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Synthesis, Structure, and Transformations of New Endic Anhydride Derivatives

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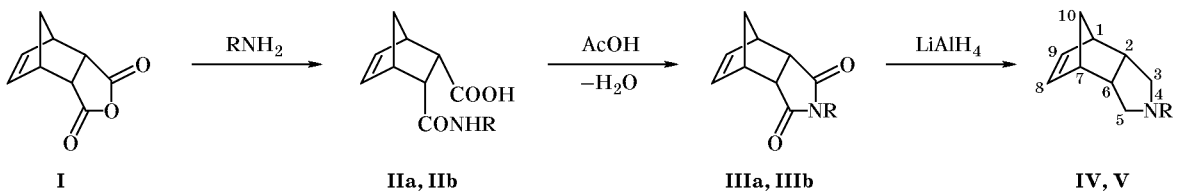
Abstract—4-Azatricyclo[5.2.1.$0^{2,6}$]dec-8-ene and its *N*-phenyl derivative were synthesized by reaction of endic anhydride with amines, transformation of the amido acids thus obtained to imides, and subsequent reduction of the latter with lithium aluminum hydride. The unsubstituted tricyclic amine was brought into reactions with electrophilic reagents: *p*-toluenesulfonyl chloride, *p*-toluoyl chloride, *m*-tolyl isocyanate, phenyl isothiocyanate, and endic anhydride to obtain a number of new derivatives; also, the corresponding salt with 1-adamantanecarboxylic acid was isolated. *N*-(*p*-Tolylsulfonyl)- and *N*-(*m*-tolylcarbamoyl)-4-azatricyclo-[5.2.1.$0^{2,6}$]dec-8-enes were oxidized to the corresponding 8,9-epoxy derivatives with monoperoxyphthalic acid. The structure of the products was confirmed by the data of IR, ^{1}H and ^{13}C NMR, and mass spectra. The molecular structures of *N*-(*p*-iodophenyl)bicyclo[2.2.1]hept-2-ene-*endo*-5,*endo*-6-dicarboximide and *N*-phenyl-4-azatricyclo[5.2.1.$0^{2,6}$]dec-8-ene were established by X-ray analysis.

In the recent years, a number of publications were concerned with search for new biologically active compounds among norbornene and norbornane derivatives, specifically among amines containing these bicyclic fragments. Rigid cage-like structures of such molecules with a fixed spatial orientation of substituents are convenient models dor studying the relations between their structure and pharmacological activity [1]. We previously examined derivatives of *exo*- and *endo*-5-aminomethylbicyclo[2.2.1]hept-2-enes [2] and *exo*- and *endo*-2-aminomethylbicyclo[2.2.1]heptanes [3] and found that compounds belonging to these series exhibit neurotropic activity. The goal of the present work was to synthesize stereochemically pure derivatives of 4-azatricyclo[5.2.1.$0^{2,6}$]dec-8-ene (**IV**) on the basis of accessible endic anhydride (**I**).

Derivatives of amine **IV** exhibit various kinds of pharmacological activity, e.g., hypotensive and tranquilizing) [4, 5]. The presence of a hydrogenated isoindole fragment makes them structurally related to lysergic acid whose derivatives are known as hypotensive drugs. Salts of amines related to amine **IV** possess ganglioblocking ability and are wholesome for central nervous system [5, 6]. Starting from amine **IV** as a key compound, a large number of derivatives exhibitng an antiglycemic effect were prepared [6, 7]. Saturated analog of amine **IV** was used to synthesize substances active against Gram-positive and Gram-negative bacteria [8], as well as morphine antagonists [9]. The above data provide a support to the reasonability of developing methods of synthesis of new 4-azatricyclo[5.2.1.$0^{2,6}$]dec-8-ene derivatives.

Scheme 1.



IIa, **IIIa**, **IV**, R = H; **IIb**, **IIIb**, R = C_6H_4I-*p*; **V**, R = C_6H_5.

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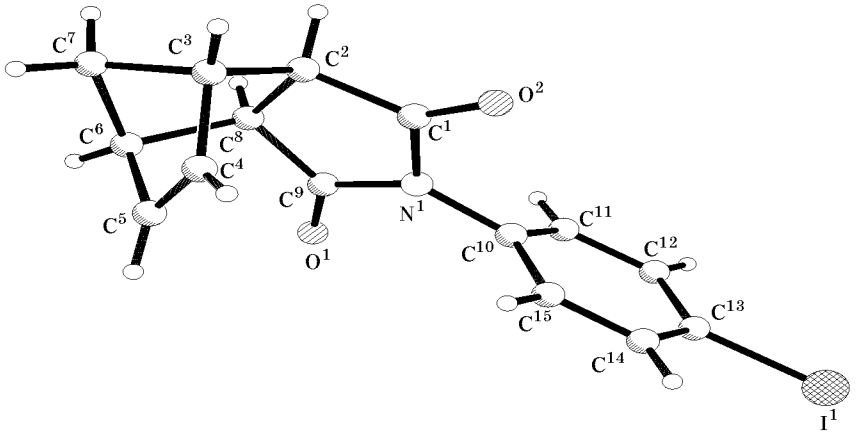


Fig. 1. Structure of the molecule of *N*-(*p*-iodophenyl)bicyclo[2.2.1]hept-2-ene-*endo*-5,*endo*-6-dicarboximide (**IIIb**) according to the X-ray diffraction data.

