Acid-induced dimerization of 3-(1*H*-indol-3-yl)maleimides. Formation of cyclopentindole derivatives

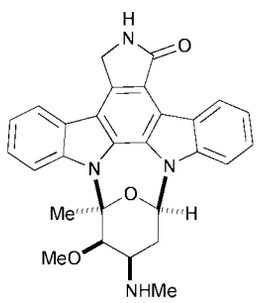
Jan Bergman,* Tomasz Janosik, Eva Koch † and Benjamin Pelcman †

Department of Biosciences at Novum, Karolinska Institute, Novum Research Park, SE-141 57 Huddinge, Sweden and Södertörn University College, SE-141 04 Huddinge, Sweden

Received (in Cambridge, UK) 19th May 2000, Accepted 9th June 2000
Published on the Web 28th July 2000

Acid-induced dimerizations of 3-substituted maleimides have been investigated, leading to *e.g.* the cyclopentindole **9** and the deeply coloured spiro compounds **24** and **25** in good yields. 3-(1*H*-Indol-3-yl)maleimide **6b** readily gave the cycloaddition products **13**–**15** on treatment with appropriate dienophiles. In addition, several related 3,3-di-(1*H*-indol-3-yl)succinimides have been prepared and studied.

Quite a number of indolo[2,3-*a*]pyrrolo[3,4-*c*]carbazoles have been identified as natural products,[1] and several of these alkaloids show pronounced physiological activity. Staurosporine[2] **1**, for example, is an extremely potent PKC inhibitor, and rebeccamycin[3] **2** is an interesting antitumour antibiotic, and several synthetic approaches to indolo[2,3-*a*]-pyrrolo[3,4-*c*]carbazoles have been published.[4]



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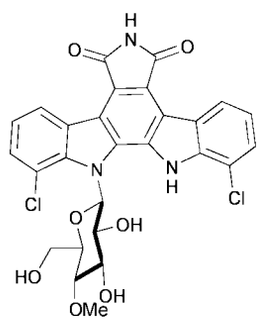

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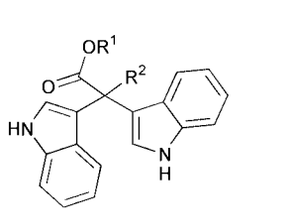
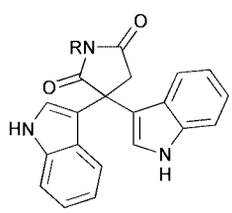
As previously reported from our group,[5] indole reacts readily with diethyl oxalacetate producing **3b**, which is in harmony with the previously reported formation of the ester **3a** by condensation of indole with ethyl pyruvate.[6]

Results and discussion

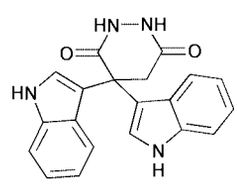
Preparation of **3b** was particularly cheap and easy because simple heating at reflux (acetic acid) of the commercially available sodium salt of diethyl oxalacetate with 2 molar equivalents of indole produced **3b** which separated directly from the reaction solution. A similar condensation between ethyl 2,4-dioxopentanoate and indole similarly selectively gave **3c**. The dimethyl ester **3e** had previously been obtained in a low yield by Lange[7] and by Johnson[8] by reaction of indole with dimethyl acetylenedicarboxylate. However, at the time the adduct was considered, incorrectly, to be dimethyl 2,3-diindolylsuccinate. A few years later (1965) Noland and Landucci[9] obtained the NMR spectrum of the adduct and reassigned it to structure **3e**. Several years later Acheson[10] made the same adduct and arrived at the same conclusion. The reaction involving dimethyl acetylenedicarboxylate gives a plethora of products and for preparative purposes the route using dimethyl oxalacetate is the method



3a R^1 = Et, R^2 = Me
3b R^1 = Et, R^2 = CH_2COOEt
3c R^1 = Et, R^2 = CH_2COMe
3d R^1 = Me, R^2 = CH(OMe)COOMe
3e R^1 = Me, R^2 = CH_2COOMe



4a R = Bn
4b R = $(CH_2)_2$–N⟨⟩NH
4c R = NH_2
4d R = H



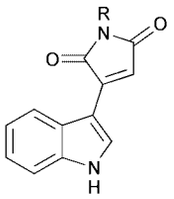
5

of choice.[10] When the diester **3b** was refluxed in benzylamine for 12 h, the succinimide **4a** was formed. The more basic amine *N*-(2-aminoethyl)piperazine also reacted easily and cleanly, giving compound **4b**. This straightforward approach could, however, not be applied to the preparation of **4d**, as reaction of **3b** with ammonia (not using pressure vessel) did not lead to the desired product. However, **3b** reacted readily with hydrazine hydrate when refluxed for 3 h to yield compound **4c**, which was subsequently transformed into **4d** by treatment with Raney nickel in 1,4-dioxane. Compound **4c** displayed interesting ^1H–^{15}N correlation spectra; only two different ^1J (^1H–^{15}N) couplings were detected (indole NH and the NH_2 group), which is consistent with the assigned structure and thus ruling out the isomeric structure **5**. The ^1H NMR data of the 3,3-*gem*-diindolyl compound **4d** were identical with those of a compound previously incorrectly assigned[11] the isomeric 3,4-diindolylsuccinimide structure **7b**. Interestingly, a compound closely related to **4d**, namely 3,3-diphenylsuccinimide has been reported to possess anticonvulsant activity.[12]

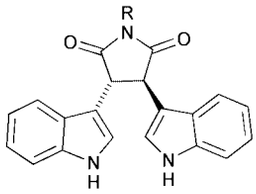
The intention now was to provoke acid-induced dimerization as had been done in some related systems, or possibly an acid-induced cleavage yielding indole and **6a**, which might add

† *Present address*: Karo Bio AB, Novum, SE-141 57 Huddinge, Sweden

DOI: 10.1039/b004030o

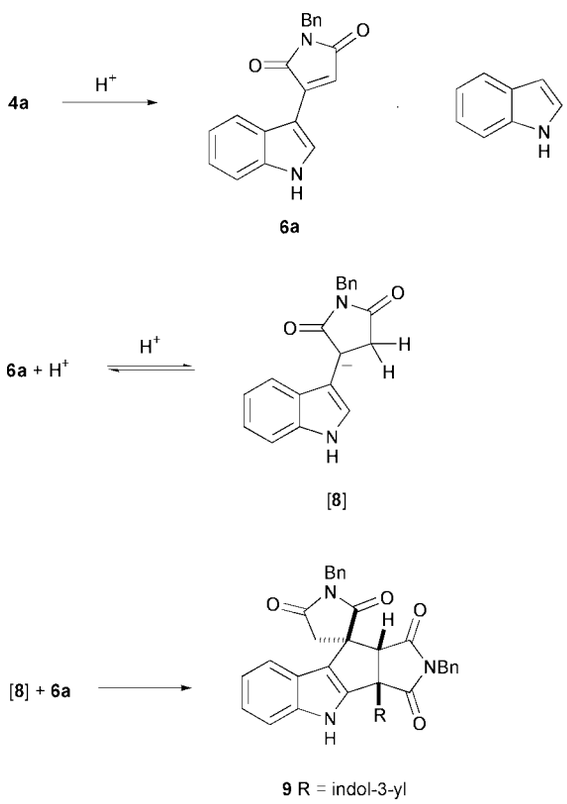


6a R = Bn
6b R = H



7a R = Bn
7b R = H

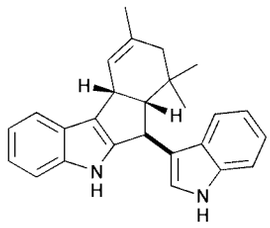
indole again and eventually yield an isomer of **4a**, *i.e.* **7a**, which in turn might undergo acid-induced 2,2′-coupling,[13] thus producing a desired indolo[2,3-*a*]pyrrolo[3,4-*c*]carbazole system. However, the outcome of the treatment of **4a** with strong acid (trifluoroacetic acid, TFA) was unexpected, as a product with the composition $C_{38}H_{28}N_4O_4$ was obtained, which is composed of two different indole rings and two different benzyl groups, and also features two quaternary signals in the aliphatic region of the ^{13}C NMR spectrum, as well as three methylenes. After analysis of the spectral data structure **9** was assigned. A rationalization of the events leading to compound **9** is given in Scheme 1.



