Coupling reactions of indole-3-acetic acid derivatives. Synthesis of arcyriaflavin A

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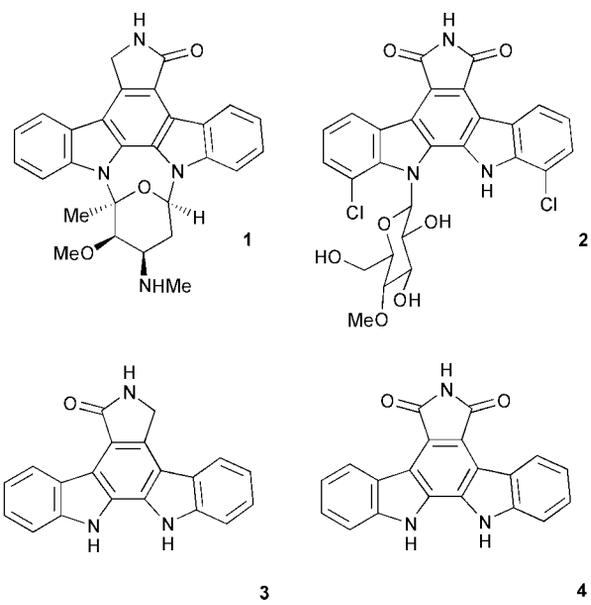
The bisindolesuccinic acid methyl ester **10** was obtained by an iodine-promoted coupling of the dianion **9**. The diester was converted to the *N*-benzylimide **12**, which was oxidatively cyclized to the indolo[2,3-*a*]pyrrolo[3,4-*c*]-carbazole **15**. The diester **10** could be directly transformed to the known indolocarbazole diester **27** *via* acid-induced intramolecular cyclization in TFA. The same methodology gave arcyriaflavin A **4** from the succinimide **18b.**

Introduction

The interesting biological activities of indolocarbazole alkaloids, such as the protein kinase C inhibitor staurosporine[1] and the tumour-growth inhibitor rebeccamycin,[2] have stimulated the development of a number of synthetic approaches towards indolo[2,3-*a*]pyrrolo[3,4-*c*]carbazoles such as the aglycon of **1**, staurosporinone **3**, and arcyriaflavin A **4**.[3–7]

Both staurosporine **1** and rebeccamycin **2** have been shown by labelling experiments to be biosynthetically derived from two tryptophan units.[8,9] This notion has been used by us[10,11] and others[12] in the synthetic strategy to this type of compounds.



Results and discussion

Our first approach towards arcyriaflavin A **4** involves the oxidative coupling of anions α to the carbonyl group of either indole-3-acetic acid or its methyl ester as shown in Scheme 1. Sequential addition of 2 eq. of BuLi and 1 eq. of *t*-BuLi to

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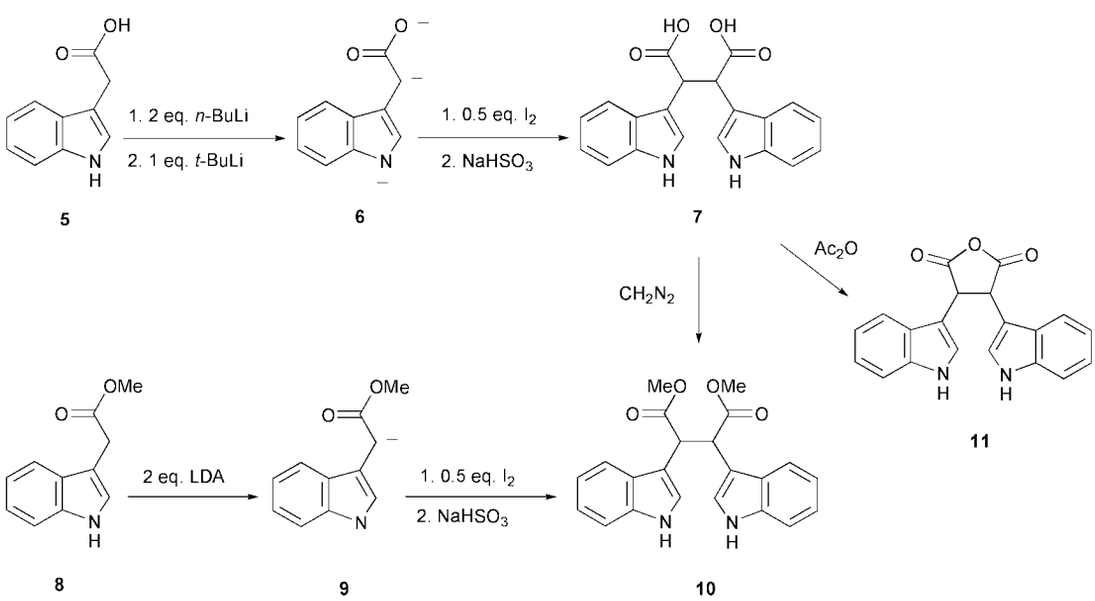

