ISSN 1070-4280, Russian Journal of Organic Chemistry, 2007, Vol. 43, No. 9, pp. 1297–1304. © Pleiades Publishing, Ltd., 2007.
Original Russian Text © I.N. Tarabara, Ya.S. Bondarenko, A.A. Zhurakovskii, L.I. Kas'yan, 2007, published in Zhurnal Organicheskoi Khimii, 2007, Vol. 43, No. 9, pp. 1303–1310.

New Derivatives of 2-(3,5-Dioxo-4-azatricyclo[5.2.1.0$^{2,6\text{-}endo}$]-dec-8-en-4-yl)acetic Acid. Synthesis and Reactivity

I. N. Tarabara, Ya. S. Bondarenko, A. A. Zhurakovskii, and L. I. Kas'yan

Dnepropetrovsk National University, per. Nauchnyi 13, Dnepropetrovsk, 49625 Ukraine

Received July 28, 2006

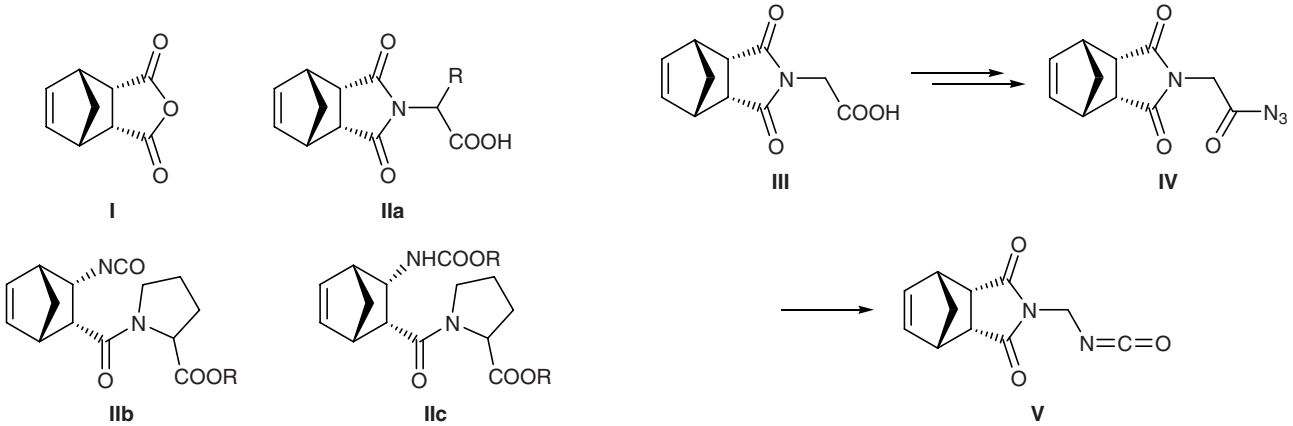
Abstract—New urea, carbamates, and carboxamides of the norbornene series were synthesized on the basis of 4-isocyanatomethyl-4-azatricyclo[5.2.1.0$^{2,6\text{-}endo}$]dec-8-ene-3,5-dione, and their behavior in reactions with various electrophiles was studied. The structure of the isolated compounds was confirmed by the IR and ^{1}H NMR spectra.

DOI: 10.1134/S1070428007090072

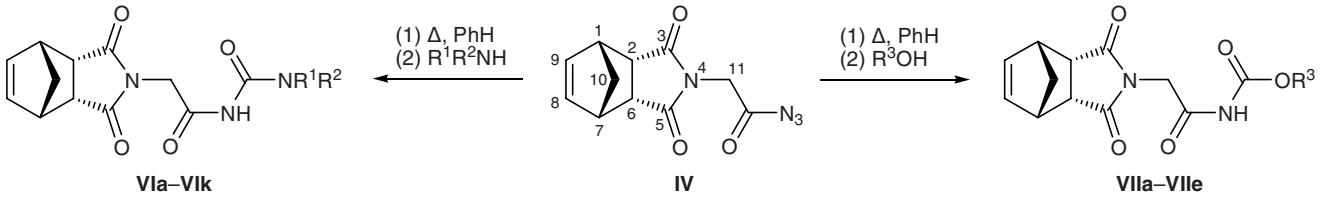
The use in organic synthesis of compounds containing several reaction centers differing in their electronic nature offers wide possibilities for further functionalization. Among such compounds, an important place is occupied by amino acids. The role of amino acids as building blocks for protein molecules is well known; in addition, many examples were reported on the application of amino acids in the synthesis of pharmacologically active compounds [1], including those derived from alicyclic hydrocarbons and containing amino acid residues. While synthesizing Thalidomide analogs, Koch et al. [2] isolated and characterized compounds obtained from endic anhydride (**I**) and amino acids and described products of the reactions of the resulting imido acids **IIa** (R = H, Me, Et) with ammonia. Biagini et al. [3] studied reactions of anhydride **I** with both racemic and optically active glycine, alanine, phenylglycine, valine, isoleucine, serine, and cystine methyl ester hydrochlorides. Important products were synthesized on the basis of proline esters [4, 5]; they included conformationally rigid enzyme analogs, peptides, pseudopeptides, and the corresponding synthons **IIb** and **IIc** [6].

We previously showed that the condensation products of endic anhydride with some natural amino acids can be transformed into a variety of biologically active structures [7]. In particular, 2-(3,5-dioxo-4-azatricyclo-[5.2.1.0$^{2,6\text{-}endo}$]dec-8-en-4-yl)acetic acid (**III**) available via condensation of endic anhydride with glycine was chemoselectively converted into the corresponding isocyanate **V** through intermediate azide **IV** (Scheme 1), and compound **V** was used to prepare a series of new urea derivatives of the norbornene series [8]. Taking into account that the properties of isocyanate **V** were studied very poorly, the present work was aimed at investigating in detail the reactivity of this compound and products derived therefrom.

Scheme 1.



Scheme 2.



VI, R^1 = H, R^2 = 1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1*H*-pyrazol-4-yl (**a**), 2-HOC_6H_4 (**b**), pyridin-2-yl (**c**), pyridin-3-yl (**d**), 1,3-thiazol-2-yl (**e**), 1,3,4-thiadiazol-2-yl (**f**), 5-ethyl-1,3,4-thiadiazol-2-yl (**g**), 5-propyl-1,3,4-thiadiazol-2-yl (**h**), $PhCH_2$ (**i**), R^1R^2N = piperidino (**j**), morpholino (**k**); **VII**, R^3 = Me (**a**), Et (**b**), *i*-Pr (**c**), *n*-Bu (**d**), *cyclo*-C_6H_{11} (**e**).

