Asymmetric Reduction of Prochiral Ketones with Chiral Hydride Reagents Prepared from Lithium Aluminium Hydride and (*S*)-2-(*N*-Substituted aminomethyl)pyrrolidines

Masatoshi Asami, Hiroyasu Ohno, Susumu Kobayashi, and Teruaki Mukaiyama
The University of Tokyo, Hongo, Bunkyo-ku, Tokyo 113
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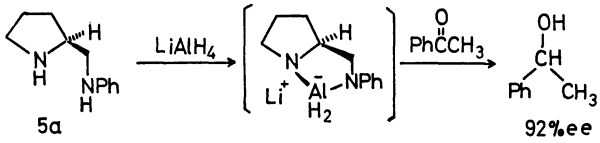
Asymmetric reduction of prochiral ketones with various hydride reagents prepared from lithium aluminium hydride and (*S*)-2-(*N*-substituted aminomethyl)pyrrolidines, derived easily by four steps from commercially available (*S*)-proline, yields optically active alcohols with 13—92% optical purity having the *S*-configuration.

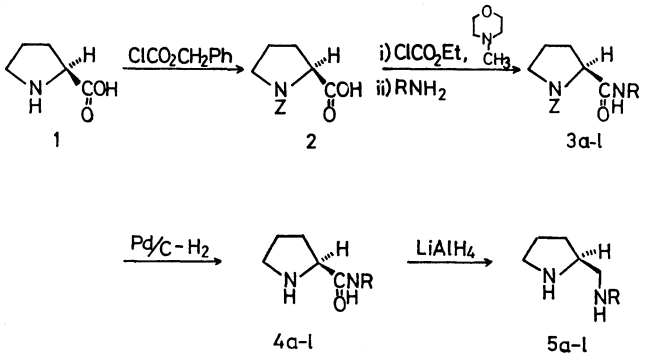
Asymmetric reduction of prochiral carbonyl compounds by chiral hydride reagents has been the object of extensive work and a number of methods have been reported.[1] Most of such works have been developed based on the use of chiral hydride reagents obtained by reaction of $LiAlH_4$ and chiral ligands such as alkaloids,[2] sugar derivatives,[3] amino alcohols,[4,5] chiral oxazolines,[6] tartaric acid derivatives,[7] chiral diols,[8] or chiral amines.[9] Relatively high optical yield (<83%) was achieved in the case of the reduction of acetophenone by using these ligands.

On the other hand, during the course of our synthetic investigation utilizing the onium salts of azaaromatics, we have reported the convenient and efficient methods for the optical interconversion of chiral secondary alcohols,[10a] and transformation of the alcohols to chiral halides,[10b] thiols,[10c] and primary amines.[10d] This prompted us to study on the exploration of a new and efficient chiral ligand, and (*S*)-2-(anilinomethyl)pyrrolidine (**5a**) is found to be efficient for the reduction of acetophenone to yield (*S*)-1-phenylethanol with 92% optical purity as briefly reported in the previous communication.[11] (Scheme 1).

(*S*)-2-(*N*-substituted aminomethyl)pyrrolidines (**5a**—**l**) were easily prepared from readily available (*S*)-proline as shown in the following scheme (Scheme 2): (*S*)-Proline (**1**) was converted to (*S*)-*N*-(benzyloxycarbonyl)-proline (**2**) by treatment with benzyloxycarbonyl chloride and sodium hydrogencarbonate. Then it was transformed into the corresponding amides (**3a**—**l**) by treatment with *N*-methylmorpholine, ethyl chloroformate and amines. *N*-Substituted (*S*)-prolinamides (**4a**—**l**) were obtained by the hydrogenolysis of the amides **3a**—**l** in the presence of 5% Pd–C catalyst under hydrogen atmosphere at ordinary pressure. The amides **4a**—**l** were further reduced to the required chiral diamines, (*S*)-2-(*N*-substituted aminomethyl)pyrrolidines **5a**—**l**, tabulated in Table 1.



Scheme 1.



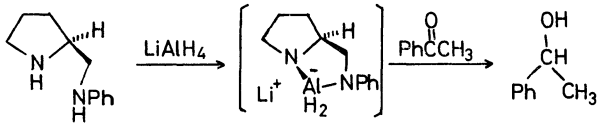
Scheme 2.