Imides **IIIa** and **IIIb** as precursors of amines **IV** and **V** were synthesized following the most convenient way which includes synthesis of amido acids **IIa** and **IIb** as intermediate products. The latter were obtained under mild conditions by reaction of equimolar amounts of endic anhydride and appropriate amine in benzene (Scheme 1); in the synthesis of **IIa**, an aqueous solution of ammonia was used. In the IR spectra of **IIa** and **IIb** we observed a set of absorption bands typical of unsaturated fragments (3050 and 700 cm^{-1}) and carboxy and carboxamide groups (3450, 3362, 1700, 1670, 1540, and 1250 cm^{-1}) [10].

Crystalline amido avids **IIa** and **IIb** were converted into imides **IIIa** and **IIIb** by heating in glacial acetic acid. The IR spectra of **IIIa** and **IIIb** lack carboxy group absorption, but bands typical of imide carbonyl groups (1775–1750 and ~1710 cm^{-1}) and unsaturated norbornene fragments are present. The N–H stretching vibrations of imide **IIIa** give rise to IR band in the region of 3190 cm^{-1} [10].

Table 1 gives the ^{1}H NMR spectral parameters of compounds **I**–**III**, which indicate variation of chemical shifts of protons attached to the tricyclic skeleton. The lowest chemical shifts of protons on C^1, C^4, C^5, C^6, and C^7 are typical of amido acid **IIa**. The olefinic protons in **IIa** are nonequivalent, δ 6.19 and 5.94 ppm; the corresponding vicinal coupling constants are as follows: $^3J_{2,3}$ = 5.5, $^3J_{2,1}$ = $^3J_{3,4}$ = 3.0 Hz. Closure of the imide ring is accompanied by an upfield shift of the bridge 7-H signal (by 0.5–0.6 ppm) and by increase of the geminal coupling constant $J_{syn\text{-}7,anti\text{-}7}$ to 8.8 Hz. Table 2 contains the ^{13}C NMR spectral parameters of imides **IIIa** and **IIIb**. The most characteristic are signals from carbon atoms at the double bond (δ_C 134.32 and 134.83 ppm) and carbonyl carbon atoms (δ_C 180.11 and 176.56 ppm for compounds **IIIb** and **IIIa**, respectively).

Imides **IIIa** and **IIIb** were reduced with lithium aluminum hydride in boiling ether; the reduction of **IIIb** was accompanied by hydrodehalogenation, as

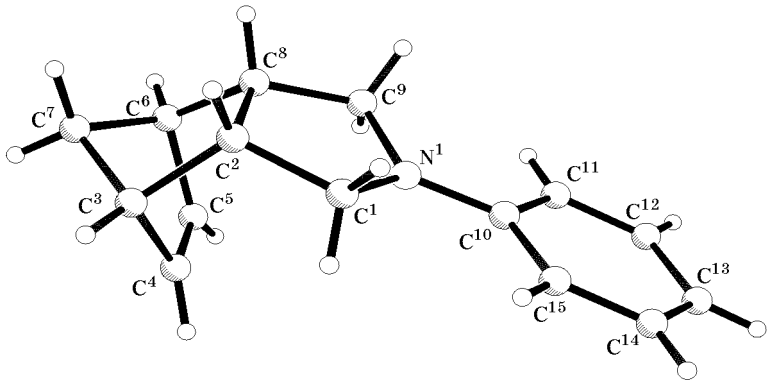


Fig. 2. Structure of the molecule of *N*-phenyl-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene (**V**) according to the X-ray diffraction data.

Table 1. Parameters of the ^{1}H NMR spectra (chemical shifts δ, ppm, and coupling constants *J*, Hz) of compounds **I**, **IIa**, **IIIa**, and **IIIb**

Comp. no.	2-H, 3-H	1-H, 4-H	5-H, 6-H	7-H$_{syn}$, 7-H$_{anti}$	Substituent R
I	6.32	3.51	3.60, $^3J_{5,4} = {}^3J_{6,1} = 3.0$	1.79, 1.58, $^2J_{syn\text{-}7,anti\text{-}7} = 9.0$	–
IIa	6.19, 5.94, $^3J_{2,3} = 5.5$, $^3J_{2,1} = {}^3J_{3,4} = 3.0$	3.14	2.99	1.21, 1.12, $^2J_{syn\text{-}7,anti\text{-}7} = 8.3$	7.27, 6.58 (2H, NH_2)
IIIa	6.14	3.26	3.31, $^3J_{5,4} = {}^3J_{6,1} = 3.0$	1.67, 1.55, $^2J_{syn\text{-}7,anti\text{-}7} = 8.8$	4.82 (1H, NH)
IIIb	6.24	3.41	3.49, $^3J_{5,4} = {}^3J_{6,1} = 3.0$	1.78, 1.60, $^2J_{syn\text{-}7,anti\text{-}7} = 8.8$	7.74 (2H, H_{arom}), 6.90 (2H, H_{arom})

Table 2. Parameters of the ^{13}C NMR spectra (chemical shifts δ_C, ppm) of compounds **IIa**, **IIIa**, and **IIIb**

Comp. no.	C^2, C^3	C^1, C^4	C^5, C^6	C^7	Substituent R
IIa	136.16, 134.03	47.55, 46.20	49.45, 49.32	48.92	176.00 (CO); 174.56 (CO)
IIIa	134.32	44.91	47.27	52.07	180.11 (CO)
IIIb	134.83	45.87	46.16	52.63	176.56 (CO); 138.42, 128.56 (C_{arom})

Table 3. Parameters of the ^{1}H NMR spectra (chemical shifts δ, ppm, and coupling constants *J*, Hz) of 4-azatricyclo-[5.2.1.0^{2,6}]dec-8-enes **V**–**VI**, **IX**, **X**, **XII**, and **XIII**[a]

