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Enantioselective Borane Reduction of Acetophenone Catalysed by Oxazaborolidines Derived from Chiral Diethanolamines

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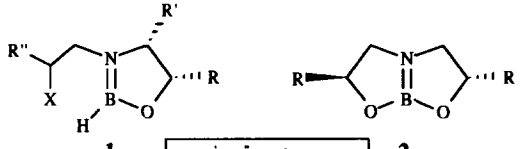
***Abstract** : The synthesis of oxazaborolidines of types **1** and **2**, derived from chiral diethanolamines and their behaviour, as catalysts for the asymmetric reduction of acetophenone by borane has been investigated. Bicyclic oxazaborolidines of type **2** afforded the expected alcohol in good yield but with modest ee's (ee<40%). Monocyclic oxazaborolidines of type **1** gave better results. For instance, catalyst **16** allowed the isolation of (S) α-methyl benzyl alcohol with 72% ee while oxazaborolidine **26**, structurally close to **16**, produced a remarkable reversal of enantiofacial selectivity. The origin of the enantioselectivity of these catalysts is discussed on the basis of transition state models.*

Chiral oxazaborolidine-borane adducts have been shown to be highly effective for the catalytic enantioselective reduction of many prochiral ketones.[1] The exact nature of the reaction mechanism still remains under investigation.[2] Although several efficient catalysts have been developed, most of them are derived, with few exceptions,[3] from L-amino acids.[1a,4] The resulting (*S*) amino alcohol-borane systems have been reported to reduce acetophenone to an alcohol having (*R*) configuration with high asymmetric induction. The use of more expensive D-amino acids is thus required to obtain (*S*) alcohol.

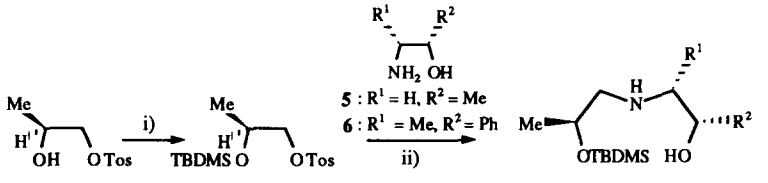
In the course of our study concerning the behaviour of diethanolamines as tridentate boron ligands,[5] we decided to prepare and to test new oxazaborolidines **1** and dioxazaborolidines **2** as chiral catalysts in the asymmetric borane reduction of acetophenone. We wish to report herein our results.



Diethanolamine synthesis

Oxazaborolidines **1** and **2** are derived from chiral diethanolamines. In the field of asymmetric reduction of ketones, several diethanolamines have previously been used as chiral ligands of aluminum hydrides,[6a-c] for borohydrides [5] or for samarium complexes in the Meerwein-Ponndorf reaction.[6d] However, chiral diethanolamines have never been employed for the preparation of catalysts for ketone reduction by boranes.

Oxazaborolidines of type **1** were prepared from diethanolamines **7-8** which were in turn prepared as shown in Scheme 1. Thus, the hydroxyl group of the monotosylated diol **3** [7] was protected using *tert*-butyldimethylsilyl triflate[8] to afford **4** in 92% yield. Nucleophilic substitution of **4** by amino alcohols **5** or **6** was achieved in good yield in refluxing *n*-butanol, giving compounds **7** and **8**.



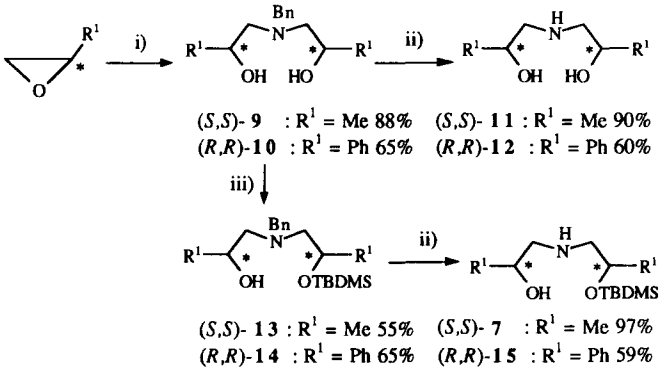
(*S*)-**3** **4** 92%

7 : R^1 = H, R^2 = Me 82%
8 : R^1 = Me, R^2 = Ph 78%

i) TBDMSOTf; 2,6 lutidine; CH_2Cl_2; 0°C. ii) n-BuOH; 48h; Δ

Scheme 1: Preparation of monoprotected diethanolamines **7**, **8**

Oxazaborolidines of type **2** were prepared from diethanolamines **11** and **12**, themselves obtained by aminolysis of the appropriate epoxides followed by debenzylation (Scheme 2).[5] Moreover, diethanolamines **9** and **10** were monosilylated to afford, after debenzylation, compounds **7** and **15**, respectively.



