ISSN 1070-4280, Russian Journal of Organic Chemistry, 2010, Vol. 46, No. 5, pp. 678–684. © Pleiades Publishing, Ltd., 2010.
Original Russian Text © E.V. Beletskii, O.A. Ignatenko, M.A. Kuznetsov, S.I. Selivanov, 2010, published in Zhurnal Organicheskoi Khimii, 2010, Vol. 46, No. 5, pp. 678–684.

Oxidative Addition of *N*-Aminophthalimide to Styryl-1,2,4-oxadiazoles

E. V. Beletskii, O. A. Ignatenko, M. A. Kuznetsov, and S. I. Selivanov

St. Petersburg State University, St. Petersburg,198504 Russia
e-mail: mak@mail.wplus.net

Received August 26, 2009

Abstract—The oxidation of *N*-aminophthalimide with lead tetraacetate in the presence of 5-[(*E*)-2-arylethenyl]-3-(4-methylphenyl)-1,2,4-oxadiazoles and 5-(4-methylphenyl)-3-[(*E*)-2-phenyl-ethenyl]-1,2,4-oxadiazole led to the formation of the corresponding (3-aryl-1-phthalimidoaziridin-2-yl)-(4-methylphenyl)-1,2,4-oxadiazoles. In the reaction with 3,5-distyryl-1,2,4-oxadiazole a mixture was obtained of two regioisomeric monoadducts and a diadduct in the ratio 80 : 15 : 5; at the use of 3 equiv of the aziridinating reagents only diadduct was isolated as a mixture of two diastereoisomers in the ~3 : 2 ratio that were separated by recrystallization.

DOI: 10.1134/S1070428010050143

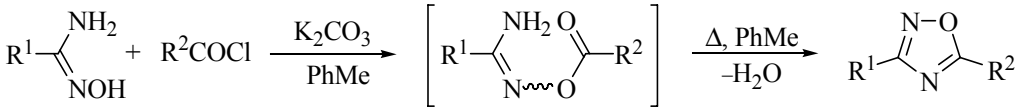
The oxidative phthalimido-aziridination of alkenyl-substituted pyrazoles and 1,3,4-oxadiazoles proceeds at the exocyclic C=C bond and affords cleanly the corresponding aziridinylazoles [1, 2]. In this connection the evaluation of the applicability range and revealing the regular trends of this reaction as a general method for designing linearly connected polyheterocyclic systems containing aziridine fragment is an urgent task. To this end we selected styryl-substituted 1,2,4-oxadiazoles fairly different from its isomers, symmetric 1,3,4-oxadiazoles.

Initial unsaturated 1,2,4-oxadiazoles **IIa–IIe** were obtained by procedure [3] through the thermal cyclization of acylation products of amidoximes **Ia, Id** prepared from *p*-tolunitrile or cinnamonitrile and hydroxylamine (Scheme 1) [3].

The ^{1}H NMR spectra of styryl-1,2,4-oxadiazoles **IIa–IIe** in the region δ 7.0–8.0 ppm contain doublets of the olefin protons with ^{3}J 15–17 Hz indicating the retention of the trans-location of these protons in the course of the cyclization. In their ^{13}C NMR spectra the carbon atoms of the heterocycle at δ 168–169 (C^3) and ~175 ppm (C^5) are characteristic; they are shifted downfield by 5–10 ppm compared with the carbon atoms of the isomeric 1,3,4-oxadiasoles (cf. [2]).

The oxidative addition of the N-aminophthalimide to styryloxadiazoles **IIa–IIe** was carried out by the standard procedure adding in turns by small portions *N*- amino-phthalimide and lead tetraacetate to the solution of the unsaturated compound in dichloromethane [2]. We established in the preliminary runs with **IIa** substrate (from the ^{1}H NMR spectra of the reaction mixtures) that at cooling the solution from the room temperature to –10°C the conversion of the initial compound considerably grew, but further cooling practically did not affect the rate of the process, therefore all subsequent reactions were performed at–10°C. The composition of separated

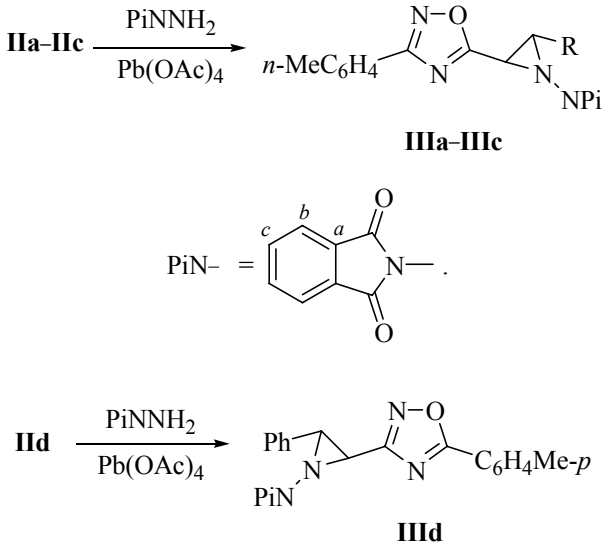
Scheme 1.



Ia, Id **IIa–IIe**, 40–75%

R^1 = C_6H_4Me-*p*, R^2 = CH=CH–Ph (**a**), CH=CH–C_6H_4OMe-*p* (**b**), CH=CH–$C_6H_4NO_2$-*p* (**c**); R^1 = CH=CH–Ph, R^2 = C_6H_4Me-*p* (**d**), CH=CH–Ph (**e**).

Scheme 2.



R = Ph (**a**), C_6H_4OMe-*p* (**b**), $C_6H_4NO_2$-*p* (**c**);

products was confirmed by elemental analyses, and their structure, by ^1H, ^{13}C NMR and mass spectra.

