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The Cycloaddition of the *N*-Arylmaleimides to Aryl(3,4-dihydroisoquinolinium-2-yl)amides

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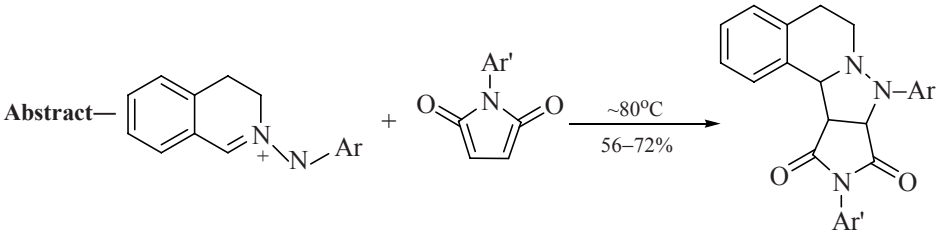
Abstract—



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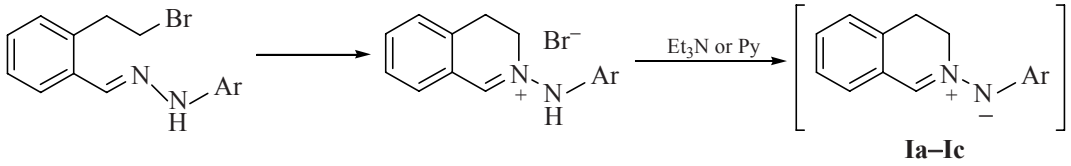
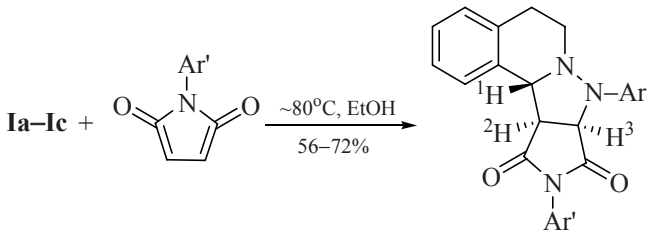
1,3-Dipolar cycloaddition is an effective procedure for the synthesis of 5-membered heterocycles providing a highly stereo- and regioselective preparation of the polyfunctional compounds having several asymmetric centers simultaneously [1]. Azomethine imines are very reactive 1,3-dipoles which can react even with the low active dipolarophiles like nitriles and Schiff bases [2] giving various nitrogen-containing heterocyclic, fused, and spiro-joined systems [3]. One of the method to generate azomethine imines with a structural fragment of 3,4-dihydroisoquinoline *in situ* is a deprotonation of tertiary hydrazonium derivatives under basic conditions [4, 5].



Ar = Ph (**a**), 4-$NO_2C_6H_4$ (**b**), 2,4-$(NO_2)_2C_6H_3$ (**c**).

The cycloaddition of *N*-methylmaleimide to azomethine imine **Ia** prepared by a catalytic dehydration of 2-phenylamino-3,4-dihydroisoqionoline leads exclusively to the *trans*-adduct [6], whereas for the analogous azomethine imines with a phenanthridine moiety the formation of the *cis*-adduct is only observed [7]. However the interaction of *N*-arylmaleimides with azomethine imines generated by the thermolysis of *cis*-*N,N*'-dialkylsubstituted diaziridines, 6-aryl-1,5-diazabicyclo[3.1.0]hexanes [8] or *trans*-*N,N*'-dialkylsubstituted diaziridines with a skeleton of 3,4-dihydroisoquinoline [9], resulted in the formation of *cis*- and *trans*-isomers mixtures in the absence of any substituents in the *ortho*-positions of the arylmaleimide and led to the *trans*-adducts only in the case of 2,6-disubstituted *N*-arylmaleimides.

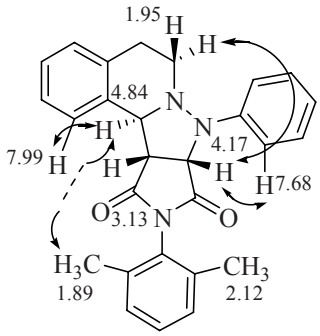
In the present work we investigated a stereoselectivity of *N*-arylmaleimides cycloaddition to azomethine imines (**Ia–Ic**) generated *in situ*. Azomethine imines (**Ia–Ic**) reacted with *N*-arylmaleimides (**IIa–IIg**) to form exclusively *trans*-cycloadducts (**IIIa–IIIj**) irrespective of a character and location of the benzene ring substituents both in imide and azomethine imine. At the same time no azomethine imine dimers similar to the dimers described in the literature [5] were observed in the reaction mixtures.