(*S*,*S*)- **9** : R^1 = Me 88% (*S*,*S*)- **11** : R^1 = Me 90%
(*R*,*R*)-**10** : R^1 = Ph 65% (*R*,*R*)-**12** : R^1 = Ph 60%

(*S*,*S*)- **13** : R^1 = Me 55% (*S*,*S*)- **7** : R^1 = Me 97%
(*R*,*R*)-**14** : R^1 = Ph 65% (*R*,*R*)-**15** : R^1 = Ph 59%

i) Benzylamine; methanol; Δ ii) Pd/C; H_2 (1 atm); methanol iii) TBDMSOTf; 2.6-lutidine; CH_2Cl_2.

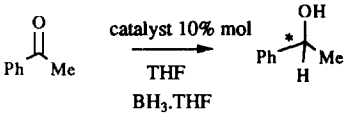
Scheme 2 : Preparation of diethanolamines by epoxide aminolysis

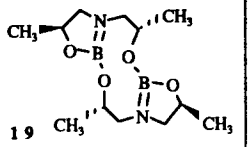
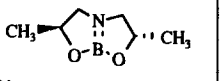
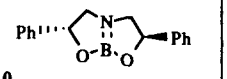
Oxazaborolidine synthesis :

Oxazaborolidines **16-21** (Tables 1 and 2) were obtained by reacting the corresponding diethanolamines (**7**, **8**, **11**, **12**, **15**) with 1.1 equivalents of borane dimethylsulfide complex in THF (BMS) for one hour at room temperature followed by six hours reflux. These reactions were monitored by measuring the amount of H_2-gas evolved (3 or 2 equivalents for the formation of **2** and **1** respectively) and by ^{11}B NMR.[9] The solutions, which where quite unstable, [10] were then cooled to room temperature and used without purification. Under these conditions, diethanolamine (*S*,*S*)-**11** afforded the dimeric structure **19** (MS $_{(EI)}$ m/z 282 $[M]^+$). The symmetry of compound **19** was illustrated by its simple ^{13}C and ^{11}B NMR spectra. Surprisingly, diethanolamine (*R*,*R*)-**12**, which is the phenyl analogue of **11**, afforded a monomeric compound (*R*,*R*)-**20** (MS $_{(EI)}$ m/z 265 $[M]^+$). Oxazaborolidine **19'** was synthesized by adding to a THF solution of equimolar amounts of BMS and diethanolamine (*S*,*S*)-**11**, one equivalent of *n*-BuLi and, after 30 minutes, one equivalent of methyl iodide.[5] The monomeric structure of **19'** was assigned on the basis of its ^{11}B NMR and mass spectra (MS $_{(EI)}$ m/z 141 $[M]^+$).

Results :

When acetophenone was reduced by borane, in the presence of a catalytic amount (0.1 equiv.) of bicyclic oxazaborolidines (*S,S*)-**19, 19'** or (*R,R*)-**20**, complete reaction was observed after a few minutes and the products (*S*)- and (*R*)-phenylethanol, respectively, were isolated in high yield (Table 1).

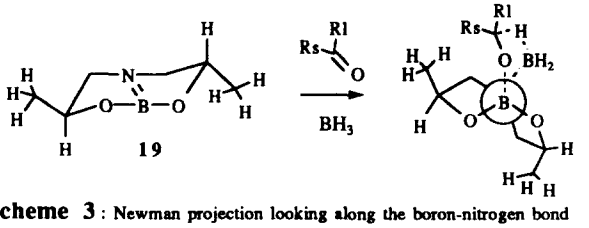


Catalyst	T°C	Yield[a]	ee[b] (conf)
 **19**	25	95%	28% (*S*)
	40	94%	31% (*S*)
	66	90%	69% (*S*)
	110[c]	41%	55% (*S*)
 **19'**	25	92%	49% (*S*)
	40	90%	65% (*S*)
	66	82%	55% (*S*)
 **20**	25	92%	38% (*R*)
	40	96%	27% (*R*)
	66	85%	35% (*R*)

a) Isolated yields, crude yields were quantitative (TLC)
b) Determined by HPLC-analysis, using a CHIRACEL OD column (flow rate : 0.5 mL/min; eluent : hexane / 2-propanol = 9 / 1
c) This reaction was performed in toluene

