Unusual reaction of α-diketones of the indole series with hydrazine

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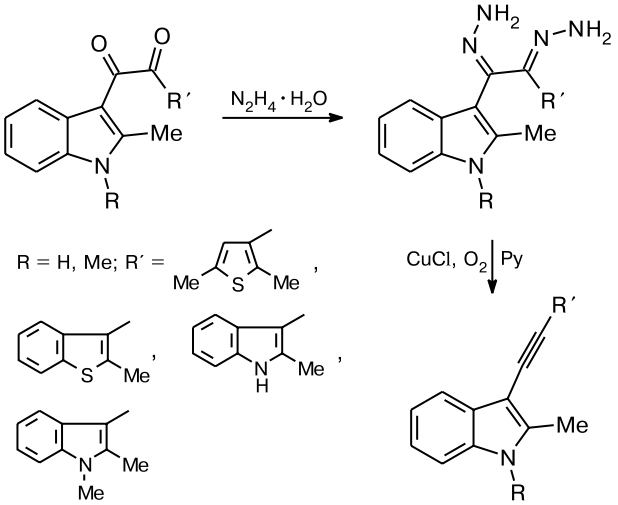
Symmetrical and unsymmetrical α-diketones of the indole series were synthesized by the Friedel—Crafts reaction of 3-indolylglyoxyl chlorides with heterocycles. A nonconventional reaction of *N*-unsubstituted diketones with hydrazine producing 3*H*-pyrazolo[3,4-*c*]quinoline derivatives was found.

Key words: indol-3-ylglyoxyl chlorides, α-diketones, hydrazine hydrate, 3*H*-pyrazolo[3,4-*c*]quinolines, heterocyclization.

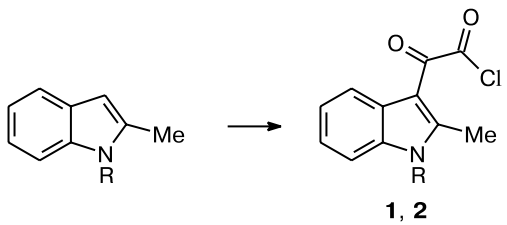
Recently, we have synthesized[1] 4-hetaryl-2-phenyl-5,6-dithienyl-4*H*-1,3-thiazines by cycloaddition of bis(2,5-dimethyl-3-thienyl)acetylene with heteroaromatic aldehydes and thiobenzamide. Earlier, we have prepared[2] the above-mentioned acetylene by oxidation of bis(2,5-dimethyl-3-thienyl)ethanedione bis-hydrazone. The aim of the present study was to apply this approach[2] to the synthesis of new acetylene derivatives from symmetrical and unsymmetrical 1,2-diketones bearing the indolyl, benzothiophenyl, or thienyl substituents (Scheme 1).

Scheme 1



We synthesized α-diketones starting from (2-methyl-3-indolyl)glyoxyloyl chloride[3] **1** and (1,2-dimethyl-3-indolyl)glyoxyloyl chloride **2**, which were prepared by the reaction of equimolar amounts of the substrate and oxalyl chloride in diethyl ether (Scheme 2).

Scheme 2



1, **2**

R = H (**1**), Me (**2**)
Reagents and conditions: $(ClCO)_2$, diethyl ether.

Acid chlorides **1** and **2** were used to acylate 2,5-dimethylthiophene and 2-methylbenzo[*b*]thiophene, respectively. To decrease the polarity of the medium (which leads to a decrease in the solvation energy of the transition state resulting in an increase in the selectivity of the process), we used a mixture of 1,2-dichloroethane (DCE) and hexane (*cf.* lit. data[2,4—6]). The optimal $AlCl_3$: substrate : acid chloride ratio was 4.5 : 1.5 : 1. The reactions with the use of smaller amounts of the Lewis acid or an equimolar amount of the substrate produced the target compounds in lower yields.

The reaction of acid chloride **1** with 2,5-dimethylthiophene affords 1-(2,5-dimethyl-3-thienyl)-2-(2-methyl-3-indolyl)ethanedione (**3**), and the reaction with 2-methylbenzo[*b*]thiophene gives 1-(2-methyl-3-benzo[*b*]thienyl)-2-(2-methyl-3-indolyl)ethanedione (**4**).