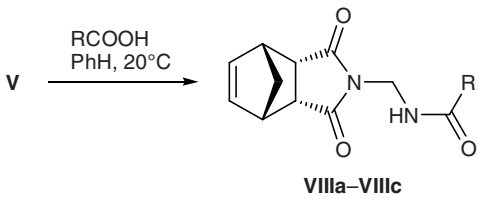
Azide **IV** was prepared according to the procedures described in [8] and was converted into isocyanate **V** by heating in boiling anhydrous benzene over a period of 1.5–2 h. Despite low stability of compound **V** (especially as individual substance), we succeeded in recording its IR spectrum which contained an absorption band at 2270 cm^{-1} due to stretching vibrations of the N=C=O group, as well as bands at 3080 and 730 cm^{-1} arising from stretching and bending vibrations of C–H bonds in the strained unsaturated bicyclic fragment [9].

Isocyanate **V** was brought (without isolation) into reactions with various nucleophiles, in particular with amines, alcohols, and carboxylic acids; the reactions were carried out with equimolar amounts of the reactants in anhydrous benzene. Isocyanate **V** reacted with amines and alcohols in a fairly selective fashion; as a result, we isolated the corresponding ureas **VIa**–**VIk** and carbamates **VIIa**–**VIIe** (Scheme 2). The IR spectra of **VIa**–**VIk** were sufficiently informative to identify the nature of functional groups present in their molecules. All ureas **VIa**–**VIk** showed in the IR spectra absorption bands in the region 3410–3240 cm^{-1}, which belong to stretching vibrations of the NH groups. Carbonyl groups in the imide fragment gave rise to two bands at 1790–1765 and 1735–1720 cm^{-1}, corresponding to their antisymmetric and symmetric stretching vibrations. The spectra of all compounds **VIa**–**VIk** also contained bands typical of substituted urea fragments at 1660–1615, 1590–1550, and 1270–1215 cm^{-1}. The substituted carbamate fragment in compounds **VIIa**–**VIIe** was characterized by IR absorption bands at 1720, 1560–1555, and 1240–1230 cm^{-1} [9].

Convincing proofs for the assumed structure of compounds **VI** and **VII** were obtained by analysis of their ^{1}H NMR spectra which were fairly simple due to high symmetry of their molecules. In the spectra of ureas **VI** we observed signals from protons attached to the bicyclic skeleton and those present in the substituents. Two nonequivalent NH protons resonated as a triplet and singlet at δ 6.81–7.41 and 8.74–10.72 ppm, respectively, and the signal from the exocyclic methylene group appeared at δ 3.99–4.72 ppm. Unlike ureas **VI**, protons of the bridging methylene group (*syn*-10-H and *anti*-10-H) in carbamates **VII** were nonequivalent (Δδ = 0.1 ppm), presumably due to unsymmetrical orientation of the carbamate fragment with respect to the bicyclic skeleton.

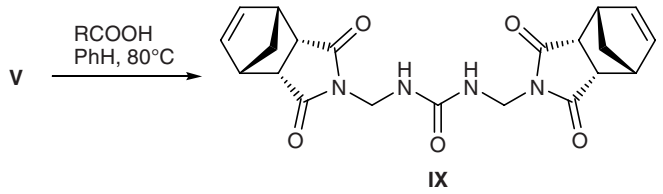
In keeping with published data, aliphatic isocyanates react with carboxylic acids to give the corresponding amides as major products; the reaction scheme includes formation of mixed aliphatic carbamic anhydride, followed by decarboxylation at elevated temperature [10]. By contrast, aromatic isocyanates usually produce the corresponding amides in a poor yield, whereas the major products are symmetric ureas [10]. In our case, isocyanate **V** reacted with aliphatic carboxylic acids in benzene at room temperature (20°C) to give the corresponding amides **VIIIa**–**VIIIc** in high yields (Scheme 3). The IR spectra of **VIIIa**–**VIIIc** contained absorption bands due to stretching vibrations of the imide carbonyl groups (1790–1780 and 1725–1720 cm^{-1}) and NH groups (3390–3300 cm^{-1}) and three amide bands at 1680–1660, 1580–1565, and 1240–1225 cm^{-1} [9]. In the ^{1}H NMR spectra of amides **VIIIb** and **VIIIc**, signals from protons in the bicyclic fragment, exocyclic methylene groups (δ 4.51 and 4.71 ppm), and amide NH fragment (δ 6.73 and 8.28 ppm, respectively) were present. By heating iso-

Scheme 3.



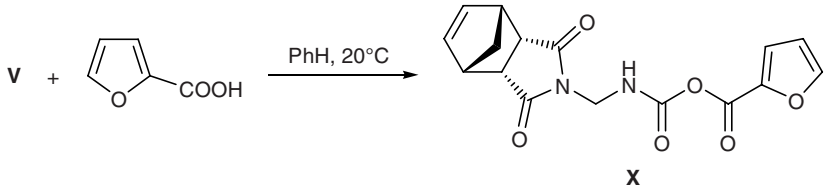
R = H (**a**), Me (**b**), $ClCH_2$ (**c**).

Scheme 4.



R = Ph, 2-furyl.

Scheme 5.



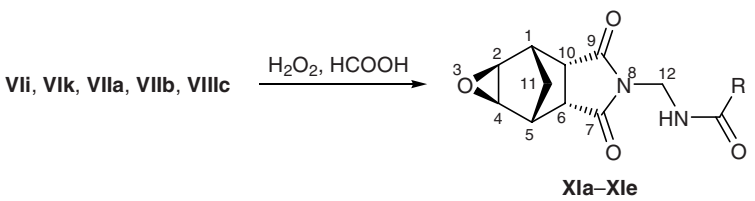
cyanate **V** with an equimolar amount of benzoic or furan-2-carboxylic acid in boiling anhydrous benzene we obtained symmetric urea **IX** as the only product (Scheme 4). The product was identified on the basis of its elemental composition and ^{1}H NMR spectrum. The latter contained no aromatic proton signals, but those belonging to protons in the bicyclic and urea fragments were present.

However, in the reaction of isocyanate **V** with furan-2-carboxylic acid in anhydrous benzene at 20°C we isolated a low-melting substance which was assigned the structure of mixed anhydride **X** on the basis of the IR data (Scheme 5). In the IR spectrum of the product we observed absorption bands arising from imide and carbamate fragments and a strong band at 1815 cm^{-1} which is likely to belong to the anhydride carbonyl group [9].

