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Synthesis of Chiral Lithium Dialkoxyaminoborohydrides.

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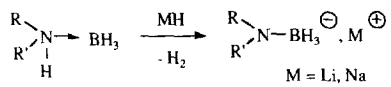
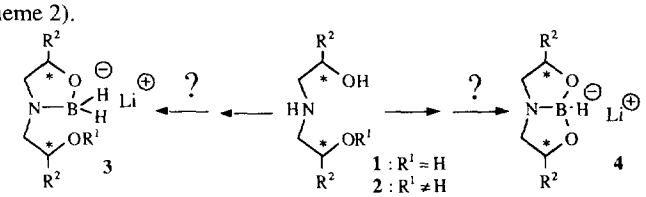
Abstract : A convenient synthesis of chiral dialkoxyaminoborohydrides from borane and some diethanolamines is described. This is a novel class of reducing agents which react with acetophenone to afford α-methyl benzyl alcohol in good yields but in low ee's .

Sodium aminoborohydrides were first synthesized by Hutchins by deprotonating a preformed secondary amine-borane with sodium hydride.[1] Singaram has published several papers describing the preparation and the use of lithium aminoborohydrides.[2] These compounds were described as safe and powerful reducing agents, being air and heat stable (Scheme 1).



Scheme 1

We were interested in exploring the synthesis of optically active aminoborohydrides [3] from chiral diethanolamines using Singaram's procedure. In particular, the synthesis of monoalkoxyaminoborohydrides of type **3** and dialkoxyaminoborohydrides of type **4**, starting from chiral diethanolamines **2** or **1** , respectively, was investigated (Scheme 2).

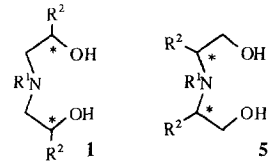


Scheme 2

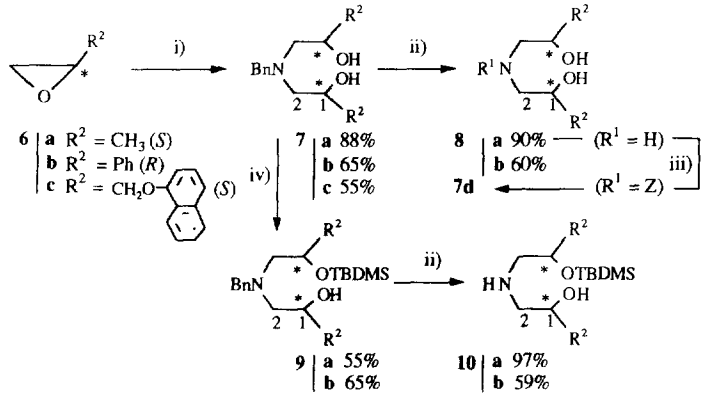
These ligands allow introduction of chirality as well as modulation of the number of reactive hydrides. As the first step in the preparation of aminoborohydrides **4**, it was expected that both alcohol functionalities of diethanolamines **1** would react with borane to yield the corresponding dialkoxyamine-borane.

Trifunctional ligands have not been studied as extensively as bidentate auxiliaries.[4] Because the third liganding atom can coordinate to the reagent to produce a highly defined stereochemical environment, chiral diethanolamines are increasingly used in asymmetric synthesis.[5]

The preparation and the use of diethanolamines **1**, bearing chiral centers α to the oxygen atoms being less common [5a,6] than those of diethanolamines of type **5** [5b,5d] (Scheme 3), the former family was selected for investigation.



Aminolysis of epoxides is a well documented method of preparing β-amino alcohols and it appeared reasonable to synthesize diethanolamines **1** by treating chiral epoxides with a primary amine.[7] However, direct reaction, i.e. heating the epoxide in the presence of amine, is often limited by the low nucleophilicity of amines.[8] Not surprisingly then, initial attempts using toluene [5c] as solvent resulted in formation of a mixture of secondary and tertiary amines. On the assumption that reaction would be favoured by a polar solvent capable of stabilizing the transition state, the various chiral diethanolamines **7a,b,c** were prepared in good yield and in high enantiomeric excess [9], by refluxing a methanolic solution of 2.2 equivalents of epoxide **6** and 1 equivalent of benzylamine. Reactions took from 6 to 48 hours depending on the steric hindrance presented by the epoxide substituents (Scheme 3).



