Russian Journal of Organic Chemistry, Vol. 38, No. 4, 2002, pp. 553–563. Translated from Zhurnal Organicheskoi Khimii, Vol. 38, No. 4, 2002, pp. 578–590.

New *N*-(Arylsulfonyl)-5-aminomethylbicyclo[2.2.1]hept-2-enes. Synthesis, ^{1}H and ^{13}C NMR Spectra, and Chemical Reactions

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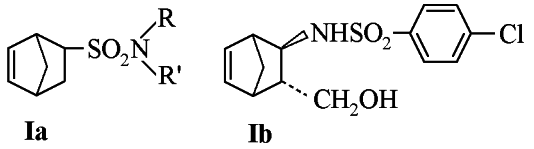
Received July 12, 2000

Abstract—A synthesis of new *N*-(arylsulfonyl)-5-aminomethylbicyclo[2.2.1]hept-2-enes obtained by reaction of stereoisomeric *exo*- and *endo*-5-aminomethylbicyclo[2.2.1]hept-2-enes with arylsulfonyl chlorides is described. With the use of the data of ^{1}H and ^{13}C NMR spectra, including those of two-dimensional spectra recorded in COSY and NOESY mode, the contribution of stereochemical features of sulfonamides into the spectra structure of *endo*- and *exo*-isomers was evaluated. Applying various methods of the phase-transfer catalysis alkylation and acylation of the stereoisomeric arylsulfonamides containing a norbornene fragment was carried out. The reactions of alkylated stereoisomeric sulfonamides, *N*-(benzyl)-*N*-(3,4-dichlorophenylsulfonyl)-5-aminomethylbicyclo[2.2.1]hept-2-enes, with peroxyphthalic acid provide epoxides; the orientation of substituents in the cage norbornene fragment does not affect the direction of the process. The structure of the products obtained by sulfonamides transformations was confirmed by IR, ^{1}H and ^{13}C NMR spectra.

Sulfonamide drugs were introduced into medical practice in nineteen thirties as efficient preparations against staphylococcosis and streptococcal infections [1]. Later sulfonamides belonging to norbornene series were prepared, both amides of sulfonic acids **Ia** and amine derivatives with a norbornene fragment, among them compound **Ib**. Among the derivatives of sulfonic acid **Ia** stimulators of brain functions, analeptics, antagonists of hypnotic and narcotic agents were found [2]. Compound **Ib** possessed antithrombic, antisclerotic, and aniischemic function [3].



Ia **Ib**

Both the mentioned groups of compounds are promising due to the presence in their structure of two pharmacophoric moieties, sulfonamide and norbornene fragments; the latter is characteristic of a terpenoid series of plant origin. G.Krieger [4] believes that the rigid molecules of substituted norbornenes (and norbornanes) with fixed spatial orientation of substituents are the most suitable objects for investigation of relations between pharmacological activity and the chemical structure. Therefore it is regretful that in many cited studies was not investigated and even was not paid attention to the stereochemical configuration of the bicyclic compounds. As exception the recent synthetic studies can be indicated [5–7] and investigations of the biological activity [8] of a group of stereochemically individual sulfonamides originating from exo-5-(**IIa**) and *endo*-5-aminomethylbicyclo[2.2.1]hept-2-ene (**IIb**), and from their saturated analogs can be indicated.

The analysis of publications shows that most of them consider the saturated norbornane systems. Just among them compounds inhibiting thromboxane A_2 (TXA_2) biosynthesis were found and blocking action of TXA_2 on the receptrors of living organisms was revealed [10]. Since the formation of TXA_2 plays an important role in pathogenesis of thrombosis and ischemia the synthesis of TXA_2 antagonists is an important field of chemical studies. In [5, 7, 11] syn theses of arylsulfonamides from unsaturated amines **IIa, b** containing unsubstituted phenyl and *p*-methyl, *o*,*o*',*p*-triisopropyl, *p*-methoxycarbonyl, *p*-bromo, *p*-chloro, and *p*-fluorophenyl sulfonylderivatives of amines **IIa, b** are described. By example of sulfonamide **IIIb** and the corresponding *exo*-isomer **IIIa** a neurotropic (analgetic, anti-spasmotic, antihypoxic, tranquillizing) activity and clear distinctions of the pharmacological characteristics of the mentioned

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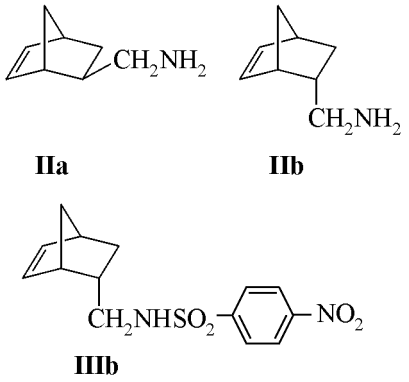
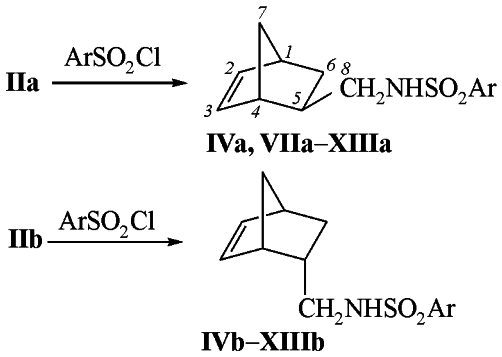
amide pair **IIIa, b** and also of their *p*-chlorophenylsulfonyl analogs was demonstrated [8, 12].



The goal of this study was investigation of a new group of stereoisomeric arylsulfonyl derivatives of amines **IIa, b** containing prevailingly the promising nitrophenylsulfonyl moieties. A special attention was paid to the synthesis of *o*-methylated arylsulfonamides for in the other groups of compounds they displayed specific pharmacological properties [11].



Ar = *m*-$NO_2C_6H_4$ (**IV**) *o*-$NO_2C_6H_4$ (**V**), 2,4-$(NO_2)_2C_6H_3$ (**VI**), *o*-NO_2, *p*-$CH_3C_6H_3$ (**VII**), *p*-NO_2, *o*-$CH_3C_6H_3$ (**VIII**), 2-CH_3O, 5-$NO_2C_6H_3$ (**IX**), 4-F, 2-$CH_3C_6H_3$ (**X**), *m3-*$CF_3C_6H_4$ *(***XI**), 3,4-$Cl_2C_6H_3$ (**XII**), β-$C_{10}H_7$ (**XIII**).

