2-Phenyl-1-boraadamantane complexes. Crystal structure and use in the synthesis of cage compounds

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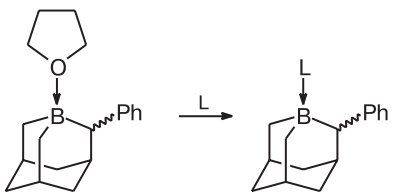
Complexes of 2-phenyl-1-boraadamantane with trimethylamine and pyridine were studied by X-ray diffraction analysis. The 2-phenyl-1-boraadamantane adduct with tetrahydrofuran (**1**) was transformed to 1-hydroxy-2-phenyladamantane *via* a carbonylation—oxidation sequence. The intramolecular version of the organoborane reaction with organic azides was employed as a key step in the transformation of 2-phenyl-1-boraadamantane adduct (**1**) into 2-phenyl-1-azaadamantane (**5**).

Key words: boraadamantanes, 2-phenyl-1-boraadamantane, 1-hydroxy-2-phenyladamantane, 2-phenyl-1-azaadamantane, X-ray study, amine complexes, carbonylation—oxidation, iodination, azides, cyclization.

Recently, we reported[1] the synthesis of 2-phenyl-1-boraadamantane complexes **1**—**3**, in one of which through-space interaction of the substituent in position 2 with the ligand, trimethylamine molecule, was clearly manifested. In particular, for 2-phenyl-1-boraadamantane complex with trimethylamine (**2**), steric inhibition of free rotation of the Ph group was found by dynamic ^{13}C and ^{1}H NMR spectroscopy, and the activation parameters of the rotation were calculated. In this work, we report the results of X-ray diffraction study of 2-phenyl-1-boraadamantane complexes with trimethylamine (**2**) and pyridine (**3**); the transformation of 1-boraadamantane cage into the adamantane and 1-azaadamantane cage was carried out.

Adducts **2** and **3** were prepared from tetrahydrofuran complex **1** on treatment with Me_3N and Py, respectively[1] (Scheme 1).

Scheme 1



1 **2**, **3**

L = Me_3N (**2**), Py (**3**)

According to X-ray diffraction data, complexes **2** and **3** crystallize as racemates. It should be noted that for complex **2**, seldom encountered quasi-racemic crystals are formed. Adduct **2** crystallizes in the chiral noncentrosymmetric space group $P2_1$ but the crystallographically independent molecule is a superposition of two enantiomers in which the 1-boraadamantane fragments are turned with respect to one another through 45° around the B—N bond (Fig. 1). This means that the crystal contains both enantiomers in 1 : 1 ratio.

Unfortunately, the disordered structure of complex **2**, resulting in rather high correlations, precludes detailed analysis of the structure of the 1-boraadamantane fragment.

The structural features of the complex with Py (**3**) (Fig. 2) could be studied in more detail. This compound is characterized by clear-cut steric interaction between the ligand and the phenyl substituent.

As in the previously studied complexes of unsubstituted 1-boraadamantane[2] and 2,2′-ethylenebis-1-boraadamantane with Py[3], distortion of the boraadamantane fragment was noted for structure **3** (Tables 1, 2); in particular, the B(1)—C(2) and B(1)—C(9) bonds are elongated (1.640(4) and 1.636(4) Å, respectively) with respect to the B(1)—C(8) bond (1.618(4) Å) and the B—C—C bond angles (the mean value is 110.1°) are greater than the C—C—C angles (the mean value is 106.6°). Yet another feature is elongation of the C(2)—C(3), C(9)—C(5), and C(8)—C(7) side bonds,

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 8, pp. 1437—1441, August, 2002.

