The first chiral derivatives of 1-boraadamantane

Mikhail E. Gurskii,[a] Vladimir A. Ponomarev,[a] Konstantin A. Lyssenko,[b] Mikhail Yu. Antipin,[b] Philippe Renaud[c] and Yurii N. Bubnov*[a,b]

[a] *N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 119991 Moscow, Russian Federation. Fax: +7 095 135 5328; e-mail: bor@ioc.ac.ru*

[b] *A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, 119991 Moscow, Russian Federation. Fax: +7 095 135 5085*

[c] *Department of Chemistry and Biochemistry, University of Bern, CH-3000 Bern 9, Switzerland. Fax: +41 (0)31 631 3426; e-mail: philippe.renaud@ioc.unibe.ch*

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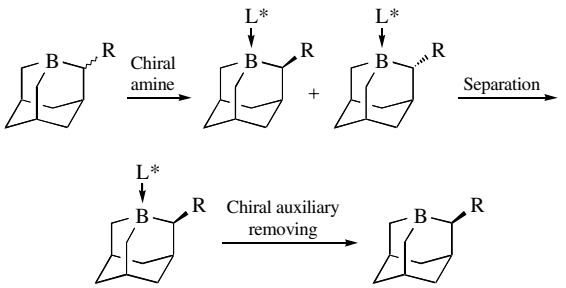
Both (*S*)-(+)- [(*S*)-5**] and (*R*)-(–)-2-methyl-1-boraadamantane [(*R*)-**5**] were isolated in 96% and 92% *ee*, respectively, by the crystallization of corresponding (*S*)-(–)- and (*R*)-(+)-phenylethylamine adducts from hexane and transformed into optically active 1-hydroxy-2-methyladamantanes by the carbonylation–oxidation sequence.**

2-Substituted 1-boraadamantanes, which are available from triallylborane and terminal acetylenes,[1] contain an asymmetric carbon centre (C-2), and they can be resolved to enantiomers by fractional crystallization of diastereomeric complexes with a chiral amine ligand. The subsequent removal of a chiral auxiliary (amine) from the isolated diastereomer should furnish enantiopure 2-substituted adamantane (Scheme 1).



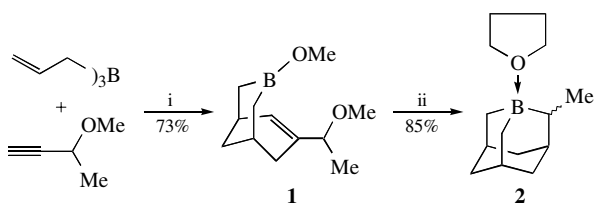
Scheme 1

Using this approach, we resolved the enantiomers of 2-methyl-1-boraadamantane and transformed it into corresponding chiral cage alcohols.

2-Methyl-1-boraadamantane was synthesised previously from triallylborane and vinylacetylene in several steps.[2] In this work, we used a modified protocol for the preparation of unsubstituted 1-boraadamantane.[3]

Condensation of triallylborane and 3-methoxybut-1-yne led, after treatment with methanol, to 7-(1-methoxyethyl)-3-methoxy-3-borabicyclo[3.3.1]non-6-ene **1**.† The hydroboration and isomerization of compound **1** with a THF solution of borane gave THF complex of 2-methyl-1-boraadamantane **2**† in 85% yield (Scheme 2).

The treatment of **2** with (*S*)-(–)-phenylethylamine (PEA) gave a mixture of diastereomeric complexes **3a**,† which were isolated as white well-shaped crystals. Six step-by-step crystallizations of this mixture from hexane are required to obtain (*S*,*S*)-**3**† with ≥ 96% diastereomeric excess (in all cases, the diastereomeric excess was determined by ^{13}C NMR spectroscopy, see Figures 2 and 3). The same diastereomeric excess can be achieved only by three crystallizations if the sample of (*S*,*S*)-**3** is used as a seed for crystallization. Note that the diastereomeric excess obtained and the *ee* of the chiral amine used are the same (Scheme 3).



Scheme 2 *Reagents and conditions*: i, 135–140 °C, then MeOH, 1 equiv. at room temperature; ii, BH_3·THF in THF, reflux for 2 h.

