Russian Journal of Organic Chemistry, Vol. 38, No. 11, 2002, pp. 1606–1614. Translated from Zhurnal Organicheskoi Khimii, Vol. 38, No. 11, 2002, pp. 1661–1670.

Reactions of *p*-Nitrophenyloxirane with Amines Containing Fragments with Bicyclic Skeleton

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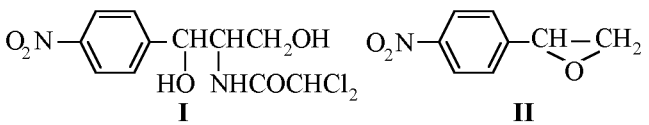
Received July 7, 2001

Abstract—Reactions of *p*-nitrophenyloxirane with amines containing fragments with bicyclic skeleton of norbornene, norbornane, epoxynorbornane (stereoisomeric *exo*- and *endo*-5-aminomethylbicyclo[2.2.1]hept-2-enes, *N*-benzyl-*endo*-5-aminomethylbicyclo[2.2.1]hept-2-ene, *endo*-5-(2-aminoethyl)bicyclo[2.2.1]hept-2-ene, stereoisomeric *exo*- and *endo*-2-aminomethylbicyclo[2.2.1]heptanes, 2-(1-aminoethyl)bicyclo[2.2.1]-heptane, *exo*-5-aminomethyl-*exo*-2,3-epoxybicyclo[2.2.1]heptane) were investigated. The aminolysis of *p*-nitrophenyloxirane occurred regioselectively according to Krasusky rule as was proved by ^{1}H and ^{13}C NMR data. As shown by ^{1}H and ^{13}C NMR spectroscopy the oxyalkylation product obtained from *N*-benzyl-*endo*-5-aminomethylbicyclo[2.2.1]hept-2-ene was composed of two diastereomers originating from the presence of a chiral nitrogen atom in the rear part of the rigid bicyclic skeleton. New products of amino groups transformation in the molecules of hydroxyamines were obtained by reaction with *p*-methylbenzoyl chloride and *p*-nitrophenylsulfonyl chloride. Regioselectivity of the attack of electrophilic reagents on the nitrogen in the hydroxyamines was confirmed by IR and ^{1}H NMR spectra of the products. The data on pharmacological activity tests of *N*-2-hydroxyethyl(*p*-nitrophenyl)-5-aminomethylbicyclo[2.2.1]hept-2-ene are reported.

A lot of antibiotics from aromatic series is currently known. The most important among them, chloramphenicol or Levomycetin (**I**), contains a structural fragment related to *p*-nitrophenyloxirane (**II**) [1].



I **II**

The *p*-nitrophenyl group significantly affects the antibiotic activity first of all by its electronic character. This fact was proved by comparative investigation of analogs with different substituents in the p-position of the benzene ring [1]. The biological activity of derivatives turned epoxide **II** into a promising synthon that was studied in detail by various spectral methods [2]. Although epoxide **II** is usually prepared by halohydrin procedure [3, 4], an epoxidizing method was recently developed consisting in reacting *p*-nitrostyrene with dimethyldioxirane that provided epoxide **II** in 95% yield. Among the reactions of epoxide **II** are described reduction [3, 5], and also aminolysis. The latter consisting in treating epoxide **II** with water solution of ammonia is the first stage of its transformation into Levomycetin [6]. A large group of *p*-nitrophenylethanolamine derivatives was obtained by treating epoxide **II** in anhydrous alcohol with threefold or greater excess of amines [7].

Although as amines were tested ethylenimines [8] and 2-mercapto-4,5-diphenyldiazole [9], still many amines capable of forming biologically active hydroxyamines were not studied in this respect. The goal of this study was investigation of reaction between *p*-nitrophenyloxirane with amines **III**–**VIII** containing skeleton fragments of norbornene and norbornane. Into the first group of amines are included *exo*- and *endo*-5-aminomethylbicyclo[2.2.1]hept-2-enes (**IIIa, b**), *N*-benzyl-*endo*-5-aminomethylbicyclo-[2.2.1]hept-2-ene (**IV**), and *endo*-5-(2-aminoethyl)-bicyclo[2.2.1]hept-2-ene (**V**). The group of saturated bicyclic amines contains *exo*- and *endo*-2-aminomethylbicyclo[2.2.1]heptanes (**VIa, b**), and 2-(1-aminoethyl)bicyclo[2.2.1]heptane (**VII**). For comparison also an epoxy derivative of amine **IIIa**, *exo*-5-aminomethyl-*exo*-2,3-epoxybicyclo[2.2.1]heptane (**VIII**) was also studied. Stereoisomeric amines **IIIa, b** were prepared by reduction with lithium aluminum hydride [10] of individual *exo*- and *endo*-5-cyanobicyclo[2.2.1]hept-2-enes (**IXa, b**) which in their turn were isolated by fractional distillation from the adduct of cyclopentadiene with acrylonitrile [11].