1066-5285/02/5108-1562 $27.00

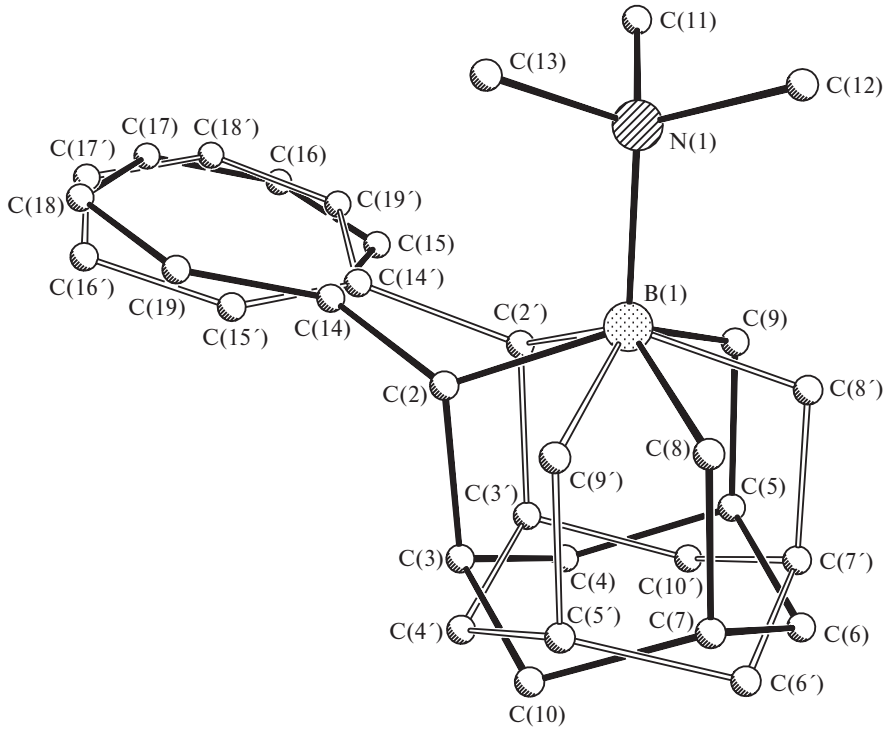


Fig. 1. General view of molecule **2**.

whose lengths range from 1.543(3) to 1.563(3) Å (the mean value is 1.553 Å), with respect to the bonds in the C(3)C(4)C(5)C(6)C(7)C(10) six-membered ring, which vary in the 1.517(4)—1.540(4) Å range (the mean value is 1.530 Å).

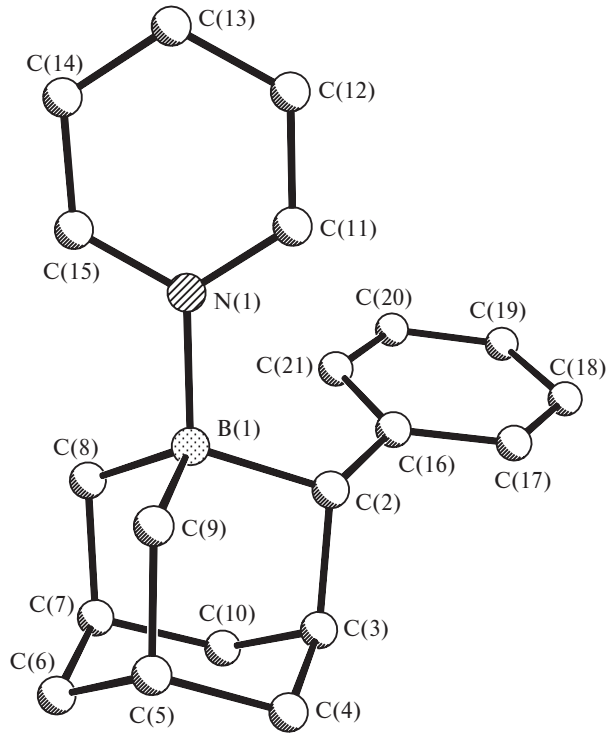


Fig. 2. General view of molecule **3**.