Scheme 1

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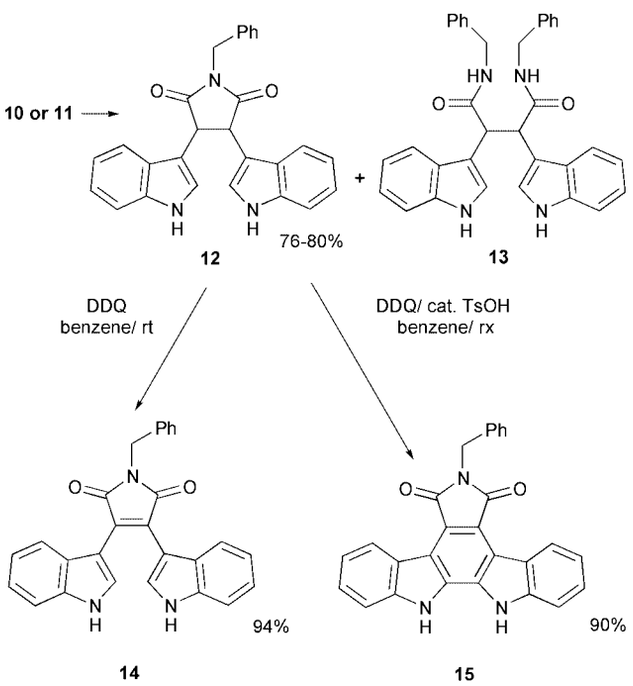
indole-3-acetic acid **5** afforded the trianion **6**. Quenching an aliquot of the reaction mixture with D_2O and subsequent examination of the reaction product with ^1H NMR showed 95% incorporation of deuterium α to the carbonyl group. It was also found that **6** was stable at −40 °C in THF for at least 18 h. Addition of 0.5 eq. of iodine to a solution of **6** in THF at −70 °C followed by an acidic work-up gave 2,3-di(indol-3-yl)succinic acid **7**. The reaction mixture was treated, without any attempts to purify the diacid, with diazomethane or acetic anhydride to give a diastereomeric mixture (the ±-pair and the *meso*-form) of the diester **10** or the diastereomerically pure anhydride **11**, respectively. However, the yields of **10** and **11** were not satisfactory (38% and 32%, respectively). Fortunately, the diester **10** could be obtained in a much higher yield (85%), as a diastereomeric mixture (1 : 1), by the iodine-promoted coupling of the dianion **9**, prepared from indole-3-acetic acid methyl ester **8** and lithium diisopropylamide (LDA). Heating (200 °C; N_2) of the diester **10** or the anhydride **11** with benzylamine gave the bisindolesuccinimide **12** together with some of the bisamide **13** (Scheme 2). The imide **12** was readily