Scheme 1

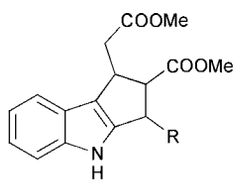
In harmony with this formulation the simple molecule **6a**,[14] when treated with TFA at 25 °C, yielded within 30 seconds a quantitative yield of **9** as one single diastereomer. The bulky benzyl group seems to be important for this outcome because experiments starting with *N*-methyl-3-(1*H*-indol-3-yl)-maleimide gave mixtures of diastereomers. The stereochemistry at the spiro centre of **9** was assigned on the basis of NOE observations; irradiation of the methine proton at δ 4.32 produced only a small positive NOE (0.38%) for one of the methylene signals of the spiro ring. The structural similarities between **9** and the indole alkaloid yuehchukene **10** should be noted.[15]

A reaction of related interest with that in Scheme 1 had previously been reported by Inhoffen,[16] who obtained the dimer **11** as a mixture of diastereomers (which readily under-

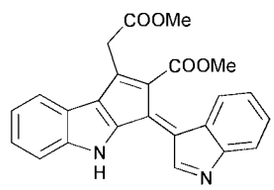


10

went dehydrogenation to the highly coloured compound **12**) by treatment of methyl 3-(1*H*-indol-3-yl)acrylate with strong acid.

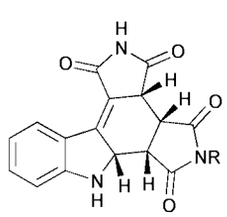


11 R = indol-3-yl

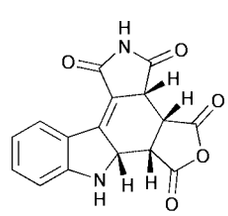


12

3-Vinylindoles are interesting partners in cycloadditions, as has been demonstrated in particular by both Noland[17] and Condoluci.[18] Some additional examples such as **13**–**15** are provided by the present work by refluxing compound **6b**[14] with an appropriate dienophile. However, in the presence of acids, the cycloadditions were not observed because of quick acid induced dimerizations, as outlined in Scheme 1. A 1,3-proton shift was induced by heating compound **13** with TFA in 1,4-dioxane, giving the indole **16** in quantitative yield. It is noteworthy that **13** is remarkably stable under acidic conditions, *e.g.* it was found to be unaffected by TFA at room temperature.



13 R = H
14 R = Et



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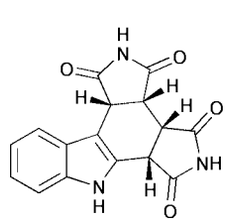
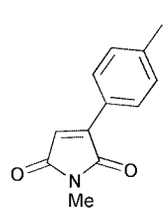
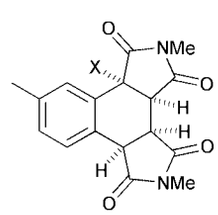


16

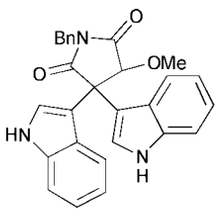
Dimerizations of monoarylmaleimides with electron-donating substituents (CH_3, OCH_3) have been reported previously, but those reactions took a somewhat different course. Thus heating (100 °C) of **17** gave the dimer **18**, whose structure has been confirmed rigorously by X-ray crystallography.[19]



17

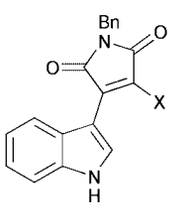


18 X = *p*-tolyl

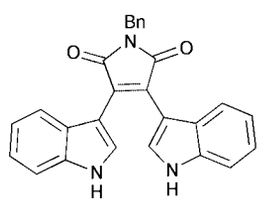


19

As discussed above, the desired rearrangement of the *gem*-diindolyl derivative **4a** failed, and at this point it was argued that the situation might be more prosperous with a precursor such as **19**. In such a case protonation of the methoxy group followed by migration of one of the indole rings might successfully compete with elimination of one of the indole rings in analogy with Scheme 1. The necessary starting material **19** could readily be prepared by condensation of dimethyl methoxyoxalacetate with indole in hot acetic acid, followed by cyclization of the intermediate diester **3d** obtained by reflux in benzylamine (in this case catalyzed by potassium cyanide). Dimethyl methoxyoxalacetate, which is used in production of, *e.g.*, the drug sulfadoxin,[20] was prepared as described by Holton.[21] Treatment of **19** with TFA led to a quick cleavage yielding a mixture of the expected and easily separated products **20a** and **21** (a known molecule).[11,22] The structure of **20a**, which did not show any propensity for dimer formation, was correlated with that of **20b** by a nucleophilic displacement of chlorine with methoxide (see ref. 23).

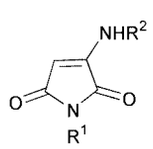


20a X = OMe
20b X = Cl



21

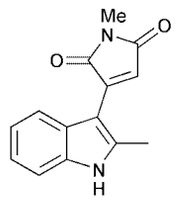
Within the frame of this work another class of maleimides containing electron-donating substituents have been studied, *viz*. **22**, which were readily prepared by addition of an aniline derivative to dimethyl acetylenedicarboxylate,[24] followed by cyclization with an appropriate amine. Some related derivatives, (*e.g.*, R^1 = Pr, R^2 = pyrazol-1-yl) have been reported by Katritzky; these compounds were, however, prepared from the corresponding 3-bromomaleimide.[25]



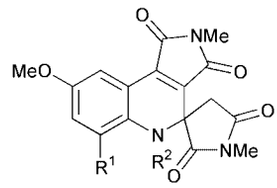
22a R^1 = Me, R^2 = 2,**4**-di-MeOC_6H_3
22b R^1 = Et, R^2 = 4-MeOC_6H_4
22c R^1 = Me, R^2 = **4**-MeOC_6H_4
22d R^1 = $(CH_2)_3NMe_2$, R^2 = **4**-MeOC_6H_4
22e R^1 = H, R^2 = **4**-MeOC_6H_4

Upon heating of **22c** with 2-methylindole in acetic acid at reflux, an exchange reaction occurred, yielding compound **23**. The precursor to **22c** also underwent exchange reactions; thus, heating of indole and dimethyl 2-(4-methoxyphenylamino)maleate in acetic acid gave the 2:1 product **3e**.

