Chemistry of Heterocyclic Compounds, Vol. 47, No. 2, May, 2011 (Russian Original Vol. 47, No. 2, February, 2011)

INTRA- AND INTERMOLECULAR THERMAL TRANSFORMATIONS OF 2-ACYL- AND 2-ALKOXYCARBONYL-N-PHTHALIMIDOAZIRIDINES*

M. A. Kuznetsov[1] and V. V. Voronin[1]**

Heating 2-acyl- and 2-alkoxycarbonyl-N-phthalimidoaziridines leads to substituted oxazoles in 45-65% yield. Only esters of oxazolecarboxylic acids are formed when the aziridine contains acyl and alkoxy groups. The thermolysis of the same aziridines in the presence of N-phenylmaleimide and the dimethyl ester of acetylenedicarboxylic acid gives both oxazoles and the products of 1,3-dipolar cycloaddition from aziridines with two substituents at the carbon atoms but only oxazoles from trisubstituted aziridines.

Keywords: N-aminopyrrolidines, N-aminopyrrolines, aziridines, azomethinylids, 1,3-oxazoles, pyrroles, 1,3-dipolar cycloaddition.

The thermally or photochemically induced dissociation of the C−C bond in the strained aziridine ring leads to 1,3-dipoles, which have been termed azomethinylids [1]. The addition of these species at multiple bonds of dipolarophiles yields various five-membered nitrogen heterocycles [2]. The generation of azomethinylids upon heating derivatives of N-phthalimidoaziridine and subsequent 1,3-dipolar cycloaddition have been demonstrated experimentally [3-5]. On the other hand, heating N-phthalimidoaziridines having acyl [6] or alkoxycarbonyl substituents [7] at the carbon atoms of the aziridine ring in the absence of dipolarophiles leads to oxazoles, which may be attributed to a 1,5-electrocyclization of the intermediate acylazomethinylids accompanied by loss of the phthalimide group.

Thus, two types of thermal transformations are possible for acyl and alkoxycarbonyl derivatives of N-phthalimidoaziridine: 1) 1,3-dipolar cycloaddition and 2) rearrangement to give oxazoles. These reactions may compete and their preparative value will depend on which pathway predominates. In the present work, we studied both the intra- and intermolecular thermal transformations of 2-acyl- and 2-alkoxy-N-phthalimido-aziridines.

We selected aziridines **1a-f** for this study. The corresponding oxazole has already been obtained in 60% yield upon heating aziridine **1a** [6]. However, the reaction of this aziridine with dipolarophiles has not been investigated. Aziridines **1b**,**c** were selected in light of the possibility of obtaining not readily available spiro-fused heterocyclic structures as the result of 1,3-dipolar cycloaddition. We considered the possibility of

* Dedicated to Leonid Isaakovich Belen'kii on the occasion of his eightieth birthday.

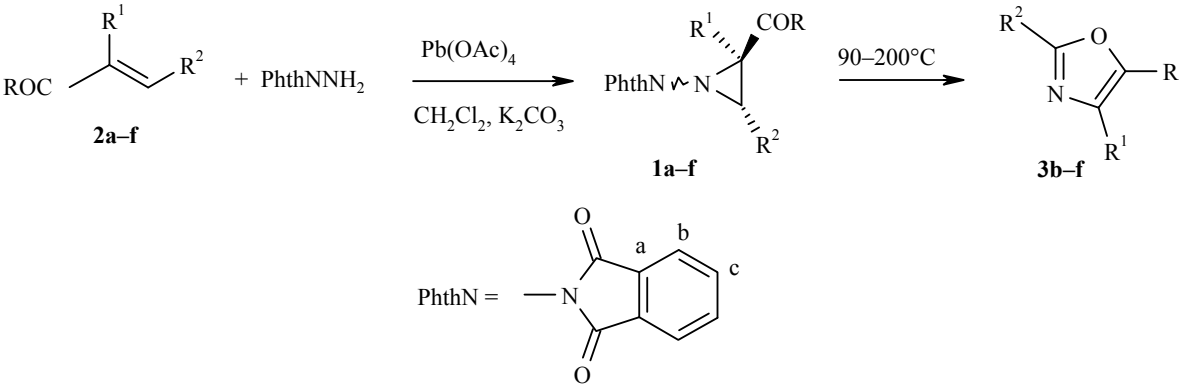
** To whom correspondence should be addressed, e-mail: mak@mail.wplus.net.

[1]St. Petersburg State University, 26 Universitetskii Pr., Stary Petergof, St. Petersburg 198504, Russia.

Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 2, pp. 219-230, February, 2011. Original article submitted January 26, 2011.

alternative transformations in the case of aziridine **1d** due to the presence of a C=C bond in the side chain. In the case of aziridines **1e**,**f**, we attempted to clarify which of the acyl or alkoxycarbonyl group would be more active in the rearrangement to an oxazole. N-Phenylmaleimide and the dimethyl ester of acetylenedicarboxylic acid (DMAD) served as the very active dipolarophiles. These reagents often serve as traps.

N-Phthalimidoaziridines **1a-f** were obtained by oxidative aminoaziridination of the corresponding unsaturated carbonyl compounds using a 50% excess of N-aminophthalimide at -20°C by a standard procedure [8].



1a, **2a** R = Me, R^1 = H, R^2 = Ph, **1**–**3 b**–**d** R^2 = Ph, **b** R+R^1 = $(CH_2)_4$, **c** R+R^1 = $(CH_2)_3$,
d R = $C^{\alpha}H{=}C^{\beta}HPh$, R^1 = H; **e** R = Ph, R^1 = H, R^2 = CO_2Me; **f** R = Me, R^1 = CO_2Et, R^2 = Ph

Aziridines **1b-f** had not been described previously or were only noted in the literature. Hence, these compounds were characterized by elemental analysis and spectral data. Two pairs of doublets at 3.7-5.0 ppm, corresponding to the protons of the aziridine ring of the two invertomers, are seen in the ^{1}H NMR spectra of **1a**,**d,** and **1e** due to slow inversion of the endocyclic nitrogen atom [9] on the NMR time scale. The ratio of these invertomers is 1:0.06 for **1a**, 1:0.07 for **1d**, and 1:0.7 for **1e**. Only the signals of the major invertomer were reliably identified in the ^{13}C NMR spectra of compounds **1a**,**d**. The content of the minor invertomer is apparently so small for **1b**,**c**, and **1f** that its signals could not be detected in the NMR spectra.

