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Features of Reactions between (3,5-Dioxo-4-azatricyclo-[5.2.1.0$^{2\text{-}endo,6\text{-}endo}$]dec-8-en-4-yl)carboxylic Acids and *p*-Nitrophenyl Azide

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Abstract—Reactions were performed of (3,5-dioxo-4-azatricyclo[5.2.1.0$^{2\text{-}endo,6\text{-}endo}$]dec-8-en-4-yl)carboxylic acids and their derivatives with *p*-nitrophenyl azide. A significant fact of the involvement of the carboxy group into the formation of aziridine ring was established and the intermolecular character of this process was confirmed. The structure of compounds synthesized was proved by IR and ^{1}H NMR spectra.

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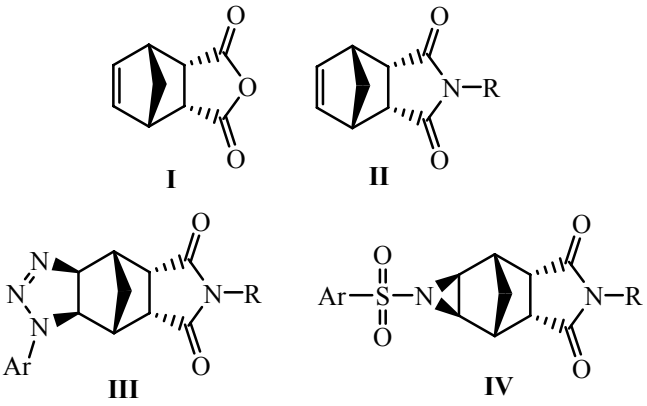
The reaction of organic azides with compounds containing multiple bonds is extensively used in designing various heterocyclic systems, in partcular, three-membered and five-membered nitrogen heterocycles and their numerous derivatives [1, 2]. Among the unsaturated substrates used in these reactions a special place belongs to norbornene and its derivatives: due to the enhanced reactivity of the strained double bond the reaction of these compounds with azides proceeds especially readily and as a rule takes a single route affording substituted triazolines or aziridines depending on the structure (type) of the applied azide. The readiness of this reaction makes it possible to use it for analytical detection of strained double bonds [3], and norbornene proper as a convenient reagent for testing the reactions of new azides [4]. The reactions of norbornene and its numerous derivatives with aryl azides proceeds along the mechanism of [3+2]-cycloaddition and in the most cases results in the formation of the corresponding triazoline systems [5]; reactions with azides containing electron-withdrawing substituents at the azide function (sulfonyl-, carbonylazides etc.), as a rule provide the corresponding aziridines or the products of deeper transformations [2, 6].

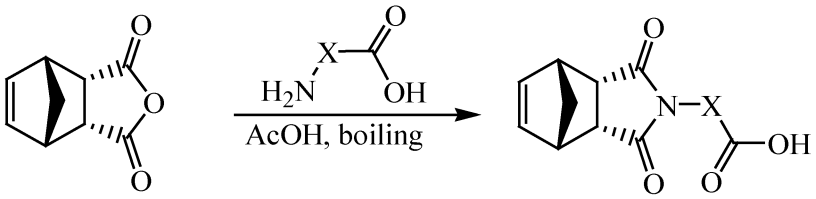
Among the compounds with a strained double bond included into a rigid bicyclic system a special attention attracts endic anhydride (**I**); owing to the presence of the reactive anhydride ring it is extensively used for preparation organic compounds of versatile structure. In

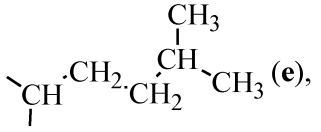
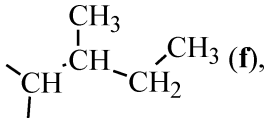


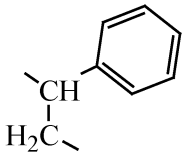
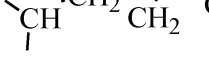
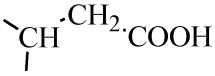
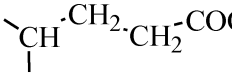
[7] the possibility was demonstrated to transform anhydride **I** into sophisticated polycyclic systems by reactions with arylsulfonyl azides. The reactions of imides **II** (R=Alk, Ar, Ht) with a series of aryl azides and arylsulfonyl azides were used to synthesize new heteropolycyclic compounds **III** and **IV** [8]. The behavior of the other derivatives of anhydride **I** in reactions with azides was not investigated and thus became the goal of this study.

We chose as objects of the research (3,5-dioxo-4-azatricyclo[5.2.1.0$^{2\text{-}endo,6\text{-}endo}$]dec-8-en-4-yl)carboxylic acids, the known and obtained for the first time products of endic anhydride (**I**) condensations with natural amino acids [9–11] employed as valuable "building blocks" in organic synthesis [12–14], and also their derivatives. The

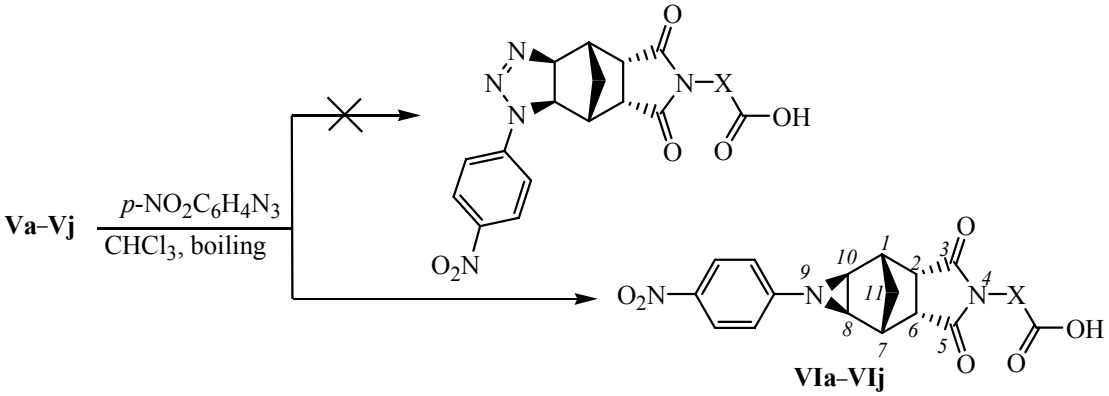
Scheme 1.