Table 1 : Borane reduction of acetophenone catalysed by bicyclic oxazaborolidines **19**, **19'** and **20**

The observed asymmetric induction was very dependent on the reaction temperature in the case of the dimeric catalyst (*S,S*)-**19** (ee's increase from 28% at room temperature up to 69% when the reaction mixture is heated at 66°C).[11] Changing the reaction temperature has little effect on the resulting asymmetric induction in the case of monomeric oxazaborolidines (*S,S*)-**19'** and (*R,R*)-**20**. The moderate asymmetric induction (ee_{max}: 65%) afforded by monomeric catalysts **19'** and **20** can be rationalised by the pyramidalization of both boron and nitrogen atoms which occurs when the nitrogen atom of the catalyst binds to free borane while the ketone coordinates to boron (Scheme 3).[12] The cis relationship between the two reactants forces the catalyst to take a roof shape. The catalysed reaction develops on the top of this roof where the chiral environment is not defined enough to provide good asymmetric induction.

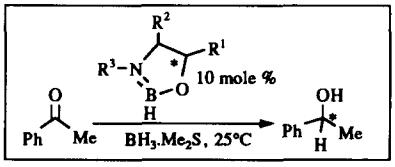


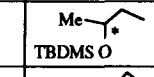
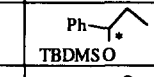
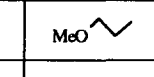
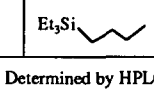
Scheme 3 : Newman projection looking along the boron-nitrogen bond

Monocyclic oxazaborolidine **16** gave better results as a catalyst for the asymmetric reduction of acetophenone. The observed enantioselectivity (72% ee) and the (*S*) configuration of the resulting alcohol (requiring, in Corey's system, the use of (*R*) diphenylprolinol, derived from an unnatural amino acid[1a])

encouraged us to investigate the structural features of this new oxazaborolidine which influence the enantioselectivity (Table 2).

Table 2 : Borane reduction of acetophenone catalysed by monocyclic oxazaborolidines.



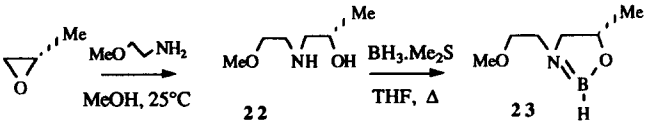
Catalysts					*Products*	
N°	R^1	R^2	R^3	(*config*)	Yield[a]	ee[b](*conf*)
16	Me	H		(S,S)	98%	72% (*S*)
17	Ph	H		(*R*,*R*)	93%	20% (*R*)
18	Ph	Me		(*S*,*R*,*S*)	45%	3% (*S*)
21	Me	H	H	(*S*)	95%	26% (*S*)
23	Me	H		(*S*)	92%	15% (*S*)
26	Me	H		(*S*)	91%	52% (*R*)

a) Isolated yields b) Determined by HPLC-analysis, using a CHIRACEL OD-H column (flow rate : 0.5 mL/min; eluent : 2-propanol/n-hexane = 1/9).

Compounds **16**, **17**, **21**, **23**, **26** (Table 2) represent, as far as we know, the first example of the class of oxazaborolidines bearing only chiral centers α to the oxygen. However, this structural feature does not seem to favour asymmetric induction as can be seen with catalyst **21** (R^3 = H), derived from commercially available (*S*)-2-aminopropanol. The predominance of the (*S*) enantiomer (26% ee) obtained in this case may be explained by a slight preference for borane to bind to the nitrogen atom from the face opposite to that of the methyl substituent.

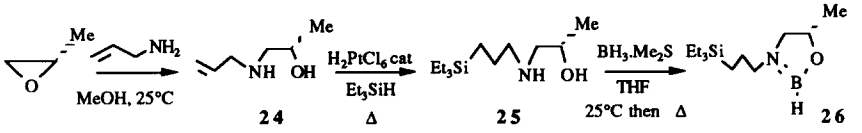
Asymmetric induction is more favourable when the stereogenic center is located on the carbon adjacent to the nitrogen.[1b] However, the presence of an additional R^2 group α to the nitrogen atom is not compatible with our N-substituted catalysts as can be seen in the case of **18** (Table 2). The poor asymmetric induction displayed in this example probably results from a retarded complexation of borane by the oxazaborolidine.

