Russian Journal of Organic Chemistry, Vol. 37, No. 4, 2001, pp. 583–591. Translated from Zhurnal Organicheskoi Khimii, Vol. 37, No. 4, 2001, pp. 617–625.

3-Azabicyclo[3.3.1]nonane Derivatives: IV.* Synthesis of Amino Acids with 3-Azabicyclo[3.3.1]nonane Fragment**

I. V. Shakhkel'dyan[1], E. G. Nikiforova[1], Yu. D. Grudtsyn[1], Yu. M. Atroshchenko[1], O. Ya.Borbulevich[2], Yu. A. Efremov[1], S. S. Gitis[1], D. N. Moiseev[1], E. N. Alifanova[1], P. V. Chudakov[1], and A. Yu. Kovalevskii[2]

[1]*Lev Tolstoi Tula State Pedagogical University, Tula, 300600 Russia*
[2]*Nesmeyanov Institute of Organoelemental Compounds, Russian Academy of Sciences, Moscow, Russia*

Received November 15, 1999

Abstract—A series of 1.5-dinitro-3-azabicyclo[3.3.1]non-6-enes was prepared by reduction of 1-R-2,4- and 1-R-3,5-dinitrobenzenes with potassium borohydride followed by Mannich reaction with formaldehyde and amino acids. The molecular structure of (6-bromo-1,5-dinitro-3-azabicyclo[3.3.1]non-6-en-3-yl)acetic acid was studied by X-ray diffraction analysis. The mechanism of decomposition under electron impact was determined for (7-methoxy-1,5-dinitro-3-azabicyclo[3.3.1]non-6-en-3-yl)acetic acid.

Azaanalogs of bicyclo[3.3.1]nonane are known to possess biological activity [2]. On the other hand the amino acids as necessary components of the living body also are interesting physiologically active substances. Among their synthetic derivatives were found compounds with characteristics of important farmaceuticals [3]. In this connection it seemed interesting to prepare derivatives of azabicyclo-[3.3.1]nonane containing in their structure amino acid fragments.

We formerly synthesized (1,5-dinitro-3-azabicyclo-[3.3.1]non-6-en-3-yl)acetic acid starting with hydride complex of *m*-dinitrobenzene prepared from the nitro compound and potassium borohydride, then introducing it into Mannich reaction with formaldehyde and aminoacetic acid [4]. Similarly from hydride adducts of 1-R-2,4- and 1-R-3,5-dinitrobenzenes we prepared compounds **Ia–k** (see the Scheme).

The reduction of nitro compounds with KBH_4 was carried out in a mixture THF–water (1 : 1 by volume) ensuring sufficient solubility of both reagents. The optimum temperature is within 10–20°C range providing both fair reduction rate and preventing decomposition of the arising dipotassium salts of 3,5-bis(aci-nitro)cyclohex-1-ene. The aminomethylation was performed without isolation of the hydride diadducts from the reaction mixture. The target products were obtained at adding double excess of formaldehyde and glycine (molar ratio of *m*-nitrobenzene–CH_2O-amino acid 1 : 4 : 2). The further increase in amount of aminomethylating reagents does not result in notable increase in the yield of compounds **I**; their yield is lower when the reaction is carried out with substituted m-dinitrobenzene disregarding the character of the substituent.

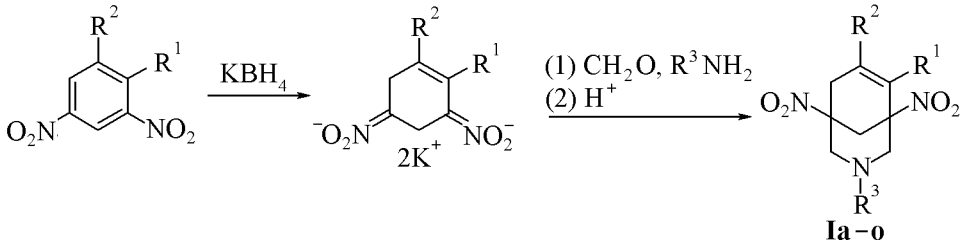
The structure and composition of compounds obtained was established from IR and ^1H NMR spectra and elemental analyses (Tables 1–3). In the IR spectra of compounds **Ia–k** (Table 3) are observed absorption bands in the region 2500–3400 (νOH), 2830–2990 (νC–H aliph.), 1710–1755 (νC=O), 1340–1380 and 1540– 1560 cm^{-1} (ν_s and ν_{as} NO_2).

In analysis of ^1H NMR spectra (300 MHz) of compounds **I** (Table3, Fig.1) we regarded piperidine ring as having *chair* conformation with no eclipsed positions, and the cyclohexene fragment as being close to planar. In all structures the methylene protons H^8 are nonequivalent due to dissimilar localization with respect to the equatorial plane of the piperidine ring and to the nitro group at C^1 atom. The methylene groups protons are coupled with a geminal constant 17.5–18,5 Hz. In the spectra of compounds **Ia–d** the signal of each such proton appears as a doublet of doublets due to the coupling with the H^7 proton (^3J 3.5 Hz). The signal of H^7 proton is split into a doublet of doublets or into a triplet. The

* Communication III see [1].

** The study was carried out under financial support of the Russian Foundation for Basic Research (grant no. 97-03-33783), and of the Program Supporting the Leading Scientific Schools (grant no. 96-15-97367).

Scheme.