In the first place, we examined suitable reaction conditions using chiral diamine **5a** as ligand and acetophenone as model substrate. The reactions were carried out as follows: The diamine **5a** in ether, THF, or toluene was added to the standardized $LiAlH_4$

Table 1. Physical property of (*S*)-2-(*N*-substituted aminomethyl)pyrrolidines **5a**—**l**

No.	Chiral diamines substituent	$[\alpha]_D$ (EtOH)	Bp
5a	Ph	$[\alpha]_D^{24}$+19.7° (*c* 1.04)	111—112 °C/0.55 mmHg
5b	Isopropyl	$[\alpha]_D^{26}$+16.5° (*c* 1.07)	59—62 °C/4 mmHg
5c	Hexyl	$[\alpha]_D^{24}$+13.9° (*c* 1.13)	66—70 °C/0.25 mmHg
5d	Cyclohexyl	$[\alpha]_D^{24}$+10.3° (*c* 1.01)	78—80 °C/0.4 mmHg
5e	(*R*)-1-Phenylethyl	$[\alpha]_D^{24}$+53.5° (*c* 1.02)	110—118 °C/1 mmHg
5f	(*S*)-1-Phenylethyl	$[\alpha]_D^{24}$−43.0° (*c* 1.10)	106—116 °C/0.7 mmHg
5g	1-Naphtyl	$[\alpha]_D^{24}$+29.5° (*c* 1.03)	159—161 °C/0.3 mmHg
5h	2-Methoxyphenyl	$[\alpha]_D^{24}$+25.2° (*c* 1.08)	150 °C/0.6 mmHg
5i	4-Methoxyphenyl	$[\alpha]_D^{24}$+14.4° (*c* 0.97)	130—132 °C/0.25 mmHg
5j	2-Pyridyl	$[\alpha]_D^{24}$+21.3° (*c* 1.16)	102—106 °C/0.025 mmHg
5k	4-Pyridyl	$[\alpha]_D^{24}$+1.90° (*c* 0.68)	130—140 °C/0.04 mmHg
5l	3,4-Dichlorophenyl	$[\alpha]_D^{24}$+9.46° (*c* 0.96)	150—153 °C/0.25 mmHg

Table 2. Asymmetric reduction of acetophenone with $LiAlH_4$-chiral diamine **5a** complex



Exp	Solvent	Temp (°C)	Molar ratio[a)]	Additive	Yield (%)	$[\alpha]_D$ (*c*, cyclopentane)	Optical purity (%)[b)]
1	Ether	−40	B	—	68	$[\alpha]_D^{31}$ −35.5° (7.30)	82
2	Ether	−78	A	—	68	$[\alpha]_D^{22}$ −33.8° (7.27)	78
3	Ether	−78	B	—	84	$[\alpha]_D^{22}$ −36.1° (7.39)	84
4	Ether	−78	C	—	88	$[\alpha]_D^{22}$ −38.2° (7.17)	89
5	Ether	−100	B	—	81	$[\alpha]_D^{25}$ −37.5° (7.25)	87
6	Ether	−100	C	—	93	$[\alpha]_D^{26}$ −39.8° (7.28)	92
7	THF	−78	B	—	54	$[\alpha]_D^{24}$ + 8.3° (4.00)	19
8	Toluene	−78	B	—	—[c)]		
9	Ether	−78	B	TMEDA	67	$[\alpha]_D^{25}$ − 7.6° (6.88)	18
10	Ether	−78	B	DME	84	$[\alpha]_D^{24}$ −16.6° (7.39)	38
11	Ether	−78	B	$MgBr_2$	85	$[\alpha]_D^{24}$ −10.7° (7.17)	25

a) $LiAlH_4$: **5a**: Acetophenon A 1.3: 1.5: 1, B 1.75: 2.00: 1, C 2.36: 2.73: 1. b) Based on $[\alpha]_D^{21}$ −43.1° (*c* 7.19, C_5H_{10}) reported by S. Yamaguchi and H.S. Mosher, *J. Org. Chem.*, **38**, 1970 (1973). c) Only trace of alcohol was detected by TLC.

solution. On addition of the diamine **5a**, *ca.* 2 mol of hydrogen gas evolved and white precipitates, presumably, the diamine **5a**–$LiAlH_4$ complex appeared in ether or toluene. But, in the case of THF, almost homogeneous solution resulted. After the evolution of gas had been completed, the mixture was stirred at room temperature for 1 h. Then it was cooled and was added acetophenone. Stirring was continued for additional 3 h at the temperature and it was hydrolyzed to yield 1-phenylethanol. In the cases when additives (*N,N,N',N'*-tetramethylethylenediamine (TMEDA), 1,2-dimethoxyethane (DME), or $MgBr_2$) were used, they were added before lowering the temperature and the mixture was stirred at room temperature for about 1 h. Then it was cooled to −78 °C and added acetophenone and treated similarly. The results are summarized in Table 2.