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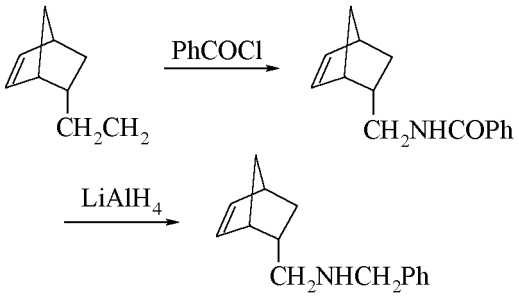
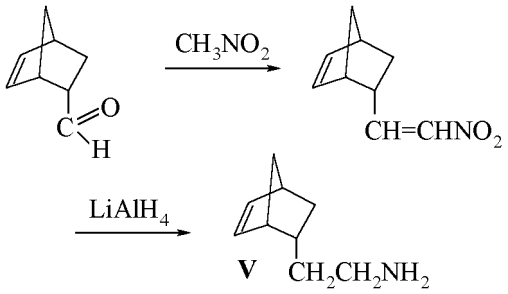
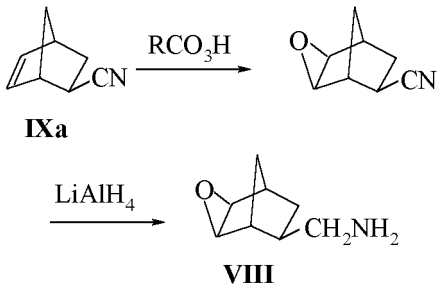


The same nitriles by hydrogenation on nickel catalyst in the presence of ammonia furnished stereoisomeric saturated amines **VIa, b**. Amine **IV** obtained from compound **IIIb** [13] was selected to study the effect of electronic and steric characteristics of benzyl group on the course of reaction with epoxide **II**.

Amine **V** was synthesized along modified procedure [14] in keeping with a scheme given below.

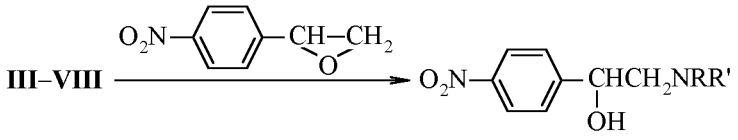


The synthesis of epoxyamine **VIII** was described in [15] and was carried out using the stereoisomerically homogeneous nitrile **IXa**.



Aminolysis of epoxide **II** with amines **III**–**VIII** was carried out at equimolar reagents ratio in 2-propanol solution at room temperature with monitoring by TLC. Aminoalcohols were obtained containing skeleton fragments of norbornene, norbornane, and epoxynorbornane **X**–**XV**.

The characteristics of aminoalcohols with bicyclic fragments are reported in Table 1. Save the oily product **XI** all the other compounds are crystalline substances with R_f in 0.45–0.82 range. In the IR spectra the bands are observed of symmetric and asymmetric vibrations of nitro group (1535–1520, 1360–1340 cm^{-1}), and also of hydroxy group and the N–H bond in the secondary amines (3400–3100 cm^{-1}); however the exact assignment of the bands is dif-



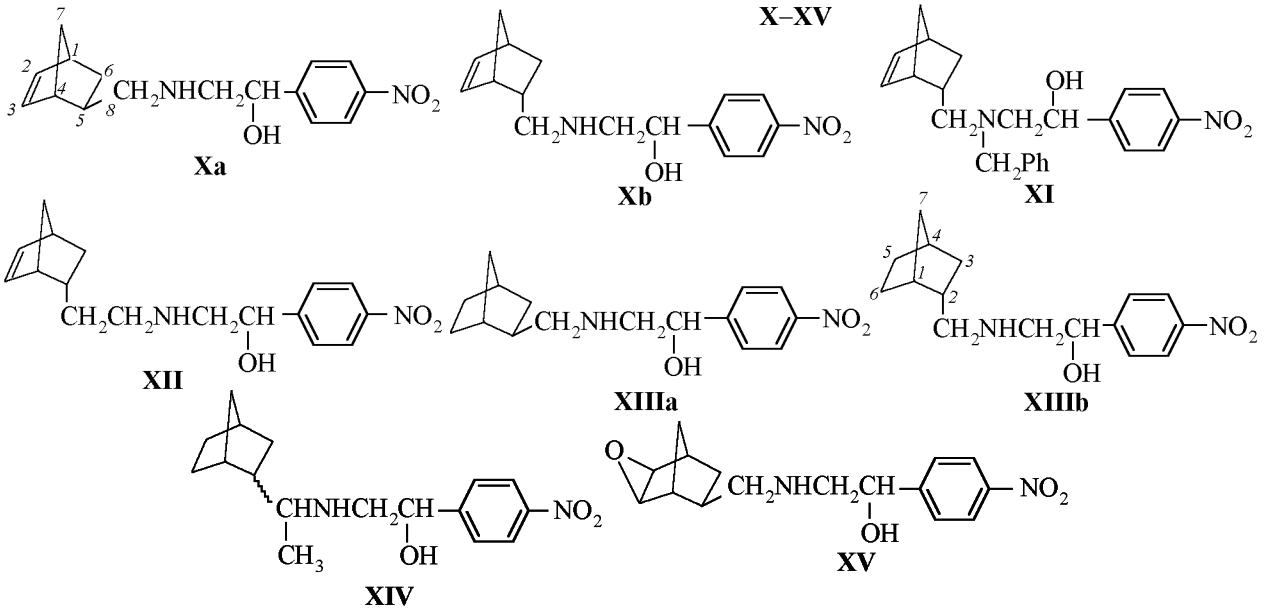


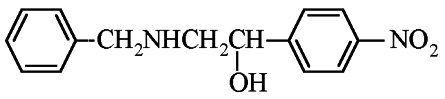
Table 1. Reaction products obtained from *p*-nitrophenyloxirane and amines with bicyclic fragments **X**–**XV**

