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THERMAL TRANSFORMATIONS OF 7-ARYL-1,6-DIAZABICYCLO[4.10]HEPTANES AND 6,13-DIARYLPERHYDRODIPYRIDAZINO-[1,2-*a*:1',2'-*d*]-1,2,4,5-TETRAZINES*

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The thermolysis of 7-aryl-1,6-diazabicyclo[4.1.0]heptanes in the absence of 1,3-dipolarophiles leads to dimers of the initially formed azomethineimines, namely, 6,13-diaryloctahydrodipyridazino[1,2-a:1',2'-d]-1,2,4,5-tetrazines The thermolysis of such diaziridines in the presence of N-arylmaleimides leads predominantly to the trans cycloaddition adducts. The trans adducts are the only products of the thermolysis in the presence of 2,6-disubstituted N-phenylmaleimides. The cis adducts predominated in the thermolysis of 6,13-diaryloctahydrodipyridazino[1,2-a:1',2'-d]-1,2,4,5-tetrazines in the presence of N-arylmaleimides without substituents in the ortho position of the benzene ring.

Keywords: azomethineimine, N-arylmaleimide, 1,6-diazabicyclo[4.1.0]heptane, tetrazine, 1,3-dipolar cycloaddition.

Azomethineimines are a convenient synthone for obtaining five-membered heterocycles with two nitrogen atoms. These reagents undergo 1,3-dipolar cycloaddition, permitting the formation of polyfunctional pyrazole derivatives, including polycyclic systems already with several new chiral sites in a single synthetic step [1]. Readily available 1,(*n*+2)-diazabicyclo[*n*.1.0]alkanes serve as precursors for reactive azomethineimines: the thermal opening of the diaziridine fragment, for example, in 1,5-diazabicyclo[3.1.0]hexanes, which occurs above 100°C at the carbon–nitrogen bond, leads to unstable cyclic azomethineimines. Under the reaction conditions, these cyclic species may either isomerize to give the corresponding 2-pyrazolines [2] or, in the presence of active 1,3-dipolarophiles, give products of 1,3-dipolar cycloaddition [3-5]. The steric interactions between the reagent and substrate in the *endo* or *exo* approach of the 1,3-dipolarophile are probably the determining factor in the steric selectivity of the cycloaddition leading to *trans* isomers as the major products [6].

In the present work, we studied possible changes in the reactivity and direction of stabilization of the intermediate labile azomethineimines as well as the steric selectivity of the cycloaddition of N-arylmaleimides with increasing size of the N,N'-polymethylene bridge in going from 6-aryl-1,5-diazabicyclo[3.1.0]hexanes studied in our previous work to 7-aryl-1,6-diazabicyclo[4.1.0]heptanes **1a-c** obtained according to Kuznetsov et al. [7].

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

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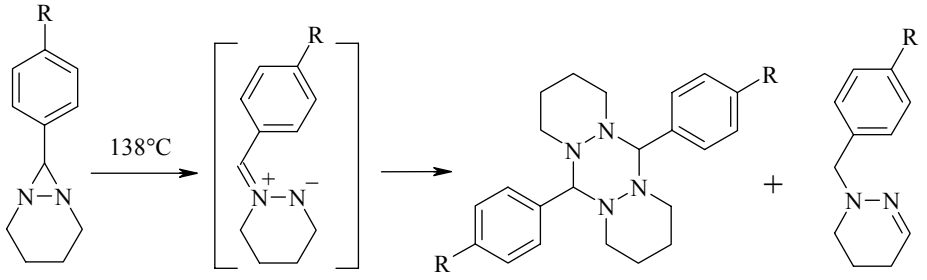
The thermolysis of diaziridines **1a**,**b** in *p*-xylene for 1 h gave good yields of 6,13-diaryloctahydrodipyridazino[1,2-*a*:1',2'-*d*]-1,2,4,5-tetrazines **2a**,**b** instead of 1-arylmethyl-1,4,5,6-tetrahydropyridazines **3a** and **3b** expected by analogy to the thermolysis of 1,5-diazabicyclo[3.1.0]hexanes. Nevertheless, the ^{1}H NMR spectrum of the reaction mixture obtained in the thermolysis of **1b** shows signals for benzylic protons (4.17 ppm) and imino group protons (6.74 ppm) of **3b** present in trace amounts [8]; these signals correspond to the literature values.

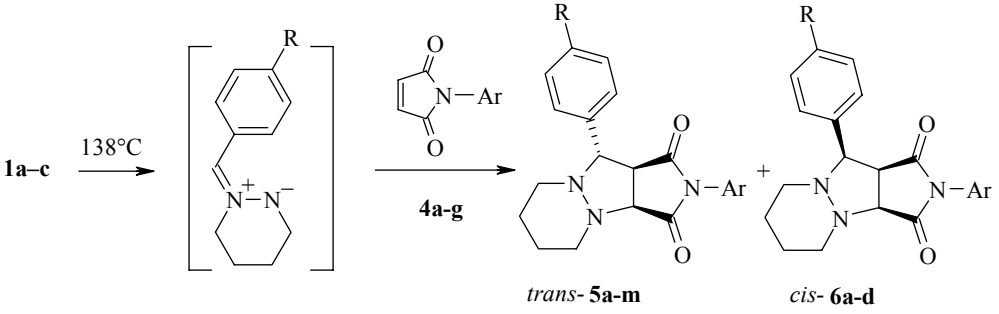


1a,b **2a,b** **3a,b** traces

1–3 a R = Me, **b** R = H

The stabilization of the azomethineimines formed in the thermal opening of the diaziridine ring in **1a** and **1b** by dimerization rather than a [1,4-H] shift was somewhat unexpected since we observed dimerization for 1,5-diazabicyclo[3.1.0]hexanes only in the catalytic opening of the diaziridine fragment [9, 10]. According to literature data [11, 12], dimer **2b** has been obtained in the reaction of benzaldehyde with hexahydropyridazine. We should note that, under conditions similar to those used for obtained **1a-c**, a dimer of the corresponding azomethineimine, namely, 6,13-bis(4-methoxyphenyl)octahydrodipyridazino[1,2-*a*:1'2'-*d*]-1,2,4,5-tetrazine (**2c**, R = OMe) was also obtained from anisaldehyde instead of the diazabicycloheptane.