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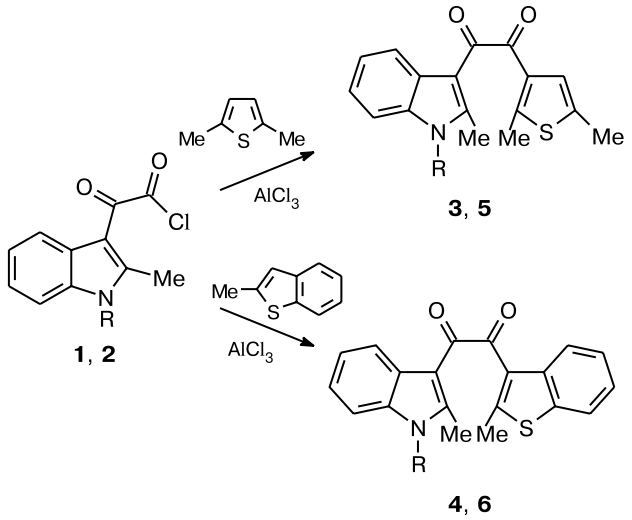
Analogously, acid chloride **2** is transformed into 1-(1,2-dimethyl-3-indolyl)-2-(2,5-dimethyl-3-thienyl)ethanedione (**5**) and 1-(1,2-dimethyl-3-indolyl)-2-(2-methyl-3-benzo[*b*]thienyl)ethanedione (**6**) (Scheme 3). The yields of the diketones are 40—65%.

Scheme 3

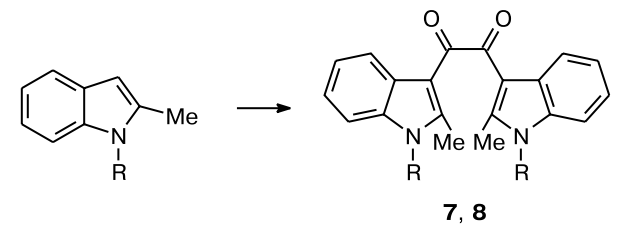


R = H (**1**, **3**, **4**), Me (**2**, **5**, **6**)

Reaction conditions and yields of products: DCE : hexane = 10 : 3, 1.2 h, the yield of **3** was 64%; DCE : hexane = 27 : 7, 6 h, the yield of **4** was 59% (86%); DCE : hexane = 24 : 7, 3 h, the yield of **5** was 45%; DCE : hexane = 10 : 3, 7 h, the yield of **6** was 40% (71%). The yield with respect to unconsumed 2-methylbenzo[*b*]thiophene is given in parentheses.

We synthesized symmetrical diketones, *viz.*, 1,2-bis(2-methyl-3-indolyl)ethanedione (**7**) and 1,2-bis(1,2-dimethyl-3-indolyl)ethanedione (**8**), in high yields (Scheme 4) according to a modified procedure developed for the synthesis of 1,2-bis(1-methyl-3-indolyl)ethanedione[7] (heating of an ethereal solution of a mixture of the substrate and oxalyl chloride in the absence of a catalyst). The known procedure for the synthesis of 1,2-bis(3-indolyl)ethanedione[8] and 1,2-bis(2-methyl-3-indolyl)ethanedione[9] by the reaction of oxalyl chloride with the corresponding indolylmagnesium bromides is inconvenient because of low yields.

Scheme 4

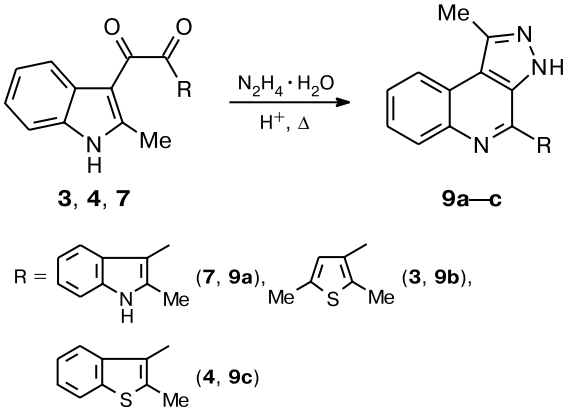


R = H (**7**, 81%), Me (**8**, 88%)
Reagents and conditions: $(ClCO)_2$, diethyl ether.

Our next aim was to synthesize bis-hydrazones (osazones) from α-diketones **3**—**8** according to Scheme 1 and transform the resulting compounds into acetylenes. Data on osazones of α-diketones of the indole series are lacking in the literature. Let us only mention the synthesis of 1,2-bis(2-methyl-3-indolyl)ethanedione bis-phenylhydrazone by refluxing a solution of 1,2-bis(2-methyl-3-indolyl)ethanedione in the presence of phenylhydrazine in acetic acid.[8]

We found that diketone **7** remained intact after refluxing with a 16-fold excess of hydrazine hydrate in ethanol in the presence of a catalytic amount of *p*-TsOH for 1 day. Refluxing in glacial acetic acid for 21 h unexpectedly afforded 4-(2-methyl-3-indolyl)-1-methyl-3*H*-pyrazolo[3,4-*c*]quinoline (**9a**) in 34% yield (Scheme 5) rather than hydrazone. Raising the temperature to 170—175 °C and the use of higher-boiling ethylene glycol in the presence of an equivalent amount of hydrazine hydrochloride led to a decrease in the reaction time to 2 h and an increase in the yield of the reaction product to 63%.