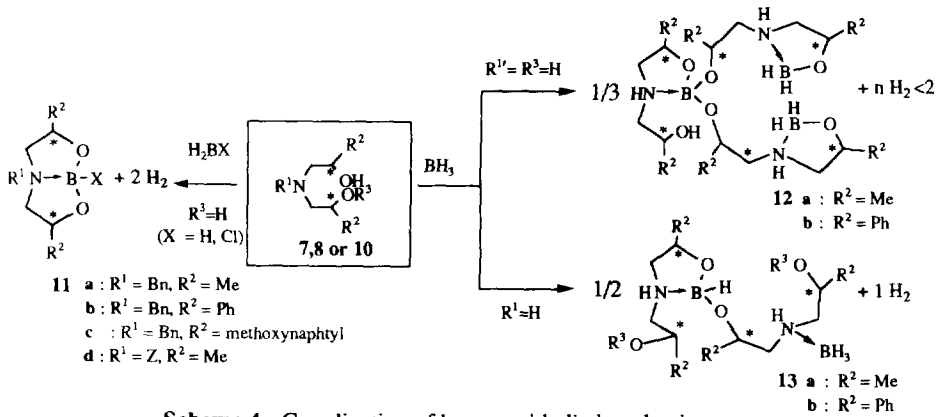
i) Benzylamine; methanol; Δ ii) Pd/C; H_2 (1 atm); methanol iii) Benzylchloroformate (ZCl); triethylamine; DMAP; CH_2Cl_2. iv) TBDMSOTf; 2,6-lutidine; CH_2Cl_2.

Scheme 3 : Preparation of chiral diethanolamines

Under these conditions, aminolysis of **6a** and **6c** resulted in clean disubstitution by benzylamine at the less hindered carbon of each of the two epoxides. In contrast, aminolysis of styrene oxide **6b** is known to give a 75:25 mixture of C-2 and C-3 substitution products.[10] Debenzylation of **7a,b** by hydrogenolysis allowed the preparation of the C_2-symmetric secondary amines **8a,b**. Furthermore, **8a** was selectively converted to the benzyl carbamate **7d** in order to study electronic effects at the nitrogen atom on coordination with borane (*vide infra*). Moreover, diethanolamines **7a** and **7b** were monosilylated to afford, after debenzylation, compounds **10a** and **10b** respectively.

Coordination of diethanolamines 7-8, 10 to borane .

The reaction of borane with simple amino alcohols has previously been described.[11] Reaction of an equimolar amount of borane:THF complex with an amino alcohol, at room temperature,[11c] brings on the evolution of an amount of H_2 gas corresponding to a B-O bond formation, while covalent N-B bond formation is observed after several hours (and sometimes only after heating). Monomeric,[11a] as well as oligomeric structures[11b] have already been evocated. Our aim was to deprotonate a preformed amine-borane (Scheme 4) in order to convert the dative N→B bond into a covalent bond and thus create the wanted tetravalent boron species of types **3** or **4** (Scheme 2).



Scheme 4 : Coordination of borane with diethanolamines

The synthesis of compounds of type **11** have previously been described by esterification of boronic acid with diethanolamine (X = alkyl, aryl).[12] In our case, the preparation of the wanted lithium borohydrides **4** requires the synthesis of an amine-borane **11** with X and R^1 = H . With this in mind, we investigated the coordination of ligands **7**, **8**, **10** with borane as the first step in the synthesis of aminoborohydrides **3** and **4**. Thus, one equivalent of borane (BH_3:THF, BH_3:Me_2S, or BH_2Cl:THF), was added dropwise, at room temperature, to a solution of the diethanolamine. The reaction was monitored by measuring the amount of H_2 gas evolved and by ^{11}B NMR spectroscopy (results are reported in Table 1).

Table 1: Coordination of borane with diethanolamines

Substrates					*Products*		
n°	R^1	R^2	R^3	config.	n°	n H_2 [a]	δ ^{11}B [b]
7a	Bn	Me	H	*S,S*	11a	2	+11.3
7b	Bn	Ph	H	*R,R*	11b	2	+19.1
7c	Bn	1-naphthyloxy methyl	H	*S,S*	11c	2	+13
7d	Z	Me	H	*S,S*	11d	2	+14.6
8a	H	Me	H	*S,S*	12a	1.66	+9.7 [c] / -15.6
8b	H	Ph	H	*R,R*	12b	1.33	+8.1 [c] / -17.5
10a	H	Me	TBDMS	*S,S*	13a	1	+5.8 [d] / -18.1
10b	H	Ph	TBDMS	*R,R*	13b	1	+3.04 [d] / -17.7

a) Amounts in mol equiv. evolved after two hours at room temperature. b) In $CDCl_3$, $BF_3.OEt_2$ as an external standard. c) Two signals in 1:2 ratio d) Two signals in 1:1 ratio

It was observed that tertiary amines **7a,b,c,d** react with borane, regardless of the nature of the borane complex, the solvent (THF, CH_2Cl_2) or the R^2 substituents, to yield the dialkoxyamine-boranes **11a,b,c,d** (Scheme 4). Two equivalents of H_2 gas were evolved almost instantaneously in these cases. Mass and NMR spectroscopy (^{11}B, ^1H, ^{13}C) are in accordance with the assigned structures (Table 1).