From monostyryl-substituted oxadiazoles **IIa–IId** the products of addition to the exocyclic C=C bonds were obtained in 34–70% yield. These compounds are the first representatives of the series of aziridinyl-1,2,4-oxadiazoles **IIIa–IIId**, a new class of linearly connected polyheterocyclic compounds (Scheme 2).

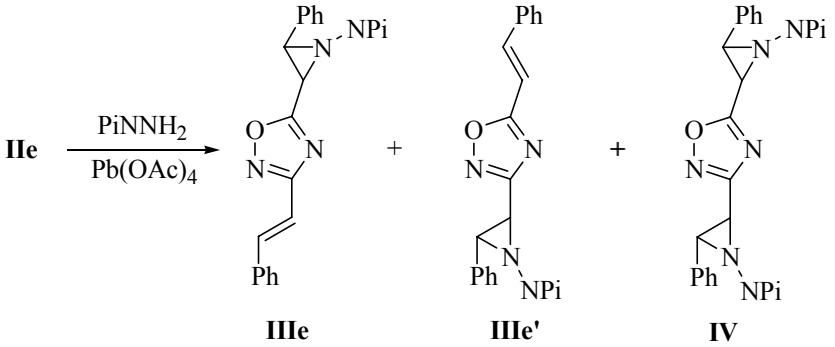
Because of the slow inversion in the NMR time scale of the aziridine nitrogen atom [4] in the middle part of the ^1H NMR spectra (δ 4.2–5.4 ppm) of compounds **IIIa–IIId** two pairs of doublets are present corresponding to the protons of the aziridine ring belonging to two invertomers with the *syn*- and *anti*-position of the phthalimide group and the heterocycle. The vicinal coupling constants (5.0–5.9 Hz) observed there indicate the *trans*-location of the aziridine protons as is expectable for the configuration of the double bond is always retained at the oxidative aminoaziridination [4]. The ratio of invertomers varied from ~5 : 1 to ~10 : 1; therewith in the ^1H NMR spectra the signals of the aziridine protons belonging to the main invertomer are located upfield with respect to the minor invertomer, and the vicinal coupling constant of the aziridine protons in the major invertomer is always somewhat smaller than in the minor one. The available data do not allow the reliable assignment of the configuration of these invertomers to the *syn* or *anti* structure, but however analogously to the aziridinyl-1,3,4-oxadiazoles [2] it is presumable that the major invertomer possesses the *syn*-orientation of the heterocycle and the phthalimide residue.

The comparison of the ^{13}C NMR spectra of adducts **IIIa–IIId** and initial styryl-1,2,4-oxadiazoles **IIa–IId** shows that the replacement of the styryl substituent by the aziridinyl residue leads to the upfield shift of the contiguous carbon atom of the oxadiazole molety by 2.5–2.8 ppm, but practically does not affect the position of the signal of the carbon atom attached to the *para*-tolyl substituent.

The ^1H NMR spectrum of the reaction mixture containing 3,5-distyryl-1,2,4-oxadiazole (**IIe**) at the equimplar ratio of all reagents demonstarated the formation of two regioisomeric monoadducts **IIIe, IIIe'**, and diadduct **IV** in the ratio 80 : 15 : 5 (Scheme 3).

The double recrystallization of the residue after the evaporation of the reaction mixture made it possible to get rid of the diadduct and to obtain in 35% yield of the compound containing the monoadducts **IIIe** and **IIIe'** in the ratio 95 : 5. However at further recrystallization the composition of the mixture did not change, and the attempt at the separation of the regioisomers by column chromatography on silica gel failed for these aziridine

Scheme 3.



like the adducts **IIIa–IIId** quickly decomposed on silica gel.

In the middle part of the ^{1}H NMR spectra (δ 4.1–5.4 ppm) of the monoadducts mixture the doublets of aziridine protons of both invertomers of compound **IIIe** are clearly seen (in the ratio 87 : 17) and of the main invertomer of the minor regioisomer **IIIe'**. In the downfield region for each invertomer of compound **IIIe** the doublets appear belonging to one of the olefin protons (δ 6.9–7.1 ppm, ^3J 16–17 Hz), but the signals of the second proton are overlapped by the complex aromatic multiplets. In the ^{13}C NMR spectrum only the signals of the aziridine carbon atoms of the main invertomer of compound **IIIe** were reliably identified.

The assignment of the regioisomers structures provided a certain problem. It is seen that the ranges of the chemical shifts of the aziridine protons in the compounds **IIIe** and **IIIe'** like those in the spectra of regioisomeric aziridinyl-oxadiazoles **IIIa, IIId** are overlapped and cannot be used for assignment. However the comparison of δ values for the carbon atoms of the oxadiazole fragment in initial compound **IIe** and in the main regioisomer of the mono-adduct shows that the formation of the aziridine ring causes an upfield shift of the signal of atom C^5 (by 2.7 ppm), and the position of the signal of atom C^3 nearly remains the same. This fact makes it possible to ascribe with a high probability to the main regioisomer **IIIe** the structure of the adduct to the C=C bond of the styryl group linked to the atom C^5.

The additional confirmation to this assumption was obtained from the comparison of the relative reactivity of regioisomeric 5- and 3-styryl-1,2,4-oxadiazoles (**IIa, IId**). Although the yields of adducts **IIIa, IIId** in the preparative runs were practically similar (69 and 66%), in the reaction of the equimolar mixture of compounds **IIa, IId** with the aziridinating reagents at the large deficit of the latter the obtained ratio of aziridines **IIIa, IIId** was ~3.5 : 1, which means that in the studied reaction 5-styryl-oxadiazole **IIa** is 3.5 times more active than its regioisomer **IId**. 3,5-Distyryl-oxadiazole **IIe** may be regarded as resulting from the replacement of the *para*-tolyl substituent by the similar in its electronic effect styryl substituent (close values of constants σ_m and σ_p; although σ_p^+ are strongly different [5]) on the one hand, at the atom C^3 of oxadiazole **IIa**, and on the other hand, at the atom C^5 of oxadiazole **IId**. Inasmuch as this substitution at the atom C^3 should relatively weakly affect the C=C bond at the atom C^5 (and vise versa), we are able to consider that the relative activity of the C=C bonds in the distyryloxadiazole **IIe** is approximately similar to the relative reactivity of compounds **IIa, IId**. Therefore the main monoadduct should be regioisomer **IIIe** in agreement with the above assignment.

