with $LiAlH_4$. Thus, the reduction of **27** with $LiAlH_4$ gave 6-benzyloxy-7-methoxy-*N*-methyl-1,2,3,4-tetrahydroisoquinoline (**29**) selectively in 83% yield. *N*-Formyl group on 1,2,3,4-tetrahydroisoquinolines can be removed readily by acid catalyzed hydrolysis. Thus, when *N*-formyl compound **27** was allowed to react with sulfuric acid in methanol (1/9) at

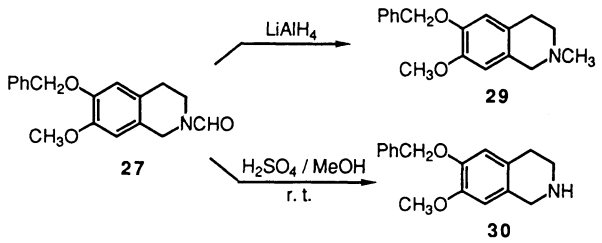
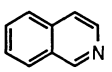
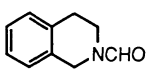
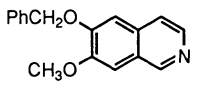
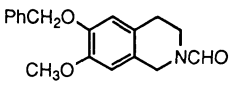
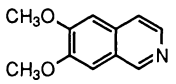
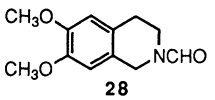


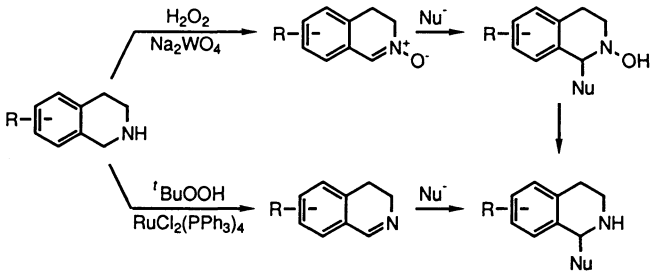
Table 5. Hydrogenation of Isoquinolines under Water-Gas Shift Conditions[a]

Entry	Isoquinoline	Tetrahydroisoquinoline	Yield[b]/%
1		 **25**	69
2		 **27**	65
3		 **28**	66

a) A mixture of isoquinoline (2.31 mmol), $Rh_6(CO)_{16}$ (0.0188 mmol), and water (0.5 ml) in 2-methoxyethanol (2 ml) was heated at 150 °C for 24 h under the pressure of CO (56 kg cm^{-2}). b) Isolated yield.

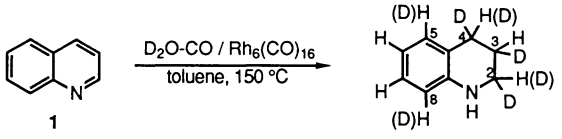
room temperature, 6-benzyloxy-7-methoxy-1,2,3,4-tetrahydroisoquinoline (**30**) was obtained in 95% yield. 6,7-Dimethoxy-1,2,3,4-tetrahydroisoquinoline (**31**) was also obtained upon hydrolysis of *N*-formyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (**28**) in 96% yield.

The tetrahydroisoquinolines thus obtained are quite useful synthetic intermediates. Introduction of substituents at position 1 of tetrahydroisoquinolines can be performed readily by using our recently developed methods, that is, oxidation of secondary amines to give either imines[20] or nitrones[21] and subsequent treatment of these intermediates with nucleophiles as shown in Scheme 1.



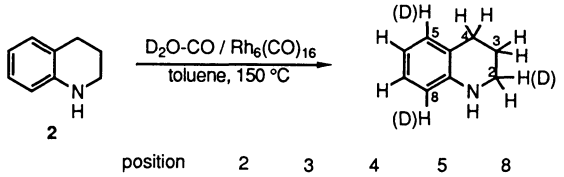
Scheme 1.

Mechanisms. The hydrogenation of quinoline **1** using deuterium oxide in place of water in toluene was examined. The product of deuterated 1,2,3,4-tetrahydroquinoline was analyzed by 270 MHz ^{1}H NMR spectroscopy, and the results were shown in Scheme 2. The product obtained after 5 h had 1.2 deuteriums at position 2, 1.0 deuterium at position 3, 1.2 deuteriums at position 4, and 0.2 deuterium at each positions 5 and 8. The product obtained after 24 h had 1.7 deuteriums at position 2, 1.0 deuterium at position 3, 1.2 deuteriums at position 4, and 0.9 deuterium at each positions 5 and 8. When 1,2,3,4-tetrahydroquinoline (**2**) was subjected to the same conditions for 5 h, the product had 0.1 deuterium at position 2 and 0.8 deuterium each at positions 5 and 8, and no deuterium incorporation was observed at positions 3 and 4 as shown in Scheme 3. Thus, water must be the hydrogen source in the present hydrogenation reaction, and each 1.0 deuterium was introduced at the positions of 2, 3, and 4. The deuterium incorporation at positions 5 and 8 may be due to the exchange of the aromatic hydrogen of **2** rather than **1**. The deuterium incorporation at positions 5 and 8 in **2** is noteworthy, although specific reason has not been clarified yet. The deuterium incorporation at position 2 in **2** is derived from dehydrogenation–hydrogenation process of **2** via intermediacy imine metal complex.[22,23]