Compd. no.	Yield, %	mp, °C	R_f, ether	IR spectrum, cm^{-1}	Found, %			Formula	Calculated, %		
					C	H	N		C	H	N
Xa	79.4	125–126	0.79	3388, 3264, 3032, 1600, 1524, 1330, 1102, 800, 696	66.64	6.99	9.68	$C_{16}H_{20}N_2O_3$	66.67	6.94	9.72
Xb	84.2	150–151	0.68	3374, 3266, 3030, 1602, 1520, 1342, 1104, 856, 722	66.63	6.90	9.69	$C_{16}H_{20}N_2O_3$	66.67	6.94	9.72
XI	82.4	Oil[a]	0.82	3462, 3061, 1602, 1534, 1359, 1228, 1118, 708			7.31	$C_{23}H_{26}N_2O_3$	73.02	6.88	7.41
XII	67.4	155–156.5	0.66	3430, 3266, 3054, 1535, 1348, 1240, 1120, 713			9.20	$C_{17}H_{22}N_2O_3$	67.55	7.28	9.27
XIIIa	79.6	79.0–80.5	0.63	3368, 3120, 1610, 1532, 1354, 1115			9.61	$C_{16}H_{22}N_2O_3$	66.21	7.59	9.65
XIIIb	88.6	111–113	0.45	3355, 3110, 1612, 1530, 1352, 1116	66.18	7.51	9.58	$C_{16}H_{22}N_2O_3$	66.21	7.59	9.65
XIV	90.9	119–120	0.64	3325, 3111, 3090, 1530, 1352, 1088	67.03	7.83	9.14	$C_{17}H_{24}N_2O_3$	67.10	7.89	9.21
XV	74.8	138–140	0.54	3410, 3251, 3080, 1640, 1524, 1320, 1130, 870, 715	63.11	6.53	9.15	$C_{16}H_{20}N_2O_4$	63.16	6.58	9.21

[a] For compound **XI** n_D^{45} 1.5718.

ficult. In the spectra appear the bands of unsaturated moieties (ν =C–H 3060–3030 cm^{-1}) that in the spectra of compounds **XIII**–**XV** are attributed to the vibrations of the aromatic fragment, and in the spectra of hydroxyamines **X**–**XII** correspond also to the vibrations of C–H at the strained double bond.

The ^1H NMR spectra of compounds **Xa, b, XI** were far more informative. The assignment of signals from the aminoalcohol moiety was done with the use of the spectrum of compound **XVI** obtained by aminolysis of epoxide **II** with benzylamine under conditions described above.



XVI

The parameter of signals from the protons at carbon atoms attached to hydroxy and amino groups and to phenyl substituent in the molecules **Xa, b, XI, XVI** are listed in Table 2. In the spectra recorded in DMSO from products of reaction with primary amines **Xa, b, XVI** appear doublets of protons from hydroxy group (3.10–2.82 ppm) and triplets of protons from amino group (2.30–2.60 ppm) confirming that amines give with the oxirane 1:1 adducts. The position of the three one-proton signals (one in the 4.71–4.77 ppm region and two at 2.20–2.95 ppm) evidences that the epoxy ring opens in keeping with Krasusky rule [16]. The regioselective course of the reaction conforming to the rules of the bimolecular nucleophilic substitution originates first of all from the nature of the reaction medium and also from the structural features of the epoxide with a spatially accessible terminal carbon in the epoxy ring. The presence of a *p*-nitrophenyl substituent is liable to destabilize additionally the transition state that might result in the anti-Krasusky products [17].

The spectrum of compound **XI** unlike those mentioned above reveals the presence of two kinds of molecules with close but not identic values of the chemical shifts from protons neighboring with the hydroxy group and of methylene group protons in the benzyl substituent. In the ^{13}C NMR spectrum of hydroxyamine **XI** is also observed double set of signals, in particular, the doubled signal from the methylene group linked to nitrogen (59.59 and 59.32 ppm) (Table 3).