These results indicate that ether is preferred as solvent and the optical purity increased by lowering the reaction temperature [Exp. 1, 3, 5, and 4, 6]. The molar ratio of each substances also affect both synthetic and optical yields. The presence of additives such as TMEDA, DME or $MgBr_2$ caused the decrease of optical purity, which indicates that lithium ion plays an important role in the present asymmetric reductions.

The effect of the *N*-substituents in the ligand diamines **5a**—**l** on the enantioselectivity in the present asymmetric reduction were examined with various *N*-substituted diamines **5a**—**l**–$LiAlH_4$ complexes under the same reaction conditions as Exp. 3 by employing the asymmetric reduction of acetophenone as a model. The results are summarized in Table 3. Relatively high optical purities were attained when *N*-aryl substituted diamines–$LiAlH_4$ complexes were employed as chiral hydride reagent. Electron-withdrawing group (3,4-dichloro) or electron-donating group (4-methoxyl) in *N*-aryl substituent did not cause the remarkable effect both on the synthetic and optical yields, but methoxyl group on the *o*-position (2-methoxyl) in *N*-aryl substituent which can coordinate to the metal atom, either lithium or aluminium of the bicyclic hydride reagents, deactivated the reagent.

Table 3. Asymmetric reduction of acetophenone with $LiAlH_4$-chiral diamines **5a**—**l** complex

Exp.	Diamines **5** R	Alcohol Yield (%)	Alcohol $[\alpha]_D$ (*c*, cyclopentane)	Optical purity (%)
3	**a** Ph	84	$[\alpha]_D^{22}$ −36.1° (7.39)	84
12	**b** Isopropyl	65	$[\alpha]_D^{24}$ −20.1° (7.13)	47
13	**c** Hexyl	45	$[\alpha]_D^{25}$ −21.3° (2.11)	49
14	**d** Cyclohexyl	78	$[\alpha]_D^{26}$ −25.5° (6.74)	59
15	**e** (*R*)-1-Phenylethyl	69	$[\alpha]_D^{22}$ −22.2° (7.67)	52
16	**f** (*S*)-1-Phenylethyl	72	$[\alpha]_D^{23}$ −23.0° (7.53)	54
17	**g** 1-Naphtyl	67	$[\alpha]_D^{28}$ −33.3° (5.80)	77
18	**h** 2-Methoxyphenyl	18	$[\alpha]_D^{25}$ 0° (5.37)	0
19	**i** 4-Methoxyphenyl	63	$[\alpha]_D^{28}$ −32.5° (5.75)	76
20	**j** 2-Pyridyl	88	$[\alpha]_D^{24}$ − 1.0° (7.23)	2
21	**k** 4-Pyridyl[a)]	64	$[\alpha]_D^{28}$ + 3.0° (6.75)	7
22	**l** 3,4-Dichlorophenyl	66	$[\alpha]_D^{28}$ −33.3° (5.74)	77

a) Small amount of THF was used.

Further, the diamine–$LiAlH_4$ complex was applied to the asymmetric reduction of various ketones by choosing diamine **5a**–$LiAlH_4$ complex and diamine **5d**–$LiAlH_4$ complex as the chiral hydride reagents. In every case, the reactions were carried out according to a similar procedure as mentioned above and corresponding alcohols were obtained as summarized in Table 4.

