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Synthesis of Spiroheterocyclic Systems from Barbituric Acids and *N*,*N*-Disubstituted *o*-Aminobenzaldehydes

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Abstract—Reactions of barbituric, 1,3-dimethylbarbituric, and 2-thiobarbituric acids with 2-(1-pyrrolidinyl)-benzaldehyde, its 6- and 7-membered homologs, and 4-phenylpiperazine and morpholine analogs lead to formation of fused systems with a spirocyclic 2,4,6-trioxopyrimidine fragment. The process involves intermediate formation of labile 5-arylmethylidenebarbituric acids which exhibit *t*-amino effect and undergo spontaneous isomerization to give the final products. The observed spirocyclizations are characterized by an anomalously high rate.

It is known [1–3] that reactions of barbituric acids with aromatic aldehydes give as a rule either the corresponding 5-arylmethylidene derivatives or bis(pyrimidin-5-yl)arylmethanes. Condensations of barbituric acid (**Ia**) with aldehydes containing a nucleophilic group, e.g., NH_2 or OH, in the *ortho* position [1, 4] may be accompanied by further cyclization of 5-arylmethylidenebarbituric acids with formation of fused systems.

In the reaction of acid **Ia** with an equimolar amount of 2-(1-pyrrolidinyl)benzaldehyde (**IIa**) in aqueous ethanol, instead of the expected 5-[2-(1-pyrrolidinyl)-phenylmethylidene]hexahydropyrimidine-2,4,6-trione like **A**, we isolated in 96% yield an unusual product, 2,4,6-trioxospiro[perhydropyrimidine-5,5'-1',2',3',3a',-4',5'-hexahydropyrrolo[1,2-*a*]quinoline] (**IIIa**), as a colorless crystalline substance (Scheme 1). The structure of **IIIa** was determined on the basis of its ^{1}H NMR and mass spectra. Further study of this unexpected reaction allowed us to detect formation of an intensely red intermediate, assumingly 5-arylmethylidenehexahydropyrimidine-2,4,6-trione **A**. After mixing colorless solutions of compounds **Ia** and **IIa**, the mixture instantaneously turned red, the color became more intense during the first 10–20 s and then lost its intensity, and final product **IIIa** separated from the mixture as colorless crystals. The reaction performed in 60% ethanol at 50°C (concentrations of **Ia** and **IIa** 0.2 and 0.22 M, respectively) was complete in about 2 min.

The observed pattern led us to presume that the first step in the reaction of acid **Ia** with aldehyde **IIa** is a normal Knoevenagel condensation yielding 5-arylmethylidene-2,4,6-pyrimidinetrione **A**. It is known that compounds possessing an analogous π-system are characterized by an intense red–orange color. A model of such chromophore is 5-(4-dimethylaminobenzylidene)barbituric acid (λ_{max} 447 nm, ε = 33500 [5]). The subsequent rearrangement of intermediate **A** to spirocyclic system **IIIa** can be regarded as a sort of an anomalous cyclizations which were discussed in [6] under the generic name "*tert*-amino effect." This term almost was not used in Russian literature. However, we believe that the *t*-amino effect implies primarily electronic factors favoring hydride ion abstraction from the α-carbon atom of a tertiary amine and that the use of this term as applied to a reaction is not quite correct. Therefore, the rearrangement discussed in the present article is referred to as *t*-spirocyclization, and reactions involving *tert*-amino effect are generically called *t*-reactions.

It is known that *t*-amino effect is inherent to tertiary aromatic amines possessing a π-acceptor substituent (carbonyl, nitro, α- or β-cyanovinyl group, etc.) in the *ortho* position. At elevated temperature these compounds undergo cyclization with participation of the α-carbon atom in the alkylamino group to form a new heterocyclic system. The activation barrier to *t*-reactions is fairly high; therefore, they require severe conditions (as a rule, prolonged heating at 100–150°C and,

