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NEW CHIRAL HETEROCYCLES: 5-[(R)-(+)-1'-METHYLBENZYL]-1,3,5-DITHIAZINE AND 3,7-DI-[(R)-(+)-1'-METHYLBENZYL]-3,7-DIAZA-1,5-DITHIACYCLOOCTANE. CONFORMATIONAL STUDIES AND THEIR REACTIONS WITH BORANE.

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Abstract. We report herein the syntheses of a new 5-[(R)-(+)-1'-methylbenzyl]-1,3,5-dithiazine **1**, the 5-isopropyl-1,3,5-dithiazine **2** and the 3,7-di-[(R)-(+)-1'-methylbenzyl]-3,7-diaza-1,5-dithiacyclooctane **3**, two of them (**1** and **3**) are new sulfur and nitrogen heterocycles bearing a chiral N-substituent. Compounds **1** and **2** were found in conformational equilibrium when observed at rt at ^{1}H-270 MHz or ^{13}C-67.8 MHz, when cooling a preferred chair conformation was observed with the N-substituent in the axial position. Heterocycle **3** was in an anchored crown conformation at rt. A conformational study of ring inversions for **1** and **3** was performed and their thermodynamic data were obtained, $\Delta G^{\ddagger}$ = 48.1 ± 0.8 for **1** and $\Delta G^{\ddagger}$ = 64.8 ± 1.2 kJ/mol for **3**. The reactivity of **1-3** with BH_3-THF was investigated, the N- or S-BH_3 adducts were not stable, the reactions afforded cleanly the N-borane-N-dimethyl-N-alkylamine adducts. The reaction of **3** with BD_3 gave the N-BD_3 adduct of $[CH_2D]_2N$-$CH[CH_3]C_6H_5$. An X-ray diffraction study of **3** confirmed its crown conformation with the N-substituents in *pseudo*-axial position.

INTRODUCTION

We are currently studying the synthesis, reactivity and conformation of heterocycles rich in lone pairs of electrons[1]. In previous studies of some other dithiazines[1], it was found that at low temperature, the conformation of these compounds is frozen and two different protons (axial and equatorial positions) are observed for C-2 and two for C-4 and C-6. The coalescence temperatures of the two groups of protons were used to calculate the ring inversion. The energy of the N-alkyl derivatives of dithiazine was found to be[1a-b,2], $\Delta G^{\ddagger}$ = 46.0 for N-methyl, $\Delta G^{\ddagger}$ = 43.5 for N-*iso*propyl and $\Delta G^{\ddagger}$ = 38.9 KJ/mol for N-*tert*butyl. Working with these heterocycles, we have discovered that formation of N-borane adducts freezes the ring conformation at room temperature[1,3]. Therefore, we were interested in knowing how the stereogenic center affected the symmetry, the conformational behavior and the spectroscopical data of the free heterocycles and their borane adducts.

SYNTHESIS

Compounds **1** and **3**, fig. 1, were prepared from the optically active (R)-(+)-1-methyl-

benzylamine, CH_2O and NaHS hydrate, see the experimental part. The compounds were obtained in 6 and 77% of yield, respectively. Fortunately, we have found that the acidic treatment of compound **3** afforded easily compound **1** (60% after purification). This process could involve the elimination of an unstable imine which by hydrolysis also afforded the HCl of (R)-(+)-1-methyl benzylamine [^{1}H NMR δ(ppm) 1.62 (d, J= 6.8 Hz), 4.36 (q, J= 6.8 Hz), 7.2-7.56 (m)].

