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# Epoxidation and Heterocyclization of Arenesulfonamides of the Norbornene Series

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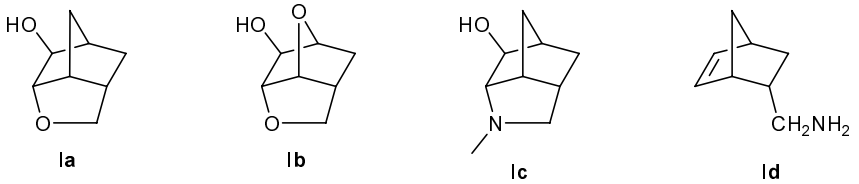
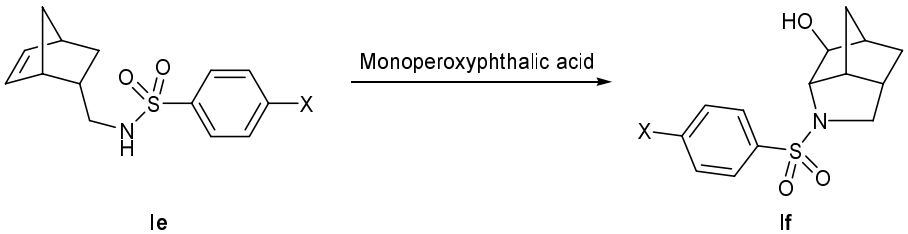
**Abstract**—Reactions of previously known and newly synthesized *N*-(bicyclo[2.2.1]hept-5-en-*endo*-2-ylmethyl)arenesulfonamides with monoperoxyphthalic acid generated *in situ* from phthalic anhydride and 30% hydrogen peroxide lead mostly to the corresponding *N*-arylsulfonyl-*exo*-2-hydroxy-4-azatricyclo[4.2.1.$0^{3,7}$]-nonanes (azabrendanes). In some cases, *N*-(*exo*-5,6-epoxybicyclo[2.2.1]hept-5-en-*exo*-2-ylmethyl)arenesulfonamides were isolated as the only products or mixtures of alternative oxidation products were obtained. The presence of electron-acceptor nitro groups in the benzene ring and bulky substituents, primarily in the *ortho* position, is considered to be a structural factor preventing the primary oxidation products (epoxy derivatives) from undergoing heterocyclization.

Compounds with a cage-like structure are extensively studied due to their high biological activity [1]. Such polycyclic compounds can be synthesized on the basis of substituted norbornenes [2]. As compared to oxabrendane **Ia** and its analog **Ib** having an oxygen bridge [3], substituted azabrendanes, *exo*-2-hydroxy-4-azatricyclo[4.2.1.$0^{3,7}$]nonanes **Ic** have been studied relatively poorly. These compounds were synthesized mainly from stereochemically pure bicyclo[2.2.1]hept-5-en-*endo*-2-ylmethylamine (**Id**). *N*-Arylsulfonyl-substituted azabrendanes **If** were obtained for the first time by reactions of *N*-(bicyclo[2.2.1]hept-5-en-*endo*-2-ylmethyl)arenesulfonamides having a *para*-substituent (X = $CH_3$, F, Cl, Br, $NO_2$, NHCOOMe, COOEt, etc.) with monoperoxyphthalic acid (both prepared preliminarily and generated *in situ* from phthalic anhydride and aqueous hydrogen peroxide) [4] (Scheme 1).

Examples of epoxidation of *endo*-sulfonamides of the norbornene series, which is not accompanied by heterocyclization, have also been reported. Epoxy derivatives were obtained from perfluoroalkanesulfonamides like **Ig** [5], sulfonamides **Ih** in which the amino group is more distant from the norbornane fragment [6], and N,N-disubstituted sulfonamides like **Ii** [7]. Epoxy derivatives were also formed in reactions of all sulfonamides with *exo* configuration of the norbornene




**Scheme 1.**

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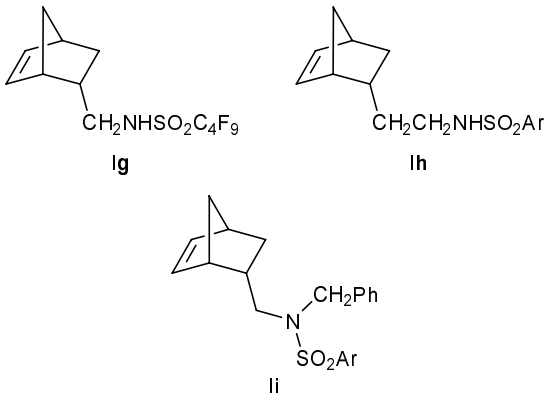
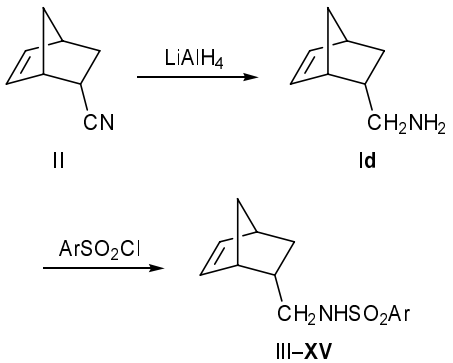



moiety [8]. The ability of compounds derived from amine **Id** to undergo heterocyclization in reactions with peroxy acids strongly depends on the substituent on the nitrogen atom. For example, epoxidation of the corresponding *N*-arylureas and phosphonamides leads to substituted azabrendanes [9, 10], while carboxamides give rise to epoxy derivatives [11].