Comp. no.	8-H, 9-H	1-H, 7-H	2-H, 6-H	3*A*-H, 3*B*-H, 5*A*-H, 5*B*-H	10-H$_{syn}$, 10-H$_{anti}$	Substituent
IV	6.20	2.82	2.70	2.68, 2.57, $^2J_{3A,3B} = 11.7$, $^3J_{3A,2} = 7.5$, $^3J_{3B,2} = 1.2$	1.46, 1.42, $^2J_{syn\text{-}10,anti\text{-}10} = 7.8$	–
V	6.16	3.08	2.97	3.23, 2.90, $^2J_{3A,3B} = 9.6$	1.61, 1.52, $^2J_{syn\text{-}10,anti\text{-}10} = 8.2$	6.45–7.20 (5H, H_{arom})
VI	5.95	2.80	2.80	3.03, 2.69	1.46, 1.36	2.45 (CH_3), 7.55 (2H, H_{arom}), 7.32 (2H, H_{arom})
IX	6.16	2.92	2.92	3.27, 3.06	1.53, 1.43	2.27 (CH_3), 7.00–7.50 (2H, H_{arom})
X	6.20	2.90	2.98	3.40–3.65	1.54, 1.39, $^2J_{syn\text{-}10,anti\text{-}10} = 8.5$	7.10–7.26 (5H, H_{arom}), 6.74 (NH)
XII	3.31	2.57	2.57	3.46, 2.70, $^2J_{3A,3B} = 10.4$	1.46, 0.76, $^2J_{syn\text{-}10,anti\text{-}10} = 10.0$	2.43 (3H, CH_3), 7.33 (2H, H_{arom}), 7.65 (2H, H_{arom})
XIII	3.67, 3.64	3.25	2.59	3.27, 2.78	1.47, 0.86, $^2J_{syn\text{-}10,anti\text{-}10} = 9.9$	2.29 (3H, CH_3), 6.82–7.26 (H_{arom})

[a] The spectra of compounds **IV**, **V**, **X**, **XII**, and **XIII** were measured in chloroform-*d* (400 MHz), and of **VI** and **IX**, in DMSO-d_6 (500 MHz).

Table 4. Parameters of the ^{13}C NMR spectra (chemical shifts δ_C, ppm) of 4-azatricyclo[5.2.1.0^{2,6}]dec-8-enes **V**, **X**, **XII**, and **XIII**

Comp. no.	C^8, C^9	C^1, C^7	C^2, C^6	C^3, C^5	C^{10}	Substituent
V	136.06	46.85	45.85	50.87	30.07	129.25, 115.61, 112.15 (C_{arom})
X	128.91	46.98	46.98	52.07	52.07	177.47 (CS), 139.56, 128.80, 125.79, 125.56 (C_{arom})
XII	49.68	44.06	40.76	48.15	29.59	21.92 (CH_3), 143.89, 131.99, 129.81, 128.12 (C_{arom})
XIII	48.97, 46.95	44.20	40.69	48.83, 45.81	29.84	21.86 (CH_3), 153.89 (SO), 138.99, 135.81, 128.87, 124.16, 120.86, 117.18 (C_{arom})

follows from the data of elemental analysis and ^1H (Table 3) and ^{13}C NMR spectra (Table 4). The NMR spectra of amines **IV** and **V** contain signals from protons at C^3 and C^5 (δ 2.5–3.2 ppm) but no signals from carbonyl carbon atoms. Amine **V** shows signals from phenyl protons in the region δ 6.45–7.20 ppm, while aromatic protons of imide **IIIb** appear as two doublets (2H each) at δ 7.74 and 6.90 ppm.

The steric structure of cyclic amine **V** was studied by X-ray analysis. For comparison, the structure of initial imide **IIIb** was also examined (Figs. 1, 2).

Table 5. Coordinates ($\times 10^4$) of nonhydrogen atoms and their equivalent isotropic thermal parameters (Å$^2 \times 10^3$) in molecule **IIIb**

Atom	*x*	*y*	*z*	U_{eq}
I^1	263(1)	8063(2)	4186(1)	125(1)
N^1	2538(4)	3487(11)	6454(5)	29(2)
O^1	2420(4)	817(11)	5602(5)	52(2)
O^2	2880(4)	5751(13)	7563(5)	61(3)
C^1	2954(6)	4222(16)	7308(7)	41(3)
C^2	3419(5)	2663(18)	7730(6)	40(3)
C^3	4052(6)	3350(18)	7934(7)	48(4)
C^4	3995(6)	4300(2)	7154(8)	64(4)
C^5	3885(5)	2995(17)	6563(8)	44(3)
C^6	3858(6)	984(18)	6974(8)	53(4)
C^7	4348(6)	1330(2)	7909(8)	65(4)
C^8	3266(5)	1064(14)	7068(6)	32(3)
C^9	2707(6)	1655(15)	6294(7)	41(3)
C^{10}	2003(6)	4496(15)	5891(6)	34(3)
C^{11}	1463(7)	3706(16)	5661(6)	51(4)
C^{12}	942(6)	4739(15)	5167(7)	44(3)
C^{13}	976(6)	6539(16)	4853(8)	46(4)
C^{14}	1532(6)	7344(15)	5069(6)	38(3)
C^{15}	2037(6)	6337(14)	5567(7)	39(3)

The coordinates of non-hydrogen atoms in structures **IIIb** and **V** and their equivalent isotropic thermal parameters are given in Tables 5 and 6.