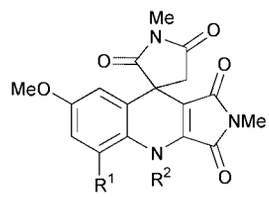
Formation of the deeply coloured (blue-violet) spiro compounds **24** and **25** was observed on heating **22a** or **22c** respectively in TFA at reflux. The structures were assigned on the basis of HMBC experiments, as well as ^2J and ^3J (^{1}H–^{15}N) correlations, which ruled out the isomeric system **27** as an alternative, since, *e.g.*, compound **26** displayed a ^3J coupling between the methylene protons and the acetylated nitrogen atom. Donation of electron density from the NH group *via* the aromatic ring to the maleimide carbonyls is possibly the cause of the blue-violet colour of **24** and **25**. A simple experiment was performed to test this hypothesis; acetylation of **25** gave the yellow compound **26**, which featured a visible light absorption maximum at 429 nm, in contrast to **25**, which has a λ_{max} at 562 nm. A similar shift in absorption maxima is displayed by the red *N*,*N*′-diacetylindigo (λ_{max} = 557 nm) and the dye indigo (λ_{max} = 610 nm).[26]



23



24 R^1 = OMe, R^2 = H
25 R^1 = H, R^2 = H
26 R^1 = H, R^2 = Ac



27

Experimental

NMR spectra were recorded on a Bruker DPX 300 (300 MHz) spectrometer or on a Bruker AM 400 (400 MHz). *J*-Values are given in Hz. IR spectra were recorded with a Perkin-Elmer 1600 FT-IR spectrometer. UV/VIS data were acquired using a Pharmacia Biotech Ultrospec 3000 spectrophotometer. Elemental analyses were performed by H. Kolbe Mikroanalytisches Laboratorium, Mülheim an der Ruhr, Germany. High-resolution mass spectroscopic (HRMS) analyses were performed by Sveriges Lantbruksuniversitet (SLU), Uppsala, Sweden. MS (ESI) analyses were obtained on a Perkin-Elmer API 150 EX spectrometer. Mps were taken on a Büchi Melting Point B-545 apparatus or a Reichert Kofler hot stage and are uncorrected. All solvents were purified by distillation or were of analytical grade. Chromatography was performed on Merck Silica Gel 60.

Diethyl 2,2-di(1*H*-indol-3-yl)succinate 3b

Indole (23.2 g, 0.2 mol) and sodium ethyl oxalacetate (23.0 g, 0.22 mol) in acetic acid (150 cm^3) were refluxed for 10 h, whereupon the solvent was removed, and the residue washed with water. The residue was treated with warm propan-2-ol containing 10–20% water to give white crystals of **3b** (20.5 g, 51%); mp 171–172 °C (lit.,[10] 170–172 °C) (Found: C, 70.98; H, 6.07; N, 6.97. Calc. for $C_{24}H_{24}N_2O_4$: C, 71.27; H, 5.98; N, 6.92%); ν_{max}(KBr)/cm^{-1} 3365, 2987w, 1715br, 1456, 1372, 1341, 1240, 1190, 1020, 747; δ_H (300 MHz; DMSO-d_6) 10.98 (2H, d, *J* 1.8, 2 × NH), 7.53 (2H, d, *J* 2.5, ArH), 7.27 (2H, d, *J* 8.1, ArH), 7.00 (2H, d, *J* 8.0, ArH), 6.90 (2H, dd, *J* 7.9, 7.5, ArH), 6.64 (2H, dd, *J* 7.9, 7.5, ArH), 4.06 (2H, q, *J* 7.1, O$CH_2$$CH_3$), 3.88 (2H, q, *J* 7.1, O$CH_2$$CH_3$), 3.64 (2H, s, CH_2), 1.09 (3H, t, *J* 7.1,

OCH_2CH_3), 1.01 (3H, t, *J* 7.1, OCH_2CH_3); δ_C (75.4 MHz; DMSO-d_6) 172.3 (s), 170.3 (s), 136.3 (s), 125.7 (s), 124.1 (d), 120.4 (d), 120.0 (d), 117.9 (d), 114.6 (s), 111.3 (d), 60.2 (t), 59.6 (t), 47.7 (s), 42.5 (t), 13.9 (q), 13.8 (q); *m*/*z* (ESI) 403 ($[M - H]^-$, 100%).

Ethyl 2,2-di(1*H*-indol-3-yl)-4-oxopentanoate 3c

The procedure above was used starting with indole and ethyl 2,4-dioxopentanoate. Yield 70%; mp 208–209 °C (Found: C, 73.72; H, 5.93; N, 7.40. $C_{23}H_{22}N_2O_3$ requires C, 73.78; H, 5.92; N, 7.48%); ν_{max}(KBr)/cm^{-1} 3396, 3330, 2976w, 1720, 1456, 1362, 1339, 1274, 1238, 1202, 1173, 1089, 744; δ_H (400 MHz; DMSO-d_6) 10.93 (2H, s, 2 × NH), 7.46 (2H, d, *J* 2.4, ArH), 7.26 (2H, d, *J* 8.1, ArH), 7.02 (2H, d, *J* 8.0, ArH), 6.89 (2H, dd, *J* 7.9, 7.9, ArH), 6.63 (2H, dd, *J* 7.9, 7.9, ArH), 4.03 (2H, q, *J* 7.1, OCH_2CH_3), 3.83 (2H, s, CH_2), 1.94 (3H, s, CH_3), 1.06 (3H, t, *J* 7.1, OCH_2CH_3); δ_C (100.6 MHz; DMSO-d_6) 205.5 (s), 172.6 (s), 136.2 (s), 125.8 (s), 123.8 (d), 120.2 (d), 120.1 (d), 117.8 (d), 115.0 (s), 111.1 (d), 59.9 (t), 50.7 (t), 47.0 (s), 30.1 (q), 13.8 (q); *m*/*z* (ESI) 373 ($[M - H]^-$, 62%), 315 (100).

Dimethyl 2,2-di(1*H*-indol-3-yl)-3-methoxysuccinate 3d

The procedure above was used starting with dimethyl methoxyoxalacetate.[20,21] Yield 66%, mp 225–227 °C; ν_{max}(KBr)/cm^{-1} 3433, 3358, 3124w, 3057w, 2952w, 2907w, 2831w, 1726, 1643, 1457, 1434, 1339, 1225, 1104, 1004, 729; δ_H (300 MHz; DMSO-d_6) 11.03 (1H, s, NH), 11.00 (1H, s, NH), 7.38 (1H, d, *J* 2.5, ArH), 7.30–7.28 (3H, m, ArH), 6.92–6.77 (4H, m, ArH), 6.64–6.58 (2H, m, ArH), 5.09 (1H, s, CH), 3.55 (3H, s, OCH_3), 3.36 (3H, s, OCH_3), 3.28 (3H, s, OCH_3); δ_C (75.4 MHz; DMSO-d_6) 171.7 (s), 170.4 (s), 136.0 (s), 136.0 (s), 126.9 (s), 126.8 (s), 125.4 (d), 125.3 (d), 121.1 (d), 121.0 (d), 120.3 (d), 120.2 (d), 117.9 (d), 117.9 (d), 112.2 (s), 111.5 (s), 111.1 (d), 111.1 (d), 84.8 (d), 58.5 (q), 55.1 (s), 52.0 (q), 51.4 (q); *m*/*z* (EI) 406 (M^+, 5%), 304 (22), 303 (100), 243 (15) [Found: HRMS (EI) *m*/*z* 406.1524. $C_{23}H_{22}N_2O_5$ requires *M*, 406.1529].

Dimethyl 2,2-di(1*H*-indol-3-yl)succinate 3e

The procedure above was used starting with dimethyl oxalacetate.[20,21] Yield 62%; mp 197–198 °C (lit.,[10] 196–198 °C); ν_{max}(KBr)/cm^{-1} 3396, 3059, 2945, 1724, 1457, 1440, 1356, 1346, 1243, 1107, 1084, 967, 744; δ_H (300 MHz; DMSO-d_6) 11.03 (2H, d, *J* 2.0, NH), 7.56 (2H, d, *J* 2.5, ArH), 7.31 (2H, d, *J* 8.1, ArH), 7.02 (2H, d, *J* 8.1, ArH), 6.93 (2H, app. t, *J* 7.3, ArH), 6.67 (2H, app. t, *J* 7.3, ArH), 3.71 (2H, s, CH_2), 3.59 (3H, s, CH_3), 3.44 (3H, s, CH_3); δ_C (75.4 MHz; DMSO-d_6) 172.9 (s), 170.9 (s), 136.4 (s), 125.7 (s), 124.1 (d), 120.5 (d), 120.0 (d), 118.1 (d), 114.6 (s), 111.4 (d), 51.8 (q), 51.2 (q), 47.7 (s), 42.4 (t).