The B(1)—N(1) bond length in the adduct with Py (**3**) is 0.045 Å shorter than that in adduct **2**; this is in full agreement with the results of comparison of the stability of triorganoborane adducts with tertiary amines and pyridine.[4]

Due to the presence of the phenyl substituent in position 2 of complex **3**, the pyridine ring is

Table 1. Selected bond lengths (*d*) in structures **2** and **3**

Bond	*d*/Å	
	2*	**3**
B(1)—N(1)	1.691(2)	1.646(3)
B(1)—C(2)	1.624(5) [1.654(5)]	1.640(4)
B(1)—C(8)	1.628(7) [1.596(6)]	1.618(4)
B(1)—C(9)	1.669(6) [1.667(6)]	1.635(3)
C(2)—C(3)	1.581(8) [1.563(9)]	1.563(3)
C(3)—C(4)	1.552(9) [1.506(9)]	1.538(3)
C(3)—C(10)	1.52(1) [1.525(9)]	1.524(4)
C(4)—C(5)	1.58(1) [1.499(9)]	1.540(4)
C(5)—C(6)	1.52(1) [1.56(1)]	1.517(4)
C(5)—C(9)	1.53(1) [1.559(8)]	1.543(3)
C(6)—C(7)	1.55(1) [1.52(1)]	1.536(3)
C(7)—C(8)	1.55(1) [1.547(8)]	1.548(3)
C(7)—C(10)	1.55(1) [1.48(1)]	1.537(3)

* The bond lengths for the second enantiomer are given in brackets.

Table 2. Selected bond angles (ω) in structures **2** and **3**

Angle	ω/deg	
	2*	**3**
C(2)—B(1)—N(1)	112.3(2) [112.4(2)]	111.0(2)
C(8)—B(1)—N(1)	108.7(3) [109.4(2)]	110.8(2)
C(8)—B(1)—C(2)	106.8(4) [109.7(4)]	114.0(2)
C(8)—B(1)—C(9)	108.9(3) [104.7(3)]	107.7(2)
C(9)—B(1)—N(1)	108.9(3) [110.4(3)]	106.4(2)
C(9)—B(1)—C(2)	111.2(3) [111.2(3)]	106.4(2)
C(3)—C(2)—B(1)	106.3(4) [104.6(4)]	105.0(2)
C(4)—C(3)—C(2)	112.0(5) [113.6(5)]	110.0(2)
C(10)—C(3)—C(2)	110.6(5) [109.4(6)]	111.0(2)
C(10)—C(3)—C(4)	107.5(5) [109.2(6)]	109.5(2)
C(3)—C(4)—C(5)	111.0(5) [111.5(5)]	110.5(2)
C(4)—C(5)—C(9)	110.4(5) [110.1(4)]	109.1(2)
C(6)—C(5)—C(4)	105.3(6) [111.4(6)]	109.3(2)
C(6)—C(5)—C(9)	112.7(6) [112.1(6)]	110.8(2)
C(5)—C(6)—C(7)	112.3(7) [108.8(6)]	111.1(2)
C(6)—C(7)—C(8)	112.4(7) [106.4(6)]	108.7(2)
C(6)—C(7)—C(10)	106.3(6) [112.1(6)]	110.2(2)
C(10)—C(7)—C(8)	109.0(7) [111.2(6)]	109.8(2)
C(7)—C(8)—B(1)	108.6(4) [110.0(4)]	107.0(2)
C(5)—C(9)—B(1)	107.6(4) [107.4(4)]	107.9(2)
C(3)—C(10)—C(7)	111.5(5) [111.4(6)]	111.7(2)

*The bond angles for the second enantiomer are given in brackets.