Ia–o

R^1 = CH_3, R^2 = H, R^3 = CH_2COOH (**a**), R^1 = Cl, R^2 = H, R^3 = CH_2COOH (**b**), R^1 = Br, R^2 = H, R^3 = CH_2COOH (**c**), R^1 = OCH_3, R^2 = H, R^3 = CH_2COOH (**d**), R^1 = H, R^2 = OCH_3, R^3 = CH_2COOH (**e**), R^1 = H, R^2 = COOH, R^3 = CH_2COOH (**f**), R^1 = H, R^2 = $COOCH_3$, R^3 = CH_2COOH (**g**), R^1 = H, R^2 = $CONH_2$, R^3 = CH_2COOH (**h**), R^1 = H, R^2 = $CON(C_2H_5)_2$, R^3 = CH_2COOH (**i**), R^1 = H, R^2 = piperidinocarbonyl, R^3 = CH_2COOH (**j**), R^1 = H, R^2 = morpholinocarbonyl, R^3 = CH_2COOH (**k**), R^1 = R^2 = H, R^3 = CH_2CH_2COOH (**l**), R^1 = R^2 = H, R^3 = $CH(COOH)CH_2COOH$ (**m**), R^1 = R^2 = H, R^3 = $CH(COOH)CH_2CONH_2$ (**n**), R^1 = R^2 = H, R^3 = $CH(COOH)CH_2CH_2COOH$ (**o**).

Table 1. Yields, melting points, retention factors, and elemental analyses of compounds **Ia**–**o**

Compd. no.	Yield, %	mp, °C	R_f	Found, %			Formula	Calculated, %		
				C	H	N		C	H	N
Ia	38	167–168	0.61	46.42, 46.27	5.23, 5.34	14.70, 14.70	$C_{11}H_{15}N_3O_6$	46.32	5.30	14.73
Ib	23	172–173	0.67	39.48, 39.33	4.00, 3.79	14.00, 13.89	$C_{10}H_{12}ClN_3O_6$	39.29	3.96	13.75
Ic	36	176–177	0.62	34.60, 34.38	3.66, 3.74	12.10, 12.12	$C_{10}H_{12}BrN_3O_6$	34.31	3.46	12.00
Id	33	185–186	0.65	43.57, 43.60	5.32, 5.11	14.03, 14.10	$C_{11}H_{15}N_3O_7$	43.86	5.02	13.95
Ie	26	192–193	0.67	43.97, 43.72	5.45, 5.25	14.02, 14.12	$C_{11}H_{15}N_3O_7$	43.86	5.02	13.95
If	40	219–220	0.43	42.20, 41.95	4.58, 4.49	13.38, 13.31	$C_{11}H_{13}N_3O_8$	41.91	4.16	13.33
Ig	42	170–171	0.60	43.91, 43.89	4.67, 4.66	12.84, 12.79	$C_{12}H_{15}N_3O_8$	43.77	4.59	12.76
Ih	30	234–235	0.23	42.61, 42.53	4.93, 4.72	18.05, 17.98	$C_{11}H_{14}N_4O_7$	42.04	4.49	17.83
Ii	36	169–170	0.63	48.98, 49.24	5.72, 5.89	15.24, 15.31	$C_{15}H_{22}N_4O_7$	48.65	5.99	15.13
Ij	38	203–205	0.65	50.76, 50.57	5.88, 5.79	14.75, 14.80	$C_{16}H_{22}N_4O_7$	50.26	5.20	14.65
Ik	48	242–244	0.59	47.01, 46.96	5.37, 5.32	14.62, 14.64	$C_{15}H_{20}N_4O_8$	46.88	5.25	14.58
Il	53	223–224	0.55	46.18, 46.55	5.42, 5.31	14.85, 14.64	$C_{11}H_{15}N_3O_6$	46.32	5.30	14.73
Im	28	224–225	0.42	45.00, 44.75	4.65, 4.77	12.70, 12.75	$C_{12}H_{15}N_3O_8$	43.77	4.56	12.77
In	19	159–160	0.13	44.09, 43.72	4.98, 4.95	17.03, 16.89	$C_{12}H_{16}N_4O_7$	43.90	4.91	17.07
Io	32	166–167	0.46	45.25, 46.39	4.93, 5.01	11.96, 12.19	$C_{13}H_{17}N_3O_8$	45.48	4.99	12.24

Table 2. IR spectra, cm^{-1}, of compounds **Ia**–**o**

Compd. no.	$\nu_s(NO_2)$	$\nu_{as}(NO_2)$	ν(C=O)	ν(O–H)	ν(C–H aliph.)	Other bands
Ia	1347	1546	1716	2500–3200	2836, 2893, 2980	
Ib	1356, 1377	1565	1721	2500–3300	2867, 2923, 2951	
Ic	1349, 1374	1551	1721	2700–3300	2859, 2925, 2963	
Id	1340, 1383	1539	1713	2600–3300	2856, 2927	
Ie	1340, 1373	1544	1720	2500–3200	2836, 2913, 2964	
If	1340	1535	1708	2700–3400	2873, 2955	
Ig	1360, 1381	1541	1727	2500–3400	2856, 2921, 2960	
Ih	1343	1540	1665, 1702	2600–3300	2852, 2927, 2956	1633 [$\delta(NH_2)$]; 3365, 3469 [$\nu(NH_2)$]
Ii	1356, 1377	1546, 1593	1735	2500–3300	2845, 2940, 2973	
Ij	1351, 1367	1541, 1589	1733	2500–3200	2867, 2947	
Ik	1357	1549, 1569	1732	2700–3400	2859, 2922	
Il	1340	1535	1724	2500–3100	2877, 2928	
Im	1363	1553	1717	2750–3300	2873, 2937	
In	1356	1531	1700	2500–3400	2867, 2927	1657 [$\delta(NH_2)$]; 3200, 3347, 3443 [$\nu(NH_2)$]
Io	1363	1547	1719	2500–3400	2959	