X = CH_2 (**à**), $CH(CH_3)$ (**b**), $(CH_2)_2$ (**c**), $(CH_2)_5$ (**d**),  (**e**),  (**f**),

 (**g**),  (**h**),  (è),  (**j**).

Scheme 2.



synthesis of known (**Va–Vc, Vi, Vj**) and new (**Vd–Vh**) acids was carried out by the previously developed procedure consisting in boiling equimolar mixtures of anhydride **I** and appropriate amino acids in the glacial acetic acid [12]; the target products were obtained in a good yield and a high purity (Scheme 1).

p-Nitrophenyl azide synthesized by a known procedure [15] was used as reagent. The reaction of azide with acids **Va–Vj** was performed by boiling equivalent amounts of reagents in anhydrous chloroform. Notwithstanding the type of amino acid we obtained unexpectedly as the only reaction products aziridines **VIa–VIj** (Scheme 2). The formation of the aziridine ring in reactions of norbornene and its various derivatives with common aryl azides was possible only under special conditions: either at sufficiently high temperature (therewith transformation occurred with stable at common circumstances products of [3+2]-cycloaddition), or under UV-irradiation of the reaction mixtures [1, 2]. In both events the aziridines were not the only reaction products.

In reactions of acids **Va–Vj** with azides in other solvents (benzene, acetonitrile) only insignificant changes in the yield of the corresponding aziridines was observed; the reaction in chloroform at room temperature required considerably longer time and resulted in lower yield of aziridines.

We studied by an example of acid **Va** the behavior of its derivatives in reaction with *p*-nitrophenyl azide. By reaction of acid **Va** with anhydrous methanol or ethanol in the presence of catalytic quantity of phosphorus oxychloride we obtained previously described esters **VIIa** and **VIIb** [10, 13]. Using chloride of acid **Va** obtained by standard procedure we synthesized amides **VIIIa–VIIIc** described in [12] (Scheme 3).

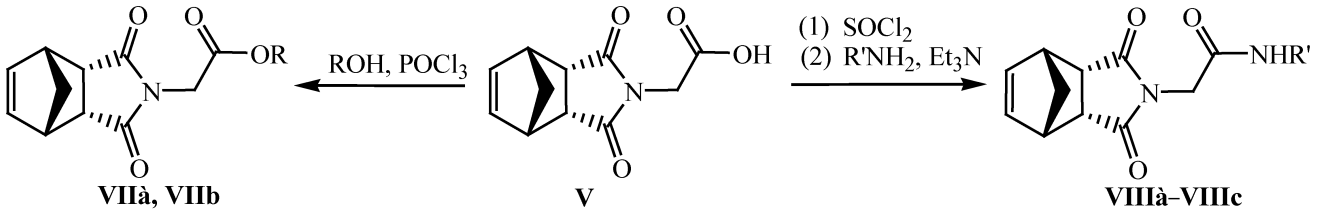
It was established that in reactions of compounds **VIIa, VIIb**, **VIIIa–VIIIc** with *p*-nitrophenyl azide under the same conditions the only products obtained were the corresponding triazolines **IXa–IXe** (Scheme 4).

Similar facts were reported in one of our recent papers: synthesized from acid **Va** derivatives with sub-stituted

carbamide, carbamate, and carbamoyl fragments in reaction with *p*-nitrophenyl azide yielded exclusively the corresponding triazolines **Xa–Xd** [16] (Scheme 5).

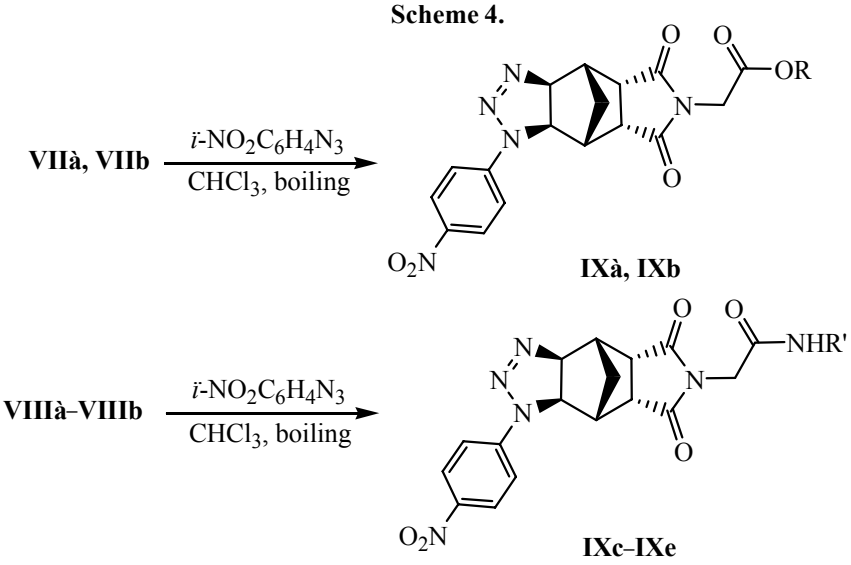
Conclusive proofs of the structure of heterocyclic compounds synthesized was obtained by analysis of their ^{1}H NMR spectra. The main criteria determining the character of the heterocycle formed (triazoline or aziridine) are the multiplicity and the position of the signals corresponding to the protons in this ring. In the spectra of aziridines **VIa–VIj** due to the high symmetry of the

Scheme 3.