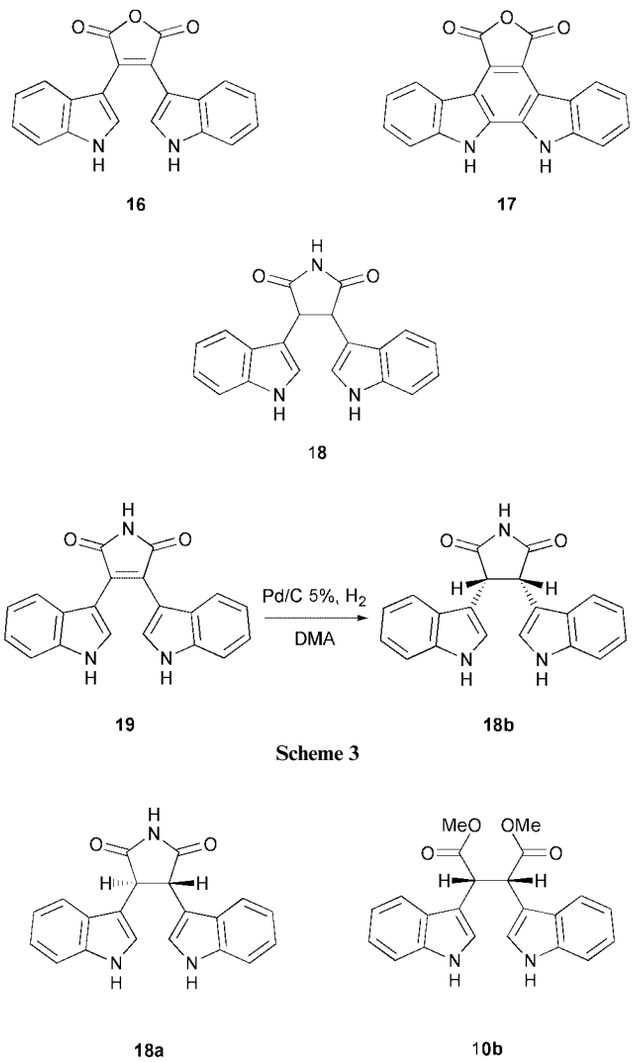
Scheme 2

dehydrogenated with one equivalent of DDQ at room temperature to give the bisindolemaleimide **14**. Compound **12** could also serve as precursor for the indolocarbazole **15**, by the use of two equivalents of DDQ and a catalytic amount of *p*-TsOH in refluxing benzene.

The same set of transformations could be exerted on the anhydride **11**, thus establishing a route to compounds **16**[13] and **17**. A somewhat higher temperature (refluxing chlorobenzene, 132 °C) was, however, required.

The diester **10** was formed as a mixture of the ±-pair and the *meso*-form. On trituration with 1,4-dioxane one of them crystallized in pure form. When the mixture of **10** was treated with ammonium formate in refluxing triglyme only one of the two diastereomers cyclized to the imide **18**. The other diastereomer of **10**, identical with the one obtained from trituration with 1,4-dioxane, could be recovered intact from the reaction mixture.

To assign the structure of the diastereomers we synthesized the *cis*-succinimide **18b** from arcyriarubin A **19** (see Scheme 3), an experiment previously described by Davis.[14] The *cis*-succinimide **18b** was not identical with our sample obtained from the diester and thereby we can conclusively ascertain the *trans* stereochemistry of the imide **18a** and thus deduce



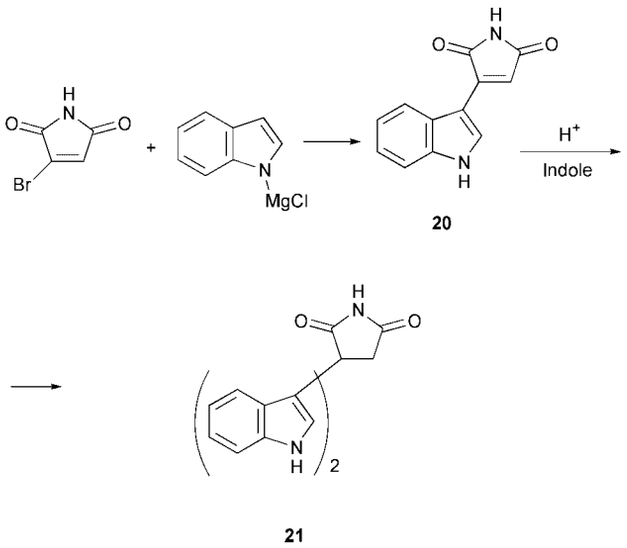
Scheme 3

that the pure dimer **10b**, obtained by crystallization of the diastereometric mixture of **10** from 1,4-dioxane, is the *meso*-form.