The presence of a reactive strained double bond in the molecules of the synthesized compounds makes them capable of undergoing various further transformations in reactions with electrophilic reagents. As examples, we examined their reactions with peroxyformic acid and *p*-nitrophenyl azide; these electrophiles were used by us previously while studying the reactivity of other norbornene derivatives. Peroxyformic acid was generated *in situ* from 98% formic acid and 50% hydrogen peroxide. Following this procedure, compounds **VIi**, **VIk**, **VIIa**, **VIIb**, and **VIIIc** were converted into the corresponding epoxy derivatives **XIa**–**XIe** (Scheme 6). The structure of **XIa**–**XIe** was confirmed by spectral methods. The IR spectra of epoxides **XI** contained strong absorption bands at 856–850 cm^{-1}, which are typical of C–O stretching vibrations in epoxynorbornane molecules [11]. Epoxy derivatives **XIa**–**XIc** and **XIe** characteristically showed in the ^{1}H NMR spectra upfield shift of the 2-H and 4-H signals to the region δ 3.00–3.23 ppm; in addition, the signal from one proton in the methylene bridge (*anti*-11-H) was displaced from δ 1.16–1.62 to 1.02–1.04 ppm as a result of magnetically anisotropic effect of the three-membered oxygen-containing ring [12].

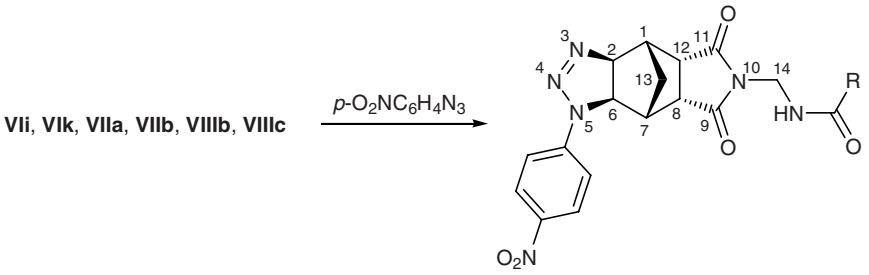
The reactions of compounds **VIi**, **VIk**, **VIIa**, **VIIb**, **VIIIb**, and **VIIIc** with *p*-nitrophenyl azide were carried out by heating equimolar amounts of the reactants in boiling anhydrous chloroform, the progress of the reaction being monitored by TLC. The only products were the corresponding fused triazole derivatives **XIIa**–**XIIf** whose structure was confirmed by spectral data. Like the initial norbornenes, compounds **XIIa**–**XIIf** displayed IR absorption bands from the imide

Scheme 6.



XI, R = PhCH$_2$NH (**a**), morpholino (**b**), MeO (**c**), EtO (**d**), ClCH$_2$ (**e**).

Scheme 7.



XIIa–XIIf

XII, R = $PhCH_2NH$ (**a**), morpholino (**b**), MeO (**c**), EtO (**d**), Me (**e**), $ClCH_2$ (**f**).

carbonyl groups (1780–1770, 1728–1712 cm^{-1}) and NH group (3400–3298 cm^{-1}). A medium-intensity band was observed in the region 1600–1594 cm^{-1}. No such band was present in the IR spectra of the initial compounds; presumably, it belongs to stretching vibrations of the N=N bond in the triazole fragment [13].

The presence of an unsymmetrically substituted dihydrotriazole fragment makes molecules **XII** strongly asymmetric, and their ^1H NMR spectra differ considerably from the spectra of the corresponding epoxy derivatives. In particular, the 2-H/6-H, 1-H/7-H, and 8-H/12-H protons in the bicyclic skeleton become nonequivalent, the largest nonequivalence being observed for the 2-H and 6-H protons in the dihydrotriazole fragment. These protons resonate at δ 4.62–4.67 and 3.81–3.97 ppm, respectively (^3J = 8.7–9.4 Hz), which is typical of systems with the *exo*-oriented heteroring [14]. The spectra of compounds **XIIa**–**XIIc** and **XIIf** are also characterized by a small downfield shift of the *syn*-13-H signal (δ 1.58–1.61 against 1.47–1.61 ppm in the spectra of the initial compounds), whereas the second proton in the methylene bridging group (*anti*-13-H) resonates in a stronger field (δ 1.07–1.08 ppm). These findings indicate that the *anti*-13-H proton appears directly above the triazole ring plane; therefore, the reaction of compounds **VI**–**VIII** with aryl azides follows the Alder rule [15].

EXPERIMENTAL

The IR spectra were recorded in KBr on UR-20 and Paragon 500 FT-IR spectrometers. The ^1H NMR spectra were measured from solutions in DMSO-d_6 on Bruker DAX-500 (500 MHz) and Varian VXR-Unity (200 MHz) spectrometers using tetramethylsilane as internal reference. The progress of reactions and the purity of products were monitored by TLC on Silufol UV-254 plates using chloroform as eluent; development with iodine vapor. The elemental compositions were determined on a Carlo Erba analyzer.

4-Isocyanatomethyl-4-azatricyclo[5.2.1.0$^{2,6\text{-}endo}$]-dec-8-ene-3,5-dione (V). A solution of 0.50 g (2 mmol) of azide **IV** [8] in 5 ml of anhydrous benzene was heated for 2 h under reflux. The mixture was cooled, the solvent was removed under reduced pressure (water-jet pump), and the residue was recrystallized from a large volume of anhydrous hexane. Yield 0.44 g (98%), mp 72–74°C. IR spectrum, ν, cm^{-1}: 3080, 2270, 1770, 1700, 1660, 1445, 1355, 1200, 730. Found, %: C 60.73; H 5.01; N 13.16. $C_{11}H_{10}N_2O_3$. Calculated, %: C 60.55; H 4.59; N 12.84.

***N*-(Aryl, hetaryl, cycloalkyl)-*N′*-(3,5-dioxo-4-azatricyclo[5.2.1.0$^{2,6\text{-}endo}$]dec-8-en-4-ylmethyl)ureas VIa–VIk (*general procedure*).** A solution of 0.50 g (2 mmol) of azide **IV** in 5 ml of anhydrous benzene was heated for 2 h under reflux; it was then cooled, an equimolar amount of the corresponding amine was added, and the mixture was left to stand until a solid precipitated. The precipitate was filtered off, washed with benzene on a filter, dried, and recrystallized from benzene or 2-propanol.

***N*-(1,5-Dimethyl-3-oxo-2-phenyl-1*H*-pyrazol-4-yl)-*N′*-(3,5-dioxo-4-azatricyclo[5.2.1.0$^{2,6\text{-}endo}$]dec-8-en-4-ylmethyl)urea (VIa).** Yield 92%, mp 283–284°C, R_f 0.14. IR spectrum, ν, cm^{-1}: 3340, 3220, 1785, 1725, 1660, 1610, 1570, 1350, 1250, 710. ^1H NMR spectrum, δ, ppm: 9.21 s (1H, NH), 7.50–7.33 (5H, H_{arom}), 6.06 m (2H, 8-H, 9-H), 3.99 d (2H, 11-H), 3.41 m (2H, 2-H, 6-H), 3.26 m (2H, 1-H, 7-H), 3.03 s (3H, CH_3), 2.08 s (3H, CH_3), 1.58 m (2H, *syn*-10-H, *anti*-10-H). Found, %: N 16.56. $C_{22}H_{23}N_5O_4$. Calculated, %: N 16.62.