position	2	3	4	5	8
5 h	1.2	1.0	1.2	0.2	0.2
24 h	1.7	1.0	1.2	0.9	0.9

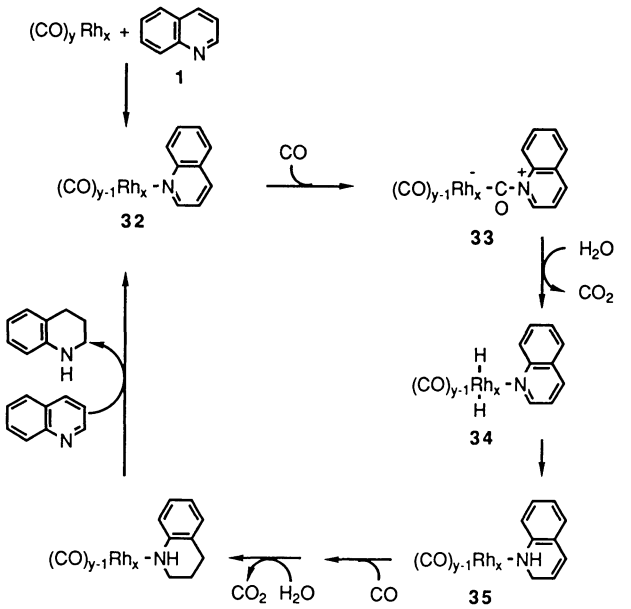
Scheme 2.



position	2	3	4	5	8
5 h	0.1	0	0	0.8	0.8

Scheme 3.

Although the exact nature of the active species still remains unspecified, a hydrido rhodium carbonyl species[24] seems to be the active catalyst. Recently Fish[25] reported that **1** reacts with mononuclear rhodium dication complex to form N-bounded rhodium–quinoline complex, while **2** complexes with π-bonding rather than N-bonding. Laine[26] and Fish[27] isolated ruthenium–quinoline complexes by the reaction of **1** with $Ru_3(CO)_{12}$, and the structure of the complexes has been characterized as triangle of ruthenium atoms with **1** bound to the cluster to the nitrogen and the 2-carbon atoms. The catalytic cycle is rationalized by assuming Scheme 4. The first step is the coordination of quinoline to the rhodium catalyst to give the N-bounded rhodium–quinoline complex **32**. Water-gas shift reactions induced by rhodium and ruthenium catalysts are promoted by amines, and hence amine-coordinated complexes have been considered to be active species.[14a,c] The water-gas shift reaction gives quinoline-coordinated rhodium hydride species **34**. Subsequent intramolecular addition of nitrogen-bounded rhodium hydride to the pyridine ring of



Scheme 4.

quinoline results in regioselective reduction to give **35**, Similar reaction of **35** with carbon monoxide and water gives 1,2,3,4-tetrahydroquinoline along with **32**.

In summary, the rhodium carbonyl cluster catalyzes the hydrogenation of a wide variety of quinolines by means of water and carbon monoxide. The hydrogenation proceeds regioselectively to give 1,2,3,4-tetrahydroquinolines efficiently. Similar treatment of isoquinolines affords the corresponding *N*-formyl-1,2,3,4-tetrahydroisoquinolines.

Experimental

General. All melting points were determined in capillary tubes and are uncorrected. IR spectra were recorded on a Hitachi 215 spectrometer. NMR spectra were obtained on JEOL JNM PMX-60SI (60 MHz for ^{1}H) and JEOL JNM GSX-270 (270 MHz for ^{1}H and 67.9 MHz for ^{13}C) spectrometers; chemical shifts (δ) were expressed in parts per million down field from tetramethylsilane. Analytical GLC evaluations of products mixtures were carried out on Shimadzu GC-9A flame ionization gas chromatograph by using a 1 m×4 mm analytical column (10% SE-30 on 60—80 mesh Uniport HP). Preparative TLC was performed on glass plates coated with Merck silica gel 60 PF_{254} (art. 7747). Mass spectra were obtained on a Hitachi RMS-4 or Shimadzu GCMS-QP1000 mass spectrometers. Elemental analyses were performed on a Yanagimoto MT-3 CHN corder.

Materials. $Rh_6(CO)_{16}$ (Nippon Engelhald Co., Ltd.) and other metal catalysts were commercially available and used as received, except $Fe(CO)_5$ which was distilled prior to use and $Mo(CO)_6$ which was sublimed prior to use. 2-Methoxyethanol was commercially available and used as received. Quinolines and isoquinolines were commercially available and used as received except 8-aminoquinoline, 5- and 8-nitroquinoline,[28] 6-benzyloxy-7-methoxyisoquinoline, and 6,7-dimethoxyisoquinoline[29] which were prepared according to the reported procedure.

Catalytic Activity of Various Metal Complexes. A mixture of quinoline (**1**), metal complex, H_2O (0.5 mL), and 2-methoxyethanol (2 mL) was heated at 150 °C for 12 h in a 10-mL stainless-steel autoclave under the pressure of CO (56 kg cm^{-2}). The conversion of **1** and the yield of 1,2,3,4-tetrahydroquinoline (**2**) were determined by the GLC analysis of the reaction mixture using an internal standard (dodecane). The results with various catalysts are shown in Table 1.

