Available online at www.sciencedirect.com
SCIENCE DIRECT
Journal of Organometallic Chemistry 691 (2006) 1993–1997
Journal of Organometallic Chemistry
www.elsevier.com/locate/jorganchem

Novel boracycles from 2-amino-2-methylpropan-1-ol and borane methyl sulfide: Synthesis and X-ray crystal structures

Ofir Baum [a], Israel Goldberg [b], Morris Srebnik [a,*]

[a] Department of Natural Products and Medicinal Chemistry, School of Pharmacy, POB 12065, Hebrew University in Jerusalem, 91120, Israel
[b] School of Chemistry, Sackler Faculty of Exact Science, Tel-Aviv University, Ramat-Aviv, Israel

Received 22 November 2005; received in revised form 15 December 2005; accepted 3 January 2006
Available online 17 February 2006

Abstract

On reacting the simple 1,2-amino alcohol: 2-amino-2-methylpropan-1-ol, with borane methyl sulfide (BMS), the expected five member oxazaborolidine ring is not obtained. Instead, two polycyclic structures with trigonal boron atoms **6** and **7** were obtained, and their structure were determined by X-ray crystallography. Compound **6** was obtained in 39% yield and compound **7** was obtained in 7% yield.

Keywords: Boranes'methyl sulfide; Oxazaborolidine; Crystal structure

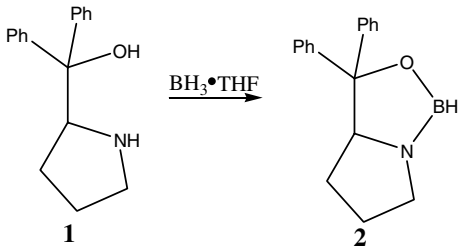
1. Introduction

1,3,2-Oxazaborolidines play an important role in organic chiral transformations. They catalyze the enantioselective reduction of prochiral ketones by borane sources, as in the well known CBS catalyst [1]. Other important applications of oxazaborolidines are the catalytic reductions of C=N bonds like ketoxime and imine [2,3]. In addition oxazaborolidines act as Lewis acid catalysts in many enantioselective reactions [2–4]. Oxazaborolidines are usually prepared by reacting an amino alcohol with borane methyl sulfide (BMS). While for the most part the corresponding oxazaborolidines are obtained, unexpected structures are sometimes encountered. As part of ongoing research in our laboratory to synthesize novel organic boron structures, we began to explore the reaction of borane methyl sulfide (BMS) with the simple 1,2-amino alcohol: 2-amino-2-methylpropan-1-ol [5–10]. There are many reports on the use and preparation of oxazaborolidines. However, due to their sensitivity to air and moisture, oxazaborolidines are usually prepared in situ without isolation and characterization. The majority of the papers that report the isolation and characterization of oxazaborolidines do so with the more stable tetragonal boron derivatives. In this regard, an early and important paper is the report of Corey on the mechanism of enantioselective catalytic reduction of prochiral ketones by borane and amino alcohols. His mechanism suggested the in situ existence of the oxazaborolidine **2**. The mechanism was corroborated by isolation of **2** and demonstrating its catalytic character (Scheme 1) [1].

Based on ^{11}B NMR, Corey also reported on the existence of a dimer (δ 28.3 ppm for the monomer and a doublet at 7.6 ppm for dimer) [1]. Corey did not isolate the dimer or suggest a structure. Nöth's group showed interest in this dimer and achieved some insight in to the associative character of oxazaborolidines. They determined the structure of the dimer **3**, by X-ray crystallography [11]. Nöth also determined the structure of the prolinol derived oxazaborolidine dimer **4**, and referred to those structures as "abnormal dimers" [11].

