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1-Boraadamantane derivatives with functional groups in the side chain

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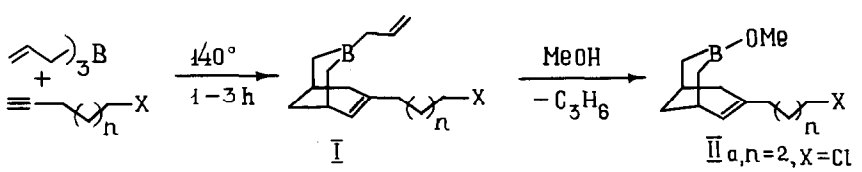
Abstract

1-Boraadamantane derivatives containing ω-functionalized substituents in the position 2 have been synthesized by hydroboration-isomerization of 7-(ω-X-alkyl)-3-borabicyclo[3.3.1]non-6-enes. The application of the method permitted the previously unreported preparation of intra-complexes of the 1-boraadamantane series (X, XI, XIII).

In the course of a study of 1-boraadamantane derivatives [1–4] we have synthesized a number of novel compounds of this type containing functional groups in the side chain (see ref. 5 for the preliminary report).

Previously unknown 7-(ω-haloalkyl)-3-borabicyclo[3.3.1]non-6-enes, used as starting substances, were prepared on the basis of an allylboron-acetylene condensation, specifically the reaction of triallylborane with ω-haloacetylenes.

ω-Bromo- and ω-chloroalkylacetylenes proved to react with triallylborane in an expected way [2] (at 130–140 °C, 1.5–3 h) to form bicyclic compounds, I. The latter were immediately, and without isolation, treated with methanol, which resulted in the cleavage of the $B-C_{allyl}$ bond, evolution of propylene and the formation of methyl esters, II, in about 80% yield.



I

II a, n=2, X=Cl

II б, n=1, X=Br

These data provide further evidence of the resistance of organic halides towards allylic derivatives of boron.

The transformations of bicyclic halides II into 2-(ω-aminoalkyl)-1-boraadamantanes were performed in two ways:

1. by hydroboration–isomerization to the corresponding 2-(ω-haloalkyl)-1-boraadamantanes followed by the replacement of the halogen by amino-group;

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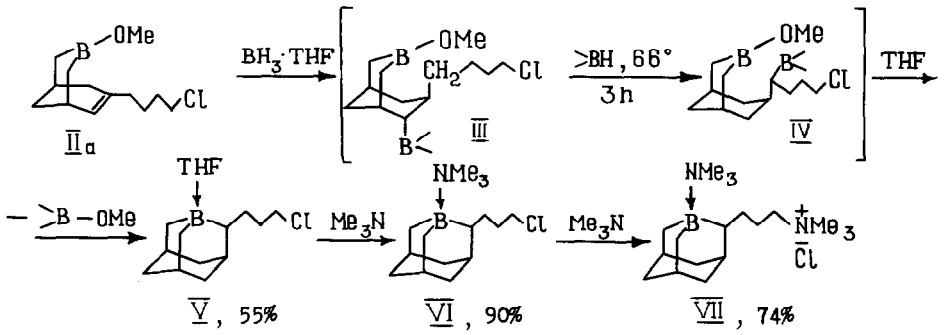
2. by the replacement of the halogen by amino group with successive hydroboration–isomerization.

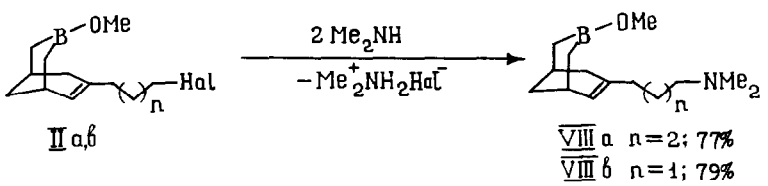
Hydroboration of the ester IIa with a tetrahydrofuran solution of BH_3 according to a standard method [3] gave, via intermediates III and IV, the tetrahydrofuran complex V, which was converted into the trimethylamine complex of 2-(3-chloropropyl)-1-boraadamantane, VI. Heating the latter with an excess of trimethylamine led to the 1-boraadamantane derivative VII, which is readily soluble in water.



Unlike compound VII, which contains three carbon atoms in the side chain, the ethyl analogue, on dissolution in water or methanol, underwent γ-elimination to form the cyclopropyl compound [6].