Table 3. ^{1}H NMR spectra, δ, ppm (*J*, Hz) (CCl_4–DMSO-d_6) of compounds **Ia**–**k**

Compd. no.	H_e^2	H_a^2	H_e^4	H_a^4	H^6 (H^7)	H_e^8	H_a^8
Ia	3.27 d (11.2)	3.02 d (11.1)	3.31 d (11.1)	2.97 d (11.2)	5.71 m	2.77 m	2.70 m
Ib	3.25 d (11.2)	3.15 d (11.1)	3.36 d (11.1)	3.03 d (11.2)	6.22 d.d (4.6, 3.5)	2.99 d.d (18.3, 3.5)	2.83 d.d (18.3, 4.6)
Ic	3.20 d (11.2)	3.11 d (10.5)	3.36 d (10.5)	3.04 d (11.2)	6.41 d.d (4.6, 3.6)	2.96 d.d (18.4, 3.6)	2.79 d.d (18.4, 4.6)
Id	3.27 d (11.1)	3.03 d (11.1)	3.35 d (11.1)	2.96 d (11.1)	4.95 t (3.38)	2.86 d.d (17.7, 2.6)	2.75 d.d (17.7, 3.9)
Ie	3.05 d (11.1)	3.00 d (11.1)	3.34 d (11.2)	3.01 d (11.2)	5.00 s	2.83 d (17.7)	2.72 d (17.7)
If	3.20 d (10.5)	3.14 d (10.5)	3.37 d (10.5)	3.07 d (10.5)	6.96 s	2.98 d (18.4)	2.86 d (18.4)
Ig	3.21 d (11.2)	3.17 d (11.2)	3.37 d (10.5)	3.08 d (10.5)	7.03 s	3.00 d (18.4)	2.93 d (18.4)
Ih	3.17 d (11.2)	3.11 d (11.2)	3.36 d (10.5)	3.05 d (10.7)	6.76 s	2.98 d (18.4)	2.85 d (18.4)
Ii	3.20 d (11.2)	3.08 d (11.2)	3.43 d (10.6)	3.03 d (10.6)	5.95 s	3.00 d (18.3)	2.77 d (18.3)
Ij	3.21 d (10.5)	3.04 d (10.5)	3.40 d (10.5)	3.00 d (10.5)	5.94 s	2.99 d (18.4)	2.78 d (18.4)
Ik	3.22 d (10.5)	2.97 d (10.5)	3.40 d (10.5)	2.93 d (10.5)	6.01 s	3.01 d (17.7)	2.78 d (17.7)

Table 3 (Contd.)

Compd. no.	H^9_e	H^9_a	H^α	H^β	COOH	R^1 (R^2)
Ia	2.94 d (11.2)	2.53 d (11.2)	3.45 d (17.1)	3.38 d (17.1)	12.26 s	1.58 s (3H)
Ib	3.15 d (11.2)	2.78 d (11.2)	3.52 d (17.1)	3.47 d (17.1)	12.32 s	–
Ic	3.14 d (11.1)	2.80 d (11.1)	3.52 d (17.1)	3.41 d (17.1)	12.35 s	–
Id	3.12 d (11.1)	2.56 d (11.1)	3.46 d (17.7)	3.37 d (17.7)	12.28 s	3.53 s (3H)
Ie	2.75 d (11.2)	2.63 d (11.2)	3.49 d (17.7)	3.37 d (17.7)	12.23 s	3.59 s (3H)
If	2.81 d (11.8)	2.73 d (11.8)	3.47 d (17.7)	3.36 d (17.7)	12.48 s	12.48 s
Compd. no.	H^9_e	H^9_a	H^α	H^β	COOH	R^1 (R^2)
Ig	2.81 d (11.8)	2.75 d (11.8)	3.46 d (17.7)	3.35 d (17.7)	12.29 s	3.76 s (3H)
Ih	2.80 d (11.2)	2.68 d (11.2)	3.48 d (17.7)	3.37 d (17.7)	12.30 s	7.00 s (1H, NH), 7.45 s (1H, NH')
Ii	2.84 d (11.2)	2.73 d (11.2)	3.48 d (17.7)	3.38 d (17.7)	12.35 s	1.12 t (3H, CH_3), 3.44 q (2H, CH_2, 7.2)
Ij	2.85 d (11.2)	2.73 d (11.2)	3.46 d (17.7)	3.36 d (17.7)	12.33 s	1.54 m, 1.64 m, 3.51 m
Ik	2.86 d (11.2)	2.73 d (11.2)	3.43 d (17.7)	3.35 d (17.7)	12.32 s	3.58 m