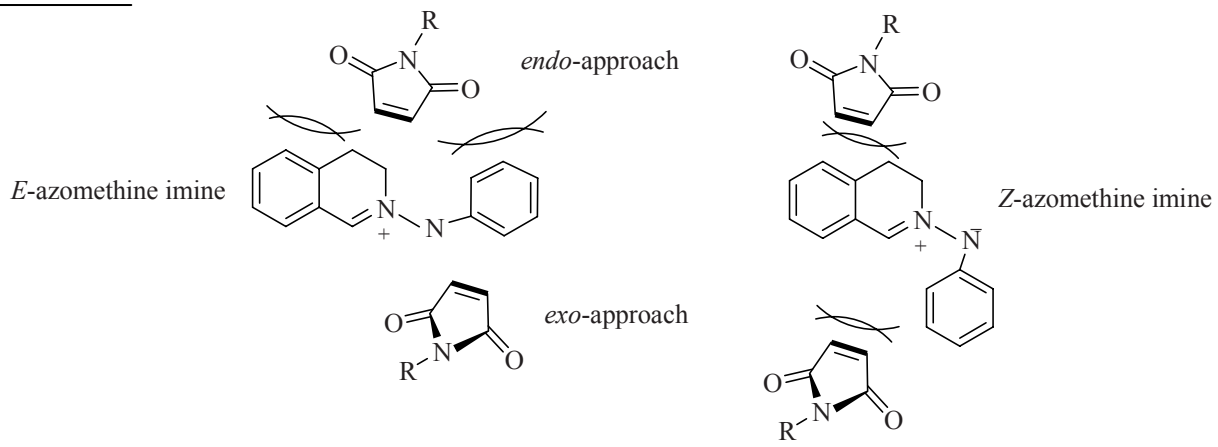
IIa–IIg **IIIa–IIIj**

II: Ar' = Mes (**a**), Ph (**b**), 4-BrC_6H_4 (**c**), 4-$MeOC_6H_4$ (**d**), 4-$NO_2C_6H_4$ (**e**), 2,6-$(CH_3)_2C_6H_3$ (**f**), 2,6-$Cl_2C_6H_3$ (**g**); **III**: Ar = Ph, Ar' = Mes (**a**), Ph (**b**), 4-BrC_6H_4 (**c**), 4-$MeOC_6H_4$ (**d**), 4-$NO_2C_6H_4$ (**e**), 2,6-$(CH_3)_2C_6H_3$ (**f**), 2,6-$Cl_2C_6H_3$ (**g**); Ar = 4-$NO_2C_6H_4$, Ar' = Ph (**h**), Mes (**i**); Ar = 2,4-$(NO_2)_2C_6H_3$, Ar' = Mes (**j**).

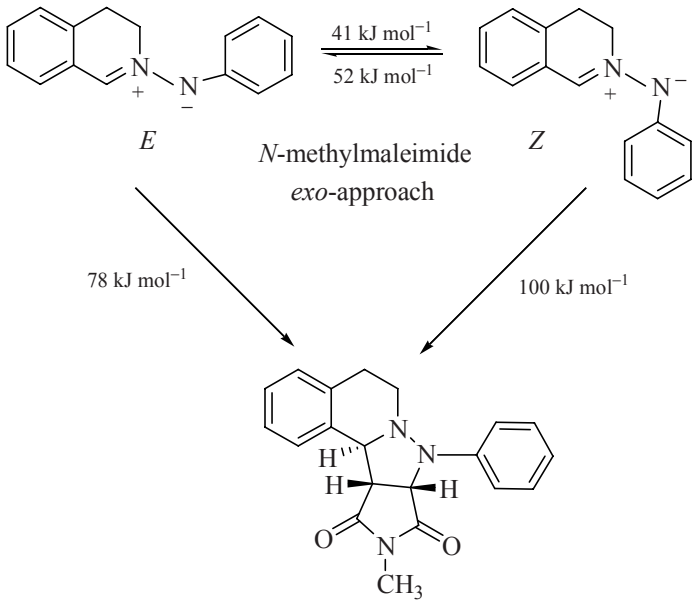
A typical ^{1}H NMR spectrum of the adduct **IIIf** in deuterobenzene contained the following signals (δ, ppm; *J*, Hz): singlets of the protons of methyl groups at 1.89 (3H) and 2.12 (3H), multiplets of methylene protons in the regions 1.87–2.03 (1H), 2.29–2.41 (1H), 2.76–2.92 (1H) and 2.97–3.08 (1H), proton H^2 at 3.13 d.d (1H, ~8.0 and ~8.0), proton H^3 at 4.17 d (1H, ~8.0) and proton H^1 at 4.84 d (1H, ~8.0), and also aromatic protons in the regions 6.74–6.81 (1H), 6.84–7.20 (6H), 7.23–7.24 (2H), 7.63–7.73 (2H) and at 7.99 d (1H, 7.4). There were no very broad signals in this spectrum recorded at room temperature as were observed in the cases of cycloadducts of arylmaleimides with methyl-(3,4-dihydroisoquinolinium-2-yl)amides [9], because the introduction of an aryl group instead of methyl significantly decreased the flexibility of the adduct skeleton. However, in our case it was not possible to determine a relative configuration of the adduct directly from the spin-spin coupling constants between protons H^1 and H^2, because the value $J \sim 8$ Hz for the fused 5-membered cycles could be attributed both to *trans*-, and *cis*-adducts. Therefore, the *trans*-configuration of the prepared cycloaddition products was unequivocally established with the aid of 2D ^{1}H NMR spectrum (NOESY, C_6D_6) of the adduct (3f). In this spectrum a cross-peak of the through-space interaction between proton at δ 4.84 ppm and methyl protons at δ 1.89 ppm was observed, but there were no cross-peaks for the interaction between methyl protons at δ 1.89 and protons at δ 3.13 and 4.17 ppm, that could only be pos-sible in the case of *trans*-configuration of the adduct. Main through-space interactions observed in the NOESY spectrum of the adduct **IIIf** are shown below.



