ISSN 1070-4280, Russian Journal of Organic Chemistry, 2007, Vol. 43, No. 11, pp. 1642–1650. © Pleiades Publishing, Ltd., 2007.
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Carboxamides and Amines Having Two and Three Adamantane Fragments

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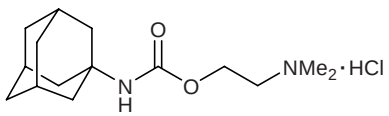
Received October 11, 2006; revised July 31, 2007

Abstract—New carboxamides having two and three adamantane fragments were synthesized from adamantanecarboxylic acid chlorides and adamantane-containing amines. The amides were reduced to the corresponding amines, and the latter were converted into *N*-*p*-nitrophenylsulfonyl and *N*-*p*-tolylsulfonylcarbamoyl derivatives by treatment with *p*-nitrobenzenesulfonyl chloride and *p*-toluenesulfonyl isocyanate, respectively. The structure of the newly synthesized compounds was confirmed by IR and ^{1}H NMR spectroscopy. Some carboxamides turned out to be inactive in the reduction with lithium tetrahydridoaluminate, which was discussed in terms of the results of semiempirical quantum-chemical calculations.

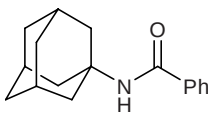
DOI: 10.1134/S1070428007110103

Nowadays, the scope of thorough chemical and biomedical studies includes polyamines that are necessary for the design of medical agents acting on the central nervous system [1, 2]. Polyamines of the adamantane series were not studied. Therefore, the goal of the present work was to synthesize such amines by reduction of the corresponding carboxamides obtained from adamantane-containing amines and adamantanecarboxylic acid chlorides. This approach was applied by us previously to prepare amines containing two bicyclic fragments [3], as well as mono- and diamines having norbornene, epoxynorbornane, and adamantane fragments [4, 5].

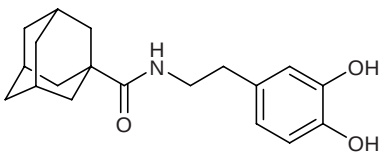
Amines and their derivatives constitute a considerable number of adamantane derivatives that have passed clinical trials and have been introduced into medical practice. Examples are Amantadine, Rimantadine, Adapromine, Memantine, Dimantine, etc., which



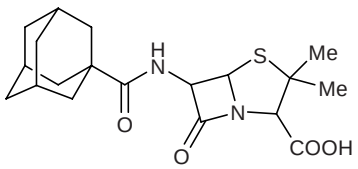
Ia



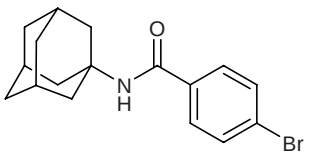
Ib



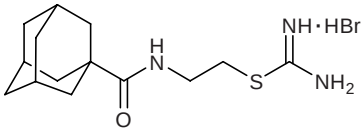
Ic



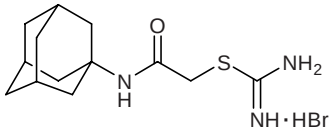
Id



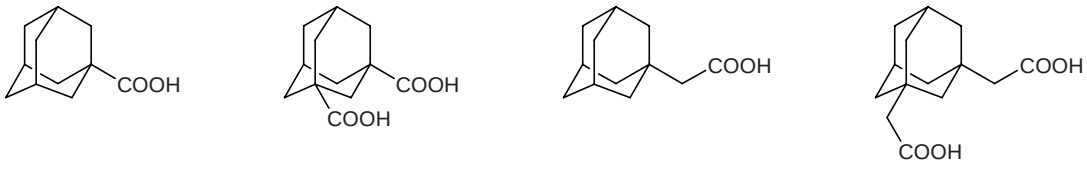
Ie



If



Ig



IIa **IIb** **IIc** **IId**

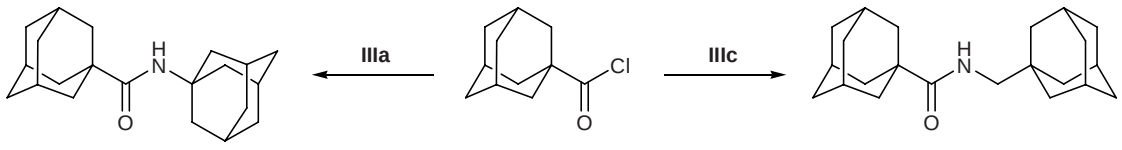
IIIa **IIIb** **IIIc** **IIId**

exhibit anti-influenza, anti-Parkinson, antidepressant, and anti-herpes activity [1, 6]. Specificity of biological action of adamantane derivatives is largely determined by the presence in their molecules of a bulky cage-like fragment [1, 6, 7] whose lipophilicity (hydrophobicity) facilitates direct interaction with biological membranes having a lipid layer, as well as with hydrophobic domains in proteins, including those constituting receptor structures. Both *N*-adamantyl carboxamides, such as Tromantadine (**Ia**) and Bemantine (**Ib**), and adamantanecarboxamides, such as anti-Parkinson Dopamantine (**Ic**) and antibiotic Amantocillin (**Id**), have passed clinical trials [1]. In addition to vast data on biological activity of amides of the adamantane series, high neuropsychotropic activity of amide **Ie** was noted [1]. Analogous biological action of amides derived from adamantanecarboxylic acids and adamantane-containing amines was proved by comparison of hypotensive properties of thiuronium salts **If** and **Ig**; in this case, amide **If** showed a stronger activity which even exceeded that of novocainamide [8].