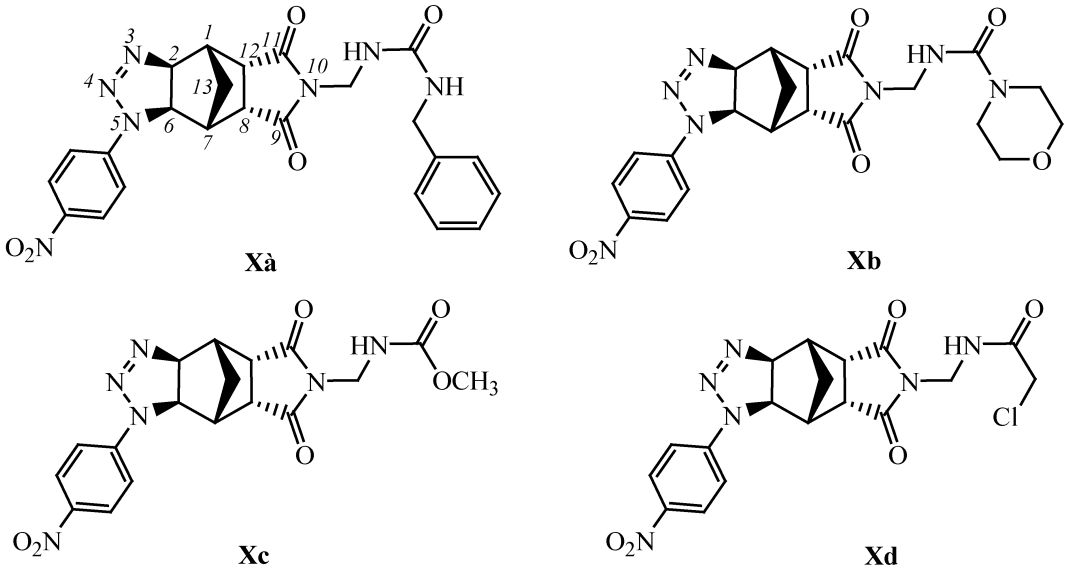


R = CH_3 (**a**), C_2H_5 (**b**); R' = CH_2Ph (**a**), C_6H_4Br-*p* (**b**), 2-thiazolyl (**c**).

Scheme 4.



Scheme 5.



R = CH_3 (**a**), C_2H_5 (**b**); R' = CH_2Ph (**c**), C_6H_4Br-*p* (**d**), 2- thiazolyl (**e**).

molecule the protons H^{8} and H^{10} are equivalent and resonate in the region 3.1–3.2 ppm. The lack of splitting of these signals that might be caused by the coupling with the bridgehead protons H^{1}, H^{7} indicates their *endo*-orientation and does not contradict the known Alder rule of the *exo*-attack [17, 18]. The additional proof of the *exo*-orientation of the formed heterocyclic fragment with respect to the bicyclic framework is the essential nonequivalence of the bridging protons and the upfield shift of the signal of one of them (H^{11an}) as compared to the position of this signal in the spectra of the initial olefins. The proton (H^{11an}) is located directly over the plane of the three-membered ring and suffered from the magnetically anisotropic effect of the latter.

Owing to the significant asymmetry of molecules of compounds **IXa–IXe** caused by the presence of asymmetrically substituted triazoline fragment their ^{1}H NMR spectra are essentially different from the aziridine spectra and are characterized by the nonequivalence of the skeleton protons (H^{2} and H^{6}, H^{1} and H^{7}, H^{8} and H^{12}). This nonequivalence is especially large for the protons of the triazoline fragment (H^{2}, H^{6}) that resonate in the regions 4.88–4.62 and 4.28–3.81 ppm; their coupling is characterized by vicinal constants 8.6–9.4 Hz common for the like systems containing an *exo*-oriented triazoline fragment [19]. The *exo*-orientation of the formed triazoline ring is also confirmed by the strong nonequivalence and by the position of the signals from the bridging protons (H^{13s}, H^{13an}).

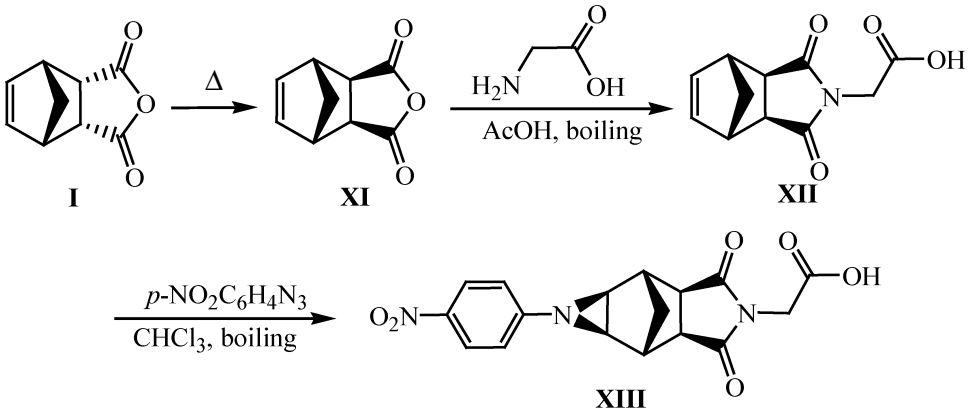
The results obtained suggest that the carboxy group is directly involved in the formation of the aziridine ring. We believe that the product of [3+2]-cycloaddition formed in the first stage suffers protonation that induces its further transformation into aziridine. Owing to the conformational rigidity of the bicyclic framework and spatially close location of the olefin fragment and the carboxy group the involvement of the latter in the process of aziridine ring formation may be both inter- and intramolecular.

In order to test the assumption on the probable intramolecular involvement of the carboxy group we synthesized acid **XII** with the *exo*-configuration of the substituted imide fragment proceeding from *exo*-anhydride **XI** obtained by the known method of *endo*-isomer **I** isomerization [20] (Scheme 6). The investigation of the behavior of acid **XII** in the reaction with *p*-nitrophenyl azide showed that in this case also formed the corresponding aziridine **XIII**. The structure of the latter is confirmed by the appearance in its ^{1}H NMR spectrum of a two-proton singlet in the region 3.10 ppm belonging to the protons H^{8}, H^{10} of the aziridine ring.