Insofar as cage-like sulfonamides and their oxidation products are known to exhibit high biological activity (specifically neurotropic) [12], alternative procedures for the synthesis of substituted azabrendanes have been proposed. Among these, functionalization at the nitrogen atom of the parent compound, *exo*-2-hydroxy-4-azatricyclo[4.2.1.$0^{3,7}$]nonane [13] and alkylation of arenesulfonamides with *exo*-5,6-epoxybicyclo[2.2.1]heptan-*endo*-2-ylmethyl bromide under conditions of phase-transfer catalysis [14]. Taking into account that *N*-sulfonyl derivatives of amine **Id** are capable of undergoing alternative transformations and

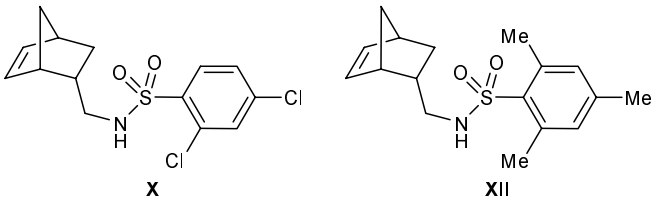
**Scheme 2.**

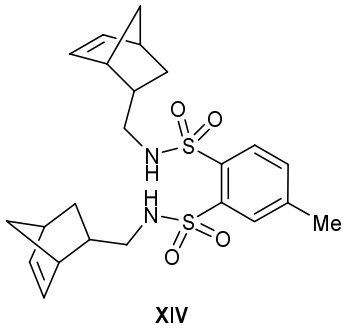



**III**, Ar = 2-$O_2NC_6H_4$; **IV**, Ar = 3-$O_2NC_6H_4$; **V**, Ar = 2-$O_2N$-4-$MeC_6H_3$; **VI**, Ar = 2,4-$(O_2N)_2C_6H_3$; **VII**, Ar = 2-$O_2N$-4-Cl-$C_6H_3$; **VIII**, Ar = 2-MeO-5-$O_2NC_6H_3$; **IX**, Ar = 2-Me-4-$O_2N$-$C_6H_3$; **X**, Ar = 2,4-$Cl_2C_6H_3$; **XI**, Ar = 3,4-$Cl_2C_6H_3$; **XII**, Ar = 2,4,6-$Me_3C_6H_2$; **XIII**, Ar = 2,4,6-(*i*-Pr)$_3C_6H_2$; **XIV**, Ar = 4-Me-2-($C_7H_9CH_2NHSO_2$)$C_6H_3$ ($C_7H_9$ stands for bicyclo[2.2.1]hept-*endo*-2-yl); **XV**, Ar = 2-naphthyl.

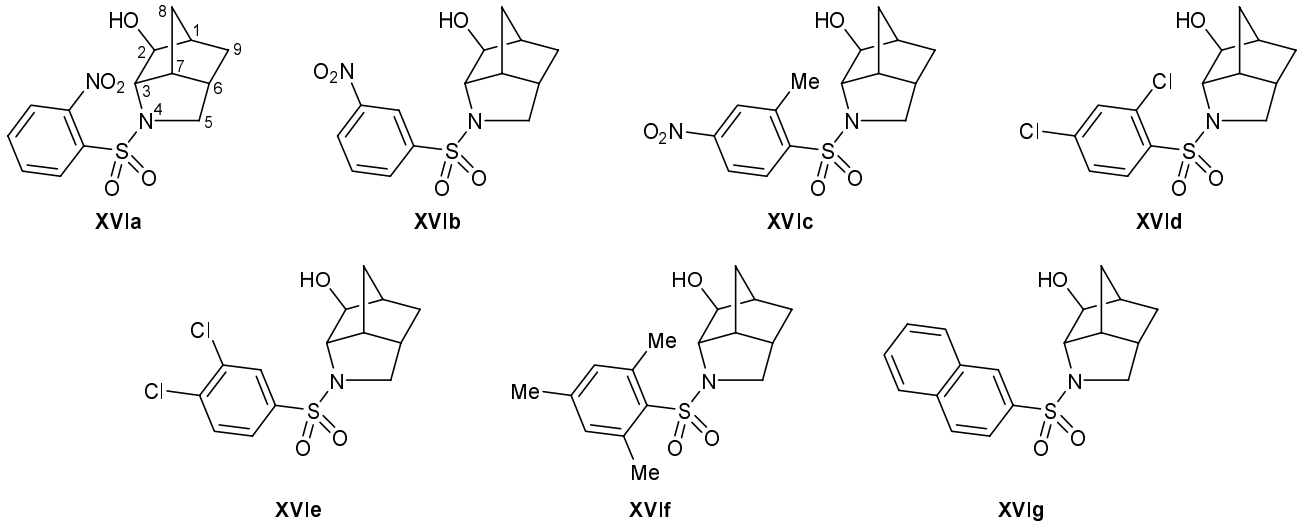
that their structure is closely related to the behavior in reactions with peroxy acids, in the present work we examined epoxidation of *N*-(bicyclo[2.2.1]hept-5-en-*endo*-2-ylmethyl)arenesulfonamides **III**–**XV** containing one, two, or three substituents in different position of the aromatic ring.

Sulfonamides **III**–**XV** were synthesized according to Scheme 2 from bicyclo[2.2.1]hept-5-ene-*endo*-2-carbonitrile (**II**) which is the Diels–Alder adduct of cyclopentadiene and acrylonitrile (it was separated from the *exo*-2 isomer by fractional distillation) [15]. The reduction of bicyclic nitrile **II** to amine **Id** with lithium tetrahydridoaluminate was described in [15, 16]. Treatment of amine **Id** with arenesulfonyl chlorides afforded the corresponding arenesulfonamides **III**–**XV** containing various substituents in the benzene ring (nitro, methyl, isopropyl, and methoxy groups and chlorine atoms). Specific attention was given to the reactions involving *ortho*-substituted benzenesulfonamides of the norbornene series. Mesityl, 2,4,6-triisopropylphenyl, and β-naphthyl groups were involved as bulky aromatic fragments. Compounds **III**–**VI**, **VIII**, **IX**, **XI**, and **XV** were reported in [7], compounds **VII** and **XIII** were described in [4], and sulfonamides **X**, **XII**, and **XIV** were synthesized for the first time.