Exclusively high stereoselectivity of the cycloaddition in the case of aryl(3,4-dihydroisoquinolinium-2-yl)amides in comparison with methyl(3,4-dihydroisoquinolinium-2-yl)amide and methyl(3,3-dimethyl-3,4-dihydroisoquinolinium-2-yl)amide [9] can be caused by an increase in the steric hindrance when a methyl group was replaced by an aryl one. Model analysis of the spatial course of this reaction shows that the *trans*-adduct should be formed in the case of *exo*-approach of maleimide to the corresponding azomethine imine. At the same time, azomethine imine can exist both in *Z*-, and *E*-forms. As it is shown in the scheme given below, the *exo*-approach of a dipolarophile to *E*-azomethine imine seems more preferable, whereasthe *endo*-approach leading to the *cis*-adducts should suffer a significant steric hindrance.



In accordance with a quantum-chemical calculation (DFT, basis 6-31G(d), B3LYP, Gaussian-03 [10]) *Z*-azomethine imine is more stable than *E*-azomethine imine, and a difference in the activation barrier values for the *Z/E*-isomerization is ~11 kJ mol^{-1} ($\Delta G^{\neq}_{Z\text{-}E}$ = 52 kJ mol^{-1} and $\Delta G^{\neq}_{Z\text{-}E}$ = 41 kJ mol^{-1}), so that in the reaction mixture at the temperature ~80°C about 97–98% of *Z*-form and ~2-3% of *E*-form should be in equilibrium. At the same time, activation barrier for the *exo*-approach of methylmaleimide to *E*-azomethine imine is on ~22 kJ mol^{-1} smaller than in the case of *Z*-azomethine imine ($\Delta G^{\neq}_{Z\text{-}E}$ ~100 kJ mol^{-1} and $\Delta G^{\neq}_{Z\text{-}E}$ ~78 kJ mol^{-1}, respectively). From this we can evaluate that cycloaddition to *E*-azomethine imine proceeds ~2000 times faster than to *Z*-azomethine imine. For the *endo*-approach of methylmaleimide *Z*-azomethine imine the activation barrier is ~97 kJ mol^{-1}.



As a result we can assume that azomethine imines **Ia–Ic** react with *N*-arylmaleimides in the less stable but more active *E*-form, where the phenyl group rotated relative to the azomethine imine plane prevents the *endo*-approach of a dipolarophile. For the *exo*-approach this steric hindrance is absent, therefore exclusively *trans*-isomers are formed.

EXPERIMENTAL

Elemental analyses were done on C, H, N-analyser Hewlett-Packard-185B. IR spectra were obtained for 1–2% solutions in chloroform. NMR spectra of compounds were recorded on Bruker DPX-300 instrument [300.13 (^{1}H), 75.468 MHz (^{13}C)] in $CDCl_3$, DMSO-d_6, C_6D_6. Chemical shifts were given relative to the residual proton signals of deuterochloroform, DMSO-d_6, benzene-d_6 (7.26 ppm, 2.50 ppm, 7.16 ppm for ^{1}H NMR, respectively [11]) or carbons signals of deuterochloroform, DMSO-d_6 (77.16 ppm and 39.52 ppm for ^{13}C NMR, respectively).

General procedure for the preparation of compounds (IIIa–IIIg). To a solution of 1 mmol of phenylhydrazine in 1 ml of ethanol a solution of 1 mmol of 2-(2-bromoethyl)benzaldehyde in 1 ml of ethanol was added at stirring. Then the reaction mixture was heated up to 80°C on a water bath, and a warm solution of 1 mmol of *N*-arylmaleimide and 200 μl of pyridine in a small volume of ethanol (5–7 ml) was added. The mixture was refluxed for about 1.5 h, then the mixture was cooled, the precipitate was filtered off and refluxed with 5–7 ml of ethanol for about 20 min. Then the precipitate was filtered off and dried in air.

