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Asymmetric Reductions of Imines and Ketones by Chiral Oxaborolidines†

Masako Nakagawa,* Tomohiko Kawate, Taro Kakikawa, Hideki Yamada, Teruaki Matsui, and Tohru Hino*

Faculty of Pharmaceutical Sciences, Chiba University, 1-33, Yayoi-cho, Inage-ku, Chiba-shi, 263, Japan.

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Abstract: Asymmetric reduction of imines were studied using dialkoxyborane **1**. Dihydro-β-carboline **5a** showed moderate (42%ee) and *N*-phenylketimine **10** higher enantioselectivity (73%ee). Asymmetric reduction of ketones with oxazaborolidine **33** showed high enantioselectivites.

As a part of our continued effort to synthesize various biologically important alkaloids and other medicinally relevant molecules,[1] our attention has been focused on the development of efficient methods for the construction of enantiopure amines, which would provide an effective route to optically active these compounds.[2]

Despite the enormous progress made in the asymmetric alkylation and reduction of prochiral carbonyl compounds to chiral alcohols,[3] the development of the corresponding studies of useful enantioselective conversion of prochiral imines to chiral amines remains a challenging area of research.[4,5] Our first attention was drawn towards a new chiral borane reagent **1** for the asymmetric reduction of imines.[2] On the other hand, recent progress [6] in the search for the high enantioselectivity and broad applicability of oxazaborolidines as reducing agents or catalysts has led us to explore the asymmetric reduction of imines and ketones by a new oxazaborolidine reagent **33** having a sterically rigid tetracyclic structure. We now report moderate to high enantioselectivity obtained in the reduction of a prochiral C=N group and C=O group with new chiral reducing reagents **1** and **33**, respectively.

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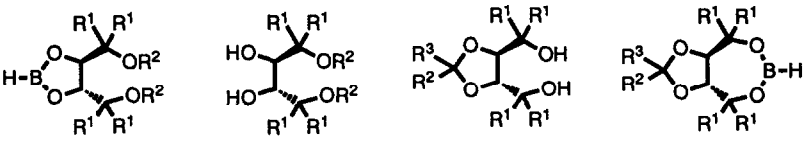
† Dedicated to Professor Emeritus Shun-ichi Yamada on the occasion of his 77th birthday.

Asymmetric Reduction of Imines with Dialkoxyborane 1.

The reaction conditions initially chosen to mimic those found most successful for corresponding studies with ketones[7] failed to reduce imines. This can be in part a consequence of the low electrophilicity of the C=N group of imines compared with the corresponding carbonyl group, which often requires activation by a Lewis acid to proceed. After several trials, we found various dialkoxyborane reagents **1** reduce 3,4-dihydro-1-methyl-β-carboline **5a** which has been selected as a stable imine as well as considerable potential in the synthesis of biologically important indole alkaloids.

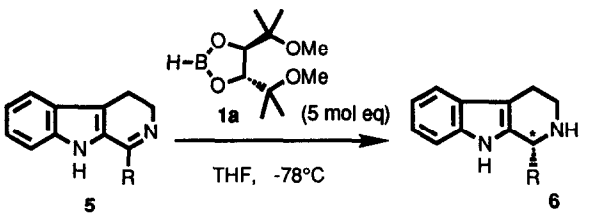


1 **2** **3** **4**

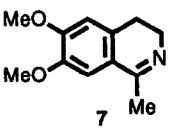
1, 2: **a**, R^1=R^2=Me
b, R^1=Et, R^2=Me
c, R^1=H, R^2=Me
d, R^1=Me, R^2=Ph

3, 4: **a**, R^1=R^2=R^3=Me
b, R^1=Et, R^2=R^3=Me
c, R^1=R^2=Me, R^3=Ph

Table 1: Reduction of Dihydro-β-carbolines with **1a**



5 **1a** (5 mol eq) THF, -78°C **6**



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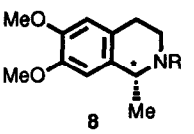

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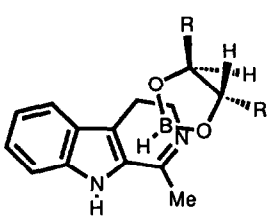
a: R=H
b: R =CO_2Me

