ISSN 1070-4280, Russian Journal of Organic Chemistry, 2009, Vol. 45, No. 8, pp. 1200–1207. © Pleiades Publishing, Ltd., 2009.
Original Russian Text © M.A. Kuznetsov, A.V. Ushkov, S.I. Selivanov, A.S. Pan'kova, A. Linden, 2009, published in Zhurnal Organicheskoi Khimii, 2009, Vol. 45, No. 8, pp. 1209–1216.

Thermolysis of Dimethyl *cis*- and *trans*-1 Pthalimidoaziridine-2,3-dicarboxylates in the Presence of Dipolarophiles

M. A. Kuznetsov[a], A. V. Ushkov[a], S. I. Selivanov[a], A. S. Pan'kova[a], and A.Linden[b]

[a]*St. Petersburg State University, St. Petersburg, 198504 Russia*
e-mail: mak@mail.wplus.net
[b]*Organisch-chemisches Institut der Universität Zürich*

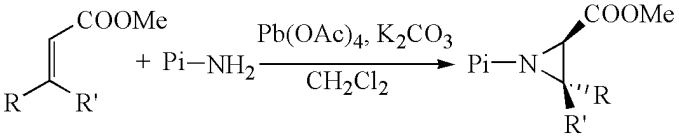
Received September 24, 2008

Abstract—Thermolysis of dimethyl esters of stereoisomeric phthalimidoaziridine-2,3-dicarboxylic acids in the presence of dimethyl fumarate, dimethyl maleate, and *N*-phenylmaleimide occurred stereo-specifically and stereoselectively led to the formation of derivatives of 1-phthalimidopyrrolidine, products of 1,3-dipolar additrion of intermediately arising azomethine ylides. In keeping with the rules of the conservation of orbital symmetry the thermal opening of the 2,3-disubstituted 1-phthalimidoaziridines into azomethine ylides occurred conrotatory. The relative positions of the substituents in the dipolarophiles is retained in the reaction products indicating the concerted addition mechanism.

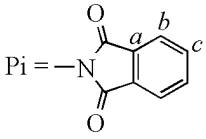
DOI: 10.1134/S1070428009080144

We recently showed that the thermolysis of *trans*-2,3-disubstituted *N*-phthalimidoaziridines with nitrile substituents in the presence of various dipolarophiles proceeded stereospecifically, stereoselectively, and afforded in good yields the corresponding derivatives of *N*-aminopyrrolidine and therefore might underlie a general preparation method of these unavailable compounds [1]. The target of this study was the extension of the approach to 2,3-disubstituted *N*-phthalimidoaziridines **I** and **II** with methoxycarbonyl substituents that far weaker activated the cleavage of the C–C bond than the cyano group (cf. [1] and references therein). Besides we aimed to reveal the spatial relationships of this process not only by the example of *trans*- **I**, but also *cis*-2,3-disubstituted aziridine **II** in combination with dipolarophiles **IIIa–IIIc** with electron-deficient double carbon-carbon bonds differing in activity and spatial arrangement.

Aziridines **I** and **II** were obtained from *N*-amino-phthalimide and the appropriate unsaturated esters by oxidative aminoaziridination [2]. Inasmuch as the strained three-membered ring possesses a low stability the oxidative addition of the *N*-aminophthalimide to unsaturated compounds is commonly performed at low temperature. It turned out however that at –15...–18°C the reaction with dimethylfumarate gave aziridine **I** in only 13–20% yield. Yet at the room temperature (18–23°C) its yield grew to 85%. Aziridine **II** was obtained at 0°C.



I (85%), **II** (34%)



; R = COOMe, R' = H (**I**);

R = H, R' = COOMe (**II**).

The characteristics of N-phthalimidoaziridines **I** and **II** are well consistent with the published data [3–5]. The inversion of the endocyclic nitrogen atom slow in the NMR time scale [6] is degenerate for aziridine **I**, and in its ^{1}H NMR spectrum in the region δ 4.8–4.9 ppm two characteristic doublets are present of *AX* system from the protons of the aziridine ring existing in a single form. Aziridine **II**, in keeping with the NMR data, at room temperature existed as an only invertomer, evidently, with

the *syn*-orientation of the aziridine proton and the phthalimide group.

The thermolysis of aziridines **I** and **II** was carried out in sealed ampoules and/or in an air-tight glass reactor in the presence of a 50% excess of the dipolarophile. Benzene or chlorobenzene served as solvents. The reaction of aziridines **I** and **II** with dipolarophiles **IIIa–IIIc** started with appreciable velocity only at heating to 220°C. TLC monitoring showed that under these conditions in about 3 h aziridines **I** and **II** completely converted into the thermolysis products (Scheme 1).

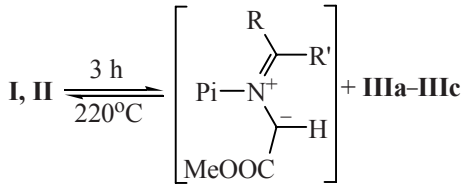
Similarly to the previous reaction series [1] we observed in the process a strong tarring and phthalimide formation. On workup of the reaction mixtures in all cases we obtained from aziridines **I** and **II** the products of 1,3-dipolar cycloaddition: previously unknown *N*-phthalimidopyrrolidines **IVa–IVc** and **Va–Vc** respectively nearly always as a single stereoisomer. The reaction of aziridine **II** with dimethyl fumarate **IIIa** was an exception for it gave a mixture of diastereomers **Va**[1] and **Va**[2] and also oxazole **VII** formed apparently through an intramolecular cyclization of the intermediate azomethine ylide followed by aromatization of oxazoline **VI** by elimination of a phthalimide molecule (Scheme 2).