Amines **IIa, b** were synthesized proceeding from stereoisomeric 25-cyanobicyclo[2.2.1]hept-2-enes prepared by diene condensation of cyclopentadiene with acrylonitrile [5, 13]. The individual *exo*- and *endo*-nitriles were separated from a mixture by fractional distillation to the isomeric purity of 99%. The nitriles were reduced into amines **IIa, b** by lithium aluminum hydride in anhydrous ether, and the amines characteristics were published in [5, 7, 13]. As was shown in [14], amine **IIb** contained up to 10% of *exo*-isomer **IIa**, and amine **IIa** formed as individual compound (according to ^1H and ^{13}C NMR spectra). The different purity of amines originated from isomerization of the *endo*-nitrile under conditions of reduction with lithium aluminum hydride.

The sulfonamides were prepared by two procedures. In procedure *a* the amines **IIa, b** were reacted with arenesulfonyl chlorides in a heterogeneous system (water, ether) at vigorous stirring with equimolar ratio of reagents (amine, sulfonyl chloride, and alkali [11]. By procedure *b* the reaction was carried out under homogeneous conditions (in solution of triethylamine in ethyl ether) [9]. The yields, procedures applied, and some properties of the *exo*-sulfonamides are given in Table 1, those of the corresponding *endo*-stereoisomers in Table 2. Sulfonamide **Va** was previously described in detail in [7], and we studied dinitrosulfonamide by an example of *endo*-isomer **Vb**.

In the IR spectra of compounds appear the absorption bands of the sulfonamide group (1330–1310, 1150–1140, 3290–3200 cm^{-1}) corresponding to symmetric and asymmetric vibrations of the O=S=O fragment and to the stretching vibrations of NH group [15]. The assignment of bands is complicated by the presence of two unsaturated moieties: of a strained double bond and aromatic ring. The absorptions in the region 1575–1550 cm^{-1} [ν(C=C) of norbornene] and over 3000 cm^{-1} [ν(=C–H)] are screened respectively by that of sulfonamide group [ν(NH)] and of aromatic system. However in the spectra of compounds the characteristic for norbornene double bond absorption bands of bending vibrations of =C–H bond are observed. The location of these bands is slightly different in the *exo*- and *endo*-isomers (715–700 and 725–720 cm^{-1} respectively). In the IR spectra appear the absorption bands corresponding to the substituents in the benzene ring: nitro group (1520–1510, 1330–1310 cm^{-1}) and methoxy group (2860, 1200 cm^{-1}).

More important information was provided by analysis of ^1H and ^{13}C NMR spectra (Tables 3 and 4 respectively). The signals were assigned with the use of two-dimensional spectra of compounds **XIIa, b** in COSY and NOESY mode (Figs. 1, 2), and also of the data of earlier studies [16, 17]. Two-dimensional spectra were measured for this group of sulfonamides (derivatives of amines **IIa, b**) for the first time, and they provided a possibility of clearing up all the dubious points and confirmed the validity of criteria advanced earlier for assignment of conformation of

Table 1. Physico-chemical characteristics and elemental analyses of *N*-(arylsulfonyl)-*exo*-5-aminomethylbicyclo[2.2.1]hept-2-enes **IVa, VIIa**–**XIIIa**

Compd. no.	Yield, % (Method of synthesis)	mp, °C	R_f (ether)	IR spectrum, cm^{-1}	Found, %			Formula	Calcd., %		
					C	H	N		C	H	N
IVa	77 (b)	110–112	0.76	3280, 3043, 1571, 1511, 1450, 1328, 1151, 712	54.55	5.13	9.11	$C_{14}H_{16}N_{204}S$	54.54	5.19	9.09
VIIa	63 (b)	105–107	0.55		55.93	5.52	8.63	$C_{15}H_{18}N_{204}S$	55.90	5.59	8.70
VIIIa	98 (b)	121–122	0.43	3270, 3040, 1570, 1510, 1400, 1310, 1150, 712	55.89	5.63	8.75	$C_{15}H_{18}N_{204}S$	55.90	5.59	8.70
IXa	78 (b)	177–179	0.47	3267, 3052, 2860, 1523, 1345, 1200, 1164, 725	54.74	6.07	8.23	$C_{15}H_{18}N_{205}S$	53.25	5.33	8.28
Xa	75 (b)	95–97	0.71		61.06	6.13	4.78	$C_{15}H_{18}FN_{02}S$	61.02	6.10	4.75
XIa	76 (a)	[a]	0.576[b]	3258, 3052, 1602, 1530, 1326, 1156, 848, 698	54.27	4.92	4.14	$C_{15}H_{16}F_3N_{02}S$	54.38	4.83	4.23
XIIa	96 (b)	120–122	0.53	3251, 3042, 1626, 1552, 1325, 1152, 865, 832, 813, 700	50.88	4.79	4.26	$C_{14}H_{14}C_{12}N_{02}S_b$	50·76	4.23	4.23
XIIIa	59 (a)	137–138	0.54[b]	3394, 3070, 1588, 1450, 1356, 1158, 718	68.94	6.15	4.52	$C_{18}H_{19}N_{02}S$	69.01	6.07	4.47

[a] bp 146–147°C (3.5 mm Hg), n_9D^{20} 1.5028. [b] *R*f in the system ether–hexane, 2:1. [c] Found S, %: 9.64 (**IXa**), 9.59 (**XIIa**). Calculated, %: 9.47 (**IXa**), 9.67 (**XIIa**).

Table 2. Physico-chemical characteristics and elemental analyses of *N*-(arylsulfonyl)-*endo*-5-aminomethylbicyclo[2.2.1]hept-2-enes **IVb**–**XIIIb**