abnormal chemical shift ot this proton in the spectrum of compound **Id** (δ 4.95 ppm) is probably caused by the additional screening by a methyl group fixed in a syn-configuration. In the spectra of compounds **Ie–k** the constants $^4J_{6,8}$ are apparently small, and thus the signal of H^6 proton is observed as a slightly broadened singlet. The upfield chemical shift of the signal from proton H^6 in the spectrum of compound **Ie** (δ 5.00 ppm) also may be caused by additional screening with a methyl group. The signals of methylene protons in positions 2, 4, and 9 of the piperidine ring appear as three pairs of broadened doublets from equatorial and axial protons (^2J 10.5–11.5 Hz) since the coupling constants ^4J are close to the resolution limit of the NMR spectrometer. The doublets at δ 3.35–3.40 ppm were assigned to H^4_e protons that suffer the strongest anisotropic effect from the double bond. The chemical shifts of all the doublets are also affected by the torsion angles of the nitro groups. In compounds **Ia–d** the R^1 substituent effects a deshielding influence on the H^9_e proton resulting in the downfield shift of the corresponding doublet as compared with its position in the spectra of compounds **Ie–k**. As in the same plane should be located two carbon and two oxygen atoms we believe that the carboxymethyl group at the nitrogen atom in compounds **Ia–k** cannot be present in the *endo*-configuration. The methylene protons therein become nonequivalent due to asymmetrical position with respect to the C^2NC^4 plane, and their signals are split into doubles by the mutual coupling with the constant ^2J 17.1–17.7 Hz. The broad singlet from the carboxy group proton is located in the 12.2–12.5 ppm region. The protons from R substituents give the expected signals. In the spectrum of compound **Ih** the amide group protons are nonequivalent due to no free rotation around C–N bond because of a hydrogen bond between one of these protons and one oxygen of a nitro group attached to C^4 carbon. Thus the ^{1}H NMR spectra confirm the structure of compounds synthesized.

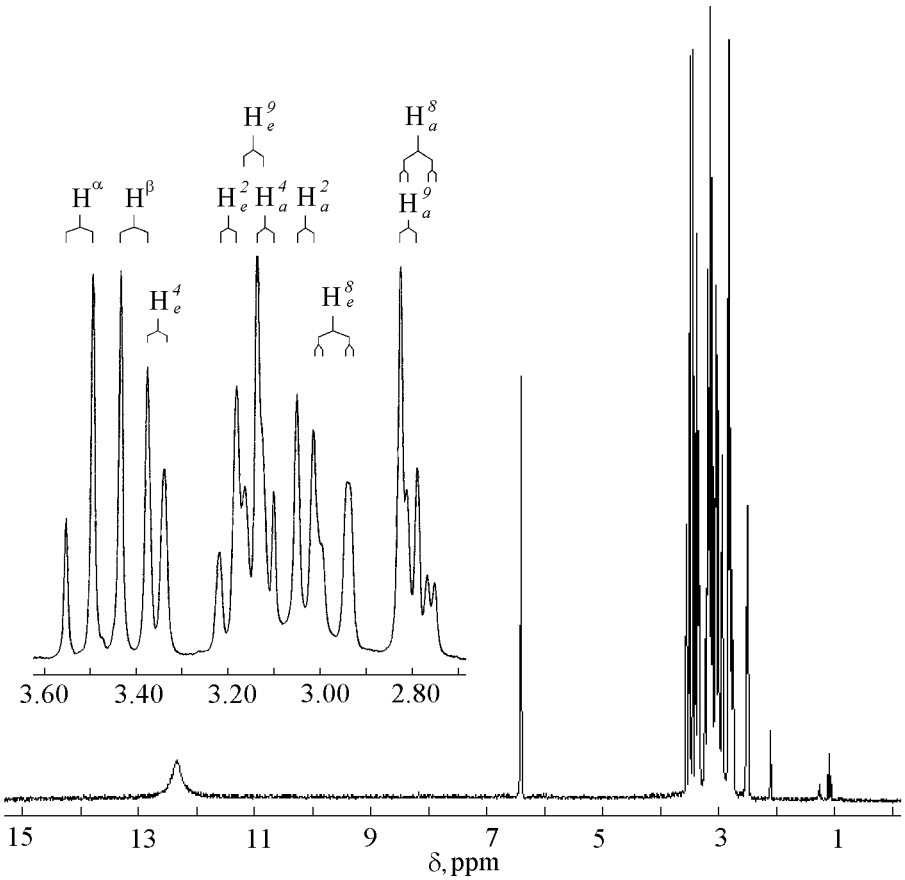


Fig. 1. ^{1}H NMR spectrum (CCl_4–DMSO-d_6) (300 MHz) of (6-bromo-1,5-dinitro-3-azabicyclo[3.3.1]non-6-en-3-yl)acetic acid (**Ic**).

The series of the bicyclo[3.3.1]nonanes synthesized was extended by using in the Mannich condensation of the other amino acids: 9β-alanine, DL-asparagine, DL-aspartic acid, D,L-glutamic acid). Thus we synthesized compounds **Il–o**. The structure thereof also follows from the spectral data (Tables 2, 4). In the ^{1}H NMR spectra of these compounds the signals of protons H^6 and H^7 appear at 5.87–5.97 ppm ($J_{6,7}$ ~10 Hz) respectively, and those from the carboxy group in the region 11.95–12.53 ppm. A specific feature of the spectra of compounds **Im–o** is a double set of signals from H^α proton of the substituent attached to nitrogen. This is due to the existence of stereoisomers differing in the position of this proton with respect to the equatorial plane of the piperidine ring. In all conformers are also different the chemical shifts of H_e^4 protons (Table 4).

