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SYNTHESIS OF N-SUBSTITUTED 9-[2-(3,4-METHYLENEDIOXYPHENYL)-2-OXOETHYL]-1,5-DINITRO-7,8-BENZO-3-AZABICYCLO[3.3.1]NON-7-EN-6-ONES

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Aminomethylation has been accomplished of the anionic Yanovskii adduct of 2,4-dinitronaphthol and 3,4-dimethylenedioxyacetophenone. The structure of the 3-substituted 9-[2-(3,4-methylenedioxyphenyl)-2-oxoethyl]-1,5-dinitro-7,8-benzo-3-azabicylo[3.3.1]non-7-en-6-one was determined by two-dimensional homo- and heteronuclear correlation spectroscopy.

Keywords: 3-azabicyclo[3.3.1]nonanes, anionic Yanovskii adducts, homo- and heteronuclear correlation spectroscopy, aminomethylation reaction, Mannich reaction.

One of the interesting classes of heterocyclic compounds are azabicyclo[3.3.1]nonanes. First of all this is because the azabicyclo skeleton is found as a structural unit in the composition of natural biologically active compounds possessing neurotropic, antiarrhythmic, and anticancer properties [1-5]. Many compounds which predominantly affect the κ-opioid receptors have found practical use after clinical testing [6-9]. Moreover, bicyclononanes and their heteroanalogs are suitable models for the study of the influence of intramolecular interactions on the conformational behavior of organic compounds.

Nitro derivatives of aromatic hydrocarbons are unique sources for the synthesis of heterocyclic compounds [10]. On addition of nucleophilic agents to 1,3-dinitroarenes stable σ-complexes are formed which possess high reactivity in electrophilic reactions, and take part as CH-acid components in the Mannich reaction with the formation of 3-azabicyclo[3.3.1]nonanes. We have previously studied the aminomethylation of the anionic Yanovskii adduct of 2,4-dinitronaphthol and acetone [11]. In a continuation of this work we have investigated the possibility of using 3,4-methylenedioxyacetophenone as the source of the carbanion in this reaction.

The method of synthesis includes several stages, the first of which consists of the preparation of the disodium salt of the Yanovskii σ-adduct **1** by the reaction of sodium ethoxide on the solution of 2,4-dinitronaphthol and 3,4-methylenedioxyacetophenone in ethanol. The anionic intermediate was precipitated from the reaction mixture with ether. The orange-red crystals in the precipitate were washed first with absolute ethanol and then with absolute ether. The reaction occurred in almost quantitative yield. In the next stage the

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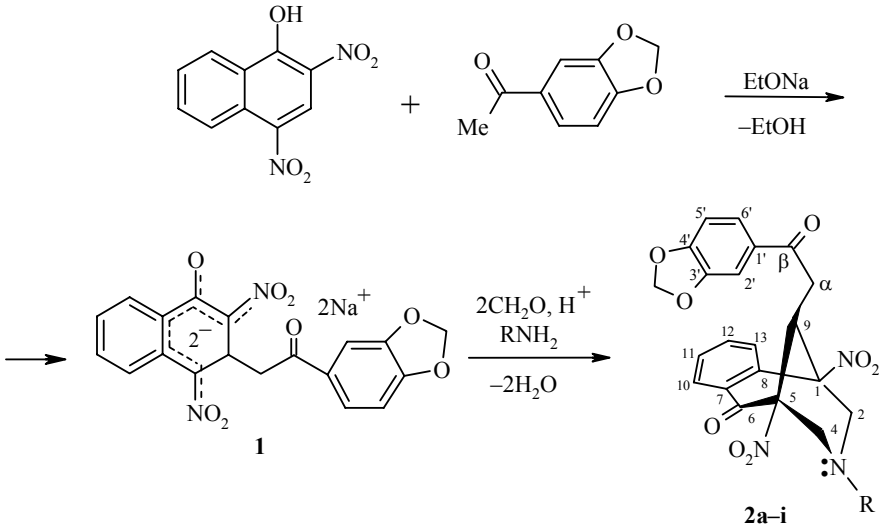
disodium salt **1** underwent aminomethylation with formaldehyde and primary amines. With weak acidification with 20% phosphoric acid (pH 5-6) the required products precipitated from the reaction mixture as crystals which were purified by column chromatography to give 40-60% yields of 3-substituted 9-[2-(3,4-methylene-dioxyphenyl)-2-oxoethyl]-1,5-dinitro-7,8-benzo-3-azabicyclo[3.3.1]non-7-en-6-ones **2a-i**.



2 a R = Me, **b** R = Et, **c** R = Pr, **d** R = *i*-Pr, **e** R = Bu, **f** R = C_5H_{11}, **g** R = $(CH_2)_2OH$, **h** R = $(CH_2)_2Br$, **i** R = CH_2Ph

It should be noted that the determining factor in the synthesis of the heterocycles is the acidity of the medium in the aminomethylation step. When the reaction is carried out in acidic or strongly acidic media the yield of reaction products is considerably decreased, not only because of the instability of the anionic intermediate **1** under these conditions [12], but also because of a concurrent reaction, the protonation of the σ-complex. Probably the formation of products of C-protonation occurs as a result of isomerization of the intermediate bisnitronic acid.

In the IR spectra of the azabicyclononanes **2a-i** a series of bands were observed which are completely indicative of the proposed structure. There are bands at 3050 cm^{-1} in the region of aromatic CH stretching vibrations. Intense absorption bands at 2840-2960 cm^{-1} are assigned to CH stretching vibrations of the methylene groups. The ν_{CO} band has two submaxima which indicates the presence of nonequivalent carbonyl groups in the molecule. Vibrations of the C=C bond were observed in the 1598 cm^{-1} region. Bands at ~1340 and 1365, and ~1555 cm^{-1} correspond to symmetric and antisymmetric vibrations of the nitro groups.