Carrying out the thermolysis of diazabicycloheptanes **1a-c** for 40 min in *p*-xylene at reflux in the presence of an equimolar amount of N-arylmaleimides **4a-g** gave adducts **5a-m** and **6a-d** in total preparative yields of 66-91%.

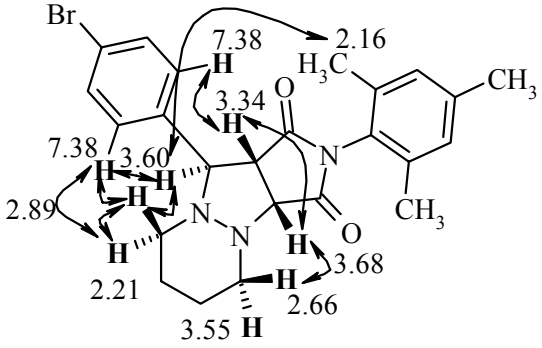


trans- **5a-m** *cis*- **6a-d**

1 a R = Me, **b** R = H, **c** R = Br; **4**–**6 a** Ar = 4-$MeOC_6H_4$, **b** Ar = 4-MeC_6H_4, **c** Ar = Ph, **d** Ar = 4=BrC_6H_4; **4**, **5 e** Ar = 2,6-$Me_2C_6H_3$, **f** Ar = 2,6-$Cl_2C_6H_3$, **g** Ar = 2,4,6-$Me_3C_6H_2$; **5 h**, **k** Ar = 2,6-$Me_2C_6H_3$, **i**, **l** Ar = 2,6-$Cl_2C_6H_3$, **j**, **m** Ar = 2,4,6-$Me_3C_6H_2$; **5 a**–**g** R = Me, **h**–**j** R = H, **k**–**m** R = Br; **6 a**–**d** R = Me

The relative *trans* configuration of adduct **5m** was established using the NOESY 2D ^{1}H NMR spectrum. The major through-space interactions between the protons of this compound seen as the corresponding cross peaks are given in the scheme below. The most important such peak here is observed for the interaction between the proton at 3.60 ppm and the methyl protons at 2.16 ppm, which is possible only for the *trans* isomer.

The configuration of the remaining cycloaddition products **5a-l** and **6a-d** was also determined using the assignments for the ^{1}H NMR signals for adduct **5m**. ^{1}H NMR spectroscopy shows that the ratio of the *trans* and *cis* isomers **5a-d/6a-d** in the reaction mixture was about 3-4:1 but only 1.5-3:1 for the 6-aryl-1,5-diaza-bicyclo[3.1.0]hexanes in the presence of the same maleimides [4, 10], which indicates a slight increase in the steric selectivity with increasing size of the N,N'-polymethylene bridge. On the other hand, the time required for the complete conversion of starting compounds **1a-c** is virtually the same as for the 6-aryl-1,5-diaza-bicyclo[3.1.0]hexanes.



The thermolysis of diaziridines **1a-c** in the presence of 2,6-disubstituted N-arylmaleimides **4e-g** led to the exclusive formation of the *trans* products of 1,3-dipolar cycloaddition. The planes of the benzene and pyrrole rings in these maleimides are virtually orthogonal. Thus, steric hindrance may arise as the *ortho* substituents in the maleimide benzene ring approaches the cyclic azomethinimine. In the case of *Z*-configuration of the virtually planar azomethineimine formed, the strong steric interactions between the *ortho* substituents in the maleimide and the benzene ring of the azomethineimine upon *exo* approach of the dipolarophile should hinder the formation of the *cis* adduct, while such hindrance probably does not obtain in the formation of the *trans* adduct upon *endo* approach of the dipolarophile (from the side of the polymethylene bridge), such that the only products of the cycloaddition are the *trans* adducts.

The thermolysis of azomethineimine dimers **2a-c** in the presence of N-arylmaleimides in *p*-xylene also lead to products of the 1,3-dipolar cycloaddition but requires more prolonged heating (12 h instead of 40 min). Inversion of the steric selectivity is noted for the N-arylmaleimides lacking substituents in the *ortho* position of the benzene ring. The ^{1}H NMR spectra of the reaction mixtures obtained in the thermolysis of dimers **2a** and **2c** in the presence of maleimide **4a** indicated predominance of the corresponding *cis* adducts. On the other hand, the exclusive formation of *trans* adduct **5n** (R = OMe, Ar = 2,4,6-$Me_3C_6H_2$) was found in the thermolysis of dimer **2c** in the presence of N-mesitylmaleimide **4g**.

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra were taken on a Bruker DPX-300 spectrometer at 300 and 75 MHz, respectively, in $CDCl_3$. The chemical shifts are given relative to the signal of the residual chloroform proton (7.26 ppm for ^{1}H NMR) or the $CDCl_3$ signal (77.16 for ^{13}C NMR) [13]. The C, H, N analysis was carried out on a Hewlett-Packard 185B analyzer. The thin-layer chromatographic analysis was carried out on Silufol UV-254 plates with development by UV light or in an iodine chamber. A sample of *p*-xylene was heated at reflux using a Dean-Stark trap, then for 2 h with sodium, and distilled. A sample of *t*-BuOCl was obtained according to Mintz and Walling [14]. The melting points of diazabicycloheptanes **1b** and **1c** coincided with the literature data [7].