Scheme 5



Refluxing of α-diketone **3** in glacial acetic acid in the presence of a catalytic amount of *p*-TsOH for 22 h afforded traces of 3*H*-pyrazolo[3,4-*c*]quinoline **9b** (TLC data), and 53% of the starting compound was recovered. The use of ethylene glycol instead of acetic acid led to an increase in the yield of compound **9b** to 60%.

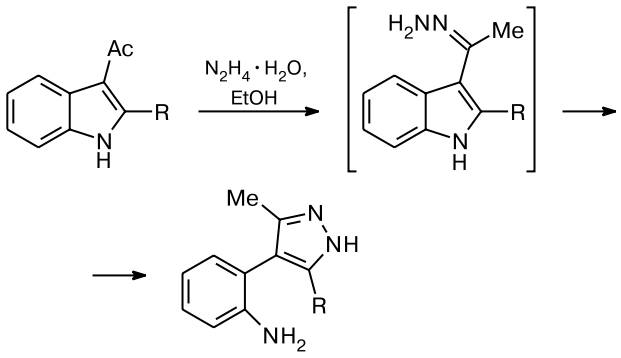
The reaction of 1-(2-methyl-3-benzo[*b*]thienyl)-2-(2-methyl-3-indolyl)ethanedione (**4**) with hydrazine hydrate in *n*-butanol in the presence of *p*-TsOH for 8.5 h produces 1-methyl-4-(2-methyl-3-benzo[*b*]thienyl)-3*H*-pyrazolo[3,4-*c*]quinoline **9c** in 27% yield (see Scheme 5). In acetic acid, the yield of the latter product is lower.

The reaction in ethylene glycol affords 3*H*-pyrazolo[3,4-*c*]quinoline **9c** in 14% yield.

Heating of *N*-methylindolyl-substituted α-diketones **5** and **8** with an excess of hydrazine hydrate in the presence of an equimolar amount of hydrazine hydrochloride in ethylene glycol gave rise to a complex mixture of products, which is apparently attributed to the fact that the 3*H*-pyrazolo[3,4-*c*]quinoline system cannot be formed.

The above-described transformations of α-diketones **3**, **4**, and **7** are analogous to the reaction of 3-acetylindole with hydrazine hydrate (heating in a sealed tube at 150—160 °C for 5 h) giving rise to 4-(2-aminophenyl)-3-methylpyrazole[10] (Scheme 6) as a result of the nucleophilic attack on position 2 of the indole system. Refluxing in ethanol in an open flask for 2 h afforded only hydrazone. Heating of the latter with an eightfold excess of hydrazine hydrate in a sealed tube at 150—160 °C for 3 h gave the corresponding (aminophenyl)pyrazole. Hydrazones of 2-methyl- and 2-phenyl-substituted 3-acetylindoles were not isolated; instead, the corresponding (aminophenyl)pyrazoles were obtained.

Scheme 6



R = H, Me, Ph

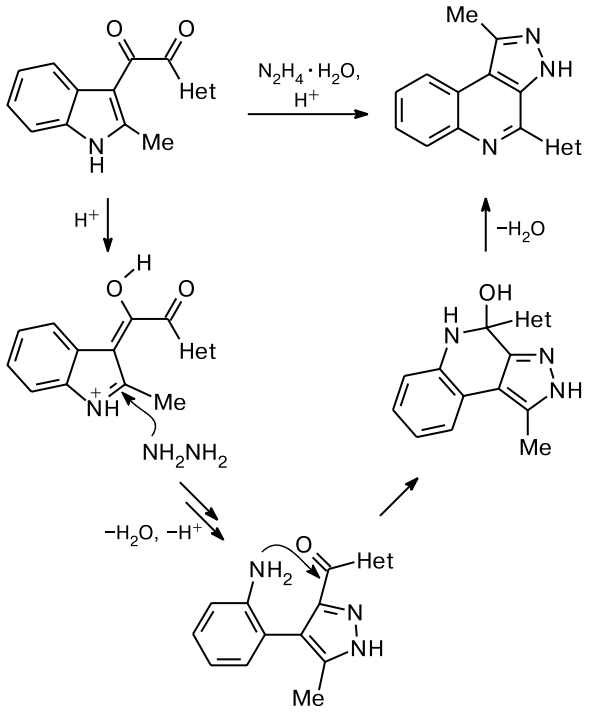
Heating of 3-benzoylindole and 3-benzoyl-2-methylindole with an eightfold excess of hydrazine hydrate in the presence of an equimolar amount of hydrazine hydrochloride in ethanol in an autoclave at 150—160 °C afforded 4-(2-aminophenyl)-5-phenylpyrazole and 4-(2-aminophenyl)-3(5)-methyl-5(3)-phenylpyrazole, respectively, in almost quantitative yields.[11]

Presumably, 4-(2-aminophenyl)-3(5)-hetaroyl-5(3)-methylpyrazoles formed from compounds **3**, **4** and **7** undergo intramolecular cyclization giving rise to the quinoline system. In further studies, we used the modified conditions of the reaction of 3-benzoylindole[11] with hydrazine hydrate.