General procedure for the preparation of compounds (IIIh–IIIi). A solution of 1 mmol of 4-nitrophenylhydrazine in 5 ml of ethanol was heated up to 80°C with stirring on a water bath, then a solution of 1 mmol of 2-(2-bromoethyl)benzaldehyde in 1 ml of ethanol was added. A warm solution of 1 mmol of *N*-arylmaleimide and 200 μl pyridine in a small volume of ethanol (5–7 ml) was added in 5–10 min. After that a mixture was treated as described above.

***rel*-(8a*R*,11a*S*,11b*R*)-10-Mesityl-8-phenyl-5,6,-11a,11b-tetrahydro-8*H*-pyrrolo[3',4':3,4]-pyrazolo-[5,1-*a*]isoquinoline-9,11(8a*H*,10*H*)-dione (IIIa).** Yield 346 mg (79%). mp 241–242°C. IR spectrum, ν, cm^{-1}: 1040, 1240, 1310, 1340, 1380, 1455, 1495, 1600, 1725 s, 1790, 2860, 2930, 3070. ^{1}H NMR spectrum, δ, ppm, $CDCl_3$: 2.12 s (6H, $2CH_3$), 2.31 s (3H, CH_3), 2.38–2.56 m (1H, CH_2CH_2), 2.75–2.88 m (1H, CH_2CH_2), 3.02–3.19 m (1H, CH_2CH_2), 3.23–3.37 m (1H, CH_2CH_2), 3.97 d.d (1H, *J* ~8.0 and ~8.0, CH), 4.80 d (1H, *J* ~8.0, CH), 4.92 d (1H, *J* ~8.0, CH), 6.91–7.01 m ($3H_{arom}$), 7.12–7.20 m ($1H_{arom}$), 7.21–7.39 m ($4H_{arom}$), 7.42–7.50 m ($2H_{arom}$), 7.77 d ($H_{arom.}$, *J* 6.8). ^{13}C NNR spectrum, δ, ppm, $CDCl_3$: 17.9 ($2CH_3$), 21.2 (CH_3), 29.1 (CH_2), 41.6 (CH_2), 54.6 (CH), 61.6 (CH), 65.3 (CH), 117.9 ($2CH_{arom}$), 121.2 (CH_{arom}), 126.9 (CH_{arom}), 127.1 (C_{arom}), 127.6 (CH_{arom}), 128.3 (CH_{arom}), 128.5 (CH_{arom}), 129.2 ($2CH_{arom}$), 129.4 (CH_{arom}), 129.5 (CH_{arom}), 133.5 (C_{arom}), 134.2 (C_{arom}), 135.5 (C_{arom}), 135.6 (C_{arom}), 139.6 (C_{arom}), 144.5 (C_{arom}), 172.2 (C=O), 175.0 (C=O). Found, %: C 76.89; H 6.26; N 9.75. $C_{28}H_{27}N_3O_2$. Calculated, %: C 76.86; H 6.22; N 9.60.

***rel*-(8a*R*,11a*S*,11b*R*)-8,10-Diphenyl-5,6,11a,11b-tetrahydro-8*H*-pyrrolo[3',4':3,4]pyrazo-lo[5,1-*a*]-isoquinoline-9,11(8a*H*,10*H*)-dione (IIIb).** Yield 245 mg (62%). mp 233–234°C. IR spectrum, ν, cm^{-1}: 1040, 1170, 1260, 1305, 1390, 1500, 1520, 1600, 1720 s, 1785, 2840, 2915, 2940, 2965, 3045. ^{1}H NMR spectrum, δ, ppm, $CDCl_3$: 2.34–2.55 m (1H, CH_2CH_2), 2.73-2.87 m (1H, CH_2CH_2), 3.02–3.19 m (1H, CH_2CH_2), 3.20–3.38 m (1H, CH_2CH_2), 3.95 d.d (1H, *J* ~8.0 and ~8.0, CH), 4.80 d (1H, *J* ~8.0, CH), 4.88 d (1H, *J* ~8.0, CH), 6.92–7.02 m ($1H_{arom}$), 7.13–7.21 m ($1H_{arom}$), 7.22–7.53 m ($11H_{arom}$), 7.78 d ($1H_{arom.}$, *J* 6.7). ^{13}C NNR spectrum, δ, ppm, $CDCl_3$: 29.1 (CH_2), 41.7 (CH_2), 54.4 (CH), 61.1 (CH), 64.9 (CH), 117.9 ($2CH_{arom}$), 121.3 (CH_{arom}), 126.6 ($2CH_{arom}$), 126.9 (CH_{arom}), 127.6 (CH_{arom}), 128.3 (CH_{arom}), 128.5 (CH_{arom}), 128.9 (CH_{arom}), 129.3 ($4CH_{arom}$), 131.6 (C_{arom}), 133.5 (C_{arom}), 134.2 (C_{arom}), 144.2 (C_{arom}), 172.1 (C=O), 175.0 (C=O). Found, %: C 76.03; H 5.41; N 10.61. $C_{25}H_{21}N_3O_2$. Calculated, %: C 75.93; H 5.35; N 10.63.