General Procedure for Hydrogenation of Quinolines and Isoquinoline under Water-Gas Shift Conditions. In a 10-mL stainless-steel autoclave equipped with a magnetic stirring bar were placed quinoline (2.31 mmol), $Rh_6(CO)_{16}$ (0.020 g, 0.0188 mmol), H_2O (0.5 mL, 27.8 mmol), and 2-methoxyethanol (2.0 mL). The autoclave was sealed and degassed by three 5 kg cm^{-2} pressurization/depressurization cycles with CO. The autoclave was then charged to 56 kg cm^{-2} of CO and heated with stirring a 150 °C for 24 h. After the autoclave was cooled to room temperature, the pressure was released. The reaction mixture was taken up with chloroform and filtered through a pad of Florisil (3 g, 14×55 mm). After removal of the solvent under reduced pressure, the product was purified by means of silica-gel column chromatography (ca. 5 g, eluents are described below) or Kugelrohr distillation. These results are summarized in Tables 2, 3, and 5.

1,2,3,4-Tetrahydroquinoline (2): Bp 126—127 °C/3 mmHg (1 mmHg≈133.3 Pa) (Kugelrohr); R_f 0.83 (SiO_2, ethyl acetate); ^{1}H NMR ($CDCl_3$, 270 MHz) δ=1.91 (2H, tt, J=6.3 and 5.8 Hz, H^3), 2.74 (2H, t, J=6.3 Hz, H^4), 3.26 (2H, t, J=5.8 Hz, H^2), 3.76 (1H, br-s, NH), 6.43 (1H, d, J=7.4 Hz, H^8), 6.58 (1H, t, J=7.2 Hz, H^6), and 6.90—6.98 (2H, m, H^5 and H^7).

Found: C, 81.26; H, 8.34; N, 10.41%. Calcd for $C_9H_{11}N$: C, 81.16; H, 8.33; N, 10.52%.

2-Methyl-1,2,3,4-tetrahydroquinoline (3): Bp 126 °C/5 mmHg (Kugelrohr); R_f 0.69 (SiO_2, ethyl acetate–hexane=1:4); IR (neat) 3400 (NH), 2940, 2860, 1615, 1500, 1320, and 775 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ=1.19 (3H, d, J=6.3 Hz, CH_3), 1.57 (1H, dddd, J=12.8, 11.4, 9.9, and 5.5 Hz, H^{3a}), 1.91 (1H, dddd, J=12.8, 5.6, 3.5, and 2.9 Hz, H^{3e}), 2.71 (1H, ddd, J=16.4, 5.5, and 3.5 Hz, H^{4e}), 2.83 (1H, J=16.4, 11.4, and 5.6 Hz, H^{4a}), 3.38 (1H, ddq, J=9.9, 6.3, and 2.9 Hz, H^2), 3.60 (1H, br-s, NH), 6.45 (1H, dd, J=8.1 and 1.2 Hz, H^8), 6.59 (1H, ddd, J=7.3, 7.3, and 1.2 Hz, H^6), and 6.90—6.99 (2H, m, H^5 and H^7); ^{13}C NMR ($CDCl_3$, 67.9 MHz) δ=22.6, 26.6, 30.2, 47.2, 114.0, 117.0, 121.1, 126.7, 129.3, and 144.8.

Found: C, 81.36; H, 8.80; N, 9.43%. Calcd for $C_{10}H_{13}N$: C, 81.58; H, 8.90; N, 9.52%.

4-Methyl-1,2,3,4-tetrahydroquinoline (5): Bp 150 °C/5 mmHg (Kugelrohr); IR (neat) 3400 (NH), 2960, 2860, 1610, 1585, 1500, 1360, 1315, 1070, and 740 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ=1.25 (3H, d, J=7.1 Hz, CH_3), 1.62 (1H, dddd, J=12.8, 6.4, 6.4, and 3.8 Hz, H^{3e}), 1.92 (1H, J=12.8, 8.2, 5.3, and 4.2 Hz, H^{3a}), 2.80—2.92 (1H, m, H^4), 3.17 (1H, ddd, J=11.2, 6.4, and 4.2 Hz, H^{2e}), 3.25 (1H, ddd, J=11.2, 8.2, and 3.8 Hz, H^{2a}), 3.75 (1H, br-s, NH), 6.39 (1H, dd, J=7.9 and 1.2 Hz, H^8), 6.59 (1H, ddd, J=7.5, 7.5, and 1.2 Hz, H^6), 6.92 (1H, ddd, J=7.9, 7.5, and 1.2 Hz, H^7), and 7.01 (1H, d, J=7.5 Hz, H^5); ^{13}C NMR ($CDCl_3$, 67.9 MHz) δ=22.6, 29.9, 30.2, 39.0, 114.1, 116.8, 126.5, 126.7, 128.3, and 144.3; mass spectrum (80 eV), m/z (relative intensity) 147 (M^+, 44), 146 (M^+-1, 10), 133 (100), and 118 (26).

Found: C, 81.46; H, 8.95; N, 9.46%. Calcd for $C_{10}H_{13}N$: C, 81.58; H, 8.90; N, 9.52%.