The possible mechanism of the formation of compounds **9a**—**c** is presented in Scheme 7.

3*H*-Pyrazolo[3,4-*c*]quinolines, unlike their 2*H* isomers, were not described in the literature. 1-Methyl- and

Scheme 7



1-phenyl-substituted 4-methyl-2-phenyl-2*H*-pyrazolo[3,4-*c*]quinolines[12] were synthesized by the rearrangement of phenylhydrazones of 2-methyl- and 2-phenyl-substituted 1-(3-indolyl)propane-1,2-diones occurring under reflux of their ethanolic solutions in the presence of catalytic amounts of hydrochloric acid. The above-mentioned phenylhydrazones were prepared by the addition of 2-methyl- and 2-phenylindole to the corresponding nitrile imine.[13]

The structures of 3*H*-pyrazolo[3,4-*c*]quinolines **9a**—**c** were confirmed by ^{1}H NMR spectra, which show the characteristic signals for the quinoline protons at positions 6 and 9 at δ 8.2—8.5 and the pyrazole methyl at δ 2.9. The mass spectra contain the molecular ion peaks $[M]^+$ and the fragment ions formed as a result of the loss of the methyl group from the molecular ion, as well as peaks of the $H_2C{=}N{-}CH_2$ species characteristic of alkylpyrazoles.

Since the known 3-methyl-1*H*-pyrazole exists in the equilibrium with its tautomer, *viz.*, 5-methyl-1*H*-pyrazole, there is, presumably, an equilibrium between 3*H*-pyrazolo[3,4-*c*]quinolines **9a**—**c** and their 2*H*-tautomers. However, it is necessary to perform additional investigations.

Thus, we demonstrated the possibility of preparing the previously unknown 4-hetaryl-substituted 1-methyl-3*H*-pyrazolo[3,4-*c*]quinolines, which was exemplified by the synthesis of NH-unsubstituted α-diketones of the indole series **3**, **4**, and **7**. Apparently, the series of these compounds can be extended with the use of other heterocyclic substituents.

Experimental

The ^1H and ^{13}C NMR spectra were recorded on Bruker AM-200 and Bruker AM-250 spectrometers in $CDCl_3$, DMSO-d_6, and acetone-d_6. The mass spectra (EI) were measured on a Kratos instrument (70 eV) using a direct inlet system.

The high-resolution mass spectra were obtained on an LTQ FT hybrid mass spectrometer (Thermo Finnigan, Germany) consisting of a linear quadrupole ion trap and a Fourier transform ion cyclotron resonance mass spectrometer. A universal electrospray ionization (ESI) source Finnigan Ion Max Source was used as the ion source. Electrospraying of samples was carried out at a voltage of the needle emitter of 4 kV; samples were injected into the needle emitter at a rate of 1 μL min^{-1}. The samples were dissolved in a 50 : 50 acetonitrile—water mixture with the addition of 1% acetic acid.

The melting points were measured on a Boetius hot-stage apparatus and are uncorrected. The course of the reactions was monitored by TLC on Merck plates (Silica gel 60 F_{254}, visualization with UV light). Column chromatography was performed on Merck SiO_2-60 silica gel (0.060—0.200 mm).

Aluminum chloride, 2-methylindole, oxalyl chloride, and hydrazine hydrate were purchased from Merck.

1,2-Dimethylindole was synthesized from 2-methylindole and iodomethane.[14] 2-Methylbenzo[*b*]thiophene was prepared from benzothiophene and iodomethane.[15] (2-Methyl-3-indolyl)glyoxyloyl chloride (**1**) was synthesized from oxalyl chloride and 2-methylindole.[3]

(1,2-Dimethyl-3-indolyl)glyoxyloyl chloride (2). Oxalyl chloride (7.10 g, 4.8 mL, 55.92 mmol) was added dropwise to a solution of 1,2-dimethylindole (7.00 g, 48.21 mmol) in anhydrous diethyl ether (100 mL) at 0—2 °C. The resulting suspension was stirred at 0—5 °C for 2.5 h. The precipitate that formed was filtered off and washed with anhydrous diethyl ether. The mother liquor was concentrated to 10% of the initial volume and petroleum ether was added. The precipitate that formed was combined with the first portion of the precipitate and dried in a vacuum desiccator. Acid chloride **2** was obtained in a yield of 10.27 g (90%), m.p. 83 °C. Found (%): C, 61.47; H, 4.60; Cl, 14.98; N, 5.30. $C_{12}H_{10}ClNO_2$. Calculated (%): C, 61.16; H, 4.28; Cl, 15.04; N, 5.94. ^1H NMR ($CDCl_3$), δ: 2.73 (s, 3 H, 2-Me); 3.75 (s, 3 H, 1-Me); 7.30—7.40 (m, 3 H, H_{Het}(5,6,7)); 7.90 (d, 1 H, H_{Het}(4), $J_{4,5}$ = 7.2 Hz).

