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Synthesis of 6*H*-pyrrolo[3′,4′:2,3][1,4]diazepino[6,7,1-*hi*]indole-8,10(7*H*,9*H*)-diones using 3-bromo-4-(indol-1-yl)maleimide scaffold

Sergey A. Lakatosh, Yuri N. Luzikov and Maria N. Preobrazhenskaya *

Gause Institute of New Antibiotics, Russian Academy of Medical Sciences, B. Pirogovskaya 11, Moscow 119021, Russia. E-mail: lcta@space.ru; Fax: 7 095 245 02 95; Tel: 7 095 245 37 53

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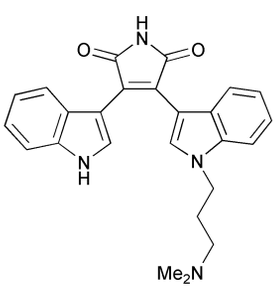
Series of 3-arylalkyl- or 3-alkylamino-4-(indol-1-yl)maleimides and bis(indol-1-yl)maleimides were synthesised. The cyclization of the 3-substituted 4-(indol-1-yl)maleimides under the action of acids resulted in the formation of diazepine[1,4] derivatives with indoline and maleimide nuclei annelated. These compounds readily produced the corresponding indolomaleimidodiazepines[1,4] after dehydrogenation.

Introduction

Interest in bis(indol-3-yl)maleimides and related compounds comes from their valuable biological properties, especially high cytotoxicity and inhibitory activity towards protein kinase C, the key enzyme that transduces a variety of extracellular signals from cell periphery to gene transcription mechanisms.[1] 3-[(3-Dimethylaminopropyl)indol-3-yl]-4-(indol-3-yl)maleimide (**1**), which is a potent inhibitor of protein kinase C represents one of the most investigated compounds of this type.[1] Bis(indol-3-yl)-maleimides are closely related to the derivatives of maleimido-indolo[2,3-*a*]carbazole. Antibiotic rebeccamycin (**2**) and some other compounds of this type (*e.g.* **3**) are of great biological importance due to their inhibitory activities towards topoisomerase I and protein kinase C.[2]



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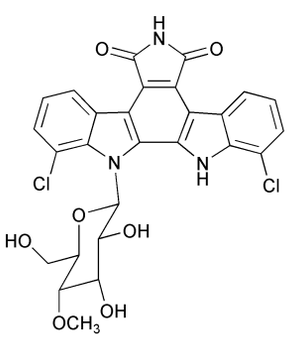

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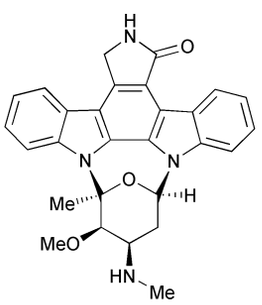

3

Maleimidoindolo[2,3-*a*]carbazoles (**8**) have been obtained from the corresponding bis(indol-3-yl)maleimides (**4**) *via* bis-(indol-3-yl)succinimides (**5**) by cyclization in acidic media with subsequent oxidation.[3] 2,2′-Cyclization of bis(indol-3-yl)maleimide (**4**) under the action of acids was successful in the presence of an oxidant (*e.g.* DDQ) (Scheme 1).[4] Bis(indol-3-yl)-maleimides under the action of TFA formed aminophenyl-carbazoles **7** accompanied by the opening of one of the indole rings.[5]

Although many derivatives of this type have been studied, their bis(indol-1-yl)analogues remain to be investigated. The goal of this work was the synthesis of bis(indol-1-yl)maleimides and 3-arylalkyl- or 3-dialkylamino-4-(indol-1-yl)maleimides and the study of the possibility to obtain from them poly-condensed heterocyclic compounds.

Results and discussion

The initial step of this work was the synthesis of bis(indol-1-yl)maleimides and 3-(indol-1-yl)maleimides substituted at position 4 with arylalkyl-, dialkyl- or alkylamino- moieties. The interaction of 3,4-dibromomaleimides (**9a**–**c**) with indoline in DMF in the presence of Et_3N afforded the corresponding 3-bromo-4-[2,3-dihydroindol-1-yl]maleimides (**10a**–**c**) in 75–80% yields. Only monosubstituted products were obtained; the second bromine atom could not be substituted by various amines or the indole Grignard reagent. The surprisingly low reactivity of the second bromine atom in compounds **10a**–**c** can be explained by masking the electron withdrawing effect of the carbonyl groups by the neighbouring indoline introduced into the maleimide ring. However after the dehydrogenation of the indoline moiety the bromine atom in 3-bromo-4-(indol-1-yl)maleimides (**11a**–**c**) was substituted successfully with indoline or various amines (*N*-ethylaniline, diethylamine, benzylamine) to give compounds **12a**–**e** in 70–80% yields (Scheme 2). 3-(Indol-1-yl)-4-[2,3-dihydroindol-1-yl]maleimides **12a** and **b** were dehydrogenated with the use of DDQ in boiling toluene to give the corresponding bis(indol-1-yl)maleimides (**13a**,**b**) (Scheme 3).

In an attempt to effect the 2,2′-ring closure **13a**,**b** were treated with an excess of TFA in CH_2Cl_2 at rt or in toluene at 90 °C until the full conversion of the starting material was observed by TLC (~2 h). The ^{1}H-NMR spectra of the isolated products (**14a** and **b**) displayed the signals of the indole nucleus substituted at positions 1 and 7 (4 and 9a on Scheme 3) and the indoline nucleus substituted at positions 1 and 2 (15 and 9b on Scheme 3). The significant downfield shift of the C5-H hydrogen signal can be explained by the influence of the neighbouring carbonyl group at C3. In ^{13}C-NMR spectra the signals corresponding to indoline C9b and C10 carbons were identified in the high field area. According to the APT-experiments the C9b atom is bonded with one hydrogen atom, and C10 with two hydrogens. Based on these data we assigned the structures of

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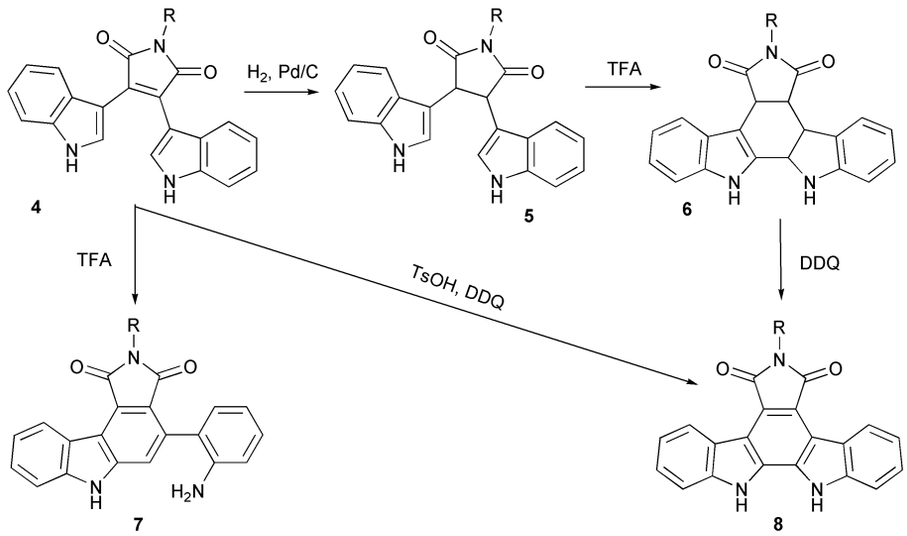
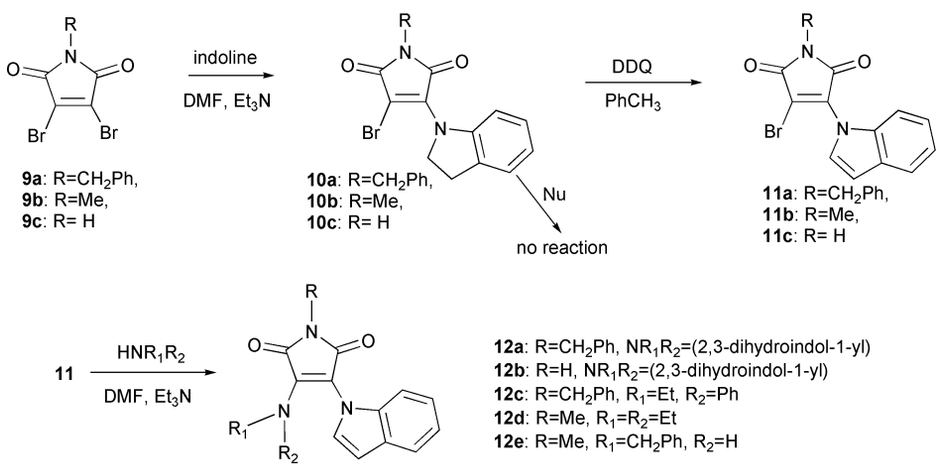
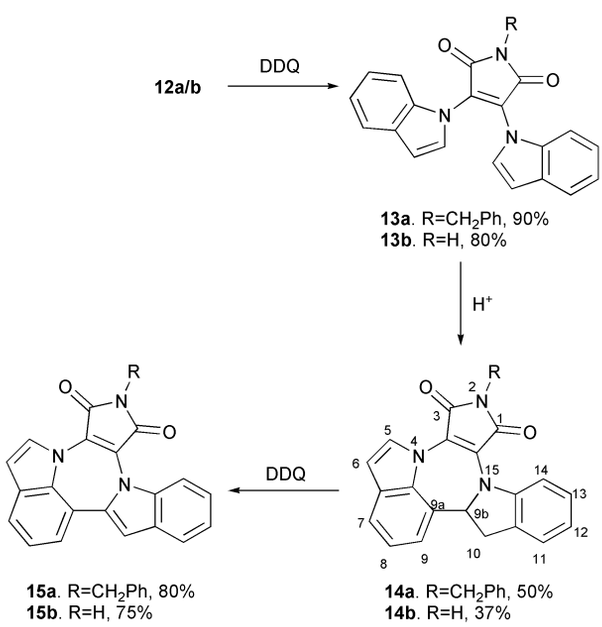


