

A New Synthesis of Polyheterocyclic Compounds Containing Nitrogen and Boron Atoms [†]

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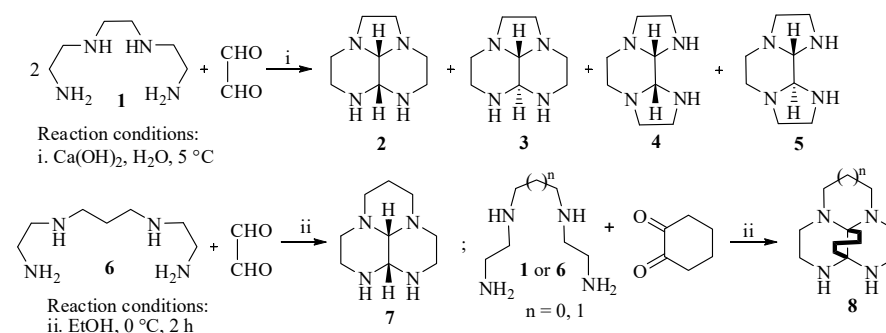
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Abstract: Tetraazatricyclanes containing two boron atoms in the molecular framework were synthesized for the first time via the heterocyclization reaction of tetraamines with tetrakis(dimethylamino)diborane. Tetrakis(dimethylamino)diborane is a new starting reagent in the synthesis of polyheterocyclic compounds that may be of interest as cytotoxic agents.

Keywords: heterocyclization; polyamines; tetrakis(dimethylamino)diborane; polyheterocyclic compounds

1. Introduction

Organic nitrogen compounds occupy a special place among synthetic substances. The number of new heterocyclic compounds containing nitrogen atoms and possessing pharmacological properties [1] is constantly growing. Earlier, refs. [2,3] it was shown that the condensation of triethylenetetramine **1** with glyoxal under optimal conditions (H₂O, 5 °C) in the presence of Ca(OH)₂ (Scheme 1) leads to the preparation of different tetraazatricyclanes, namely *cis/trans*-octahydrodiazaphthalenes **2**, **3** and *cis/trans*-decahydrodiimidazopyrazines **4**, **5**. Replacing the solvent and increasing the reaction temperature affect the ratio and yield of the resulting tricyclanes [4–6]. *N,N'*-bis(aminoethyl)propane-1,3-diamine **6** can be used as another linear tetramine [7]. As a result, the condensation of tetramine **6** with glyoxal (EtOH, 0 °C) allows one to obtain tetraazatricyclane **7**. Non-trivial framework *bis*-aminals **8** were synthesized using the electrophilic agent cyclohexane-1,2-dione [8] (Scheme 1).



Scheme 1. Condensation of polyamines with dialdehyde [2–7] and diketone [8] in the synthesis of tetraazatricyclanes.

The inclusion of boron in the molecular framework of azapolycycles is of undoubted interest. Tetraamino-substituted diborane compounds are important in diborane chemistry. It is worth highlighting the tetrakis(dimethylamino)diborane B₂(NMe₂)₄ **9**, which is used as the synthetic precursor to most other derivatives. It has been demonstrated [9,10] that



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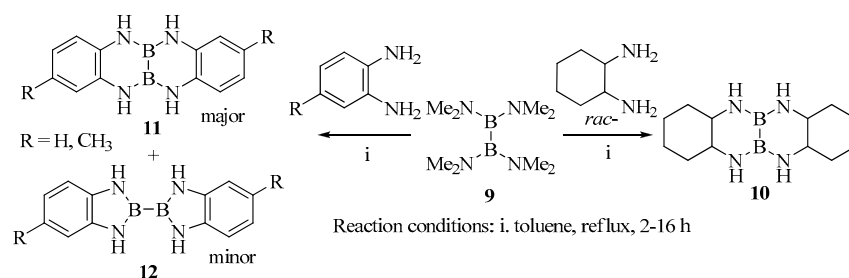
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that reaction of $B_2(NMe_2)_4$ with 1,2-diamines yields different products **10–12** depending on the diamine employed (Scheme 2).

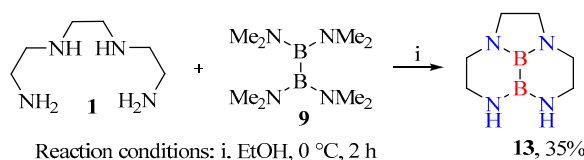


Scheme 2. Reaction of 1,2-diamines [9,10] with tetrakis(dimethylamino)diborane.