The absolute configuration of a chiral centre in the 1-boraadamantane moiety was found by X-ray diffraction (XRD) analysis as (*S*,*S*)-**3** on the basis of a comparison with the known stereo structure of the chiral amine ligand (*S*)-(–)-phenylethylamine (Figure 1).‡

We found using XRD that the principal geometry of (*S*,*S*)-**3** is close to the donor–acceptor complexes of 1-boraadamantane derivatives. In particular, the B(1)←N(1) bond lengths in (*S*,*S*)-**3**

† *Characterization data of* **1** (as a diastereomeric 1:1 mixture): 73% yield from triallylborane and 3-methoxybut-1-yne. Bp 78–80 °C (2 Torr). ^{1}H NMR (200 MHz, $CDCl_3$) δ: 0.6–2.4 (m, 28H, intricate multiplet of aliphatic protons), 3.12 (d, 6H, CH–O*Me*), 3.50 (s, 3H, B–OMe), 5.51 (ex s, 1H, C=C*H*OMe). ^{11}B NMR (64.21 MHz, $CDCl_3$) δ: 52.3. ^{13}C NMR (50.32 MHz, $CDCl_3$) δ: 19.5 and 19.9 (Me), 26.8 and 26.9 (C-5), 29.0 and 29.1 (C-1), 30.9 and 31.3 (C-8), 32.6 (C-9), 52.7 (B–OMe), 54.8 and 55.2 (CH–O*Me*), 81.1 and 81.2 (*C*H–OMe) 130.49 and 131.5 (C-6), 133.8 and 134.2 (C-7). Found (%): C, 68.57; H, 10.09; B, 5.05. Calc. for $C_{12}H_{21}O_2B$ (%): C, 69.26; H, 10.17; B, 5.19.

2: 85% yield from **1**, bp 83 °C (2 Torr). ^{1}H NMR (200 MHz, $CDCl_3$) δ: 0.7–2.3 (m, intricate multiplet of aliphatic protons), 3.88 (m, 4H, CH_2OCH_2 of THF). ^{11}B NMR (64.21 MHz, $CDCl_3$) δ: 11.6. ^{13}C NMR (50.32 MHz, $CDCl_3$) δ: 16.6 (Me) 24.5 [C(3)–C(4) of THF], 25.0 (C-9), 27.5 (C-8), 31.4 (C-2), 33.9 and 34.0 (C-5,7), 33.2 (C-4), 40.5 and 41.4 (C-6,10), 41.1 (C-3), 68.6 (CH_2OCH_2 fragment of THF).

(±)-**3a** (as a diastereomeric 1:1 mixture): yield 81% from **2** and (*S*)-(–)-phenylethylamine. Mp 75–77 °C. ^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 0.3–2.7 [m, 17H, intricate multiplet of cage protons with strongly pronounced equal signals of both diastereomeric forms at 0.75 and 0.87 (d, BCH–*Me* of *S*,*R*- and *S*,*S*- forms, respectively, *J* 7 Hz) and at 1.50 and 1.52 (d, Ph–CH*Me*NH_2, *S*,*R*- and *S*,*S*- forms respectively, *J* 7 Hz)]; 4.17–4.22 (q, 1H, Ph–C*H*MeNH_2, *J* 7 Hz), 7.2–7.4 (m, 5H, Ph). ^{11}B NMR (64.21 MHz, $CDCl_3$) δ: –6.32. Found (%): C, 80.33; H, 10.59; B, 3.91. Calc. for $C_{18}H_{28}BN$ (%): C, 80.30; H, 10.48; B, 4.09.

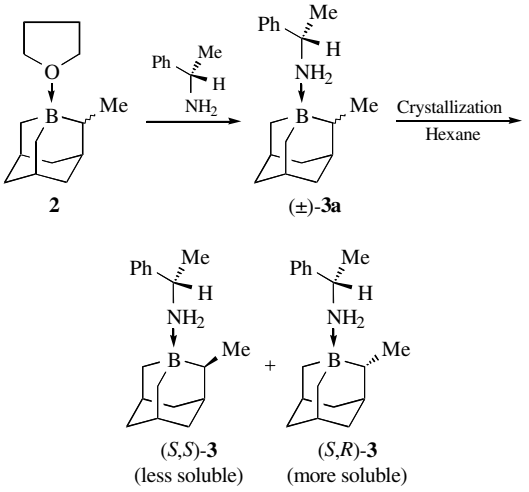
(*S*,*S*)-**3**: Mp 105–106 °C. ^{13}C NMR (100.13 MHz, $CDCl_3$) δ: 16.4 (Me), 22.6 (*Me*–CH–NH_2Ph), 25.8 (C-9), 26.4 (C-8), 30.6 (C-2), 32.8 and 33.1 (C-5,7), 33.6 (C-4), 39.9 (C-10), 40.9 (C-6), 41.7 (C-3), 50.7 (Me–*C*H–NH_2Ph), 126.2 (*o*-Ph), 128.4 (*p*-Ph), 129.3 (*m*-Ph), 142.8 (*ipso*-Ph).

