DOI 10.1007/s10593-018-2194-1

Chemistry of Heterocyclic Compounds **2017**, *53*(11), 1199–1206

[3+2] Cycloaddition of *o*-nitrophenyl azide to 3a,6-epoxyisoindoles

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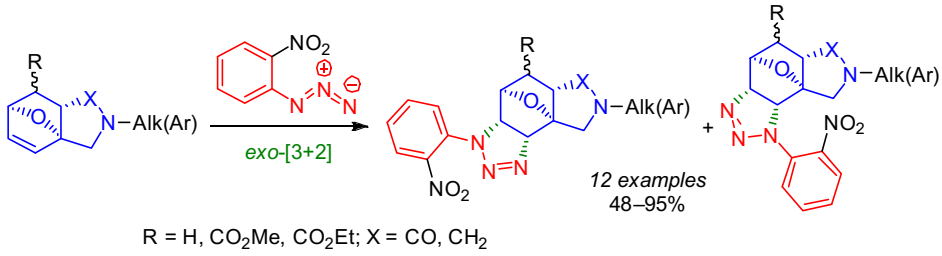
Translated from Khimiya Geterotsiklicheskikh Soedinenii, 2017, *53*(11), 1199–1206

Submitted June 22, 2017
Accepted July 20, 2017



[3+2] Cycloaddition of *o*-nitrophenyl azide to the multiple bond of oxabicyclo[2.2.1]heptene moiety in substituted 3a,6-epoxyisoindoles was performed. The 1,3-dipolar addition reaction proceeded stereoselectively, producing a pair of isomeric *cis*-4,8a-epoxy[1,2,3]triazolo-[4,5-*e*]isoindoles. This approach demonstrated synthetic access to isomeric epoxy-1,2,3-benzotriazoles fused with a γ-butyrolactam moiety.

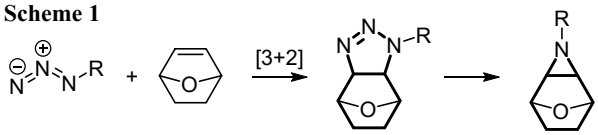
Keywords: 1,2,3-benzotriazoles, 3a,6-epoxyisoindoles, 4,8a-epoxy[1,2,3]triazolo[4,5-*e*]isoindoles, *o*-nitrophenyl azide, [3+2] cycloaddition, 1,3-dipolar cycloaddition.

[3+2] Cycloaddition reactions are widely used for the synthesis of five-membered heterocycles containing from one to three heteroatoms.[1] The development of click chemistry concept since 2001 has led to a particularly frequent use of organic azides as 1,3-dipoles for rapid assembly of molecules on the basis of disubstituted 1,2,3-triazole rings. A suitable dipolarophile for these reactions can be a triple or double carbon–carbon bond. In the latter case, the double bond can also be an endocyclic C=C bond, enabling the preparation of triazoles annulated with other rings.

The cycloaddition of azides to oxabicycloheptene moiety was first described in 1944 and is still relevant due to the possible transformations of triazole ring to other groups, in particular the pharmacophoric aziridine ring (Scheme 1).[2]

It is known that substituted hexahydro-1,2,3-benzotriazoles inhibit the human enzymes autotaxin[3a,b] and SMG1,[3c] while 4,7-methano-1,2,3-benzotriazoles decrease the biosynthesis of gibberellins and metabolic degradation of abscisic acid in plants.[3d] Despite the lack of data about the biological activity of epoxy-1,2,3-benzotriazoles

Scheme 1

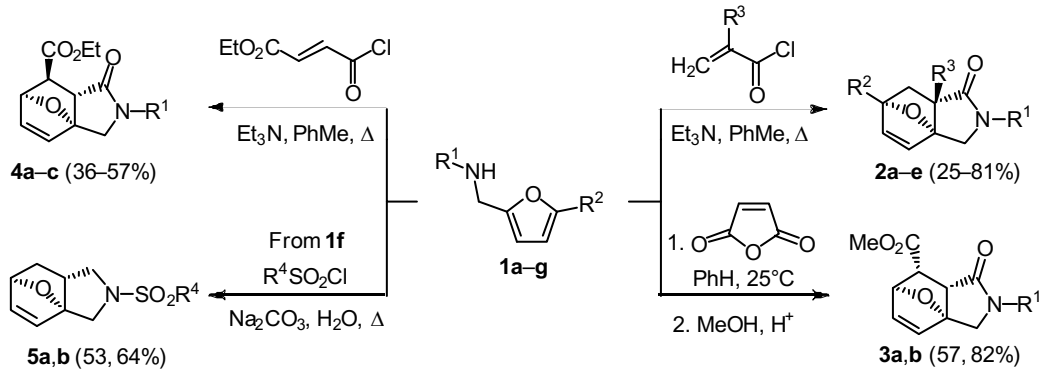


themselves, their easy transformation to 8-oxa-3-azatricyclooctanes, which are analogs of the aforementioned benzotriazoles, provide motivation to develop methods for the preparation of such epoxy derivatives.[4]

Reactions between organic azides and oxabicycloheptenes fused with a γ-butyrolactam ring have not yet been described, but the ambiguous results obtained with [3+2] cycloaddition to similar systems require a detailed study of the stereoselectivity in such processes.

The objects of this study, epoxyisoindoles **2**–**4** and their *N*-arylsulfonyl derivatives **5a**,**b**, are available in two or three synthetic steps. These compounds were obtained according to previously described procedures from the furfurylamines **1a**–**g** and halides or anhydrides of α,β-un-

Scheme 2



1a,**f**, **2a**,**c**,**d**, **4a** R^1 = Ph; **1b**, **2b**,**e**, **3a** R^1 = Bn; **1c**, **4b** R^1 = Furan-2-ylmethyl; **1d**, **4c** R^1 = 3,4-$(MeO)_2C_6H_3(CH_2)_2$; **1e**, **3b** R^1 = Me, **1f** R^1 = Allyl; **1a–f**, **2a**,**b**,**d**,**e** R^2 = H, **1g**, **2c** R^2 = Me; **2a–c** R^3 = H; **2d**,**e** R^3 = Me; **5a** R^4 = Ph; **5b** R^4 = 4-MeC_6H_4

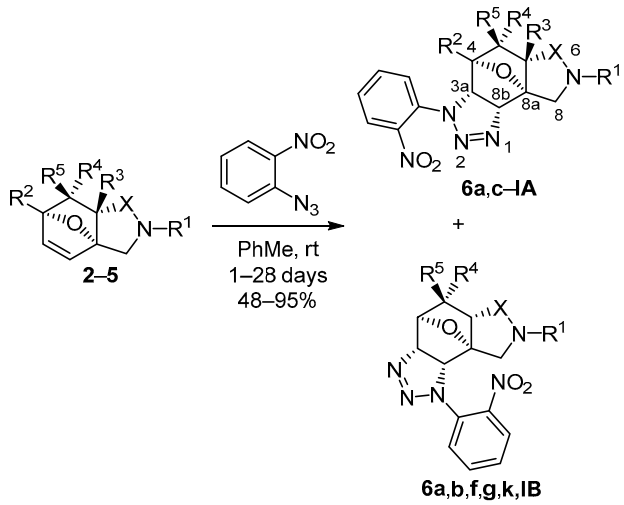
saturated carboxylic acids,[5] or by a reaction of allylfurfurylamine **1f** (R^1 = allyl, R^2 = H) with arylsulfonyl chlorides[6] (Scheme 2). In order to improve the solubility, the starting carboxylic acids were converted to methyl esters **3a**,**b**.