The reaction of borane with the unprotected alcohol functionality of **10a,b** led, as expected, to the release of one equivalent of H_2 gas. The ^{11} B NMR spectrum of the resulting intermediates revealed the presence of two signals which suggested the formation of the compound **13**, structurally closed from previously described dimers.[11b, 13]

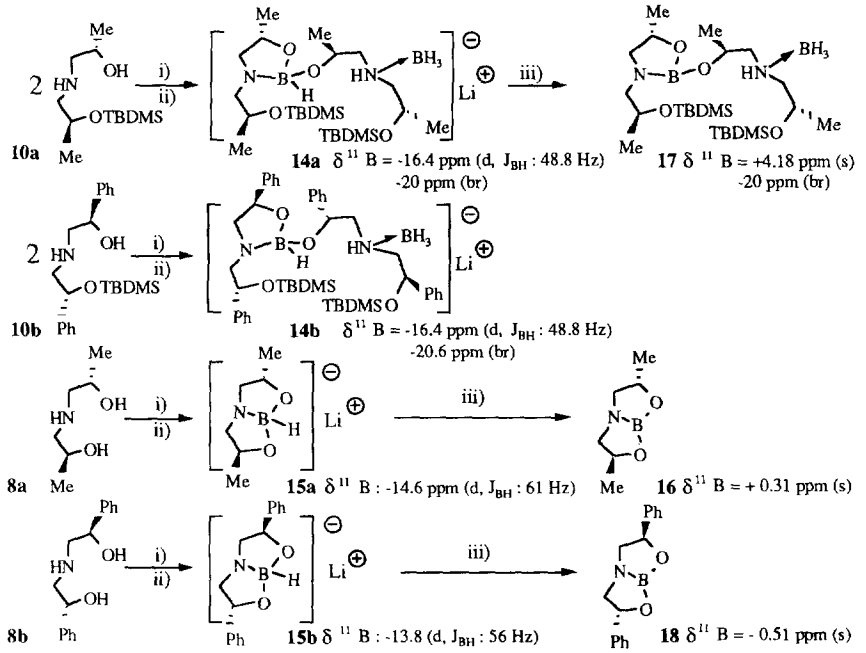
Surprisingly, the amount of H_2 gas evolved in the case of secondary amines of type **8** did not reach 2 equivalents. The ^{11} B NMR spectrum of an equimolar mixture of **8a,b** and BMS revealed two peaks. The signals at +9.7 or +8.1 are typical of a dialkoxyamine-borane ($R_3N\rightarrow BH(OR')_2$) while the signals at -15.6 and -17.5 ppm are indicative of an amine-borane ($R_3N\rightarrow BH_3$).[11b]

The trimeric structure **12** displayed in Scheme 4 was deduced from a ^1H NMR titration experiment using an equimolar amount of dichloromethane as an internal standard.[14]

The basicity of the amine cannot explain this incomplete cyclisation because the presence of an electron withdrawing (**7d**, R^1 = Z) or donating (**7a**, R^1 = Bn) substituent on nitrogen results in both cases in the release of two equivalents of H_2 gas. The formation of the second boron-oxygen covalent bond is apparently easier in the presence of a bulky nitrogen substituent close to the hydroxyl group.

Synthesis of chiral lithium aminoborohydrides.

The preparation of aminoborohydrides **14a,b** and **15a,b** was achieved by first mixing equimolar amounts of aminoalcohols **10a,b** or **8a,b** and borane:THF. After 30 minutes at 25°C was added the required amount of *n*-BuLi to deprotonate both NH and OH. [15] It was hoped that converting the alcohol function into an alkoxide would increase the nucleophilicity of the oxygen atom and facilitate the cyclisation.



i) BH_3 :THF 1 equiv.; 25°C ii) *n*-BuLi; 0°C iii) MeI, 25°C

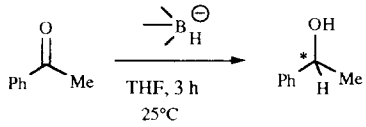
Scheme 5 : Preparation of chiral aminoborohydrides.

These aminoborohydrides exhibit, in THF solution, ^{11}B NMR chemical shifts in the -13 to -16 ppm range upfield to BF_3:Et_2O as a reference (Scheme 5). The coupling constants range from 48-61 Hz (in contrast, amine-borane generally exhibit coupling constant of about 100 Hz). These results correlate well with the reported values of ^{11}B NMR chemical shifts for LiH_3BNR_2 ranging from -16 to -23 ppm.[2] The ^{11}B NMR signals of **15a,b** appear as doublets (coupling with one hydrogen) and are clearly in accordance with the assigned structures. ^{11}B NMR spectrum of **14a,b** displayed a doublet signal at -16.4 ppm corresponding to the B-H bond and a broad signal at -20 ppm wich result from the presence of the N-BH_3 moiety. [16]

Aminoborohydrides are known to react vigorously with methyl iodide to liberate methane and the corresponding amine-borane.[2] This property was verified with compounds **14a** and **15a,b** which react with methyl iodide to afford the oxazaborolidines **17**, **16** and **18** (Scheme 5).[17]

Reduction of acetophenone was then investigated in order to determine the potential of these modified borohydrides as chiral reducing agents (Table 2). Complete reduction occurred in less than two hours at room temperature to afford the resulting alcohol but with poor asymmetric induction (ee<10%). Decreasing the reaction temperature to -78°C resulted in 40% conversion after 12 hours without improving the asymmetric induction. Moreover, changing methyl substituents (**15a**) for phenyl (**15b**) did not increase the stereoselectivity.

