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Tetrahedron 61 (2005) 8241–8248

Synthesis of 4-substituted 3-(indol-3-yl)maleimides and azepines with annelated indole and maleimide nuclei

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Received 30 January 2005; revised 31 May 2005; accepted 9 June 2005

Abstract—A series of 4-substituted 3-(indole-3-yl)maleimides has been synthesized. Upon the action of CH_3SO_3H in TFA, the 3-(indole-3-yl)-4-(arylalkylamino)-maleimides undergo cyclization to give 12b,13-dihydro-4b*H*-indolo[3,2-*d*]pyrrolo[3,4-*b*][1]benzazepine-5,7(6*H*, 8*H*)-dione derivatives.

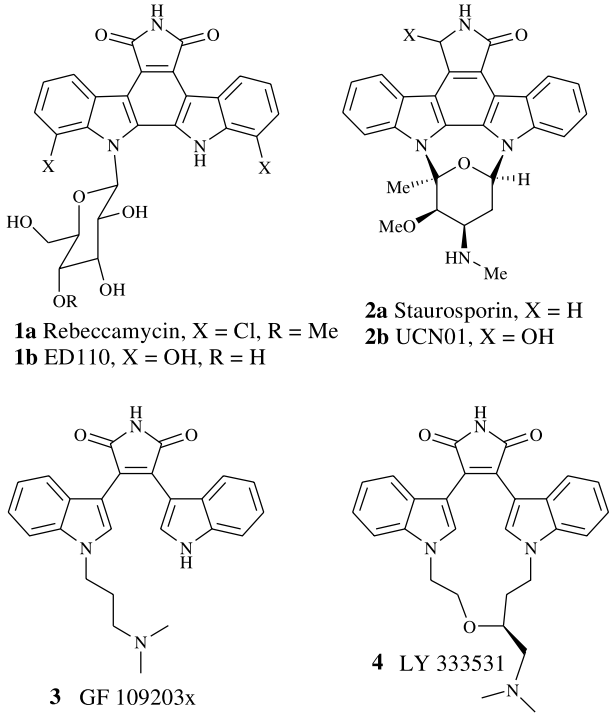
1. Introduction

Bisindolylmaleimide derivatives, their analogues, and related polycondensed compounds are known to have valuable biological properties. Some of them are inhibitors of topoisomerase I (e.g., rebeccamycin **1a** and ED110 **1b**) and the enzymes of proteinkinase C family (staurosporin **2a**, UCN01 **2b**, and some bis(indol-3-yl)maleimides, for example, **3** and **4**) as well as other types of protein kinases[1] (Scheme 1).

Under the action of protic acids, bis(indol-3-yl)maleimides **5** undergo 2,2′-cyclization accompanied by the opening of one of the indole rings to form aminophenylcarbazoles **7**.[2] However, in the presence of an oxidant (e.g., DDQ) they are transformed into indolo[2,3-*a*]pyrrolo[3,4-*c*]carbazol-5,7-diones **8**.[3] Previously, we showed that bis(indol-1-yl)maleimides **9** and 3-dialkyl-(3-arylalkyl-)amino-4-(indol-1-yl)maleimides **11** under the action of protic acids form diazepine[1,4] derivatives **10** and **12** (Scheme 2).[4]

The transformation of **11** into **12** proceeds with a hydride shift followed by an intramolecular electrophilic substitution reaction (Scheme 3).[5]

In this work, the synthesis of 4-substituted 3-(indole-3-yl) maleimides and new polycondensed heterocyclic systems derived from them are described.



Scheme 1.

2. Results and discussion

1-Methyl-3-bromo-4-(indol-3-yl)maleimide and its *N*-Boc-derivative were obtained as previously described.[6] However, the bromine atoms in these bromomaleimides were inert to nucleophilic substitution by primary or secondary amines in contrast to the easy substitution of bromine atoms

Keywords: Indoles; Bisindolylmaleimides; Cyclization.
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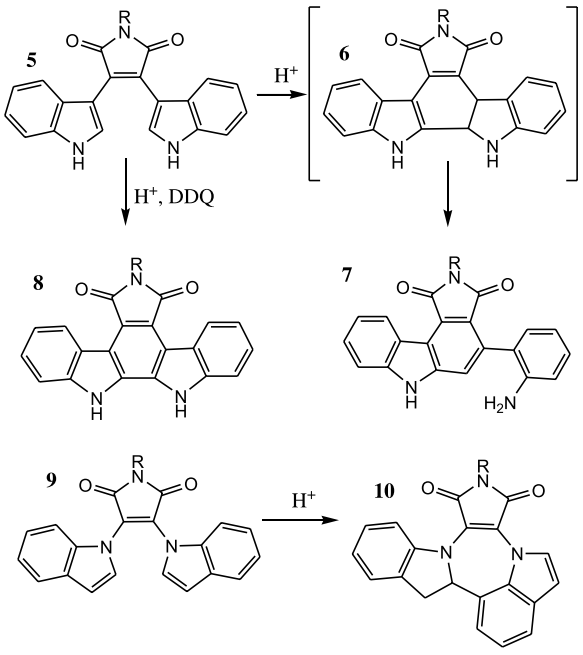
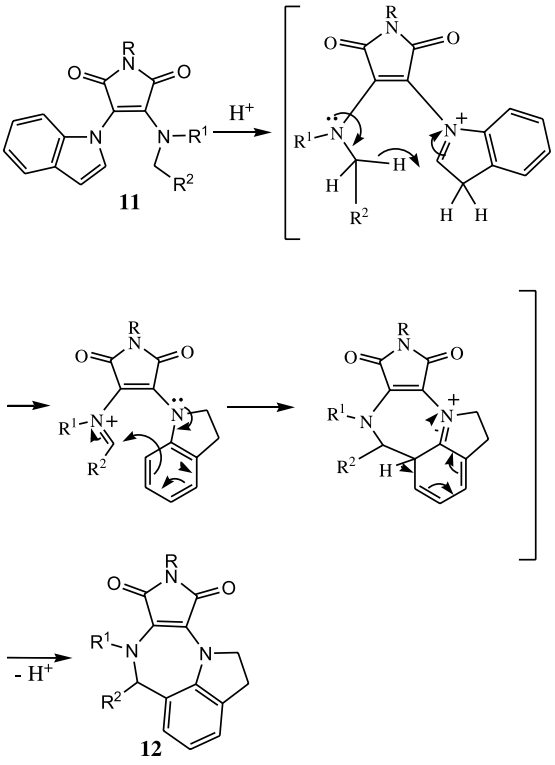
0040–4020/$ - see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2005.06.027



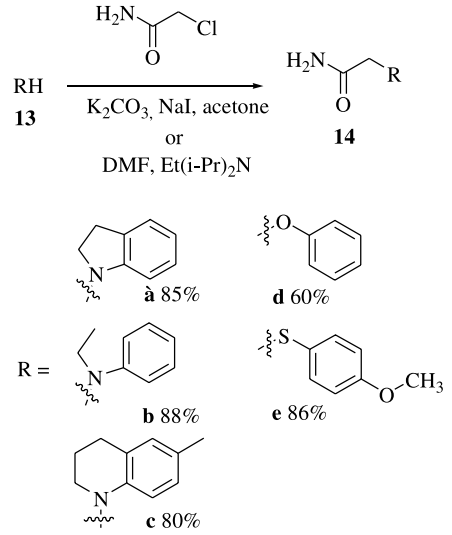
Scheme 2.