As the result, in the case of the ketones having aromatic ring attached to the carbonyl group gave fairly good optical purities (50—85% with diamine **5a**–$LiAlH_4$ complex), but satisfactory results could not be obtained in the case of normal aliphatic ketones. We assume that enantioselectivities were induced by both electronic

Table 4. Asymmetric reduction of various ketones with $LiAlH_4$–chiral diamine **5a** complex and $LiAlH_4$–chiral diamine **5d** complex

Exp	Ketone	Diamine 5 R		Alcohol[a] Yield (%)	Alcohol[a] $[\alpha]_D$ (*c*. solv.)	Alcohol[a] Optical Purity (%)
23	PhCOEt	**a**	Ph	90	$[\alpha]_D^{25}$ −23.7° (neat)	85[b]
24	$PhCOCHMe_2$	**a**	Ph	80	$[\alpha]_D^{23}$ −27.0° (6.79, ether)	57[c]
25	α-Tetralone	**a**	Ph	94	$[\alpha]_D^{22}$ +16.3° (4.12, $CHCl_3$)	50[d]
26	$PhCH_2COMe$	**a**	Ph	85	$[\alpha]_D^{25}$ +12.9° (5.19, C_6H_6)	31[e]
27	n-$C_6H_{13}COMe$	**a**	Ph	77	$[\alpha]_D^{25}$ + 1.27° (neat)	13[f]
28	PhCOEt	**d**	Cyclohexyl	40	$[\alpha]_D^{28}$ −28.9° (5.40, $CHCl_3$)	63[b]
29	$PhCOCHMe_2$	**d**	Cyclohexyl	83	$[\alpha]_D^{28}$ −24.0° (7.20, ether)	51[c]
30	α-Tetralone	**d**	Cyclohexyl	80	$[\alpha]_D^{28}$ + 1.36 (4.42, $CHCl_3$)	4[d]

a) All these alcohols have *S*-configuration. b) Based on $[\alpha]_D^{25}$ 27.7° (neat), $[\alpha]_D$ 45.45° (*c* 5.15, $CHCl_3$) reported by R. H. Pickard and J. Kenyon, *J. Chem. Soc.*, **99**, 45 (1911); *ibid* **105**, 1115 (1914). c) Based on $[\alpha]_D^{20}$ 47.7° (*c* 7, ether) reported by R. MacLeod, F. J. Welch and H. S. Mosher, *J. Am. Chem. Soc.*, **82**, 876 (1960). d) Based on $[\alpha]_D^{17}$ 32.7° (*c* 4.1, $CHCl_3$) reported by A. G. Davies and A. M. White, *J. Chem. Soc.*, **1952**, 3300. e) Based on $[\alpha]_D^{20}$ 41.8° (*c* 5.26, C_6H_6) reported by R. H. Pickard and J. Kenyon *J. Chem. Soc.*, **105**, 1115 (1914), f) Based on $[\alpha]_D^{25}$ 9.57° (neat) reported by S. J. Cristol, B. Franzus, A. Shadan, *J. Am. Chem. Soc.*, **77**, 2512 (1955).

and steric effects of the aromatic ring in the ketones attached to the carbonyl group. That is, the conjugation effect puts the aromatic ring and carbonyl group on the same plane. This makes possible to distinguish a sharp steric difference of the two substituents and enantioface of unsymmetrical ketones during hydride transfer to attain relatively high optical yield.

Although the precise mechanism of this asymmetric reduction is not clear, we assume that high enantioselectivity, namely, all of the produced alcohols have *S*-configuration (except the case THF was used as solvent) with high optical purity, in the present asymmetric reduction of prochiral ketones is due to the following factors: 1) The diamines, a simple structure having only one asymmetric carbon, produce the effective chiral environment by the treatment with $LiAlH_4$. This may be due to the formation of sterically restricted *cis*-fused bicyclic hydride reagents, creating the additional chiral center on the nitrogen atom in the pyrrolidine ring. 2) The reactivity of the two hydrogen atoms contained in this chiral reagent is remarkably different. Actually only one hydrogen atom was consumed by the reaction with ketones, but the other remained unreacted because of large steric hinderance. 3) Lithium ion, presumably coordinating to the nitrogen atoms on the pyrrolidine ring and/or on the side chain in the diamine–$LiAlH_4$ complex, restrict the direction of approach of the ketones.

Table 5. Comparison of various chiral reducing reagents prepared from $LiAlH_4$ and chiral ligands (optical purity)

Ketone	Ligand: Sugar[3a] derivative	Darbon[a] [4]	Chiral oxazoline[6]	Chiral amine[9]	**5a**
PhCOMe	71	75	65	43	84 (92)[b]
PhCOEt	46	—	62	52	85
$PhCOCHMe_2$	—	48	43	—	57
α-Tetralone	—	—	4	—	50
$PhCH_2COMe$	—	—	1	—	31
n-$C_6H_{13}COMe$	25	—	4 (6)	—	13

a) (+)-(2*S*,3*R*)-4-Dimethylamino-3-methyl-1,2-diphenyl-2-butanol. b) at −100 °C.