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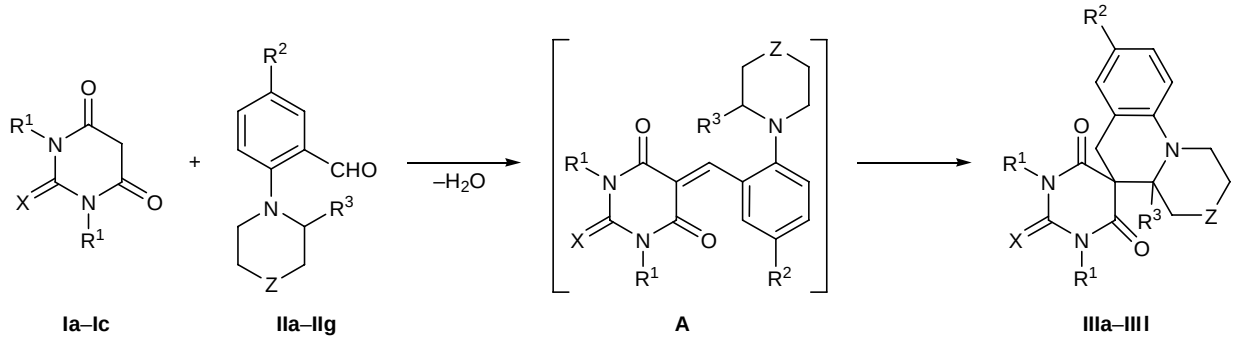
Scheme 1.



Ia–Ic **IIa–IIg** **A** **IIIa–IIIl**

I, R^1 = H (**a**, **c**), Me (**b**); X = O (**a**, **b**), S (**c**); **II**, R^2 = H (**a**, **e**, **f**), NO_2 (**b**–**d**, **g**); R^3 = H (**a**–**f**), Me (**g**); Z = bond (**a**, **b**), CH_2 (**c**, **g**), $(CH_2)_2$ (**d**), NPh (**e**), O (**f**); **III**, R^1 = H (**a**–**g**, **l**), Me (**h**–**k**); R^2 = H (**a**, **e**–**g**, **j**), NO_2 (**b**–**d**, **h**, **i**, **k**); R^3 = H (**a**–**f**, **h**–**l**), Me (**g**); X = O (**a**–**k**), S (**l**); Z = bond (**a**, **b**, **h**), CH_2 (**c**, **g**), $(CH_2)_2$ (**d**, **i**, **k**), NPh (**e**, **j**), O (**f**).

in some cases, addition of a Lewis acid). The mechanism of activation of the alkylamino group in *t*-reactions remains not quite clear.

Several types of *t*-reactions are known. Among these, the closest analog to the reaction under study is thermal isomerization of 2-vinyl-1-phenylpyrrolidine derivatives **IV**, which involves 1,5-hydride shift to give intermediate dipolar ion **B** and subsequent cyclization to fused pyrroloquinoline system **V** [7] (Scheme 2).

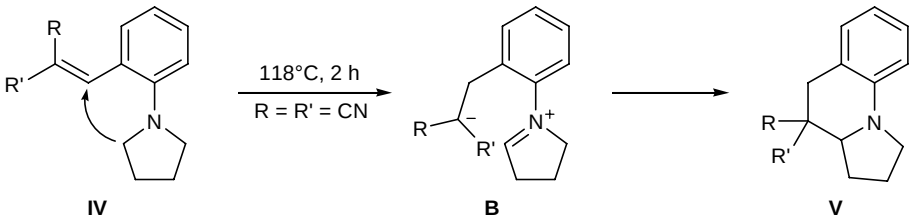
t-Reactions with cyclic CH acid derivatives were studied to a considerably lesser extent; synthesis of spirocyclic systems from CH acids was reported only in [8, 9]. Therefore, the reaction of barbituric acid (**Ia**) with aldehyde **IIa** attracts interest not only as a synthetic route to difficultly accessible spirocyclic system **IIIa** but also as an example of anomalously fast *t*-reaction. The isomerization of the corresponding 5-arylmethylidene-2,4,6-pyrimidinetrione **A** was so fast that we did not succeed in isolating it and even detecting by ^{1}H NMR spectroscopy when the reaction was performed in an NMR ampule at 20°C in DMSO-d_6, the initial reactant concentration being 0.2 M. Under these conditions, the *t*-spirocyclization occurred at a considerably higher rate than the first condensation stage.

The reaction of acid **Ia** with 5-nitro-2-(1-pyrrolidinyl)benzaldehyde (**IIb**) gave spirocyclic derivative **IIIb**, and the rate of the process was as high as in the reaction of **Ia** with **IIa**. Theoretically, the presence of a nitro group should sharply reduce the electron density on the amino nitrogen atom in the *para* position, and the rate of *t*-spirocyclization should decrease due to both hindered hydride ion abstraction and destabilization of intermediate zwitterion **B**. Nevertheless, the overall rate of the process was limited by the formation of the corresponding 5-arylmethylidene-2,4,6-pyrimidinetrione **A**, while its subsequent rearrangement was faster than the initial condensation stage.

