

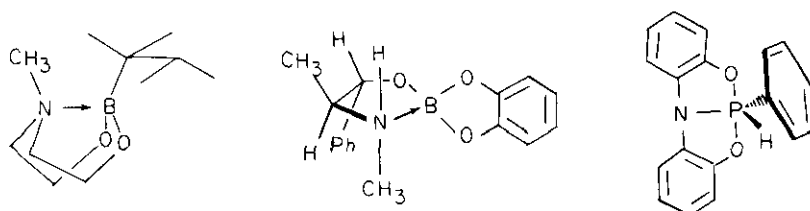
NEW BORON HETEROPENTACYCLIC COMPOUNDS OF  $C_2$  SYMETRY BEARING TWO CHIRAL ATOMS: NITROGEN AND BORON

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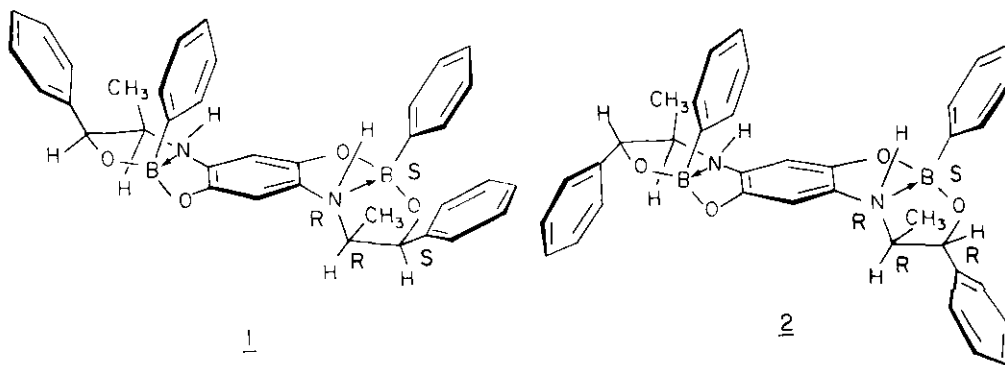
Abstract - The preparation and spectroscopic characterization of two new boron heteropentacyclic compounds derived from 2,5-diaminoquinone ephedrine is described. Although the nitrogen boron coordination affords four new chiral centers, stereoselective ring closure proceeds to give only one isomer.

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

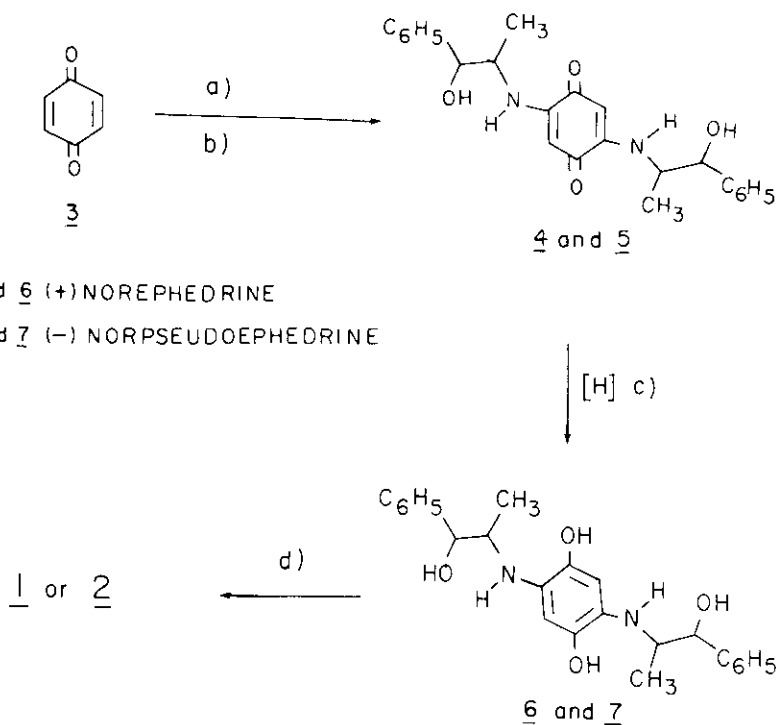


SCHEME 1

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.



Compounds 1 and 2 were prepared according to scheme 2.



1, 4 and 6 (+) NOREPHEDRINE

2, 5 and 7 (-) NORPSEUDOEPHEDRINE

Scheme 2

a) Boric ester of (+)-norephedrine or (-)-norpseudoephedrine in ethanol at room temperature, 24 h.<sup>4</sup>

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

c) [10% Pd/C] and H<sub>2</sub> at atmospheric pressure in ethylacetate.

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

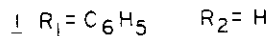
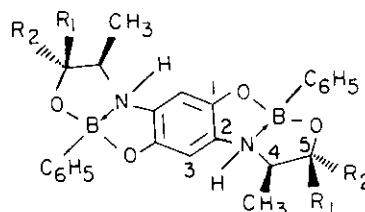
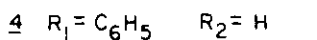
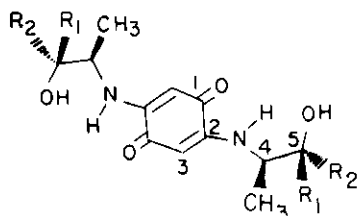
Scheme 2

Compound 4 was a red crystalline compound, mp 193-195°C. IR (KBr)  $\nu_{\text{C=O}}$  1563;  $\nu_{\text{N-H;OH}}$  3300 cm<sup>-1</sup>. Mass spectrum: M<sup>+</sup> 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)  $\nu_{\text{C=O}}$  1566;  $\nu_{\text{NH,OH}}$  3330, 3263 cm<sup>-1</sup>. Mass spectrum: M<sup>+</sup> 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)  $\nu_{\text{B}\rightarrow\text{N}}$  1100 cm<sup>-1</sup>. For NMR see tables.