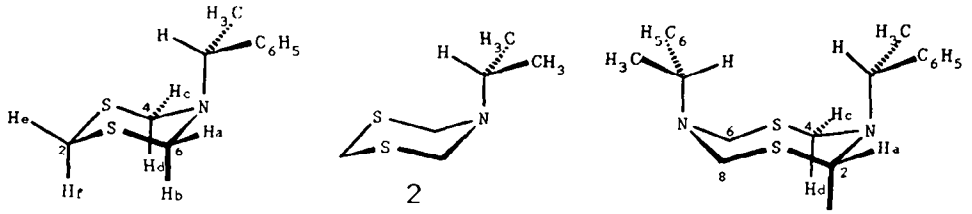

Figure 1

NMR STUDY

Compound 1. At rt (in C_6D_6, $CDCl_3$, C_2D_6SO or C_4D_8O) **1** was in a conformational equilibrium, therefore, we decided to cool the solution of **1** in C_4D_8O and to observe the spectra. The ^{13}C NMR spectrum (-100°C) showed two different signals for C-4 and C-6. By heating the solution both signals coalesce and give a new one ($\Delta G^{\neq}$= 48.5 KJ/mol). It was possible to assign all the protons, by HETCOR $^{13}C/^1H$ and COSY $^1H/^1H$ experiments at -100°C, taking into account the shielding effect of the phenyl group and by comparison with the N-*iso*propyldithiazine spectra at the same temperature. In the ^{1}H NMR at -100°C six different protons were observed since ring inversion was frozen and the chiral center makes the methylene protons (C-4 and C-6) diasterotopic. By heating the solution from -100°C, the temperatures of coalescence of protons in C-2, and C-4 and C-6 were determined. After the coalescence one singlet and two doublets emerged (Tc at -20°C, $\Delta G^{\neq}$= 48.1 KJ/mol). At room temperature, the spectrum of ^{1}H NMR exhibits, two doublets with the appearance of an AB system (J= 13.2 Hz). By HETCOR $^{13}C/^1H$ and COSY $^1H/^1H$ experiments at 27°C we were able to determine that each doublet is an average of one equatorial hydrogen with an axial hydrogen both in different carbon atoms (C-4 and C-6); the signal at 4.26 (Tc at -10°C, $\Delta G^{\neq}$= 49.4 ± 0.8 KJ/mol) was the average of Hb and Hc, fig. 1. And Ha and Hd were at 4.56 (Tc= -35°C, $\Delta G^{\neq}$= 48.5 ± 0.8 KJ/mol). The explanation is that the ring inversion followed by nitrogen epimerization exchanges Ha by Hd and Hc by Hb. The two doublets for the C-4 and C-6 methylene groups do not coalesce even at +90°C. It means that the N-inversion, in order to put the N-substituent in equatorial position, is an energetically disfavored process. This is not consistent with the behavior of (R)-(+)-1-methylbenzylamine which does not exhibit diasterotopic N-Hs owing to the fast N-inversion. On the other hand, the N-BH_3 adduct of the N-[(R)-(+)-1-methylbenzyl]-N,N-di-methylamine reported in this work has diasterotopic methyl groups since there is no lone pair on the nitrogen and inversion is not possible.

Compound 2. As compound **1**, **2** is in conformational equilibrium at rt. By -90°C the preferred conformation can be studied, the N-substituent is in axial position in agreement with results from similar compounds[1].

Compound 3. The NMR study (^{1}H-270 MHz or ^{13}C-67.8 MHz) performed on **3** shows an anchored heterocycle. The preferred crown conformation has the N-substituents in *pseudo*-axial position. The molecular mechanics calculations afforded the same results[4]. By the effect of the chiral group, compound **3** presents in ^{1}H NMR four different methylene protons, which were assigned by comparison with **1** and **2** and by HETCOR ^{13}C/^{1}H and COSY ^{1}H/^{1}H experiments. By heating, coalescence of the methylene groups occurs in the same way as in **1**. These experiments allowed us to calculate the ring inversion energy as $\Delta G^{\neq}$ = 65.3 ± 1.2 KJ/mol. The inversion of this eight membered ring **3** demands more energy than in N,N'-di*iso*propyldithiadiazacyclooctane ($\Delta G^{\neq}$ = 56.0 KJ/mol)[5] and in the corresponding dithiazine **1** ($\Delta G^{\neq}$ = 48.5. KJ/mol).

X-RAY DIFFRACTION STUDY OF COMPOUND 3.