(*S*,*R*)-**3**: ^{13}C NMR (100.13 MHz, $CDCl_3$) δ: 16.7 (Me), 22.4 (*Me*–CH–NH_2Ph), 25.8 (C-9), 26.4 (C-8), 30.6 (C-2), 32.8 and 33.1 (C-5,7), 33.6 (C-4), 40.0 (C-10), 40.9 (C-6), 41.7 (C-3), 51.1 (Me–*C*H–NH_2Ph), 126.1 (*o*-Ph), 128.4 (*p*-Ph), 129.3 (*m*-Ph), 142.7 (*ipso*-Ph).

(*S*)-**5**: 85% yield from (*S*)-**4**, mp 92–94 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 0.5–2.3 (m, 17H, intricate multiplet of adamantane protons), 7.49 (t, 2H, *m*-Py), 7.87 (t, 1H, *p*-Py), 8.47 (d, 2H, *o*-Py). ^{11}B NMR (64.21 MHz, $CDCl_3$) δ: –2.85. ^{13}C NMR (50.32 MHz, $CDCl_3$) δ: 16.1 (Me), 25.3 (C-9), 32.77 and 33.1 (C-5,7), 33.5 (C-4), 34.4 (C-2,8), 39.7 (C-10), 40.1 (C-6), 41.8 (C-3), 124.9 (*m*-Py), 138.4 (*p*-Py), 144.4 (*o*-Py). MS, *m*/*z* (*I*, %): 227 $[M]^+$ (41.1), 148 $[M - Py]^+$ (17.7). Found (%): C, 79.56; H, 9.81; B, 4.72. Calc. for $C_{15}H_{22}BN$ (%): C, 79.31; H, 9.76; B, 4.76.

(*S*)-**6**: yield 35% from **2**. Mp 204–206 °C (lit.,[4] 206–208 °C). ^{1}H NMR for (*S*)-**6** (200 MHz, $CDCl_3$) δ: 1.07 (d, 3H, Me, *J* 7 Hz), 1.4–2.2 (m, 15H, intricate multiplet of adamantane cage protons). ^{13}C NMR for (*S*)-**6** and (*R*)-**6** (200 MHz, $CDCl_3$) δ: 13.6 (Me), 30.0 (C-4), 30.7 (C-5), 31.4 (C-7), 36.5 (C-3), 37.0 (C-6), 38.2 (C-10), 38.7 (C-9), 45.0 (C-2), 47.2 (C-8), 70.0 (C-1). Found (%): C, 79.46; H, 10.91. Calc. for $C_{11}H_{18}O$ (%): C, 79.53; H, 11.15.

(*S*)-**7**: ^{11}B NMR (64.21 MHz, $CDCl_3$) δ: –18 (d, $J_{^1H^{11}B}$ 73 Hz).



Scheme 3

[1.641(3) Å] is significantly shorter than the corresponding lengths in a complex of 2-phenyl-1-boraadamantane with trimethylamine [1.691(2) Å][4(a)] and in a complex of 1-boraadamantane with 3,5-dimethyl-1-azaadamantane [1.690(2) Å].[4(b)] The observed variation clearly indicates that the B←N bond length in donor–acceptor complexes of boraadamantane is governed by steric rather than electronic characteristics of Lewis bases.