Other *o*-aminobenzaldehydes **IIc**–**IIg** reacted with barbituric acid (**Ia**) according to a similar scheme. As a result, spirocyclic systems **IIIc**–**IIIg** were obtained directly. In the reaction with 5-nitro-2-(2-methylpiperidino)benzaldehyde (**IIg**) the cyclization selectively involved the tertiary carbon atom despite formation of more sterically strained structure **IIIg**.

1,3-Dimethylbarbituric acid (**Ib**) is a close analog of acid **Ia**. Compound **Ib** reacted with aldehydes **IIa**, **IIb**, **IId**, and **IIf** under similar conditions to afford compounds **IIIh**–**IIIk**. Likewise, the reaction of 2-thiobarbituric acid (**Ic**) with aldehyde **IId** gave

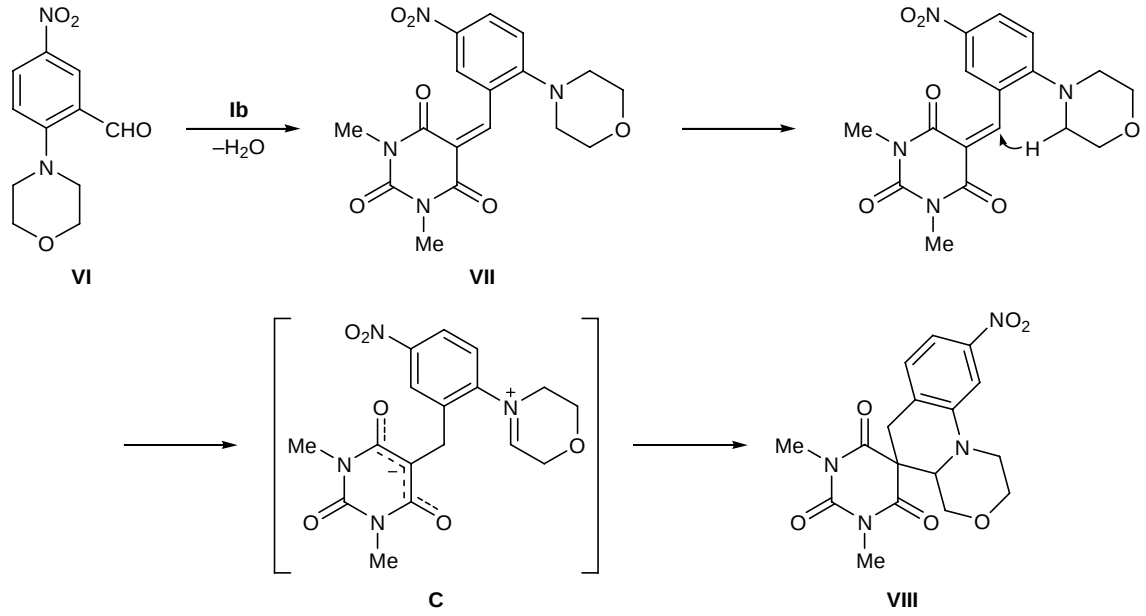
Scheme 2.



IV **B** **V**

R, R' = CN, COOEt.

Scheme 3.



2-thioxo-4,6-dioxopyrimidine derivative **IIIl**. In all the above reactions, the *t*-spirocyclization of intermediate 5-arylmethylidene derivatives **A** occurred through a negligible activation barrier, and its rate was so high that these intermediates could not be isolated.

In the condensation of 1,3-dimethylbarbituric acid (**Ib**) with 2-morpholino-5-nitrobenzaldehyde (**VI**) in ethanol at 50°C we succeeded in isolating intermediate 1,3-dimethyl-5-(2-morpholino-5-nitrobenzylidene)-hexahydropyrimidine-2,4,6-trione (**VII**). This provides an additional support to the assumption that 5-arylmethylidenebarbituric acids are formed as intermediates in the reactions under study. Compound **VII** is stable under standard conditions, while it undergoes isomerization into spirocyclic derivative **VIII** at elevated temperature, e.g., on heating for 1 min at 100°C in acetic acid (Scheme 3). Presumably, the reason for the lower rate of *t*-spirocyclization of compound **VII**, as compared to the other analogs like **A**, is reduction of the electron density on the α-carbon atom in the alkylamino group due to acceptor effects of the nitro group and morpholine oxygen atom. Nevertheless, even in this case the isomerization rate is anomalously high in comparison with the known [6–9] examples of *t*-reactions, the fastest of which are slower by three orders of magnitude under analogous conditions.