The presence of two stereoisomers in the sample of hydroxyamine **XI** is obvious from the analysis of ^1H signals from the protons belonging to the skeleton of the molecule. In Table 4 are presented doubled signals of protons H^8 and H^6, in particular of H^{6n} spatially close to the *endo*-oriented substituent of hydroxyamine **XI** (the chemical shifts of protons H^{6n} are 0.59 and 0.43 ppm). Notably different are the chemical shifts of the olefin protons; in one of the stereoisomers the resonance is observed at 5.6–5.8 ppm that is uncommon for substituted norbornenes. It is presumable that the displacement of the

Table 2. Fragments of ^{1}H NMR spectra of aminolysis products of *p*-nitrophenyloxirane **Xa, b, XI, XVI**, δ, ppm, coupling constants, Hz

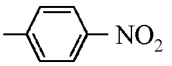
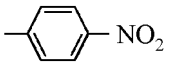
Compd. no.	C<u>H</u>–OH *X*	C<u>H$_2$</u>–N (*A*, *B*)	C<u>H$_2$</u>–Ph	CH$_2$–<u>Ph</u>		NH, OH
Xa	**4.75,** $^3J_{XA}$ 9.2, $^3J_{XB}$ 3.8	2.70, 2.95, $^2J_{AB}$ 12.2	–	–	8.12, 7.53, ^3J 8.8	2.30, 2.96
Xb	**4.71,** $^3J_{XA}$ 9.2, $^3J_{XB}$ 3.8	2.33, 2.84, $^2J_{AB}$ 11.2	–	–	8.17, 7.51, ^3J 8.8	2.52, 3.10
XIA, B	**4.71,** $^3J_{XA}$ 9.9, $^3J_{XB}$ 4.3 4.77, $^3J_{XA}$ 10.5, $^3J_{XB}$ 3.6	2.64, 2.20–2.40, $^2J_{AB}$ 12.9, $^3J_{AX}$ 10.5	3.97, 3.51, ^2J 13.3 3.84, 3.37, ^2J 13.3	7.10–7.20 (5H)	8.14, 7.43, ^3J 8.8	2.40–2.65 2.70–2.85
XVI	**4.77,** $^3J_{XA}$ 9.0, $^3J_{XB}$ 3.7	2.66, 2.95, $^2J_{AB}$ 12.3	3.84, 3.78, ^2J 13.3	7.32 (5H)	8.16, 7.49, ^3J 8.6	2.60, 2.82

Table 3. Fragments of ^{13}C NMR spectra of compounds **Xa, b, XI, XVI**, δ, ppm

Compd. no.	<u>C</u>H–OH	<u>C</u>H$_2$–N	<u>C</u>H$_2$–Ph	CH$_2$<u>Ph</u>	
Xa	70.77	57.16	–	–	150.39, 147.46, 127.70, 123.84
Xb	70.67	57.21	–	–	150.47, 147.44, 126.68, 123.81
XIA, B	68.85 68.47	49.73 49.46	59.59 59.32	138.24, 128.63, 128.60, 127.61	150.39, 147.45, 126.56, 123.65
XVI	70.76	53.38	56.05	139.54, 128.66, 128.18, 127.42	150.13, 147.42, 126.58, 123.63

signals is caused by a magnetically anisotropic influence of the structural fragments in the *endo*-oriented substituent, probably of the benzene ring in the CH_2Ph group (Table 4).

The double set of signals observed on various nuclei may be ascribed to the presence in the sample of compound **XI** of diastereomers **XIA, XIB** with chiral atoms of carbon in the skeleton and of nitrogen. The diastereomers might arise as a result of alternative by stereochemistry attack of epoxide **II** molecules on the nitrogen in amine **IV**; the stability and a high barrier to inversion for the isomers is probably due to the heavy sterical loading on the nitrogen atom, and also by additional spatial shielding of the arising chiral center with the norbornene skeleton for the tertiary amino group is located in the rear (endo) part thereof.

In Table 4 are also given the chemical shifts and coupling constants of the protons attached to carbon skeleton of hydroxyamines **Xa, b**. The difference in the spectra of these stereoisomers are also seen of Figs. 1, 2. The comparison of proton spectra (Table 4, Fig. 1) reveals the common difference in the spectra of *exo*- and *endo*-isomers that has been previously found in isomeric sulfonamides, ureas, and carboxamides of norbornene series [10, 13, 18]: significant distinctions are observed in resonances of olefin protons (H^2, H^3), bridgehead protons (H^1, H^4), and also protons linked to C^6 atom. As in the earlier described cases, in the *endo*-isomer **Xb** as compared with *exo*-isomer was observed stronger nonequivalence of H^2, H^3 protons and weaker nonequivalence of H^1, H^4 protons. In the spectrum of *endo*-isomer **Xb** the signal from H^{6n} proton appears at 0.52 ppm, and the similar signal in the spectrum of *exo*-isomer **Xa** is located at 1.12 ppm (Fig. 1).

The difference was also revealed in the ^{13}C NMR spectra of stereoisomeric aminoalcohols **Xa, b** (Fig. 2). As with the other stereoisomeric substituted norbornenes first of all are dissimilar the signals of olefin carbons C^2 and C^3 (136.96 and 136.54 ppm in the spectrum of *exo*-isomer **Xa**, 137.76 and 132.14 in the spectrum of *endo*-isomer **Xb**), and also those of carbon nuclei C^6, of the bridge carbons (C^7) and of substituent (C^8). In particular, the chemical shifts of bridging carbon atoms are 45.58 and 49.89 ppm for *exo*- and *endo*-isomers respectively; the difference is

Table 4. Parameters of ^{1}H NMR spectra of norbornene fragments of compounds **Xa, b, XI**, δ, ppm, coupling constants, Hz