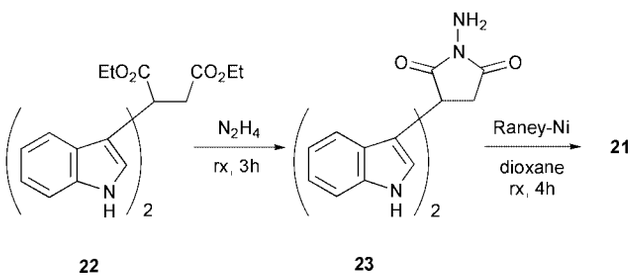
A compound claimed to be the *trans*-imide **18a** has been reported in the literature.[14] This purported compound was obtained in a low reported yield (6%) by reaction of indolylmagnesium chloride with bromomaleimide followed by acidic (2 M HCl) work-up. Repetition of this experiment showed, however, that this product is in fact 3,3-di(indol-3-yl)succinimide **21** which was first indicated by the appearance of a CH_2 group in the ^{13}C NMR spectrum. The previous workers did not report any ^{13}C NMR data and interpreted the CH_2 singlet in the ^1H NMR spectrum as two coinciding CH signals. This result can be rationalized as initial formation of **20** followed by acid-catalyzed addition of a second molecule of indole during the acidic work-up (Scheme 4).

In harmony with this scheme it was found that interaction of **20** with indole under acidic conditions indeed gave **21**. The structure of **21** was also confirmed by an independent synthesis starting with the known diester **22**, which readily underwent cyclization with hydrazine yielding **23**, which in turn upon treatment with Raney nickel in 1,4-dioxane gave the imide **21** (Scheme 5).[15] It should also be noted that compound **21**, still written as **18b**, recently has been tested for activity against human cytomegalovirus.[16] The discussion in this paper thus at this point might be somewhat misleading.

The *trans*-imide **18a** could be dehydrogenated to arcyriarubin A **19**, but arcyriaflavin A **4** could not be obtained with the same methodology which gave **15** and **17**. Whereas indole in acidic media dimerizes to 2-(indol-3-yl)indoline, 3-substituted indoles will form 2,2′-coupled dihydrodimers by rearrangement.[17–19]



Scheme 4

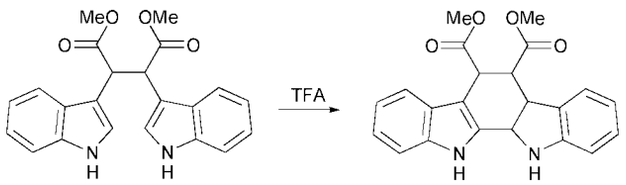


Scheme 5

Such couplings are known for simple indoles, *e.g.* skatole, and, as we presented in an earlier communication,[11] for indole-3-acetic acid and several related derivatives (see Scheme 6).

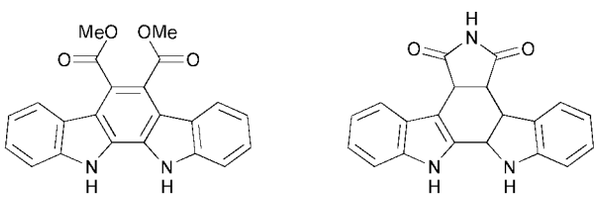
It was shown that the dimer **24b** was readily formed by treatment of methyl indole-3-acetate with trifluoroacetic acid (TFA) and readily underwent cyclization to the lactam **25**, whose structure has been confirmed by X-ray crystallography.[20] Interestingly, unsuccessful attempts to prepare the dimer **24b** had been reported as early as 1965.[21] Dehydrogenation of **24b** with DDQ readily gave the corresponding 2,2′-biindolyl derivative **26**.

As compounds **10** and **18b** each have two unsubstituted 2-positions they should (*cf.* Scheme 6) be able to undergo intramolecular acid-promoted ring closure as they also did upon treatment with TFA, and indeed **10** gave the tetrahydroindolocarbazole **27** (Scheme 7) in excellent yield.



