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Design of Bicyclic and Cage Boron Compounds Based on Allylboration of Acetylenes with Allyldichloroboranes

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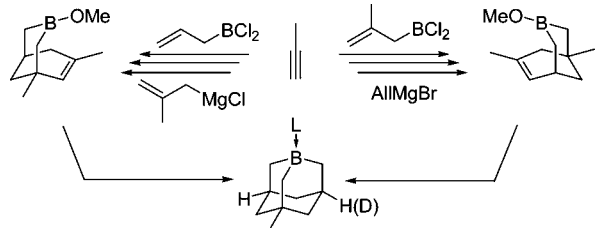
ABSTRACT



Allylboration of acetylenes with allyldichloroboranes has been proposed as a first step of allylboron−acetylene condensation and a way to design condensation products from stage to stage. The chemistry has been applied to the synthesis of isomeric 3-borabicyclo[3.3.1]non-6-enes transformed into 3-methyl-1-boraadamantane and [5-D]-3-methyl-1-boraadamantane derivatives.

The allylboron−acetylene condensation (ABAC)−thermal regio- and stereospecific reaction of triallyl- and trimethallylborane with terminal acetylenes presents an efficient approach to 7-substituted 3-borabicyclo[3.3.1]non-6-enes (3-BBN) and 1-boraadamantane derivatives[1] including optically active forms.[2] Organoboranes of these types were applied as precursors for various compounds, such as cyclohexene derivatives, bicyclic carbo- and heterocycles,[1,3] 1-adamantanols,[1] 1-azaadamantanes,[4] 1-borahomoadamantanes,[5] and 1-adamantylboronates,[1,2b,6] that are difficult to access by classical synthetic methods. Polyhomologation of 1-boraadamantane was used in the synthesis of polymethylene poly-

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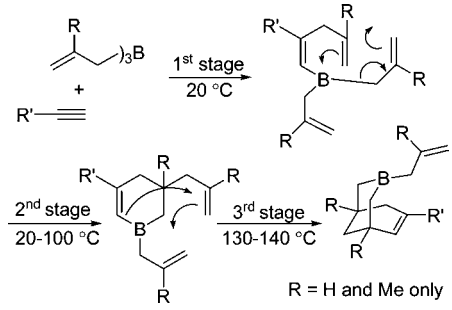
mers.[7] Complexes of 1-boraadamantanes were found to possess antiviral[8] and antihepatitis C activity.[9]

The general character of ABAC is not limited by the availability of hydrocarbon precursors, and a number of different acetylene derivatives were utilized in this reaction.[1,3,10] On the other hand, modification of the allylborane component is quite nontrivial. Classical variants of the condensation make it possible to synthesize only 7-substituted 1,5-H- and 1,5-dimethyl-3-borabicyclo[3.3.1]non-6-enes (when triallyl- or trimethallylborane are used, Scheme 1).

Scheme 1. Classical Allylboron−acetylene Condensation

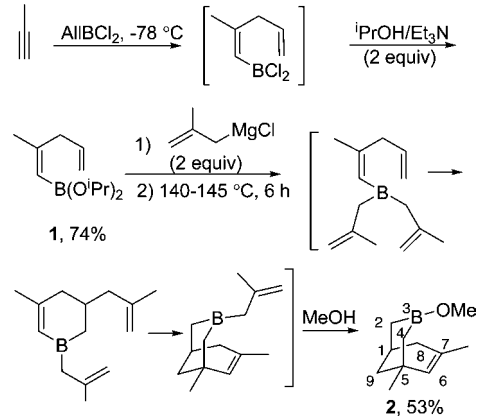


The condensation was found to proceed in three consecutive stages shown in Scheme 1 (temperature ranges are given for R′ = Alk).

Our idea was to apply a consecutive procedure, wherein two different allylic groups could be introduced in a molecule separately. Obviously, allylic borane used at the first stage must be able to allylborate C−C triple bond and bear two functional groups at the boron atom. The reagents of choice for this purpose seemed to be highly electrophilic allyldihaloboranes, capable for allylboration of not only activated multiple bonds[11] but also allenes,[12] acetylenes,[13,14a] and even simple alkenes[13,14] as well.

The starting allyldichloro- and methallyldichloroboranes were generated in situ by the redistribution reaction of triallyl- or trimethallylborane with BCl_3.[12,13] Allylboration of propyne with $AllBCl_2$ readily proceeds under mild conditions (−78 °C). The penta-1,4-dienyldichloroborane formed initially was detected and characterized by ^1H, ^{13}C, and ^{11}B NMR and IR spectroscopy of the reaction mixture. This allylboration product should be used at once without isolation because its distillation in vacuo gives rise to 1,5-dichloro-2-borinene derivative (formed via intramolecular haloboration[13]). Alcoholeysis of the reaction mixture with isopropyl alcohol in the presence of triethylamine afforded 1,4-pentadienylboronate **1** in 74% yield (Scheme 2).