7-(4-Tolyl)-1,6-diazabicyclo[4.1.0]heptane (1a). *t*-BuOCl (22 mmol) in methanol (10 ml) was added slowly dropwise to a solution of 1,4-diaminobutane (0.04 mol) in methanol (60 ml) cooled to -10°C. Then, *p*-tolualdehyde (20 mmol) was added dropwise over 30 min. The mixture was stirred for an additional 1 h, left for 24 h in a refrigerator, and filtered through 1 cm Merck 60 (35-70 μm) silica gel. Methanol was removed in vacuum and 100 ml water was added. The mixture was extracted with three ether portions (30 ml) after saturating the solution with NaCl. Ether was evaporated off and the residue was recrystallized from ether to give 3.1 g (82%) **1a**, mp 72°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.78 (4H, m, $(CH_2)_2$); 2.32 (3H, s, CH_3); 2.88 (2H, m, CHN); 3.47 (1H, s, NCHN); 3.50 (2H, m, CHN); 7.13 (2H, d, *J* = 8, H arom); 7.21 (2H, d, *J* = 8, H arom). ^{13}C NMR, δ, ppm: 24.7 (CH_3); 23.4 (2C, CH_3); 51.1 (2C, CH_2); 53.8 (CH); 121.3 (2C); 125.0 (2C); 136.7, 137.5. Found, %: C 76.07; H 8.51; N 14.76. $C_{12}H_{16}N_2$. Calculated, %: C 76.55; H 8.57; N 14.88.

Thermolysis of 7-Aryl-1,5-diazabicyclo[4.1.0]heptanes in the Absence of Dipolarophiles (General Method). A solution of diazabicycloheptane (0.8 mmol) in absolute *p*-xylene (3 ml) was heated for 1 h at 140°C in an argon stream. The solvent was distilled off in vacuum and the residue was recrystallized from ether.

6,13-Bis(4-methylphenyl)octahydrodipyridazino[1,2-*a*:1',2'-*d*]-1,2,4,5-tetrazine (2a) was obtained in 55% yield (77 mg); mp 197°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.48 (8H, m, CH_2CH_2); 2.14 (4H, m, CHN); 2.35 (6H, s, CH_3); 2.46 (4H, m, CHN); 4.03 (2H, s, NCHN); 7.13 (4H, m, H arom); 7.56 (4H, m, H arom). Found, %: C 76.41; H 8.50; N 14.80. $C_{24}H_{32}N_4$. Calculated, %: C 76.55; H 8.57; N 14.88.

6,13-Diphenyloctahydrodipyridazino[1,2-a:1',2'-*d*]-1,2,4,5-tetrazine (2b) [11, 12] was obtained in 57% yield (65 mg); mp 187°C (244°C [11]). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.39 (8H, m, CH_2CH_2); 2.17 (4H, m, CHN); 2.45 (4H, m, CHN); 4.06 (2H, s, NCHN); 7.31 (8H, m, H arom); 7.69 (2H, m, H arom).

6,13-Bis(4-methoxyphenyl)octahydrodipyridazino[1,2-a:1',2'-d]-1,2,4,5-tetrazine (2c) was obtained by a procedure similar to the preparation of **1b** but the addition of the solution of 4-methoxybenzaldehyde in methanol (30 ml) to the solution of 1,4-diaminobutane cooled to -12°C was carried out over 1.5 h. After treatment of the reaction mixture and removal of the solvent, the residue was recrystallized from methanol to give 2.08 g (51%) **2c**; mp 210°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.38 (8H, m, CH_2CH_2); 2.16 (4H, m, CHN); 2.46 (4H, m, CHN); 3.81 (6H, s, OCH_3); 3.97 (2H, s, NCHN); 6.86 (4H, m, H arom); 7.15 (2H, m, H arom), 7.58 (2H, m, H arom). Found, %: C 70.58; H 7.93; N 13.69. $C_{24}H_{32}N_4O_2$. Calculated, %.: C 70.56; H 7.90; N 13.71

Thermolysis of 7-aryl-1,6-diazabicyclo[4.1.0]heptanes in the Presence of N-Arylmaleimides (General Method). N-Arylmaleimide **4a-g** (0.75 mmol) was added to a solution of diazabicycloheptane **1a-c** (0.8 mmol) in absolute *p*-xylene (3 ml) and heated for 1 h at 140°C in an argon stream. The solvent was removed in vacuum and the residue was subjected to chromatography on a column packed with Merck 60 silica gel (35-70 μm) using 2:1 hexane–ethyl acetate as the eluent. The reaction was monitored by thin-layer chromatography; the *trans* isomers have higher R_f values.

(3aR,10R,10aS)-2-(4-Methoxyphenyl)-10-(4-methylphenyl)hexahydropyrrolo[3',4':3,4]pyrazolo-[1,2-*a*]pyridazine-1,3(2H,3aH)-dione (5a) was obtained in 65% yield (208 mg); mp 159°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.49-1.69 (4H, m, CH_2CH_2); 2.23 (1H, t, *J* = 10, CHN); 2.37 (3H, s, CH_3); 2.68 (1H, t, *J* = 8, CHN); 2.88 (1H, t, *J* = 10, CHN); 3.36 (1H, t, *J* = 7.2, CHC=O); 3.50 (1H, d, *J* = 3.6, CHN); 3.58 (1H, d, *J* = 10, CHN); 3.65 (1H, d, *J* = 8, CHN); 3.84 (3H, s, OCH_3); 6.99 (2H, d, *J* = 8, H arom); 7.19 (2H, d, *J* = 7.2, H arom); 7.27 (2H, d, *J* = 7.2, H arom); 7.38 (2H, d, *J* = 8, H arom). ^{13}C NMR spectrum, δ, ppm: 21.5 (CH_3); 24.1 (2C, CH_2); 53.3 (CH_2); 55.6 (CH_2); 55.9 (CH); 66.5 (CH); 71.9 (CH); 114.8 (OCH_3); 124.7, 128.1 (2C); 129.9 (2C); 135.9 (2C); 138.3 (2C); 159.9; 174.1 (C=O); 176.1 (C=O). Found, %: C 70.42; H 6.85; N 10.56. $C_{23}H_{25}N_3O_3$. Calculated, %.: C 70.57; H 6.44; N 10.73.