1-(2,5-Dimethyl-3-thienyl)-2-(2-methyl-3-indolyl)ethanedione (3). Acid chloride **1** (0.44 g, 2 mmol) was added portionwise to a stirred suspension of $AlCl_3$ (1.20 g, 9 mmol) in a mixture of hexane (3 mL) and 1,2-dichloroethane (5 mL) for 10 min. Then a solution of 2,5-dimethylthiophene (0.34 g, 0.34 mL, 3 mmol) in 1,2-dichloroethane (5 mL) was added at room temperature. The resulting crimson solution was stirred at the same temperature for 70 min and poured onto ice. Then dichloromethane (30 mL) was added. The organic layer was separated and washed with water, an aqueous solution of sodium hydrocarbonate, and water. The solvent was evaporated. Diketone **3** was obtained in a yield of 0.38 g (64%), m.p. 172—173 °C (ethanol). Found (%): C, 68.86; H, 5.25; S 10.58. $C_{17}H_{15}NO_2S$. Calculated (%): C, 68.66; H, 5.08; S, 10.78. ^1H NMR ($CDCl_3$), δ: 2.34 (s, 3 H, 5-Me_{thioph}); 2.52 (s, 3 H, 2-Me_{thioph}); 2.75 (s, 3 H, 2-Me_{indole}); 6.97 (s, 1 H, 4-H_{thioph}); 7.16—7.25 (m, 3 H, 5,6,7-H_{indole}); 7.98 (d, 1 H, 4-H_{indole}, $J_{4,5}$ = 7.70 Hz); 9.25 (br.s, 1 H, NH). ^{13}C NMR ($CDCl_3$), δ: 14.75 (5-Me_{thioph}); 14.89 (2-Me_{thioph}); 15.96 (2-Me_{indole}); 110.41 (C(3)); 111.19 (C(7)), 120.96, 122.98, 123.38 (C(4), C(5), C(6)), 126.99, 127.06 (C(4′), C(3a)), 132.29 (C(5′)), 135.12 (C(7a)), 136.46 (C(3′)), 147.11 (C(2)), 151.55 (C(2′)), 190.60, 190.83 (2 CO). MS (EI, 70 eV), *m/z* (I_{rel} (%)): 297 $[M]^+$ (6), 158 $[(C_9H_8N)CO]^+$ (100), 139 $[(C_6H_7S)CO]^+$ (21), 130 $[C_9H_8N]^+$ (25), 111 $[C_6H_7S]^+$ (21).

1-(2-Methyl-3-benzo[*b*]thienyl)-2-(2-methyl-3-indolyl)ethanedione (4). Acid chloride **1** (1.00 g, 4.51 mmol) was added portionwise to a stirred suspension of $AlCl_3$ (2.70 g, 20.30 mmol) in a mixture of 1,2-dichloroethane (12 mL) and hexane (7 mL) at 15—17 °C for 10 min. Then a solution of 2-methylbenzo[*b*]thiophene (1.02 g, 6.77 mmol) in 1,2-dichloroethane (15 mL) was added for 40 min. The resulting dark solution with a reddish tint was stirred at the same temperature for 5 h and poured onto ice. Then dichloromethane (30 mL) was added. The organic layer was separated and washed with water, an aqueous solution of sodium hydrocarbonate, and water. The solvent was evaporated. Column chromatography (AcOEt—petroleum ether, 1 : 3, as the eluent) of the residue (1.72 g) afforded the starting benzothiophene in a yield of 0.55 g and diketone **4** in a yield of 0.89 g (59%), m.p. 178—179 °C (ethanol). Found (%): C, 71.69; H, 4.73; S, 9.92; N, 4.03. $C_{20}H_{15}NO_2S$. Calculated (%): C, 72.05; H, 4.53; S, 9.62; N, 4.20. ^1H NMR ($CDCl_3$), δ: 2.47 (s, 3 H, 2-Me_{thioph}); 2.70 (s, 3 H, 2-Me_{indole}); 7.14—7.24 (m, 3 H, 5,6-H_{indole}, 5-H_{thioph}); 7.33—7.44 (m, 2 H, 7-H_{indole}, 6-H_{thioph}); 7.76 (d, 1 H, 4-H_{thioph}, $J_{4,5}$ = 7.9 Hz); 7.97 (d, 1 H, 4-H_{indole}, $J_{4,5}$ = 7.6 Hz); 8.51 (d, 1 H, 7-H_{thioph}, $J_{6,7}$ = 7.9 Hz); 9.58 (br.s, 1 H, NH). MS (EI, 70 eV), *m/z* (I_{rel} (%)): 332 $[M - 1]^+$ (3), 317 $[M - Me - 1]^+$ (1), 175 $[(C_9H_7S)CO]^+$ (16), 158 $[(C_9H_8N)CO]^+$ (100), 130 $[C_9H_8N]^+$ (15).

