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THERMAL OPENING OF THE DIAZIRIDINE FRAGMENT IN 1-METHYL- AND 1,3,3-TRIMETHYL-1,3,4,8b-TETRAHYDRO-[1,2]DIAZIRINO[3,1-*a*]ISOQUINOLINES IN THE PRESENCE OF N-ARYLMALEIMIDES*

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The thermal opening of the diaziridine ring in 1-methyl- and 1,3,3-trimethyl-1,3,4,8b-tetrahydro[1,2]diazirino[3,1-a]isoquinolines in the presence of N-arylmaleimides leads to the predominant or exclusive formation of the trans isomers of the products of 1,3-dipolar cycloaddition. In the absence of dipolarophile, the conversion of the starting diaziridines is incomplete over the same time period, while the thermolysis products are N-[3,4-dihydro-2(1H)-isoquinolyl]- and N-[3,3-dimethyl-3,4-dihydro-2(1H)-isoquinolyl]-N-methyleneamines formed as the result of isomerization of intermediate labile azomethineimines.

Keywords: azomethineimines, N-arylmaleimides, diaziridine, 3,4-dihydroisoquinoline, 1,3-dipolar cycloaddition.

Azomethineimines are convenient synthones for the construction of various functionally-substituted condensed and spiro-fused heterocyclic systems [1]. A method permitting the generation of azomethineimines *in situ* involves the thermal opening of the diaziridine fragment at the carbon–nitrogen bond, which may be accompanied by isomerization of the resultant azomethineimine [2-4] or its reverse dimerization [5]. Azomethinimines are extremely reactive and may undergo cycloaddition even with such relatively inactive dipolarophiles as nitriles and Schiff bases [6]. The steric selectivity is usually very high [1, 7].

Labile azomethineimines, obtained in the thermolysis of *cis*-N,N'-dialkyldiaziridines, namely, 6-aryl-diazabicyclo[3.1.0]hexanes, irreversibly isomerize to give the corresponding 2-pyrazolines or undergo 1,3-dipolar cycloaddition in the presence of active dipolarophiles [8-10]. For example, in the presence of N-arylmaleimides lacking substituents in the *ortho* positions of the benzene ring, the reaction leads to a mixture of two diastereomers [9, 10]. The only reaction products in the case of *ortho* substituents are the *trans* adducts [11].

* Dedicated to the memory of A. A. Potekhin.

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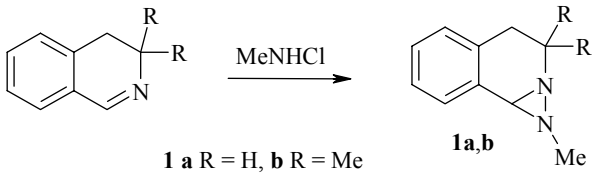
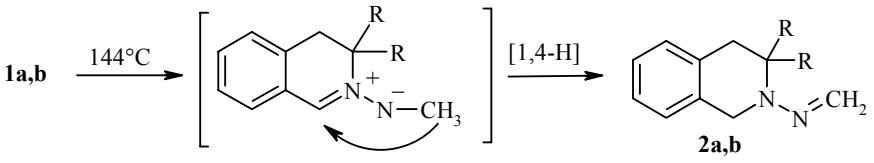
In contrast to 1,5-diazabicyclo[3.1.0]hexanes, monocyclic N,N'-dialkyldiaziridines exist predominantly in the more stable *trans* configuration [12, 13]. The bicyclic diaziridine, 1-methyl-1,3,4,8b-tetrahydro-[1,2]diazirino[3,1-*a*]isoquinoline (**1a**) [14], probably should have the same *trans* configuration and, similar to 6-phenyl-1,5-diazabicyclo[3.1.0]hexane, possesses the 3-phenyldiaziridine fragment but differs from the latter in its alkyl substitution topology. Thus, we undertook a study of the thermal behavior of diaziridine **1a** and its 3,3-dimethyl analog **1b** relative to 6-aryl-1,5-diazabicyclo[3.1.0]hexanes, which have been studied extensively in our laboratory. We also investigated the steric selectivity of the cycloaddition to azomethineimines generated from diaziridines **1a**,**b** since, according to the literature data, the cycloaddition of N-methylmaleimide to azomethinimines with the isoquinoline structural fragment leads exclusively to *trans* adducts [15] or *cis* adducts [16].



Diaziridines **1a**,**b** were obtained from the corresponding 3,4-dihydroisoquinolines under conditions similar to those given in the literature [14]. We note that we could not obtain the corresponding diaziridines under analogous conditions from 1,3,3-trimethyl- and 3,3-dimethyl-1-phenyl-3,4-dihydroisoquinolines.

The thermolysis of **1a** and **1b** in the absence of 1,3-dipolarophiles was carried out in *o*-xylene at reflux (144°C). Diaziridine **1a** was heated for 10 h, while **1b** was heated for 9 h. After removal of the solvent, the reaction mixtures were analyzed by ^{1}H NMR spectroscopy.