***rel*-(8a*R*,11a*S*,11b*R*)-10-(4-Bromophenyl)-8-phenyl-5,6,11a,11b-tetrahydro-8*H*-pyrrolo-[3',4':3,4]pyrazolo[5,1-*a*]isoquinoline-9,11(8a*H*,10*H*)-dione (IIIc).** Yield 266 mg (56%). mp 225–226°C. IR spectrum, ν, cm^{-1}: 1040, 1080, 1240, 1310, 1380, 1495, 1600, 1725 s, 1790, 2845, 2910, 3080. ^{1}H NMR spectrum, δ, ppm, $CDCl_3$: 2.35–2.56 m (1H, CH_2CH_2), 2.73–2.90 m (1H, CH_2CH_2), 3.01–3.19 m (1H, CH_2CH_2), 3.20–3.36 m (1H, CH_2CH_2), 3.92 d.d (1H, *J* ~8.0 and ~8.0, CH), 4.79 d (1H, *J* ~8,0, CH), 4.87 d (1H, *J* ~8,0, CH), 6.94–7.02 m ($1H_{arom}$), 7.13–7.20 m ($1H_{arom}$), 7.22–7.39 m ($6H_{arom}$), 7.40–7.48 m ($2H_{arom}$), 7.55–7.64 m ($2H_{arom}$), 7.75 d ($1H_{arom.}$, *J* 6.7). ^{13}C NNR spectrum, δ, ppm, $CDCl_3$: 28.9 (CH_2), 41.7 (CH_2), 54.4 (CH), 61.1 (CH), 64.9 (CH), 118.0 ($2CH_{arom}$), 121.5 (CH_{arom}), 122.8 (C_{arom}), 126.9 (CH_{arom}), 127.7 (CH_{arom}), 128.1 ($2CH_{arom}$), 128.4 ($2CH_{arom}$), 129.3 ($2CH_{arom}$), 130.6 (C_{arom}), 132.4 ($2CH_{arom}$), 133.4 (C_{arom}), 134.0 (C_{arom}), 144.1 (C_{arom}), 171.8 (C=O), 174.7 (C=O). Found, %: C 63.30; H 4.32; N 8.70. $C_{25}H_{20}BrN_3O_2$. Calculated, %: C 63.30; H 4.25; N 8.86.

***rel*-(8a*R*,11a*S*,11b*R*)-10-(4-Methoxyphenyl)-8-phenyl-5,6,11a,11b-tetrahydro-8*H*-pyrrolo[3',4':3,4]-pyrazolo[5,1-*a*]isoquinoline-9,11(8a*H*,10*H*)-dione (IIId).** Yield 250 mg (58.5%). mp 223–224°C. IR spectrum, ν, cm^{-1}: 1040, 1170, 1260, 1305, 1390, 1500, 1520, 1600, 1720 s, 1785, 2840, 2915, 2940, 2965, 3045. ^{1}H NMR spectrum, δ, ppm, $CDCl_3$: 2.35-2.56 m (1H, CH_2CH_2), 2.74–2.88 m (1H, CH_2CH_2), 3.03–3.19 m (1H, CH_2CH_2), 3.22–3.36 m (1H, CH_2CH_2), 3.83 s (3H, OCH_3), 3.92 d.d (1H, *J* ~8.0 and ~8.0, CH), 4.78 d (1H, *J* ~8.0, CH), 4.87 d (1H, *J* ~8.0, CH), 6.92–7.03 m ($3H_{arom}$), 7.13–7.20 m ($1H_{arom}$), 7.21-7.39 m ($6H_{arom}$), 7.42-7.51 m ($2H_{arom}$), 7.78 d ($H_{arom.}$, *J* 6.7). ^{13}C NNR spectrum, δ, ppm, $CDCl_3$: 29.1 (CH_2), 41.8 (CH_2), 54.3 (CH), 55.6 (OCH_3), 61.1 (CH), 64.9 (CH), 114.5 ($2CH_{arom}$), 117.9 ($2CH_{arom}$), 121.2 (CH_{arom}), 124.2 (C_{arom}), 126.9 (CH_{arom}), 127.6 (CH_{arom}), 127.9 ($2CH_{arom}$), 128.3 (CH_{arom}), 128.5 (CH_{arom}), 129.3 ($2CH_{arom}$), 133.5 (C_{arom}), 134.2 (C_{arom}), 144.3 (C_{arom}) 159.7 (C_{arom}), 172.4 (C=O), 175.3 (C=O). Found, %: C 73.36; H 5.59; N 9.84. $C_{26}H_{23}N_3O_3$. Calculated, %: C 73.39; H 5.45; N 9.88.