Entry		R	Time	Yield(%)		$[\alpha]_D$	%ee[a]
1	**5a**	Me	10 min	**6a**	98	+22.0°	42(R)
2	**5b**	nBu	10 min	**6b**	100	+18 5°	23(R)
3	**5c**	iBu	10 min	**6c**	100	+18.5°	23(R)
4	**5d**	Ph	7.5 h	**6d**	96	+4.37°	27(R)

a) Optical purities were calculated by comparison of optical rotaion with reported value(**6a**) or authentic sample(**6b** ~**d**).[12]



favoured ***si*-face attack**

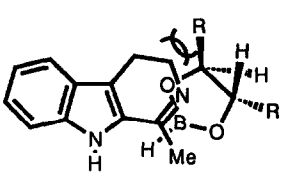


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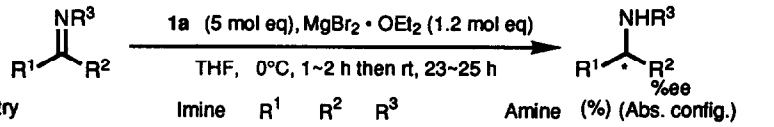
Figure 1

Table 2: Reduction of Various Imines with **1a**



Entry	Imine	R^1	R^2	R^3	Amine	(%)	(Abs. config.)
1	**9**	Me	Ph	Ph	**21**	89	56(R)[a]
2	**10**	Et	Ph	Ph	**22**	91	73(S)[b]
3	**11**	Pr	Ph	Ph	**23**	94	65(S)[a]
4	**12**	Bu	Ph	Ph	**24**	95	65(-)[a,d]
5	**13**	iPr	Ph	Ph	**25**	85	18(-)[a,d]
6	**14**	α-tetralone		Ph	**26**	79	12(+)[a,d]
7	**15**	Me	Ph	C_6H_4-*p*OMe	**27**	99	59(+)[a,d]
8	**16**	iPr	Me	Ph	**28**	75	71(-)[a,d]
9	**17**	Ph	Me	CH_2Ph	**29**	70	72(R)[b]
10	**18**	Ph	Pr	CH_2Ph	**30**	81	36(+)[c,d]
11	**19**	Ph	Me	OMe		N R	
12	**20**	Ph	Me	OCH_2Ph		N R	

a) Determined by HPLC using a chiral column (Daicel chiralcel OD, hexane:^{i}PrOH=95. 5 or 98:2 as eluent).
b)Calculated by comparison of optical rotation with reported value· **22**, ref 14; **29**, ref15
c) Determined by ^{1}H-NMR using a chiral shift reagent, (R)-2,2,2-trifluoro-1-(9-anthranyl)ethanol.
d) Absolute configuration was not determined

The requisite chiral dialkoxyboranes **1** were prepared by treatment of BH_3•THF with chiral diols **2**, obtained straightforward manner from L-or D-dialkyl tartrate.[8] The reaction of **5a** with **1a** in THF at -78°C proceeded within 10 min to give tetrahydro-β-carboline **6a** in 42%ee. This reduction was applied to a range of 1-substituted-β-carboline **5b~5d**. In all cases the corresponding amines **6** were obtained in excellent yield but all gave low optical yields. (Table 1) The results led us to investigate the steric bulkiness of the substituents of **1** which may control the reduction course effectively and improve the enantioselectivity. All the dialkoxyborane **1b~d** and **4a~c** examined provided **6a** in essentially quantitative chemical yields, but proved to be less effective. The *si*-face directing effect for the formation of **6a** may be explained considering a transition state which avoids nonbonded interaction between the methylene protons of **5a** and the substituent of dialkoxyborane **1**.(Figure 1) Consequently, when **5a** was treated with **D-1a**, the enantiomer of **1a**, (S)-**6a** was obtained in 48%ee.

Characteristic feature of this reagent **1a**, however, is the capability of reducing a representative cyclic imine, 3,4-dihydroisoquinoline **7** to (+)-(R)-salsolidine **8** (50% yield,[9] 28%ee) which was not reduced by Itsuno's reagent **31**.[5a] These investigations have now been extended to the reduction of the structurally related *N*-phenylazomethines (**9-20**) with the aim of obtaining chiral secondary amines (**21-30**). In contrast

to **5**, **1a** alone failed to reduce *N*-phenylpropiophenone imine **10** under the similar reaction conditions. However, addition of $MgBr_2$•OEt_2 (1.2 mol eq) gave a remarkable effect on the asymmetric reduction of **10** with **1a** in 91% yield with 73%ee. Table 2 summarizes the results.

Treatment of the imines **9**, **11**, **12** and **15**, derived from phenyl primary alkyl ketones and aniline, with **1a** and $MgBr_2$•OEt_2 gave modest to good enantioselectivity with high chemical yields. (entries 1,3,4, and 7) Better enantioselectiveties were observed when an dialkyl ketimine, 3-methyl-2-butanone anil **16** and *N*-benzyl imine **17** were reduced under similar conditions.(entries 8 and 9) The reagent **1a** did not reduce the oxime ethers. Although no clear-cut explanations for the stereochemical outcome of the present reduction are available at the moment, similar reduction of **10** with **D-1a** cleanly produced (R)-**22** in corresponding chemical (94%) and optical yields having the specific rotation opposite in sign (71%ee).