Diadduct **IV** was obtained and isolated in a pure state by using the three-fold excess of the aziridinating reagents. Its identification and confirmation of the structure is complicated by its formation in the form of two diastereomers, 3-[rel-(2*R*,3*S*)-3-phenyl-1-phthalimidoaziridin-2-yl]-5-[(2*R*,3*S*)-3-phenyl-1-phthal-imidoaziridin-2-yl]-1,2,4-oxadiazole and 3-[rel-(2*R*,3*S*)-]-5-[(2*S*,3*R*)-]-isomer; each of them can fundamentally exist as four invertomers (*anti-anti-, anti-syn-, syn-anti-*, and *syn-syn-*). As a result in the middle part of the ^{1}H NMR spectrum of the reaction mixture over a score of aziridine protons signals are observed corresponding to two diastereomeric diadducts present in the ratio ~3 : 2. This is quite in contrast to the formation of a single diastereomer of analogous diadduct from 2,5-distyryl-1,3,4-oxadiazole [2].

The obtained diastereomers mixture was separated by recrystallization. In the middle part of the ^{1}H NMR spectrum (δ 3.5–5.2 ppm) of the solution of the major diastereomer of diaziridinyl-oxadiazole **IV** in $CDCl_3$ three set of signals (at the four theoretically probable invertomers) of aziridine protons are observed in the ratio 85 : 11 : 4 (in DMSO d_6 the ratio is 88 : 9 : 3). In the spectrum of the minor diastereomer of compound **IV** the aziridine signals of all four invertomers are present in the region δ 3.9–5.4 ppm with the ratio 62 : 18 : 13 : 7 (in $CDCl_3$). The considerable difference in the ratio of invertomers is apparently due to the steric interactions of phthalimide groups in one aziridine moiety with that in another seemingly remote aziridine substituent. If these interactions were insignificant the ratio of invertomers would be the same for both diastereomers **IV**, and in event of weak influence of the substituents at the heterocycle on the invertomer stability taking into account the invertomers ratio in $CDCl_3$ solutions for aziridines **IIIa** (88 : 12) and **IIId** (85 : 15) it would be 75 : 13 : 10 : 2.

The purity of obtained samples of diadduct **IV** diastereomers was proved by the absence in the ^{1}H NMR spectrum of one diastereomer the signals of the main form of the other diastereomer. Besides for both diadduct **IV** diastereomers spectra EXSY-NOESY were registered that proved the presence in each spectrum of several forms of a single compound.

It can be stated in conclusion that the oxidative phthalimidoazirination of styryl-substituted 1,2,4-

oxadiazoles at –10°C cleanly affords the corresponding aziridinyloxadiazoles, and the reactivity of the C=C bond at the atom C^5 is significantly higher, than at the atom C^3. Under the same conditions the phthalimidoaziridination of 1,3,4-oxadiazoles proceeded to a lower conversion of the initial compounds, and the yield of adducts not exceeded 15–20% [2] demonstrating the different effect of the isomeric heterocycles on the activity of the multiple bond linked to the oxadiazole ring, although both 1,2,4-oxadiazole and 1,3,4-oxadiazole are π acceptor heterocycles.

EXPERIMENTAL

^{1}H (300 MHz) and ^{13}C (75.4 MHz) were registered on a spectrometer DPX-300 Bruker C using as internal reference the signals of residual protons (δ 7.26 and 2.50 ppm) or of carbon atoms (δ 77.0 and 39.5 ppm respectively) of the deuterated solvent. The assignment of the signals in the ^{13}C NMR spectra was performed with the help of DEPT spectra. Mass spectra were measured on instruments MKh-1321 (electron impact ionization, energy of ionizing electrons 70 eV) and Finnigan MAT 95 (electrospray ionization for methanol solutions). The elemental analyses were carried out on an automatic CHN-analyzer HP-185B. The composition of the reaction mixtures and the purity of compounds obtained was checked by TLC on Alugram SIL G/UV_{254} plates. *N*-Aminophthalimide was obtained by procedure [6].

4-Toluoylamidoxime (Ia) and cinnamoylamidoxime (Id). A solution of 7.22 g (44 mmol) of hydroxylamine sulfate in 10 ml of water was added to a dispersion of 12 g (90 mmol) potassium carbonate in the solution of 44 mmol of carboxylic acid nitrile in 50 ml of methanol. The mixture was heated at reflux for 2 h, cooled, and diluted with water. The precipitated colorless crystals were filtered off. Yield of amidoxime **Ia** 75%, mp 140°C (mp 141°C [7]). Yield of amidoxime **Id** 58%, mp 91°C (mp 93°C [8]). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 4.77 br.s (2H, NH_2), 6.52 d (1H, =CH, *J* 16.0 Hz), 6.86 d (1H, =CH, *J* 16.0 Hz), 7.30–7.48 m (5H, Ph).

5-Styryl-3-*p*-tolyl-1,2,4-oxadiazoles IIa–IIc. A dispersion of 1.50 g (10 mmol) of *p*-toluoylamidoxime (**Ia**), 1.45 g (11 mmol) of K_2CO_3, and 10 mmol of the corresponding cinnamoyl chloride in 30 ml of benzene was heated at reflux with stirring for 3 h. The reaction mixture was filtered, the solvent was distilled off in a vacuum. The obtained light-yellow powder was washed with 1 ml of ethyl ether, was dissolved in 50 ml of dichloromethane, and washed with 0.1 N HCl (2 × 30 ml). The solvent was distilled off in a vacuum.