***rel*-(8a*R*,11a*S*,11b*R*)-10-(4-Nitrophenyl)-8-phenyl-5,6,11a,11b-tetrahydro-8*H*-pyrrolo-[3',4':3,4]pyrazolo[5,1-*a*]isoquinoline-9,11(8a*H*,10*H*)-dione (IIIe).** Yield 301 mg (68%). mp 232–233°C. IR spectrum, ν, cm^{-1}: 1040, 1240, 1305, 1350, 1375, 1500, 1535, 1600, 1725 s, 1790, 2845, 2920, 2940, 3060. ^{1}H NMR spectrum, δ, ppm, $CDCl_3$: 2.37–2.61 m (1H, CH_2CH_2), 2.76–2.94 m (1H, CH_2CH_2), 3.01–3.20 m (1H, CH_2CH_2), 3.22–3.41 m (1H, CH_2CH_2), 3.90–4.09 m (1H, CH), 4.75–4.88 m (1H, CH), 4.89–5.02 m (1H, CH), 6.94–7.08 m ($1H_{arom}$), 7.13–7.23 m ($1H_{arom}$), 7.24–7.54 m ($6H_{arom}$), 7.67 d ($2H_{arom.}$, *J* 7.8), 7.71–7.82 m (H_{arom}), 8.34 d ($2H_{arom.}$, *J* 7.8). ^{13}C NNR spectrum, δ,

ppm, $CDCl_3$: 28.9 (CH_2), 42.0 (CH_2), 54.5 (CH), 55.6 (OCH_3), 61.1 (CH), 65.0 (CH), 118.1 ($2CH_{arom}$), 121.7 (CH_{arom}), 124.5 ($2CH_{arom}$), 127.0 (CH_{arom}), 127.2 ($2CH_{arom}$), 127.8 (CH_{arom}), 128.3 (CH_{arom}), 128.4 (CH_{arom}), 129.4 ($2CH_{arom}$), 133.4 (C_{arom}), 133.8 (C_{arom}), 137.1 (C_{arom}), 143.9 (C_{arom}) 147.2 (C_{arom}), 171.4 (C=O), 174.4 (C=O). Found, %: C 68.39; H 4.65; N 12.39. $C_{25}H_{20}N_4O_4$. Calculated, %: C 68.17; H 4.58; N 12.72.

***rel*-(8a*R*,11a*S*,11b*R*)-10-(2,6-Dimethylphenyl)-8-phenyl-5,6,11a,11b-tetrahydro-8*H*-pyrrolo[3',4':3,4]-pyrazolo[5,1-*a*]isoquinoline-9,11(8a*H*,10*H*)-dione (IIIf).** Yield 288 mg (68%). mp 212–213°C. IR spectrum, ν, cm^{-1}: 1040, 1170, 1275, 1310, 1375, 1455, 1475, 1495, 1720 s, 1785, 2845, 2930, 2980, 3040. ^1H NMR spectrum, δ, ppm, C_6D_6: 1.89 s (3H, CH_3), 1.87–2.03 m (1H, CH_2CH_2), 2.12 s (3H, CH_3), 2.29–2.41 m (1H, CH_2CH_2), 2.76–2.92 m (1H, CH_2CH_2), 2.97–3.08 m (1H, CH_2CH_2), 3.13 d.d (1H, *J* ~8.0 and ~8.0, CH), 4.17 d (1H, *J* ~8.0, CH), 4.84 d (1H, *J* ~8.0, CH), 6.74–6.81 m ($1H_{arom}$), 6.84–7.20 m ($6H_{arom}$), 7.23–7.24 m ($2H_{arom}$), 7.63–7.73 m ($2H_{arom}$), 7.99 d ($1H_{arom.}$, *J* 7.4). ^{13}C NNR spectrum, δ, ppm, $CDCl_3$: 18.0 ($2CH_3$), 29.1 (CH_2), 41.7 (CH_2), 54.7 (CH), 61.5 (CH), 65.3 (CH), 118.0 ($2CH_{arom}$), 121.3 (CH_{arom}), 126.9 (CH_{arom}), 127.7 (CH_{arom}), 128.3 (CH_{arom}), 128.4 (CH_{arom}), 128.7 (CH_{arom}), 128.8 (CH_{arom}), 129.2 ($2CH_{arom}$), 129.7 (CH_{arom}), 129.8 (C_{arom}), 133.4 (C_{arom}), 134.1 (C_{arom}), 135.9 (C_{arom}), 136.0 (C_{arom}), 144.4 (C_{arom}), 172.1 (C=O), 174.9 (C=O). Found, %: C 76.57; H 5.97; N 9.96. $C_{27}H_{25}N_3O_2$. Calculated, %: C 76.57; H 5.95; N 9.92.