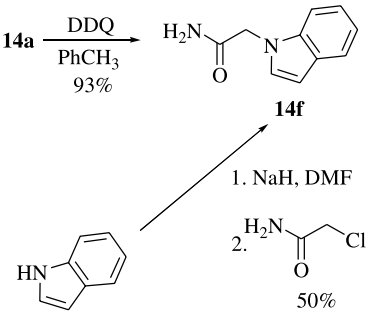


Scheme 3.

by primary or secondary amines in 3-bromo-4-(indol-1-yl)maleimides.[4] Another known method for the synthesis of bis(aryl)maleimides is based on condensation of methyl arylglyoxylates with acetamides using KO^{t}Bu.[7]

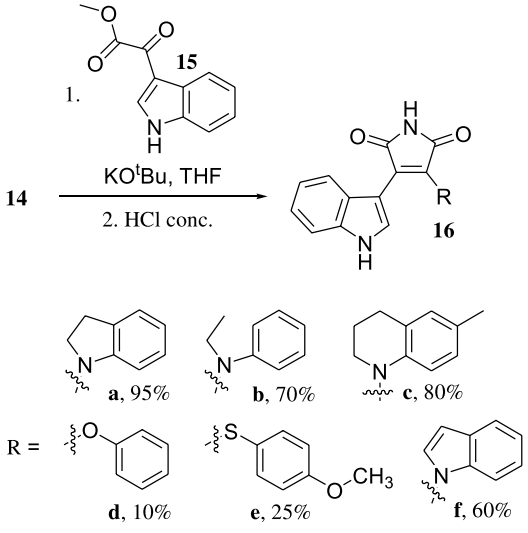
2-Substituted acetamides **14** were obtained in a good yield from the corresponding amines **13a–c**, phenol **13d** and 4-methoxythiophenole **13e** and 2-chloroacetamide in acetone in the presence of anhydrous K_2CO_3 or in DMF in the presence of Hünig's base (Scheme 4). Indol-1-ylacetamide **14f** was prepared by dehydrogenation of **14a** with DDQ in boiling toluene. It was also prepared in lower yield by alkylation of indolyl sodium with 2-chloroacetamide.



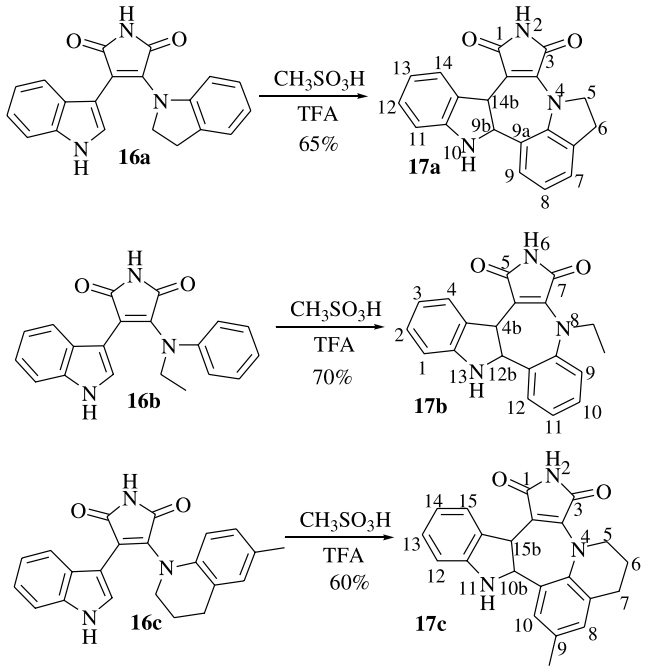


Scheme 4.

Compounds **14a–f** were condensed with methyl indole-3-glyoxylate **15** to give the corresponding 4-substituted 3-(indol-3-yl)maleimides **16** (Scheme 5).



Scheme 5.



Scheme 6.

Maleimides **16a–c** were treated with TFA in CH_2Cl_2. Although the color of the reaction mixture changed from red to dark violet, starting materials were recovered after stirring for 2 h followed by neutralization of the acid by aq $NaHCO_3$. These compounds were also stable in neat TFA. However, after treatment with the mixture of TFA/CH_3SO_3H (5:1) for ~2 h the cyclization products **17a–c** were isolated and purified by crystallization or column chromatography. The analysis of the NMR spectra of **17a–c** indicated that intramolecular electrophilic substitution occurred to form azepine derivatives with indoline and maleimide nuclei annelated (Scheme 6). In the ^1H NMR spectra of cyclization products **17a–c** two 1H signals coupled with each other were present corresponding to the hydrogens at the positions 2 and 3 of 2,3-disubstituted indoline subfragment. One of them was coupled with 1H doublet, in the area δ 5–6 ppm, corresponding to the indoline NH hydrogen. The signals corresponding to four hydrogens at the positions 4–7 of 2,3-disubstituted indoline subfragment (two doublets and two triplets) and one hydrogen singlet of NH imide hydrogen were present in the low field area of the spectrum. It differs from the earlier described[4] cyclization of 3-dialkyl-(3-arylalkyl-)amino-4-(indol-1-yl)maleimides **11** (Scheme 3), proceeding with hydride shift and transfer of electrophilic center from indole nucleus to alkylamino moiety. In the case of 3-aryl-alkylamino-4-(indol-3-yl)maleimides **16a–c**, the hydride shift was not observed.

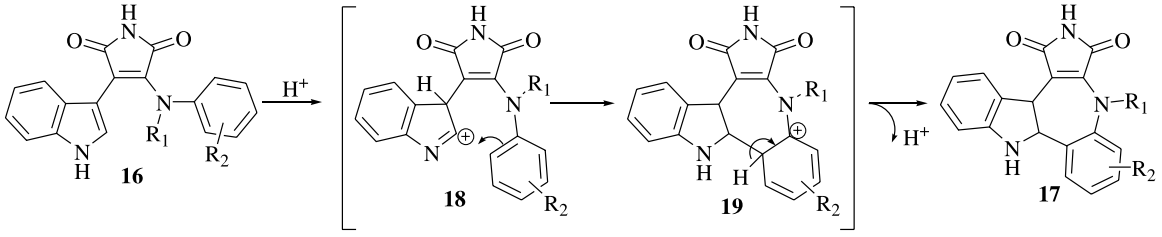
The mechanism of this transformation apparently consists of the following steps: (1) protonation of the indole nucleus to form the iminium electrophilic center at position-2 (**18**) and (2) attack of the electrophile on the position adjacent (*ortho*) to the alkylamino substituent in the benzene ring leading to the formation of azepine ring (**19**) (Scheme 7).

We failed to obtain a product of the cyclization of 3-(indol-3-yl)-4-phenoxymaleimide **16d** upon the action of CH_3SO_3H in TFA. 3-(Indol-3-yl)-4-(4-methoxythiophenyl)maleimide **16e** under the same conditions gave a complex mixture.

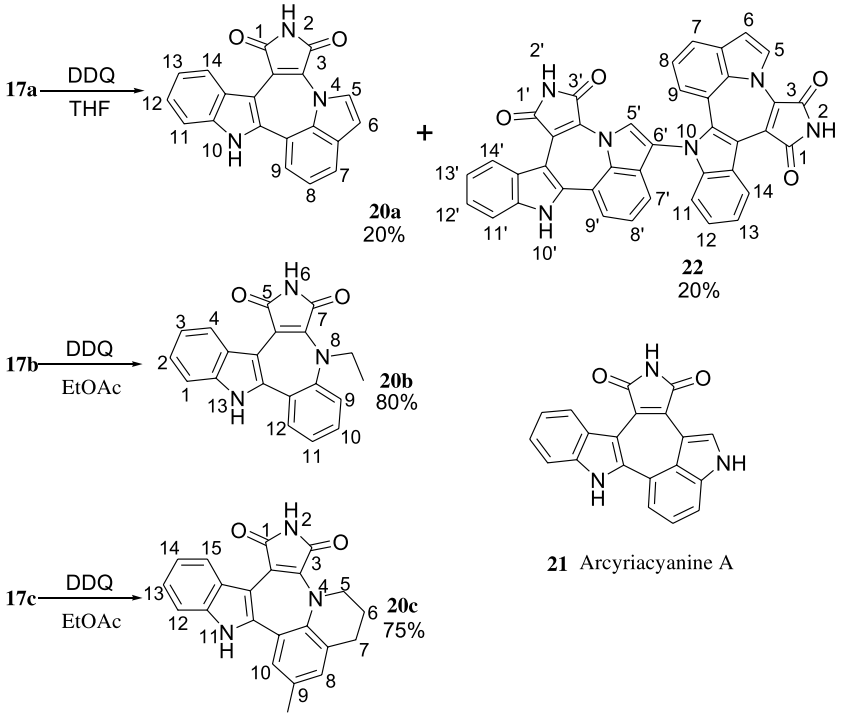
Dehydrogenation of **17a** with an excess of DDQ in THF led to the corresponding aromatic derivative **20a** in 20% yield, isomeric to the natural antibiotic arcyriacyanine A **21**.[2] From the reaction mixture, the dimer **22** of **20a** was also isolated in 20% yield (Scheme 8). When 2 equiv of DDQ were used, a mixture of starting **17a**, and the reaction products **20a** and **22** was formed. In the ^1H NMR spectrum of **22** two broad singlets corresponding to two imide hydrogens (N2–H and N2′–H) at δ 11.2 and δ 11.14 and only one singlet corresponding to the indole NH hydrogen (N10′–H) at δ 11.7 were present. Also present were one singlet signal for C5′–H δ 8.06 and two doublet signals coupled with each other corresponding to C5–H and C6–H. The signals corresponding to the hydrogens of the benzene moieties of four indole subfragments (four doublets and four triplets of C11–H, C12–H, C13–H, C14–H, and C11′–H, C12′–H, C13′–H, C14′–H, as well as four doublets and two triplets of C7–H, C8–H, C9–H, and C7′–H, C8′–H, C9′–H) were seen. The structure of the dimer **22** was supported by HRMS and EI MS data. The dehydrogenation of **17a** by Pd/C in boiling toluene proceeded slowly, however, the dimer **22** was not formed. It suggests that the dimerization was induced by the presence of dichlorodicyanohydroquinone formed from DDQ in the process of the reaction. The dehydrogenation of indoline derivatives **17b**,**c** with 1 equiv of DDQ in EtOAc gave the corresponding indoloazepines **20b**,**c** in good yield (Scheme 8).