Taking the above into account, of specific interest are the mechanism of *t*-spirocyclization and factors producing anomalous *t*-amino effect in systems like **A** and **VIII**. We believe that the processes occurring therein are related to addition of nucleophiles at the exocyclic C=C bond in 5-arylmethylidenebarbituric acids; very strong polarization of that bond endows these compounds with Lewis acid properties [10]. Reactions of amines at the C=C bond leads to formation of stable zwitterionic systems with a structure analogous to hypothetical intermediate **C**. The 1,5-hydride shift in **VII** with formation of zwitterion **C** may be treated as intramolecular capture of a nucleophilic species, i.e., hydride ion, from the NCH_2 group. Most probably, hydride ion abstraction occurs through a 6-membered cyclic transition state.

To conclude, it should be noted that *t*-spirocyclization of barbituric acid derivatives not only provides a new synthetic approach to difficultly accessible heterocyclic systems with a spiropyrimidine fragment but also demonstrates an unusual example of *t*-amino effect. Further studies on *t*-amino effect in derivatives of cyclic CH acids are expected to considerably extend the scope of application of *t*-reactions in organic chemistry.

EXPERIMENTAL

The ^1H and ^{13}C NMR spectra were recorded on a Bruker AM-500 spectrometer at 500 and 125 MHz, respectively. The mass spectra (electron impact, 70 eV) were obtained on an MKh-1303 instrument with direct sample admission into the ion source (150°C). The purity of the products was checked by the analytical data, ^1H NMR spectra, and TLC [Silufol UV-254

plates; solvent systems: chloroform, chloroform–ethyl acetate (1:1), or 2-propanol–water (4:1)].

Compounds **Ia**–**Ic**, **IIc**, and **IIf** were commercial products. Aldehydes **IIa** and **IIe** were synthesized from *o*-fluorobenzaldehyde and the corresponding amines according to the procedures described in [7] and [11].

5-Nitro-2-(1-pyrrolidinyl)benzaldehyde (IIb). To a solution of 0.1 mol of 2-chloro-5-nitrobenzaldehyde in 40 ml of DMF we added 0.11 mol of anhydrous K_2CO_3 and 0.11 mol of pyrrolidine. The mixture was stirred for 6 h at 75–90°C, cooled, and diluted with 150 ml of water, and the precipitate was filtered off and washed with water. The crude product was dissolved in 20% hydrochloric acid, the undissolved material was filtered off, and the filtrate was diluted with water and made alkaline by adding aqueous ammonia. The precipitate was filtered off, washed with water, recrystallized from aqueous ethanol, and dried at 30°C under reduced pressure. Yield 18.5 g (84%), yellow crystalline substance, mp 131°C.

5-Nitro-2-(1-azepanyl)benzaldehyde (**IId**) was synthesized in a similar way. Yield 95%, yellow crystalline substance, mp 133°C.

5-Nitro-2-(2-methylpiperidino)benzaldehyde (**IIg**) was synthesized in a similar way from 2-chloro-5-nitrobenzaldehyde and 2-methylpiperidine. Yield 95%, yellow crystalline substance, mp 69°C.