***rel*-(8a*R*,11a*S*,11b*R*)-10-(2,6-Dichlorophenyl)-8-phenyl-5,6,11a,11b-tetrahydro-8*H*-pyrrolo[3',4':3,4]-pyrazolo[5,1-*a*]isoquinoline-9,11(8a*H*,10*H*)-dione (IIIg).** Yield 405 mg (87%). mp 227–228°C. IR spectrum, ν, cm^{-1}: 1105, 1245, 1310, 1380, 1470, 1500, 1600, 1725 s, 1795, 2920, 3080. ^1H NMR spectrum, δ, ppm, $CDCl_3$: 2.35–2.57 m (1H, CH_2CH_2), 2.76–2.93 m (1H, CH_2CH_2), 3.05–3.22 m (1H, CH_2CH_2), 3.26–3.44 m (1H, CH_2CH_2), 4.00 d.d (1H, *J* ~8.0 and ~8.0, CH), 4.90 d (1H, *J* ~8.0, CH), 5.02 d (1H, *J* ~8.0, CH), 6.91–7.01 m ($1H_{arom}$), 7.13–7.21 m ($1H_{arom}$), 7.22–7.50 m ($9H_{arom}$), 7.70 d ($H_{arom.}$, *J* 6.5). ^{13}C NNR spectrum, δ, ppm, $CDCl_3$: 29.1 (CH_2), 41.8 (CH_2), 54.5 (CH), 61.8 (CH), 65.0 (CH), 117.5 ($2CH_{arom}$), 121.0 (CH_{arom}), 126.8 (CH_{arom}), 127.8 (CH_{arom}), 127.9 (C_{arom}), 128.3 (C_{arom}), 128.4 (CH_{arom}), 128.8 (CH_{arom}), 128.9 (CH_{arom}), 129.3 ($2CH_{arom}$), 131.5 (CH_{arom}), 133.4 (C_{arom}), 133.8 (C_{arom}), 134.7 (C_{arom}), 134.8 (C_{arom}), 144.2 (C_{arom}), 170.7 (C=O), 173.1 (C=O). Found, %: C 64.77; H 4.21; N 9.27. $C_{25}H_{19}Cl_2N_3O_2$. Calculated, %: C 64.66; H 4.12; N 9.05.

***rel*-(8a*R*,11a*S*,11b*R*)-8-(4-Nitrophenyl)-10-phenyl-5,6,11a,11b-tetrahydro-8*H*-pyrrolo[3',4':3,4]pyrazolo[5,1-*a*]isoquinoline-9,11(8a*H*,10*H*)-dione (IIIh).** Yield 329 mg (75%). mp 244–245°C. IR spectrum, ν, cm^{-1}: 1120, 1200, 1245, 1320, 1340, 1380, 1520, 1595, 1720 s, 1805, 3070. ^1H NMR spectrum, δ, ppm, DMSO-d_6: 2.64–2.77 m (1H, CH_2CH_2), 2.80–2.93 m (1H, CH_2CH_2), 3.00–3.12 m (1H, CH_2CH_2), 3.13–3.25 m (1H, CH_2CH_2), 4.10 d.d (1H, *J* ~8.5 and ~8.5, CH), 4.97 d (1H, *J* ~8.5, CH), 5.49 d (1H, *J* ~8.5, CH), 7.18–7.30 m ($3H_{arom}$), 7.30–7.39 m ($2H_{arom}$), 7.40–7.57 m ($6H_{arom}$), 8.12–8.21 m ($2H_{arom}$). ^{13}C NNR spectrum, δ, ppm, DMSO-d_6: 28.5 (CH_2), 43.4 (CH_2), 52.8 (CH), 62.1 (CH), 63.2 (CH), 114.7 ($2CH_{arom}$), 125.6 ($2CH_{arom}$), 126.2 (CH_{arom}), 127.5 ($2CH_{arom}$), 127.6 (CH_{arom}), 127.8 (CH_{arom}), 128.2 (CH_{arom}), 128.4 (CH_{arom}), 128.9 (CH_{arom}), 129.0 ($2CH_{arom}$), 132.0 (C_{arom}), 133.2 (C_{arom}), 133.3 (C_{arom}), 138.4 (C_{arom}), 149.1 (C_{arom}), 172.4 (C=O), 173.9 (C=O). Found, %: C 68.39; H 4.65; N 12.39. $C_{25}H_{20}N_4O_4$. Calculated, %: C 68.17; H 4.58; N 12.72.