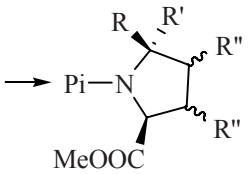
The formation of 5-alkoxyoxazoles from alkoxycarbonyl-substituted *N*-phthalimidoaziridines was already described [7], but here we report on the first example of this conversion of 2,3-disubstituted *N*-phthalimidoaziridines.

The formation in the thermolysis only of the above listed compounds was confirmed by ^{1}H NMR spectra of the reaction mixtures taken just after their cooling. Compound **Vb** is a viscous oily fluid, all other products of these reactions are crystalline substances. The composition of *N*-phthalimidopyrrolidines **IV** and **V** was proved by elemental analysis, and the structure was in total agreement with the ^{1}H, ^{13}C NMR, and mass spectra where the same regularities were observed as in the spectra of compounds with the cyano substituents [1]. In particular, the rotation of phthalimide group slow in the NMR time scale is characteristic of these compounds; therefore at the lack of axial symmetry of the molecule the ^{13}C signals of the imide carbon atoms (δ 164–165 ppm) are strongly broadened or totally absent, and the other signals from the phthalimide fragment are also broadened.

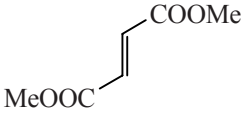
The spatial arrangement of compounds obtained was established mostly in the same way that we had applied before [1]. Obviously for pyrrolidines **IV** and **V** with identical in pairs substituents at α- and β-carbon atoms 6 diastereomeric structures are theoretically possible: two with a symmetry plane σ (symmetry C_s), two with the second order symmetry axis C_2, and two without symmetry elements. Therewith in adducts **IVa** and **Vb, Vc** all four protons of the pyrrolidine ring are anisochronous and form *ABXY* system. Consequently in their ^{1}H NMR spectra the signals of H^3 and H^4 appear as doublets of doublets or triplets indicating that pyrrolidines **IVa** and **Vb, Vc** lack any symmetry elements. In contrast, in compounds **IVb**, **IVc**, and **Va**[1,2] the four ring protons appear as only two signals of *AA'XX'* system demonstrating the symmetry of their molecules. These

Scheme 1.

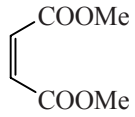




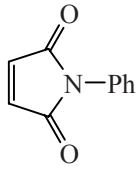
IVa–IVc (29–48%),
Va–Vc (22–88%)



IIIa

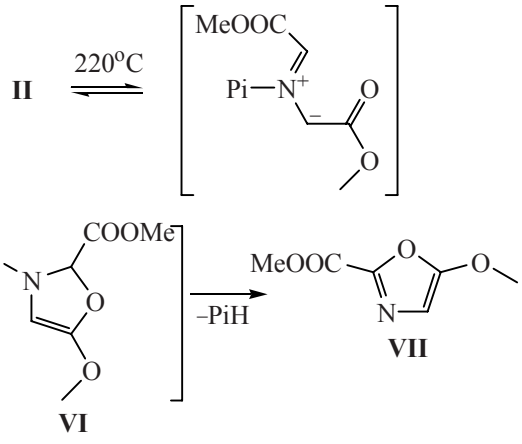


IIIb

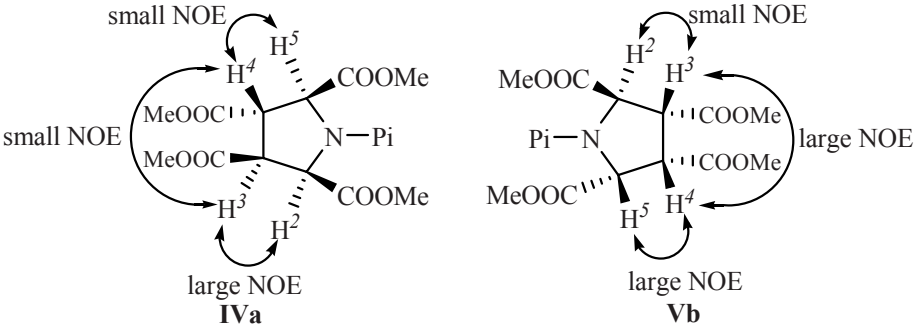


IIIc

Scheme 2.



Scheme 3.



data are in agreement with the presence in the ^{13}C NMR spectra of four carbon signals of pyrrolidine ring for adduct **IVa**, three for adducts **Vb, Vc** (signals of atoms C^3 and C^4 coincide), and only two for compounds **IVb**, **IVc**, and **Va**[1,2].