***N*-(2-Hydroxyphenyl)-*N′*-{(3,5-dioxo-4-azatricyclo[5.2.1.0$^{2,6\text{-}endo}$]dec-8-en-4-ylmethyl)urea (VIb).** Yield 87%, mp 215–216°C. ^1H NMR spectrum, δ,

ppm: 9.62 s (1H, NH); 7.84, 6.77, and 6.68 (3H, H_{arom}); 7.41 t (1H, NH); 5.99 m (2H, 8-H, 9-H); 4.63 d (2H, 11-H), 3.33 m (2H, 2-H, 6-H), 3.24 m (2H, 1-H, 7-H), 1.52 m (2H, *syn*-10-H, *anti*-10-H). Found, %: N 12.74. $C_{17}H_{17}N_3O_4$. Calculated, %: N 12.84.

***N*-(3,5-Dioxo-4-azatricyclo[5.2.1.0$^{2,6\text{-}endo}$]dec-8-en-4-ylmethyl)-*N*′-(2-pyridyl)urea (VIc).** Yield 66%, mp 201–202°C. IR spectrum, ν, cm^{-1}: 3250, 3160, 1790, 1735, 1615, 1600, 1570, 1340, 1225, 730. ^{1}H NMR spectrum, δ, ppm: 9.20 s (1H, NH); 8.50, 8.18, 7.68, and 7.40 (4H, pyridine); 6.93 t (1H, NH); 5.96 m (2H, 8-H, 9-H); 4.72 d (2H, 11-H); 3.32 m (2H, 2-H, 6-H); 3.23 m (2H, 1-H, 7-H); 1.53 m (2H, *syn*-10-H, *anti*-10-H). Found, %: N 17.90. $C_{16}H_{16}N_4O_3$. Calculated, %: N 17.95.

***N*-(3,5-Dioxo-4-azatricyclo[5.2.1.0$^{2,6\text{-}endo}$]dec-8-en-4-ylmethyl)-*N*′-(3-pyridyl)urea (VId).** Yield 86%, mp 195–196°C. ^{1}H NMR spectrum, δ, ppm: 8.74 s (1H, NH); 8.48, 8.13, 7.84, and 7.23 (4H, pyridine); 6.81 t (1H, NH); 5.98 m (2H, 8-H, 9-H); 4.67 d (2H, 11-H); 3.32 m (2H, 2-H, 6-H); 3.25 m (2H, 1-H, 7-H); 1.52 m (2H, *syn*-10-H, *anti*-10-H). Found, %: N 17.92. $C_{16}H_{16}N_4O_3$. Calculated, %: N 17.95.

***N*-(3,5-Dioxo-4-azatricyclo[5.2.1.0$^{2,6\text{-}endo}$]dec-8-en-4-ylmethyl)-*N*′-(1,3-thiazol-2-yl)urea (VIe).** Yield 63%, mp 159–160°C. ^{1}H NMR spectrum, δ, ppm: 10.29 s (1H, NH), 7.30 and 7.03 (2H, 4′-H, 5′-H), 7.12 t (1H, NH), 5.96 m (2H, 8-H, 9-H), 4.68 d (2H, 11-H), 3.34 m (2H, 2-H, 6-H), 3.22 m (2H, 1-H, 7-H), 1.52 m (2H, *syn*-10-H, *anti*-10-H). Found, %: N 17.71. $C_{14}H_{14}N_4O_3S$. Calculated, %: N 17.61.

***N*-(3,5-Dioxo-4-azatricyclo[5.2.1.0$^{2,6\text{-}endo}$]dec-8-en-4-ylmethyl)-*N*′-(1,3,4-thiadiazol-2-yl)urea (VIf).** Yield 89%, mp 240–241°C. IR spectrum, ν, cm^{-1}: 3240, 3130, 1790, 1725, 1620, 1590, 1240. ^{1}H NMR spectrum, δ, ppm: 10.72 s (1H, NH), 9.00 (1H, 5′-H), 7.18 t (1H, NH), 5.96 m (2H, 8-H, 9-H), 4.70 d (2H, 11-H), 3.34 m (2H, 2-H, 6-H), 3.23 m (2H, 1-H, 7-H), 1.51 m (2H, *syn*-10-H, *anti*-10-H). Found, %: N 21.99. $C_{13}H_{13}N_5O_3S$. Calculated, %: N 21.94.

***N*-(3,5-Dioxo-4-azatricyclo[5.2.1.0$^{2,6\text{-}endo}$]dec-8-en-4-ylmethyl)-*N*′-(5-ethyl-1,3,4-thiadiazol-2-yl)-urea (VIg).** Yield 66%, mp 141–142°C. ^{1}H NMR spectrum, δ, ppm: 10.55 s (1H, NH), 7.13 t (1H, NH), 5.98 m (2H, 8-H, 9-H), 4.70 d (2H, 11-H), 3.33 m (2H, 2-H, 6-H), 3.23 m (2H, 1-H, 7-H), 2.92 q (2H, CH_2), 1.53 m (2H, *syn*-10-H, *anti*-10-H), 1.27 t (3H, CH_3). Found, %: N 20.09. $C_{15}H_{17}N_5O_3S$. Calculated, %: N 20.17.

***N*-(3,5-Dioxo-4-azatricyclo[5.2.1.0$^{2,6\text{-}endo}$]dec-8-en-4-ylmethyl)-*N*′-(5-propyl-1,3,4-thiadiazol-2-yl)-urea (VIh).** Yield 74%, mp 136–138°C. IR spectrum, ν, cm^{-1}: 3400, 3270, 1790, 1735, 1660, 1585, 1340, 1250, 1220, 730. ^{1}H NMR spectrum, δ, ppm: 10.53 s (1H, NH), 7.13 t (1H, NH), 5.96 m (2H, 8-H, 9-H), 4.68 d (2H, 11-H), 3.34 m (2H, 2-H, 6-H), 3.20 m (2H, 1-H, 7-H), 2.88 t (2H, CH_2), 2.70 m (2H, CH_2), 1.52 t (2H, *syn*-10-H, *anti*-10-H), 0.93 t (3H, CH_3). Found, %: N 19.28. $C_{16}H_{19}N_5O_3S$. Calculated, %: N 19.39.