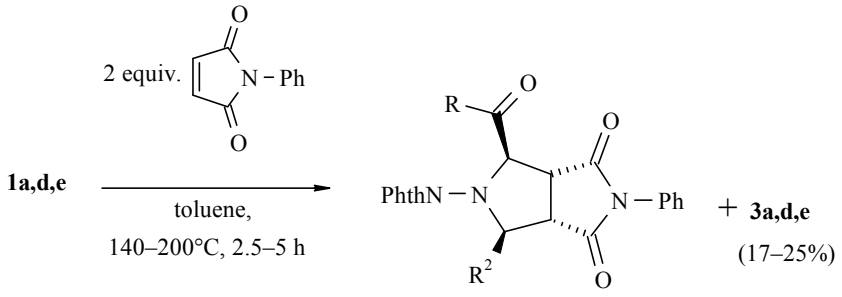
Steric considerations suggest that the invertomer, in which the phthalimide group is in the *cis* position relative to the less bulky COR group is the major form for aziridines **1a**,**d**, while the only observed invertomer in the case of trisubstituted aziridines **1b**,**c**, and **1f** has *cis* orientation of the phthalimide group and aziridine proton. The invertomers of aziridine **1e** exist in comparable amounts since the effective volumes of the substituents at the carbon atoms of the aziridine ring in this case are similar (both substituents have a carbonyl group next to the three-membered ring). The coupling constants of compounds **1a**,**d**, and **1e** (4.4-4.9 Hz for the major invertomer and 4.7-5.8 Hz for the minor invertomer) indicate *trans* arrangement of the aziridine protons, which is in accord with the well-known steric specificity of oxidative aminoaziridination [3-10]. We should also note that the signals of the phthalimide group carbon atoms in the ^{13}C NMR spectra of aziridines **1a-f** are broadened as a consequence of a second hindered process, which is slow on the NMR time scale, namely, rotation about the tetrasubstituted N–N bond [4, 5, 10]. The signals for atoms C(a) and NCO in the spectrum of aziridine **1c** are not seen at all due to strong broadening.

Heating aziridines **1b-f** in toluene at 90-200°C in hermetically sealed vessels for from 45 min to 5 h leads to oxazoles **3b-f** in 45-65% yield. The transformation to oxazoles for aziridines **1e**,**f**, which have both acyl and alkoxycarbonyl substituents, proceeds only with involvement of the acyl groups. Oxazoles **3b**,**f** have already been reported and identified by comparison of the NMR spectra with literature data. We fully characterized oxazoles **3c-e** since **3c**,**e** were obtained for the first time and only the melting point of oxazole

3d had been reported. It is interesting that aziridines **1b**,**c** begin to decompose at a significant rate already at 150°C but considerable tar formation is noted and the yields of oxazoles **3b**,**c** are only 20-28%. By raising the reaction temperature to 180°C, we were able to increase the yields of the desired oxazole products to 45-54%. This finding suggests that the rate of ring opening of aziridines to azomethinylids increases more rapidly with increasing temperature than the rate of competing side reactions.

Thus, the thermolysis of all the acylazirdines obtained in this study leads to the corresponding oxazoles. When the aziridine molecule has both acyl and alkoxycarbonyl groups, the reaction proceeds only with involvement of the acyl group.

The thermolysis of aziridines **1a**,**d**, and **1e** under the same conditions but in the presence of two equivalents of N-phenylmaleimide leads to mixtures of adducts **4a**,**4d**, and **4e** and oxazoles **3a**,**d**, and **3e**.

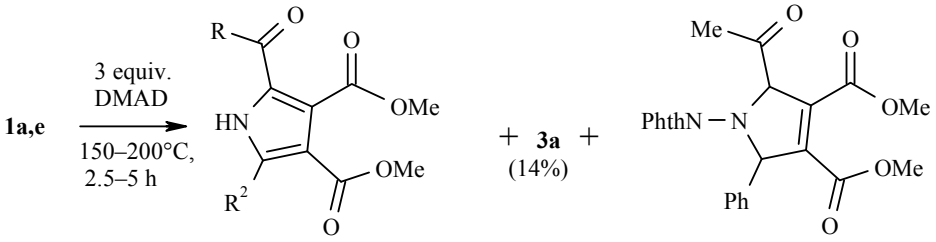


4a,d,e (32–59%)

4 a R = Me, R^2 = Ph; **d** R = –CH=CHPh, R^2 = Ph; **e** R = Ph, R^2 = CO_2Me

We should note that, as in the case of the starting N-phthalimidoaziridines, the signals for the phthalimide group NCO atoms are lacking in the ^{13}C NMR spectra of pyrrolidines **4a**,**d**,**e**, while the signals for C(a) atoms are lacking in the spectra of compounds **4d**,**e**. In addition, the signals for the C(b) atoms are also lacking in the spectrum of **4d**. These findings are attributed to hindered rotation about the N-N bond of the tetrasubstituted hydrazine fragment in these compounds.

The three-dimensional structure of cycloadducts **4a**,**d**, and **4e** was established from the two-dimensional ^1H NOESY spectra. Comparison of the NOE data for the protons of pyrrolidine rings in **4a**,**d**,**e** indicated that these compounds are *exo* adducts with *cis* orientation of the substituents of the former aziridine ring.



