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Dedicated to Full Member of the Russian Academy of Sciences V.I. Minkin on his Jubilee

Synthesis and Structure of 5-Indolyl-6-thienyl-1,2,4-triazines

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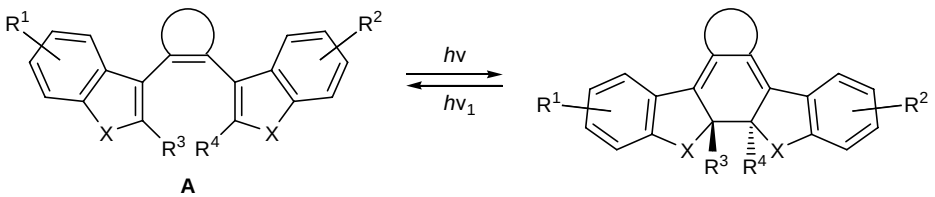
Abstract—Acylation of indole and 2,5-dimethylthiophene with 2-(3-indolyl)-2-oxoacetyl chloride afforded the corresponding diketones. 1-(2,5-Dimethyl-3-thienyl)-2-(3-indolyl)ethanedione reacted with thiosemicarbazide under atmosperic and elevated pressure to give 6-(2,5-dimethyl-3-thienyl)-5-(3-indolyl)-2,3-dihydro-1,2,4-triazine-3-thione whose structure was studied in detail by the X-ray diffraction method. Reactions of 6-(2,5-dimethyl-3-thienyl)-5-(3-indolyl)-2,3-dihydro-1,2,4-triazine-3-thione with amines and hydrazine resulted in formation of fused triazolo- and tetrazolotriazines.

Bisindolylethenes **A** attract interest as photochromic compounds [1]; in addition, they exhibit a broad spectrum of biological activity [2, 3]. Most frequently, the bridging group in these compounds is a maleic anhydride or maleimide fragment. It is known that structural variations of the bridging group in bisindolylethenes strongly affect their activity [3]. Another promising approach to building up new biologically active derivatives implies synthesis of bishetarylethenes in which the ring in the bridge is connected not only to indole group but also to a different heterocyclic [4] or aromatic substituent [5].

In the present work we applied both approaches and synthesized unsymmetrical compounds containing indole and thiophene fragments bridged through a 1,2,4-triazine heteroring. We previously described synthesis of 1,2,4-triazines **III**–**V** from accessible diketone **II** [6] which was prepared by oxidation of the corresponding hydroxy ketone **I** (Scheme 1). We have found that diketones **VIIa** and **VIIb** are formed in good yields by reaction of 2-(3-indolyl)-2-oxoacetyl chloride (**VI**) [7] with indole or 2,5-dimethylthiophene, respectively, in a mixture of heptane with dichloroetane in the presence of aluminum chloride (Scheme 2). According to published data, chloride **VI** reacts with aromatic and heteroaromatic compounds in a mixture of dichloroethane and nitromethane in the presence of $AlCl_3$ [8]. However, the yields did not exceed 60%. Using the acylation of 2,5-dimethylthiophene as an example, we showed in [9] that reduction of the polarity of the medium decreases the energy of solvation of the corresponding transition complexes and thus increases the yield of the target product and suppresses side reactions [9]. In fact, by replacing nitromethane by less polar heptane we succeeded in obtaining diketones **VIIa** and **VIIb** in higher yields. Furthermore, the procedure proposed by us seems to be more convenient from the preparative viewpoint, as compared to the



A

X = NH, NR.

