Pergamon

Tetrahedron 58 (2002) 1443–1452

TETRAHEDRON

Synthesis of indolocarbazole quinones; potent aryl hydrocarbon receptor ligands

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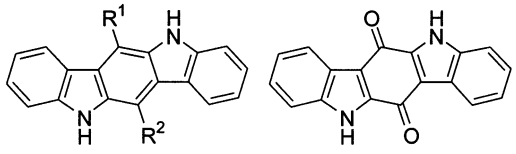
Received 12 October 2001; revised 21 November 2001; accepted 20 December 2001

Abstract—Syntheses of indolo[2,3-*b*]carbazole-6,12-dione and the isomeric indolo[3,2-*b*]carbazole-6,12-dione, an extremely efficient inducer of the aryl hydrocarbon (Ah) receptor are described. Initial oxidation of the parent indolo[3,2-*b*]carbazole followed by several different ring-closing strategies produced the latter compound. Entries into syntheses of unsymmetrical 6,12-disubstituted indolo[2,3-*b*]carbazoles are also described.

1. Background and introduction

In our continuous research directed towards the understanding of the aryl hydrocarbon (Ah) receptor,[1] two extremely efficient ligands, 6-formylindolo[3,2-*b*]carbazole[2] (**1**) and 6,12-diformylindolo[3,2-*b*]carbazole[3] (**2**) have been synthesised recently, thereby also confirming the structure of the products previously obtained upon UV-irradiation of an aqueous L-tryptophan solution.[4] The former compound (**1**) displays an affinity for the Ah receptor at picomolar concentration, thus being more potent than the highly toxic environmental pollutant 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD). As both **1** and **2** have been suggested to be endogenous ligands for the receptor,[5] the breakdown of these molecules in vitro and in vivo must be further studied. In addition, recent findings show that **1** acts as an anticarcinogen on benzo[*a*]pyrene induced mutagenesis both in vitro and in vivo (Fig. 1).[6]

The quinone **3** has previously been reported to possess low affinity for the Ah receptor,[7] which is in sharp contrast to recent studies which have established the compound to be extremely potent in the Ah receptor induced induction of CYP1A1 mRNA.[8] In this context, we became interested in its isomer indolo[2,3-*b*]carbazole-6,12-dione (**4**). Both these molecules are potential in vivo degradation products from the parent indolo[3,2-*b*]carbazole (**5**) and indolo[2,3-*b*]carbazole (**6**), respectively. We therefore set out to establish synthetic routes to **3** and **4**, which now has been accomplished (Fig. 2).



1 R^1=H, R^2=CHO
2 R^1=R^2=CHO
3

Figure 1.

2. Results

2.1. Indolo[3,2-*b*]carbazole-6,12-dione (3)

Since we wanted the corresponding quinone **3** as the precursor for the syntheses of various indolo[3,2-*b*]carbazoles, we started out according to the existing procedure reported in the literature for this compound.[9] Thus the reaction of chloroanil or bromoanil with aniline in pyridine was reported to give **3** in 50% yield, something that we could not repeat under a variety of conditions. Formation of the corresponding 2,5-dianilino-3,6-dibromo-*p*-benzoquinone using ethanol as the solvent has been established earlier.[10] Later, preparation of similar products from *N*-methylaniline confirmed that the attack of the aniline on chloroanil (or

Keywords: indole; quinone; carbazole; Ah receptor.

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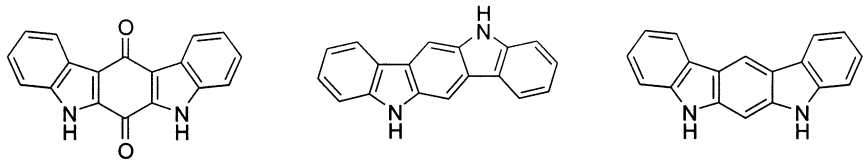
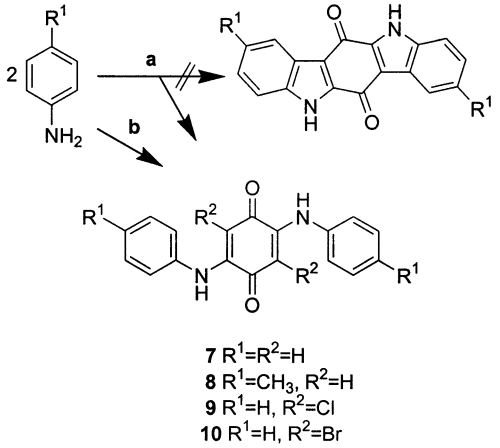
PII: S0040-4020(02)00006-6



4 **5** **6**

Figure 2.

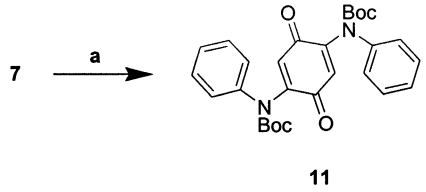


7 $R^1=R^2=H$
8 $R^1=CH_3$, $R^2=H$
9 $R^1=H$, $R^2=Cl$
10 $R^1=H$, $R^2=Br$

Scheme 1. (a) 1.0 equiv. bromoanil, pyridine, rx. (b) 3.0 equiv. *p*-benzoquinone, EtOH, rx.

bromoanil) occurs in the 2 and 5 positions.[11] Furthermore, the other possible isomer (2,6-disubsituted) was not detected in this study. In contrast to the claimed quinone structures, we could only obtain a small amount of the dehalogenated compound 2,5-dianilino-*p*-benzoquinone[12] (**7**) (Scheme 1). A similar result was observed if *p*-toluidine and bromoanil were reacted in pyridine, thus producing 2,5-di(*p*-toluidino)-*p*-benzoquinone (**8**), which could also be obtained from *p*-toluidine and *p*-benzoquinone in ethanol[13] (Scheme 1). Similar reductive dehalogenations have previously been reported, wherein dibromodiiodoquinone upon treatment with a large excess of aniline in toluene produced **7**.[14] Further, it has been reported that 2,5-dianilino-3,6-diiodo-*p*-benzoquinone produced iodine vapour and small quantities of **7** upon heating in nitrobenzene.[15] In connection with all these studies, we have also developed a quick and convenient technique for the preparation of 2,5-dianilino-3,6-dichloro-*p*-benzoquinone (**9**). Attempts to produce the corresponding 2,5-dianilino-3,6-dibromo-*p*-benzoquinone (**10**) with the same procedure instead produced the debrominated quinone **7** in a good yield. This reductive elimination of bromine is similar to the one reported by Hallas and co-workers who established that in the reaction between bromoanil and two aromatic amines the first step involves an addition–elimination and the second step is a reduction, thus producing a product free from bromine.[16]

In the reaction between aniline and *p*-benzoquinone in ethanol, **7** is produced.[12a] However, the very limited solubility of **7** prevents further transformations. To increase the solubility, **7** was protected with *tert*-butyloxycarbonyl groups to produce **11** in 87% yield as outlined in



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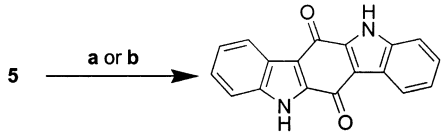
Scheme 2. (a) Boc_2O, DMAP, THF, 21°C (87%).

Scheme 2. Since the syntheses of various substituted indoloquinones have previously frequently been effected using $Pd(OAc)_2$ in acetic acid as the ring cyclisation reagent,[17] we subjected **7** and **11** to similar conditions, which however failed to produce **3**. In a series of experiments using a microwave reactor, several substituted 2,5-di(anilino)-1,4-benzoquinones were irradiated in $Pd(OAc)_2$–AcOH mixtures without satisfactory results. With these discomforting results, other approaches obviously had to be considered.