Scheme 7

Gentle warming of a TFA solution of the tetrahydro compound **27** gave the known, fully aromatized diester **28**.[22] The imide **18b** similarly gave the tetrahydroindolocarbazole **29** when treated with TFA. Here it might be added that some related dehydrogenations leading to indolo[3,2-*a*]pyrrolo[3,4-*c*]-carbazoles have recently been described by us.[23]

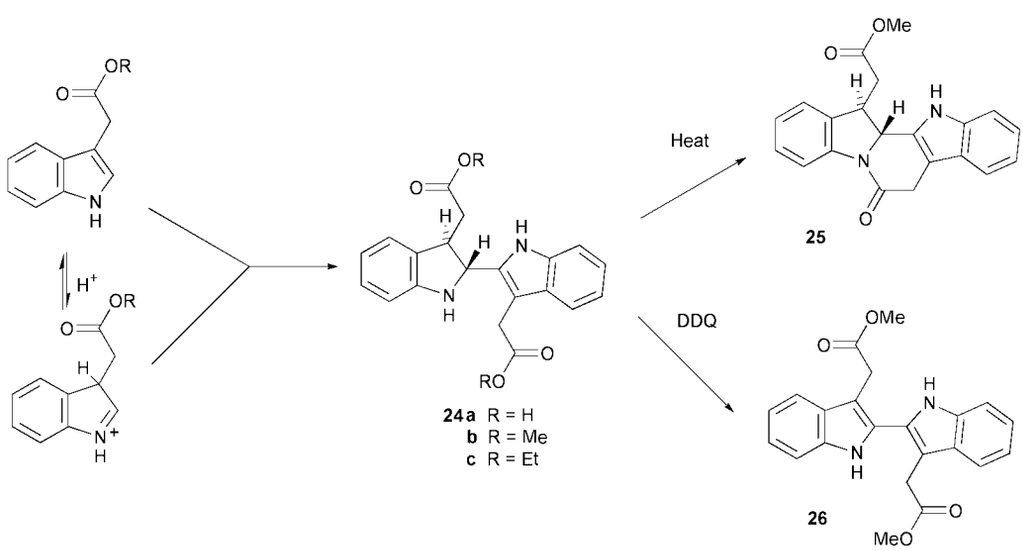


Arcyriaflavin A **4** was obtained in quantitative yield by refluxing a TFA solution of **29** for 8 h.

Experimental

General

NMR spectra were recorded on a Bruker DPX 300 (300 MHz) spectrometer and a Bruker VP-200. IR spectra were recorded with a Perkin-Elmer 1600 FT-IR. *J*-values are in Hz. HRMS analyses were performed by Sveriges Lantbruksuniversitet (SLU), Uppsala, Sweden, MS ESI analyses were obtained on a Perkin-Elmer API 150 EX spectrometer. MS (EI^+) analyses were performed on a Micromass Platform II spectrometer or a LKB-9000, both with a direct inlet at 70 eV. Mps were taken on a Büchi Melting Point B-545 apparatus or a Reichert WME Kofler hot stage and are uncorrected. All solvents were purified by distillation or were HPLC grade. Diisopropylamine (DIPA)



Scheme 6

and THF were distilled immediately before use from CaH_2 and benzophenone ketyl, respectively. Chromatography was performed on Merck Silica Gel 60. All reactions, except the TFA-induced dimerizations and the DDQ dehydrogenations, were performed under a positive pressure of nitrogen.