Compd. no.	H^1	H^2, H^3	H^4	H^5	H^{6x}	H^{6n}	H^{7s}, H^{7a}	H^{8A}, H^{8B}
Xa	2.80	6.05	2.61	1.51	1.18, $^2J_{6x,6n}$ 12.0	1.12	1.31, 1.28, $^2J_{7s,7a}$ 8.0	≈2.62
Xb	2.81	6.13, 5.89, $^3J_{2,3}$ 5.6, $^3J_{2,1}$ 3.0, $^3J_{3,4}$ 3.0	2.78	2.18	1.84, $^2J_{6x,6n}$ 11.4, $^3J_{6x,5}$ 8.6, $^3J_{6x,1}$ 3.6	0.52, $^3J_{6n,5}$ 4.1, $^4J_{6n,7s}$ 2.2	1.42, 1.22, $^2J_{7s,7a}$ 8.0	2.50–2.60
XIA, B	2.77	6.04–6.10	2.93	≈2.35	1.88, $^2J_{6x,6n}$ 11.4, $^3J_{6x,5}$ 8.8, $^3J_{6x,1}$ 4.0	0.59, $^3J_{6n,5}$ 4.5, $^4J_{6n,7s}$ 2.7	1.47, 1.27, $^2J_{7s,7a}$ 8.2	2.20–2.60
	2.80	5.80, 5.62, $^3J_{2,3}$ 5.7, $^3J_{2,1}$ 2.7, $^3J_{3,4}$ 2.9	2.77	≈2.35	1.85, $^2J_{6x,6n}$ 11.4, $^3J_{6x,5}$ 9.0, $^3J_{6x,1}$ 4.1	0.43, $^3J_{6n,5}$ 4.3, $^4J_{6n,7s}$ 2.7	1.42, 1.26, $^2J_{7s,7a}$ 8.2	2.20–2.60

just like that observed in the previously described spectra of stereoisomeric substituted norbornenes [13, 18, 19].

The structure of hydroxyamine **XIIIb** was also confirmed by ^{1}H and ^{13}C NMR spectra. In its ^{1}H NMR spectrum appear the key signals of protons near the hydroxy group (4.78 ppm) and amino group (2.99 and 2.67 ppm) confirming that the opening of the epoxy ring by amine **VIb** occurs in keeping to Krasusky rule. The corresponding carbons give signals in the ^{13}C NMR spectrum at 70.66 and 57.27 ppm, the methylene and methine carbons of the skeleton appear as signals at 52.41, 38.91, 35.62, 30.33, 22.84 and 40.57, 38.78, 35.70 ppm respectively. In the ^{1}H NMR spectrum of compound **XIIIb** are observed all the proton signals from the saturated norbornane skeleton: equivalent bridgehead protons H^1, H^4 (2.17 ppm), bridge protons H^{7s}, H^{7a} (1.30 ppm), proton at carbon atom C^2, linked to the substituent (1.94 ppm), and protons H^{3x} and H^{3n} (1.72 and 0.62 ppm), protons of the exocyclic fragment H^{8A}, H^{8B} (2.55–2.65 ppm). In contrast to the spectrum of unsaturated analog **Xb** here the anisotropic influence of the exocyclic bond C^5–C^8 is spread not only to H^{3n} atom but also to more remote H^{6n} (1.06 ppm).

The compounds synthesized contain several nucleophilic sites, in particular, amino and hydroxy groups.

Table 5. Products of aminoalcohols sulfonylation and acylation

Compd. no.	Yield, %	mp, °C	R_f, ether	IR spectrum, cm^{-1}	Found N, %	Formula	Calculated N, %
XVIIa	69.0	100–102	0.73	3380, 3259, 3030, 1611, 1525, 1385, 1333, 1258, 1112, 805, 700	8.82	$C_{22}H_{23}N_3O_7S$	8.88
XVIIb	64.1	110–111	0.75	3378, 3271, 3033, 1609, 1525, 1390, 1355, 1245, 1116, 860, 720	8.83	$C_{22}H_{23}N_3O_7S$	8.88
XVIII	65.3	118–120	0.65		8.80	$C_{22}H_{25}N_3O_7S$	8.84
XIXa	84.1	153.5–155	0.77	3466, 3070, 1620, 1522, 1450, 1365, 1112, 810, 715	6.95	$C_{24}H_{26}N_2O_4$	6.90
XIXb	77.0	126.5–127.5	0.78	3400, 3075, 1620, 1522, 1360, 1112, 870, 718	6.94	$C_{24}H_{26}N_2O_4$	6.90
XXa	74.5	121–122	0.68	3400, 2978, 1620, 1532, 1332, 1111	6.82	$C_{24}H_{28}N_2O_4$	6.86
XXb	78.2	103.5–104.5	0.71	3422, 3013, 2901, 1616, 1530, 1331, 1099	6.81	$C_{24}H_{28}N_2O_4$	6.86