Table 2 : Lithium aminoborohydride reduction of acetophenone



N°	14a	14b	15a	15b
Equiv.[a]	1.1	1.1	1.1	1.8
Yield[b] %	95	85	93	90
ee[c] %	6 (*R*)	8 (*S*)	9 (*R*)	5 (*S*)

a) Borohydrides were prepared in situ
b) Isolated yields. Yields of crude product were quantitative (TLC)
c) Determined by HPLC analysis, using a Chiracel OD column
(flow rate : 0.5 mL/min; eluent : 2-propanol / hexane = 1 / 9

In conclusion, a convenient procedure for the synthesis of various chiral aminoborohydrides from borane and diethanolamines is described. The preparation of the intermediate alkoxyamine-borane was found very substrate dependant. The resulting intermediates **12a,b** are transformed, under basic conditions, into the monomeric borohydrides **15a,b** while amine-borane **13a,b** led to the dimeric structures **14a,b** containing an aminoborohydride functionnality and an amine-borane site. These modified reagents reduce acetophenone at room temperature in high yields although with low ee's. Contrary to our expectations, the rigid, bicyclic structure of borohydrides **15a,b** does not appear to favour the delivery of hydride selectively to one enantioface of acetophenone.

The design and synthesis of more highly enantioselective borohydrides of this type are now in progress.

Acknowledgement : We are grateful to SIPSY for financial support of this work. We also thank the R&D team of SIPSY for stimulating discussions and one of the referee for useful comments and for calling reference 11c to our attention.

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. Mass spectra were recorded on a Delsi/Nermag spectral 30 spectrometer. 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.

Chemicals

Commercially available chemicals were used, with the exception of **8c** which was synthesised by a previously described methodology.[18] THF was freshly distilled from benzophenone/sodium prior to use.

General procedure for the preparation of diethanolamines 7

25 mmol of distilled benzylamine were added to a methanolic solution of 55 mmol of chiral epoxide and the reaction mixture was refluxed for 6 to 48 h. After complete reaction, the mixture was concentrated *in vacuo* and the crude material was purified as described below.

Bis [(2S)-hydroxypropan-1-yl] benzylamine ***7a***

This compound, prepared from (*S*)-propylene oxide, was obtained in 88% yield, after chromatography on silica gel (eluent : dichloromethane / methanol 95 / 5).
$[\alpha]_D^{20}$ +144 (c = 2, $CHCl_3$). **^{1}H NMR** δ (ppm) : 7.28 (m, 5H, Ar), 3.85 (m, 3H, J = 6.25 Hz, 13 Hz, CH + CH_2 benzyl), 3.50 (d, 1H, J = 13Hz, CH_2 benzyl), 2.65 (br s, 2H, OH), 2.41 (d, 4H, J = 5.62 Hz, CH_2), 1.11 (d, 6H, J = 6.25 Hz, CH_3). **^{13}C NMR** δ (ppm) :138.5, 129.1, 128.6, 127.5 (Ar), 64 (CH), 62.1, 59.8 (CH_2), 20.4 (CH_3). **Anal.Calcd.** for $C_{13}H_{21}NO_2$, 1/3 CH_3OH : C, 68.48; H, 9.55; N, 5.99; O, 15.96; found : C, 68.42; H, 9.38; N, 6.19; O, 15.79;

Bis N-[(1R)-1-hydroxyphenylethan-2-yl] benzylamine ***7b***

This compound was prepared starting from (*R*)-styrene oxide in 65% yield after purification on silica gel (pentane / ethyl acetate 8 / 2). This product was identical to that described by Trost *et al.*[10] 20 % of the other regioisomer were also isolated.

Bis N-[(1S)-1-hydroxy-(1-naphthyloxymethyl)-ethan-2-yl] benzylamine ***7c***

This compound was prepared from epoxide **6c**[18] in 55% yield after chromatography on silica gel (pentane / ethyl acetate 8 / 2).
$[\alpha]_D^{20}$ -21.3 (c = 2.5, $CHCl_3$). **^{1}H NMR** δ (ppm) : 8.05 (d, 2H, J = 8.75 Hz, Ar), 7.70 (d, 2H, J = 7.2 Hz, Ar), 6.60 (d, 2H, J = 8.75 Hz, Ar), 4.2 (m, 2H, J = 4.5 Hz, CHOH), 3.95 (m, 3H, CH_2 benzyl + CH_2O), 3.6 (m, 3H, J = 5 Hz, CH_2 benzyl + 2OH), 2.8 (m, 4H, CH_2). **^{13}C NMR** δ (ppm) : 154.2, 138.3, 134.5, 129.2, 128.6, 127.5, 126.5, 125.8, 25.3, 121.9, 120.6, 104.8 (Ar), 70.1 (CH), 67.5(OCH_2), 60.1, 57.2 (NCH_2).
Anal.Calcd. for $C_{33}H_{33}NO_4$, 1/2 H_2O : C, 76.74; H, 6.85; N, 2.71. found : C, 76.75; H, 6.65; N, 2.53