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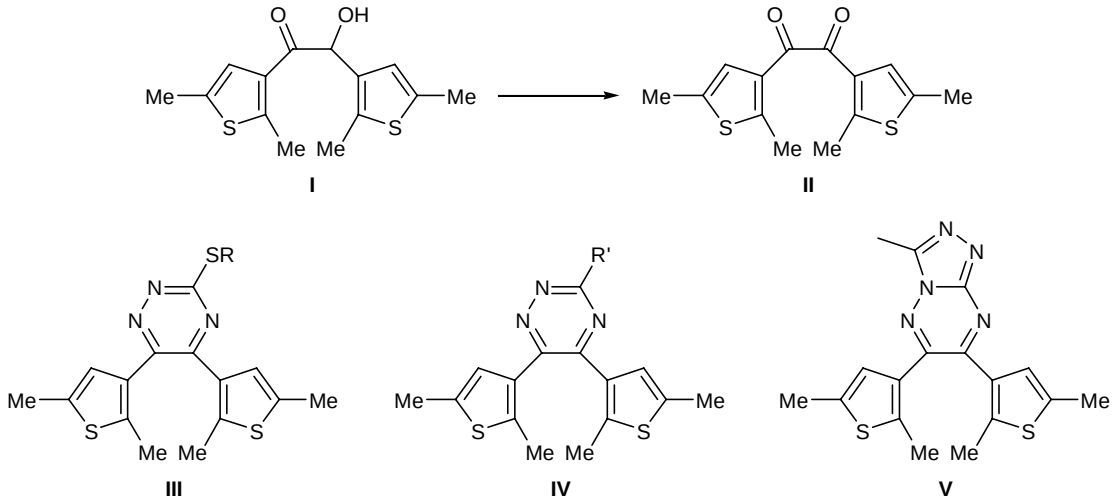
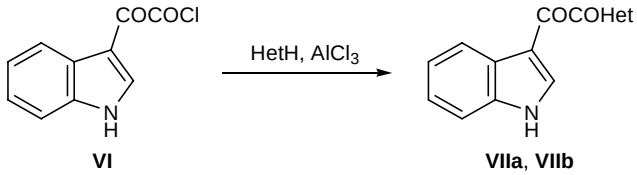
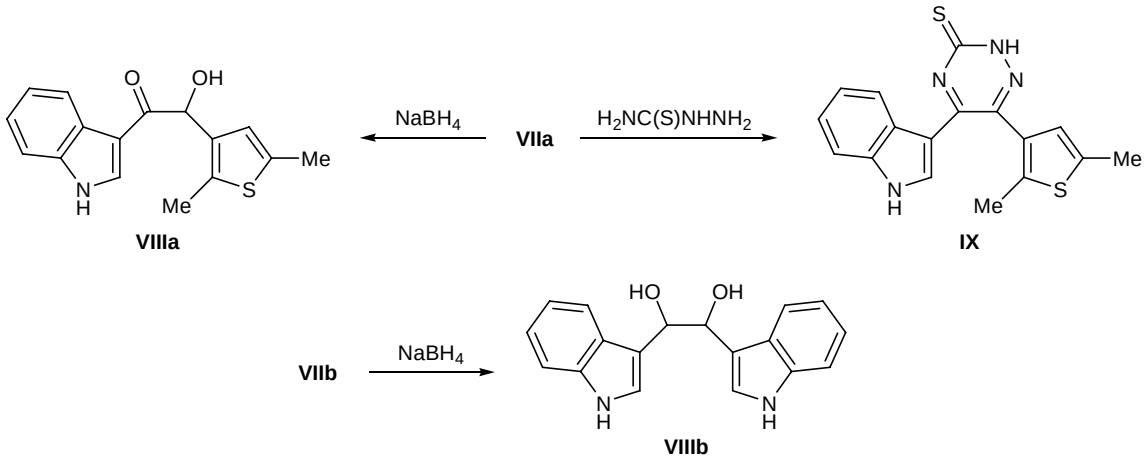
Scheme 1.



Scheme 2.



VII, Het = 2,5-dimethyl-3-thienyl (**a**), 3-indolyl (**b**).



synthesis of diketone **VIIb** via reaction of chloride **VI** with magnesium derivative of indole [3, 7].

Diketones **II**, **VIIa**, and **VIIb** are characterized by considerably different reactivities. For instance, we failed to obtain the corresponding 1,2,4-triazinethione from symmetric diketone **VIIb**. When the reaction was performed under the conditions described for the synthesis of **II** and **III**, the initial diketone was recovered from the reaction mixture, while more severe conditions (elevated temperature, the use of acids as solvent or of thiosemicarbazide hydrochloride) resulted in tarring. No triazinethione was formed from diketone **VIIb** even at elevated pressure (up to 1000 MPa).

Diketone **VIIa** was more reactive than bisindolyl derivative **VIIb**; however, it was much less reactive than dithienylethanedione **II**. Below are given the yields of compound **IX** in the reaction of diketone **VIIa** with thiosemicarbazide at 75°C, depending on the pressure and reaction time (according to the ^{1}H NMR data).

The yield of triazinethione **IX** in the reaction of **VIIa** with thiosemicarbazide under atmospheric pres-

sure (6 h) was only 46% (run no. 2), whereas analogous bisthienyl derivative **III** was formed almost quantitatively under the same conditions [6]. We succeeded in considerably raising the yield of **IX** by increasing the reaction time (run no. 3). It is known that in some cases high pressure favors formation of heterocyclic compounds [10–12]. In our case, carrying out the reaction under high pressure allowed us to shorten the reaction time and increase the product yield (run nos. 4–6). Such effect of high pressure on the formation of triazinethiones was not reported previously.

Run no.	Pressure, MPa	Time, h	Yield, %
1	0.1	2	30
2	0.1	6	46
3	0.1	48	86
4	500	2	60
5	1000	2	78
6	1000	6	94

We were the first to synthesize triazines having vicinal indolyl and thienyl substituents. Therefore, it was reasonable to determine the steric structure and geometric parameters of molecule **IX** by X-ray analysis and compare the obtained data with those available from the Cambridge Crystallographic Data Center (CCDC) [13], namely for 3,4-bis(3-indolyl)-1*H*-pyrrole-2,5-dione [5] and dithienylethenes [14] which include structural fragments of **IX**.

Compound **IX** crystallized from a mixture of methanol with acetone as solvate with the composition $C_{17}H_{14}N_4S_2 \cdot MeOH$ (**IXa**). The structure of molecule **IX** is shown in Fig. 1. The triazine, indole, and thiophene rings are planar within ±0.05, ±0.005, and ±0.008 Å, respectively. The dihedral angles between their planes are as follows: 55.8° between the triazine and thiophene rings, 18.96° between the triazine and indole rings, and 59.88° between the thiophene and indole rings. These parameters are typical of dithienylethenes with such heterocyclic bridging fragments as maleic anhydride and maleimide [15].