(3aR,10S,10aS)-2-(4-Methoxyphenyl)-10-(4-methylphenyl)hexahydropyrrolo[3',4':3,4]pyrazolo-[1,2-*a*]-pyridazine-1,3(2H,3aH)-dione (6a) was obtained in 21% yield (48 mg); mp 139°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.46-1.79 (4H, m, CH_2CH_2); 2.06 (1H, m, CHN); 2.34 (3H, s, CH_3); 3.02 (1H, d, *J* = 10, CHN);

3.19 (1H, t, *J* = 10, CHN); 3.40 (1H, d, *J* = 6.5, CHN); 3.50 (1H, d, *J* = 6.5, CHN); 3.63 (1H, m, CHN); 3.82 (3H, s, OCH_3); 4.25 (1H, m, CHC=O); 6.99 (2H, d, *J* = 8, H arom); 7.19 (2H, d, *J* = 7.2, H arom); 7.27 (2H, d, *J* = 7.2, H arom); 7.38 (2H, d, *J* = 8, H arom). ^{13}C NMR spectrum, δ, ppm: 21.7 (CH_3); 24.9 (CH_2); 50.6 (CH_2); 55.9 (CH_2); 114.8 (OCH_3); 124.6, 127.8 (2C); 129.7 (2C); 132.8 (2C); 138.5 (2C); 159.7; 173.9 (C=O); 174.4 (C=O). Found, %: C 70.20; H 6.00; N 10.79. $C_{23}H_{25}N_3O_3$. Calculated ,%: C 70.57; H 6.44; N 10.73.

(3a*R*,10*R*,10a*S*)-2,10-Bis(4-methylphenyl)hexahydropyrrolo[3',4':3,4]pyrazolo[1,2-a]pyridazine-1,3(2H3aH)-dione (5b) was obtained in 41% yield (69 mg) as an oil. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.46-1.79 (4H, m, CH_2CH_2); 2.06 (1H, m, CHN); 2.34 (3H, s, CH_3); 2.19 (3H, s, CH_3); 2.69 (1H, t, *J* = 10, CHN); 2.89 (1H, d, *J* = 10, CHN); 3.37 (1H, t, *J* = 7.2, CHN); 3.63 (1H, m, CHN); 3.80 (1H, m, CHC=O); 4.25 (1H, m, CHC=O); 7.20 (2H, d, *J* = 8, H arom); 7.28 (2H, d, *J* = 8.7, H arom); 7.37 (2H, d, *J* = 8, H arom); 7.62 (2H, d, *J* = 8.7, H arom).

(3a*R*,10*S*,10a*S*)-2,10-Bis(4-methylphenyl)hexahydropyrrolo[3',4':3,4]pyrazolo[1,2-*a*]pyridazine-1,3(2H,3aH)-dione (6b) was obtained in 29% yield (49 mg); mp 148°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.46-1.79 (4H, m, CH_2CH_2); 2.06 (1H, m, CHN); 2.19 (3H, s, CH_3); 2.34 (3H, s, CH_3); 3.02 (1H, d, *J* = 10, CHN); 3.18 (1H, t, *J* = 10, CHN); 3.41 (1H, d, *J* = 6.5, CHN); 3.63 (1H, m, CHN); 3.80 (1H, m, CHC=O); 4.25 (1H, m, CHC=O); 7.20 (2H, d, *J* = 8, H arom); 7.28 (2H, d, *J* = 8.7, H arom); 7.37 (2H, d, *J* = 8, H arom); 7.62 (2H, d, *J* = 8.7, H arom). ^{13}C NMR spectrum, δ, ppm: 21.6 (CH_3); 21.7 (CH_3); 24.9 (CH_3); 31.3 (CH_2); 50.3 (CH_2); 50.6 (CH_2); 126.4, 129.3 (2C); 129.7 (2C); 130.1 (2C); 132.7 (2C); 138.2, 138.5, 138.9, 173.8 (C=O); 174.3 (C=O). Found, %: C 73.57; H 6.71; N 11.19. $C_{23}H_{25}N_3O_2$. Calculated, %: C 73.43; H 6.56; N 11.33.

(3a*R*,10*R*,10a*S*)-10-(4-Methylphenyl)-2-phenylhexahydropyrrolo[3',4':3,4]pyrazolo[1,2-*a*]pyridazine-1,3(2H,3aH)-dione (5c) was obtained in 66% yield (190 mg); mp 154°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.49-1.69 (4H, m, CH_2CH_2); 2.24 (1H, t, *J* = 10, CHN); 2.38 (3H, s, CH_3); 2.69 (1H, t, *J* = 8, CHN); 2.90 (1H, d, *J* = 10, CHN); 3.38 (1H, t, *J* = 7.2, CHC=O); 3.60 (1H, d, *J* = 10, CHN); 3.66 (1H, d, *J* = 8, CHN); 3.77 (1H, d, *J* = 7.2, CHC=O); 7.20 (2H, d, *J* = 8, H arom); 7.35-7.43 (5H, m, H arom); 7.47-7.52 (2H, m, H arom). ^{13}C NMR spectrum, δ, ppm: 21.6 (CH_3); 24.2 (2C, CH_2); 53.2 (CH_2); 53.4 (CH_2); 55.5 (CH); 66.5 (CH); 71.9 (CH); 126.8, 128.2 (2C); 128.9 (2C); 129.9 (2C); 132.0 (2C); 132.0 (2C); 135.9; 138.2; 138.3; 173.8 (C=O); 175.9 (C=O). Found, %: C 73.18; H 6.39; N 11.64. $C_{22}H_{23}N_3O_2$. Calculated, %: C 73.11; H 6.41; N 11.63.