The IR spectra of these compounds contain absorption bands at 1330–1310, 1150–1140, and 3290–3200 $cm^{-1}$, belonging, respectively, to symmetric and antisymmetric stretching vibrations of the sulfonyl group and stretching vibrations of the N–H bond [17]. The IR bands were difficult to assign due to the presence of two unsaturated fragments, aromatic system and strained double bond [18]. Bending vibrations of



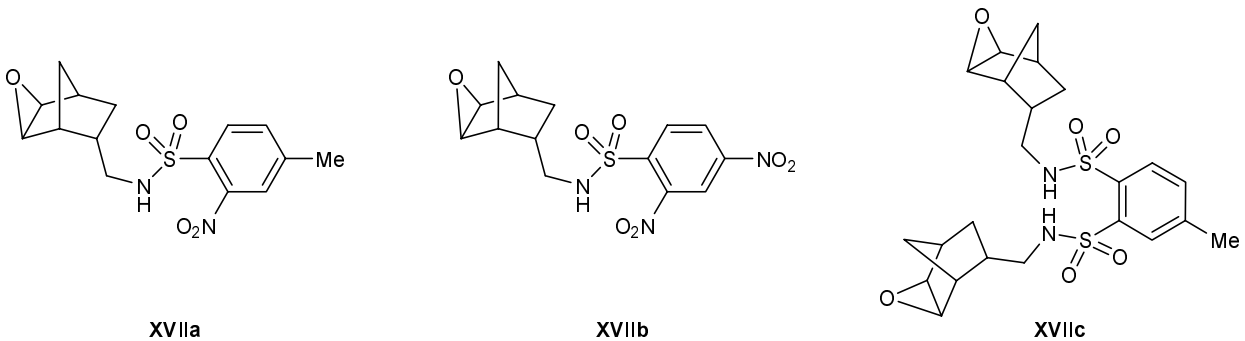

the norbornene =C–H bond appeared in the region 725–715 $cm^{-1}$, indicating *endo* orientation of the substituent in the bicyclic skeleton [4].

The *endo* configuration of sulfonamides **III**–**XV** also follows from the position of the 2-H (δ 2.05–2.20 ppm) and *endo*-3-H signals (δ 0.42–0.44 ppm), as well as from considerable nonequivalence of protons at the double bond (5-H and 6-H, Δδ = 0.21–0.33 ppm) and at $C^3$ (δ 1.27–1.35 ppm) [4]. Introduction of substituents to the nitrogen atom affects the position of signals from 2-H and 8-H which are spatially close to the arylsulfonyl group.

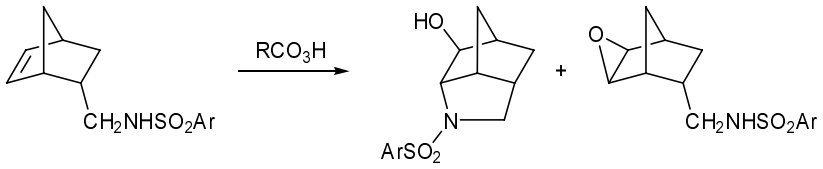
Sulfonamides **III**–**XV** were subjected to epoxidation according to the standard procedure [4, 8] with the use of monoperoxyphthalic acid which was generated *in situ* from phthalic anhydride and 30% aqueous hydrogen peroxide. The reactions were carried out in ethyl acetate in the presence of urea (to adjust proton-acceptor power of the medium); the progress of the reactions was monitored by thin-layer chromatography. Most oxidation products had the structure of *N*-arylsulfonyl-4-azatricyclo[4.2.1.$0^{3,7}$]nonanes (azabrendanes **XVIa**–**XVIg**) which were isolated as individual compounds in high yields. Some oxidation products were epoxy derivatives **XVIIa**–**XVIIc**.

Repeated epoxidation of sulfonamides **VII** and **XIII** allowed us to detect in the reaction mixture both possible oxidation products, the corresponding azabrendane and epoxy derivative (Scheme 3). These findings contradict our previous data reported in [4] where compounds **XVIII** and **XX** were assigned the azabrendane structure by analogy with other cases. A mixture of oxidation products was also obtained from sulfonamide **VIII**. We failed to separate isomeric products by chromatography. According to the $^1$H NMR data, the ratio of azabrendane and epoxy derivative in the product mixtures obtained from sulfonamides **VII**, **VIII**, and **XIII** was 2:1, 1:4, and 2:3, respectively.

The IR spectra of all oxidation products lacked absorption in the region 725–715 $cm^{-1}$, which corresponds to bending vibrations of the strained double C=C bond in the bicyclic skeleton [18]. The spectra contained absorption bands belonging to sulfonyl groups at 1360–1320 and 1170–1125 $cm^{-1}$. Epoxy derivatives characteristically showed in the IR spectra



**Scheme 3.**

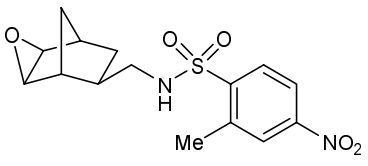



**VII**, **VIII**, **XIII** **XVIII–XX** **XXI–XXIII**

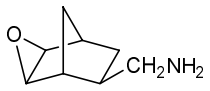
**XVIII**, **XXI**, Ar = 2-$O_2N$-4-$ClC_6H_3$; **XIX**, **XXII**, Ar = 2-MeO-5-$O_2NC_6H_3$; **XX**, **XXIII**, Ar = 2,4,6-(*i*-Pr)$_3C_6H_2$.

strong absorption bands in the region 860–845 $cm^{-1}$ due to stretching vibrations of oxirane C–O bonds [19]. No analogous band was present in the spectra of substituted azabrendanes. Different positions of the OH and NH stretching vibration bands did not allow us to distinguish between the isomeric products.

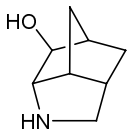
The structure of the oxidation products was determined by $^1H$ and $^{13}C$ NMR spectroscopy. Signals were assigned on the basis of published data [20] and two-dimensional spectra (COSY and NOESY) of *N*-(*exo*-5,6-epoxybicyclo[2.2.1]hept-5-en-*exo*-2-ylmethyl)-4-methyl-2-nitrobenzenesulfonamide (**XVIIa**).




**XXIV**




**XXV**




**XXVI**

The $^1H$ NMR spectra of epoxides contained doublet signals at δ 3.10–3.20 ppm ($^3J$ = 3.0–3.4 Hz), belonging to protons in the oxirane ring (5-H, 6-H). Unusual position of the 5-H and 6-H signals from diepoxy derivative **XVIIc** is likely to result from anisotropic effect of the neighboring fragments in its sterically strained molecule. Quite characteristic is the position of the *anti*-7-H signal (δ 0.7–0.9 ppm); this proton is located directly above the *exo*-oriented (according to the Alder rule [20, 21]) oxirane fragment which exerts shielding effect. In the spectrum of dinitrobenzenesulfonamide **XVIIb**, a number of signals are displaced appreciably downfield (especially those from 8-$H_A$, 8-$H_B$, 2-H and *exo*-3-H) relative to the corresponding signals of other epoxy derivatives. The largest difference is observed for compound **XXV** (δ 2.55, 2.47, 1.46, and 1.41 ppm).

