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NEW BORON HETEROPENTACYCLIC COMPOUNDS OF C_2 SYMETRY BEARING TWO CHIRAL ATOMS: NITROGEN AND BORON

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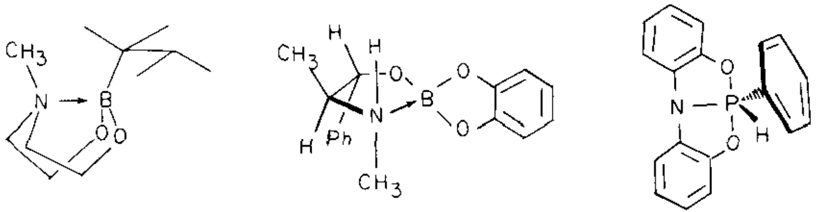
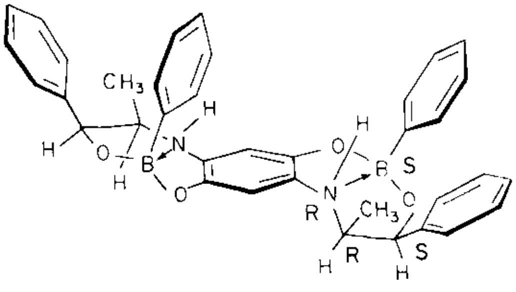
Abstract – The preparation and spectroscopic characterization of two new boron heteropentacyclic compounds derived from 2,5-diaminohydroquinone ephedrines is described. Although the nitrogen boron coordination affords four new chiral centers, stereoselective ring closure proceeds to give only one isomer.

We are interested in the syntheses of boron and phosphorus heterocyclic compounds such as the ones depicted in scheme 1[1-3]. These atoms, contrary to the carbon atoms, are capable of bonding to several electronegative atoms affording interesting heterocyclic structures.



SCHEME 1

In the present communication we report the synthesis of two pentacyclic compounds 1 and 2 of C_2 symmetry, in which the boron and nitrogen atoms are chiral. The synthesis is stereoselective and affords only one isomer in each case.



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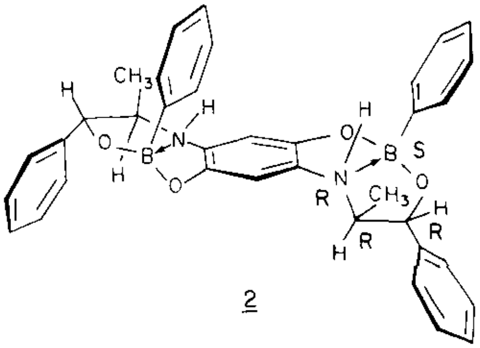

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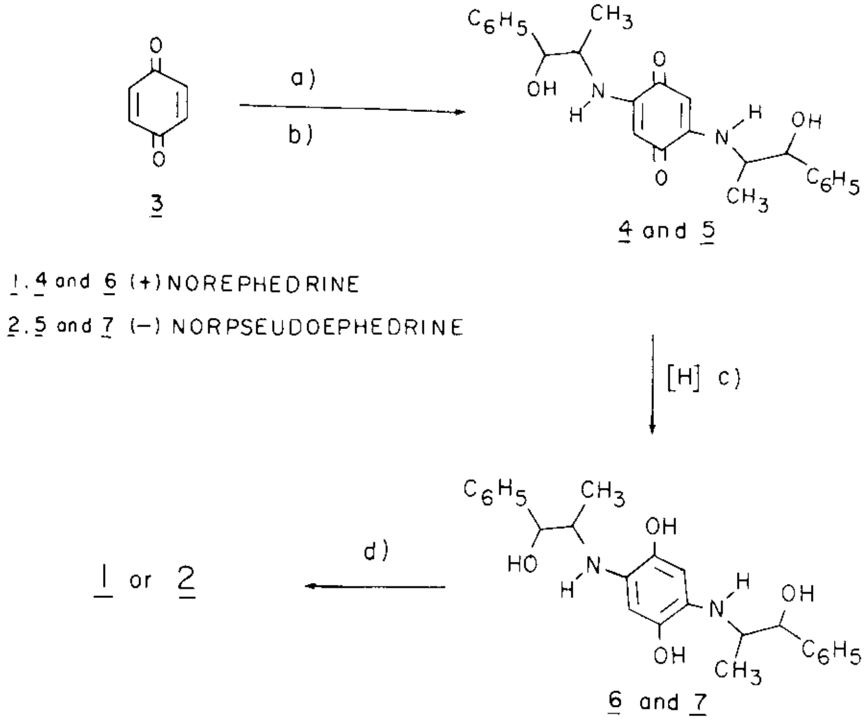
Compounds 1 and 2 were prepared according to scheme 2.