Bis [(2S)-2-hydroxy-propan-1-yl] amine ***8a***

A mixture of 100 mg of 10% palladium on activated carbon and 2.23 g (10 mmol) of **7a** in 50 mL of methanol was stirred for 3h under a hydrogen atmosphere (1 atm). The solution was then filtered on a pad of celite, the filtrate was concentrated under reduced pressure and the residue was distilled *in vacuo* (155°C, 0.5 Torr) to afford 1.19g of **8a** (90%).
$[\alpha]_D^{20}$ +74.3 (c 1.3, $CHCl_3$). **^{1}H NMR** δ (ppm) : 4.21 (m, 3H, OH + NH), 3.80 (m, 2H, CH), 2.51 (d, 4H, J = 3.75 Hz, CH_2), 1.08 (d, 6H, J = 5 Hz, CH_3). **^{13}C NMR** δ (ppm) : 66.1 (CH), 56.3 (CH_2), 20.8 (CH_3).**Anal.Calcd.** for $C_6H_{15}NO_2$, 0.16 H_2O : C, 53.12; H, 11.27; N, 10.33; O, 25.26; found : C, 53.48; H, 10.85; N, 10.32; O, 25.29;

Bis [(1R)-1-hydroxyphenyl-ethan-2-yl] amine ***8b***

Following the same procedure as for **8a** except that THF was used as the solvent, **8b** was prepared from **7b** in 80% yield. NMR data and optical rotation were similar to values reported by de Vries.[5a]

Bis N-[(2RS)-2-hydroxy-propan-2-yl] benzyloxycarbonylamine ***7d***

To a solution of 133 mg (1 mmol) of racemic **8a**, 282 µL (2 mmol) of triethylamine and 25 mg (0.2 mmol) of 4-dimethylaminopyridine in 100 mL of CH_2Cl_2, were added at room temperature, 210 µL (1.5 mmol) of benzylchloroformate and the mixture was stirred for six hours. After completion of the reaction, the solution was concentrated *in vacuo*. 100 mL of ethyl acetate and 100 mL of water were added to the residue, the organic layer was extracted and dried with magnesium sulfate. The solvent was removed *in vacuo* and the crude product was purified by flash chromatography (eluent : ethyl acetate) affording 177 mg of **7d** (67%).

^{1}H NMR δ (ppm) : 7.30 (m, 5H, Ar), 5.09 (s, 2H, CH_2), 4.09 (m, 4H, OH + CH), 3.24 (m, 4H, NCH_2), 1.12 (dd, 6H, J = 6 Hz, CH_3). **^{13}C NMR** δ (ppm) : 157.5 (C=O), 136.4, 128.5, 128.1, 127.8 (Ar), 67.4 (OCH_2), 66.3 (CH), 56.9, 56.6 (CH_2N), 20.8, 20.5 (CH_3).

N-benzyl-N-[(2S)-2-(tert-butyldimethylsilyloxy)-propan-1-yl]-(2S)-aminopropan-2-ol ***9a***

To a solution of 2.23 g (10 mmol) of **7a** and 2.2 mL (18.9 mmol) of 2,6-lutidine in 100 mL of CH_2Cl_2 were added dropwise, at 0°C, 3.7 mL (16.1 mmol) of tert-butyldimethylsilyl triflate. The mixture was stirred at 0°C for 2h. 100 mL of a saturated solution of $NaHCO_3$ were then added and the organic layer was extracted, washed with water (3x100mL), dried with magnesium sulfate and concentrated *in vacuo*. Flash chromatography (eluent : pentane / ethyl acetate 9 / 1) of the crude material afforded 1.4 g of **9a** (55%).
$[\alpha]_D^{20}$ +31 (c = 5.7, $CHCl_3$). **^{1}H NMR** δ (ppm) : 7.27 (m, 5H, Ar), 3.9 (m, 2H, J = 13.75 Hz, 4.5 Hz, 6.25 Hz, CH_2 benzyl + CH), 3.75 (sext, 1H, J = 6.75 Hz, 6.25 Hz, CH), 3.55 (br s, 1H, OH), 3.45 (d, 1H, J = 13.75 Hz, CH_2 benzyl), 2.6 (dd, 1H, J = 6.75 Hz, CH_2), 2.4 (m, 3H, J = 6.75 Hz, 4.5 Hz, CH_2), 1.08 (dd, 6H, J = 4.5 Hz, 6.25 Hz, CH_3), 0.85 (s, 9H, t-Bu), 0.02 (ds, 6H, $SiCH_3$). **^{13}C NMR** δ (ppm) : 138.7, 129.1, 128.4, 127.2 (Ar), 67.2, 63.5 (CH), 63.3, 62.4, 60 (CH_2), 26 ($C(\underline{C}H_3)_3$), 22.2, 19.9 (CH_3), 18.1 ($\underline{C}(CH_3)_3$), -4.2 (Si CH_3). **Anal.Calcd.** for $C_{19}H_{35}NO_2Si$, 1/4 H_2O : C, 66.76; H, 10.39; N, 4.09 found : C, 66.65; H, 10.06; N, 3.78

N-benzyl-N-[(1R)-1-(tert-butyldimethylsilyloxy)-1-phenylethan-2-yl]-(1R)-2-amino-1-phenylethan-1-ol ***9b***