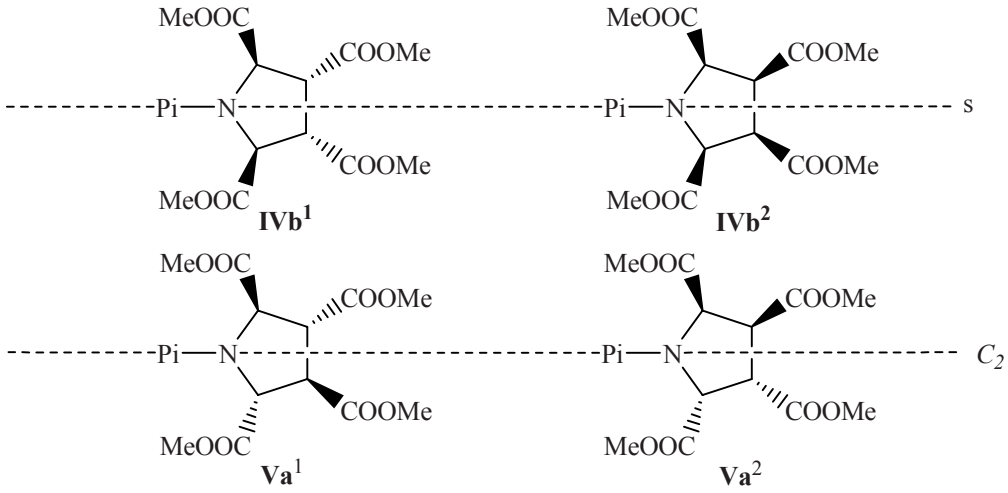
The assignment of structures of two unsymmetrical stereoisomeric compounds **IVa** and **Vb** was performed owing to 2D NOESY spectra. In the spectrum 2D NOESY of compound **Vb** obviously the relative NOE value for the pair of protons H^2–H^3 is considerably smaller that for the pairs H^3–H^4 and H^4–H^5 leading at once just to the assumed structure. Besides a cross-peak appears for the protons pair H^3–H^5 indicating their location on the same side of the pyrrolidine ring plane; this additionally confirms the validity of the assignment.

Inasmuch as with the given set of substituents only two structures without symmetry elements are possible the assignment to the second unsymmetrical adduct structure **IVa** with a pair of *cis*- and two pairs of *trans*-vicinal protons would be possible simply by exclusion. In full agreement with the above in 2D ^1H NOESY spectrum of compound **IVa** the relative NOE value for the pair of the *cis*-located vicinal protons H^2–H^3 is essentially larger than for the other two pairs of the *trans*-located protons H^3–H^4 and H^4–H^5 (Scheme 3).

For the three symmetrical stereoisomeric adducts **IVb** and **Va**[1,2] the choice should be made from four theoretically possible structures: **IVb**[1], **IVb**[2] with a mirror plane and protons enantiotopic in pairs, and **Va**[1], **Va**[2] with the second order rotation axis and protons equivalent in pairs (Scheme 4).

To distinguish the symmetry type of these compounds molecules we registered their ^{13}C NMR spectra at low temperature. At reduced temperature the sterically hampered rotation around the N–N bond became even slower; then the spectra of molecules lacking the axial symmetry (C_2 axis) should reveal the nonequivalence of two halves of the phthalimide fragment (cf. [1]). Thus in the ^{13}C NMR spectrum of compound **IVb** already at –10°C two signals of N–C=O appeared that at room temperature coincided with the base line, split in two the signal of atom C^b, and the signals of atoms C^a and C^c

Scheme 4.



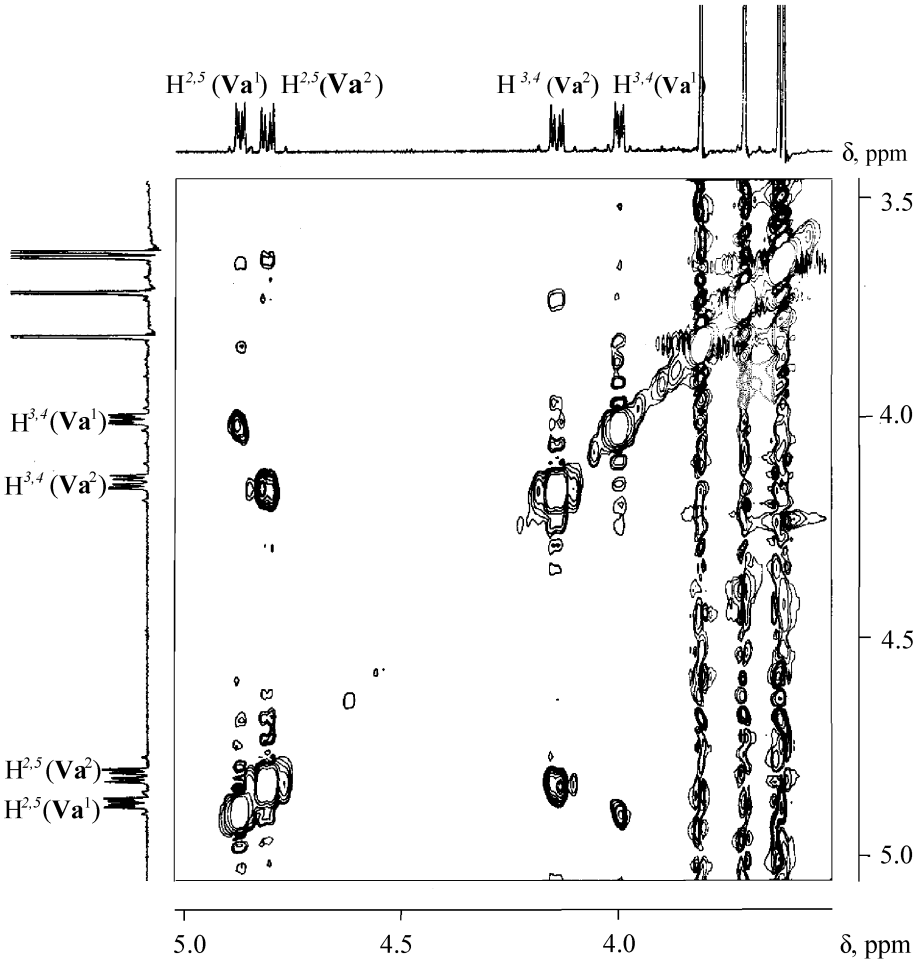


Fig. 1. 2D NOESY spectrum of the mixture of compounds **Va[1], Va[2]**, 1 : 1.

significantly broadened. At –40°C all the four signals were split in two unambiguously indicating that in the molecules of adduct **IVb** the mirror plane and not the symmetry axis was present. On the contrary, the spectra of compounds **Va[1]** and **Va[2]** remained virtually unchanged on cooling to –40°C. Therefore their molecules possess a symmetry axis C_2.