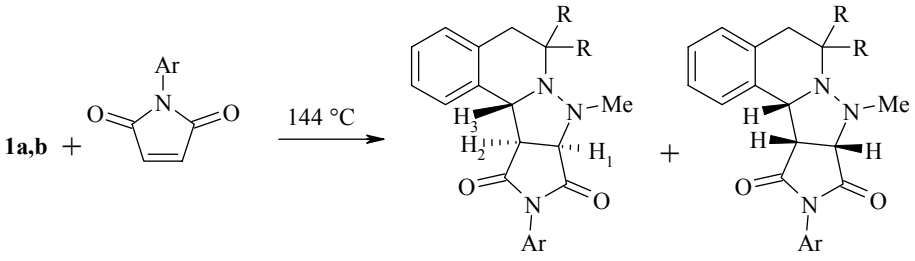


The spectra of these reaction mixtures showed only signals of the starting compounds **1a** and **1b** and the products of their thermal conversion **2a** and **2b. W**e obtained a 4:1 mixture of **1a** and **2a** and a 3:2 mixture of **1b** and **2b**. By analogy with the product obtained in the thermolysis of 6-aryl-1,5-diazabicyclo[3.1.0]hexanes, which results from a formal [1,4-H]-shift in the initially formed azomethineimine and using the spectral data of the reaction mixtures, we assigned the structures of N-(3,4-dihydro-2(1H)-isoquinolyl)-N-methyleneamine (**2a**) and N-(3,3-dimethyl-3,4-dihydro-2(1H)-isoquinolyl)-N-methyleneamine (**2b**) to the products of the thermolysis of diaziridines **1a** and **1b**, respectively. Products of the dimerization of the azomethineimines, which might have been expected in light of the example described for an analog of diaziridine **1a** with a *p*-tolyl group instead of a methyl group at the nitrogen atom [5], were not found in the reaction mixture.

Our results showed that complete conversion of the starting compounds is not observed under comparable conditions in the thermolysis of diaziridines **1a** and **1b** in the absence of 1,3-dipolarophiles even over a significantly longer time (9-10 h) than in the thermolysis of 6-aryl-1,5-diazabicyclo[3.1.0]hexanes (20-30 min). This result indicates the greater thermal stability of *trans*-N,N'-dialkyldiaziridines in comparison with *cis*-diaziridines.

The thermolysis of diaziridines **1a** and **1b** in the presence of N-arylmaleimides **3a-f** was also carried out in *o*-xylene at reflux with monitoring of the reaction course by thin-layer chromatography. In this case, the starting diaziridines were entirely converted to the products of 1,3-dipolar cycloaddition **4a-k** and **5a-d** after 10 h in the case of **1a** and 8 h in the case of **1b**.

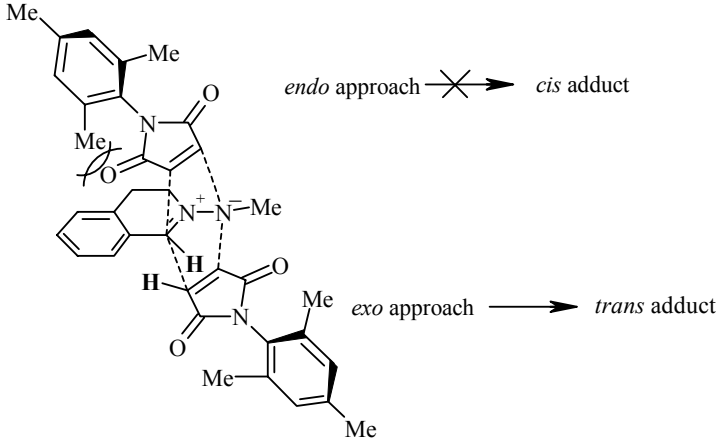
The thermolysis of **1a** in the presence of imides **3a**,**b** gave ~3-3.5:1 mixtures of *trans* adducts **4a**,**b** and *cis* adducts **5a**,**b**. The introduction of two methyl groups at C-3 in the isoquinoline system creates steric hindrance for the *endo* approach of the dipolarophile, i.e., approach from the side of the 3,4-dihydroisoquinoline system. As a consequence, the thermolysis of diaziridine **1b** in the presence of imides **3a**,**b** leads to a ~7-8:1 *trans:cis* product ratio in favor of *trans* isomers **4c,d**.



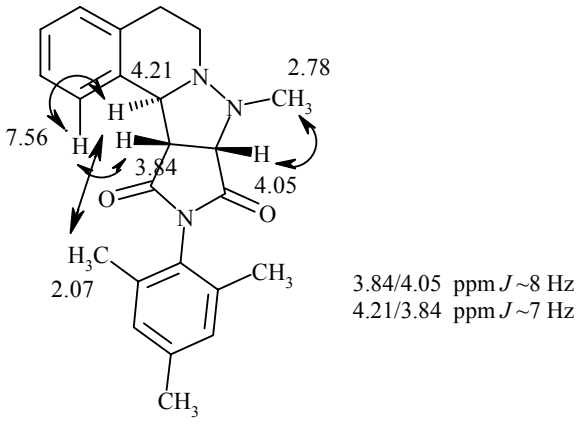
3 **a** Ar = 4-BrC_6H_4, **b** Ar = 4-$MeOC_6H_4$, **c** Ar = 2,6-$Cl_2C_6H_3$, **d** Ar = 1-naphthyl **e** Ar = Mes, **f** Ar = 2,6-$Me_2C_6H_3$; **4, 5** **a** Ar = 4-BrC_6H_4, R = H; **b** Ar = 4-$MeOC_6H_4$, R = H; **c** Ar = 4-BrC_6H_4, R = Me; **d** Ar = 4-$MeOC_6H_4$, R = Me; **4** **e** Ar = Mes, R = H; **f** Ar = 1-naphthyl, R = H; **g** Ar = 2,6-$Me_2C_6H_3$, R = H; **h** Ar = 2,6-$Cl_2C_6H_3$, R = H; **i** Ar = Mes, R = Me; **j** Ar = 2,6-$Me_2C_6H_3$, R = Me; **k** Ar = 2,6-$Cl_2C_6H_3$, R = Me

Hence, the steric selectivity of the cycloaddition of N-arylmaleimides, lacking *ortho* substituents in the benzene ring, to azomethineimines generated in the thermolysis of diaziridines **1a**,**b** is rather high but 100% steric specificity in the addition described in the literature for reactions with N-methylmaleimide [15, 16] was not observed in our case.