Interestingly, in the late 1920s, Clar and John had already oxidised pentacene to the corresponding pentacene-6,13-dione with CrO_3 in acetic acid.[18] A similar treatment of **5** afforded the desired product **3** in 34% (Scheme 3). The spectroscopic data, (IR), given by Osman et al.[9] were different from ours, thus indicating that all the purported penta and heptacyclic quinones obtained from chloroanil (or bromoanil) and anilines must be reconsidered.



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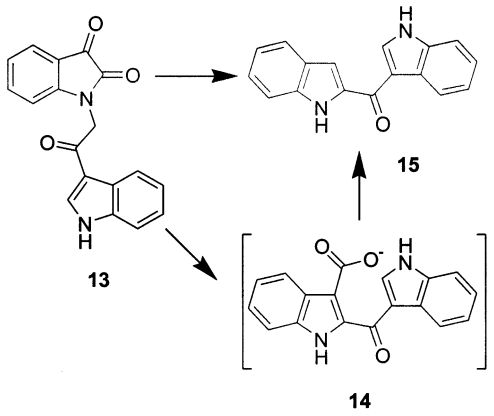
Scheme 3. (a) CrO_3, H_2O, AcOH, 21°C (34%). (b) DMSO, H_2O_2, UV-light, heat.

In this context, we noted that indolo[3,2-*b*]carbazole (**5**) upon standing for several months in DMSO-d_6 with access to light/air started to decompose. In the ^1H NMR spectrum of **5**, signals from **3** could be recognised. This led us to add a drop of 30% hydrogen peroxide to see if the process could be speeded up. As expected, the oxidation process was much faster and within a week, **5** had been completely converted into **3**. To further accelerate this oxidation, a solution of **5** in DMSO-d_6, together with a drop of 30% hydrogen peroxide, were exposed to moderate heating and UV-light to transform **5** into **3** as the main product in only 6 h when monitored by ^1H NMR spectroscopy. This procedure does produce hydroxyl radicals among other reactive species and



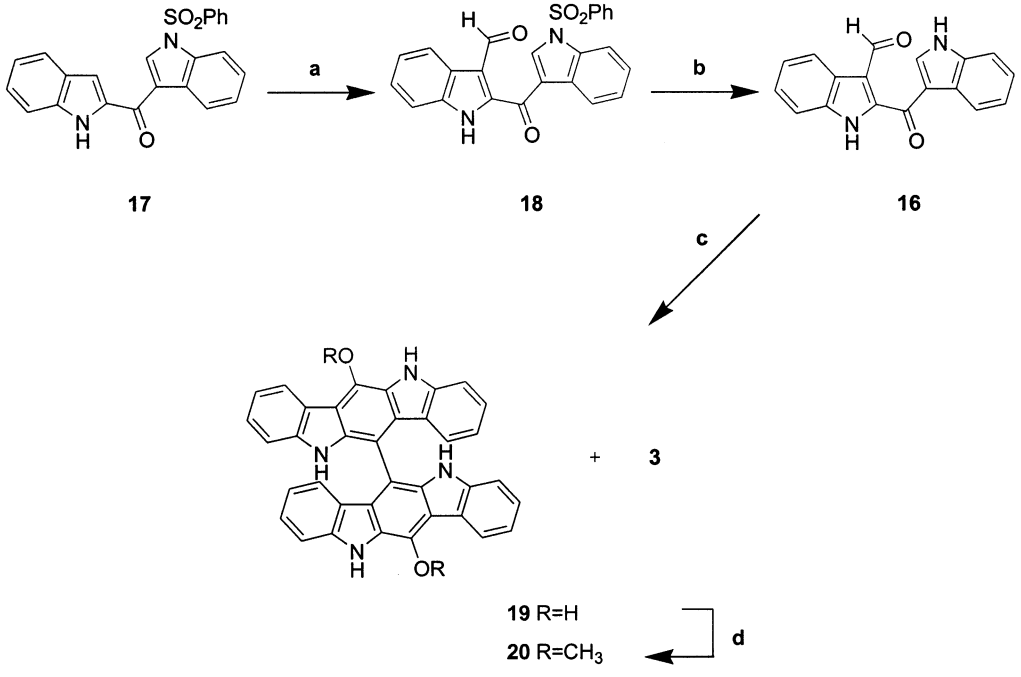
Scheme 4. Formation of 2,3-diindolylketone **15**.

would thus mimic the mode of action of certain P450 cytochromes[19] involved in the oxidation of aromatic molecules. It seems likely that **3** can be one of the degradation products from **5** formed in vivo.

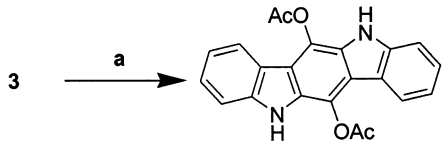
We have also prepared 5,11-dimethylindolo[3,2-*b*]carbazole-6,12-dione (**12**) according to Szmuszkovicz[20] in a double condensation of 1-methylindole-2-carbonyl chloride, catalysed by $AlCl_3$. As the removal of a methyl group from an indole nitrogen has been reported to proceed using forcing conditions, **12** was treated with strong acids[21] and oxidising agents,[22] but no satisfactory demethylation to **3** took place. In order to facilitate deprotection, we prepared 1-benzylindole-2-carbonyl chloride[23] and reacted this compound at different temperatures with Lewis acids. As debenzylation of 1-benzyl-2-acylindoles induced by $AlCl_3$ has been reported previously,[24] we hoped that a ring closure would precede this reaction. However, we could only observe degradation of the starting material. Use of $ZnCl_2$ as catalyst did in fact lead to 5,11-dibenzylindolo[3,2-*b*]carbazole-6,12-dione, as judged by NMR spectroscopy and low-resolution mass, but the low yield (1%) did not encourage further efforts towards this precursor. In a last attempt in this cyclisation strategy, we prepared *tert*-butyloxycarbonylindole-2-carbonyl chloride in situ from the corresponding acid using oxalyl chloride–DMF in CH_2Cl_2, and treated this compound under several different conditions without detecting any trace of **3**.

One interesting precursor for a ring closure, which might produce **3**, had earlier been prepared in situ. By reacting isatin and 3-chloroacetylindole, Jackson and co-workers obtained the indole-2,3-dione derivative **13** in low yield. After basic hydrolysis, **15** could be obtained in 81% yield via the indoledione–indole rearrangement[25] and an in situ decarboxylation of **14** (Scheme 4).[26]

To obtain a substrate suitable for ring closure similar to **14**, we started out with **15**, prepared according to an alternative route.[2b] Formylation using Vilsmeier–Arnold–Haack conditions now produced a complex reaction mixture and the desired **16** could only be obtained in 16% yield. To prevent possible side reactions, the *N*-benzensulfonyl protected ketone **17** was reacted with chloromethylenemorpholinium chloride[27] (freshly prepared) to produce **18** in 89% yield. Deprotection of **18** with K_2CO_3 in MeOH–H_2O, produced the desired aldehyde **16** in 88% yield (Scheme 5). Ring closure of **16** using EtOH–HCl at reflux produced the anticipated quinone **3** after oxidation in situ together with the symmetrical dimer **19**. As the isolation of **19** was troublesome, this product was first *O*-methylated to produce **20** and then finally isolated by chromatography on aluminium oxide. The yields of **3** and **20** varied depending on the workup procedure. Upon reacting **16** with aq. HCl in EtOH at reflux for 0.5 h followed by stirring of the resulting



Scheme 5. (a) Chloromethylenemorpholinium chloride, $CHClCCl_2$, 22–50°C (89%). (b) K_2CO_3, MeOH–H_2O, 21°C (88%). (c) HCl, EtOH, rx, (58% of **3**). (d) CH_2N_2, Et_2O, 21°C (17% of **20**).



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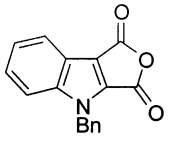
Scheme 6. (a) Ac_2O, NaOAc, Zn (s) (68%).