3-(4-Methylphenyl)-5-[(E)-2-phenylethenyl]-1,2,4-oxadiazole (IIa). Yield 75%. Colorless powder, mp 108–109°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.43 s (3H, CH_3), 7.06 d (1H, =CH, *J* 16.8 Hz), 7.27 d[a] (2H, *p*-Tol, H^m, *J* 8.4 Hz), 7.40–7.45 m (3H, Ph, $H^{m,p}$), 7.58–7.63 m (2H, Ph, H°), 7.87 d (1H, =CH, $H^{m,p}$), 7.58–7.63 m (2H, Ph, H°), 7.87 d (1H, =CH, *J* 16.8 Hz), 8.02 d (2H, *p*-Tol, H°, *J* 8.4 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 21.69 (CH_3), 110.44 (=CH–Ht), 124.25 (*p*-Tol, C^p), 127.50, 128.03, 129.17, 129.68, 130.59, 134.60 (Ph, C^i), 141.57 (*p*-Tol, C^i), 142.65 (=CH–Ph), 168.83 (C^3), 175.17 (C^5). Mass spectrum, electron impact, *m/z* (I_{rel}, %): 262 (87) $[M]^+$, 261 (100), 145 (11), 133 (51) $[C_7H_7CNO]^+$, 128 (46), 103 (26), 77 (31), 71 (10), 57 (12), 51 (13), 41 (10). Found, %: C 77.59; H 5.33; N 10.66. $C_{17}H_{14}N_2O$. Calculated, %: C 77.86; H 5.34; N 10.69. M 262.31.

3-(4-Methylphenyl)-5-[(*E*)-2-(4-methoxyphenyl)-ethenyl]-1,2,4-oxadiazole (IIb). Yield 53%. Colorless powder, mp 120–121°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.42 s (3H, CH_3), 3.85 s (3H, OCH_3), 6.88–6.98 m (3H, =CH and *p*-$MeOC_6H_4$, H^m), 7.29 d (2H, *p*-Tol, H^m, *J* 8.4 Hz), 7.55 d (2H, *p*-$MeOC_6H_4$, H°, *J* 8.4 Hz), 7.82 d (1H, =CH, *J* 16.8 Hz), 8.01 d (2H, *p*-Tol, H°, *J* 8.4 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 21.60 (CH_3), 55.66 (OCH_3); 108.00, 114.66 (=CH–Ht and *p*-$MeOC_6H_4$, C^m); 124.39 (*p*-Tol, C^p), 127.39, 127.50 (*p*-$MeOC_6H_4$, C^i), 129.68, 129.72, 141.50 (*p*-Tol, C^i), 142.32 (=CH–Ar), 161.71 (C–O), 168.76 (C^3), 175.58 (C^5). Mass spectrum, electron impact, *m/z* (I_{rel}, %): 292 (66) $[M]^+$, 291 (37), 205 (24), 161 (100) $[M - C_7H_7CN_2]^+$, 133 (37) $[C_7H_7CNO]^+$, 89 (13), 77 (27). Found, %: C 73.89; H 5.52; N 9.39. $C_{18}H_{16}N_2O_2$. Calculated, %: C 73.97; H 5.48; N 9.59. M 292.34.

3-(4-Methylphenyl)-5-[(*E*)-2-(4-nitrophenyl)-ethenyl]-1,2,4-oxadiazole (IIc). Yield 40%. Yellow powder, mp 189–190°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 2.39 s (3H, CH_3), 7.38 d (2H, *p*-Tol, H^m, *J* 8.9 Hz), 7.58 d (1H, =CH, *J* 16.8 Hz), 7.93 d (2H, *p*-$NO_2C_6H_4$, H°, *J* 7.9 Hz), 8.00 d (1H, =CH, *J* 16.8 Hz), 8.07 d (2H, *p*-Tol, H°, *J* 8.9 Hz), 8.26 d (2H, *p*-$NO_2C_6H_4$,

[a] Here and hereinafter in describing the signals of aromatic protons whose spectra belong to the second order we report the apparent multiplicity of complex signals and the distance between the main peaks of the complex multiplets and not the calculated values of coupling constants.

H^{m}, *J* 7.9 Hz). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 21.08 (CH_3), 114.40 (CH=), 123.30 (C^{i}), 123.99, 126.96, 129.40, 129.81, 140.11 (CH=), 140.62 (C^{i}), 141.61 (*p*-Tol, C^{i}), 148.04 (C^{i}), 168.12 (C^{3}), 174.64 (C^{5}). Mass spectrum, electron impact, *m/z* (I_{rel}, %): 307 (100) $[M]^+$, 306 (43), 176 (38) $[M–C_7H_7CN_2]^+$, 133 (95) $[C_7H_7CNO]^+$, 102 (24), 91 (14), 77 (33), 51 (10). Found, %: C 66.20; H 4.37; N 13.50. $C_{17}H_{13}N_3O_3$. Calculated, %: C 66.45; H 4.23; N 13.68. M 307.31.

3-Styryl-1,2,4-oxadiazoles IId and IIe. To a solution of 810 mg (5 mmol) of cinnamoylamidoxime (**Id**) and 5 mmol of *p*-toluoyl or cinnamoyl chloride in 10 ml of dichloromethane was added dropwise at stirring 0.62 ml (560 mg, 5.5 mmol) of *N*-methylmorpholine. The solution was stirred for 10 min, heated to boiling, washed with 1N HCl (3 × 10 ml). The organic layer was dried with anhydrous magnesium sulfate, the solvent was distilled off in a vacuum. To the residue 30 ml of toluene was added and the solution was heated at reflux for 10 h. The solvent was distilled off in a vacuum, the residue was recrystallized from ethanol.