For the final assignment of structures of compounds **IVb** and **Va[1,2]** we registered the NOESY spectra of mixtures of equal amounts of compounds **Va[1], Va[2]** (Fig. 1) and **IVb,Va[1]**.

In the spectrum of the pair of compounds **Va[1], Va[2]** whose molecules have the axial symmetry it is well seen that the relative NOE value for proton pairs $H^{2,5}$-$H^{3,4}$ for compound **Va[2]** is essentially larger than in compound **Va[1]** that unambiguously indicates the *cis*-position of proton pairs $H^{2,5}$-$H^{3,4}$ in compound **Va[2]** and their more favorable *trans*-location in the main product, compound **Va[1]**. It turned out for the mixture **IVb** and **Va[1]** that the NOE values for proton pairs $H^{2,5}$-$H^{3,4}$ were nearly identical in both compounds. It shows their *trans*-position also in compound **IVb** that therefore has the structure **IVb[1]**, expectedly, for the formation under the severe thermolysis conditions the sterically strained structure **IVb[2]** as the sole product seems highly improbable.

In the analysis of the spatial structure of bicyclic compounds **IVc** and **Vc** we excluded from the consideration the versions with very unfavorable *trans*-junction of two five-membered rings. Under this restriction the structure of compound **Vc** unambiguously follows directly from the lack of symmetry elements in its molecule, and for adduct **IVc** only structures of the type **IVb[1]** or **IVb[2]** can be regarded having a symmetry plane and distinguished by the position of methoxy-carbonyl groups and N phenylmaleimide fragment with respect to the plane of the pyrrolidine ring. Evidently the *exo*-

structure is more probable, and it was assigned to compound **IVc**.

This assignment is well consistent with the already proved spatial structure of adduct **IVb** obtained from aziridine **I** with dimethyl maleate (**IIIb**). An additional argument to its validity are the results of XRD analysis of compound **IX** (Fig. 2) that we have obtained formerly [1] from (*E*)-1-phthalimidoaziridine-2,3-dinitrile (**VIII**) and dimethyl maleate (**IIIb**).

It is clear from Fig. 2, that in total agreement with the above stated the cyano and methoxycarbonyl groups in adduct **IX** are removed from each other. We can add to this statement that in no cases up till now (see [1]) we have detected the formation in such reactions of "*all-cis*" adducts (adducts of *endo*-type) having all four substituents on one side of the pyrrolidine ring.

The results obtained completely correspond to the two-stage mechanism we had previously suggested [1]: The beginning of the process was the permitted in the thermolysis by the rules of orbital symmetry conservation conrotatory opening, probably, reversible, of 2,3-disubstituted 1-phthal-imidoaziridines **I, II** into the corresponding azomethine ylides. Then the concerted cycloaddition of these 1,3-dipoles occurred to the multiple bonds of dipolarophiles **IIIa–IIIc**, and both stages proceeded completely stereo-specifically, and the cycloaddition was highly stereoselective. Thus in the reactions of *trans*-disubstituted aziridine **I** with dimethyl maleate (**IIIb**) and *N*-phenylmaleimide (**IIIc**) formed only the less sterically strained adducts **IVb, IVc** of *exo*-type. When the cycloaddition products are of comparable stability, like in the reaction of *cis*-aziridine **II** with dimethyl fumarate

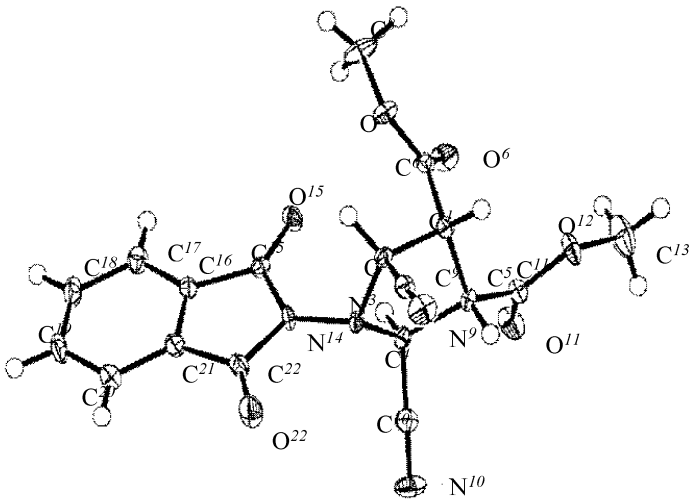
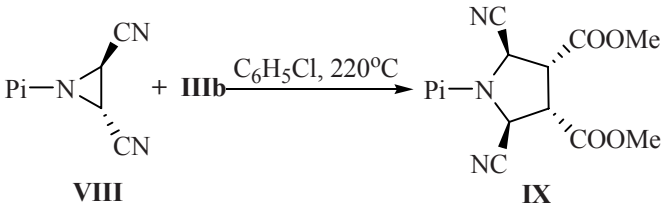


Fig. 2. Structure of compound **IX** according to XRD analysis.