The bicycloheptene fragment in imides **IIIa** and **IIIb** is a sterically strained system. Presumably, this is the reason for elongation of skeletal C–C bonds, especially in molecule **IIIb**. The C^3–C^7, C^5–C^6, and C^6–C^8 bond lengths in **IIIb** are 1.64(2), 1.62(2), and 1.65(2) Å, respectively; i.e., they are longer than standard single C–C bond (1.53 Å). The C–C bonds in the carbon skeleton of **V** are elongated to a lesser extent: the corresponding bond lengths are 1.554(8), 1.548(8), and 1.579(9) Å, respectively. These data may be explained by change of the substitution pattern in the nitrogen-containing five-membered ring.

The C^7H_2 methylene bridge inclines almost equally with respect to the other parts of the norbornane fragment: the bond angles $C^4C^3C^7$ and $C^2C^3C^7$ are, respectively, 101.0(1) and 100.0(6)° in molecule **IIIb** and 101(1) and 99.5(5)° in **V**. In going from **IIIb** to **V**, the degree of puckering of the six-membered norbornane ring increases: the bond angles $C^2C^3C^4$ are 108(1) and 105.5(5)°, respectively. In addition, structure **V** is characterized by greater declination of the five-membered ring from the bicyclic skeleton: the $C^3C^2C^1$ angles in molecules **IIIb** and **V** are 112(1) and 117.3(5)°, respectively. Taking into account *cis*-junction of the bicycloheptene and tetrahydropyrrole rings (the torsion angle $H^2C^2C^8H^8$ is 64°), structure **V** is characterized by shortened intramolecular contacts $H^{1a}\cdots C^4$ 2.75 Å and $H^{9a}\cdots C^5$ 2.67 Å; the corresponding sum of the van der Waals radii is 2.87 Å [11].

The main differences between structures **IIIb** and **V** are observed for the conformation of the nitrogen-contaning heteroring and mutual arrangement of the heteroring and benzene ring. The conjugation between the π-systems of the benzene ring at N^1 and heteroring

in molecule **IIIb** is essentially disturbed: the torsion angle $C^9N^1C^{10}C^2$ is 61(1)°, and the N^1-C^{10} bond is elongated to 1.46(1) Å relative to the average value 1.371 Å [12].

Unlike the planar imide fragment in **IIIb**, the tetrahydropyrrole ring in **V** adopts an *envelope* conformation. The N^1 atom deviates by 0.17 Å from the mean-square plane including the other pyrrole ring atoms. Despite shortened intramolecular contacts $H^{1a}\cdots C^{15}$ 2.85 Å, $H^2\cdots C^9$ 2.66 Å, and $H^{15}\cdots C^1$ 2.58 Å (the sum of the van der Waals radii is 2.87 Å [11]), the phenyl ring on N^1 is coplanar to the five-membered heteroring plane: the torsion angle $C^1N^1C^{10}C^{11}$ is 178.4(6)°. However, the N^1-C^{10} is also elongated [1.413(7) Å against the standard value 1.371 Å [12].

Molecules **V** in crystal are stacked along the *100* crystallographic axis, and molecules **IIIb** are stacked along the *010* axis. In the latter case, the stacking is favored by shortened intermolecular contacts $I^1\cdots H^{3a'}$ (x – 0.5, y – 1.5, z – 0.5) 3.04 Å (the sum of van der Waals radii is 3.31 Å [12]), $I^1\cdots C^{3'}$ (x – 0.5, y – 1.5, z – 0.5) 3.82 Å (3.86 Å), and $I^1\cdots H^{7b'}$ (x – 0.5, y – 0.5, z – 0.5) 3.24 Å (3.31 Å).

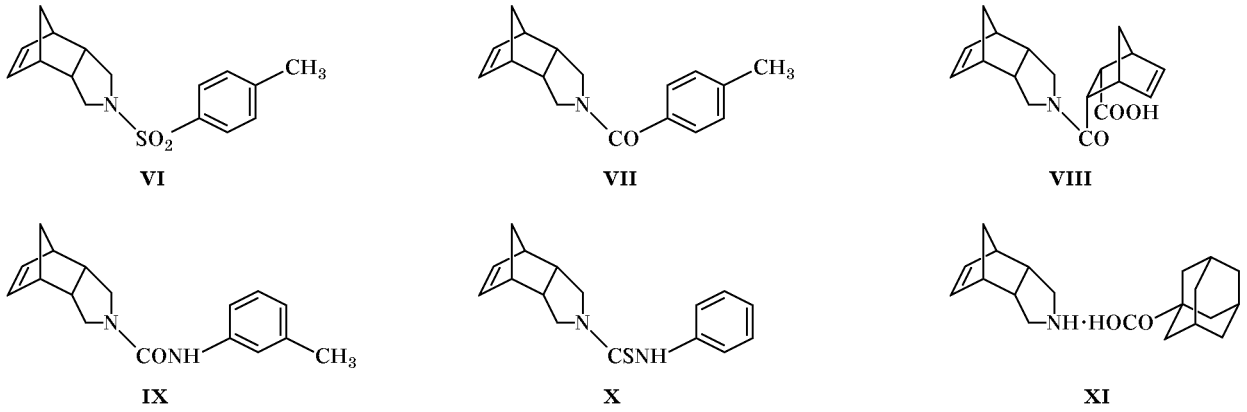
Using unsubstituted amine **IV** as initial compound, we obtained a series of its derivatives. Previously, *N*-alkyl derivatives of **IV** were mainly synthesized and studied [5, 6]. In the present work we obtained products of reactions of **IV** with a series of electrophilic reagents, specifically with *p*-toluenesulfonyl chloride, *p*-toluoyl chloride, endic anhydride, *m*-tolyl isocyanate, and phenyl isothiocyanate; also, a salt of **IV** with 1-adamantanecarboxylic acid was prepared (Scheme 2). The yields, melting points, IR spectra, and elemental analyses of compounds **VI**–**XI** are given in Table 7. Most reactions leading to products **VI**–**XI** occurred without heating, which suggests a fairly high reactivity of amine **IV** in which the nitrogen atom is located at the *endo* side of the rigid bicyclic carbon skeleton. Sulfonamide **VI** was synthesized in a two-phase system (ether–water) using equimolar amounts of the reactants (amine **IV**, *p*-toluenesulfonyl chloride, and sodium hydroxide). Amide **VII** was prepared by an analogous procedure. Amido acid **VIII**, urea and thiourea derivatives **IX** and **X** were synthesized in benzene from equimolar amounts of the reactants, and salt **XI** was obtained in acetone.