1-(1,2-Dimethyl-3-indolyl)-2-(2,5-dimethyl-3-thienyl)ethanedione (5). Acid chloride **2** (1.00 g, 4.24 mol) was added with stirring to a suspension of $AlCl_3$ (2.54 g, 19.09 mmol) in a mixture of petroleum ether (7 mL) and 1,2-dichloroethane (12 mL) at 10 °C for 10 min. Then a solution of 2,5-dimethylthiophene (0.71 g, 0.73 mL, 6.37 mmol) in 1,2-dichloroethane (12 mL) was added for 15 min (the temperature of the mixture raised to 18 °C). The reaction mixture was stirred at the same temperature for 3 h and poured onto ice. Then dichloromethane (30 mL) was added. The organic layer was separated, and the aqueous layer was extracted with dichloromethane. The combined extracts were washed with water, an aqueous solution of sodium hydrocarbonate, and water. After evaporation of the solvent, a dark remainder (1.73 g) was obtained. Column chromatography of the latter (ethyl acetate—light petroleum ether, (1 : 3)—(1 : 2), as the eluent) afforded diketone **5** in a yield of 0.60 g (45%), m.p. 123—125 °C (ethanol). Found (%): C, 69.32; H, 5.68; S, 10.32; N, 4.33. $C_{18}H_{17}NO_2S$. Calculated (%): C, 69.43; H, 5.50; S, 10.30; N, 4.50. M = 311.41. ^1H NMR ($CDCl_3$), δ: 2.34 (s, 3 H, 5-Me_{thioph}); 2.62 (s, 3 H, 2-Me_{thioph}); 2.76 (s, 3 H, 2-Me_{indole}); 3.65 (s, 3 H, 1-Me_{indole}); 6.97 (s, 1 H, 4-H_{thioph}); 7.19-7.30 (m, 3 H, 5,6,7-H_{indole}); 7.92 (d, 1 H, $J_{4,5}$ = 7.98 Hz, 4-H_{indole}). MS (EI, 70 eV), *m/z* (I_{rel} (%)): 311 $[M]^+$ (3), 172 $[1/2\ M]^+$ (100), 144 $[1/2\ M - CO]^+$ (9).

1-(1,2-Dimethyl-3-indolyl)-2-(2-methyl-3-benzo[*b*]thienyl)ethanedione (6). Acid chloride **2** (1.00 g, 4.24 mmol) was added portionwise to a stirred suspension of $AlCl_3$ (2.54 g, 19.09 mmol) in a mixture of 1,2-dichloroethane (12 mL) and hexane (7 mL) at 10 °C for 10 min. Then a solution of 2-methylbenzo[*b*]thiophene (0.94 g, 6.37 mmol) in 1,2-dichloroethane (12 mL) was added for 17 min (the temperature raised

to 18 °C). The resulting solution was stirred at the same temperature for 7 h and poured onto ice. Then dichloromethane (30 mL) was added. The organic layer was separated and washed with water, an aqueous solution of sodium hydrocarbonate, and water. The solution was concentrated. Column chromatography (ethyl acetate—light petroleum ether, (1 : 3)—(1 : 2), as the eluent) of the residue (1.53 g) afforded the starting benzothiophene in a yield of 0.55 g and diketone **6** in a yield of 0.60 g (40%), m.p. 202—203 °C (ethanol). Found (%): C, 72.87; H, 5.13; S, 8.54. $C_{21}H_{17}NO_2S$. Calculated (%): C, 72.60; H, 4.93; S, 9.23. ^{1}H NMR ($CDCl_3$), δ: 2.72 (s, 3 H, 2-Me_{thioph}); 2.74 (s, 3 H, 2-Me_{indole}); 3.74 (s, 3 H, 1-Me_{indole}); 7.17—7.47 (m, 5 H, 5,6,7-H_{indole}, 5,6-H_{thioph}); 7.78 (d, 1 H, 7-H_{thioph}, $J_{6,7}$ = 7.2 Hz); 7.92 (d, 1 H, 4-H_{indole}, $J_{4,5}$ = 7.6 Hz); 8.55 (d, 1 H, 4-H_{thioph}, $J_{4,5}$ = 7.9 Hz). MS (EI, 70 eV), *m/z* (I_{rel} (%)): 347 $[M]^+$ (3), 332 $[M - Me]^+$ (3), 175 $[(C_9H_7S)CO]^+$ (6), 172 $[(C_{10}H_{10}N)CO]^+$ (100), 147 $[C_9H_7S]^+$ (6), 144 $[C_{10}H_{10}N]^+$ (10).