(3a*R*,10*S*,10a*S*)-10-(4-Methylphenyl)-2-phenylhexahydropyrrolo[3',4':3,4]pyrazolo[1,2-*a*]-pyridazine-1,3(2H,3aH)-dione (6c) was obtained in 15.6% yield (37 mg); mp 152°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.49-1.69 (4H, m, CH_2CH_2); 2.24 (1H, m, CHC=O); 2.34 (3H, s, CH_3); 3.03 (1H, d, *J* = 10, CHN); 3.19 (1H, t, *J* = 10, CHN); 3.36 (1H, d, *J* = 6.5, CHN); 3.47 (1H, d, *J* = 6.5, CHN); 3.65 (1H, m, CHN); 3.72-3.96 (1H, m, CHC=O); 7.20 (2H, d, *J* = 8, H arom); 7.35-7.43 (5H, m, H arom); 7.47-7.52 (2H, m, H arom). ^{13}C NMR spectrum, δ, ppm: 21.7 (CH_3), 24.0 (CH_2); 24.9 (CH_2); 50.3 (CH_2); 50.6 (CH_2); 54.8 (CH); 64.7 (CH); 73.2 (CH); 126.6; 128.4 (2C); 128.8 (2C); 129.4 (2C); 129.7 (2C); 131.9, 132.7, 138.5; 173.7 (C=O); 174.2 (C=O). Found, %: C 73.08; H 6.39; N 11.64. $C_{22}H_{23}N_3O_2$. Calculated, %: C 73.11; H 6.41; N 11.63.

(3a*R*,10*R*,10a*S*)-2-(4-Bromophenyl)-10-(4-methylphenyl)hexahydropyrrolo[3',4':3,4]pyrazolo[1,2-*a*]-pyridazine-1,3(2H,3aH)-dione (5d) was obtained in 68% yield (237 mg); mp 140°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.49-1.69 (4H, m, CH_2CH_2); 2.24 (1H, t, *J* = 10, CHN); 2.38 (3H, s, CH_3); 2.69 (1H, t, *J* = 8, CHN); 2.88 (1H, t, *J* = 10, CHN); 3.40 (1H, t, *J* = 7.2, CHC=O); 3.57 (1H, d, *J* = 10, CHN); 3.62 (1H, d, *J* = 7.2, CHN); 3.77 (1H, d, *J* = 8, CHC=O); 7.20 (2H, d, *J* = 8, H arom); 7.28 (2H, d, *J* = 8.7, H arom); 7.37 (2H, d, *J* = 8, H arom); 7.62 (2H, d, *J* = 8.7, H arom). ^{13}C NMR spectrum, δ, ppm: 21.6 (CH_3); 24.0 (CH_2); 24.2 (CH_2); 53.1 (CH_2); 53.3 (CH_2); 55.6 (CH), 66.4 (CH); 71.9 (CH); 122.8; 128.2 (2C); 128.4 (2C); 129.9 (2C); 131.0 (2C); 132.6, 135.7, 138.4, 173.4 (C=O); 175.5 (C=O). Found, %: C 60.14; H 5.36; N 9.89. $C_{22}H_{22}BrN_3O_2$. Calculated, %: C 60.01; H 5.04; N 9.54.

(3aR,10S,10aS)-2-(4-Bromophenyl)-10-(4-methylphenyl)hexahydropyrrolo[3',4':3,4]pyrazolo-[1,2-*a*]pyridazine-1,3(2H,3aH)-dione (6d) was obtained in 24% yield (66 mg); mp 154°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.62 (4H, m, CH_2CH_2); 2.06 (1H, m, CHN); 2.34 (3H, s, CH_3); 3.02 (1H, d , *J* = 10, CHN); 3.16

(1H, t, *J* = 10, CHN); 3.42 (1H, m, CHN); 3.64 (1H, m, CHN); 3.82 (1H, m, CHC=O); 4.26 (1H, m, CHC=O); 7.20 (2H, d, *J* = 8, H arom); 7.28 (2H, d, *J* = 8.7, H arom); 7.37 (2H, d, *J* = 8, H arom); 7.62 (2H, d, *J* = 8.7, H arom). ^{13}C NMR spectrum, δ, ppm: 21.6 (CH_3); 24.0 (CH_2); 24.2 (CH_2); 53.1 (CH_2); 53.3 (CH_2); 55.6 (CH); 66.4 (CH); 71.9 (CH); 122.8; 128.2 (2C); 128.4 (2C); 129.9 (2C); 131.0 (2C); 132.6; 135.7; 138.4; 173.4 (C=O); 175.5 (C=O). Found, %: C 60.33; H 5.19; N 9.76. $C_{22}H_{22}BrN_3O_2$, Calculated, %: C 60.01; H 5.04; N 9.54.