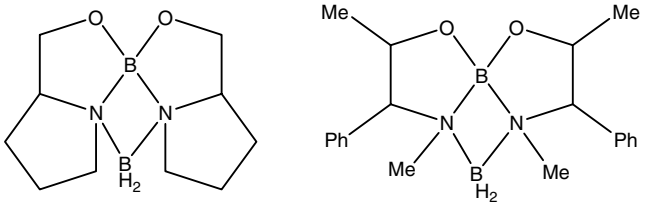
* Corresponding author. Tel.: +97226757301; fax: +97226758201.
E-mail address: msrebni@md.huji.ac.il (M. Srebnik).

0022-328X/$ - see front matter © 2006 Elsevier B.V. All rights reserved.
doi:10.1016/j.jorganchem.2006.01.003



1 2

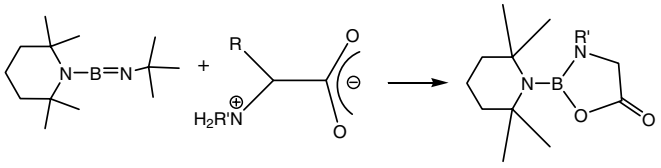
Scheme 1.



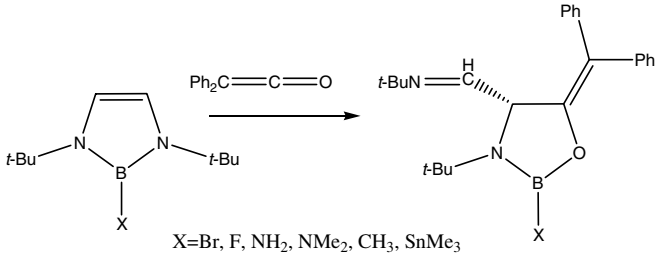
3 4

Nöth also reported the preparation of trigonal boron atoms in an oxazaborolidine ring using (*tert*-butylimino)(2,2,6,6-tetramethylpiperidino)-borane and amino acid as reactants (Scheme 2) [12].

More complex oxazaborolidines containing trigonal boron atoms were prepared by L. Weber et al. using a different method. The products have various boron substituents, such as halogens (Scheme 3) [13].



Scheme 2.



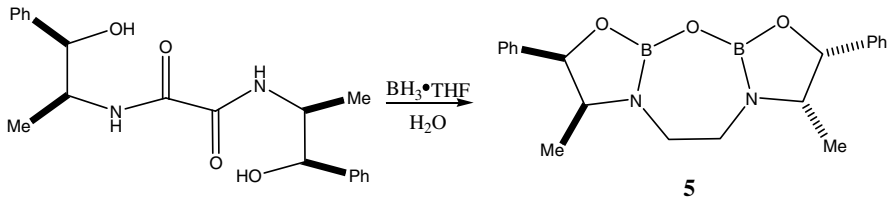
Scheme 3.

Advancement in the field of polycyclic oxazaborolidines was recently reported by E.M. Cruz et al. They used an oxalylamide derivative to produce a tri-cyclic compound **5** (Scheme 4) [14].

2. Results and discussion

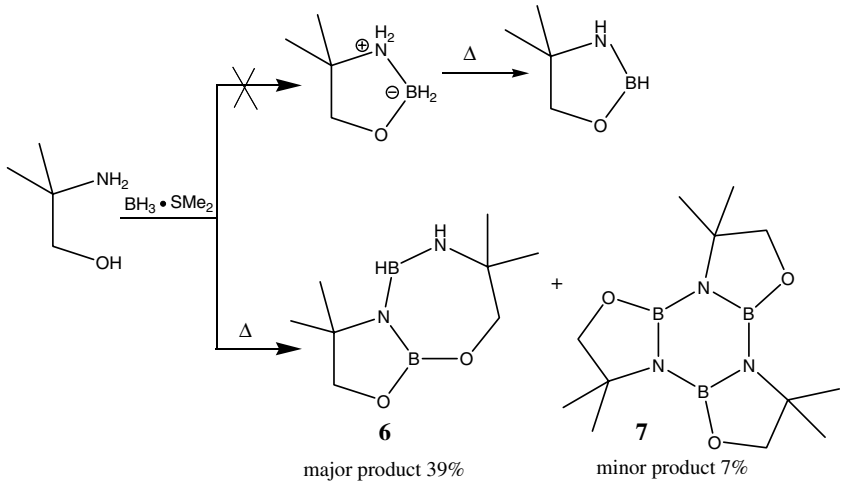
Mixing 2-amino-2-methylpropan-1-ol with borane methyl sulfide (BMS) according to the procedure reported by Corey resulted in two compounds neither of which was the expected oxazaborolidine (Scheme 5) [1]. The resulting compounds of this reaction were not in accordance even with the findings of Nöth who reported the formation of an "abnormal" dimer with a similar amino alcohol. We used 2-amino-2 methylpropan-1-ol which contains two hydrogens attached to nitrogen, as opposed to prolinol or ephedrine derivatives that contain only one hydrogen. It is apparently this additional hydrogen that leads to the products we encountered. The structures were very unusual and could only be deduced by the use of X-ray crystallography (Scheme 5).