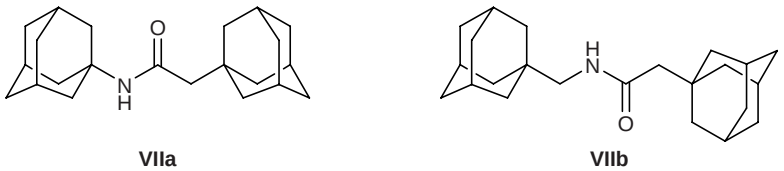
For the synthesis of adamantane-containing amides we used adamantane-1-carboxylic acid (**IIa**), adamantane-1,3-dicarboxylic acid (**IIb**), (1-adamantyl)acetic acid (**IIc**) and adamantane-1,3-diyldiacetic acid (**IId**); the amine components were adamantan-1-amine (**IIIa**), *N*-methyladamantan-1-amine (**IIIb**), 1-adamantylmethanamine (**IIIc**), and 1-(1-adamantyl)ethanamine (**IIId**). Amines **IIIa**–**IIId** were used by us previously to obtain adamatane-containing arensulfonamides, carboxamides, phosphonic amides, ureas, thioureas, and amino alcohols (via reaction with epoxy derivatives) [9]. The reactivity of adamantane-containing amines toward *p*-toluenesulfonyl chloride and diphenyl chlorophosphate was estimated by kinetic methods [10]. Amides having several adamantane fragments were synthesized through intermediate acid chlorides **Va**–**Vd** which were preliminarily isolated [4, 5]. Their reactions with amines were carried out in chloroform in the presence of triethylamine at room temperature. Crystalline amides **VIa** [11] and **VIb** were obtained from adamantane-1-carbonyl chloride (**Va**) (Scheme 1). (1-Adamantyl)acetyl chloride (**Vc**) reacted with amines **IIIa** and **IIIc** to give amides **VIIa** and **VIIb**. Amides **VIIIa**, **VIIIb**, **IXa**, and **IXb** were synthesized by treatment of dicarboxylic acid chlorides **Vb** and **Vd** with the same amines, and the reactions of dichloride **Vd** with amines **IIIb** and **IIId** gave diamides **IXc** and **IXd**, respectively.

In all cases, the reaction conditions were the same (room temperature), regardless of the number of adamantane fragments in the resulting molecule (two or

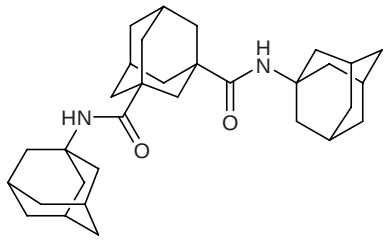
Scheme 1.