To prove the structures of bicyclo[3.3.1]nonanes we also carried out a ray diffraction study of one among the compounds synthesized, (6-bromo-1,5-dinitro-3-azabicyclo[3.3.1]non-6-en-3-yl)acetic acid (**Ic**)

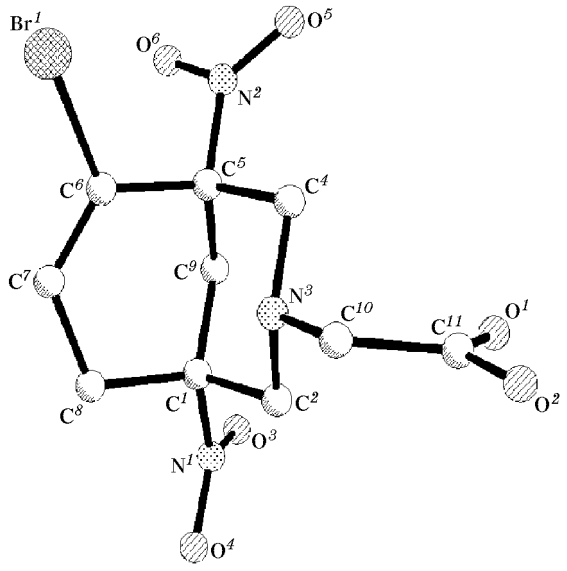
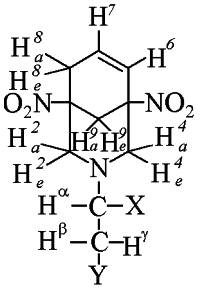


Fig. 2. Molecular structure of (6-bromo-1,5-dinitro-3-azabicyclo[3.3.1]non-6-en-3-yl)acetic acid (**Ic**).

Table 4. ^{1}H NMR spectra δ, ppm (*J*, Hz) (CCl_4–DMSO-d_6) of compounds **Il**–**o**



Compd. no.	H^2_e	H^2_a	H^4_e	H^4_a	H^6	H^7	H^8_e	H^8_a
Il	3.07 d (10.2)	2.70 d (10.2)	3.31 d (10.2)	2.65 d (10.2)	5.92 d (10.4)	5.98 d.t (10.4, 3.1)	2.75 d (16.5)	2.68 d (16.5)
Im	3.18 d (10.1)	2.82 d (10.1)	3.35 d (10.6), 3.29 d (10.6)	2.72 d (10.6)	5.87 d (10.0)	5.97 d.t (10.0, 2.4)	3.06 d.d (16.2, 2.4)	2.82 d.d (16.2, 2.4)
In	3.15 d (10.3)	2.72 d (10.3)	3.35 d (10.6), 3.33 d (10.6)	2.65 d (10.6)	5.87 m (10.0)	5.96 m (10.0)	2.74 d (16.0)	2.66 d (16.0)
Io	3.05 m (10.2)	2.72 d (10.2)	3.27 m (11.0)	3.17 m (11.0)	5.97 d (10.0)	6.06 m (10.0)	2.78 d (15.0)	2.72 d (15.0)

Compd. no.	H^9_e	H^9_a	H^α	H^β	H^γ	X[a]	Y[b]
Il	2.71 d (10.2)	2.65 d (10.2)	2.85 m	2.36 t (7.0)	2.36 t (7.0)	2.82 m	11.95 s
Im	3.05 d (10.4)	2.65 d (10.4)	3.80 d.d (8.1, 6.8), 3.71 d.d (8.1, 6.8)	2.65 d.d (16.0, 6.8)	2.39 d.d (16.0, 8.1)	12.35	12.35 s
In	3.09 d (11.1)	3.04 d (11.1)	3.84 t (7.1), 3.76 t (8.5)	2.45 d.d (15.0, 7.1)	2.36 d.d (15.0, 8.5)	12.53 s	7.26 s, 7.15 s, 6.65 s, 6.60 s
Io	2.90 d (10.6)	2.68 d (10.6)	3.44 d.d (10.6, 5.0), 3.30 d.d (10.6, 5.6)	1.91 m	1.80 m	12.17 s	12.17 s, 2.26 t (7.2)

[a] X = H (**Il**), COOH (**Im**–**o**). [b] X = COOH (**l, m, o**), $CONH_2$ (**n**).

(Fig. 2). The piperidine ring in compound **Ic** is in the *chair* conformation. The deviations of atoms N^3 and C^9 from the plane going through all the other atoms of the ring amount to –0.667(5) and 0.759(5) Å respectively. The cyclohexene fragment is in *sofa* conformation with C^9 deviating from the plane of the other atoms by 0.770(5) Å. The conformation of the eight-membered ring C^1–C^8 is similar to that observed in analogous compounds [5–6]. The nitro groups attached to atoms C^1 and C^3 have a synclinal orientation with respect to the C^1–C^8 and C^5–C^6 bonds respectively [torsion angles $C^8C^1N^1O^4$ and $C^6C^5N^2O^6$ are equal respectively to –54.4(5) and –57.6(5)°]. The nitrogen atom N^3 is in the trigonal-pyramidal configuration. Its deviation from the plane going through three atoms linked thereto amounts to –0.369(5) Å [the sum of bond angles equals 341.5(4)°]. The CH_2COOH group is in equatorial

position [torsional angle $C^{10}N^3C^2C^1$ 166.9(4)°] and possesses a synclinal orientation with respect to C^2–N^3 bond [torsional angle $C^2N^3C^{10}C^{11}$ 64.4(5)°]. The carboxy group is oriented synperiplanar [torsional angle $N^3C^{10}C^{11}O'$ 2.8(7)°].