Several examples of the second method for the synthesis of 2-(ω-aminoalkyl)-1-boraadamantane compounds are described further, with particular reference to their previously unknown intracomplex derivatives.

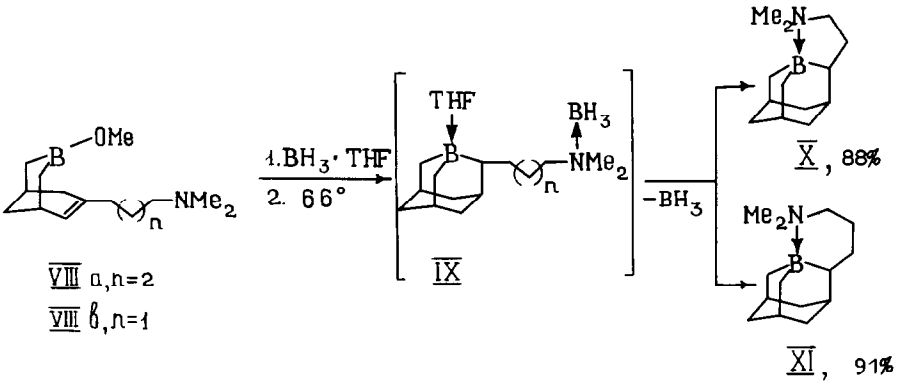
On heating (in an ampoule) compound IIa with an excess of dimethylamine in benzene, 3-methoxy-7-(4-dimethylaminobutyl)-3-borabicyclo[3.3.1]non-6-ene (VIIIa) was obtained:



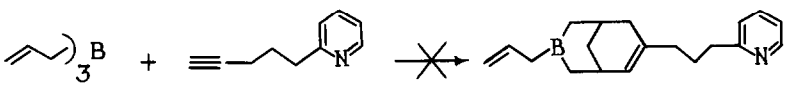
Similarly, the amino-compound VIIIb was synthesized from 3-methoxy-7-(3-bromopropyl)-3-borabicyclo[3.3.1]non-6-ene (IIb). In this case, the replacement of the halogen by dimethylamino group proceeded at room temperature, taking several days to complete.

Hydroboration–isomerization of amino derivatives VIIIa and VIIIb gave at first diboron complexes IX, whose vacuum sublimation produced the intracomplex compounds X and XI.

We attempted to apply the methods described to the synthesis of the pyridine analogues of compounds X and XI. It immediately became clear, however, that the condensation of triallylborane with 5-(2-pyridyl)-1-pentyne (130–140 °C) was



attended by pronounced resin formation and gave no individual compound XII:



It should be noted that this reaction is the first reported failure of an allylboron-acetylene condensation [2].

The bicyclic compound XII was prepared (without isolation in the pure state) by the consecutive treatment of the bromide IIc with α-picolyllithium (2 equivalents) and with a solution of HCl in ether. The successive hydroboration ($BH_3 \cdot THF$) and sublimation carried out directly from the reaction mixture gave the intramolecular 1-boraadamantane complex XIII:

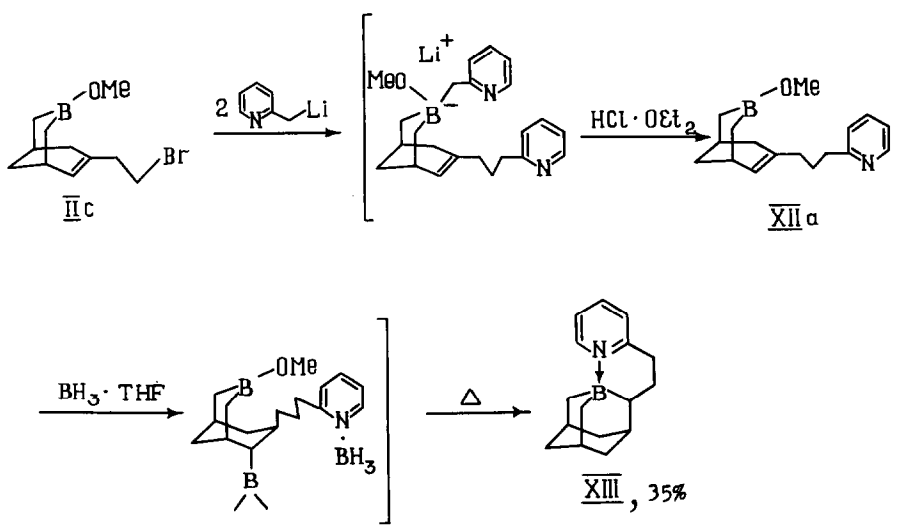
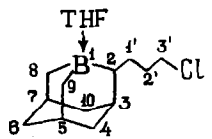


