ELSEVIER

Available online at www.sciencedirect.com

ScienceDirect

Mendeleev Commun., 1994, **4(2)**, 45–47

Mendeleev Communications

Synthesis of Novel Methyl-substituted 1-Azaadamantanes from 1-Boraadamantane Derivatives

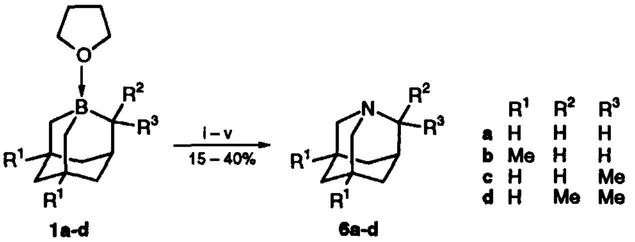
Yurii N. Bubnov,* Mikhail E. Gurskii and Dmitrii G. Pershin

N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 117913 Moscow, Russian Federation.
Fax: +7 095 135 5328

Three new homologues of 1-azaadamantane (2-Me, 2,2- and 3,5-Me_2) have been prepared from the corresponding 1-boraadamantane compounds; the key stage in the transformation is an intramolecular 1,2-anionotropic rearrangement of the ω-azidoalkylborane intermediate.

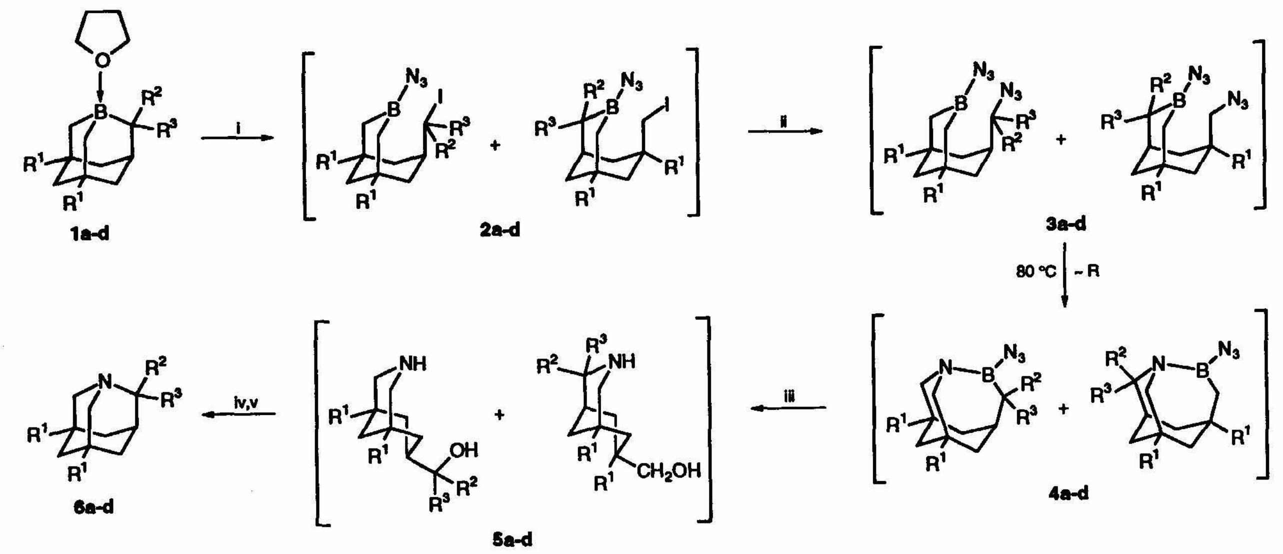
1-Azaadamantane is attracting much attention due to the high symmetry of the molecule[1,2] as well as to the biological activity of its derivatives.[3–5] However, these studies have been hampered by the difficulties in assembling the 1-azaadamantane framework (6–8 stages in a 5–7% overall yield[6,7]).

Recently we have elaborated the most effective route so far to 1-azaadamantane from its 'electronic antagonist'—1-boraadamantane.[8] The key stage in the method is a thermal intramolecular 1,2-anionotropic rearrangement (transfer of an organic moiety from boron to nitrogen) in 3-azido-7α-azidomethyl-3-borabicyclo[3.3.1]nonane, which is readily generated by iodination of 1-boraadamantane in the presence of sodium or lithium azide (2.5–3M). The subsequent oxidation and



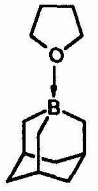
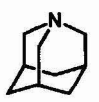
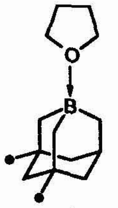
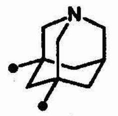
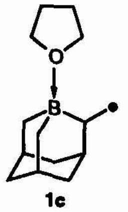
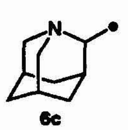
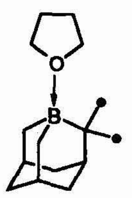
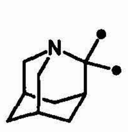
Scheme 1 *Reagents and conditions*: i, NaN_3 (1M), I_2 (1M), diglyme 80 °C; ii, NaN_3 (1.5–2M), diglyme, 80 °C, 1 h; iii, NaOH, H_2O_2, Et_2O/H_2O, 0–5 °C, then 35 °C, 0.5 h; iv, $SOCl_2$, C_6H_6,80 °C, 0.5 h; v, NaOH, H_2O/Et_2O, 20 °C.