Assignments of signals in the ^1H and ^{13}C NMR spectra of the synthesized compounds can be made more reliably by use of two-dimensional homo- (COSY) and heteronuclear (HSQC, HMBC) correlation spectroscopy. The starting point for deciphering the NMR spectra of compound **2d** is the doublet of doublets at 0.77 and 0.87 ppm (^3J = 6.41, ^4J = 1.83 Hz) of the two methyl groups of the substituent on the nitrogen atom, which are correlated in the HSQC spectrum as a result of the direct constant $^1J_{CH}$ with the signal in the strongest field at δ_C 17.68 ppm.

The multiplet at δ 2.69 ppm may be assigned to the CH proton of the isopropyl group; it is determined by the vicinal constants $^3J_{CH\text{-}CH3}$ in the COSY spectrum and also by the correlation peaks resulting from spin-spin coupling through two $^2J_{CH}$ bonds with carbon atoms of the CH_3 groups.

For the methyne proton in the HMBC spectrum (Table 1) there is also observed an interaction with the signals at δ_C 56.54 and 57.46 ppm with the corresponding spin-spin coupling constant $^3J_{CH}$. Hence it can be concluded that these signals belong to atoms $C_{(4)}$ and $C_{(2)}$ of the piperidine ring. In its turn, the group of four doublets (^2J = 10.90 Hz) at 3.22, 3.33, 3.42, and 3.63 ppm are assigned to the diastereotopic protons of the methylene groups H-2*e*, H-4*a*, H-2*a*, and H-4*e* respectively, on the basis of the direct CH constants in the HQSC spectrum, with cross peaks H-2/$CHMe_2$ and H-4/$CHMe_2$ on account of the more distant $^3J_{CH}$. In addition, for the axial and equatorial protons of the NCH_2 groups the following correlation peaks can be identified in the HMBC spectrum: H-2/$C_{(1)}$ and H-4/$C_{(5)}$ ($^2J_{CH}$), H-2/$C_{(4)}$, H-2/$C_{(9)}$, H-2/$C_{(8)}$, H-4/$C_{(2)}$, H-4/$C_{(9)}$, H-4/$C_{(6)}$ ($^3J_{CH}$), which not only permits distinction of these signals, but also identifies the corresponding signals of the quaternary carbon atoms $C_{(1)}$ and $C_{(5)}$ (91.63 and 92.33), $C_{(8)}$ (136.89), the bridge carbon $C_{(9)}$ (45.64), and also the atom $C_{(6)}$ of the endocyclic carbonyl group (187.15 ppm).

The signals of protons H-α and H-α′ of the ketone group form a three-spin ABX system with the bridge proton H-9 which appears in the ^{1}H NMR spectrum as two doublets of doublets at 3.25 and 3.36 ppm (^2J = 17.77, ^3J = 5.34, ^3J = 1.98 Hz). In the HSQC spectrum correlation peaks are observed for the methylene protons H-α and H-α' with a signal at 36.97 ppm which may be assigned to the atom $C_{(α)}$. The presence of correlation peaks due to $^2J_{CH}$ spin-spin coupling in the HMBC spectrum (Table 1) – H-α/$C_{(9)}$, H-α/$C_{(8)}$, H-α'/$C_{(9)}$, H-α′/$C_{(8)}$ – confirm these assignments.

The signals of the protons of the methylene groups of the dioxolane ring were fixed at 5.97 ppm, they have correlation peaks with the carbon atoms $C_{(3')}$ and $C_{(4')}$ in the HMBC spectrum.

Table 1. Correlation Peaks in the HMBC Spectrum of 3-Isopropyl-9-[2-(3,4-methylenedioxyphenyl)-2-oxoethyl]-1,5-dinitro-7,8-benzo-3-aza-bicyclo[3.3.1]non-7-en-6-one (**2d**)

Atom No	δ_H, ppm	δ_C, ppm	HMBC	J_{H-H}, Hz
1	—	91.63	—	—
2	3.42, d; 3.42, d	57.46	1, 8, 4, 9, CH	10.99
4	3.63, d; 3.33, d	56.54	5, 9, 2, CH, 6	10.99
5	—	92.33	—	—
6	—	187.15	—	—
7	—	133.33	—	—
8	—	136.89	—	—
9	4.2, dd	45.64		5.34; 1.98
10	8.16, d	127.09	8, 12, 6	7.02
11	7.58, t	129.48	7, 13	7.02
12	7.70, t	134.85	8, 10	7.02
13	7.30, d	125.38	7, 11, 1	7.02
α	3.36, ddd; 3.25, ddd	36.97	9, β	17.77; 5.34; 1.98
β	—	192.63	—	—
1′	—	130.64	—	—
2′	7.24	107.93	6′, β, 4′	
3′	—	148.11	—	—
4′	—	152.08	—	—
5′	6.72, dd	107.82	1′, 3′	8.24; 2.14
6′	7.31	124.34	2′, β, 4′	
NCH	2.69, m	54.35	2, 4, Me	
Me	0.87, dd; 0.77, dd	17.68	CH, Me	6.41; 1.83
OCH_2O	5.97, d	101.89	3′, 4′	2.13