Compound **Ic** forms a crystal solvate with toluene of 1:1 composition; therewith the solvent is disordered by two positions with population density of 0.5. Thus the data of the X-ray structural analysis are well consistent with the spectral data.

Additional proofs of the structure of azabicyclononanes synthesized we obtained from the study of fragmentation under electron impact by an example of (7-methoxy-1,5-dinitro-3-azabicyclo[3.3.1]non-6-en-3-yl)acetic acid (**Ie**). Mass spectrum of compound **Ie** revealed the low stability of the molecular ion to the electron impact (I_{rel} 1.5%). This fact is apparently caused by easy rupture of the molecular ion in two places: with elimination of a nitro and a carboxy groups. Therewith in the mass spectrum are observed fairly abundant fragment ions with *m*/*z* 255 $[M–NO_2]^+$ and 256 $[M–COOH]^+$. The nitro-nitrite rearrangement characteristic of nitro compounds [8] is relatively weakly pronounced both at the first and the second stage of the molecular ions degradation. Relative intensity of peaks belonging to ions with *m*/*z* 271 $[M–NO]^+$ and 255 $[M–NO_2–NO]^+$ in both cases corresponds to 0.1% of the total ion current. In the latter fragment a hydrogen atom migrates from the bicycle to the remaining oxygen of a nitro group. As a result arises a hydroxy group whose cleavage from the fragment $[M–NO]^+$ provides a relatively abundant ion peak with *m*/*z* 208 of diene structure. The loss of a CO_2 molecule by the carboxymethyl group gives rise of an ion peak of *m*/*z* 164, and the subsequent cleavage of a CH_2 species results in ions with *m*/*z* 150. This fragment ion undergoes a rearrangement that results in formation of a C–N bond between a carbon in the bicycle and a nitrogen. Thus forms an NCH_2 group that is eliminated. This process is energetically feasible to such extent that the resulting ion peak of *m*/*z* 122 is the most abundant in the mass spectrum of compound **Ie**. Note that no elimination of methoxy group occurs at the electron impact either in the first stage or in the further stages of the decomposition of the molecular ions.