The R^3 side chain of catalyst **16** seemed to be beneficial to the observed stereoselectivities (compare **16** with **21**). This prompted us to evaluate different types of side chain in order to better understand the results obtained with **16**. Thus, monosubstitution of (*S*)-isopropylene oxide by excess of methoxymethylamine afforded (*S*)-diethanolamine **22** in 62% yield after distillation (Scheme 4). Amino alcohol **22** was then converted into oxazaborolidine **23** and used to catalyse the borane reduction of acetophenone. The low enantioselectivity induced by **23** (15% ee) further illustrates the importance of the TBDMS group in inducing the enantioselectivity observed with **16** (Table 2).



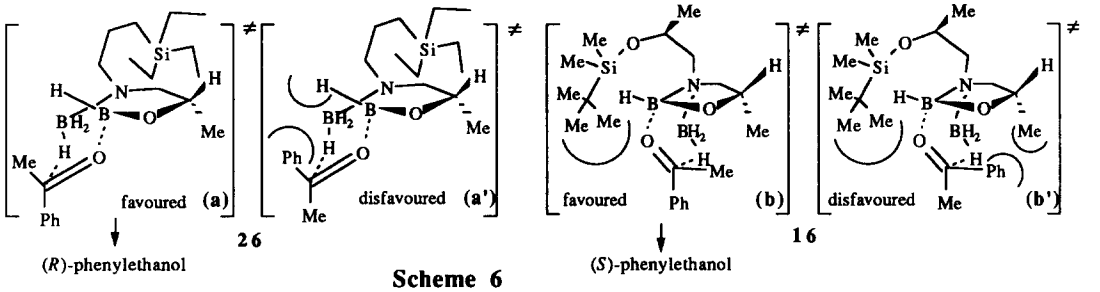
Scheme 4 : Preparation of oxazaborolidine 23

We next investigated the role of the oxygen atom located on the R^3 side chain of **16** by preparing a carbon analog **26**. Monosubstitution of (*S*)-isopropylene oxide by excess allylamine provided allylamino alcohol **24** in 80% yield after distillation (Scheme 5). Regioselective hydrosilylation of **24** using triethylsilane and a catalytic amount of hexachloroplatinic acid[13] then afforded the desired amino alcohol **25**.



Scheme 5 : Preparation of oxazaborolidine 26

Amino alcohol **25** was converted into oxazaborolidine **26** following the procedure described above, and subsequently used as catalyst in the borane reduction of acetophenone. The resulting alcohol was obtained in good yield and with an asymmetric induction (52% ee) close to that induced by **16**, suggesting that the trialkylsilyl group of this side chain is of major importance in displaying stereoselectivity (Table 2). The fact that (*R*) enantiomer predominates in this case suggests that the reaction occurs via a different transition state. By analogy with the established mechanism,[1a,12] we propose, for **26** and **16**, transition state models which account for the configuration of the major formed enantiomer. When the oxazaborolidine nitrogen atom is substituted as in **26**, a free borane approach towards the α face of the catalyst should be favoured in order to set the bulky triethylpropylsilyl chain anti to the oxazaborolidine methyl substituent (Scheme 6, transition state (**a**)). The ketone should then approach anti to the large nitrogen substituent.



Scheme 6

The asymmetric induction provided by **26** may be explained by a better coordination of the electrophilic boron to the ketone oxygen with the oxazaborolidine B-H bond anti to the larger carbonyl appendage. As shown above, **16** allowed formation of (*S*)-phenylethanol with 72% ee. This result rules out the involvement of an exo complex of type (**a**) but suggests that enantiomer (*S*) may arise from an endo complex (**b**).[12] The bulky *tert*-

butyl substituent may hinder the exo coordination and force acetophenone to approach the α face of the catalyst. The reaction can proceed through a six-membered ring "boat-like" transition state with the phenyl group in an axial position in order to minimise steric interactions. This interpretation is substantiated by the result obtained with oxazaborolidine **17**. Thus, changing the ring substituent from methyl (**16**) to phenyl (**17**) hinders the α face of the catalyst and creates a mismatched effect.[14] The difference of enantiofacial selectivity observed between **26** and **16** arises from a different orientation of the nitrogen side chain (Scheme 6). In the case of **16**, a possible internal coordination of the silyl ether oxygen with the boron atom[15] and an attractive dipole-dipole interaction between the oxazaborolidine hydride and the silicon atom[16] suggest the transition state (**b**) where the side chain is oriented as depicted in Scheme 6.