The ^{1}H NMR spectra of the reaction mixtures in the thermal opening of the diaziridine fragment in **1a**,**b** in the presence of *ortho*-substituted N-arylmaleimides, as in the thermolysis of 6-aryl-1,5-diaza-bicyclo[3.1.0]hexanes [11], show signals exclusively for the *trans* adducts **4e-k**. The planes of the benzene and pyrrole rings in 2,6-disubstituted N-arylmaleimides and in N-(1-naphthyl)maleimide are virtually orthogonal. Thus, strong steric interactions between the *ortho* substituents in the imide benzene ring and the 3,4-dihydroisoquinoline fragment, especially when substituents are present at C-3, which hinder formation of the *cis* adduct, should obtain upon the *endo* approach of such dipolarophiles to the initially formed azomethinimine. No such hindrance exists for the *exo* approach so that *trans* isomers **4e-k** are exclusively formed.



We should note that the signals for H-1, H-2, and H-3 in the ^{1}H NMR spectra of adducts **4a-k** at room temperature are considerably broadened, while the coupling constant of H-2 and H-3 at elevated temperature is about 7 Hz, which prevents an unequivocal assignment of the configuration. Thus, the NOESY 2D ^{1}H NMR spectrum of **4e** was obtained in DMSO-d_6 at 80°C in order to clarify the configuration of the adducts obtained. Modeling of the structure of *trans* isomer **4e** using the PM3 method [17] showed that the proton at 4.21 ppm and protons of the mesityl methyl protons at 2.07 ppm are approximated (~2.6 Å), such that the corresponding cross peak is seen in the 2D ^{1}H NMR spectrum. On the other hand, the distances between the mesityl methyl group protons and the protons at 3.84 and 4.05 ppm exceed 3.5 Å, such that the corresponding cross peaks are absent. The major spatial interactions observed in the spectrum of adduct **4e** are shown below:



The configuration of the remaining protons of cyclic products **4a-k** and **5a-d** was determined using the assignments of the ^{1}H NMR signals for adduct **4e.**

Diaziridine **1a** does not react with imide **3e** at room temperature over a period of at least 11 days, which supports the formation of the adducts not as the result of nucleophilic attack of the hydrazine fragment of **1a** at the double bond of **3e**, but rather as the result of cycloaddition of maleimide to the initially formed azomethinimine.

EXPERIMENTAL

The elemental analyses were carried out on a Hewlett-Packard 185B C, H, N-analyzer. The ^{1}H and ^{13}C NMR spectra were taken on a Bruker DPX-300 spectrometer at 300 and 75MHz, respectively, in $CDCl_3$ and DMSO-d_6. The chemical shifts were given relative to the residual deuterochloroform or DMSO-d_6 protons (7.26 and 2.50 ppm, respectively, for the ^{1}H NMR spectra [18]). The thin-layer chromatography was carried out on Silufol UV-254 plates with development in UV light or in an iodine chamber. A sample of absolute *o*-xylene was heating at reflux with a Dean-Stark trap and 2 h with sodium, followed by distillation.

1-Methyl-1,3,4,8b-tetrahydro[1,2]diazirino[3,1-*a*]isoquinoline (1a) was obtained from 3,4-dihydroisoquinoline (13.2 g, 0.1 mol) as described by Schmitz [14]. The yield of **1a** was 6.0 g (37.5%); bp 58-60°C (0.2 mm Hg). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 2.41 (1H, dd, $J = 4.0$, $J = 15.3$, CH_2); 2.57 (3H, s, NCH_3); 2.54-2.66 (1H, m, CH_2); 2.83-2.96 (1H, m, CH_2); 3.36 (1H, s, CH); 3.62 (1H, dd, $J = 5.9$, $J = 13.0$, CH_2); 7.07-7.12 (1H, m, H arom); 7.23-7.29 (2H, m, H arom); 7.41-7.45 (1H, m, H arom).

1,3,3-Trimethyl-1,3,4,8b-tetrahydro[1,2]diazirino[3,1-*a*]isoquinoline (1b) was obtained from 3,3-dimethyl-3,4-dihydroisoquinoline (2.5 g, 15.6 mmol) [19] in methanol (30 ml) by treatment with an ice-cooled solution of N-chloromethylamine (0.6 mol). The mixture was stirred for 5 h. Over the first 15 min,

the mixture temperature rose to 35°C. The mixture was left at 5-6°C for two days and then, methanol was removed at reduced pressure. The residue was extracted with ether. Ether was distilled off in a weak vacuum and the residue was distilled through a short Vigret column, taking the fraction with bp 78-80°C (0.25 mm Hg), to give 2.0 g (68%) **1b**. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 0.83 (3H, s, CCH_3); 1.41 (3H, s, CH_3); 2.22 (1H, d, *J* = 15.3, CH_2); 2.58 (3H, s, NCH_3); 2.74 (1H, d, *J* = 15.3, CH_2); 3.36 (1H, s, CH); 6.99-7.06 (1H, m, H arom); 7.17-7.28 (2H, m, H arom); 7.36-7.43 (1H, m, H arom). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 25.0 ($C\underline{C}H_3$); 29.2 ($C\underline{C}H_2$), 37.9 (CH_2); 48.5 (NCH_3); 53.8 ($\underline{C}CH_3$); 63.5 (CH); 126.5 (CH); 128.5 (CH); 129.0 (CH); 129.1 (CH); 131.4 (C); 134.9 (C). Found, %: C 76.15; H 8.53; N 14.67. $C_{12}H_{16}N_2$. Calculated, %: C 76.55; H 8.57; N 14.88.