In conclusion, it is noteworthy that the diamine **5a** produces effective chiral hydride reagent with $LiAlH_4$ and reduces prochiral ketones, including acetophenone, propiophenone, phenyl isopropyl ketone, α-tetralone, benzyl methyl ketone and 2-octanone, to afford corresponding chiral alcohols with 13—92% optical purity having *S*-configuration.

Experimental

Spectra. NMR were obtained on a Hitachi R-24 spectrometer. Infrared spectra were taken using a Hitachi EPI-G2 spectrometer. Mass spectra were taken using a Hitachi RMU-6 spectrometer. Optical rotations were taken on a JASCO DIP-SL automatic polarimeter using 1-dm or 1-cm thermostated microcell. Products were identified by NMR and IR with authentic samples.

Materials. All solvents used were distilled according to the general methods and stored over sodium metal as a drying agent. Further ether and THF were distilled from $LiAlH_4$ prior to use. A supernatant of etheral $LiAlH_4$ solution was stored in a flask closed with a rubber septum.

(S)-N-(Benzyloxycarbonyl)prolinanilide ***3a.*** Commercial *(S)*-proline **1** (11.5 g, 0.1 mol), sodium hydrogencarbonate (20.16 g) and benzyloxycarbonyl chloride (32 g, 30—35% toluene solution) in 150 ml of water were stirred for 2 h at room temperature. Then sodium hydrogencarbonate (10.08 g) and benzyloxycarbonyl chloride (32 g, 30—35% toluene solution) were added and stirred for 3 h at room temperature. The reaction mixture was washed two times with 50 ml of ether and the aqueous layer was acidified (pH 3—4) by 6M HCl. The mixture was extracted four times with ethyl acetate (250 ml) and the extracts were dried over Na_2SO_4. The solvent was evaporated and *(S)-N-*(benzyl-

oxycarbonyl)proline **2** (24.1 g, 96.8%, $[\alpha]_D^{22}-40.4°$ (*c* 1.027, EtOH) was obtained. Under an argon atmosphere (*S*)-*N*-(benzyloxycarbonyl)proline **2** (18.7 g) in 250 ml of ethyl acetate was added *N*-methylmorpholine (7.6 g) in 10 ml of ethyl acetate at −15 °C. And ethyl chloroformate (8.1 g) in 10 ml of ethyl acetate was added slowly to the solution at −15 °C during 5 minutes then aniline (7.0 g) in 20 ml of ethyl acetate was added to the reaction mixture at −15 °C. The mixture was kept at −15 °C for 1 h and at 0 °C for 1 h then gradually up to room temperature and it was stirred overnight. To the mixture was added 150 ml of ethyl acetate, and 100 ml of water. Then organic layer was washed with aqueous 4% sodium hydrogencarbonate solution, saturated sodium chloride solution, 2% hydrochloric acid, and saturated sodium chloride solution (50 ml each) successively. Then organic layer was dried over Na_2SO_4 and concentrated to give crude (*S*)-*N*-(benzyloxycarbonyl)prolinanilide **3a** (22.8 g). Recrystallyzation from acetone afforded 18.7 g (77%, mp 141—141.5 °C, $[\alpha]_D^{23}-63.2°$ (*c* 0.997, EtOH). Found: C, 70.07; H, 6.18; N, 8.65%. Calcd for $C_{19}H_{20}O_3N_2$: C, 70.35; H, 6.22; N, 8.64%. By similar prodecure amides **3b**—**1** were obtained.