Table 6. Coordinates ($\times 10^4$) of nonhydrogen atoms and their equivalent isotropic thermal parameters ($Å^2 \times 10^3$) in molecule **V**

Atom	x	y	z	U_{eq}
N^1	1809(7)	4433(7)	1431(5)	57(2)
C^1	2968(9)	5424(9)	2357(5)	56(2)
C^2	1858(9)	5006(8)	3419(5)	56(2)
C^3	3248(10)	3847(8)	4369(5)	60(2)
C^4	3911(9)	2317(9)	3721(5)	66(2)
C^5	2249(10)	1394(8)	3376(5)	54(2)
C^6	383(9)	2290(8)	3755(6)	57(2)
C^7	1427(9)	3072(10)	4876(6)	70(2)
C^8	–15(9)	3880(8)	2973(6)	55(2)
C^9	–118(8)	3672(8)	1708(6)	57(2)
C^{10}	2318(10)	4415(9)	327(6)	49(2)
C^{11}	1155(10)	3484(8)	–572(6)	55(2)
C^{12}	1752(10)	3454(8)	–1654(7)	67(2)
C^{13}	3503(10)	4344(8)	–1885(5)	56(2)
C^{14}	4606(10)	5303(10)	–988(6)	60(2)
C^{15}	4046(9)	5359(9)	83(6)	60(2)

The IR spectra of compounds **VI**–**XI** are given in Table 7. The molecules of all products contain an unsaturated fragment whose vibrations give rise to absorption bands in the regions 1575–1550 (C=C),

Scheme 2.



VI **VII** **VIII**

IX **X** **XI**

Table 7. Yields, melting points, IR frequencies, and elemental analyses of 4-azatricyclo[5.2.1.$0^{2,6}$]dec-8-enes **VI**–**XIII**

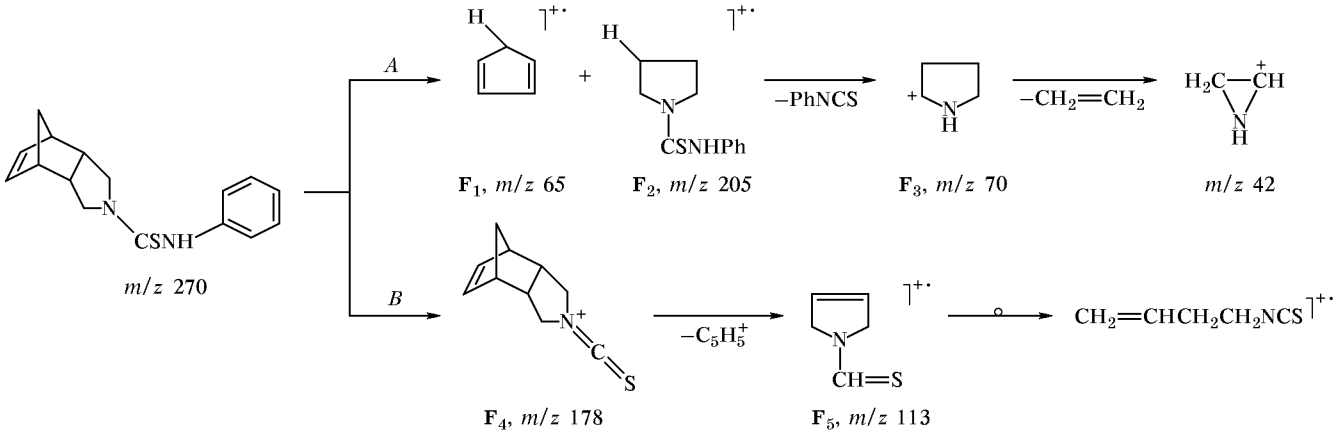
Comp. no.	Yield, %	mp, °C	IR spectrum, ν, cm^{-1}	Calculated, %			Formula	Found, %		
				C	H	N		C	H	N
VI	81.9	113–114	3050, 1610, 1485, 1330, 1154, 1120, 1085, 720	66.44	6.57	4.84	$C_{16}H_{19}NO_2S$	66.53	6.66	4.93
VII	88.3	Oily substance	3070, 1640, 1600, 1440, 1349, 1240, 1060, 723	80.63	7.51	5.53	$C_{17}H_{19}NO$	80.71	7.59	5.62
VIII	87.4	145–146		72.24	7.02	4.68	$C_{18}H_{21}NO_3$	72.37	7.17	4.80
IX	87.5	133–134	3300, 3030, 1635, 1610, 1548, 1484, 1230, 718	76.12	7.46	10.45	$C_{17}H_{20}N_2O$	76.16	7.49	10.47
X	75.0	195–196	3254, 3048, 1535, 1452, 1337, 1294, 1240, 698	71.10	6.67	10.37	$C_{16}H_{18}N_2S$	71.02	6.57	10.31
XI	65.0	214–215	3055, 2440, 1600, 1574, 1415, 720	76.19	9.21	4.44	$C_{20}H_{29}NO_2$	76.23	9.29	4.48
XII	90.9	168–169	3045, 1596, 1481, 1329, 1160, 1111, 1088, 854	62.95	6.23	4.59	$C_{16}H_{19}NO_3S$	62.19	6.19	4.64
XIII	95.2	150–152	3291, 3032, 1640, 1608, 1549, 1489, 1300, 1233, 973, 907, 850	71.83	7.04	9.86	$C_{17}H_{20}N_2O_2$	71.90	7.12	9.95