There are considerable differences in the chemical shifts of protons in the bicyclic skeleton of compound **XVIIa** and its isomer **XXIV** with *exo* orientation of the substituent on $C^2$, δ, ppm: 2.16 and 1.71 (2-H), 1.76 and 1.49 (*exo*-3-H), and 0.80 and 1.06 (*endo*-3-H); the chemical shifts of 5-H and 6-H in these compounds are similar. The $C^5$ and $C^6$ signals in the $^{13}C$ NMR spectra of compounds **XVIIa**–**XVIIc** appear in the $\delta_C$ range from 48.8 to 51.4 ppm [22]. The difference in the chemical shifts of $C^5$ and $C^6$ in **XVIIa**–**XVIIc** is larger than in compounds **XXIV** and **XXV** with *exo* orientation of the arylsylfonylaminomethyl group. The $C^7$ signal is displaced considerably upfield ($\Delta\delta_C$ = 20–25 ppm), as compared to substituted norbornenes; and the difference is smaller by 4–4.5 ppm than that for *exo* isomers **XXIV** and **XXV** [20, 22].

The $^1H$ NMR spectra of azabrendanes **XVI** and **XVIII**–**XX** contain a one-proton singlet from 2-H (δ 3.6–3.8 ppm) and a doublet from 3-H (δ 3.5–3.7 ppm), the latter signal is split due to coupling with 7-H ($^3J$ = 4.8–5.2 Hz). Signals from the diastereotopic 5-$H_A$ and 5-$H_B$ protons are located in the δ region 3.1–3.4 ppm; they appear as quartet and doublet due to coupling with each other and (one of these) with 6-H. Also, signals from two pairs of geminal protons on $C^8$ and $C^9$ are present. The corresponding geminal coupling constants differ considerably due to rigid structure of the tricyclic skeleton: $^2J_{HH}$ = 8.9–9.8, 9.4–11.6, and 12.5–13.4 Hz for 5-H, 8-H, and 9-H, respectively. Protons in the bridgehead positions (1-H and 7-H) are also nonequivalent (δ 2.04–2.20 and 2.29–2.60 ppm, respectively), for the 7-H proton suffers deshielding effect from the five-membered nitrogen-containing ring. As compared to parent *exo*-2-hydroxy-4-azatricyclo[4.2.1.$0^{3,7}$]nonane (**XXVI**), signals from protons on $C^5$, $C^2$, and $C^3$, i.e., those located in the vicinity of the nitrogen atom attached to electron-acceptor sulfonyl group, are displaced downfield.

Characteristic signals in the $^{13}C$ NMR spectra of azabrendanes **XVIe**, **XVIf**, and **XX** are observed in the $\delta_C$ regions 80.2–81.7 ($C^2$), 68.4–69.9 ($C^3$), and 53.4–54.8 ppm ($C^5$); the corresponding carbon atoms are neighboring to oxygen and nitrogen. Carbon signals from the other methylene groups ($C^8$, $C^9$) are located in a stronger field close to each other ($\delta_C$ 33.6–36.1 ppm). The bridgehead carbon atoms ($C^1$ and $C^7$), as well as protons attached thereto, considerably differ in chemical shifts (by 4.5 ppm).

Our results essentially differ from published data for epoxidation of *para*-substituted sulfonamides of the norbornane series [4]. The reaction direction depends only on the sulfonamide structure, namely on the nature, number, and position of substituents in the aromatic ring. Among the examined compounds, heterocyclization occurred with those having free *ortho* positions in the benzene ring (compounds **IV** and **XI**) and 2-naphthalenesulfonamide **XV**. The formation of azabrendanes **XVIc**, **XVId**, and **XVIf** in the oxidation of sulfonamides **V**, **X**, and **XII** suggests that steric hindrances created by chlorine atom and methyl group in the *ortho* position are insufficient to prevent heterocyclization or that these substituents increase the nucleophilicity of the nitrogen atom. The probability for heterocyclization of arenesulfonamides in the oxidation with monoperoxyphthalic acid increases in the following series of *ortho* substituents: bicyclo[2.2.1]-hept-5-en-*endo*-2-ylmethylaminosulfonyl < $NO_2$ < *i*-Pr < MeO < Me < Cl < H.

Comparison of the chemical behavior of *o*-nitrobenzenesulfonamide **III** and its analogs **V** and **VI** having an additional substituent (methyl or nitro group, respectively) in the *para* position of the benzene ring demonstrates an important role of steric factor in the heterocyclization of epoxy intermediate. The same also follows from comparison of mesitylenesulfonamide **XII** with its triisopropyl-substituted analog **XIII**. On the one hand, the role of steric factor in reactions of bicyclic compounds increases, for nucleophilic attack by the nitrogen atom on electrophilic centers (carbon atoms in the oxirane ring) occurs from the sterically loaded internal (*endo*) area of the bicyclic skeleton [10]. On the other hand, stereoelectronic (polar) effect of sulfonyl and nitro groups is also important: this effect leads to reduction of electron density on the nitrogen atom and hence of nucleophilic reactivity of substituted amino group in sulfonamide molecules. However, our experimental results, as well as the results of quantum-chemical calculations of the electron density distribution in *N*-(*exo*-5,6-epoxybicyclo[2.2.1]-heptan-*endo*-2-ylmethyl)arenesulfonamides [23], did not allow us to estimate separately the contributions of stereoelectronic (polar) and steric factors to the reaction under study.

## EXPERIMENTAL

The IR spectra were measured in the range from 4000 to 400 $cm^{-1}$ on a Specord 75IR spectrometer from samples prepared as thin films or KBr pellets. The $^1H$ NMR spectra were recorded on Varian-VXR (300 MHz) and Gemini-BB instruments (500 MHz) from solutions in chloroform-*d* or DMSO-$d_6$ using TMS or HMDS as internal reference. The $^{13}C$ NMR spectra, including two-dimensional COSY and NOESY experiments, were run on a Gemini-BB spectrometer at 100.7 MHz. The progress of reactions and the purity of products were monitored by TLC on Silufol UV-254 plates using diethyl ether as eluent (development with iodine vapor). The elemental compositions were determined on a Carlo Erba analyzer.

Bicyclo[2.2.1]hept-5-en-*endo*-2-ylmethylamine (**Id**) was prepared by the procedure reported in [16]. Sulfonamides **III**–**VI**, **VIII**, **IX**, **XI**, and **XV** were described previously in [4], and compounds **VII** and **XIII**, in [7].