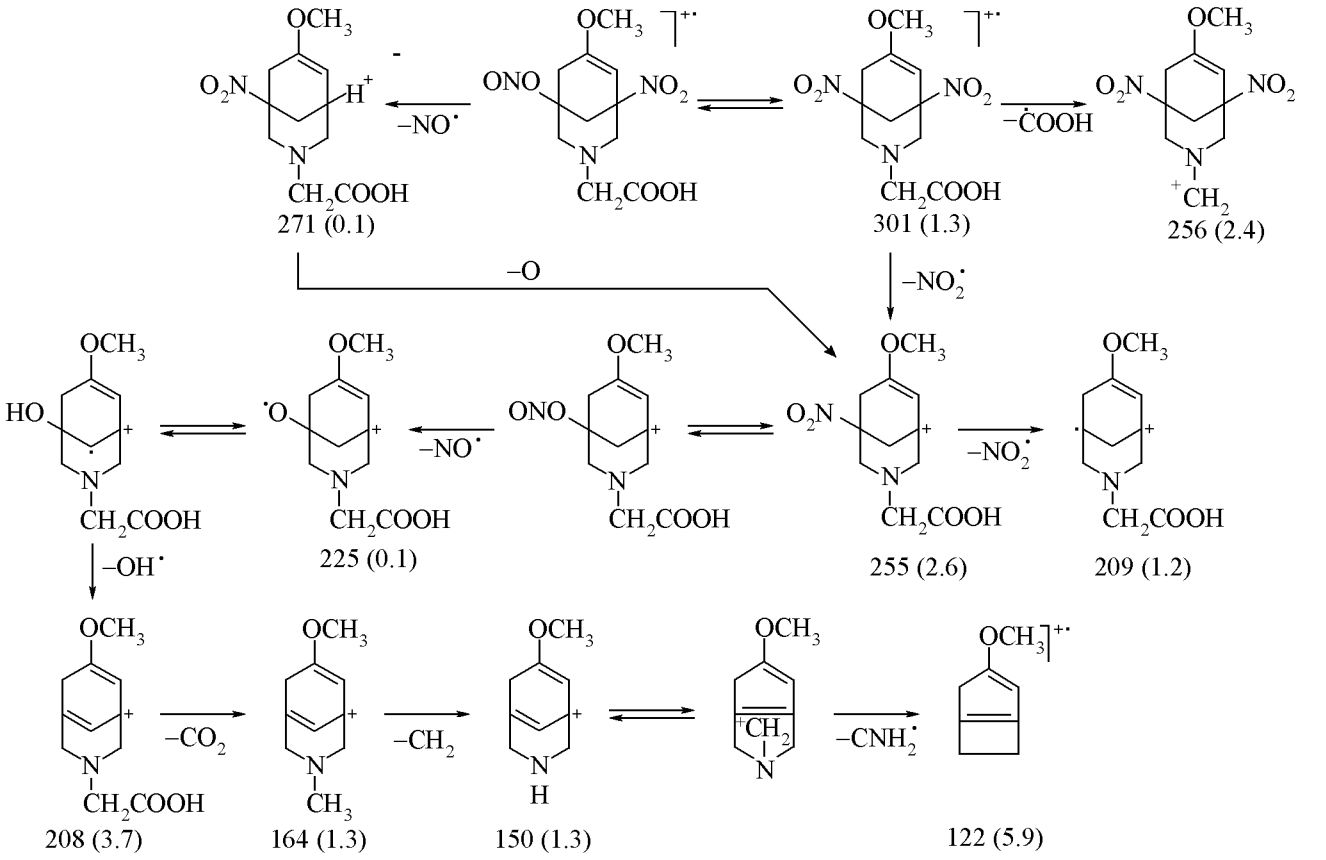


Table 5. Coordinates ($\times 10^4$) and equivalent isotropic thermal parameters ($Å^2 \times 10^3$) of nonhydrogen atoms in the structure of (6-bromo-1,5-dinitro-3-azabicyclo[3.3.1]non-6-en-3-yl)acetic acid (**Ic**)

Atom	*x*	*y*	*z*	U_{eq}
Br^1	469(1)	9180(1)	6509(1)	38(1)
N^1	6445(5)	11354(4)	7715(4)	30(1)
N^2	2283(5)	11764(4)	5272(3)	26(1)
N^3	1678(4)	11494(3)	8682(3)	21(1)
O^1	1120(4)	14066(3)	9049(3)	33(1)
O^2	–895(5)	13461(3)	10848(3)	36(1)
O^3	7371(5)	12011(5)	6803(4)	62(1)
O^4	6859(5)	10924(5)	8664(3)	45(1)
O^5	1201(5)	12581(4)	5161(3)	39(1)
O^6	3182(6)	11297(4)	4408(3)	47(1)
C^1	4666(5)	11033(4)	7688(4)	22(1)
C^2	3427(5)	11718(4)	8675(4)	23(1)
C^4	1342(5)	11985(4)	7488(4)	22(1)
C^5	2559(5)	11278(4)	6537(3)	19(1)
C^6	2303(6)	9836(4)	6897(4)	24(1)
C^7	3192(5)	9089(4)	7562(4)	24(1)
C^8	4531(6)	9571(4)	8019(4)	27(1)
C^9	4431(5)	11555(4)	6420(4)	23(1)
C^{10}	373(5)	11832(4)	9749(4)	25(1)
C^{11}	251(5)	13240(4)	9831(4)	24(1)
C_S^1(A)	3108(40)	14135(39)	11491(22)	107(12)
C_S^2(A)	4568(26)	14595(21)	10406(18)	84(7)
C_S^3(A)	5782(23)	13865(14)	9680(15)	58(4)
C_S^4(A)	7132(21)	14340(20)	8654(15)	76(5)
C_S^5(A)	2754(68)	14657(49)	11563(49)	189(32)
C_S^6(A)	3638(38)	13585(16)	11147(32)	115(16)
C_S^7(A)	5044(32)	14049(28)	10138(27)	91(9)
C_S^1(B)	4202(23)	15587(19)	6354(17)	67(5)
C_S^2(B)	5845(26)	15161(24)	5785(16)	39(4)
C_S^3(B)	6188(22)	14762(10)	4648(12)	45(3)
C_S^4(B)	7897(27)	14271(17)	4080(16)	69(6)
C_S^1(C)	5133(34)	15181(22)	5847(23)	55(7)
C_S^2(C)	6788(30)	14751(17)	5311(27)	82(7)
C_S^3(C)	7021(26)	14383(26)	4173(23)	76(7)

The assumed scheme of compound **Ie** degradation under the electron impact also supports the structure of the bicyclononanes obtained.

Thus the use of amino acids in the Mannich condensation with hydride diadducts of *m*-dinitrobenzene provides a possibility to prepare new derivatives of 3-azabicyclo[3.3.1]nonane that can be interesting as potential biologically active substances.

EXPERIMENTAL

IR spectra (from a film prepared from acetone solution) were recorded on spectrophotometer Specord 75IR. ^{1}H NMR spectra were registered on spectrometer Bruker AC-300, mixed solvent CCl_4–DMSO-d_6, internal reference HMDS. The retention factors (R_f) were determined on Silufol UV-254 plates, eluent toluene–acetone (2 : 1), development under UV irradiation or in iodine vapor. Mass spectrum of compound **Ie** was measured on Varian MAT-311 instrument, ionizing electrons energy 70 eV.

General procedure of synthesis of 3-R^3-6-R^1-7-R^2-1,5-dinitro-3-azabicyclo[3.3.1]non-6-enes Ia–o. In 10 ml of THF-water mixture (1 : 1 by volume) was dissolved 0.4 mmol of dinitro compound. At cooling with ice water and continuous stirring 1.08 g (20 mmol) of KBH_4 was added within 10–15 min, and the stirring was carried out for 15 min more maintaining the temperature of the reaction mixture in 5–15°C range. After the end of the reduction was added 1.5 ml of cooled 30% aqueous solution of formaldehyde (16 mmol) and 8 mmol of an appropriate amino acid in 50 ml of water, then the reaction mixture was acidified with acetic acid to pH 6. The separated precipitate of compounds **Ij, l** was filtered off and crystallized from ethanol; with the rest of the reaction products was performed extraction with several portions of dichloroethane, and the solvent was evaporated in a vacuum. The raw products **Ii, m–o** were dissolved in ethanol, the solution was treated with activated carbon, filtered, the filtrate was diluted with a double volume of water, and the product was salted out with sodium chloride. Compounds **If, h** were crystallized from an acetone–dichloroethane mixture, compound **Ik** from a mixture acetone–DMF. Compounds **Ia–e, g** were purified by column chromatography on silica gel (ASKG) (eluent toluene–acetone, 10 : 1) followed by crystallization from ethanol.