Asymmetric Reduction of Imines and Ketones with Oxazaborolidine 33.

Our attention has now been focused on the reduction of imines and ketones with a new chiral oxazaborolidine **33** which is readily prepared from the chiral aminoalcohol **34** and BH_3•THF since recent report[10] reveals that Corey's reagent **32** as well as Itsuno's reagent **31** also serve as an reducing agent for *N*-phenylketimines to chiral amines.

The formation of **33** was accomplished by Corey's conditions (3 mol eq of BH_3•THF, reflux 3 h, solvent evaporation). We first carried out the reduction of the imine **10**, but the asymmetric induction was only 13%ee. The other conditions attempted to improve the enantioselectivity was unsuccessful.

On the other hand, oxazaborolidine **33** was shown to be highly effective reagent for reduction of prochiral ketones to chiral secondary alcohols. The results for the reduction of acetophenone **35** and a range of other ketones by **33** with BH_3•THF (0.6 mol eq) are summarized in Table 3. The ketone reductions readily occur (5 min) with high enantioselectivities. While the best enantioselectivity was obtained with α-tetralone **41**, the induction was poor with β-tetralone **42**.

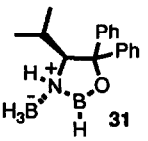
Further studies are in progress to fully evaluate the potential of these new reducing reagents.

Acknowledgments .

Financial support of this work by the Ministry of Education, Science, and Culture in the form of a Grant-in-Aid for Scientific Research is gratefully acknowledged. Thanks also due to the Hayashi Memorial Foundation for Female Natural Scientists, Japan Research Foundation for Optically Active Compounds, and the Uehara Memorial Foundation for financial support. We also thank Dr. K. Ogata, Mrs. H. Seki, Miss R. Hara, Mr. T. Kuramochi, and Mrs. S. Imamoto at the Chemical Analysis Center of Chiba University for measurement of spectroscopic data (NMR and mass) and elemental analysis.

EXPERIMENTAL

Instrumental technique, etc., were as described in the preceding paper.[1f] HPLC analysis was performed on a Hitachi 655 instrument, using a Daicel chiralcel OD and the following solvent system was used as a eluent: A) hexane:^{i}PrOH= 95:5, B) hexane:^{i}PrOH=98:2, or C) hexane:^{i}PrOH=90:10.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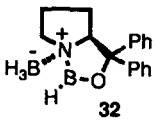
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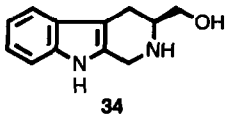
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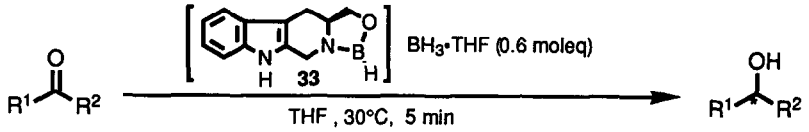
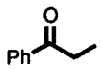
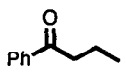
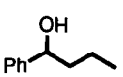
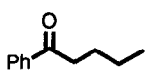
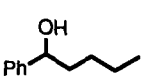
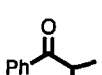
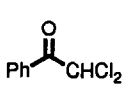
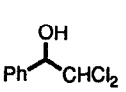
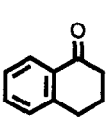
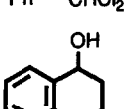
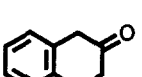
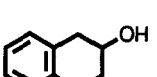
Table 3: Reduction of Various Ketones with **33** [a]



Entry	Ketone		Alcohol		Yield(%)	%ee
1	**35**		**43**		85	88 (R)[b]
2	**36**		**44**		97	78 (R)[b]
3	**37**		**45**		96	89 (R)[b]
4	**38**		**46**		95	80 (R)[b]
5	**39**		**47**		85	50 (S)[c]
6	**40**		**48**		100	8 (+)[b]
7	**41**		**49**		99	96 (R)[b]
8	**42**		**50**		99	11(R)[c]

a) **33** was prepared *in situ* from **34** (1.1 mol eq) and BH_3•THF(3 mol eq) in THF.[6h-k]

b) Determined by HPLC using a chiral column (Daicel chiralcel OD, hexane:iPrOH=95:5 as eluent).

c) Calculated by comparison of optical rotation with reported value: **47**, ref17; **50**, ref18.