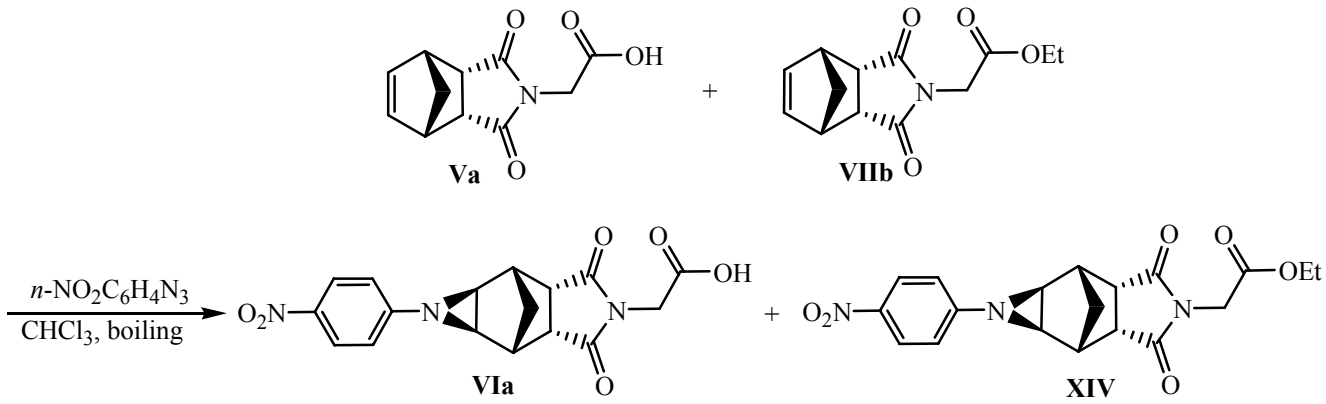
These data are likely to suggest that the participation of the carboxy group in the aziridine formation is of the intermolecular character. The additional proof of this type of behavior was obtained by the reaction of ester **VIIb** with *p*-nitrophenyl azide in the presence of acid **Va**. The treatment of a mixture containing equivalent amounts of compounds **Va** and **VIIb** with a slight excess *p*-nitrophenyl azide alongside aziridine **VIa** was obtained aziridine **XIV** (Scheme 7) whose structure was proved by spectral data.

Thus the study of unusual proceeding of reactions of (3,5-dioxo-4-azatricyclo[5.2.1.$0^{2\text{-}endo,6\text{-}endo}$]dec-8-en-4-yl)carboxylic acids with *p*-nitrophenyl azide made it possible to propose a simple procedure for introducing an aziridine ring into molecules of polycyclic framework compounds. An intermolecular character of the carboxy group participation in the aziridine ring formation was confirmed.

Scheme 6.



Scheme 7.



EXPERIMENTAL

IR spectra were measured on a spectrophotometer UR-20 from samples of compounds pelletized with KBr. ^{1}H NMR spectra were registered on spectrometers Bruker DAX-500 at operating frequency 500 MHz and Varian VXR at operating frequencies 200 and 300 MHz, internal reference TMS. The reaction progress was monitored and the homogeneity of compounds obtained was checked by TLC on Silufol UV-254 plates, eluents ether and acetone, development in iodine vapor. Elemental analyses were performed on an analyzer Carlo Erba.

(3,5-Dioxo-4-azatricyclo[5.2.1.0$^{2\text{-}endo,6\text{-}endo}$]dec-8-en-4-yl)carboxylic acids **Vd–Vh** were synthesized by procedure [12].

6-(3,5-Dioxo-4-azatricyclo[5.2.1.0$^{2\text{-}endo,6\text{-}endo}$]-dec-8-en-4-yl)hexanoic acid (Vd). Yield 81%, oily substance, R_f 0.43 (ether). IR spectrum, cm^{-1}: 3510, 1760, 1735, 1700, 1240, 740. Calculated, %: C 64.98; H 6.86; N 5.05. $C_{15}H_{19}NO_4$. Found, %: C 65.17; H 6.71; N 5.15.

4-Methyl-2-(3,5-dioxo-4-azatricyclo[5.2.1.0$^{2\text{-}endo,6\text{-}endo}$]-dec-8-en-4-yl)pentanoic acid (Ve). Yield 85%, oily substance, R_f 0.48 (ether). IR spectrum, cm^{-1}: 3510, 1760, 1735, 1700, 1240, 740. Calculated, %: C 65.96; H 7.27; N 4.81. $C_{16}H_{21}NO_4$. Found, %: C 65.71; H 6.82; N 5.10.

3-Methyl-2-(3,5-dioxo-4-azatricyclo-[5.2.1.0$^{2\text{-}endo,6\text{-}endo}$]-dec-8-en-4-yl)pentanoic acid (Vf). Yield 87%, mp 101–102°C (water), R_f 0.60 (ether). IR spectrum, cm^{-1}: 3240, 3080, 1760, 1740, 1690, 1250, 725. Calculated, %: C 65.96; H 7.27; N 4.81. $C_{16}H_{21}NO_4$. Found, %: C 65.77; H 7.12; N 5.05.

3-Phenyl-3-(3,5-dioxo-4-azatricyclo[5.2.1.0$^{2\text{-}endo,6\text{-}endo}$]-dec-8-en-4-yl)propanoic acid (Vg). Yield 85%, mp 85–86°C (benzene), R_f 0.33 (ether). IR spectrum, cm^{-1}: 3460, 3080, 1760, 1720, 1700, 1590, 1260, 720. ^{1}H NMR spectrum (300 MHz, $CDCl_3$), δ, ppm: 1.47 d (1H, H^{10an}), 1.51 d (1H, H^{10s}), 3.15 d (1H, CH), 3.17 d (1H, CH), 3.21 m (2H, H^1, H^7), 3.30 m (2H, H^2, H^6), 5.37 t (1H, CH), 5.79 m (1H, H^9), 5.90 m (1H, H^8), 7.23–7.34 m (5H$_{arom}$), 12.38 s (1H, COOH). Calculated, %: C 69.44; H 5.50; N 4.50. $C_{18}H_{17}NO_4$. Found, %: C 69.19; H 5.44; N 4.35.