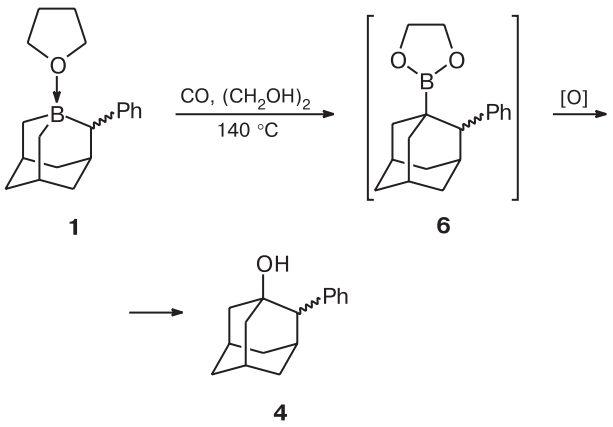
turned relative to the boraadamantane bisecting plane (B(1)C(2)C(3)C(6)) through 25°. The angle between the root-mean-square planes of the Ph group and the pyridine ring is equal to 76.4°. Due to these positions of pyridine and 1-boraadamantane cage, the H(11)...H(2) and H(15)...H(8A) distances are shortened to 2.19 and 2.10 Å, respectively. The observed conformation of complex **3** indicates that the steric repulsion between the phenyl group and the pyridine ligand predominates over the repulsion between the H atoms located in the pyridine *ortho*-positions and the α-positions of the 1-boraadamantane fragment.

We carried out the transformation of the 2-phenyl-1-boraadamantane complex with tetrahydrofuran (**1**) into 1-hydroxy-2-phenyladamantane (**4**) and 2-phenyl-1-azaadamantane (**5**).

Consecutive carbonylation and oxidation of 1-boraadamantane derivatives is among the best methods for the synthesis of 1-adamantanol derivatives.[5]

Carbonylation of complex **1** was carried out in two steps. First, a solution of compound **1** in THF was heated in an autoclave with CO (100 atm) for 3 h at 140 °C. Then ethylene glycol was added to the reaction mixture (to facilitate migration of the "third group"), and the mixture was heated for an additional 3 h at 140 °C under a CO pressure of 75 atm. The intermediate ethylene glycol ester **6** was immediately oxidized without isolation (Scheme 2). The yield of 1-hydroxy-2-phenyladamantane (**4**) was 47%.

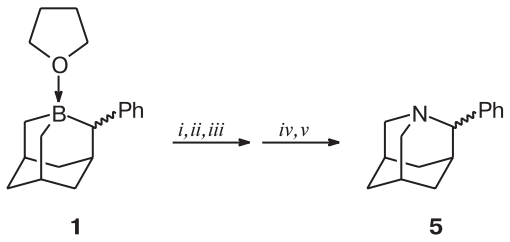
Scheme 2



Previously, we developed an efficient method for the transformation of 1-boraadamantanes into the corresponding 1-azaadamantanes[6] based on the intramolecular version of the reaction of organoboranes with organic azides, resulting in secondary amines. The application of this method to 2-phenyl-1-boraadamantane afforded 2-phenyl-1-azaadamantane (**5**), difficult to synthesize, in a moderate yield.

The transformation **1** → **5** is accomplished as a two-pot procedure using simple and readily available reagents (Scheme 3).