Spiro[perhydropyrimidine-5,5'-1',2',3',3a',4',5'-hexahydropyrrolo[1,2-*a*]quinoline]-2,4,6-trione (IIIa). A hot solution of 0.01 mol of barbituric acid (**Ia**) in 40 ml of 60% ethanol was added under stirring to a solution of 0.01 mol of aldehyde **IIa** in 20 ml of ethanol, heated to 50°C. The mixture was stirred for 5 min at 50°C and was kept for 1 h at room temperature. The precipitate was filtered off, washed with aqueous ethanol, and dried at 40°C under reduced pressure. Yield 2.74 g (96%), mp 252°C (from aqueous DMF). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 1.64 m and 2.11 m (2H, *AB* system, C**H**$_2$CH), 2.00 m (2H, CH_2), 3.01 d and 3.31 d (2H, *AB* system, C**H**$_2$Ar, *J* = 16.9), 3.21 m and 3.52 m (2H, *AB* system, NCH_2), 3.70 d.d (1H, NCH, ^1J = 8.5, ^2J = 6.0), 6.46 d (1H, H_{arom}, *J* = 8.3), 6.52 t (1H, H_{arom}, *J* = 7.2), 6.93 d (1H, H_{arom}, *J* = 7.2), 7.98 t (1H, H_{arom}, *J* = 8.3), 11.10 s (1H, NH), 11.37 s (1H, NH). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm (*J*, Hz): 22.62 (CH_2), 27.30 (**C**H$_2$CH), 34.44 (**C**H$_2$Ar), 47.32 (NCH_2), 47.93 (C^5), 62.72 (NCH), 110.89 ($C^{9'}$), 115.22 ($C^{7'}$), 119.45 ($C^{6a'}$), 126.42 ($C^{8'}$), 127.70 ($C^{6'}$), 143.29 ($C^{9a'}$), 150.13 (C^2), 168.67 and 172.04 (C^4 and C^6). Found, %: C 63.13; H 5.31; N 14.70. $C_{15}H_{15}N_3O_3$. Calculated, %: C 63.15; H 5.30; N 14.73.

Compounds **IIIb**–**IIIl** were synthesized in a similar way; they were isolated as yellow (**IIIb**–**IIId**, **IIIg**, **IIIi**, **IIIj**, **IIIl**) or colorless crystalline substances (**IIIe**, **IIIf**, **IIIh**, **IIIk**).

7'-Nitrospiro[perhydropyrimidine-5,5'-1',2',3',-3a',4',5'-hexahydropyrrolo[1,2-*a*]quinoline]-2,4,6-trione (IIIb). Yield 84%, mp 305°C (decomp.; from aqueous DMF). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 1.65 m and 2.03 m (2H, *AB* system, CH_2), 2.18 m (2H, C**H**$_2$CH), 2.96 d and 3.27 d (2H, *AB* system, C**H**$_2$Ar, *J* = 17.2), 3.30 m and 3.69 m (2H, *AB* system, NCH_2), 3.88 d.d (1H, NCH, J_1 = 10.3, J_2 = 5.8), 6.51 d (1H, H_{arom}, *J* = 9.2), 7.88 d (1H, H_{arom}, *J* = 2.2), 7.95 d.d (1H, H_{arom}, J_1 = 9.2, J_2 = 2.2), 11.25 s (1H, NH), 11.51 s (1H, NH). Found, %: C 54.51; H 4.30; N 16.92. $C_{15}H_{14}N_4O_5$. Calculated, %: C 54.55; H 4.27; N 16.96.

8'-Nitrospiro[perhydropyrimidine-5,5'-1',2',3',-3a',4',5'-hexahydropyrido[1,2-*a*]quinoline]-2,4,6-trione (IIIc). Yield 81%, mp 265°C (decomp.; from aqueous DMF). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 1.30–1.90 m (6H, $3CH_2$), 3.04 d and 3.35 d (2H, *AB* system, C**H**$_2$Ar, *J* = 17.3), 3.09 d.d and 3.71 d.d (2H, *AB* system, NCH_2, J_1 = 12.7, J_2 = 10.9), 4.22 d.d (1H, NCH, J_1 = 13.8, J_2 = 5.6), 6.90 d (1H, H_{arom}, *J* = 9.2), 7.85 d (1H, H_{arom}, *J* = 2.3), 7.90 d.d (1H, H_{arom}, J_1 = 9.2, J_2 = 2.3), 11.27 s (1H, NH), 11.28 s (1H, NH). Found, %: C 55.90; H 4.63; N 16.22. $C_{16}H_{16}N_4O_5$. Calculated, %: C 55.81; H 4.68; N 16.27.

3'-Nitrospiro[perhydropyrimidine-5,5'-5',6',6a',-7',8',9',10',11'-octahydroazepino[1,2-*a*]quinoline]-2,4,6-trione (IIId). Yield 90%, mp >320°C (decomp.; from aqueous DMF). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 1.25–1.99 m (8H, $4CH_2$), 2.93 d and 3.45 d (2H, *AB* system, C**H**$_2$Ar, *J* = 18.2), 3.28 m and 3.90 m (2H, *AB* system, NCH_2), 3.94 d.d (1H, NCH, J_1 = 11.0, J_2 = 3.7), 6.68 d (1H, H_{arom}, *J* = 9.7), 7.88 d.d (1H, H_{arom}, J_1 = 9.7, J_2 = 2.4), 7.93 d (1H, H_{arom}, *J* = 2.4), 11.06 s (1H, NH), 11.25 s (1H, NH). Found, %: C 56.94; H 5.09; N 15.59. $C_{17}H_{18}N_4O_5$. Calculated, %: C 56.98; H 5.06; N 15.63.