Table 1

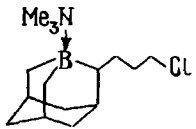
^{13}C NMR chemical shifts of 1-boraadamantane functionalized derivatives [a,b]

Compound	C-3	C-4	C-5	C-6	C-7	C-10	C′-1	C′-2	C′-3	Remainder
V	35.2	33.1	33.6	40.5	33.9	41.0	31.6	26.0	46.2	24.7 (CH_2, THF) 68.6 (CH_2O, THF)
VI	33.9	33.5	32.6	40.6	33.0	41.4	31.0	28.3	46.2	48.8 (CH_3N)
VII	33.6	33.3	32.2	40.2	32.6	41.1	27.8	21.3	67.8	48.8 (CH_3N) 53.1 (CH_3N^+)
X	34.4	33.5	32.5	41.0	33.1	41.8	25.3	64.4		46.5 47.8 (CH_3N)
XI	37.7	33.9	33.2	41.2	33.7	42.0	28.3	24.6	60.6	44.2 47.8 (CH_3N)
XIII	37.7	34.4 [c]	33.4	41.3	33.9	41.6	25.0	34.6 [c]		122.1 (C″-4) 126.7 (C″-2) 137.7 (C″-3) 144.5 (C″-5) 159.4 (C″-1)

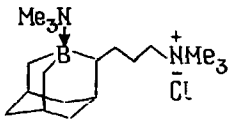
[a] CDCl. [b] Signals from C-2, C-8 and C-9 are very broad. [c] These CS may be interchanged.



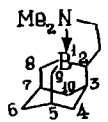
(V)



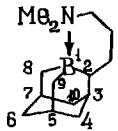
(VI)



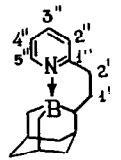
(VII)



(X)



(XI)



(XIII)

Tetrahydrofuran complexes of 1-boraadamantanes are stable in an inert atmosphere but in air they are readily oxidized. At the same time, their amine and pyridine analogues, as well as their intramolecular complexes, are as a rule stable substances.

Structures of all of the compounds synthesized were confirmed by IR and NMR spectra and elemental analyses. ^{13}C NMR data of the functionalized 1-boraadamantanes are listed in Table 1. Spectral data on the chemical ionizations of intracomplex compounds X, XI, XIII have been given in ref. 7.

Experimental

All organoboron compounds were manipulated under dry argon. The PMR spectra were recorded on a Bruker WM-250 (250 MHz) instrument. The ^{13}C and ^{11}B NMR spectra were obtained with a Bruker AM-300 spectrometer (75.47 MHz for carbon and 96.3 MHz for boron).

3-Methoxy-7-(3-bromopropyl)-3-borabicyclo[3.3.1]non-6-ene (IIb) was prepared by a standard method [6].

3-Methoxy-7-(4-chlorobutyl)-3-borabicyclo[3.3.1]non-6-ene (IIa)

To 18.31 g of triallylborane at 130–140 °C, 15.25 g of 5-chloro-1-hexyne was added drop by drop, followed by heating for 2 h at 140 °C. Methanol (16 ml) was then added carefully and the reaction mixture was refluxed for 1 h. Subsequent distillation gave 21.07 g (67%) of IIa, b.p. 110–112 °C (1 mmHg), n_D^{20} 1.4980. Found: C, 65.17; H, 9.27; B, 4.56; Cl, 14.34. $C_{13}H_{22}BClO$ calc.: C, 64.90; H, 9.21; B, 4.49; Cl, 14.74%.

^1H NMR ($CDCl_3$, δ, ppm): 0.75–1.10 m (4H, 2-,4-H), 1.40–1.95 m (10H), 2.25 and 2.45 m (1-,5-H), 3.52 t (2H, HCCl, $^3J = 6.5$ Hz), 3.62 s (3H, HCO), 5.42 m (1H, 6-H).

