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Tetrahedron: *Asymmetry* 9 (1998) 3991–3996

TETRAHEDRON: *ASYMMETRY*

1,3-Heterazolidin-2-ones as starting materials for optically active 1,3,2-oxazaborolines and 1,3,2-diazaboroline derived from ephedrines

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Abstract

(4*R*,5*R*)-3,4-Dimethyl-5-phenyl-1,3,2-oxazaboroline (**1a**) derived from pseudoephedrine and (4*R*,5*S*)-1,3,4-trimethyl-5-phenyl-1,3,2-diazaboroline (**1d**) derived from ephedrine have been prepared from the corresponding 1,3-heterazolin-2-one. Hydrolysis of **1d** afforded the 1-methyl-3-(methylamine)-2-phenyl-propylamine **5**. The structures were established from ^{1}H, ^{13}C and ^{11}B NMR data. The X-ray diffraction analysis of (4*R*,5*S*)-(+)-3,4-dimethyl-5-phenyl-1-hydro-1,3-diazolidine-2-one (**4e**) was performed. Isomeric N-monoborane adducts of the 1,3,2-diazaboroline **1d** were prepared, and their structures were deduced from the NMR data.

1. Introduction

We are interested in the synthesis and structural analysis of optically active B–H heteroazaborolines derived from ephedrines.[1–5] We have synthesized the 1,3,2-thiazaboroline **1b** derived from bis-ephedrine disulfide and determined the structure of its N-borane adduct **2b**[4] (Scheme 1). Recently, preparation of 1,3,2-heterazaborolines **1a–c** from BH_3–THF reduction of the corresponding 1,3,2-heterazoline-2-imines and formation of their N-borane adducts **2a–c** were reported.[5]

Continuing our research in the chemistry of optically active boron hydrides, we are interested in preparing new heterocycles bearing different heteroatoms, as well as looking for easier ways to prepare them. Therefore, we have explored the borane reduction of 1,3-heterazolidin-2-one compounds **4e** and **4t** as a synthetic alternative on the formation of 1,3,2-heterazaborolines **1a** and **1d**. Thus, we have prepared the 1,3-diazolidin-2-one **4e** reported previously by Close[6] and the 1,3-oxazolidin-2-one **4t**.

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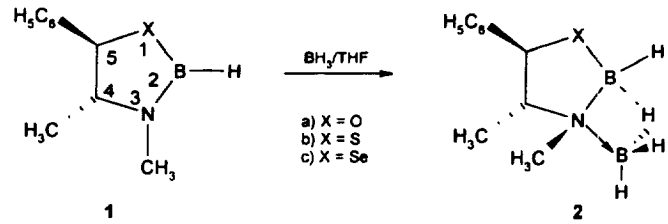
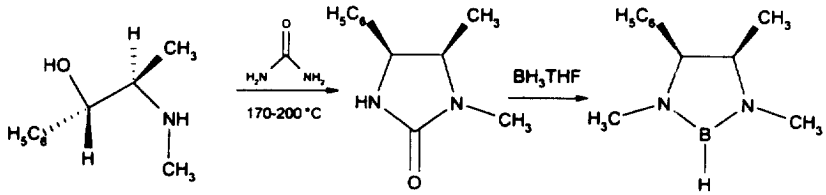


1 2

Scheme 1.

In his report, Close assumed that the reaction depicted in Scheme 2 produced the *trans* isomer of **4**. However, the analysis of the structure indicated that it is the *cis* isomer **4e** as was determined by ^{1}H and ^{13}C NMR. Its X-ray diffraction molecular structure confirmed the *cis* stereochemistry (Fig. 1). Atoms C5, N1, C2(O) and the N1–Me group are coplanar. The C4–N3 [1.457(4)] and C5–N1 [1.453(4)] bond lengths are typical of single bonds. However, N1–C2 [1.341(5)] and N3–C2 [1.380(4)] have some double bond character.



ephedrine 3e 4e 1d

Scheme 2.

The reaction of heterocycles **4e** and **4t** with three equivalents of BH_3–THF in refluxing THF afforded the B–H heterocycles **1a** and **1d**, respectively (Schemes 2 and 3), which were purified by distillation at reduced pressure. Both compounds present a doublet in the ^{11}B NMR spectrum: **1a** δ +29 ppm [^{1}J(B–H)=153 Hz][2] and **1d** δ +29 ppm [^{1}J(B–H)=138 Hz]. The ^{13}C NMR spectrum of **1d** shows two signals for N–Me, which have similar chemical shifts. These signals were assigned by NOESY and