***N*-Benzyl-*N*′-(3,5-dioxo-4-azatricyclo-[5.2.1.0$^{2,6\text{-}endo}$]dec-8-en-4-ylmethyl)urea (VIi).** Yield 88%, mp 124–125°C, R_f 0.27. IR spectrum, ν, cm^{-1}: 3375, 3320, 1765, 1720, 1635, 1570, 1260, 730. ^{1}H NMR spectrum, δ, ppm: 7.32–7.19 m (5H, H_{arom}), 6.55 t (2H, NH), 5.95 m (2H, 8-H, 9-H), 4.58 d (2H, 11-H), 4.18 d (2H, CH_2), 3.30 m (2H, 2-H, 6-H), 3.23 m (2H, 1-H, 7-H), 1.51 t (2H, *syn*-10-H, *anti*-10-H). Found, %: N 12.85. $C_{18}H_{19}N_3O_3$. Calculated, %: N 12.91.

***N*-(3,5-Dioxo-4-azatricyclo[5.2.1.0$^{2,6\text{-}endo}$]dec-8-en-4-ylmethyl)piperidine-1-carboxamide (VIj).** Yield 81%, mp 108–109°C. IR spectrum, ν, cm^{-1}: 3430, 3080, 1785, 1720, 1660, 1550, 1355, 1250, 1220, 735. Found, %: N 13.92. $C_{16}H_{21}N_3O_3$. Calculated, %: N 13.86.

***N*-(3,5-Dioxo-4-azatricyclo[5.2.1.0$^{2,6\text{-}endo}$]dec-8-en-4-ylmethyl)morpholine-4-carboxamide (VIk).** Yield 76%, mp 159–160°C, R_f 0.22. IR spectrum, ν, cm^{-1}: 3410, 1780, 1725, 1660, 1550, 1360, 1270, 1230, 730. ^{1}H NMR spectrum, δ, ppm: 7.00 t (1H, NH); 5.98 m (2H, 8-H, 9-H); 4.58 d (2H, 11-H); 3.50, 3.48, and 3.22 (8H, NCH_2CH_2O); 3.31 m (2H, 2-H, 6-H); 3.23 m (2H, 1-H, 7-H); 1.52 m (2H, *syn*-10-H, *anti*-10-H). Found, %: N 13.71. $C_{15}H_{19}N_3O_4$. Calculated, %: N 13.77.

Alkyl (3,5-dioxo-4-azatricyclo[5.2.1.0$^{2,6\text{-}endo}$]dec-8-en-4-ylmethyl)carbamates VIIa–VIIe (*general procedure*)**.** A solution of 0.50 g (2 mmol) of azide **IV** in 5 ml of anhydrous benzene was heated for 2 h under reflux; it was then cooled, an equimolar amount of the corresponding anhydrous alcohol was added, and the mixture was left to stand until the reaction was complete (TLC). The solvent was removed, and the residue was purified by column chromatography on silica gel using diethyl ether as eluent.

Methyl (3,5-dioxo-4-azatricyclo[5.2.1.0$^{2,6\text{-}endo}$]-dec-8-en-4-ylmethyl)carbamate (VIIa). Yield 68%, mp 97–98°C, R_f 0.38. IR spectrum, ν, cm^{-1}: 3430, 3010, 1780, 1760, 1720, 1555, 1360, 1270, 1230, 730.

^{1}H NMR spectrum, δ, ppm: 7.11 t (1H, NH), 6.00 m (2H, 8-H, 9-H), 4.54 d (2H, 11-H), 3.56 s (3H, CH_3), 3.26 m (2H, 2-H, 6-H), 3.22 m (2H, 1-H, 7-H), 1.62 d (1H, *syn*-10-H), 1.53 d (1H, *anti*-10-H). Found, %: N 11.28. $C_{12}H_{14}N_2O_4$. Calculated, %: N 11.20.

Ethyl (3,5-dioxo-4-azatricyclo[5.2.1.0$^{2,6\text{-}endo}$]dec-8-en-4-ylmethyl)carbamate (VIIb). Yield 74%, mp 76–77°C. IR spectrum, ν, cm^{-1}: 3420, 3015, 1780, 1765, 1720, 1565, 1360, 1265, 1235. ^{1}H NMR spectrum, δ, ppm: 6.96 t (1H, NH), 5.99 m (2H, 8-H, 9-H), 4.51 d (2H, 11-H), 4.00 q (2H, CH_2), 3.28 m (2H, 2-H, 6-H), 3.22 m (2H, 1-H, 7-H), 1.63 d (1H, *syn*-10-H), 1.53 d (1H, *anti*-10-H), 1.22 t (3H, CH_3). Found, %: N 10.58. $C_{13}H_{16}N_2O_4$. Calculated, %: N 10.61.

Isopropyl (3,5-dioxo-4-azatricyclo[5.2.1.0$^{2,6\text{-}endo}$]-dec-8-en-4-ylmethyl)carbamate (VIIc). Yield 62%, mp 134–135°C. IR spectrum, ν, cm^{-1}: 3400, 3020, 1775, 1760, 1720, 1560, 1365, 1270, 1230. ^{1}H NMR spectrum, δ, ppm: 7.32 t (1H, NH), 5.98 m (2H, 8-H, 9-H), 4.72 m (1H, CH), 4.48 d (2H, 11-H), 3.30 m (2H, 2-H, 6-H), 3.20 m (2H, 1-H, 7-H), 1.54 d (1H, *syn*-10-H), 1.51 d (1H, *anti*-10-H), 1.14 d (6H, CH_3). Found, %: N 10.04. $C_{14}H_{18}N_2O_4$. Calculated, %: N 10.07.

Butyl (3,5-dioxo-4-azatricyclo[5.2.1.0$^{2,6\text{-}endo}$]dec-8-en-4-ylmethyl)carbamate (VIId). Yield 69%, mp 124–125°C. ^{1}H NMR spectrum, δ, ppm: 6.97 t (1H, NH), 5.98 m (2H, 8-H, 9-H), 4.52 d (2H, 11-H), 3.93 t (2H, CH_2), 3.30 m (2H, 2-H, 6-H), 3.24 m (2H, 1-H, 7-H), 1.63 d (1H, *syn*-10-H), 1.53 d (1H, *anti*-10-H), 1.52 m (2H, CH_2), 1.34 m (2H, CH_2), 0.92 t (3H, CH_3). Found, %: N 9.47. $C_{15}H_{20}N_2O_4$. Calculated, %: N 9.59.