Reduction of imines with dialkoxyborane (General procedure, typically described for the reduction of 10 with 1a) The chiral borane reagents were prepared as follow: To a solution of chiral diol **2a** (3753 mg, 18.2 mmol) in THF (24 ml), was added BH_3•THF (1 M in THF, 16 ml) at 0°C. The reaction mixture was stirred for 2 h at 0°C, then allowed to stand at ca. 4°C for 22 h. The resulting solution was used as a ca. 0.4 M solution of **1a** in THF without further manipulation. For further purification, **1a** was distilled under reduced pressure, bp 49~51°C (2 x 10^{-3} mmHg). $[\alpha]_D^{22}$ -81.3°(c 4.77, $CHCl_3$). IR ν_{max}(neat)

2580(B-H) cm^{-1}. ^{1}H-NMR δ 1.12(6H, s, Me x 2), 1.16(6H, s, Me x 2), 3.23(6H, s, OMe x 2), 4.14(2H, s, CH x 2).

The reduction was performed as follow: **1a** (18.8 ml, 7.52 mmol, prepared as above) was added to the mixture of *N*-phenyl imine **10** (315 mg, 1.5 mmol) and $MgBr_2$•OEt_2 (465 mg, 1.8 mmol) in THF (30 ml) at 0°C under an argon atmosphere. After stirred for 23 h at room temperature, saturated $NaHCO_3$ aqueous solution was added and concentrated *in vacuo*, and extracted with CH_2Cl_2. The extracts were washed, dried, and evaporated to gave a residue, which was chromatographed on silica gel ($CHCl_3$:hexane= 1:3~1:2) to give the amine **22** (289 mg, 91%, $[\alpha]_D^{25}$ +6.40°, 73%ee[5a]).

1-Methyl-tetrahydro-β-carboline 6a: orange solid. $[\alpha]_D^{27}$ +22.0°(c 0.91, EtOH), 42%ee(R)(lit. for (S)-**6a**, $[\alpha]_D^{25}$ -52°(c 2.0, EtOH)[11]). ^{1}H-NMR δ 1.46(3H, d, *J*=6.8 Hz, Me), 1.58(1H, brs, N_b-H), 2.72(1H, dddd, *J*=1.7, 3.4, 5.1, 15.4 Hz, 4-H_a), 2.78(1H, dddd, *J*=2.0, 5.3, 9.0, 15.4 Hz, 4-H_b), 3.06(1H, ddd, *J*=5.1, 9.0, 13.1 Hz, 3-H_a), 3.37(1H, ddd, *J*=3.4, 5.4, 13.0 Hz, 3-H_b), 4.19(1H, tq, *J*=2.0, 6.8 Hz, 1-H), 7.09(1H, dt, *J*=1.0, 7.9 Hz, aromatic), 7.15(1H, dt, *J*=1.2, 8.0 Hz, aromatic), 7.31(1H, dd, *J*=1.0, 8.0 Hz, aromatic), 7.48(1H, d, *J*=7.8 Hz, aromatic), 7.75(1H, brs, N_a-H). EIMS *m/z* 186(M^+), 171(100).

1-Butyl-tetrahydro-β-carboline 6b[12]: yellow caramel. $[\alpha]_D^{25}$ +18.51°(c 1.14, EtOH), 23%ee(R)[for (S)-**6b**: $[\alpha]_D^{22}$ -80.86°(c 0.55, EtOH)]. ^{1}H-NMR δ 0.94(3H, t, *J*=7.42 Hz, Me), 1.33-1.71(6H, m, $CH_aCH_2CH_2Me$ and N_b-H), 1.88(1H, m, 1-CH_b), 2.74(2H, m, 4-H_2), 3.03(1H, ddd, *J*=5.22, 8.52, 13.75 Hz, 3-H_a), 3.36(1H, m, 3-H_b), 4.06(1H, m, 1-H),, 7.75(1H, brs, N_a-H). EIMS *m/z* 228(M^+), 170(M^+-Bu). HR-FABMS Calcd for $C_{15}H_{20}N_2$+H: 229.1706. Found: 229.1709.