Dimethyl 2,3-di(indol-3-yl)succinate 10 from 8

To a solution of LDA [prepared from DIPA (5.61 ml, 40 mmol), *n*-BuLi (10 M; 4 ml, 40 mmol) and THF (100 ml)] was added a solution of **8** (3.78 g, 20 mmol) in THF (40 ml) over a period of 75 min, keeping the temperature below −65 °C (sometimes a viscous precipitate formed, making stirring difficult). After 2 h at −75 °C, the mixture was allowed to come to −40 °C, kept at that temperature for 30 min and recooled to −75 °C. A solution of iodine (2.53 g, 10 mmol) in THF (40 ml) was added over a period of 75 min at −70 °C whereafter the mixture was stirred at −75 °C for 1 h and then allowed to reach room temperature overnight. The purple solution was poured into $NaHSO_3$ (aq., saturated) and, after separation, the aqueous phase was extracted with EtOAc. The combined organic phases were washed successively with water and brine and dried with $MgSO_4$. Concentration gave a brown foam, which was triturated with hot 1,4-dioxane to give dimer **10b** (0.79 g) as fine white needles (only one diastereomer), mp 270–273 °C; δ_H (200 MHz; DMSO-d_6) 11.10 (2H, s, NH), 7.74 (2H, d, *J* 7, ArH), 7.41 (2H, d, *J* 2, ArH), 7.36 (2H, d, *J* 8, ArH), 7.01–7.13 (4 H, m, ArH), 4.77 (2H, s, CH), 3.26 (6H, s, CH_3); δ_C (50 MHz; DMSO-d_6) 172.0 (s), 136.0 (s), 126.1 (s), 123.6 (d), 121.2 (d), 118.8 (2d), 111.5 (d), 110.1 (s), 51.4 (q), 45.4 (d); ν_{max}(KBr)/cm^{-1} 3350, 1714, 1432, 1313, 1161, 749; *m*/*z* (ESI) [M + H$^+$] 377. Found: HRMS (EI) *m*/*z* 376.1410. $C_{22}H_{20}N_2O_4$ requires *M*, 376.1423. Concentration of the 1,4-dioxane solution followed by flash chromatography (CH_2Cl_2–MeOH, 99:1) gave **10** (2.44 g) as a mixture of diastereomers. Total yield of **10a** plus **10b**: 85%.

Dimethyl 2,3-di(indol-3-yl)succinate 10 from 5

n-BuLi (1.6 M; 25 ml, 40 mmol) was added to a solution of **5** (3.50 g, 20 mmol) in THF (150 ml) over a period of 15 min, keeping the temperature below −60 °C. After 20 min at −75 °C the mixture was treated with *t*-BuLi (1.6 M; 13 ml, 20 mmol) over a period of 15 min, keeping the temperature below −70 °C. After 2 h at −75 °C the yellow solution was allowed to come to −40 °C, kept at that temperature for 30 min, and recooled to −75 °C. A solution of iodine (2.53 g, 10 mmol) in THF (10 ml) was added over a period of 10 min at −70 °C, whereafter the mixture was stirred at −75 °C for 1 h and was then allowed to reach room temperature overnight. The purple solution was poured into $NaHSO_3$ (aq., saturated) and, after separation, the aqueous phase was extracted with EtOAc. The combined organic phases were washed successively with water and brine and dried with $MgSO_4$. A solution of diazomethane (≈30 mmol) in diethyl ether was added and after 1 h unchanged diazomethane was quenched with acetic acid. Concentration and chromatography (CH_2Cl_2–MeOH, 99:1) gave **10** as a mixture of diastereomers; *m*/*z* (EI$^+$) 376. IR and NMR data as above.

3,4-Di(indol-3-yl)succinic anhydride 11

The diacid **7** was prepared as above but the combined organic phases were concentrated, and dissolved in acetic anhydride (50 ml). After reflux for 5 h, the dark brown solution was allowed to cool and after concentration it was triturated with hot ethanol to give **11** (1.07 g, 32%) as a slightly reddish solid, mp 250–255 °C; δ_H (300 MHz; DMSO-d_6) 11.16 (2H, s, NH), 7.57 (2H, d, *J* 8, ArH), 7.51 (2H, d, *J* 2, ArH), 7.38 (2H, d, *J* 8, ArH), 7.10 (2H, app t, ArH), 6.99 (2H, app t, ArH), 5.28 (2H, s, CH); δ_C (75 MHz; DMSO-d_6) 172.7 (s), 137.1 (s), 127.2 (s), 125.5 (d), 122.3 (d), 119.8 (d), 119.5 (d), 112.6 (d), 108.1 (s), 46.1 (d); ν_{max}(KBr)/cm^{-1} 3410, 3390, 1860, 1775, 1455, 1420, 1340, 1250, 1180, 1025, 935, 920, 795, 740; *m*/*z* (EI$^+$) 330. Found: HRMS (EI) *m*/*z* 330.1025. $C_{20}H_{14}N_2O_3$ requires *M*, 330.1004.