Thermolysis of 1a,b in the Absence of Dipolarophiles. A sample solution of diaziridine **1a** or **1b** (1 ml, 0.6-0.7 M) was heated with stirring in *o*-xylene at 144°C bath temperature. The ratio of the products in the reaction mixture was determined by ^{1}H NMR spectroscopy.

N-[3,4-Dihydro-2(1H)-isoquinolinyl]-N-methyleneamine (2a). Diaziridine **1a** was heated for 10 h. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 3.01 (2H, t, *J* = 6, CH_2); 3.51 (2H, t, *J* = 6, CH_2); 4.21 (2H, s, CCH_2N); 6.29 (1H, d, *J* = 10.9, N=CH_2); 6.49 (1H, d, *J* = 10.9, N=CH_2); 7.09-7.21 (4H). The **1a-2a** ratio was 4:1.

N-[3,3-Dimethyl-3,4-dihydro-2(1H)-isoquinolyl]-N-methyleneamine (2b). Diaziridine **1b** was heated for 9 h. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.24 (6H, s, $C(CH_3)_2$); 2.90 (2H, s, CCH_2C); 4.10 (2H, s, CCH_2N); 6.28 (1H, d, *J* = 11.5, N=CH_2); 6.41 (1H, d, *J* = 11.5, N=CH_2); 7.08-7.21 (4H, m, H arom). The **1b-2b** ratio was 3:2.

Thermolysis of Diaziridines in the Presence of N-Arylmaleimides. Equimolar amounts of diaziridine and dipolarophile were heated in 1 ml *o*-xylene at 144°C bath temperature for 8 h. The solvent was distilled off in vacuum. Products **4** and **5a-d** were separated on a Merck 60 silica gel column (35-70 μm) or by extraction. In column chromatography, the crude product/adsorbent weight ratio was 1:150. The gradient elution for **4a,b** and **5a**,**b** was 4:1 hexane–ethyl acetate, 2:1 hexane–ethyl acetate. The gradient elution for **4c,d** and **5c,d** was 2:1 hexane–ethyl acetate, 1:1 hexane–ethyl acetate. The solid residue of **4e-g** was extracted 5-6 times with hexane. These products were recrystallized from ethanol (**4ab,f-h** and **5a,b**), from methanol (**4c, d,i-k)**, or from ether (**4e**). In the case of strong tar formation, the residue was initially dissolved in chloroform and filtered through a thin silica gel layer.

***rel*-(8a*R*,11a*S*,11b*R*)-10-(4-Bromophenyl)-8-methyl-5,6,11a,11b-tetrahydro-8H-pyrrolo[3',4':3,4]-pyrazolo[5,1-*a*]isoquinoline-9,11-(8aH,10H)-dione (4a) and *rel*-(8a*R*,11a*S*,11b*S*)-10-(4-Bromophenyl)-8-methyl-5,6,11a,11b-tetrahydro-8H-pyrrolo[3',4':3,4]pyrazolo[5,1-*a*]isoquinoline-9,11-(8aH,10H)-dione (5a)** were obtained from diaziridine **1a** (130 mg, 0.81 mmol) and imide **3a** (204 mg, 0.81 mmol).

The yield of compound **4a** was 190 mg (57%); mp 179°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 2.88 (3H, s, NCH_3); 2.68-3.28 (4H, m, CH_2CH_2); 3.62-3.72 (1H, m, CH); 3.79-4.01 (1H, m, CH); 4.08-4.88 (1H, m, CH); 7.10-7.33 (5H, m, H arom); 7.58-7.72 (5H, m, H arom). Found, %: C 58.41; H 4.43; N 10.22. $C_{20}H_{18}BrN_3O_2$. Calculated, %: C 58.26; H 4.40; N 10.19. The yield of compound **5a** was 9% (30 mg); mp 155°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 2.58-2.78 (2H, m, CH_2); 2.90 (3H, s, NCH_3); 2.94-3.12 (1H, m, CH_2); 3.23-3.36 (1H, m, CH_2); 4.00-4.11 (2H, m, CH); 4.99-5.14 (1H, m, CH); 7.00 (2H, d, *J* = 7.3, H arom); 7.06-7.14 (1H, m, H arom); 7.15-7.32 (2H, m, H arom); 7.36-7.44 (1H, m, H arom); 7.49 (2H, d, *J* = 7.3, H arom). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 30.2 (CH_2); 46.8 (CH_3); 50.4 (CH_2); 52.4 (CH); 63.2 (CH); 69.9 (CH); 122.4 (C); 125.9 (CH); 127.4 (2CH); 127.5 (CH); 128.6 (CH); 129.3 (CH); 130.1 (C); 130.2 (C); 132.4 (2CH); 134.1 (C); 173.6 (C=O); 175.3 (C=O). Found, %: C 58.30; H 4.30; N 10.21. $C_{20}H_{18}BrN_3O_2$. Calculated, %: C 58.26; H 4.40; N 10.19.