Compd. no.	Yield, % (Method of synthesis)	mp, °C	R_f (ether)	IR spectrum, cm^{-1}	Found, %			Formula	Calcd., %		
					C	H	N		C	H	N
IVb	55 (b)	115–116	0.48		54.51	5.10	9.12	$C_{14}H_{16}N_{204}S$	54.54	5.19	9.09
Vb	68 (a)	107–108	0.25[a]	3296, 3073, 1552, 1376, 1332, 1168, 860, 720	54.41	5.17	9.16	$C_{14}H_{16}N_{204}S$	54.54	5.19	9.09
VIb	72 (a)	94–95	0.47[a]	3368, 3092, 1592, 1560, 1552, 1336, 1144, 720	47.62	4.19	12.00	$C_{14}H_{15}N_{306}S$	47.59	4.25	11.90
VIIb	70 (b)	110–111		3314, 3061, 1600, 1537, 1330, 1158, 720	55.81	5.65	8.75	$C_{15}H_{18}N_{204}S$	55.90	5.59	8.70
VIIIb	96 (b)	125–126	0.42	3280, 3040, 1580, 1520, 1320, 1160, 720	55.85	5.65	8.76	$C_{15}H_{18}N_{204}S$	55.90	5.59	8.70
IXb	76 (b)	180–182	0.42	3270, 3050, 2810, 1500, 1330, 1200, 1155, 720	53.21	5.38	8.16	$C_{15}H_{18}N_{205}S$	53.25	5.33	8.28
Xb	82 (6)	100–101	0.54	3270, 3045, 2925, 1568, 1515, 1320, 720	61.08	6.15	4.78	$C_{15}H_{18}FN_{02}S$	61.02	6.10	4.75
XIb	73 (a)	177–178	0.42[a]	3250, 3052, 1610, 1540, 1326, 1158, 722	54.47	4.89	4.30	$C_{15}H_{16}F_3N_{02}S$	54.38	4.83	4.23
XIIb	87 (b)	141–142	0.67	3262, 3061, 1602, 1562, 1322, 1162, 722	50.60	4.28	4.22	$C_{14}H_{14}C_{12}N_{02}S_6$	50.76	4.23	4.23
XIIIb	85 (a)	170–171	0.34[a]	3248, 3038, 1582, 1498, 1322, 1154, 722	68.92	6.10	4.59	$C_{18}H_{19}N_{05}S$	69.01	6.07	4.47

[a] R_f values in the system ether–hexane, 2:1. [b] Found, %: S 9.55; Cl 21.05. Calculated, %: S 9.67; Cl 21.45.

Table 3. ^{1}H NMR spectra of compounds **Va, b, VIb, Xb, XIIa, b**, 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}
Va	2.76	5.99, 5.94, $^3J_{2,3}$ 5.3, $^3J_{2,1}$ 2.4, $^3J_{3,4}$ 2.5	2.58	1.50	1.20	1.03, $^2J_{6x,6n}$ 11.7, $^3J_{6n,5}$ 4.2,	1.25, 1.15, $^2J_{7s,7a}$ 8.8	3.09, 2.99, $^2J_{8A,8b}$ 12.4, $^3J_{8A,5}$ 8.4, $^3J_{8b,5}$ 7.3
Vb	2.79	6.07, 5.74, $^3J_{2,3}$ 5.8, $^3J_{2,1}$ 2.8, $^3J_{3,4}$ 3.1	2.73	2.18	1.76, $^2J_{6x,6n}$ 11.6, $^3J_{6x,5}$ 8.8, $^3J_{6x,1}$ 3.5	0.42, $^3J_{6n,5}$ 4.2, $^4J_{6n,7s}$ 2.6	1.38, 1.16, $^2J_{7s,7a}$ 8.4	2.68, 2.62, $^2J_{8A,8b}$ 9.1, $^3J_{8A,5}$ 6.0, $^3J_{8b,5}$ 6.0
VIb	3.01	6.28, 5.98, $^3J_{2,3}$ 5.7, $^3J_{2,1}$ 3.0, $^3J_{3,4}$ 2.7	2.91	2.51	2.03, $^2J_{6x,6n}$ 11.7, $^3J_{6x,5}$ 9.3, $^3J_{6x,1}$ 3.9	0.70, $^3J_{6n,5}$ 4.2, $^4J_{6n,7s}$ 2.7	1.56, 1.36, $^2J_{7s,7a}$ 7.6	3.55, 3.36, $^2J_{8A,8b}$ 12.9, $^3J_{8A,5}$ 6.3, $^3J_{8b,5}$ 5.1
Xb	2.78	6.03, 5.72, $^3J_{2,3}$ 5.1, $^3J_{2,1}$ 2.7, $^3J_{3,4}$ 2.7	2.72	2.15	1.78	0.36, $^2J_{6x,6n}$ 11.0, $^3J_{6n,5}$ 4.1, $^4J_{6n,7s}$ 3.4	1.35, 1.17, $^2J_{7s,7a}$ 7.4	2.38, 2.28, $^2J_{8A,8b}$ 13.0, $^3J_{8A,5}$ 6.2, $^3J_{8b,5}$ 5.5
XIIa	2.77	6.03	2.67	1.53	1.17, $^2J_{6x,6n}$ 11.4, $^3J_{6x,5}$ 8.1	1.06, $^3J_{6n,5}$ 4.7	1.31, 1.27, $^2J_{7s,7a}$ 8.4	3.05, 2.96, $^2J_{8A,8b}$ 12.7, $^3J_{8A,5}$ 7.0, $^3J_{8b,5}$ 6.3
XIIb	2.84	6.14, 5.82, $^3J_{2,3}$ 5.1, $^3J_{2,1}$ 3.3, $^3J_{3,4}$ 2.7	2.81	2.18	1.82, $^2J_{6x,6n}$ 11.4, $^3J_{6x,5}$ 9.0, $^3J_{6x,1}$ 3.7	0.48, $^3J_{6n,5}$ 3.9, $^4J_{6n,7s}$ 2.4	1.45, 1.23, $^2J_{7s,7a}$ 8.1	3.00, 2.73, $^2J_{8A,8b}$ 12.0, $^3J_{8A,5}$ 6.3, $^3J_{8b,5}$ 6.3

Table 4. ^{13}C NMR spectra of compounds **IIa, b, XIIa, b**, δ, ppm

Compd. no.	C^1	C^2	C^3	C^4	C^5	C^6	C^7	C^8	Substituent
IIa	42.9	137.2	136.5	43.9	41.6	31.1	44.9	47.8	–
IIb	42.7	137.3	131.8	43.8	42.3	30.0	49.5	46.4	–
XIIa	41.7	137.0	135.9	44.0	39.2	30.9	44.9	48.5	139.9, 137.4, 133,7 131.2, 129.0, 126.1
XIIb	42.3	138.2	131.5	43.9	38.9	30.0	49.5	47.2	139.8, 137.4, 133,7 131.1, 129.0, 126.1

stereoisomeric sulfonamides that were tested in this study on a new group of sulfonamides. A significant feature of ^{1}H NMR spectra of *endo*-isomers **Vb, VIb, Xb, XIb** distinguishing them from that of *exo*-isomer **XIIa** is a clear separation of the signals of olefin protons (H^2, H^3). For the sake of comparison the spectral parameters of sulfonamide **Va** are also presented [7]. In the groups of *exo*- and *endo*-isomers can be also used other criteria developed earlier for analysis of ^{1}H NMR spectra of sulfonamides from the norbornene series can also be used [18]. Actually the contribution from the magnetic anisotropy of the exocyclic C^5–C^8 bond results in an upfield shift of H^4 proton in the spectra of *exo*-isomers **Va, XIIa** to the region 2.58– 2.67 ppm. Therefore in the *exo*-isomers the nonequivalence of the bridgehead protons H^1, H^4 is considerably greater than in the *endo*-isomers (~0.10–0.29 and ~0.03–0.10 respectively).