(3a*R*,10*R*,10a*S*)-2-(2,6-Dimethylphenyl)-10-(4-methylphenyl)hexahydropyrrolo[3',4':3,4]pyrazolo-[1,2-*a*]pyridazine-1,3(2H,3aH)-dione (5e) was obtained in 66% yield (205 mg), mp 137°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.46-1.79 (4H, m, CH_2CH_2); 2.09 (3H, s, CH_3); 2.24 (3H, s, CH_3); 2.27 (1H, m, CHN); 2.36 (3H, s, CH_3); 2.68 (1H, t, *J* = 8, CHN); 2.93 (1H, t, *J* = 10, CHN); 3.42 (1H, t, *J* = 7.2, CHC=O); 3.57 (1H, d, *J* = 10, CHN); 3.63 (1H, d, *J* = 7.2, CHN); 3.72 (1H, d, *J* = 7.2, CHC=O); 7.15 (2H, t, *J* = 7, H arom); 7.19 (2H, d, *J* = 8, H arom); 7.23 (1H, d, *J* = 8, H arom); 7.39 (2H, d, *J* = 8, H arom). ^{13}C NMR spectrum, δ, ppm: 18.1 (CH_3); 18.2 (CH_3); 21.5 (CH_3); 24.1 (CH_2); 24.3 (CH_2); 51.2 (CH_2); 53.7 (CH_2); 55.3 (CH); 66.8 (CH); 72.3 (CH); 128.2 (2C); 128.8 (2C); 128.9 (2C); 129.8 (2C); 136.0; 136.3; 136.7; 138.3 (2C); 173.8 (C=O); 175.9 (C=O). Found, %: C 74.20; H 7.00; N 10.79. $C_{24}H_{27}N_3O_2$. Calculated, %: C 74.01; H 6.99; N 10.79.

(3a*R*,10*R*,10a*S*)-2-(2,6-Dichlorophenyl)-10-(4-methylphenyl)hexahydropyrrolo[3',4':3,4]pyrazolo-[1,2-*a*]pyridazine-1,3(2H,3aH)-dione (5f) was obtained in 70% yield (240 mg), mp 150°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.49-1.69 (4H, m, CH_2CH_2); 2.24 (1H, m, CHN); 2.32 (3H, s, CH_3); 2.67 (1H, t, *J* = 8, CHN); 2.91 (1H, t, *J* = 10, CHN); 3.36 (1H, t, *J* = 7.2, CHC=O); 3.56 (1H, d, *J* = 10, CHN); 3.62 (1H, d, *J* = 7.2, CHC=O); 3.69 (1H, d, *J* = 7.2, CHN); 7.19 (2H, d, *J* = 7.2, H arom); 7.37 (1H, t, *J* = 3, H arom); 7.39 (2H, d, *J* = 2, H arom); 7.45 (1H, d, *J* = 7.2, H arom); 7.47 (1H, d, *J* = 8, H arom). ^{13}C NMR spectrum, δ, ppm: 21.5 (CH_3); 24.1 (CH_2); 24.3 (CH_2); 53.6 (CH_2); 53.8 (CH_2); 55.3 (CH); 66.7 (CH); 71.7 (CH); 122.4; 127.3 (2C); 129.3 (2C); 129.7 (2C); 129.8, 129.9 (2C); 132.3 (2C); 136.2, 138.3, 173.6 (C=O); 175.9 (C=O). Found, %: C 61.42; H, 4.85; N 9.56. $C_{22}H_{21}Cl_2N_3O_2$. Calculated, %: C 61.40; H 4.92; N 9.76.

(3a*R*,10*R*,10a*S*)-2-Mesityl-10-(4-methylphenyl)hexahydropyrrolo[3',4':3,4]pyrazolo[1,2-*a*]pyrida-zine-1,3(2H,3aH)-dione (5g) was obtained in 74% yield (238 mg); mp 142°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.46-1.79 (4H, m, CH_2CH_2); 2.05 (3H, s, CH_3); 2.20 (3H, s, CH_3); 2.22 (1H, m, CHN); 2.32 (3H, s, CH_3); 2.37 (3H, s, CH_3); 2.68 (1H, t, *J* = 8, CHN); 2.93 (1H, t, *J* = 10, CHN); 3.41 (1H, t, *J* = 7.2, CHC=O); 3.57 (1H, d, *J* = 10, CHN); 3.63 (1H, d, *J* = 7.2, CHN); 3.70 (1H, d, *J* = 7.2, CHC=O); 6.97 (2H, m, H arom); 7.19 (2H, d, *J* = 8, H arom); 7.30 (2H, d, *J* = 8, H arom). ^{13}C NMR spectrum, δ, ppm: 18.1 (CH_3); 21.5 (CH_3); 24.1 (CH_3); 24.4 (CH_3); 53.7 (CH_2); 55.3 (CH); 66.8 (CH); 72.3 (CH); 127.4 (2C); 128.2; 129.6 (2C); 129.8; 135.9 (2C); 136.3; 138.2 (2C); 139.7; 173.9 (C=O); 176.1 (C=O). Found, %: C 74.20; H 7.00; N 10.79. $C_{25}H_{29}N_3O_2$. Calculated, %: C 74.41; H 7.24; N 10.41.