***rel*-(8a*R*,11a*S*,11b*R*)-10-(4-Methoxyphenyl)-8-methyl-5,6,11a,11b-tetrahydro-8H-pyrrolo[3',4':3,4]-pyrazolo[5,1-*a*]isoquinoline-9,11-(8aH,10H)-dione (4b) and *rel*-(8a*R*,11a*S*,11b*S*)-10-(4-Methoxyphenyl)-8-methyl-5,6,11a,11b-tetrahydro-8H-pyrrolo[3',4':3,4]pyrazolo[5,1-*a*]isoquinoline-9,11-(8aH,10H)-dione (5b)**

were obtained from diaziridine **1a** (320 mg, 2 mmol) and imide **3b** (406 mg, 2 mmol). The yield of compound **4b** was 53.6% (390 mg); mp 219-220°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 2.90 (3H, s, NCH_3); 2.68-3.28 (4H, m, CH_2CH_2); 3.61-3.71 (1H, m, CH); 3.83 (3H, s, OCH_3); 3.77-4.01 (1H, m, CH); 4.08-4.88 (1H, m, CH), 6.95-7.04 (2H, m, H arom); 7.10-7.17 (1H, m, H arom); 7.18-7.32 (4H, m, H arom);7.66-7.75 (H, m, H arom). Found, %: C 69.26; H 5.70; N 11.29. $C_{21}H_{21}N_3O_3$. Calculated, %: C 69.41; H 5.82; N 11.56.

The yield of compound **5b** was 80 mg (11%); mp 181-182°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 2.62-2.78 (2H, m, CH_2); 2.90 (3H, s, NCH_3); 2.95-3.13 (1H, m, CH_2); 3.23-3.38 (1H, m, CH_2); 3.76 (3H, s, OCH_3); 4.0-4.08 (2H, m, CH); 4.98-5.12 (1H, m, CH); 6.88 (2H, d, *J* = 8.7, H arom); 7.01 (2H, m, H arom); 7.06-7.13 (1H, m, H arom); 7.14-7.27 (2H, m, H arom); 7.36-7.44 (1H, m, H arom). ^{13}C NMR spectrum ($CDCl_3$); δ, ppm: 30.2 (CH_2); 46.8 (CH_3); 50.3 (CH_2); 52.3 (CH); 55.6 (OCH_3); 63.0 (CH); 69.9 (CH); 114.5 (2C); 124.4 (C); 125.9 (C); 127.1 (2C); 127.4 (C), 128.5 (C); 129.4 (C); 130.3 (C); 159.5 (C); 134.1 (C); 174.1 (C=O); 175.9 (C=O). Found, %: C 69.76; H 5.91; N 11.41. $C_{21}H_{21}N_3O_3$. Calculated, %: C 69.41; H 5.82; N 11.56.

***rel*-(8a*R*,11a*S*,11b*R*)-10-(4-Bromophenyl)-6,6,8-trimethyl-5,6,11a,11b-tetrahydro-8H-pyrrolo[3',4':3,4]-pyrazolo[5,1-*a*]isoquinoline-9,11-(8aH,10H)-dione (4c) and *rel*-(8a*R*,11a*S*,11b*S*)-10-(4-Bromophenyl)-6,6,8-trimethyl-5,6,11a,11b-tetrahydro-8H-pyrrolo[3',4':3,4]pyrazolo[5,1-*a*]isoquinoline-9,11-(8aH,10H)-dione (5c)** were obtained from diaziridine **1b** (134 mg, 0.71mmol) and imide **3a** (180 mg, 0.71 mmol). The yield of compound **4c** was 145 mg (46%); mp 181°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 0.93 (3H, br. s, CCH_3); 1.38 (3H, s, CCH_3); 2.54 (1H, d, *J* = 14.5, CH_2); 2.82 (3H, s, NCH_3); 2.95 (1H, d, *J* = 14.5, CH_2); 3.66-3.80 (1H, m, CH); 4.48-4.64 (1H, m, CH); 4.90-5.06 (1H, m, CH); 7.02-7.12 (1H, m, H arom); 7.15-7.35 (4H, m, H arom); 7.56-7.70 (2H, m, H arom); 7.80-7.92 (1H, m, H arom). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 21.8 (CH_3); 29.2 (CH_3); 41.9 (NCH_3); 44.4 (CH_2); 56.0 (C); 60.1 (CH); 61.0 (CH); 68.4 (CH); 122.9 (C); 126.7 (CH); 127.2 (CH); 127.8 (CH); 128.1 (2CH); 128.3 (CH); 130.5 (C); 132.6 (2CH); 133.5 (C); 134.9 (C); 172.6 (C=O); 176.0 (C=O). Found, %: C 60.05; H 5.16; N 9.67. $C_{22}H_{22}BrN_3O_2$. Calculated, %: C 60.01; H 5.04; N 9.54.

Isomer **5c** was not isolated as a pure compound. Individual signals for this compound in the ^{1}H NMR spectrum of the mixture in $CDCl_3$, δ, ppm: 4.11-4.20 (2H, m, CH); 5.25-5.30 (1H, m, CH).