5-(4-Methylphenyl)-3-[(*E*)-2-phenylethenyl]-1,2,4-oxadiazole (IId). Yield 55%. Colorless powder, mp 100–101°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.46 s (3H, CH_3), 7.09 d (1H, =CH, *J* 16.7 Hz), 7.33 m ($5H_{apom}$), 7.61 d (2H, Ph, H°, *J* 8.7 Hz), 7.81 d (1H, =CH, *J* 16.7 Hz), 8.08 d (2H, *p*-Tol, H°, *J* 8.7 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 21.87 (CH_3), 113.20 (=CH–Ht), 121.63 (*p*-Tol, C^{p}), 127.58, 128.25, 128.99, 129.50 (Ph, C^{p}), 129.93, 135.60 (Ph, C^{i}), 139.16 (=CH–Ph), 143.62 (p-Tol, C^{i}), 168.49 (C^{3}), 175.28 (C^{5}). Mass spectrum, electron impact, *m/z* (I_{rel}, %): 262 (52) $[M]^+$, 261 (100), 128 (28), 119 (58) $[C_7H_7CO]^+$, 116 (14), 91 (28), 65 (22), 63 (12), 52 (11), 39 (13). Found, %: C 77.93; H 5.32; N 10.66. $C_{17}H_{14}N_2O$. Calculated, %: C 77.86; H 5.34; N 10.69. M 262.31.

3,5-Bis[(*E*)-2-phenylethenyl]-1,2,4-oxadiazole (IIe). Yield 56%. Colorless powder, mp 114–115°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 7.03 d (1H, =CH, *J* 16.0 Hz), 7.09 d (1H, =CH, *J* 16.7 Hz), 7.36–7.44 m (6H, H^{m} and H^{p}), 7.58–7.62 m (4H, H°), 7.75 d (1H, =CH, *J* 16.7 Hz), 7.86 d (1H, =CH, *J* 16.0 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 110.29 (=CH–Ht), 113.09 (=CH–Ht), 127.59, 128.06 (Ph, C^{p}), 129.02, 129.21 (Ph, C^{p}), 129.57, 130.68, 134.54 (Ph, C^{i}), 135.54 (Ph, C^{i}), 139.15 (=CH–Ph), 142.92 (=CH–Ph), 168.33 (C^{3}), 174.66 (C^{5}). Mass spectrum, electron impact, m/z (I_{rel}, %): 274 (58) $[M]^+$, 273 (100), 245 (18), 131 (38), 128 (42), 115 (80), 103 (38), 89 (16), 77 (31), 63 (11), 51 (15). Found, %: C 78.58; H 5.17; N 10.25. $C_{18}H_{14}N_2O$. Calculated, %: C 78.83; H 5.11; N 10.22. M 274.32.

General procedure of addition of *N*-aminophthalimide to styryl-1,2,4-oxadiazoles IIa–IIe. Into a solution of 1 mmol of oxadiazole **IIa–IIe** in 30 ml of dichloromethane cooled to –10°C where was dispersed 0.7 g (5 mmol) of potassium carbonate was added in turns by small portions within 15 min 162 mg (1 mmol) of N-aminophthalimide and 443 mg (1 mmol) of lead tetraacetate. Then the stirring was continued for 10 min, the mixture was filtered, the precipitate of the inorganic salt was washed with 20 ml of dichloromethane. The solvent was distilled off in a vacuum. The reaction product was recrystallized from a mixture of ethanol with DMF, 5 : 1.

3-(4-Methylphenyl)-5-[rel-(2*R*,3*S*)-3-phenyl-1-phthalimidoaziridin-2-yl]-1,2,4-oxadiazole (IIIa), invertomers mixture, 88 : 12. Yield 69%. Colorless powder, mp 178–180°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.35 s, 4.24 d (*J* 5.1 Hz), 4.86 d (*J* 5.1 Hz) CH_3 group and aziridine protons of the main invertomer; 2.42 s, 4.43 d (*J* 5.8 Hz), 5.37 d (*J* 5.8 Hz) the same of minor invertomer, overall 5H; 7.14 d (*J* 8.0 Hz), 7.28–7.32 m, 7.39–7.47 m, 7.55 d (J 8.0 Hz), 7.54–7.65 m, 8.04 d (*J* 8.0 Hz) overall 13H, 2Ar + PiN. ^{13}C NMR spectrum of the main invertomer ($CDCl_3$), δ, ppm: 21.63 (CH_3), 42.62 (CHN), 51.62 (CHN), 123.41 (PiN, C^{b}), 123.46 (*p*-Tol, C^{p}), 127.31, 127.68, 128.96, 129.11, 129.56, 130.14 (PiN, C^{a}), 134.18 (Ph, C^{i}), 134.33 (PiN, C^{c}), 141.78 (*p*-Tol, C^{i}), 164.83 (NCO), 168.45 (C^{3}), 172.70 (C^{5}). Mass spectrum, electrospray, *m/z* (I_{rel}, %): 422.3 (31) $[M]^+$, 276.2 (23) $[M – PiN]^+$, 221.2 (27), 202.2 (92), 173.1 (56), 159.1 (31), 147.1 (31) $[PiNH]^+$, 132.1 (62), 104.1 (100) $[C_6H_4CO]^+$, 76.1 (51). Found, %: C 71.09; H 4.21; N 13.30. $C_{25}H_{18}N_4O_3$. Calculated, %: C 71.08; H 4.29; N 13.26. M 422.44.