The bond lengths in the triazine ring indicate the absence of a common conjugation system. Electron density delocalization is observed only in the C^6–N^1–N^2–C^3–N^4–C^5 fragment; the bond lengths therein correspond to C–N and N–N bonds with an order of 1.5: 1.312, 1.349, 1.340, 1.353, and 1.333 Å, respectively. On the other hand, the C^5–C^6 bond (1.446 Å) is a typical single C_{sp^2}–C_{sp^2} bond [16]. This strongly

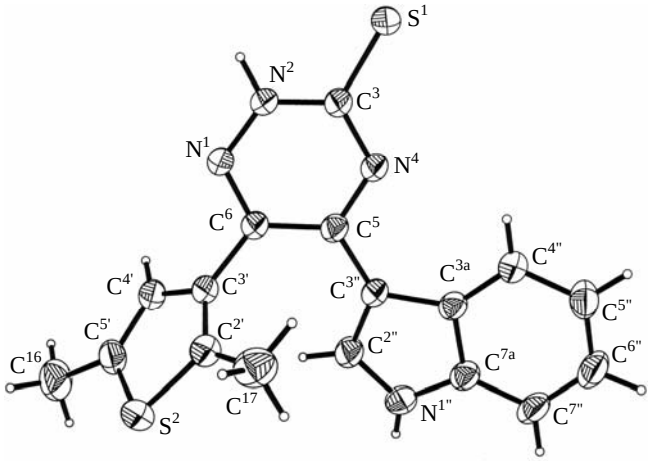


Fig. 1. Structure and conformation of the molecule of 6-(2,5-dimethyl-3-thienyl)-5-(3-indolyl)-2,3-dihydro-1,2,4-triazine-3-thione (**IX**).

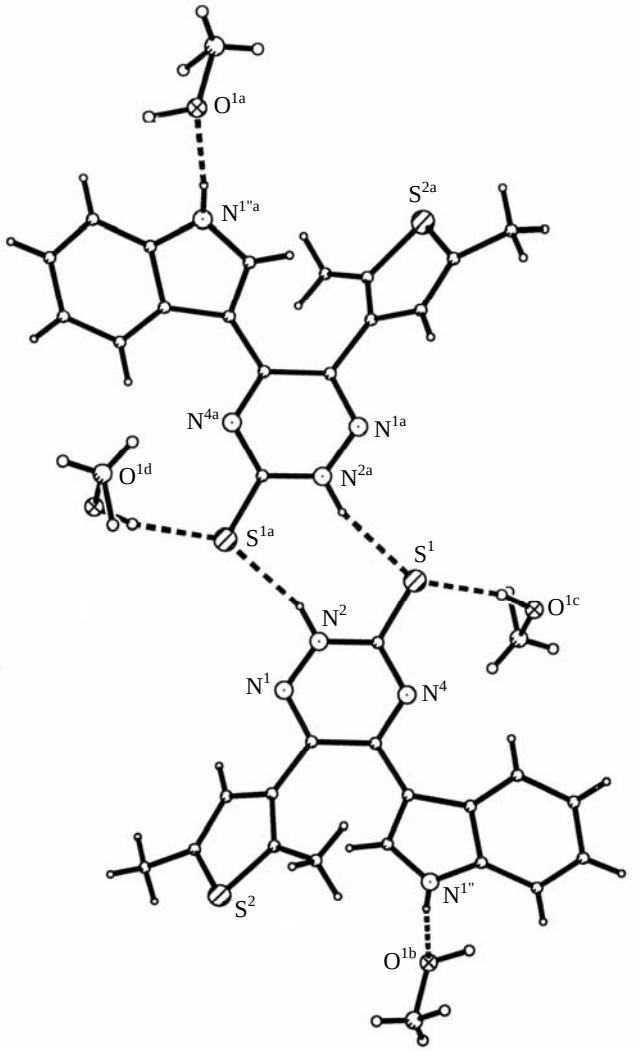


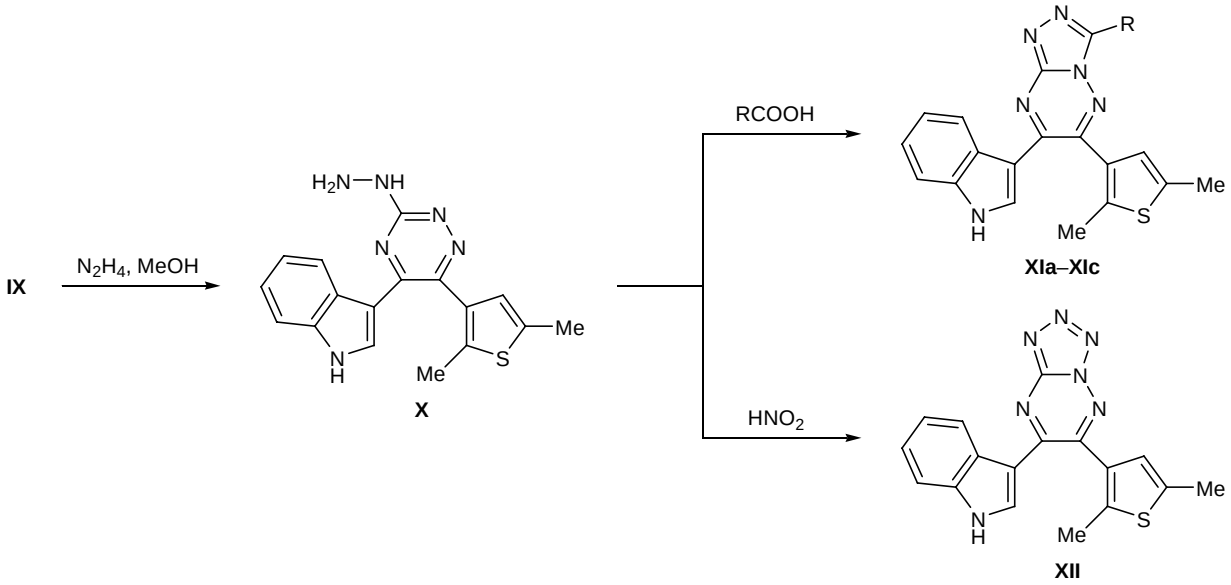
Fig. 2. Intermolecular hydrogen bonds in the crystalline structure of 6-(2,5-dimethyl-3-thienyl)-5-(3-indolyl)-2,3-dihydro-1,2,4-triazine-3-thione–methanol solvate (**IXa**).