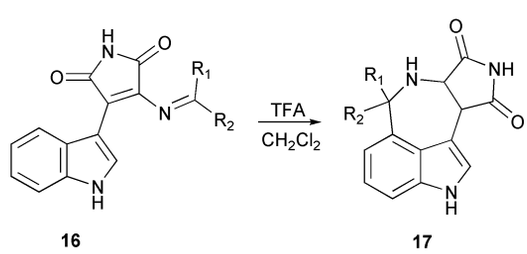
Scheme 1



Scheme 2



Scheme 3

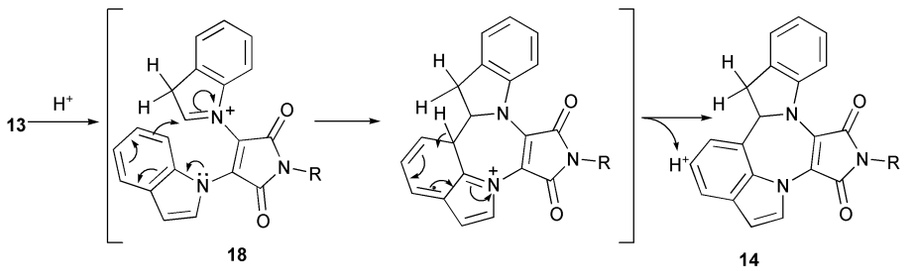


Scheme 4

9b,10-dihydro-2-benzyl-1*H*-indolo[1′,7′:4,5,6]pyrrolo[3′,4′:2,3]-[1,4]diazepino[1,7-*a*]indole-1,3(2*H*)-dione (**14a**) and the corresponding N^2H- derivative (**14b**) to the compounds formed from bisindolylmaleimides **13a** and **b** respectively through the 2–7′ cyclization (Scheme 3). Compounds **14a**,**b** were dehydrogenated with DDQ in boiling toluene to produce 1*H*-indolo-[1′,7′:4,5,6]pyrrolo[3′,4′:2,3][1,4]diazepino[1,7-*a*]indole-1,3-(2*H*)-diones **15a** and **15b**. A significant NOE between C10-H of the 1,2-disubstituted indole nucleus and C9-H of the 1,7-disubstituted indole ring in the NMR spectra of compounds **15a** is strongly indicative of the diazepine[1,4] framework with two indoles and maleimide nuclei annelated (the enhancement of intensity of C9-H was about 20%).

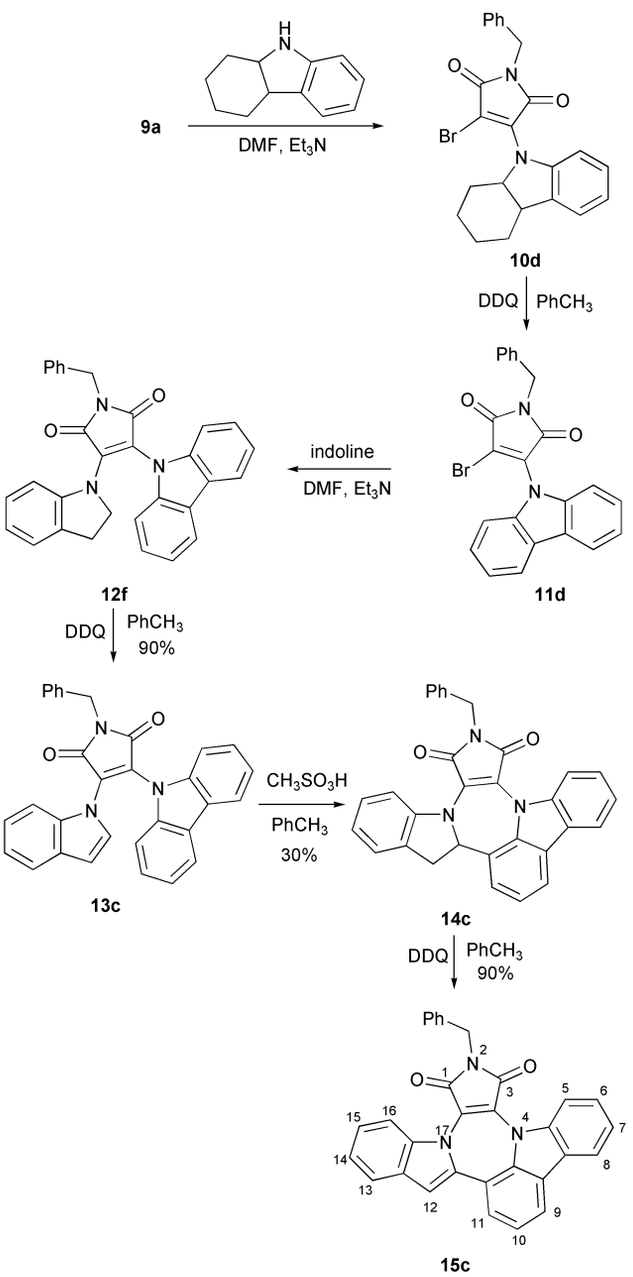
Similar reactivity was described by Mahboobi *et al.*[6] for 3-(indol-3-yl)-4-iminomaleimides **16**, which under the action of TFA in CH_2Cl_2 at −78 °C formed 7-membered azepine cycles with the maleimide and indole nuclei annelated (**17**) (Scheme 4).

We suggest that in acidic media bisindolylmaleimide **13** is protonated at position 3 of one of the indole nuclei. The intermediate **18** then undergoes the intramolecular electrophilic attack of the iminium ion on the position 7 of the non-protonated indole nucleus to give **14** (Scheme 5).



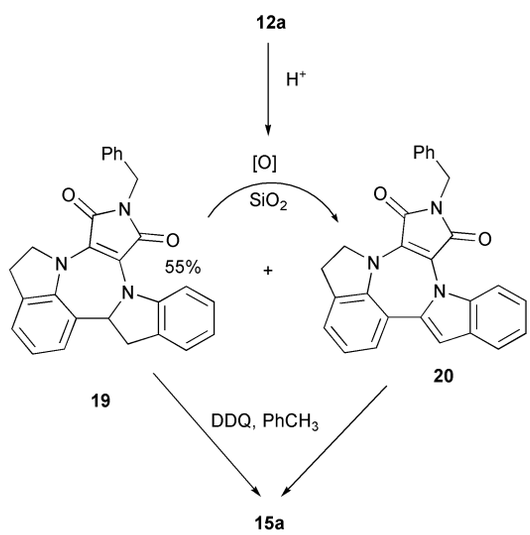
Scheme 5

1-Benzyl-3-(2,3-dihydroindol-1-yl)-4-(carbazol-9-yl)maleimide (**12f**) was obtained from 1-benzyl-3-(1,2,3,4,4a,9a-hexahydrocarbazol-9-yl)-4-bromomaleimide (**10d**) *via* 1-benzyl-3-(carbazol-9-yl)-4-bromomaleimide (**11d**). Dehydrogenation of **12f** afforded 1-benzyl-3-(indol-1-yl)-4-(carbazol-9-yl)maleimide (**13c**). The treatment of the latter with CH_3SO_3H in boiling toluene for 1 h led to the cyclization product **14c** in 30% yield. The indoline moiety of the latter was dehydrogenated to **15c** (Scheme 6). The poor yield and the necessity of relatively harsh cyclization conditions can be due to the steric hindrance.



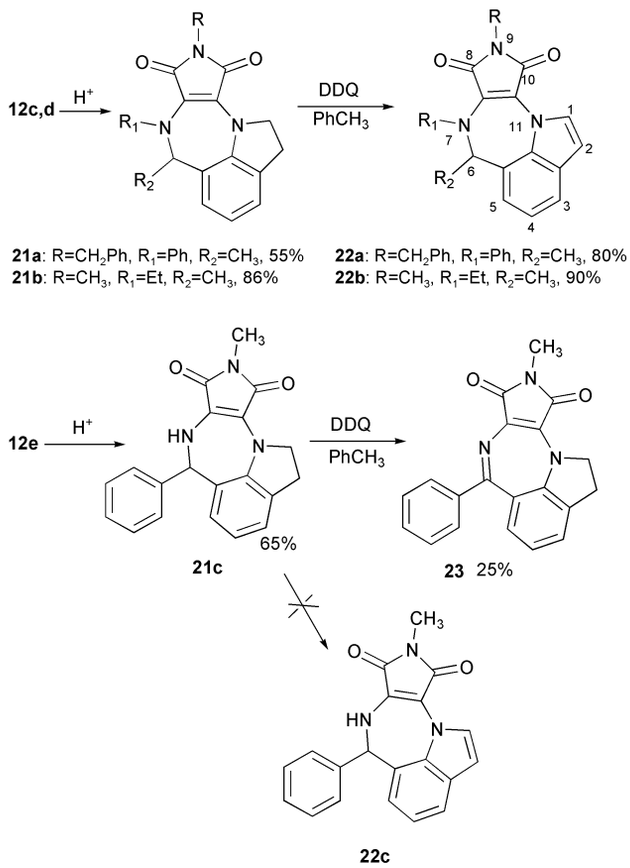
Scheme 6

3-(Indol-1-yl)-4-(2,3-dihydroindol-1-yl)maleimide (**12a**) treated with TFA in CH_2Cl_2 gave maleimido[1,4]diazepine with two indoline nuclei annelated (**19**) in 55% yield. The TLC analysis of the reaction mixture showed the presence of a minor product of the reaction that was identified as **20**. Compound **20**, isomeric to **14a**, was formed presumably by the partial aromatization of diindolinodiazepine **19**. Attempts to separate the products **19** and **20** by column chromatography ($CHCl_3$) led to the full conversion of **19** to **20** (isolated in 45% yield from **12a**), although compound **19** was successfully isolated by the crystallisation from n-heptane. The ^{1}H-NMR spectrum of the product **19** exhibited signals characteristic of 1,7- and 1,2-disubstituted indolines, whereas signals corresponding to 1,7-disubstituted indoline and 1,2-disubstituted indole were present in the spectrum of **20**. Compounds **19** and **20** were smoothly converted into bisindolodiazepine **15a** identical with the compound obtained from **14a** by treatment with DDQ (two or one equivalent respectively) (Scheme 7).