2-(3,5-Dioxo-4-azatricyclo[5.2.1.0$^{2\text{-}endo,6\text{-}endo}$]-dec-8-en-4-yl)-3-methylsulfanylbutanoic acid (Vh). Yield 87%, mp 64–65°C (2-propanol), R_f 0.69 (ether). IR spectrum, cm^{-1}: 3450, 3090, 1760, 1720, 1705, 1250, 725. ^{1}H NMR spectrum (200 MHz, DMSO-d_6), δ, ppm: 1.58 d (1H, H^{10an}), 1.64 d (1H, H^{10s}), 2.03 s (3H, CH_3), 1.92–2.38 m (4H, 2CH_2), 3.30 m (2H, H^1, H^7), 3.35 m (2H, H^2, H^6), 4.47 t (1H, CH), 6.03 m (2H, H^8, H^9), 11.78 br.s (1H, COOH). Calculated, %: C 56.95; H 5.76; N 4.75. $C_{14}H_{17}NO_4S$. Found, %: C 56.70; H 5.61; N 4.44.

Reaction of (3,5-dioxo-4-azatricyclo[5.2.1.0$^{2\text{-}endo,6\text{-}endo}$]-dec-8-en-4-yl)carboxylic acids and their derivatives with *p*-nitrophenyl azide. *General procedure.* A mixture of 0.003 mol of *p*-nitrophenyl azide and 0.003 mol of an appropriate olefin in 10–15 ml of anhydrous chloroform was boiled till the completion of the reaction (TLC monitoring). On cooling the reaction mixture the separated precipitate was filtered off, thoroughly washed with chloroform on the filter, dried, and crystallized from ethanol or 2-propanol.

2-{9-(4-*p*-Nitrophenyl)-3,5-dioxo-4,9-diazatetracyclo[5.3.1.0$^{2\text{-}endo,6\text{-}endo}$.0$^{8\text{-}exo,10\text{-}exo}$]-undec-4-yl}-

ethanoic acid (VIa). Yield 76%, mp 286–287°C (acetone). IR spectrum, cm^{-1}: 3360, 1760, 1730, 1700, 1590, 1505, 1335, 860. ^{1}H NMR spectrum (500 MHz, DMSO-d_6), δ, ppm: 1.32 d (1H, H^{11an}), 1.85 d (1H, H^{11s}), 2.62 m (2H, H^1, H^7), 3.09 m (2H, H^8, H^{10}), 3.30 m (2H, H^2, H^6), 3.99 d.d (2H, CH_2COOH), 7.07 d (2H$_{arom}$), 8.02 d (2H$_{arom}$), 12.70 br.s (1H, COOH). Calculated, %: C 57.14; H 4.20; N 11.76. $C_{17}H_{15}N_3O_6$. Found, %: C 56.35; H 4.11; N 11.38.

2-{9-(4-*p*-Nitrophenyl)-3,5-dioxo-4,9-diazatetracyclo[5.3.1.0$^{2\text{-}endo,6\text{-}endo}$.0$^{8\text{-}exo,10\text{-}exo}$]undec-4-yl}propanoic acid (VIb). Yield 72%, mp 281–282°C (2-propanol). IR spectrum, cm^{-1}: 3400, 1780, 1750, 1720, 1610, 1515, 1345, 865. ^{1}H NMR spectrum (500 MHz, DMSO-d_6), δ, ppm: 1.30 d (1H, H^{11an}), 1.42 d (3H, CH_3), 1.82 d (1H, H^{11s}), 2.72 m (2H, H^1, H^7), 3.08 m (2H, H^8, H^{10}), 3.26 m (1H, H^6), 3.28 m (1H, H^2), 4.54 q (1H, CHCOOH), 7.05 d (2H$_{arom}$), 8.03 d (2H$_{arom}$), 12.55 br.s (1H, COOH). Mass spectrum, *m/z* (I_{rel}, %) 371 (4) $[M]^+$, 201 (100), 170 (15), 155 (28), 124 (12), 91 (15), 83 (23), 66 (42), 44 (15). Calculated, %: C 58.22; H 4.58; N 11.32. $C_{18}H_{17}N_3O_6$. Found, %: C 57.69; H 4.47; N 10.98.

3-{9-(4-*p*-Nitrophenyl)-3,5-dioxo-4,9-diazatetracyclo[5.3.1.0$^{2\text{-}endo,6\text{-}endo}$.0$^{8\text{-}exo,10\text{-}exo}$]-undec-4-yl}propanoic acid (VIc). Yield 66%, mp 190–191°C (2-propanol). IR spectrum, cm^{-1}: 3340, 1770, 1730, 1710, 1615, 1505, 1345, 860. ^{1}H NMR spectrum (500 MHz, DMSO-d_6), δ, ppm: 1.18 d (1H, H^{11an}), 1.70 d (1H, H^{11s}), 2.36 m (2H, H^1, H^7), 2.98 m (2H, H^8, H^{10}), 3.20 m (2H, CH_2), 3.22 m (2H, H^2, H^6), 3.50 m (2H, CH_2), 7.09 d (2H$_{arom}$), 8.04 d (2H$_{arom}$), 12.18 s (1H, COOH). Calculated, %: C 58.22; H 4.58; N 11.32. $C_{18}H_{17}N_3O_6$. Found, %: C 57.81; H 4.39; N 11.09.