The azide model compound selected by us for the study of cycloaddition reactions with alkenes **2**–**4** was the readily available and sufficiently stable 2-nitrophenyl azide.[7]

The reaction of *o*-nitrophenyl azide at the double bond of oxabicycloheptenes **2**–**5** in toluene occurred at room temperature over several days. The target compounds – 4,8a-epoxy[1,2,3]triazolo[4,5-*e*]isoindoles **6a**–**l** were isolated in good yields predominantly as single isomers of 3-(2-nitrophenyl)triazoloisoindole **6c**–**e**,**h**–**jA** or 1-(2-nitrophenyl)-triazoloisoindole **6bB** (Scheme 3). In the case of [3+2] cycloaddition to isoindoles **2a**, **3a**,**b**, **5a**,**b**, mixtures of triazoloisoindoles **A** and **B** were formed, which were isomers with respect to the position of nitrophenyl substituent (Table 1). The analysis of data presented in Table 1 did not provide clear conclusions about the effect of substituents R^1–R^5 in isoindoles **2**–**5** on the yields and stereochemistry of cycloaddition products.

The cycloaddition products **6** theoretically can have four alternate structures **6A**, **6B**, **6A***, **6B*** (Fig. 1).

Scheme 3



Even though the literature analogies and spectral data were not sufficient for determining the position of nitrophenyl substituent in adducts **6**, the *cis* configuration of triazole ring relative to the oxygen atom of oxabicycloheptane moiety could be established unequivocally on the

Table 1. Substituents, reaction time, and yields of epoxy[1,2,3]triazolo[4,5-*e*]isoindoles **6**

Epoxy-isoindole	Triazole	R^1	R^2	R^3	R^4	R^5	X	Reaction time, h	Yield, % (**A**:**B**)
2a	**6a**	Ph	H	H	H	H	CO	30	78 (1:0.6)
2b	**6b**	Bn	H	H	H	H	CO	0.5	90 (**B**)
2c	**6c**	Ph	Me	H	H	H	CO	672	63 (**A**)
2d	**6d**	Ph	H	Me	H	H	CO	432	57 (**A**)
2e	**6e**	Bn	H	Me	H	H	CO	432	48 (**A**)
3a	**6f**	Bn	H	H	CO_2Me	H	CO	2	93 (0.85:1)
3b	**6g**	Me	H	H	CO_2Me	H	CO	168	80 (0.75:1)
4a	**6h**	Ph	H	H	H	CO_2Et	CO	312	53 (**A**)
4b	**6i**	Furan-2-ylmethyl	H	H	H	CO_2Et	CO	432	67 (**A**)
4c	**6j**	3,4-$(MeO)_2C_6H_3(CH_2)_2$	H	H	H	CO_2Et	CO	24	53 (**A**)
5a	**6k**	$PhSO_2$	H	H	H	H	CH_2	24	85 (1:0.5)
5b	**6l**	Ts	H	H	H	H	CH_2	72	91 (0.5:1)

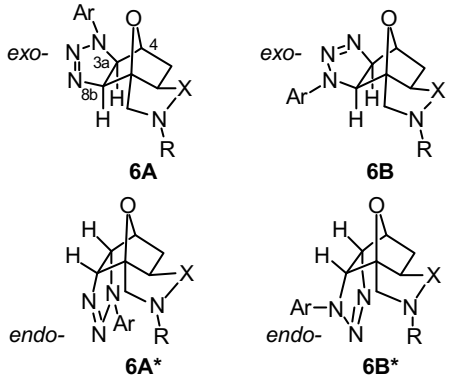


Figure 1. The possible structures of [3+2] cycloaddition products.

basis of ^{1}H NMR spectral data. The values of spin-spin coupling constants for doublet signals of 3a-CH and 8b-CH protons ($J_{3a,8b}$ = 8.2–8.9 Hz) and the absence of vicinal spin-spin coupling constants ^{3}J with the 4-CH proton at the bridgehead position adjacent to oxygen atom confirmed the *exo* orientation of triazine ring in the oxabicycloheptane system (structures **6A** and **6B**).

In order to unequivocally establish the positions of 2-nitrophenyl substituent in adducts **6**, the molecular structures of triazoloisoindoles **6b**,**c** were studied by X-ray structural analysis (Figs. 2 and 3).

Compounds **6b**,**c** included tetracyclic fused systems composed of five-membered rings – 1,2,3-triazole, pyrrolidin-2-one, and two tetrahydrofuran units, which were isomeric with respect to each other. The triazole ring was planar, while the pyrrolidinone and tetrahydrofuran rings assumed a typical envelope conformation.

The molecules of compounds **6b**,**c** contained five asymmetric centers at the C-3a, C-4, C-5a, C-8a, and C-8b carbon atoms, and could potentially form sixteen pairs of diastereomers. The crystals of compound **6b** were racemic and consisted of enantiomeric pairs of molecules with the following relative configuration at the stereocenters – *rac*-3a*S*,4*R*,5a*S*,8a*R*,8b*R*. The crystals of compound **6c** were chiral, but it was not possible in this case to objectively determine the absolute configuration of its molecules by method of X-ray structural analysis (the value of Flack parameter was equal to –0.3(5)). Nevertheless, the relative configuration of molecules in compounds **6b**,**c** was the same.

The data obtained by X-ray structural analysis of compounds **6b**,**c** provided reference parameters for their ^{1}H and ^{13}C NMR spectra, which allowed to assign the isomeric epoxytriazoloisoindoles **6a**–**l** to the series **A** or **B**. In particular, the largest difference of chemical shifts was observed for the doublet signals of geminal protons in the 8-CH_2 methylene group. The signals of these protons in isomers **A** were shifted downfield by 0.7–1.4 ppm relative to the spectra of isomers **B**. For example, ^{1}H NMR spectrum of 4,8a-epoxy[1,2,3]triazolo[4,5-*e*]isoindole **6a** showed signals of 8-CH_2 protons at 3.43 and 3.75 ppm (isomer **B**) or at 4.21 and 4.62 ppm (isomer **A**).

The largest difference of ^{13}C NMR chemical shifts ($\Delta\delta$ ~ 2 ppm) was observed for the C-8a carbon atoms. Thus, the signals of these atoms in spectra of 3-(2-nitrophenyl)triazoloisoindoles **A** were found in the range of 83.9–86.9 ppm, while the chemical shifts of the respective atoms in spectra of 1-(2-nitrophenyl)triazoloisoindoles **B** were in the range of 85.5–88.7 ppm.

The structure of the latter was also in good agreement with the data of IR spectroscopy and mass spectrometry. Mass spectra featured molecular ion peaks that were in agreement with the expected molecular formulas. IR spectra of compounds **6** contained absorption bands due to asymmetric (1537–1523 cm^{-1}) and symmetric (1362–1350 cm^{-1}) stretching vibrations of the nitro group.

Thus, in the current work we studied the stereo- and regioselectivity of 1,3-dipolar cycloaddition reaction of *o*-nitrophenyl azide to oxabicycloheptenes that were fused with γ-butyrolactam ring. The target compounds, 4,8a-epoxy-[1,2,3]triazolo[4,5-*e*]isoindoles, were obtained in high yields as single regioisomers or mixtures of two regioisomers.