***N*-(Bicyclo[2.2.1]hept-5-en-*endo*-2-ylmethyl)-2,4-dichlorobenzenesulfonamide (X).** Amine **Id**, 0.40 g (0.0033 mol), was dispersed in a mixture of 8 ml of diethyl ether and 0.65 g (0.54 ml, 0.0033 mol) of 20% aqueous sodium hydroxide, and a solution of 0.80 g of 2,4-dichlorobenzenesulfonyl chloride in 5 ml of diethyl ether was added dropwise under stirring. When the reaction was complete (TLC), the crude product containing an impurity of sodium chloride was dissolved in 20 ml of a 1:1 chloroform–water mixture, the organic phase was separated and dried over calcined magnesium sulfate, and the solvent was removed. Yield 90.2%, mp 143–145°C, $R_f$ 0.86 (diethyl ether). IR spectrum, ν, $cm^{-1}$: 3285, 3100, 3079, 1470, 1335, 1173, 850, 731. $^1H$ NMR spectrum ($CDCl_3$), δ, ppm: 8.01 s (1H, $H_{arom}$), 7.52 d (1H, $H_{arom}$), 7.36 d (1H, $H_{arom}$), 6.11 d.d (1H, 5-H), 5.78 d.d (1H, 6-H), 5.12 t (1H, NH), 2.81 m (1H, 1-H), 2.77 m (1H, 4-H), 2.66 m (1H, 8-$H_A$), 2.54 m (1H, 8-$H_B$), 2.19 m (1H, 2-H), 1.79 m (1H, *exo*-3-H), 1.44 d.d (1H, *syn*-7-H), 1.20 d (1H, *anti*-7-H), 0.44 m (1H, *endo*-3-H). Found, %: N 4.31. $C_{14}H_{15}Cl_2NO_2S$. Calculated, %: N 4.22.

***N*-(Bicyclo[2.2.1]hept-5-en-*endo*-2-ylmethyl)-mesitylenesulfonamide (XII)** was synthesized in a similar way. Yield 86.8%, mp 139–141°C, $R_f$ 0.61

(diethyl ether). $^1$H NMR spectrum ($CDCl_3$), δ, ppm: 6.96 s (2H, $H_{arom}$), 6.08 d.d (1H, 5-H), 5.68 d.d (1H, 6-H), 4.51 t (1H, NH), 2.78 m (1H, 1-H), 2.75 m (1H, 4-H), 2.70 m (1H, 8-$H_A$), 2.63 s (6H, $CH_3$), 2.51 m (1H, 8-$H_B$), 2.30 s (3H, $CH_3$), 2.15 m (1H, 2-H), 1.77 m (1H, *exo*-3-H), 1.30 d.d (1H, *syn*-7-H), 1.24 d (1H, *anti*-7-H), 0.43 m (1H, *endo*-3-H). Found, %: N 4.65. $C_{17}H_{23}NO_2S$. Calculated, %: N 4.59

***N*,*N*′-Bis(bicyclo[2.2.1]hept-5-en-*endo*-2-ylmethyl)-4-methylbenzene-1,2-disulfonamide (XIV)** was synthesized in a similar way. Yield 83.5%, mp 145–147°C, $R_f$ 0.86 (diethyl ether). IR spectrum, ν, cm$^{-1}$: 2982, 2872, 1347, 1170, 1051, 832, 725. Found, %: N 6.15. $C_{23}H_{30}N_2O_4S_2$. Calculated, %: N 6.06.

***exo*-2-Hydroxy-4-(2-nitrophenylsulfonyl)-4-azatricyclo[4.2.1.0$^{3,7}$]nonane (XVIa).** Finely powdered phthalic anhydride, 1.48 g (0.01 mol), was gradually added under stirring to a mixture of 1.54 g (0.005 mol) of sulfonamide **III**, 0.15 g (0.0025 mol) of urea, 0.20 g (0.17 ml, 0.01 mol) of 30% aqueous hydrogen peroxide, and 10 ml of ethyl acetate. When the reaction was complete (TLC), the mixture was neutralized with a saturated solution of sodium carbonate to pH 7–8. The organic phase was separated, the aqueous phase was washed with three portions of chloroform, the extracts were combined with the organic phase and dried over calcined magnesium sulfate, and the solvent was removed. Yield 80.1%, mp 49–50°C. $R_f$ 0.39 (diethyl ether). IR spectrum, ν, cm$^{-1}$: 3322, 3068, 1588, 1562, 1434, 1330, 1156. $^1$H NMR spectrum ($CDCl_3$), δ, ppm: 7.96 d.d (1H, $H_{arom}$), 7.68 d.d (1H, $H_{arom}$), 7.56 m (2H, $H_{arom}$), 3.70 d (1H, 3-H), 3.57 s (1H, 2-H), 3.32 d (1H, 5-$H_B$), 3.28 d.d (1H, 5-$H_A$), 2.51 m (1H, 7-H), 2.30 m (1H, 6-H), 2.12 d (1H, 1-H), 1.90 d.d (1H, *syn*-8-H), 1.86 m (1H, *exo*-9-H), 1.38 d (1H, *anti*-8-H), 0.93 m (1H, *endo*-9-H). Found, %: N 8.55. $C_{14}H_{16}N_2O_5S$. Calculated, %: N 8.64.

***exo*-2-Hydroxy-4-(3-nitrophenylsulfonyl)-4-azatricyclo[4.2.1.0$^{3,7}$]nonane (XVIb)** was synthesized in a similar way from compound **IV**. Yield 79.8%, mp 147–148°C, $R_f$ 0.46 (diethyl ether). IR spectrum, ν, cm$^{-1}$: 3310, 3230, 3060, 1510, 1350, 1180, 1145, 900, 880, 760. $^1$H NMR spectrum ($CDCl_3$), δ, ppm: 8.43 d (1H, $H_{arom}$), 8.20 d.d (1H, $H_{arom}$), 7.56 m (2H, $H_{arom}$), 3.72 s (1H, 2-H), 3.60 d (1H, 3-H), 3.38 d (1H, 5-$H_B$), 3.14 d.d (1H, 5-$H_A$), 2.32 m (1H, 7-H), 2.30 m (1H, 6-H), 2.19 d (1H, 1-H), 1.90 d.d (1H, *syn*-8-H), 1.90 m (1H, *exo*-9-H), 1.44 d (1H, *anti*-8-H), 1.01 m (1H, *endo*-9-H). Found, %: N 8.58. $C_{14}N_{16}N_2O_5S$. Calculated, %: N 8.64.