The mentioned contribution from the magnetic anisotropy of the exocyclic bond C^5–C^8 affects also the resonance of protons attached to atom C^6. As a result the signals of proton H^{6x} in the *exo*-isomer and of H^{6n} proton in the *endo*-isomer shift upfield. There-

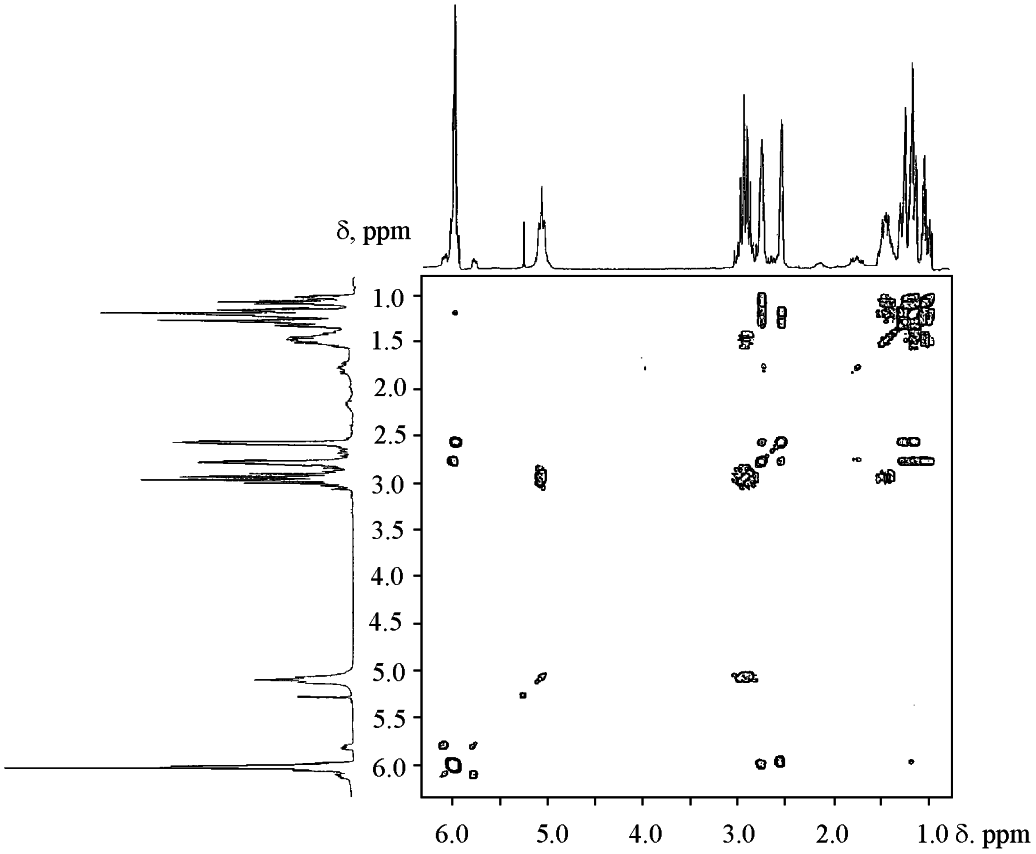


Fig. 1. HH–COSY spectrum of *N*-(3,4-dichlorophenylsulfonyl)-*exo*-5-aminomethylbicyclo[2.2.1]hept-2-ene (**XIIa**).

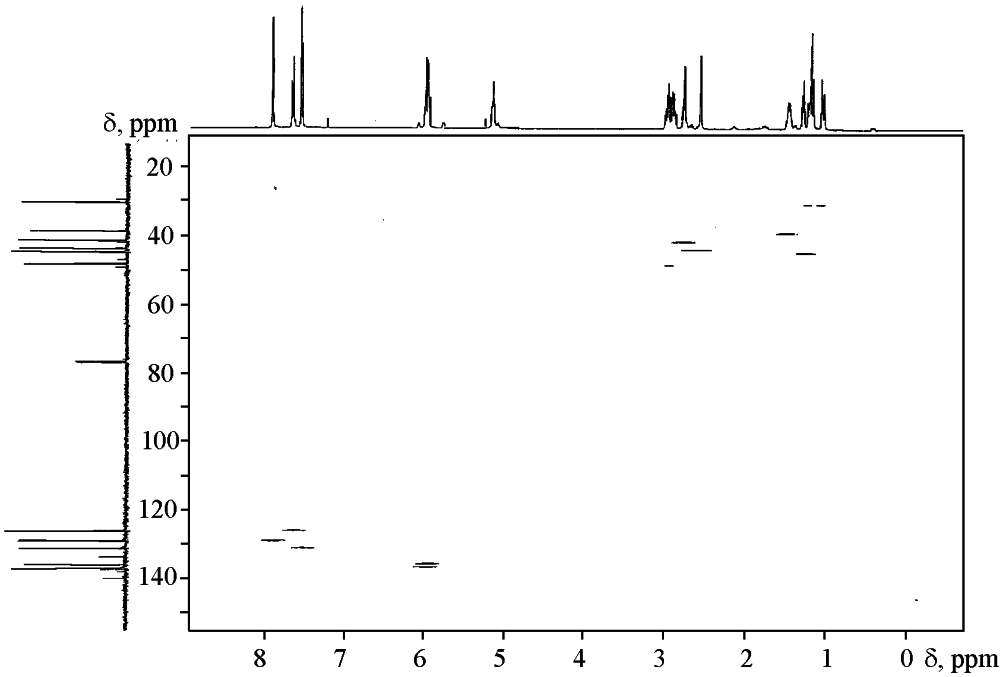


Fig. 2. CH–NOESY spectrum of *N*-(3,4-dichlorophenylsulfonyl)-*exo*-5-aminomethylbicyclo[2.2.1]hept-2-ene (**XIIa**).