1,2-Bis(2-methyl-3-indolyl)ethanedione (7). Oxalyl chloride (3.20 g, 2.10 mL, 25.16 mmol) was added to a solution of 2-methylindole (6.00 g, 45.74 mmol) in anhydrous diethyl ether (38 mL) at 1—7 °C for 30 min, which led to the formation of a red precipitate. The resulting suspension was stirred at 30 °C for 3.3 h and kept for 16 h. The black precipitate that formed was filtered off, washed with diethyl ether, and dried. Filtration of the crude diketone in a 1 : 2 mixture of ethyl acetate and petroleum ether through a layer of silica gel afforded colorless diketone **7** in a yield of 5.82 g (81%), m.p. 272—274 °C (ethanol). Found (%): C, 75.81; H, 5.51; N, 8.59. $C_{20}H_{16}N_2O_2$. Calculated (%): C, 75.93; H, 5.10; N, 8.85. ^{1}H NMR ($(CD_3)_2CO$), δ: 2.63 (s, 3 H, 2-Me); 7.13—7.23 (m, 2 H, 5,6-H_{Het}); 7.44 (d, 1 H, 7-H_{Het}, $J_{6,7}$ = 6.7 Hz); 8.10 (d, 1 H, 4-H_{Het}, $J_{4,5}$ = 7.9 Hz); 11.09 (br.s, 1 H, NH). ^{13}C NMR ($(CD_3)_2CO$), δ: 14.78 (2-Me), 111.62 (C(3)), 112.45 (C(8)), 122.07, 123.29, 123.90 (C(5,6,7)), 128.75 (C(4)), 136.85 (C(2)), 192.93 (CO). MS (EI, 70 eV), *m/z* (I_{rel} (%)): 316 $[M]^+$ (3), 158 $[1/2\ M]^+$ (100), 130 $[1/2\ M - CO]^+$ (19).

1,2-Bis(1,2-dimethyl-3-indolyl)ethanedione (8). A solution of oxalyl chloride (0.57 g, 0.39 mL, 4.48 mmol) in diethyl ether (10 mL) was added dropwise to a solution of 1,2-dimethylindole (1.48 g, 9.85 mmol) in anhydrous diethyl ether (12 mL) at −1—2 °C for 20 min. The reaction mixture was stirred at 27—30 °C for 2 h and kept for 16 h. The red precipitate that formed was filtered off, washed with diethyl ether, and dried. The yield of the compound was 1.50 g (97%). Recrystallization from DMF afforded colorless diketone **8**, m.p. 274—276 °C. Found (%): C, 76.59; H, 5.94 N, 8.12. $C_{22}H_{20}N_2O_2$. Calculated (%): C, 76.72; H, 5.85; N, 8.13. ^{1}H NMR ($CDCl_3$), δ: 2.70 (s, 3 H, 2-Me); 3.70 (s, 3 H, 1-Me); 7.14—7.35 (m, 3 H, 5,6,7-H_{Het}); 8.06 (d, 1 H, 4-H_{Het}, $J_{4,5}$ = 7.2 Hz). ^{13}C NMR ($CDCl_3$), δ: 12.68 (2-Me); 29.83 (1-Me), 109.41 (C(3)), 110.57 (C(7)), 121.34 (C(4)), 122.85 (C(5,6)), 126.76 (C(3a)), 137.15 (C(7a)), 147.25 (C(2)), 191.49 (CO). MS (EI, 70 eV), *m/z* (I_{rel} (%)): 344 $[M]^+$ (2), 172 $[1/2\ M]^+$ (100), 144 $[1/2\ M - CO]^+$ (14), 129 $[1/2\ M - CO - Me]^+$ (5).