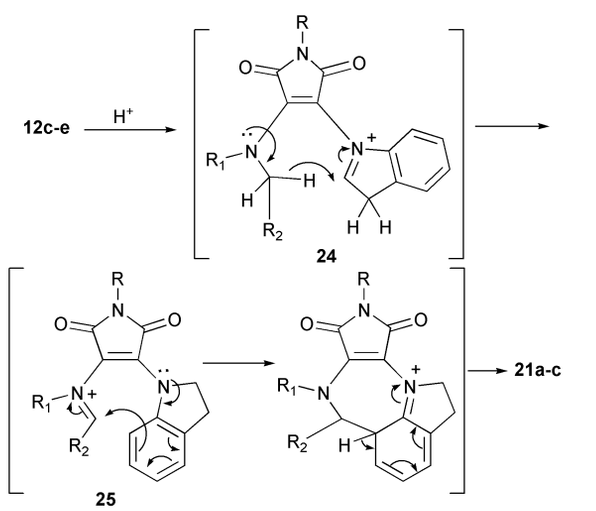
Scheme 7

When treated with TFA in CH_2Cl_2 at rt or in toluene at 90 °C the N-substituted 3-amino-4-(indol-1-yl)maleimides **12c**–**e** produced the corresponding 1,2-dihydro-6*H*-pyrrolo[3′,4′:2,3]-[1,4]diazepino[6,7,1-*hi*]indole-8,10(7*H*,9*H*)-diones **21a**–**c** in good yields (Scheme 8). Indolinodiazepines **21a**,**b**, were converted into the corresponding indolodiazepines **22a**,**b** by treatment with DDQ in boiling toluene. The ^{1}H-NMR spectra of compounds **21a**,**b** exhibit signals characteristic of a 1,7-disubstituted indoline ring and a single hydrogen quartet in the area 4–4.5 ppm (C6-H) coupled with three hydrogen doublet at 1.3–1.5 ppm (C6–CH_3), which is indicative of the diazepine[1,4] structure of the products. The spectra of dehydrogenated compounds **22a**,**b** exhibit signals of the 1,7-disubstituted indole. Contrary to the compounds **21a**,**b**, compound **21c** gave, upon the treatment with DDQ, two products according to TLC. During an attempt to separate them by column chromatography (toluene–acetone) only indolinodiazepine **23** was isolated.



Scheme 8

The structure of compounds **21a–c** suggests the intramolecular electrophilic attack of iminium ion **25** formed by a proton shift from the protonated indolomaleimide **24** to position 7 of the indoline nucleus as a cyclization step (Scheme 9).



Scheme 9

In conclusion a convenient method for the synthesis of 3-arylalkyl- or 3-alkylamino-4-indolo-maleimides or bis(indol-1-yl)-maleimides is developed. These compounds undergo cyclization under the action of acids to form diazepines[1,4] with a common structural motif of 1,2-dihydropyrrolo[3′,4′:2,3]-[1,4]diazepino[6,7,1-*hi*]indole-8,10(7*H*,9*H*)-dione.

Experimental

Mps were determined on a Buchi SMP-20 apparatus and are uncorrected. NMR spectra were recorded with Varian VXR-400 instrument at 400 MHz (^{1}H-NMR) or at 75 MHz (^{13}C-NMR) with internal reference. Chemical shifts are given in ppm and coupling constants in Hz. Assignment of the signals was based on the decoupling experiments for ^{1}H-NMR and APT-experiments for ^{13}C-NMR spectra, signals corresponding to the quaternary carbon atoms are marked (q). Electron impact mass-spectra (EI-MS) were obtained on an SAQ 710 Finnigan instrument at 70 eV (direct introduction, ion source temperature 150 °C). HRMS mass spectra were registered on a MAT 8430 Finnigan instrument with data operating system SS-300 (EI, 70 eV, direct introduction, ion source temperature 250 °C). Analytical TLC was performed on Kieselgel F_{254} plates (Merck) and column chromatography on Silica Gel Merck 60. Elemental analyses were performed in Organic Analysis Laboratory of Nesmeyanov Institute of Elemento-organic Compounds, Moscow, Russia. Extracts were dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. Solvents and reagents were obtained from commercial suppliers. 3,4-Dibromomaleimide[7], 1-methyl- and 1-benzyl-3,4-dibromomaleimide[8] were obtained as previously described.

1-Benzyl-3-bromo-4-(2,3-dihydro-1*H*-indol-1-yl)-1*H*-pyrrole-2,5-dione (10a)

To a stirred solution of 1-benzyl-3,4-dibromomaleimide **9a** (3.4 g, 10 mmol) in DMF (5 mL) were added dropwise indoline (1.8 mL, 15 mmol) and then Et_3N (2.5 mL) and the mixture was stirred at rt overnight and then poured into 1 N HCl (50 mL). The water phase was extracted with EtOAc (2 × 50 mL), extracts were washed with 1 N HCl (3 × 30 mL), aq. $NaHCO_3$ (2 × 20 mL), water and brine, dried and evaporated. The residue was crystallised from EtOH to give **10a** as dark red crystals (4 g, 10.5 mmol, 70%); mp 114–116 °C (EtOH); R_f 0.56 (n-heptane–EtOAc 6:1); (Found C. 59.50; H. 3.99; N 7.38. $C_{19}H_{15}BrN_2O_2$ requires C. 59.55; H. 3.95; N 7.31%); δ_H (d_6-DMSO) 3.12 (2H, t, *J* 7.95), 4.32 (2H, t, *J* 7.95), 4.66 (2H, s, CH_2Ph), 6.99 (1H, t, *J* 7.47), 7.01 (1H, d, *J* 7.7), 7.16 (1H, t, *J* 7.47), 7.26 (1H, t, *J* 7.7), 7.29–7.36 (5H, m, -$CH_2C_6H_6$); δ_C (d_6-DMSO) 28.9, 41.4, 54.0, 89.1 (q), 116.2, 123.1, 124.8, 126.1, 127.4, 127.5, 128.5, 132.9 (q), 136.6 (q), 141.8 (q), 141.9 (q), 165.4 (q), 166.2 (q); *m*/*z* (EI MS) M^+ 382 (100%).

1-Methyl-3-bromo-4-(2,3-dihydro-1*H*-indol-1-yl)-1*H*-pyrrole-2,5-dione (10b)

Obtained similarly from 1-methyl-3,4-dibromomaleimide **9b** as a yellow solid in 78% yield, mp 139–141 °C (decomp.) (EtOH); R_f 0.27 n-heptane–EtOAc, 5:1; (Found C. 50.87; H. 3.68; N 9.19. $C_{13}H_{11}BrN_2O_2$ requires C. 50.84; H. 3.61; N 9.12%); δ_H ($CDCl_3$) 3.08 (3H, s, N-CH_3), 3.18 (2H, t, *J* 8.02, indoline CH_2), 4.38 (2H, t, *J* 8.04, indoline CH_2), 6.98 (1H, d, *J* 8.06), 7.01 (1H, t, *J* 7.46), 7.19 (1H, t, *J* 7.87), 7.23 (1H, d, *J* 7.33); δ_C ($CDCl_3$) 24.5, 29.5, 54.2, 89.8 (q), 116.1, 123.4, 124.8, 126.5, 132.5 (q), 141.4 (q), 142.0 (q), 166.2 (q), 166.7 (q); *m*/*z* (EI MS) M^+ 306 (100%).

3-Bromo-4-(2,3-dihydro-1*H*-indol-1-yl)-1*H*-pyrrole-2,5-dione (10c)

Obtained similarly from 3,4-dibromomaleimide **9c** as dark red crystals in 60% yield, mp 125–127 °C (decomp.) (n-heptane–EtOAc), R_f 0.49 (n-heptane–EtOAc 5:2), δ_H (d_6-acetone) 3.20 (2H, t, *J* 7.95, indoline CH_2), 4.40 (2H, t, *J* 8.02, indoline CH_2), 7.00 (1H, t, *J* 7.36), 7.03 (1H, d, *J* 8.01), 7.18 (1H, t, *J* 7.55), 7.27 (1H, d, *J* 7.36), 9.83 (1H, s, N*H*); δ_C (d_6-acetone) 29.9, 54.8, 92.1 (q), 116.8, 123.7, 125.6, 127.0, 133.7 (q), 143.1 (q), 143.3 (q), 167.1 (q), 167.2 (q); *m*/*z* (EI MS) M^+ 294 (90), 292 (100); $M^+ - Br$ 213 (35); $M^+ - Br - CO$ 185 (20); $M^+ - Br - CONH$ 170 (50); $M^+ - Br - (CO)_2NH$ 142 (30%).