3065–3040 ($C_{sp^2}-H$), and 720–700 cm^{-1} ($\delta C_{sp^2}-H$). The unusual frequency of the C=C band is explained by steric strain, and its low intensity, by high symmetry of the unsaturated fragment [13]. Moreover, this band is obscured by absorption of both N–H (δN–H) and aromatic moieties. Sulfonamide **VI** shows in the IR spectrum absorption bands from the sulfonyl group (1330 and 1120 cm^{-1}), and compounds **VII**–**IX** are characterized by the presence of amide bands arising from stretching vibrations of the carbonyl group (1635–1610 cm^{-1}), bending vibrations of the N–H bonds (1548–1535 cm^{-1}), and stretching vibrations of the C–N bonds (1240–1230 cm^{-1}). The spectrum of **X** lacks amide I band, but an absorption band at 1337 cm^{-1} is present, which belongs to stretching vibrations of the thiocarbonyl group [10]. In the IR spectrum of salt **XI** we clearly observed a broad "ammonium" band in the region 3000–2300 cm^{-1} ($\nu_{as}NH_2^+$ and $\delta_sNH_2^+$), which overlaps with the νC–H bands. Bending vibrations of the NH_2^+ group appear at about 1600 cm^{-1}. The carboxylate moiety gives rise to absorption bands at 1580–1560 and 1415 cm^{-1}, which belong, respectively, to its asymmetric and symmetric stretching vibrations.

Table 3 contains ^{1}H NMR spectral parameters of compounds **VI**, **IX**, and **X**. These, as well as amines **IV** and **V**, are characterized by equivalent signals of protons at C^8/C^9, C^1/C^7, and C^3/C^5 and by a weak difference in the chemical shifts of 2-H and 6-H. A considerable nonequivalence (up to 0.4 ppm) was observed for the 3-H_A and 3-H_B protons and also for protons on C^5; a similar pattern was observed previously in the ^{1}H NMR spectrum of amine **V**. The spectra of **VI**, **IX**, and **X** also contain signals from substituents on the nitrogen atom, namely aromatic fragments and methyl groups (δ 2.45 and 2.27 ppm) in compounds **VI** and **IX**.

The ^{13}C NMR parameters of compound **X** (Table 4) indicate the presence in its molecule of a double bond (δ_C 128.91 ppm), benzene ring, and thiocarbonyl group (δ_C 177.47 ppm); the signals from C^1, C^7, C^2, and C^6 characteristically coincide with each other (δ_C 46.98 ppm). The signals from the skeletal carbon

Scheme 3.

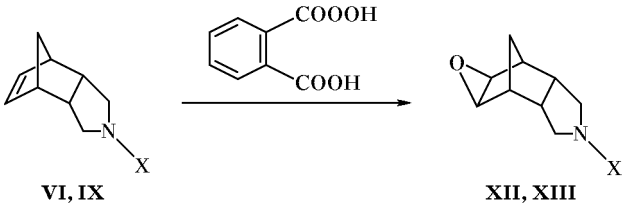


atoms are very similar to those observed in the spectrum of amine **V**.

Analysis of the mass spectrum of compound **X** showed that fragmentation of its molecular ion follows two main pathways (Scheme 3). The first of these (*A*) involves retro-Diels–Alder decomposition with formation of ions $\mathbf{F}_1$ and $\mathbf{F}_2$; elimination of phenyl isothiocyanate from the latter gives ion $\mathbf{F}_3$. According to pathway *B*, ion $\mathbf{F}_4$ is formed in the first stage via elimination of PhNH species. Ion $\mathbf{F}_4$ thus formed is converted into $\mathbf{F}_5$ which is likely to exist as more stable isothiocyanate. In keeping with the spectral data, pathway *A* prevails: the abundance of $\mathbf{F}_2$ (*m*/*z* 205) approaches 100%.

Compounds **VI** and **IX** were brought into reaction with monoperoxyphthalic acid generated *in situ* from phthalic anhydride and 40% hydrogen peroxide. As a result, epoxy derivatives **XII** and **XIII** were obtained (Scheme 4, Table 7).

Scheme 4.



XII, X = $SO_2C_6H_4CH_3$-*p*; **XIII**, X = $CONHC_6H_4CH_3$-*m*.

The IR spectra of compounds **XII** and **XIII** contain a characteristic band at 854 and 850 cm^{-1}, respectively, which belongs to vibrations of the oxirane C–O bond [14]. In the ^1H NMR spectra of epoxynorbornanes with *exo* orientation of the epoxy group, one proton of the methylene bridge, which is located directly above the oxirane ring plane (10-H_{anti}), shows an upfield shift due to magnetically anisotropic effect of the epoxy fragment. The data in Table 3 indicate that such effect is also typical of compounds **XII** and **XIII**: the corresponding upfield shift relative to unsaturated analogs **VI** and **IX** is 0.60 and 0.57 ppm, in keeping with the assumed structures. An additional proof is given by the ^{13}C NMR spectra (Table 4), where the upfield shift of the C^{10} signal (δ_C 29–30 ppm) attains 20 ppm, as compared with compounds **V** and **X** [15].