5a,e (35–44%) **6a**

5a R = Me, R^2 = Ph; **e** R = Ph, R^2 = CO_2Me

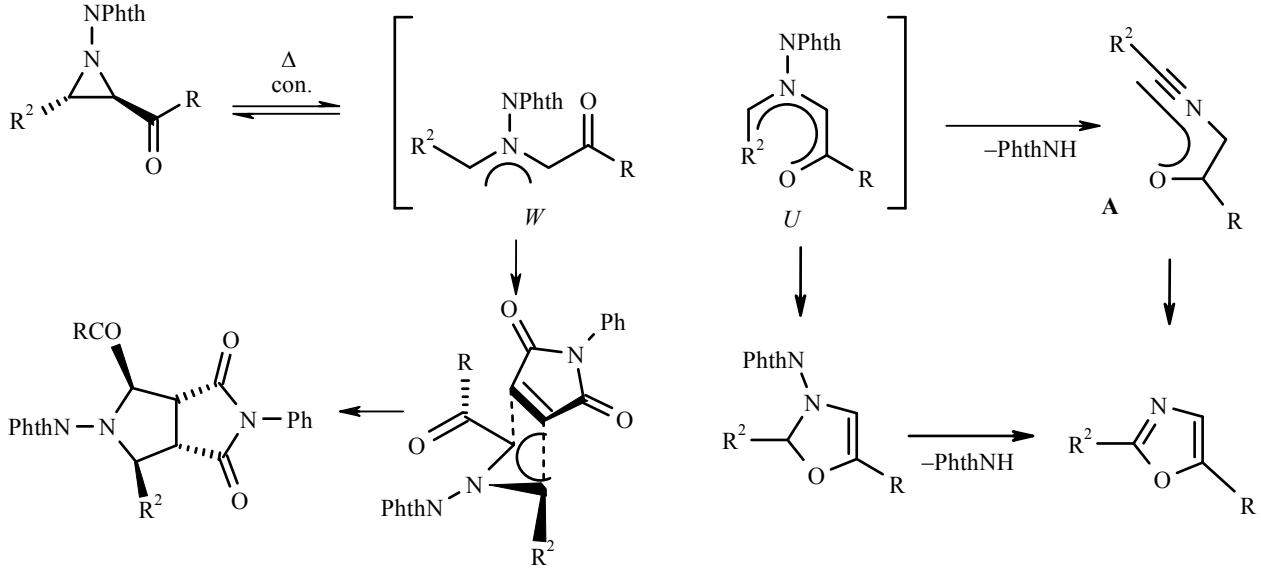
Heating aziridines **1a**,**e** in the presence of DMAD leads to pyrroles **5a**,**e**. While oxazole **3a** was isolated from the reaction with aziridine **1a**, no formation of oxazole **3e** was detected for aziridine **1e**. Furthermore, in the case of aziridine **1a**, the ^1H NMR spectrum of the reaction mixture showed an additional set of signals with singlets at 2.55, 3.64, and 3.79 ppm and doublets at 5.05 and 6.10 with coupling constant 5.8 Hz; the intensity

ratio was 175 3:3:3:1:1. The chemical shifts and coupling constant of the doublets correspond to protons H-2 and H-5 of the pyrroline ring in 1-phthalimido-2,3,4,5-tetrasubstituted 3-pyrrolines [10], while the singlets clearly correspond to the protons of the acetyl and two methoxycarbonyl groups. Hence, we assigned the structure of 3-pyrroline **6a** to this product. Unfortunately, this unstable compound could not be isolated either by chromatography or crystallization. One of the products of the decomposition of this product is apparently pyrrole **5a** since its preparative yield proved much higher than expected from the ^{1}H NMR spectrum of the reaction mixture*.

Thermolysis of aziridines **1b**,**c** in the presence of both N-phenylmaleimide and DMAD did not give the expected cycloadducts. Heavy tar formation was noted in the course of these reactions. Chromatographic separation of the reaction mixtures gave benzaldehyde, phthalimide, and oxazoles **3b**,**c**. Varying the reaction temperature in the range 150-190°C and the excess of dipolarophiles from two to nine equivalents did not yield cycloadducts.

The ^{1}H NMR spectra taken immediately after cooling and evaporation of the reaction mixtures indicated that the only product in the thermolysis of aziridine **1f** in the presence of the same dipolarophiles was oxazole **3f**. Heating aziridine **1d** in the presence of DMAD also did not lead to the expected cycloadduct. Only the signals of oxazole **3d** were reliably identified in the ^{1}H NMR spectrum of the reaction mixture.

As already noted in our previous work [4, 5], the reaction of *trans*-disubstituted aziridines **1a**,**d**, and **1e** with N-phenylmaleimide leads to *exo*-adducts with *cis* orientation of the substituents at the carbon atoms of the former aziridine ring, which is in accord with the reaction scheme given below.



con. - conrotary opening

The first reaction step features conrotatory opening of aziridine ring to give *U*- and *W*-azomethinylids. The observed steric specificity of the addition of the dipoles to N-phenylmaleimide indicates that, under the reaction conditions, their isomerization to *S*-dipoles does not occur. In principle, both the *W*-dipole and *U*-dipole can add to the dipolarophiles but the reaction for N-phenylmaleimide involving the *W*-dipole is more likely since a sterically unhindered *exo* approach to the dipolarophiles is possible for this form. Evidence for such a steric course of the reaction is also found in the *exo* arrangement of the substituents in the cycloadducts. The *U*-dipole may cyclize to give an oxazoline, from which an oxazole is formed through loss of a phthalimide

* The ^{1}H NMR spectrum of the reaction mixture indicated the **5a/3a/6a** product ratio was 22:38:40.

molecule or rearrange into nitrilylid **A**, which then is capable of cyclizing directly into the oxazole. The completely analogous formation of pyrroles observed in the reactions with DMAD may proceed either through loss of a phthalimide molecule from initially-formed pyrrolines or as a result of addition to DMAD of nitrilylid **A**.

The lack of cycloadducts and heavy tar formation in the thermolysis of the spiroaziridines probably occur since conversion to an oxazole is preferred for the (*Z,Z*)-dipole, which is analogous to the *U*-dipole, while the addition of the (*E,E*)-dipole to the dipolarophiles does not proceed due to steric hindrance.

In the case of trisubstituted aziridine **1f**, the rate of addition of the intermediate azomethinylid to the dipolarophiles under the reaction conditions is apparently low but, the decomposition reactions also proceed slowly due to good stabilization of the dipole by the electron-withdrawing substituents so that conversion of **1f** into an oxazole proves the most rapid process.