1-Benzyl-3-(1,2,3,4,4a,9a-hexahydro-9*H*-carbazol-9-yl)-4-bromo-1*H*-pyrrole-2,5-dione (10d)

Obtained similarly to **10a** (1,2,3,4,4a,9a-hexahydrocarbazole[9] used instead of indoline) in 80% yield as orange crystals, mp 115–117 °C (n-heptane–EtOAc); R_f 0.53 n-heptane–EtOAc 6:1; δ_H ($CDCl_3$) 1.18–1.28 (4H, m), 1.48–1.56 (2H, m), 1.75–1.83 (1H, m), 2.21 (1H, m), 2.36 (1H, m), 3.50 (1H, m), 4.71 (2H, s, C*H*$_2$Ph), 6.97 (1H, d, *J* 8.59), 7.07 (1H, t, *J* 7.36), 7.17 (1H, d, *J* 7.56), 7.18 (1H, t, *J* 8.42), 7.27–7.29 (1H, m, phenyl, H4), 7.31–7.34 (2H, 2 t, phenyl-H3 and -H5), 7.39–7.42 (2H, 2 d, phenyl, H2 and H6); δ_C ($CDCl_3$) 20.5, 22.3, 24.6, 27.2, 41.7, 42.0, 67.3, 87.2, 118.8, 122.8, 124.0, 125.8, 127.7, 128.6, 136.0, 136.2, 140.8, 141.1, 165.7, 166.5; *m*/*z* (EI MS) M^+ 436 (100%).

1-Benzyl-3-bromo-4-(1*H*-indol-1-yl)-1*H*-pyrrole-2,5-dione (11a)

To a solution of **10a** (380 mg, 1 mmol) in toluene (50 mL) was added DDQ (340 mg, 1.5 mmol). The mixture was refluxed for 6 h, diluted to 100 mL with EtOAc, washed with aq. $NaHSO_3$ (2 × 30 mL), Na_2CO_3 solution (3 × 30 ml) water, brine, dried and evaporated. The residue was purified by flash chromatography (n-heptane ⟶ n-heptane–EtOAc, 6:1) to give **11a** as a yellow solid (360 mg, 0.95 mmol, 95%), mp 122–123 °C (*n*-heptane–acetone), R_f 0.41 (*n*-heptane–EtOAc, 7:1); δ_H (d_6-acetone) 4.85 (2H, s, C*H*$_2$Ph), 6.86 (1H, dd, J_{32} 3.49, J_{34} 0.89, H3), 7.25 (1H, t, *J* 7.71) 7.30 (1H, t, *J* 8.28) 7.33–7.39 (3H, m), 7.45 (2H, d, *J* 8.4), 7.53, 1H, dd, J_{45} 8.12, J_{43} 0.9, H4), 7.61 (1H, d, J_{23} 3.48, H2), 7.68 (1H, d, J_{76} 7.51, H7) δ_C (d_6-acetone) 43.0, 107.9, 112.0 (q), 114.8, 121.9, 122.9, 123.6, 128.5, 128.7, 128.8, 129.4, 130.5 (q), 135.6 (q), 137.2 (q), 139.8 (q), 165.6 (q), 166.3 (q); *m*/*z* (EI MS) M^+ 380 (100%).

1-Methyl-3-bromo-4-(1*H*-indol-1-yl)-1*H*-pyrrole-2,5-dione (11b)

Obtained from **10b** similarly to **11a** as a yellow solid, mp 121–123 °C (n-heptane–EtOAc); R_f 0.3 (n-heptane–EtOAc, 5:1); δ_H (d_6-DMSO) 3.07 (3H, s, N-C*H*$_3$), 6.85 (1H, d, *J* 3.48, H3), 7.22 (1H, t, *J* 7.71), 7.28 (1H, t, *J* 7.55), 7.47 (1H, d, *J* 8.01), 7.53 (1H, d, *J* 3.47, H2), 7.66 (1H, t, *J* 7.93); δ_C (d_6-DMSO) 24.6, 106.6, 111.9 (q), 113.7, 120.9, 121.7, 122.6, 128.0, 128.9 (q), 134.1 (q), 138.5 (q), 165.1 (q), 165.6 (q); *m*/*z* (EI MS) M^+ 304 (100%).

3-Bromo-4-(1*H*-indol-1-yl)-1*H*-pyrrole-2,5-dione (11c)

Obtained from **10c** similarly to **11a** in 85% yield as a yellow solid, mp 197–199 °C (n-heptane–EtOAc); R_f 0.39 (n-heptane–EtOAc 3:1); δ_H (d_6-DMSO) 6.83 (1H, d, *J* 3.48, H3), 7.21 (1H, t, *J* 7.16, H5 or H6), 7.27 (1H, t, *J* 7.23, H5 or H6), 7.46 (1H, d, *J* 7.88, H4), 7.55 (1H, d, *J* 3.49, H2), 7.66 (1H, d, *J* 7.76, H7) 11.66 (1H, s, N-*H*); δ_C (d_6-DMSO) 106.4, 112.9 (q), 113.8, 121.0, 121.8, 122.6, 128.2, 129.0 (q), 134.3 (q), 138.8 (q), 165.8 (q), 166.7 (q); *m*/*z* (EI MS) M^+ 290 (100%).

1-Benzyl-3-bromo-4-(9*H*-carbazol-9-yl)-1*H*-pyrrole-2,5-dione (11d)

Obtained similarly to **11a** (3.6 eq. of DDQ were used) in 90% yield as a yellow solid, mp 175–177 °C (n-heptane–EtOAc), R_f 0.36 (n-heptane–EtOAc, 7:1); δ_H (d_6-DMSO) 4.8 (2H, s, C*H*$_2$Ph), 7.32 (1H, t, *J* 7.68, phenyl H4), 7.37 (2H, t, *J* 7.64, carbazole H2 and H7), 7.39 (2H, d, *J* 7.51, phenyl H2 and H6), 7.43 (2H, t, *J* 7.54, phenyl H3 and H5), 7.49 (2H, t, *J* 7.61, carbazole H3 and H6), 7.57 (2H, d, *J* 8.24, carbazole H4 and H5), 8.23 (2H, d, *J* 7.69, carbazole H1 and H8); δ_C (d_6-DMSO) 42.1, 112.9, 120.4 (q), 120.5, 121.7, 123.9 (q), 126.3, 127.5, 128.6, 136.2 (q), 137.7 (q), 138.1, 164.7 (q), 165.6 (q); *m*/*z* (EI MS) M^+ 430 (100%).

1-Benzyl-3-(indol-1-yl)-4-(2,3-dihydroindol-1-yl)-1*H*-pyrrole-2,5-dione (12a)

To the stirred solution of **11a** (1.14 g, 3 mmol) in DMF (10 ml) were added indoline (550 mg, 4.5 mmol) and TEA (0.6 ml). The reaction mixture was stirred at 90 °C while monitoring by TLC. Upon the full conversion of **11a** the solution was poured into 1 N HCl (50 mL). The resulting mixture was extracted with EtOAc (2 × 50 mL), extracts were washed with 1 N HCl (2 × 30 mL), aq. $NaHCO_3$ (2 × 20 mL), water and brine, dried and evaporated. Residue was crystallised from n-heptane–EtOAc to give **12a** (870 mg, 2.1 mmol, 69%) as yellow crystals, mp 133–135 °C (n-heptane–EtOAc); R_f 0.27 (n-heptane–EtOAc, 7:1); (Found C. 77.36; H. 5.01; N. 10.06. $C_{27}H_{21}N_3O_2$ requires C. 77.31; H. 5.05; N. 10.02%); δ_H (d_6-acetone) signals assigned to indoline nucleus: 3.18 (2H, t, *J* 8.06), 4.40 (2H, t, *J* 8.05), 6.09 (1H, d, *J* 8.06, H4), 6.49 (1H, t, *J* 7.00, H5), 6.66 (1H, t, *J* 7.42, H6), 7.05 (1H, d, *J* 7.36, H7), signals assigned to indole nucleus: 6.62 (1H, d, *J* 3.35, H3), 6.95 (1H, t, *J* 7.10, H6), 7.00 (1H, t, *J* 7.00, H5), 7.20 (1H, d, *J* 7.69, H4), 7.39 (1H, d, *J* 3.32, H2), 7.46 (1H, d, *J* 7.01, H7); benzyl: 4.78 (2H, s, C*H*$_2$Ph), 7.31 (1H, t, *J* 7.14, Ph, H4), 7.38 (2H, t, *J* 7.55, Ph, H3 and H5), 7.45 (2H, d, *J* 7.51, Ph, H2 and H6); δ_C (d_6-acetone) 29.9 (-CH_2*C*H_2N-), 42.0 (-*C*H_2CH$_2$N-), 53.8 (*C*H$_2$Ph), 105.2, 109.1 (q), 111.9, 113.1, 121.2, 121.3, 122.9, 123.5, 125.1, 127.0, 128.3, 128.9, 129.0 (q), 129.3, 129.4, 133.1 (q), 133.4 (q), 138.0 (q), 138.1 (q), 143.7 (q), 167.2 (q), 168.1 (q); *m*/*z* (EI MS) M^+ 419 (100%);

3-(Indol-1-yl)-4-(2,3-dihydroindol-1-yl)-1*H*-pyrrole-2,5-dione (12b)

Obtained from **11c** similarly to **12a** in 67% yield as a red solid, mp 174–176 °C (EtOH) (d); R_f 0.1 (n-heptane–EtOAc, 6:1); (Found C. 72.99; H. 4.66; N. 12.69. $C_{20}H_{15}N_3O_2$ requires 72.94; H. 4.59; N. 12.76%); δ_H (d_6-DMSO) 3.04 (2H, t, *J* 8.05, indoline -C*H*$_2$-), 4.20 (2H, t, *J* 8.05, indoline -C*H*$_2$-), 6.05 (1H, d, *J* 8.06), 6.46 (1H, d, *J* 7.57), 6.58 (1H, d, *J* 3.24, indole C3–*H*), 6.61 (1H, t, *J* 7.32), 6.93 (1H, t, *J* 7.57), 6.98 (1H, t, *J* 7.81), 7.01 (1H, d, *J* 7.21), 7.16 (1H, d, *J* 7.81), 7.37 (1H, d, *J* 3.41, indole C2-*H*), 7.45 (1H, d, *J* 7.57), δ_C (d_6-DMSO) 28.8, 52.4, 103.9, 108.6 (q), 110.9, 111.8, 120.1, 120.2, 121.9, 122.2, 124.2, 125.9, 127.4 (q), 128.7, 131.8 (q), 132.9 (q), 136.5 (q), 142.5 (q), 167.3 (q), 168.4 (q); *m*/*z* (EI MS) M^+ 329 (100%).