differentiates electronic structure of the bridge in molecule **IX** from that in dihetarylethenes with fixed double $C^5=C^6$ bond [14].

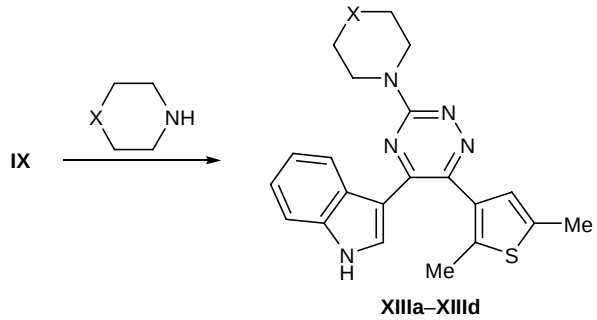
Some specific features were also found in the indole fragment. First of all, the $C^{2"}$–$C^{3"}$ (1.384 Å) and $N^{1"}$–C^{7a} bonds (1.378 Å) are appreciably longer than the corresponding bonds in unsubstituted indole (1.345 and 1.365 Å, respectively) [17]. This suggests reorganization of the electronic system in the indole fragment, which is induced by the triazine π-electron system. Taking into account that the angle between the indole and triazine ring planes is only ~19°, such effect is quite admissible. An analogous effect on the indole ring (i.e., bond lengths therein) is produced by the carbonyl group in position 3 of, e.g., 1*H*-indole-3-carbaldehyde, where the corresponding bond lengths are 1.389 and 1.382 Å, respectively [18]. On the other hand, the electronic system of the indole fragment may be influenced by intermolecular hydrogen bond between the pyrrole NH atom and oxygen atom of the solvate methanol molecule (Fig. 2). According to the crystallo-graphic criteria [19], this hydrogen bond is referred to as strong; its parameters are as follows: $O^{1b}\cdots N^{1"}$ 2.820 Å, $O^{1b}\cdots H–N^{1"}$ 1.98 Å, $\angle O^{1b}\cdots H–N^{1"}$ 171°. It is quite probable that electron density redistribution in the indole fragment changes the electronic state of the $C^{2"}$ atom. As a result, the hydrogen atom on $C^{2"}$ becomes more labile, and anomalously short intramolecular $C^{2'}$–$C^{2"}$ contact (3.183 Å) is observed.

In addition, there are two weak intermolecular hydrogen bonds in the crystalline structure of solvate **IXa**. Molecules **IX** in crystal are related through a symmetry center, and they form dimers via intermolecular hydrogen bonding between the thione sulfur atom of one molecule and NH hydrogen atom in the triazine ring of the other molecule. These hydrogen

Scheme 3.



XI, R = Me (**a**), 2-thienyl (**b**), 3-indolylmethyl (**c**).



XIII, X = bond (**a**), O (**b**), NMe (**c**), CH_2 (**d**).

bonds are characterized by the following parameters: $S^1\cdots N^{2a}$ 3.248 Å, $S^1\cdots H–N^{2a}$ 2.40 Å, $\angle S^1\cdots H–N^{2a}$ 155°. A weak intermolecular hydrogen bond is also formed between the thione sulfur atom and hydroxy proton of the solvate methanol molecule: $S^1\cdots O^{1c}$ 3.289 Å, $S^1\cdots H–O^{1c}$ 2.32 Å, $\angle S^1\cdots H–O^{1c}$ 161°. Thus the triazine and indole fragments in molecule **IX** are involved in various intramolecular hydrogen bonds, which is quite untypical of dithienylethenes [14].

A strong difference in the reactivity of the carbonyl groups in diketone **VIIa** favors formation of only one isomer of triazinethione **IX**. The X-ray diffraction data unambiguously show that nucleophilic attack by thiosemicarbazide is directed exclusively at the "thienyl" carbonyl group. Neither excess thiosemicarbazide nor high pressure conditions affect the regioselectivity of the process.

The carbonyl groups in diketone **VIIa** behave differently in reactions with reducing agents. We succeeded in effecting regioselective reduction of one carbonyl group in **VIIa** by the action of $NaBH_4$ in alcohol. The product was compound **VIIIa** containing an acyloin fragment. This compound is an analog of **I** which (as shown previously) attracts considerable interest from the viewpoint of design of various heterocyclic bridging fragments in bishetarylethenes [20, 21]. According to the ^{1}H NMR data, the reduction involves the carbonyl group neighboring to the thiophene ring. The indole proton signals in the spectrum of **VIIIa** appear at the same positions as in the spectrum of initial diketone **VIIa**, while the singlet from 4-H in the thiophene ring shifts appreciably upfield. It should be noted that the formation of a hydroxy ketone moiety was observed previously only in the electrochemical reduction of diketone **VIIb** [3] and that attempts to accomplish selective reduction of only one carbonyl group in the same diketone by the action of both $NaBH_4$ and other reducing agents (effective in the reduction of benzil to benzoin [22, 23]) resulted in formation of diol **VIIIb**.