1-Isobutyl-tetrahydro-β-carboline 6c[12]: yellow caramel. $[\alpha]_D^{25}$ +18.50°(c 1.14, MeOH), 23%ee(R)[for (S)-**6c**: $[\alpha]_D^{19.5}$ -79.8°(c 1.01, MeOH). ^{1}H-NMR δ 1.00(3H, d, *J*=6.60 Hz, Me), 1.03(3H, d, *J*=6.32 Hz, Me), 1.63(2H, m, 1-CH_2), 1.87(1H, brs, N_b-H, exchangeable), 1.98(1H, m, Me_2CH), 2.74(2H, m, 4-H_2), 3.03(1H, ddd, *J*=5.50, 8.25, 12.92 Hz, 3-H_a), 3.35(1H, td, *J*=4.40, 12.92 Hz, 3-H_b), 4.12(1H, ddd, *J*=2.20, 4.68, 6.88 Hz, 1-H), 7.74(1H, brs, N_a-H, exchangeable). EIMS *m/z* 228(M^+), 170(M^+-iBu, 100).

1-Phenyl-tetrahydro-β-carboline 6d[12]: yellow solid. $[\alpha]_D^{25}$ +4.37°(c 1.19, EtOH), 27%ee(R)[for (S)-**6d**: $[\alpha]_D^{24}$ -16.4°(c 0.38, EtOH). ^{1}H-NMR δ 1.73(1H, br, N_b-H), 2.88(1H, dddd, *J*=1.7, 3.9, 4.7, 15.4 Hz, 4-H_a), 2.92(1H, dddd, *J*=1.9, 5.4, 9.0, 15.4 Hz, 4-H_b), 3.14(1H, ddd, *J*=4.7, 9.1, 12.5 Hz, 3-H_a), 3.38(1H, ddd, *J*=3.9, 5.4, 12.7 Hz, 3-H_b), 5.16(1H, brt, 1-H). EIMS *m/z* 248(M^+, 100).

Salsolidine 8a: pale yellow oil. 28%ee(R)[HPLC, hexane:^{i}PrOH:Et_2NH=800:200:0.1, 0.5 ml/min]. t_R(major)=21.47 min, (minor)=18.19 min. $[\alpha]_D^{19}$ +14.83°(c 1.09, EtOH)(lit. for (S)-**8a**, $[\alpha]_D^{25}$ -59.3°(EtOH)[13]). ^{1}H-NMR δ 1.46(3H, d, *J*=6.7 Hz, Me), 2.28(1H, brs, NH), 2.67(1H, m, 4-H_a), 2.81(1H, m, 4-H_b), 3.01(1H, m, 3-H_a), 3.25(1H, m, 3-H_b), 3.85(6H, s, OMe x 2), 4.07(1H, q, *J*=6.7 Hz, 1-H), 6.57(1H, s, 5-H), 6.62(1H, s, 8-H)

***N*-Methoxycarbonyl-salsolidine 8b:** colorless prisms. mp. 67.5~70.5°C(AcOEt-hexane). ^{1}H-NMR δ(50°C) 1.44(3H, d, *J*=6.6 Hz, Me), 2.64(1H, m, 4-H_a), 2.86(1H, m, 4-H_b), 3.23(1H, brs, 3-H_a), 3.73(3H, s, COOMe), 3.85(6H, s, OMe x 2), 4.11(1H, brs, 3-H_b), 5.13(1H, brs, 1-H), 6.58(2H, s, aromatic). Anal. Calcd for $C_{14}H_{19}NO_4$: C, 63.38; H, 7.22; N, 5.28. Found: C, 63.30; H, 7.04; N, 5.65.

***N*-Phenyl-1-phenylethylamine 21**: pale yellow oil. 56%ee(R)[HPLC, A), 0.5 ml/min]. t_R(major)=16.99 min, (minor)=14.69 min. $[\alpha]_D^{26}$ -9.89°(c 1.76, EtOH)(lit. $[\alpha]_D^{25}$ -26.1°(c 2.15, EtOH)[14]). ^{1}H-NMR δ 1.51(3H, d, *J*=6.6 Hz, Me), 4.02(1H, brs, NH), 4.48(1H, q-like, *J*=6.6 Hz, CH),

6.51(2H, td-like, *J*=1.1, 7.5 Hz, Ph), 6.64(1H, tt, *J*=1.0, 7.4 Hz, Ph), 7.08(2H, m, Ph), 7.20-7.37(5H, m, Ph). EIMS *m/z* 197(M^+).

***N*-Phenyl-1-phenylpropylamine 22**: pale yellow oil. $[\alpha]_D^{25}$ +6.40°(c 2.89, MeOH), 73%ee(S).(lit. $[\alpha]_D^{22}$ -7.71°(c 1.06, MeOH) for 87%ee(R)[5a]). ^{1}H-NMR δ 0.95(3H, t, *J*=7.42 Hz, Me), 1.82(2H, m, CH_2), 4.04(1H, brs, NH, exchangeable), 4.22(1H, t, *J*=6.60 Hz, CH), 6.51(2H, d, *J*=7.70 Hz, Ph), 6.62(1H, m, Ph), 7.07(2H, dt, *J*=1.93, 7.01 Hz, Ph), 7.21(1H, m, Ph), 7.32(4H, m, Ph). HR-FABMS: Calcd for $C_{15}H_{17}N$+H: 212.1440. Found: 212.1427.