Following the same procedure as for **9a**, **9b** was prepared from **7b** in 65% yield. $[\alpha]_D^{20}$ -46 (c = 4.5, $CHCl_3$). MS (CI/NH_3) m/z 463 $[MH]^+$. **^{1}H NMR** δ (ppm) : 7.3 (m, 15H, Ar), 4.78 (dd, 1H, J = 7.5 Hz, 4.37 Hz, 6.25 Hz, CH), 4.61 (dd, 1H, J = 8.75 Hz, 5 Hz, CH), 4.0 (d, 1H, J = 13.75 Hz, CH_2 benzyl), 3.82 (broad singlet, 1H, OH), 3.6 (d, 1H, J = 13.75 Hz, CH_2 benzyl), 3.1 (dd, 1H, J = 7.5 Hz, CH_2), 2.7 (m, 3H, J = 4.37 Hz, 5 Hz, CH_2), 0.9 (s, 9H, t-Bu), 0.1 (s, 3H, $SiCH_3$), -0.1 (s, 3H, $SiCH_3$). **^{13}C NMR** δ (ppm) :143.6, 142.2, 138.3, 129.2, 128.5, 128.3, 127.5, 127.4, 126.5, 126 (Ar), 73.8, 69.9 (CH), 63.9, 63, 59.5 (CH_2), 26.0 ($C(\underline{C}H_3)_3$), 18.2 ($\underline{C}(CH_3)_3$), -4.4, -4.6 (Si CH_3). **Anal.Calcd.** for $C_{29}H_{39}NO_2Si$, 1/6 H_2O : C, 75.00; H, 8.47; N, 3.03 found : C, 74.93; H, 8.28; N, 3.01

N-[(2S)-2-(tert-butyldimethylsilyloxy)propan-1-yl]-(2S)-aminopropan-2-ol ***10a***

A mixture of 50 mg of 10% palladium on activated carbon and 1g (2.96 mmol) of **9a** in 50 mL of methanol was stirred for 2h under a hydrogen atmosphere (1 atm). The solution was then filtered on a pad of celite, the filtrate was concentrated in vacuo and the residue was chromatographed on silica gel (eluent : ethyl acetate / methanol 8 / 2) to afford 710 mg of **10a** (97%).
$[\alpha]_D^{20}$ +20.8 (c = 5.7, $CHCl_3$). **^{1}H NMR** δ (ppm) : 4.5 (br s, 2H, OH + NH), 4.0 (m, 1H, J = 6.25 Hz, CH), 3.83 (m, 1H, J = 2.75 Hz, 6.25 Hz, CH), 2.65 (m, 4H, J = 12.25 Hz, 8.75 Hz, 2.75, CH_2), 1.12 (dd, 6H, J = 6.25 Hz, CH_3), 0.75 (s, 9H, t-Bu), 0.15 (s, 6H, $SiCH_3$). **^{13}C NMR** δ (ppm) : 66.9, 64.7 (CH), 56.38, 56.21 (CH_2), 25.9 (t-Bu), 21.8, 20.5 (CH_3), 18.1 (($CH_3)_3\underline{C}Si$), -4.2, -4.8 ($SiCH_3$). **Anal.Calcd.** for $C_{12}H_{29}NO_2Si$ +1/12CCl_4: C, 55.80; H, 11.16; N, 5.38; found : C, 56.13; H, 10.80; N, 5.09;

N-[(1R)-1-(tert-butyldimethylsilyloxy)-1-phenylethan-2-yl]-(1R)-2-amino-1-phenylethan-1-ol ***10b***

This compound was prepared in the same manner as **10a**, using **10b** as the starting material and THF as the solvent. The crude product was chromatographed (eluent pentane / ethyl acetate 1 / 1) to afford **10b** in 59% yield. $[\alpha]_D^{20}$ -37 (c = 4.1, $CHCl_3$). **^{1}H NMR** δ (ppm) :7.29 (m, 10H, Ar), 4.81 (dd, 1H, J = 8 Hz, 3.75 Hz, CH), 4.58 (dd, 1H, J= 8.75 Hz, 3.75 Hz, CH), 3.05 (br s, 2H, OH + NH), 2.9 (m, 2H, J = 8 Hz, CH_2), 2.75 (m, 2H, J = 8.75 Hz CH_2), 0.85 (s, 9H, t-Bu), 0.02 (s, 3H, $SiCH_3$), -0.15 (s, 3H, $SiCH_3$). **^{13}C NMR** δ (ppm) : 142.8, 128.5, 128.3, 128, 127.6, 126.4, 126.1 (Ar), 74.0, 71.6 (CH), 57.8, 56.5 (CH_2), 25.9 ($C(\underline{C}H_3)_3$), 18.2 ($\underline{C}(CH_3)_3$), -4.4, -4.6 (Si CH_3). **Anal.Calcd.** for $C_{22}H_{33}NO_2Si$, 1/2 H_2O : C, 68.92; H, 8.94; N, 3.68 found : C, 69.13; H, 8.71; N, 3.44

General procedure for the preparation of dialkoxyamine-borane ***11*** *and* ***12***

To a solution of amino alcohol or diethanolamine (1 mmol) in THF, was added dropwise under an argon atmosphere, BH_3:Me_2S complex (1 mmol). The mixture was then stirred for 5 min at room temperature.