3-(4-Methylphenyl)-5-[rel-(2*R*,3*S*)-3-(4-methoxyphenyl)-1-phthalimidoaziridin-2-yl]-1,2,4-oxadiazole (IIIb), invertomers mixture, 82 : 18. Yield 64%. Colorless powder, mp 162–163°C (decomp). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.34 s, 3.83 s, 4.22 d (*J* 5.0 Hz), 4.79 d (*J* 5.0 Hz) CH_3, CH_3O groups and aziridine protons of the main invertomer; 2.42 s, 3.74 s, 4.38 d (*J* 5.9 Hz), 5.30 d (*J* 5.9 Hz) the same of minor invertomer, overall 8H; 6.81 d (*J* 8.4 Hz), 6.96 d (*J* 8.4 Hz), 7.13 d (*J* 8.4 Hz), 7.26–7.32 m, 7.47 d (*J* 8.4 Hz), 7.63–7.74 m, 8.02 d (J 8.4 Hz) overall 12H, 2Ar + PiN. ^{13}C NMR spectrum of the main invertomer ($CDCl_3$), δ, ppm: 21.63 (CH_3), 42.49 (CHN), 51.50

(CHN), 55.50 (OCH_3), 114.40 (*p*-Anys, C^m), 123.39 (PiN, C^b), 123.45 (*p*-Tol, C^p), 126.10 (*p*-Anys, C^i), 127.28, 128.62, 129.55, 130.12 (PiN, C^a), 134.31 (PiN, C^c), 141.77 (*p*-Tol, C^i), 160.29 (C–O), 164.87 (NCO), 168.43 (C^3), 172.81 (C^5). Mass spectrum, electrospray, *m/z* (I_{rel}, %): 452.3 (6) $[M]^+$, 319.2 (100) $[M–C_7H_7CNO]^+$, 305.2 (13) $[M–PiNH]^+$, 187.1 (13), 147.1 (15) $[PiNH]^+$, 132.1 (56), 104.1 (35) $[C_6H_4CO]^+$, 76.0 (11). Found, %: C 69.01; H 4.46; N 12.40. $C_{26}H_{20}N_4O_4$. Calculated, %: C 69.02; H 4.46; N 12.38. M 452.47.

3-(4-Methylphenyl)-5-[rel-(2*R*,3*S*)-3-(4-nitrophenyl)-1-phthalimidoaziridin-2-yl]-1,2,4-oxadiazole (IIIc), invertomers mixture, 91:9. Yield 34%. Light yellow powder, t_{decomp} 173–175°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.35 s, 4.25 d (*J* 5.1 Hz), 4.91 d (*J* 5.1 Hz) CH_3 group and aziridine protons of the main invertomer, 2.42 s, 4.52 d (*J* 5.9 Hz), 5.37 d (*J* 5.9 Hz) the same of minor invertomer, overall 5H; 7.14 d (*J* 7.6 Hz), 7.28–7.35 m, 7.64–7.75 m, 8.00 d (*J* 7.6 Hz), 8.17 d (*J* 7.6 Hz), 8.30 d (*J* 8.4 Hz) overall 12H, 2Ar + PiN. ^{13}C NMR spectrum of the main invertomer ($CDCl_3$), δ, ppm: 21.66 (CH_3), 42.92 (CHN), 50.42 (CHN), 123.20 (*p*-Tol, C^p), 123.61 (PiN, C^b), 124.19, 127.31, 128.34, 129.64, 129.94 (PiN, C^a), 134.58 (PiN, C^c); 141.33, 142.03 (*p*-Tol, C^i and *p*-$C_6H_4NO_2$, C^i); 148.45 (CNO_2), 164.68 (NCO), 168.46 (C^3), 171.89 (C^5). Mass spectrum, electrospray, m/z (I_{rel}, %): 467.3 (10) $[M]^+$, 319.2 (16), 202.2 (11), 173.1 (20), 147.1 (92) $[PiNH]^+$, 132.1 (25), 117.1 (37), 104.1 (100) $[C_6H_4CO]^+$, 76.1 (71). Found, %: C 64.19; H 3.80; N 14.96. $C_{25}H_{17}N_5O_5$. Calculated, %: C 64.24; H 3.67; N 14.98. M 467.44.

5-(4-Methylphenyl)-3-[rel-(2*R*,3*S*)-3-phenyl-1-phthalimidoaziridin-2-yl]-1,2,4-oxadiazole (IIId), invertomers mixture, 85 : 15. Yield 66%. Colorless powder, mp 208–210°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.38 s, 4.20 d (*J* 5.2 Hz) and 4.82 d (*J* 5.2 Hz) aziridine protons and CH_3 group of the main invertomer; 2.45 s, 4.41 d (*J* 5.8 Hz) and 5.28 d (*J* 5.8 Hz) the same of minor invertomer, overall 5H; 7.20 d (J 7.8 Hz), 7.25–7.46 m, 7.55–7.76 m, 8.08 d (*J* 8.0 Hz) overall 13H, 2Ar + PiN. ^{13}C NMR spectrum of the main invertomer ($CDCl_3$), δ, ppm: 21.83 (CH_3), 43.62 (CHN), 49.84 (CHN), 121.02 (*p*-Tol, C^p), 123.21 (PiN, C^b), 127.36, 128.06, 128.74, 128.84, 129.85, 130.31 (PiN, C^a), 134.09 (PiN, C^c), 135.07 (Ph, C^i), 143.91 (*p*-Tol, C^i), 164.96 (NCO), 165.74 (C^3), 175.82 (C^5). Mass spectrum, electron impact, *m/z* (I_{rel}, %): 422 (5) $[M]^+$, 395 (4), 319 (19), 318 (12), 276 (19) $[M–PiN]^+$, 262 (11), 236 (13), 200 (19), 147 (20) $[PiNH]^+$, 132 (15), 119 (100) $[C_7H_7CO]^+$, 104 (56) $[C_6H_4CO]^+$, 91 (20), 77 (32). Found, %: C 70.97; H 4.17; N 13.11. $C_{25}H_{18}N_4O_3$. Calculated, %: C 71.08; H 4.29; N 13.26. M 422.44.