The diffraction measurements were carried out on a Nonius KappaCCD diffractometer, using graphite monochromated Mo Kα radiation ($\lambda = 0.7107$ Å). The crystalline samples of the analyzed compounds were covered with a thin layer of light oil and freeze-cooled to ca. 110 K in order to minimize solvent escape, structural disorder and thermal motion effects, and increase the precision of the results. The crystal structures were solved by direct methods, and refined by full-matrix least squares on F^2. All non-hydrogen atoms were refined anisotropically. The hydrogen atoms were located in idealized positions, and were refined using a riding model, with $U_{iso} = 1.2$ or 1.5 U_{eq} of the parent atom. The crystal and experimental data for all the compounds are summarized in Table 1. The results represent precise determinations of the molecular structures of compounds **6** and **7**. The latter crystallized in a hexagonal $P6_3$ space group as a racemic twin. There are two molecules of **7** per unit cell, residing on trigonal rotation axes (C_3) passing through the centers of the $(BN)_3$ rings at $(0, 0, z)$ and $(0, 0, 1/2 + z)$, respectively. Thus, the crystallographically independent asymmetric unit consist of one third of this molecule (7 non-hydrogen atoms), and to the total number of refined parameters amounts to 65 (21 positional



5

Scheme 4.



Scheme 5.

Table 1
Crystal data and structure refinement for compounds **6** and **7**

Compound	**6**	**7**
Formula	$C_8H_{18}B_2N_2O_2$	$C_{12}H_{24}B_3N_3O_3$
F_w	195.86	290.76
Habit	Plates	Rods
Color	Colorless	Colorless
Temperature (K)	110(2)	110(2)
Radiation	Mo Kα	Mo Kα
Crystal size (mm)	$0.40 \times 0.25 \times 0.10$	$0.40 \times 0.15 \times 0.15$
Crystal system	Monoclinic	Hexagonal
Space group	$P2_1/c$	$P6_3$
a (Å)	9.3151 (2)	9.6781 (8)
b (Å)	15.8565 (2)	9.6781 (8)
c (Å)	7.4846 (5)	9.8218 (4)
α (°)	90.0000 (10)	90.00
β (°)	90.5830 (9)	90.00
γ (°)	90.000 (2)	120.00
V (Å^3)	1105.46 (8)	796.71 (10)
Z	4	2
D_{calcd} (g cm^{-3})	1.177	1.212
$F(000)$	424	312
μ (mm^{-1})	0.080	0.083
θ Range (°)	3.01–27.91	1.407–26.88
Number of unique reflections	2551	1024
Number of restraints	0	1
hkl Limits	−12, 12/−20, 20/−9, 0	−12, 12/−10, 10/−9, 12
Number of parameters	127	65
Number of reflections with $[I > 2\sigma(I)]$	1916	899
Final R indices $[I > 2\sigma(I)]$	0.0476	0.0696
R_1	0.1254	0.1824
wR_2 $\lvert\Delta\rho\rvert$ (e Å^{-3})	⩽0.052	⩽0.073
Goodness-of-fit	1.049	1.111

parameters, 42 anisotropic thermal displacement parameters, overall scale factor, and one twinning batch scale factor) (see Figs. 1 and 2).