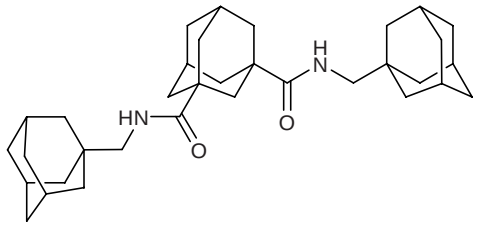
VIa **Va** **VIb**



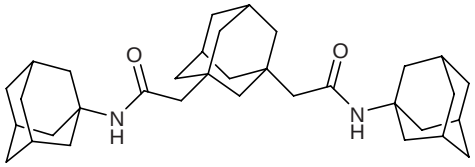
VIIa **VIIb**



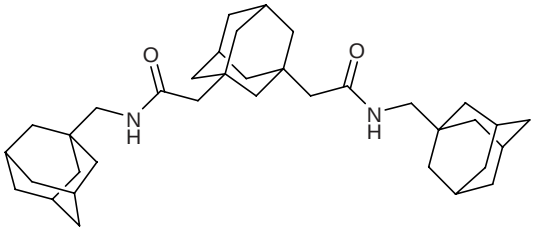
VIIIa



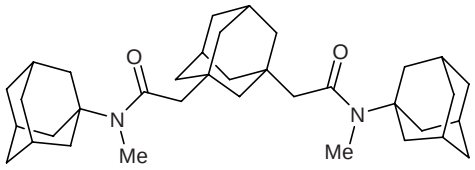
VIIIb



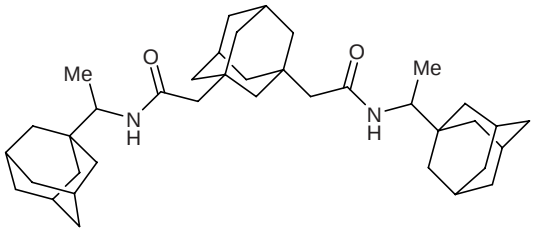
IXa



IXb



IXc

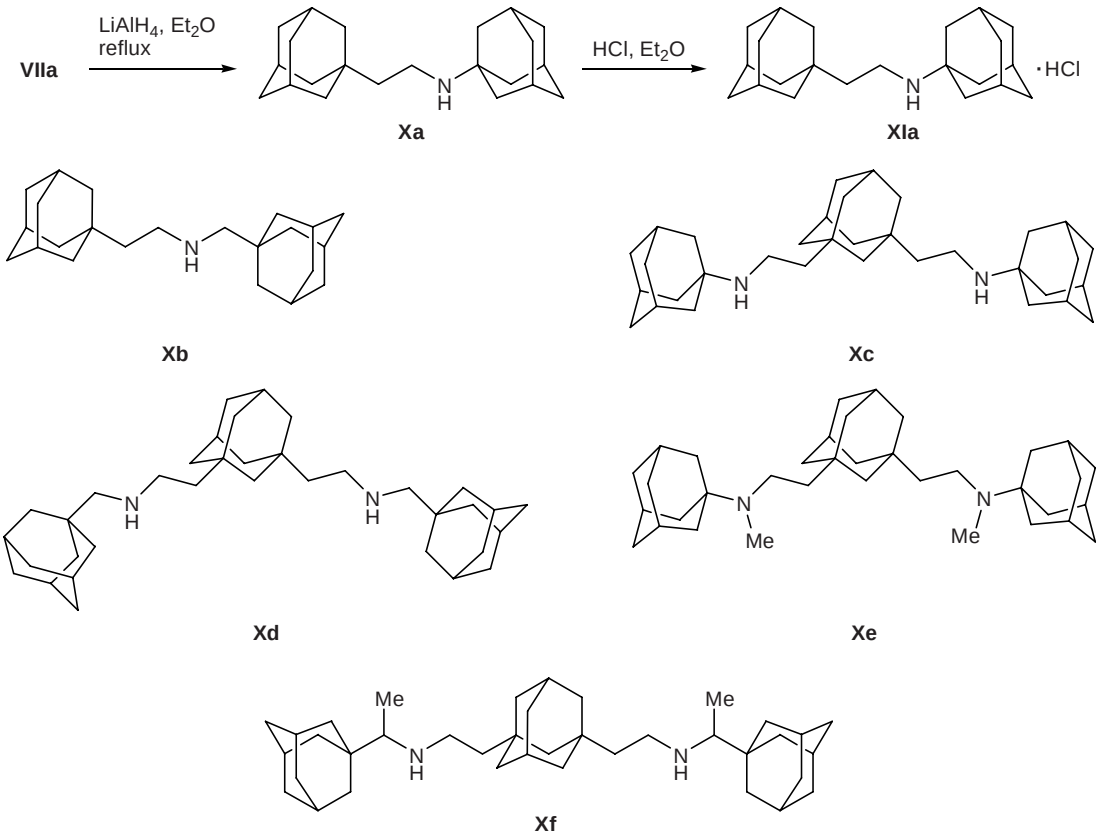


IXd

three) and the presence of additional steric hindrances (methyl group on the nitrogen atom in amide **IXc** or at the neighboring carbon atom in **IXd**). The structure of compounds **VI**–**IX** was confirmed by the IR data. Their IR spectra contained absorption bands in the regions 1650–1622, 1544–1526, and 1273–1270 cm^{-1}, corresponding to stretching vibrations of the carbonyl group (amide I), bending vibrations of the NH group (amide II), and stretching vibrations of the amide C–N bond (amide III) [12, 13]. Stretching vibrations of the secondary NH group gave rise to absorption at 3380–3320 cm^{-1}. In the ^1H NMR spectra of amides **VIa**, **VIb**, **IXb**, and **IXd**, the NH proton resonated in the δ range from 2.09 to 3.18 ppm. In the downfield region (δ 3.40–4.12 ppm) we observed signals from methylene protons in the CH_2CO group of **IXa**, **IXb**, and **IXd**. Signals from the C**H**$_2$NH and C**H**NH protons appeared at δ 2.85–2.95 ppm, and protons in the adamantane fragments were characterized by chemical shifts δ of 1.20–2.10 ppm.

With a view to obtain amines containing several adamantane fragments, we examined reduction of the synthesized amides with lithium tetrahydridoaluminate in boiling diethyl ether. The progress of reactions was monitored by TLC; when the reaction was complete, the mixture was quenched with moist diethyl ether and ice-cold water. According to [14], the reduction of 1 mol of secondary amide requires 0.75 mol of $LiAlH_4$. Taking into account that some excess of the reducing agent is necessary to reduce cage-like amides [15], we used 2 mol of the reagent per mole of monoamide and 4 mol in the reduction of dicarboxamides. Amide **VIa** failed to undergo reduction under the above conditions. Likewise, no reaction occurred in dimethoxyethane at 80°C (the amount of the reducing agent being the same), and initial amide **VIa** was recovered from the reaction mixture. Our further experiments showed that amides **VIb**, **VIIIa**, and **VIIIb** derived from adamantane-1-carboxylic and adamantane-1,3-dicarboxylic acids cannot be reduced to the corresponding amides under the given conditions. Presumably, the reason is that the reaction center (carbonyl group) in their molecules is directly attached to the adamantane framework. By contrast, 1-adamantylacetamides **VIIa** and **VIIb** and adamantane-1,3-diyldiacetamides **IXa** and **IXb** were smoothly reduced to give amines **Xa**–**Xd**; and in some cases the yields of the latter exceeded 90%. The reduction of amides **IXc** and **IXd** obtained from adamantane-1,3-diyldiacetic acid and *N*-methyladamantan-1-amine and Rimantadine showed that the

Scheme 2.



presence of a methyl group on the nitrogen atom or on the neighboring carbon atom does not hinder formation of the corresponding amines **Xe** and **Xf** (Scheme 2).

Amines **Xa**–**Xf** were isolated as oily substances which were purified by conversion into the corresponding hydrochlorides, followed by alkalization, extraction, and removal of the solvent. The R_f values of compounds **Xa**–**Xf** (0.57–0.87; diethyl ether) were higher than those of the initial amides; therefore, their purity can be monitored by TLC. Amines **Xa**–**Xf** were characterized as crystalline hydrochlorides **XIa**–**XId** and **XIf** which were obtained by passing dry hydrogen chloride through a solution of amine **X** in anhydrous diethyl ether. Spots of hydrochlorides **XI** remained at the start of chromatograms after elution.