3-[(*E*)-2-phenylethenyl]-5-[rel-(2*R*,3*S*)-3-phenyl-1-phthalimidoaziridin-2-yl]-1,2,4-oxadiazole (IIIe), invertomers mixture, 87 : 13, and 5% of regioisomer **IIIe'**. The reaction product was twice recrystallized from ethanol. Yield 35%. Colorless powder, mp 155–156°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 4.23 d (J 5.1 Hz), 4.85 d (*J* 5.1 Hz), 6.90 d (*J* 16.0 Hz) aziridine protons and =CH of the main invertomer; 4.42 d (*J* 5.8 Hz), 5.34 d (*J* 5.8 Hz), 7.11 d (*J* 16.7 Hz) the same of minor invertomer, overall 3H; 7.24–7.50 m, 7.55–7.60 m, 7.64–7.82 m, overall 15H, 2Ph + =CH + PiN; 4.19 (*J* 5.1 Hz), 4.81 (*J* 5.1 Hz) aziridine protons of compound **IIIe'**. ^{13}C NMR spectrum of the main invertomer ($CDCl_3$), δ, ppm: 42.43 (CHN), 51.48 (CHN), 113.03 (=CH–Ht), 123.39 (PiN, C^b), 127.14, 127.34, 128.79, 128.83, 128.99, 129.53 (PiN, C^a), 129.99, 133.94 (Ph, C^i), 134.23 (PiN, C^c), 134.96 (Ph, C^i), 139.39 (=CH–Ph), 164.67 (NCO), 167.79 (C^3), 172.02 (C^5). Mass spectrum, electron impact, *m/z* (I_{rel}, %): 434 (1.5) $[M]^+$, 331 (4), 302 (1), 262 (5), 247 (5), 186 (3), 147 (100) $[PiNH]^+$, 129 (42), 104 (79) $[C_6H_4CO]^+$, 76 (71). Found, %: C 71.79; H 4.08; N 12.75. $C_{26}H_{18}N_4O_3$. Calculated, %: C 71.88; H 4.18; N 12.90. M 434.45.

Estimation of the relative reactivity of oxadiazoles IIa and IId in the oxidative addition of *N*-aminophthalimide. To a solution of equimolar amounts of oxadiazoles **IIa** and **IId** (each 131 mg, 0.5 mmol) in 30 ml of dichloromethane and containing dispersed potassium carbonate (0.5 g) cooled to –10°C was added at stirring in turns by small portions 16 mg (0.1 mmol) of *N*-aminophthalimide and 44 mg (0.1 mmol) of lead tetraacetate. The mixture was stirred for 10 min more, then filtered through a thin layer of Na_2SO_4. The precipitate of inorganic salts was washed with 20 ml of dichloromethane. The solvent was distilled off in a vacuum. The ratio of aziridines **IIIa** and **IIId** in the dry residue was evaluated at 3.5 : 1 by ^{1}H NMR from the intensity ratio of the aziridine protons belonging to the main invertomers (for aziridine **IIIa** δ 4.24 ppm, invertomer content 88%; for compound **IIId** δ 4.20 ppm, invertomer content 85%).

Addition of a triple excess of *N*-aminophthalimide to oxadiazole IIe. To a solution of 274 mg (1 mmol) of oxadiazole **IIe** in 30 ml of dichloromethane where was dispersed 0.7 g of potassium carbonate cooled to –10°C was added at stirring in turns by small portions within

15 min 486 mg (3 mmol) of *N*-aminophthalimide and 1.33 g (3 mmol) of lead tetraacetate. The mixture was stirred for 10 min more, then filtered , and the precipitate of inorganic salts was washed with 20 ml of dichloromethane. The solvent was distilled off in a vacuum. The recrystallization from the mixture of ethanol with DMF, 5 : 1, furnished a mixture of diastereomers of 3,5-bis-[rel-(2*R*,3*S*)-3-phenyl-1-phthalimido-aziridin-2-yl]-1,2,4-oxadiazole (**IV**) in a ratio 5 : 1 (^{1}H NMR spectrum). Yield 69%. Colorless powder, mp 210°C (decomp.). Mass spectrum, *m/z* (I_{rel}, %): 594 (4) $[M]^+$, 447 (10) $[M–PiNH]^+$, 289 (13), 248 (25), 220 (37), 147 (67) $[PiNH]^+$, 117 (33), 104 (100) $[C_6H_4CO]^+$, 103 (83), 77 (88). Found, %: C 68.64; H 3.70; N 14.07. $C_{34}H_{22}N_6O_5$. Calculated, %: C 68.68; H 3.73; N 14.13. M 594.59.