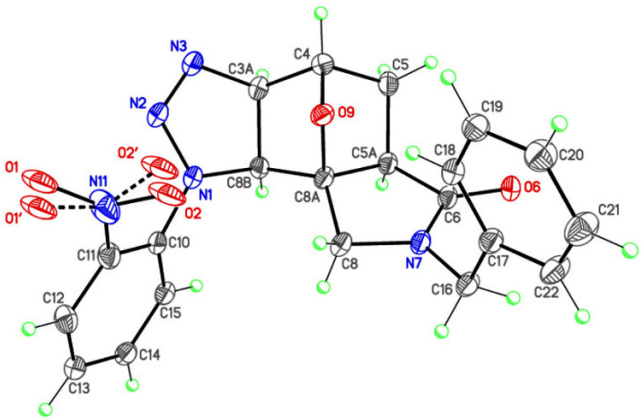


Figure 2. The molecular structure of compound **6b** with atoms represented by thermal vibration ellipsoids of 50% probability.

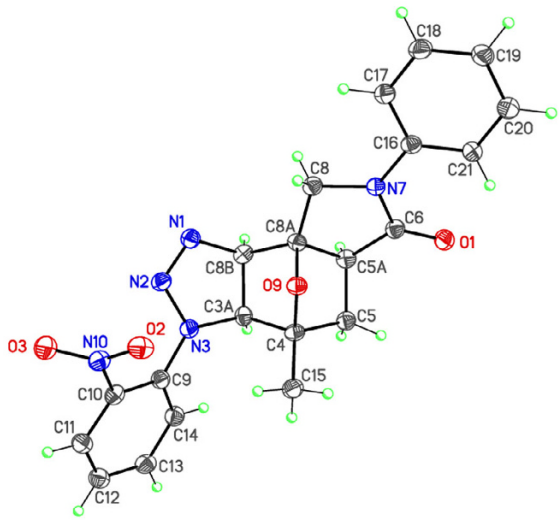


Figure 3. The molecular structure compound **6c** with atoms represented by thermal vibration ellipsoids of 50% probability.

Experimental

IR spectra were recorded on an InfraLUM FT-801 FTIR spectrometer for samples in KBr pellets. ^{1}H NMR spectra were acquired on a JEOL JNM-ECA600 instrument (600 MHz), using TMS as internal standard. ^{13}C NMR spectra were acquired on a Bruker Avance 600 spectrometer (150 MHz), using the central peak of $CDCl_3$ triplet (77.4 ppm) or DMSO-d_6 multiplet (40.0 ppm) as internal standard. Mass spectra of compounds **3b** and **4c** were recorded on a Thermo Trace DSQ mass spectrometer (EI ionization, 70 eV, source temperature 200°C, direct introduction of sample) or Thermo DSQ II – Focus GC gas chromate-mass spectrometer (EI ionization, 70 eV, source temperature 200°C, carrier gas – helium, RTX-5MS column). Mass spectra with electrospray ionization for the rest of the compounds were recorded on a Shimadzu LCMS-8040 quadrupole mass spectrometer (Chromolith HighResolution RP-18 reversed-phase chromatography column, mobile phase – acetonitrile (80%) and water (20%), flow rate – 0.6 ml/min, temperature 40°C). Elemental analysis was performed on a EuroVector EA 3000 CHNS-analyzer. Melting points were determined on Stuart SMP 10 and SMP 30 instruments and were not corrected. TLC analysis was performed on Sorbfil PTSH-AF-A-UV-254 plates, visualization in iodine vapor or with $KMnO_4$ solution. The product ratios in isomer mixtures were determined by ^{1}H NMR spectra as the ratios of integrated intensities for protons of the same type. The reagents were purchased from Acros Organics and Alfa Aesar and were used without additional purification. The solvents were distilled prior to use.

The synthesis with spectral and physicochemical characterization, as well as elemental analysis data for compounds **2a**,**c**,[5a] **2b**,[5d] **2d**,[5b] **2e**,[5c] **3a**,[5a] **4a**,**b**,[5d] **5a**,[6a,6c] **5b**[6b,6c] have been described previously.

Methyl (3a*S,6*R**,7*S**,7a*R**)-2-methyl-1-oxo-1,2,3,6,7,7a-hexahydro-3a,6-epoxyisoindole-7-carboxylate (3b)**. A solution of methylfurfurylamine **1e** (2.0 g, 18 mmol) and maleic anhydride (1.8 g, 18 mmol) in benzene (150 ml) was stirred at room temperature for 2 days. The obtained precipitate was filtered off, washed with benzene (2×10 ml), ether (2×10 ml), and recrystallized from EtOH. Yield 2.4 g (63%), light-beige prismatic crystals, mp 177–178°C. IR spectrum, ν, cm^{-1}: 1703 (CO_2), 1638 (N–C=O). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 2.44 (1H, d, *J* = 9.1) and 2.72 (1H, d, *J* = 9.1, 7,7a-CH); 2.74 (3H, s, NCH_3); 3.55 (1H, d, *J* = 11.3) and 3.99 (1H, d, *J* = 11.3, 3-CH_2); 4.97 (1H, d, *J* = 1.5, 6-CH); 6.41 (1H, dd, *J* = 6.0, *J* = 1.5, 5-CH); 6.56 (1H, d, *J* = 6.0, 4-CH); 12.13 (1H, br. s, CO_2H). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 29.4; 44.4; 49.8; 50.0; 81.1; 88.3; 135.7; 136.7; 170.3; 173.0. Mass spectrum, *m*/*z*: 210 $[M+H]^+$. Found, %: C 57.37; H 5.27; N 6.81. $C_{10}H_{11}NO_4$. Calculated, %: C 57.41; H 5.30; N 6.70.

A suspension of the obtained acid (2.0 g, 9.6 mmol) in methanol (40 ml) was treated by adding 2 drops of concd H_2SO_4 and then stirred for 8 days at room temperature while monitoring by TLC. The reaction mixture was poured into water (100 ml), neutralized with aqueous 25% NH_3 solution, and extracted with CH_2Cl_2 (3×50 ml). The combined organic extracts were dried over anhydrous Na_2SO_4. The drying agent was separated by filtration, and the solvent was removed by evaporation. Yield 1.8 g (82%), light-beige powder, mp 95–96°C (hexane–EtOAc). IR spectrum, ν, cm^{-1}: 1746 (CO_2), 1678 (N–C=O). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 2.57 (1H, d, *J* = 9.2) and 2.64 (1H, d, *J* = 9.2, 7,7a-CH); 2.73 (3H, s, NCH_3); 3.60 (3H, s, OCH_3); 3.57 (1H, d, *J* = 11.4) and 3.86 (1H, d, *J* = 11.4, 3-CH_2); 4.99 (1H, d, *J* = 1.8, 6-CH); 6.30 (1H, dd, *J* = 5.9, *J* = 1.8, 5-CH); 6.40 (1H, d, *J* = 5.9, 4-CH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 29.9; 44.5; 50.6; 50.8; 52.0; 81.3; 88.4; 135.3; 136.7; 170.5; 172.2. Mass spectrum, *m*/*z* (I_{rel}, %): 223 (2) $[M]^+$, 164 (10), 113 (24), 110 (100), 85 (20), 81 (40), 59 (16), 53 (40), 42 (24). Found, %: C 59.15; H 5.83; N 6.34. $C_{11}H_{13}NO_4$. Calculated, %: C 59.19; H 5.87; N 6.27.