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra were taken on a Bruker DPX-300 spectrometer at 300 and 75 MHz, respectively, for solutions in $CDCl_3$ using the signal of the residual protons in the solvent as the internal standard (δ 7.26 ppm) in the ^{1}H NMR spectra and signal of the solvent carbon atom (δ 77.16 ppm) as the internal standard in the ^{13}C NMR spectra [11]. The elemental analyses were carried out using a Hewlett-Packard HP-185B automatic CHN analyzer. The high-resolution ESI mass spectra were taken on a Bruker micrOTOF mass spectrometer. The composition of the reaction mixtures and separation fractions as well as the purity of the isolated products were monitored by thin-layer chromatography on Macherey-Nagel POLYGRAM SIL G/UV_{254} and ALUGRAM SIL G/UV_{254} plates.

N-Aminophthalimide was obtained according to Drew and Hatt [12]. (*E*)-2-Benzylidenecyclohexanone (**2b**) [13] and (*E*)-2-benzylidenecyclopentanone (**2c**) [14] were synthesized by a method analogous to the procedure of Tietze and Eicher [15]. Benzalacetone (**2a**) and dibenzalacetone (**2d**) were prepared according to Golodnikov and Mandel'shtam [16]. Treatment of β-benzoylacrylic [(2*E*)-4-oxo-4-phenylbut-2-enoic] acid [17] with thionyl chloride and subsequent addition of excess methanol gave the corresponding methyl ester **2e** [18]. The ethyl ester of (*Z*)-2-benzylidene-3-oxobutanoic acid **2f** was prepared according to Anaç et al. [19]. The pure (*Z*)-isomer was obtained by chromatographic separation of the initially obtained mixture of diastereomers and its configuration was demonstrated by comparison with the ^{1}H NMR spectra with literature data [19].

N-Phthalimidoaziridines 1a-f (General Method). N-aminophthalimide (0.729 g, 4.5 mmol) and lead tetraacetate (1.995 g, 4.5 mmol) were added consecutively in small portions over 30 min to a stirred suspension of potassium carbonate (1.863 g, 13.5 mmol) in a solution of unsaturated compound (3.0 mmol) in anhydrous dichloromethane (30 ml) cooled to -20°C. The mixture was stirred for an additional 20 min at room temperature and filtered through a 1.5-cm-thick silica gel layer. The residue was washed with 100-150 ml dichloromethane. The combined filtrates were evaporated in vacuum. The residue was separated by chromatography on a column packed with 30 g silica gel using dichloromethane as the eluent.

(2*R′*,3*S′*)-2-Acetyl-3-phenyl-1-phthalimidoaziridine (1a) was obtained in 74% yield (0.679 g) as greenish-yellow crystals, mp 192°C (mp 192-193°C [6]). The ^{1}H NMR spectrum indicated that this product was a mixture of two invertomers in 1:0.06 ratio. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.55 (s, CH_3 maj) and 2.47 (s, CH_3 min) (total 3H); 3.72 (d, *J* = 4.4) and 4.37 (d, *J* = 4.4) (H-2, H-3 maj); 4.02 (d, *J* = 5.8) and 4.54 (d, *J* = 5.8) (H-2, H-3 min) (total 2H); 7.37-7.43 (5H, m, C_6H_5); 7.66-7.77 (4H, m, PhthN). ^{13}C NMR of the major invertomer, δ, ppm: 31.51 (CH_3); 49.92, 51.07 (C-2, C-3); 123.07 (C-b); 127.06 and 128.60 (C-*m*, C-*o*); 128.52 (C-*p*); 130.18 (C-a); 133.98 (C-c); 134.91 (C-*ipso*); 164.67 (NCO); 198.50 (CO). The literature ^{1}H and ^{13}C NMR spectra [6] were in good accord with these data.

(2*R′*,3*S′*)-2-Phenyl-1-phthalimido-1-azaspiro[2.5]octan-4-one (1b) was obtained in 99% yield (1.027 g) as greenish-yellow crystals, mp 162°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.63 (1H, ddd, *J* = 14.5, *J* = 10.6, *J* = 3.9); 1.71-1.88 (3H, m) and 2.10-2.25 (2H, m) (H-6, H-7, H-8); 2.49 (1H, ddd, *J* = 18.0, *J* = 5.2, *J* = 5.2, H-5); 2.77 (1H, ddd, *J* = 18.0, *J* = 10.1, *J* = 7.5, H-5); 4.81 (1H, s, H-2); 7.32-7.43 (5H, m, C_6H_5); 7.65-7.75 (4H, m, PhthN). ^{13}C NMR spectrum, δ, ppm: 21.21, 23.12, 28.77, 39.47 (C-5, C-6, C-7, C-8); 54.14 (C-2); 55.22 (C-3); 123.14 (C-b); 127.92 (C-*p*); 128.02 and 128.42 (C-*m*, C-*o*); 130.42 (C-a); 133.59 (C-*ipso*); 134.08 (C-c); 164.95 (NCO); 203.09 (CO). Found: *m/z* 347.1340 $[M+H]^+$. Calculated: $[M+H]^+$ 347.1390. Found, %: C 72.85; H 5.20; N 8.04. $C_{21}H_{18}N_2O_3$. Calculated, %: C 72.82; H 5.24; N 8.09

(2*R′*,3*S′*)-2-Phenyl-1-phthalimido-1-azaspiro[2.4]heptan-4-one (1c) was obtained in 92% yield (0.920 g) as colorless crystals, mp 114-116°C. ^{1}H NMR spectrum, δ, ppm: 1.87-2.02 (2H, m); 2.31-2.50 (3H, m); 2.69-2.80 (1H, m) (H-5, H-6, H-7); 4.36 (1H, s, H-2); 7.34-7.40 (5H, m, C_6H_5); 7.65-7.74 (4H, m, PhthN). ^{13}C NMR spectrum, δ, ppm: 19.35, 27.06, 38.56 (C-5, C-6, C-7); 54.71 (C-2); 57.32 (C-3); 123.17 (C-b); 127.68 (C-*p*); 128.29 and 128.61 (C-*m*, C-*o*); 133.57 (C-*ipso*); 134.09 (C-c); 209.72 (CO). The signals of carbon atom C-a and NCO of the phthalimide group are not visible due to strong broadening. Found: *m/z* 333.1203 $[M+H]^+$. Calculated: $[M+H]^+$ 333.1234. Found, %: C 72.29; H 4.78; N 8.45. $C_{20}H_{16}N_2O_2$. Calculated, %: C 72.28; H 4.85; N 8.43.