Major diatereomer of diadduct IV. To a solution of 274 mg (1 mmol) of oxadiazole **IIe** in 30 ml of dichloromethane where was dispersed 0.7 g of potassium carbonate cooled to –10°C was added at stirring in turns by small portions within 15 min 486 mg (3 mmol) of *N*-aminophthalimide and 1.33 g (3 mmol) of lead tetraacetate. The mixture was stirred for 10 min more, then filtered , and the precipitate of inorganic salts was washed with 20 ml of dichloromethane. The solvent was distilled off in a vacuum. The residue was recrystallized from the mixture of ethanol with DMF, 5:1, filtered at 40°C, minor diastereomer was isolated from the filtrate. Yield of the major diastereomer 22%. Colorless powder, mp 221–223°C (decomp.). According to the ^{1}H NMR spectrum exists as a mixture of three invertomers , 85 : 11 : 4 in $CDCl_3$ and 88 : 9 : 3 in DMSO-d_6. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.92 d (*J* 5.5 Hz), 3.94 d (*J* 5.2 Hz), 4.03 m (two doublets overlapped into a broadened triplet) aziridine protons of the main invertomer; 3.53 d (*J* 5.5 Hz), 4.26 m, 4.79 d (*J* 5.5 Hz), 4.84 d (*J* 5.5 Hz), 5.07 d (*J* 5.5 Hz), 5.14 d (*J* 5.5 Hz) aziridine protons of minor invertomers, overall 4H; 7.10–7.18 m, 7.22–7.45 m, 7.50–7.65 m, 7.72–7.88 m, overall 18H, 2Ph + 2PiN. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.47–3.52 br.s, 4.52 d (*J* 4.6 Hz), 4.80 d (*J* 5.5 Hz) aziridine protons of the main invertomer; 4.63 d (*J* 4.6 Hz), 4.71 d (*J* 5.5 Hz), 4.91 d (*J* 4.6 Hz), 5.01 d (*J* 5.5 Hz) aziridine protons of the first minor invertomer, overall 4H; 7.05–7.12 m, 7.32–7.47 m, 7.55–7.75 m, 7.77–7.95 m, overall 18H, 2Ph + 2PiN. ^{13}C NMR spectrum of the main invertomer (DMSO-d_6), δ, ppm: 39.48 (CHN), 41.02 (CHN), 49.38 (CHN), 52.33 (CHN), 123.13 (PiN, C^b), 123.32 (PiN, C^b), 127.24, 128.40, 128.46, 128.50, 128.64, 128.91, 129.13 (PiN, C^a), 129.26 (PiN, C^a), 133.17 (Ph, C^i), 133.83 (Ph, C^i), 134.67 (PiN, C^c), 134.87 (PiN, C^c), 163.88 (NCO), 165.04 (C^3), 173.28 (C^5). Found, %: C 68.60; H 3.91; N 14.00. $C_{34}H_{22}N_6O_5$. Calculated, %: C 68.68; H 3.73; N 14.13.

Minor diastereomer of diadduct IV. The filtrate after recrystallization of the diastereomers mixture was poured into 50 ml of water, the precipitate was filtered off and recrystallized ftom ethyl acetate. Yield 8%. Colorless powder, mp 195–196°C. According to ^{1}H NMR spectrum it exists as a mixture of four invertomers, 62 : 18 : 13 : 7 in $CDCl_3$, 54 : 25 : 17 : 4 in DMSO-d_6. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.90 d (*J* 5.7), 4.07 d (*J* 5.7 Hz), 4.66 d (J 5.7 Hz), 4.69 d (J 5.7 Hz) aziridine protons of the main invertomer; 3.83 d (5.7 Hz), 4.13 d (*J* 5.7 Hz), 4.21 d (*J* 5.7 Hz), 4.27 d (*J* 5.7 Hz), 4.41 d (*J* 5.7 Hz), 4.78–4.83 br.t, 5.05 d (*J* 5.7 Hz), 5.16 d (*J* 5.7 Hz) aziridine protons of minor invertomers, overall 4H; 7.22–7.35 m, 7.38–7.48 m, 7.52–7.60 m, 7.62–7.77 m, overall 18H, 2Ph + 2PiN. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 4.26 d (*J* 5.5 Hz), 4.46 d (*J* 5.5 Hz), 4.57 d (J 5.5 Hz), 4.72 d (*J* 5.5 Hz) aziridine protons of the main invertomer; 3.95 d (*J* 5.5 Hz), 4.88 d (*J* 5.5 Hz), 4.94 d (*J* 5.5 Hz), 4.05 d (J 5.5 Hz), 5.19 d (J 5.5 Hz), 5.39 d (*J* 5.5 Hz) aziridine protons of minor invertomers, overall 4H; 7.15–7.27 m, 7.30–7.55 m, 7.60–7.77 m, overall 18H, 2Ph + 2PiN. ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 40.96 (CHN), 41.98 (CHN), 49.70 (CHN), 51.16 (CHN), 122.83 (PiN, C^b), 122.91 (PiN, C^b), 122.99 (PiN, C^b), 123.07 (PiN, C^b), 127.34, 127.47, 127.55, 127.59, 127.86, 128.42, 128.47, 128.50, 128.72, 129.27 (PiN, C^a), 129.30 (PiN, C^a), 129.37, 129.40 (PiN, C^a), 129.45, 133.83 (Ph, C^i), 134.13 (PiN, C^c), 134.28 (PiN, C^c), 134.50 (Ph, C^i), 134.56 (PiN, C^c), 134.68 (PiN, C^c), 164.22 (NCO), 164.28 (NCO), 164.34 (NCO), 164.84 (C^3), 172.85 (C^5). Found, %: C 68.52; H 3.89; N 14.08. $C_{34}H_{22}N_6O_5$. Calculated, %: C 68.68; H 3.73; N 14.13.

REFERENCES

1. Ignatenko, O.A., Blandov, A.N., and Kuznetsov, M.A., *Zh. Org. Khim*., 2005, vol. 41, p. 1830.
2. Ignatenko, O.A., Kuznetsov, M.A., and Selivanov, S.I., *Zh. Org. Khim*., 2007, vol. 43, p. 1048.
3. Clapp, B.L. *Adv. Heterocycl. Chem.,* 1976, vol. 20, p. 65.
4. Atkinson, R.S. and Malpass, J.R., *J. Chem. Soc., Perkin Trans. I,* 1977, p. 2242.
5. Hansch, C., Leo, A., and Taft, R.W., *Chem. Rev.,* 1991, vol. 91, p. 165.
6. Drew, N.D.K. and Hatt, N.H., *J. Chem. Soc.,* 1937, p. 16.
7. Quan, C. and Kurth, M., *J. Org. Chem.,* 2004, vol. 69, p. 1470.
8. Wolff, H., *Ber.,* 1886, 19, p. 1507.