Taking into account the above data indicating stereoselective *exo* attack by peroxy acid on the double bond of new tricyclic compounds **VI** and **IX**, unusual position of the 8-H and 9-H signals should be noted (δ 3.31–3.70 ppm). Such signals are more typical of *endo*-epoxy derivatives of the same series [16], whereas analogous signals of the *exo* isomers were usually observed at δ 3.00–3.20 ppm [14]. Presumably, this pattern is explained by magnetically anisotropic effect of the *endo*-oriented hydrogenated pyrrole fragment or benzene ring in the arylsulfonyl or aroyl group.

EXPERIMENTAL

The IR spectra were recorded on a Specord 75IR spectrometer from samples pelleted with potassium bromide. The ^1H NMR spectra were obtained on Varian VXR-300 (300 MHz) and Gemini-BB instruments (400 and 500 MHz) from solutions in $CDCl_3$ or DMSO-d_6 using hexamethyldisiloxane as internal reference. The ^{13}C NMR spectra were measured on a Gemini-BB spectrometer operating at 50.3 and 100.7 MHz. The progress of reactions was monitored, and the purity of products was checked, by TLC on

Silufol UV-254 plates using diethyl ether as eluent; the chromatograms were developed with iodine vapor. The elemental analyses were obtained on a Karlo Erba analyzer.

X-Ray diffraction data for compound IIIb. Monoclinic crystals. $C_{15}H_{12}INO_2$. Unit cell parameters (20°C): a = 26.241(5), b = 7.042(1), c = 18.328(4) Å; β = 119.4(1)°; V = 2949(1) Å^3; M_r = 365.16; Z = 8; space group $C2/c$; d_{calc} = 1.645 g/cm^3; μ(MoK_α) = 2.168 mm^{-1}, F(000) = 1424. The unit cell parameters and intensities of 2113 reflections (2062 independent reflections with R_{int} = 0.098) were measured on a Siemens P3/PC automatic four-circle diffractometer (MoK_α, graphite monochromator, 2θ/θ scanning to $2\theta_{max}$ = 50°). The structure was solved by the direct method using SHELX97 software package [17]. The absorption was taken into account by semi-empirical procedure from the results of Ψ-scanning, T_{min} = 0.037, T_{max} = 0.44. The positions of hydrogen atoms were determined from the difference synthesis of electron density and were refined according to the "rider" model with $U_{iso} = 1.2U_{eq}$ of nonhydrogen atom attached to the given hydrogen atom. The structure was refined with respect to F^2 by the full-matrix least-squares procedure in anisotropic approximation for nonhydrogen atoms [to wR_2 = 0.293 from 2062 reflections; R_1 = 0.089 from 800 reflections with $F > 4\sigma(F)$, S = 0.899].

X-Ray diffraction data for compound V. Monoclinic crystals. $C_{15}H_{17}N$. Unit cell parameters (20°C): a = 6.530(2), b = 8.046(3), c = 11.943(5) Å; β = 99.77(3)°; V = 618.4(4) Å^3; M_r = 160.19; Z = 2; space group $P2(1)$; d_{calc} = 0.860 g/cm^3; μ(MoK_α) = 0.056 mm^{-1}; F(000) = 170. The unit cell parameters and intensities of 1112 reflections (1023 independent reflections with R_{int} = 0.088) were measured on a Siemens P3/PC automatic four-circle diffractometer (MoK_α, graphite monochromator, 2θ/θ scanning to $2\theta_{max}$ = 50°). The structure was solved by the direct method using SHELX97 software package. The positions of hydrogen atoms were determined from the difference synthesis and were refined using the "rider" model with $U_{iso} = 1.2U_{eq}$ of nonhydrogen atom attached to the given hydrogen atom. The structure was refined with respect to F^2 by the full-matrix least-squares procedure in anisotropic approximation for nonhydrogen atoms [to wR_2 = 0.124 from 1023 reflections; R_1 = 0.051 from 483 reflections with $F > 4\sigma(F)$, S = 0.86].

***endo*-5-Carbamoylbicyclo[2.2.1]hept-2-ene-*endo*-6-carboxylic acid (IIa).** To a solution of 13.1 g (0.08 mol) of endic anhydride (**I**) in 70 ml of benzene we added dropwise with stirring 8.2 g (0.12 mol) of 25% aqueous ammonia, and the mixture was stirred until the reaction was complete (TLC). The resulting amido acid was filtered off, washed with benzene, and subjected to further purification. Yield 81.7%, mp 137–138°C. IR spectrum, ν, cm^{-1}: 3450, 3362, 3080, 3050, 1700, 1670, 1540, 1395, 1338, 1252, 1200, 790, 700. Found, %: C 59.73; H 6.16; N 7.86. $C_9H_{11}NO_3$. Calculated, %: C 59.67; H 6.08; N 7.73.

***endo*-5-(*p*-Iodophenylcarbamoyl)bicyclo[2.2.1]-hept-2-ene-*endo*-6-carboxylic acid (IIb)** was synthesized in a similar way from 0.82 g (0.005 mol) of endic anhydride and 1.09 g (0.005 mol) of *p*-iodoaniline. Yield 71.9%, mp 145–146°C. IR spectrum, ν, cm^{-1}: 3350, 3078, 1710, 1665, 1548, 1246, 708.