N-Benzyl-3,3-di(1*H*-indol-3-yl)succinimide 4a

A mixture of **3b** (8.08 g, 20 mmol) and benzylamine (20 cm^3) was refluxed under N_2 for 16 h. The mixture was allowed to cool, and diluted with ethanol (25 cm^3). The solution was slowly added to vigorously stirred aq. hydrochloric acid (2 M; 200 cm^3). The pinkish precipitate was collected, dried and crystallized from diisopropyl ether–propan-2-ol (2:1; approx. 200 cm^3) to give a white solid, which was dried at 130 °C (9 mmHg). Yield 5.88 g (70%); mp 177–180 °C (Found: C, 77.36; H, 5.06; N, 9.66. $C_{27}H_{21}N_3O_2$ requires C, 77.31; H, 5.05; N, 10.02%); ν_{max}(KBr)/cm^{-1} 3380, 1770, 1690, 1390, 1335, 1165, 750, 700; δ_H (300 MHz; DMSO-d_6) 11.10 (2H, d, *J* 1.9, 2 × NH), 7.38 (2H, d, *J* 8.1, ArH), 7.33–7.27 (5H, m, ArH), 7.24 (2H, d, *J* 8.0, ArH), 7.18 (2H, d, *J* 2.5, ArH), 7.05 (2H, app. t, *J* 7.2, ArH), 6.83 (2H, app. t, *J* 7.5, ArH), 4.73 (2H, s, $CH_2C_6H_5$), 3.66 (2H, s, CH_2); δ_C (75.4 MHz; DMSO-d_6) 178.4 (s), 175.4 (s), 137.1 (s), 136.1 (s), 128.5 (d), 127.8 (d), 127.6 (d), 125.3 (s), 123.6 (d), 121.3 (d), 119.9 (d), 118.7 (d), 114.7 (s), 111.9 (d), 47.5 (s), 43.6 (t), 41.8 (t); *m*/*z* (ESI) 418 ($[M - H]^-$, 100%).

3,3-Di(1*H*-indol-3-yl)-*N*-(2-piperazinoethyl)succinimide 4b

The diester **3b** (1.11 g, 2.75 mmol) was heated in *N*-(2-aminoethyl)piperazine (6 cm^3) at 200 °C under N_2 for 18 h. After cooling, the mixture was poured into water (30 cm^3), producing a white precipitate. The product was collected by filtration, washed with water, and dried. Yield 0.99 g (82%), white solid; mp 145–148 °C; ν_{max}(KBr)/cm^{-1} 3406, 3055, 2942, 2816, 1771, 1698, 1458, 1400, 1336, 1151, 743; δ_H (300 MHz; DMSO-d_6) 11.07 (2H, d, *J* 1.4, 2 × NH), 7.37 (4H, m, ArH), 7.15 (2H, d, *J* 2.3, ArH), 7.06 (2H, app. t, *J* 7.5, ArH), 6.87 (2H, app. t, *J* 7.7, ArH), 3.63 (2H, m, CH_2), 3.55 (2H, s, CH_2), 2.66 (4H, m, 2 × CH_2), 2.48 (2H, m, CH_2), 2.28 (4H, m, 2 × CH_2); δ_C (75.4 MHz; DMSO-d_6) 178.5 (s), 175.3 (s), 137.0 (s), 125.2 (s), 123.7 (d), 121.2 (d), 119.8 (d), 118.6 (d), 114.8 (s), 111.8 (d), 55.3 (t), 54.0 (t), 47.3 (s), 45.5 (t), 43.6 (t), 35.5 (t); *m*/*z* (ESI) 442 ($[M + H]^+$, 100%) [Found: HRMS (EI) *m*/*z* 441.2173. $C_{26}H_{27}N_5O_2$ requires *M*, 441.2165].

N-Amino-3,3-di(1*H*-indol-3-yl)succinimide 4c

Diethyl 2,2-di(1*H*-indol-3-yl)succinate **3b** (4.32 g, 10 mmol) and hydrazine hydrate (20 cm^3) were heated at reflux under nitrogen for 3 h. The clear solution was cooled and poured into water. The solid formed was collected, washed with water, and dried. Recrystallization from ethanol gave **4c** as a white solid (2.90 g, 78%); mp 274–275 °C (Found: C, 69.65; H, 4.72; N, 16.47. $C_{20}H_{16}N_4O_2$ requires C, 69.76; H, 4.68; N, 16.27%); ν_{max}(KBr)/cm^{-1} 3346, 3302, 3243, 1783, 1706br, 1196, 1112, 754, 744; δ_H (300 MHz; DMSO-d_6) 11.04 (2H, d, *J* 1.6, 2 × NH), 7.36 (2H, d, *J* 8.1, ArH), 7.30 (2H, d, *J* 8.0, ArH), 7.19 (2H, d, *J* 2.5, ArH), 7.05 (2H, app. t, *J* 7.2, ArH), 6.86 (2H, app. t, *J* 7.3, ArH), 5.16 (2H, s, NH_2), 3.51 (2H, s, CH_2); δ_C (75.4 MHz; DMSO-d_6) 176.5 (s), 173.2 (s), 137.0 (s), 125.2 (s), 123.4 (d), 121.2 (d), 119.9 (d), 118.6 (d), 114.9 (s), 111.7 (d), 45.7 (s), 42.1 (t); *m*/*z* (ESI) 343 ($[M - H]^-$, 100%).

3,3-Di(1*H*-indol-3-yl)succinimide 4d

N-Amino-3,3-di(1*H*-indol-3-yl)succinimide **4c** (744 mg, 2 mmol) was dissolved in 1,4-dioxane (20 cm^3). Raney-nickel (≈8 g) was added and the mixture was refluxed for 4 h. After filtration and concentration water was added, and the solid formed was collected, dried and finally purified by column chromatography (ethyl acetate) on silica gel to yield **4d** as a white solid (400 mg, 58%), mp 268–269 °C (Found: C, 72.86; H, 4.69; N, 12.63. $C_{20}H_{15}N_3O_2$ requires C, 72.94; H, 4.59; N, 12.76%); ν_{max}(KBr)/cm^{-1} 3413, 3366, 3184, 3057w, 1762, 1715br, 1458, 1419, 1339, 1184, 742; δ_H (300 MHz; DMSO-d_6) 11.48 (1H, br s, NH), 11.05 (2H, d, *J* 1.9, 2 × NH), 7.36 (2H, d, *J* 8.1, ArH), 7.30 (2H, d, *J* 8.0, ArH), 7.19 (2H, d, *J* 2.5, ArH), 7.04 (2H, app. t, *J* 7.2, ArH), 6.87 (2H, app. t, *J* 7.5, ArH), 3.52 (2H, s, CH_2); δ_C (75.4 MHz; DMSO-d_6) 180.2 (s), 177.1 (s), 137.1 (s), 125.4 (s), 123.4 (d), 121.3 (d), 120.0 (d), 118.7 (d), 115.1 (s), 111.9 (d), 48.8 (s), 44.9 (t); *m*/*z* (ESI) 328 ($[M - H]^-$, 100%).