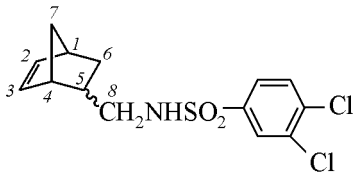
fore nonequivalence of signals from protons attached to C^6 amounts to 0.1–0.2 ppm for *exo*-isomers and 1.3 ppm for the corresponding *endo*-isomers; this difference was used previously [18] and in this study as a criterion in the analysis of the spectra belonging to stereoisomeric sulfonamides of the norbornene series. The chosen objects provided a possibility of evaluating the contribution from two nitro groups in the benzene ring of sulfonamide **VIb**: the effect consisted in a significant downfield shift of all the signals from the norbornene skeleton (Table 3).

In Table 4 are presented the ^{13}C NMR spectra of sulfonamides **XIIa, b** and the spectra of original amines **IIa, b** for the sake of comparison. The application of two-dimensional NMR spectroscopy to compounds **XIIa, b** (Fig. 2) provided a solution of the difficult problem of signals assignment for the nuclei C^1, C^4, and C^5. The carbon spectra of stereoisomeric sulfonamides **XIIa, b** and those of the key amines **IIa, b** are very similar: the introduction of an arylsulfonyl substituents affected first of all the position of signal from C^5 atoms (upfield shift of 2.5 ppm) and less that from C^8 atoms (downfield shift of 1.5 ppm).

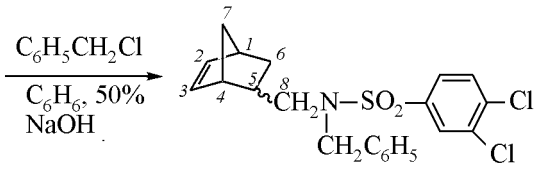
The spectra of compounds **IIa, XIIa**, and **IIb, XIIb** contain enough information for evaluation of the stereochemical features of the molecules. The observed difference is related prevailingly to the position of signals from C^3, C^7, and C^8 atoms. Unlike the *exo*-isomers *endo*-isomers **IIb, XIIb** are characterized firstly, by considerable nonequivalence of signals from the carbon atoms of the double bond (5–7 ppm), secondly, by significant deshielding (up to 4–5 ppm) of the bridging carbon (C^7), and finally, by small additional shielding of the carbon atom in the substituent (C^8). The use of two-dimensional spectra revealed the inversion of signal position from C^7 and C^8 depending on the stereochemical features of the molecule.

In this study were investigated some chemical transformations of sulfonamides in alkylation, acylation, and oxidation with perphthalic acid.

The alkylation and acylation of sulfonamides was carried out under conditions of phase-transfer catalysis that had been previously described for compounds with norbornene fragments [19]. Reactions of compounds containing rigid cage fragments, among them of norbornene derivatives, are of special interest because of high steric requirements of the substrate with respect to attacking reagent. Alkylation of sulfonamides **IIIb, XIIa, b** with benzyl chloride was carried out in a system benzene–water solution containing 50% of sodium hydroxide and 10% of tetrabutylammonium bromide.

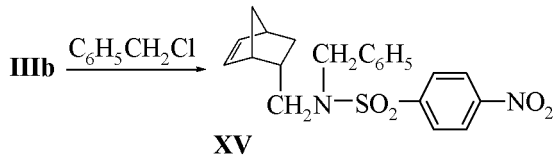


exo-**IIa,**
endo-**IIb**

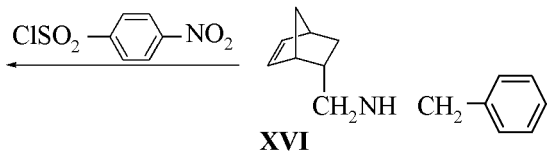


exo-**XIVa,**
endo-**XIVb**

Compound **XV** was obtained similarly from sulfonamide **IIIb**, and it was identical to the arylsulfonylation product of amine **XVI** described in [17].



XV



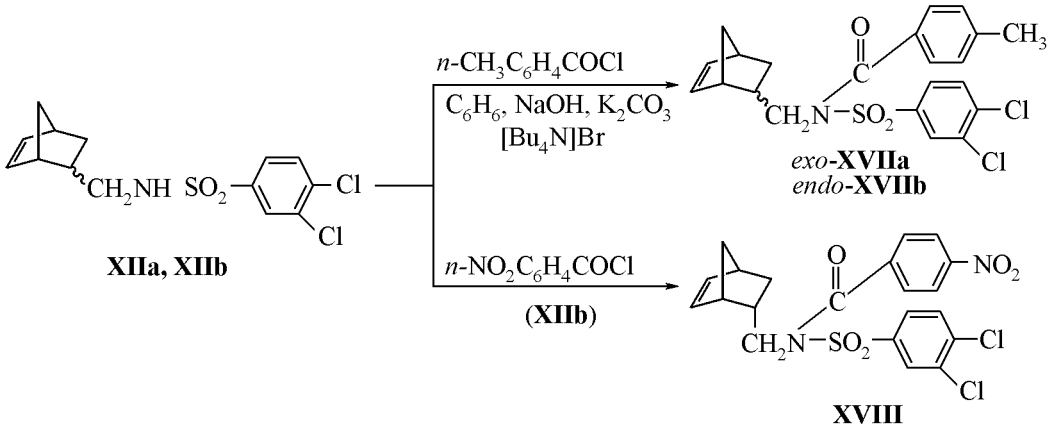
XVI

All attempts to alkylate sulfonamide **XIIb** with 1-bromoadamantane were unsuccessful, among them the two series of experiments carried out at 70°C in benzene under phase-transfer catalysis with tetrabutylammonium bromide both in liquid–liquid and in liquid–solid phase systems. In the first series the catalyst was used in amounts 10 and 20 mol%, in the second series in the presence of crystalline sodium hydroxide and potassium carbonate the same catalyst was used in amounts 10, 20, 50, and 100 mol%. The failure apparently is due to the sterical hindrances arising in the transition state in the presence of two bulky cage fragments. Physico-chemical characteristics of alkylated sulfonamides **XIVa, b, XV** are presented in Table 5.