3'-Phenylspiro[perhydropyrimidine-5,5'-1',2',3',3a',4',5'-hexahydro-1*H*-pyrazino[1,2-*a*]-quinoline]-2,4,6-trione (IIIe). Yield 95%, mp 296°C (decomp.; from aqueous DMF). ^{1}H NMR spectrum

(DMSO-d_6), δ, ppm (*J*, Hz): 2.72 t (1H, NCH_2, *J* = 10.3), 2.95 m (1H, NCH_2), 3.14 d and 3.27 d (2H, *AB* system, C**H**$_2$Ar, *J* = 16.1), 3.15 m (1H, NCH_2), 3.46 m and 4.07 m (2H, *AB* system, NCH_2), 3.63 m (1H, NCH_2), 3.69 d.d (1H, NCH, ^1J = 10.4, ^2J = 5.1), 6.64 t (1H, H_{arom}, *J* = 6.9), 6.77 t (1H, H_{arom}, *J* = 6.9), 6.84 d (2H, H_{arom}, *J* = 9.2), 6.88 d (1H, H_{arom}, *J* = 8.0), 6.94 d (1H, H_{arom}, *J* = 6.9), 7.04 t (1H, H_{arom}, *J* = 8.1), 7.18 d.d (2H, H_{arom}, *J* = 8.1), 11.21 s (1H, NH), 11.40 s (1H, NH). Found, %: C 67.04; H 5.37; N 14.85. $C_{21}H_{20}N_4O_3$. Calculated, %: C 67.01; H 5.36; N 14.88.

Spiro[perhydropyrimidine-5,5'-1',3',4',9',-10',10a'-hexahydro-2'-oxa-4a'-azaphenanthrene]-2,4,6-trione (IIIf). Yield 92%, mp 320°C (decomp.; from aqueous DMF). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 2.93 m and 3.57 m (2H, *AB* system, NCH_2), 3.08 d and 3.28 d (2H, *AB* system, C**H**$_2$Ar, *J* = 15.0), 3.31 m and 3.40 m (2H, *AB* system, OC**H**$_2$CH, J_1 = 11.5, J_2 = 8.1), 3.72 d.d (1H, NCH, J_1 = 11.5, J_2 = 5.2), 3.81 m and 3.89 m (2H, *AB* system, OC**H**$_2$CH$_2$), 6.66 t (1H, H_{arom}, *J* = 6.9), 6.83 d (1H, H_{arom}, *J* = 9.2), 6.93 d (1H, H_{arom}, *J* = 8.1), 7.04 t (1H, H_{arom}, *J* = 8.1), 11.23 s (1H, NH), 11.44 s (1H, NH). Found, %: C 59.77; H 5.05; N 16.88. $C_{15}H_{15}N_3O_4$. Calculated, %: C 59.80; H 5.02; N 13.95.

5'-Methyl-8'-nitrospiro[perhydropyrimidine-5,5'-1',2',3',3a',4',5'-hexahydropyrido[1,2-*a*]quinoline]-2,4,6-trione (IIIg). Yield 79%, mp 203°C (decomp.; from aqueous DMF). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 1.16 s (3H, Me), 1.47–1.94 m (5H, CH, $2CH_2$), 2.94 d.d and 3.79 d.d (2H, *AB* system, NCH_2, J_1 = 12.8, J_2 = 4.1), 3.06 d and 3.58 d (2H, *AB* system, C**H**$_2$Ar, *J* = 17.9), 6.84 d (1H, H_{arom}, *J* = 9.0), 7.88 d (1H, H_{arom}, *J* = 2.3), 7.93 d.d (1H, H_{arom}, J_1 = 9.0, J_2 = 2.3), 11.24 s (1H, NH), 11.36 s (1H, NH). Found, %: C 57.02; H 5.10; N 15.56. $C_{17}H_{18}N_4O_5$. Calculated, %: C 56.98; H 5.06; N 15.63.