Preparation of compound 9 from 6a

Compound **6a** (604 mg, 2 mmol) was dissolved in TFA (3 cm^3) at 25 °C. A red solution was quickly obtained and the dimeric product started to precipitate within 2 min. The solid formed was collected after 30 min, washed with propan-2-ol and dried; yield 602 mg (100%); mp 338–339 °C (Found: C, 75.28; H, 4.77; N, 9.25. $C_{38}H_{28}N_4O_4$ requires C, 75.48; H, 4.67; N, 9.27%); ν_{max}(KBr)/cm^{-1} 3385, 3320, 3030w, 1770w, 1697s, 1433, 1339, 1177, 740, 701; δ_H (300 MHz; DMSO-d_6) 11.88 (1H, s, NH), 11.24 (1H, d, *J* 2.2, NH), 7.43–7.39 (2H, m, ArH), 7.33

(5H, m, ArH), 7.26 (5H, m, ArH), 7.16–7.06 (3H, m, ArH), 6.97–6.90 (2H, m, ArH), 6.85 (1H, d, *J* 7.9, ArH), 6.74 (1H, app. t, *J* 7.2, ArH), 4.78 (1H, d, *J* 14.6, C*H*H), 4.72 (1H, d, *J* 14.6, CH*H*), 4.67 (1H, d, *J* 14.8, C*H*H), 4.63 (1H, d, *J* 14.8, CH*H*), 4.31 (1H, s, CH), 3.60 (1H, d, *J* 18.0, C*H*H), 3.00 (1H, d, *J* 18.0, CH*H*); δ_C (75.4 MHz; DMSO-d_6) 178.1 (s), 175.3 (s), 174.9 (s), 174.6 (s), 141.7 (s), 139.8 (s), 136.6 (s), 135.8 (s), 135.5 (s), 128.6 (d), 128.4 (d), 128.3 (d), 127.9 (d), 127.7 (d), 127.5 (d), 124.9 (d), 124.4 (s), 122.0 (d), 121.4 (d), 120.5 (s), 119.7 (d), 119.0 (d), 118.1 (s), 118.1 (d), 117.3 (d), 112.9 (d), 112.0 (d), 111.4 (s), 62.0 (d), 55.8 (s), 51.9 (s), 42.6 (t), 42.0 (t), 37.1 (t); *m*/*z* (ESI) 605 ([M + H]$^+$, 58%), 488 (60), 303 (100).

Preparation of compound 9 from 4a

Compound **4a** (838 mg, 2 mmol) was dissolved in TFA (5 cm^3) at 25 °C. After 24 h at rt the solvent was evaporated and the residue was treated with propan-2-ol, yielding a pinkish solid, which was recrystallized from acetonitrile–*N*,*N*-dimethylacetamide; 450 mg (67%). This material was identical with that from the preparation above.

2,3,3a,3b,4,5,6,6a,6b,7-Decahydro-1*H*-dipyrrolo[3,4-*a*:3,4-*c*]-carbazole-1,3,4,6-tetraone 13

A mixture of (1*H*-indol-3-yl)maleimide[14] **6b** (106 mg, 0.5 mmol) and maleimide (56 mg, 0.58 mmol) in xylene (10 cm^3) was refluxed for 12 h. After cooling, the yellow precipitate was collected, washed with xylene and dried, yield 137 mg (89%); mp >260 °C; ν_{max}(KBr)/cm^{-1} 3368, 3198, 3026, 2792w, 1746, 1716br, 1642, 1466, 1351, 1286, 1149, 755; δ_H (300 MHz; DMSO-d_6) 11.14 (1H, s, NH), 11.02 (1H, s, NH), 8.37 (1H, d, *J* 7.7, ArH), 7.43 (1H, d, *J* 1.7, NH), 7.24 (1H, app. t, *J* 7.7, ArH), 6.75 (1H, d, *J* 8.2, ArH), 6.65 (1H, app. t, *J* 7.3, ArH), 4.51–4.47 (1H, m, CH), 3.71 (1H, dd, *J* 8.4, 5.5, CH), 3.64–3.58 (1H, m, CH), 3.33–3.30 (1H, partially obscured dd, CH); δ_C (75.4 MHz; DMSO-d_6) 177.3 (s), 175.1 (s), 175.1 (s), 168.0 (s), 157.0 (s), 147.1 (s), 133.8 (d), 127.3 (d), 120.1 (s), 116.8 (d), 113.3 (s), 109.9 (d), 60.3 (d), 43.9 (d), 42.4 (d), 39.6 (d); *m*/*z* (EI) 310 (M$^+$ + 1, 19%), 309 (M$^+$, 100), 238 (79), 212 (57), 167 (68), 141 (36), 84 (26) [Found: HRMS (EI) *m*/*z* 309.0761. $C_{16}H_{11}N_3O_4$ requires *M*, 309.0750].

5-Ethyl-2,3,3a,3b,4,5,6,6a,6b,7-decahydro-1*H*-dipyrrolo[3,4-*a*:3,4-*c*]carbazole-1,3,4,6-tetraone 14

The procedure above was used, but with *N*-ethylmaleimide (64 mg, 0.51 mmol) as the dienophile. Yellow solid; yield 136 mg (81%); mp >260 °C; ν_{max}(KBr)/cm^{-1} 3420, 3205br, 3058w, 2981w, 1775, 1746, 1702br, 1644, 1606, 1465, 1411, 1344, 1292, 1146, 1103, 754; δ_H (300 MHz; DMSO-d_6) 11.16 (1H, s, NH), 8.32 (1H, d, *J* 7.7, ArH), 7.46 (1H, d, *J* 1.5, NH), 7.22 (1H, dd, *J* 8.2, 7.6, ArH), 6.75 (1H, d, *J* 8.2, ArH), 6.62 (1H, app. t, *J* 7.2, ArH), 4.53–4.47 (1H, m, CH), 3.73–3.64 (2H, m, 2 × CH), 3.36 (1H, dd, *J* 5.4, 2.2, CH), 3.11 (2H, q, *J* 7.1, CH_2), 0.58 (3H, t, *J* 7.1, CH_3); δ_C (75.4 MHz; DMSO-d_6) 175.4 (s), 175.1 (s), 173.4 (s), 167.8 (s), 157.0 (s), 147.1 (s), 133.8 (d), 127.1 (d), 120.1 (s), 116.8 (d), 113.1 (s), 109.8 (d), 60.5 (d), 42.8 (d), 42.6 (d), 38.4 (d), 32.6 (t), 12.3 (q); *m*/*z* (EI) 338 (M$^+$ + 1, 21%), 337 (M$^+$, 100), 266 (39), 238 (18), 212 (45), 167 (65), 141 (21) [Found: HRMS (EI) *m*/*z* 337.1064. $C_{18}H_{15}N_3O_4$ requires *M*, 337.1063].

1,2,3,3a,3b,4,6,6a,6b,7-Decahydrofuro[3,4-*a*:3,4-*c*]carbazole-1,3,4,6-tetraone 15

(1*H*-Indol-3-yl)maleimide[14] **6b** (108 mg, 0.51 mmol) and maleic anhydride (73 mg, 0.74 mmol) were heated in xylene (12 cm^3) at reflux for 12 h. After cooling, the yellow precipitate was collected, washed with xylene and dried; yield 140 mg (88%); mp >260 °C; ν_{max}(KBr)/cm^{-1} 3434, 3158, 3062, 1777, 1704br, 1651, 1467, 1351, 1290, 1148, 980, 756; δ_H (300 MHz; DMSO-d_6) 11.38 (1H, s, NH), 8.37 (1H, d, *J* 7.7, ArH), 7.61 (1H, d, *J* 1.4, NH), 7.29 (1H, dd, *J* 8.2, 7.7, ArH), 6.80 (1H, d, *J* 8.1, ArH), 6.70 (1H, app. t, *J* 7.5, ArH), 4.61–4.57 (1H, m, CH), 4.13–4.02 (2H, m, 2 × CH), 3.51–3.49 (1H, m, CH); δ_C (75.4 MHz; DMSO-d_6) 174.4 (s), 171.5 (s), 168.3 (s), 167.7 (s), 157.0 (s), 147.1 (s), 134.3 (d), 127.4 (d), 120.0 (s), 117.5 (d), 113.6 (s), 110.3 (d), 59.9 (d), 44.1 (d), 42.4 (d), 39.8 (d); *m*/*z* (EI) 310 (M$^+$, 53%), 238 (66), 212 (50), 167 (100), 141 (23), 84 (20) [Found: HRMS (EI) *m*/*z* 310.0609. $C_{16}H_{10}N_2O_5$ requires *M*, 310.0590].