Table 5. Physico-chemical characteristics and elemental analyses of sulfonamides **XIVa, b, XV, XVIIa, b, XVIII** and epoxides **XXa, b**

Compd. no.	Yield, %	mp, °C	IR spectrum, cm^{-1}	Found, %			Formula	Calculated, %		
				C	H	N		C	H	N
XIVa	79	143–145	3078, 3042, 1626, 1552, 1325, 1152, 700	59.73	4.91	3.36	$C_{21}H_{21}Cl_2NO_2S$	59.72	4.98	3.32
XIVb	71	150–151	3081, 3061, 1562, 1322, 1162, 714	59.70	4.83	3.35	$C_{21}H_{21}Cl_2NO_2S$	59.72	4.98	3.32
XV	86	135–137	3060, 1605, 1550, 1340, 1320, 1160, 718	–	–	6.95	$C_{21}H_{22}N_2O_4S$	–	–	7.04
XVIIa	88	80–82	3054, 1675, 1600, 1565, 1500, 1368, 1163, 710	58.69	4.73	3.15	$C_{22}H_{21}Cl_2NO_3S$	58.67	4.67	3.11
XVIIb	88	85–86	3054, 1683, 1602, 1570, 1502, 1337, 1162, 726	58.63	4.82	3.10	$C_{22}H_{21}Cl_2NO_3S$	58.67	4.67	3.11
XVIII	70	90–91		52.43	3.78	5.88	$C_{21}H_{18}Cl_2N_2O_5S$	52.39	3.74	5.82
XXa	82	164–165	3035, 1580, 1460, 1380, 1360,1347,1170,850,740	–	–	3.41	$C_{21}H_{21}Cl_2NO_3S$	–	–	3.20
XXb	79	145–146	3030, 1580, 1460, 1380, 1350, 1170, 850, 775	–	–	3.46	$C_{21}H_{21}Cl_2NO_3S$	–	–	3.20

Acylation of sulfonamides was studied by an example of compounds **XIIa, b** and *p*-methyl- and *p*-nitrobenzoyl chlorides as acylating agents. Acylation consisted in preparation of the sulfonamide sodium salt followed by heating of the latter with acyl chloride at 65–70°C. The experiments along the above described procedures in the liquid–liquid systems resulted in the hydrolysis of the acylating reagents.



In the IR spectra of products of sulfonamides alkylation and acylation (Table 5) are lacking the bands of the stretching vibrations of N–H bond (3300–3200 cm^{-1}). In the spectra of acylation products **XVIIa, b** appear the characteristic absorption bands of the amide carbonyl (1680–1670 cm^{-1}). In spectra of all compounds were observed the absorption bands corresponding to unsaturated part of the molecule, to sulfonyl group, and in the spectrum of compound **XVIII** also to nitro group [15].

The ^1H NMR spectra of sulfonamides substituted at nitrogen (Table 6) lack the signal of NH proton and possess signals of methylene protons of benzyl group (4.30–4.40 ppm) (compounds **XIVa, b, XV**), and of

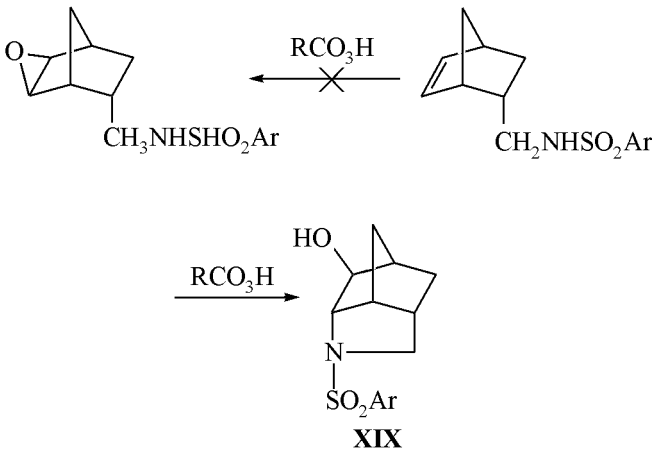
Table 6. ^{1}H NMR spectra of compounds **XIVa, b, XV, XVIIa, b, XVIII,** δ, ppm, coupling constants, Hz

Compd. no.	H^1	H^2, H^3	H^4	H^5	H^{6x}	H^{6n}	H^{7s}, H^{7an}	H^{8A}, H^{8B}	Substituent
XIVa[a]	2.75	5.97, 5.81, $^3J_{2,3}$ 5.5, $^3J_{2,1}$ 2.8, $^3J_{3,4}$ 2.5	2.48	1.46	1.04	1.02	1.27, 1.18, $^2J_{7s,7an}$ 9.2	3.21, 3.24, $^2J_{8A,8B}$ 12.6 $^3J_{8A,5}$ 7.1, $^3J_{8B,5}$ 6.5	4.43, 4.28, $^2J_{H,H}$ 15.3
XIVb[a]	2.70	6.10, 5.74, $^3J_{2,3}$ 5.2 $^3J_{2,1}$ 2.8, $^3J_{3,4}$ 2.5	2.64	2.20	1.63, $^2J_{6x,6n}$ 11.4, $^3J_{6x,5}$ 9.1, $^3J_{6x,1}$ 4.6	0.41, $^3J_{6n,5}$ 3.4, $^4J_{6n,7s}$ 1.9,	1.35, 1.09, $^2J_{7s,7an}$ 7.8	2.90, 2.83, $^2J_{8A,8B}$ 13.6, $^3J_{8A,5}$ 8.7, $^3J_{8B,5}$ 7.5	4.40, 4.30, $^2J_{H,H}$ 14.3
XVa	2.71	6.11, 5.79, $^3J_{2,3}$ 5.7, $^3J_{2,1}$ 2.7	2.64	2.21	1.25, $^2J_{6x,6n}$ 10.8, $^3J_{6x,5}$ 8.4, $^3J_{6x,1}$ 3.6	0.41, $^3J_{6n,5}$ 3.3, $^4J_{6n,7s}$ 2.1	1.34, 1.09, $^2J_{8A,8B}$ 14.1, $^2J_{7s,7an}$ 8.4	2.93, 2.87, $^2J_{H,H}$ 12.6 $^3J_{8A,5}$ 9.0, $^3J_{8B,5}$ 7.5	4.44, 4.37,
XVIIa[b]	2.76	6.04, 5.96, $^3J_{2,3}$ 5.1, $^3J_{2,1}$ 3.0 $^3J_{3,4}$ 2.8	2.50	1.79	1.18, $^2J_{6x,6n}$ 11.1	1.07	1.22, 0.93, $^2J_{7s,7an}$ 8.4	3.90, 3.15, $^2J_{8A,8B}$ 14.0, $^3J_{8A,5}$ 9.0, $^3J_{8B,5}$ 6.9	2.41
XVIIb[b]	2.75	6.09, 5.70, $^3J_{2,3}$ 5.4, $^3J_{2,1}$ 2.7, $^3J_{3,4}$ 2.7	2.75	2.45	1.80, $^2J_{6x,6n}$ 11.7, $^3J_{6x,5}$ 8.1, $^3J_{6x,1}$ 3.3	0.50, $^3J_{6n,5}$ 3.5, $^4J_{6n,7s}$ 2.0	1.39, 1.18, $^2J_{7s,7an}$ 8.4	3.53, 3.44, $^2J_{8A,8B}$ 12.0 $^3J_{8A,5}$ 8.2, $^3J_{8B,5}$ 6.6	2.42 –
XVIII	2.80	6.15, 5.82, $^3J_{2,3}$ 5.7, $^3J_{2,1}$ 4.2, $^3J_{3,4}$ 4.2	2.80	2.48	1.85, $^2J_{6x,6n}$ 11.7, $^3J_{6x,5}$ 8.4, $^3J_{6x,1}$ 3.6	0.54, $^3J_{6n,5}$ 4.2, $^4J_{6n,7s}$ 2.4	1.48, 0.87, $^2J_{7s,7an}$ 8.4	3.46, 3.44, $^2J_{8A,8B}$ 12.6, $^3J_{8A,5}$ 8.4, $^3J_{8B,5}$ 7.5	–