(2*R′*,3*S′*)-2-Phenyl-3-[(*E*)-3-phenylprop-2-enoyl]-1-phthalimidoaziridine (1d). The reaction was carried out for dibenzalacetone **2d** (0.702 g, 3 mmol) with N-aminophthalimide (0.486 g, 3.0 mmol) and lead tetraacetate (1.329 g, 3.0 mmol). Dichloromethane was distilled off. The resultant residue was separated on a column packed with 40 g silica gel using 1:4 ethyl acetate–hexane as the eluent to give 0.415 g (35%) aziridine **1d** as yellowish crystals, mp 141°C. The ^{1}H NMR spectrum indicated that this product was a 1:0.07 mixture of two invertomers. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.98 (d, *J* = 4.9) and 4.60 (d, *J* = 4.9) (H-2, H-3 maj); 4.15 (d, *J* = 5.5) and 4.93 (d, *J* = 5.5) (H-2, H-3 min) (total 2H); 7.12 (d, *J* =16.1, H-α maj) and 7.23 (d, *J* = 16.2, H-α min) (total 1H); 7.34-7.67 (m, 2Ph, PhthN and H-β maj) and 8.02 (d, *J* = 16.2, H-β min) (total 15H). ^{13}C NMR spectrum of the major invertomer, δ, ppm: 50.32 and 50.92 (C-2, C-3); 123.25 (C-b); 125.96 (C-α); 127.27, 128.79, 128.87, 129.11 (C-*m*, C-*o*); 128.67 and 131.17 (C-*p*); 130.38 (C-a); 134.09 (C-c); 134.23 and 135.37 (C-*ipso*); 144.75 (C-β); 164.70 (NCO); 189.32 (CO). Found: *m/z* 395.1442 $[M+H]^+$. Calculated: $[M+H]^+$ 395.1390. Found, %: C 76.38; H 4.77; N 7.11. $C_{25}H_{18}N_2O_3$. Calculated, %: C 76.13; H 4.60; N 7.10.

Methyl Ester of (2*R′*,3*S′*)-3-Benzoyl-1-phthalimidoaziridine-2-carboxylic Acid (1e). The reaction was carried out at 0°C to give 0.885 g (84%) **1e** as colorless crystals, mp 142°C. The ^{1}H NMR spectrum indicated that this product was a 1:0.7 mixture of two invertomers. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.77 (s, CH_3 min) and 3.89 (s, CH_3 maj) (total 3H); 3.85 (d, *J* = 4.7) and 4.87 (d, *J* = 4.7) (H-2, H-3 min); 4.27 (d, *J* = 4.7) and 4.51 (d, *J* = 4.7) (H-2, H-3 maj) (total 2H); 7.51-7.82 (7H, m, PhthN, H-*m*, H-*p*); 8.08-8.11 (m, H-*o* maj) and 8.25-8.28 (m, H-*o* min) (total 2H). ^{13}C NMR spectrum, δ, ppm: 43.69, 44.81, 45.35, 46.49, 53.28; 53.40 (CH_3, C-2, C-3); 123.47 and 123.49 (C-b); 128.98, 129.08, 129.27, 134.16, 134.30, 134.41 (C-*m*, C-*o*, C-*p*, C-c); 130.07 and 130.13 (C-a); 136.09 and 136.81 (C-*ipso*); 164.14 and 164.51 (NCO); 166.12 and 167.34 (CO_2); 188.97 and 191.34 (CO). Found: *m/z* 373.0763 $[M+Na]^+$. Calculated: $[M+Na]^+$ 373.0795. Found, %: C 65.03; H 4.18; N 8.20. $C_{19}H_{14}N_2O_5$.. Calculated, %: C 65.14; H 4.03; N 8.00.

Ethyl Ester of (2*R′*,3*S′*)-2-acetyl-3-phenyl-1-phthalimidoaziridine-2-carboxylic Acid (1f). The reaction was carried out at 20°C. Column chromatography gave fractions containing product **1f**, which were combined and evaporated to volume ~3 ml. Then, 4 ml ether was added. Hexane was added dropwise until the onset of precipitation. After 3 h, the precipitate was filtered off and dried in the air to give 0.882 g (78%) **1f** as greenish crystals, mp 138-139°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.96 (3H, t, *J* = 7.1, CH_3); 2.57 (3H, s, $COCH_3$); 4.10 (2H, q, *J* = 7.1, CH_2); 4.78 (1H, s, H-3); 7.30-7.37 (3H, m, H-*m*, H-*p*); 7.42-7.45 (2H, m, H-*o*); 7.66-7.77 (4H, m, PhthN). ^{13}C NMR spectrum, δ, ppm: 13.82 (CH_3); 29.36 ($CO\underline{C}H_3$); 54.27 (C-3); 60.07 (C-2); 62.25 (CH_2); 123.39 (C-b); 127.67 and 128.47 (C-*m*, C-*o*); 128.75 (C-*p*); 130.26 (C-a); 132.08 (C-*ipso*); 134.31 (C-c); 164.39 (NCO); 165.53 (CO_2); 194.19 (CO). Found: *m/z* 401.1083 $[M + Na]^+$. Calculated: $[M + Na]^+$ 401.1108. Found, %: C 66.43, H 4.78; N 7.18. $C_{21}H_{18}N_2O_5$. Calculated, %: C 66.66; H 4.79; N 7.40.

Thermal Transformations of Aziridines 1b-f in the Absence of Dipolarophiles (General Method). A solution of aziridine **1b-f** (0.5 mmol) in anhydrous toluene (10 ml) was heated in a thick-walled glass reactor. The solvent was then distilled off in vacuum. The residue was subjected to chromatography on column packed with 10 g silica gel, eluting with from 10:1 to 4:1 hexane–ethyl acetate.