Mendeleev Commun., 1994, 4(2), 45–47



Scheme 2 *Reagents and conditions*: i, NaN_3(1M), I_2(1M), diglyme, 80 °C; ii, NaN_3 (1.5–2M), diglyme, 80 °C, 1 h; iii, NaOH, H_2O_2, Et_2O/H_2O, 0–5 °C, then 35 °C, 0.5 h; iv, $SOCl_2$, C_6H_6, 80 °C, 0.5 h; v, NaOH, H_2O/Et_2O, 20 °C.

Table 1 Synthesis and properties of 1-azaadamantanes **6a–d**.

Starting organoborane	1-Azaadamantane	Yield (%), from **1a–d**	M.p. /°C	HRMS, $[M]^+$ Found/calc.	Formula
 **1a**	 **6a** [1,2]	40	260–262	137.12038 137.12043	$C_9H_{15}N$
 **1b**	 **6b**	15	*a*	165.15148 165.15173	$C_{11}H_{19}N$
 **1c**	 **6c**	36	98–101	151.13579 151.13608	$C_{10}H_{17}N$
 **1d**	 **6d**	30	67– 70	165.15137 165.15173	$C_{11}H_{19}N$

[a] Liquid, b.p. 55–57 °C/15 mmHg, n_D^{20} 1.4893.

transannular cyclization lead to 1-azaadamantane in 40% overall yield.

We have now expanded upon and demonstrated the generality of the methodology[8] for the transformation of 2-methyl-2,2-and 3,5-dimethyl-1-boraadamantane **1b–d** into the corresponding 1-azaadamantane derivatives **6b–d** (Scheme 1, Table 1). The starting methylated 1-boraadamantanes **1b–d** were obtained from triallyl- and trimethallylborane according to literature procedures[9,10] (three stages, 50–70% overall yields).

The reaction pathway from **1** to **6** is presented in Scheme 2.[†,‡]

Iodination of tetrahydrofuran complexes **1b–d** in the presence of sodium azide (2.5–3M) in diglyme at 80 °C proceeds with cleavage of one B–C bond to give a mixture of the corresponding intermediate diazido compounds **3b–d**. Under these reaction conditions (80 °C), the latter undergo rearrangement to produce a mixture of cage azidoboranes **4b–d**. Treatment of mixtures **4b–d** with sodium hydroxide and hydrogen peroxide leads to mixtures of aminoalcohols **5b–d**, treatment of which with $SOCl_2$ followed by treatment with sodium hydroxide solution yields the target 1-azaadamantanes **6b–d**.

Solid **6c** and **6d** readily sublime *in vacuo*; 3,5-dimethyl-1-azaadamantane **6b** is a liquid.

This work was supported by the Russian Fundamental Research Foundation (grant no. 93–03–18193).

References

1 T. Sasaki, *Adv. Heterocycl. Chem.*, 1982, **30**, 79.

2 A. I. Kuznetsov and N. S. Zefirov, *Usp. Khim.*, 1989, **58**, 1815 (*Russ. Chem. Rev.*, 1989, **58**, 1033).

3 F. X. Jarreau and J. J. Koenig, *Fr. Patent.* 2,543,954 (*Chem. Abstr.*, 1985, **102**, 31937h).

4 *Jap. Patent*, 62 77.386 [87 77.386] (*Chem. Abstr.*, 1988, **108**, 5870s).

5 *Jap. Patent*, 02 01.943 [90 01.943] (*Chem. Abstr.*, 1990, **113**, 114940m).

6 R. M. Black, *Synthesis*, **1981**, 829.

7 W. N. Speckamp, J. Dijkink and H. O. Huisman, *J. Chem. Soc., Chem. Commun.*, 1970, 197.

8 Yu. N. Bubnov, M. E. Gursky and D. G. Pershin, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1990, 952 (in Russian); Yu. N. Bubnov, M. E. Gursky and D. G. Pershin, *J. Organomet. Chem.*, 1991, **412**, 1.

9 Yu. N. Bubnov, M. E. Gurskii, A. I. Grandberg and D. G. Pershin, *Tetrahedron*, 1986, **42**, 1079.

10 B. M. Mikhailov, T. V. Potapova and A. S. Shashkov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1979, 2724 (*Bull Acad. Sci. USSR, Div. Chem. Sci.*, 1979, 2533).