6-Methyl-1,2,3,4-tetrahydroquinoline (8): Bp 144—145 °C/5 mmHg (Kugelrohr); IR (neat) 3350 (NH), 3000, 2900, 2830, 1610, 1510, 1260, and 800 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ=1.87—1.96 (2H, m, H^3), 2.19 (3H, s, CH_3), 2.72 (2 H, t, J=6.5 Hz, H^4), 3.25 (2H, t, J=5.5 Hz, H^2), 3.51 (1H, br-s, NH), 6.38 (1H, d, J=8.5 Hz, H^8), and 6.75—6.78 (2H, m, H^5 and H^7); ^{13}C NMR ($CDCl_3$, 67.9 MHz) δ=20.4, 22.5, 26.9, 42.2, 114.5, 121.6, 126.2, 127.3, 130.1, and 142.4.

Found: C, 81.64; H, 8.80; N 9.44%. Calcd for $C_{10}H_{13}N$: C, 81.58; H, 8.90; N, 9.52%.

8-Methyl-1,2,3,4-tetrahydroquinoline (9): Bp 148—150 °C/5 mmHg (Kugelrohr); R_f 0.79 (SiO_2, ethyl acetate); IR (neat) 3400 (NH), 2930, 2840, 1600, 1490, 1360, 1310, 1270, 1190, 1110, 750, and 730 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ=1.92 (2H, tt, J=6.4 and 5.5 Hz, H^3), 2.05 (3H, s, CH_3), 2.77 (2H, t, J=6.4 Hz, H^4), 3.34 (2H, t, J=5.5 Hz, H^2), 3.60 (1H, br-s, NH), 6.54 (1H, dd, J=7.4 and 7.4 Hz, H^6), and 6.80—6.88 (2H, m, H^5 and H^7); ^{13}C NMR ($CDCl_3$, 67.9 MHz) δ=17.1, 22.1, 27.3, 42.3, 116.4, 120.8, 121.1, 127.3, 127.8, and 142.7.

Found: C, 81.60; H, 8.87; N, 9.41%. Calcd for $C_{10}H_{13}N$: C, 81.58; H, 8.90; N, 9.52%.

2,4-Dimethyl-1,2,3,4-tetrahydroquinoline (11): Bp 143—144 °C/4 mmHg (Kugelrohr); R_f 0.70 (SiO_2, ethyl acetate);

IR (neat) 3370 (NH), 3040, 2960, 2850, 1610, 1580, 1480, 1300, 1260, 1170, 1160, 1130, 1040, and 840 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ=1.17 (3HX0.7, d, J=6.2 Hz, cis-2-CH_3), 1.19 (3HX0.3, d, J=6.2 Hz, trans-2-CH_3), 1.26 (3HX0.3, d, J=7.2 Hz, trans-4-CH_3), 1.31 (3HX0.7, d, J=6.7 Hz, cis-4-CH_3), 1.34 (1HX0.7, ddd, J=12.8, 11.2, and 11.1 Hz, cis-H^{3a}), 1.636 (1HX0.3, dd, J=6.5 and 4.0 Hz, trans-H^{3a}), 1.638 (1HX0.3, dd, J=7.5 and 5.0 Hz, trans-H^{3e}), 1.91 (1HX0.7, ddd, J=12.8, 5.3, and 2.6 Hz, cis-H^{3e}), 2.80—3.00 (1H, m, H^4), 3.30—3.55 (1H, m, H^2), 3.47 (1H, br-s, NH), 6.44 (1HX0.7, dd, J=7.9 and 1.2 Hz, cis-H^8), 6.47 (1HX0.3, dd, J=7.9 and 1.2 Hz, trans-H^8), 6.58—6.66 (1HX0.3, m, trans-H^6), 6.64 (1HX0.7, ddd, J=7.6, 7.5, and 1.2 Hz, cis-H^6), 6.91—6.99 (1HX0.3, m, trans-H^7), 6.96 (1HX0.7, ddd, J=7.9, 7.5, and 1.2 Hz, cis-H^7), 6.99—7.04 (1HX0.3, m, trans-H^5), and 7.12 (1HX0.7, ddd, J=7.6, 1.2, and 1.2 Hz cis-H^5); ^{13}C NMR ($CDCl_3$, 67.9 MHz) δ=20.3 (cis-4-CH_3), 22.7 (2-CH_3), 24.8 (trans-4-CH_3), 30.1 (trans-C^4), 30.8 (cis-C^4), 37.1 (trans-C^3), 40.6 (cis-C^3), 42.3 (trans-C^2), 47.3 (cis-C^2), 113.9 (cis-C^8), 114.0 (trans-C^8), 116.9 (trans-C^6), 117.2 (cis-C^{6a}), 126.2 (C^{4a}), 126.6 (trans-C^7), 126.7 (cis-C^7), 126.8 (cis-C^5), 129.1 (trans-C^5), 144.1 (trans-C^{8a}), and 144.7 (cis-C^{8a}).

Found: C, 82.05; H, 9.39; N, 8.57%. Calcd for $C_{11}H_{15}N$: C, 81.93; H, 9.38; N, 8.69%.

8-Amino-1,2,3,4-tetrahydroquinoline (13): Bp 172 °C/5 mmHg (Kugelrohr); R_f 0.62 (SiO_2, ethyl acetate); IR (neat) 3330 (NH), 3050, 2930, 2850, 1600, 1500, 1330, 1290, 1250, 1180, 1100, 990, 760, and 730 cm^{-1}; ^1H NMR ($CDCl_3$, 60 MHz) δ=1.65—2.15 (2H, m, H^3), 2.73 (2H, t, J=6.0 Hz, H^4), 3.13 (3H, br-s, NH and NH_2), 3.10—3.43 (2H, m, H^2), and 6.50 (3H, s, ArH).