2,3,3a,3b,4,5,6,6a,7,11c-Decahydro-1*H*-dipyrrolo[3,4-*a*:3,4-*c*]-carbazole-1,3,4,6-tetraone 16

Compound **13** (30 mg, 0.097 mmol) was heated in 1,4-dioxane (6 cm^3) containing TFA (0.1 cm^3) at reflux for 18 h. After evaporation of the solvent, **16** was collected as an orange solid (30 mg, 100%); mp >260 °C; ν_{max}(KBr)/cm^{-1} 3373, 3241, 3070w, 1778, 1761br, 1455, 1359, 1327, 1178, 1118, 870, 745; δ_H (300 MHz; DMSO-d_6) 11.38 (1H, s, NH), 11.29 (1H, s, NH), 11.11 (1H, s, NH), 7.77 (1H, d, *J* 7.8, ArH), 7.38 (1H, d, *J* 8.0, ArH), 7.10 (1H, dd, *J* 8.0, 7.5, ArH), 7.00 (1H, dd, *J* 7.9, 7.5, ArH), 4.31 (1H, dd, *J* 8.0, 1.9, CH), 4.24 (1H, dd, *J* 7.3, 1.9, CH), 3.84 (1H, app. t, *J* 7.3, CH), 3.71 (1H, app. t, *J* 7.5, CH); δ_C (75.4 MHz; DMSO-d_6) 177.5 (s), 177.5 (s), 177.2 (s), 176.2 (s), 137.0 (s), 127.5 (s), 125.7 (s), 121.9 (d), 120.3 (d), 119.1 (d), 111.5 (d), 103.8 (s), 41.0 (d), 40.9 (d), 40.1 (d), 40.0 (d); *m*/*z* (EI) 310 (M$^+$ + 1, 18%), 309 (M$^+$, 100), 305 (17), 238 (43), 167 (60), 166 (15), 84 (28) [Found: HRMS (EI) *m*/z 309.0716. $C_{16}H_{11}N_3O_4$ requires *M*, 309.0750].

N-Benzyl-3,3-di(1*H*-indol-3-yl)-4-methoxysuccinimide 19

The diester **3d** (20.3 g, 50 mmol) was refluxed with benzylamine (25 cm^3) under nitrogen for 24 h in the presence of a catalytic amount of potassium cyanide (49 mg, 1 mmol). The mixture was allowed to cool and was then diluted with ethanol (25 cm^3). This solution was slowly added to vigorously stirred aq. hydrochloric acid (2 M; 250 cm^3). The precipitate formed was collected, dried and crystallized from propan-2-ol–water to yield **19** as a whitish solid (20.2 g, 90%), mp 186 °C; ν_{max}(KBr)/cm^{-1} 3394, 3347, 3062w, 2941w, 1695s, 1458, 1430, 1392, 1338, 1132, 1107, 1074, 744; δ_H (300 MHz; DMSO-d_6) 11.18 (1H, s, NH), 11.05 (1H, s, NH), 7.39–7.22 (7H, m, ArH), 7.12–6.97 (6H, m, ArH), 6.82 (1H, app. t, *J* 7.4, ArH), 6.71 (1H, app. t, *J* 7.4, ArH), 5.08 (1H, s, CH), 4.68 (2H, s, CH_2), 3.42 (3H, s, CH_3); δ_C (75.4 MHz; DMSO-d_6) 176.4 (s), 175.7 (s), 137.7 (s), 137.1 (s), 136.6 (s), 129.3 (d), 128.4 (d), 128.3 (d), 127.4 (s), 126.5 (s), 125.7 (d), 124.5 (d), 122.1 (d), 121.6 (d), 121.4 (d), 119.5 (d), 119.1 (d), 113.8 (s), 112.5 (d), 112.3 (d), 111.3 (d), 84.3 (d), 60.5 (q), 54.0 (s), 42.2 (t); *m*/*z* (EI) 449 (M$^+$, 31%), 332 (33), 273 (21), 245 (23), 243 (28), 156 (100), 128 (62), 117 (84), 91 (88) [Found: HRMS (EI) *m*/*z* 449.1745. $C_{28}H_{23}N_3O_3$ requires *M*, 449.1739].

Treatment of 19 with TFA

Compound **19** (2.25 g, 5 mmol) was dissolved in TFA (10 cm^3). After 24 h the solution was poured into water and the reddish solid was collected, washed with water, and dried. The mixture obtained was subjected to gradient chromatography on silica gel, starting with dichloromethane with slowly increasing amounts of methanol. This operation gave a yellowish solid identified as the cleavage product *N*-benzyl-3-(1*H*-indol-3-yl)-4-methoxymaleimide **20a** (0.75 g, 2.25 mmol) and a reddish-violet compound (mp 286–287 °C) identified as **21** (1.60 g, 3.84 mmol). The spectral data of **21** were identical with those previously published.[22] Data for compound **20a**: mp 174–176 °C (Found: C, 72.08; H, 4.76; N, 8.34. $C_{20}H_{16}N_2O_3$ requires C, 72.28; H, 4.85; N, 8.43%); ν_{max}(KBr)/cm^{-1} 3294, 1700br, 1655, 1529, 1455, 1438, 1423, 1360, 1236, 748; δ_H (300 MHz; DMSO-d_6) 11.72 (1H, br s, NH), 7.87–7.84 (2H, m, ArH), 7.44

(1H, d, *J* 8.0, ArH), 7.36–7.26 (5H, m, ArH), 7.16 (1H, app. t, *J* 8.1, ArH), 7.08 (1H, app. t, *J* 8.0, ArH), 4.65 (2H, s, CH_2), 4.17 (3H, s, CH_3); δ_C (75.4 MHz; DMSO-d_6) 169.8 (s), 166.1 (s), 145.0 (s), 136.9 (s), 136.1 (s), 128.5 (d), 128.0 (d), 127.2 (d), 125.6 (s), 121.8 (d), 121.4 (d), 119.7 (d), 112.3 (s), 111.8 (d), 103.1 (s), 59.7 (q), 40.4 (t); *m*/*z* (ESI) 333 ($[M + H]^+$, 100%).

N-Benzyl-3-chloro-4-(1*H*-indol-3-yl)maleimide 20b

Indole (2.34 g, 20 mmol) as a solution in benzene (20 cm^3) was added under nitrogen to ethylmagnesium bromide (20 mmol) in diethyl ether (30 cm^3). The solution was stirred for 30 min, whereupon a solution of *N*-benzyl-3,4-dichloromaleimide (5.12 g, 20 mmol) in benzene (20 cm^3) was added dropwise at reflux. After a reflux period of 4 h the mixture was cooled and treated with saturated aq. ammonium chloride (60 cm^3). The organic layer was separated, washed with water, and dried ($MgSO_4$). The crude product obtained after evaporation was purified on a silica gel column using dichloromethane as eluent to give **20b** (4.50 g, 65%) as orange-red crystals, mp 203 °C; ν_{max}(KBr)/cm^{-1} 3283br, 1770, 1699br, 1595, 1430, 1400, 1185, 1117, 742; δ_H (300 MHz; DMSO-d_6) 12.20 (1H, s, NH), 8.13 (1H, d, *J* 3.0, ArH), 7.97 (1H, d, *J* 7.8, ArH), 7.53 (1H, d, *J* 7.8, ArH), 7.34–7.14 (7H, m, ArH), 4.72 (2H, s, CH_2); δ_C (75.4 MHz; DMSO-d_6) 168.3 (s), 165.8 (s), 136.6 (s), 136.5 (s), 133.5 (s), 131.6 (d), 128.6 (d), 127.4 (d), 127.4 (d), 124.7 (s), 122.6 (d), 122.2 (d), 121.4 (s), 120.7 (d), 112.4 (d), 103.3 (s), 41.5 (t); *m*/*z* (EI) 338 (34%), 336 (100), 273 (23), 245 (9), 204 (10), 177 (12), 175 (21), 168 (27), 149 (11), 140 (16), 113 (13), 91 (20) [Found: HRMS (EI) *m*/*z* 336.0664. $C_{19}H_{13}{}^{35}ClN_2O_2$ requires *M*, 336.0666].