(**IIIa**), both possible stereo-isomers, **Va[1]** and **Va[2]**, are present in the reaction mixture, but even here significantly prevails the less strained "*all-trans*" adduct **Va[1]**.

The limiting stage of the whole process is apparently the opening of the aziridine ring into the azomethine ylide whose rate should mainly be governed by the substituents in the three-membered ring. In this connection it is curious that the temperature of the start of the reaction with dipolarophiles of 1-phthalimidoaziridines **I, II** containing two methoxycarbonyl substituents is practically the same (220°C) as for the previously studied dinitrile [1], although it is assumed that CN group activates this process far stronger. The complete stereospecificity of both stages also should be stressed for it does not always occur with aziridines having other substituents at the nitrogen. It may be stated in conclusion that disregarding the severe reaction conditions the thermolysis of 2,3-disubstituted *N* phthalimidoaziridines in the presence of dipolarophile can really serve as a general stereospecific and highly stereoselective method of synthesis of *N*-aminopyrrolidine derivatives.

EXPERIMENTAL

^{1}H and ^{13}C NMR spectra were registered on a spectrometer Bruker DPX-300 (300 MHz), as internal reference served the signals of residual protons (δ 7.26 and 2.50 ppm) and carbon atoms (δ 77.16 and 39.50 ppm respectively) of solvents. Mass spectra were obtained on an instrument MKh-1303, the energy of ionizing electrons 70 eV. Elemental analysis was carried out on an automatic CHN-analyzer HP-185B. The composition of reaction mixtures and the fractions obtained at their separation, and also the purity of isolated products were checked by TLC on Polygram sil G/UV_{254} and Alugram sil G/UV_{254} plates purchased from Macherey-Nagel. Melting points were measured on a device Buchi Melting point B-540. *N*-Aminophthalimide was obtained by procedure [8].

Dimethyl *trans*-1-phthalimidoaziridine-2,3-dicarboxylate I. To a dispersion of 1.3 g (9.4 mmol) of anhydrous potassium carbonate in solution of 432 mg

(3 mmol) of dimethyl fumarate (**IIIa**) in 40 ml of dichloromethane at room temperature (18–23°C) within 40 min was added by portions of 10–15 mg by turns 486 mg (3 mmol) of *N*-aminophthalimide and 1.33 g (3 mmol) of lead tetraacetate. The reaction mixture was stirred for 1 h more, filtered through a thin bed of silica gel, and the solution was distilled off on a rotary evaporator. Yield 775 mg (85%), mp 158°C (149–150°C [3], 151°C [4, 5]). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.60 d (1H, CH, *J* 4.8 Hz), 3.74 s (3H, MeO), 3.86 s (3H, MeO), 3.96 d (1H, CH, *J* 4.8 Hz), 7.65–7.79 m (4H, Pi). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 42.65 and 44.65 (2CH), 53.13 and 53.27 (2MeO), 123.33 (C^b), 129.90 (C^a), 134.21 (C^c), 164.01 (CON), 165.25 and 166.52 (2COO). Mass spectrum, *m/z* (I_{rel}, %): 304 (30) $[M]^+$, 245 (100), 201 (40), 132 (38), 130 (38), 113 (60), 105 (92), 76 (100). Found, %: C 55.42; H 3.99; N 9.21. $C_{14}H_{12}N_2O_6$. Calculated, %: C 56.27; H 3.98; N 9.21.

Dimethyl *cis*-1-phthalimidoaziridine-2,3-dicarboxylate II. To a dispersion of 1.3 g (9.4 mmol) of anhydrous potassium carbonate in cooled to 0°C solution of 1.13 ml (1.3 g, 9 mmol) of dimethyl -maleate (**IIIb**) in 40 ml of dichloromethane at room temperature (18–23°C) within 40 min was added by portions of 10–15 mg by turns 486 mg (3 mmol) of *N*-aminophthalimide and 1.33 g (3 mmol) of lead tetraacetate. The reaction mixture was stirred for 1 h more, filtered through a thin bed of silica gel, and the solution was distilled off on a rotary evaporator. The oily residue was dissolved in 5 ml of ethyl ether and was left overnight in a refrigerator. On the next day the separated precipitate was recrystallized from methanol. Yield 310 mg (34%), mp 140°C (137°C [4, 5]). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.64 s (2H, 2CH), 3.86 s (6H, 2MeO), 7.70–7.85 m (4H, Pi). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 44.93 (CH), 53.05 (MeO), 123.52 (C^b), 129.72 (C^a), 134.53 (C^c), 163.98 (CON), 165.45 (COO). Mass spectrum, *m/z* (I_{rel}, %): 304 (5) $[M]^+$, 245 (60), 213 (12), 113 (20), 104 (100), 76 (80). Found, %: C 55.26; H 4.03; N 9.10. $C_{14}H_{12}N_2O_6$. Calculated, %: C 56.27; H 3.98; N 9.21.