In summary, this paper describes the preparation of several monocyclic and bicyclic oxazaborolidines derived from chiral diethanolamines and their use as chiral catalysts in the borane reduction of acetophenone. Bicyclic oxazaborolidines (*S,S*)-**19** and (*R,R*)-**20** were efficient catalysts and afforded the expected alcohol in good yields but with modest ee's (ee < 40%). Monocyclic oxazaborolidine (*S,S*)-**16** behaved as a more effective chirality inducer and afforded (*S*)-phenylethanol with 72% ee. The presence of a trialkylsilyl group was shown to be crucial for the stereoselection. Interestingly, a slight structural modification of the silylated nitrogen side chain (**26**) led to a reversal of the stereoselectivity of reduction giving the (*R*)-alcohol. In the proposed transition state model (**b**), the major enantiomer could arise from an endo conformation favoured both by steric hindrance and dipolar interaction. Although the introduction of an additional coordinating atom to the classical oxazaborolidine structure has been shown to decrease the enantioselectivity of this reaction,[17] it may be possible to improve our results by modifying the structure of our catalysts and the nature of the substrate. This subject is currently being studied.

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Experimental

^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AM 250 MHz spectrometer. Samples were measured in $CDCl_3$ using TMS as internal standard for ^{1}H NMR, and $CDCl_3$ as internal standard for ^{13}C NMR. ^{11}B NMR spectra were recorded on a Bruker AM 250 MHz spectrometer. Samples were measured in THF or $CDCl_3$, with BF_3:OEt_2 as external standard. The ee values were determined by chiral hplc on a Chiracel OD-H (Daicel) column (eluent : 2-propanol / hexane = 1:9). Optical rotations were measured on a Perkin Elmer 241 polarimeter. Commercially available chemicals were used. Compounds **7**, **9-15** were synthesised by a previously described methodology.[5] THF was freshly distilled from benzophenone / sodium prior to use.

(S)-propyleneglycol-2-tert-butyldimethylsilyloxy-1-tosylate 4 :

To a solution of 322 mg of (*S*)-propyleneglycol-1-tosylate **3** [7] (1.4 mmol) and 326 µL of 2,6-lutidine (2.8 mmol) in 50 mL of CH_2Cl_2 were added at 25°C, 0.48 mL of *tert*-butyldimethylsilyl triflate (2.1 mmol). The reaction mixture was stirred at ambient temperature for 2 h. 100 mL of 2N $NaHCO_3$ were then added to the solution. The mixture was extracted with ethyl acetate and the organic layer was washed with brine. The solvents were then dried on $MgSO_4$ and concentrated *in vacuo*. Flash chromatography (eluent : CH_2Cl_2 / cyclohexane = 2:1) afforded 442 mg (92%) of **4**. $[\alpha]_D^{20}$ -3.8 (c = 2, $CHCl_3$). **^{1}H NMR** δ (ppm) : 7.78 (d, 2H, J = 8.25Hz, Ar), 7.32 (d, 2H, J = 8.25Hz, Ar), 3.97 (q, 1H, J = 6.25Hz, CH), 3.78 (d, 2H, J = 6.25Hz, CH_2), 1.07 (d, 3H, J = 6.25Hz, CH_3), 0.8 (s, 9H, t-Bu), 0.2 (d, 6H, $SiCH_3$). **^{13}C NMR** δ (ppm) :144.7, 133.1, 129.8, 127.9 (Ar), 74.3 (CH), 66.2 (CH_2), 25.8 (t-Bu), 26.6 (CH_3), 20.2 (CH_3), 18.0 ($(CH_3)_3\underline{C}Si$), -4.8 ($SiCH_3$). Anal.Calcd. for $C_{16}H_{28}SiSO_4$: C, 55.81; H, 8.13; S, 9.3; found : C, 56.07; H, 8.20; S, 9.32;

General procedure for the preparation of monosubstituted diethanolamines 7, 8 :

To a solution of 11 mmol of tosylate **4** in 50 mL of *n*-butanol were added 10 mmol of (*S*)-aminopropan-2-ol **5** or (1*S*,2*R*)-norephedrine **6**. The solution was heated at reflux during 48 h and concentrated. The resulting mixture was dissolved in 100 mL of

ethyl acetate and 100 mL of a saturated solution of $NaHCO_3$. The organic layer was extracted, washed with 50 mL of brine, dried over $MgSO_4$ and concentrated *in vacuo*.