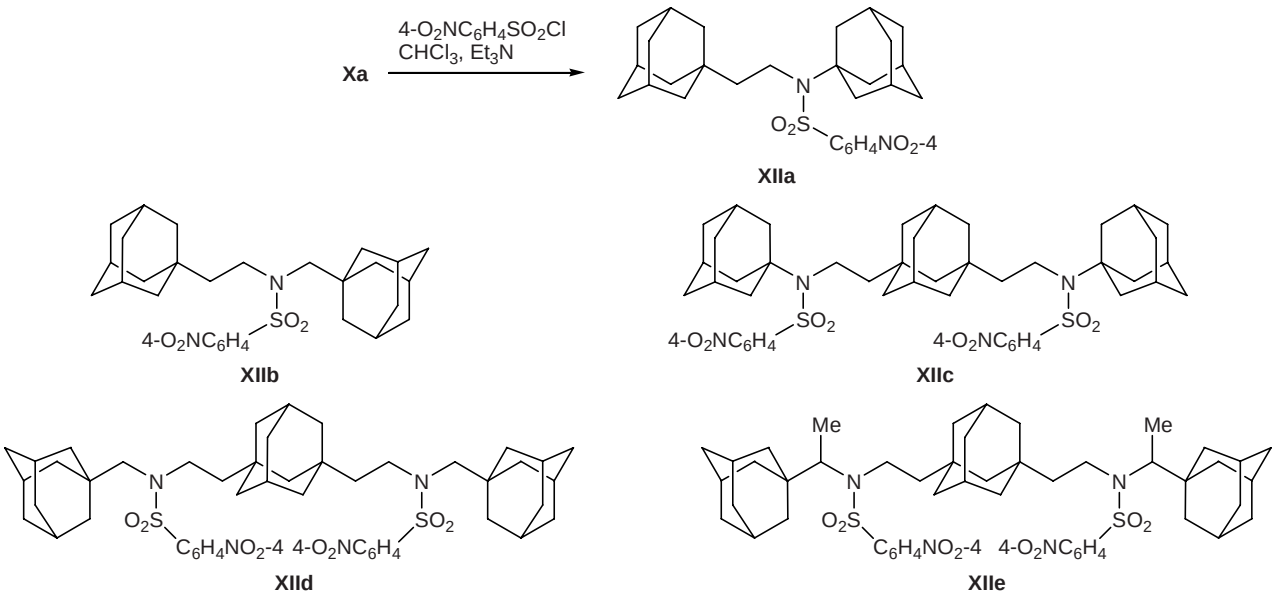
The IR spectra of **Xa**–**Xf** lacked amide I bands but contained absorption bands due to NH stretching vibrations [12, 13]. In the IR spectra of amine hydrochlorides **XI** we observed no absorption assignable to free amino groups; instead, absorption bands in the region 2725–2700 cm^{-1} were present [$\nu_{as}(NH_2)$, $\nu_s(NH_2)$] together with medium-intensity bands at 1440 cm^{-1}, belonging to stretching vibrations of the CH_2N^+ group [12].

The obtained secondary amines were brought into reactions with some electrophilic reagents, namely *p*-nitrobenzenesulfonyl chloride and *p*-toluenesulfonyl isocyanate. Sulfonamides **XIIa**–**XIIe** were obtained in chloroform at room temperature in the presence of an equimolar amount of triethylamine (Scheme 3). In the reactions with diamines **Xc**, **Xd**, and **Xf**, 2 equiv of *p*-nitrobenzenesulfonyl chloride and triethylamine was used. Sulfonamides **XIIa**–**XIIe** were isolated as crystalline or oily substances. Their IR spectra contained absorption bands due to asymmetric and symmetric stretching vibrations of the nitro groups (1560–1545 and 1330–1320 cm^{-1} [12]) and sulfonyl groups (1370–1355 and 1175–1130 cm^{-1}).

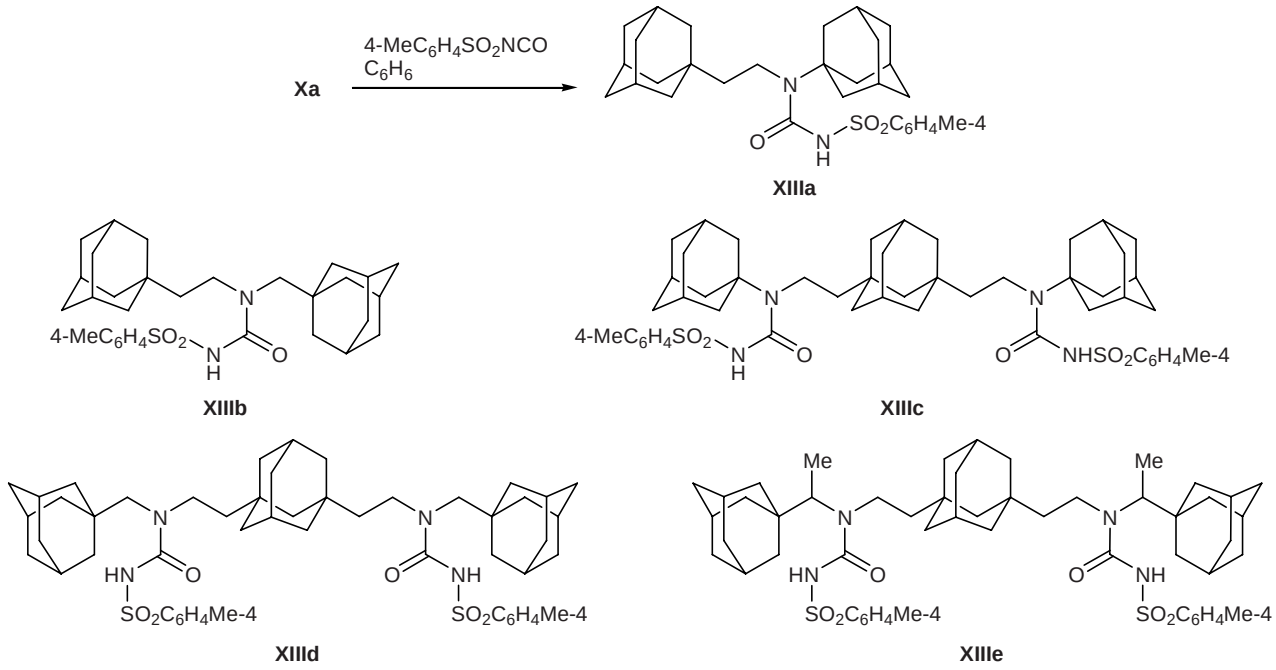
Sulfonylureas **XIIIa**–**XIIIe** were synthesized by reaction of amines **Xa**–**Xd** and **Xf** with *p*-toluenesulfonyl isocyanate in benzene at room temperature. In the IR spectra of crystalline ureas **XIIIa**–**XIIIe** we observed absorption bands from stretching and bending vibrations of the NH (3280–3250, 1560–1540 cm^{-1}), sulfonyl (1355–1350, 1180–1170 cm^{-1}), and carbonyl groups (1650–1645 cm^{-1}) [12, 13].