Found: C, 72.85; H, 8.20; N, 18.73%. Calcd for $C_9H_{12}N_2$: C, 72.94; H, 8.16; N, 18.90%.

5-Amino-1,2,3,4-tetrahydroquinoline (15): Mp 102 °C; R_f 0.76 (SiO_2, ethyl acetate); IR (Nujol) 2870, 1580, 1340, 1250, 1170, 1130, and 760 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ=2.00 (2H, tt, J=6.6 and 5.4 Hz, H^3), 2.47 (2H, t, J=6.6 Hz, H^4), 3.23 (2H, t, J=5.4 Hz, H^2), 3.52 (3H, br-s, NH and NH_2), 5.99 (1H, d, J=7.9 Hz), 6.07 (1H, d, J=7.9 Hz), and 6.79 (1H, dd, J=7.9 and 7.9 Hz, H^7); ^{13}C NMR ($CDCl_3$, 67.9 MHz) δ=21.5, 22.4, 41.4, 104.7, 105.6, 106.8, 127.0, 144.9, and 145.8.

Found: C, 72.77; H, 8.13; N, 18.82%. Calcd for $C_9H_{12}N_2$: C, 72.94; H, 8.16; N, 18.90%.

2-Methoxyethyl 1,2,3,4-Tetrahydroquinoline-2-carboxylate (16): Bp 230—232 °C/7 mmHg (Kugelrohr); R_f 0.81 (SiO_2, ethyl acetate); IR (neat) 3400 (NH), 2930, 1740 (C=O), 1610, 1590, 1500, 1200, 1120, 1040, and 740 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ=2.01 (1H, dddd, J=12.9, 8.9, 8.9, and 5.5 Hz, H^{3a}), 2.31 (1H, dddd, J=12.9, 5.6, 5.6, and 3.8 Hz, H^{3e}), 2.74 (1H, ddd, J=16.5, 5.6, and 5.5 Hz, H^{4e}), 2.83 (1H, J=16.5, 8.9, and 5.6 Hz, H^{4a}), 3.38 (3H, s, OCH_3), 3.61 (2H, t, J=4.7 Hz), 4.0 (1H, br, NH), 4.08 (1H, dd, J=8.9 and 3.8 Hz, H^2), 4.33 (2H, t, J=4.7 Hz), 6.58 (1H, dd, J=7.9 and 0.9 Hz, H^8), 6.64 (1H, ddd, J=7.4, 7.3, and 1.2 Hz, H^6), and 6.92—7.03 (2H, m, H^5 and H^7); ^{13}C NMR ($CDCl_3$, 67.9 MHz) δ=24.7, 25.8, 53.9, 59.0, 64.2, 70.3, 114.6, 117.6, 120.5, 127.0, 129.1, 143.0, and 173.3.

Found: C, 66.31; H, 7.27; N, 5.85%. Calcd for $C_{13}H_{17}NO_3$: C, 66.35; H, 7.30; N, 5.95%.

6-Chloro-1,2,3,4-tetrahydroquinoline (17): Reaction time was 12 h: IR (neat) 3400 (NH), 2930, 2840, 1600, 1580, 1495, 1470, 1350, 1300, 1270, 1180, 1080, 950, 890, and 800 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ=1.89 (2H, tt, J=6.4 and 5.5 Hz, H^3), 2.71 (2H, t, J=6.4 Hz, H^4), 3.26 (2H, t, J=5.5 Hz, H^2), 3.75 (1H, br-s, NH), 6.36 (1H, dd, J=7.2 and 1.7 Hz, H^8), and 6.86—6.91 (2H, m, H^5 and H^7); ^{13}C NMR ($CDCl_3$, 67.9 MHz) δ=21.6, 26.8, 41.7, 115.0, 120.8, 122.7, 126.3, 128.9, and 143.3.

17·HCl: Found: C, 52.89; H, 5.39; N, 6.82; Cl, 34.35%. Calcd for $C_9H_{11}NCl_2$: C, 52.97; H, 5.43; N, 6.86; Cl, 34.74%.

6-Methoxy-1,2,3,4-tetrahydroquinoline (20): Bp 162—168 °C/6 mmHg (Kugelrohr); IR (neat) 3380 (NH), 2940, 2840, 1520, 1470, 1300, 1260, 1240, 1200, 1160, 1040, and 810 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ=1.86—1.95 (2H, m, H^3), 2.73 (2H, t, J=6.5 Hz, H^4), 3.20—3.25 (2H, m, H^2), 3.43 (1H, br-s, NH), 3.71 (3H, s, OCH_3), 6.42 (1H, d, J=8.4 Hz, H^8), and 6.53—6.60 (2H, m, H^5 and H^7); ^{13}C NMR ($CDCl_3$, 67.9 MHz) δ=22.5, 27.2, 42.4, 55.8, 113.0, 115.0, 115.6, 122.9, 138.9, and 151.9.

Found: C, 73.68; H, 8.08; N , 8.46%. Calcd for $C_{10}H_{13}NO$: C, 73.59; H, 8.03; N, 8.58%.