(S)-2-(Anilinomethyl)pyrrolidine **5a**. *(S)-N*-(Benzyloxycarbonyl)prolinanilide **3a** (21 g) and 5% Pd—C catalyst (1g) were stirred vigorously in methanol (120 ml) under hydrogen atmosphere for 3 h. Then reaction mixture was filtered through celite and the filtrate was concentrated to give crude (*S*)-prolinanilide **4a**, which was recrystallized from cyclohexane to afford pure **4a** (11.5 g, 94%, mp 76—77 °C, $[\alpha]_D^{27}-71.0°$ (c 1.025, EtOH)). Found: C, 69.53; H, 7.58; N, 14.84%. Calcd for $C_{11}H_{14}ON_2$: C, 69.44; H, 7.42; N, 14.73%. **4a** (10.5 g) in 35 ml of THF was added to the $LiAlH_4$ (4.2 g) in 40 ml of THF at 0 °C under an argon atmosphere. The reaction mixture was stirred overnight at 0 °C and hydrolyzed with saturated sodium sulfate solution. After removal of the inorganic material and concentration of organic layer, fractional distillation under reduced pressure afforded a colorless oil **5a** (7.2 g, 81%, bp 111—112 °C/0.55 mmHg, $[\alpha]_D^{24}+19.7°$ (*c* 1.087, EtOH); IR 3280 cm^{-1} (N-H); NMR ($CDCl_3$) δ=0.93—2.13 (m, 5H), 2.35—3.46 (m, 5H), 4.10 (br, 1H), 6.33—6.86 (m, 3H), 6.86—7.38 (m, 2H). MS (70 eV), *m/e*, 176 (M^+), 107, 77, 70, and 43. By similar procedure diamines **5b**—**1** were also prepared. **5b**; IR 3280 cm^{-1} (N-H); NMR ($CDCl_3$) δ=1.00 (d, 6H), 1.32 (s, 2H), 1.20—2.03 (m, 4H), 2.30—3.34 (m, 6H). Found: C, 67.84; H, 13.00; N, 19.64%. Calcd for $C_8H_{18}N_2$: C, 67.55; H, 12.75; N, 19.64%. **5c**; IR 3280 cm^{-1} (N-H); NMR ($CDCl_3$) δ=0.62—1.95 (m, 15H), 1.21 (s, 2H), 1.91—3.32 (m, 7H); MS (70 eV), *m/e*, 185 (M^++1), 114, 70, 43. Found: C,71.49; H, 13.42; N, 15.48%. Calcd for $C_{11}H_{24}N_2$: C, 71.68; H, 13.12; N, 15.20%. **5d**; IR 3270 cm^{-1} (N-H); NMR ($CDCl_3$) δ=0.59—2.06 (m, 14H), 1.40 (s, 2H), 2.06—3.29 (m, 6H); MS (70 eV), *m/e*, 183 (M^++1), 112, 70, 43. Found: C, 72.50; H, 12.42; N, 15.30%. Calcd for $C_{11}H_{22}N_2$: C, 72.47; H, 12.61; N, 15.37%. **5e**; IR 3280 cm^{-1} (N-H); NMR ($CDCl_3$) δ=0.76—1.91 (m, 4H), 1.27 (d, 3H), 1.64 (s, 2H), 2.20—3.06 (m, 5H), 3.65 (q, 1H), 6.99—7.39 (m, 5H). Found: C, 76.67; H, 10.04; N, 13.77%. Calcd for $C_{13}H_{20}N_2$: C, 76.42; H, 9.87; N, 13.71%. **5f**; IR 3280 cm^{-1} (N-H); NMR ($CDCl_3$) δ=0.69—2.05 (m, 4H), 1.29 (d, 3H), 1.83 (s, 2H), 2.29—3.13 (m, 5H), 3.70 (q, 1H), 6.88—7.43, (m 5H). Found: C, 76.36; H, 9.65; N, 13.79%. Calcd for $C_{13}H_{20}N_2$: C, 76.42, H, 9.87, N, 13.71%. **5g**; IR 3350 cm^{-1} (N-H); NMR ($CDCl_3$) δ=0.90—1.98 (m, 5H), 2.42—3.55 (m, 5H), 4.92 (br, 1H), 6.49 (dd, 1H), 6.99—7.97 (m, 6H); MS (70 eV), *m/e*, 226 (M^+), 157, 70, 43. **5h**; IR 3400 cm^{-1} (N-H); NMR ($CDCl_3$) δ=1.05—2.20 (m, 5H), 2.52—3.63 (m, 6H), 3.79 (s, 3H), 6.25—6.94 (m, 4H); MS (70 eV), *m/e*, 206 (M^+), 137, 70, 43. **5i**; IR 3330 cm^{-1} (N-H); NMR ($CDCl_3$) δ=1.03—2.10 (m, 4H), 2.50—3.50 (m, 7H), 3.63 (s, 3H), 6.20—6.77 (m, 4H); MS (70 eV), *m/e*, 206 (M^+), 137, 70, 43. **5j**; IR 3300 cm^{-1} (N-H); NMR ($CDCl_3$) δ= 1.00—2.50 (m, 5H), 2.55—3.85 (m, 5H), 4.25 (br, 1H), 6.27—6.75 (m, 2H), 7.33 (dt, 1H), 8'08 (d, 1H); MS (70 eV), *m/e*, 178 (M^++1), 108, 70, 43. Found: C, 68.01; H, 8.51; N, 24.01%. Calcd for $C_{10}H_{15}N_3$: C, 67.76; H, 8.53; N, 23.71%. **5k**; IR 3300 cm^{-1} (N-H); NMR ($CDCl_3$) δ= 0.50—2.23 (m, 4H), 2.44 (s, 1H), 2.59—3.78 (m, 5H), 5.04 (br, 1H), 6.41 (d, 2H), 8.14 (d, 2H); MS (70 eV), *m/e*, 178 (M^++1), 108, 70, 43. **5l**; IR 3350 cm^{-1} (N-H); NMR ($CDCl_3$) δ=0.97—2.13 (m, 5H), 2.35—3,50 (m, 5H), 4.41 (br, 1H), 6.29 (dd, 1H), 6.55 (dd, 1H), 7.03 (d, 1H); MS (70 eV), *m/e*, 244 (M^+), 175, 70, 43.