6-{9-(4-*p*-Nitrophenyl)-3,5-dioxo-4,9-diazatetracyclo[5.3.1.0$^{2\text{-}endo,6\text{-}endo}$.0$^{8\text{-}exo,10\text{-}exo}$]undec-4-yl}-hexanoic acid (VId). Yield 61%, mp 130–131°C (2-propanol). IR spectrum, cm^{-1}: 3390, 1760, 1720, 1710, 1590, 1505, 1330, 855. ^{1}H NMR spectrum (300 MHz, $CDCl_3$), δ, ppm: 1.08 m (4H, 2CH_2), 1.26 d (1H, H^{11an}), 1.25–1.43 m (4H, 2CH_2), 1.68 d (1H, H^{11s}), 2.48 m (2H, H^1, H^7), 3.05 m (2H, H^8, H^{10}), 3.27 m (2H, H^2, H^6), 3.29 d.d (2H, CH_2COOH), 7.18 d (2H$_{arom}$), 8.05 d (2H$_{arom}$), 11.99 s (1H, COOH). Calculated, %: C 61.02; H 5.57; N 10.17. $C_{21}H_{23}N_3O_6$. Found, %: C 60.35; H 5.48; N 9.94.

4-Methyl-2-{9-(4-*p*-nitrophenyl)-3,5-dioxo-4,9-diazatetracyclo[5.3.1.0$^{2\text{-}endo,6\text{-}endo}$.0$^{8\text{-}exo,10\text{-}exo}$]-undec-4-yl}pentanoic acid (VIe). Yield 73%, mp 195–197°C (2-propanol). IR spectrum, cm^{-1}: 3410, 1780, 1740, 1710, 1610, 1525, 1350, 1275, 860. ^{1}H NMR spectrum (300 MHz, DMSO-d_6), δ, ppm: 1.04 m (6H, 2CH_3), 1.29 d (1H, H^{11an}), 1.71 d (1H, H^{11s}), 1.89 m (2H, CH_2), 2.44 m (1H, H^7), 2.60 m (1H, H^1), 3.08 m (2H, H^8, H^{10}), 3.37 m (2H, H^2, H^6), 4.44 m (1H, CH), 7.19 d (2H$_{arom}$), 8.06 d (2H$_{arom}$), 12.93 br.s (1H, COOH). Calculated, %: C 61.82; H 5.90; N 9.83. $C_{22}H_{25}N_3O_6$. Found, %: C 62.03; H 6.09; N 9.90.

3-Methyl-2-{9-(4-*p*-nitrophenyl)-3,5-dioxo-4,9-diazatetracyclo[5.3.1.0$^{2\text{-}endo,6\text{-}endo}$.0$^{8\text{-}exo,10\text{-}exo}$]undec-4-yl}pentanoic acid (VIf). Yield 75%, mp 203–205°C (2-propanol). IR spectrum, cm^{-1}: 3390, 1760, 1730, 1700, 1595, 1520, 1340. ^{1}H NMR spectrum (300 MHz, $CDCl_3$), δ, ppm: 0.77 d (3H, CH_3), 1.27 d (1H, H^{11an}), 1.69 d (1H, H^{11s}), 1.89–1.99 m (2H, CH_2), 2.43 m (1H, H^7), 2.61 m (1H, H^1), 3.08 m (2H, H^8, H^{10}), 3.37 m (2H, H^2, H^6), 4.51 m (1H, CH), 7.18 d (2H$_{arom}$), 8.05 d (2H$_{arom}$), 13.03 s (1H, COOH). Calculated, %: C 61.82; H 5.90; N 9.83. $C_{22}H_{25}N_3O_6$. Found, %: C 61.93; H 5.88; N 9.80.

3-Phenyl-3-{9-(4-*p*-nitrophenyl)-3,5-dioxo-4,9-diazatetracyclo[5.3.1.0$^{2\text{-}endo,6\text{-}endo}$.0$^{8\text{-}exo,10\text{-}exo}$]-undec-4-yl}propanoic acid (VIg). Yield 70%, mp 169–171°C (decomp.) (2-propanol). IR spectrum, cm^{-1}: 3410, 3025, 1780, 1740, 1610, 1525, 1350, 1280, 860. ^{1}H NMR spectrum (300 MHz, DMSO-d_6), δ, ppm: 0.88 d (1H, H^{11an}), 1.27 d (1H, H^{11s}), 1.79–1.99 m (2H, CH_2), 2.65 m (2H, H^1, H^7), 2.82 m (2H, H^8, H^{10}), 3.14 m (2H, H^2, H^6), 4.24 t (1H, CH), 6.99 d (2H$_{arom}$), 7.20–7.26 m (5H, H^{Ph}), 8.12 d (2H$_{arom}$), 13.50 br.s (1H, COOH). Calculated, %: C 64.42; H 4.73; N 9.39. $C_{24}H_{21}N_3O_6$. Found, %: C 64.20; H 4.60; N 9.44.

2-{9-(4-*p*-Nitrophenyl)-3,5-dioxo-4,9-diaza-tetracyclo[5.3.1.0$^{2\text{-}endo,6\text{-}endo}$.0$^{8\text{-}exo,10\text{-}exo}$]undec-4-yl}-3-methylsulfanylbutanoic acid (VIh). Yield 64%, mp 153–155°C (2-propanol). IR spectrum, cm^{-1}: 3400, 1775, 1740, 1725, 1610, 1525, 1360, 860. ^{1}H NMR spectrum (300 MHz, DMSO-d_6), δ, ppm: 1.28 d (1H, H^{11an}), 1.70 d (1H, H^{11s}), 1.91 s (3H, CH_3), 2.17 m (2H, CH_2), 2.37 m (2H, CH_2), 2.45 m (1H, H^7), 2.63 m (1H, H^1), 3.07 m (2H, H^8, H^{10}), 3.34 m (2H, H^2, H^6), 4.64 t (1H, CHCOOH), 7.17 d (2H$_{arom}$), 8.05 d (2H$_{arom}$), 12.95 br.s (1H, COOH). Calculated, %: C 55.68; H 4.87; N 9.74. $C_{20}H_{21}N_3O_6S$. Found, %: C 55.28; H 4.72; N 9.51.