***exo*-2-Hydroxy-4-(2-methyl-4-nitrophenylsulfonyl)-4-azatricyclo[4.2.1.0$^{3,7}$]nonane (XVIc)** was synthesized in a similar way from compound **IX**. Yield 87.6%, mp 141–142°C, $R_f$ 0.65 (diethyl ether). IR spectrum, ν, cm$^{-1}$: 3245, 3043, 1575, 1520, 1460, 1350, 1330, 1160, 1085, 845. $^1$H NMR spectrum ($CDCl_3$), δ, ppm: 7.85 d.d (1H, $H_{arom}$), 7.63 d (1H, $H_{arom}$), 7.41 d (1H, $H_{arom}$), 3.76 s (1H, 2-H), 3.68 d (1H, 3-H), 3.32 d (1H, 5-$H_B$), 3.28 d.d (1H, 5-$H_A$), 2.67 s (3H, $CH_3$), 2.42 m (1H, 7-H), 2.22 m (1H, 6-H), 2.04 d (1H, 1-H), 1.96 d.d (1H, *syn*-8-H), 1.86 m (1H, *exo*-9-H), 1.48 d (1H, *anti*-8-H), 1.06 m (1H, *endo*-9-H). Found, %: N 8.37. $C_{15}H_{18}N_2O_5S$. Calculated, %: N 8.28.

**4-(2,4-Dichlorophenylsulfonyl)-*exo*-2-hydroxy-4-azatricyclo[4.2.1.0$^{3,7}$]nonane (XVId)** was synthesized in a similar way from compound **X**. Yield 90.5%, mp 116–118°C, $R_f$ 0.66 (diethyl ether). IR spectrum, ν, cm$^{-1}$: 3520, 3280, 3100, 1460, 1350, 1178, 825. $^1$H NMR spectrum ($CDCl_3$), δ, ppm: 7.93 d (1H, $H_{arom}$), 7.68 d.d (1H, $H_{arom}$), 7.59 d (1H, $H_{arom}$), 3.70 s (1H, 2-H), 3.56 d (1H, 3-H), 3.30 d (1H, 5-$H_B$), 3.10 d.d (1H, 5-$H_A$), 2.29 m (1H, 7-H), 2.26 m (1H, 6-H), 2.16 d (1H, 1-H), 1.92 d.d (1H, *syn*-8-H), 1.90 m (1H, *exo*-9-H), 1.40 d (1H, *anti*-8-H), 0.98 m (1H, *endo*-9-H). Found, %: N 4.15. $C_{14}H_{15}Cl_2NO_3S$. Calculated, %: N 4.02.

**4-(3,4-Dichlorophenylsulfonyl)-*exo*-2-hydroxy-4-azatricyclo[4.2.1.0$^{3,7}$]nonane (XVIe)** was synthesized in a similar way from compound **XI**. Yield 83.3%, mp 125–126°C, $R_f$ 0.76 (diethyl ether). IR spectrum, ν, cm$^{-1}$: 3512, 3271, 2881, 1460, 1370, 1331, 1170, 860. $^1$H NMR spectrum ($CDCl_3$), δ, ppm: 7.88 s (1H, $H_{arom}$), 7.61 d.d (1H, $H_{arom}$), 7.55 d (3H, $H_{arom}$), 3.65 s (1H, 2-H), 3.51 d (1H, 3-H), 3.23 d (1H, 5-$H_B$), 3.05 d.d (1H, 5-$H_A$), 2.43 m (1H, 7-H), 2.22 m (1H, 6-H), 2.12 d (1H, 1-H), 1.86 d.d (1H, *syn*-8-H), 1.67 m (1H, *exo*-9-H), 1.35 d (1H, *anti*-8-H), 0.92 m (1H, *endo*-9-H). $^{13}$C NMR spectrum ($CDCl_3$), $\delta_C$, ppm: 138.4, 137.0, 132.6, 130.0, 127.7, 124.8, ($C_{arom}$); 80.2 ($C^2$); 68.4 ($C^3$); 53.4 ($C^5$); 45.8 ($C^7$); 41.3 ($C^1$); 37.9 ($C^6$); 35.9 ($C^8$). Found, %: N 4.12. $C_{14}H_{15}Cl_2NO_3S$. Calculated, %: N 4.02.

***exo*-2-Hydroxy-4-(2,4,6-trimethylphenylsulfonyl)-4-azatricyclo[4.2.1.0$^{3,7}$]nonane (XVIf)** was synthesized in a similar way from sulfonamide **XII**. Yield 71.2%, oily substance, $R_f$ 0.27 (diethyl ether). $^1$H NMR spectrum ($CDCl_3$), δ, ppm: 6.94 s (2H, $H_{arom}$), 3.67 s (1H, 2-H), 3.63 d (1H, 3-H), 3.17 d (1H, 5-$H_B$), 3.11 d.d (1H, 5-$H_A$), 2.62 m (1H, 7-H), 2.61 s (6H,

$CH_3$), 2.33 m (1H, 6-H), 2.28 s (3H, $CH_3$) 2.15 d (1H, 1-H), 1.95 d.d (1H, *syn*-8-H), 1.91 m (1H, *exo*-9-H), 1.41 d (1H, *anti*-8-H), 0.98 m (1H, *endo*-9-H). Found, %: N 4.28. $C_{17}H_{23}NO_3S$. Calculated, %: N 4.36.