1-Benzyl-3-(*N*-ethylanilino)-4-(indol-1-yl)-1*H*-pyrrole-2,5-dione (12c)

Obtained from **11a** and *N*-ethylaniline similarly to **12a** in 85% yield as yellow crystals, mp 112–114 °C (n-heptane–EtOAc); (Found C. 76.95; H. 5.50; N. 9.98. $C_{27}H_{23}N_3O_2$ requires C. 76.94; H. 5.50; N. 9.97%); R_f 0.42 (n-heptane-EtOAc 6:1); δ_H ($CDCl_3$) 1.16 (3H, t, *J* 7.1, NCH$_2$C*H*$_3$), 4.00 (2H, q, *J* 7.09, NC*H*$_2$CH$_3$), 4.75 (2H, s, C*H*$_2$Ph), 6.33 (1H, d, *J* 3.29, indole H3), 6.76–6.79 (2H, m), 6.80–6.85 (4H, m) includes 6.81 (1H, d, *J* 3.34, assigned to indole H2), 7.00 (1H, t, *J* 6.86), 7.01 (1H, d, *J* 7.65), 7.10 (1H, t, *J* 6.86), 7.32–7.39 (4H, m), 7.45 (2H, d, *J* 6.92); δ_C ($CDCl_3$) 14.1, 41.5, 47.3, 104.0, 104.1, 106.4 (q), 110.7, 120.1, 120.5, 121.9, 122.9, 125.4, 127.7, 127.9, 128.2 (q), 128.6, 128.7, 136.3 (q), 136.4 (q), 137.2 (q), 141.2 (q), 165.8 (q), 167.2 (q); *m*/*z* (EI MS) M^+ 421 (100%).

1-Methyl-3-(*N*-diethylamino)-4-(1*H*-indol-1-yl)-1*H*-pyrrole-2,5-dione (12d)

Obtained from **11b** and diethylamine similarly to **12a** in 90% yield as yellow crystals, mp 88–90 °C (EtOH); R_f 0.19 (n-heptane–EtOAc 6:1); (Found C. 68.67; H. 6.44; N. 14.19. $C_{17}H_{19}N_3O_2$ requires C. 68.67; H. 6.44; N. 14.13%); δ_H (d_6-acetone) 1.02 (6H, t, *J* 7.08, N-CH$_2$C*H*$_3$), 2.05 (4H, m, N-C*H*$_2$CH$_3$), 2.99 (3H, s, N-C*H*$_3$), 6.60 (1H, d, *J* 3.23, H3), 7.08 (1H, t, *J* 6.92), 7.12 (1H, t, *J* 7.03), 7.24 (1H, d, *J* 3.22, H2), 7.27 (1H, d, *J* 7.21), 7.59 (1H, d, *J* 7.81); δ_C (d_6-acetone) 5.25, 14.7, 37.0,

94.8, 102.5, 111.9, 112.6, 113.9, 120.2 (q), 122.6, 122.7 (q), 130.9 (q), 133.7 (q), 157.6 (q), 159.9 (q); *m/z* (EI MS) M^+ 297 (100%).

1-Methyl-3-(benzylamino)-4-(indol-1-yl)-1*H*-pyrrole-2,5-dione (12e)

Obtained from **11b** and benzylamine similarly to **12a** in 87% yield as yellow crystals, mp 124–125 °C (EtOH); (Found C. 72.52; H. 5.16; N. 12.63. $C_{20}H_{17}N_3O_2$ requires C. 72.49; H. 5.17; N. 12.68%); R_f 0.24 (n-heptane–EtOAc, 3:1); δ_H (d_6-acetone) 2.98 (3H, s, -CH_3), 4.15 (2H, br d, -NHCH_2Ph), 6.56 (1H, dd, J_{32} 3.23, J_{34} 0.87, indole H3), 6.83–6.87 (2H, m), 7.06–7.16 (6H, m), 7.24 (1H, d, *J* 8.05), 7.44 (1H, br, N*H*), 7.59 (1H, d, *J* 7.51); δ_C (d_6-acetone) 14.8, 38.1, 94.8, 102.5, 111.9, 112.4, 113.9, 118.9, 119.1, 120.0, 120.1 (q), 122.4, 129.4 (q), 130.9 (q), 133.5 (q), 157.7 (q), 160.9 (q); *m/z* (EI) M^+ 331 (100%).

1-Benzyl-3-(2,3-dihydro-1*H*-indol-1-yl)-4-(9*H*-carbazol-9-yl)-1*H*-pyrrole-2,5-dione (12f)

Obtained from **11d** and indoline similarly to **12a** in 77% yield as an orange solid, mp 177–179 °C (n-heptane–EtOAc); R_f 0.24 (n-heptane–EtOAc 7:1); (Found C. 79.33; H. 4.97; N. 8.97. $C_{31}H_{23}N_3O_2$ requires C. 79.30; H. 4.94; N. 8.95%); δ_H (d_6-DMSO) indoline: 3.02 (2H, t, *J* 7.82), 4.23 (2H, t, *J* 7.82), 6.09 (1H, d, *J* 7.77, H4), 6.25 (1H, t, *J* 7.77, H5), 6.57 (1H, t, *J* 7.36, H6), 6.97 (1H, d, *J* 7.34, H7), carbazole: 7.19 (2H, t, *J* 7.54, H2 and H7), 7.36 (2H, d, *J* 7.66, H4 and H5), 7.45 (2H, t, *J* 7.65, H3 and H6), 8.06 (2H, d, *J* 7.61, H1 and H8), benzyl: 4.78 (2H, s, CH_2Ph), 7.32 (1H, t, *J* 6.95, Ph, H4), 7.37–7.44 (4H, m); δ_C (d_6-DMSO) 28.0, 41.0, 53.1, 104.2, 110.9, 113.1, 120.2, 120.4, 122.8 (q), 123.0, 124.4, 125.7, 126.1, 127.4, 127.5, 128.6, 132.6 (q), 136.4 (q), 137.0 (q), 140.0 (q), 141.9 (q), 165.8 (q), 167.2 (q); *m/z* (EI) M^+ 469 (100%).

1-Benzyl-3,4-bis(1*H*-indol-1-yl)-1*H*-pyrrole-2,5-dione (13a)

Obtained by the dehydrogenation of **12a** in the conditions described for **11a** in 91% yield as a red solid, R_f 0.51 (n-heptane–EtOAc 5:1); *m/z* (EI HRMS) M^+ 417,1484 ($C_{27}H_{19}N_3O_2$ requires 417,1477) (100), δ_H (d_6-acetone) 4.90 (2H, s, CH_2Ph), 6.61 (2H, d, J_{45} 8.38, H4), 6.72 (2H, t, *J* 7.85, H5), 6.79 (2H, d, J_{32} 3.5, H3), 6.93 (2H, t, *J* 7.5, H6), 7.31–7.41 (3H, m, *Ph*), 7.47–7.52 (4H, m, indole H7 and *Ph*), 7.71 (2H, d, J_{23} 3.51, H2); δ_C (d_6-acetone) 42.5, 107.9, 111.9, 121.6, 122.5 (4C), 123.5, 123.8, 128.5, 129.0, 129.4, 129.8, 136.4, 137.5, 167.3; *m/z* (EI MS) M^+ 417 (100), (M^+ − CH_2Ph) 326 (20%).

3,4-Bis(1*H*-indol-1-yl)-1*H*-pyrrole-2,5-dione (13b)

Obtained by the dehydrogenation of **12b** in the conditions described for **11a** in 90% yield as an orange solid, mp 147–148 °C (n-heptane–EtOAc), R_f 0.12 (n-heptane–EtOAc 6:1), (Found C. 73.42; H. 3.96; N. 12.81. $C_{20}H_{13}N_3O_2$ requires C. 73.38; H. 4.00; N. 12.84%); δ_H (d_6-DMSO) 6.59 (2H, d, *J* 7.69, H4), 6.71 (2H, t, *J* 7.75, H5), 6.77 (2H, d, *J* 3.46, H3), 6.91 (2H, t, *J* 7.44, H6), 7.46 (2H, d, *J* 7.73, H7), 7.65 (2H, d, *J* 3.46, H2), 11.61 (1H, s, N*H*); δ_C (d_6-DMSO) 106.6, 110.8, 120.7, 121.5, 122.5, 123.4, 128.3, 135.1, 167.6; *m/z* (EI MS) M^+ 327 (100%).

1-Benzyl-3-(1*H*-indol-1-yl)-4-(9*H*-carbazol-9-yl)-1*H*-pyrrole-2,5-dione (13c)

Obtained by dehydrogenation of **12f** in the conditions described for **11a** in 91% yield as an orange solid, mp 205–206 °C (n-heptane–EtOAc), R_f 0.3 (n-heptane–EtOAc 6:1); (Found C. 79.64; H. 4.53; N. 9.05. $C_{31}H_{21}N_3O_2$ requires 79.64; H. 4.53; N. 8.99%); δ_H (d_6-DMSO) 4.90 (2H, s, CH_2Ph), 6.49 (2H, d, *J* 3.66), 6.78 (1H, d, *J* 3.49, indole H3), 6.85 (1H, m), 7.22 (2H, t, *J* 7.33), 7.28 (2H, t, *J* 8.24), 7.34 (1H, t, *J* 7.32), 7.38–7.45 (5H, m), 7.54 (2H, d, *J* 7.18), 7.48 (1H, d, *J* 3.49, indole H2), 8.09 (2H, d, *J* 8.09); δ_C (d_6-DMSO) 41.6, 107.2, 111.2, 111.5, 120.0 (q), 120.2, 120.8, 121.5, 121.7, 122.4, 123.7, 126.2 (q), 127.5, 127.7, 128.0, 128.6, 128.7 (q), 128.8 (q), 134.6 (q), 136.4 (q), 138.5, 166.1 (q), 166.4 (q); *m/z* (EI MS) M^+ 467 (100%).