***N*-Phenyl-1-phenylbutylamine 23**: pale yellow oil. 94%. 65%ee(S)[HPLC, A), 0.5 ml/min]. t_R(major)=13.44 min, (minor)=11.44 min. $[\alpha]_D^{25}$ +1.84°(c 2.12, MeOH)[(-)-rotation for R-configuration[5a]]. ^{1}H-NMR δ 0.93(3H, t, *J*=7.51 Hz, Me), 1.39(2H, m, CH_2), 1.77(2H, m, CH_2), 4.05(1H, brs, NH), 4.30(1H, t, *J*=6.78 Hz, CH). EIMS *m/z* 225(M^+). HR-FABMS: Calcd for $C_{16}H_{19}N$+H: 226.1597. Found: 226.1594.

***N*-Phenyl-1-phenylpentylamine 24**: pale yellow oil. 95%. 65%ee[HPLC, A), 0.5 ml/min]. t_R(major)=12.64 min, (minor)=10.88 min. $[\alpha]_D^{24}$ -2.72°(c 1.14, MeOH). ^{1}H-NMR δ 0.88(3H, t, *J*=7.14 Hz, Me), 1.34(4H, m, CH_2 x 2), 1.78(2H, m, CH_2), 4.05(1H, brs, NH, exchangeable), 4.28(1H, t, *J*=6.78 Hz, CH). HR-FABMS: Calcd for $C_{17}H_{21}N$+H: 240.1754. Found: 240.1743.

***N*-Phenyl-2-methyl-1-phenylpropylamine 25**: pale yellow oil. 18%ee[HPLC, C), 0.5 ml/min]. t_R(major)=11.52 min, (minor)=12.72 min. $[\alpha]_D^{25}$ -4.75°(c 1.98, MeOH). ^{1}H-NMR δ 0.91(3H, d, *J*=6.78 Hz, Me), 0.98(3H, d, *J*=6.77 Hz, Me), 2.02(1H, m, Me_2CH), 4.12(2H, brd, *J*=5.86 Hz, CH and NH(exchangeable)). HR-FABMS: Calcd for $C_{16}H_{19}N$+H: 226.1597. Found: 226.1594.

1-Phenylamino-1,2,3,4-tetrahydronaphthalene 26: orange oil. 79%. 12%ee[HPLC, C), 0.5 ml/min]. t_R(major)=18.32 min, (minor)=16.83 mim. $[\alpha]_D^{25}$ +1.46°(c 0.89, MeOH). ^{1}H-NMR δ 1.81(1H, m, 3-H_a), 1.88(1H, m, 3-H_b), 1.97(2H, m, 2-H_2), 2.80(2H, m, 4-H_2), 3.86(1H, brs, NH), 4.63(1H, t, *J*=4.76 Hz, 1-CH), 6.68(3H, m, Ph), 7.11-7.22(5H, m, Ph), 7.40(1H, d, *J*=6.96 Hz, Ph). FABMS *m/z* 224(MH^+). HR-FABMS: Calcd for $C_{16}H_{17}N$+H: 224.1440. Found: 224.1432.

***N*-(*p*-Methoxyphenyl)-1-phenylethylamine 27**: pale yellow oil. 99%. 59%ee[HPLC, A), 0.5 ml/min]. t_R(major)=17.81 min, (minor)=20.05 min. $[\alpha]_D^{21}$ +4.54°(c 3.24, MeOH). ^{1}H-NMR δ 1.49(3H, d, *J*=6.59 Hz, Me), 3.69(3H, s, OMe), 3.77(1H, brs, NH, exchangeable), 4.41(1H, q, *J*=6.78 Hz, CH), 6.47(2H, d, *J*=8.98 Hz, Ph), 6.69(2H, d, *J*=8.98 Hz, Ph), 7.21-7.35(5H, m, Ph). HR-EIMS: Calcd for $C_{15}H_{17}NO$: 227.1311. Found: 227.1312.