Tetramethyl *rel*-(2*R*,3*S*,4*S*,5*S*)-1-phthalimidopyrrolidine-2,3,4,5-tetra-carboxylate (IVa). A solution of 304 mg (1 mmol) of aziridine **I** and 216 mg (1.5 mmol) of dimethyl fumarate (**IIIa**) in 10 ml of anhydrous benzene in a sealed ampule was heated at 220°C for 3 h. On completion of the reaction the solvent was distilled off in a vacuum on a rotary evaporator. The obtained dry residue was subjected to chromatography on a column packed with 45 g of silica gel (gradient elution with a mixture CH_2Cl_2–THF, from 1:0 to 20:1 v/v). We obtained 100 mg (33%) of initial *N*-phthalimidoaziridine **I** (R_f 0.65, CH_2Cl_2), 40 mg (27%) of phthalimide (R_f 0.25, CH_2Cl_2), and 130 mg (29%) of compound **IVa** (R_f 0.1, CH_2Cl_2), mp 136–138°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.68 s (3H, MeO), 3.70 s (6H, 2MeO), 3.79 s (3H, MeO), 4.06 t (1H, H^4, *J* 8.4 Hz), 4.14 t (1H, H^3, *J* 8.4 Hz), 4.50 d (2H, $H^{2,5}$, *J* 8.4 Hz), 7.50–7.90 m (4H, Pi). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 46.82 and 47.17 ($C^{3,4}$); 52.66, 52.72, 52.91, 52.96 (4MeO); 66.39 and 66.67 ($C^{2,5}$); 123.87 (C^b), 129.97 (C^a), 134.75 (C^c), 169.00, 169.51, 169.64, 170.92 (4COO). Signal of NC=O was not seen due to slow rotation of phthalimide fragment. Mass spectrum, *m/z* (I_{rel}, %): 448 (1) $[M]^+$, 357 (31), 302 (34), 297 (100), 270 (41), 59 (25). Found, %: C 53.33; H 4.49; N 6.21. $C_{20}H_{20}N_2O_{10}$. Calculated, %: C 53.57; H 4.50; N 6.25.

Tetramethyl *rel*-(2*R*,3*R*,4*S*,5*S*)-1-phthalimidopyrrolidine-2,3,4,5-tetracarboxylate (IVb). A solution of 304 mg (1 mmol) of aziridine **I** and 0.19 ml (216 mg, 1.5 mmol) of dimethyl maleate (**IIIb**) in 10 ml of anhydrous chlorobenzene was heated for 3 h in a thick-walled glass reactor at 220°C. On completion of the reaction the solvent was distilled off in a vacuum on a rotary evaporator. The obtained dry residue was subjected to chromatography on a column packed with 45 g of silica gel (gradient elution with a mixture CH_2Cl_2–Et_2O, from 1:0 to 9:1 v/v). We obtained 35 mg (20%) of phthalimide (R_f 0.25, CH_2Cl_2), and 170 mg (38%) of compound **IVb** (R_f 0.15, CH_2Cl_2), mp 121–124°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.68 s (6H, 2MeO), 3.78 s (6H, 2MeO), 3.86 m (2H, $H^{3,4}$), 4.64 m (2H, $H^{2,5}$), 7.70–7.90 m (4H, Pi). ^{13}C NMR spectrum ($CDCl_3$, 20–25°C), δ, ppm: 45.64 ($C^{3,4}$), 52.72 (2MeO), 53.02 (2MeO), 65.81 ($C^{2,5}$), 123.80 (C^b), 129.95 (C^a), 134.70 (C^c), 169.51 (2COO), 170.39 (2COO). Signal of NC=O was not seen due to slow rotation of phthalimide fragment. ^{13}C NMR spectrum ($CDCl_3$, –40°C), δ, ppm: 45.04 ($C^{3,4}$), 53.10 (2MeO), 53.46 (2MeO), 65.46 ($C^{2,5}$), 123.60 and 124.22 ($C^{b,b'}$), 129.07 and 129.28 ($C^{a,a'}$), 134.81 and 135.02 ($C^{c,c'}$), 165.29 and 166.49 (CON and C′ON), 169.58 (2COO), 170.53 (2COO). Mass spectrum, *m/z* (I_{rel}, %): 448 (1) $[M]^+$, 302 (100), 297 (86), 270 (15), 239 (25), 130 (11), 104 (19), 76 (15), 59 (27). Found, %: C 53.63; H 4.46; N 6.28. $C_{20}H_{20}N_2O_{10}$. Calculated, %: C 53.57; H 4.50; N 6.25.

Dimethyl *rel*-(1*R*,2*R*,4*S*,5*S*)-6,8-dioxo-7-phenyl-3-phthalimido-3,7-diazabicyclo-[3.3.0]octane-2,4-dicarboxylate (IVc). A solution of 304 mg (1 mmol) of aziridine **I** and 260 mg (1.5 mmol) of phenylmaleimide

(**IIIc**) in 10 ml of anhydrous benzene was heated for 3 h in a sealed ampoule at 220°C. On completion of the reaction the solvent was distilled off in a vacuum on a rotary evaporator. The obtained dry residue was subjected to chromatography on a column packed with 45 g of silica gel (eluent a mixture CH_2Cl_2–dioxane, 70 : 3 v/v). We obtained 30 mg (20%) of phthalimide (R_f 0.25, CH_2Cl_2) and 230 mg (48%) of compound **IVc** (R_f 0.20, CH_2Cl_2), mp 237–239°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.76 s (6H, 2MeO), 4.18 m (2H, H^{1,5}), 4.57 m (2H, H^{2,4}), 7.40–7.48 m (3H, H^{m,p}), 7.48–7.55 m (2H, H^{o}), 7.75–7.95 m (4H, Pi). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 46.38 (C^{1,5}), 53.35 (2MeO), 67.61 (C^{2,4}), 124.03 (C^{b}), 126.78 and 129.42 (C^{o,m}), 129.11 (C^{p}), 129.70 (C^{a}), 131.72 (C^{i}), 134.92 (C^{c}), 169.07 (COO), 174.86 (CON). Signal of NC=O was not seen due to slow rotation of phthalimide fragment. Mass spectrum, *m/z* (I_{rel}, %): 477 (4) $[M]^+$, 447 (62), 445 (74), 419 (21), 418 (79), 390 (100), 389 (52), 333 (58), 239 (100), 152 (33), 119 (25), 104 (42), 76 (35), 59 (31). Found, %: C 60.25; H 4.03; N 8.67. $C_{24}H_{19}N_3O_8$. Calculated, %: C 60.38; H 4.01; N 8.80.