***rel*-(8a*R*,11aS,11b*R*)-10-(4-Methoxyphenyl)-6,6,8-trimethyl-5,6,11a,11b-tetrahydro-8H-pyrrolo-[3',4':3,4]pyrazolo[5,1-*a*]isoquinoline-9,11-(8aH,10H)-dione (4d) and *rel*-(8a*R*,11a*S*,11b*S*)-10-(4-Methoxy-phenyl)-6,6,8-trimethyl-5,6,11a,11b-tetrahydro-8H-pyrrolo[3',4':3,4]pyrazolo[5,1-*a*]isoquinoline-9,11-(8aH,10H)-dione (5d)** were obtained from diaziridine **1b** (200 mg, 1.06 mmol) and imide **3b** (216 mg, 1.06 mmol) in *o*-xylene (2 ml). The yield of compound **4d** was 214 mg (51%); mp 214-215°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 0.94 (3H, br. s, CCH_3); 1.38 (3H, s, CCH_3); 2.54 (1H, d, *J* = 15.3, CH_2); 2.84 (3H, s, NCH_3); 2.96 (1H, d, *J* = 15.3, CH_2); 3.72 (1H, dd, *J* = 6.5, *J* = 7.3, CH); 3.84 (3H, s, CH_3O); 4.56 (1H, d, *J* = 7.3, CH); 5.00 (1H, d, *J* = 6.5, CH); 6.96-7.10 (3H, m, H arom); 7.16-7.32 (4H, m, H arom), 7.56-7.70 (2H, m, H arom), 7.85-7.93 (1H, m, H arom). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 21.7 ($C\underline{C}H_3$); 29.2 ($C\underline{C}H_3$); 41.9 (NCH_3); 44.4 (CH_2); 55.7 (OCH_3); 55.9 (C); 60.4 (CH); 61.2 (CH); 68.7 (CH); 115.0 (2CH); 124.5 (C); 126.9 (CH); 127.4 (CH); 128.1 (2CH); 128.2 (CH); 128.5 (2CH); 133.7 (C); 135.3 (C); 160.1 (C); 173.5 (C=O); 176.9 (C=O). Found, %: C 70.51; H 6.37; N 10.72. $C_{23}H_{25}N_3O_3$. Calculated, %: C 70.57; H 6.44; N 10.73.

Isomer **5d** was not isolated as a pure compound. Individual signals for this compound in the ^{1}H NMR spectrum of the mixture in $CDCl_3$, δ, ppm: 4.11-4.20 (2H, m, CH); 5.25-5.30 (1H, m, CH).

***rel*-(8a*R*,11aS,11b*R*)-10-Mesityl-8-methyl-5,6,11a,11b-tetrahydro-8H-pyrrolo[3',4':3,4]pyrazolo-[5,1-*a*]isoquinoline-9,11-(8aH,10H)-dione (4e)** was obtained from diaziridine **1a** (111 mg, 0.69 mmol) and imide **3e** (149 mg, 0.69 mmol). The yield of compound **4e** was 192 mg (74%); mp 140-140°C. ^{1}H NMR spectrum (DMSO-d_6) at 100°C, δ, ppm (*J*, Hz): 2.07 (3H, s, CH_3); 2.08 (3H, s, CH_3); 2.30 (3H, s, CH_3); 2.78 (3H, s, NCH_3); 2.85-3.20 (4H, m, CH_2CH_2); 3.84 (1H, dd, *J* = 7.0, *J* = 8.0, CH); 4.05 (1H, d, *J* = 8.0, CH); 4.21 (1H, d, *J* = 7.0, CH); 7.00 (2H, s, H arom); 7.13-7.28 (3H, m, H arom); 7.55-7.57 (1H, m, H arom). ^{1}H NMR

spectrum ($CDCl_3$) at 25°C, δ, ppm (*J*, Hz): 2.10 (3H, s, CH_3); 2.15 (3H, s, CH_3); 2.31 (3H, s, CH_3); 2.89 (3H, s, NCH_3); 2.68-3.28 (4H, m, CH_2CH_2), 3.61-3.77 (1H, m, CH), 3.78-4.08 (1H, m, CH), 4.20-4.98 (1H, m, CH), 6.98 (2H, s, H arom); 7.10-7.31 (3H, m, H arom); 7.60-7.80 (1H, m, H arom). ^{13}C NMR spectrum (DMSO-d_6) at 80°C, δ, ppm: 18.0 ($2CH_3$); 21.3 (CH_3); 28.0 (CH_2); 39.1 (NCH_3); 43.7 (CH_2); 53.9 (CH); 66.4 (CH); 67.1 (CH); 126.9 (C); 127.5 (C); 127.6 (C); 128.8 (C); 129.6 (C); 129.7 (C); 134.96 (C); 136.2 (C); 136.3 (C); 136.5 (C); 139.4 (C); 174.7 (C=O); 176.8 (C=O). Found, %: C 73.52; H 6.60; N 11.22. $C_{23}H_{25}N_3O_2$. Calculated, %: C 73.57; H 6.71; N 11.19.

***rel*-(8a*R*,11a*S*,11b*R*)-8-Methyl-10-(2-naphthyl)-5,6,11a,11b-tetrahydro-8H-pyrrolo[3',4':3,4]pyrazolo[5,1-*a*]isoquinoline-9,11-(8aH,10H)-dione (4f)** was obtained from diaziridine **1a** (90 mg, 0.56 mmol) and imide **3d** (120 mg, 0.56 mmol). The yield of compound **4f** was 144 mg (69%); mp 165-170°C. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.95 (3H, s, NCH_3); 2.78-3.58 (4H, m, CH_2CH_2); 3.70-3.92 (1H, m, CH); 3.93-4.29 (1H, m, CH); 4.38-5.28 (1H, m, CH); 6.97-8.05 (11H, m, H arom). Found, %: C 75.11; H 5.68; N 11.15. $C_{24}H_{21}N_3O_2$. Calculated, %: C 75.18; H 5.52; N 10.96.