As far as we know, there are no data about the involvement of polyamines in the heterocyclization reaction with (dimethylamino)diborane in the scientific literature. In this regard, the goal of this work was to study the possibility of using (dimethylamino)diborane as a key reagent in the synthesis of tetraazatricyclanes containing boron atoms in the molecular framework.

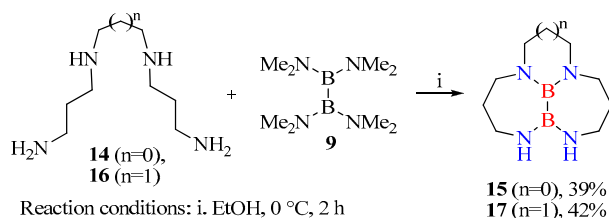
2. Results and Discussion

With preliminary experiments, we established that the interaction of triethylenetetraamine **1** with tetrakis(dimethylamino)diborane **9** in a molar ratio of 1:1 under reaction conditions (EtOH, 0 °C, 2 h) leads to the selective formation of hexahydro-3*H*,6*H*-2*a*,5,6,8*a*-tetraaza-5*a*,8*b*-diboracacenaphthylene **13** in 35% yield, the molecule of which is a 6/5/6 tricyclic system (Scheme 3).



Scheme 3. Synthesis of perhydro tetraazadiboracacenaphthylene.

The application of other linear polyamines, namely 1,2-bis(3-aminopropylamino)ethane **14** and *N,N'*-bis(3-aminopropyl)-1,3-propanediamine **16**, in such a reaction under the optimal conditions gave previously unknown analogous products—decahydro-2*a*,6,7,10*a*-tetraaza-6*a*,10*b*-diboracyclopenta[*ef*]heptalene **15** and decahydro-1*H*-3*a*,7,8,11*a*-tetraaza-7*a*,11*b*-diborabenz[*ef*]heptalene **17**, respectively, in 39–42% yields (Scheme 4).



Scheme 4. Heterocyclization of polyamines with tetrakis(dimethylamino)diborane.

3. Conclusions

Thus, in the present study we have demonstrated that the intermolecular heterocyclization of polyamines with tetrakis(dimethylamino)diborane provides for the synthesis of novel diboron-containing tetraazatricyclanes. The obtained compounds may be of interest as precursors in the further synthesis of functionally-substituted tetracyclanes, which have potential cytotoxic and antitumor activity [11–13].

4. Experimental Part

The ^1H and ^{13}C NMR spectra, including two-dimensional homo- (COSY) and heteronuclear (HSQC, HMBC) spectra, were recorded using a Bruker Avance 500 spectrometer (500.17 MHz for ^1H and 125.78 MHz for ^{13}C) according to standard Bruker protocols, using DMSO- d_6 as solvent and TMS as internal standard. Commercially available reagents used in this work were purchased from Sigma–Aldrich (St. Louis, MO, USA) and Acros Organics (Geel, Belgium).

Heterocyclization of polyamines with tetrakis(dimethylamino)diborane (general procedure). A round-bottom flask mounted on a magnetic stirrer was charged with a solution of corresponding polyamine (2.00 mmol) in 5 mL of ethanol and was cooled in an ice bath at 0 °C, then tetrakis(dimethylamino)diborane (2.00 mmol) in 5 mL of ethanol was added. The mixture was stirred at 0 °C for 2 h and was left in the cold for 12 h. The resulting precipitate was filtered off. Pure compounds **13**, **15**, **17** were thus isolated as white powders.

Hexahydro-3H,6H-2a,5,6,8a-tetraaza-5a,8b-diboraacenaphthylene (13): Yield 35%. ^1H NMR: δ 2.53–2.59 (m, 8H), 2.62–2.65 (m, 4H). ^{13}C NMR spectrum: δ 41.0, 49.0, 51.1. $^{11}\text{B}\{^1\text{H}\}$ NMR: δ 1.40 (br. s).

Decahydro-2a,6,7,10a-tetraaza-6a,10b-diboracyclopenta[ef]heptalene (15): Yield 39%. ^1H NMR: δ 2.43–2.47 (m, 4H), 2.54–2.59 (m, 8H), 2.64–2.69 (m, 4H). ^{13}C NMR spectrum: δ 35.7, 46.5, 46.9, 50.2.

Decahydro-1H-3a,7,8,11a-tetraaza-7a,11b-diborabenzof[ef]heptalene (17): Yield 42%. ^1H NMR: δ 2.15–2.19 (m, 2H), 2.47–2.51 (m, 4H), 2.57–2.63 (m, 8H), 2.66–2.69 (m, 4H). ^{13}C NMR spectrum: δ 28.2, 32.4, 45.2, 45.7, 49.5.

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Conflicts of Interest: The authors declare no conflict of interest.

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