Although ^1H NMR spectra of adamantane derivatives are not so informative as the spectra of substitut-

Scheme 3.

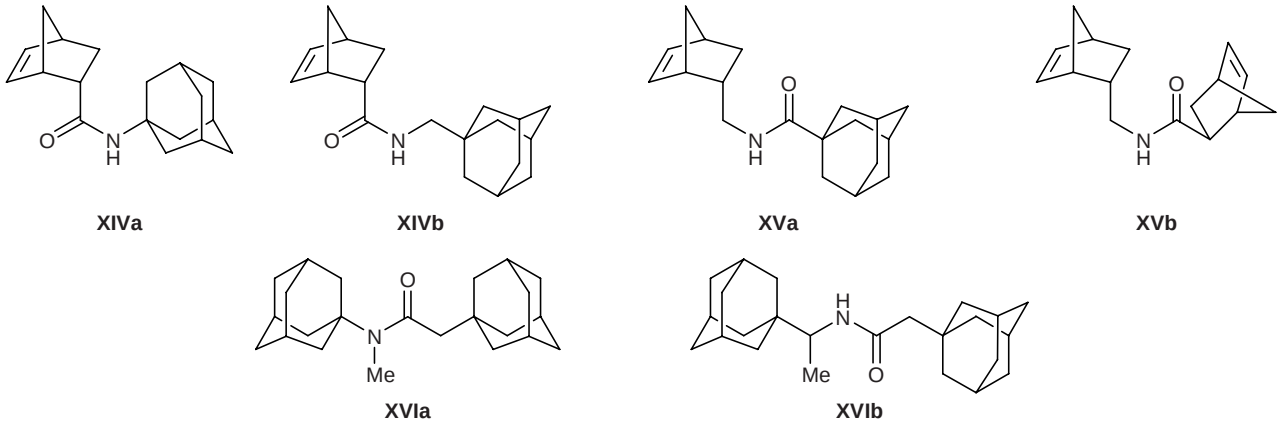


Scheme 4.



ed norbornenes, we examined the spectra of compounds **XIId** and **XIIId**. Sulfonamide **XIId** displayed four-proton multiplets at δ 3.20, 2.87, and 2.05 ppm; the first two signals were assigned to methylene protons at the nitrogen atom. Analogous signals in the spectrum of sulfonylurea **XIIId** are located at δ 3.18, 2.91, and 2.10 ppm. Adamantane protons in both compounds resonated in the regions δ 1.25–1.65, 1.90–1.98, and 2.16 ppm; protons in the *ortho* positions with respect to the nitro and sulfonyl groups gave doublets at δ 8.35, 8.03, and 7.91 ppm; signals from protons in the *ortho* positions with respect to the methyl group were observed at δ 7.29 ppm; and the methyl and NH protons resonated as singlets at δ 2.43 and 4.08 ppm, respectively. The positions of signals and their intensity ratios were consistent with structures including three adamantane fragments.

As noted above, amides **VIa**, **VIb**, **VIIIa**, and **VIIIb** in which the carbonyl group is directly attached to the adamantane framework were not reduced with



XIVa **XIVb** **XVa** **XVb**

XVIa **XVIb**

lithium tetrahydridoaliminate. Such inertness of secondary amides toward $LiAlH_4$ is a fairly rare case, although it was reported for some bis-crown ethers [16]. On the other hand, structurally related amides **XIVa**, **XIVb**, and **XVa** [4, 5] having norbornene and adamantane fragments, as well as amide **XVb** [3] with two norbornene fragments, are known to undergo reduction under the same conditions. With a view to rationalize different behaviors of cage-like amides in the reduction with $LiAlH_4$ we resorted to quantum-chemical calculations which were performed using semiempirical PM3 method [17, 18]. In order to facilitate consideration of conformational properties, instead of adamantane-1,3-diacetamides **IXc** and **IXd** we examined structurally simpler amides **XVIa** and **XVIb** derived from 1-adamantylacetic acid. The results of calculations are given in table. Analysis of these data showed that charges on the carbonyl carbons cannot be regarded as the main factor responsible for different reactivities of the amides, for its variation is insignificant. It is more probable that the reaction is orbital-controlled. The energies of the lowest unoccupied molecular orbitals (E_{LUMO}) decrease in the series **XIVb** > **XVb** > **XIVa** > **XVIa** > **XIIa** > **XVa** > **VIb** > **VIIb** > **XVIb** > **VIa**, which generally corresponds to the reactivity series observed experimentally. In fact, the results of calculations predict ready reduction of amides containing only norbornene (**XVb**) or norbornene and adamantane fragments (**XIVa**, **XIVb**) and low reactivity of amide **VIa**. An exception is the position in the above series of inactive amide **VIb**, which is closer to the middle of the series than to its end. Presumably, the inertness of amides **VIa** and **VIb** results from spatial proximity of two adamantane fragments to the carbonyl group; these fragments exert electron-donating effect and simultaneously create steric hindrances to attack by nucleophile (AlH_4^-) on the electrophilic carbonyl carbon atom.