Scheme 2

a) Boric ester of (+)-norephedrine or (-)-norpseudoephedrine in ethanol at room temperature, 24 h.[4]

b) Hydrolysis by water, the reaction mixture was chromatographed on silica gel.

c) [10% Pd/C] and H_2 at atmospheric pressure in ethylacetate.

d) Phenylboronic acid in ethyl acetate, by azeotropic distillation of water.

Scheme 2

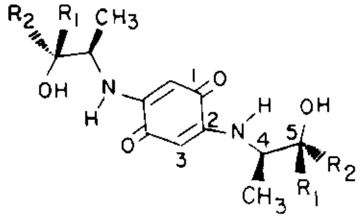
Compound 4 was a red crystalline compound, mp 193-195°C. IR (KBr) $\nu_{C=O}$ 1563; $\nu_{N-H;OH}$ 3300 cm^{-1}. Mass spectrum: M^{+} 406.4 (0.5); 193.2 (100); 79.2 (54.5); 77.2 (43.4); 177.2 (32.4); 300.3 (18.0). For NMR see tables.

Compound 5 was a pink powder, mp 186-188°C. IR (KBr) $\nu_{C=O}$ 1566; $\nu_{NH,OH}$ 3330, 3263 cm^{-1}. Mass spectrum: M^{+} 406.2 (1.1); 193.2 (100); 300.1 (33.8); 79.1 (30.0); 77.1 (27.8). For NMR see tables.

Compound 1 was a colourless compound, mp 243-245°C. IR (KBr) $\nu_{B\to N}$ 1100 cm^{-1}. For NMR see tables.

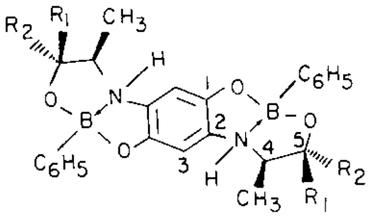
Compound 2 was a colourless compound, mp 207-210°C. For NMR see tables.

TABLE ^{13}C, ^{1}H and ^{11}B NMR DATA



4 $R_1 = C_6H_5$ $R_2 = H$

5 $R_1 = H$ $R_2 = C_6H_5$



1 $R_1 = C_6H_5$ $R_2 = H$

2 $R_1 = H$ $R_2 = C_6H_5$

^{13}C NMR VALUES

COMPOUND	(atom number)	1	2	3	4	5	CH_3		C-C_6H_5		
								ipso	orto	meta	para
1	(Acetone-d_6)	134.9	130.9	107.4	67.2	77.0	14.4	140.7	126.8	127.9[a]	127.8[a]
									B-C_6H_5		
								c	133.4	128.9[a]	128.2[a]
									C-C_6H_5		
2	(DMSO-d_6)	133.9	129.7	106.2	65.2	75.7	13.5	139.5	125.7	127.0[b]	127.2[b]
									B-C_6H_5		
								143.2	132.4	128[b]	127.8[b]
									C-C_6H_5		
4	(Acetone-d_6)	177.1	149.6	92.2	52.9	73.0	13.4	142.1	126.1	127.7	126.9
									C-C_6H_5		
5	(Acetone-d_6)	178.8	151.8	93.2	55.0	75.6	17.4	143.6	127.3	129.2	128.5

^{1}H-NMR VALUES

		N-H	3	4	5	CH_3	Aromatic Protons
1	(Acetone-d_6)	-	7.02s	4.00d,d (J=4,6 Hz)	4.35d (J=4 Hz)	1.05d (J=6 Hz)	7.20-7.80
1	(DMSO-d_6)	8.70 broad signal	6.95s	3.90m	5.20d (J=4 Hz)	0.95d (J=6 Hz)	7.20-7.80
2	(DMSO-d_6)	9.00d (6 Hz)[d]	6.90s	3.40m	4.58d (J=9 Hz)	1.10d (J=6 Hz)	7.10-7.75
4	(Acetone-d_6)	7.00d (J=8 Hz)[d]	5.33s	4.95	5.00	1.05d (J=6 Hz)	7.30-7.62
5	(Acetone-d_6)	7.00d (J=9 Hz)[d]	5.25s	3.72m	4.90d (J=4 Hz)	1.38d (J=6 Hz)	7.25-7.60

^{11}B NMR VALUES

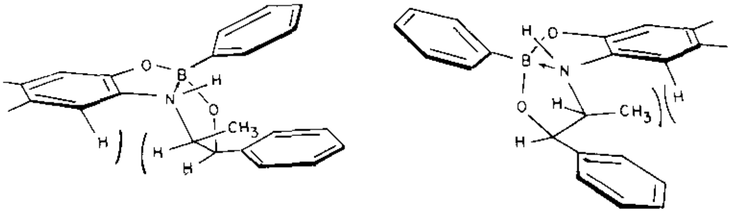
1	(THF)	+12.7 ppm
2	(THF)	+12.1 ppm

a) and b) Assignments may be interchanged. c) Not observed. d) Coupled with C_4-H.