22

Figure 3.

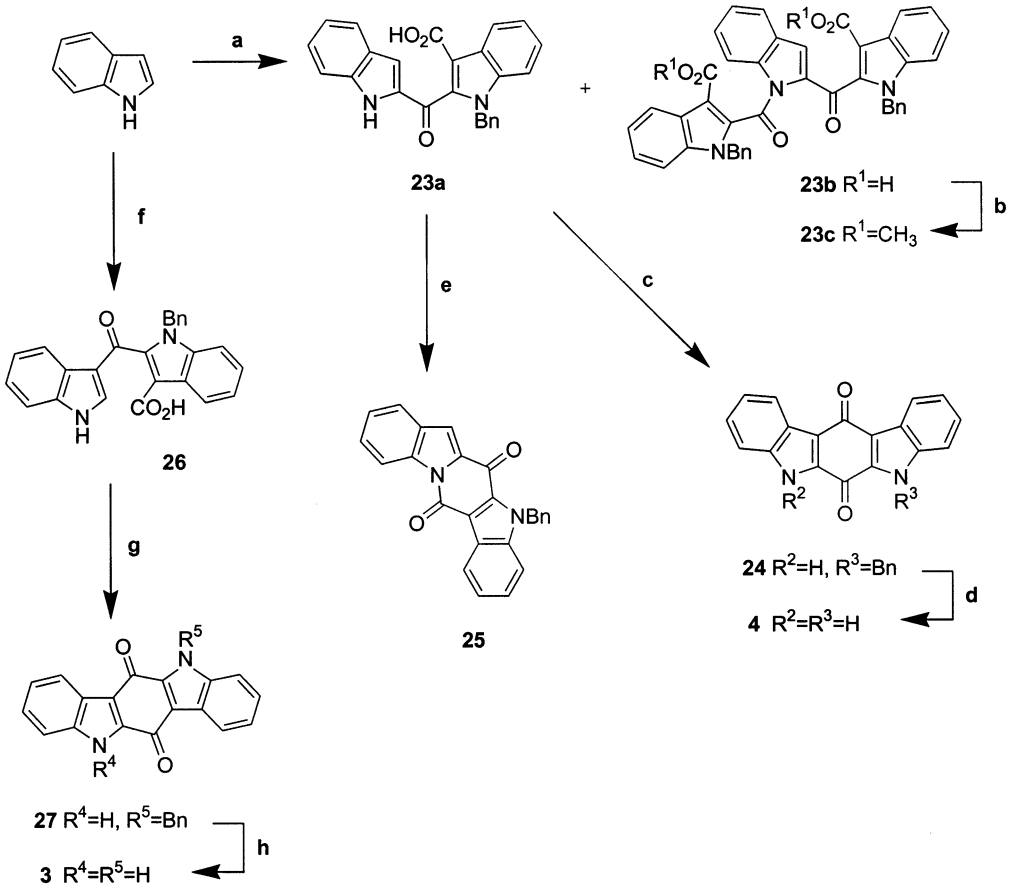
suspension at room temperature for 24 h with access to air, **3** could be isolated in 58% yield. In contrast to this result, **20** could be isolated in 17% yield together with 34% of **3** if the reaction mixture upon cooling was treated with ethereal diazomethane after a quick workup procedure. A similar process of dimerisation has earlier been observed in the case of hydroxy and methoxy-anthracenes by Cameron and Schütz,[28] and recently, Bringmann and co-workers reported a 4,4′-dimer of murrayafoline-A.[29] Oxidative couplings in the indolocarbazole series have not been reported yet, and thus the isolated product **20** represents the first example of a 6,6′-diindolo[3,2-*b*]carbazole coupling product.

In a further investigation of the properties of **3**, initial attempts to reduce **3** to the hydroquinone using AcOH–zinc failed. Thus **3** was treated with Ac_2O–zinc dust together with AcONa to give the diacetyl compound **21** in 68% yield. Attempts to remove the acetyl groups in order to produce the hydroquinone resulted in complex mixtures even under mild conditions (Scheme 6).

2.2. Indolo[2,3-*b*]carbazole-6,12-dione (4)

In analogy with the synthesis of **3** from **16**, we wanted to produce a suitable precursor for a ring closure to the pentacyclic system **4**, thus the anhydride **22** was considered as a suitable electrophile in the reaction with indole. The necessary 1-benzylindole-2,3-dicarboxylic acid was prepared according to Baiocchi,[30] and further transformed into **22**. Addition of Grignard reagents to **22** has been reported to result in addition mainly in the 2-position (Fig. 3).[31]

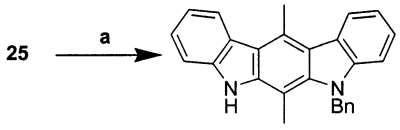
Using the Katritzky protocol for sequential N-protection and 2-lithiation of indole,[32] **22** was used as the electrophile to give the ketone **23a** in 63% yield (Scheme 7). From this reaction, we could also isolate the product **23b** in 5% that must have arisen from a double attack of the indole nucleus



Scheme 7. (a) (i) THF, −78°C, BuLi; (ii) CO_2 (g); (iii) *t*-BuLi; (iv) **22** (63%). (b) CH_2N_2, Et_2O, 21°C (89%). (c) TFAA, Ac_2O, 21°C (85%). (d) $AlCl_3$, PhH, rx (63%). (e) Ac_2O, rx (71%). (f) (i) EtMgBr, Et_2O, 21°C; (ii) $ZnCl_2$; (iii) **22** (69%). (g) PPSE, $MeNO_2$, rx (61%). (h) $AlCl_3$, PhH, rx (71%).

on two molecules of **22**. To facilitate the characterisation, **23b** was isolated as its dimethyl ester **23c** in 89% yield after treatment with an ethereal diazomethane solution (Scheme 7). Subsequent treatment of **23a** in trifluoroacetic anhydride–acetic anhydride (1:5) produced the *N*-benzylated product **24** in 85% yield. Treatment of **24** with $AlCl_3$ in refluxing benzene afforded indolo[2,3-*b*]carbazole-6,12-dione (**4**) (63% based on recovered starting material) (Scheme 7). Reaction of **23a** with oxalyl chloride–DMF in CH_2Cl_2 resulted in a 2:1 mixture of the two possible products **24** and **25**. The use of Ac_2O at reflux gave selective formation of the thermodynamic product **25** in 71% yield. Reaction with an indolyl zinc Grignard reagent by the method of Bergman et al.[33] with the anhydride **22** as electrophile resulted in the isomer (of **23a**) **26** in 69% yield. To effect ring closure, **26** was initially treated with neat polyphosphoric acid (PPA), which resulted in a complex mixture. As polyphosphoric acid trimethylsilyl ester (PPSE)[34] is a milder alternative to PPA and has been used for related ring closures,[35] we reacted **26** with this reagent in refluxing nitromethane, thereby producing the cyclised product *N*-benzylindolo[3,2-*b*]carbazole-6,12-dione (**27**) in 61% yield. Subsequent debenzylation of **27** with $AlCl_3$ in benzene at reflux afforded **3** in 71% yield (Scheme 7).

In analogy with similar structures,[36] compound **25** has been used as a precursor for the synthesis of an unsymmetrical 6,12-disubstituted indolo[2,3-*b*]carbazole as outlined in Scheme 8. Reaction with MeLi followed by reductive aromatisation produced *N*-benzyl-6,12-dimethylindolo[2,3-*b*]carbazole (**28**) in 64% yield.



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Scheme 8. (a) (i) MeLi, THF, rx; (ii) $NaBH_4$, EtOH, rx (64%).