Calculated (PM3) electronic structure parameters of compounds **VI**, **VII**, and **XIV**–**XVI**

Compound no.	Charges on atoms *q*, a.u.			HOMO		LUMO	
	N	C	O	*E*, eV	localization	*E*, eV	localization
VIa	–0.06	0.25	–0.36	–9.613	N 5.68; O 7.93	1.145	C_{carb} 52.24; O 17.93
VIb	–0.06	0.24	–0.37	–9.564	N 6.93; O 7.71	1.065	C_{carb} 53.77; O 27.26
VIIa	–0.05	0.25	–0.35	–9.662	N 5.19; O 6.34	1.019	C_{carb} 51.88; O 26.86
VIIb	–0.06	0.24	–0.36	–9.612	N 7.92; O 5.09	1.076	C_{carb} 53.31; O 27.17
XIVa	–0.06	0.25	–0.36	–9.633	N 66.17; O 17.11	0.834	C=C 46.92, 44.19
XIVb	–0.06	0.25	–0.36	–9.611	N 66.29; O 16.33	0.746	C=C 47.02, 43.99
XVa	–0.05	0.24	–0.36	–9.606	N 4.76; O 7.01	1.049	C=C 47.20, 45.13
XVb	–0.10	0.27	–0.34	–9.690	N 7.67; O 0.34	0.756	C_{carb} 46.40; O 24.88; C=C 9.16, 8.33
XVIa	–0.09	0.28	–0.35	–9.388	N 68.64; O 10.01	0.972	C_{carb} 55.43; O 28.18
XVIb	–0.06	0.24	–0.36	–9.684	N 70.48; O 15.73	1.096	C_{carb} 53.37; O 26.95

EXPERIMENTAL

The IR spectra were recorded in the range from 4000 to 400 cm^{-1} on a UR-20 spectrometer from samples prepared as thin films (neat) or KBr pellets. The ^1H NMR spectra were measured from solutions in $CDCl_3$ or DMSO-d_6 on a Varian VXR instrument (300 MHz) using tetramethylsilane as internal reference. The progress of reactions was monitored, and the purity of products was checked, by TLC on Silufol $60F_{254}$ plates using diethyl ether as eluent; chromatograms were developed with iodine vapor. Elemental analyses were obtained on a Carlo Erba analyzer.

Adamantanecarboxylic acid amides (*general procedure***).** A solution of 2 mmol of the corresponding acid chloride in chloroform was added dropwise under stirring to a mixture of 2 mmol of amine **IIIa–IIId** and 2 mmol of triethylamine in 5 ml of chloroform, and the mixture was stirred at room temperature until the reaction was complete (TLC). The mixture was treated in succession with water, 5% hydrochloric acid, and water again, the organic phase was separated and dried over anhydrous magnesium sulfate, the solvent was removed, and the residue was purified by recrystallization from aqueous isopropyl alcohol.

***N*-(1-Adamantyl)adamantane-1-carboxamide (VIa).** Yield 55%, mp 242–243°C, R_f 0.26. IR spectrum, ν, cm^{-1}: 3340, 1650, 1531, 1241. ^1H NMR spectrum, δ, ppm: 1.37–2.12 m (30H, Ad), 3.18 s (1H, NH). Found, %: N 4.44. $C_{21}H_{31}NO$. Calculated, %: N 4.47.

***N*-(1-Adamantylmethyl)adamantane-1-carboxamide (VIb).** Yield 52%, mp 270–272°C, R_f 0.74. IR spectrum, ν, cm^{-1}: 3363, 1631, 1527, 1450, 1270. ^1H NMR spectrum, δ, ppm: 1.48–2.08 m (30H, Ad), 2.95 d (2H, C**H**$_2$NH), 2.96 t (1H, NH). Found, %: N 4.35. $C_{22}H_{33}NO$. Calculated, %: N 4.28.

***N*-(1-Adamantyl)(1-adamantyl)acetamide (VIIa).** Yield 53%, mp 235–237°C, R_f 0.38. IR spectrum, ν, cm^{-1}: 3371, 1627, 1565, 1280. Found, %: N 4.06. $C_{22}H_{33}NO$. Calculated, %: N 4.28.

***N*-(1-Adamantylmethyl)(1-adamantyl)acetamide (VIIb).** Yield 57%, mp 210–212°C, R_f 0.65. IR spectrum, ν, cm^{-1}: 3371, 1653, 1560, 1461, 1280. Found, %: N 4.06. $C_{23}H_{35}NO$. Calculated, %: N 4.11.

***N*,*N*′-Bis(1-adamantyl)adamantane-1,3-dicarboxamide (VIIIa).** Yield 59%, mp 191–192°C, R_f 0.32. IR spectrum, ν, cm^{-1}: 3382, 1641, 1533, 1445, 1270. Found, %: N 5.65. $C_{32}H_{46}N_2O_2$. Calculated, %: N 5.71.

***N*,*N*′-Bis(1-adamantylmethyl)adamantane-1,3-dicarboxamide (VIIIb).** Yield 65%, mp 222–223°C, R_f 0.69. IR spectrum, ν, cm^{-1}: 3320, 1625, 1541, 1440, 1265. Found, %: N 5.47. $C_{34}H_{50}N_2O_2$. Calculated, %: N 5.41.