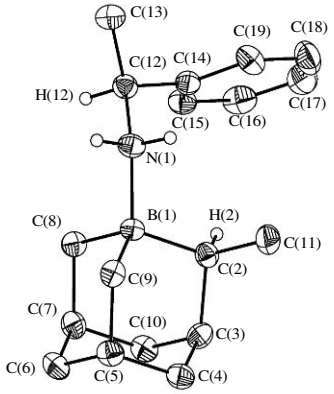


Figure 1 The general view of (*S*,*S*)-**3**. Selected bond lengths (Å): B(1)–N(1) 1.641(3), B(1)–C(2) 1.626(3), B(1)–C(8) 1.621(3), B(1)–C(9) 1.632(3), N(1)–C(12) 1.512(3); selected bond angles (°): C(8)–B(1)–C(2) 110.6(2), C(8)–B(1)–C(9) 108.4(2), C(2)–B(1)–C(9) 109.9(2), C(8)–B(1)–N(1) 109.8(2), C(2)–B(1)–N(1) 112.5(2), C(9)–B(1)–N(1) 105.4(2), C(12)–N(1)–B(1) 122.1(2), C(11)–C(2)–B(1) 116.5(2), C(3)–C(2)–B(1) 105.6(2), C(7)–C(8)–B(1) 107.3(2), C(5)–C(9)–B(1) 107.5(2).

‡ *Crystallographic data for* (*S*,*S*)-**3**: at 110 K, the crystals of $C_{18}H_{28}BN$ are orthorhombic, space group $P2_12_12_1$, a = 7.210(3) Å, b = 14.586(6) Å, c = 14.781(6) Å, V = 1554.5(12) Å^3, Z = 4, M = 269.22, d_{calc} = 1.150 g cm^{-3}, μ(MoKα) = 0.65 cm^{-1}, F(000) = 592. Intensities of 7133 reflections were measured with a Smart 1000 CCD diffractometer at 110 K [λ(MoKα) = = 0.71072Å, ω-scans with a 0.3° step in ω and 10 s per frame exposure, $2\theta < 58°$] and 3919 independent reflections (R_{int} = 0.0330) were used in a further refinement. The structure was solved by a direct method and refined by the full-matrix least-squares technique against F^2 in the anisotropic–isotropic approximation. Hydrogen atoms were located from the Fourier synthesis and refined in the isotropic approximation. The refinement converged to wR_2 = 0.1164 and GOF = 0.977 for all independent reflections [R_1 = 0.0558 was calculated against F for 2834 observed reflections with $I > 2\sigma(I)$]. All calculations were performed using SHELXTL PLUS 5.0 on IBM PC AT.

Atomic coordinates, bond lengths, bond angles and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). These data can be obtained free of charge *via* www.ccdc.cam.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336 033; or deposit@ccdc.cam.ac.uk). Any request to the CCDC for data should quote the full literature citation and CCDC reference number 212040. For details, see 'Notice to Authors', *Mendeleev Commun.*, Issue 1, 2003.

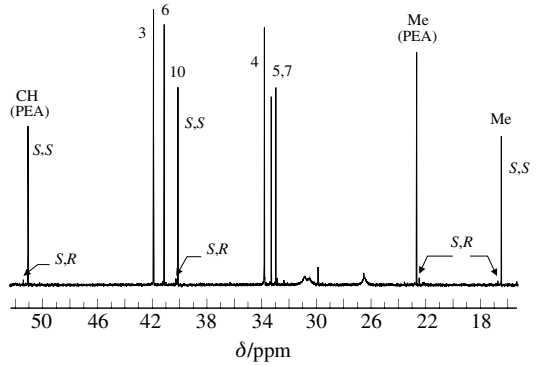


Figure 2 The ^{13}C NMR spectra of (*S*,*S*)-**3** (125.75 MHz, $CDCl_3$).

Amine ligands were removed from (*S*,*S*)-**3** and (*R*,*R*)-**3** by the treatment with a THF solution of $BF_3{\cdot}Et_2O$. Thus, both enantiomers of 2-methyl-1-boraadamantane as adducts with THF **4** were obtained (Scheme 4). By the interaction of isolated chiral complexes **4** with pyridine, air stable pyridinates (*S*)-**5**† and (*R*)-**5** were obtained with $[\alpha]_D^{20}$ +40.1 (*c* 1, hexane) and –38.5 (*c* 1, hexane), respectively.