2-Formyl-1,2,3,4-tetrahydroquinoline (25): R_f 0.44 (SiO_2 ethyl acetate); IR (neat) 2850, 1660 (C=O), 1440, 1400, 1190, 930, and 750 cm^{-1}; ^1H NMR ($CDCl_3$, 60 MHz) δ=2.90 (2H, t, J=6.0 Hz, H^4), 3.58 (2HX0.6, t, J=6.0 Hz, H^3), 3.73 (2HX0.4, t, J=6.0 Hz, H^3), 4.47 (2HX0.4, s, H^1), 4.62 (2HX0.6, s, H^1), 7.00 (4H, s, ArH), 8.10 (1HX0.6, s, NCHO), and 8.15 (1HX0.4, s, NCHO).

Found: C, 74.41; H, 6.80; N, 8.55%. Calcd for $C_{10}H_{11}NO$: C, 74.51; H, 6.88; N, 8.69%.

2-Formyl-6-benzyloxy-7-methoxy-1,2,3,4-tetrahydroisoquinoline (27): IR (neat) 2940, 1665 (C=O), 1620, 1520, 1450, 1260, 1225, 1115, 1020, 860, 750, and 700 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ=2.72 (2HX0.4, t, J=6.1 Hz, H^4), 2.75 (2HX0.6, t, J=5.9 Hz, H^4), 3.57 (2HX0.6, t, J=5.9 Hz, H^3), 3.74 (2HX0.4, t, J=6.1 Hz, H^3), 3.84 (3HX0.6, s, OCH_3), 3.85 (3HX0.4, s, OCH_3), 4.44 (2HX0.4, s, H^1), 4.59 (2HX0.6, s, H^1), 5.10 (2H, s), 6.59 (1HX0.4, s), 6.62 (2HX0.6, s), 6.65 (1HX0.4, s), 7.26—7.45 (5H, m, Ph), 8.16 (1HX0.6, s, NCHO), and 8.22 (1HX0.4, s, NCHO); ^{13}C NMR ($CDCl_3$, 67.9 MHz) δ=27.5, 29.2, 38.0, 42.0, 43.3, 47.1, 56.18, 56.24, 71.25, 71.32, 109.5, 110.0, 114.7, 114.8, 124.5, 124.7, 125.5, 126.4, 127.3, 127.86, 127.90, 128.5, 137.0, 137.1, 147.1, 148.9, 161.1, and 161.5; mass spectrum (80 eV), m/z (relative intensity) 297 (M^+, 4), 265 (3), 206 (M^+-CH_2Ph, 5), 178 (5), and 91 (100).

Found: C, 72.97; H, 6.68; N, 4.63%. Calcd for $C_{18}H_{19}NO_3$: C, 72.71; H, 6.44; N, 4.71%.

2-Formyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (28) Mp 127—128 °C; R_f 0.26 (SiO_2, ethyl acetate); ^1H NMR ($CDCl_3$, 270 MHz) δ=2.79 (2HX0.4, t, J=6.1 Hz, H^4), 2.83 (2HX0.6, t, J=5.8 Hz, H^4), 3.63 (2HX0.6, t, J=5.8 Hz, H^3), 3.78 (2HX0.4, t, J=6.1Hz, H^3), 3.85 (6HX0.6, s, OCH_3), 3.86 (6HX0.4, s, OCH_3), 4.47 (2HX0.4, s, H^1), 4.61 (2HX0.6, s, H^1), 6.58 (1HX0.4, s), 6.60 (2HX0.6, s), 6.62 (1HX0.4, s), 8.19 (1HX0.6, s, NCHO), and 8.25 (1HX0.4, s, NCHO); ^{13}C NMR ($CDCl_3$, 67.9 MHz) δ=27.6, 29.3, 38.1, 42.0, 43.4, 47.1, 56.0, 56.05, 56.10, 108.9, 109.4, 111.7, 112.0, 123.8, 124.0, 125.4, 126.4, 148.0, 148.2, 148.3, 161.1, and 161.6.

Found: C, 65.02; H, 6.76; N, 6.07%. Calcd for $C_{12}H_{15}NO_3$: C, 65.13; H, 6.85; N, 6.33%.

Hydrogenation of 4 Using Molecular Hydrogen. A mixture of **4** (1.57 g, 11.0 mmol) and $Rh_6(CO)_{16}$ (0.024 g, 0.023 mmol) was heated at 200 °C for 20 h under the pressure of H_2 (10 kg cm^{-2}). After cooling to room temperature, the reaction mixture was taken up with ether and filtered. After removal of the solvent under reduced pressure, silica-gel column chromatography (ethyl acetate–hexane=3:7) afforded

4-methyl-5,6,7,8-tetrahydroquinoline (**6**) (0.680 g, 47%): R_f 0.50, (SiO_2, ethyl acetate); ^1H NMR ($CDCl_3$, 270 MHz) δ=1.82—1.88 (4H, m, H^6 and H^7), 2.20 (3H, s, CH_3), 2.64 (2H, t, J=6.1 Hz), 2.91 (2H, t, J=6.1 Hz), 6.89 (1H, d, J=4.8 Hz, H^3), and 8.22 (1H, d, J=4.8 Hz, H^2); ^{13}C NMR ($CDCl_3$, 67.9 MHz) δ=18.8, 22.86, 22.91, 25.8, 33.0, 122.6, 131.1, 145.8, 146.1, and 156.7.