Analysis of the two-dimensional COSY spectra of compound **2d** reveals two separate closed spin systems in the region of resonance of aromatic protons. The protons H-10, H-11, H-12, and H-13 of the condensed benzene ring form a four-spin ABCD system which is observed in the ^{1}H NMR spectrum as two doublets at 8.16 (H-10) and 7.30 (H-13) and two triplets at 7.58 (H-11) and 7.70 ppm (H-12). To distinguish the signals of the similar multiplicity of protons H-10 and H-13 is allowed by cross-peaks in the HMBC spectrum (Table 1): H-10/$C_{(12)}$, H-8/$C_{(12)}$, H-10/$C_{(6)}$, and H-13/$C_{(11)}$, H-13/$C_{(7)}$, H-13/$C_{(1)}$, respectively. The signals of the carbon atoms of the condensed benzene ring are unambiguously assigned from the HSQC spectrum: 134.85 ($C_{(12)}$), 129.48 ($C_{(11)}$), 127.00 ($C_{(10)}$), and 125.39 ppm ($C_{(13)}$). The signals of the quaternary atoms $C_{(7)}$ (133.33) and $C_{(8)}$ (136.89 ppm) can be distinguished by the presence of the correlation peaks H-2*e*/$C_{(8)}$ and H-2*a*/$C_{(8)}$ in the HMBC spectrum (Table 1).

The protons H-2', H-5', and H-6' of the 3',4'-methylenedioxyphenyl group form a three-spin system in the ^{1}H NMR spectrum, consisting of three doublet or doublets at 6.72 (H-5', ^2J = 8.24, ^5J = 2.14 Hz), 7.31 (H-6', ^2J = 8.24, ^4J = 1.53 Hz), 7.24 ppm (H-2', ^4J = 1.53, ^5J = 2.14 Hz). The assignment of the signals for these aromatic protons follows from the presence of cross-peaks in the HMBC spectrum resulting from distant spin-spin coupling: H-5'/$C_{(1')}$, H-5'/$C_{(3')}$, H-6'/$C_{(2')}$, H-6'/$C_{(4')}$, H-6'/$C_{(\beta)}$, H-2′/$C_{(4')}$, H-2'/$C_{(6')}$, H-2'/$C_{(\beta)}$ (Table 1). Carbon atoms correspond to the following signals in the ^{13}C NMR, also confirmed with the help of two-dimensional HSQC and HMBC spectra: 152.08 ($C_{(4')}$), 148.11 ($C_{(3')}$), 130.64 ($C_{(1')}$), 124.34 ($C_{(6')}$), 107.93 ($C_{(5')}$), 107.82 ppm ($C_{(2')}$).

So as a result of the aminomethylation of the anionic adduct of 2,4-dinitronaphthol and 3,4-methylenedioxyacetophenone 10 new derivatives of 3-azabicyclo[3.3.1]nonane have been synthesized and their spectra have been investigated in detail.

EXPERIMENTAL

R_f values were determined on Silufol UV-254 plates using 1:4:1 acetone–toluene–hexane as eluent, and UV light and iodine vapor for development. Melting points were measured with a Boetius Kofler plate, with a rate of heating of 4 deg/min. Electronic spectra were recorded on a Specord UV-vis spectrophotometer. IR spectra of KBr disks (compounds **2a-i)** or nujol mulls (compound **1**) with a Specord IR-75 spectrophotometer, ^{1}H and ^{13}C NMR spectra were recorded on Bruker AC-300 (300 and 75 MHz) (compounds **2a-c,f, h**), Bruker WM-250 (250 and 63 MHz) (compounds **2e,i**) in DMSO-d_6, and Bruker DRX-500 machines (500 and 127 MHz) (compound **2d** in $CDCl_3$) with HMDS as internal standard.

Disodium Salt of 3-[2-(3,4-methylenedioxyphenyl)-2-oxoethyl]-2,4-bis(acinitro)-5,6-benzoyl-cyclohex-5-en-1-one (1). A freshly prepared solution of sodium ethoxide (sodium (0.022 mol) in absolute ethanol (15 ml)) was added to a solution of 2,4-dinitronaphthol (0.005 mol) in 3,4-methylenedioxyacetophenone (0.109 mol) with vigorous stirring and stirring was continued for 30 min at 20-25°C. The precipitate was filtered off, washed with absolute ethanol and ether, and dried in a vacuum dessicator. Yield 87%. IR spectrum, ν, cm^{-1}: 1485 (NO_2^-), 1280, 1283 (NO_2^-), 1700, 1706 (C=O), 1606 (C=C), 2845, 2920 (CH). UV spectrum (DMSO), λ_{max} : 598 nm.

9-[2-(3,4-Methylenedioxyphenyl)-2-oxoethyl]-1,5-dinitro-7,8-benzo-3-azabicyclo[3.3.1]non-7-en-6-ones 2a-i (General Method). To a solution of the corresponding hydrochloride (hydrobromide) or free amine (0.016 mol) in 50% ethanol (10 ml) on cooling with ice, 32% formaldehyde (3 ml, 0.038 mol) was added. The disodium salt **1** (0.0027 mol) was added in portions to this mixture at -5°C with stirring and was acidified with 20% orthophosphoric acid to pH 5.0-6.0. The precipitate was filtered off, washed with water and dried to constant mass. It was purified by column chromatography on silica gel (ASKG) with toluene and 10:1 toluene-acetone (for compound **2g**) as eluents. The solvent was evaporated in vacuum, the product was precipitated by addition of acetone, and crystallized from ethanol.