Bisindolylmaleimide **16f** was obtained by the dehydrogenation of **16a** with DDQ in 80% yield or by condensation of methyl (indol-3-yl)glyoxylate **15** with acetamide **14f** in 60% yield.

Upon the action of the excess of CH_3SO_3H in TFA, bisindolylmaleimide **16f** afforded 8b,9-dihydroindolo[4′,3′:3,4,5]pyrrolo[3′,4′:6,7]azepino[1,2-*a*]indol-



Scheme 7.



Scheme 8.

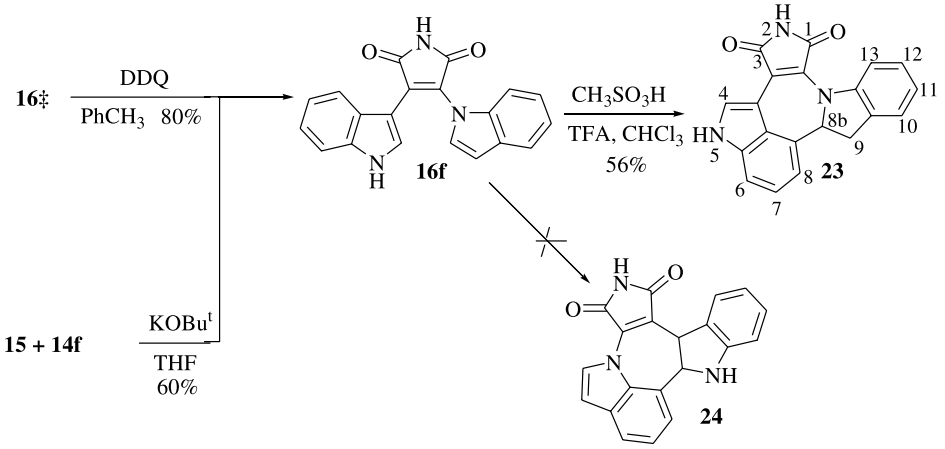
1,3(2*H*,5*H*)dione **23** in 56% yield. In the ^{1}H NMR-spectrum of **23**, the signals corresponding to the hydrogen atoms of 3,4-disubstituted indole and 1,2-disubstituted indoline fragments are present. It is interesting to note the difference in reactivity between 1- and 3-subsituted indole fragments of the bisindolylmaleimide **16f**, as the formation of the azepine derivative **24** isomeric to **23** was not observed (Scheme 9).

3. Conclusion

3-(Indol-3-yl)maleimides containing an *N*-alkylaryl substituent (including *N*-tetrahydroquinolinyl or *N*-indolinyl moiety) in position 4 of the maleimide ring produced azepines annelated with maleimide, indoline, and arylamine (including indoline or tetrahydroquinoline) nuclei under acid treatment. Subsequent dehydrogenation led to the corresponding azepines annelated with maleimide and indole nuclei.

4. Experimental

Mps were determined on a Buchi SMP-20 apparatus. 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 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 a 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



Scheme 9.

operating system SS-300 (EI, 70 eV, direct introduction, ion source temperature 250 °C). Infrared spectra were recorded with Nicolet Avatar 330 FTIR spectrometer using KBr discs. UV–vis spectra were recorded using Hitachi U-2000 spectrophotometer using THF as a solvent. Analytical TLC was performed on Silica Gel F254 plates (Merck) and column chromatography on Silica Gel Merck 60. Extracts were dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. Solvents and reagents were obtained from commercial suppliers unless otherwise specified.

4.1. Acetamides 14

(A) Compound **13** (70 mmol) and an excess of anhydrous K_2CO_3 were added to the solution of 2-chloroacetamide (3 g, 32.2 mmol) in acetone (200 mL). The reaction mixture was refluxed with intensive stirring for 3 h. After cooling to rt the reaction mixture was filtered and the filtrate evaporated. The residue was dissolved in EtOAc (200 mL), the solution was washed with 1 N HCl (2× 50 mL), 0.5 N Na_2CO_3 solution (2×50 mL), water (2× 50 mL), dried, and evaporated. The residue was recrystallized from an appropriate solvent.

(B) Compound **13** (70 mmol) and Et(^{i}Pr)$_2$N (4.5 g, 35 mmol) were added to the solution of 2-chloroacetamide (3 g, 32.2 mmol) in dry DMF (40 mL). The reaction mixture was left to stir overnight at 60 °C. After cooling to rt the reaction mixture was poured into 1 N HCl (100 mL) and extracted with EtOAc (2×100 mL). The organic layer was washed with 1 N HCl (100 mL), water (50 mL), dried, and evaporated. The residue was recrystallized from an appropriate solvent.

4.1.1. 2-(2,3-Dihydroindol-1-yl)acetamide (14a). Compound **14a** was obtained by method A as colorless crystals (from EtOAc) (4.8 g, 27.4 mmol, 85%); mp 146–147 °C (EtOAc); [Found: C, 68.26; H, 7.97; N, 15.75. $C_{10}H_{12}N_2O$ requires C, 68.16; H, 7.86; N, 15.90%]; R_f 0.61 ($CHCl_3$–MeOH 10:1); ν_{max}: 1242, 1305, 1335, 1385, 1398, 1458, 1473, 1489, 1605, 1653, 2842, 2897, 3185, 3377 cm^{-1}; δ_H (d_6-DMSO) 2.92 (2H, t, J=8.3 Hz), 3.41 (2H, t, J=8.3 Hz), 3.61 (2H, s), 6.44 (1H, d, J=7.6 Hz), 6.60 (1H, t, J= 7.4 Hz), 6.98 (1H, t, J=7.4 Hz), 7.04 (1H, d, J=7.1 Hz), 7.16 (1H, s), 7.44 (1H, s); δ_C (d_6-DMSO) 28.1, 52.1, 53.6, 106.5, 117.3, 124.1, 127.0, 129.4 (q), 152.0 (q), 171.4 (C=O); *m/z* (EI-MS) M$^+$176 (35), 132 M$^+$ −CONH$_2$ (100%).

4.1.2. 2-(*N*-Ethylphenylamino)acetamide (14b). Compound **14b** was obtained by method B as colorless crystals (from ^{i}PrOH) (5.05 g, 28.3 mmol, 88%); mp 104–106 °C (^{i}PrOH); [Found: C, 67.26; H, 7.97; N, 15.78. $C_{10}H_{14}N_2O$ requires C, 67.39; H, 7.92; N, 15.72%]; R_f 0.62 ($CHCl_3$–MeOH 25:1); ν_{max}: 1239, 1257, 1340, 1405, 1502, 1654, 2976, 3182, 3417 cm^{-1}; δ_H (d_6-DMSO) 1.10 (3H, m, –CH$_2$C*H*$_3$), 3.42 (2H, m, –C*H*$_2$CH$_3$), 3.78 (2H, s, –C*H*$_2$C(O)NH$_2$), 6.59–6.64 (3H, m), 7.13 (1H, s, N*H*), 7.15–7.19 (2H, m), 7.32 (1H, s, N*H*); δ_C (d_6-DMSO) 11.8, 45.4, 53.5, 111.7, 115.8, 147.9 (q), 172.3 (C=O); *m/z* (EI-MS) M$^+$178 (55), 134 M$^+$ −CONH$_2$ (100%).