***rel*-(8aR,11a*S*,11b*R*)-10-(2,6-Dimethylphenyl)-8-methyl-5,6,11a,11b-tetrahydro-8H-pyrrolo-[3',4':3,4]pyrazolo[5,1-*a*]isoquinoline-9,11-(8aH,10H)-dione (4g)** was obtained from diaziridine **1a** (90 mg, 0.56 mmol) and imide **3f** (113 mg, 0.56 mmol). The yield of compound **4g** was 144 mg (71%); mp 161°C. ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 2.15 (3H, s, CH_3); 2.20 (3H, s, CH_3); 2.90 (3H, s, NCH_3); 2.88-3.08 (4H, m, CH_2CH_2); 3.68-3.77 (1H, m, CH); 3.83-4.10 (1H, m, CH); 4.38-4.88 (1H, m, CH); 7.07-7.34 (6H, m, H arom); 7.61-7.77 (1H, m, H arom). Found, %: C 72.80; H 6.35; N, 11.36. $C_{22}H_{23}N_3O_2$. Calculated, %: C 73.11; H 6.41; N 11.63.

***rel*-(8a*R*,11a*S*,11b*R*)-10-(2,6-Dichlorophenyl)-8-methyl-5,6,11a,11b-tetrahydro-8H-pyrrolo[3',4':3,4]-pyrazolo[5,1-*a*]isoquinoline-9,11-(8aH,10H)-dione (4h)** was obtained from diaziridine **1a** (110 mg, 0.69 mmol) and imide **3c** (166 mg, 0.69 mmol). The yield of compound **3c** was 177 mg (64%); mp 170-171°C. ^1H NMR spectrum (DMSO-d_6) at 120°C, δ, ppm (*J*, Hz): 3.02 (3H, s, NCH_3); 2.87-3.06 (4H, m, CH_2CH_2); 3.91 (1H, dd, $J = 6.9$, $J = 8.4$, CH); 4.18 (1H, d, $J = 8.4$, CH); 4.30 (1H, d, $J = 6.9$, CH); 7.12-7.27 (3H, m, H arom); 7.50-7.69 (4H, m, H arom). ^{13}C NMR spectrum (DMSO-d_6) at 80°C, δ, ppm: 27.1 (CH_2); 37.9 (NCH_3); 42.6 (CH_2); 52.7 (CH); 64.8 (CH); 66.0 (CH); 125.6 (C); 126.1 (C); 126.4 (C); 127.4 (C); 127.5 (C); 128.4 (C); 128.5 (C); 131.7 (C); 133.3 (C); 133.4 (C); 133.5 (C); 134.4 (C); 171.8 (C=O); 173.7 (C=O). Found, %: C 59.75; H 4.41; N 10.38. $C_{20}H_{17}Cl_2N_3O_2$. Calculated, %: C 59.71; H 4.26; N 10.45.

***rel*-(8a*R*,11aS,11b*R*)-10-Mesityl-6,6,8-trimethyl-5,6,11a,11b-tetrahydro-8H-pyrrolo[3',4':3,4]pyrazolo[5,1-*a*]isoquinoline-9,11-(8aH,10H)-dione (4i)** was obtained from diaziridine **1b** (100 mg, 0.53 mmol) and imide **3e** (114 mg, 0.53 mmol). The yield of compound **4i** was 120 mg (56%); mp 208-209°C. ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 0.98 (3H, br. s, CH_3); 1.39 (3H, br. s, CH_3); 2.07 (3H, s, CH_3); 2.18 (3H, s, CH_3); 2.32 (3H, s, CCH_3); 2.58 (1H, d, $J = 15.3$, CH_2); 2.91 (3H, s, NCH_3); 2.97 (1H, d, $J = 15.3$, CH_2); 3.70-3.82 (1H, m, CH); 4.53-4.71 (1H, m, CH); 4.88-5.03 (1H, m, CH); 6.99 (2H, s, H arom); 7.04-7.11 (1H, m, H arom); 7.17-7.30 (2H, m, H arom); 7.87-7.96 (1H, m, H arom). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 17.9 (CH_3); 18.3 (CH_3); 21.1 (CH_3); 22.3 (CH_3); 28.9 (CH_3); 42.8 (NCH_3); 44.3 (CH_2); 56.3 (C); 59.4 (CH); 61.2 (CH); 68.8 (CH); 126.7 (CH); 127.3 (CH); 127.7 (C); 128.0 (CH); 128.3 (CH); 129.6 (2CH); 133.7 (C); 134.9 (C); 135.4 (C); 135.6 (C); 139.6 (C); 172.9 (C=O); 175.8 (C=O). Found, %: C 74.23; H 7.17; N 10.57. $C_{25}H_{29}N_3O_2$. Calculated, %: C 74.41; H 7.24; N 10.41.

***rel*-(8a*R*,11a*S*,11b*R*)-10-(2,6-Dimethylphenyl)-6,6,8-trimethyl-5,6,11a,11b-tetrahydro-8H-pyrrolo-[3',4':3,4]pyrazolo[5,1-*a*]isoquinoline-9,11-(8aH,10H)-dione (4j)** was obtained from diaziridine **1b** (100 mg, 0.53 mmol) and imide **3c** (107 mg, 0.53 mmol). The yield of compound **4j** was 124 mg (60%); mp 209°C. ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.00 (3H, br. s, CH_3); 1.40 (3H, s, CH_3); 2.11 (3H, s, CH_3); 2.23 (3H, s, CH_3), 2.58 (1H, d, $J = 15.3$, CH_2); 2.91 (3H, s, $NC\underline{H}_3$); 2.97 (1H, d, $J = 15.3$, CH_2); 3.73-3.83 (1H, m, CH); 4.58-4.68 (1H, m, CH); 4.90-5.02 (1H, m, CH); 7.01-7.35 (6H, m, H arom); 7.84-7.96 (1H, m, H arom).