***N*-Phenyl-1,2-dimethylpropylamine 28**: pale yellow oil. 75%. 71%ee[HPLC, hexane, 0.5 ml/min]. t_R(major)=30.35 min, (minor)=32.40 min. $[\alpha]_D^{23}$ -27.90°(c 1.24, MeOH). ^{1}H-NMR δ 0.91(3H, d, *J*=6.77 Hz, Me), 0.97(3H, d, *J*=6.96 Hz, Me), 1.09(3H, d, *J*=6.41 Hz, Me), 1.84(1H, m, Me_2CH), 3.34(1H, m, CH), 3.47(1H, brs, NH, exchangeable), 6.57(2H, dd, *J*=0.92, 8.61 Hz, Ph), 6.64(1H, tt, *J*=1.10, 7.33 Hz, Ph), 7.15(2H, m, Ph). EIMS *m/z* 163(M^+). HR-EIMS: Calcd for $C_{11}H_{17}N$: 163.1362. Found: 163.1367.

***N*-Benzyl-1-phenylethylamine 29**: pale yellow oil. 70%. $[\alpha]_D^{22}$ +28.57°(c 0.63, $CHCl_3$), 72%ee(R)(lit. for (S) $[\alpha]_D^{20}$ -39.8°($CHCl_3$)[15]). ^{1}H-NMR δ 1.37(3H, d, *J*=6.60 Hz, Me), 1.57(1H, brs, NH, exchangeable), 3.59(1H, d, *J*=13.19 Hz, $PhCH_a$), 3.66(1H, d, *J*=13.16 Hz, $PhCH_b$), 3.81(1H, q, *J*=6.60 Hz, CH). EIMS *m/z* 211(M^+). HR-EIMS: Calcd for $C_{15}H_{17}N$: 211.1362. Found: 211.1361.

***N*-Benzyl-1-phenylbutylamine 30**: pale yellow oil. 81%. 36%ee[^{1}H-NMR analysis using (R)-2,2,2-trifluoro-1-(9-anthranyl)ethanol]. $[\alpha]_D$21 +16.63°(c 2.64, $CHCl_3$). ^{1}H-NMR δ 0.85(3H, t, *J*=7.3 Hz, Me),

1.15(1H, m, $MeCH_a$), 1.30(1H, m, $MeCH_b$), 1.57-1.74(3H, m, CH_2 and NH), 3.53(1H, d, *J*=13.2 Hz, $PhCH_a$), 3.61(1H, m, CH), 3.64(1H, d, *J*=13.2 Hz, $PhCH_b$). FABMS *m/z* 240(MH^+). HR-FABMS: Calcd for $C_{17}H_{21}N$+H: 240.1754. Found: 240.1750.

Reduction of ketones and imines with 33 and BH_3•THF. (general procedure for 49) BH_3•THF(1 M in THF, 1.5 ml, 1.5 mmol) was added to a solution of **34** [16](111 mg, 0.55 mmol) in THF (5 ml) and the mixture was refluxed for 3 h under argon atmosphere. After cooling to room temperature, solvent and excess borane were removed *in vacuo* to give a white amorphous solid, crude **33**, which was used without further purification. **33** was dissolved in THF (5 ml) and BH_3•THF(1 M in THF, 0.3 ml, 0.3 mmol) was added. To this solution, a solution of α-tetralone **41** (73 mg, 0.5 mmol) in THF (5 ml) was added dropwise over 40 min at 30°C. The resulting mixture was stirred further 5 min at the same temperature, and sat. $NaHCO_3$ aqueous solution was added to the mixture. After removal of THF *in vacuo*, Aqueous layer was extracted with CH_2Cl_2 and combined organic layers were washed with H_2O and brine and dried. Evaporation of the solvent gave a residue, which was chromatographed on a silica gel to afford alcohol **49** (73 mg, 99%); 96%ee(S) [HPLC, A), 0.3 ml/min].

1-Phenyl-ethanol 43: colorless oil. 88%ee (R)[HPLC, A), 1.0 ml/min]: t_R (major)=8.76 min, (minor)=10.40 min. IR ν_{max}(neat) 3350 cm^{-1}. ^{1}H-NMR δ 1.50(3H, d, *J*=6.4 Hz, Me), 1.85(1H, brs, OH), 4.90(1H, q, *J*=6.4 Hz, CH), 7.25~7.38(5H, m, Ph). EIMS *m/z* 122(M^+).

1-Phenyl-1-propanol 44: colorless oil. 78%ee (R)[HPLC, A), 1.0 ml/min]: t_R (major)=9.28 min, (minor)=11.20 min. IR ν_{max}(neat) 3350, 3025 cm^{-1}. ^{1}H-NMR δ 0.92(3H, t, *J*=7.5 Hz, Me), 1.71-1.85(2H, m, CH_2), 1.88(1H, brs, OH), 4.59(1H, t, *J*=6.6 Hz, CH). EIMS *m/z* 136(M^+).