4.1.3. 2-(6-Methyl-3,4-dihydroquinolin-1-yl)acetamide (14c). Compound **14c** was obtained by method B as colorless crystals (from ^{i}PrOH) (5.3 g, 25.8 mmol, 80%); mp 175–177 °C (^{i}PrOH); [Found: C, 70.43; H, 8.03; N, 13.79. $C_{12}H_{16}N_2O$ requires C, 70.56; H, 7.90; N, 13.71%]; R_f 0.6 ($CHCl_3$–MeOH 25:1); ν_{max}: 1209, 1243, 1331, 1387, 1403, 1512, 1619, 1655, 2837, 2886, 2924, 3169, 3345 cm^{-1}; δ_H (d_6-DMSO) 1.9 (2H, m, –NCH$_2$C*H*$_2$CH$_2$), 2.14 (3H, s, PhC*H*$_3$), 2.67 (2H, t, J=6.4 Hz, –NCH$_2$CH$_2$C*H*$_2$), 3.30 (2H, t, J=6.2 Hz, –NC*H*$_2$CH$_2$CH$_2$), 3.69 (2H, s, –C*H*$_2$-C(O)NH$_2$), 6.26 (1H, d, J=8.1 Hz, C8–*H*), 6.72 (1H, d, J=1.9 Hz, C5–*H*), 6.76 (1H, dd, J=8.2, 1.9 Hz, C7–*H*), 7.18 (1H,s, N*H*), 7.26 (1H, s, N*H*); δ_C (d_6-DMSO) 20.0, 21.9, 27.4, 50.3, 55.0, 110.6, 122.1 (q), 124.3 (q), 127.1, 129.4, 143.1 (q), 172.3 (C=O); *m/z* (EI-MS) M$^+$204 (100), 160 M$^+$ −CONH$_2$ (33%).

4.1.4. 2-Phenoxyacetamide (14d). Compound **14d** was obtained by method A as colorless crystals (from ^{i}PrOH) (3 g, 19.4 mmol, 60%); mp 96–98 °C (^{i}PrOH); [Found: C, 63.65; H, 6.10; N, 9.39. $C_8H_9NO_2$ requires C, 63.56; H, 6.00; N, 9.27%]; R_f 0.56 ($CHCl_3$–MeOH 10:1); ν_{max}: 1243, 1292, 1354, 1415, 1458, 1497, 1586, 1679, 2923, 3062, 3141, 3457 cm^{-1}; δ_H ($CDCl_3$) 4.52 (2H, s), 6.65 (2H, br s), 6.96 (2H, d, J=7.8 Hz), 7.06 (1H, t, J=7.3 Hz), 7.35 (2H, m); δ_C ($CDCl_3$) 67.0, 114.5, 122.0, 129.7, 157.0 (q), 171.3 (C=O); *m/z* (EI-MS) M$^+$151 (100), 107 M$^+$ −CONH$_2$ (75%).

4.1.5. 2-(4-Methoxythiophenyl)acetamide (14e). Compound **14e** was obtained by method A as yellowish crystals (from ^{i}PrOH) (5.4 g, 27.6 mmol, 86%); mp 100–102 °C (^{i}PrOH); [Found: C, 54.85; H, 5.72; N, 7.18. $C_9H_{11}NO_2S$ requires C, 54.80; H, 5.62; N, 7.10%]; R_f 0.4 ($CHCl_3$–MeOH 10:1); ν_{max}: 1237, 1288, 1383, 1420, 1456, 1496, 1573, 1626, 2919, 2961, 3199, 3383 cm^{-1}; δ_H (d_6-DMSO) 3.49 (2H, s), 3.74 (3H, s), 6.92 (2H, d), 7.11 (1H, br s), 7.36 (2H, d), 7.48 (1H, br s); δ_C (d_6-DMSO) 38.3, 55.2, 114.7 (2C), 126.0 (q), 131.7 (2C), 158.4 (q), 170.1 (C=O); *m/z* (EI-MS) M$^+$197 (100), 153 M$^+$ −CONH$_2$ (55), 139 M$^+$ − CH$_2$CONH$_2$ (20%).

4.1.6. Indol-1-ylacetamide (14f). (A) The solution of **14a** (500 mg, 2.8 mmol) in the mixture of toluene and THF (2:1, 150 mL) was treated with DDQ (770 mg, 3.4 mmol), and the reaction mixture was refluxed for 2 h. The cooled to rt reaction mixture was diluted with EtOAc (50 mL), washed with aq $NaHSO_3$ (2×30 mL), aq Na_2CO_3 (2×30 mL), water (50 mL), brine (30 mL), dried and evaporated. The residue was purified by flash chromatography ($CHCl_3$). The product was obtained as a grey colored solid (453 mg, 2.6 mmol, 93%); mp 158–160 °C ($CHCl_3$); [Found: C, 69.06; H, 5.84; N, 16.19. $C_{10}H_{10}N_2O$ requires C, 68.95; H, 5.79; N, 16.08%]; R_f 0.51 ($CHCl_3$–MeOH 10:1); ν_{max}: 1311, 1325, 1405, 1466, 1484, 1515, 1626, 1668, 3183, 3382 cm^{-1}; δ_H (d_6-acetone) 4.87 (2H, s), 6.50 (1H, d, J=3.1 Hz, C3–*H*), 6.63 (2H, br s), 7.06 (1H, t, J=7.5 Hz), 7.17 (1H, t, J= 7.6 Hz), 7.31 (1H, d, J=3.1 Hz), 7.39 (1H, d, J=8.2 Hz), 7.59 (1H, d, J=7.9 Hz); δ_C (d_6-acetone) 49.6, 102.3, 110.3, 120.2, 121.4, 122.2, 129.7 (q), 130.0, 137.5 (q), 170.4 (C=O); *m/z* (EI-MS) M$^+$174 (90), M$^+$ −CONH$_2$ 130 (100%).

(B) A solution of indole (580 mg, 5 mmol) in DMF (3 mL) was added to the stirred suspension of NaH (60% in mineral oil, 200 mg, 5 mmol) in DMF (4 mL), the mixture was left

to stir at rt for 30 min. The reaction mixture was then treated with the solution of 2-chloroacetamide (470 mg, 5 mmol) in DMF (5 mL) and left to stir overnight. The reaction mixture was poured into ice and extracted with EtOAc (2×50 mL). The organic layer was washed with water (3×30 mL), dried and evaporated. The residue was purified by flash chromatography ($CHCl_3$) to give **14f** (435 mg, 50%). The obtained product was identical to **14f**, obtained by method A according to TLC and NMR data.

4.2. 4-Substituted 3-(indol-3-yl)maleimides 16

The stirred solution or suspension of acetamide **14** (200–500 mg) and equimolar amount of methyl (indol-3-yl)glyoxylate **15** in THF (20 mL) was treated with KO^{t}Bu (1.5 equiv). The reaction mixture was left to stir for 2.5–3 h at 50 °C, cooled to 0 °C, and concd HCl (3 equiv) was added. The mixture was stirred for 15 min, diluted with water (50 mL), and extracted with EtOAc (2×50 mL). The organic layer was separated, washed with water up to neutral pH, dried, and evaporated. The residue was worked up as indicated below.