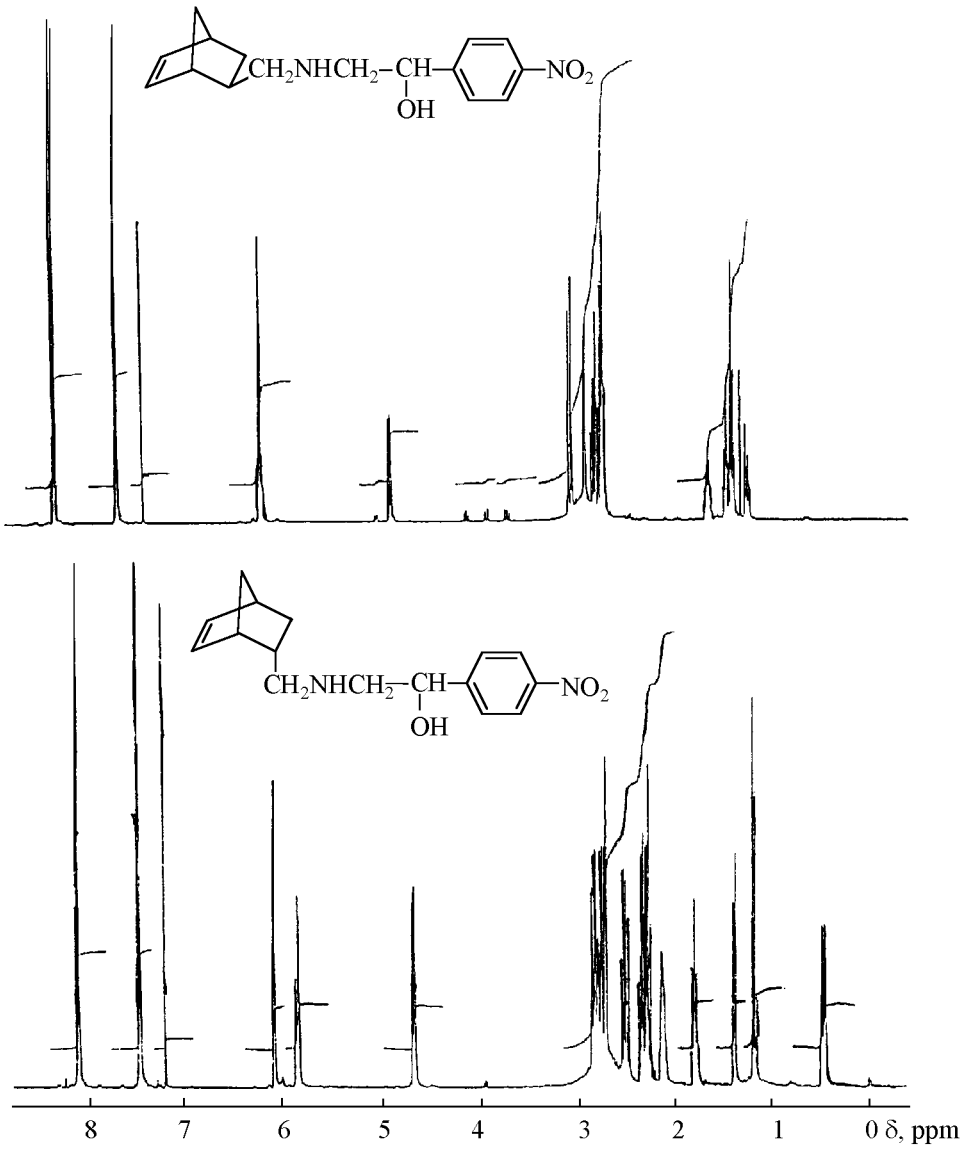
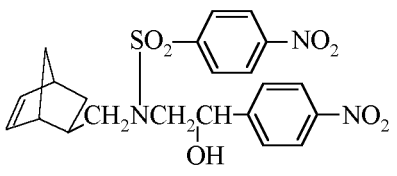
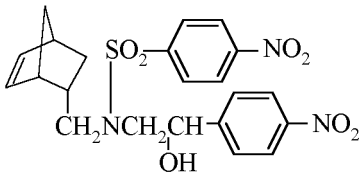


Fig. 1. ^{13}C NMR spectra of stereoisomeric *N*-(2-hydroxy-2-*p*-nitrophenylethyl)-5-aminomethylbicyclo[2.2.1]hept-2-enes (**Xa, b**).

To test the reactivity of amino alcohols we carried out reactions of some among them with *p*-nitrobenzenesulfonyl chloride and *p*-methylbenzoyl chloride. The aminoalcohols **Xa, b, XIIIb** were treated with *p*-nitrobenzenesulfonyl chloride in chloroform in the presence of triethylamine at equimolar amounts of reagents and with monitoring by TLC. The yield of sulfonamides **XVIIa, b, XVIII** amounted to 64–69% (Table 5). Concurrently performed sulfonylation of compounds **Xa, b** in a two-phase system (ether, aqueous alkali) previously successfully carried out with the original amines **IIIa, b** was less lucky and furnished the respective sulfonamides in 38.1 and 37.6% yield. The isolation and purification of reaction products **XVIIa, b** was difficult at this procedure.