3-Methoxy-7-(2-bromoethyl)-3-borabicyclo[3.3.1]non-6-ene (IIc)

To 14.47 g of triallylborane at 140–145 °C 14.06 g of 4-bromo-1-butyne was added slowly; the mixture was heated at 145 °C for 2 h and then cooled to 0 °C. After adding 12.8 ml of methanol followed by boiling for 1 h, the mixture was distilled to give 21.1 g (78%) of IIc, b.p. 105–106 °C (15 mmHg), n_D^{20} 1.5218. Found: C, 51.81; H, 7.16; B, 4.12; Br, 30.84. $C_{11}H_{18}BrO$ calc.: C, 51.41; H, 7.06; B, 4.21; Br, 31.09%.

^1H NMR ($CDCl_3$, δ, ppm): 0.77–1.1 m (4H, 2-,4-H), 1.55–1.80 m (3H, 8-,9-H), 2.21–2.55 m (3H, 1-,5-,8-H), 2.42 m (2H, 1-H), 3.38 m (2H, 2-H′), 3.61 s (3H, HCO), 5.51 m (1H, 6-H).

Tetrahydrofuran complex of 2-(3-chloropropyl)-1-boraadamantane (V)

A solution of 15.45 g of IIa in 33 ml of THF at 0 °C was added to 21.18 ml of a $BH_3 \cdot THF$ solution in THF (2.09 *M*), and the mixture was refluxed for 2 h. The solvent was removed in vacuum and the residue distilled to yield 9.94 g (55%) of V, b.p. 108–110 °C (0.6 mmHg). Found: C, 67.85; H, 10.09; B, 3.99; Cl, 12.22%. $C_{16}H_{28}BClO$ calc.: C, 67.98; H, 9.93; B, 3.83; Cl, 12.54%.

^1H NMR ($CDCl_3$, δ, ppm): 0.48–2.2 m (18H), 1.94 m (4H, CH_2–C, THF), 3.55 m (2H, HCCl), 3.89 m (4H, CH_2–O, THF). ^{11}B NMR δ 12.5 ppm.

Trimethylamine complex of 2-(3-chloropropyl)-1-boraadamantane (VI)

To a solution of 6.78 g of V in 10 ml of THF was added a slight excess of trimethylamine at −30 to −35 °C followed by heating to 10 °C and removal in vacuum of the solvent and of the excess amine. Low-temperature crystallization of the residue from methanol gave 5.82 g (90%) of VI, m.p. 87–88 °C. Found: C, 66.50; H, 10.88; B, 4.09; Cl, 13.07. $C_{15}H_{29}BClN$ calc.: C, 66.81; H, 10.84; B, 4.01; Cl, 13.15%.

^{1}H NMR ($CDCl_3$, δ, ppm): 0.3–2.2 m 918H), 2.42 s (6H, CH_3N), 3.58 m (2H, HCCl). ^{11}B NMR δ −1.05 ppm.

Trimethylamine complex of 2-(3-trimethylammoniopropyl)-1-boraadamantane (VII)

5.45 g of VI and 4.78 g of Me_3N in 50 ml of benzene were placed into an ampoule and heated on a water bath for 8 days. After opening the ampoule, the precipitate was filtered and washed with hexane affording 4.9 g (74%) of colourless crystals of VII, m.p. 168 °C (decomp.). Found: C, 65.22; H, 11.66; B, 3.42; Cl, 10.76. $C_{18}H_{38}BClN$ calc.: C, 65.74; H, 11.65; B, 3.29; Cl, 10.79%.

^{1}H NMR (CD_3OD, δ, ppm): 0.4–2.15 m (18H), 2.39 s (9H, CH_3N), 3.40 s (9H, CH_3N^+), 3.62 m (2H, CH_2N^+). ^{11}B NMR δ −0.8 ppm.

7-(3-Dimethylaminopropyl)-3-methoxy-3-borabicyclo[3.3.1]non-6-ene (VIIIb)

6.47 g of 3-methoxy-7-(3-bromopropyl)-3-borabicyclo[3.3.1]non-6-ene IIb and 4.3 g of trimethylamine in 85 ml of benzene were left in an ampoule for 5 days. The ampoule was then opened, and the precipitate filtered and washed with hexane. The filtrate was evaporated and the residue distilled to yield 4.43 g (79%) of VIIIb, b.p. 92–93 °C (1 mmHg), n_D^{20} 1.4910. Found: C, 72.38; H, 11.03; B, 4.25. $C_{14}H_{26}BNO$ calc.: C, 71.50; H, 11.14; B, 4.60%.