2-{9-(4-*p*-Nitrophenyl)-3,5-dioxo-4,9-diazatetracyclo[5.3.1.0$^{2\text{-}endo,6\text{-}endo}$.0$^{8\text{-}exo,10\text{-}exo}$]undec-4-yl}butan-1,4-dioic acid (VIi). Yield 75%, mp 187–190°C (2-propanol). IR spectrum, cm^{-1}: 3355, 1770, 1740, 1710, 1610, 1530, 1350, 870. ^{1}H NMR spectrum (300 MHz,

DMSO-d_6), δ, ppm: 1.26 d (1H, H^{11an}), 1.67 d (1H, H^{11s}), 2.42–2.60 m (2H, CH_2), 2.67 m (1H, H^7), 2.93 m (1H, H^1), 3.04 m (2H, H^8, H^{10}), 3.31 m (2H, H^2, H^6), 4.85 d.d (1H, CHCOOH), 7.12 d ($2H_{arom}$), 8.03 d ($2H_{arom}$), 12.95 br.s (2H, 2COOH). Calculated, %: C 54.94; H 4.10; N 10.12. $C_{19}H_{17}N_3O_8$. Found, %: C 54.51; H 3.81; N 9.86.

2-{9-(4-*p*-Nitrophenyl)-3,5-dioxo-4,9-diazatetracyclo[5.3.1.0$^{2\text{-}endo,6\text{-}endo}$.0$^{8\text{-}exo,10\text{-}exo}$]undec-4-yl}pentan-1,5-dioic acid (VIj). Yield 70%, mp 188–189°C (2-propanol). ^{1}H NMR spectrum (300 MHz, DMSO-d_6), δ, ppm: 1.25 d (1H, H^{11an}), 1.65 d (1H, H^{11s}), 1.94–2.26 m (4H, $2CH_2$), 2.40 m (1H, H^7), 2.59 m (1H, H^1), 3.03 m (2H, H^8, H^{10}), 3.32 m (2H, H^2, H^6), 4.78 d.d (1H, CHCOOH), 7.13 d ($2H_{arom}$), 8.02 d ($2H_{arom}$), 12.79 br.s (2H, 2COOH). Calculated, %: C 55.94; H 4.43; N 9.79. $C_{20}H_{19}N_3O_8$. Found, %: C 55.75; H 4.37; N 9.58.

Reactions of derivatives of 2-(3,5-dioxo-4-azatricyclo[5.2.1.0$^{2\text{-}endo,6\text{-}endo}$]dec-8-en-4-yl}ethanoic acid (Va) with *p*-nitrophenyl azide. *General procedure.* A mixture of 0.003 mol of *p*-nitrophenyl azide and 0.003 mol of an appropriate ester **VIIa, VIIb** or amide **VIIIa–VIIIc** in 10–15 ml of anhydrous chloroform was boiled till the completion of the reaction (TLC monitoring). The solvent was removed in a vacuum, to the residue 5–7 ml of ether was added, the precipitate separated after grinding was filtered off, washed with , ether on the filter, dried in air, and recrystallized from 2-propanol.

Methyl {5-(4-nitrophenyl)-9,11-dioxo-3,4,5,10-tetraazatetracyclo[5.5.1.0$^{2\text{-}exo,6\text{-}exo}$.0$^{8\text{-}endo,12\text{-}endo}$]-tridec-3-en-11-yl}ethanoate (IXa). Yield 93%, mp 206–208°C (ethanol). IR spectrum, cm^{-1}: 3490, 1770, 1730, 1615, 1535, 1520, 1345, 1235, 855. ^{1}H NMR spectrum (300 MHz, DMSO-d_6), δ, ppm: 1.12 d (1H, H^{13an}), 1.65 d (1H, H^{13s}), 3.08 m (1H, H^7), 3.19 m (1H, H^1), 3.49 m (2H, H^8, H^{12}), 3.66 s (3H, CH_3), 3.92 d (1H, H^6), 4.28 m (2H, CH_2COOCH_3), 4.71 d (1H, H^2), 8.30 d ($2H_{arom}$), 7.29 d ($2H_{arom}$). Calculated, %: C 54.14; H 4.26; N 17.54. $C_{18}H_{17}N_5O_6$. Found, %: C 53.95; H 4.07; N 17.32.

Ethyl {5-(4-nitrophenyl)-9,11-dioxo-3,4,5,10-tetraazatetracyclo[5.5.1.0$^{2\text{-}exo,6\text{-}exo}$.0$^{8\text{-}endo,12\text{-}endo}$]-tridec-3-en-11-yl}ethanoate (IXb). Yield 87%, mp 181–182°C (ethanol). IR spectrum, cm^{-1}: 1770, 1740, 1710, 1680, 1595, 1520, 1510, 1340, 1245, 855. ^{1}H NMR spectrum (300 MHz, DMSO-d_6), δ, ppm: 1.12 t (3H, CH_3), 1.14 d (1H, H^{13an}), 1.68 d (1H, H^{13s}), 3.10 m (1H, H^7), 3.20 m (1H, H^1), 3.50 m (2H, H^8, H^{12}), 3.93 d (1H, H^6), 4.11 q (2H, CH_2), 4.26 m (2H, CH_2COOEt), 4.77 d (1H, H^2, $^3J_{2,6}$ 9.0), 7.32 d ($2H_{arom}$), 8.33 d ($2H_{arom}$). Calculated, %: C 55.21; H 4.60; N 16.95. $C_{19}H_{19}N_5O_6$. Found, %: C 55.15; H 4.47; N 16.87.

***N*-(Benzyl)-2-{5-(4-nitrophenyl)-9,11-dioxo-3,4,5,10-tetraazatetracyclo[5.5.1.0$^{2\text{-}exo,6\text{-}exo}$.0$^{8\text{-}endo,12\text{-}endo}$]-tridec-3-en-11-yl}ethaneamide (IXc).** Yield 76%, mp 176–177°C (decomp.) (ethanol). IR spectrum, cm^{-1}: 3100, 3020, 1710, 1595, 1515, 1430, 1380, 1335, 855. ^{1}H NMR spectrum (500 MHz, DMSO-d_6), δ, ppm: 1.23 d (1H, H^{13an}), 1.70 d (1H, H^{13s}), 3.08 m (1H, H^7), 3.20 m (1H, H^1), 3.48 m (2H, H^8, H^{12}), 4.03 d (1H, H^6), 4.30 m (2H, CH_2), 4.88 d (1H, H^2), 7.28 t (1H, NH), 7.33 d ($2H_{arom}$), 8.04 m (5H, H^{Ph}) 8.23 d ($2H_{arom}$). Calculated, %: C 60.76; H 4.64; N 17.72. $C_{24}H_{22}N_6O_5$. Found, %: C 61.02; H 4.50; N 17.49.