(3a*R*,10*R*,10a*S*)-2-(2,6-Dimethylphenyl)-10-phenylhexahydropyrrolo[3',4':3,4]pyrazolo[1,2-a]pyrida-zine--1,3(2H,3aH)-dione (5h) was obtained in 72% yield (216 mg); mp 139°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.49-1.69 (4H, m, CH_2CH_2); 2.09 (3H, s, CH_3); 2.22 (1H, t, *J* = 10, CHN); 2.25 (3H, s, CH_3); 2.69 (1H, t, *J* = 8, CHN); 2.95 (1H, d, *J* = 10, CHN); 3.44 (1H, t, *J* = 7.2, CHC=O); 3.57 (1H, d, *J* = 10, CHN); 3.68 (1H, d, *J* = 7.2, CHN); 3.72 (1H, d, *J* = 7.2, CHC=O); 7.16 (2H, t, *J* = 6.5); 7.25 (2H, d, *J* = 8, H arom); 7.32 (1H, d, *J* = 7.2, H arom); 7.39 (2H, t, *J* = 7.2, H arom); 7.51 (2H, d, *J* = 6.5, H arom). ^{13}C NMR spectrum, δ, ppm: 18.1 (CH_3); 18.2 (CH_3); 24.1 (CH_2); 24.3 (CH_2); 53.7 (CH_2); 55.3 (CH); 66.8 (CH); 72.4 (CH); 128.5; 128.8 (2C); 129.0 (2C); 129.2 (2C); 129.8 (2C); 136.3; 136.7; 139.2; 173.6 (C=O); 175.9 (C=O). Found, %: C 73.59; H 6.79; N 10.91. $C_{23}H_{25}N_3O_2$. Calculated, %: C 73.57; H 6.71; N 11.19.

(3a*R*,10*R*,10a*S*)-2-(2,6-Dichlorophenyl)-10-phenylhexahydropyrrolo[3',4':3,4]pyrazolo[1,2-a]pyrida-zine-1,3(2H,3aH)-dione (5i) was obtained in 75% yield (249 mg); mp 131°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.49-1.69 (4H, m, CH_2CH_2); 2.25 (1H, t, *J* = 8, CHN); 2.68 (1H, t, *J* = 8, CHN); 2.91 (1H, d, *J* = 10, CHN); 3.47 (1H, t, *J* = 7.2, CHC=O); 3.57 (1H, d, *J* = 10, CHN); 3.68 (1H, d, *J* = 7.2, CHN); 3.76 (1H, d, *J* = 7.2, CHC=O); 7.19 (2H, d, *J* = 8, H arom); 7.37 (2H, d, *J* = 8, H arom); 7.39 (2H, d, *J* = 8, H arom);

7.46 (2H, t, J = 8, H arom). ^{13}C NMR spectrum, δ, ppm: 23.5 (CH_2); 23.7 (CH_2); 52.9 (CH_2); 53.2 (CH_2); 54.9 (CH); 66.3 (CH); 71.3 (CH); 127.7, 128.4 (2C); 128.5 (2C); 129.3 (2C); 130.9 (2C); 134.4; 134.8; 135.1; 171.7 (C=O); 173.6 (C=O). Found, %: C 60.68; H 4.84; N 9.92. $C_{21}H_{19}Cl_2N_3O_2$; Calculated, %: C 60.59; H 4.60; N 10.09.

(3a*R*,10*R*,10a*S*)-2-Mesityl-10-phenylhexahydropyrrolo[3',4':3,4]pyrazolo[1,2-a]pyridazine-1,3(2H,3aH)- dione (5j) was obtained in 75% yield (233 mg); mp 130°C. ^{1}H NMR spectrum, δ, ppm (J, Hz): 1.49-1.69 (4H, m, CH_2CH_2); 2.05 (3H, s, CH_3); 2.20 (3H, s, CH_3); 2.25 (1H, t, J = 10, CHN); 2.32 (3H, s, CH_3); 2.69 (1H, t, J = 8, CHN); 2.94 (1H, t, J = 10, CHN); 3.42 (1H, t, J = 7.2, CHC=O); 3.67 (1H, d, J = 7.2, CHN); 3.71 (1H, d, J = 7.2, CHC=O); 6.97 (2H, m, H arom); 7.33 (1H, d, J = 7.2, H arom); 7.38 (2H, t, J = 7.2, H arom); 7.51 (2H, d, J = 7.2, H arom). ^{13}C NMR spectrum, δ, ppm: 17.4 (CH_3); 17.5 (CH_3); 20.9 (CH_3); 23.6 (CH_2); 23.8 (CH_2); 53.1 (CH_2); 53.2 (CH_2); 54.7 (CH); 66.2 (CH); 71.8 (CH); 126.8; 127.7 (2C); 128.6 (2C); 129.0 (2C); 129.2; 135.3; 135.7; 173.2 (C=O); 175.5 (C=O). Found, %: C 74.09; H 6.97; N 10.71. $C_{24}H_{27}N_3O_2$. Calculated, %: C 74.01; H 6.99; N 10.79.

(3a*R*,10*R*,10a*S*)-10-(4-Bromophenyl)-2-(2,6-dimethylphenyl)hexahydropyrrolo[3',4':3,4]pyrazolo-[1,2-*a*]pyridazine-1,3(2H,3aH)-dione (5k) was obtained in 73% yield (265 mg); mp 146°C. ^{1}H NMR spectrum, δ, ppm (J, Hz): 154-1.79 (4H, m, CH_2CH_2); 2.23 (3H, s, CH_3); 2.24 (3H, s, CH_3); 2.68 (1H, t, J = 8, CHN); 2.91 (1H, t, J = 10, CHN); 3.37 (1H, t, J = 7.2, CHC=O); 3.52 (1H, d, J = 10, CHN); 3.63 (1H, d, J = 7.2, CHN); 3.71 (1H, d, J = 7.2, CHC=O); 7.16 (2H, m, H arom); 7.17 (2H, d, J = 6, H arom); 7.24 (1H, d, J = 8, H arom); 7.51 (2H, d, J = 8, H arom). ^{13}C NMR spectrum, δ, ppm: 18.1 (CH_3); 18.2 (CH_3); 24.0 (CH_2); 24.2 (CH_2); 53.6 (CH); 53.8 (CH_2); 55.3 (CH_2); 66.7 (CH); 71.7 (CH); 122.4; 128.8 (2C); 129.0 (2C); 129.9 (2C); 132.3 (2C); 136.2; 136.5; 138.2; 173.4 (C=O); 173.4 (C=O). Found, %: C 60.70; H 5.95; N 9.15. $C_{23}H_{24}BrN_3O_2$. Calculated, %: C 60.80; H 5.32; N 9.25.