Scheme 2

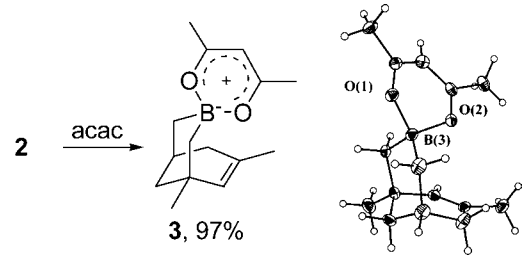


Replacement of ^{i}PrO groups in **1** under the action of methallylmagnesium chloride (2 equiv) followed by thermal bicyclization (140−145 °C, 6 h) and methanolysis gave rise to 5,7-dimethyl-3-methoxy-3-borabicyclo[3.3.1]non-6-ene **2** as a colorless air- and moisture-sensitive liquid in 39% overall yield. The product was purified by vacuum distillation (65−68 °C, 2 mmHg).

The synthesis of boron bicycle **2** is the first example of the step-by-step controlled version of ABAC and presents an efficient way to regulate the structure of final products from stage to stage.

Addition of acetylacetone to **2** in methanol after evaporation of the solvent provided the formation of green fluorescent crystals of the boron chelate **3** (Scheme 3). Crystalli-

Scheme 3



zation of **3** from pentane affords crystals suitable for X-ray analysis.[15]

Then we carried out the synthesis of the other isomer using methallyldichloroborane and allylmagnesium bromide as the

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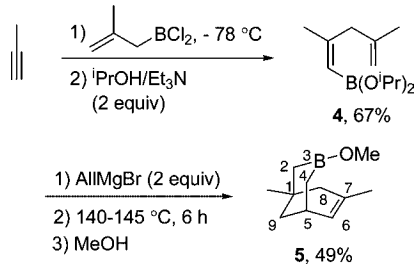
key reagents and synthesized 3-borabicyclo[3.3.1]non-6-ene **5**, which differs from **2** only by location of the methyl group at the ring junction carbon relative to the double bond (Scheme 4). Allylboration of propyne with methallyldichloroborane followed by treatment with 2 equiv of ^{i}PrOH and Et_3N gave 67% of boronate **4**. Compound **4** under the action of allylmagmesium bromide (2 equiv) with further thermal bicyclization (140−145 °C, 6 h) and methanolysis yielded 49% of target bicycle **5** (bp 66−69 °C, 2 mmHg).

Scheme 4

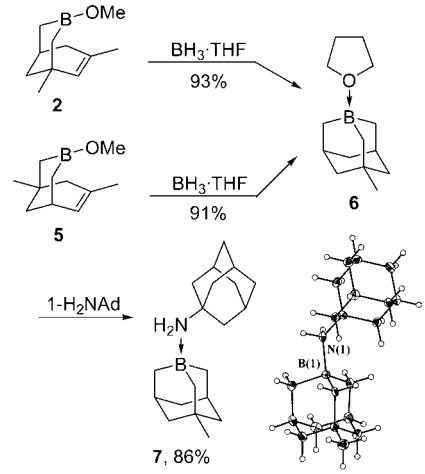


Apparently, the isolation of boronates (**1** and **4**) is not necessary, and the initially formed mixture of chloroboranes may be directly treated with allylic Grignards, simplifying the total experimental procedure.

Isomeric 3-borabicyclo[3.3.1]non-6-enes **2** and **5** were transformed into derivatives of earlier unavailable 3-methyl-1-boraadamantane. Hydroboration−isomerization ring-closure[1] of bicycles **2** and **5** with borane−THF afforded THF-3-methyl-1-boraadamantane, isolated as a colorless liquid by vacuum distillation (66−69 °C, 2 mmHg). The structure of the resulting 1-boraadamantane does not depend on the double-bond location in starting bicycles **2** and **5**. Addition of 1-aminoadamantane to a THF solution of **6** gave the air-stable 1-aminoadamantane complex **7** isolated as the colorless needles after removal of the solvent and washing with pentane (Scheme 5). A single-crystalline sample, suitable for X-ray study, was obtained from methanol.[16]