4.2.1. 3-(2,3-Dihydroindol-1-yl)-4-(indol-3-yl)maleimide (16a). Compound **16a** was obtained from **14a** (240 mg, 1.4 mmol) and **15** (280 mg, 1.4 mmol) as a red colored oil, that crystallized upon storage to give dark violet crystals (440 mg, 1.3 mmol. 95%); mp 198–200 °C (EtOH); [Found: C, 73.04; H, 4.51; N, 12.80. $C_{20}H_{15}N_3O_2$ requires C, 72.94; H, 4.59; N, 12.76%]; R_f 0.61 ($CHCl_3$–MeOH 10:1); ν_{max}: 1214, 1239, 1320, 1340, 1429, 1461, 1486, 1517, 1599, 1634, 1680, 1754, 3051, 3356 cm^{-1}; δ_H (d_6-DMSO) 3.10 (2H, t, J=8.2 Hz, indoline C3–*H*), 4.16 (2H, t, J=8.2 Hz, indoline C2–*H*), 6.21 (1H, dd, J=8.2 Hz, indoline C4–*H*), 6.59–6.63 (2H, two triplets, indoline C5–*H* and C6–*H*), 6.84 (1H, t, J=7.4 Hz, indole C6–*H* or C5–*H*), 7.00 (1H, t, J=8.1 Hz, indole C6–*H* or C5–*H*), 7.07 (1H, dd, J=8.3 Hz, indoline C7–*H*), 7.31 (1H, d, J=8.0 Hz, indole C4–*H* or C7–*H*), 7.33 (1H, d, J=8.2 Hz, indole C4–*H* or C7–*H*), 7.42 (1H, d, J=2.6 Hz, indole C2–*H*), 10.72 (1H, s, imide N*H*), 11.49 (1H, br d, J=2.5 Hz, indole N*H*); δ_C (d_6-DMSO) 28.7 (indoline C3), 52.2 (indoline C2), 104.7 (q), 111.59, 111.61 (q), 112.0, 119.4, 120.1, 120.6, 121.4, 124.1, 125.8, 126.8 (q), 127.6, 131.1 (q), 134.3 (q), 135.5 (q), 143.7 (q), 169.6 (C═O), 171.8 (C═O); EI HRMS calcd M^+ for $C_{20}H_{15}N_3O_2$ 329.1164, found 329.1177 (100), $M^+-(CO)_2NH$ 285 (13%).

4.2.2. 3-(Indol-3-yl)-4-(*N*-ethylanilino)maleimide (16b). Compound **16b** was obtained from **14b** (200 mg, 1.12 mmol) and **15** (230 mg, 1.12 mmol) as dark red crystals (300 mg, 0.78 mmol, 70%); mp 248–250 °C (EtOH); [Found: C, 72.80; H, 5.39; N, 12.72. $C_{20}H_{17}N_3O_2$ requires C, 72.49; H, 5.17; N, 12.68%]; R_f 0.29 ($CHCl_3$–MeOH 25:1); ν_{max}: 1223, 1239, 1262, 1311, 1340, 1398, 1435, 1499, 1509, 1594, 1615, 1625, 1694, 1756, 3040, 3223, 3377 cm^{-1}; δ_H (d_6-DMSO) 1.05 (3H, m, ethyl C*H*$_3$), 3.55 (2H, m, ethyl C*H*$_2$), 6.87 (1H, t, J=7.2 Hz, Ph), 6.91 (1H, t, J=7.9 Hz, Ph), 6.99 (2H, d, J=7.9 Hz, Ph, C2–*H* and C6–*H*), 7.09 (1H, t, J=7.6 Hz, indole), 7.17–7.20 (2H, t and t, indole and Ph C4–*H*), 7.28 (1H, d, J=8.0 Hz, indole), 7.42 (1H, d, J=8.0 Hz, indole), 7.96 (1H, d, J=2.8 Hz, indole C2–*H*), 10.74 (1H, s, imide N*H*), 11.70 (1H, d, J=2.8 Hz, indole N*H*); δ_C (d_6-DMSO) 13.5 (ethyl *C*H$_3$), 44.7 (ethyl *C*H$_2$), 104.1 (q), 112.0, 118.1 (2C, Ph), 119.2 (q), 120.0, 120.4, 120.8, 121.7, 126.3 (q), 128.4, 128.7 (2C, Ph), 135.7 (q), 136.0 (q), 145.1 (q), 169.7 (C═O), 171.6 (C═O); *m*/*z* (EI-MS) M^+ 331 (100) M^+- NH 316 (20%).

4.2.3. 3-(1*H*-Indol-3-yl)-4-(3,4-dihydro-6-methylquinolin-1-yl)maleimide (16c). Compound **16c** was obtained from **14c** (220 mg, 1.08 mmol) and **15** (220 mg, 1.08 mmol) as dark red crystals (308 mg, 0.86 mmol, 80%); mp 260–262 °C (EtOH); [Found: C, 73.81; H, 5.49; N, 11.87. $C_{22}H_{19}N_3O_2$ requires C, 73.93; H, 5.36; N, 11.76]; R_f 0.36 ($CHCl_3$–MeOH 20:1); ν_{max}: 1243, 1299, 1329, 1398, 1433, 1502, 1522, 1613, 1630, 1674, 1760, 2920, 3186, 3342 cm^{-1}; δ_H (d_6-DMSO) 1.73 (2H, m, $CH_2CH_2CH_2$), 2.18 (3H, s, PhC*H*$_3$), 2.67 (2H, t, J=6.2 Hz, PhC*H*$_2$CH$_2$–), 3.25 (2H, t, J=5.9 Hz, NC*H*$_2$CH$_2$), 6.70 (1H, d, J=8.2 Hz, Ph C6–*H*), 6.77 (1H, dd, J=8.2, 1.5 Hz, Ph C5–*H*), 6.82 (1H, d, J=1.5 Hz, Ph C3–*H*), 6.91 (1H, t, J=7.6 Hz, indole), 7.10 (1H, t, J=7.6 Hz, indole), 7.32 (1H, d, J=8.2 Hz, indole), 7.45 (1H, d, J=8.2 Hz, indole), 7.70 (1H, d, J=2.8 Hz, indole C2–*H*), 10.64 (1H, s, imide N*H*), 11.7 (1H, br s, indole N1–*H*); δ_C (d_6-DMSO) 20.2, 21.9, 26.4, 48.6, 104.2 (q), 112.0, 118.5 (q), 119.6 (q), 119.9, 120.4, 121.8, 124.8 (q), 126.1 (q), 126.8, 128.3, 128.9 (q), 129.4, 136.1 (q), 136.4 (q), 138.3 (q), 169.2 (C═O), 171.6 (C═O); *m*/*z* (EI-MS) M^+ 357 (100) M^+- C(O)NHC(O) 286 (15%).

4.2.4. 3-(Indol-3-yl)-4-phenyloxymaleimide (16d). The residue after solvent evaporation was chromatographed ($CHCl_3$–MeOH 20:1), the fractions containing **16d** were pooled and evaporated, the residue was purified by the preparative TLC ($CHCl_3$–MeOH 20:1), to give **16d** as a yellow solid (52 mg, 0.17 mmol, 10% from **14d**, 250 mg, 1.7 mmol); R_f 0.5 ($CHCl_3$–MeOH 10:1), EI HRMS, found M^+ 304.0837 (100%). $C_{18}H_{12}N_2O_3$ requires 304.0848; ν_{max}: 1221, 1251, 1318, 1353, 1379, 1444, 1488, 1590, 1642, 1671, 1716, 2925, 3170, 3359 cm^{-1}; δ_H (d_6-DMSO) 6.99 (2H, d, J=8.5 Hz), 7.1 (1H, t J=7.6 Hz), 7.15 (1H, t, J=7.6 Hz), 7.19 (1H, m), 7.28–7.32 (2H, m), 7.46 (1H, d, J=8.0 Hz), 7.9 (1H, d, J=8.2 Hz), 8.13 (1H, d, J=2.9 Hz), 11.0 (1H, s), 11.92 (1H, br d).