(3a*R*,10*R*,10a*S*)-10-(4-Bromophenyl)-2-(2,6-dichlorophenyl)hexahydropyrrolo[3'4':3,4]pyrazolo-[1,2-*a*]pyridazine-1,3(2H,3aH)-dione (5l) was obtained in 74% yield (293 mg); mp 151°C. ^{1}H NMR spectrum, δ, ppm (J, Hz): 1.46-1.79 (4H, m, CH_2CH_2); 2.27 (1H, m, CHN); 2.68 (1H, t, J = 8, CHN); 2.90 (1H, t, J = 10, CHN); 3.42 (1H, t, J = 7.2, CHC=O); 3.57 (1H, d, J = 10, CHN); 3.69 (1H, d, J = 7.2, CHN); 3.77 (1H, d, J = 7.2, CHC=O); 7.35 (2H, d, J = 8, H arom); 7.41 (2H, d, J = 8, H arom); 7.45 (2H, d, J = 8, H arom); 7.50 (2H, d, J = 6.5, H arom); 7.53 (2H, d, J = 8, H arom). ^{13}C NMR spectrum, δ, ppm: 24.0 (CH_2); 24.2 (CH_2); 53.6 (CH); 55.5 (CH); 66.7 (CH); 122.5; 128.2 (2C); 129.0 (2C); 129.1 (2C); 130.0 (2C); 131.6; 132.3 (2C); 134.9; 135.2 (2C); 137.9; 172.0 (C=O); 174.0 (C=O). Found, %: C 50.62; H 3.78; N 8.16. $C_{21}H_{18}BrCl_2N_3O_2$. Calculated, %: C 50.93; H 3.66; N 8.49.

(3a*R*,10*R*,10a*S*)-10-(4-Bromophenyl)-2-mesitylhexahydropyrrolo[3',4':3,4]pyrazolo[1,2-*a*]pyridazine-1,3(2H,3aH)-dione (5m) was obtained in 77% yield (288 mg); mp 147°C. ^{1}H NMR spectrum, δ, ppm (J, Hz): 1.49-1.69 (4H, m, CH_2CH_2); 2.02 (3H, s, CH_3); 2.16 (3H, s, CH_3); 2.21 (1H, m, CHN); 2.30 (3H, s, CH_3); 2.66 (1H, t, J = 8, CHN); 2.89 (1H, t, J = 10, CHN); 3.34 (1H, t, J = 7.2, CHC=O); 3.55 (1H, d, J = 10, CHN); 3.60 (1H,d , J = 7.2, CHC=O); 3.68 (1H, d, J = 7.2, CHN); 6.94 (1H, s, H arom); 6.96 (1H, s, H arom); 7.38 (2H, d, J = 8, H arom); 7.49 (2H, d, J = 8, H arom). ^{13}C NMR spectrum, δ, ppm: 18.0 (CH_3); 18.1 (CH_3); 21.5 (CH_3); 24.1 (CH_2); 24.3 (CH_2); 53.6 (CH); 66.7 (CH); 71.7 (CH); 122.4 (2C); 129.8 (2C); 129.9; 132.3; 135.8 (2C); 136.2 (2C); 138.3; 139.8; 173.6 (C=O); 175.9 (C=O). Found, %: C 61.66; H 5.70, N 8.73. $C_{24}H_{26}BrN_3O_2$. Calculated, %: C 61.54; H 5.60; N 8.97.

Thermolysis of Tetrazines 2a-c in the Presence of N-Arylmaleimides. N-Arylmaleimide (0.8 mmol) was added to a solution of tetrazine (0.4 mmol) in absolute *p*-xylene (3 ml) and heated for 12 h at 140°C in an argon stream. After removal of the solvent, the residue was recrystallized from ether.

(3a*R*,10*R*,10a*S*-2-Mesityl-10-(4-methoxyphenyl)hexahydropyrrolo[3',4':3,4]pyrazolo[1,2-*a*]pyridazine-1,3(2H,3aH)-dione (5n) was obtained in 85% yield (284 mg); mp 125°C. ^{1}H NMR spectrum, δ, ppm (J, Hz): 1.46-1.79 (4H, m, CH_2CH_2); 2.05 (3H, s, CH_3); 2.19 (3H, s, CH_3); 2.22 (1H, t, J = 10, CHN); 2.32 (3H, s, CH_3); 2.67 (1H, t, J = 8, CHN); 2.92 (1H, t, J = 10, CHN); 3.39 (1H, t, J = 7.2, CHC=O); 3.57 (1H, d, J = 10,

CHN); 3.63 (1H, d, J = 7.2, CHN); 3.70 (1H, d, J = 7.2, CHC=O); 3.83 (3H, s, OCH_3); 6.91 (2H, d, J = 8, H arom); 6.94 (1H, s, H arom); 6.96 (1H, s, H arom); 7.42 (2H, d, J = 8, H arom). ^{13}C NMR spectrum, δ, ppm: 18.0 (CH_3); 18.1 (CH_3); 21.5 (CH_3); 24.13 (CH_3); 24.36 (CH_2); 24.9 (CH_2); 50.3 (CH_2); 50.6 (CH_2); 54.8 (CH); 64.7 (CH); 73.2 (CH); 126.6; 128.4 (2C); 128.8 (2C); 129.4 (2C); 129.7 (2C); 131.9; 132.7; 138.5; 173.9 (C=O); 176.2 (C=O). Found, %: C 72.01; H 6.49; N 10.34. $C_{25}H_{29}N_3O_3$, Calculated, %: C 71.57; H 6.97; N 10.02.

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