The X-ray diffraction study of orthorhombic crystal of compound **3**[8] showed that in solid state has a similar structure to that deduced in solution and to that of the N-methyl derivative[6], fig. 2.

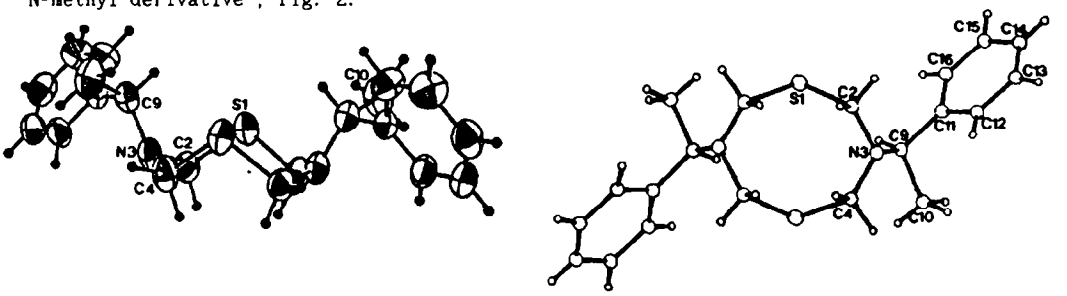

Figure 2. Crystal X-ray diffraction of compound **3**: a) ORTEP diagram and b) an other view of **3**. Selected interatomic distances and angles are as follows: S(1)-C(2) 1.842(2), S(1)-C(4) 1.856(2), N(3)-C(2) 1.437(2), N(3)-C(9) 1.477(2), C(9)-C(10) 1.529(2), C(9)-C(11) 1.515(2), C(11)-C(12) 1.387(2), C(11)-C(16) 1.381(2), C(2)-S(1)-C(4) 101.58(8), C(2)-N(3)-C(9) 112.7(1), S(1)-C(2)-N3 119.6(1), N(3)-C(9)-C(10) 113.3(1), N(3)-C(9)-C(11) 109.3(1), C(10)-C(9)-C(11) 109.5(1), C(9)-C(11)-C(12) 121.1(1), C(9)-C(11)-C(16) 121.5(1).

The molecule has a C2 axis in a crown conformation with the N-substituents in axial position. The methyl and phenyl groups are directed toward the outside in an alternated rotamer (N-C bond) with each C9-H proton directed to one sulfur atom, the distance H-9-S1 (2.91 Å) suggests the presence of a hydrogen bonding of H-9 with the S axial lone pairs. The N-N and S-S distances are 4.230 Å and 3.557 Å respectively, Table 1. The sulfur atoms are pushed towards the outside in order to avoid repulsion between the lone pairs which remain parallel and perpendicular to the ring plane, the N-substituents are also pushed towards the outside to avoid steric hindrance, this effect is clear on the geometry of

nitrogen atoms which are almost planar (57% of sp^2). The open angle between C9-N3-C4' [118(1)°, Table 2], larger than the angle C2-N3-C9 [112.7(1)°] is indicative of a more important steric effect of the methyl group when compared with the phenyl group. In the solid state, the plane of the phenyl group is in front of C-2. This geometry must also be favored in solution because it is in agreement with the shielding effect found in NMR in the methylene of C-2.

REACTIVITY OF COMPOUNDS 1 AND 3 WITH BH_3-THF AND BD_3-THF

We were interested in studying the effect of N-BH_3 adduct formation on the conformational equilibrium of nitrogen and sulfur heterocycles. Therefore, we reacted the heterocycles **1** and **3** with BH_3-THF, fig. 3. In any case the N-BH_3 adduct was not observed but a fast opening reaction of the heterocycles occurred that gave the N-borane-N,N-dimethyl-N-[(R)-(+)-1-methyl]benzylamine in high yield (71%). This is a good method to perform the dimethylation of amines[1b]. The N-BH_3 adduct and the free dimethylated amine were identified by the NMR spectra. In the ^1H and ^{13}C NMR, the diastereotopic N-methyl groups of the N-BH_3 adduct are distinguished ($\Delta\delta$ in ^{13}C NMR is 7.48 ppm). When BD_3-THF is added to **3**, the N-BD_3 adduct of $(CH_2D)_2NCH(CH_3)(C_6H_5)$ was obtained. The latter compound could be relevant for stereochemical studies[7].