N-Benzyl-3,4-di(indol-3-yl)succinimide 12

A mixture of **10** (1.47 g, 3.9 mmol) and benzylamine (6 ml) was heated at 200 °C for 18 h. The orange solution which solidified on cooling was dissolved in EtOH. The EtOH solution was added dropwise with stirring to aq. HCl (2 M; 100 ml), and the precipitate which formed was collected, washed with ethanol and dried. Purification by chromatography (CH_2Cl_2–MeOH, 98:2) gave **12** (1.30 g, 80%), mp 184–187 °C; δ_H (200 MHz; DMSO-d_6) 10.95 (2H, s, NH), 7.4–7.3 (11H, m, ArH), 7.07 (2H, m, ArH), 6.89 (2H, m, ArH), 4.78 (2H, s, CH_2), 4.62 (2H, s, CH); δ_C (75 MHz; DMSO-d_6) 176.9 (s), 136.5 (s), 136.35 (s), 128.6 (d), 128.0 (d), 127.7 (d), 126.1 (s), 124.3 (d), 121.4 (d), 118.8 (d), 118.6 (d), 111.8 (d), 109.7 (s), 67.3 (d), 42.1 (t); ν_{max}(KBr)/cm^{-1} 3400, 1775, 1695, 1460, 1430, 1395, 1345, 1155, 740 and 700; *m*/*z* (ESI) [M + H]$^+$ 420. Found: HRMS (EI) *m*/*z* 419.1627. $C_{27}H_{21}N_3O_2$ requires *M*, 419.1634.

N-Benzyl-3,4-di(indol-3-yl)maleimide 14

DDQ (0.16 g, 0.069 mmol) was added at room temperature in small portions to a stirred solution of **12** (0.29 g, 0.69 mmol) in benzene (10 ml). After 1 h at room temperature the mixture was concentrated and subjected to chromatography (CH_2Cl_2–MeOH, 98:2) to give **14** (0.27 g, 94%) as a red solid, δ_H (200 MHz; Me_2CO-d_6) 10.9 (2H, br s, NH), 7.89 (2H, s, ArH), 7.5-7.3 (7H, m, ArH), 7.0–6.9 (4H, m, ArH), 6.63 (2H, m, ArH), 4.84 (2H, s, CH_2); ν_{max}(KBr)/cm^{-1} 3400, 1760, 1685, 1530, 1400, 1345, 1245, 810, 750, 700. These data are in agreement with those published.[24]

N-Benzylarcyriaflavin A 15

DDQ (1 g, 4.4 mmol) and a catalytic amount of *p*-TsOH were added to a solution of **12** (0.82 g, 1.96 mmol) in benzene (20 ml). The red mixture was stirred at room temperature for 1 h and heated at reflux for 2 h. Concentration and chromatography (CH_2Cl_2–MeOH, 98:2) gave **15** (0.73 g, 90%) as red solid, mp >260 °C; δ_H (DMSO-d_6) 11.75 (2H, s, NH), 8.99 (2H, d, *J* 7, 8, ArH), 7.82 (2H, d, *J* 8.1, ArH), 7.56 (2H, app t, ArH), 7.56–7.30 (7H, m, ArH), 4.92 (2H, s, CH_2); ν_{max}(KBr)/cm^{-1} 3315, 1750, 1680, 1570, 1380, 750, 700. MS (EI$^+$) *m*/*z* 415. These data are in agreement with those published.[24]