Cyclohexyl (3,5-dioxo-4-azatricyclo[5.2.1.0$^{2,6\text{-}endo}$]-dec-8-en-4-ylmethyl)carbamate (VIIe). Yield 86%, mp 139–140°C. IR spectrum, cm^{-1}: 3375, 3015, 1780, 1740, 1720, 1560, 1340, 1265, 1240. ^{1}H NMR spectrum, δ, ppm: 7.36 t (1H, NH); 5.96 m (2H, 8-H, 9-H); 4.48 d (2H, 11-H); 3.31 m (2H, 2-H, 6-H); 3.23 m (2H, 1-H, 7-H); 1.75, 1.66, 1.52, and 1.30 (11H, cyclohexyl); 1.54 d (1H, *syn*-10-H), 1.50 d (1H, *anti*-10-H). Found, %: N 8.84. $C_{17}H_{22}N_2O_4$. Calculated, %: N 8.81.

Reaction of compound V with organic acids. A solution of 0.50 g (2 mmol) of azide **IV** in 5 ml of anhydrous benzene was heated for 2 h under reflux; it was then cooled, an equimolar amount of the corresponding carboxylic acid was added, and the mixture was stirred until the reaction was complete (TLC). The solvent was removed, and the residue was recrystallized from appropriate solvent.

***N*-(3,5-Dioxo-4-azatricyclo[5.2.1.0$^{2,6\text{-}endo}$]dec-8-en-4-ylmethyl)formamide (VIIIa).** Yield 77%, mp 148–149°C, R_f 0.28. IR spectrum, ν, cm^{-1}: 3390, 3295, 1790, 1720, 1660, 1565, 1290, 1225, 740. Found, %: N 12.89. $C_{11}H_{12}N_2O_3$. Calculated, %: N 12.73.

***N*-(3,5-Dioxo-4-azatricyclo[5.2.1.0$^{2,6\text{-}endo}$]dec-8-en-4-ylmethyl)acetamide (VIIIb).** Yield 75%, mp 105–106°C. IR spectrum, ν, cm^{-1}: 3300, 1780, 1720, 1660, 1580, 1235, 730. ^{1}H NMR spectrum, δ, ppm: 6.73 t (1H, NH), 5.91 m (2H, 8-H, 9-H), 4.51 d (2H, 11-H), 3.25 m (2H, 2-H, 6-H), 3.01 m (1H, 1-H), 2.52 m (1H, 7-H), 1.89 s (3H, CH_3), 1.49 m (2H, *syn*-10-H, *anti*-10-H). Found, %: N 12.17. $C_{12}H_{14}N_2O_3$. Calculated, %: N 11.97.

Chloro-*N*-(3,5-dioxo-4-azatricyclo[5.2.1.0$^{2,6\text{-}endo}$]-dec-8-en-4-ylmethyl)acetamide (VIIIc). Yield 46%, mp 143–144°C, R_f 0.29. IR spectrum, ν, cm^{-1}: 3340, 3030, 1780, 1725, 1680, 1575, 1240. ^{1}H NMR spectrum, δ, ppm: 8.28 t (1H, NH), 6.05 m (2H, 8-H, 9-H), 4.71 d (2H, 11-H), 4.02 s (2H, CH_2), 3.37 m (2H, 2-H, 6-H), 2.87 m (1H, 1-H), 2.72 m (1H, 7-H), 1.47 d (1H, *syn*-10-H), 1.16 d (1H, *anti*-10-H). Found, %: N 10.37. $C_{12}H_{13}ClN_2O_3$. Calculated, %: N 10.43.

***N*,*N*′-Bis(3,5-dioxo-4-azatricyclo[5.2.1.0$^{2,6\text{-}endo}$]-dec-8-en-4-ylmethyl)urea (IX).** A solution of 0.50 g (2 mmol) of azide **IV** in 5 ml of anhydrous benzene was heated for 2 h under reflux; it was then cooled, an equimolar amount of benzoic or furan-2-carboxylic acid was added, and the mixture was heated under reflux until the reaction was complete (TLC). The solvent was removed, and the residue was recrystallized from ethanol. Yield 56%, mp 239–240°C, R_f 0.11. IR spectrum, ν, cm^{-1}: 3370, 1770, 1710, 1670, 1580, 1260, 1230. ^{1}H NMR spectrum, δ, ppm: 6.72 t (2H, NH), 5.94 m (4H, 8-H, 9-H), 4.51 d (4H, 11-H), 3.28 m (4H, 2-H, 6-H), 3.22 m (4H, 1-H, 7-H), 1.53 d (2H, *syn*-10-H), 1.49 d (2H, *anti*-10-H). Found, %: N 13.72. $C_{21}H_{22}N_4O_5$. Calculated, %: N 13.66.

(3,5-Dioxo-4-azatricyclo[5.2.1.0$^{2,6\text{-}endo}$]dec-8-en-4-ylmethyl)carbamic furan-2-carboxylic anhydride (X). A solution of 0.50 g (2 mmol) of azide **IV** in 5 ml of anhydrous benzene was heated for 2 h under reflux; it was then cooled, an equimolar amount of furan-2-carboxylic acid was added, and the mixture was stirred until the reaction was complete (TLC). The solvent was removed, and the residue was dried on a filter for a short time and recrystallized from anhydrous benzene. Yield 85%, mp 75–76°C, R_f 0.13. IR spectrum, ν, cm^{-1}: 3280, 3065, 1815, 1790, 1740, 1720, 1560, 1230.

Found, %: C 58.12; H 4.18; N 8.69. $C_{16}H_{14}N_2O_6$. Calculated, %: C 58.18; H 4.24; N 8.48.

Epoxy derivatives XIa–XIe (*general procedure*)**.** Urea **VIi** or **VIk**, carbamate **VIIa** or **VIIb**, or amide **VIIIc**, 1 mmol, was dissolved in 10 ml of 98% formic acid, 0.06 ml (2 mmol) of 50% aqueous hydrogen peroxide was added under stirring, and the mixture was stirred until the reaction was complete (TLC). Volatile substances were removed under reduced pressure (water-jet pump), and the residue was recrystallized from water or propan-2-ol.

***N*-Benzyl-*N′*-(7,9-dioxo-3-oxa-8-azatetracyclo-[5.3.1.0$^{2,4\text{-}exo}$.0$^{6,10\text{-}endo}$]undec-8-ylmethyl)urea (XIa).** Yield 66%, mp 99–100°C, R_f 0.18. IR spectrum, ν, cm^{-1}: 3370, 1774, 1712, 1690, 1648, 1566, 1258, 850. ^{1}H NMR spectrum, δ, ppm: 7.31–7.14 (5H, H_{arom}), 6.71 t (1H, NH), 6.53 t (1H, NH), 4.70 d (2H, 12-H), 4.14 d (2H, CH_2), 3.21 m (2H, 6-H, 10-H), 3.00 m (2H, 2-H, 4-H), 2.88 m (2H, 1-H, 5-H), 1.35 d (1H, *syn*-11-H), 1.03 d (1H, *anti*-11-H). Found, %: N 12.43. $C_{18}H_{19}N_3O_4$. Calculated, %: N 12.32.