1-Methyl-4-(2-methyl-3-indolyl)-3*H*-pyrazolo[3,4-*c*]quinoline (9a). A solution of ethanedione **7** (1.04 g, 3.28 mmol) and hydrazine hydrate (2.30 mL, 45.99 mol) in ethylene glycol (15 mL) in the presence of hydrazine hydrochloride (0.23 g, 3.28 mmol) was heated with stirring at 170—175 °C for 2 h. Then the reaction mixture was cooled and poured into water. The precipitate that formed (0.47 g) was filtered off and recrystallized from DMF. Compound **9a** was obtained in a yield of 0.64 g (63%), m.p. 332—334 °C. ^{1}H NMR (DMSO-d_6), δ: 2.09 (s, 3 H, 2-Me_{indole}); 2.88 (s, 3 H, 1-Me); 6.98—7.07 (m, 1 H, 6-H_{indole}); 7.08—7.17 (m, 1 H, 5-H_{indole}); 7.42 (d, 1 H, 7-H_{indole}, $J_{6,7}$ = 7.4 Hz); 7.51—7.72 (m, 3 H, 4-H_{indole}, 7-H, 8-H); 8.10 (m, 1 H, 9-H); 8.36 (m, 1 H, 6-H); 11.46 (br.s, 1 H, NH_{indole}); 13.15 (br.s, 1 H, NH). MS (EI, 70 eV), *m/z* (I_{rel} (%)): 312 $[M]^+$ (100), 311 $[M - 1]^+$ (58), 297 $[M - Me]^+$ (15), 270 $[M - H_2C{=}N - CH_2]^+$ (15). High-resolution mass spectrum: found: *m/z* $[M + H]^+$ 313.144, $[MH + 1]^+$ 314.149; $C_{20}H_{16}N_4$; calculated: M + H = 313.145.

4-(2,5-Dimethyl-3-thienyl)-1-methyl-3*H*-pyrazolo[3,4-*c*]quinoline (9b). A solution of α-diketone **3** (0.32 g, 1.08 mmol) and hydrazine hydrate (0.75 mL, 15.06 mmol) in ethylene glycol (7 mL) was heated with stirring in the presence of *p*-TsOH (~20 mg) at 185—190 °C for 3 h. After cooling, the reaction mixture was poured into water and the white precipitate that formed was filtered off in a yield of 0.31 g. The precipitate was recrystallized from ethanol. Quinoline **9b** was obtained in a yield of 0.19 g (60%), m.p. 176—177 °C. Found (%): C, 69.57; H, 5.58; N, 13.85. $C_{17}H_{15}N_3S$. Calculated (%): C, 69.60; H, 5.15; N, 14.32. ^{1}H NMR (DMSO-d_6), δ: 2.48 (s, 3 H, 5-Me_{thioph}); 2.58 (s, 3 H, 2-Me_{thioph}); 2.86 (s, 3 H, 1-Me); 7.15 (s, 1 H, 4-H_{thioph}); 7.57—7.74 (m, 2 H, 7-H, 8-H); 8.03—8.15 (m, 1 H, 9-H); 8.25—8.40 (m, 1 H, 6-H); 13.38 (br.s, 1 H, NH). MS (EI, 70 eV), *m/z* (I_{rel} (%)): 294 $[M + 1]^+$ (34), 293 $[M]^+$ (98), 278 $[M - Me]^+$ (65), 251 $[M - H_2C{=}N - CH_2]^+$ (40).

1-Methyl-4-(2-methyl-3-benzo[*b*]thienyl)-3*H*-pyrazolo[3,4-*c*]quinoline (9c). A mixture of 1,2-ethanedione **4** (0.24 g, 0.72 mmol) and hydrazine hydrate (0.52 mL, 10.80 mmol) in *n*-butanol (2 mL) in the presence of *p*-TsOH was refluxed for 8.5 h, poured into water, and extracted with dichloromethane. The organic layer was separated, washed several times with water, and concentrated. The residue (0.35 g) was recrystallized from ethanol. 1-Methyl-4-(2-methyl-3-benzo[*b*]thienyl)-3*H*-pyrazolo[3,4-c]quinoline **9c** was obtained in a yield of 61 mg (26.5%), m.p. 228—230 °C. After repeated recrystallization from dioxane, m.p. 234—235 °C. ^{1}H NMR (DMSO-d_6), δ: 2.63 (s, 3 H, 2-Me_{thioph}); 2.91 (s, 3 H, 1-Me); 7.23 (1H, m, 5-H_{thioph}); 7.65 (m, 3 H, 7-H, 8-H, 6-H_{thioph}); 7.89 (d, 1 H, 4-H_{thioph}, J = 8.2 Hz); 8.15 (m, 1 H, 9-H); 8.32 (m, 1 H, 7-H_{thioph}); 8.45 (m, 1 H, 6-H); 8.99 (br.s, 1 H, NH), m.p. 234—235 °C (dioxane). MS (EI, 70 eV), *m/z* (I_{rel} (%)): 329 $[M + 1]^+$ (100), 314 $[M - Me]^+$ (47), 300 $[M - N_2 - 1]^+$ (12), 287 $[M - H_2C{=}N - CH_2]^+$ (28). High-resolution mass spectrum: found *m/z* $[M + H]^+$ 330.097, $[MH + 1]^+$ 331.100; $C_{20}H_{15}N_3S$; calculated: M = 330.106.

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