***N*,*N*′-Bis(1-adamantyl)adamantane-1,3-diyldiacetamide (IXa).** Yield 72%, mp 245–246°C, R_f 0.81. IR spectrum, ν, cm^{-1}: 3355, 1640, 1535, 1445, 1270. ^1H NMR spectrum, δ, ppm: 1.23–2.06 m (44H, Ad), 2.09 s (2H, NH), 4.11 s (4H, CH_2CO). Found, %: N 5.45. $C_{34}H_{50}N_2O_2$. Calculated, %: N 5.41.

***N*,*N*′-Bis(1-adamantylmethyl)adamantane-1,3-diyldiacetamide (IXb).** Yield 75%, oily substance, R_f 0.85. IR spectrum, ν, cm^{-1}: 3351, 1635, 1535, 1444, 1271. ^1H NMR spectrum, δ, ppm: 1.19–2.08 m (44H, Ad), 2.94 d (4H, CH_2NH), 3.20 t (2H, NH), 4.05 s and 4.12 s (2H each, CH_2CO). Found, %: N 5.20. $C_{36}H_{54}N_2O_2$. Calculated, %: N 5.13.

***N*,*N*′-Bis(1-adamantyl)-*N*,*N*′-dimethyladamantane-1,3-diyldiacetamide (IXc).** Yield 63%, oily substance, R_f 0.75. IR spectrum, ν, cm^{-1}: 1638, 1442, 1268. Found, %: N 5.23. $C_{36}H_{54}N_2O_2$. Calculated, %: N 5.13.

***N*,*N*′-Bis[1-(1-adamantyl)ethyl]adamantane-1,3-diyldiacetamide (IXd).** Yield 81%, mp 173–175°C, R_f 0.80. IR spectrum, ν, cm^{-1}: 3343, 1654, 1561, 1460, 1270, 769. ^1H NMR spectrum, δ, ppm: 0.91 d (6H, CH_3), 1.43–2.10 m (44H, Ad), 2.85 m (2H, C**H**NH), 3.05 d (2H, NH), 3.40 s and 3.52 s (4H, CH_2CO). Found, %: N 4.95. $C_{38}H_{58}N_2O_2$. Calculated, %: N 4.48.

Reduction of amides VIIa, VIIb, and Xa–Xf (*general procedure***).** A solution of 2 mmol of amide **VIIa**, **VIIb**, or **Xa–Xd** in 10 ml of anhydrous diethyl ether was added dropwise under stirring to a suspension of 4 mmol of lithium tetrahydridoaluminate in 10 ml of anhydrous diethyl ether, and the mixture was stirred for 10 h, maintaining it moderately boiling (TLC). Excess reducing agent was decomposed by treatment with moist diethyl ether and ice water. The organic layer was separated and dried over calcined magnesium sulfate, and the solvent was removed.

***N*-(1-Adamantyl)-2-(1-adamantyl)ethanamine (Xa).** Yield 83%, oily substance, R_f 0.65. IR spectrum, ν, cm^{-1}: 3301, 1570, 1462, 1370. Found, %: N 4.55. $C_{22}H_{35}N$. Calculated, %: N 4.47. Hydrochloride **XIa** was obtained by passing dry hydrogen chloride through a solution of amine **Xa** in diethyl ether. Yield 84%, mp 250°C. IR spectrum, ν, cm^{-1}: 2710, 1465.

***N*-(1-Adamantylmethyl)-2-(1-adamantyl)ethanamine (Xb).** Yield 90%, oily substance, R_f 0.88. IR spectrum, ν, cm^{-1}: 3354, 1460, 1361, 1058. Found, %:

N 4.20. $C_{23}H_{37}N$. Calculated, %: N 4.28. Hydrochloride **XIb**: yield 73%, mp 231–233°C. IR spectrum, ν, cm^{-1}: 2700, 1460.

***N,N′*-Bis(1-adamantyl)-2,2′-(adamantane-1,3-diyl)diethanamine (Xc).** Yield 91%, oily substance, R_f 0.62. IR spectrum, ν, cm^{-1}: 3295, 1581, 1455, 1370, 1115. Found, %: N 5.78. $C_{34}H_{54}N_2$. Calculated, %: N 5.71. Hydrochloride **XIc**: yield 91%, mp 230–231°C. IR spectrum, ν, cm^{-1}: 2710, 1465.

***N,N′*-Bis(1-adamantylmethyl)-2,2′-(adamantane-1,3-diyl)diethanamine (Xd).** Yield 91%, oily substance, R_f 0.83. IR spectrum, ν, cm^{-1}: 3345, 1571, 1460, 1360, 1119. Found, %: N 5.53. $C_{36}H_{58}N_2$. Calculated, %: N 5.40. Hydrochloride **XId**: yield 83%, mp 225–227°C. IR spectrum, ν, cm^{-1}: 2705, 1464.

***N,N′*-Bis(1-adamantyl)-*N,N′*-dimethyl-2,2′-(adamantane-1,3-diyl)diethanamine (Xe).** Yield 89%, oily substance, R_f 0.55. IR spectrum, ν, cm^{-1}: 1480, 1380, 1355, 1120. Found, %: N 5.51. $C_{36}H_{58}N_2$. Calculated, %: N 5.40. Hydrochloride **XIe**: yield 85%, oily substance. IR spectrum, ν, cm^{-1}: 2700, 1460.

***N,N′*-Bis[1-(1-adamantyl)ethyl]-2,2′-(adamantane-1,3-diyl)diethanamine (Xf).** Yield 94%, oily substance, R_f 0.57. IR spectrum, ν, cm^{-1}: 3325, 1564, 1460, 1170. Found, %: N 5.23. $C_{38}H_{62}N_2$. Calculated, %: N 5.13.