2-Phenyl-4,5,6,7-tetrahydrobenzo[*d*]oxazole (3b) was obtained in 54% yield (54 mg) after heating aziridine **1b** for 45 min at 180°C as yellowish crystals, mp 74°C. ^{1}H NMR spectrum, δ, ppm: 1.83-1.91 (4H, m, H-5, H-6); 2.60-2.69 (4H, m, H-4, H-7); 7.40-7.43 (3H, m, H-*m*, H-*p*); 7.99-8.01 (2H, m, H-*o*). ^{13}C NMR spectrum, δ, ppm: 22.05, 23.02, 23.10, 23.24 (C-4, C-5, C-6, C-7); 125.98 and 128.76 (C-*m*, C-*o*); 129.76 (C-*p*); 128.17, 135.25 (C-*ipso*, C-3a); 146.97 (C-7a); 159.81 (C-2). The ^{1}H and ^{13}C NMR spectra given by Nicolaou et al. [20] for this compound are in good accord with these results.

2-Phenyl-5,6-dihydro-4H-cyclopenta[*d*]oxazole (3c) was obtained in 45% yield (42 mg) after heating aziridine **1c** for 1 h at 180°C as a yellow oil. ^{1}H NMR spectrum, δ, ppm: 2.50-2.60 (2H, m, CH_2); 2.63-2.68 (2H, m, CH_2); 2.76-2.81 (2H, m, CH_2); 7.38-7.44 (3H, m, H-*m*, H-*p*); 7.97-8.00 (2H, m, H-*o*). ^{13}C NMR spectrum, δ, ppm: 22.62, 22.77, 27.10 (C-4, C-5, C-6); 125.86 and 129.82 (C-*m*, C-*o*); 128.80 (C-*p*); 128.63 (C-*ipso*); 145.41 (C-3a); 154.74 (C-7a); 165.63 (C-2). Found: *m/z* 186.0967 $[M+H]^+$. $C_{12}H_{12}NO$. Calculated: $[M+H]^+$ 186.0919.

(*E*)-2-Phenyl-5-styryloxazole (3d) was obtained in 65% yield (80 mg) after heating aziridine **1d** for 4 h at 140°C and separation by column chromatography, eluting with from 6:1 to 3:1 hexane–ethyl acetate as yellow crystals, mp 82°C (mp 105°C [21]). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 6.95 (1H, d, *J* = 16.3, =CH); 7.17 (1H, s, H-4); 7.18 (1H, d, *J* = 16.3, =CH); 7.27-7.53 (8H, m, H arom); 8.10-8.13 (2H, m, 2-Ph, H-*o*). ^{13}C NMR spectrum, δ, ppm: 113.21, 126.54, 126.64, 126.72, 127.48 (C-*ipso*); 128.38, 128.97, 129.60, 130.58, 136.52 (C-*ipso*); 150.48 (C-5); 161.22 (C-2). Found: *m/z* 248.1089 $[M+H]^+$. Calculated: $[M+H]^+$ 248.1070. Found, %: C 82.68; H 5.39; N 5.43. $C_{17}H_{13}NO$. Calculated, %: C 82.57; H 5.30; N 5.66.

Methyl Ester of 5-Phenyloxazole-2-carboxylic Acid (3e) was obtained in 62% yield (63 mg) after heating aziridine **1e** for 150 min at 200°C and separation by column chromatography, eluting with from 6:1 to 3:1 hexane–ethyl acetate as colorless crystals, mp 89-90°C. ^{1}H NMR spectrum, δ, ppm: 4.01 (3H, s, CH_3); 7.38-7.48 (3H, m, H-*m*, H-*p*); 7.52 (1H, s, H-4); 7.73-7.76 (2H, m, H-*o*). ^{13}C NMR spectrum, δ, ppm: 53.24 (CH_3); 124.05 (C-4); 126.74 (C-*ipso*); 125.24 and 129.20 (C-*m*, C-*o*); 129.98 (C-*p*); 151.52, 154.52, 156.20 (C-2, C-5, CO). Found: *m/z* 226.0450 $[M+Na]^+$. Calculated: $[M+H]^+$ 226.0474. Found, %: C 65.07; H 4.47; N 6.89. $C_{11}H_9NO_3$. Calculated, %: C 65.02; H 4.46; N 6.89.

Ethyl Ester of 5-Methyl-2-phenyloxazole-4-carboxylic Acid (3f) was obtained in 65% yield (75 mg) after heating aziridine **1f** for 5 h at 90°C and separation by column chromatography with dichloromethane as the eluent as yellow crystals, mp 52-53°C (mp 48-49°C [21]). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.41 (3H, t, *J* = 7.1, CH_3); 2.70 (3H, s, Het-CH_3); 4.42 (2H, q, *J* = 7.1, CH_2); 7.42-7.47 (3H, m, H-*m*, H-*p*); 8.04-8.08 (2H, m, H-*o*). ^{13}C NMR spectrum, δ, ppm: 12.35 (CH_3); 14.51 (CH_3); 61.14 (CH_2); 126.69 and 128.82 (C-*m*, C-*p*); 126.72, 128.91 (C-*ipso*, C-4); 130.83 (C-*p*); 156.27, 159.75, 162.61 (C-2, C-5, CO). The ^{1}H and ^{13}C NMR spectra given by Wan et al. [22] are in good accord with our results.

Thermal Reactions of Aziridines 1a, 1d, and 1e with N-phenylmaleimide (General Method). A solution of aziridine (0.5 mmol) and N-phenylmaleimide (173 mg, 1 mmol) in anhydrous toluene (10 ml) was heated in a thick-wall glass reactor. The solvent was then distilled off in vacuum and the residue was separated on a column packed with 20 g silica gel.

Aziridine **1a** was heated for 5 h at 150°C. The reaction products were subjected to column chromatography, eluting with from 4:1 to 1:1 hexane–ethyl acetate. The fraction containing adduct **4a** was again separated on a column packed with 6 g silica gel, eluting with dichloromethane. The crude product was crystallized from methanol to give 141 mg (59%) adduct **4a** and 16 mg (20%) oxazole **3a**.