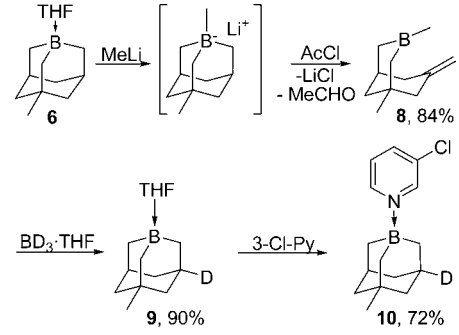
It was of interest to synthesize a 1-boraaadamantane molecule bearing three different substituents at the cage junctions. The stereogenic center in this case is located in the center of the adamantyl moiety. For this purpose, we have utilized a β-hydride elimination reaction.[17] Treatment

Scheme 5



of **6** with MeLi, followed by acetyl chloride addition to 3-methyl-1-boraadamantane "ate" complex (Scheme 6),

Scheme 6



resulted in the formation of 84% of 3,5-dimethyl-7-methylene-3-borabicyclo[3.3.1]nonane **8** (a colorless air-sensitive liquid, bp 38−40 °C, 2 mmHg).

Compound **8** was converted to 1-boraadamantane again, but in this case BD_3·THF was applied. Deuteroboration and subsequent ring closure afforded 90% of [5-D]-3-methyl-1-boraadamantane THF adduct **9**, which was transformed into the air-stable complex **10** (72%) by action of 3-chloropyridine.

The location of the deuterium in the complexes **9** and **10** was determined by ^{1}H, ^{2}H, and ^{13}C NMR spectroscopy as well as elemental analysis and MS. The ^{1}H NMR spectra contain signals of only one junctional H, and the signals with the same δ are observed in ^{2}H NMR spectra (2.23 ppm for **9**, 2.28 ppm for **10**). The lines of C(5) in ^{13}C NMR are split by the D atom (33.5 ppm t, J = 19.7 Hz for **9** and 32.7 ppm t, J = 19.5 Hz for **10**). It should be stressed that derivatives **9** and **10** are the first chiral derivatives of 1-boraadamantane with molecular tetrahedron-type asymmetry. The classical version of ABAC makes it possible to synthesize 1-boraadamantanes chiral due to the asymmetric C(2)-carbon[2b] only.

(15) Crystal data for **3**: $C_{15}H_{23}BO_2$, M = 246.14, at 100 K, triclinic, space group P-1, a = 9.4826(6) Å, b = 11.5606(8) Å, c = 14.2207(9) Å, α = 68.110(1)°, β = 78.325(1)°, γ = 84.522(1)°, V = 1416.3(2) Å^3, $Z(Z')$ = 4(2), R1 = 0.0568 (for 4716 reflections with $I > 2\sigma(I)$), wR2 = 0.1680 (for all independent reflections 6821 with $2\theta_{max}$ = 56°).

(16) Crystal data for **7**: $C_{20}H_{34}BN$, M = 299.29, at 100 K, triclinic, space group P-1, a = 11.202(2) Å, b = 13.174(2) Å, c = 13.299(2) Å, a = 66.300(3)°, b = 79.906(3)°, g = 72.084(3)°, V = 1707.0(4) Å^3, $Z(Z')$ = 4(2), R1 = 0.0635 (for 4249 reflections with $I > 2\sigma(I)$), wR2 = 0.1634 (for all independent reflections 8231 with $2\theta_{max}$ = 56°).

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In conclusion, we have suggested an efficient way to regulate the structure of allylboron−acetylene condensation products based on allylboration of acetylenes with different allyldichloroboranes. Utilization of allyldichloroboranes offers wide possibilities in the modification of 3-borabicyclo-[3.3.1]non-6-ene and 1-boraadamantane derivatives. Whereas only several synthetic triallylboranes are available, a wide variety of allyldialkylboranes and allylboronates (linear, cyclic, cage, with functionalized allylic group) were used in organic synthesis[18] and could be converted in situ with boron halides to the corresponding allyldihaloboranes.[13]

The chemistry proposed was applied to the synthesis of isomeric 1- and 5-methyl-substituted 3-borabicyclo[3.3.1]non-6-enes. Both of them were transformed into previously unavailable 3-methyl-1-boraadamantane derivatives and [5-D]-3-methyl-1-boraadamantane with molecular tetrahedron asymmetry.

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Supporting Information Available: Experimental procedures and full spectroscopic data for all new compounds. X-ray crystallographic data of compounds **3** and **7** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org. X-ray data for **3** and **7** have been also deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC 720055 and 720056 and can be obtained upon request (phone +44 1223 336408; fax +44 1223 336033).

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