Reactions of dimethyl *cis*-1-phthalimidoaziridine-2,3-dicarboxylate II with dimethyl fumarate. A solution of 304 mg (1 mmol) of aziridine **II** and 216 mg (1.5 mmol) of dimethyl fumarate (**IIIa**) in 10 ml of anhydrous benzene in a sealed ampule was heated at 220°C for 3 h. On completion of the reaction the solvent was distilled off in a vacuum on a rotary evaporator. The obtained dry residue was subjected to chromatography on a column packed with 45 g of silica gel (gradient elution with a mixture CH_2Cl_2–Et_2O, from 1 : 0 to 9 : 1 v/v). We obtained 35 mg (22%) of **methyl 5-methoxy-1,3-oxazole-2-carboxylate (VII)** (R_f 0.35, CH_2Cl_2), 55 mg (37%) of phthalimide (R_f 0.25, CH_2Cl_2), 50 mg (11%) **tetramethyl *rel*-(2*R*,3*R*,4*R*,5*R*)-1-phthalimidopyrrolidine-2,3,4,5-tetra-carboxylate (Va^1)** (R_f 0.15, CH_2Cl_2), and 50 mg (11%) of a mixture of compound **Va^1** and **tetramethyl *rel*-(2*R*,3*S*,4*S*,5*R*)-1-phthalimidopyrrolidine-2,3,4,5-tetracarboxylate (Va^2)** (R_f 0.13, CH_2Cl_2) in a ratio 7:4 (according to ^{1}H NMR data). Overall yield of adduct **Va^1** 18%, of its stereoisomer **Va^2** 4%.

Pyrrolidine Va^1. mp 115–117°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.63 s (6H, 2MeO), 3.82 s (6H, 2MeO), 4.00 m (2H, H^{3,4}), 4.87 m (2H, H^{2,5}), 7.70–7.90 m (4H, Pi). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 46.93 (C^{3,4}), 52.92 (2MeO), 53.09 (2MeO), 64.37 (C^{2,5}); 123.74 (C^{b}), 130.01 (C^{a}), 134.67 (C^{c}), 166.49 (CON), 169.32 (2COO), 171.02 (2COO). Mass spectrum, *m/z* (I_{rel}, %): 448 (2) $[M]^+$, 389 (12), 357 (43), 302 (57), 297 (100), 270 (62), 239 (23), 210 (12), 166 (12), 130 (14), 104 (18), 76 (16), 59 (25). Found, %: C 53.62; H 4.54; N 6.15. $C_{20}H_{20}N_2O_{10}$. Calculated, %: C 53.57; H 4.50; N 6.25.

Pyrrolidine **Va^2** in the mixture with compound **Va^1**. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.62 s (6H, 2MeO), 3.71 s (6H, 2MeO), 4.15 m (2H, H^{3,4}), 4.82 m (2H, H^{2,5}), 7.70–7.90 m (4H, Pi). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 45.80 (C^{3,4}), 52.69 (4MeO), 63.46 (C^{2,5}), 123.82 (C^{b}), 129.91 (C^{a}), 134.77 (C^{c}), 166.24 (CON), 169.35 (2COO), 170.27 (2COO).

Oxazole (VII). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.96 s (3H, MeO), 4.00 s (3H, MeO), 6.35 s (1H, CH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 53.02 (MeO), 59.00 (MeO), 102.0 (CH), 143.12 (C=N), 155.79 (COO), 162.11 (COO). Mass spectrum, *m/z* (I_{rel}, %): 157 (38) $[M]^+$, 126 (15), 68 (28), 59 (89), 55 (23), 54 (38), 43 (100). Found, %: C 46.20; H 4.70; N 8.81. $C_6H_7NO_4$. Calculated, %: C 45.86; H 4.46; N 8.92.