4.2.5. 3-(Indol-3-yl)-4-[(4-methoxyphenyl)thio]maleimide (16e). Compound **16e** was obtained from **14e** (300 mg, 1.5 mmol) and **15** (305 mg, 1.5 mmol). The residue after solvent evaporation was chromatographed ($CHCl_3$) and left to crystallize. **22e** crystallized from $CHCl_3$ as orange crystals as a solvate with $CHCl_3$ (178 mg, 0.38 mmol, 25%); mp 185–186 °C ($CHCl_3$); [Found: C, 51.43; H, 3.21; N, 6.06. $C_{20}H_{15}Cl_3N_2O_3S$ requires C, 51.13; H, 3.22; N, 5.96%]; R_f 0.46 ($CHCl_3$–MeOH 10:1); ν_{max}: 1231, 1292, 1303, 1338, 1425, 1489, 1579, 1701, 1762, 3251, 3374, 3539, 3635 cm^{-1}; δ_H (d_6-DMSO) 3.7 (3H, s), 6.81 (2H, d, J=8.8 Hz), 7.11 (1H, dt, ^4J=1.1, 7.9 Hz), 7.18 (1H, dt, ^4J=1.1, 8.2 Hz), 7.21 (C*H*Cl$_3$), 7.26 (2H, d, J=8.8 Hz), 7.46 (1H, d, J=8.1 Hz), 7.85 (1H, d, J=2.9 Hz, indole C2–*H*), 7.88 (1H, d, J=8.0 Hz), 11.09 (1H, s), 11.97 (1H, br d, J=2.9 Hz); δ_C (d_6-DMSO) 55.2 (O*C*H$_3$), 79.2 (*C*HCl$_3$), 104.8 (q), 112.0, 114.6 (2C), 120.1, 122.1, 122.3, 122.8 (q), 125.0 (q), 126.0 (q), 131.1, 131.6 (2C), 136.4 (q), 137.9 (q), 158.7 (q), 169.2 (*C*═O), 170.4 (*C*═O); *m*/*z* (EI-MS) M^+ 350 (100), M^+-C(O)NHC(O) 279 (10%).

4.2.6. 3-(Indol-1-yl)-4-(indol-3-yl)maleimide (16f). (A) To the solution of **16a** (100 mg, 0.3 mmol) in toluene (50 mL) was added the solution of DDQ (76 mg, 0.33 mmol) in toluene (3 mL). The reaction mixture was refluxed for 3 h. After cooling to rt it was diluted with EtOAc (50 mL), washed with saturated aq $NaHSO_3$ (30 mL), aq $NaHCO_3$ (2×30 mL), water (30 mL), brine (30 mL), dried and evaporated. The product was isolated by flash chromatography ($CHCl_3$) as a red solid (78 mg, 0.24 mmol, 80%); mp 160–161 °C (EtOH–$CHCl_3$); [Found: C, 73.45; H, 4.10; N, 12.96. $C_{20}H_{13}N_3O_2$ requires C, 73.38; H, 4.00; N, 12.84%]; EI HRMS, found M^+ 327.1016 (100), $M^+ - (CO)_2NH$ 256 (30%). $C_{20}H_{13}N_3O_2$ requires 327.1008; R_f 0.5 ($CHCl_3$–MeOH 10:1); ν_{max}: 1207, 1238, 1329, 1420, 1457, 1513, 1616, 1712, 1761, 2925, 3342 cm^{-1}; δ_H (d_6-DMSO) 6.05 (1H, d, J=8.2 Hz), 6.49 (1H, t, J=7.6 Hz), 6.76 (1H, d, J=3.3 Hz), 6.86 (1H, t, J=8.2 Hz), 6.93 (1H, t, J=8.1 Hz), 6.95–7.00 (2H, t and d), 7.34 (1H, d, J=8.2 Hz), 7.56 (1H, d, J=3.3 Hz), 7.57 (1H, d, J=7.7 Hz), 8.06 (1H, d, J=3.0 Hz), 11.23 (1H, s), 11.97 (1H, br s); δ_C (d_6-DMSO) 103.8 (q), 105.1, 111.8, 112.0, 119.7, 120.3, 120.6, 120.7, 122.1, 122.2, 125.3 (q), 126.0 (q), 126.4 (q), 128.1 (q), 128.4, 131.1, 136.6 (q), 136.1 (q), 169.3 (C=O), 171.0 (C=O).

(B) Bisindolylmaleimide **16f** was also obtained by condensation of (indol-1-yl)acetamide **14f** and **15** by the action of $KOBu^t$ in 60% yield after column chromatography ($CHCl_3$). It was identical to **16f** obtained by method A according to TLC and NMR data.

4.3. Transformation of 4-substituted 3-(indol-3-yl)maleimides 16 upon the action of CH_3SO_3H

To the solution of **16** (200–300 mg) in TFA (5 mL) was added CH_3SO_3H (1 mL) and the reaction mixture was stirred for 3 h at rt and then was poured into aq $NaHCO_3$/EtOAc (1:1, 100 mL), $NaHCO_3$ was added up to neutral pH. The organic layer was separated, washed with water (50 mL), dried, and worked up as indicated below.

4.3.1. 5,6,10,14b-Tetrahydro[1′,7′:1,2,3]pyrrolo[3′,4′:6,7]azepino[4,5-*b*]indol-1,3(2*H*,9b*H*)-dione (17a). The solution was concentrated and left to crystallize at 0 °C. The precipitate was filtered, washed with EtOAc (2×5 mL) and dried to give **23a** as a dark yellow solid (130 mg, 0.4 mmol, 65%, from **22a** 200 mg, 0.61 mmol); mp 254–255 °C (EtOAc, decomp.); EI HRMS, found 329.1173 (100), $M^+ - CO$ 301 (13), $M^+ - (CO)_2NH$ 258 (40%). $C_{20}H_{15}N_3O_2$ requires M^+ 329.1164; R_f 0.7 ($CHCl_3$–MeOH 10:1); ν_{max}: 1245, 1303, 1334, 1355, 1415, 1462, 1586, 1623, 1679, 1757, 2877, 3044, 3249, 3359 cm^{-1}; λ_{max}: 243 nm (ε 13,337 $cm^{-1}\,M^{-1}$), 293 (4225), 413 (8464); δ_H (d_6-DMSO) 3.09–3.13 (2H, m, C6–H), 4.42–4.49 (3H, m), 4.66 (1H, d, J=6.6 Hz, C14b–*H*), 6.48 (1H, br s, N10–*H*), 6.52 (1H, t, J=7.5 Hz), 6.55 (1H, d, J=7.3 Hz), 6.91 (1H, t, J=7.6 Hz), 6.98 (1H, t, J=7.6 Hz), 7.00 (1H, d, J=7.1 Hz), 7.17 (1H, d, J=7.1 Hz), 7.42 (1H, d, J=7.8 Hz, C14–*H*), 10.63 (1H, s, N2–*H*); δ_C (d_6-DMSO) 27.5, 42.5, 49.6, 62.6, 103.1 (q), 108.9, 117.2, 122.8, 124.1, 124.2, 127.4, 129.6, 131.6 (q), 133.0 (q), 138.1 (q), 142.1 (q), 149.5 (q), 168.3 (*C*=O), 171.9 (*C*=O).

4.3.2. 8-Ethyl-12b,13-dihydro-4b*H*-indolo[3,2-*d*]pyrrolo[3,4-*b*][1]benzazepine-5,7(6*H*,8*H*)-dione (17b). The extract was evaporated and the residue was chromatographed ($CHCl_3$) to give **17b** as a yellow crystals (140 mg, 0.42 mmol, 70%, from **16b**, 200 mg, 0.6 mmol); mp 209–210 °C ($CHCl_3$); [Found: C, 72.42; H, 5.31; N, 12.40. $C_{20}H_{17}N_3O_2$ requires C, 72.49; H, 5.17; N, 12.68%]; R_f 0.27 ($CHCl_3$); ν_{max}: 1249, 1279, 1348, 1409, 1481, 1492, 1598, 1650, 1701, 1755, 2924, 2972, 3350, 3380 cm^{-1}; λ_{max}: 240 nm (ε 19,332 $cm^{-1}\,M^{-1}$), 276 (8254), 404 (4934); δ_H (d_6-DMSO) 1.10 (3H, m, CH_2CH_3), 4.03 (2H, m, CH_2CH_3), 4.25 (1H, d, J=7.1 Hz C4b–*H*), 4.94 (1H, dd, J_{12b-4b}=7.3 Hz, J_{12b-13}=2.6 Hz, C12b–*H*), 6.12 (1H, d, J_{13-12b}=2.6 Hz, N13–*H*), 6.54 (1H, dt, J=7.5, 1.0 Hz, C3–*H*), 6.57 (1H, d, J=6.8 Hz, C1–*H*), 6.95 (1H, dt, J=7.6, 1.3 Hz, C2–*H*), 7.08–7.12 (1H, m), 7.19 (1H, d, J=7.3 Hz, C4–*H*), 7.31–7.39 (3H, m), 10.5 (1H, s, N6–*H*); δ_C (d_6-DMSO) 14.3 (CH_2CH_3), 41.6 (*C*4b), 44.7 (N–CH_2–), 64.9 (*C*12b), 108.6, 113.1 (q), 116.8, 122.4, 123.5, 124.4, 127.4, 130.5 (q), 131.4 (q), 131.5, 141.1 (q), 145.6 (q), 150.9 (q), 169.0 (C=O), 171.4 (C=O); *m/z* (EI-MS) M^+ 331 (100) $M^+ - C(O)NH$ 288 (15), $M^+ - C(O)NHC(O)$ 260 (20%).