Ethyl (3a*S,6*R**,7*R**,7a*R**)-2-[2-(3,4-dimethoxyphenyl)-ethyl]-1-oxo-1,2,3,6,7,7a-hexahydro-3a,6-epoxyisoindole-7-carboxylate (4c)**. A solution of amine **1d** (0.06 mol) and ethyl fumaroyl chloride (0.06 mol) (prepared *in situ* by stirring monoethyl fumarate (13.0 g, 0.09 mol) with thionyl chloride (39.0 ml, 0.54 mol) in anhydrous benzene (100 ml) for a week, followed by removal of solvent and the excess of thionyl chloride by distillation at reduced pressure at 50°C) and triethylamine (16.7 ml, 0.12 mol) in toluene (100 ml) was refluxed for 10 h while monitoring by TLC, cooled, and poured into water (100 ml). The organic layer was separated and the aqueous layer was extracted with ethyl acetate (3×50 ml). The organic phases were combined and dried over anhydrous $MgSO_4$, filtered, evaporated, and the residue was crystallized from hexane–EtOAc mixture. Yield 8.35 g (36%), light-beige rhombic crystals, mp 108–109°C. IR spectrum, ν, cm^{-1}: 1723 (CO_2), 1687 (N–C=O). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.22 (3H, t, *J* = 7.6, $OCH_2C\underline{H}_3$); 2.75–2.81 (2H, m, $NCH_2C\underline{H}_2$); 2.82 (1H, d, *J* = 3.4, 7a-CH); 3.39 (1H, dd, *J* = 3.4, *J* = 4.4, 7-CH); 3.38–3.42 (1H, m) and 3.64–3.70 (1H, m, NCH_2); 3.49 (1H, d, *J* = 11.7) and 3.79 (1H, d, *J* = 11.7, 3-CH_2); 3.83 (3H, s) and 3.84 (3H, s, $2OCH_3$); 4.07–4.10 (2H, m, $OC\underline{H}_2CH_3$); 5.18 (1H, dd, *J* = 2.1, *J* = 4.4, 6-CH); 6.26 (1H, dd, *J* = 6.2, *J* = 2.1, 5-CH); 6.45 (1H, *J* = 6.2, 4-CH); 6.72 (1H, s, H-2 Ar); 6.73 (1H, d, *J* = 8.9, H-6 Ar); 6.77 (1H, d, *J* = 8.9, H-5 Ar). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 14.1; 33.3; 44.4; 46.5; 49.9; 51.3; 55.7; 55.8; 61.0; 80.2; 90.4; 111.2; 111.8; 120.5; 131.0; 134.8; 135.0; 147.6; 148.9; 170.3; 172.3. Mass spectrum, *m*/*z* (I_{rel}, %): 387 $[M]^+$ (4), 165 (12), 164 (100), 151 (20), 149 (8), 99 (8), 81 (58). Found, %: C 65.02; H 6.43; N 3.73. $C_{21}H_{25}NO_6$. Calculated, %: C 65.10; H 6.50; N 3.62.

Preparation of 4,8a-epoxy[1,2,3]triazolo[4,5-*e*]isoindoles 6a–l (General method). A solution of the appropriate 3a,6-epoxyisoindole **2**–**5** (0.5 g) in toluene (30 ml) was treated by adding an equimolar amount of *o*-nitrophenyl azide.[7] The obtained reaction mixture was stirred at room temperature for 1–28 days, while monitoring by TLC. The target adducts were isolated by filtration in the form of fine, yellow precipitates (compounds **6a**,**b**,**d**–**h**,**j**–**l**) or by removing toluene by distillation at reduced pressure (compounds **6c**,**i**).

(3a*S,4*R**,5a*S**,8a*R**,8b*R**)-3-(2-Nitrophenyl)-7-phenyl-3,3a,4,5,5a,7,8,8b-octahydro-6*H*-4,8a-epoxy[1,2,3]triazolo-[4,5-*e*]isoindol-6-one (6aA) and (3a*S**,4*R**,5a*S**,8a*R**,8b*R**)-1-(2-nitrophenyl)-7-phenyl-1,3a,4,5,5a,7,8,8b-octahydro-6*H*-4,8a-epoxy[1,2,3]triazolo[4,5-*e*]isoindol-6-one (6aB)** (1:0.6 mixture of isomers). Yield 0.62 g (78%), bright-yellow amorphous material. IR spectrum, ν, cm^{-1}: 1698 (N–C=O), 1530 (NO_2 ν as), 1349 (NO_2 ν s), 1600 (N=N). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.98 (1H, dd, *J* = 13.0, *J* = 9.4), 2.15 (0.6H, dd, *J* = 12.8, *J* = 9.4), 2.22 (1H, dt, *J* = 13.0, *J* = 5.0) and 2.32 (0.6H, dt, *J* = 12.8, *J* = 5.0, 5-CH_2); 2.91 (0.6H, dd, *J* = 9.4, *J* = 4.3) and 3.00 (1H, dd, *J* = 9.2, *J* = 4.1, 5a-CH); 3.43 (0.6H, d, *J*= 11.4), 3.75 (0.6H, d, *J*= 11.4), 4.21 (1H, d, *J*= 11.9) and 4.62 (1H, d, *J* = 11.9, 8-CH_2); 4.35 (1H, d, *J* = 8.2), 4.51 (0.6H, d, *J* = 8.7), 5.20 (0.6H, d, *J* = 8.7) and 5.26 (1H, d, *J* = 8.2, 3a,8b-CH); 4.39 (1H, d, *J* = 5.0) and 4.94 (0.6H, d, *J* = 5.0, 4-CH); 7.19 (1H, t, *J* = 7.3, H Ar); 7.47 (0.6H, td, *J* = 8.2, *J* = 7.3, H Ar), 7.30–7.33 (3.2H, m, H Ar); 7.37–7.41 (3.2H, m, H Ar); 7.55–7.71 (4.8H, m, H Ar); 7.93 (1H, dd, *J* = 8.2, *J* = 1.4, H Ar); 8.00 (0.6H, dd, *J* = 8.2, *J* = 1.4, H Ar). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 30.3; 31.5; 48.2; 48.3; 48.4; 48.7; 58.9; 61.5; 79.6; 80.2; 85.5; 88.6; 88.7; 89.1; 119.4; 119.5; 119.8; 120.5; 124.1; 124.2; 124.3; 124.9; 125.0; 125.4; 128.8(2C); 130.9; 131.7; 133.1; 133.5; 138.9; 139.2; 141.0; 142.0; 172.8; 172.9. Mass spectrum, *m*/*z*: 392 $[M]^+$. Found, %: C 61.31; H 4.32; N 17.98. $C_{20}H_{17}N_5O_4$. Calculated, %: C 61.38; H 4.38; N 17.89.