Substituent as follows: [a] N–$\underline{CH}_2$–Ph, [b] CH_3.

a methyl group (~2.4 ppm) (compounds **XVIIa, b**). Also were observed changes in the signals of protons attached to cage skeleton as compared with the resonances in the spectra of the original sulfonamides. In the spectra of compounds **XIVa, b, XVIIa, b** the proton signals from H^4 and H^{7ap} shift upfield, and the signals of protons H^{8A} and H^{8B} are displaced downfield as compared with the corresponding peaks in the spectra of sulfonamides **XIIa, b**. The protons at C^5 were slightly screened by alkyl groups and notably deshielded by acyl groups as show the respective shifts to strong and weak field. The substituents introduced to nitrogen increase the nonequivalence of proton in pairs H^1 and H^4, H^2 and H^3; the difference in the chemical shifts of protons H^1 and H^4 in the spectrum of compound **XVII** attains the value 0.26 ppm, quite uncommon for substituted norbornenes. All the criteria presented above for estimation of the stereochemical features of arylsulfonamides from the norbornene series are completely valid for the analysis of the new group of their derivatives.

It was recently shown that stereoisomeric arylsulfonamides with different substituent orientation with respect to the norbornene skeleton behaved differently in reactions with perphthalic acid. The *exo*-isomers afford epoxy compounds, and the reaction of *endo*-isomers includes heterocyclization that



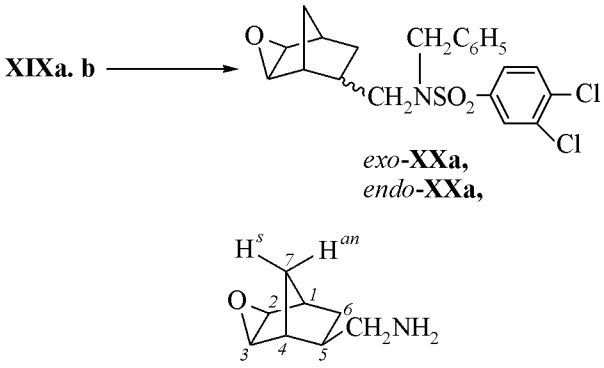
XIX

Table 7. ^{1}H NMR spectra of epoxy compounds **XXa, b, XXI**, δ, ppm, coupling constants, Hz

Compd. no.	H^1	H^2, H^3	H^4	H^5	H^{6x}	H^{6n}	H^{7s}, H^{7an}	H^{8A}, H^{8B}	Substituent (N–$\underline{CH}_2$–Ph)
XXa	2.63	2.95	2.37	1.50	1.18, $^2J_{6x,6n}$ 12.3, $^3J_{6x,5}$ 9.6, $^3J_{6x,1}$ 3.3	0.97, $^3J_{6n,5}$ 3.8	1.26, 0.68, $^2J_{7s,7a}$ 10.5	3.10, 2.95, $^2J_{8A,8B}$ 13.2, $^3J_{8A,5}$ 9.0 $^3J_{8B,5}$ 6.3	4.42, 4.18, $^2J_{H,H}$ 15.3
XXb	2.39	3.18, 3.07, $^3J_{2,3}$ 3.0	2.26	2.06	1.52, $^2J_{6x,6n}$ 12.6, $^3J_{6x,5}$ 9.0, $^3J_{6x,1}$ 3.9	0.87, $^4J_{6n,7s}$ 2.1	1.16, 0.58, $^2J_{7s,7a}$ 10.5	3.28, 3.07, $^2J_{8A,8B}$ 13.5 $^3J_{8A,5}$ 8.7, $^3J_{8B,5}$ 6.6	4.41, 4.25, $^2J_{H,H}$ 15.3
XXI	2.37	3.01	2.31	1.46	1.41 $^3J_{6x,5}$ 8.1 $^3J_{6x,1}$ 2.7	1.02, $^3J_{6n,5}$ 3.8	1.17, 0.74, $^2J_{7s,7a}$ 10.2	2.55, 2.47, $^2J_{8A,8B}$ 12.5 $^3J_{8A,5}$ 7.7, $^3J_{8B,5}$ 6.8	–

finally furnishes *N*-(arylsulfonyl)-*exo*-2-hydroxy-4-azatricyclo[4.2.1.0^{3,7}]nonanes (substituted azabrendanes, **XIX**). The structure of the latter was proved by spectral methods and X-ray diffraction study [11].

The investigation of structures of epoxidation products obtained from sulfonamides **XIVa, b**



XXI

revealed the decisive importance of the benzyl substituent at nitrogen for the direction of reaction between these compounds and perphthalic acid. The reaction of both sulfonamides, *exo*- and *endo*-isomers with perphthalic acid affords epoxy derivatives **XXa, b**, whose physico-chemical characteristics are given in Table 5.