Sulfonamides XIIa–XIIe (*general procedure*). A solution of 0.2 mmol of *p*-nitrobenzenesulfonyl chloride in 6 ml of chloroform was added dropwise under stirring at room temperature to a mixture of 0.2 mmol of amine **Xa**–**Xd** or **Xf** and 0.2 mmol of triethylamine in 10 ml of anhydrous chloroform, and the mixture was stirred until the reaction was complete (TLC). The mixture was then treated with water, 15% hydrochloric acid, and water again, the organic phase was separated and dried over anhydrous magnesium sulfate, the solvent was removed, and the residue was purified by recrystallization from aqueous isopropyl alcohol.

***N*-(1-Adamantyl)-*N*-[2-(1-adamantyl)ethyl]-4-nitrobenzenesulfonamide (XIIa).** Yield 56%, mp 118–120°C, R_f 0.73. IR spectrum, ν, cm^{-1}: 1559, 1465, 1362, 1184, 1130. Found, %: N 5.70. $C_{28}H_{38}N_2O_4S$. Calculated, %: N 5.62.

***N*-(1-Adamantylmethyl)-*N*-[2-(1-adamantyl)ethyl]-4-nitrobenzenesulfonamide (XIIb).** Yield 64%, oily substance, R_f 0.56. IR spectrum, ν, cm^{-1}: 1558, 1460, 1361, 1325, 1190, 1131. Found, %: N 5.40. $C_{29}H_{40}N_2O_4S$. Calculated, %: N 5.47.

***N,N′*-Bis(1-adamantyl)-*N,N′*-[2,2′-(adamantane-1,3-diyl)diethylene]bis(4-nitrobenzenesulfonamide) (XIIc).** Yield 53%, mp 138–140°C, R_f 0.91. IR spectrum, ν, cm^{-1}: 1545, 1460, 1355, 1321, 1200, 1140. Found, %: N 6.63. $C_{46}H_{60}N_4O_8S_2$. Calculated, %: N 6.51.

***N,N′*-Bis(1-adamantylmethyl)-*N,N′*-[2,2′-(adamantane-1,3-diyl)diethylene]bis(4-nitrobenzenesulfonamide) (XIId).** Yield 67%, oily substance, R_f 0.82. IR spectrum, ν, cm^{-1}: 1550, 1465, 1366, 1328, 1175. Found, %: N 6.20. $C_{48}H_{64}N_4O_8S_2$. Calculated, %: N 6.31.

***N,N′*-Bis[1-(1-adamantyl)ethyl]-*N,N′*-[2,2′-(adamantane-1,3-diyl)diethylene]bis(4-nitrobenzenesulfonamide) (XIIe).** Yield 62%, oily substance, R_f 0.78. IR spectrum, ν, cm^{-1}: 1550, 1464, 1361, 1328, 1193, 1130. Found, %: N 6.01. $C_{50}H_{68}N_4O_8S_2$. Calculated, %: N 6.11.

Sulfonylureas XIIIa–XIIIe (*general procedure*). Amine **Xa**–**Xd** or **Xf**, 0.2 mmol, was dissolved in 5 ml of benzene, 0.2 mmol of *p*-toluenesulfonyl isocyanate was added at room temperature, and the mixture was stirred until the reaction was complete (TLC). The precipitate was filtered off, washed with benzene on a filter, dried, and recrystallized from benzene–hexane.

***N*-(1-Adamantyl)-*N*-[2-(1-adamantyl)ethyl]-*N′*-(4-tolylsulfonyl)urea (XIIIa).** Yield 68%, mp 92–93°C, R_f 0.92. IR spectrum, ν, cm^{-1}: 3274, 1655, 1545, 1460, 1351, 1170. Found, %: N 5.56. $C_{30}H_{42}N_2O_3S$. Calculated, %: N 5.49.

***N*-[2-(1-Adamantyl)ethyl]-*N*-(1-adamantylmethyl)-*N′*-(4-tolylsulfonyl)urea (XIIIb).** Yield 70%, mp 93–94°C, R_f 0.78. IR spectrum, ν, cm^{-1}: 3268, 1650, 1560, 1460, 1355, 1170. Found, %: N 5.40. $C_{31}H_{44}N_2O_3S$. Calculated, %: N 5.34.

***N*^{1},*N*^{2}-[2,2′-(Adamantane-1,3-diyl)diethylene]bis-[*N*-(1-adamantyl)-*N′*-(4-tolylsulfonyl)urea] (XIIIc).** Yield 74%, mp 90–91°C, R_f 0.43. IR spectrum, ν, cm^{-1}: 3255, 1651, 1541, 1460, 1350, 1170. Found, %: N 6.45. $C_{50}H_{68}N_4O_6S_2$. Calculated, %: N 6.33.

***N*^{1},*N*^{2}-[2,2′-(Adamantane-1,3-diyl)diethylene]bis-[*N*-(1-adamantylmethyl)-*N′*-(4-tolylsulfonyl)urea] (XIIId).** Yield 71%, mp 96–97°C, R_f 0.58. IR spectrum, ν, cm^{-1}: 3261, 1650, 1561, 1465, 1355, 1171. Found, %: N 6.25. $C_{52}H_{72}N_4O_6S_2$. Calculated, %: N 6.14.

***N*^{1},*N*^{2}-[2,2′-(Adamantane-1,3-diyl)diethylene]bis-{*N*-[1-(1-adamantyl)ethyl]-*N′*-(4-tolylsulfonyl)urea}

(XIIIe). Yield 81%, mp 92–94°C, R_f 0.65. IR spectrum, ν, cm^{-1}: 3281, 1660, 1555, 1470, 1362, 1173. Found, %: N 6.10. $C_{54}H_{76}N_4O_6S_2$. Calculated, %: N 5.96.

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