(3a*S,4*R**,5a*S**,8a*R**,8b*R**)-7-Benzyl-1-(2-nitrophenyl)-1,3a,4,5,5a,7,8,8b-octahydro-6*H*-4,8a-epoxy[1,2,3]triazolo-[4,5-*e*]isoindol-6-one (6b)**. Yield 0.75 g (90%), lemon-yellow needles, mp 173–174°C (EtOAc–EtOH). IR spectrum, ν, cm^{-1}: 1694 (N–C=O), 1526 (NO_2 ν as), 1353 (NO_2 ν s), 1602 (N=N). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 2.07 (1H, dd, *J* = 13.0, *J* = 9.3) and 2.21 (1H, dt, *J* = 13.0, *J* = 5.0, 5-CH_2); 2.73 (1H, dd, *J* = 9.3, *J* = 5.0, 5a-CH); 2.89 (1H, d, *J* = 11.5) and 3.14 (1H, d, *J* = 11.5, 8-CH_2); 4.24 (1H, d, *J* = 15.1) and 4.40 (1H, d, *J* = 15.1, NCH_2); 4.36 (1H, d, *J* = 8.7) and 5.13 (1H, d, *J* = 8.7, 3a,8b-CH); 4.88 (1H, d, *J* = 5.0, 4-CH); 7.05 (2H, d, *J* = 6.4, H Ar); 7.22–7.28 (3H, m, H Ar); 7.33–7.36 (1H, m, H Ar); 7.44 (1H, dd, *J* = 8.3, *J* = 1.4, H Ar); 7.53–7.56 (1H, m, H Ar); 7.86 (1H, dd, *J* = 8.3, *J* = 1.4, H Ar). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 30.9; 45.2; 46.7; 46.8; 58.4; 79.3; 88.4; 90.2; 119.5; 124.4; 125.3; 127.2; 127.3; 128.5; 131.5; 133.3; 136.5; 141.6; 173.0. Mass spectrum, *m*/*z*: 406 $[M+H]^+$. Found, %: C 62.15; H 4.64; N 17.35. $C_{21}H_{19}N_5O_4$. Calculated, %: C 62.22; H 4.72; N 17.27.

(3a*S,4*R**,5a*S**,8a*R**,8b*R**)-4-Methyl-3-(2-nitrophenyl)-7-phenyl-3,3a,4,5,5a,7,8,8b-octahydro-6*H*-4,8a-epoxy[1,2,3]triazolo[4,5-*e*]isoindol-6-one (6c)**. Yield 0.54 g (63%), transparent lemon-yellow rhombic crystals, mp 185°C (EtOAc–DMF). IR spectrum, ν, cm^{-1}: 1703 (N–C=O), 1530 (NO_2 ν as), 1359 (NO_2 ν s), 1602 (N=N). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 1.26 (3H, s, CH_3); 1.73 (1H, dd, *J* = 12.4, *J* = 4.4) and 2.28 (1H, dd, *J* = 12.4, *J* = 9.4, 5-CH_2); 3.31 (1H, dd, *J* = 9.4, *J*= 4.4, 5a-CH); 4.01 (1H, d, *J* = 11.5) and 4.65 (1H, d, *J* = 11.5, 8-CH_2); 4.75 (1H, d, *J* = 8.7) and 5.43 (1H, d, *J* = 8.7, 3a,8b-CH); 7.15 (1H, t, *J* = 7.3, H Ar); 7.28 (1H, t, *J* = 7.8, H Ar); 7.39 (2H, t, *J* = 7.8, H Ar); 7.59 (1H, d, *J* = 8.2, H Ar); 7.67 (1H, t, *J* = 8.2, H Ar); 7.74 (2H, d, *J* = 7.8, H Ar); 7.82 (1H, d, *J* = 8.2, H Ar). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 16.4; 36.3; 48.6; 50.0; 61.5; 86.9; 87.3; 88.9; 118.1; 119.4; 123.6; 124.1; 125.1; 128.8; 132.1; 133.0; 139.2; 141.0; 173.0. Mass spectrum, *m*/*z*: 406 $[M+H]^+$. Found, %: C 62.15; H 4.67; N 17.36. $C_{21}H_{19}N_5O_4$. Calculated, %: C 62.22; H 4.72; N 17.27.

(3a*S,4*R**,5a*S**,8a*R**,8b*R**)-5a-Methyl-3-(2-nitrophenyl)-7-phenyl-3,3a,4,5,5a,7,8,8b-octahydro-6*H*-4,8a-epoxy[1,2,3]triazolo[4,5-*e*]isoindol-6-one (6d)**. Yield 0.49 g (57%), light-yellow amorphous powder, mp 174–175°C. IR spectrum, ν, cm^{-1}: 1704 (N–C=O), 1523 (NO_2 ν as), 1350 (NO_2 ν s), 1595 (N=N). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.43 (3H, s, CH_3); 1.51 (1H, d, *J* = 13.0) and 2.49 (1H, dd, *J* = 13.0, *J* = 5.8, 5-CH_2); 4.26 (1H, d, *J* = 5.8, 4-CH); 4.33 (1H, d, *J* = 8.2) and 5.36 (1H, d, *J* = 8.2, 3a,8b-CH); 4.19 (1H, d, *J* = 11.7) and 4.51 (1H, d, *J* = 11.7, 8-CH_2); 7.18 (1H, t, *J* = 7.6, H Ar), 7.38–7.40 (3H, m, H Ar), 7.56 (1H, d, *J* = 8.2, H Ar), 7.62–7.65 (3H, m, H Ar); 7.93 (1H, d, *J* = 8.2, H Ar). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 19.1; 38.7; 47.4; 53.8; 62.2; 79.9; 83.9; 90.8; 119.8; 124.9; 125.1; 125.4; 126.3; 128.9; 133.0; 133.7; 139.0; 141.9; 175.6. Mass spectrum, *m*/*z*: 406 $[M+H]^+$. Found, %: C 62.16; H 4.66; N 17.38. $C_{21}H_{19}N_5O_4$. Calculated, %: C 62.22; H 4.72; N 17.27.

(3a*S,4*R**,5a*S**,8a*R**,8b*R**)-7-Benzyl-5a-methyl-3-(2-nitrophenyl)-3,3a,4,5,5a,7,8,8b-octahydro-6*H*-4,8a-epoxy[1,2,3]triazolo[4,5-*e*]isoindol-6-one (6e)**. Yield 0.40 g (48%), lemon-yellow plates, mp 161–162°C. IR spectrum, ν, cm^{-1}: 1688 (NC=O), 1535 (NO_2 ν as), 1360 (NO_2 ν s), 1603 (N=N). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.34 (3H, s, CH_3); 1.45 (1H, d, *J*= 13.0) and 2.39 (1H, dd, *J* = 13.0, *J* = 5.8, 5-CH_2); 3.57 (1H, d, *J* = 12.4) and 3.86 (1H, d, *J* = 12.4, 8-CH_2); 4.21 (1H, d, *J* = 5.8, 4-CH); 4.25 (1H, d, *J* = 8.2) and 5.22 (1H, d, *J* = 8.2, 3a,8b-CH); 4.38 (1H, d, *J* = 15.1) and 4.61 (1H, d, *J* = 15.1, NCH_2); 7.22 (2H, d, *J* = 6.9, H Ar); 7.30 (1H, t, *J* = 6.9, H Ar); 7.34–7.38 (3H, m, H Ar); 7.55 (1H, d, *J* = 8.2, H Ar); 7.62 (1H, t, *J* = 8.2, H Ar); 7.90 (1H, d, *J* = 8.2, H Ar). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 19.2; 30.9; 38.1; 45.6; 46.7; 62.1; 79.8; 84.2; 89.3; 120.5; 125.1; 125.4; 126.1; 127.8; 128.0; 128.8; 133.2; 133.7; 135.7; 176.2. Mass spectrum, *m*/*z*: 420 $[M+H]^+$. Found, %: C 62.95; H 4.99; N 16.82. $C_{22}H_{21}N_5O_4$. Calculated, %: C 63.00; H 5.05; N 16.70.