Received: Moscow, 13th December 1993
Cambridge, 21st January 1994; Com. 3/07670I

[†] *General details.* All manipulations with organoboron compounds were performed in dry argon. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker WM–250 spectrometer (68.69 MHz carbon). ^{11}B NMR spectra were obtained on a Bruker AC–200P spectrometer (Standard $BF_3 \cdot Et_2O$). High resolution mass-spectra were recorded on a Varian-MAT instrument.

Typical experimental procedure for the synthesis of the 1-azaadamantanes **6b–d**. From two dropping funnels, a solution of 12 g (54.5 mmol) of **1c** in 30 ml of diglyme and 13.8 g (54.5 mmol) of iodine in 60 ml of diglyme were simultaneously added dropwise to a stirred suspension of 10.9 g (168 mmol) of NaN_3 in 90 ml of diglyme at 70–80 °C for 1 h. The mixture was stirred at 80 °C for 0.5 h. Nitrogen (985 ml, 72%) was evolved. The resulting white solid was filtered off and diglyme was distilled off *in vacuo* (35–37 °C/1 mmHg). The solid residue was extracted with diethyl ether (3 × 120 ml) and the organic phase was concentrated to 150 ml. A solution of 6.6 g (165 mmol) NaOH in 80 ml of water (at 20 °C) and 21 ml of 30% H_2O_2 (over 1 h at 0 °C) were added with stirring. The reaction mixture was refluxed over a period of 0.5 h. The ether layer was separated while the aqueous layer was saturated with potassium carbonate and extracted with ether (2 × 100 ml). The combined ether extracts were dried (Na_2SO_4) and ether was distilled off *in vacuo* (12 mmHg). Judging from TLC SiO_2 (100/160μ, MeOH–aqueous NH_3, 8:1), 4.0 g (43.5%) of an isomeric mixture of aminoalcohols **6c** was isolated.

A solution of 4.0 g (23.7 mmol) of a mixture of azabicyclononanes **5c** in 55 ml of benzene was added to 6.5 ml of $SOCl_2$ in 90 ml of benzene. The mixture was refluxed for 0.5 h. Benzene and an excess of $SOCl_2$ were distilled off *in vacuo*, then the solid residue was suspended in 100 ml of ether, filtered, washed with ether (2 × 40 ml) and dried *in vacuo* to give 3.8 g of the hydrochloride of **6c** (86% from **5c** or 37% from **1c**). To a solution of the hydrochloride in 30 ml of water, 10 ml of 10% NaOH was added and the product was extracted with ether. The ether was distilled off and drying *in vacuo* (9 mmHg) gave 3.0 g **6c** (84% from **5c** or 36% from **1c**), m.p. 98–101 °C.

[‡] *Selected spectral data for:*

5a: ^{1}H and ^{13}C NMR data are identical with that presented in ref. 2.

5b: ^{1}H NMR ($CDCl_3$) 0.70 (s, 6H, Me), 1.29 (s, 2H, $C^{4}H$), 1.44–1.60 (AB system, 4H, $C^{6,10}H$, J_{AB} 25.8 Hz), 1.86 (m, 1H, $C^{7}H$), 2.58–2.76 (AB system, 4H, $C^{2,9}H$, J_{AB} 24.4 Hz), 2.91 (s, 2H, $C^{8}H$); ^{13}C NMR ($CDCl_3$) 27.6 (Me), 28.2 (C^{5}), 28.6 ($C^{3,7}$), 42.6 ($C^{4,6}$), 50.5 (C^{10}), 57.2 (C^{9}), 64.1 ($C^{2,8}$).

5c: ^{1}H NMR ($CDCl_3$) 1.09 (d, 3H, Me, J 7.4 Hz), 2.71 (d, 1H, $C^{9}H^{\beta}$, J 12.4 Hz), 3.05 [m, 4H, C(2,8)H, $C^{9}H^{\alpha}$]; ^{13}C NMR ($CDCl_3$) 18.0 (Me), 26.4 (C^{5}), 26.85 (C^{7}), 29.85 (C^{4}), 30.7 (C^{3}), 37.2 (C^{6}), 38.1 (C^{10}), 50.5 (C^{9}), 58.6 (C^{2}), 60.6 (C^{8}).

5d: ^{1}H NMR ($CDCl_3$) 1.20 (s, 6H, Me), 1.34 (w.s., 1H, $C^{3}H$), 2.87 (d, 2H, NCH_2^{α}, J 12.6 Hz), 3.46 (d, 2H, NCH_2^{β}, J 12.6 Hz); ^{13}C NMR ($CDCl_3$) 26.2 ($C^{5,7}$), 27.0 (Me), 32.3 ($C^{4,10}$), 33.5 (C^{3}), 38.4 (C^{6}), 53.35 ($C^{8,9}$), 54.9 (C^{2}).