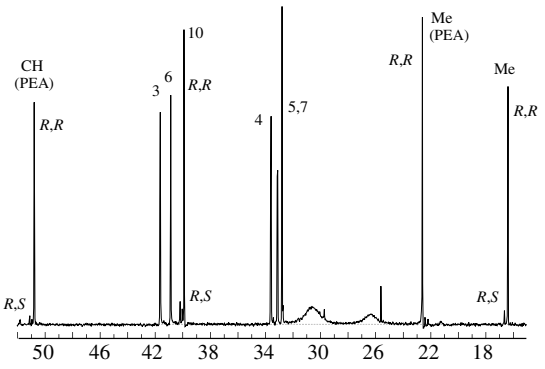
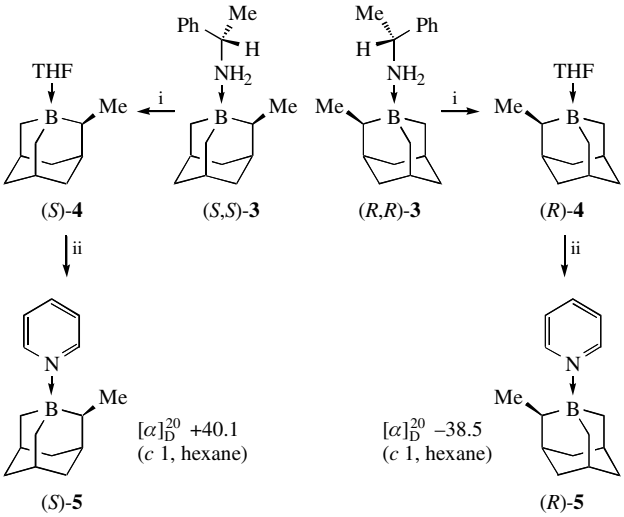
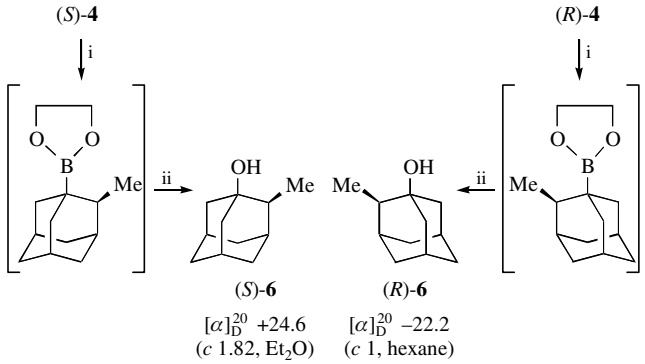


Figure 3 The ^{13}C NMR spectra of (*R*,*R*)-**3** (125.75 MHz, $CDCl_3$).

THF complexes (*S*)-**4** and (*R*)-**4** were converted into optically active 1-hydroxy-(*S*)-(+)-2-methyladamantane (*S*)-**6**† and 1-hydroxy-(*R*)-(–)-2-methyladamantane (*R*)-**6** with 96% and 92% *ee*, respectively, using a carbonylation–oxidation procedure (Scheme 5). Enantiomerical purity was determined by ^{13}C NMR



Scheme 4 *Reagents and conditions*: i, $BF_3{\cdot}Et_2O$, hexane, reflux for 3 h; ii, pyridine, Et_2O, room temperature.



Scheme 5 *Reagents and conditions*: i, CO, $(HOCH_2)_2$, 150 °C, 2 h; ii, OH^-, H_2O_2, 0→36 °C.

spectroscopy in the presence of the chiral paramagnetic shift reagent tris[3-(heptafluorobutyryl)-l-camphorato]europium(III).

Chiral potassium (*S*)-(+)-2-methyl-1-boraadamantylhydride (*S*)-**7**† was prepared as a 0.081 M solution in THF by the treatment of (*S*)-**4** with potassium hydride (Scheme 6). In the ^{11}B NMR spectrum of the compound, a characteristic doublet at –18 ppm ($J_{^1H^{11}B}$ 73 Hz) was observed.

Compound (*S*)-**7** is the first chiral cage hydroborate. This superhydride might be useful for the asymmetric reduction of aldehydes, imines, *etc*.

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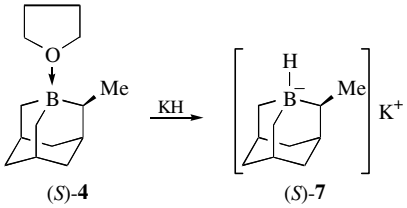

Scheme 6

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