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

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

 $^{13}\text{C}$  NMR VALUES

COMPOUND	(atom number)	1	2	3	4	5	CH <sub>3</sub>	C-C <sub>6</sub> H <sub>5</sub>					
								ipso	ortho	meta	para		
<u>1</u>	(Acetone-d <sub>6</sub> )	134.9	130.9	107.4	67.2	77.0	14.4	140.7	126.8	127.9 <sup>a</sup>	127.8 <sup>a</sup>		
<u>2</u>	(DMSO-d <sub>6</sub> )	133.9	129.7	106.2	65.2	75.7	13.5	139.5	125.7	127.0 <sup>b</sup>	127.2 <sup>b</sup>		
<u>4</u>	(Acetone-d <sub>6</sub> )	177.1	149.6	92.2	52.9	73.0	13.4	142.1	126.1	127.7	126.9		
<u>5</u>	(Acetone-d <sub>6</sub> )	178.8	151.8	93.2	55.0	75.6	17.4	143.6	127.3	129.2	128.5		

 $^1\text{H}$ -NMR VALUES

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

 $^{11}\text{B}$  NMR VALUES

<u>1</u>	(THF)	+12.7 ppm
<u>2</u>	(THF)	+12.1 ppm

a) and b) Assignments may be interchanged. c) Not observed. d) Coupled with C<sub>4</sub>-H.

Structures 1 and 2 are proposed based on spectroscopic measurements. In  $^{11}\text{B}$  NMR, compounds 1 and 2 give an absorption near +12 ppm characteristic of a coordinated boronic ester <sup>1-2</sup>. In  $^1\text{H}$  NMR, the  $\text{C}_3$  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  $\text{C}_4$ -H. In  $^{13}\text{C}$  NMR,  $\text{C}_3$  shows chemical shifts of 106.2 and 107.4 ppm for 1 and 2 respectively, that agree with calculated values based on substituent effects<sup>5</sup>. An infrared absorption at  $\nu = 1100\text{ cm}^{-1}$  shows a N $\rightarrow$ B bond. All this information allows us to propose the bicyclic structure produced by a B $\leftarrow$ 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 epinephrine 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  $\text{C}_2$  and  $\text{C}_3$  of the central aromatic ring, see figure 1.

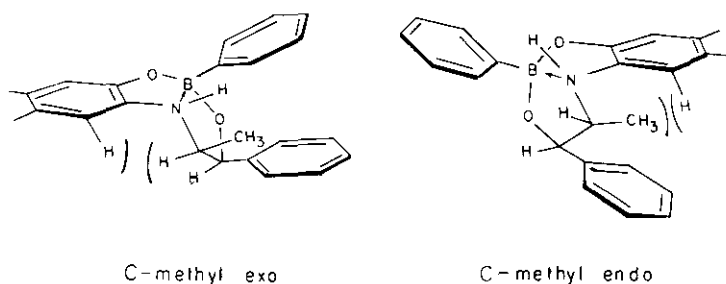


FIGURE 1

Moreover, since in  $^{13}\text{C}$  NMR a similar chemical shift is observed for the C-methyl of 1 and 2 ( $\delta = 14.4$  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<sup>2</sup> (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.

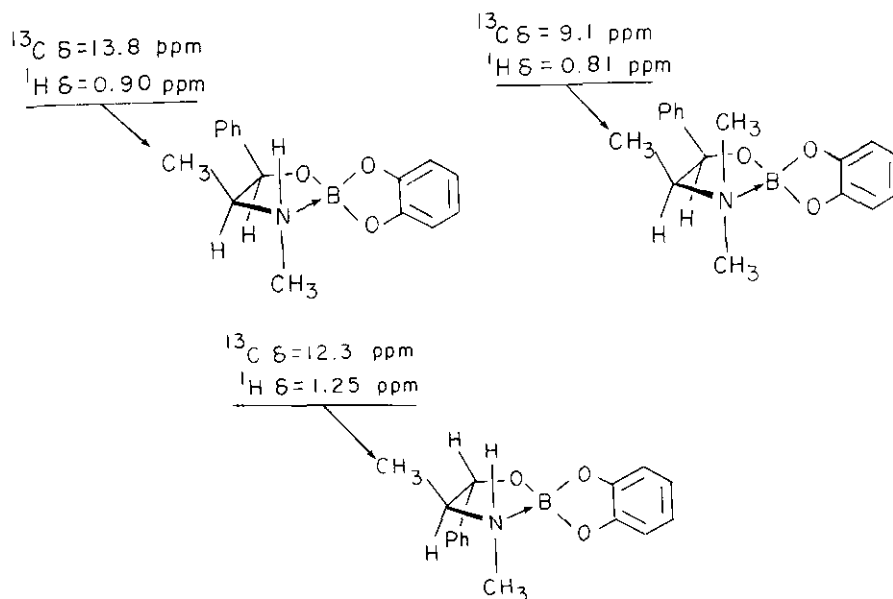


FIGURE 2 (reference 2)

Furthermore, it was observed that steric compression originated by the presence of the N-methyl shifts the C<sub>4</sub>-methyl signal to high field<sup>2</sup>. Comparison of the δ of C<sub>4</sub> methyls in 1 and 2 with the model compounds<sup>2</sup> allows us to propose the structures with a C-methyl exo for each isomer. In <sup>1</sup>H NMR the C<sub>4</sub>-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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