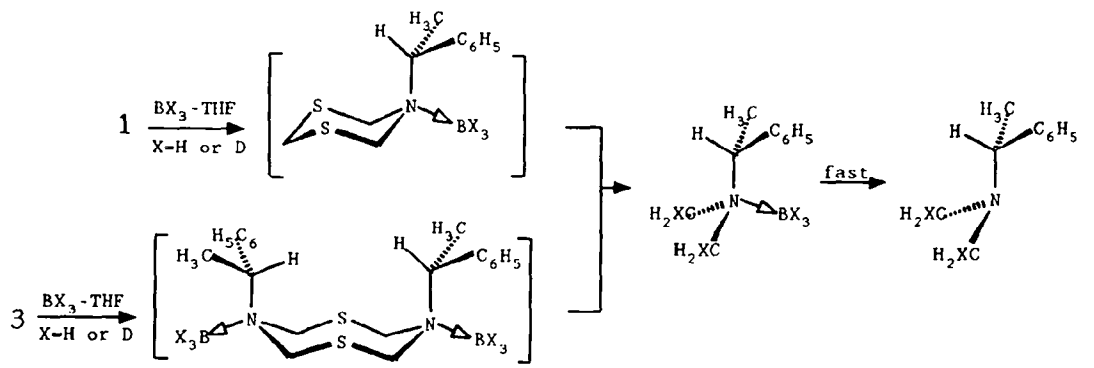

Figure 3

REACTIVITY OF COMPOUND 2 WITH BH_3-THF AND BD_3-THF

The reaction of **2** with BH_3-THF is very interesting because several reaction products, determined by NMR, are obtained depending on **2** and BH_3-THF ratio. When one equivalent of borane is added at -78°C and observed immediately in NMR, the N-BH_3 adduct **4** is the main product accompanied by a minor quantity of heterocycle **5**. If two equivalents of BH_3-THF are used and the reaction is warmed to 25°, the main reaction product is **5**. With three equivalents of BH_3-THF, heating at 50°C for 12 h and evaporation of solvent, the reaction product is the borate of the ammonium salt **6**, this result is the consequence of the N-BH_3

adduct of N,N-dimethyl-N-*iso*propylamine (^{11}B NMR δ = -10.9 ppm, q, 105 Hz) being very sensitive to hydrolysis, fig. 4.

The NMR data show that the N-BH3 adduct **4** is an anchored molecule with the BH3 in axial position as is deduced from the δ ^{11}B NMR (-14.3 ppm, q, J_{BH}= 100 Hz). This behavior contrasts with that observed for N-methyldithiazine in which the N-BH3 adduct is very stable and the BH3 group prefers the equatorial position (δ= -8.0 ppm, q, J_{BH}= 100 Hz)[1a,b]. Heterocycle 5 has exchanged a CH_2 for a BH_2 group (^{11}B NMR δ= -4.1 ppm, t, J_{BH}= 114 Hz) but the *iso*propyl group remains in equatorial position, fig. 4. The configuration of the nitrogen atom in 5 was also deduced from the δ ^{13}C NMR of N-CH3 (41.39 ppm) similar to that of the axial N-CH3 group (44.34 ppm) in heterocycle 7[1b]. These results give evidence of the different weights of methyl, borane and *iso*propyl groups in the conformational equilibrium of the dithiazine ring.

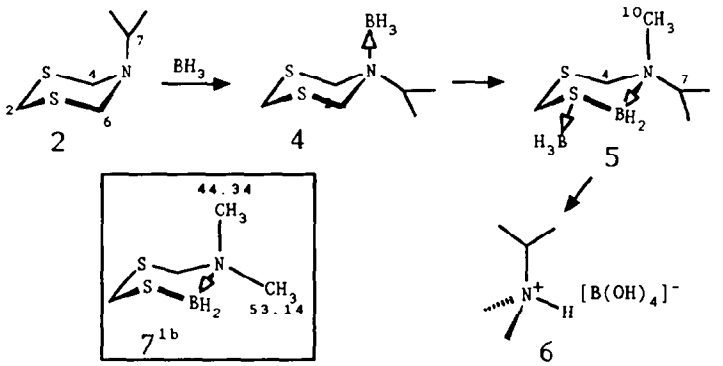

Figure 4

EXPERIMENTAL.