1-Phenyl-1-butanol 45: colorless solid. 89%ee (R)[HPLC, A), 0.3 ml/min]: t_R (major)=28.04 min, (minor)=30.56 min. IR ν_{max}(KBr) 3370, 3275 cm^{-1}. ^{1}H-NMR δ 0.93(3H, t, *J*=7.3 Hz, Me), 1.25-1.36(1H, m, CH_aMe), 1.38-1.49(1H, m, CH_bMe), 1.64-1.72(1H, m, CH_aCH_2Me), 1.75-1.83(1H, m, CH_bCH_2Me), 1.84(1H, brs, OH), 4.68(1H, t, *J*=6.6 Hz, C*H*OH). EIMS *m/z* 150(M^+).

1-Phenyl-1-pentanol 46: colorless oil. 80%ee (R)[HPLC, A), 0.5 ml.min]: t_R (major)=16.16 min, (minor)=18.20 min. IR ν_{max}(neat) 3350, 3025 cm^{-1}. ^{1}H-NMR δ 0.88(3H, t, *J*=7.4 Hz, Me), 1.21-1.43(4H, m, CH_2CH_2Me), 1.67-1.85(2H, m, CH_2), 1.85(1H, s, OH), 4.66(1H, t, *J*=6.6 Hz, C*H*OH). EIMS *m/z* 164(M^+).

2-Methyl-1-phenyl-1-propanol 47: colorless oil. $[\alpha]_D^{21}$ -24.06°(c 0.64, Et_2O), 50%ee (S)[for (R) $[\alpha]_D^{20}$ +47.7°[17)]. IR ν_{max}(neat) 3400, 3045 cm^{-1}. ^{1}H-NMR δ 0.80(3H, d, *J*=6.8 Hz, Me), 0.99(3H, d, *J*=6.6 Hz, Me), 1.85(1H, brs, OH), 1.91-2.00(1H, m, C*H*Me_2), 4.35(1H, d, *J*=6.9 Hz, C*H*OH). EIMS *m/z* 150(M^+).

2,2-Dichloro-1-phenyl-ethanol 48: colorless oil. 8%ee (+) [HPLC, A), 1.0 ml/min]: t_R (major)=17.31 min, (minor)=19.95 min. IR ν_{max}(neat) 3400, 3030 cm^{-1}. ^{1}H-NMR δ 2.94(1H, d, *J*=3.1 Hz, OH), 4.98(1H, dd, *J*=2.5, 6.2 Hz, C*H*OH), 5.82(1H, d, *J*=5 4 Hz, $CHCl_2$). EIMS *m/z* 192(M^++2), 190(M^+).

1-Hydroxytetralone 49: colorless oil. 96%ee (R)|HPLC, A), 0.3 ml/min]: t_R (major)=31.52 min, (minor)=28.81 min. IR ν_{max}(neat) 3300, 3025 cm^{-1}. ^{1}H-NMR δ 1.73-1.83(2H, m, 2-H_a, 3-H_a), 1.87-2.03(3H, m, 2-H_b, 3-H_b, OH), 2.69-2.75(1H, m, 4-H_a), 2.82(1H, dd, *J*=5.6, 16 6 Hz, 4-H_b), 4.78(1H, d, *J*=3.7 Hz, C*H*OH), 7.09-7.12(1H, m, Ph), 7.17-7.22(2H, m, Ph), 7.41-7.44(1H, m, Ph). EIMS *m/z* 148(M^+).

2-Hydroxytetralone 50: colorless oil. $[\alpha]_D^{21}$ +7.88°(c 0.66, EtOH), 11%ee (R)[for (S): $[\alpha]_D^{19}$ -72.2°[18)] IR ν_{max}(neat) 3350, 3020 cm^{-1}. ^{1}H-NMR δ 1.71(1H, s, OH), 1.78-1.85(1H, dddd, *J*=5.8, 8.2, 11.8, 14.3 Hz, 3-H_a), 2.03(1H, m, 3-H_b), 2.76(1H, dd, *J*=8.0, 16.2 Hz, 1-H_a), 2.84(1H, dd, *J*=6.1, 9.2, 17.1 Hz, 4-H_a), 2.95(1H, ddd, *J*=5.8, 11.8, 17.1 Hz, 4-H_b), 3.08(1H, dd, *J*=4.9, 16.2 Hz, 1-H_b), 4.15-4.17(1H, m, C*H*OH), 7.07-7.24(4H, m, Ph). EIMS *m/z* 148 (M^+).

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