*Dialkoxyamine-borane **11a***

^{1}H NMR δ (ppm) : 7.35 (m, 5H, arom.), 4.25 (m, 1H, J = 6.25 Hz, 2.75 Hz, CH), 4.15 (d, 1H, J = 13.75 Hz, CH_2 benzyl), 4.00 (m, 2H, J = 13.75 Hz, CH + CH_2 benzyl), 3.40 (dd, 1H, J = 12.5 Hz, 4.25 Hz, CH_2), 2.75 (dd, 1H, J = 11 Hz, 2.75 Hz, CH_2), 2.55 (t, 1H, J = 11 Hz, CH_2), 2.16 (t, 1H, J = 11 Hz, CH_2), 1.25 (dd, 6H, J = 6.25 Hz, CH_3). **^{13}C NMR** δ (ppm) : 131.8, 130.4, 128.6, 128.5 (Ar), 67.6 (CH_2 benzyl), 65.7, 65.1 (CH), 60.8, 60.7 (CH_2), 19.1, 18.7 (CH_3). **^{11}B NMR** δ (ppm) : + 11.3. MS (CI/NH_3) m/z 234 $[MH]^+$.

*Dialkoxyamine-borane **11b***

^{1}H NMR δ (ppm) : 7.35 (m, 15H, arom.), 5.29 (dd, 1H, J = 11.25 Hz, 3.75 Hz, CH), 5.00 (dd, 1H, J = 12.25 Hz, 4.5 Hz, CH), 4.30 (d, 1H, J = 13.75 Hz, CH_2 benzyl),4.11 (d, 1H, J = 13.75 Hz, CH_2 benzyl), 3.63 (dd, 1H, J = 12.25 Hz, 4.5 Hz, CH_2), 2.95 (dd, 1H, J = 11.25 Hz, 3.75 Hz, CH_2), 2.80 (t, 1H, J = 11.25 Hz, CH_2), 2.56 (t, 1H, J = 11.25 Hz, CH_2). **^{13}C NMR** δ (ppm) : 132.0, 131.2, 128.9, 128.5, 127, 126, 125.7 (Ar), 74.6, 72.6, (CH), 66 (CH_2 benzyl), 61.5, 61.4 (CH_2) **^{11}B NMR** δ (ppm) : + 19.1.

*Dialkoxyamine-borane **12a***

^{1}H NMR δ (ppm) : 4.5 (m, 1H, OH), 4.3 (m, 1H, CH), 4.00 (m, 8H, CH + NH), 3.6 (m, 1H, CH_2), 2.5 (m, 10H, CH_2), 2.1 (m, 1H, CH_2), 1.2 (m, 18H, CH_3). **^{11}B NMR** δ (ppm) : +9.7, -15.6

*Dialkoxyamine-borane **12b***

^{1}H NMR δ (ppm) : 7.35 (m, 10H, arom.), 5.35 (m, 1H, CH), 5.15 (m, 1H, CH), 3.50 (m, 2H, OH + NH), 3.16 (m, 2H, CH_2), 2.80 (m, 2H, CH_2),.**^{11}B NMR** δ (ppm) : +8.1, -17.5

*General procedure for the preparation of lithium aminoborohydrides **14a,b** and **15a,b***

To a solution of amino alcohol or diethanolamine (1 mmol) in THF, was added dropwise under an argon atmosphere, BH_3:THF complex (1 mmol). The mixture was then stirred for 30 min at room temperature. *n*-BuLi (1.1 mmol in the case of amino alcohols and 1.8 mmol when using diethanolamines) was then added to the reaction mixture at 0°C and stirring was continued at 0°C for 2h. Aminoborohydrides can be stored at 5°C under an argon atmosphere during several months without noticeable decomposition. These aminoborohydrides were caracterised by ^{11}B NMR : **14a** : δ -16.4 (d, J = 48.8 Hz), -20 (broad singlet), **14b** : δ -16.4 (d, J = 48.9 Hz), -21 (broad singlet), **15a** : δ -14.6 (d : J_{BH} = 61 Hz), **15b** : δ -13.8 (d : J_{BH} = 56 Hz).

*General procedure for the reduction of acetophenone using lithium aminoborohydrides **14a,b** and **15a,b***

To a THF solution of preformed lithium aminoborohydride was added, at room temperature, 1 mmol of acetophenone. The reacting mixture was stirred for 3h. 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 are reported in Table 2).

REFERENCES

1. Hutchins, R.O.; Learn, K.; El Telbany, F.; Stercho, Y.P.; *J.Org.Chem.*, **1984**, *49*, 2438.
2. Fisher, G.B.; Fuller, J.C.; Harrison, J.; Alvarez, S.G.; Burkhardt, E.R.; Goralski, C.T.; Singaram, B.; *J.Org.Chem.*, **1994**, *59*, 6378 and references therein.