^{1}H (270 MHz) and ^{13}C (67.8 MHz) NMR spectra were recorded with TMS as internal reference and ^{11}B NMR (86.55 MHz) spectra with BF_3-OEt_2 as external reference. Mass spectra were recorded on a Hewlett Packard 5989 mass spectrometer. Melting points are uncorrected. Crystal data[8]: Computations for compound 3 were performed by using MOLEN[9] adapted for a Micro Vax II. Atomic form factors for neutral S, C, N, O and H were taken from ref. 10. Hydrogen atoms were found on difference electron density maps.

Synthesis of 5-*iso*propyl-1,3,5-dithiazine, 2. *Iso*propylamine (13 ml, 0.30 mol) in water (20 ml) was added to aqueous CH_2O (37%, 76.69 ml, 0.94 mol) and stirred 5 min at rt. Another solution of NaSH (19.38 g, 0.35 mol) in 70 ml of water was added and the mixture was stirred 35 h, the whole was extracted with (5 x 50 ml) CH_2Cl_2. The extracts were dried with Na_2SO_4 and evaporated to give a green oil which was distillated at 120°C/13 mm. The distillated crystallized and the crystals were washed with cold hexane at -78°C. A pure compound (2) was obtained (18.2 g, 64%). ^{1}H NMR (C_4D_8O, 270.05 MHz, at 27°C) δ 1.09 (d, J= 6.6, 6H; CH_3), 3.75 (m, 1H, H-7), 4.11 (s, 2H, 2H-2), 4.50 (s, 4H, 2H-4 and 2H-6). ^{1}H

NMR (C_4D_8O, 270.05 MHz, at -90°C) δ 1.07 (d, J_{AB}= 6.0, 6H, CH_3), 3.68 (d br, J_{AB}= 13.2, 1H, H-2eq), 3.73 (sept, J= 6.0, 1H, H-7), 4.29 (d, J_{AB}= 13.2, 2H, H-4eq and H-6eq), 4.65 (d, J_{AB}= 13.2, 1H, H-2ax), 4.80 (d, J_{AB}= 13.2, 2H, H-4ax and H-6ax). ^{13}C NMR (C_4D_8O, 67.8 MHz, at 27°C) δ 21.11 ($\underline{C}H_3$, 2C), 34.28 (C-2), 45.81 (C-7), 56.89 (C-4 and C-6). ^{13}C NMR (C_4D_8O, 67.8 MHz, at -90°C) δ 20.99 ($\underline{C}H_3$, 2C), 33.62 (C-2), 44.86 (C-7), 56.50 (C-4 and C-6).