3. Conclusion

In summary, we have developed syntheses of indolo[2,3-*b*]carbazole-6,12-dione (**4**) and indolo[3,2-*b*]carbazole-6,12-dione (**3**), an extremely potent ligand to the aryl hydrocarbon receptor. The synthetic strategies followed in the construction of these systems produce several derivatives that might be used in further syntheses of both unsymmetrical and symmetrical indolo[3,2-*b*]carbazoles and indolo[2,3-*b*]carbazoles as exemplified in Scheme 8, thus producing further SARs for the Ah receptor.

4. Experimental

4.1. General aspects

NMR spectra were recorded at 300 or 500 MHz for ^1H and 75 or 125 MHz for ^{13}C at 298 K if not stated otherwise; δ values are given in ppm and coupling constants are reported in Hz. IR spectra were recorded on a Perkin–Elmer FT-IR 1600 spectrophotometer. Melting points were determined using the capillary method on a Büchi B-545 and are uncorrected. Mass spectra were recorded using an LC/MS system operating in the electron spray ionisation (ESI) mode at 70 eV. FAB-MS and HRMS experiments were performed by E. Nilsson, Kemicentrum, Lund, Sweden. The elemental analyses were performed by H. Kolbe Microanalytisches Laboratorium, Mühlheim an der Ruhr, Germany. All reagents were of commercial quality and used as received from Lancaster, Aldrich, or Merck. Solvents were purified by distillation or were of HPLC grade. Chromatographic separations were performed on silica gel 60 (230–400 mesh) and on aluminium oxide (activity grade II-III, 70–230 mesh). Reactions were monitored by thin-layer chromatography on silica gel coated plates and on aluminium oxide coated plates, both with a fluorescent indicator.

4.1.1. 2,5-Dianilino-*p*-benzoquinone (7). This compound was prepared according to Ref. 12a and was recrystallised twice from DMA followed by drying at 150°C/1 mmHg for 12 h thereby producing lustrous purple crystals. Mp 357–360°C (345°C);[12b] IR (KBr) cm^{-1}: 3224, 1638, 1565, 1488, 1442, 1357, 1286, 1174, 741, 725, 692; ^1H NMR (DMSO-d_6, 125°C) δ 8.81 (2H, bs), 7.45 (4H, dd, J=7.8, 7.3 Hz), 7.37 (4H, d, J=7.8 Hz), 7.24 (2H, t, J=7.3 Hz), 5.81 (2H, s); ^{13}C NMR (DMSO-d_6, 125°C) δ 179.1 (s), 146.7 (s), 137.3 (s), 128.6 (d), 124.8 (d), 122.8 (d), 95.2 (d).

4.1.2. 2,5-Di(*p*-toluidino)-*p*-benzoquinone (8). This compound was prepared according to Ref. 13 and purified by sublimation at 260°C/1 mmHg to produce purple–blue needles. Mp 329–332°C (318°C);[13] IR (KBr) cm^{-1}: 3444, 3237, 1634, 1558, 1516, 1479, 1354, 1282; ^1H NMR (DMSO-d_6, 125°C) δ 8.74 (2H, bs), 7.26 (8H, s), 5.75 (2H, s), 2.35 (6H, s); ^{13}C NMR (DMSO-d_6, 125°C) δ 178.9 (s), 147.0 (s), 134.7 (s), 134.4 (s), 129.1 (d), 122.7 (d), 94.7 (d), 19.7 (q).

4.1.3. 2,5-Dianilino-3,6-dichloro-*p*-benzoquinone (9). To a stirred solution of chloroanil (24.5 g, 0.1 mol) in DMA (120 mL), sodium acetate (25.0 g, 0.3 mol) and aniline (18.6 g, 0.2 mmol) were added. After a period at 25–40°C, the mixture was refluxed for 15 min. The precipitate formed was collected and carefully washed with water to yield the quinone **9**, 31.8 g (89%). Mp 315.5–316°C (315°C).[37]

4.1.4. *N,N′*-(*tert*-Butyloxycarbonyl)-2,5-dianilino-*p*-benzoquinone (11). To a suspension of **7** (393 mg, 1.35 mmol) in THF (40 mL) under argon at 21°C, Boc_2O (1116 mg, 5.11 mmol) was added. The suspension was cooled on ice followed by addition of DMAP (166 mg, 1.36 mmol). The resulting suspension was stirred at 21°C for 20 h and was then evaporated. The crude product was subjected to chromatography on silica gel, eluent EtOAc–hexane (0–20%) to give 580 mg (87%) of **11** as an orange solid. Crystallisation of this substance can be done from either EtOH or *i*-Pr_2O to produce fine orange–red crystals. Mp 179.5–180.5°C (*i*-Pr_2O); IR (KBr) cm^{-1}: 3052, 2984, 1728, 1718, 1666, 1591, 1368, 1325, 1237, 1148, 762, 698; ^1H NMR (acetone-d_6) δ 7.44–7.37 (4H, m), 7.31–7.27 (6H, m), 6.50 (2H, s), 1.42 (18H, s); ^{13}C NMR (acetone-d_6) δ 183.5 (s), 153.1 (s),

149.8 (s), 142.7 (s), 130.1 (d), 127.9 (d), 127.8 (d), 127.7 (d), 83.0 (s), 28.1 (q); FABHRMS Calcd for $C_{28}H_{30}KN_2O_6$ 529.1741 $[M+K]^+$ found 529.1731.

4.1.5. 5*H*,11*H*-Indolo[3,2-*b*]carbazole-6,12-dione (3). To a solution of CrO_3 (2.00 g, 20 mmol) in H_2O (3 mL) stirred at −5°C, a suspension of **5** (256 mg, 1 mmol) in glacial AcOH (3 mL) was added together with pieces of ice to the reaction mixture, ensuring that the temperature did not exceed 5°C during the exothermic reaction. The resulting black solution was stirred for 2 h at 0–5°C whereupon it was filtered through a porous frit. The solid obtained was washed with water and small portions of EtOH. Drying overnight at reduced pressure produced **3** as a brown solid 97 mg (34%). Mp>400°C; IR (KBr) cm^{-1}: 3209, 1632, 1614, 1434, 747; ^1H NMR (DMSO-d_6) δ 12.91 (2H, s), 8.07 (2H, d, J=7.8 Hz), 7.54 (2H, d, J=7.8 Hz), 7.36–7.31 (4H, m); ^{13}C NMR (DMSO-d_6) δ 175.8 (s), 139.6 (s), 137.4 (s), 125.4 (d), 124.0 (s), 123.9 (d), 121.3 (d), 114.8 (s), 113.9 (d); MS EI (30 V) $[M+H]^+$ 287 (9%), $[M]^+$ 286 (41%); Anal. Calcd for $C_{18}H_{10}N_2O_2$: C, 75.52; H, 3.52; N, 9.79; found C, 75.65; H, 3.65; N, 9.68.

4.1.6. From 5-benzyl-5*H*,11*H*-indolo[3,2-*b*]carbazole-6,12-dione (27). 5-benzyl-5*H*,11*H*-indolo[3,2-*b*]carbazole-6,12-dione (**27**) (82 mg, 0.22 mmol) was suspended in PhH (7.5 mL) at 21°C followed by addition of $AlCl_3$ (s) (290 mg, 2.20 mmol) in one portion. The bluish-black reaction mixture was heated at reflux for 5.5 h and then poured on ice/H_2O, diluted with THF (100 mL) and the water phase was extracted with EtOAc (3×50 mL). After washing the combined organic extracts with brine (100 mL), the solvents were evaporated under reduced pressure. The solid obtained was suspended in DMF (10 mL), heated to reflux and cooled. Filtration and washing with water (3×30 mL), followed by drying in an oven overnight at 140°C produced **3**, 44 mg (71%) as a brown solid.