4.3.3. 9-Methyl-6,7,11,15b-tetrahydro-5*H*-indolo[2′,3′:4,5]pyrrolo[3′,4′:6,7]azepino[3,2,1-*ij*]quinoline-1,3(2*H*,10b*H*)-dione (17c). Compound **17c** was obtained from **16c** (200 mg, 0.56 mmol) as described for **17b** as a yellow solid (120 mg, 0.42 mmol, 60%,); EI HRMS, found M^+ 357.1489 (100%). $C_{22}H_{19}N_3O_2$ requires 357.1477; R_f 0.27 ($CHCl_3$); ν_{max}: 1263, 1337, 1405, 1437, 1454, 1477, 1606, 1637, 1706, 1753, 2729, 2926, 3424 cm^{-1}; λ_{max}: 245 nm (ε 13,059 $cm^{-1}\,M^{-1}$), 294 (4515), 408 (3253); δ_H (d_6-DMSO) 1.93 (1H, m, C6–*H*), 2.08 (1H, m, C6–*H*), 2.26 (3H, s, $PhCH_3$), 2.81–2.89 (2H, m, C7–*H*), 3.32–3.40 (1H, m, C5–*H*), 4.48 (1H, dt, J=13.0, 4.0 Hz, C5–*H*), 4.85 (1H, d, J=7.3 Hz, C10b–*H*), 6.01 (1H, br s, N11–*H*), 6.52–6.57 (2H, t and d, C14–*H* and C12–*H*), 6.93 (1H, d, J=1.9 Hz, C8–*H* or C10–*H*), 6.95 (1H, dt, J_{13-15}=1.4, 7.7 Hz, C13–*H*), 7.19 (1H, d, J=7.22 Hz, C15–*H*), 10.45 (1H, s, N2–*H*); δ_C (d_6-DMSO) 20.1 (CH_3), 22.7, 26.5, 42.0 (*C*15b), 46.8 (*C*5), 65.8 (*C*10b), 109.4, 110.8 (q), 117.4, 124.9, 127.8, 129.8, 129.9 (q), 130.3 (q), 130.4, 131.7 (q), 132.3 (q), 140.5 (q), 141.5 (q), 151.2 (q), 168.7 (C=O), 171.8 (C=O); *m/z* (EI-MS) M^+ 357 (100), $M^+ - C(O)NHC(O)$ 286 (23%).

4.3.4. Indolo[1′,7′:1,2,3]pyrrolo[3′,4′:6,7]azepino[4,5-*b*]indol-1,3(2*H*,10*H*)-dione (20a) and its dimer (22). The solution of **17a** (200 mg, 0.61 mmol) in THF (100 mL) was treated with DDQ (300 mg, 1.3 mmol) in THF (2 mL). The reaction mixture was stirred at 60 °C for 3 h, concentrated to the volume 5 mL, and the residue was dissolved in EtOAc (150 mL). The solution was washed with aq $NaHSO_3$ (2×30 mL), aq $NaHCO_3$ (2×30 mL), water (50 mL), dried and evaporated. The residue was chromatographed ($PhCH_3$–acetone 20:1) to give **20a** as a dark blue solid (40 mg, 0.12 mmol, 20%); mp 248–250 °C (EtOH); EI HRMS, found M^+ 325.0857 (100), $M^+ - (CO)_2NH$ 254 (16%). $C_{20}H_{11}N_3O_2$ requires 325.0851; R_f 0.57 ($CHCl_3$–MeOH 10:1); ν_{max}: 1208, 1232, 1283, 1359, 1419, 1449, 1523, 1587, 1649, 1704, 1757, 2974, 3057, 3165, 3414 cm^{-1}; λ_{max}: 245 nm (ε 27,191 $cm^{-1}\,M^{-1}$), 350 (23,491), 586 (1933); δ_H (d_6-DMSO) 6.5 (1H, d, J=3.6 Hz, C6–H), 6.91 (1H, t, J=7.7 Hz, C8–H), 6.99 (1H, t, J=7.1 Hz), 7.07 (1H, t, J=7.1 Hz), 7.11 (1H, d, J=7.5 Hz), 7.15 (1H, d, J=

8.1 Hz), 8.01 (1H, d, J=8.1 Hz), 8.12 (1H, d, J=3.6 Hz, C5–H); δ_C (d_6-DMSO) 104.3 (q), 106.2, 118.1, 118.8 (q), 121.09, 121.14 (q), 121.4, 123.0, 123.5, 123.8, 125.8, 126.0 (q), 130.5 (q), 132.7 (q), 137.2 (q), 138.2 (q), 141.8 (q), 166.8 (C=O), 169.6 (C=O); and **22** as a green solid (80 mg, 0.12 mmol, 20%); mp>330 °C ($PhCH_3$/acetone); EI HRMS, found M^+ 648.1555 (100%). $C_{40}H_{20}N_6O_4$ requires 648.1546; R_f 0.25 ($CHCl_3$–MeOH 10:1); ν_{max}: 1214, 1231, 1313, 1360, 1431, 1578, 1618, 1646, 1707, 2870, 2956, 3386, 3641 cm^{-1}; λ_{max}: 246 nm (ε 23,257 cm^{-1} M^{-1}), 301–368 (24,561–23,307), 602 (1950); δ_H (d_6-DMSO) 5.93 (1H, d, J=8.1 Hz), 6.65 (1H, t, J=7.9 Hz), 6.92 (1H, td, J=7.7, 1.1 Hz), 6.92 (1H, d, J=3.8 Hz), 6.97 (1H, d, J=7.5 Hz), 7.01 (1H, td, J=7.0, 1.0 Hz), 7.21 (1H, d, J=7.8 Hz), 7.24 (1H, td, J=7.5, 0.9 Hz), 7.33 (1H, t, J=7.7 Hz), 7.70 (1H, d, J=7.3 Hz), 7.76 (1H, d, J=7.1 Hz), 7.79 (1H, d, J=7.1 Hz), 7.95 (2H, two doublets, J=7.7 Hz), 8.06 (1H, s), 8.41 (1H, d, J=3.7 Hz); δ_C (d_6-DMSO) 104.1 (q), 109.0, 109.2 (q), 111.6, 114.3 (q), 117.9, 118.4, 119.2 (q), 119.3 (q), 120.4, 121.1, 121.4 (q), 123.1, 123.3, 123.4, 124.0, 124.6, 124.8, 124.9, 125.0, 125.6 (q), 125.8 (q), 128.0, 129.0, 129.2, 130.1 (q), 131.0 (q), 131.6 (q), 136.6 (q), 136.7 (q), 138.1 (q), 142.8 (q), 154.9 (q), 166.1 (C=O), 166.4 (C=O), 168.9 (C=O), 169.3 (C=O); *m/z* (EI-MS) M^+ 648 (100), $M^+ - (CO)_2NH$ 577 (10), $M^+ - ((CO)_2NH)_2$ 508 (10), $M^+/2$ 324 (20%).