2-Benzyl-9b,10-dihydro-1*H*-indolo[1′,7′:4,5,6]pyrrolo[3′,4′:2,3]-[1,4]diazepino[1,7-*a*]indole-1,3(2*H*)-dione (14a)

To the stirred solution of **13a** (100 mg, 0.24 mmol) in CH_2Cl_2 (20 mL) was added TFA (2 mL) and the reaction mixture was left to stir at rt for 2 h, then it was poured into the mixture of EtOAc (50 mL) and saturated $NaHCO_3$ solution (50 mL). The organic layer was separated and washed with saturated $NaHCO_3$ solution (2 × 50 mL), water (30 mL) and brine, dried and evaporated. The product was isolated by flash chromatography (n-heptane ⟶ *n*-heptane–acetone, 10:1) as a violet solid (56 mg, 56%), R_f 0.53 ($PhCH_3$), *m/z* (EI HRMS) M^+ 417.1469 ($C_{27}H_{19}N_3O_2$ requires 417.1477) (100), M^+ − $PhCH_2N(CO)_2$ 256 (10%); δ_H (d_6-DMSO) signals assigned to indoline ring: 3.74–3.89 (2H, m, C10-H), 5.35 (1H, dd, J_{9b-10} 4.48, J_{9b-10} 9.66, C9b-H), 6.83 (1H, t, *J* 7.33, C12-H or C13-H), 6.87 (1H, d, *J* 7.86, C11-H), 7.04 (1H, t, *J* 7.69, C12-H or C13-H),7.21 (1H, d, *J* 7.65, C14-H); signals assigned to indole ring: 6.85 (1H, d, *J* 3.62, C6-H), 7.18 (1H, t, *J* 7.70, C8-H), 7.26–7.40 (6H, m, 5H benzyl hydrogens and C7-H), 7.66 (1H, d, *J* 7.73, C9-H), 8.45 (1H, d, *J* 3.62, C5-H); 4.73 (2H, s, CH_2Ph); δ_C (d_6-DMSO) 31.3, 40.8, 63.2, 106.2, 111.8, 119.8, 120.1 (q), 120.7, 121.1, 123.4 (q), 124.6, 125.6, 126.9, 127.4 (2C, quaternary and tertiary), 128.1 (q), 128.2, 128.6, 130.0 (q), 134.0 (q), 136.8 (q), 143.5 (q), 164.4 (q), 165.6 (q).

9b,10-Dihydro-1*H*-indolo[1′,7′:4,5,6]pyrrolo[3′,4′:2,3][1,4]-diazepino[1,7-*a*]indole-1,3(2*H*)-dione (14b)

Obtained from **13b** similarly to **14a** as a red solid, R_f 0.19 (n-heptane–EtOAc 3:1), *m/z* (EI HRMS) M^+ 327.1021 ($C_{20}H_{13}N_3O_2$ requires 327.1008); δ_H (d_6-DMSO) signals assigned to indoline nucleus: 3.75 (1H, dd, J_{10-9b} 9.61, J_{gem} 16.7, C10-H), 3.85 (1H, dd, J_{10-9b} 4.33, J_{gem} 16.8, C10-H), 5.30 (1H, dd, J_{9b-10} 9.59, J_{9b-10} 4.33, C9b-H), 6.81 (1H, t, *J* 7.24), 6.86 (1H, d, *J* 8.05), 7.03 (1H, t, *J* 7.73), 7.26 (1H, d, *J* 7.25); signals assigned to indole nucleus: 6.83 (1H, d, *J* 3.5, C6-H), 7.19 (1H, t, *J* 7.65, C8-H), 7.32 (1H, d, *J* 7.65, C7-H), 7.65 (1H, d, *J* 7.65, C9-H), 8.43 (1H, d, *J* 3.5, C5-H), 10.96 (1H, s, N*H*); δ_C (d_6-DMSO) 31.3, 63.1, 106.0, 111.6, 119.7, 120.5, 120.6, 121.1, 121.3, 123.9, 124.6, 125.6, 126.9, 127.4, 128.0, 130.0, 134.0, 143.6, 165.5, 166.8.

2-Benzyl-11b,12-dihydro-1*H*-indolo[1′,2′:4,5]pyrrolo[3′,4′:2,3]-[1,4]diazepino[6,7,1-*jk*]carbazole-1,3(2*H*)-dione (14c)

To a refluxing solution of **13c** (200 mg, 0.43 mmol) in toluene (30 mL) was added CH_3SO_3H (0.2 mL) the reaction mixture was refluxed for 1 h diluted with EtOAc to 100 mL and washed with aq. $NaHCO_3$ (2 × 50 mL), water (50 mL), brine, dried and evaporated. The residue was subjected to flash chromatography (n-heptane ⟶ n-heptane–acetone 10:1) to give **14c** in 30% yield as a red solid, mp 149–150 °C (n-heptane–acetone); R_f 0.26 (n-heptane–EtOAc, 6:1); (Found: C, 79.71; H, 4.55; N, 9.04. $C_{31}H_{21}N_3O_2$ requires C, 79.64; H, 4.53; N, 8.99%) δ_H (d_6-DMSO) signals assigned to indoline nucleus: 3.43 (1H, dd, J_{12-11b} 9.29, J_{gem} 16.52, C12-H), 4.15 (1H, dd, J_{12-11b} 9.78, J_{gem} 16.51, C12-H), 5.65 (1H, t, J_{11b-12} 9.23, C11b-H), 6.82 (1H, t, *J* 7.32, C15-H), 7.00 (1H, d, *J* 7.87, C13-H), 7.07 (1H, t, *J* 6.64, C14-H), 7.20 (1H, d, *J* 7.28, C16-H); carbazole and phenyl moieties: 7.29 (1H, t, *J* 7.28), 7.34–7.49 (9H, m), 7.88 (1H, d, *J* 8.42), 8.20 (2H, d, *J* 7.5); δ_C (d_6-DMSO) 36.3 (C12), 40.7 (*C*H_2Ph), 64.1 (C11b), 112.6, 115.2, 119.5, 119.8, 120.7, 121.7, 122.3, 123.4 (q), 124.3, 124.4 (q), 124.7, 124.9 (q), 125.8, 126.7, 127.3, 127.37 (2C), 127.44 (q), 127.5, 128.3 (q), 128.5 (2C), 128.8 (q), 135.0 (q), 136.8 (q), 137.3 (q), 144.0 (q), 164.0 (q), 164.2 (q); *m/z* (EI MS) M^+ 467 (100%).

2-Benzyl-1*H*-indolo[1′,7′:4,5,6]pyrrolo[3′,4′:2,3][1,4]diazepino-[1,7-*a*]indole-1,3(2*H*)-dione (15a) A

To the solution of **14a** (100 mg, 0.24 mmol) in toluene (10 mL) was added DDQ (65 mg, 0.28 mmol). The reaction mixture was refluxed for 1 h, diluted with EtOAc to 70 mL and washed with $NaHSO_3$ solution (2 × 20 mL), $NaHCO_3$ solution (3 × 20 mL), water and brine. The product was purified by flash chromatography (n-heptane ⟶ n-heptane–acetone 10:1) to give **15a** as a red crystalline solid (80mg, 80%), mp 193–194 °C (n-heptane–acetone); R_f 0.37 (n-heptane–EtOAc 6:1); (Found: C, 77.79; H, 4.11; N, 9.98. $C_{27}H_{17}N_3O_2$ requires C, 78.06; H, 4.12; N, 10.11%); δ_H (d_6-DMSO) 70 °C 4.75 (2H, s, C*H*$_2$Ph), 6.79 (1H, d, *J* 3.66, C6-H), 7.10 (1H, t, *J* 7.10, C12-H or C13-H), 7.15 (1H, t, *J* 7.14, C12-H or C13-H), 7.21 (1H, s, C10-H), 7.22 (1H, t, *J* 7.73, C8-H), 7.34–7.42 (5H, m, Ph), 7.48–7.52 (3H, m, C11-H, C14-H and C7-H), 7.77 (1H, d, *J* 7.68, C9-H), 8.21 (1H, d, *J* 3.66, C5-H); δ_C (d_6-DMSO) 41.0, 107.6, 107.7, 114.6, 116.8 (q), 116.9 (q), 120.0, 120.6, 120.8, 121.9, 122.9, 123.0, 125.0 (q), 127.0, 127.1, 128.1, 129.8 (q), 130.1 (q), 135.0 (q), 135.9 (q), 136.0 (q), 137.2, 163.7 (q), 163.9 (q); *m*/*z* (EI MS) M^+ 415 (100), $M^+ - CH_2Ph$ 324 (22), $M^+ - PhCH_2N(CO)_2$ 254 (10%). **B**. A sample of **19** (50 mg, 0.12 mmol) was dehydrogenated with 2.2 eq. of DDQ in boiling toluene to give **15a** (40 mg, 80%) identical with the sample of **15a** obtained by the method **A**. A sample of **20** (50 mg, 0.12 mmol) was dehydrogenated with 1.1 eq. of DDQ in boiling toluene to give **15a** (45 mg, 90%) identical with the sample of **15a** obtained by the method **A**.