9-[2-(3,4-Dimethylenedioxyphenyl)-2-oxoethyl]-3-methyl-1,5-dinitro-7,8-benzo-3-azabicyclo[3.3.1]non-7-en-6-one (2a). Yield 70%; mp 185°C, R_f 0.63. IR spectrum, ν, cm^{-1}: 1551, 1505, 1348 (NO_2), 1708, 1682 (C=O), 1607 (C=C), 2940, 2915, 2869 ($C–H_{aliph}$), 1467, 1448 ($C–H_{aliph}$), 1250, 1118, 1042 (C–O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 8.09 (1H, d, *J* =7.3, H-10); 7.68 (1H, t, *J* = 7.3, H-11); 7.84 (1H, t, *J* = 7.3, H-12); 7.46 (1H, d, *J* = 7.3, H-13); 3.53 (1H, d, *J* = 10.3, H-4*e*); 3.24 (1H, d, *J* = 10.3, H-4*a*); 3.36 (1H, d, *J* = 10.0, H-2*a*); 3.28 (1H, d, *J* =10.0, H-2*e*); 4.24 (1H, br. s, H-9); 3.45 (1H, dd, *J* =19.1, *J* = 5.1, H-α); 3.22 (1H, dd, *J* =19.1, *J* =2.9, H-α'); 7.48 (1H, d, *J* = 8.0, H-6'); 7.32 (1H, s, H-2'); 6.92 (1H, d, *J* = 8.0, H-5'); 6.09 (2H, s, $COC_6H_3OC\underline{H}_2O$); 2.23 (3H, s, NCH_3). ^{13}C NMR spectrum, δ, ppm: 91.29 ($C_{(1)}$); 61.36 ($C_{(2)}$); 60.38 ($C_{(4)}$); 92.54 ($C_{(5)}$); 186.58 ($C_{(6)}$); 132.08 ($C_{(7)}$); 136.71 ($C_{(8)}$); 43.94 ($C_{(9)}$); 126.67 ($C_{(10)}$); 129.38 ($C_{(11)}$); 135.72 ($C_{(12)}$); 126.18 ($C_{(13)}$); 192.88 ($CH_2\underline{C}OC_6H_3OCH_2O$); 36.71 ($\underline{C}H_2COC_6H_3OCH_2O$); 129.92, 107.18, 147.67, 151.61, 107.83, 124.39 ($CH_2CO\underline{C}_6H_3OCH_2O$); 101.91 ($CH_2COC_6H_3O\underline{C}H_2O$); R [43.94, $N\underline{C}H_3$)]. Found, %: C 58.18; H 4.18; N 9.28. $C_{22}H_{19}N_3O_8$. Calculated, %: C 58.28; H 4.19; N 9.27.

3-Ethyl-9-[2-(3,4-methlenedioxyphenyl)-2-oxoethyl]-1,5-dinitro-7,8-benzo-3-azabicyclo[3.3.1]non-7-en- 6-one (2b). Yield 68%; mp 196°C, R_f 0.56. IR spectrum, ν, cm^{-1}: 1556, 1510, 1362 (NO_2), 1713, 1683 (C=O), 1607 (C=C), 2967, 2955 ($C–H_{aliph}$), 1448, 1490 ($C–H_{aliph}$), 1250, 1118, 1042 (C–O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 8.08 (1H, d, *J* = 7.3, H-10); 7.67 (1H, t, *J* = 7.3, H-11); 7.84 (1H, t, *J* = 7.3, H-12); 7.45 (1H, d, *J* =7.3, H 13); 3.58 (1H, d, *J* = 11.0, H-4*e*); 3.30 (1H, d, *J* = 11.0, H-4*a*); 3.43 (1H, d, *J* = 11.0, H-2*a*); 3.32 (1H, d, *J* = 11.0, H-2*e*); 4.25 (1H, dd, *J* = 4.4, *J* = 3.7, H-9); 3.43 (1H, dd, *J* = 19.1, *J* = 5.1, H-α); 3.21 (1H, dd, *J* = 19.1, *J* = 3.7, H-α'); 7.48 (1H, d, *J* = 8.1, H-6'); 7.34 (1H, s, H-2'); 6.92 (1H, d, *J* = 8.1, H-5'); 6.09 (2H, s, $COC_6H_3OC\underline{H}_2O$); 2.46 (2H, q, *J* = 7.7, $NC\underline{H}_2CH_3$); 0.74 (3H, t, *J* = 7.4, $NCH_2C\underline{H}_3$). ^{13}C NMR spectrum, δ, ppm: 91.40 ($C_{(1)}$); 59.07 ($C_{(2)}$); 58.18 ($C_{(4)}$); 92.57 ($C_{(5)}$); 186.69 ($C_{(6)}$); 132.31 ($C_{(7)}$); 136.66 ($C_{(8)}$); 44.35 ($C_{(9)}$); 126.41 ($C_{(10)}$); 129.29 ($C_{(11)}$); 135.02 ($C_{(12)}$); 125.97 ($C_{(13)}$); 192.83 ($CH_2\underline{C}OC_6H_3OCH_2O$); 36.81 ($\underline{C}H_2COC_6H_3OCH_2O$); 129.94, 107.13, 147.65, 151.56, 107.78, 124.33 ($CH_2CO\underline{C}_6H_3OCH_2O$); 101.86 ($CH_2COC_6H_3O\underline{C}H_2O$); R [49.56 ($N\underline{C}H_2CH_3$), 10.81 ($NCH_2\underline{C}H_3$)]. Found, %: C 59.78; H 4.45; N 9.02. $C_{23}H_{21}N_3O_8$. Calculated, %: C 59.87; H 4.49; N 8.99.