4.3.5. 8-Ethyl-8,13-dihydro-5*H*-indolo[3,2-*d*]pyrrolo[3,4-*b*][1]benzazepine-5,7(6*H*)-dione (20b). To the solution of **17b** (200 mg, 0.6 mmol) in EtOAc (50 mL) was added DDQ (140 mg (0.62 mmol) and the reaction mixture was left with stirring at rt for 3 h. The reaction mixture was diluted with EtOAc (50 mL), washed with aq $NaHSO_3$ (30 mL), aq $NaHCO_3$ (2×30 mL), water (50 mL), dried and evaporated. The residue was chromatographed ($CHCl_3$–MeOH 50:1) to give **20b** as dark blue crystals (160 mg, 0.48 mmol, 80%); mp>330 °C (^{i}PrOH); [Found: C, 72.91; H, 4.77; N, 12.72. $C_{20}H_{15}N_3O_2$ requires C, 72.94; H, 4.59; N, 12.76%]; R_f 0.58 ($CHCl_3$–MeOH 20:1); ν_{max}: 1201, 1227, 1241, 1313, 1347, 1439, 1504, 1633, 1696, 1753, 2975, 3056, 3252 cm^{-1}; λ_{max}: 244 nm (ε 25,465 cm^{-1} M^{-1}), 331 (15,850), 500 (2163); δ_H (d_6-DMSO) 1.12 (3H, m, CH_2CH_3), 3.86 (2H, m, CH_2CH_3), 7.07 (1H, d, J=7.9 Hz), 7.09 (1H, t, J=7.9 Hz, C3–*H*), 7.16 (1H, t, J=7.4 Hz), 7.20 (1H, t, J=7.3 Hz, C2–*H*), 7.39 (1H, t, J=7.5 Hz), 7.44 (2H, d+d, J=7.6 Hz, C1–*H* and Ph-*H*), 7.97 (1H, d, C4–*H*), 10.75 (1H, s, N6–*H*), 11.96 (1H, s, N13–*H*); δ_C (d_6-DMSO) 14.4, 44.3, 106.2 (q), 111.6, 120.3, 121.6, 122.1, 123.0, 124.5, 124.9 (q), 126.1 (q), 127.9 (q), 128.6, 130.8, 137.0 (q), 140.0 (q), 142.6 (q), 150.4 (q), 167.6 (C=O), 170.0 (C=O); *m/z* (EI-MS) M^+ 329 (78), $M^+ - CH_2CH_3$ 300 (100), $M^+ - CH_2CH_3$–$(CO)_2NH$ 229 (27%).

4.3.6. 9-Methyl-6,7-dihydro-5*H*-indolo[2′,3′:4,5]pyrrolo[3′,4′:6,7]azepino[3,2,1-*ij*]quinoline-1,3(2*H*,11*H*)-dione (20c). Compound **20c** was obtained from **17c** (250 mg, 0.7 mmol) as described for **20b** as dark blue crystals (186 mg, 0.53 mmol, 75%); mp>330 °C (^{i}PrOH); [Found: C, 74.33; H, 4.78; N, 11.71. $C_{22}H_{17}N_3O_2$ requires C, 74.35; H, 4.82; N, 11.82]; R_f 0.67 ($CHCl_3$–MeOH 20:1); ν_{max}: 1207, 1240, 1318, 1335, 1362, 1435, 1497, 1538, 1638, 1690, 1745, 2878, 2915, 3054, 3234, 3303, 3344 cm^{-1}; λ_{max}: 245 nm (ε 21,199 cm^{-1} M^{-1}), 340 (15,347); δ_H (d_6-DMSO) 2.01 (2H, m, C6–H_2), 2.69 (2H, t, J=2.0 Hz, C7–H_2), 3.55 (2H, m, C5–H_2), 6.83 (1H, d, J=1.3 Hz, C10–*H* or C8–*H*), 6.94 (1H, d, J=1.3 Hz, C10–*H* or C8–*H*), 6.99 (1H, dt, J=1.0, 8.1 Hz, C14–*H*), 7.10 (1H, dt, J=1.0, 8.0 Hz, C13–*H*), 7.34 (1H, d, J=8.2 Hz, C12–*H*), 7.84 (1H, d, J=8.1 Hz, C15–*H*), 10.62 (1H, s, N2–*H*), 11.65 (1H, s, N11–*H*); δ_C (d_6-DMSO) 20.0, 49.5, 51.2, 45.3, 106.1 (q), 111.5, 120.2, 122.1, 122.5 (q), 122.6, 125.1 (q), 126.7 (q), 127.0, 129.8 (q), 132.0, 133.2 (q), 137.3 (q), 139.7 (q), 145.0 (q), 146.6 (q), 166.9 (C=O), 1701.0 (C=O); *m/z* (EI-MS) M^+ 355 (100), $M^+ - CH_3$ 340 (20), M^+ 284–$(CO)_2NH$ (21%).

4.3.7. 8b,9-Dihydroindolo[4′,3′:3,4,5]pyrrolo[3′,4′:6,7]azepino[1,2-*a*]indole-1,3(2*H*,5*H*)-dione (23). The solution of **16f** (100 mg, 0.31 mmol) in $CHCl_3$ (5 mL) was treated with CH_3SO_3H (0.2 mL) and TFA (1 mL). The reaction mixture was left with stirring for 2 h and then poured into the mixture of saturated aq $NaHCO_3$/EtOAc (1:1, 150 mL). The organic layer was separated, washed with water (2× 50 mL), dried and evaporated. The residue was chromatographed (toluene–acetone 15:1), the fractions containing **23** were pooled and left for crystallization at rt for 24 h. The dark violet crystals were filtered off, washed with toluene and dried in vacuo to give pure **23** (56 mg, 0.17 mmol, 56%); mp>330 °C; [Found: C, 73.44; H, 3.84; N, 12.28. $C_{20}H_{13}N_3O_2$ requires C 73.38; H, 4.00; N, 12.84%]; R_f 0.41 ($PhCH_3$–acetone 5:2); ν_{max}: 1249, 1264, 1350, 1412, 1480, 1518, 1603, 1613, 1639, 1694, 1752, 2922, 3051, 3165, 3300 cm^{-1}; λ_{max}: 246 nm (ε 17,157 cm^{-1} M^{-1}), 337 (5417), 502 (6693); δ_H (d_6-DMSO) 3.66 (1H, dd, J_{gem}= 16.3 Hz, J_{9-8b}=10.0 Hz), 3.94 (1H, dd, J_{gem}=16.3 Hz, J_{9-8b}=2.8 Hz), 5.12 (1H, dd, J_{8b-9}=10.3, 2.5 Hz), 6.79–6.81 (2H, triplet and doublet), 7.00 (1H, t, J=7.8 Hz), 7.17–7.21 (2H, m), 7.28 (1H, d, J=7.5 Hz), 7.46 (1H, d, J= 7.7 Hz), 7.99 (1H, d, J=2.8 Hz, C4–H), 10.52 (1H, s), 11.85 (1H, br d, J=2.0 Hz, $N^{ind}H$); δ_C (d_6-DMSO) 30.2 (C9), 64.5 (C8b), 106.9 (q), 111.9, 112.0, 115.8, 117.5 (q), 120.2, 122.1, 124.0, 124.5 (q), 125.0, 126.8 (q), 128.4, 133.3 (q), 133.4 (q), 136.3 (q), 144.2 (q), 176.3 (C=O), 170.9 (C=O).

Acknowledgements

This work was supported by Russian Foundation for Basic Research grant No 03-03-32090-a, S.A. Lakatosh was also supported by Regional Social Fund for Support of Russian Medical Science.

References and notes

1. Pindur, U.; Kim, Y.-S. F.; Meharbani, F. *Curr. Med. Chem.* **1999**, *6*, 29–68.
2. Steglich, W. *Pure Appl. Chem.* **1989**, *61*, 281–288.
3. Bergman, J.; Pelcman, B. *Tetrahedron Lett.* **1987**, *28*, 4411–4444.
4. Lakatosh, S. A.; Luzhikov, Y. N.; Preobrazhenskaya, M. N. *Org. Biomol. Chem.* **2003**, *1*, 826–833.
5. Lakatosh, S. A.; Luzhikov, Y. N.; Preobrazhenskaya, M. N. *Tetrahedron* **2005**, *61*, 2017–2020.
6. Brenner, M.; Rexhausen, H.; Steffan, B.; Steglich, W. *Tetrahedron* **1988**, *44*, 2887–2892.
7. Faul, M. M.; Winneroski, L. L.; Krumrich, C. A. *J. Org. Chem.* **1998**, *63*, 6053–6058.