Asymmetric Reduction of Ketone with $LiAlH_4$–Diamine **5a** *Complex in Ether (Representative example).* The diamine **5a** (359.3 mg, 2.04 mmol) in 2 ml of ether was added to a standardized ethereal solution of $LiAlH_4$ (2.86 ml, 1.77 mmol) over ten minutes at room temperature under an argon atmosphere. On addition of **5a**, hydrogen gas evolved and white precipitates appeared. After stirring for 1 h at room temperature, propiophenone (134 mg, 1.00 mmol) in 2 ml of ether was added at −78 °C, and the reaction mixture was stirred for 3 h. The mixture was hydrolyzed with 0.4 ml of water and washed successively with 8 ml of 0.5 N hydrochloric acid and saturated sodium chloride solution. The ethereal layer was dried over Na_2SO_4 and the solvent was removed. The crude product was purified by preparative TLC to give 1-phenyl-1-propanol (120.0 mg, 90%). Further it was purified for the measurement of specific rotation by bulb to bulb distillation [175 °C (bath temperature/21 mmHg], and 104.3 mg of the alcohol was obtained, $[\alpha]_D^{25}$—23.65° (neat). Most of the chiral diamine was recovered from the aqueous layer by usual work up.

Asymmetric Reduction Acetophenone with $LiAlH_4$–Diamine **5a** *Complex in THF (or toluene).* Under an argon atmosphere, $LiAlH_4$ in ether (2.79 ml, 2.66 mmol) was transfered into the flask. The ether was removed under reduced pressure at room temperature for about 1 h, then 5.5 ml of THF was added. The diamine **5a** (540.2 mg, 3.07 mmol) in 4 ml of THF was added to the solution over ten minutes at room temperature. After stirring for 1 h at toom temperature, acetophenone (180.3 mg, 1.5 mmol) was added at —78 °C and the mixture was stirred for 3 h. The reaction mixture was treated similarly as mentioned above and 1-phenylethanol (97.3 mg, 54%) was obtained, which was further purified for the measurement of specific rotation by bulb to bulb distillation [150—160 °C (bath temperature)/21 mmHg], and 86 mg of alcohol was obtained, $[\alpha]_D^{24}+8.25°$ (*c* 4.00, cyclopentane).

Asymmetric Reduction of Acetophenone with $LiAlH_4$–Diamine **5a** *in the Presence of Additives.* The diamine **5a** (539 mg, 3.07 mmol)–$LiAlH_4$ complex (2.66 mmol) in 8 ml of ether was added TMEDA (307 mg, 2.66 mmol) in 2 ml of ether at room temperature. After stirring for 1 h, acetophenone (180.5 mg, 1.5 mmol) was added to the reaction mixture at −78 °C, which was stirred for 3 h. After the reaction mixture was treated similarly, 1-phenylethanol (122.5 mg, 67%) was obtained, which was further purified by bulb to bulb distillation [150—160 °C (bath temperature)/21 mmHg] and 115.9 mg of alcohol was obtained, $[\alpha]_D^{25}-7.6°$ (*c* 6.88, cyclopentane).

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