Synthesis of 3,7-[(R)-(+)-1'-methylbenzyl]-1,5-dithia-3,7-diazacyclooctane, 3. 8.60 ml of (R)-(+)-1-methylbenzylamine (0.06 mol) in methanol (120 ml) were added to 34.90 ml (0.46 mol) of aqueous formaldehyde (37%) and the mixture was stirred for 5 min at 0°C. Another solution of 9.33 g NaSH (0.16 mol) in 150 ml of methanol was added and the mixture was stirred 24 h at 0°C. The precipitated was filtered and washed with 100 ml of methanol at 0°C. The solid (compound 3) was dissolved in CH_2Cl_2 and crystallized in CH_2Cl_2/hexane (1:3) and 9.12 g obtained, 70%. The solution was evaporated and a green oil was obtained and compound **1** (0.83 g (6 %)) was purified by thin layer chromatography (hexane/CH_2Cl_2, 1:1). M.p. 153-5°C. Anal. for $C_{20}H_{26}N_2S_2$, Calcd. C 66.99, H 7.30, N 7.81; Found C 67.09, H 7.37, N 7.81. $[\alpha]_D^{20}$ +134.67 (c 0.02, CH_2Cl_2). ^1H NMR (C_6D_6, 270.05 MHz, at 27°C) δ 1.32 (d, J= 6.6, 3H; CH_3), 3.70 (d, J_{AB}= 14.5, 1H, H 4eq), 3.73 (d, J_{AB}= 13.8, 1H, H-2eq), 4.42 (d, J_{AB}= 14.5, 1H, H-4ax), 4.63 (q, J= 6.6, 1H, N-$\underline{C}H$), 4.90 (d, J_{AB}= 13.8, 1H, H-2ax), 7.0-7.4 (m, 5H). ^{13}C NMR (C_6D_6, 67.8 MHz, at 27°C) δ 21.84 (CH_3), 56.96 (N-$\underline{C}H$), 61.40 (C-), 63.36 (C-), 127.52 (C-*para*), 127.66, 127.99, 128.38 and 128.95 (C-*para*, C-*meta* and C-*ortho*), 144.61 (C-*ipso*). MS(60eV) *m/z* (%) 180(41), 148(43), 105(100), 41(24).

Synthesis of 5-[(R)-(+)-1'-methylbenzyl]-1,3,5-dithiazine, 1. Compound 3 (0.22 g, 0.63 mmol) was dissolved in methanol (30 ml) and treated with 0.2 ml of a water solution of HCl (37.5%). After 4 h of stirring, the solvent was evaporated and the mixture was extracted with CH_2Cl_2 and dried with Na_2SO_4. The evaporation of the solvent gave a yellow oil which was the dithiazine unpurified with the amine. The latter was extracted (0.09 g, 63%) from the oil with 10 ml of a solution CH_2Cl_2/hexane (1:4) by stirring 10 min. Anal. for $C_{11}H_{15}NS_2$, Calcd. C 58.66, H 6.66, N 6.22 Found C 58.51, H 6.51, N 6.15. $[\alpha]_D^{20}$ +72.25 (c 0.011, CH_2Cl_2). ^1H NMR (C_4D_8O, 270.05 MHz, at 27°C) δ 1.34 (d, J= 6.6, 3H, CH_3), 4.11 (s, 2H, 2H-2), 4.26 (d br, J= 13.2, 2H, H-4ax and H-6eq), 4.55 (d, J= 13.2, 2H, H-4eq and H-6ax), 4.82 (q, J= 6.6, 1H, N-$\underline{C}H$), 7.1-7.4 (m, 5H). ^1H NMR (C_4D_8O, 270.05 MHz, at -60°C) δ 1.33 (d, J_{AB}= 7.3, 3H, CH_3), 3.60 (d, J_{AB}= 12.5, 1H, H-6eq), 3.68 (d, J_{AB}= 13.2, 1H, H-2eq), 4.49 (d, J_{AB}= 13.2, 1H, H-3eq), 4.64 (d, J_{AB}= 12.5, 1H, H-6ax), 4.68 (d, J_{AB}= 13.2, 1H, H-2ax), 4.80 (q, J= 7.3, 1H, N-$\underline{C}H$), 4.92 (d, J= 13.2, 1H, H-3ax), 7.2-7.4 (m, 5H). ^{13}C NMR (C_4D_8O, 67.8 MHz, at 27°C) δ 21.46 ($\underline{C}H_3$), 33.85 (C-2), 55.50 (N-CH), 56.73 (C-4 and C-6), 127.81 (C-*para*), 128.10 and 129.22 (C-*ortho* and C-*meta*), 145.08 (C-*ipso*). ^{13}C NMR (C_4D_8O, 67.8 MHz, at -60°C) δ 21.62 ($\underline{C}H_3$), 33.53 (C-2), 55.22 (N-CH), 55.79 (C-4), 57.04 C-6), 127.89 (C-*para*), 127.99 and 129.32 (C-*ortho* and C-*meta*), 144.97 (C-*ipso*). MS(70eV) *m/z* (%) 225$[M]^{+\cdot}$(33), 179(25), 147(31), 105(100), 42(24).