Compound **6** is unique and consists of two trigonal boron atoms in a polycyclic structure. The one related

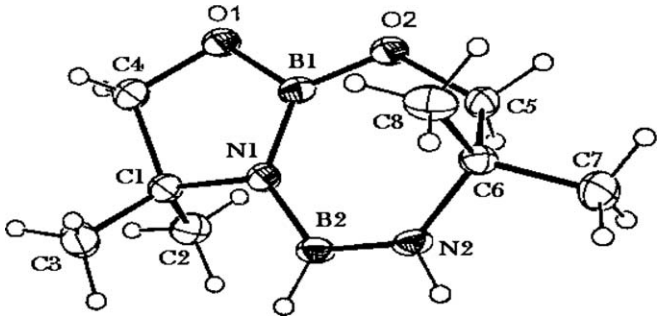


Fig. 1. Molecular structure of compound **6**. Ellipsoids represent thermal displacement parameters at the 50% probability level. The selected bond distances (Å) and angles (°) are: O1–B1 = 1.3866 (18), O2–B1 = 1.3569 (19), B1–N1 = 1.4264 (19), N1–B2 = 1.4323 (19), N2–B2 = 1.395 (2), B1–O1–C4 = 106.93 (11), B1–O2–C5 = 121.10 (11), B1–N1–B2 = 130.11 (12), B1–N1–C1 = 106.84 (12), B2–N1–C1 = 122.82 (12), B2–N2–C6 = 129.67 (11).

structure is the tricyclic structure, reported by E.M. Cruz et al. containing one trigonal boron flanked by two oxygen atoms and nitrogen [14]. Compound **6** bears the functional group of oxazaborolidine: a borane adjacent to an amine thus enables compound **6** to serve as a more complexed oxazaborolidine catalyst. This group creates a possibility for chemical activity, thus making compound **6** interesting.

Compound **7** belongs to the family of borazines [15]. The structure of this family is a six member ring of alternate boron and nitrogen atoms. Due to resonance of double bonds between nitrogen and boron, it is considered as the inorganic counterpart of benzene [15,16]. Borazines were studied intensively in the 1960s, but the interest subsided over the years. Researchers hoped that the resemblance in structure of borazines to benzene would lead to different electronic and chemical character from other borane derivatives, as benzene is different from alkanes. But it was established that the resonance of borazines is not at all as dramatic as in carbon chemistry [16]. Current interest in borazines is primarily in the fields of inorganic