The reactivity of the thioxo group in the triazine ring of **IX** its typical of thiones. Compound **IX** reacts with hydrazine to afford the corresponding hydrazino derivative **X**. By analogy with published data [24, 6], reactions of **X** with carboxylic acids led to formation of 3-substituted 6-(2,5-dimethyl-3-thienyl)-7-(3-indolyl)[1,2,4]triazolo[4,3-*b*][1,2,4]triazines **XIa**–**XIc**, and nitrosation of this compound gave 7-(2,5-dimethyl-3-thienyl)-6-(3-indolyl)tetrazolo[1,5-*b*][1,2,4]-triazine (**XII**). Also, triazinethione **IX** smoothly reacted with amines, yielding 3-aminotriazines **XIIIa**–**XIIId** (Scheme 3).

Thus the results of our study showed that 2-(3-indolyl)-1-(2,5-dimethyl-3-thienyl)ethanedione can be used as starting compound for the synthesis of 1,2-dihetarylethenes in which the indole and thiophene rings are linked through various 1,2,4-triazine-containing bridges.

EXPERIMENTAL

The ^{1}H NMR spectra were recorded on a Bruker AM-300 spectrometer in DMSO-d_6. The mass spectra (electron impact, 70 eV) were obtained on a Kratos instrument with direct sample admission into the ion source. The melting points were determined on a Boetius melting point apparatus and were not corrected. The progress of reactions was monitored by TLC on Silufol UV-254 plates using petroleum ether–ethyl acetate (1:2) as eluent. Silica gel from Acros (CAS-7631-86-9, 0.060–0.200 mm) was used for column chromatography.

Dichloroethane was heated for 3 h over P_2O_5 under reflux and distilled. Heptane and alcohols were used without additional purification. Diethyl ether and tetrahydrofuran were dried over metallic sodium. 2-(3-Indolyl)-2-oxoacetyl chloride (**VI**) was synthesized by the procedure described in [7]. High-pressure reactions were carried out in Teflon ampules using a setup described in [25].

X-Ray diffraction study of 6-(2,5-dimethyl-3-thienyl)-5-(3-indolyl)-2,3-dihydro-1,2,4-triazine-3-thione–methanol solvate (IXa). Light yellow monoclinic crystals, $C_{17}H_{14}N_4S_2\cdot$MeOH, with the following unit cell parameters: a = 7.724(1), b = 17.636(3), c = 13.594(2) Å; β = 92.88(4)°; V = 1849.3(5) Å^3; ρ_{calc} = 1.331 g/cm^3; space group $P2_1/c$; Z = 4. The unit cell parameters and intensities of 5367 independent reflections were measured on a Bruker SMART-1000 diffractometer (MoK_α, graphite monochromator, φ-ω scanning in the range $1.89 \geq \theta \leq 30.11°$). The structure was solved by the direct method which localized all non-hydrogen atoms and was refined using 3453 reflections with $I > 2\sigma(I)$ by the full-matrix least-squares procedure for non-hydrogen atoms. The positions of hydrogen atoms were determined by the difference synthesis of electron density and were refined by the least-squares procedure in isotropic approximation.

The final divergence factors were R_1 = 0.062 and wR_2 = 0.174 (R_1 = 0.084, wR_2 = 0.192 for all independent reflections). The calculations were performed using Bruker SMART [26], SHELXL-97, and Bruker SHELXTL software [27]. The coordinates and thermal parameters of atoms were deposited to the Cambridge Crystallographic Data Center (entry no. 251952).

General procedure for the synthesis of diketones VIIa and VIIb. Chloride **VI**, 4.16 g (20 mmol), was added in portions over a period of 3–5 min to a suspension of 12.0 g (90 mmol) of $AlCl_3$ in a mixture of 20 ml of dichloroethane and 10 ml of heptane under stirring at 18–20°C. A solution of 33 mmol of indole or 2,5-dimethylthiophene in 20 ml of dichloroethane was then added dropwise under stirring, and the mixture was stirred until the reaction was complete (TLC). The mixture was poured into 100 ml of an ice–water mixture, and the product was extracted into ethyl acetate (3×100 ml). The extract was dried over Na_2SO_4 and evaporated under reduced pressure, and the residue was recrystallized from alcohol.

1-(2,5-Dimethyl-3-thienyl)-2-(3-indolyl)ethanedione (VIIa). Reaction time 4 h, yield 4.27 g (75%), yellow crystals, mp 149–151°C (from MeOH). ^{1}H NMR spectrum, δ, ppm: 2.35 s (3H, CH_3), 2.67 s (3H, CH_3), 6.98 s (1H, thiophene), 7.30 m (2H, indole), 7.54 m (1H, indole), 8.15 m (2H, indole), 12.36 br.s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 283 (12) $[M]^+$, 145 (28), 144 (100), 140 (9), 139 (43), 116 (31), 89 (30), 67 (18), 59 (23), 43 (13). Found, %: C 66.94; H 4.53; N 5.02; S 11.18. $C_{16}H_{13}NO_2S$. Calculated, %: C 67.92; H 4.62; N 4.95; S 11.32. *M* 283.33.