4.1.7. From 2-(1*H*-indole-3-carbonyl)-1*H*-indole-3-carbaldehyde (16). To a suspension of 2-(1*H*-indole-3-carbonyl)-1*H*-indole-carbaldehyde (**16**) (106 mg, 0.37 mmol) in EtOH (14 mL), 2 M HCl (11 mL) was added dropwise. After the last addition, the reaction mixture was refluxed for 30 min. The resulting suspension was cooled and stirred at 21°C for 24 h. The solid obtained was washed with DMF and dried in an oven at 140°C overnight to produce **3**, 61 mg (58%) as a brown solid.

4.1.8. 5,11-Dimethyl-5*H*,11*H*-indolo[3,2-*b*]carbazole-6,12-dione (12). Prepared according to Ref. 20 and recrystallised from DMF to produce a reddish solid. Mp 373.5–375.5°C (365°C);[20] IR (KBr) cm^{-1}: 3054, 1636, 1492, 1470, 1170, 1076, 950, 744; ^1H NMR (DMSO-d_6, 125°C) δ 8.20, (2H, d, J=7.8 Hz), 7.65 (2H, d, J=8.2 Hz), 7.42 (2H, dd, J=7.8, 7.3 Hz), 7.36 (2H, t, J=7.3 Hz), 4.22 (6H, s); ^{13}C NMR (DMSO-d_6, 125°C) δ 176.1 (s), 138.8 (s), 135.8 (s), 125.0 (d), 123.6 (d), 123.0 (s), 121.1 (d), 115.7 (s), 111.2 (d), 39.2 (q); MS EI (30 V) $[M+H]^+$ 315 (9%), $[M]^+$ 314 (44%).

4.1.9. 2-(1-Benzenesulfonyl-1*H*-indole-3-carbonyl)-1*H*-indole-3-carbaldehyde (18). (1-Benzenesulfonyl-1*H*-indol-3-yl)-(1*H*-indol-2-yl)-methanone (**17**) (1.000 g, 2.5 mmol) was suspended in dry trichloroethylene (20 mL) at 21°C under argon. To this solution, freshly prepared solid chloromethylenemorpholinium chloride[27] (850 mg, 5.00 mmol) was added in one portion. After 50 min at 21°C, the mixture was heated to 50°C. After 30 min, dry trichloroethylene (10 mL) was added and the reaction stirred for further 40 min and then poured on ice (50 g) and diluted with CH_2Cl_2 (50 mL). This solution was carefully neutralised with 0.5 M NaOH and the organic phase separated. Further extraction of the water phase with CH_2Cl_2 (50 mL) followed by washing the combined organic phases with water (50 mL), brine (50 mL), drying with Na_2SO_4, and finally evaporation of the solvents produced a red solid, which was suspended in CH_2Cl_2 (30 mL) and stirred until smooth. The precipitate was filtered off and washed with small portions of CH_2Cl_2 to produce a yellow solid, 890 mg. Concentration of the CH_2Cl_2-phases to 1/3 and storage in a refrigerator overnight produced further product (61 mg), total 951 mg (89%). This substance was recrystallised from EtOAc/heptane to produce yellow crystals. Mp 256.5–258.0°C (EtOAc/heptane); IR (KBr) cm^{-1}: 3420, 3124, 1642, 1633, 1536, 1448, 1384, 1174, 747, 568; ^1H NMR ($CDCl_3$) δ 12.93 (1H, s), 10.19 (1H, s), 8.65 (1H, s), 8.33 (1H, d, J=7.9 Hz), 8.24 (1H, d, J=7.3 Hz), 8.19 (2H, d, J=7.7 Hz), 8.05 (1H, d, J=7.9 Hz), 7.76 (1H, apt t, J=7.3 Hz), 7.69–7.61 (3H, m), 7.55–7.44 (3H, m), 7.37 (1H, dd, J=8.1, 7.6 Hz); ^{13}C NMR ($CDCl_3$) δ 186.5 (d), 181.2 (s), 142.2 (s), 136.5 (d), 136.1 (s), 135.9 (s), 135.4 (d), 134.0 (s), 130.1 (d), 127.5 (d), 127.3 (s), 126.4 (d), 125.8 (d), 125.2 (d), 125.0 (s), 123.5 (d), 122.2 (d), 122.2 (d), 120.3 (s), 118.4 (s), 113.4 (d), 113.2 (d); MS (ESI) $[M+H]^+$ 429, $[M-1]^-$ 427; Anal. Calcd for $C_{24}H_{16}N_2O_4S$: C, 67.28; H, 3.76; N, 6.54; found C, 67.18; H, 3.63; N, 6.48.

4.1.10. 2-(1*H*-Indole-3-carbonyl)-1*H*-indole-carbaldehyde (16). To a suspension of the indolecarboxaldehyde **18** (1.156 g, 2.70 mmol) in MeOH (45 mL) at 21°C, K_2CO_3 (1.119 g, 8.10 mmol) dissolved in water (10 mL) was added dropwise. After the last addition, the resulting solution was stirred for 5 h and then concentrated to 1/4 on a rotary evaporator, diluted with water (30 mL) and again concentrated, now to approximately 30 mL. The pH of the obtained suspension was carefully adjusted to 7 with 1 M HCl, diluted with EtOAc (100 mL) and the aqueous phase extracted with EtOAc (3×50 mL). The combined organic phases were washed with brine (50 mL) and dried over Na_2SO_4. Evaporation of the solvents produced a solid that was triturated with Et_2O (15 mL), filtered and dried to give **16** as a yellow solid 682 mg (88%). This material slowly darkened during attempted melting point measurements, and no value could be recorded. IR (KBr) cm^{-1}: 3264, 1642, 1597, 1576, 1522, 1434, 1376, 1228, 736; ^1H NMR (DMSO-d_6) δ 12.74 (1H, s), 12.36 (1H, s), 10.13 (1H, s), 8.31–8.25 (2H, m), 8.20 (1H, d, J=2.1 Hz), 7.60–7.56 (2H, m), 7.40 (1H, dd, J=8.2, 7.0 Hz), 7.36–7.27 (3H, m); ^{13}C NMR (DMSO-d_6) δ 186.0 (d), 180.4 (s), 144.8 (s), 137.8 (d), 136.8 (s), 135.5 (s), 125.7 (s), 124.9 (d), 124.7 (s), 123.7 (d), 123.1 (d), 122.5 (d), 121.9 (d), 121.3 (d), 117.0 (s), 116.6 (s), 113.0 (d), 112.5 (d); FABHRMS Calcd for $C_{18}H_{13}N_2O_2$ 289.0977 $[M+H]^+$ found 289.0980.