***N*-(7,9-Dioxo-3-oxa-8-azatetracyclo[5.3.1.0$^{2,4\text{-}exo}$.-0$^{6,10\text{-}endo}$]undec-8-ylmethyl)morpholine-4-carboxamide (XIb).** Yield 66%, mp 192–193°C (decomp.). IR spectrum, ν, cm^{-1}: 3405, 3030, 1790, 1715, 1670, 1560, 1220, 860. ^{1}H NMR spectrum, δ, ppm: 7.21 t (1H, NH), 4.70 d (2H, 12-H), 3.49–3.45 m and 3.22–3.19 m (4H each, NCH_2CH_2O), 3.19 m (2H, 6-H, 10-H), 3.02 m (2H, 2-H, 4-H), 2.86 m (2H, 1-H, 5-H), 1.33 d (1H, *syn*-11-H), 1.02 d (1H, *anti*-11-H). Found, %: N 13.28. $C_{15}H_{19}N_3O_5$. Calculated, %: N 13.08.

Methyl (7,9-dioxo-3-oxa-8-azatetracyclo-[5.3.1.0$^{2,4\text{-}exo}$.0$^{6,10\text{-}endo}$]undec-8-ylmethyl)carbamate (XIc). Yield 78%, mp 166–167°C, R_f 0.26. IR spectrum, ν, cm^{-1}: 3312, 1778, 1736, 1728, 1690, 1538, 1252, 856. ^{1}H NMR spectrum, δ, ppm: 7.86 t (1H, NH), 4.63 d (2H, 12-H), 3.49 s (3H, CH_3), 3.22 m (2H, 6-H, 10-H), 3.03 m (2H, 2-H, 4-H), 2.87 m (2H, 1-H, 5-H), 1.34 d (1H, *syn*-11-H), 1.04 d (1H, *anti*-11-H). Found, %: N 10.64. $C_{12}H_{14}N_2O_5$. Calculated, %: N 10.53.

Ethyl (7,9-dioxo-3-oxa-8-azatetracyclo-[5.3.1.0$^{2,4\text{-}exo}$.0$^{6,10\text{-}endo}$]undec-8-ylmethyl)carbamate (XId). Yield 63%, mp 134–135°C, R_f 0.30. IR spectrum, ν, cm^{-1}: 3314, 1780, 1728, 1712, 1690, 1538, 1248, 854. Found, %: N 10.18. $C_{13}H_{16}N_2O_5$. Calculated, %: N 10.00.

Chloro-*N*-(7,9-dioxo-3-oxa-8-azatetracyclo-[5.3.1.0$^{2,4\text{-}exo}$.0$^{6,10\text{-}endo}$]undec-8-ylmethyl)acetamide (XIe). Yield 78%, mp 127–128°C, R_f 0.19. IR spectrum, ν, cm^{-1}: 3310, 3030, 1775, 1710, 1560, 1230, 1160, 860. ^{1}H NMR spectrum, δ, ppm: 8.89 t (1H, NH), 4.72 d (2H, 12-H), 4.01 s (2H, CH_2), 3.33 m (2H, 6-H, 10-H), 3.23 m (2H, 2-H, 4-H), 2.87 m (2H, 1-H, 5-H), 1.33 d (1H, *syn*-11-H), 1.04 d (1H, *anti*-11-H). Found, %: N 10.02. $C_{12}H_{13}ClN_2O_4$. Calculated, %: N 9.84.

Triazole derivatives XIIa–XIIf (*general procedure*)**.** A mixture of 1 mmol of compound **VIi**, **VIk**, **VIIa**, **VIIb**, **VIIIb**, or **VIIIc** and 0.25 g (1.5 mmol) of *p*-nitrophenyl azide in 10 ml of chloroform was heated for 5–7 h under reflux. The solvent was removed under reduced pressure (water-jet pump), the residue was ground with 10 ml of diethyl ether, and the precipitate was filtered off, dried, and recrystallized from isopropyl alcohol.

***N*-Benzyl-*N′*-(9,11-dioxo-3,4,5,10-tetraazatetracyclo[5.5.1.0$^{2,6\text{-}exo}$.0$^{8,12\text{-}endo}$]tridec-10-ylmethyl)urea (XIIa).** Yield 87%, mp 107–109°C (decomp.), R_f 0.21. IR spectrum, ν, cm^{-1}: 3374, 3300, 1774, 1712, 1690, 1598, 1516, 1334, 1250, 846. ^{1}H NMR spectrum, δ, ppm: 8.31 d (2H, H_{arom}), 7.31 d (2H, H_{arom}), 7.26–6.99 m (5H, H_{arom}), 6.88 t (1H, NH), 6.56 t (1H, NH), 4.75 d (2H, 14-H), 4.65 d (1H, 2-H, $^3J_{2,6}$ = 9.4 Hz), 4.02 (2H, CH_2), 3.81 d (1H, 6-H), 3.31 m (2H, 8-H, 12-H), 3.13 m (1H, 1-H), 3.04 m (1H, 7-H), 1.58 d (1H, *syn*-13-H), 1.07 d (1H, *anti*-13-H). Found, %: N 20.15. $C_{24}H_{23}N_7O_5$. Calculated, %: N 20.04.

***N*-(9,11-Dioxo-3,4,5,10-tetraazatetracyclo-[5.5.1.0$^{2,6\text{-}exo}$.0$^{8,12\text{-}endo}$]tridec-10-ylmethyl)morpholine-4-carboxamide (XIIb).** Yield 62%, mp 195–197°C (decomp.), R_f 0.12. IR spectrum, ν, cm^{-1}: 3405, 1790, 1725, 1710, 1665, 1610, 1530, 1340, 1260, 1225, 870, 855. ^{1}H NMR spectrum, δ, ppm: 8.33 d (2H, H_{arom}), 7.41 t (1H, NH), 7.32 d (2H, H_{arom}), 4.74 d (2H, 14-H), 4.67 d (1H, 2-H, $^3J_{2,6}$ = 8.7 Hz), 3.84 d (1H, 6-H), 3.31 m and 3.12 m (4H each, NCH_2CH_2O), 3.32 m (2H, 8-H, 12-H), 3.14 m (1H, 1-H), 3.03 m (1H, 7-H), 1.60 d (1H, *syn*-13-H), 1.07 d (1H, *anti*-13-H). Found, %: N 20.80. $C_{21}H_{23}N_7O_6$. Calculated, %: N 20.89.