1,3-Dimethylspiro[perhydropyrimidine-5,5'-1',2',3',3a',4',5'-hexahydropyrrolo[1,2-*a*]quinoline]-2,4,6-trione (IIIh). Yield 96%, mp 162°C (from EtOH–$CHCl_3$). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.49 m and 2.06 m (2H, *AB* system, C**H**$_2$CH), 2.00 m (2H, CH_2), 2.98 d and 3.56 d (2H, *AB* system, C**H**$_2$Ar, *J* = 16.7), 3.21 s and 3.37 s (3H each, NMe), 3.32 m and 3.59 m (2H, *AB* system, NCH_2), 3.70 d.d (1H, NCH, J_1 = 9.5, J_2 = 6.0), 6.57 d (1H, H_{arom}, *J* = 8.4), 6.64 t (1H, H_{arom}, *J* = 7.1), 6.99 d (1H, H_{arom}, *J* = 8.4), 7.14 t (1H, H_{arom}, *J* = 7.1). Found, %: C 65.15; H 6.11; N 13.39. $C_{17}H_{19}N_3O_3$. Calculated, %: C 65.16; H 6.11; N 13.41.

1,3-Dimethyl-7'-nitrospiro[perhydropyrimidine-5,5'-1',2',3',3a',4',5'-hexahydropyrrolo[1,2-*a*]-quinoline]-2,4,6-trione (IIIi). Yield 83%, mp 294°C (from EtOH–$CHCl_3$). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.46 m and 2.02 m (2H, *AB* system, CH_2), 2.09 m (2H, C**H**$_2$CH), 3.07 d and 3.27 d (2H, *AB* system, C**H**$_2$Ar, *J* = 16.6), 3.21 s and 3.39 s (3H each, NMe), 3.36 m and 3.71 m (2H, *AB* system, NCH_2), 3.88 d.d (1H, NCH, J_1 = 10.9, J_2 = 6.0), 6.52 d (1H, H_{arom}, *J* = 8.4), 7.95 d (1H, H_{arom}, *J* = 2.1), 8.09 d.d (1H, H_{arom}, J_1 = 8.4, J_2 = 2.1). Found, %: C 56.98; H 5.06; N 15.62. $C_{17}H_{18}N_4O_5$. Calculated, %: C 56.98; H 5.06; N 15.63.

1,3-Dimethyl-3'-nitrospiro[perhydropyrimidine-5,5'-5',6',6a',7',8',9',10',11'-octahydroazepino-[1,2-*a*]quinoline]-2,4,6-trione (IIIj). Yield 95%, mp 259°C (from EtOH–$CHCl_3$). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.40–1.65 m (6H, $3CH_2$), 1.70 m and 1.99 m (2H, *AB* system, C**H**$_2$CH), 3.15 m and 3.83 m (2H, *AB* system, NCH_2), 3.18 d and 3.45 d (2H, *AB* system, C**H**$_2$Ar, *J* = 18.5), 3.27 s and 3.32 s (3H each, NMe), 3.62 d.d (1H, NCH, J_1 = 10.0, J_2 = 5.1), 6.65 d (1H, H_{arom}, *J* = 9.9), 8.01 d.d (1H, H_{arom}, J_1 = 9.9, J_2 = 2.5), 8.04 d (1H, H_{arom}, *J* = 2.5). Found, %: C 59.06; H 5.74; N 14.49. $C_{19}H_{22}N_4O_5$. Calculated, %: C 59.06; H 5.74; N 14.50.

1,3-Dimethyl-3'-phenylspiro[perhydropyrimidine-5,5'-1',2',3',3a',4',5'-hexahydro-1*H*-pyrazino-[1,2-*a*]quinoline]-2,4,6-trione (IIIk). Yield 96%, mp 188°C (from EtOH–$CHCl_3$). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 2.72 d.d and 4.08 d.d (2H, *AB* system, NC**H**$_2$CH, J_1 = 11.5, J_2 = 9.2), 3.06 m and 3.29 m (2H, *AB* system, NCH_2), 3.10 d and 3.56 d (2H, *AB* system, C**H**$_2$Ar, *J* = 17.3), 3.21 s and 3.40 s (3H each, NMe), 3.37 m and 3.51 m (2H, *AB* system, NCH_2), 3.82 d.d (1H, NCH, J_1 = 9.2, J_2 = 3.6), 6.79 m (4H, H_{arom}), 6.88 t (1H, H_{arom}, *J* = 6.9), 6.94 d (2H, H_{arom}, *J* = 9.2), 7.02 d (1H, H_{arom}, *J* = 8.1), 7.17 t (1H, H_{arom}, *J* = 8.1), 7.25 d.d (2H, H_{arom}, *J* = 8.1). Found, %: C 68.22; H 6.01 N 13.81. $C_{23}H_{24}N_4O_3$. Calculated, %: C 68.30; H 5.98; N 13.85.