Elemental analyses, melting points, retention factors (R_f), and yields of compounds obtained are given in Table 1, IR and ^{1}H NMR spectra in Tables 2–4.

Crystals for the X-ray study were grown by slow evaporation under isothermal conditions of a solution of compound Ic in a mixture toluene–acetone (10 : 1). Crystals of $C_{10}H_{12}BrN_3O_6$–C_7H_8 (toluene) at 163(2) K triclinic, *a* 8.169(4), *b* 10.654(5), *c* 11.475(5) Å, α 78.35(4), β 72.96(4), γ 86.13(4)°, *V* 935.1(8) $Å^3$, crystal size $0.4 \times 0.4 \times 0.3$ mm, space group $P\bar{1}$, *Z* 2, d_{calc} 1.571 g cm^{-3}, *F*(000) 452, μ= 2.238 mm^{-1}.

The intensities of 3574 reflections (3316 independent, R_{int} 0.130) were measured on automatic

four-circle diffractometer Enraf–Nonius CAD4 (β-filter, MoK_α irradiation, θ/2θ-scanning to $2\theta_{max}$ 50°). The data file obtained was subjected to profile analysis by procedure [9] that considerably refined the data quality.

The structure was solved by the direct method with the use of software SHELXTL PLUS [10]. The position of hydrogen atoms was geometrically refined along "rider" model with a fixed $U_{iso} = nU_{eq}$ of a nonhydrogen atom bonded to the given hydrogen atom (n = 1.5 for hydrogen atoms in methylene and carboxy groups, n = 1.2 for all the other hydrogen atoms). In refining the disordered solvate toluene molecules we introduced the restrictions for the following bond lengths: C(Ar)–C(Ar) 1.400(9) and C(Ar)–CH_3 1.470(9) Å [11]. The refinement by F^2 in anisotropic approximation (307 parameters) for nonhydrogen atoms by full-matrix least-squares procedure for 3222 reflections was performed to R_1 0.072 [for 3015 reflections with $F > 4\sigma(F)$], wR_2 0.192, S 1.12. The coordinates of nonhydrogen atoms are presented in Table 5.

REFERENCES

1. Leonova, O.V., Atroshchenko, Yu.M., Shakhkel'dyan, I.V., Gitis, S.S., Grudtsyn, Yu.D., Nikiforova, E.G., Alekhina, N.N., Alifanova, E.N., Chudakov, P.V., and Kaminskii, A.Ya., *Zh. Org. Khim.*, 2001, vol. 37, no. 3, pp. 421–425.
2. Zefirov, N.S. and Rogozina, S.V., *Usp. Khim.*, 1973, vol. 42, no. 3, pp. 423–441.
3. Agababyan, A.G., Gevorgyan, G.A., and Mndzhoyan, O.L., *Usp. Khim.*, 1982, vol. 51, no. 4, pp. 678–695.
4. Atroshchenko, Yu.M., Nikiforova, E.G., Gitis, S.S., Grudtsyn, Yu.D., Shishkin, O.V., Andrianov, V.F., and Shakhkel'dyan, I.V., *Zh. Org. Khim.*, 1999, vol. 35, no. 9, pp. 1339–1343.
5. Evans, E.H., Newson, A.T., March, L.A., Nowell, I.W., and Wasworth, A.H., *J. Chem. Soc. Perkin Trans. I*, 1987, no. 1, pp. 137–141.
6. Shishkin, O.V., Atroshchenko, Yu.M., Gitis, S.S., Alifanova, E.N., and Shakhkeldyan, I.V., *Acta Cryst., C*, 1998, vol. 54, no. 2, pp. 271–273.
7. Atroshchenko, Yu.M., Nikiforova, E.G., Shakhkel'dyan, I.V., Grudtsyn, Yu.D., Akhmedov, N.G., Alifanova, E.N., Borbulevich, O.Ya., Shishkin, O.V., Gitis, S.S., and Kaminskii, A.Ya., *Zh. Org. Khim.*, 2000, vol. 36, no. 5, pp. 771–777.
8. Khmel'nitskii, R.A., Efremov, Yu.A., Drozd, V.N., and Kaminskii, A.Ya., *Izv. TSKhA.*, 1975, no. 1, pp. 203–207.
9. Strel'tsov, V. A. and Zavodnik, V. E., *Kristallografiya*, 1989, vol. 34, no. 6, pp. 1369–1375.
10. Sheldrick, G.M., *SHELXTL PLUS. PC Version. A System of Computer Programs for the Determination of Crystal Structure from X-ray Diffraction Data*, Siemens Analytical X-ray Instruments Inc., Germany, 1994.
11. Allen, F.H., Kennard, O., Watson, D.G., Brammer, L., Orpen, A.J., and Taylor, R., *J. Chem. Soc. Perkin Trans. II*, 1987, no. 1, pp. 1–19.