^{1}H NMR ($CDCl_3$, δ, ppm): 0.8–1.2 m (4H, 2-, 4-H), 1.4–2.6 m (12H), 2.15 s (6H, CH_3N), 3.64 s (3H, CH_3O), 5.46 m (1H, 7-H).

7-(4-Dimethylaminobutyl)-3-methoxy-3-borabicyclo[3.3.1]non-6-ene (VIIIa)

Following the same procedure as that for VIIIb, 5.76 g of IIa and 4.32 g of dimethylamine in 50 ml of benzene were heated for 6 days on a water bath, yield 4.60 g (77%) of VIIIa, b.p. 119–120 °C (1.5 mmHg), n_D^{20} 1.4888. Found: C, 71.58; H, 11.33; B, 4.03. $C_{15}H_{28}BNO$ calc.: C, 71.43; H, 11.15; B, 4.41%.

^{1}H NMR ($CDCl_3$, δ, ppm): 0.7–1.04 m (4H, 2-, 4-H), 1.25–2.50 m (14H), 2.16 s (6H, CH_3N), 3.58 s (3H, CH_3O), 5.37 m (1H, 6-H).

2-(2-Dimethylaminoethyl)-1-boraadamantane (X)

A solution of 3.9 g of VIIIb in 10 ml of THF was added at 0 °C to 16.37 ml of a solution of $BH_3 \cdot$ THF in THF (2.03 mol), and the mixture was boiled under reflux for 3 h. After the solvent had been evaporated in vacuum, the residue was sublimated (120 °C, 1.5 mmHg) with subsequent low-temperature crystallization from methanol to give 3.05 g (90%) of X, m.p. 119–120 °C. Found: C, 76.54; H 11.77; B, 5.15. $C_{13}H_{24}BN$ calc.: C, 76.11; H, 11.79; B 5.27%.

^{1}H NMR ($CDCl_3$, δ, ppm): 0.4–2.25 m (16H), 2.42 s (6H, CH_3N), 2.75 and 3.17 m (2H, CH_2N). ^{11}B NMR δ −2.0 ppm. Mass spectrum (*m/z*, ion): 205, M^+.

2-(3-Dimethylaminopropyl)-1-boraadamantane (XI)

This was prepared in a similar way from 2.87 g of VIIIa and 17.96 ml of a solution of $BH_3 \cdot THF$ in THF (1.28 *M*) in 91% yield, m.p. 65–66 °C. Found: C, 76.88; H, 11.79; B, 4.61. $C_{14}H_{26}BN$ calc.: C, 76.71; H, 11.96; B, 4.94%.

^1H NMR ($CDCl_3$, δ, ppm): 0.35–2.20 m (18H), 2.28 and 2.42 s (6H, CH_3N), 2.36 and 3.08 m (2H, CH_2N). ^{11}B NMR δ −3.7 ppm. Mass spectrum (*m/z*, ion): 219, M^+.

2-[2-(2-Pyridyl)ethyl]-1-boraadamantane (XIII)

To a solution of 5 g of IIc in 25 ml of THF was added at −70 °C a solution of α-picolyllithium [from 3.64 g of α-picoline and 22 ml of BuLi (1.76 mol)], and the mixture was allowed to stand at −60 °C for 24 h. The temperature was then raised to −30 °C and the mixture treated with methanol and 11 ml of HCl (6 *M*) in ether. After heating the solution to 20 °C, low-boiling substances were removed under reduced pressure, and the residue was dissolved in 10 ml of THF and added drop by drop to 60 ml of a solution of $BH_3 \cdot THF$ in THF (1.01 *M*). The mixture was boiled for 1.5 h. After removal of the solvent in vacuum, two-fold sublimation and low-temperature crystallization (THF–methanol), 1.86 g (35%) of XIII was obtained, m.p. 149–150 °C. Found: C, 80.31; H, 9.44; B, 4.56. $C_{16}H_{22}BN$ calc.: C, 80.35; H, 9.27; B, 4.32%.

^1H NMR ($CDCl_3$, δ, ppm): 0.33–1.39 m (16H), 3.10 m (2H, 2′-H), 7.25 m (2H, 2″-, 4″-H, Py), 7.77 t (1H, 4″-H, Py), 8.42 d (1H, 5″-H, Py). ^{11}B NMR δ −5.0 ppm. Mass spectrum (*m/z*, ion): 239, M^+.

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