In the IR spectra of products are observed strong bands in the region 850–840 cm^{-1} characteristic of epoxynorbornanes [ν(C–O) of the epoxy ring]. The ^{1}H NMR spectra contain signals of protons at the epoxy ring (3.07–3.18 ppm) and very characteristic of *exo*-epoxynorbornanes upfield signals of H^{7ap} protons (0.5–0.7 ppm) (Table 7). The H^{7ap} protons situated directly over the plane of the epoxy ring suffer magnetically-anisotropic influence and considerable shielding [7, 17].

The comparison of ^{1}H NMR spectra of epoxides **XXa, b** permits evaluation of the effect on the structure of the spectra of the substituent orientation with respect to the carbon skeleton. In the spectrum of *endo*-isomer **XXb** compared to that of *exo*-isomer **XXa** is increased the nonequivalence of protons H^2 and H^3, the signals from H^1 and H^4 are approached, and also notably grows the nonequivalence of protons attached to C^6, and the signals from protons at C^5 and C^8 are shifted downfield. The position of signals from protons at C^8 undergoes inversion as compared to the signals in the spectra of the corresponding olefins **XIVa, b**, namely, the signals of protons H^{8A} and H^{8B} belonging to *endo*-isomer **XXb** appear in a weaker field than those of *exo*-isomer **XXa**. In Table 7 are also presented the spectral parameters of the key epoxyamine **XXI** that was synthesized in [20].

EXPERIMENTAL

IR spectra were recorded on spectrophotometer Specord 75IR in the region 4000–400 cm^{-1} from thin films or KBr pellets. ^{1}H and ^{13}C NMR spectra were registered on spectrometer Varian VXR-300 at operating frequencies 300 and 75.4 MHz respectively from solutions in deuterochloroform with TMS or HMDS as internal reference. Some spectra were measured by procedures COSY and NOESY. The reaction progress was monitored and the purity of compounds synthesized was checked by TLC on Silufol UV–254 plates, eluents ether and ether–hexane mixture, development in iodine vapor.

Synthesis of stereoisomeric 5-cyanobicyclo[2.2.1]-hept-2-enes and stereoisomeric 5-aminomethylbicyclo-[2.2.1]hept-2-enes (**IIa, b**) was carried out along procedures described in [5, 13, 14]. The characteristics of compounds obtained were consistent with the published data.

***N*-(Arylsulfonyl)-*exo*- (and *endo*)-5-aminomethylbicyclo[2.2.1]hept-2-enes.** (a) To a stirred emulsion of 0.01 mol of amine **IVa, b** in 10 ml of ethyl ether and 2 ml of 20% water solution of sodium hydroxide was added dropwise a solution of 0.01 mol of an appropriate arylsulfonyl chloride in 10 ml of ether. The end of reaction was determined by TLC monitoring. The organic layer was separated, the solvent was removed. The product formed containing salt impurity was dissolved in 20 ml of chloroform–water mixture (1 : 1), the organic layer was separated, dried with calcined magnesium sulfate, the solvent was removed, and the reaction product was purified by crystallization. The characteristics of compounds and elemental analyses are given in Tables 1 and 2. This procedure was used in the synthesis of compounds **Vb, VIb, XIa, b, XIIIa, b**.

(b) To a stirred solution of 0.01 mol of an appropriate amine and 0.9 ml of triethylamine in 10 ml of ether was added dropwise the solution of 0.01 mol of an appropriate arylsulfonyl chloride in 10 ml of ether. The reaction was monitored by TLC. On completion of reaction the solvent was removed. The product formed containing salt impurity was dissolved in 20 ml of chloroform–water mixture (1 : 1), the organic layer was separated, dried with calcined magnesium sulfate, the solvent was removed, and the reaction product was purified by crystallization from a mixture 2-propanol–water (2 : 1). The characteristics of compounds obtained **IVa, b, VII, b–Xa, b, XIIa, b** are listed in Tables 1 and 2.

***N*-(Arylsulfonyl)-*N*-(benzyl)-5-aminomethylbicyclo[2.2.1]hept-2-enes (XIVa, b, XV).** To a mixture of 0.01 mol of sulfonamide **III, XIIa, b**, 1.9 g (0.015 mol) of benzyl chloride and 0.32 g (0.001 mol) of tetrabutylammonium bromide in 20 ml of benzene was added at stirring 2.3 ml of 50% water solution of NaOH. The mixture was heated at stirring (65–70°C) for 2 h till completion of reaction by TLC evidence. The cooled reaction mixture was washed 2 times with water, the organic layer was separated, and from the water layer the reaction products were extracted with ether. The combined organic solutions were dried with calcined magnesium sulfate, the solvent was removed, and the reaction products were purified by column chromatography on silica gel with subsequent crystallization. The characteristics of compounds **XIVa, b, XV** are given in Table 5, the parameters of ^{1}H NMR spectra in Table 6.

***N*-(Acyl)-*N*-(3,4-dichlorophenylsulfonyl)-5-aminomethylbicyclo[2.2.1]hept-2-enes (XVIIa, b, XVIII).** A mixture of 0.01 mol of sulfonamide **XIIa, b**, 1.4 g of powdered sodium hydroxide, 0.81 g of potassium carbonate, 0.97 g of tetrabutylammonium bromide, and 15 ml of anhydrous benzene was stirred for 2 h at 35–40°C. Then the reaction mixture was heated to 60°C, and was added dropwise 0.03 mol of an appropriate acyl chloride in 5 ml of anhydrous benzene, and the mixture was stirred at 60–70°C till the end of reaction (TLC monitoring). The cooled mixture was subjected to the above described workup, and the products were purified. The characteristics of compounds **XVIIa, b, XVIII** are given in Table 5, the parameters of ^{1}H NMR spectra in Table 6.

***N*-(Benzyl)-*N*-(3,4-dichlorophenylsulfonyl)-5-aminomethyl-*exo*-2,3-epoxybicyclo[2.2.1]heptanes (XXa, b).** To a mixture of 0.002 mol of alkylated sulfonamide **XIVa, b** in 10 ml of ethyl acetate, 0.001 mol of urea, and 0,004 mol of 50% water solution of hydrogen peroxide at 20–25°C while stirring was added by small portions 0.004 mol of powdered phthalic anhydride. The reaction mixture was stirred till the end of the process (TLC monitoring), then it was treated with saturated solution of sodium carbonate till neutral reaction of the medium. The organic layer was separated, the water layer was extracted with chloroform. The combined organic solutions were dried with calcined magnesium sulfate, the solvent was removed, and epoxides were purified by recrystallization. The characteristics of compounds obtained are given in Table 5, the parameters of ^{1}H NMR spectra in Table 7.

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