Structures 1 and 2 are proposed based on spectroscopic measurements. In ^{11}B NMR, compounds 1 and 2 give an absorption near +12 ppm characteristic of a coordinated boronic ester [1-2]. In ^{1}H NMR, the C_3 aromatic hydrogen gives rise to a singlet near 7 ppm, the N-H appears at 8.7 ppm for 1 and at 9.0 ppm for 2, the latter signal shows coupling with C_4-H. In ^{13}C NMR, C_3 shows chemical shifts of 106.2 and 107.4 ppm for 1 and 2 respectively, that agree with calculated values based on substituent effects[5]. An infrared absorption at ν= 1100 cm^{-1} shows a N→B bond. All this information allows us to propose the bicylic structure produced by a B←N coordination.

The stereochemical analysis indicates that two isomers are possible for each compound, these differ on the B and N configurations as well as the position of ephedrine substituents, which could be exo or endo relative to the dihedral angle of the two five member ring cycles. Surprisingly, only one isomer was observed in each case.

Observation of the Dreiding stereomodels shows that of the two possible isomers for each compound, the one that has a C-methyl in position exo should show no steric compression due to the fact that it is adjacent to a N-H. On the other hand the isomer that has the C-methyl in position endo should exhibit this compression caused by in space proximity of this group to the C_2 and C_3 of the central aromatic ring, see figure 1.



C-methyl exo

C-methyl endo

FIGURE 1

Moreover, since in ^{13}C NMR a similar chemical shift is observed for the C-methyl of 1 and 2 (δ= 14.4 and 13.5 ppm) we can assume that for the two structures the C-methyls have the same environment.

It has been described in related cyclic compounds[2] (figure 2) that the ephedrinic C-Me group shows distinct chemical shifts depending on whether they are adjacent to a proton or a methyl group.

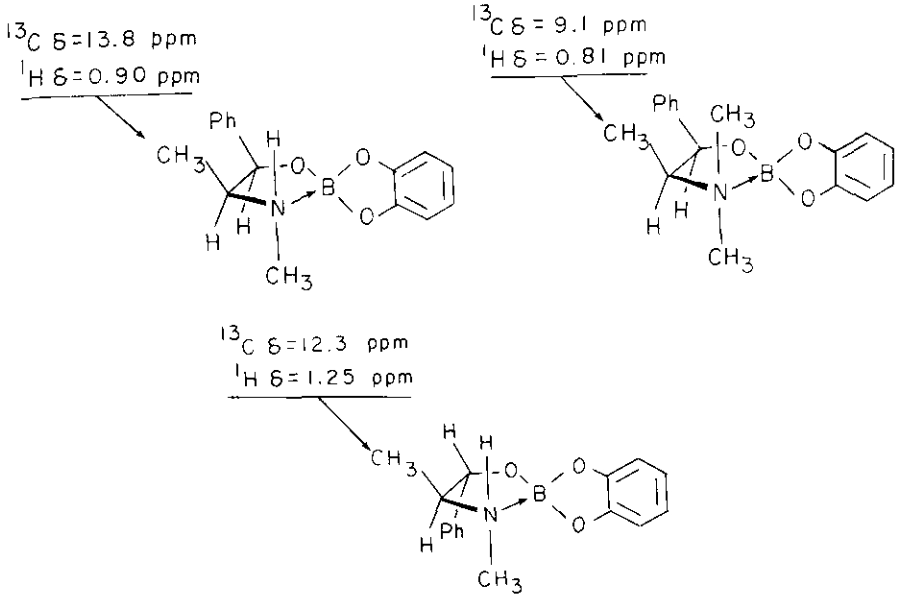


FIGURE 2 (reference 2)

Futhermore, it was observed that steric compression originated by the presence of the N-methyl shifts the C_4-methyl signal to high field[2]. Comparison of the δ of C_4 methyls in 1 and 2 with the model compounds[2] allows us to propose the structures with a C-methyl exo for each isomer. In ^{1}H NMR the C_4-methyl groups show δ= 0.95 and 1.10 ppm for 1 and 2 which are very close to the values of compounds in figure 2, thus suggesting that a shielding effect of the aromatic central ring is absent.

ACKNOWLEDGMENT

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