***exo*-2-Hydroxy-4-(2-naphthyl)-4-azatricyclo-[4.2.1.0$^{3,7}$]nonane (XVIg)** was synthesized in a similar way from sulfonamide **XV**. Yield 67.4%, oily substance, $R_f$ 0.80 (diethyl ether). IR spectrum, ν, cm$^{-1}$: 3382, 2880, 1450, 1336, 1160, 823. $^1$H NMR spectrum ($CDCl_3$), δ, ppm: 8.47–7.56 m (7H, $H_{arom}$), 3.77 s (1H, 2-H), 3.71 d (1H, 3-H), 3.34 d (1H, 5-$H_B$), 3.18 d.d (1H, 5-$H_A$), 2.31 m (1H, 7-H), 2.29 m (1H, 6-H), 2.18 d (1H, 1-H), 1.90 d.d (1H, *syn*-8-H), 1.88 m (1H, *exo*-9-H), 1.37 d (1H, *anti*-8-H), 1.00 m (1H, *endo*-9-H). $^{13}$C NMR spectrum ($CDCl_3$), $\delta_C$, ppm: 135.0–127.6 ($C_{arom}$), 81.7 ($C^2$), 69.9 ($C^3$), 54.8 ($C^5$), 46.4 ($C^7$), 41.9 ($C^1$), 37.4 ($C^6$), 34.2 ($C^8$). Found, %: N 4.36. $C_{18}H_{19}NO_3S$. Calculated, %: N 4.25.

***N*-(*exo*-5,6-Epoxybicyclo[2.2.1]hept-5-en-*endo*-2-ylmethyl)-4-methyl-2-nitrobenzenesulfonamide (XVIIa).** Finely powdered phthalic anhydride, 1.48 g (0.01 mol), was gradually added under stirring to a mixture of 1.61 g (0.005 mol) of sulfonamide **V**, 0.15 g (0.0025 mol) of urea, 0.20 g (0.17 ml, 0.01 mol) of 30% aqueous hydrogen peroxide, and 10 ml of ethyl acetate. When the reaction was complete (TLC), the mixture was subjected to standard treatment. The organic phase was separated, the aqueous phase was washed with three portions of chloroform, the extracts were combined with the organic phase and dried over calcined magnesium sulfate, and the solvent was removed. Yield 83.5%, mp 142–143°C, $R_f$ 0.63 (diethyl ether). IR spectrum, ν, cm$^{-1}$: 3410, 1661, 1550, 1430, 1370, 1350, 1172, 840. $^1$H NMR spectrum ($CDCl_3$), δ, ppm: 8.02 d (1H, $H_{arom}$), 7.68 d (1H, $H_{arom}$), 7.25 d.d (1H, $H_{arom}$), 5.25 t (1H, NH), 3.14 d.d (1H, 5-H), 3.11 d.d (1H, 6-H), 3.10 m (1H, 8-$H_A$), 3.05 m (1H, 8-$H_B$), 2.81 s (3H, $CH_3$), 2.53 m (1H, 4-H), 2.50 m (1H, 1-H), 2.16 m (1H, 2-H), 1.76 m (1H, *exo*-3-H), 1.40 d.d (1H, *syn*-7-H), 0.80 m (1H, *endo*-3-H), 0.75 d (1H, *anti*-7-H). Found, %: N 8.35. $C_{15}H_{18}N_2O_5S$. Calculated, %: N 8.28.

***N*-(*exo*-5,6-Epoxybicyclo[2.2.1]hept-5-en-*endo*-2-ylmethyl)-2,4-dinitrobenzenesulfonamide (XVIIb)** was synthesized in a similar way from compound **VI**. Yield 84.3%, mp 142–143°C, $R_f$ 0.51 (diethyl ether). IR spectrum, ν, cm$^{-1}$: 3357, 3300, 3115, 3080, 3046, 1560, 1546, 1370, 1355, 1175, 1148, 850, 775. $^1$H NMR spectrum ($CDCl_3$), δ, ppm: 8.82 d (1H, $H_{arom}$), 8.25 d.d (1H, $H_{arom}$), 7.28 d.d (1H, $H_{arom}$), 4.46 t (1H, NH), 3.18 d.d (1H, 5-H), 3.14 d.d (1H, 6-H), 3.15–3.05 m (2H, 8-$H_A$, 8-$H_B$), 2.58 m (1H, 4-H), 2.54 m (1H, 1-H), 2.18 m (1H, 2-H), 1.87 m (1H, *exo*-3-H), 1.43 d.d (1H, *syn*-7-H), 0.91 m (1H, *endo*-3-H), 0.73 d (1H, *anti*-7-H). $^{13}$C NMR spectrum ($CDCl_3$), $\delta_C$, ppm: 148.2, 132.8, 130.7, 127.3, 124.5, 121.0 ($C_{arom}$); 51.4 ($C^5$); 48.9 ($C^6$); 45.5 ($C^8$); 40.5 ($C^2$), 38.8 ($C^1$); 37.7 ($C^4$); 30.3 ($C^3$); 27.7 ($C^7$). Found, %: N 11.29. $C_{14}H_{15}N_3O_7S$. Calculated, %: N 11.38.

***N*,*N*′-Bis(*exo*-5,6-epoxybicyclo[2.2.1]hept-*endo*-2-ylmethyl)-4-methylbenzene-1,2-disulfonamide (XVIIc)** was synthesized in a similar way from bissulfonamide **XIV**. Yield 86.7%, oily substance, $R_f$ 0.49 (diethyl ether). IR spectrum, ν, cm$^{-1}$: 3323, 1580, 1420, 1342, 1168, 1131, 858. $^1$H NMR spectrum ($CDCl_3$), δ, ppm: 8.09 d (1H, $H_{arom}$), 8.00 d (1H, $H_{arom}$), 7.54 d.d (1H, $H_{arom}$), 6.20 t (1H, NH), 3.73 d.d (1H, 5-H), 3.53 d.d (1H, 6-H), 2.80–3.00 m (2H, 8-$H_A$, 8-$H_B$), 2.67 s (3H, $CH_3$), 2.57 m (1H, 4-H), 2.47 m (1H, 1-H), 2.18 m (1H, 2-H), 1.68 m (1H, *exo*-3-H), 1.34 d.d (1H, *syn*-7-H), 0.90 m (1H, *endo*-3-H), 0.71 d (1H, *anti*-7-H). Found, %: N 5.58. $C_{23}H_{30}N_2O_6S_2$. Calculated, %: N 5.67.