1*H*-Indolo[1′,7′:4,5,6]pyrrolo[3′,4′:2,3][1,4]diazepino[1,7-*a*]-indole-1,3(2*H*)-dione (15b)

Obtained from **14b** similarly to **15a** as a red solid in 75% yield, mp 135 °C (decomp.) (EtOAc); R_f 0.3 (n-heptane–EtOAc, 3:1); *m*/*z* (EI HRMS) M^+ 325.0859 ($C_{20}H_{11}N_3O_2$ requires 325.0851); $M^+ - HN(CO)_2$ 254; δ_H (d_6-DMSO) 6.79 (1H, d, *J* 3.58, C6-H), 7.09 (1H, t, *J* 7.14, C12-H or C13-H), 7.14 (1H, t, *J* 7.14, C12-H or C13-H), 7.18 (1H, s, C10-H), 7.19 (1H, t, *J* 7.75, C8-H), 7.47–7.50 (3H, m, C11-H, C14-H and C7-H), 7.74 (1H, d, *J* 7.75, C9-H), 8.16 (1H, d, *J* 3.58, C5-H), 11.31 (1H, s, N*H*); δ_C (d_6-DMSO) 107.7, 110.0, 115.2, 117.0, 117.6, 120.3, 120.9, 121.1, 122.2, 123.2, 123.3, 125.4, 126.5, 129.9, 130.3, 135.2, 136.1, 137.3, 165.1, 165.5.

2-Benzyl-1*H*-indolo[1′,2′:4,5]pyrrolo[3′,4′:2,3][1,4]diazepino-[6,7,1-*jk*]carbazole-1,3(2*H*)-dione (15c)

Obtained by the dehydrogenation of **14c** similarly to **15a** in 90% yield as a red solid, mp 138–140 °C (n-heptane–EtOAc); R_f 0.41 (n-heptane–EtOAc 6:1), *m*/*z* (EI HRMS) M^+ 465.1462 ($C_{31}H_{19}N_3O_2$ requires 465.1477), $M^+ - CH_2Ph$ 374, $M^+ - CH_2PhN(CO)_2$ 256; δ_H (d_6-DMSO) 4.69 (2H, s, C*H*$_2$Ph), 7.14 (1H, t, *J* 7.18, carbazole H3 or H6), 7.18 (1H, s, C12-H), 7.21 (1H, t, *J* 7.46, C7-H or C10-H), 7.28 (1H, t, *J* 7.33, C15-H), 7.32–7.37 (3H, m), 7.38–7.42 (3H, m), 7.45 (1H, t, *J* 7.14, C14-H), 7.55 (2H, d, *J* 8.23, C8-H and C9-H), 7.92 (1H, d, *J* 8.20, C13-H), 7.96 (1H, d, *J* 7.83, C11-H), 8.04 (1H, d, 7.65, C5-H), 8.11 (1H, d, *J* 7.77, C16-H); δ_C (d_6-DMSO) 41.1, 109.3, 114.7, 117.4, 117.6 (q), 119.85, 119.87, 120.5, 121.6 (q), 122.2, 123.2, 123.3, 123.8, 124.4, 124.9 (q), 125.8, 126.2, 127.3, 127.5, 128.3 (q), 128.4, 129.6 (q), 136.1 (q), 136.5 (q), 137.2 (q), 137.8 (q), 141.5 (q), 163.0 (q), 164.0 (q).

2-Benzyl-5,6,9b,10-tetrahydro-1*H*-indolo[1′,7′:4,5,6]pyrrolo-[3′,4′:2,3][1,4]diazepino[1,7-*a*]indole-1,3(2*H*)-dione (19)

The solution of **12a** (200 mg, 0.48 mmol) in CH_2Cl_2 (10 mL) was treated with 1 ml of TFA, the resulting dark violet mixture was allowed to stir at rt for 2 h. The reaction mixture was diluted with EtOAc (100 mL) and washed with sat. aq. $NaHCO_3$ (2 × 30 mL), water (50 mL) and brine (50 mL), dried and evaporated. The residue was refluxed in *n*-heptane for 30 min the mixture was then hot filtered and filtrate cooled to −15 °C, the precipitate was filtered off, washed with n-heptane and dried *in vacuo* to give **19** as a dark violet solid (110 mg, 55%), *m*/*z* (EI HRMS) M^+ 419.1642 ($C_{27}H_{21}N_3O_2$ requires 419.1633), $M^+ - H_2$ 417, $M^+ - H_2 - CH_2Ph$ 326; R_f 0.40 (n-heptane–EtOAc 5:1); mp 75–77 °C (n-heptane), δ_H (d_6-DMSO) 3.01–3.19 (2H, m, C6-*H*), 3.48 (1H, dd, *J* 9.53, J_{ab} 16.35, C10-H_a), 3.68 (1H, dd, *J* 3.17, J_{ba} 16.36, C10-H_b), 4.30 (1H, m, C5-H_a), 4.53–4.60 (1H, m, C5-H_b), 4.62 (2H, s, -C*H*$_2$Ph), 4.94 (1H, dd, *J* 9.52, *J* 3.17, C9b-*H*), 6.51 (1H, d, *J* 7.81), 6.65 (1H, t, *J* 7.33, C12–*H* or C13-*H*), 6.85 (1H, t, *J* 7.57, C8-*H*), 6.96 (1H, t, *J* 7.35, C12-*H* or C13-*H*), 7.16 (1H, d, *J* 7.13), 7.17 (1H, d, *J* 7.19), 7.24 (1H, d, *J* 7.88), 7.26–7.38 (5H, m, -CH_2-C_6H_6); δ_C (d_6-DMSO) 27.4, 31.0, 40.2, 50.2, 62.9, 109.0, 112.8 (q), 118.3, 121.0, 124.0, 124.2, 124.6, 126.6, 126.87 (q), 126.9, 126.95, 127.0, 128.0 (q), 128.1, 128.6 (q), 132.8 (q), 136.9 (q), 143.1 (q), 145.0 (q), 164.4 (q), 165.4 (q).

2-Benzyl-5,6-dihydro-1*H*-indolo[1′,7′:4,5,6]pyrrolo[3′,4′:2,3]-[1,4]diazepino[1,7-*a*]indole-1,3(2*H*)-dione (20)

Obtained in the attempt to isolate **19** from the reaction mixture by column chromatography (eluent $CHCl_3$). Full conversion of **19** into **20** was observed and the product **20** was obtained by the evaporation of the corresponding fractions in 45% yield from **12a** as a violet solid, mp 160–163 °C (n-heptane–$CHCl_3$); R_f 0.48 (n-heptane–EtOAc 5:1); EI HRMS M^+ 417.1467 ($C_{27}H_{19}N_3O_2$ requires 417.1477), $M^+ - CH_2Ph$ 326, $M^+ - CH_2PhN(CO)_2$ 256; δ_H (d_6-DMSO) 3.06 (2H, t, *J* 8.54, C6-H), 4.35 (2H, t, *J* 8.54, C5-H), 4.67 (2H, s, C*H*$_2$Ph), indole nucleus: 6.89 (1H, s, H3, C10-H), 6.92 (1H, t, *J* 7.54, C8-H), 7.01 (1H, t, *J* 7.28, C13-H), 7.07 (1H, t, *J* 8.34, C12-H), 7.09 (1H, d, *J* 7.65, C7-H), 7.21 (1H, d, *J* 8.28, C11-H), 7.33–7.39 (5H, m, phenyl hydrogens), 7.44 (1H, d, *J* 7.61, C14-H), 7.58 (1H, d, *J* 8.2, C9-H); δ_C (d_6-DMSO) 27.5, 40.6, 48.8, 108.9, 110.4 (q), 114.0, 116.8 (q), 120.2, 121.2, 123.0, 123.8, 125.0, 126.3, 127.2, 127.3, 128.5, 129.6 (q), 132.9 (q), 135.0 (q), 135.7 (q), 136.6 (q), 136.9 (q), 144.3 (q), 163.9 (q), 164.5 (q).

1,2-Dihydro-6-methyl-7-phenyl-9-benzyl-6*H*-pyrrolo[3′,4′:2,3]-[1,4]diazepino[6,7,1-*hi*]indole-8,10(7*H*,9*H*)-dione (21a)

To a solution of 1-benzyl-3-(ethylanilino)-4-(indol-1-yl)male-imide **12c** (200 mg, 0.47 mmol) in CH_2Cl_2 (20 mL) TFA (2 mL) was added, the reaction mixture was stirred at the ambient temperature for 2 h, then it was diluted with EtOAc (100 mL) and washed with sat. aq. $NaHCO_3$ (2 × 30 mL), water (50 mL) and brine (50 mL). The dry residue was purified by flash chromatography (n-heptane ⟶ n-heptane–acetone, 10:1) to give **21a** as dark red crystals (110 mg, 55%), mp 138–140 °C (cyclohexane); R_f 0.24 (n-heptane–EtOAc 6:1); (Found C, 76.94; H, 5.51; N, 9.91. $C_{27}H_{23}N_3O_2$ requires C, 76.94; H, 5.5; N, 9.97%); δ_H (d_6-DMSO) 1.42 (3H, d, *J* 6.77, -C*H*$_3$), 3.05–3.19 (2H, m, C2-H), 4.35 (1H, m, C1-H_a), 4.55 (1H, m, C1-H_b), 4.67 (2H, s, C*H*$_2$Ph), 5.31 (1H, m, C6-H), 6.73 (1H, t, *J* 7.32), 6.81 (1H, t, *J* 7.37), 6.92 (2H, d, *J* 8.37), 7.12 (2H, t, *J* 6.91), 7.14–7.18 (2H, m), 7.27–7.32 (3H, m, -CH_2*Ph*), 7.35–7.41 (2H, m, -CH_2*Ph*); δ_C (d_6-DMSO) 20.3, 25.7, 38.4, 48.3, 55.1, 108.9 (q), 114.2, 117.3, 120.1, 122.2, 125.0, 125.2, 125.5, 126.5, 126.9, 129.8 (q), 131.3 (q), 134.0 (q), 135.2 (q), 139.8 (q), 145.8 (q), 163.2 (q), 164.7 (q); δ_H ($CDCl_3$) 1.46 (3H, d, *J* 6.96, -C*H*$_3$), 2.96–3.14 (2H, m, C2-H), 4.35 (1H, m, C1-H_a), 4.43 (1H, m, C1-H_b), 4.62 (2H, d, *J* 5.67, -C*H*$_2$Ph), 4.97 (1H, m, C6-H), 6.69 (1H, t, *J* 7.5, C4-H), 6.74 (1H, t, *J* 7.32, N–Phenyl, C4-H), 6.82 (2H, d, *J* 7.83, phenyl C2-H and C6-H), 6.86 (1H, d, *J* 7.37, C3-H), 6.96 (1H, d, *J* 7.36, C5-H), 7.10 (2H, two triplets, N-Phenyl C3-H and C5-H), 7.18–7.22 (1H, m, -CH_2*Ph*,C4-H), 7.24–7.28 (2H, m, -CH_2*Ph*), 7.29–7.33 (2H, m, -CH_2*Ph*); δ_C ($CDCl_3$) 22.9, 28.2, 41.2, 50.5, 59.4, 112.8 (q), 117.2, 120.5, 122.0, 124.2, 127.5, 128.2, 128.4, 128.5, 128.8, 131.8 (q), 132.9 (q), 134.1 (q), 136.8