Scheme 3

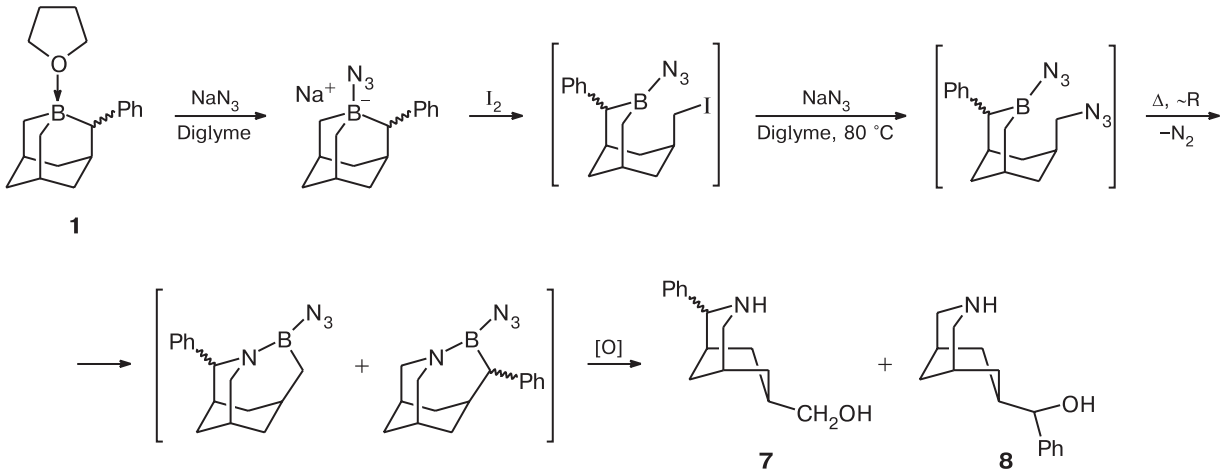


Reagents and conditions: *i*. NaN_3. *ii*. I_2, 90 °C. *iii*. NaOH, H_2O_2. *iv*. $SOCl_2$. *v*. NaOH.

The first step is the synthesis of bicyclic amino alcohols **7** and **8**. The possible mechanism for their formation is presented in Scheme 4.

The iodination of complex **1** in the presence of a threefold excess of NaN_3 in diglyme at 85 °C is accompanied by N_2 evolution and affords (after treatment of the reaction mixture with an alkaline hydrogen peroxide) a mixture (1 : 3) of regioisomeric bicyclic amino

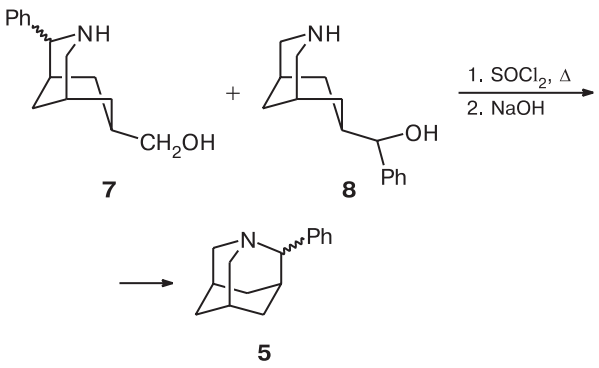
Scheme 4



alcohols **7** and **8**, which were separated by column chromatography on SiO_2 (Scheme 4). The products were formed as thick gradually crystallizing oils.

The second step, namely, cyclization of individual amino alcohols **7** and **8** (or their mixture) to give azaadamantane **5**, was attained by refluxing them with $SOCl_2$ in benzene followed by treatment of the resulting hydrochloride with NaOH (Scheme 5).

Scheme 5

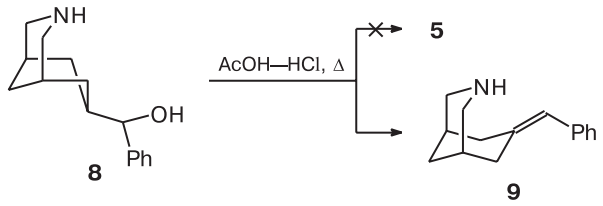


2-Phenyl-1-azaadamantane (**5**) is a colorless thin fluid. Its structure was confirmed by the data of ^1H and ^{13}C NMR spectroscopy, mass spectrometry, and elemental analysis.

We attempted to carry out the cyclization **8** → **5** in a mixture of glacial AcOH with concentrated HCl by a known procedure.[7] However, under these conditions, the 1-azaadamantane cage was not formed but dehydration of alcohol **8** took place to give compound **9** containing a benzylidene group (Scheme 6).

Thus, 2-phenyl-1-boraadamantane readily prepared from benzylacetylene can serve as the starting compound

Scheme 6



for the synthesis of difficultly accessible cage compounds of the adamantane and azaadamantane series.