4.1.11. 12,12′-Bis(6-methoxy-5*H*,11*H*-indolo[3,2-*b*]carbazole) (20). To a suspension of the indolecarboxaldehyde **16** (502 mg, 1.743 mmol) in 95% EtOH (50 mL) 2 M HCl (40 mL) was added and the mixture heated to reflux under a slow stream of argon. After refluxing the solution for 35 min, the starting material was consumed as judged by TLC (hexane–EtOAc 5:4) and the solution was allowed to cool. A fine black powder containing crude indolo[3,2-*b*]carbazole-6,12-dione (**3**), was filtered off. The pH of the filtrate was adjusted with 0.5 M NaOH to 6, diluted with 100 mL water and extracted with EtOAc (3×100 mL). The combined organic phases were washed with water (2×70 mL) and brine (70 mL), dried over Na_2SO_4, concentrated to 50 mL and immediately methylated by addition of a freshly prepared ethereal solution of diazomethane (25 mL) at 21°C. After stirring for 15 min, the solvents were evaporated and the residue purified by column chromatography on Al_2O_3 (hexane–EtOAc 5:2) to produce the indolocarbazole **20** (15 mg). The above-mentioned black powder containing **3** was washed with EtOAc (60 mL). This EtOAc phase was washed with water (2×30 mL), brine (40 mL), dried over Na_2SO_4 before concentration to 30 mL and methylated as earlier with an ethereal diazomethane solution (15 mL) to produce a crude mixture. This mixture was suspended in 20 mL acetone, filtered through a glass filter (N 4) and purified by column chromatography as earlier to produce **20** (31 mg). The powder of **3** after the EtOAc wash was washed with water until the pH of the filtrate was 7 and then suspended in DMF (10 mL), refluxed for 40 min and subsequently cooled to 21°C. Filtration and washing with acetone (50 mL) produced a brown powder of **3** that after drying in an oven at 140°C for 16 h produced **3** 169 mg (34%). The combined dark green organic phases from the washings were concentrated and dried at 1 mmHg to produce a crude mixture, which was purified as earlier to give additional **20** (39 mg). During the workup, all organic solutions and dry mixtures were kept away from light at −16°C. The total yield of **20** was 85 mg (17%). Mp 189°C (dec.); IR (KBr) cm^{-1}: 3406, 2961, 2921, 2851, 1736, 1722, 1641, 1623, 1459, 1457, 1378, 1328, 1282, 1281, 1094, 1025, 804, 744; ^1H NMR (DMSO-d_6) δ 11.27 (2H, s), 10.30 (2H, s), 8.35 (2H, d, J=7.8 Hz), 7.43 (2H, d, J=8.3 Hz), 7.28 (2H, dd, J=7.8, 7.3 Hz), 7.23 (2H, d, J=7.8 Hz), 7.17 (2H, dd, J=7.4, 7.3 Hz), 7.11 (2H, dd, J=7.8, 7.3 Hz), 6.43 (2H, dd, J=7.8, 7.3 Hz), 6.30 (2H, d, J=8.2 Hz), 4.36 (6H, s); ^{13}C NMR (DMSO-d_6) δ 141.3 (s), 141.0 (s), 138.7 (s), 135.3 (s), 127.5 (s), 125.0 (d), 124.9 (d), 123.0 (s), 123.0 (s), 122.0 (d), 121.4 (s), 120.7 (d), 117.9 (d), 117.5 (d), 114.7 (s), 110.6 (d), 110.6 (d), 107.0 (s), 60.4 (q); FABHRMS Calcd for $C_{38}H_{26}N_4O_2$ 570.2056 $[M]^+$ found 570.2048.

4.1.12. 6,12-Diacetoxy-5*H*,11*H*-indolo[3,2-*b*]carbazole (21). To a suspension of the dione **3** (286 mg, 1.00 mmol) in Ac_2O (30 mL) at 21°C, AcONa (123 mg, 1.50 mmol) was added followed by Zn dust (1.112 g, 17.00 mmol). After the last addition, the mixture was heated at reflux for 25–30 min until the dark suspension changed into a solution containing some light crystals. The crystals in the solution were carefully removed from the excess of Zn, and the Zn carefully washed with boiling Ac_2O (2×10 mL) and acetone (2×15 mL). The organic solution was concentrated to 8–10 mL and cooled in an ice bath. After 1 h, the light crystals were collected, washed with boiling water (200 mL) and dried to produce **21** (210 mg). The mother liquor was evaporated and purified by column chromatography on Al_2O_3 (hexane–EtOAc 3:2) to produce additional **21** (45 mg). In total, 255 mg (68%) of the indolocarbazole **21** was obtained. Mp 280°C (dec.); IR (KBr) cm^{-1}: 3332, 3053, 1746, 1617, 1554, 1458, 1372, 1340, 1299, 1219, 1150, 1038, 1013, 740, 686, 534; ^1H NMR (DMSO-d_6) δ 11.36 (2H, s), 8.01 (2H, d, J=7.5 Hz), 7.47 (4H, m), 7.19 (2H, dd, J=6.8, 6.5 Hz), 2.66 (6H, s); ^{13}C NMR (DMSO-d_6) δ 169.0 (s), 140.9 (s), 127.6 (s), 126.2 (d), 125.9 (s), 121.6 (d), 120.5 (s), 118.7 (d), 116.1 (s), 110.7 (d), 22.5 (q); FABHRMS Calcd for $C_{22}H_{16}N_2O_4$ 372.1110 $[M]^+$ found 372.1109.

4.1.13. 1-Benzyl-2-(1*H*-indole-2-carbonyl)-1*H*-indole-3-carboxylic acid (23a). To a solution of indole (1.170 g, 10.0 mmol) in THF (20 mL) under a positive pressure of N_2 cooled to −78°C, a 1.6 M solution of *n*-BuLi in hexanes (8.75 mL, 14.0 mmol) was added dropwise. After 40 min, at this temperature, CO_2 (g) was bubbled through the solution for 10 min whereupon the solvent was removed under reduced pressure. Fresh THF (20 mL) was added and the solution cooled to −78°C before addition of a 1.7 M solution of *t*-BuLi in pentanes (8.25 mL, 14.0 mmol). After 45 min, at −78°C, the anhydride **22** (3.750 g, 13.5 mmol) was added in one portion. After 2 h, at −78°C, the cooling bath was removed for 10 min and was then replaced again. After 1 h, at −78°C, the reaction was quenched with a solution of sat. NH_4Cl (2 mL) and the mixture was allowed to slowly reach to 21°C overnight. Upon dilution with THF (100 mL) and EtOAc (100 mL), the organic phase was washed with 2 M HCl (100 mL), water (100 mL) and dried with $MgSO_4$. Evaporation of the solvent produced a yellow solid, which was dissolved in a minimum amount of Et_2O (15 mL). Hexane was added with stirring until a yellow solid started to form. After 1 h at 21°C, the solid was collected and washed with Et_2O–hexane to give 2.490 g (63%) of the carboxylic acid **23a**. Mp 240°C (dec.); IR (KBr) cm^{-1}: 3332, 1662, 1616, 1540, 1170, 746; ^1H NMR ($CDCl_3$) δ 12.34 (1H, bs), 12.09 (1H, s), 8.16–8.12 (1H, m), 7.61 (1H, d, J=8.1 Hz), 7.57–7.53 (1H, m), 7.47 (1H, d, J=8.3 Hz), 7.34–7.29 (3H, m), 7.28–7.04 (6H, m), 6.88 (1H, s), 5.44 (2H, s); ^{13}C NMR ($CDCl_3$) δ 181.0 (s), 164.9 (s), 141.0 (s), 138.6 (s), 136.5 (s), 136.4 (s), 136.2 (s), 128.4 (d), 127.5 (d), 126.9 (s), 126.6 (d), 126.4 (d), 125.4 (s), 123.9 (d), 123.1 (d), 122.4 (d), 121.6 (d), 120.5 (d), 113.0 (d), 112.8 (d), 111.7 (d), 108.2 (s), 47.6 (t); FABHRMS Calcd for $C_{25}H_{19}N_2O_3$ 395.1396 $[M+H]^+$ found 395.1372.