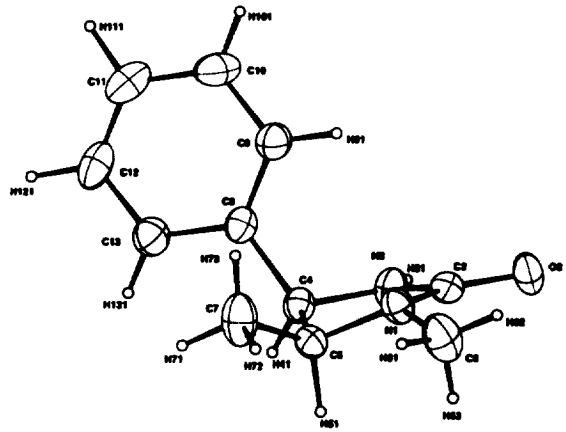
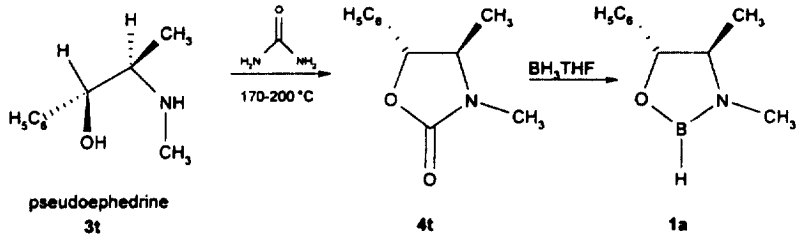
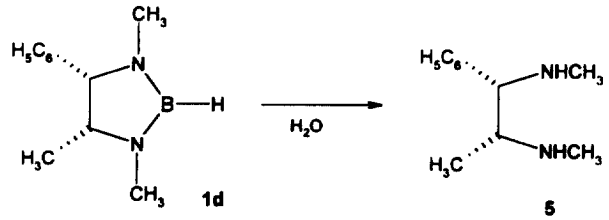


Figure 1. Molecular structure of compound **4e**. Relevant bond lengths, C5–N1, 1.453(4); N3–C4, 1.457(4); N1–C2, 1.341(5); C4–C7, 1.508(5); C2–O2, 1.225(4); C4–C5, 1.549(4); C2–N3, 1.380(4); C5–C8, 1.521(5); N3–C6, 1.440(4). Relevant bond angles (°); C4–N3–C2, 110.0(3); N3–C4–C7, 113.0(3); N3–C2–N1, 107.5(3); N3–C4–C5, 102.3(3); N3–C2–O2, 125.1(3); C5–C4–C7, 116.3(3); N1–C2–O2, 127.5(3); C4–C5–N1, 100.4(3); C2–N3–C6, 119.0(3); C4–C5–C8, 115.5(3); C2–N1–C5, 113.8(3); N1–C5–C8, 113.2(3); C4–N3–C6, 120.5(3)

HETCOR experiments. Compound **1d** is the first example of optically active 1,3,2-imidazaboroline derived from ephedrine. Its hydrolysis affords the corresponding optically active diamine **5** (Scheme 4).

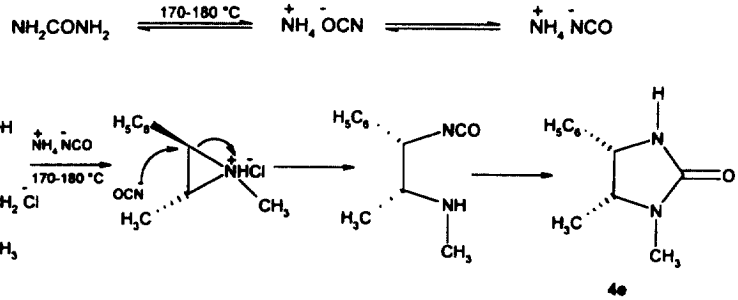


Scheme 3.



Scheme 4.

Compound **4e** was formed stereoselectively with retention of configuration at C5. An aziridine with methyl and phenyl groups in the *trans* position as an intermediate could explain this stereochemistry (Scheme 5). However, ^{1}H and ^{13}C NMR data of *cis*-1,3-diazolidin-2-one **4e** had been reported by Drewes et al.[7] but C4 and C5 were not assigned; the proximity of the chemical shifts made it very difficult. We have performed a heteronuclear correlation experiment $^{1}H/^{13}C$ (HETCOR) in order to correctly assign them (Tables 1 and 2).