Reduction of compound 2 with BH_3-THF. In an NMR tube to a solution of N-*iso*propyl dithiazine **2** (0.10 g, 0.61 mmol) in $CDCl_3$ (0.4 ml) at -78°C was added BH_3-THF in THF (2.3 M, 0.27 ml, 0.61 mmol). The reaction was followed by ^{13}C and ^{11}B NMR from -78°C. The N-BH_3 adduct **4** was the main compound. A similar reaction with two equivalents of BH_3-THF at -78°C was warmed to 25°, the heterocycle **5** appears as the main product. Compound **2** was made to react with three equivalents of BH_3-THF and heated 12 h at 50°C, then the solvent was evaporated. A sample of the reaction product was dissolved in DMSO-*d6* which was characterized by NMR as the borate of the N,N-dimethyl-N-*iso*propylammonium **6**.

5-Isopropyl-1,3,5-dithiazine N-BH_3 Adduct 4. ^{11}B NMR (C_4D_8O, 86.55 MHz, at 27°C) δ -14.3 (q, J_{BH}= 100). ^{13}C NMR (C_4D_8O, 67.8 MHz, at 27°C) δ 15.81 (CH_3), 29.90 (C2), 49.29 (N$\underline{C}$H), 60.08 (C4 and C6).

5-Isopropyl-5-methyl-1,3,6,5-dithiaborazine 5. ^{11}B NMR (C_4D_8O, 86.55 MHz, at 27°C) δ -4.1 ($\underline{B}H_2$, t, J_{BH}= 114), -23.2 ($\underline{B}H_3$, q, J_{BH}= 103). ^{13}C NMR (C_4D_8O, 67.8 MHz, at 27°C) δ 14.51 ($\underline{C}H_3$), 16.99 ($\underline{C}H_3$), 32.16 (C2), 41.39 (C10), 52.64 (C7), 62.91 (C4).

N,N-Dimethyl-N-*iso*propylammonium borate 6. ^{11}B NMR (DMSO-D_6, 86.55 MHz, at 27°C) δ +1.26 ($\underline{B}(OH)_4$, s). H^1 NMR (DMSO-D_6, 270.05 MHz, at 27°C) δ 1.18 ($C\underline{H}_3$, d, 3H, J= 6.6), 2.6 (NC$\underline{H}_3$, s, 6H), 3.58 (NC$\underline{H}$, m, 1H), 6.60 (N$\underline{H}$, s br, 1H). ^{13}C NMR (DMSO-D_6, 67.8 MHz, at 27°C) δ 16.07 ($\underline{C}H_3$), 38.47 ($\underline{C}H_3$), 56.66 (N$\underline{C}$H).

Reduction of compound 3 with BH_3-THF. To a solution of 0.5 g of heterocycle **3** (1.40 mmol) in dry CH_2Cl_2 (50 ml), at 0°C and N_2 atmosphere, was added 1.40 ml of a solution of BH_3-THF in THF (2.3 M, 3.21 mmol). The reaction mixture was stirred at rt. for 24 h. The formation of BH_3 adduct of (R)-(+)-1-methylbenzyl-N,N-dimethylamine was followed by NMR. Then 10 ml of methanol were added and the solution heated at 50°C for 12 h. The solvent was evaporated and the mixture was purified by flash chromatography (CH_2Cl_2/hexane, 6:4). The free dimethylamine (0.291 g, 71%) was obtained as a transparent oil.