(3a*R′*,4*R′*,6*S′*,6a*S′*)-4-Acetyl-2,6-diphenyl-5-phthalimidotetrahydropyrrolo[3,4-*c*]pyrrole-1,3(2H,3aH)-dione (4a) was obtained as colorless crystals, mp 231-232°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.55 (3H, s, CH_3); 3.58 (1H, dd, *J* = 9.3, *J* = 7.2, H-6a); 4.03 (1H, dd, *J* = 9.3, *J* = 4.9, H-3a); 4.72 (1H, d, *J* = 4.9, H-4); 5.13 (1H, d, *J* = 7.2, H-6); 7.28-7.64 (10H, m, $2C_6H_5$); 7.71-7.80 (4H, m, PhthN). ^{13}C NMR spectrum, δ, ppm: 27.34 (CH_3); 45.75 and 52.33 (C-3a, C-6a); 71.42 and 73.26 (C-4, C-6); 123.93 (C-b); 126.78, 127.19, 128.96, 129.41 (C-*m*, C-*o*); 128.65 and 129.04 (C-*p*); 129.56 (C-a); 131.88 (2-Ph, C-*ipso*); 134.87 (C-c); 138.36 (6-Ph, C-*ipso*); 175.10 and 175.82 (C-1, C-3); 203.68 (CO). The phthalimide NCO signals are not visible due to strong broadening. Found: 480.1529 $[M+H]^+$. Calculated: $[M+H]^+$ 480.1554. Found, %: C 69.70; H 4.26; N 8.67. $C_{28}H_{21}N_3O_5$. Calculated, %: C 70.14; H 4.42; N 8.76.

5-Methyl-2-phenyloxazole (3a) was obtained as a colorless oil. ^{1}H NMR spectrum, δ, ppm: 2.39 (3H, s, CH_3); 6.84 (1H, s, H-4); 7.41-7.46 (3H, m, H-*m*, H-*p*); 7.98-8.01 (2H, m, H-*o*). The spectrum reported by Herrera et al. [23] is in good accord with these results.

Aziridine **1d** was heated for 4 h at 140°C. Chromatographic separation eluting with from 6:1 to 2:1 hexane–ethyl acetate gave 136 mg (48%) adduct **4d** and 21 mg (17%) oxazole **3d**.

(3aR',4R',6S',6aS')-2,4-Diphenyl-6-[(E)-3-phenylprop-2-enoyl]-5-phthalimidotetrahydropyrrolo-[3,4-*c*]pyrrole-1,3(2H,3aH)-dione (4d) was obtained as colorless crystals, mp 162-163°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.61 (1H, dd, *J* = 9.4, *J* = 7.6) and 4.08 (1H, dd, *J* = 9.4, *J* = 5.7) (H-3a, H-6a); 5.04 (1H, d, *J* = 5.7) and 5.21 (1H, d, *J* = 7.6) (H-4, H-6); 7.59-7.82 (21H, m, H arom). ^{13}C NMR spectrum, δ, ppm: 46.13 and 51.91 (C-3a, C-6a); 70.89 and 71.67 (C-4, C-6); 122.07 (C-α); 126.90, 127.65, 128.84, 129.02, 129.12, 129.14, 129.20, 129.51, 131.20 (C-*m*, C-*o*, C-*p*); 131.96, 134.59, 137.94 (C-*ipso*); 134.83 (C-c); 145.83 (C-β); 175.02, 175.90 (C-1, C-3); 194.48 (CO). The signals for C-a, C-b, and the phthalimide group NCO carbon atoms are not visible due to strong broadening. Found: *m/z* 568.1804 $[M+H]^+$. Calculated: $[M+H]^+$ 568.1867. Found, %: C 74.30; H 4.51, N 7.38. $C_{35}H_{25}N_3O_5$. Calculated, %: C 74.06; H 4.44; N 7.40.

Aziridine **1e** was heated for 150 min at 200°C. Chromatographic separation eluting with from 6:1 to 2:1 hexane–ethyl acetate gave adduct **4e**, which was additionally purified by recrystallization from 8:1 ether–dichloromethane to give 84 mg (32%) **4e** and 26 mg (25%) oxazole **3e**.

Methyl Ester of (1*R′*,3*S′*,3a*S′*,6a*R′*)-3-Benzoyl-4,6-dioxo-5-phenyl-2-phthalimdooctahydropyrrolo-[3,4-*c*]pyrrole-1-carboxylic Acid (4e) was obtained as colorless crystals, mp 130-132°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.76 (3H, s, CH_3); 4.20 (1H, dd, *J* = 9.6, *J* = 3.9) and 4.29 (1H, d.d, *J* = 9.6, *J* = 4.7 (H-3a, H-6a); 4.54 (1H, d, *J* = 4.7) and 5.47 (1H, d, *J* = 3.9) (H-1, H-3); 7.32-7.56 (8H, m, H arom); 7.73-7.82 (4H, m, PhthN); 7.92-7.95 (2H, m, PhCO, H-*o*). ^{13}C NMR spectrum, δ, ppm: 47.31, 47.36, 53.33 (CH_3, C-3a, C-6a); 69.35 and 70.16 (C-1, C-3); 124.01 (C-b); 126.93, 128.83, 129.10, 129.43, 133.80 (C-*m*, C-*o*, C-*p*); 134.92 (C-c); 129.54 and 135.20 (C-*ipso*); 169.24, 175.36, 176.14 (CO_2, C-4, C-6); 193.80 (CO). The signals for C-a and the phthalimide group NCO carbon atom are not visible due to strong broadening. Found: *m/z* 546.1248 $[M+Na]^+$. Calculated: $[M+Na]^+$ 546.1272. Found, %: C 66.32; H 4.14; N 7.88. $C_{29}H_{21}N_3O_7$. Calculated, %: C 66.54; H 4.04; N 8.03.

Thermal Reactions of Aziridines 1a and 1e with DMAD (General Method). A solution of aziridine **1a** or **1e** (0.5 mmol) and DMAD (213 mg, 1.5 mmol) in anhydrous toluene (10 ml) was heated in a thick-walled glass reactor. The solvent was then distilled off and the residue was separated on a column packed with 20 g silica gel.

A mixture of DMAD and aziridine **1a** was heated for 5 h at 150°C. The reaction mixture was evaporated and the residue was separated by column chromatography eluting with from 6:1 to 1:1 hexane–ethyl acetate. The fraction containing adduct **5a** was again separated on a column packed with 10 g silica gel, eluting with dichloromethane to give 53 mg (35%) pyrrole **5a** and 11 mg (14%) oxazole **3a**.