1,2-Bis(3-indolyl)ethanedione (VIIb). Reaction time 2 h, yield 4.23 g (73%), brownish crystals, mp 275–280°C (from MeOH); published data [7]: mp 279–280°C. ^{1}H NMR spectrum, δ, ppm: 7.32 m (4H), 7.57 m (2H), 8.28 m (2H), 12.26 br.s (2H, NH). $C_{18}H_{12}N_2O_2$. Mass spectrum, *m*/*z* (I_{rel}, %): 288 (13) $[M]^+$, 144 (100), 117 (13), 116 (38), 89 (40), 63 (13), 57 (9), 43 (10). Calculated: *M* 288.30.

2-(2,5-Dimethyl-3-thienyl)-1-(3-indolyl)-2-hydroxyethanone (VIIIa). Sodium tetrahydridoborate was added in 5–10 mg portions to a solution of 60 mg (0.5 mmol) of diketone **VIIa** in 20 ml of methanol under stirring at 18–20°C until the initial compound disappeared (TLC, R_f 0.6). Total of about 30 mg of $NaBH_4$ was added. The mixture was diluted with water, and the precipitate was filtered off and washed with dilute methanol. Yield 58 mg (93%), colorless crystals, mp 203–206°C. ^{1}H NMR spectrum, δ, ppm: 2.32 s (3H, CH_3), 2.47 s (3H, CH_3), 5.30 br.s (1H, OH), 5.62 d (1H, CH), 6.56 s (1H, thiophene), 7.16 m (2H, indole), 7.43 m (1H, indole), 8.14 d (1H, indole), 8.23 m (1H, indole), 11.76 br.s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 285 (8) $[M]^+$, 145 (16), 144 (100), 140 (11), 139 (36), 116 (28), 89 (20), 67 (21), 59 (13), 43 (8). Found, %: C 67.12; H 5.24; N 4.90; S 11.25. $C_{16}H_{15}NO_2S$. Calculated, %: C 67.34; H 5.30; N 4.91; S 11.23. *M* 285.37.

1,2-Bis(3-indolyl)ethane-1,2-diol (VIIIb). Sodium tetrahydridoborate was added in 15–20 mg portions to a solution of 145 mg (0.5 mmol) of diketone **VIIb** in 10 ml of methanol, and the mixture was heated for 3–5 min under reflux until the initial compound disappeared (TLC, R_f 0.35). Total of 75 mg (2 mmol) of $NaBH_4$ was added. The mixture was diluted with water and extracted with ethyl acetate (3×50 ml). The extract was dried over Na_2SO_4, the solvent was distilled off under reduced pressure, and the residue was recrystallized from methanol. Yield 118 mg (81%), colorless crystals, mp 210–212°C. ^{1}H NMR spectrum, δ, ppm: 4.73 br.s (2H, OH), 5.14 s (2H, CH), 6.98 m (4H, indole), 7.17 s (2H, indole), 7.34 d (2H, indole), 7.59 d (2H, indole), 10.76 br.s (2H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 274 (22) $[M - H_2O]^+$, 243 (18), 144 (100), 130 (42), 116 (39), 88 (34), 57 (23), 43 (52). No molecular ion was detected in the mass spectrum. Found, %: C 74.02; H 5.50; N 9.52. $C_{18}H_{16}N_2O_2$. Calculated, %: C 73.95; H 5.52; N 9.58. *M* 292.34.

6-(2,5-Dimethyl-3-thienyl)-5-(3-indolyl)-2,3-dihydro-1,2,4-triazine-3-thione (IX). A mixture of 850 mg (3 mmol) of dione **VIIa** and 460 mg (5 mmol) of thiosemicarbazide in 5 ml of ethanol was heated for 30 min under reflux. Potassium carbonate, 450 mg (4 mmol), was then added, and the mixture was heated for 48 h under reflux, diluted with 5 ml of water, and acidified with 5 ml of acetic acid. The precipitate was filtered off, washed with a small amount of methanol, and dried. Yield 738 mg (74%), yellow crystals, mp 248–251°C (from MeOH). ^{1}H NMR spectrum, δ, ppm: 2.25 s (3H, CH_3), 2.48 s (3H, CH_3), 6.70 s (1H, thiophene), 6.92 d (1H, indole), 7.26 m (2H, indole), 7.45 m (1H, indole), 8.73 m (1H, indole), 11.96 s (1H, NH), 14.30 s (1H, NHCS). Mass spectrum, *m*/*z* (I_{rel}, %) : 338 (100) $[M]^+$, 305 (16), 280 (36), 251 (91), 236 (28), 218 (17), 142 (23), 126 (18), 117 (12), 97 (13), 77 (13), 59 (45), 43 (29). Found, %: C 59.84; H 4.13; N 16.12; S 18.61. $C_{17}H_{14}N_4S_2$. Calculated, %: C 60.33; H 4.17; N 16.55; S 18.95. *M* 338.42.