***rel*-(8a*R*,11a*S*,11b*R*)-10-Mesityl-8-(4-nitrophenyl)-5,6,11a,11b-tetrahydro-8*H*-pyrrolo[3',4':3,4]pyrazolo[5,1-*a*]isoquinoline-9,11(8a*H*,10*H*)-dione (IIIi).** Yield 370 mg (77%). mp 242–243°C. IR spectrum, ν, cm^{-1}: 1120, 1245, 1320, 1340, 1375, 1520, 1595, 1720 s, 1805, 2930, 3080. ^1H NMR spectrum, δ, ppm, DMSO-d_6: 2.05 s (3H, CH_3), 2.10 s (3H, CH_3), 2.28 s (3H, CH_3), 2.62–2.77 m (1H, CH_2CH_2), 2.82–2.95 m (1H, CH_2CH_2), 3.00–3.16 m (1H, CH_2CH_2), 3.17–3.27 m (1H, CH_2CH_2), 4.27 d.d (1H, *J* ~8.5 and ~8.5, CH), 4.67 d (1H, *J* ~8.5, CH), 5.66 d (1H, *J* ~8.5, CH), 7.01 s (H_{arom}), 7.03 s (H_{arom}), 7.20–7.33 m ($3H_{arom}$), 7.34–7.49 m ($3H_{arom}$), 8.18 m ($2H_{arom}$). ^{13}C NNR spectrum, δ, ppm, $CDCl_3$: 17.9 (CH_3), 18.0 (CH_3), 21.2 (CH_3), 29.1 (CH_2), 43.4 (CH_2), 54.0 (CH), 61.5 (CH), 65.2 (CH), 115.8 ($2CH_{arom}$), 125.8 ($2CH_{arom}$), 126.7 (C_{arom}), 127.1 (CH_{arom}), 128.1 (CH_{arom}), 128.4 (CH_{arom}), 128.5 (CH_{arom}), 129.7 ($2CH_{arom}$), 132.8 (C_{arom}), 132.9 (C_{arom}), 135.3 (C_{arom}), 135.4 (C_{arom}), 140.0 (C_{arom}), 140.6 (C_{arom}), 149.2 (C_{arom}), 171.3 (C=O), 173.8 (C=O). Found, %: C 69.73; H 5.53; N 11.67. $C_{28}H_{26}N_4O_4$. Calculated, %: C 69.70; H 5.43; N 11.61.

***rel*-(8a*R*,11a*S*,11b*R*)-8-(2,4-Dinitrophenyl)-10-mesityl-5,6,11a,11b-tetrahydro-8*H*-pyrrolo[3',4':3,4]-pyrazolo[5,1-*a*]isoquinoline-9,11(8a*H*,10*H*)-dione (IIIj).** 253 mg of 2-(2,4-dinitrophenyl)-3,4-dihydroisoquinolinium bromide [4] and 138 mg of imide **IIa**

were dissolved in 2 ml of DMF, to the mixture 300 μl of pyridine were added. The mixture was heated at 100°C under vigorous stirring for 5 h. The mixture was cooled and poured in 30 ml of distilled water, the precipitate was filtered off and refluxed with 10 ml of ethanol. The ethanol was cooled and precipitate was filtered off.

Yield 201 mg (60%). mp 250–251°C. ^{1}H NMR spectrum, δ, ppm, DMSO-d_6: 2.03 s (3H, CH_3), 2.10 s (3H, CH_3), 2.28 s (3H, CH_3), 2.71–2.94 m (4H, CH_2–CH_2), 4.27 d.d (1H, *J* ~8.0 and ~8.0, CH), 4.48 d (1H, *J* ~8.0, CH), 5.78 d (1H, *J* ~8.0, CH), 6.96–7.07 m ($2H_{arom}$), 7.17–7.35 m ($3H_{arom}$), 7.50–7.59 m ($1H_{arom}$), 7.85 d ($1H_{arom.}$, *J* ~8.7), 8.41 d ($1H_{arom.}$, *J* ~8.7), 8.56 s ($1H_{arom}$). ^{13}C NNR spectrum, δ, ppm, DMSO-d_6: 17.0 (CH_3), 17.2 (CH_3), 20.6 (CH_3), 43.7 (CH_2), 46.6 (CH_2), 54.7 (CH), 61.4 (CH), 64.5 (CH), 119.8 (CH_{arom}), 121.2 (CH_{arom}), 126.5 (CH_{arom}), 126.9 (C_{arom}), 127.2 (CH_{arom}), 127.6 (CH_{arom}), 127.7 (CH_{arom}), 128.3 (CH_{arom}), 128.9 (CH_{arom}), 129.1 (CH_{arom}), 132.8 (C_{arom}), 132.9 (C_{arom}), 135.0 (C_{arom}), 135.8 (C_{arom}), 139.0 (C_{arom}), 139.1 (C_{arom}), 139.4 (C_{arom}), 140.6 (C_{arom}), 171.3 (C=O), 174.2 (C=O). Found, %: C 63.53; H 5.16; N 13.57. $C_{28}H_{25}N_5O_6$. Calculated, %: C 63.75; H 4.78; N 13.28.

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