Scheme 5. Possible pathway to the 1,3-diazolidin-2-one **4e**

It is known that addition of BH_3 to borolines **1a–c** gives the N-borane adducts **2a–c** (Scheme 1).[5] The N-borane coordination stops the N–B retrocoordination in the cycle, allowing for a hydride bridge to compensate the endocyclic boron electronic deficiency. The structures of **2a–c** were deduced from the ^{11}B NMR data and have been attributed to diborane groups with a B–H–B bridge. The presence of the hydride bond strongly shifts the signal of the endocyclic boron to lower frequencies. This bond can also be deduced from the IR data.[5] Therefore, it was relevant to evaluate the selectivity and the stereochemistry of the borane addition to the new heterocycle 1,2,3-diazaboroline **1d**. This compound has two different nitrogen atoms and two faces, and in consequence, four isomeric N-borane adducts are possible. The reaction of compound **1d** with one equivalent of BH_3–THF at rt was followed by ^{11}B NMR. The spectrum presented five signals, one of the starting compound (+29.3 ppm, d, **1d**), a broad signal at +33.9 ppm and three quadruplets at lower frequencies in a ratio: −14.4 (70%), −18.9 (20%),

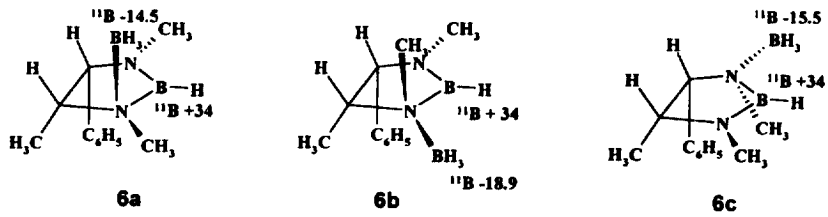
Table 1
^{1}H NMR δ (ppm), J (Hz) of compounds **1–6**

Compd.	H4(m)	H5(^{3}J)(d)	CH_3(^{3}J)(d)	N1-H or N1-CH_3	N3-CH_3	Aromatic (m)
1a	2.98	4.81(7.2)	0.88(6.1)		2.32	7.15
1d	3.75	4.43(9.4)	0.63(6.7)	2.65	2.54	7.27
4e	3.73	4.43(8.3)	0.72(6.6)	6.00	2.70	7.32
4t	3.52	4.88(7.9)	1.35(6.1)		2.85	7.26
5	3.51	3.51	0.89 (6.4)	2.24	2.35	7.26
6a	3.90	4.67(7.7)	0.81(6.3)	2.41	2.73	7.34
6b	3.63	4.52(8.8)	1.01(6.9)	2.62	2.77	7.33
6c	3.73	4.32	8.79	2.79	2.28	7.31
6d	3.73	4.2(11.3)	1.14(7.7)	2.45	2.28	7.37

Table 2
^{13}C NMR δ (ppm) of compounds **1–6**

Compd	C4	C5	CH_3	Ci	Co	Cm	Cp	N1CH_3 or C2	N3-CH_3
1a	64.5	88.1	18.8	143.5	128.7	125.7	127.7		29.8
1d	61.7	71.5	16.0	139.2	127.8	126.9	128.3	32.4	33.1
4e	57.6	58.1	14.3	138.4	128.4	127.8	127.8	162.8	28.1
4t	61.1	82.3	17.2	137.5	127.6	128.7	129.2	160.1	28.9
5	60.1	68.2	15.5	141.0	128.3	128.0	127.1	34.8	34.4
6a	65.9	70.8	12.3	135.6	127.9	127.3	128.5	33.1	39.7
6b	66.8	71.1	11.9	133.7				33.4	47.3
6c	58.6	77.9	14.4	135.0				43.0	31.4
6d	64.5	74.5	12.7	133.7	128.2	127.5	127.8	40.0	33.9

−15.5 (10%) the latter correspond to N-borane adducts **6a–c**, respectively (Scheme 6). The structures of compounds **6a–c** were determined based on the inductive and steric effect of the borane group on its neighboring atoms observed by ^{1}H and ^{13}C NMR[8–10] (Tables 1 and 2).

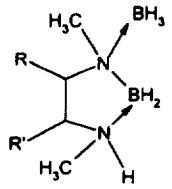


6a **6b** **6c**

Scheme 6. N-Borane monoadducts **6a–c** derived from **1d**. ^{11}B NMR data are shown

In the 1,3,2-diazaboroline heterocycles, the strong shift observed for compounds **2a–c** in the ^{11}B NMR of the endocyclic boron atom was not observed in **6a–c**. The explanation could be the absence of the BHB bond, because the intracyclic boron atom in **1d** is not acidic enough due to the retrocoordination from the free nitrogen atom.

Compound **1d** was reacted with two equivalents of BH_3–THF at rt and the reaction was followed by ^{11}B NMR. Three triplets (+3.5, −0.6, −1.8 ppm) and four quartets (−6,0, −6.7, −7.6 and +9.5 ppm) were observed in the spectrum. All of them are isomers of the N-borane adduct of 1,3,2-diazaborolidine (**7**) (Scheme 7). We were unable to assign the NMR data to the corresponding isomers. Heterocycles **7** present similar NMR data to those of the di-N-borane adducts of 1,3-diazolidine[11] (Scheme 8).