9-[2-(3,4-Methylenedioxyphenyl)-2-oxoethyl]-1,5-dinitro-3-propyl-7,8-benzo-3-azabicyclo[3.3.1]non-7-en-6-one (2c). Yield 67%; mp 150°C, R_f = 0.62. IR spectrum, ν, cm^{-1}: 1551, 1510, 1362 (NO_2), 1713, 1683 (C=O), 1607 (C=C), 2966, 2940 ($C–H_{aliph}$), 1450, 1449 ($C–H_{aliph}$), 1250, 1118, 1047 (C–O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 8.09 (1H, d, *J* = 7.4, H-10); 7.67 (1H, t, *J* = 7.4, H-11); 7.83 (1H, t, *J* = 7.4 , H-12); 7.46 (1H, d, *J* =7.4, H-13); 3.56 (1H, d, *J* = 10.3, H-4*e*); 3.28 (1H, d, *J* = 10.3, H-4*a*); 3.42 (1H, d, *J* = 10.3, H-2*a*); 3.31 (1H, d, *J* = 10.3, H-2*e*); 4.26 (1H, dd, *J* = 4.4, *J* = 3.7, H-9); 3.46 (1H, dd, *J* = 19.5, *J* = 5.2, H-α); 3.23 (1H, dd, *J* = 19.5, *J* = 3.3, H-α'); 7.48 (1H, d, *J* = 8.1, H-6'); 7.34 (1H, s, H-2'); 6.92 (1H, d, *J* = 8.1, H-5'); 6.09 (2H, s, $COC_6H_3OC\underline{H}_2O$); 2.37 (2H, t, *J* = 7.0, $NC\underline{H}_2CH_2CH_3$); 1.16 (2H, m, $NCH_2C\underline{H}_2CH_3$); 0.33 (3H, t, *J* = 7.0, $NCH_2CH_2C\underline{H}_3$). ^{13}C NMR spectrum, δ, ppm: 91.45 ($C_{(1)}$); 59.27 ($C_{(2)}$); 58.85 ($C_{(4)}$); 92.63 ($C_{(5)}$); 186.88 ($C_{(6)}$); 132.53 ($C_{(7)}$); 136.86 ($C_{(8)}$); 44.40 ($C_{(9)}$); 126.49 ($C_{(10)}$); 129.41 ($C_{(11)}$); 135.15 ($C_{(12)}$); 126.31 ($C_{(13)}$); 193.05 ($CH_2\underline{C}OC_6H_3OCH_2O$); 36.92 ($\underline{C}H_2COC_6H_3OCH_2O$); 129.94, 107.38, 147.79, 151.75, 107.86, 124.63 ($CH_2CO\underline{C}_6H_3OCH_2O$); 102.07 ($CH_2COC_6H_3O\underline{C}H_2O$); R [56.69, 18.05 ($N(\underline{C}H_2)_2CH3$); 10.62 ($N(CH_2)_2\underline{C}H_3$)]. Found, %: C 59.83; H 4.76; N 8.78. $C_{24}H_{23}N_3O_8$. Calculated, %: C 59.87; H 4.78; N 8.73.

3-Isopropyl-9-[2-(3,4-methylenedioxyphenyl)-2-oxoethyl]-1,5-dinitro-7,8-benzo-3-azabicyclo[3.3.1]non-7-en-6-one (2d). Yield 65%; mp 201-203°C, R_f = 0.65. IR spectrum, ν, cm^{-1}: 1551, 1510, 1367 (NO_2), 1708, 1683 (C=O), 1607 (C=C), 2976, 2925 ($C–H_{aliph}$), 1445 ($C–H_{aliph}$), 1260, 1103, 1042 (C–O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 8.16 (1H, d, *J* = 7.9, H-10); 7.58 (1H, t, *J* = 7.9, H-11); 7.70 (1H, t, *J* = 7.9 , H-12); 7.32 (1H, d, *J* = 7.9, H-13); 3.63 (1H, d, *J* = 11.0, H-4*e*); 3.32 (1H, d, *J* = 11.0, H-4*a*); 3.42 (1H, d, *J* = 11.0, H-2*a*); 3.21 (1H, d, *J* = 11.0, H-2*e*); 4.26 (1H, dd, *J* = 4.4, *J* = 3.7, H-9); 3.37 (1H, dd, *J* = 19.5, *J* = 5.1, H-α); 3.25 (1H, dd, *J* = 19.5, *J* = 3.3, H-α'); 6.72 (1H, d, *J* = 8.2, H-5'); 7.24 (1H, s, H-2'); 7.31 (1H, d, *J* = 8.2, H-6'); 5.97 (2H, s, $COC_6H_3OC\underline{H}_2O$); 2.69 (2H, m, $NC\underline{H}(CH_3)_2$); 0.87, 0.77 (6H, d, *J* = 6.4, $NCH(C\underline{H}_3)_2$). ^{13}C NMR spectrum,

δ, ppm: 91.63 ($C_{(1)}$); 57.46 ($C_{(2)}$); 56.54 ($C_{(4)}$); 92.40 ($C_{(5)}$); 187.15 ($C_{(6)}$); 133.33 ($C_{(7)}$); 136.89 ($C_{(8)}$); 37.05 ($C_{(9)}$); 127.09 ($C_{(10)}$); 129.48 ($C_{(11)}$); 134.85 ($C_{(12)}$); 124.71 ($C_{(13)}$); 192.63 ($CH_2\underline{C}OC_6H_3OCH_2O$); 36.97 ($\underline{C}H_2COC_6H_3OCH_2O$); 130.64, 107.85, 148.11, 127.078, 107.85, 107.93 ($CH_2CO\underline{C}_6H_3OCH_2O$); 92.40 ($CH_2COC_6H_3O\underline{C}H_2O$); R [45.64 ($N\underline{C}H(CH_3)_2$), 17.43, 17.68 ($NCH(CH_3)_2$)]. Found, %: C 59.83; H 4.76; N 8.78. $C_{24}H_{23}N_3O_8$. Calculated, %: C 59.87; H 4.78; N 8.73.