Dimethyl Ester of 2-Acetyl-5-phenyl-1H-pyrrole-3,4-dicarboxylic Acid (5a) was obtained as colorless crystals, mp 107°C. ^{1}H NMR spectrum, δ, ppm: 2.45 (3H, s, CH_3); 3.74 (3H, s, OCH_3); 3.99 (3H, s, OCH_3); 7.43-7.46 (3H, m, H-*p*, H-*m*); 7.54-7.57 (2H, m, H-*o*); 9.47 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm: 26.78

(CH_3); 51.87 (OCH_3); 53.19 (OCH_3); 113.12 and 124.10 (C-3, C-4); 128.39, 132.77, 140.06 (C-*ipso*, C-2, C-5); 128.55 and 129.28 (C-*m*, C-*o*); 129.89 (C-*p*); 163.59 (CO_2); 166.60 (CO_2); 187.86 (CO). Found: *m/z* 324.0897 $[M+Na]^+$. Calculated: $[M+Na]^+$ 324.0842. Found, %: C 63.66; H 4.99; N 4.70. $C_{16}H_{15}NO_5$. Calculated, %: C 63.78; H 5.02; N 4.65.

Trimethyl ester of 5-Benzoyl-1H-pyrrole-2,3,4-tricarboxylic Acid (5e) was obtained upon heating a mixture of aziridine **1e** and DMAD for 150 min at 200°C. Chromatographic separation eluting with 4:1 hexane–ethyl acetate gave 76 mg (44%) **5e** as colorless crystals, mp 127-128°C. ^{1}H NMR spectrum, δ, ppm: 3.31 (3H, s, OCH_3); 3.92 (3H, s, OCH_3); 3.94 (3H, s, OCH_3); 7.44-7.49 (2H, m, H-*m*); 7.57-7.62 (1H, m, H-*p*); 7.75-7.78 (2H, m, H-*o*); 10.10 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm: 51.81 (OCH_3); 52.92 (OCH_3); 53.03 (OCH_3); 118.84, 122.55, 123.41, 132.91, 137.42 (C-2, C-3, C-4, C-5, C-*ipso*); 128.66 and 129.12 (C-*m*, C-*o*); 133.60 (C-*p*); 159.50 (CO_2); 162.60 (CO_2); 164.48 (CO_2); 187.04 (CO). Found: *m/z* 368.0692 $[M+Na]^+$. Calculated: $[M+Na]^+$ 368.0741. Found, %: C 59.20; H 4.40; N 4.16. $C_{17}H_{15}NO_7$. Calculated, %: C 59.13; H 4.38; N 4.06.

REFERENCES

1. J. W. Lown, in: A. Padwa (editor), *1,3-Dipolar Cycloaddition Chemistry*, vol. 1, John Wiley & Sons, New York (1984), p. 653.
2. L. M. Harwood and R. J. Vickers, *Synthetic Applications of 1,3-Dipolar Cycloaddition Chemistry Toward Heterocycles and Natural Products,* in: A. Padwa and W. H. Pearson (editors), *The Chemistry of Heterocyclic Compounds*, vol. 59, John Wiley & Sons, Hoboken (2003), p. 169.
3. J. Charrier, A. Foucaud, H. Person, and E. Loukakou, *J. Org. Chem.*, **48**, 481 (1983).
4. M. A. Kuznetsov, A. S. Pan'kova, A. V. Ushkov, and S. I. Selivanov, *Zh. Org. Khim.*, **44**, 807 (2008).
5. M. A. Kuznetsov, A. V. Ushkov, S. I. Selivanov, A. S. Pan'kova, and A. Linden, *Zh. Org. Khim*., **45**, 1200 (2009).
6. E. V. Beletskii and M. A. Kuznetsov, *Zh. Org. Khim.*, **45**, 1237 (2009).
7. H. Person, K. Luanglath, M. Baudru, and A. Foucaud, *Bull. Soc. Chim. France*, 1989 (1976).
8. M. A. Kuznetsov, L. M. Kuznetsova, J. G. Schantl, and K. Wurst, *Eur. J. Org. Chem.*, 1309 (2001).
9. R. S. Atkinson and J. J. Malpass, *J. Chem. Soc., Perkin Trans. 1*, 2242 (1977).
10. A. S. Pan'kova, Author's Abstract of Chem. Sci. Cand. Dissertation, St. Petersburg (2009).
11. H. E. Gottlieb, V. Kotlyar, and A. Nudelman, *J. Org. Chem.*, **62**, 7512 (1997).
12. H. D. K. Drew and H. H. Hatt, *J. Chem. Soc.*, 16 (1937).
13. U. P. Kreher, A. E. Rosamilia, C. L. Raston, J. L. Scott, and C. R. Strauss, *Org. Lett.*, **5**, 3107 (2003).
14. H. O. House and H. Babad, *J. Org. Chem.*, **28**, 90 (1963).
15. L. Tietze and T. Eicher, *Preparative Organic Chemistry* [Russian translation], Mir, Moscow (1999), p. 209.
16. G. V. Golodnikov and T. V. Mandel'shtam, *Laboratory Textbook in Organic Synthesis* [in Russian], Izd. Leningradsk. Gos. Univ., Leningrad (1976), p. 358.
17. D. Papa, F. Schenk, F. Villani, and E. Klingsberg, *J. Am. Chem. Soc.*, **70**, 3359 (1948).
18. P. Chiang, M. Rommel, and J. Bode, *J. Am. Chem. Soc.*, **131**, 8714 (2009).
19. O. Anaç, Ö. Sezer, Ö. Aldaş, F. Ş. Güngör, and M. Ş. Cansever, *Tetrahedron Lett.*, **49**, 1062 (2008).
20. K. C. Nicolaou, J. Hao, M. V. Reddy, P. B. Rao, G. Rassias, S. A. Snyder, X. Huang, D. Y.-K. Chen, W. E. Brenzovich, N. Giuseppone, P. Giannakakou, and A. O'Brate, *J. Am. Chem. Soc.*, **126**, 12897 (2004).
21. R. P. Foulds and R. Robinson, *J. Chem. Soc.*, **103**, 1768 (1913).
23. C. Wan, J. Zhang, S. Wang, J. Fan, and Z. Wang, *Org. Lett.*, **12**, 2338 (2010).
24. A. Herrera, R. Martinez-Alvarez, P. Ramiro, D. Molero, and J. Almy, *J. Org. Chem.*, **71**, 3026 (2006).