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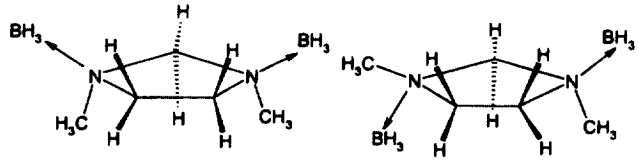
Scheme 7.



Scheme 8.

2. Experimental section

Compounds **4t** and **4e** were prepared as described in the literature.[6] Compound **4e** was recrystallized from ethanol, mp 178.5°C, $[\alpha]_D^{25}$ 45 (c 0.056 M, MeOH) or $[\alpha]_D^{25}$ 62 (c 0.059 M, $CHCl_3$). Crystallographic data: formula, $C_{11}H_{14}N_2O$; 190.179; space group, $P2_12_12_1$; a=6.193(3) Å, b=8.064(2) Å, c=20.884(2) Å, α=90.0, β=90.0 γ=90.0; V=1043.08(7) Å^3, Z=4, crystal size=0.2×0.2×0.2 mm; linear abs. coeff. 0.61 cm^{-1}; ρ (calc.) 0.95 g cm^{-3}, scan type 2/θ; scan range (deg.) 0.45+0.43 tgθ; data collected used 738.

2.1. (4R,5S)-cis-3,4-Dimethyl-5-phenyl-1,3,2-diazaboroline 1d and (4R,5R)-3,4-dimethyl-5-phenyl-1,3,2-oxazaboroline 1a

Both compounds were prepared following the same procedure: compound **4e** (5.0 g, 26.1 mmol) was dissolved in 10 ml of dry THF in an ice bath, then 30.2 ml (78.5 mmol) of 2.6 M BH_3–THF solution was added. The reaction mixture was refuxed for 4 h and distilled under vacuum (bp, 92°C at 1.0 mmHg). A viscous liquid (**1d**) was obtained (3.2 g, 65% yield); $[\alpha]_D^{25}$ −12 (c 0.1 M, THF); IR: ν 2554 cm^{-1} (BH); mass: m/z (%): 188 (46), [M$^+$] 173 (100), 158 (29).

Compound **1a** was prepared from **4t**: bp, 95°C at 1.5 mmHg; 3.0 g, 65% yield.

2.2. 1-Methyl-3-(methylamine)-2-phenyl-propylamine 5

100 mg (0.5 mmol) of **1d** were placed in a flask dissolved in 5 ml of $CHCl_3$. Water (3 ml) were added and the mixture stirred for 2 h. The chloroform was separated and evaporated to give the amine as a viscous liquid, 70 mg (78%), $[\alpha]_D^{25}$ +47.7 (c 0.1 M, $CHCl_3$), IR: ν 4200, 3600, 1205 cm^{-1}, mass: m/z (%): 179.3 (1), [M$^+$] 72 (100).

2.3. cis-3,4-Dimethyl-5-phenyl-1,3,2-diazaboroline N-boranes 6a–c

50 mg (0.3 mmol) of **1d** were placed in an NMR tube with 0.3 ml (0.3 mmol) of BH_3–THF solution (1.0 M). The solvent was eliminated under vacuum, $CDCl_3$ was added and the reaction product characterized by NMR.

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References

1. Tlahuext, H.; Contreras, R. *Tetrahedron: Asymmetry* **1992**, *3*, 727.
2. Tlahuext, H.; Contreras, R. *Tetrahedron: Asymmetry* **1992**, *3*, 1145.
3. Tlahuext, H.; Santiesteban, F.; Báez, E. G.; Contreras, R. *Tetrahedron: Asymmetry* **1994**, *5*, 1579.
4. Cruz, A.; Flores-Parra, A.; Tlahuext, H.; Contreras, R. *Tetrahedron: Asymmetry* **1995**, *6*, 1933.
5. Cruz, A.; Macías-Mendoza, D.; Barragán-Rodríguez, E.; Tlahuext, H.; Nöth, H.; Contreras, R. *Tetrahedron: Asymmetry* **1997**, *8*, 3903.
6. Close, W. J. *J. Org. Chem.* **1950**, *15*, 1131.
7. Drewes, S. E.; Malissar, D. G. S.; Roos, G. H. P. *Chem. Ber.* **1993**, *126*, 2663.
8. Contreras, R.; Morales, H. R.; Mendoza, M. L.; Domínguez, C. *Spectrochim. Acta.* **1987**, *A43*, 43.
9. Contreras, R.; Santiesteban, F.; Paz-Sandoval, M. A.; Wrackmeyer, B. *Tetrahedron* **1984**, *40*, 3829.
10. Paz-Sandoval, M. A.; Santiesteban, F.; Contreras R. *Magn. Reson. Chem.* **1985**, *23*, 428.
11. Ariza-Castolo, A.; Contreras, R. *Current Topics in the Chemistry of Boron*, volume 90; Royal Society of Chemistry, 1994.