XVIIa



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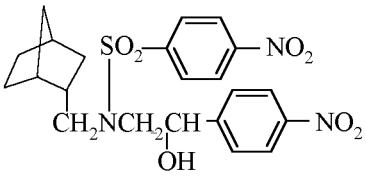

XVIII

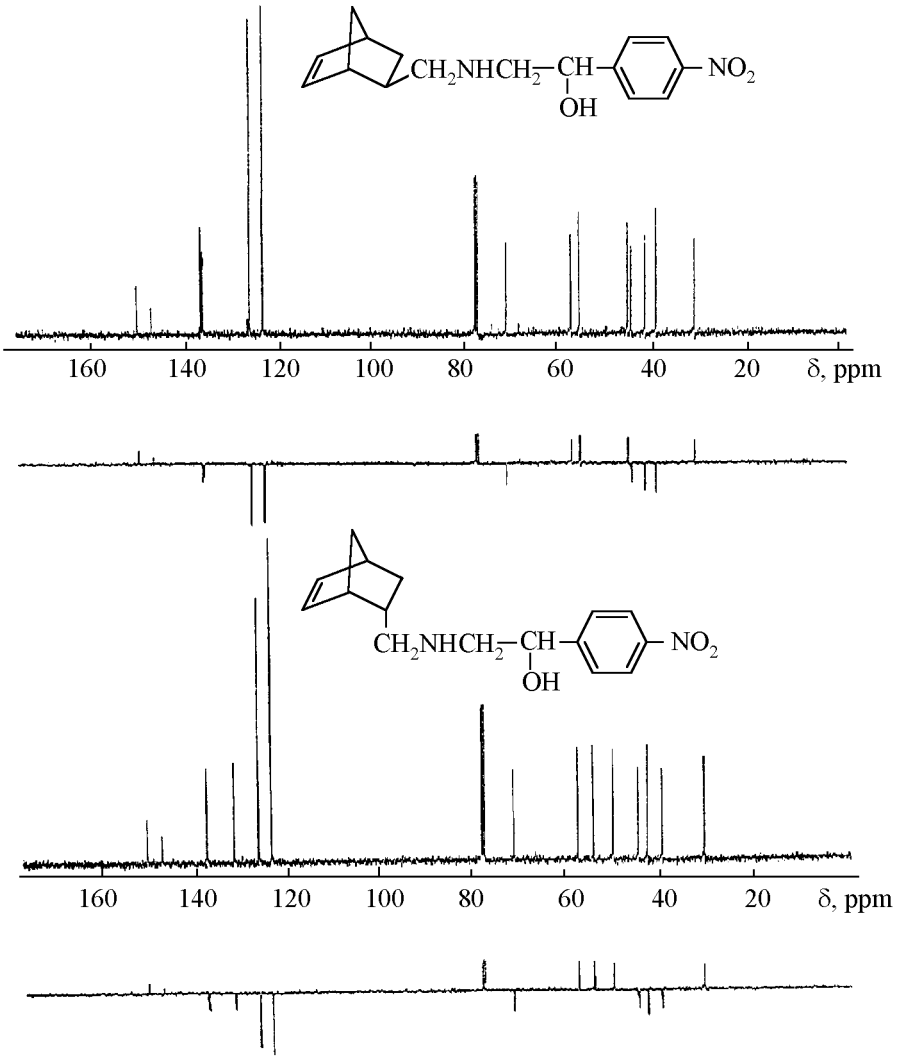

Fig. 2. ^{1}H NMR spectra of stereoisomeric *N*-(2-hydroxy-2-*p*-nitrophenylethyl)-5-aminomethylbicyclo[2.2.1]hept-2-enes (**Xa, b**).

Acylation of compounds **Xa, b, XIIIa, b** was carried out by treating with equimolar amount of *p*-methylbenzoyl chloride and pyridine in chloroform along procedure used in acylation of norbornylamines [16]; thus were prepared compounds **XIXa, b, XXa, b**.

The properties of compounds **XVII–XX** are presented in Table 5. The presence of sulfonyl group attached to nitrogen was confirmed by IR spectra (Table 5) and data of ^{1}H NMR. In the IR spectra of compounds **XVIIa, b** alongside the absorption bands of nitro group appear the bands of sulfonyl group (1385–1355, 1116–1111 cm^{-1}) and is conserved the absorption of the unsaturated fragment (700 and 720 cm^{-1}, δ = C–H) [20]. In the IR spectra of amides **XIXa, b, XXa, b** are observed bands in the region of 1620 cm^{-1} (amide I, ν C=O), but same as in the spectra of sulfonamides lack the bands of the bending vibrations of N–H bond at 1560–1540 cm^{-1} [20]. The presence of the secondary hydroxy group is confirmed both by the presence of wide bands in the region 3400–3200 cm^{-1} (ν O–H) and by absorption at 1116–1111 cm^{-1} (ν C–O) [20].

In the ^{1}H NMR spectra of unsaturated amides **XIXa, b** appear the signals of protons from methyl groups (2.38 and 2.39 ppm), of eight aromatic protons; the signals of methine and methylene groups neighboring to the *p*-nitrophenyl substituent are shifted downfield (5.2–5.3 and 3.6–3.9 ppm) as compared to the spectra of the original aminoalcohols

Table 6. Toxicity parameters and characteristic of biological activity of compound **IIIa, X**[a]

Compd. no.	LD_{50}, mg/kg	Activity relative to control, %				
		analgetic	anticonvulsant	antihypoxic	tranquilizing	antiphlogistic
IIIa	335	27.6	0	0	90.3	–[b]
X	92	68.0	113.0	18.6	80.8	37.0

[a] The effects were studied on doses equal to 0.1 of LD_{50}. [b] No data available.