N-[(2S)-2-tert-butyldimethylsilyloxypropan-1-yl]-(2S)-aminopropan-2-ol **7**:

The crude product was chromatographed on silica gel (eluent : methanol / ethyl acetate = 2 / 8) to afford **7** in 82% yield. NMR data and optical rotation were identical to the values previously reported.[5]

N-[(2S)-2-tert-butyldimethylsilyloxypropan-1-yl]-(1S,2R)-N-methyl-1-aminoethyl-benzyl alcohol **8** :

The crude product was chromatographed on silica gel (eluent : ether) to afford **8** in 78% yield.
$[\alpha]_D^{20}$ +11.8 (c = 1, $CHCl_3$). **^{1}H NMR** δ (ppm) : 7.31 (m, 5H, Ar), 4.70 (d, 1H, J = 3.9 Hz, CH), 3.97 (m, 1H, J = 3.75Hz, 5Hz, CH), 2.9 (m, 1H, J = 3.9Hz, 6.25Hz, CH), 2.65 (dxdxd, 2H, J = 11.25Hz, 3.75Hz, CH_2), 1.19 (d, 3H, J = 6.25Hz, CH_3), 0.9 (s, 9H, tBu), 0.85 (d, 3H, J = 6.25Hz, CH_3), 0.1 (2xs, 6H, $SiCH_3$). **^{13}C NMR** δ (ppm) : 141.5, 128.1, 127.0, 126.0 (Ar), 73.4, 67.6, 58.3 (CH), 54.6 (CH_2), 25.9 (tBu), 21.8 (CH_3), 18.0 ($(CH_3)_3\underline{C}Si$), 14.7 (CH_3), -4.3 -4.7($SiCH_3$). Anal.Calcd. for $C_{18}H_{33}NO_2Si$: C, 66.87; H, 10.21; N, 4.33; found : C, 66.73; H, 9.98; N, 4.30;

(S)-N-(methoxyethyl)aminopropan-2-ol **22**.

To a solution of (*S*)-propylene oxide (0.75 mL, 12.7 mmol) in methanol (10 mL) were added 1.11 mL (12.7 mmol) of methoxyethylamine. The mixture was stirred at room temperature for 12 h, concentrated *in vacuo* and distilled (100°C, 0.5Torr) to afford 630 mg of **22** (45%). $[\alpha]_D^{20}$ +53 (c = 2.3, $CHCl_3$). **^{1}H NMR** δ (ppm) : 3.58 (m, 1H, CH), 3.22 (t, 2H,J = 5Hz, CH_2O), 3.1 (s, 3H, CH_3O), 2.54 (td, 2H, J = 2.5Hz, 5Hz, NCH_2), 2.35 (dd, 1H, J = 11.25Hz, 2.75Hz, CH_2), 2.2 (m, 1H, J = 11.25Hz, CH_2), 0.9 (d, 3H, J = 6.25Hz, CH_3). **^{13}C NMR** δ (ppm) : 71.5 (CH_2O), 65.3 (CH), 58.3, 56.8 (NCH_2), 48.6 (OCH_3), 19.6 (CH_3). Anal.Calcd. for $C_6H_{15}NO_2$+ 1/4H_2O : C, 52.70; N, 10.24; O, 25.76 found : C, 57.52; N, 10.03; O, 25.49

(S)-N-(allyl)-aminopropan-2-ol **24** :

To a methanolic solution of (*S*)-propylene oxide (0.8 mL, 11.2 mmol) were added 4 mL of allylamine. The mixture was stirred at room temperature for 12 h, concentrated *in vacuo* and distilled (115°C, 0.5Torr) to afford 1g of **24** (80%). $[\alpha]_D^{20}$ +20 (c = 5, $CHCl_3$). **^{1}H NMR** δ (ppm) : 5.75 (m, 1H, J = 17.5Hz, 10Hz, 1.5Hz, CH allyl), 5 (m, 2H, J = 17.5Hz, 10Hz, 1.25Hz, CH_2 allyl), 3.7 (m, 1H, CH), 3.12 (m, 2H, J = 1.5Hz, NCH_2), 3.0 (br s, 2H, OH + NH), 2.6 (dd, 1H, J = 11.75, 2.75, CH_2), 2.3 (dd, 1H, J = 11.75Hz, 9Hz, CH_2), 1.12 (d, 3H, J = 6.25Hz, CH_3). **^{13}C NMR** δ (ppm) :136.3 (CH=), 116.1 (CH_2=), 65.5 (CH), 56.2, 51.9 (CH_2N), 20.8 (CH_3).