(q), 142.3 (q), 147.7 (q), 165.9 (q), 167.0 (q); *m*/*z* (EI MS) M^+ 421 (100%).

7-Ethyl-1,2-dihydro-6,9-dimethyl-6*H*-pyrrolo[3′,4′:2,3][1,4]-diazepino[6,7,1-*hi*]indole-8,10(7*H*,9*H*)-dione (21b)

Obtained from 1-methyl-3-(diethylamino)-4-(indol-1-yl)maleimide **12d** similarly to **21a** in 86% yield as violet crystals, mp 80–82 °C (cyclohexane); R_f 0.41 (n-heptane–EtOAc 3:1); (Found C, 68.71; H, 6.45; N, 14.16. $C_{17}H_{19}N_3O_2$ requires C, 68.67; H, 6.44; N, 14.13%); δ_H (d_6-DMSO) 1.02 (3H, t, *J* 7.03, N-CH_2CH_3), 1.23 (3H, d, *J* 6.96, C6-CH_3), 2.95 (2H, m, N-CH_2CH_3), 3.13 (2H, m, C2-H), 4.05 (1H, m, C1-H_a), 4.36 (2H, m, C1-H_b), 6.74 (1H, t, *J* 7.42, C4-H), 7.02 (1H, d, *J* 7.51, C3-H or C5-H), 7.09 (1H, d, *J* 7.38, C3-H or C5-H); δ_C (d_6-DMSO) 14.0, 22.8, 23.2, 27.6, 49.6, 50.3, 59.1, 118.2 (q), 120.8, 123.9, 127.1, 129.2 (q), 132.2 (q), 132.3 (q), 143.4 (q), 166.5 (q), 167.9 (q); *m*/*z* (EI MS) M^+ 297 (100%).

1,2-Dihydro-9-methyl-6-phenyl-6*H*-pyrrolo[3′,4′:2,3][1,4]-diazepino[6,7,1-*hi*]indole-8,10(7*H*,9*H*)-dione (21c)

Obtained from 1-methyl-3-(benzylamino)-4-(indol-1-yl)maleimide **12e** similarly to **21a** in 65% yield as dark violet crystals mp 168–170 °C (n-heptane–acetone); R_f 0.27 (n-heptane–EtOAc, 6:1); (Found C, 72.46; H, 5.17; N, 12.68. $C_{20}H_{17}N_3O_2$ requires C, 72.49; H, 5.17; N, 12.68%); δ_H ($CDCl_3$) 2.95 (3H, s, N-CH_3), 3.21 (2H, t, *J* 8.49, C2-H), 4.41 (1H, m, C1-H_a), 4.55 (1H, m, C1-H_b), 4.77 (1H, br s, N*H*), 5.35 (1H, s, C6-H), 6.70 (1H, t, *J* 7.57, C4-H), 6.77 (1H, d, *J* 7.76, C3-H), 7.09 (1H, d, *J* 7.29, C5-H), 7.13–7.16 (2H, m), 7.25–7.34 (3H, m); δ_C ($CDCl_3$) 23.5, 28.3, 50.1, 64.2, 116.8 (q), 119.9, 120.5 (q), 124.2, 125.0 (q), 127.2, 127.6, 129.0, 129.2, 132.1 (q), 142.9 (q), 144.1 (q), 167.96 (q), 167.99 (q); *m*/*z* (EI MS) M^+ 331 (100%).

6-Methyl-7-phenyl-9-benzyl-6*H*-pyrrolo[3′,4′:2,3][1,4]-diazepino[6,7,1-*hi*]indole-8,10(7*H*,9*H*)-dione (22a)

Obtained by dehydrogenation of **21a** with 1.2 eq. of DDQ similarly to **15a** as red crystals in 80% yield, mp 153–154 °C (n-heptane–acetone); R_f 0.4 (n-heptane–EtOAc, 6:1); (Found C, 77.24; H, 5.05; N, 9.97. $C_{27}H_{21}N_3O_2$ requires C, 77.31; H, 5.05; N, 10.02%); δ_H (d_6-DMSO) 1.56 (3H, d, *J* 6.97, CH-CH_3), 4.68 (2H, s, -CH_2Ph), 5.52 (1H, q, *J* 6.96, C6-H), 6.83 (1H, d, *J* 3.48, C2-H), 6.95 (1H, t, *J* 7.32, ~N-Ph H4), 7.07 (1H, t, *J* 7.33, C4-H), 7.13–7.16 (3H, m), 7.24 (2H, t, *J* 7.36, ~N-Ph H3 and H5), 7.29–7.38 (5H, m, CH_2-C_6H_6), 7.57 (1H, d, *J* 7.73, C5-H), 8.46 (1H, d, *J* 3.49, C1-H); δ_C (d_6-DMSO) 23.5, 40.8, 60.3, 106.4, 119.8, 120.5, 121.5, 121.8, 122.3, 122.9 (q), 123.8 (q), 125.2, 127.1, 127.3, 128.6, 129.0, 130.1 (q), 130.5 (q), 133.6 (q), 136.7 (q), 146.2 (q), 165.5 (q), 165.8 (q); *m*/*z* (EI MS) M^+ 419 (100%).

7-Ethyl-6,9-dimethyl-6*H*-pyrrolo[3′,4′:2,3][1,4]diazepino[6,7,1-*hi*]indole-8,10(7*H*,9*H*)-dione (22b)

Obtained similarly to **15a** by dehydrogenation of **21b** as red crystals in 90% yield, mp 99–100 °C (n-hexane); R_f 0.38 (n-heptane–EtOAc 6:1); (Found C, 69.18; H, 5.84; N, 14.21. $C_{17}H_{17}N_3O_2$ requires C, 69.14; H, 5.8; N, 14.23%); δ_H (d_6-DMSO) 1.17 (3H, t, *J* 7.03, N-CH_2CH_3), 1.33 (3H, d, *J* 6.83, N-$CHCH_3$), 2.98 (3H, s, N-CH_3), 3.54 (1H, m, *J* 7.05, N-CH_2CH_3), 3.87 (1H, m, *J* 7.05, N-CH_2CH_3), 4.62 (1H, d, *J* 6.83, C6-H), 6.69 (1H, d, *J* 3.45, C2-H), 7.01 (1H, t, *J* 7.43, C4-H), 7.08 (1H, d, *J* 6.84, C3-H), 7.51 (1H, d, *J* 7.76, C5-H), 8.48, 1H, d, *J* 3.43, C1-H); δ_C (d_6-DMSO) 14.3, 23.26, 23.31, 47.1, 60.2, 104.5, 111.3 (q), 119.9, 120.2, 120.3, 124.9, 128.5 (q), 129.2 (q), 130.0 (q), 133.4 (q), 166.2 (q), 164.4 (q); *m*/*z* (EI MS) M^+ 295 (100%).

1,2-Dihydro-9-methyl-6-phenyl-8*H*-pyrrolo[3′,4′:2,3][1,4]-diazepino[6,7,1-*hi*]indole-8,10(9*H*)-dione (23)

Compound **21c** was subjected to dehydrogenation with 1.1 eq. of DDQ in the conditions described for the synthesis of **15a**. The reaction mixture obtained exhibited the presence of two products with R_f 0.21 and 0.41 (n-heptane–EtOAc, 3:1). We suggested by analogy with the compounds **22a**,**b** that the product with R_f 0.41 has the structure of **22c**. During the attempt to separate them by column chromatography only the product with the R_f of 0.21 was isolated in 25% yield (from **12e**) as dark blue crystals, mp 235–237 °C (toluene–acetone); (Found C, 72.82; H, 4.53; N, 12.61. $C_{20}H_{15}N_3O_2$ requires C, 72.94; H, 4.59; N, 12.76%); δ_H (d_6-DMSO) 2.80 (3H, s, N-CH_3), 2.81 (2H, t, *J* 8.38, C2-H), 3.97 (2H, t, *J* 8.18, C1-H), 6.15 (1H, dd, *J* 7.69, J_{meta} 0.98, C3-H), 6.64 (1H, t, *J* 7.57, C4-H), 7.04 (1H, dd, *J* 7.48, J_{meta} 0.97, C5-H), 7.32–7.44 (5H, m, phenyl); δ_C (d_6-DMSO) 22.8, 26.7, 46.8, 124.6, 125.4, 127.4, 128.0, 129.1, 130.0, 132.6, 133.4, 137.3, 139.6, 152.4, 163.8, 166.8, 176.6; *m*/*z* (EI MS) M^+ 329 (100%).

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