(R)-(+)-1-Methylbenzyl-N,N-dimethylamine N-BH_3 Adduct. ^{11}B NMR ($CDCl_3$, 86.55 MHz, at 27°C) δ -10.05 (q, J_{BH}= 94.7). H^1 NMR ($CDCl_3$, 270.05 MHz, at 27°C) δ 1.74 (d, J= 7.25, 3H, C-C$\underline{H}_3$), 2.47 (d, J= 9.9, N-C$\underline{H}_3$), 4.07 (q, J= 7.25, 1H, N-C$\underline{H}$), 7.39 (sbr, 5H). ^{13}C NMR ($CDCl_3$, 67.8 MHz, at 27°C) δ 16.77 (q, J= 128.4, C-$\underline{C}H_3$), 44.99 (qsext, J= 139.4 and 4.4, N-$\underline{C}H_3$), 52.48 (qbr, J= 139.4, N-$\underline{C}H_3$), 70.08 (d, J= 141.58, N-$\underline{C}$H), 128.31 (dd, J= 162.9 and 6.0, C-*ortho*), 128.86 (dt, 161.4 and 6.6, C-*para*), 130.06 (dbr, J= 158.4, C-*meta*), 136.94 (sbr, C-*ipso*).

(R)-(+)-1-Methylbenzyl-N,N-dimethylamine. ^1H NMR ($CDCl_3$, 270.05 MHz, at 27°C) δ 1.39 (d, J= 6.6, 3H, C-C$\underline{H}_3$), 2.21 (s, 3H, N-C$\underline{H}_3$), 3.28 (q, J= 6.6, 1H, N-C$\underline{H}$), 7.29 (m, 5H). ^{13}C NMR ($CDCl_3$, 67.8 MHz, at 27°C) δ 20.17 (q, J= 125, C-$\underline{C}H_3$), 43.19 (q, J= 132.2, N-$\underline{C}H_3$), 65.99 (d, J= 141.0, N-$\underline{C}$H), 128.20 (dd, J= 158.6 and 6.6, C-*ortho*), 126.90 (td, J= 150.0 and 5.4, C-*para*), 127.53 (tdd, 167.5, 5.5, 6.6, C-*meta*), 143.69 (m, C-*ipso*).

Reduction and deuteration of compound 3 with BD_3-THF. A solution of 0.3 g (0.84 mmol) of **3** in dry THF (50 ml) was bubbled with 2 equivalents (1.68 mmol) of B_2D_6 [generated from

0.42 ml of BF_3-etherate and 0.095 g of $NaBD_4$] at 0°C and in N_2 atmosphere. The reaction mixture was stirred for 24 h at r.t., formation the BH_3 adduct of (R)-(+)-1-methylbenzyl-N,N-di-[methyldeuterated]amine was followed by NMR. Treatment of the mixture with 10 ml of water gave 0.20 g of the free deuterated amine (73%).

(R)-(+)-1-methylbenzyl-N,N-di-[methylmonodeuterated]amine N-BD_3 Adduct. ^{11}B NMR ($CDCl_3$, 86.55 MHz, at 27°C) δ -10.4 (s br). ^1H NMR ($CDCl_3$, 270.05 MHz, at 27°C) δ 1.72 (d, J= 7.30, 3H, C-CH_3), 2.42 (s, 3H, N-CH_3), 2.46 (s, 3H, N-CH_3) 4.04 (q, J= 7.30, 1H, N-CH), 7.36 (sbr, 5H). ^{13}C NMR ($CDCl_3$, 67.8 MHz, at 27°C) δ 16.72 (C-CH_3), 44.68 (N-CH_3), 52.06 (N-CH_3), 69.95 (N-CH), 127.50 (C-*ortho*), 126.85 (C-*para*), 128.18 (C-*meta*), 136.94 (C-*ipso*).

(R)-(+)-1-Methylbenzyl-N,N-di-[methylmonodeuterated]amine. ^1H NMR ($CDCl_3$, 270.0 MHz, at 27°C) δ 1.39 (d, J= 6.6, 3H, C-CH_3), 2.16 (s br, 6H, N-CH_3), 3.23 (q, J= 6.6, 1H, N-CH), 7.29 (m, 5H). ^{13}C NMR ($CDCl_3$, 67.8 MHz, at 27°C) δ 20.24 (C-CH_3), 42.92 (N-CH_3), 65.94 (N-CH), 129.53 (C-*ortho*), 130.20 (C-*para*), 128.98 (C-*meta*), 144.19 (C-*ipso*).

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