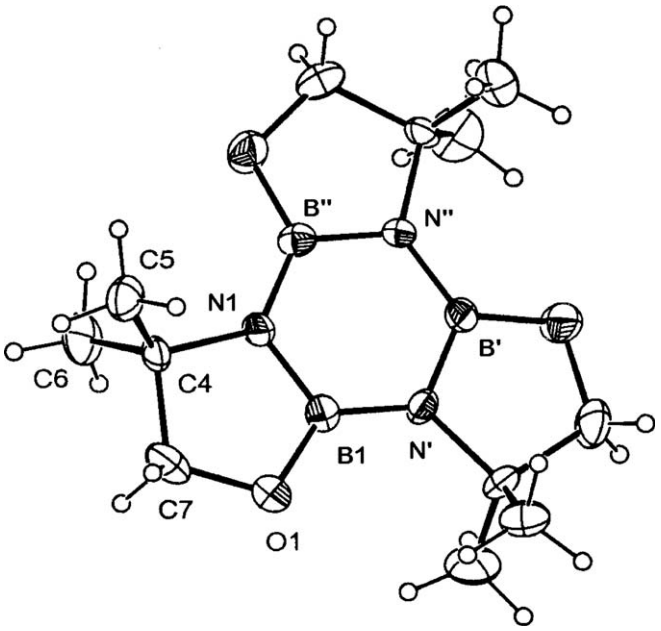


Fig. 2. Molecular structure of compound **7**. The molecule resides in the crystal on an axis of threefold rotation (C3), which passes through the center of the central six-membered ring. Atoms B′ and B″, as well as N′ and N″, are symmetry related to N1 and B1, respectively. Ellipsoids represent thermal displacement parameters at the 50% probability level. The selected bond distances (Å) and angles (°) are: O1–B1 = 1.384 (4), B1–N1 = 1.407 (4), B1–N2 = 1.442 (4), O1–C4 = 1.476 (4), N1–C1 = 1.486(3), C1–C4 = 1.564 (4), N1–B1–N2 = 120.2 (3), B1–N1–B2 = 119.8 (3), B1–N1–C1 = 129.6 (6), B1–O1–C4 = 107.9 (3).

chemistry and ceramics [16,17]. Compound **7** is very elegant molecule with a planar internal ring and a C_3 symmetry as determined from the crystallographic data. Attempts to use this compound in further applications failed due to low reactivity. A recent paper, surprising in its similarity, on obtaining borazines from a series of amino alcohols and borane by pyrolysis, was reported by Stepanenko et al. [18]. The report includes findings of low chemical reactivity of one sample in accordance with the findings reported herein.

The ^{11}B NMR spectra of other reported compounds are consisted with structures we obtained. Nöth et al. reported on boron chemical shifts of −10 and 14 ppm for tetragonal borons, and Corey et al. reported a chemical shift of 28.1 PPM for trigonal borons substituted with H, N and O atoms, in an oxazaborolidine [1,11]. The boron chemical shift of compound **6** is at 25.1 ppm and is in upfield in comparison to compound **7** (27.8 ppm) due to the partial benzene like resonance of borazines. The ^{11}B NMR of **6** shows a broad singlet with a small shoulder, due to a singlet of one boron overlapping doublet of the second boron.

3. Conclusions

This paper describes the reaction of 2-amino-2-methylpropan-1-ol with BMS. Two compounds were characterized by single crystal X-ray crystallography: a borazine **7** in low yield, and a major product, **6**, that contains a novel bicyclic structure that consists of two trigonal boron atoms. We presume that the structures are formed because the amino alcohol is a primary amine as compared to prolinol or ephedrine that are secondary amines. This enables the amino group in our study to create two bonds.

4. Experimental

^{1}H, ^{13}C and ^{11}B NMR spectra were obtained in $CDCl_3$ solution in 298 K with Me_4Si as an internal standard on a Varian unity spectrometer. Melting points were measured on a Fisher scientific melting point apparatus. All glassware was heated to 150 °C for half hour, flashed with nitrogen and assembled while hot. Solvents were distilled over sodium and benzophenone. Reactions were carried out in an inert atmosphere using glove box techniques.

*Preparation of **6** and 7*. 4.9 ml of 2-amino-2-methylpropan-1-ol were dissolved in 5 ml of THF and added with a dropping funnel, over half hour, to a solution of 5 ml of borane methyl sulfide (BMS) 10 M (50 mmol) in 5 ml of THF, that was placed in an ice bath. Hazard: evolution of hydrogen gas. The solution was then dried with vacuum resulting in a white solid. The solid was placed in an oil bath at 100 °C until liquidation of the solid, after considerable evolution of gas; (hazard: hydrogen gas). After cooling the liquid to room temperature it solidified. Adding 10 ml of pentane with tender warming the solid is dissolved and living the solution to cool to 25 °C. Cooling the solution to 0 °C for a period of 2 h gives crystals. Decanting the solution washing the crystals with 5 ml of cold pentane gives 2.20 g of **6**, yield of 39%. Drying the solute, again with vacuum giving solid residue, adding 5 ml of THF and leaving the solution for 14 days at 25 °C gives crystals of **7** 0.37 g, yield of 7%. The residue that contains the remaining of the reaction mixture is liquid with multiple unresolved ^{11}B NMR peaks, and was discarded.