Independent synthesis of *N*-benzyl-3-(1*H*-indol-3-yl)-4-methoxymaleimide 20a

The chloro compound **20b** (343 mg, 1 mmol) was dissolved in acetonitrile (10 cm^3) and added to methanol (15 cm^3) wherein sodium (50 mg, 2.2 mmol) had been dissolved. The solution was refluxed for 1 h wherewith sodium chloride precipitated. Water (30 cm^3) was slowly added and yellow-orange crystals were formed and collected (310 mg, 92%). Spectral data were identical with those of **20a** obtained by treatment of **19** with TFA.

General procedure for preparation of maleimides 22a–e

The requisite aniline (0.1 mol) was dissolved in dry diethyl ether (150 cm^3) and dimethyl acetylenedicarboxylate (0.1 mol) was added. The resulting mixture was stirred at rt for 1 h, followed by addition of the appropriate amine (0.1 mol) and gentle heating. After 24 h at rt the products **22a**–**e** were collected. Recrystallization from propan-2-ol–ethanol gave the pure maleimides.

3-(2,4-Dimethoxyanilino)-*N*-methylmaleimide 22a. Yellow solid, yield 84%; mp 187 °C; ν_{max}(KBr)/cm^{-1} 3362, 2941w, 2832w, 1770, 1705, 1655, 1610, 1536, 1488, 1450, 1391, 1238, 1119, 1046, 1015, 764; δ_H (300 MHz; DMSO-d_6) 8.16 (1H, br s, NH), 7.02 (1H, d, *J* 9.0, ArH), 6.79 (1H, d, *J* 2.9, ArH), 6.68 (1H, dd, *J* 8.9, 2.9, ArH), 5.51 (1H, s, CH), 3.81 (3H, s, OCH_3), 3.72 (3H, s, OCH_3), 2.87 (3H, s, NCH_3); δ_C (75.4 MHz; DMSO-d_6) 172.4 (s), 167.8 (s), 153.6 (s), 143.9 (s), 142.6 (s), 128.0 (s), 112.4 (d), 109.0 (d), 105.5 (d), 88.9 (d), 56.4 (q), 55.6 (q), 23.5 (q); *m*/*z* (ESI) 263 ($[M + H]^+$, 100%) [Found: HRMS (EI) *m*/*z* 262.0887. $C_{13}H_{14}N_2O_4$ requires *M*, 262.0954].

***N*-Ethyl-3-(4-methoxyanilino)maleimide 22b.** Yellow plates, yield 75%; mp 145 °C (Found: C, 63.34; H, 5.82; N, 11.35. $C_{13}H_{14}N_2O_3$ requires C, 63.40; H, 5.73; N, 11.38%); ν_{max}(KBr)/cm^{-1} 3316, 3160, 2978w, 2934w, 2829w, 1766, 1693, 1644, 1623, 1540, 1513, 1444, 1415, 1256, 1180, 1038, 823, 777; δ_H (300 MHz; DMSO-d_6) 9.61 (1H, s, NH), 7.31 (2H, d, *J* 9.0, ArH), 6.91 (2H, d, *J* 9.0, ArH), 5.44 (1H, s, CH), 3.72 (3H, s, OCH_3), 3.42 (2H, q, *J* 7.2, CH_2), 1.08 (3H, t, *J* 7.2, CH_3); δ_C (75.4 MHz; DMSO-d_6) 172.3 (s), 167.4 (s), 155.8 (s), 144.2 (s), 132.5 (s), 121.2 (d), 114.5 (d), 86.4 (d), 55.3 (q), 31.9 (t), 13.9 (q); *m*/*z* (ESI) 247 ($[M + H]^+$, 100%).

3-(4-Methoxyanilino)-*N*-methylmaleimide 22c. Yellow solid, yield 78%; mp 182 °C (Found: C, 61.95; H, 5.12; N, 12.10. $C_{12}H_{12}N_2O_3$ requires C, 62.07; H, 5.21; N, 12.06%); ν_{max}(KBr)/cm^{-1} 3298, 3133w, 3073w, 1760, 1702, 1622, 1545, 1510, 1452, 1246, 1177, 1138, 1116, 1028, 842, 692; δ_H (300 MHz; DMSO-d_6) 9.56 (1H, br s, NH), 7.31 (2H, d, *J* 7.9, ArH), 6.92 (2H, d, *J* 7.9, ArH), 5.45 (1H, s, CH), 3.72 (3H, s, OCH_3), 2.87 (3H, s, NCH_3); δ_C (75.4 MHz; DMSO-d_6) 172.7 (s), 167.8 (s), 155.8 (s), 144.4 (s), 132.5 (s), 121.2 (d), 114.6 (d), 86.5 (d), 55.4 (q), 23.4 (q); *m*/*z* (ESI) 233 ($[M + H]^+$, 100%).

***N*-[3-(Dimethylamino)propyl]-3-(4-methoxyanilino)maleimide 22d.** Yellow needles, yield 88%; mp 148 °C (Found: C, 63.21; H, 7.10; N, 13.80. $C_{16}H_{21}N_3O_3$ requires C, 63.35; H, 6.98; N, 13.85%); ν_{max}(KBr)/cm^{-1} 3384br, 3063w, 2987w, 1725, 1646, 1522, 1418, 1342, 1231, 1198, 1144, 1033, 992, 744, 727; δ_H (400 MHz; DMSO-d_6) 9.52 (1H, s, NH), 7.32 (2H, d, *J* 9.0, ArH), 6.92 (2H, d, *J* 9.0, ArH), 5.44 (1H, s, CH), 3.73 (3H, s, OCH_3), 3.42 (2H, t, *J* 7.0, CH_2), 2.17 (2H, t, *J* 7.0, CH_2), 2.08 (6H, s, NMe_2), 1.61 (2H, m, CH_2); δ_C (100.6 MHz; DMSO-d_6) 172.3 (s), 167.4 (s), 155.6 (s), 144.0 (s), 132.3 (s), 121.0 (d), 114.3 (d), 86.2 (d), 56.3 (t), 55.1 (q), 45.0 (q), 35.2 (t), 26.2 (t); *m*/*z* (ESI) 304 ($[M + H]^+$, 56%), 259 (100).

3-(4-Methoxyanilino)maleimide 22e. Pale green solid, yield 78%; mp 208 °C (Found: C, 60.49; H, 4.57; N, 12.77. $C_{11}H_{10}N_2O_3$ requires C, 60.55; H, 4.62; N, 12.84%); ν_{max}(KBr)/cm^{-1} 3274, 2969w, 2846w, 1766, 1692, 1618, 1529, 1512, 1350, 1250, 1230, 1106, 1012, 830, 777, 767; δ_H (300 MHz; DMSO-d_6) 10.48 (1H, s, NH), 9.44 (1H, s, NH), 7.31 (2H, d, *J* 9.0, ArH), 6.92 (2H, d, *J* 9.0, ArH), 5.39 (1H, d, *J* 1.1, CH), 3.74 (3H, s, OCH_3); δ_C (75.4 MHz; DMSO-d_6) 173.8 (s), 169.2 (s), 155.6 (s), 144.3 (s), 132.6 (s), 121.0 (d), 114.5 (d), 87.7 (d), 55.3 (q); *m*/*z* (ESI) 217 ($[M - H]^-$, 100%).