Experimental

All operations with organoboron compounds were carried out under dry argon. ^1H, ^{13}C, and ^{11}B NMR spectra were recorded on Bruker AC-200P (200.13, 50.32, and 64.21 MHz, respectively) and Bruker AMX-400 (400.13 (^1H) and 100.13 MHz (^{13}C)) spectrometers in $CDCl_3$. Mass spectra (EI) were recorded on a KRATOS MS30 instrument (200 eV).

The 2-phenyl-1-boraadamantane—tetrahydrofuran (**1**), 2-phenyl-1-boraadamantane—trimethylamine (**2**), and 2-phenyl-1-boraadamantane—pyridine (**3**) adducts were synthesized by a procedure published previously.[1]

2-Phenyl-1-adamantanol (4). A solution of complex **1** (9.89 g, 35 mmol) in 70 mL of THF was heated in an autoclave with CO (initial pressure 100 atm) for 3 h at 140 °C. The autoclave was cooled, and 5 mL of ethylene glycol was added to the reaction mixture. The mixture was heated at 140 °C under a CO pressure of 70 atm for an additional 4 h. The content of the autoclave was transferred into a flask, and at 0 °C, a mixture of 30 mL of EtOH and 16 mL of 10% NaOH was added, and 45% H_2O_2 (4 mL, 50 mmol) was added dropwise. The mixture was kept for 8 h and refluxed for 10 h, THF was evaporated, and the residue was extracted with Et_2O (2×20 mL) and chromatographed on SiO_2 (Et_2O—hexane, 3 : 1, as the eluent) to give 3.72 g (47%) of compound **4**, m.p. 53—55 °C. Found (%): C, 83.64; H, 8.80. $C_{16}H_{20}O$. Calculated (%):

C, 84.15; H, 8.83. ^{1}H NMR, δ: 1.30—2.40 (m, 13 H, adamantane nucleus); 3.07 (s, 1 H, CHPh); 7.40 (m, 5 H, Ph). ^{13}C NMR, δ: 30.2 and 30.9 (C(5), C(7)); 30.8 (C(4)); 36.5 (C(3)); 36.6 (C(9)); 38.9 and 39.9 (C(6), C(10)); 47.7 (C(8)); 56.6 (C(2)); 77.0 (C(1)); 125.8 (*p*-C, Ph); 127.8 and 129.6 (*o*-C and *m*-C, Ph); 141.8 (*i*-C, Ph). MS, *m*/*z* (I_{rel} (%)): 227 $[M]^+$ (100).

7-Hydroxymethyl-2-phenyl-3-azabicyclo[3.3.1]nonane (7) and 7-(α-hydroxybenzyl)-3-azabicyclo[3.3.1]nonane (8). Complex **1** (0.97 g, 38.8 mmol) in 22 mL of diglyme and I_2 (9.83 g, 38.8 mmol) in 43 mL of diglyme were added simultaneously from two dropping funnels over a period of 1.5 h to a suspension of NaN_3 (7.77 g, 119.5 mmol) in 63 mL of diglyme stirred at 80—85 °C. The mixture was stirred for 0.5 h at the same temperature (during this period, 930 mL of N_2 evolved (80%)). The solvent was evaporated *in vacuo* (35—40 °C, 1 Torr) and the residue was extracted with Et_2O (3×30 mL). The combined ethereal extracts were cooled to 0 °C, 60 mL of 10% NaOH was added, and 15 mL of 30% H_2O_2 was added with stirring. The mixture was stirred for 0.5 h at 0 °C and for 0.5 h at 20 °C and refluxed for 4 h. The ethereal layer was separated and extracted successively with 30 mL of 10% HCl and water (2×50 mL). The aqueous extract was neutralized by NaOH to pH 10 and extracted again with Et_2O (3×20 mL). The organic layers were combined and dried with Na_2SO_4, the solvent was evaporated, and the residue (3.75 g, 42%) was chromatographed on SiO_2 (MeOH—NH_4OH, 15 : 1, as the eluent) to give compounds **7** and **8**.