3-Butyl-9-[2-(3,4-methylenedioxyphenyl)-2-oxoethyl]-1,5-dinitro-7,8-benzo-3-azabicyclo[3.3.1]non-7-en-6-one (2e). Yield 58%; mp 125-127°C, R_f 0.49. IR spectrum, ν, cm^{-1}: 1551, 1510, 1367 (NO_2), 1713, 1678 (C=O), 1607 (C=C), 2966, 2935, 2900, 2869 ($C–H_{aliph}$), 1463, 1448 ($C–H_{aliph}$), 1250, 1118, 1042 (C–O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 8.08 (1H, d, *J* = 7.3, H-10); 7.67 (1H, t, *J* = 7.3, H-11); 7.83 (1H, t, *J* = 7.3, H-12); 7.45 (1H, d, *J* =7.3, H-13); 3.55 (1H, d, *J* = 11.0, H-4*e*); 3.24 (1H, d, *J* = 11.0, H-4*a*); 3.41 (1H, d, *J* = 11.0, H-2*a*); 3.30 (1H, d, *J* = 11.0, H-2*e*); 4.25 (1H, dd, *J* = 4.3, *J* = 5.5, H-9); 3.46 (1H, dd, *J* = 18.9, *J* = 5.5, H-α); 3.20 (1H, dd, *J* = 18.9, *J* = 3.6, H-α'); 6.92 (1H, d, *J* = 8.5, H-5'); 7.34 (1H, s, H-2'); 7.49 (1H, d, *J* = 8.5, H-6'); 6.09 (2H, s, $COC_6H_3OC\underline{H}_2O$); 2.41 (2H, t, *J* =6.7, $NC\underline{H}_2CH_2CH_2CH_3$); 1.14 (2H, m, $NCH_2C\underline{H}_2CH_2CH_3$); 0.68 (2H, m, $NCH_2CH_2C\underline{H}_2CH_3$); 0.54 (3H, t, ^2J = 6.7, $NCH_2CH_2CH_2C\underline{H}_3$). ^{13}C NMR spectrum, δ, ppm: 96.76 ($C_{(1)}$); 64.71 ($C_{(2)}$); 64.81 ($C_{(4)}$); 97.93 ($C_{(5)}$); 192.17 ($C_{(6)}$); 137.86 ($C_{(7)}$); 142.17 ($C_{(8)}$); 49.73 ($C_{(9)}$); 131.78 ($C_{(10)}$); 134.67 ($C_{(11)}$); 140.40 ($C_{(12)}$); 131.55 ($C_{(13)}$); 198.34 ($CH_2\underline{C}OC_6H_3OCH_2O$); 42.18 ($\underline{C}H_2COC_6H_3OCH_2O$); 135.30, 112.60, 153.10, 157.04, 113.26, 129.87 ($CH_2CO\underline{C}_6H_3OCH_2O$); 107.35 ($CH_2COC_6H_3O\underline{C}H_2O$); R [59.67 ($N\underline{C}H_2CH_2CH_2CH_3$); 32.67 ($NCH_2\underline{C}H_2CH_2CH_3$); 24.10 ($NCH_2CH_2\underline{C}H_2CH_3$); 18.41 ($NCH_2CH_2CH_2\underline{C}H_3$)]. Found, %: C 60.67; H 5.09; N 8.41. $C_{25}H_{25}N_3O_8$. Calculated, %: C 60.60; H 5.05; N 8.48.