N-Methyl-3-(2-methyl-1*H*-indol-3-yl)maleimide 23

The maleimide **22c** (232 mg, 1 mmol) and 2-methylindole (131 mg, 1 mmol) were heated at reflux in acetic acid (5 cm^3) for 3 h. The mixture was allowed to cool and the solvent was evaporated. Trituration of the residue with diethyl ether gave a solid, which was collected, washed with diethyl ether, and finally crystallized from propan-2-ol to yield **23** (110 mg, 46%) as a yellow solid, mp 213 °C (Found: C, 69.86; H, 5.12; N, 11.55. $C_{14}H_{12}N_2O_2$ requires C, 69.99; H, 5.03; N, 11.66%); ν_{max}(KBr)/cm^{-1} 3318, 1758w, 1694, 1607, 1453, 1425, 1388, 1230, 837, 746; δ_H (300 MHz; DMSO-d_6) 11.81 (1H, br s, NH), 7.73 (1H, d, *J* 7.4, ArH), 7.35 (1H, d, *J* 8.0, ArH), 7.14–7.04 (2H, m, ArH), 6.69 (1H, s, CH), 2.95 (3H, s, CH_3), 2.55 (3H, s, CH_3); δ_C (75.4 MHz; DMSO-d_6) 171.4 (s), 171.0 (s), 141.6 (s), 140.2 (s), 135.6 (s), 126.6 (s), 121.7 (d), 120.4 (d), 120.3 (d), 119.9 (d), 111.1 (d), 102.6 (s), 23.6 (q), 13.9 (q); *m*/*z* (ESI) 239 ($[M - H]^-$, 100%).

6,8-Dimethoxy-2-methyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,4-*c*]-quinoline-1,3-dione-4-spiro-3′-(1′-methylpyrrolidine-2′,5′-dione) 24

Compound **22a** (500 mg, 1.91 mmol) was dissolved in TFA (5 cm^3) and after a short period (5 min) of reflux the solvent was evaporated and the residue treated with propan-2-ol to yield **24** (284 mg, 70%) in pure form as a blue-violet solid, mp 255 °C (Found: C, 58.08; H, 4.65; N, 11.38. $C_{18}H_{17}N_3O_6$ requires C, 58.22; H, 4.61; N, 11.32%); λ_{max}(EtOH) /nm 299, 375, 582; ν_{max}(KBr)/cm^{-1} 3348, 2943w, 1764, 1701br, 1653,

1482, 1437, 1382, 1151, 990; δ_H (400 MHz; DMSO-d_6) 7.04 (1H, d, *J* 2.6, ArH), 6.58 (1H, d, *J* 2.6, ArH), 6.57 (1H, s, NH), 3.82 (3H, s, OCH_3), 3.71 (3H, s, OCH_3), 3.29 (1H, d, *J* 17.9, C*H*H), 2.91 (3H, s, NCH_3), 2.89 (3H, s, NCH_3), 2.88 (1H, d, *J* 18.0, CH*H*); δ_C (100.6 MHz; DMSO-d_6) 175.4 (s), 173.4 (s), 168.3 (s), 168.2 (s), 151.3 (s), 146.0 (s), 134.8 (s), 130.2 (s), 125.7 (s), 108.9 (s), 103.6 (d), 98.9 (d), 59.7 (s), 55.3 (q), 55.0 (q), 47.3 (t), 24.0 (q), 22.8 (q); *m*/*z* (ESI) 372 ([M + H]$^+$, 100%), 313 (91) [Found: HRMS (EI) *m*/*z* 371.1121. $C_{18}H_{17}N_3O_6$ requires *M*, 371.1117].

8-Methoxy-2-methyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,4-*c*]-quinoline-1,3-dione-4-spiro-3′-(1′-methylpyrrolidine-2′,5′-dione) 25

The maleimide **22c** (464 mg, 2 mmol) was refluxed in TFA (10 cm^3) for 90 min. After cooling, the solvent was evaporated. The residue was subjected to column chromatography (40–50% ethyl acetate in hexane) to afford **25** (251 mg, 74%) as blue-violet crystals, mp 194–196 °C; λ_{max} (EtOH)/nm 303, 357, 562; ν_{max}(KBr)/cm^{-1} 3361, 2940w, 1782w, 1697br, 1433, 1374, 1285, 1136, 1042, 984, 749; δ_H (300 MHz; DMSO-d_6) 7.34 (1H, d, *J* 2.9, ArH), 6.91 (1H, br s, NH), 6.85 (1H, dd, *J* 8.9, 2.9, ArH), 6.50 (1H, d, *J* 8.9, ArH), 3.67 (3H, s, OCH_3), 3.38 (1H, d, *J* 18.2, C*H*H), 2.91 (3H, s, NCH_3), 2.86 (3H, s, NCH_3), 2.81 (1H, d, *J* 18.2, CH*H*); δ_C (75.4 MHz; DMSO-d_6) 175.2 (s), 173.5 (s), 168.2 (s), 168.2 (s), 151.2 (s), 139.6 (s), 134.6 (s), 125.7 (s), 120.9 (d), 114.4 (d), 110.1 (s), 108.7 (d), 59.8 (s), 55.4 (q), 46.3 (t), 24.5 (q), 23.4 (q); *m*/*z* (EI) 341 (M$^+$, 18%), 282 (7), 256 (100), 241 (27), 213 (7) [Found: HRMS (EI) *m*/*z* 341.1017. $C_{17}H_{15}N_3O_5$ requires *M*, 341.1012].

Acetylation of 25

Compound **25** (400 mg, 1.17 mmol) was refluxed in acetic anhydride (5 cm^3) for 2 h. Upon cooling, **26** (380 mg, 85%) was obtained as a yellowish crystalline solid, mp 255 °C; λ_{max} (EtOH)/nm 296, 346, 429; ν_{max}(KBr)/cm^{-1} 2940w, 1774, 1703, 1673, 1500, 1438, 1379, 1366, 1290, 1269, 1038, 1026; δ_H (300 MHz; DMSO-d_6) 7.59 (1H, d, *J* 3.0, ArH), 7.36 (1H, d, *J* 9.0, ArH), 7.09 (1H, dd, *J* 9.0, 3.0, ArH), 3.82 (3H, s, OCH_3), 3.32–3.27 (1H, partially obscured d, C*H*H), 3.16 (1H, d, *J* 18.3, CH*H*), 2.99 (3H, s, NCH_3), 2.90 (3H, s, NCH_3), 2.26 (3H, s, $COCH_3$); δ_C (75.4 MHz; DMSO-d_6) 173.7 (s), 172.7 (s), 171.3 (s), 167.4 (s), 166.9 (s), 156.6 (s), 134.4 (s), 132.3 (s), 129.1 (s), 125.3 (d), 119.2 (s), 116.6 (d), 110.2 (d), 62.8 (s), 55.6 (q), 41.4 (t), 25.1 (q), 24.0 (q), 23.6 (q); *m*/*z* (EI) 383 (M$^+$, 12%), 341 (28), 282 (7), 256 (100), 241 (13), 170 (17) [Found: HRMS (EI) *m*/*z* 383.1125. $C_{19}H_{17}N_3O_6$ requires *M*, 383.1117].

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