*Compound **6***. ^{1}H NMR (300 MHz, $CDCl_3$, 298 K): δ ppm = 1.121 (s, 6H); 1.224 (s, 6H); 3.55 (broad s, 1H); 3.700 (s, 2H); 3.816 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, 298 K): δ ppm = 27.699 (s, 2C); 29.969 (s, 1C); 53.554 (s, 1C); 58.867 (s, 1C); 75.575 (s, 1C); 78.824 (s, 1C); ^{11}B NMR (96 MHz, $CDCl_3$, 298 K): δ ppm = 25.097 (broad m, 2B). Melting point 99 °C.

Compound 7. ^{1}H NMR (300 MHz, $CDCl_3$, 298 K): δ ppm = 1.2593 (s, 18H); 3.916 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, 298 K): δ ppm = 29.080 (s, 6C); 56.415 (s, 3C); 81.663 (s, 3C); ^{11}B NMR (96 MHz, $CDCl_3$, 298 K) δ ppm = 28.792 (broad s, 3B). Melting point 139 °C.

Acknowledgments

This research was supported in part by the Alex Grass Center for Drug Design and Synthesis of Novel Therapeutics, and by David R. Bloom Center of Pharmacy. O.B. thanks the Hebrew University of Jerusalem for the fellowships.

Appendix A. Supplementary data

CCDC 292053 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jorganchem.2006.01.003.

References

[1] E.J. Corey, R.K. Bakshi, S. Shibata, J. Am. Chem. Soc. 109 (1987) 5551–5552.
[2] L. Deloux, M. Srebnik, Chem. Rev. 93 (1993) 763–784.
[3] O. Baum, M. Srebnik, e-EROS (2006) in press.
[4] S. Wallbaum, J. Martens, Tetrahedron: Asymm. 3 (1992) 475–504.
[5] A. Shibli, H. Abu Ali, I. Goldberg, M. Srebnik, J. Organomet. Chem. 690 (2005) 2180–2185.
[6] K. Takrouri, E. Shalom, I. Goldberg, J. Katzhendler, M. Srebnik, J. Organomet. Chem. 690 (2005) 4150–4158.
[7] R. Smoum, A. Rubinstein, M. Srebnik, Org. Biomol. Chem. 3 (2005) 941–944.
[8] A. Shibli, H. Abu Ali, I. Goldberg, M. Srebnik, Appl. Organomet. Chem. 19 (2005) 171–172.
[9] A. Jabbour, D. Steinberg, V. Dembitsky, A. Moussaieff, B. Zaks, M. Srebnik, J. Med. Chem. 47 (2004) 2409–2410.
[10] H. Abu Ali, A.A. Al Quntar, I. Goldberg, M. Srebnik, Organometallics 21 (2002) 4533–4539.
[11] A. Lang, H. Nöth, M. Schidt, Chem. Ber. 130 (1997) 241–246.
[12] G. Geisberger, H. Nöth, Chem. Ber. 123 (1990) 953–961.
[13] L. Weber, M. Schnieder, T.C. Maciel, H.B. Wartig, M. Schimmel, Organometallics 19 (2000) 5791–5794.
[14] M. Tlahuextl, A.R. Tapia-Benevides, A. Flores-Parra, R. Contreras, H. Tlahuext, E.M. Cruz, Heteroatom Chem. 16 (2005) 513–519.
[15] H. Steinberg, R.J. Brotherton, Organoboron Chemistry, Wiley-Interscience, New York, 1966 (Chapter 8).
[16] A.J. Bridgeman, Polyhedron 17 (1998) 2279–2288.
[17] E. Framery, M. Vaultier, Heteroatom Chem. 11 (2000) 218–225.
[18] V. Stepanenko, M. Ortiz-Marciales, Abstracts of Papers, 230th ACS National Meeting, Washington, DC, United States, August 28–September 1, 2005 ORGN-689.