Methyl (9,11-dioxo-3,4,5,10-tetraazatetracyclo-[5.5.1.0$^{2,6\text{-}exo}$.0$^{8,12\text{-}endo}$]tridec-10-ylmethyl)carbamate (XIIc). Yield 85%, mp 189–191°C (decomp.), R_f 0.17. IR spectrum, ν, cm^{-1}: 3298, 1770, 1728, 1688, 1598, 1538, 1514, 1334, 1254, 848. ^{1}H NMR spectrum, δ, ppm: 8.32 d (2H, H_{arom}), 7.91 t (1H, NH), 7.32 d (2H, H_{arom}), 4.72 d (2H, 14-H), 4.62 d (1H, 2-H, $^3J_{2,6}$ = 8.7 Hz), 3.89 d (1H, 6-H), 3.46 s (3H, CH_3), 3.35 m (2H, 8-H, 12-H), 3.14 m (1H, 1-H), 3.03 m (1H, 7-H),

1.60 d (1H, *syn*-13-H), 1.08 d (1H, *anti*-13-H). Found, %: N 20.17. $C_{18}H_{18}N_6O_6$. Calculated, %: N 20.29.

Ethyl (9,11-dioxo-3,4,5,10-tetraazatetracyclo-[5.5.1.0$^{2,6\text{-}exo}$.0$^{8,12\text{-}endo}$]tridec-10-ylmethyl)carbamate (XIId). Yield 66%, mp 200–202°C (decomp.). IR spectrum, ν, cm^{-1}: 3374, 1776, 1724, 1686, 1594, 1552, 1512, 1336, 1250, 848. Found, %: N 19.53. $C_{19}H_{20}N_6O_6$. Calculated, %: N 19.58.

***N*-(9,11-Dioxo-3,4,5,10-tetraazatetracyclo-[5.5.1.0$^{2,6\text{-}exo}$.0$^{8,12\text{-}endo}$]tridec-10-ylmethyl)acetamide (XIIe).** Yield 57%, mp 110–112°C (decomp.). IR spectrum, ν, cm^{-1}: 3374, 1774, 1720, 1712, 1694, 1594, 1514, 1334, 1290, 848. Found, %: N 21.11. $C_{18}H_{18}N_6O_5$. Calculated, %: N 21.05.

Chloro-*N*-(9,11-dioxo-3,4,5,10-tetraazatetracyclo-[5.5.1.0$^{2,6\text{-}exo}$.0$^{8,12\text{-}endo}$]tridec-10-ylmethyl)acetamide (XIIf). Yield 72%, mp 192–193°C (decomp.), R_f 0.36. IR spectrum, ν, cm^{-1}: 3400, 1778, 1724, 1678, 1600, 1522, 1510, 1340, 1210, 848. ^{1}H NMR spectrum, δ, ppm: 10.00 t (1H, NH), 8.32 d (2H, H_{arom}), 7.31 d (2H, H_{arom}), 4.78 d (2H, 14-H), 4.66 d (1H, 2-H, $^3J_{2,6}$ = 9.4 Hz), 3.97 s (2H, CH_2), 3.83 d (1H, 6-H), 3.34 m (2H, 8-H, 12-H), 3.14 m (1H, 1-H), 3.05 m (1H, 7-H), 1.61 d (1H, *syn*-13-H), 1.08 d (1H, *anti*-13-H). Found, %: N 19.64. $C_{18}H_{17}ClN_6O_5$. Calculated, %: N 19.42.

REFERENCES

1. Mashkovskii, M.D., *Lekarstvennye sredstva* (Medicines), Moscow: Novaya Volna, 2002, 14th ed., vols. 1, 2.
2. Koch, H., Kotlan, J., Farkouh, E., and Linder, M., *Monatsh. Chem*., 1971, vol. 102, p. 609.
3. Biagini, S.C.G., Bush, S.M., Gibson, V.C., Mazzariol, L., North, M., Teasdale, W.G., Williams, C.M., Zagotto, G., and Zamuner, D., *Tetrahedron*, 1995, vol. 51, p. 7247.
4. Jones, I.G., Jones, W., and North, M., *Synlett*, 1997, vol. 12, p. 1478.
5. Jones, I.G., Jones, W., and North, M., *Tetrahedron*, 1999, vol. 55, p. 279.
6. Hibbs, D.E., Hursthouse, M.B., Jones, I.G., Jones, W., Abdul Malik, K.M., and North, M., *J. Org. Chem*., 1998, vol. 63, p. 1496.
7. Tarabara, I.N., Yarovoi, M.Yu., Isaev, A.K., and Kas'yan, L.I., *Visn. Dnipropetr. Univ., Khim*., 2002, no. 8, p. 36; Tarabara, I.N., Yarovoi, M.Yu., Bondarenko, Ya.S., and Kas'yan, L.I., *Visn. Dnipropetr. Univ., Khim*., 2003, no. 9, p. 35; Tarabara, I.N., Bondarenko, Ya.S., and Kas'yan, L.I., *Vopr. Khim. Khim. Tekhnol*., 2004, no. 3, p. 45; Tarabara, I.N., Bondarenko, Ya.S., Soshnikova, M.A., and Kas'yan, L.I., *Visn. Dnipropetr. Univ., Khim*., 2004, no. 10, p. 26; Tarabara, I.N., *Visn. Dnipropetr. Univ., Khim*., 2005, no. 11, p. 115.
8. Tarabara, I.N., Yarovoi, M.Yu., and Kas'yan, L.I., *Russ. J. Org. Chem*., 2003, vol. 39, p. 1676.
9. Nakanishi, K., *Infrared Absorption Spectroscopy. Practical*, San Francisco: Holden-Day, 1962.
10. Blagbrough, I.S., Mackenzie, N.E., Ortiz, C., and Scott, A.I., *Tetrahedron Lett*., 1986, vol. 27, p. 1251.
11. Kas'yan, L.I., *Usp. Khim*., 1998, vol. 67, p. 299; Kas'yan, L.I., *Russ. J. Org. Chem*., 1999, vol. 35, p. 635.
12. Tori, K., Aono, K., Kitahonoki, K., Muneyuki, R., Takano, Y., Tanida, H., and Tsuji, T., *Tetrahedron Lett*., 1966, p. 2921; Zefirov, N.S., Kasyan, L.I., Gnedenkov, L.Yu., Shashkov, A.S., and Cherepanova, E.G., *Tetrahedron Lett*., 1979, p. 949.
13. Bellamy, L.J., *The Infra-red Spectra of Complex Molecules*, London: Methuen, 1958.
14. Halton, B. and Woolhouse, A.D., *Aust. J. Chem*., 1973, vol. 26, p. 619; Shea, K.J. and Kim, J., *J. Am. Chem. Soc*., 1992, vol. 114, p. 4846.
15. Zefirov, N.S. and Sokolov, V.I., *Usp. Khim*., 1967, vol. 36, p. 243.