3'-Nitro-2-thioxospiro[perhydropyrimidine-5,5'-5',6',6a',7',8',9',10',11'-octahydroazepino[1,2-*a*]-quinoline]-4,6-dione (IIIl). Yield 77%, mp 261°C (from aqueous EtOH). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 1.35–2.03 m (8H, $4CH_2$), 3.01 d and 3.48 d (2H, *AB* system, C**H**$_2$Ar, *J* = 18.4), 3.27 m and 3.91 m (2H, *AB* system, NCH_2), 3.75 d.d (1H, NCH, J_1 = 10.4, J_2 = 5.8), 6.67 d (1H, H_{arom}, *J* = 9.2), 7.89 d.d (1H, H_{arom}, J_1 = 9.2, J_2 = 2.3), 7.95 d (1H,

H_{arom}, J = 2.3), 12.11 s (1H, NH), 12.24 s (1H, NH). Found, %: C 54.42; H 4.81; N 14.92; S 8.49. $C_{17}H_{18}N_4O_4S$. Calculated, %: C 54.53; H 4.85; N 14.96; S 8.56.

2-Morpholino-5-nitrobenzaldehyde (VI) was synthesized as described above for compounds **IIb**, **IId**, and **IIg**. Yield 90%, yellow crystalline substance, mp 116°C.

1,3-Dimethyl-5-(2-morpholino-5-nitrobenzylidene)hexahydropyrimidine-2,4,6-trione (VII). A hot solution of 0.01 mol of compound **Ib** in 20 ml of ethanol was added under stirring to a solution of 0.01 mol of aldehyde **VI** in 40 ml of ethanol, heated to 50°C. The mixture was kept at room temperature until a crystalline product began to separate, cooled to 10°C, and kept for 1 h at that temperature. The precipitate was filtered off, washed with aqueous ethanol, and dried at 20°C under reduced pressure. Yield 3.18 g (85%), yellow–orange crystalline substance, mp 231°C (decomp.; from $CHCl_3$–CCl_4). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (J, Hz): 3.16 t (4H, NCH_2, J = 4.8), 3.39 s and 3.43 s (3H each, NMe), 3.88 t (4H, OCH_2, J = 4.8), 7.06 d (1H, H_{arom}, J = 8.9), 8.29 d.d (1H, H_{arom}, J_1 = 8.9, J_2 = 2.4), 8.52 s (1H, =CH), 8.80 d (1H, H_{arom}, J = 2.4). Found, %: C 54.62; H 4.88; N 14.94. $C_{17}H_{18}N_4O_6$. Calculated, %: C 54.54; H 4.85; N 14.97.

1,3-Dimethyl-7'-nitrospiro[perhydropyrimidine-5,10'-1',3',4',9',10',10a'-hexahydro-2'-oxa-4a'-azaphenanthrene]-2,4,6-trione (VIII). A solution of 5 mmol of compound **VII** in 15 ml of glacial acetic acid was heated for 1 min at 100–110°C and was then kept at room temperature. When a crystalline product separated, the mixture was cooled to 10°C, and the precipitate was filtered off, washed with ethanol, and dried at 40°C under reduced pressure. Yield 3.18 g (82%), yellow crystalline substance, mp 256°C (from AcOH). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (J, Hz): 3.09 d and 3.55 d (2H, *AB* system, C**H**$_2$Ar, J = 16.1), 3.25 m (2H, NCH_2), 3.27 s and 3.38 s (3H each, NMe), 3.64 m and 3.72 m (2H, *AB* system, OC**H**$_2$CH$_2$, J_1 = 11.0), 3.86 m and 3.92 m (2H, *AB* system, OC**H**$_2$CH, J_1 = 10.4), 4.00 d.d (1H, NCH, J_1 = 11.0, J_2 = 3.6), 6.84 d (1H, H_{arom}, J = 9.5), 7.88 d (1H, H_{arom}, J = 2.4), 6.84 d.d (1H, H_{arom}, J_1 = 9.5, J_2 = 2.4). Found, %: C 54.58; H 4.87; N 14.95. $C_{17}H_{18}N_4O_6$. Calculated, %: C 54.54; H 4.85; N 14.97.

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