Methyl (3a*S,4*R**,5*R**,5a*S**,8a*R**,8b*R**)-7-benzyl-3-(2-nitrophenyl)-6-oxo-3a,4,5,5a,6,7,8,8b-octahydro-3*H*-4,8a-epoxy[1,2,3]triazolo[4,5-*e*]isoindole-5-carboxylate (6fA) and methyl (3a*S**,4*R**,5*R**,5a*S**,8a*R**,8b*R**)-7-benzyl-1-(2-nitrophenyl)-6-oxo-3a,4,5,5a,6,7,8,8b-octahydro-1*H*-4,8a-epoxy[1,2,3]triazolo[4,5-*e*]isoindole-5-carboxylate (6fB)** (0.85:1 mixture of isomers). Yield 0.72 g (93%), bright-yellow amorphous material. IR spectrum, ν, cm^{-1}: 1738 (CO_2), 1704 (N–C=O), 1533 (NO_2 ν as), 1368 (NO_2 ν s), 1606 (N=N). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 2.98 (1H, d, *J* = 11.7) and 3.11 (1H, d, *J* = 11.7, 8-CH_2); 3.05 (0.85H, d, *J* = 9.6) and 3.12 (1H, d, *J* = 9.6, 5-CH); 3.20 (0.85H, d, *J* = 9.6) and 3.23 (1H, d, *J* = 9.6,

5a-CH); 3.68 (0.85H, J = 12.4, NCH_2); 3.74 (2.55H, s) and 3.77 (3H, s, CH_3); 3.97 (0.85H, d, J = 11.7, 8-CH_2), 4.23 (1H, d, J = 14.7) and 4.56 (1H, d, J = 14.7, NCH_2); 4.33 (1H, d, J = 8.2, 8b-CH); 4.41–4.48 (3.55H, m, 4-CH_2, 8-CH_2, 8b-CH, NCH_2); 5.06 (0.85H, s, 4-CH); 5.17 (0.85H, d, J = 8.2) and 5.18 (1H, d, J = 8.2, 3a-CH); 7.07 (1.85H, d, J = 6.9, H Ar); 7.24–7.66 (13.1H, m, H Ar); 7.90 (1H, dd, J = 7.9, J = 1.7, H Ar); 7.95 (0.85H, dd, J = 7.9, J = 1.7, H Ar). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 45.0; 45.3; 46.0; 46.1; 47.0; 50.9; 51.1; 51.3 (2C); 58.4; 61.2; 81.2; 81.9; 85.3; 87.9; 89.2; 89.8; 119.8; 120.3; 124.3; 124.6; 125.0; 125.3; 127.0; 127.1; 127.2; 127.4; 128.4; 128.5; 130.8; 131.4; 133.1; 133.3; 136.3 (2C); 141.0; 141.6; 169.3; 169.8; 170.6; 170.7. Mass spectrum, *m*/*z*: 464 $[M+H]^+$. Found, %: C 59.57; H 4.53; N 15.20. $C_{23}H_{21}N_5O_6$. Calculated, %: C 59.61; H 4.57; N 15.11.

Methyl (3a*S,4*R**,5*R**,5a*S**,8a*R**,8b*R**)-7-methyl-3-(2-nitrophenyl)-6-oxo-3a,4,5,5a,6,7,8,8b-octahydro-3*H*-4,8a-epoxy[1,2,3]triazolo[4,5-*e*]isoindole-5-carboxylate (6gA) and methyl (3a*S**,4*R**,5*R**,5a*S**,8a*R**,8b*R**)-7-methyl-1-(2-nitrophenyl)-6-oxo-3a,4,5,5a,6,7,8,8b-octahydro-1*H*-4,8a-epoxy[1,2,3]triazolo[4,5-*e*]isoindole-5-carboxylate (6gB)** (0.75:1 mixture of isomers). Yield 0.68 g (80%), bright-yellow amorphous material. IR spectrum, ν, cm^{-1}: 1732 (CO_2), 1692 (N–C=O), 1524 (NO_2 ν as), 1347 (NO_2 ν s), 1606 (N=N). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 2.71 (3H, s) and 2.92 (2.25H, s, NCH_3); 3.01–3.07 (2.75H, m) and 3.14–3.23 (2.75H, m, 5,5a-CH, 8-CH_2); 3.72 (2.25H, s) and 3.76 (3H, s, CH_3); 3.78 (0.75H, d, J = 12.4) and 4.13 (0.75H, d, J = 12.4, 8-CH_2); 4.36 (0.75H, d, J = 8.2), 4.51 (1H, d, J = 8.2), 5.17 (1H, d, J = 8.2) and 5.22 (0.75H, d, J = 8.2, 3a,8b-CH); 4.46 (0.75H, s) and 5.04 (1H, s, 4-CH); 7.41–7.71 (5.25H, m) and 7.99 (1.75H, m, H Ar). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 29.2; 29.3; 45.8; 46.7; 48.2 (2C); 50.8; 51.0; 51.2; 51.3; 58.4; 61.1; 81.3; 81.9; 85.3; 87.8; 89.2; 89.7; 124.2; 124.8; 125.0; 125.3 (2C); 128.2; 128.9; 130.8; 131.4; 133.1; 133.4; 141.1; 141.7; 169.5; 170.7; 170.8. Mass spectrum, *m*/*z*: 388 $[M+H]^+$. Found, %: C 52.65; H 4.37; N 18.19. $C_{17}H_{17}N_5O_6$. Calculated, %: C 52.71; H 4.42; N 18.08.

Ethyl (3a*S,4*R**,5*S**,5a*S**,8a*R**,8b*R**)-3-(2-nitrophenyl)-6-oxo-7-phenyl-3a,4,5,5a,6,7,8,8b-octahydro-3*H*-4,8a-epoxy[1,2,3]triazolo[4,5-*e*]isoindole-5-carboxylate (6h)**. Yield 0.40 g (53%), light-yellow powder, mp 175–176°C. IR spectrum, ν, cm^{-1}: 1742 (CO_2), 1701 (N–C=O), 1535 (NO_2 ν as), 1355 (NO_2 ν s), 1601 (N=N). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 1.30 (3H, t, J=7.3, $CH_2C\underline{H}_3$); 3.38 (1H, t, J = 5.5, 5-CH); 3.60 (1H, d, J = 5.5, 5a-CH); 4.19–4.24 (1H, m) and 4.27–4.32 (1H, m, $C\underline{H}_2CH_3$); 4.57 (1H, d, J = 8.6) and 5.50 (1H, d, J = 8.6, 3a,8b-CH); 4.06 (1H, d, J = 11.7) and 4.71 (1H, d, J = 11.7, 8-CH_2); 4.82 (1H, d, J = 5.5, 4-CH); 7.17 (1H, t, J= 7.6, H Ar); 7.34–7.41 (4H, m, H Ar); 7.72–7.75 (3H, m, H Ar); 7.89 (1H, dd, J = 8.2, J= 1.4, H Ar). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 14.0; 48.3; 48.7; 51.6; 59.0; 61.5; 80.3; 85.4; 89.8; 119.5; 119.6; 124.5; 125.3; 128.8; 130.8; 133.3; 138.9; 140.8; 169.3; 169.4; 171.2. Mass spectrum, *m*/*z*: 464 $[M+H]^+$. Found, %: C 59.56; H 4.51; N 15.20. $C_{23}H_{21}N_5O_6$. Calculated, %: C 59.61; H 4.57; N 15.11.