4.1.14. 1-Benzyl-2-[1-(1-benzyl-3-methoxycarbonyl-1*H*-indole-2-carbonyl)-1*H*-indole-2-carbonyl]-1*H*-indole-3-carboxylic acid methyl ester (23c). Upon concentration of the filtrate, **23b** could be obtained in two crops as a yellow solid 365 mg (5%). To a solution of **23b** (67 mg, 0.1 mmol) in Et_2O (5 mL) at 21°C, an ethereal diazomethane solution (10 mL) was added. The resulting solution was left overnight in air. Evaporation of the remaining solvent and purification of the residue by chromatography on silica gel with CH_2Cl_2–hexane (0–50%) produced 62 mg (89% from **23b**) of **23c** as a yellow solid. Mp 118°C (dec.); IR (KBr) cm^{-1}: 3029, 2947, 1706, 1526, 1301, 1164, 1119,

748; ^{1}H NMR (acetone-d_6) δ 8.26 (1H, d, J=8.7 Hz), 8.13 (1H, d, J=7.4 Hz), 7.99 (1H, d, J=8.2 Hz), 7.87 (1H, d, J=7.8 Hz), 7.67 (1H, dd, J=7.4, 7.3 Hz), 7.53 (1H, s), 7.47 (1H, dd, J=7.8, 7.4 Hz), 7.35–7.28 (8H, m), 7.24–7.20 (2H, m), 7.16–7.13 (2H, m), 7.10–7.09 (2H, m), 6.87–6.85 (2H, m), 5.67 (1H, d, J=16.4 Hz), 5.04–4.99 (2H, m), 4.45 (1H, d, J=15.6 Hz), 3.57 (3H, s), 3.00 (3H, s); ^{13}C NMR (acetone-d_6) δ 180.1 (s), 164.6 (s), 163.9 (s), 163.1 (s), 142.4 (s), 140.1 (s), 139.6 (s), 138.4 (s), 138.1 (s), 137.9 (s), 137.5 (s), 137.3 (s), 130.6 (d), 129.5 (d), 129.2 (d), 128.8 (s), 128.5 (d), 128.3 (d), 128.0 (d), 127.6 (d), 126.6 (s), 126.5 (s), 126.2 (d), 125.8 (d), 125.6 (d), 125.5 (d), 124.8 (d), 123.9 (d), 123.8 (d), 123.3 (d), 123.2 (d), 116.0 (d), 112.7 (d), 112.4 (d), 109.6 (s), 108.9 (s), 51.7 (q), 51.6 (q), 50.7 (t), 49.2 (t); FABHRMS Calcd for $C_{44}H_{34}N_3O_6$ 700.2448 $[M+H]^+$ found 700.2440.

4.1.15. 5-Benzyl-5*H*,7*H*-indolo[2,3-*b*]carbazole-6,12-dione (24). The acid **23a** (986 mg, 2.5 mmol) was suspended in Ac_2O (12.5 mL) at 21°C and the resulting suspension protected under argon. Upon dropwise addition of trifluoroacetic anhydride (2.5 mL), the suspension became dark. After the last addition, the suspension was stirred at 21°C for 4 h and then ice (100 mL) was added to the flask. The combined phases were removed in vacuo and a dark solid was obtained. Recrystallisation from glacial AcOH produced, after drying at 120°C for 15 h, 800 mg (85%) **24** as a green–black solid. This substance can also be sublimed at 260°C/1 mmHg to produce blue-blackish crystals. Mp 346.5–348.5°C; IR (KBr) cm^{-1}: 3447, 3250, 1638, 1466, 1328, 1241, 1089, 743; ^{1}H NMR (DMSO-d_6) δ 12.77 (1H, bs), 8.25 (1H, d, J=7.3 Hz), 8.12 (1H, d, J=7.6 Hz), 7.68 (1H, d, J=7.9 Hz), 7.51 (1H, d, J=8.0 Hz), 7.40–7.25 (9H, m), 5.98 (2H, s); ^{13}C NMR (DMSO-d_6) δ 180.4 (s), 173.0 (s), 139.2 (s), 138.2 (s), 137.1 (s), 136.9 (s), 133.7 (s), 128.7 (d) 127.5 (d), 126.8 (d), 126.6 (d), 126.1 (d), 124.3 (d), 123.9 (s), 123.7 (d), 123.6 (s), 122.3 (d), 121.9 (d), 118.6 (s), 116.9 (s), 113.8 (d), 112.4 (d), 47.5 (t); MS (ESI) $[M+H]^+$ 377, $[M-H]^-$ 375; Anal. Calcd for $C_{25}H_{16}N_2O_2$: C, 79.77; H, 4.28; N, 7.44; found C, 79.65; H, 4.21; N, 7.29.

4.1.16. 5*H*,7*H*-Indolo[2,3-*b*]carbazole-6,12-dione (4). To a solution of 5-benzyl-5*H*,7*H*-indolo[2,3-*b*]carbazole-6,12-dione (**24**) (392 mg, 1.05 mmol) in benzene under argon, solid $AlCl_3$ (1389 mg, 10.41 mmol) was added in one portion at 21°C. After stirring at this temperature for 1 h, the suspension was gradually heated over a 20 min period to reflux. After 90 min at reflux, the suspension was allowed to cool to 21°C, poured on ice (100 mL) and diluted with EtOAc (100 mL). Upon separation of the organic phase, the water phase was extracted with EtOAc (2×50 mL). The combined organic phases were washed with water (2×50 mL), brine (2×50 mL) and dried over $MgSO_4$. Evaporation of the solvents produced a dark green-blackish solid that was subjected to column chromatography on silica gel with $CHCl_3$–hexane (50–100%) as the eluent. The first fractions contained unreacted starting material. These fractions were collected and the solvents were evaporated. The residue was recrystallised twice from glacial AcOH, filtered and dried to give **24** (38 mg). Later, fractions containing **4** were pooled and evaporated to produce 170 mg of **4** (yield 63% based on recovered starting material) was obtained. Mp>400°C; IR (KBr) cm^{-1}: 3259, 1651, 1634, 1615, 1518, 1466, 1326, 1229, 1072, 740; ^{1}H NMR (DMSO-d_6) δ 12.81 (2H, s), 8.13 (2H, d, J=7.7 Hz), 7.50 (2H, d, J=8.0 Hz), 7.34 (2H, dd, J=8.6, 6.8 Hz), 7.28 (2H, dd, J=7.8, 6.9 Hz); ^{13}C NMR (DMSO-d_6) δ 180.8 (s), 172.4 (s), 138.1 (s), 136.3 (s), 126.0 (d), 124.2 (s), 123.6 (d), 121.9 (d), 117.6 (s), 113.7 (d); FABHRMS Calcd for $C_{18}H_{11}N_2O_2$ 287.0821 $[M+H]^+$ found 287.0810.

4.1.17. 5-Benzyl-5*H*,12*H*-pyrido[1,2-*a*:4,5-*b*′]-diindolo-6,13-dione (25). Compound **23a** (1.183 g, 3.00 mmol) was suspended in Ac_2O (15 mL) at 21°C and then heated at reflux for 30 min. Upon cooling, the product crystallised out as yellow needles. Collection of the solid and washing with a small amount of cooled glacial AcOH and EtOH (2×10 mL) followed by drying at reduced pressure produced the dione **25** (800 mg, 71%) as yellow crystals. Mp 227.5–229.0°C; IR (KBr) cm^{-1}: 3124, 3062, 1687, 1649, 1543, 1469, 1318, 1308, 1172, 750, 742, 694; ^{1}H NMR (DMSO-d_6, 90°C) δ 8.49 (1H, d, J=8.3 Hz), 8.36 (1H, d, J=7.9 Hz), 7.81 (1H, d, J=7.9 Hz), 7.73 (1H, d, J=8.4 Hz), 7.64 (1H, s), 7.59 (1H, dd, J=8.0, 7.6 Hz), 7.51 (1H, dd, J=7.4, 7.1 Hz), 7.44 (1H, dd, J=7.6, 7.2 Hz), 7.37–7.24 (6H, m), 6.05 (2H, s); ^{13}C NMR (DMSO-d_6, 90°C) δ 169.4 (s), 157.4 (s), 139.2 (s), 136.4 (s), 136.4 (s), 134.9 (s), 134.1 (s), 129.2 (d), 128.1 (d), 128.0 (s), 127.0 (d), 127.0 (d), 126.3 (d), 123.9 (s), 123.8 (d), 123.7 (d), 123.5 (d), 121.8 (d), 115.3 (d), 115.3 (d), 114.8 (s), 112.0 (d), 47.3 (t); MS EI (70 eV) $[M+H]^+$ 377 (7%), $[M]^+$ 376 (44%), 105 (18%), 91 (100%), 77 (11%); Anal. Calcd for $C_{25}H_{16}N_2O_2$: C, 79.77; H, 4.28; N, 7.44; found C, 79.64; H, 4.19; N, 7.33.