6-(2,5-Dimethyl-3-thienyl)-5-(3-indolyl)-1,2,4-triazin-3-ylhydrazine (X). A solution of 150 mg (0.45 mmol) of thione **IX** in a mixture of 1 ml of methanol and 1 ml of hydrazine hydrate was heated for 6 h under reflux. The mixture was cooled, and the precipitate was filtered off, washed with water and dilute methanol, and dried. Yield 125 mg (84%), yellowish crystals, mp 126–129°C (from MeOH). ^{1}H NMR spectrum, δ, ppm: 2.18 s (3H, CH_3), 2.48 s (3H, CH_3), 3.60 br.s (2H, NH_2), 6.63 s (1H, thiophene), 6.70 d (1H, indole), 7.16 m (2H, indole), 7.39 m (1H, indole), 8.40 br.s (1H, N**H**NH_2), 8.78 m (1H, indole), 12.00 br.s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 336 (4) $[M]^+$, 321 (20), 306 (90), 273 (15), 251 (55), 236 (24), 190 (12), 142 (24), 111 (37), 67 (33), 59 (100), 43 (63). Found, %: C 60.40; H 4.65; N 25.03; S 9.41. $C_{17}H_{16}N_6S$. Calculated, %: C 60.70; H 4.79; N 24.98; S 9.53. *M* 336.35 .

6-(2,5-Dimethyl-3-thienyl)-7-(3-indolyl)-3-methyl[1,2,4]triazolo[4,3-*b*][1,2,4]triazine (XIa). A mixture of 100 mg (0.3 mmol) of hydrazine **X** and 2 ml of acetic acid was heated for 6 h under reflux. The mixture was cooled, and the precipitate was filtered off, washed with water and methanol, and dried. Yield 97 mg (95%), yellow crystals, mp >350°C (from MeOH). ^{1}H NMR spectrum, δ, ppm: 2.12 s (3H, 3-CH_3), 2.28 s (3H, CH_3), 2.48 s (3H, CH_3), 6.63 m (2H, thiophene, indole), 7.37 m (2H, indole), 7.47 m (1H, indole), 8.68 m (1H, indole), 12.00 br.s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 360 (100) $[M]^+$, 345 (34), 290 (8), 258 (14), 154 (83), 127 (68), 117 (10), 100 (18), 91 (17), 77 (34), 71 (21), 59 (76), 45 (50), 43 (53). Found, %: C 62.71; H 4.42; N 22.85; S 8.83. $C_{19}H_{16}N_6S$. Calculated, %: C 63.31; H 4.48; N 23.31; S 8.89. *M* 360.44.

Triazolotriazines XIb and XIc (*general procedure*). A mixture of 70 mg (0.2 mmol) of hydrazine derivative **X** and 0.5 mmol of 2-thiophenecarboxylic acid or (3-indolyl)acetic acid was heated until it melted, kept for 6 h at 100–120°C, and cooled. Excess acid was removed by washing in succession with a solution of potassium hydrogen carbonate and water. The melt was then washed with methanol, and the precipitate was filtered off, washed with methanol, and dried.

6-(2,5-Dimethyl-3-thienyl)-7-(3-indolyl)-3-(2-thienyl)[1,2,4]triazolo[4,3-*b*][1,2,4]triazine (XIb). Yield 56 mg (63%), brownish crystals, mp >350°C (from MeOH). ^{1}H NMR spectrum, δ, ppm: 2.32 s (3H, CH_3), 2.48 s (3H, CH_3), 6.80 m (2H, thiophene, indole), 7.26 m (2H, indole, thiophene), 7.47 m (1H, indole), 7.73 m (2H, thiophene), 8.07 d (1H, indole) 8.72 m (1H, indole), 11.90 br.s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 428 (23) $[M]^+$, 292 (8), 251 (9), 155 (15), 154 (100), 136 (28), 128 (84), 111 (96), 81 (25), 71 (23), 59 (44), 57 (49), 45 (53). Found, %: C 61.58; H 3.69; N 19.50; S 15.01. $C_{22}H_{16}N_6S_2$. Calculated, %: C 61.66; H 3.76; N 19.61; S 14.97. *M* 428.55.

6-(2,5-Dimethyl-3-thienyl)-7-(3-indolyl)-3-(3-indolylmethyl)[1,2,4]triazolo[4,3-*b*][1,2,4]triazine (XIc). Yield 76 mg (77%), yellow crystals, mp >350°C (from MeOH). ^{1}H NMR spectrum, δ, ppm: 2.22 s (3H, CH_3), 2.48 s (3H, CH_3), 4.55 s (2H, CH_2), 6.74 m (2H, thiophene, indole), 7.00 m (2H, indole), 7.24 m (3H, indole), 7.35 d (1H, indole), 7.46 m (1H, indole), 7.62 d (1H, indole), 8.69 m (1H, indole), 10.87 br.s (1H, NH), 11.82 br.s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 475 (64) $[M]^+$, 337 (7),196 (13), 156 (49), 154 (100), 142 (29), 130 (59), 101 (16), 91 (26), 77 (40), 59 (55), 43 (47). Found, %: C 68.00; H 4.39; N 20.41; S 6.57. $C_{27}H_{21}N_7S$. Calculated, %: C 68.19; H 4.45; N 20.62; S 6.74. *M* 475.58.