3. Various modified chiral borohydrides have been described : a) Yamada, K.; Takeda, M.; Iwakuma, T.; *J. Chem. Soc. Perkin Trans 1*, **1983**, 265. b) Yatagai, M.; Ohnuki, T.; *J. Chem. Soc. Perkin Trans 1*, **1990**, 1826. c) Itsuno, S.; Sakurai, Y.; Shimizu, K.; Ito, K.; *J. Chem. Soc. Perkin Trans 1*, **1990**, 1859. d) Midland, M.M.; Kazubski, A.; Woodling, R.E.; *J.Org.Chem.*, **1991**, *56*, 1068.
4. Blaser, H.U.; *Chem.Rev.*; **1992**, *92*, 935 .
5. a) Asymmetric reduction of ketones see : Morrison, J.D.; Grandbois, E.R.; Howard, S.I. and Weisman, G.R.; *Tetrahedron lett.*, **1981**, *22*, 2619; de Vries, E.F.J.; Brussee, J.; Kruse, C.G.; Van der Gen, A.; *Tetrahedron : Asymmetry*, **1994**, *5*, 377 ; Steels, I.; Declercq, P.J.; *Tetrahedron : Asymmetry*, **1992**, *3*, 599. Evans, D.A.; Nelson, S.G.; Gagné, M.R.; Muci, A.R.; *J.Am.Chem.Soc.*, **1993**, *115*, 9800. b) Aldolisation reaction see : Tanner, D.; Bigersson, B.; *Tetrahedron Lett.*, **1991**, *32*, 2533. c) Epoxide azidolysis : Nugent, W.A.; *J.Am.Chem.Soc.*, **1992**, *114*, 2768. d) Asymmetric alkylation of benzaldehyde using $ZnEt_2$: Masaki, Y.; Oda, H.; Kasuta, K.; Usui, A.; Xu, F.; *Tetrahedron Lett.*, **1992**, *33*, 5089. de Vries, E.F.J.; Brussee, J.; Kruse, C.G.; Van der Gen, A.; *Tetrahedron : Asymmetry*, **1993**, *4*, 1987.
6. de Vries, E.F.J.; Steenwinkel, P.; Brussee, J.; Kruse, C.G.; Van der Gen, A.; *J.Org.Chem.*, **1993**, *58*, 4315.
7. This methodology has been described for the synthesis of racemic β-amino alcohols : Deyrup, J.A.; Moher , C.L.; *J.Org.Chem.*, **1969**, *34*, 175.
8. This problem of reactivity can be overcome by using metal amides : a) Carre, M.C.; Houmounou, J.P.; Caubere, P.; *Tetrahedron Lett.*, **1985**, *26*, 3107. b) Yamada, J.I.; Yumoto, M.; Yamamoto, Y.; *Tetrahedron Lett.*, **1989**, *30*, 4255.
9. For each diethanolamine, a single diastereoisomer was detected by ^{1}H and ^{13}C NMR.
10. Trost, B.M.; Van Vranken, D.L.; Bingel, C.; *J.Am.Chem.Soc.*, **1992**, *114*, 9327.
11. a) Hirao, A.; Itsuno, S.; Nakahama, S.; Yamazaki, N.; *J.Chem.Soc., Chem.Commun.*, **1981**, 315. c) Mancillo, T.; Santiebastan, F.; Contreras, R.; Klaébé, A.; *Tetrahedron Lett.*, **1982**, *23*, 1561. d) The formation, at low temperature, of N-BH_3 adducts has recently been reported : Tlahuext, H.; Santiesteban, F.; Garcia Baez, E., Contreras, R.; *Tetrahedron : Asymmetry*, **1994**, *5*, 1579.
12. a) Brown, H.C.; Prasad, J.V.N.V.; *J.Am.Chem.Soc.*, **1986**, *108*, 2049. b) Rettig, S.J.; Trotter,J.; *Can.J.Chem.*, **1975**, *53*, 1393.
13. a) Mathre, D.J.; Thompson, A.S.; Douglas, A.W.; Hoogsteen, K.; Carrol, J.D.; Corley, E.G.; Grabowski, *J.Org.Chem.*, **1993**, *58*, 2880. b) Brunel, J.M.; Maffei, M.; Buono, G.; *Tetrahedron : Asymmetry*, **1993**, *4* , 2255.
14. The titration was performed by measuring the integration ratio between the dichloromethane singlet and one methine proton. Compounds **12a,b** are thermally unstable and could not be characterized by mass spectrometry.
15. The requisite amount of *n*-Buli was estimated from the volum of H_2 gas evolved.
16. The chemical shifts of these broad signals were found unchanged after addition of methyl iodide.
17. **16**, **17** and **18** were characterized by ^{11}B NMR and mass spectrometry **16** : (EI) m/z 141 $[M]^+$, **17** : (CI, isobutan) m/z 517 $[MH]^+$, **18** : (EI) m/z 265 $[M]^+$, .
18. Klunder, J.M.; Onami, T.; Sharpless, K.B.; *J.Org.Chem.*, **1989**, *54*, 1295.

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