Oxidation of 8 to 1-Hydroxy-6-methyl-1,2,3,4-tetrahydroquinolin-2-one (21): To a mixture of **8** (0.270 g, 1.83 mmol) and sodium tungstate monohydrate (0.012 g, 0.04 mmol) in methanol (25 mL) was added dropwise 30% aqueous hydrogen peroxide (0.62 mL, 6.0 mmol) at 0 °C under nitrogen. The reaction mixture was stirred at room temperature for 24 h. After removal of methanol under reduced pressure, the solidified dark brown residue was extracted with dichloromethane (10 mL×4). The combined extracts were dried over sodium sulfate and evaporated. Silica-gel column chromatography (20×80 mm, dichloromethane–ether=9:1) gave **21** (0.267 g, 82%): mp 137.8—138.5 °C; R_f 0.35 (SiO_2, ether); IR (Nujol) 2900 (O–H), 1645 (C=O), 1285, 1245, 1215, 1080, 1025, 975, 890, 850, 820, and 740 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ=2.30 (3H, s, CH_3), 2.72 (2H, dd, J=7.7 and 7.0 Hz, H^3), 2.90 (2H, dd, J=7.7 and 7.0 Hz, H^4), 6.95 (1H, s, H^5), 7.08 (1H, d, J=8.1 Hz), 7.25 (1H, d, J=8.1 Hz), and 8.0—10.0 (1H, br, OH); ^{13}C NMR ($CDCl_3$, 67.9 MHz) δ=20.7, 24.6, 30.0, 113.0, 123.4, 128.08, 128.11, 133.4, 134.8, and 164.7.

Found: C, 67.88; H, 6.22; N, 7.83%. Calcd for $C_{10}H_{11}NO_2$: C, 67.78; H, 6.26; N, 7.91%.

Synthesis of 1-Acetyl-1,2,5,6-tetrahydro-4*H*-imidazo[4,5,1-*ij*]quinolin-2-one (22). In a 25-mL round-bottomed flask equipped with a reflux condenser were placed **13** (0.148 g, 1.00 mmol), diethyl carbonate (0.13 mL, 1.07 mmol), and acetic acid (5 mL). The mixture was stirred at 100 °C for 3 h. The reaction mixture was cooled to room temperature, basified with dilute aqueous ammonia, and extracted with chloroform (10 mL×3). The combined extracts were dried over sodium sulfate and evaporated. The residue was chromatographed on silica gel (20×80 mm, ethyl acetate–hexane=1:1 and methanol) to afford **22** (0.102 g, 49%) along with unreacted **13** (0.031 g, 21%). Thus, the yield based on consumed **13** is 62%: R_f 0.69 (SiO_2, methanol); ^1H NMR ($CDCl_3$, 60 MHz) δ=2.10 (2H, tt, J=5.5 and 6.0 Hz, H^5), 2.43 (3H, s, $NCOCH_3$), 2.85 (2H, t, J=5.5 Hz, H^6), 3.90 (2H, t, J=6.0 Hz, H^4), and 6.97—7.47 (3H, m, ArH); mass spectrum (70 eV), m/z (relative intensity) 172 (M^+-COCH_3, 100), 171 (90), 144 (14), and 130 (30).

Synthesis of 6-Methyl-1,2,5,6-tetrahydro-4*H*-pyrrolo[3,2,1-*ij*]quinolin-2-one (24). In a 50-mL round-bottomed flask were placed tetrahydroquinoline **5** (0.294 g, 2.00 mmol), bromoacetyl bromide (0.20 mL, 2.30 mmol), triethylamine (0.3 mL, 2.15 mmol), and benzene (10 mL). The reaction mixture was stirred at room temperature under argon atmosphere for 3 h. The resulting mixture was washed with water (10 mL×3) and dried over magnesium sulfate. After removal of the solvent under reduced pressure, column chromatography on silica gel (18×60 mm, ethyl acetate–hexane=1:1) gave 1-bromoacetyl-4-methyl-1,2,3,4-tetrahydroquinoline (**23**) (0.512 g, 96%).

In a 50-mL round-bottomed flask were placed **23** (0.128 g, 0.478 mmol) and aluminum chloride (0.190 g, 1.43 mmol). After the mixture was heated at 150 °C for 30 min, crushed ice was added to the reaction mixture. The resulting mixture was made alkaline with dilute aqueous ammonia and extracted with chloroform (10 mL×3). Combined organic layers were dried over magnesium sulfate. After removal of the solvent under reduced pressure, the residue was sublimed (110 °C, 5 mmHg, 10 h) to give **24** (0.058 g, 65%). **23**: R_f 0.91 (SiO_2, ethyl acetate); IR (neat) 2950, 2870, 1730, 1650, 1580, 1490, 1380, 1200, 1120, and 750 cm^{-1}; ^1H NMR ($CDCl_3$, 60 MHz) δ=1.26 (3H, d, J=6.0 Hz, CH_3), 1.90—2.30 (2H, m, H^3), 2.47—3.03 (1H, m, H^4), 3.70 (2H, t, J=5.0 Hz, H^2), 4.00 (2H, s, $COCH_2$), and 7.00—7.50 (4H, m, ArH). **24:** R_f 0.61 (SiO_2, ethyl acetate); ^1H NMR ($CDCl_3$, 270 MHz) δ=1.34 (3H, d, J=7.1 Hz, CH_3), 1.72 (1H, dddd, J=13.7, 8.7, 8.6, and 4.4 Hz, H^{5a}), 2.06 (1H, J=13.7, 6.7, 4.4, and 4.2 Hz, H^{5e}), 2.90—3.03 (1H, m, H^6), 3.50 (2H, s, H^1), 3.63 (1H, ddd, J=13.2, 8.6, and 4.2 Hz, H^{4a}), 3.85 (1H, ddd, J=13.2, 6.7, and 4.4 Hz, H^{4e}), 6.95 (1H, dd, J=7.6 and 7.6 Hz, H^8), and 7.05—7.12 (2H, m, H^7 and H^9); ^{13}C NMR ($CDCl_3$, 67.9 MHz) δ=19.9, 29.3, 29.4, 36.7, 37.1, 122.0, 122.2, 123.3, 125.1, 125.2, 141.7, and 174.1.