4.1.18. 1-Benzyl-2-(1*H*-indole-3-carbonyl)-1*H*-indole-3-carboxylic acid (26). Magnesium turnings (78 mg, 3.21 mmol) were placed in a 100 mL flask under argon. Et_2O (10 mL) and EtBr (0.24 mL, 3.22 mmol) were added. After 30 min at 21°C a solution of indole (357 mg, 3.05 mmol) in Et_2O (15 mL) was added dropwise. After stirring for 15 min, an ethereal solution of $ZnCl_2$ (3.10 mmol, 3.1 mL) was added and the resulting suspension stirred for 30 min whereupon the anhydride **22** (832 mg, 3.00 mol) was added in one portion. The resulting yellow suspension was stirred for 5 h and then quenched with a saturated aq. solution of NH_4Cl (20 mL). After stirring for 30 min, the solution was taken up in EtOAc (200 mL) and acidified with 1 M HCl (200 mL). The aq. phase was separated and the organic phase was washed with water (100 mL), brine (100 mL) and dried over $MgSO_4$. Evaporation of the solvent produced a yellow solid, which was suspended in ether (25 mL). After stirring overnight, the carboxylic acid **26** was filtered off and after drying gave 813 mg (69%) as a yellow powder. Mp 234.0–235.5°C; IR (KBr) cm^{-1}: 3178, 1689, 1524, 1497, 1456, 743; ^{1}H NMR (DMSO-d_6) δ 13.21 (1H, bs), 11.88 (1H, d, J=2.3 Hz), 8.21–8.18 (1H, m), 7.67 (1H, d, J=3.0 Hz), 7.64 (1H, d, J=8.5 Hz), 7.54 (1H, d, J=8.0 Hz), 7.52–7.49 (1H, m), 7.36–7.28 (3H, m), 7.26–7.19 (3H, m), 7.17–7.13 (3H, m), 5.87 (2H, s); ^{13}C NMR (DMSO-d_6) δ 186.0 (s), 162.7 (s), 138.1 (s), 137.1 (s), 136.8 (s), 135.2 (d), 128.6 (d), 127.8 (s), 127.2 (d), 126.4 (d), 125.6 (s), 125.3 (s), 125.1 (d), 122.9 (d), 121.7 (d), 121.4 (d), 121.3 (d), 121.0 (d), 118.4 (s), 112.3 (d), 111.5 (d), 47.2 (t); FABHRMS Calcd for $C_{25}H_{19}N_2O_3$ 395.1396 $[M+H]^+$ found 395.1396.

4.1.19. 5-Benzyl-5*H*,11*H*-indolo[3,2-*b*]carbazole-6,12-dione (27). $(Me_3Si)_2O$ (3.40 mL) was added to P_4O_{10} (1.700 g, 6.0 mmol) followed by CH_2Cl_2 (20 mL) under nitrogen. After 30 min at reflux, the solvent was distilled off by gradually increasing the temperature of the oil-bath to 160°C. The resulting liquid was allowed to cool to 21°C and CH_3NO_2 (5 mL) was added followed by the carboxylic acid **27** (394 mg, 1.0 mmol) suspended in CH_3NO_2 (10 mL) The colour rapidly changed to red upon addition and as the solution was heated towards reflux the suspension darkened. After 80 min at reflux, the solution was allowed to cool to 21°C, and the formed red precipitate filtered off and washing with a small portion of DMF and repeated washings with EtOH produced the dione **28** (230 mg, 61%) as a brick red solid. Mp 376.0–378.5°C; IR (KBr) cm^{-1}: 3224, 1645, 1630, 1488, 1458, 749; ^1H NMR (DMSO-d_6, 75°C) δ 12.69 (1H, bs), 8.23–8.20 (1H, m), 8.09 (1H, d, J=7.9 Hz), 7.67–7.64 (1H, m), 7.56 (1H, d, J=7.5 Hz), 7.38–7.25 (9H, m), 6.07 (2H, s); ^{13}C NMR (DMSO-d_6, 75°C) δ 176.6 (s), 175.3 (s), 138.4 (s), 138.3 (s), 137.3 (s), 136.6 (s), 136.1 (s), 128.1 (d), 126.9 (d), 126.2 (d), 125.4 (d), 125.1 (d), 124.1 (d), 123.9 (s), 123.4 (d), 123.1 (s), 121.4 (d), 121.1 (d), 115.9 (s), 115.3 (s), 113.5 (d), 112.0 (d), 47.2 (t); MS (ESI) $[M+H]^+$ 377 $[M-H]^-$ 375; Anal. Calcd for $C_{25}H_{16}N_2O_2$, C, 79.77; H, 4.28; N, 7.44; found C, 79.85; H, 4.23; N, 7.43.

4.1.20. 5-Benzyl-6,12-dimethyl-5H,7H-indolo[2,3-*b*]carbazole (28). To a solution of the dione **25** (188 mg, 0.5 mmol) in THF (40 mL) under an argon atmosphere, MeLi 1.5 M in Et_2O (3.33 mL, 5.0 mmol) was added dropwise at 21°C. After the last addition, the solution was heated at reflux for 3.5 h, cooled to 21°C and further 4 equiv. of MeLi (1.33 mL, 2.0 mmol) were added and the reflux continued for further 1.5 h. After distilling off the solvent partially (leaving approx. 10 mL of solvent), abs. EtOH (40 mL) was added followed by $NaBH_4$ (1.892 g, 50 mmol) in one portion. After the initial frothing, the suspension was heated at reflux for 14 h, then allowed to cool to 21°C. Further, 50 equiv. of $NaBH_4$ (946 mg, 25 mmol) were added and the reflux continued for 1 h. At this time, the solution was cooled to 0–5°C and ice-water (20 mL) and acetone (50 mL) were added. The slurry obtained was concentrated to approx. 15 mL and then diluted with CH_2Cl_2 (100 mL) and water (100 mL). The organic phase was removed and the water phase extracted with CH_2Cl_2 (2×50 mL). The combined organic phases were washed with brine (100 mL) and dried with Na_2SO_4. Evaporation of the solvents gave a brown solid, which was purified by column chromatography on silica gel with CH_2Cl_2–hexane (15–50%) as eluent. The indolocarbazole **28** (120 mg, 64%) was obtained as a white powder. Mp 291°C (dec.); IR (KBr) cm^{-1}: 3440, 3050, 1601, 1461, 1451, 748, 729; ^1H NMR (DMSO-d_6) δ 11.00, (1H, s), 8.33 (1H, d, J=7.8 Hz), 8.28 (1H, d, J=7.8 Hz), 7.47 (2H, t, J=8.7 Hz), 7.36–7.32 (2H, m), 7.28 (2H, dd, J=7.8, 7.3 Hz), 7.24–7.20 (2H, m), 7.16 (1H, dd, J=7.8, 7.3 Hz), 7.02 (2H, d, J=7.8 Hz), 5.91 (2H, s), 3.33 (3H, s), 2.73 (3H, s); ^{13}C NMR (DMSO-d_6) δ 142.1 (s), 140.7 (s), 140.1 (s), 139.4 (s), 138.5 (s), 128.7 (d), 126.7 (d), 125.4 (d), 125.0 (s), 124.0 (d), 124.0 (d), 123.8 (s), 123.8 (s), 121.6 (d), 119.0 (d), 118.3 (d), 116.6 (s), 116.3 (s), 110.3 (d), 108.5 (d), 97.3 (s), 47.7 (t), 17.1 (q), 12.6 (q); MS EI (70 eV) $[M]^+$ 374 (10%), 283 (35%), 105 (29%), 91 (97%), 77 (100%); Anal. Calcd for $C_{27}H_{22}N_2$, C, 86.60; H, 5.92; N, 7.48; found C, 86.49; H, 5.84; N, 7.37.

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