9-[2-(3,4-Methylenedioxyphenyl)-2-oxoethyl]-1,5-dinitro-3-pentyl-7,8-benzo-3-azabicyclo[3.3.1]non-7-en-6-one (2f). Yield 52%; mp 106-108°C, R_f 0.54. IR spectrum, ν, cm^{-1}: 1556, 1505, 1367 (NO_2), 1708, 1678 (C=O), 1607 (C=C), 2967, 2900, 2869 ($C–H_{aliph}$), 1444 ($C–H_{aliph}$), 1205, 1103, 1047 (C–O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 8.08 (1H, d, *J* = 7.3, H-10); 7.68 (1H, t, *J* = 7.3, H-11); 7.82 (1H, t, *J* = 7.3 , H-12); 7.46 (1H, d, *J* =7.3, H-13); 3.55 (1H, d, *J* = 11.0, H-4*e*); 3.30 (1H, d, *J* = 11.0, H-4*a*); 3.40 (1H, d, *J* = 11.0, H-2*a*); 3.27 (1H, d, *J* = 11.0, H-2*e*); 4.25 (1H, br. s, H-9); 3.46 (1H, dd, *J* = 19.1, *J* = 5.1, H-α); 3.21 (1H, dd, *J* = 19.1, *J* = 3.3, H-α'); 7.49 (1H, d, *J* = 8.1, H-5'); 7.34 (1H, s, H-2'); 6.91 (1H, d, *J* = 8.1, H-6'); 6.09 (2H, s, $COC_6H_3OC\underline{H}_2O$); 2.40 (2H, br. s, $NC\underline{H}_2(CH_2)_3CH_3$); 1.14 (2H, br. s, $NCH_2C\underline{H}_2(CH_2)_2CH_3$); 0.92 (2H, br. s, $N(CH_2)_2C\underline{H}_2CH_2CH_3$), 0.65 (2H, br. s, $N(CH_2)_3C\underline{H}_2CH_3$); 0.62 (3H, t, ^2J = 6.6, $N(CH_2)_4C\underline{H}_3$). ^{13}C NMR spectrum, δ, ppm: 91.39 ($C_{(1)}$); 59.27 ($C_{(2)}$); 58.87 ($C_{(4)}$); 92.51 ($C_{(5)}$); 186.63 ($C_{(6)}$); 132.45 ($C_{(7)}$); 136.75 ($C_{(8)}$); 44.38 ($C_{(9)}$); 126.33 ($C_{(10)}$); 129.18 ($C_{(11)}$); 134.91 ($C_{(12)}$); 126.06 ($C_{(13)}$); 192.80 ($CH_2\underline{C}OC_6H_3OCH_2O$); 36.76 ($\underline{C}H_2COC_6H_3OCH_2O$); 129.94, 107.14, 147.65, 151.56, 107.79, 124.34 ($CH_2CO\underline{C}_6H_3OCH_2O$); 101.86 ($CH_2COC_6H_3O\underline{C}H_2O$); R [54.50 ($N\underline{C}H_2(CH_2)_3CH_3$); 27.70 ($NCH_2\underline{C}H_2(CH_2)_2\ CH_3$); 24.93 ($N(CH_2)_2\underline{C}H_2CH_2CH_3$); 21.18 ($N(CH_2)_3\underline{C}H_2CH_3$); 13.56 ($N(CH_2)_4\underline{C}H_3$)]. Found, %: C 61. 34; H 5.31; N 8.29. $C_{26}H_{27}N_3O_8$. Calculated, %: C 61.29; H 5.30; N 8.25.

3-(2-Hydroxyethyl)-9-[2-(3,4-methylenedioxyphenyl)-2-oxoethyl]-1,5-dinitro-7,8-dibenzo-3-aza-bicyclo[3.3.1]non-7-en-6-one (2g). Yield 45%; mp 81-83°C. IR spectrum, ν, cm^{-1}: 1554, 1515, 1368 (NO_2), 1707, 1700 (C=O), 1601 (C=C), 2965, 2930, 2898 ($C–H_{aliph}$), 1447 ($C–H_{aliph}$), 1255, 1118, 1042 (C–O), 3530 (O–H). Found, %: C 57.12; H 4.34; N 8.68. $C_{23}H_{21}N_3O_9$. Calculated, %: C 57.14; H 4.35; N 8.69.

3-(2-Bromoethyl)-9-[2-(3,4-methylenedioxyphenyl)-2-oxoethyl]-1,5-dinitro-7,8-benzo-3-azabicyclo-[3.3.1]non-7-en-6-one (2h). Yield 65%; mp 202-203°C. IR spectrum, ν, cm^{-1}: 1551, 1505, 1369 (NO_2), 1704, 1683 (C=O), 1602 (C=C), 2965, 2940 ($C–H_{aliph}$), 1449 ($C–H_{aliph}$), 1255, 1118, 1036 (C–O), 812 (C–Br). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 8.09 (1H, d, *J* = 7.4, H-10); 7.66 (1H, t, *J* = 7.4, H-11); 7.83 (1H, t, *J* = 7.4 , H-12); 7.47 (1H, d, *J* =7.4, H-13); 3.68 (1H, d, *J* = 11.0, H-4*e*); 3.48 (1H, d, *J* = 11.0, H-4*a*); 3.61 (1H, d, *J* = 11.0, H-2*a*); 3.40 (1H, d, *J* = 11.0, H-2*e*); 4.26 (1H, dd, *J* = 5.1, *J* = 3.7, H-9); 3.45 (1H, dd, *J* = 14.0, *J* = 5.1, H-α); 3.22 (1H, dd, *J* = 14.0, *J* = 3.7, H-α'); 6.92 (1H, d, ^3J = 8.1, H-5'); 7.35 (1H, s, H-2'); 7.48 (1H, d, *J* = 8.1, H-6'); 6.09 (2H, s $COC_6H_3OC\underline{H}_2O$); 2.84 (2H, t, *J* =5.9, $NC\underline{H}_2CH_2Br$); 3.24 (2H, m, $NCH_2C\underline{H}_2Br$). ^{13}C NMR spectrum, δ, ppm: 91.44 ($C_{(1)}$), 58.88 ($C_{(2)}$); 58.02 ($C_{(4)}$); 92.54 ($C_{(5)}$); 186.61 ($C_{(6)}$); 132.61 ($C_{(7)}$); 136.66 ($C_{(8)}$); 44.34 ($C_{(9)}$);

126.77 ($C_{(10)}$); 129.56 ($C_{(11)}$); 135.13 ($C_{(12)}$); 126.77 ($C_{(13)}$); 193.05 ($CH_2\underline{C}OC_6H_3OCH_2O$); 36.87 ($\underline{C}H_2COC_6H_3OCH_2O$); 129.93, 107.26, 147.80, 151.75, 107.88, 124.62 ($CH_2CO\underline{C}_6H_3OCH_2O$); 102.08 ($CH_2COC_6H_3O\underline{C}H_2O$); R [56.07 ($N\underline{C}H_2CHBr$); 30.01 ($NCH_2\underline{C}H_2Br$)]. Found, %: C 50.56; H 3.70; Br 14.63; N 7.70. $C_{23}H_{20}BrN_3O_8$. Calculated, ,%: C 50.55; H 3.66; Br 14.65; N 7.69.