Ethyl (3a*S,4*R**,5*S**,5a*S**,8a*R**,8b*R**)-7-(2-furan-2-ylmethyl)-3-(2-nitrophenyl)-6-oxo-3a,4,5,5a,6,7,8,8b-octahydro-3*H*-4,8a-epoxy[1,2,3]triazolo[4,5-*e*]isoindole-5-carboxylate (6i)**. Yield 0.52 g (67%), fine yellow prismatic crystals, mp 142–143°C. IR spectrum, ν, cm^{-1}: 1725 (CO_2), 1701 (N–C=O), 1537 (NO_2 ν as), 1359 (NO_2 ν s), 1603 (N=N). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.32 (3H, t, J= 7.2, $CH_2C\underline{H}_3$); 3.31 (1H, d, J = 5.1, 5a-CH); 3.32 (1H, dd, J = 5.1, J = 4.1, 5-CH); 3.68 (1H, d, J = 12.4) and 4.09 (1H, d, J = 12.4, 8-CH_2); 4.19–4.25 (1H, m) and 4.27–4.31 (1H, m, $C\underline{H}_2CH_3$); 4.35 (1H, d, J = 8.2) and 5.21 (1H, d, J = 8.2, 3a,8b-CH); 4.36 (1H, d, J = 15.4) and 4.64 (1H, d, J = 15.4, NCH_2); 4.44 (1H, d, J = 4.1, 4-CH); 6.27 (1H, d, J = 3.0, H-3 furan); 6.34 (1H, dd, J = 3.0, J = 1.7, H-4 furan); 7.35 (1H, ddd, J = 8.2, J = 7.9, J = 1.4, H Ar); 7.39 (1H, br. s, H-5 furan); 7.54 (1H, dd, J = 8.2, J = 1.4, H Ar); 7.61 (1H, ddd, J = 8.2, J = 7.9, J = 1.4, H Ar); 7.89 (1H, dd, J = 8.2, J = 1.4, H Ar). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 14.0; 39.5; 47.2; 48.5; 50.8; 59.3; 62.2; 80.0; 86.4; 90.8; 108.8; 110.4; 124.0; 125.6; 125.8; 132.9; 133.7; 141.0; 142.8; 149.0; 169.4; 170.9. Mass spectrum, *m*/*z*: 468 $[M+H]^+$. Found, %: C 56.49; H 4.49; N 15.08. $C_{22}H_{21}N_5O_7$. Calculated, %: C 56.53; H 4.53; N 14.98.

Ethyl (3a*S,4*R**,5*S**,5a*S**,8a*R**,8b*R**)-7-[2-(3,4-dimethoxyphenyl)ethyl]-3-(2-nitrophenyl)-6-oxo-3a,4,5,5a,6,7,8,8b-octahydro-3*H*-4,8a-epoxy[1,2,3]triazolo[4,5-*e*]isoindole-5-carboxylate (6j)**. Yield 0.38 g (53%), fine lemon-yellow needles, mp 185–186°C. IR spectrum, ν, cm^{-1}: 1736 (CO_2), 1694 (N–C=O), 1534 (NO_2 ν as), 1362 (NO_2 ν s), 1604 (N=N). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.32 (3H, t, J = 7.3, $CH_2C\underline{H}_3$); 3.22 (1H, d, J = 4.4, 5a-CH); 3.28 (1H, dd, J = 5.5, J= 4.4, 5-CH); 2.78–2.86 (1H, m), 3.43–3.49 (1H, m) and 3.66–3.70 (2H, m, NCH_2CH_2); 3.87 (3H, s, OCH_3); 3.88 (3H, s, OCH_3); 3.62 (1H, d, J = 12.0) and 4.02 (1H, d, J= 12.0, 8-CH_2); 4.20–4.25 (1H, m) and 4.28–4.33 (1H, m, $C\underline{H}_2CH_3$); 4.35 (1H, d, J = 8.2) and 5.19 (1H, d, J = 8.2, 3a,8b-CH); 4.42 (1H, d, J = 5.5, 4-CH); 6.73 (1H, d, J= 2.1, H Ar); 6.76 (1H, dd, J = 8.2, J = 2.1, H Ar); 6.82 (1H, d, J = 8.2, H Ar); 7.36 (1H, td, J = 7.9, J = 1.4, H Ar); 7.54 (1H, dd, J = 8.2, J = 1.4, H Ar); 7.61–7.63 (1H, m, H Ar); 7.90 (1H, dd, J = 8.2, J = 1.4, H Ar). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 14.0; 33.2; 44.4; 47.8; 48.5; 50.9; 55.8; 55.9; 59.3; 62.2; 79.9; 86.4; 90.9; 111.4; 111.9; 120.5; 124.0; 125.6; 125.8; 130.6; 132.9; 133.6; 141.1; 147.7; 149.0; 169.4; 171.1. Mass spectrum, *m*/*z*: 552 $[M+H]^+$. Found, %: C 58.75; H 5.26; N 12.78. $C_{27}H_{29}N_5O_8$. Calculated, %: C 58.80; H 5.30; N 12.70.

(3a*S,4*R**,5a*R**,8a*R**,8b*R**)-3-(2-Nitrophenyl)-7-phenylsulfonyl-3a,4,5,5a,6,7,8,8b-octahydro-3*H*-4,8a-epoxy[1,2,3]triazolo[4,5-*e*]isoindole (6kA) and (3a*S**,4*R**,5a*R**,8a*R**,8b*R**)-1-(2-nitrophenyl)-7-phenylsulfonyl-3a,4,5,5a,6,7,8,8b-octahydro-3*H*-4,8a-epoxy[1,2,3]-triazolo[4,5-*e*]isoindole (6kB)** (1:0.5 mixture of isomers). Yield 0.68 g (85%). Compound **6kA** was isolated by fractional crystallization, fine lemon-yellow needles, mp 174–175°C (EtOAc). IR spectrum, ν, cm^{-1}: 1532 (NO_2 ν as), 1336 (SO_2 ν as, NO_2 ν s), 1165 (SO_2 ν s). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.55 (1H, ddd, J = 13.1, J = 5.5, J = 3.5) and 1.70 (1H, dd, J = 13.1, J = 8.1,

5-CH_2); 2.42–2.47 (1H, m, 5a-CH); 2.67 (1H, t, *J* = 9.3) and 3.82 (1H, td, *J* = 9.3, *J* = 8.3, 6-CH_2); 3.57 (1H, d, *J* = 12.6) and 4.15 (1H, d, *J* = 12.6, 8-CH_2); 4.16 (1H, d, *J* = 8.6) and 5.01 (1H, d, *J* = 8.6, 3a,8b-CH); 4.23 (1H, d, *J* = 5.5, 4-CH); 7.32–7.34 (1H, m, H Ar); 7.50–7.63 (5H, m, H Ar); 7.83–7.87 (3H, m, H Ar). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 31.4; 44.0; 48.0; 52.8; 62.0; 80.7; 87.3; 95.2; 124.5; 125.2; 125.3; 125.8; 127.4; 128.1; 129.0; 129.2; 132.9; 133.6. Mass spectrum, *m*/*z*: 442 $[M+H]^+$. Found, %: C 54.38; H 4.32; N 15.93. $C_{20}H_{19}N_5O_5S$. Calculated, %: C 54.41; H 4.34; N 15.86.