***N*-(4-Bromophenyl)-2-{5-(4-nitrophenyl)-9,11-dioxo-3,4,5,10-tetraazatetracyclo[5.5.1.0$^{2\text{-}exo,6\text{-}exo}$.0$^{8\text{-}endo,12\text{-}endo}$]tridec-3-en-11-yl}ethaneamide (IXd).** Yield 89%, mp 213–215°C (decomp.) (ethanol). IR spectrum, cm^{-1}: 3380, 1690, 1590, 1540, 1520, 1425, 1335, 1250, 1080, 855. Calculated, %: C 51.21; H 3.53; N 15.58. $C_{23}H_{19}BrN_6O_5$. Found, %: C 51.07; H 3.37; N 15.62.

***N*-[2-(1,3-Thiazolyl)]-2-{5-(4-nitrophenyl)-9,11-dioxo-3,4,5,10-tetraazatetracyclo[5.5.1.0$^{2\text{-}exo,6\text{-}exo}$.0$^{8\text{-}endo,12\text{-}endo}$]tridec-3-en-11-yl}ethaneamide (IXe).** Yield 82%, mp 234–235°C decomp. (ethanol). IR spectrum, cm^{-1}: 3300, 1760, 1690, 1590, 1515, 1395, 1335, 1175, 860. Calculated, %: C 51.39; H 3.64; N 20.98. $C_{20}H_{17}N_7O_5S$. Found, %: C 51.15; H 3.88; N 20.72.

(3,5-Dioxo-4-azatricyclo[5.2.1.0$^{2\text{-}exo,6\text{-}exo}$]-dec-8-en-4-yl)ethanoic acid (XII). A mixture of 0.33 g (2 mmol) of anhydride **XI** and 0.15 g (2 mmol) of aminoacetic acid was boiled in 7–10 ml of glacial acetic acid. On completion of the reaction (~8 h, TLC monitoring) the volatile reaction products were removed in a vacuum, and 5 ml of water was added to the residue. The precipitate was filtered off, dried in air, and recrystallized from water. Yield 78%, mp 120–122°C (149–150°C [10]). ^{1}H NMR spectrum (300 MHz, DMSO-d_6), δ, ppm: 1.35 d (1H, H^{10an}), 1.62 d (1H, H^{10s}), 2.76 m (2H, H^1, H^7), 3.13 m (2H, H^2, H^6), 4.07 d (2H, CH_2), 6.32 m (2H, H^8, H^9), 13.14 br.s (1H, COOH).

2-{9-(4-Nitrophenyl)-3,5-dioxo-4,9-diazatetracyclo[5.3.1.0$^{2\text{-}exo,6\text{-}exo}$.0$^{8\text{-}exo,10\text{-}exo}$]undec-4-yl}ethanoic acid (XIII). A mixture of 0.22 g (1 mmol) of acid **XII** and 0.25 g (1.5 mmol) of *p*-nitrophenyl azide in 10 ml of chloroform was boiled till the completion of the reaction (TLC monitoring). The precipitate separated on cooling was filtered off, washed with chloroform on the filter,

dried in air, and recrystallized from acetone. Yield 67%, mp 186–188°C (decomp.) (2-propanol). IR spectrum, cm^{-1}: 3410, 3030, 1760, 1725, 1610, 1520, 1345, 1285, 860. ^1H NMR spectrum (300 MHz, $CDCl_3$), δ, ppm: 0.88 d (1H, H^{11an}), 1.65 d (1H, H^{11s}), 2.65 m (2H, H^1, H^7), 2.83 m (2H, H^2, H^6), 3.10 m (2H, H^8, H^{10}), 4.25 d (2H, CH_2), 6.99 d ($2H_{arom}$), 8.12 d ($2H_{arom}$), 12.80 s (1H, COOH). Calculated, %: C 57.14; H 4.20; N 11.76. $C_{17}H_{15}N_3O_6$. Found, %: C 57.07; H 4.17; N 11.55.

Ethyl-2-{9-(4-nitrophenyl)-3,5-dioxo-4,9-diaza-tetracyclo[5.3.1.0$^{2\text{-}endo,6\text{-}endo}$.0$^{8\text{-}exo,10\text{-}exo}$]-undec-4-yl}ethanoate (XIV). A mixture of 0.50 g (2 mmol) of ester **VIIb**, 0.44 g (2 mmol) of acid **Va**, and 0.82 g (5 mmol) of *p*-nitrophenyl azide in 15 ml of chloroform was boiled till the completion of the reaction (TLC monitoring). The precipitate of aziridine **VIa** separated on cooling was filtered off, washed with chloroform on the filter, the organic layer was twice washed with a saturated solution of sodium hydrogen carbonate and dried with calcined magnesium sulfate. The solvent was removed in a vacuum, the residue was recrystallized from 2-propanol. Yield 71%, mp 158–160°C (2-propanol). IR spectrum, cm^{-1}: 1785, 1760, 1725, 1610, 1520, 1345, 1270, 860. ^1H NMR spectrum (300 MHz, DMSO-d_6), δ, ppm: 0.91 t (3H, CH_3), 1.27 d (1H, H^{11an}), 1.67 d (1H, H^{11s}), 2.52 m (2H, H^1, H^7), 3.06 m (2H, H^8, H^{10}), 3.33 m (2H, H^2, H^6), 3.86 q (2H, CH_2), 4.10 s (2H, CH_2), 7.17 d ($2H_{arom}$), 8.04 d ($2H_{arom}$). Calculated, %: C 59.22; H 4.93; N 10.91. $C_{19}H_{195}N_3O_6$. Found, %: C 59.17; H 5.03; N 11.07.

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