Found: C, 76.62; H, 6.98; N, 7.50%. Calcd for $C_{12}H_{13}NO$: C, 76.96; H, 7.01; N, 7.48%.

Hydrogenation of 1 by Using Deuterium Oxide. The reaction of **1** with D_2O was carried out according to the general procedure by using toluene in place of 2-methoxyethanol. The product was analyzed by 270 MHz ^1H NMR and the results were shown in Scheme 2.

Preparation of 6-Benzyloxy-7-methoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline (29). In a 200-mL three-necked flask equipped with a reflux condenser and a dropping funnel were placed lithium aluminum hydride (0.339 g, 0.892 mmol) and anhydrous tetrahydrofuran (15 mL). To the suspension was added cautiously a solution of **27** (1.34 g, 4.51 mmol) in anhydrous tetrahydrofuran (26 mL). After addition was complete, the reaction mixture was refluxed for 15 h. Stirring was continued while the mixture was cooled in an ice bath and a saturated aqueous solution of sodium sulfate was added cautiously until the hydrogen evolution ceased. The mixture was then filtered and evaporated to afford **29** (1.06 g, 83%). An analytical sample after recrystallization from hexane showed following properties: mp 93—94 °C; IR (Nujol) 3300 (N–H), 1610, 1520, 1225, 1130, 1010, 750, and 700 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ=2.44 (3H, s, CH_3), 2.64 (2H, t, J=5.9 Hz), 2.78 (2H, t, J=5.9 Hz), 3.50 (2H, s, H^1), 3.83 (s, 3H, OCH_3), 5.09 (2H, s, OCH_2Ph), 6.53 (1H, s), 6.63 (1H, s), and 7.25—7.50 (5H, m, Ph); ^{13}C NMR ($CDCl_3$, 67.9 MHz) δ=28.7, 46.0, 52.9, 56.2, 57.6, 71.3, 110.2, 114.7, 125.9, 127.37, 127.41, 127.7, 128.5, 137.4, 146.9, and 148.1.

Preparation of 6-Benzyloxy-7-methoxy-1,2,3,4-tetrahydroisoquinoline (30). In a 50-mL round-bottomed flask were placed **28** (0.947 g, 3.18 mmol) and a mixture of sulfuric acid and methanol (1/9) (20 mL). After the mixture was stirred at room temperature for 48 h, the solution was basified with diluted aqueous ammonia. After methanol was removed under reduced pressure, the resulting aqueous solution was extracted with chloroform (10 mL×3). The combined organic layers were dried over sodium sulfate and evaporated to give **30**: mp 78 °C; ^1H NMR ($CDCl_3$, 270 MHz) δ=1.81 (1H, br-s, NH), 2.64 (2H, t, J=5.8 Hz), 3.08 (2H, t, J=5.8 Hz), 3.83 (3H, s, OCH_3), 3.93 (2H, s, H^1), 5.10 (2H, s, OCH_2Ph), 6.53 (1H, s), 6.61 (1H, s), and 7.25—7.46 (5H, m, Ph); ^{13}C NMR ($CDCl_3$, 67.9 MHz) δ=28.6, 44.0, 48.0, 56.2, 71.4, 110.0, 115.3, 126.7, 127.3, 127.8, 128.5, 128.6, 137.4, 146.8, and 148.2; mass spectrum (80 eV), m/z (relative intensity) 269

(M^+, 9), 178 (M^+-CH_2Ph), 150 (27), and 91 (100).

Found: C, 75.49; H, 7.12; N, 5.04%. Calcd for $C_{17}H_{19}NO_2$: C, 75.81; H, 7.11; N, 5.20%.

6,7-Dimethoxy-1,2,3,4-tetrahydroisoquinoline (31). ^1H NMR ($CDCl_3$, 270 MHz) δ=2.02 (1H, br-s, NH), 2.71 (2H, t, J=5.9 Hz, H^4), 3.12 (2H, t, J=5.9 Hz, H^3), 3.83 (3H, s, OCH_3), 3.84 (3H, s, OCH_3), 3.94 (2H, s, H^1), 6.51 (1H, s), and 6.58 (1H, s); ^{13}C NMR ($CDCl_3$, 67.9 MHz) δ=28.7, 44.0, 48.0, 56.0, 109.3, 112.2, 126.6, 127.8, 147.4, and 147.6.

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