7-Hydroxymethyl-2-phenyl-3-azabicyclo[3.3.1]nonane (7). Yield 1.49 g (16.5%), thick oil, R_f 0.75. Found (%): C, 77.50; H, 9.47. $C_{15}H_{21}ON$. Calculated (%): C, 77.54; H, 9.54. ^{1}H NMR, δ: 1.25—3.90 (m, 15 H, H bicyclic fragment); 7.10—7.49 (m, 5 H, Ph). ^{13}C NMR, δ: 26.1, 30.2 (C(1), C(5)); 23.1, 30.5, 32.4 (C(6), C(8), C(9)); 32.1 (C(7)); 48.5 (C(4)); 61.1 (C(2)); 69.3 (HCOH); 126.3, 127.8, 126.7, 140.6 (Ph). MS, *m*/*z* (I_{rel} (%)): 231 $[M]^+$ (72).

7-(α-Hydroxybenzyl)-3-azabicyclo[3.3.1]nonane (8). Yield 0.29 g (5%), m.p. 73—75 °C, R_f 0.50. Found (%): C, 77.49; H, 9.57. $C_{15}H_{21}ON$. Calculated (%): C, 77.54; H, 9.54. ^{1}H NMR, δ: 1.25—1.70 (m, 3 H, $H(6)_{ax}$, $H(8)_{ax}$, $H(9)_{ax}$); 1.75—7.49 (m, 6 H, $H(6)_{eq}$, $H(8)_{eq}$, $H(9)_{eq}$, H(1), H(5), H(7)); 2.65—2.85 (q, 4 H, 2 CH_2N); 4.10—4.30 (br.s, 2 H, OH, NH (residual)); 4.60 (s, 1 H, CHOHPh); 7.11—7.41 (m, 5 H, Ph). ^{13}C NMR, δ: 25.8, 26.2 (C(1), C(5)); 26.5, 28.5, 30.7 (C(6), C(8), C(9)); 36.1 (C(7)); 52.6 (C(2), C(4)); 78.9 (HCOHPh); 126.2, 127.8, 126.5, 145.2 (Ph). MS, *m*/*z* (I_{rel} (%)): 231 $[M]^+$ (76).

2-Phenyl-1-azaadamantane (5). ***A.*** A solution of $SOCl_2$ (1.73 mL) in 15 mL of benzene was added with stirring over a period of 0.5 h to a solution of compound **7** (1.65 g, 7.13 mmol) in 25 mL of benzene. The mixture was stirred for 0.5 h at 20 °C, refluxed for 4 h, and worked-up by a standard procedure for amine isolation. The residue (0.5 g) as a thick liquid was chromatographed on SiO_2 (Et_2O—NH_4OH, 99 : 1, as the eluent) to give 0.312 g (1.46 mmol, 20%) of compound **5**, n_D^{20} 1.5579. Found (%): C, 84.10; H, 9.31. $C_{15}H_{19}N$. Calculated (%): C, 84.06; H, 9.41. ^{1}H NMR, δ: 0.90—4.00 (m, 14 H, H adamantane cage); 7.10—7.49 (m, 5 H, Ph). ^{13}C NMR, δ: 26.9, 27.2 (C(5), C(7)); 27.9 (C(3)); 30.9 (C(4)); 37.0 (C(6)); 38.1 (C(10)); 51.7 (C(9)); 60.7 (C(8)); 60.7 (C(2)); 125.8, 126.4, 128.1, 141.6 (Ph). MS, *m*/*z* (I_{rel} (%)): 213 $[M]^+$ (100).