Xa, b. In the complicated spectra of compounds **XIXa, b** certain features are observed that permit attribution the amides to exo and endo isomers (the difference in the signals of bridgehead protons H^1, H^4 and in those of the olefin fragment). The bridgehead protons (H^1 and H^4) of the *exo*-isomer have different chemical shifts (2.71 and 2.59 ppm) whereas in the *endo*-isomer their signals coincide (δ 2.72 ppm). The protons of the olefin fragment in the *exo*-isomer resonate at 6.07 ppm, and the proton signals from (H^2 and H^3) atoms of the *endo*-isomer are shifted downfield (to 5.95 and 5.22 ppm) under the effect of the spatially close substituent with a magnetically anisotropic carbonyl group. The nonequivalence of the latter atoms is more pronounced than in compound **XI** with a benzyl substituent at the nitrogen atom.

Aminoalcohols with bicyclic fragments are promising objects for testing their biological activity [21]. We carried out a pharmacological investigation of a sample of compound **X** containing equal amounts of stereoisomers **Xa, b**. The sample possessed analgetic, anticonvulsant, tranquilizing, antiphlogistic, and weak antihypoxic activity. The results of comparison of aminoalcohol **X** activity with the closest analog, *exo*-5-aminomethylbicycl[2.2.1]hept-2-ene (**IIIa**) taken as hydrochloride, are presented in Table 6. The study showed that the introduction of a substituent to the nitrogen atom resulted in appearance of new kinds of activity (anticonvulsant and antihypoxic), and also to considerable increase in the analgetic action. The data on toxicity of compounds **IIIa, X** that is fairly high are also included in Table 6.

At the comparison of pharmacological effects of two related compounds were found both principally similar characteristics and differences revealed in the degree of activity and in the increased field of neurotropic action of aminoalcohol **X** as compared to amine **IIIa**.

EXPERIMENTAL

IR spectra were measured on spectrophotometer Specord 75-IR from samples prepared as thin films or pelletized with KBr. ^{1}H NMR spectra were registered on spectrometer Varian VXR-300 (300 MHz) from compounds solutions in deuterochloroform or DMSO, internal standard TMS or HMDS. ^{13}C NMR spectra were recorded on Gemini-BB instrument at operating frequency 75.4 MHz. The reaction course was monitored and the purity of products obtained was checked by TLC on Silufol UV-254 plates, eluent ether, development in iodine vapor. Elemental analysis was carried out on Karlo Erba analyzer.

***N*-(2-Hydroxy-2-*p*-nitrophenylethyl)-*exo*-5-aminomethylbicyclo[2.2.1]hept-2-ene (Xa).** A mixture of 1.60 g (0.01 mol) of *p*-nitrostyrene oxide and 1.23 g (0.01 mol) of amine **IIIa** was dissolved in 10 ml of 2-propanol. The reaction completion was monitored by TLC. The separated precipitate was filtered, washed with 2-propanol on the filter, and dried. The aminoalcohol was purified by recrystallization from a mixture 2-propanol–water (2 : 1). Compounds **Xb, XI–XV** were prepared similarly. The characteristic of compounds obtained are given in Table 1.

***N*-(2-Hydroxy-2-*p*-nitrophenylethyl)-*N*-(*p*-nitrobenzenesulfonyl)-*exo*-5-aminomethylbicyclo[2.2.1]-hept-2-ene (XVIIa).** To a stirred mixture of 0.29 g (0.001 mol) of aminoalcohol **Xa** and 0.31 g (0.42 ml, 0.003 mol) of triethylamine in 15 ml of anhydrous chloroform was added dropwise 0.22 g (0.001 mol) of *p*-nitrobenzenesulfonyl chloride in 10 ml of anhydrous chloroform. The stirring of the mixture was continued at room temperature till completion of the reaction (TLC monitoring). Then the reaction mixture was washed in succession three times with water, with 20% solution of HCl and again with water. The organic layer was separated and dried on calcined $MgSO_4$. On removing the solvent the sulfonamide was recrystallized from a mixture 2-propanol–water (2 : 1). In a similar way were prepared compounds **XVIIb, XVIII**. The properties of compounds obtained are listed in Table 5.

***N*-(2-Hydroxy-2-p-nitrophenylethyl)-*N*-(*p*-methylbenzoyl)-*exo*-5-aminomethylbicyclo[2.2.1]-hept-2-ene (XIXa).** To a stirred mixture of 0.29 g (0.001 mol) of aminoalcohol **Xa** and 0.003 mol of pyridine or triethylamine in 15 ml of anhydrous chloroform was added dropwise 0.15 g (0.001 mol) of *p*-methylbenzoyl chloride in 5 ml of anhydrous chloroform. The stirring of the mixture was continued at room temperature till completion of the reaction (TLC monitoring). Then the reaction mixture was washed in succession three times with water, with 20% solution of HCl and again with water. The organic layer was separated and dried on calcined $MgSO_4$. On removing the solvent the sulfonamide was recrystallized from a mixture 2-propanol–water (2:1). In a similar way were prepared compounds **XIXb, XXa, b**. The characteristics of compounds obtained are given in Table 5.

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