7-(2,5-Dimethyl-3-thienyl)-6-(3-indolyl)tetrazolo-[1,5-*b*][1,2,4]triazine (XII). Compound **X**, 70 mg (0.2 mmol), was dissolved in 2 ml of 5% hydrochloric acid, and a solution of 15 mg (0.2 mmol) of sodium nitrite was added. The precipitate was filtered off, washed with water, and recrystallized from methanol. Yield 62 mg (77%), yellow crystals, mp 260°C (decomp.). ^{1}H NMR spectrum, δ, ppm: 2.32 s (3H, CH_3), 2.48 s (3H, CH_3), 6.80 s (1H, thiophene), 6.87 d (1H, indole), 7.32 m (2H, indole), 7.52 m (1H, indole), 8.69 m (1H, indole), 12.25 br.s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 347 (18) $[M]^+$, 321 (47), 291 (45), 263 (83), 250 (100), 238 (36), 223 (26), 117 (16), 91 (18), 84 (80), 66 (96), 59 (37), 43 (33). Found, %: C 53.34; H 4.53; N 23.08; S 15.05. $C_{17}H_{13}N_7S$. Calculated, %: C 53.63; H 4.50; N 23.04; S 15.07. *M* 347.40.

3-Aminotriazines XIIIa–XIIId (*general procedure*). A mixture of 70 mg (0.2 mmol) of thione **IX** and 2 ml of the corresponding amine was heated for 6 h at the boiling point. The mixture was cooled and treated with water, and the precipitate was filtered off and washed with water and methanol, and dried.

6-(2,5-Dimethyl-3-thienyl)-5-(3-indolyl)-3-(1-pyrrolidinyl)-1,2,4-triazine (XIIIa). Yield 61 mg (78%), yellowish crystals, mp 284–287°C (from MeOH). ^{1}H NMR spectrum, δ, ppm: 2.10 t (4H, CH_2CH_2), 2.14 s (3H, CH_3), 2.48 s (3H, CH_3), 3.76 t (4H, CH_2N),

6.64 s (1H, thiophene), 6.83 d (1H, indole), 7.16 m (2H, indole), 7.43 m (1H, indole), 8.58 m (1H, indole), 11.57 br.s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 375 (64) $[M]^+$, 252 (18), 251 (100), 236 (15), 191 (18), 189 (16), 142 (25), 96 (8), 55 (8). Found, %: C 66.94; H 5.61; N 18.52; S 8.59. $C_{21}H_{21}N_5S$. Calculated, %: C 67.17; H 5.64; N 18.65; S 8.54. *M* 375.49.

6-(2,5-Dimethyl-3-thienyl)-5-(3-indolyl)-3-morpholino-1,2,4-triazine (XIIIb). Yield 57 mg (70%), yellowish crystals, mp 220–224°C (from MeOH). ^{1}H NMR spectrum, δ, ppm: 2.16 s (3H, CH_3), 2.47 s (3H, CH_3), 3.82 t (4H, CH_2N), 3.93 t (4H, CH_2O), 6.63 s (1H, thiophene), 6.84 d (1H, indole), 7.18 m (2H, indole), 7.43 m (1H, indole), 8.40 m (1H, indole), 11.70 br.s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 391 (83) $[M]^+$, 334 (12), 252 (22), 251 (98), 250 (27), 139 (22), 111 (9), 100 (17), 91 (24), 86 (18), 69 (16), 59 (80), 43 (100). Found, %: C 64.04; H 5.41; N 17.14; S 8.20. $C_{21}H_{21}N_5OS$. Calculated, %: C 64.43; H 5.41; N 17.89; S 8.19. *M* 391.49.

6-(2,5-Dimethyl-3-thienyl)-5-(3-indolyl)-3-(4-methyl-1-piperazinyl)-1,2,4-triazine (XIIIc). Yield 56 mg (67%), yellowish crystals, mp 218–220°C (from MeOH). ^{1}H NMR spectrum, δ, ppm: 2.14 s (3H, CH_3), 2.27 s (3H, NCH_3), 2.47 s (3H, CH_3), 2.53 t (4H, CH_2), 3.94 t (4H, CH_2), 6.62 s (1H, thiophene), 6.83 d (1H, indole), 7.18 m (2H, indole), 7.42 m (1H, indole), 8.42 m (1H, indole), 11.68 br.s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 404 (30) $[M]^+$, 335 (27), 334 (98), 322 (15), 251 (40), 236 (13), 143 (25), 100 (30), 91 (26), 83 (42), 71 (57), 70 (100), 59 (70), 57 (60), 43 (32). Found, %: C 65.06; H 5.91; N 20.70; S 7.88. $C_{22}H_{24}N_6S$. Calculated, %: C 65.32; H 5.98; N 20.77; S 7.93. *M* 404.54.

6-(2,5-Dimethyl-3-thienyl)-5-(3-indolyl)-3-piperidino-1,2,4-triazine (XIIId). Yield 57 mg (71%), yellowish crystals, mp 244–246°C (from MeOH). ^{1}H NMR spectrum, δ, ppm: 1.72 m (6H, CH_2), 2.16 s (3H, CH_3), 2.47 s (3H, CH_3), 3.96 m (4N, NCH_2), 6.62 s (1H, thiophene), 6.84 d (1H, indole), 7.16 m (2H, indole), 8.40 m (1H, indole), 11.62 br.s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 389 (67) $[M]^+$, 252 (15), 251 (100), 236 (8), 165 (5), 142 (8), 110 (6), 84 (15), 69 (6), 59 (12), 55 (14), 43 (9). Found, %: C 66.99; H 5.85; N 17.91; S 8.11. $C_{22}H_{23}N_5S$. Calculated, %: C 67.84; H 5.95; N 17.98; S 8.23. *M* 389.52.

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