**4-(4-Chloro-2-nitrophenylsulfonyl)-*exo*-2-hydroxy-4-azatricyclo[4.2.1.0$^{3,7}$]nonane (XVIII) and *N*-(*exo*-5,6-epoxybicyclo[2.2.1]hept-*endo*-2-ylmethyl)-4-chloro-2-nitrobenzenesulfonamide (XXI)** (a mixture of isomers) were obtained by oxidation of sulfonamide **VII** according to the above procedure. Overall yield 94.2% (ratio **XVIII**:**XXI** = 1:2, according to the $^1$H NMR data), mp 123–124°C (mixture), $R_f$ 0.40 (diethyl ether). IR spectrum, ν, cm$^{-1}$: 3536, 1552, 1472, 1376, 1335, 1168, 843. $^1$H NMR spectrum ($CDCl_3$), δ, ppm: **XVIII**: 8.23–7.57 m (3H, $H_{arom}$), 3.70 d (1H, 3-H), 3.65 s (1H, 2-H), 3.34 d (1H, 5-$H_B$), 3.06 d.d (1H, 5-$H_A$), 2.60 m (1H, 7-H), 2.36 m (1H, 6-H), 2.20 d (1H, 1-H), 1.94 d.d (1H, *syn*-8-H), 1.93 m (1H, *exo*-9-H), 1.44 d (1H, *anti*-8-H), 1.00 m (1H, *endo*-9-H); **XXI**: 7.95 d (1H, $H_{arom}$), 7.66 d.d (1H, $H_{arom}$), 7.60 d (1H, $H_{arom}$), 5.40 t (1H, NH), 3.11 d.d (1H, 5-H), 3.04 d.d (1H, 6-H), 2.96 m (2H, 8-$H_A$, 8-$H_B$), 2.65 m (1H, 4-H), 2.63 m (1H, 1-H), 2.19 m (1H, 2-H), 1.72 m (1H, *exo*-3-H), 1.44 d.d (1H, *syn*-7-H), 1.08 m (1H, *endo*-3-H), 0.76 d (1H, *anti*-7-H). Found, %: N 7.92. $C_{14}H_{15}ClN_2O_5S$. Calculated, %: N 7.81.

***exo*-2-Hydroxy-4-(2-methoxy-5-nitrophenylsulfonyl)-4-azatricyclo[4.2.1.0$^{3,7}$]nonane (XIX) and *N*-(*exo*-5,6-epoxybicyclo[2.2.1]hept-5-en-*endo*-2-ylmethyl)-2-methoxy-5-nitrobenzenesulfonamide**

**(XXII)** (mixture of isomers) were obtained in a similar way by oxidation of sulfonamide **VIII**. Overall yield 83.5% (ratio **XIX**:**XXII** = 1:4, according to the $^1$H NMR data), mp 164–168°C (mixture), $R_f$ 0.59 (diethyl ether). IR spectrum, ν, cm$^{-1}$: 3450, 1498, 1351, 1300, 1175, 835. $^1$H NMR spectrum ($CDCl_3$), δ, ppm: **XXII**: 8.80 d (1H, $H_{arom}$), 8.44 d.d (1H, $H_{arom}$), 7.25 d (1H, $H_{arom}$), 4.95 t (1H, NH), 4.13 s (3H, $OCH_3$), 3.09 m (2H, 5-H, 6-H), 3.00–2.80 m (2H, 8-$H_A$, 8-$H_B$), 2.50 m (1H, 4-H), 2.46 m (1H, 1-H), 2.10 m (1H, 2-H), 1.71 m (1H, *exo*-3-H), 1.36 d.d (1H, *syn*-7-H), 0.75 m (1H, *endo*-3-H), 0.72 d (1H, *anti*-7-H). Found, %: N 7.82. $C_{15}H_{18}N_2O_6S$. Calculated, %: N 7.91.

***exo*-2-Hydroxy-4-(2,4,6-triisopropylphenylsulfonyl)-4-azatricyclo[4.2.1.0$^{3,7}$]nonane (XX) and *N*-(*exo*-5,6-epoxybicyclo[2.2.1]hept-5-en-*endo*-2-ylmethyl)-2,4,6-triisopropylbenzenesulfonamide (XXIII)** (mixture of isomers) were obtained in a similar way by oxidation of sulfonamide **XIII**. Overall yield 91.4% (ratio **XX**:**XXIII** = 3:2, according to the $^1$H NMR data), mp 160–161°C (mixture), $R_f$ 0.91 (diethyl ether). IR spectrum, ν, cm$^{-1}$: 3296, 3046, 1608, 1464, 1328, 1152, 848. $^1$H NMR spectrum ($CDCl_3$), δ, ppm: **XX**: 7.26 m (2H, $H_{arom}$), 3.82 s (1H, 2-H), 3.70 d (1H, 3-H), 3.22 d (1H, 5-$H_B$), 3.15 d.d (1H, 5-$H_A$), 2.39 m (1H, 7-H), 2.35 m (1H, 6-H), 2.19 d (1H, 1-H), 1.95 d.d (1H, *syn*-8-H), 1.72 m (1H, *exo*-9-H), 1.44 d (1H, *anti*-8-H), 0.76 m (1H, *endo*-9-H); **XXIII**: 7.17 s (2H, $H_{arom}$), 4.42 t (1H, NH), 3.08 d.d (1H, 5-H), 3.06 d.d (1H, 6-H), 2.99–2.90 m (2H, 8-$H_A$, 8-$H_B$), 2.81 m (3H, CH), 2.47 m (1H, 4-H), 2.46 m (1H, 1-H), 2.09 m (1H, 2-H), 1.91 m (1H, *exo*-3-H), 1.38 d.d (1H, *syn*-7-H), 1.27 d (6H, $CH_3$), 1.06 m (1H, *endo*-3-H), 0.74 d (1H, *anti*-7-H). $^{13}$C NMR spectrum ($CDCl_3$), $\delta_C$, ppm: **XX**: 153.1, 152.9, 151.2, 150.5, 124.1, 123.9 ($C_{arom}$); 80.2 ($C^2$); 69.3 ($C^3$); 53.8 ($C^5$); 45.6 ($C^7$); 41.9 ($C^1$); 37.3 ($C^6$); 33.7 ($C^8$); 25.2 (CH); 23.9 ($CH_3$); **XXIII**: 153.1, 152.9, 151.2, 150.5, 124.1, 123.9 ($C_{arom}$); 51.3 ($C^5$); 49.1 ($C^6$); 45.6 ($C^8$); 41.3 ($C^2$); 38.6 ($C^1$); 37.5 ($C^4$); 30.2 ($C^3$); 27.6 ($C^7$); 25.2 (CH); 23.9 ($CH_3$). Found, %: N 3.55. $C_{23}N_{35}NO_3S$. Calculated, %: N 3.46.

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