Bicyclo[2.2.1]hept-2-ene-*endo*-5,*endo*-6-dicarboximide (IIIa). A mixture of 11.0 g (0.061 mol) of amido acid **IIa** and 50 ml of glacial acetic acid was refluxed for 6 h. When the reaction was complete (TLC), the solvent was distilled off, the residue was treated with water, and the precipitate was filtered off and purified. Yield 78.4%, mp 174–175°C. IR spectrum, ν, cm^{-1}: 3190, 3151, 3064, 1751, 1728, 1695, 1353, 1274, 1184, 728. Found, %: C 66.43; H 5.71; N 8.76. $C_9H_9NO_2$. Calculated, %: C 66.26; H 5.52; N 8.59.

***N*-(*p*-Iodophenyl)bicyclo[2.2.1]hept-2-ene-*endo*-5,*endo*-6-dicarboximide (IIIb)** was synthesized in a similar way from 1.2 g (0.003 mol) of amido acid **IIb**. Yield 70.1%, mp 178–180°C. IR spectrum, ν, cm^{-1}: 3082, 2981, 1774, 1709, 1456, 1391, 1125, 1056, 838. Found, %: C 49.22; H 3.24; N 3.93. $C_{15}H_{12}INO_2$. Calculated, %: C 49.32; H 3.29; N 3.84.

4-Azatricyclo[5.2.1.0^{2,6}]dec-8-ene (IV). Imide **IIIa**, 7.5 g (0.046 mol), was added in small portions under stirring to a suspension of 7.0 g (0.184 mol) of lithium aluminum hydride in 100 ml of dry diethyl ether. The mixture was stirred at 35°C until the reaction was complete (TLC). Excess reducing agent was decomposed with cold water, the precipitate was filtered off, the organic phase was dried over calcined magnesium sulfate, the solvent was removed, and the product was subjected to purification. Yield 80.5% mp 55–56°C; published data [18]: mp 59–60°C. IR spectrum, ν, cm^{-1}: 3350, 3050, 2720, 1625, 1512, 1255, 1230, 820, 720.

***N*-Phenyl-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene (V)** was synthesized in a similar way. Yield 68.3%, mp 82–84°C. IR spectrum, ν, cm^{-1}: 1600, 1510, 1480, 1373, 1200, 746. Found, %: C 85.25; H 7.94; N 6.71. $C_{15}H_{17}N$. Calculated, %: C 85.31; H 7.94; N 6.64.

***N*-(*p*-Tolylsulfonyl)-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene (VI).** A solution of 0.28 g (0.0015 mol) of *p*-toluenesulfonyl chloride in 5 ml of ether was added dropwise under stirring to a mixture of 0.20 g (0.0015 mol) of amine **IV** in 10 ml of ether and 0.25 ml (0.0015 mol) of 20% aqueous NaOH. The mixture was stirred until the reaction was complete (TLC). The ether was removed, the solid residue was dissolved in 20 ml of a 1:1 chloroform–water mixture, the organic layer was separated and evaporated, and the product was recrystallized from isopropyl alcohol.

***N*-(*p*-Toluoyl)-4-azatricyclo[5.2.1.0^{2,6}]-dec-8-ene (VII)** was synthesized in a similar way from 0.20 g of amine **IV** and 0.26 g of *p*-toluoyl chloride. The physical properties and spectral parameters of compounds **VI** and **VII** are given in Tables 3, 4, and 7.

***N*-(*endo*-6-Carboxybicyclo[2.2.1]hept-2-ene-*endo*-5-carbonyl)-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene (VIII).** Endic anhydride, 0.12 g (0.00074 mol), was added to a solution of 0.1 g (0.00074 mol) of amine **IV** in 10 ml of benzene, and the mixture was left to stand until the reaction was complete (TLC). The precipitate was filtered off, washed with benzene, dried, and recrystallized from benzene (Table 7).

***N*-(*m*-Tolylcarbamoyl)-4-azatricyclo[5.2.1.0^{2,6}]-dec-8-ene (IX) and *N*-[phenyl(thiocarbamoyl)]-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene (X)** were synthesized by a similar procedure from 0.2 g (0.0015 mol) of amine **IV** and an equimolar amount of *m*-tolyl isocyanate or phenyl isothiocyanate, respectively. The yields, melting points, and analytical and spectral data of compounds **IX** and **X** are given in Tables 3, 4, and 7.

4-Azoniatricyclo[5.2.1.0^{2,6}]dec-8-ene 1-adamantanecarboxylate (XI). To a solution of 0.10 g (0.00074 mol) of amine **IV** in 5 ml of acetone we added a solution of 0.13 g (0.00074 mol) of 1-adamantanecarboxylic acid in 5 ml of acetone. Crystals separated and were filtered off, dried, and recrystallized from acetone (Table 7).

***exo*-8,9-Epoxy-*N*-(*p*-tolylsulfonyl)-4-azatricyclo-[5.2.1.0^{2,6}]decane (XII).** To a mixture of 0.2 g (0.65 mmol) of sulfonamide **VI**, 0.19 g (1.29 mmol) of phthalic anhydride, and 0.02 g (0.32 mmol) of urea in 15 ml of ethyl acetate we added under stirring 0.125 g (1.29 mmol) of 35% hydrogen peroxide, and the mixture was stirred until the reaction was complete (TLC). The mixture was neutralized with a saturated solution of sodium hydrogen carbonate, the organic layer was separated and dried over calcined magnesium sulfate, the solvent was removed, and the residue was recrystallized from isopropyl alcohol.

***exo*-8,9-Epoxy-*N*-(*m*-tolylcarbamoyl)-4-azatricyclo[5.2.1.0^{2,6}]decane (XIII)** was synthesized in a similar way. The properties of compounds **XII** and **XIII** are given in Tables 3, 4, and 7.

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