^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 18.0 (CH_3); 18.4 (CH_3); 22.3 (CH_3); 28.9 (CH_3); 42.9 (NCH_3); 44.3 (CH_2); 56.3 (C); 59.5 (CH); 61.2 (CH); 68.8 (CH); 126.7 (CH); 127.3 (CH); 127.9 (CH); 128.4 (CH); 128.8 (2CH); 129.7 (CH); 130.4 (C); 133.7 (C); 134.9 (C); 135.8 (C); 136.0 (C); 172.7 (C=O); 175.6 (C=O). Found, %: C 74.25; H 7.03; N 10.97. $C_{24}H_{27}N_3O_2$. Calculated, %: C 74.01; H 6.99; N 10.79.

***rel*-(8a*R*,11a*S*,11b*R*)-10-(2,6-Dichlorophenyl)-6,6,8-trimethyl-5,6,11a,11b-tetrahydro-8H-pyrrolo-[3',4':3,4]pyrazolo[5,1-*a*]isoquinoline-9,11-(8aH,10H)-dione (4k)** was obtained from diaziridine **1b** (143 mg, 0.76 mmol) and imide **3c** (180 mg, 0.76 mmol). The yield of compound **4k** was 162 mg (50%); mp 223°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 0.96 (3H, br. s, CH_3); 1.40 (3H, s, CH_3); 2.56 (1H, d, *J* = 15.8, CH_2); 2.93 (3H, s, NCH_3); 2.97 (1H, d, *J* = 15.8, CH_2); 3.82 (1H, dd, *J* = 8.0, *J* = 8.2, CH); 4.69 (1H, d, *J* = 8.2, CH); 5.04 (1H, d, *J* = 8.0, CH); 7.04-7.09 (1H, m, H arom); 7.16-7.29 (2H, m, H arom); 7.35-7.42 (1H, m, H arom); 7.45-7.51 (2H, m, H arom); 7.86-7.91 (1H, m, H arom). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 21.6 (CH_3); 29.3 (CH_3); 42.7 (NCH_3); 44.3 (CH_2); 56.2 (C); 60.2 (CH); 60.8 (CH); 68.8 (CH); 126.6 (CH); 127.3 (C); 128.0 (C); 128.1 (C); 128.3 (C); 128.9 (2C); 131.5 (C); 133.5 (C); 134.5 (2C); 134.7 (C); 171.2 (C=O); 174.3 (C=O). Found, %: C 61.67; H 5.15; N 9.97. $C_{22}H_{21}Cl_2N_3O_2$. Calculated, %: C 61.40; H 4.92; N 9.76.

REFERENCES

1. R. Grashey, in: A. Padwa (editor), *1,3-Dipolar Cycloaddition Chemistry*, vol. 1, John Wiley & Sons, New York (1984), p. 733.
2. V. V. Trofimov, Yu. B. Koptelov, A. P. Molchanov, and R. R. Kostikov, *Zh. Org. Khim.*, **30**, 1389 (1994).
3. H. W. Heine, L. M. Baclawski, S. H. Bonser, and G. D. Wachob, *J. Org. Chem.*, **41**, 3229 (1976).
4. H. W. Heine and L. Heitz, *J. Org. Chem.*, **39**, 3192 (1974).
5. G. Tomaschewski, V. Klein, and G. Geissler, *Tetrahedron Lett.*, **21**, 4877 (1980).
6. R. Grashey, H. Leitermann, R. Schmidt, and K. Adelsberger, *Angew. Chem.*, **74**, 491 (1962).
7. F. Roussi, M. Bonin, A. Chiaroni, L. Micouin, C. Riche, and H. P. Husson, *Tetrahedron Lett.*, **40**, 3727 (1999).
8. A. P. Molchanov, D. I. Sipkin, Yu. B. Koptelov, and R. R. Kostikov, *Synlett*, 1779 (2000).
9. A. P. Molchanov, D. I. Sipkin, Yu. B. Koptelov, and R. R. Kostikov, *Zh. Org. Khim.*, **37**, 888 (2001).
10. Yu. B. Koptelov, M. Kh. Kim, A. P. Molchanov, and R. R. Kostikov, *Zh. Org. Khim.*, **35**, 116 (1999).
11. A. P. Molchanov, D. I. Sipkin, Yu. B. Koptelov, J. Kopf, and R. R. Kostikov, *Zh. Org. Khim.*, **39**, 1410 (2003).
12. G. V. Shustov, S. N. Denisenko, I. I. Chervin, N. L. Astandiarov, and R. G. Kostyanovsky, *Tetrahedron*, **41**, 5719 (1985).
13. C. A. Renner and F. D. Greene, *J. Org. Chem.*, **41**, 2813 (1976).
14. E. Schmitz, *Chem. Ber.*, **95**, 676 (1962).
15. R. Grigg, F. Heaney, J. Idle, and A. Somasunderam, *Tetrahedron Lett.*, **31**, 2797 (1990).
16. Y. Tamura, Y. Miki, and M. J. Ikeda, *J. Chem. Soc., Perkin Trans. 1*, 1702 (1976).
17. J. J. P. Stewart, *J. Comput. Chem.*, **10**, 209 (1989).
18. H. E. Gottlieb, V. Kotlyar, and A. Nudelman, *J. Org. Chem.*, **62**, 7512 (1997).
19. E. Seeger, E. Wolfhard, H. Teufel, and H. Machleidt, *Chem. Ber.*, **103**, 1674 (1970).