B. A solution of $SOCl_2$ (2.6 mL) in 20 mL of benzene was added with stirring over a period of 0.5 h to a solution of a mixture of compounds **7** and **8** (2.47 g, 10.67 mmol) in 40 mL of benzene. The mixture was stirred for 0.5 h at 20 °C, refluxed for 4 h, and worked-up by the standard procedure for amine isolation to give 0.6 g (2.8 mmol, 27%) of compound **5**, b.p. 105 °C (0.03 Torr), n_D^{20} 1.5582. Found (%): C, 84.10; H, 9.31. $C_{15}H_{19}N$. Calculated (%): C, 84.06; H, 9.41. The ^{1}H and ^{13}C NMR spectra were identical to those presented in the previous procedure. MS, *m*/*z* (I_{rel} (%)): 213 $[M]^+$ (60).

7-Benzylidene-3-azabicyclo[3.3.1]nonane (9). Glacial AcOH (16 mL) was added with stirring to a solution of compound **8** (0.21 g, 0.97 mmol) in 16 mL of concentrated HCl. The extract was neutralized with NaOH to pH 10 and extracted with Et_2O (3×20 mL). The organic layers were combined and dried with Na_2SO_4, and the solvent was evaporated. Sublimation (70 °C, 2 Torr) gave 0.12 g (0.56 mmol, 58%) of compound **9**, m.p. 44 °C (0.03 Torr). Found (%): C, 82.97; H, 9.81. $C_{15}H_{19}N$. Calculated (%): C, 84.06; H, 9.41. ^{1}H NMR, δ: 0.80—3.40 (m, 12 H, H bicyclic fragment); 5.56 (br.s, 1 H, CHPh); 7.10—7.40 (m, 5 H, Ph). ^{13}C NMR, δ: 29.6 (C(1), C(5)); 30.3 (C(9)); 34.2 (C(6), C(8)); 44.3 (C(2), C(4)); 125.0, 126.0 (C(10), *p*-C); 128.3, 128.7 (*o*-C, *m*-C); 140.2, 141.4 (C(7), *i*-C). MS, *m*/*z* (I_{rel} (%)): 213 $[M]^+$ (64).

X-ray diffraction study of compounds 2, 3. Single crystals suitable for X-ray diffraction analysis were prepared by slow evaporation from solutions in $CDCl_3$ (adduct **2**) or by recrystallization from hexane (adduct **3**). The main crystallographic data and refinement parameters for structures **2** and **3** are listed in Table 3. The structures were solved by the direct method and refined in the anisotropic-isotropic full-matrix approximation over F^2. The H atoms in complex **3** were identified from difference electron density syntheses, whereas in complex **2**, these

Table 3. Crystallographic data and structure refinement parameters for **2** and **3**

Parameter	**2**	**3**
Molecular formula	$C_{18}H_{28}B_1N_1$	$C_{20}H_{24}B_1N_1$
M	269.22	289.21
Space group	$P2_1$	$P2_1/n$
Radiation	Mo-Kα (λ = 0.71072 Å)	
Scan mode	θ/2θ	
Diffractometer	«Syntex $P2_1$»	
T/K	193	
a/Å	8.291(5)	9.950(4)
b/Å	11.167(4)	6.539(3)
c/Å	8.685(3)	24.001(9)
β/deg	100.09(4)	94.61(3)
V/Å^3	791.7(6)	1556.5(12)
Z	2	4
d_{calc}/g cm^{-3}	1.129	1.234
$2\theta_{max}$/deg	66	50
The number of independent reflections (over F for reflections with $I > 2\sigma(I)$)	3079	2738
wR_2 (over F^2 for all reflections)	0.0641 (2267)	0.0641 (1922)
	0.1756 (3041)	0.1753 (2703)

atoms were located geometrically. All calculations were carried out on a SHELXTL PLUS program package (Ver. 5.0).

This work was financially supported by the Russian Foundation for Basic Research (Projects Nos. 02-03-32248, 01-03-32465 and 99-03-31125a), the State Foundation for the Support of Leading Scientific Schools (Project No. 00-15-97378), and the "Integratsia" program (Project 234).

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Received March 7, 2002