(S) N-(3-triethylsilyl-propyl)aminopropan-2-ol **25** :

To a mixture of 480 mg (4.17 mmol) of **24** and 5 mL of triethylsilane were added, at room temperature, 5 mg of hexachloroplatinic acid. The mixture was refluxed during 2 h. The resulting solution was then concentrated *in vacuo*. 100 mL of ether and 100 mL of 4M HCl were added and the mixture was stirred for 1 h at room temperature. The aqueous layer was extracted and washed three times with 50 mL of ether. 100 mL of chloroform were then added and the pH of the aqueous layer was made basic with caution by addition of several portions of a saturated aqueous solution of potassium carbonate. The organic layer was then extracted, dried on magnesium sulfate and concentrated *in vacuo* to afford 588 mg of **25** (61%). $[\alpha]_D^{20}$ +4.1 (c = 1.3, $CHCl_3$). **^{1}H NMR** δ (ppm) : 3.78 (m, 1H, J = 3Hz,CH), 3.6 (m, 2H, OH + NH), 2.6 (m, 4H, J = 12Hz, 3Hz, CH_2N), 1.42 (m, 2H, CH_2), 1.05 (d, 3H, J = 6Hz, CH_3), 0.82 (t, 9H, J = 7.6Hz, $\underline{CH_3}CH_2$), 0.4 (q, 8H, J = 7.6Hz, $SiCH_2$). **^{13}C NMR** δ (ppm) : 63.9 (CH), 55.3, 52 (CH_2N), 21.8 ($SiCH_2\underline{CH_2}$), 20.8 (CH_3), 8.6 ($SiCH_2$), 7.4 ($SiCH_2\underline{CH_3}$), 3.2 ($Si\underline{CH_2}CH_3$). Anal.Calcd. for $C_{12}H_{29}NOSi$+ 0.32 $CHCl_3$: C, 53.62; H, 10.81; N, 5.16 found : C, 53.60; H, 10.88; N, 5.19

General procedure for the preparation of oxazaborolidines **16-21, 23 and 26**

Every oxazaborolidines were prepared as follow with the exception of **19'** that was synthesized according a previously repported procedure :[5] To a solution of aminoalcohol or diethanolamine (1 mmol) in THF (5 mL), was added at room temperature under an argon atmosphere, BH_3:Me_2S complex (1.1 mmol). The mixture was then stirred for 1 h at room temperature and 6 h under reflux. The solution was cooled to room temperature and used without purification. Oxazaborolidines were characterised by mass and ^{11}B NMR spectroscopy : **16** : $\delta_{(ppm)}$ + 29.3 (d, J_{BH} = 153 Hz, $CDCl_3$), **19'** : $\delta_{(ppm)}$ + 0.31 (s , THF), **19** : $\delta_{(ppm)}$ + 9.7 (s , THF), **20** : $\delta_{(ppm)}$ - 0.51 (s, THF), **23** : $\delta_{(ppm)}$ + 6.4 (br s, THF), **26** : $\delta_{(ppm)}$ + 5.8 (br s, THF).

General procedure for the reduction of acetophenone using oxazaborolidines **16-21, 23 and 26**

To a THF solution of preformed oxazaborolidine (0.5 mmol) were added, at room temperature, 3.5 mmol of $BH_3.Me_2S$ complex (the use of BH_3.THF complex lead to the same results). Acetophenone (5 mmol) was then added dropwise over 1 h. The reaction mixture was stirred for 15 min. 50 mL of ethyl acetate and 50 mL of 0.5M HCl were then added to the solution. The organic layer was extracted, dried over magnesium sulfate, the solvents were removed *in vacuo* and the residue was chromatographed on silica gel (pentane / ethyl acetate : 9 / 1) to afford pure α-methyl benzyl alcohol (yields and ee's are reported in Tables 1 and 2).

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