Compound 6kB. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.67 (1H, ddd, *J* = 12.6, *J*= 5.0, *J* = 3.5) and 1.87 (1H, dd, *J* = 12.6, *J* = 8.3, 5-CH_2); 2.31–2.36 (1H, m, 5a-CH); 2.66 (1H, t, *J* = 9.6) and 3.69 (1H, td, *J* = 9.6, *J* = 8.3, 6-CH_2); 3.18 (1H, d, *J* = 12.6) and 3.28 (1H, d, *J* = 12.6, 8-CH_2); 4.27 (1H, d, *J* = 8.8) and 5.04 (1H, d, *J* = 8.8, 3a,8b-CH); 4.82 (1H, d, *J* = 5.0, 4-CH); 7.44–7.64 (5H, m, H Ar); 7.67–7.70 (1H, m, H Ar); 7.83–7.86 (3H, m, H Ar); 7.98 (1H, dd, *J*= 8.1, *J* = 1.5, H Ar). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 33.0; 44.0; 48.0; 52.7; 60.9; 80.8; 89.3; 96.0; 124.6; 125.0; 125.4; 125.7; 127.0; 127.2; 127.3; 129.1; 133.0; 133.9.

(3a*S,4*R**,5a*R**,8a*R**,8b*R**)-7-[(4-Methylphenyl)sulfonyl]-3-(2-nitrophenyl)-3a,4,5,5a,6,7,8,8b-octahydro-3*H*-4,8a-epoxy[1,2,3]triazolo[4,5-e]isoindole (6lA) and 3a*S**,4*R**,5a*R**,8a*R**,8b*R**)-7-[(4-methylphenyl)sulfonyl]-1-(2-nitrophenyl)-3a,4,5,5a,6,7,8,8b-octahydro-1*H*-4,8a-epoxy[1,2,3]triazolo[4,5-*e*]isoindole (6lB)** (0.5:1 mixture of isomers). Yield 0.71 g (91%), lemon-yellow amorphous material. IR spectrum, ν, cm^{-1}: 1526 (NO_2 ν as), 1344 (NO_2 ν s), 1605 (N=N), 1278 (SO_2 ν as), 1158 (SO_2 ν s). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.55 (1H, ddd, *J* = 12.8, *J* = 5.5, *J* = 3.5), 1.67 (0.5H, ddd, *J* = 12.8, *J* = 5.5, *J* = 3.5), 1.69 (1H, dd, *J* = 12.8, *J* = 8.1) and 1.86 (0.5H, dd, *J* = 12.8, *J* = 8.1, 5-CH_2); 2.30–2.35 (0.5H, m) and 2.40–2.45 (1H, m, 5a-CH); 2.43 (3H, s) and 2.44 (1.5H, s, CH_3); 2.62–2.66 (1.5H, m), 3.66 (0.5H, td, *J* = 9.6, *J* = 8.6), 3.79 (1H, td, *J* = 9.6, *J* = 8.1, 6-CH_2); 3.16 (0.5H, d, *J* = 12.6), 3.26 (0.5H, d, *J* = 12.6), 3.55 (1H, d, *J* = 12.6) and 4.15 (1H, d, *J* = 12.6, 8-CH_2); 4.16 (1H, d, *J* = 8.6), 4.26 (0.5H, d, *J* = 8.6), 5.00 (1H, d, *J* = 8.6) and 5.04 (0.5H, d, *J* = 8.6, 3a,8b-CH); 4.23 (1H, d, *J* = 5.5) and 4.82 (0.5H, d, *J* = 5.5, 4-CH); 7.31–7.34 (4H, m, H Ar); 7.45–7.60 (4H, m, H Ar); 7.68 (0.5H, td, *J* = 8.1, *J* = 1.5, H Ar); 7.71–7.73 (2H, m, H Ar); 7.85 (1H, dd, *J*= 8.6, *J* = 1.5, H Ar); 7.98 (0.5H, dd, *J* = 8.1, *J* = 1.5, H Ar). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 21.4; 21.5; 31.4; 32.9; 44.0 (2C); 47.9; 48.0; 52.7; 52.8; 60.9; 62.0; 80.7; 80.8; 87.4; 89.3; 95.2; 96.0; 124.3; 124.8; 125.2; 125.3; 125.7 (2C); 126.9; 127.3; 127.4; 128.1; 128.9; 129.8; 133.0; 133.3; 133.5; 133.9; 137.8; 141.5; 143.0; 143.8; 143.9. Found, %: C 55.32; H 4.60; N 15.47. $C_{21}H_{21}N_5O_5S$. Calculated, %: C 55.37; H 4.65; N 15.38.

X-ray structural analysis of compounds 6b,c. Compound **6b** ($C_{21}H_{19}N_5O_4$, *M* 405.41): monoclinic needles of lemon-yellow color, space group $P2_1/n$, at 100 K: *a* 10.219(2), *b* 8.0416(16), *c* 23.362(5) Å; β 91.67(3)°; *V* 1919.0(7) $Å^3$; *Z* 4; d_{calc} 1.403 g/cm^3; *F*(000) 848; μ 0.212 mm^{-1}. A total of 11232 reflections were collected, of which 3851 were independent (R_{int} 0.0717). The final values of probability factors R_1 0.0790 for 2283 independent reflections with $I \geq 2\sigma(I)$ and wR_2 0.2041 for all independent reflections, *S* 1.057. The peak values of residual electron density $\rho_{min/max}$ –0.242/0.285.

Compound **6c** ($C_{21}H_{19}N_5O_4$, *M* 405.41): transparent lemon-yellow rhombic crystals, space group $P2_12_12_1$, at 100 K: *a* 8.8358(18), *b* 13.074(3), *c* 16.772(3) Å; *V* 1937.5 (7) $Å^3$; *Z* 4; d_{calc} 1.390 g/cm^3; *F*(000) 848; μ 0.210 mm^{-1}. A total of 12501 reflections were collected, including 3993 independent reflections (R_{int} 0.0901). The final values of probability factors R_1 0.0537 for 2960 independent reflections with $I \geq 2\sigma(I)$ and wR_2 0.1459 for all independent reflections, *S* 1.034. The peak values of residual electron density $\rho_{min/max}$ –0.271/0.241.

The unit cell parameters and intensities of reflections were measured at the BELOK beamline of the Kurchatov synchrotron radiation source, using two-dimensional Rayonix SX165 CCD array (λ 0.96990 Å, φ-scanning with a step of 1.0°). The experimental data were processed by using the *iMOSFLM* program, which is a part of the CCP4 software suite.[8] The X-ray absorption for the obtained data was accounted for by using the *Scala* program.[9] The structures were solved by direct method and refined by full-matrix method of least squares in anisotropic approximation for non-hydrogen atoms. The hydrogen atom positions were calculated geometrically and included in the refinement according to the "rider" model with fixed isotropic displacement parameters (U_{iso}(H) = 1.5U_{eq}(C) for the methyl group and 1.2U_{eq}(C) for the rest of the groups). All calculations were performed by using the SHELXTL software suite.[10]

The tables of atomic coordinates, bond lengths, bond angles, torsion angles, and anisotropic displacement parameters for compounds **6b**,**c** were deposited at the Cambridge Crystallographic Data Center (deposits CCDC 1555312 (compound **6b**) and CCDC 1555313 (compound **6c**)).

*The synthesis of starting isoindoles **2**–**5** was performed with financial support from the Russian Foundation for Basic Research (grant 16-33-00389), the synthesis of triazoles **6** and X-ray structural analyses received support from the Ministry of Education and Science of the Russian Federation (project 4.1154.2017/4.6).*

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