Tetramethyl *rel*-(2*R*,3*R*,4*S*,5*R*)-1-phthalimidopyrrolidine-2,3,4,5-tetracarboxylate (Vb). A solution of 304 mg (1 mmol) of aziridine **II** and 0.19 ml (216 mg, 1.5 mmol) of dimethyl maleate (**IIIb**) in 10 ml of anhydrous chlorobenzene was heated for 3 h in a thick-walled glass reactor at 220°C. On completion of the reaction the solvent was distilled off in a vacuum on a rotary evaporator. The obtained dry residue was subjected to chromatography on a column packed with 40 g of silica gel (gradient elution with a mixture CH_2Cl_2–Et_2O, from 1:0 to 9:1 v/v). We obtained 30 mg (10%) of initial aziridine **II** (R_f 0.27, CH_2Cl_2), 60 mg (41%) of phthalimide (R_f 0.25, CH_2Cl_2), and 154 mg (34%) of oily product **Vb** (R_f 0.15, CH_2Cl_2). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.57 s (3H, MeO), 3.68 s (3H, MeO), 3.74 s (3H, MeO), 3.76 s (3H, MeO), 3.86 d.d (1H, H^4, *J* 8.0, 6.5 Hz), 4.05 d.d (1H, H^3, *J* 8.0, 8.0 Hz), 4.89 d (1H, H^5, *J* 6.5 Hz), 5.08 d (1H, H^2, *J* 8.0 Hz). 7.70–7.90 m (4H, Pi). ^{13}C NMR spectrum ($CDCl_3$, 20–25°C), δ, ppm: 45.43 (C^{3,4}), 52.38, 52.65, 52.94 (4MeO), 62.84 and 64.71 (C^{2,5}), 123.67 (C^{b}), 129.94 (C^{a}), 134.61 (C^{c}), 166.51 (CON), 168.90 (COO), 169.51 (COO), 169.55 (COO), 169.81 (COO). Mass spectrum, *m/z* (I_{rel}, %): 448 (3) $[M]^+$, 389 (51), 313 (12), 302 (100), 297 (73), 270 (27), 242 (17), 239 (46), 236 (17), 198 (15), 166 (12), 130 (22), 104 (29). Found, %: C 52.09; H 4.55; N 5.92. $C_{20}H_{20}N_2O_{10}$. Calculated, %: C 53.57; H 4.50; N 6.25.

Dimethyl *rel*-(1*R*,2*R*,4*R*,5*S*)-6,8-dioxo-7-phenyl-3-phthalimido-3,7-diazabicyclo-[3.3.0]octane-2,4-

dicarboxylate (Vc). A solution of 304 mg (1 mmol) of aziridine **II** and 260 mg (1.5 mmol) of phenylmaleimide (IIIc) in 10 ml of anhydrous chlorobenzene was heated for 3 h in a thick-walled glass reactor at 220°C. On completion of the reaction the solvent was distilled off in a vacuum on a rotary evaporator. The obtained dry residue was subjected to chromatography on a column packed with 40 g of silica gel (gradient elution with a mixture CH_2Cl_2–Et_2O, from 1 : 0 to 3 : 1 v/v). Yield 420 mg (88%), mp 215–216°C, R_f 0.3 (CH_2Cl_2–Et_2O, 10 : 1 v/v). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.67 s (3H, MeO), 3.72 s (3H, MeO), 3.84 d.d (1H, H^1, *J* 8.7, 1.6 Hz), 3.93 d.d (1H, H^5, *J* 8.5, 8.0 Hz), 4.62 d (1H, H^2, *J* 1.5 Hz), 5.31 d (1H, H^4, *J*8.0 Hz), 7.23–7.55 m (5H, Ph), 7.70–7.85 m (4H, Pi). ^{1}H NMR spectrum (CD_3CN), δ, ppm: 3.57 s (3H, MeO), 3.62 s (3H, MeO), 3.84 d.d (1H, H^1, *J* 8.7, 1.5 Hz), 4.04 d.d (1H, H^5, *J* 8.7, 8.0 Hz), 4.41 d (1H, H^2, *J* 1.5 Hz), 5.25 d (1H, H^4, *J* 8.0 Hz), 7.20–7.30 m (2H, H^m), 7.40–7.60 m (3H, $H^{o,p}$), 7.91 C (4H, Pi). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 44.81 ($C^{1,5}$), 52.73 (MeO), 53.32 (MeO), 61.66 and 64.66 ($C^{2,4}$), 123.78 (C^b), 126.92 (C^o), 129.25 (C^p), 129.50 (C^m), 129.90 (C^a), 131.75 (C^i), 134.76 (C^c), 166.18 (CON Pi); 168.68, 174.43, 175.00 (2COO and 2CON). Mass spectrum, *m/z* (I_{rel}, %): 477 (5) $[M]^+$, 418 (63), 330 (77), 239 (100), 152 (20), 104 (26), 80 (17), 76 (20). Found, %: C 59.98; H 4.10; N 8.62. $C_{24}H_{19}N_3O_8$. Calculated, %: C 60.38; H 4.01; N 8.80.

REFERENCES

1. Kuznetsov, M.A., Pan'kova, A.S., Ushkov, A.V., and Selivanov, S.I., *Zh. Org. Khim.,* 2008, vol. 44, p. 1807.
2. Gladstone, W.A.F., Norman, R.O.C. *J. Chem. Soc. C,* 1966, p. 1536.
3. Siu, T., Yudin, A.K., *J. Am. Chem. Soc.,* 2002, vol. 124, p. 530.
4. Loznevaya, Yu.G., Belov, V.N., and Kuznetsov, M.A., Abstracts of Papers, *IV Vsesoyuzn. konf. po khimii karbenov* (4th All-Union Conf. on Carbene Chemistry), Moscow: Nauka, 1987, p. 56.
5. Semenovskii, V.V., *Cand. Sci. (Chem.) Dissertation*, Leningrad, 1991.
6. Atkinson, R.S. and Malpass, J.R., *J. Chem. Soc., Perkin Trans. 1,* 1977, p. 2242.
7. Person, H., Luanglath, K., Baudru, M., and Foucaud, A., *Bull. Soc. Chim*., 1976, p. 1989.
8. Drew, N.D.K. and Hatt, N.H., *J. Chem. Soc.,* 1937, p. 16.