3-Benzyl-9-[2-(3,4-methylenedioxyphenyl)-1,5-dinitro-2-oxoethyl]-7,8-benzo-3-azabicyclo[3.3.1]-non-7-en-6-one (2i). Yield 57%; mp 211-212°. IR spectrum, ν, cm^{-1}: 1550, 1503, 1369 (NO_2), 1700, 1693 (C=O), 1601 (C=C), 2966, 2941, 2880, 2827 ($C–H_{aliph}$), 1449, 1410 ($C–H_{aliph}$), 1255, 1118, 1042 (C–O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 8.19 (1H, d, *J* = 6.7, H-10); 7.75 (1H, t, *J* = 6.7, H-11); 7.85 (1H, t, *J* = 6.7, H-12); 7.43 (1H, d, *J* = 6.7, H-13); 3.22 (1H, d, *J* = 10.4, H-4*e*); 3.40 (1H, d, *J* = 10.4, H-4*a*); 3.47 (1H, d, *J* = 10.4, H-2*a*); 3.22 (1H, d, *J* = 10.4, H-2*e*); 4.30 (1H, dd, *J* = 6.1, *J* = 4.3, H-9); 3.52 (1H, dd, *J* = 19.0, *J* = 5.5, H-α); 3.25 (1H, dd, *J* = 19.0, *J* = 3.7, H-α'); 6.92 (1H, d, ^3J = 7.9, H-5'); 7.36 (1H, s, H-2'); 7.47 (1H, d, *J* = 8.1, H-6'); 6.09 (2H, s, $COC_6H_3OC\underline{H}_2O$); 3.71, 3.61 (2H, d, *J* = 13.4, $NC\underline{H}_2Ph$); 6.66 (2H, d, *J* = 6.1, *o*-$PhCH_2$); 7.11 (1H, t, *J* = 6.1, *p*-$PhCH_2$); 7.16 (2H, d, *m*-$PhCH_2$). ^{13}C NMR spectrum, δ, ppm: 91.41 ($C_{(1)}$); 59.06 ($C_{(2)}$); 58.34 ($C_{(4)}$); 92.67 ($C_{(5)}$); 186.73 ($C_{(6)}$); 132.64 ($C_{(7)}$); 136.48 ($C_{(8)}$); 44.30 ($C_{(9)}$); 126.57 ($C_{(10)}$); 129.55 ($C_{(11)}$); 135.25 ($C_{(12)}$); 126.43 ($C_{(13)}$); 193.04 ($CH_2\underline{C}OC_6H_3OCH_2O$); 36.84 ($\underline{C}H_2COC_6H_3OCH_2O$); 129.97, 107.31, 147.78, 151.75, 107.94, 124.57 ($CH_2CO\underline{C}_6H_3OCH_2O$); 102.03 ($CH_2COC_6H_3O\underline{C}H_2O$); R [58.91 ($N\underline{C}H_2Ph$); 136.86, 127.70, 128.15, 127.18 ($NCH_2\underline{Ph}$)]. Found, %: C 63.42; H 4.52; N 7.92. $C_{28}H_{24}N_3O_6$. Calculated,%: C 63.39; H 4.53; N 7.92.

REFERENCES

1. P. A. Cootes, I. S. Blagbrough, M. G. Rowan, D. J. Pearson, T. Lewis, and B. V. L. Potter, *J. Pharm. Pharmacol.,* **48**, 210 (1996).
2. J. B. Gloer, B. L. Rinderknecht, D. T. Wicklow, and P. F. Dowd, *J. Amer. Chem. Soc.,* **114**, 1015 (1992).
3. F. Kong and R. J. Andersen, *J. Amer. Chem. Soc.,* **116**, 6007 (1994).
4. K. Samamoto, E. Tsuiji, F. Abe, T. Nakanishi, M. Yamashita, N. Shigematsi, S. Izumi, and M. Okuhara, *J. Antibiotics,* **49**, 37 (1966).
5. I. Ipiepa, B. Gil-Alberdi, E. Galvez, J. Bellanato, and P. Carmona, *J. Mol. Struct.,* **408-409**, 487 (1997).
6. W. Brandt, S. Drosihn, M. Haurand, U. Holzgrabe, and C. Nachstheim, *Arch. Pharm. Pharm. Med. Chem.,* **329**, 311 (1996).
7. P. S. Salve, G. J. Hite, R. A. Heyman, and G. Gianusos, *J. Med. Chem.,* **29**, 2111 (1986).
8. C. R. Clark, B. Birchmore, N. A. Sharif, J. C. Hunter, R. G. Hill, and J. Hugher, *Br. J. Pharmacol.,* **93**, 618 (1988).
9. G. F. Costello, B. G. Main, J. J. Barlow, J. A. Carroll, and J. S. Shaw, *Eur. J. Pharmacol.,* **151**, 475 (1988).
10. N. Ono, *The Nitro Group in Organic Synthesis*, Wiley, New York, 2001.
11. I. E. Yakunina, I. V. Shakhkeldyan, Yu. M. Atroshchenko, O. Ya. Borbulevich, V. V. Nesterov, M V Kopyshev, N. A. Troitskii, Yu. E. Efremov, E. N. Alifanova, and V. A. Subbotin, *Zh. Org. Khim.,* **40**, 266 (2004).
12. M. Arend, B. Westerman, and N. Risch, *Angew. Chem. Int. Ed.,* **37**, 1045 (1998).