trans-3,4-Di(indol-3-yl)succinimide 18a from 10

A diastereomeric mixture of **10** (0.75 g, 2 mmol), HCO_2NH_4 (10 g) and triglyme (5 ml) was refluxed for 4 days. The solution was allowed to cool and was then poured into water. The precipitate formed was collected by filtration. Chromatography (CH_2Cl_2–MeOH, 95:5) gave **18a** (0.36 g, 55%) as a colourless foam, mp 239–242 °C; δ_H (300 MHz; DMSO-d_6) 11.56 (1H, s, NH), 11.05 (2H, d, *J* 1.5, ArH), 7.42–7.35 (6H, m, ArH), 7.08 (2H, app t, ArH), 6.86 (2H, app t, ArH), 4.56 (2H, s, C*H*); δ_C (75 MHz; DMSO-d_6) 178.5 (s), 136.5 (s), 126.3 (s), 124.1 (d), 121.3 (d), 118.8 (d), 118.6 (d), 111.7 (d), 110.0 (s), 47.0 (d); ν_{max}(KBr)/cm^{-1} 3430, 3340, 3180, 3060, 1770, 1700, 1550, 755, 740; *m*/*z* (ESI) [M + H$^+$] 330. Found: HRMS (EI) *m*/*z* 329.1155. $C_{20}H_{15}N_3O_2$ requires *M*, 329.1164.

Further elution gave unchanged **10b** (0.11 g, 15%).

***cis*-3,4-Di(indol-3-yl)succinimide 18b.** The experiment (hydrogenation[14] of **19**) by Davis *et al.* was repeated. Yield 33% (lit., 70%); δ_H (300 MHz; DMSO-d_6) 11.59 (1H, s), 10.64 (2H, s), 7.39 (2H, d, *J* 8), 7.12 (2H, d, *J* 8), 6.95–6.8 (6H, m), 4.9 (2H, s); δ_C (75 MHz; DMSO-d_6) 179.6, 135.4, 127.0, 124.4, 120.7, 118.5, 118.3, 111.3, 108.2, 44.7.

General procedure for dimerization of the 3-substituted indoles

The indole (1 mmol) was dissolved in TFA (2.5 ml) and the solution was kept at room temperature for 3 h, when water (15 ml) was added. The pH of the opaque solution was adjusted to 4 with 2 M NaOH and the crude product was collected by filtration. The precipitate can be recrystallized from propan-2-ol.

2-(Indol-2′-yl)indoline-3,3′-diacetic acid 24a. Yield 91%; mp 156–160 °C; δ_H (300 MHz; DMSO-d_6) 11.12 (1H, s, NH), 7.46 (1H, d, *J* 7.8, ArH), 7.33 (1H, d, *J* 8.0), 7.11–6.96 (4H, m), 6.79–6.71 (2H, m, ArH), 4.92 (1H, d, *J* 7.5, CH), 3.78 (1H, m, CH), 3.73 (2H, s, CH_2), 2.61 (1H, dd, *J* 8.4 and 16.4, CHH), 2.70 (1H, dd, *J* 4.5 and 16.4, CHH); δ_C (300 MHz; DMSO-d_6) 173.4 (s), 173.4 (s), 149.0 (s), 135.9 (s), 135.5 (s), 131.6 (s), 127.9 (s), 127.9 (d), 123.6 (d), 121.5 (d), 119.4 (d), 118.6 (d), 118.5 (d), 111.3 (d), 110.3 (d), 106.8 (s), 60.4 (d), 45.5 (d), 36.7 (t), 29.9 (t); ν_{max}(KBr)/cm^{-1} 3089 br, 1703, 1682, 1200, 745; *m*/*z* (ESI) [M + H$^+$] 351.

These data are in agreement with those published.[20]

Dimethyl 2-(indol-2′-yl)indoline-3,3′-diacetate 24b. Yield 97%, mp 112–114 °C; δ_H (DMSO-d_6) 11.14 (1H, s, NH), 7.41 (1H, d, *J* 8, ArH), 7.31 (1H, d, *J* 8, ArH), 6.94–7.1 (4H, m, ArH), 6.62–6.70 (2H, m, ArH), 4.85 (1H, d, *J* 11, CH), 3.79 (2H, s, CH_2), 3.71 (1H, dd, *J* 6 and 11, CHH), 3.58 (3H, s, CH_3), 3.51 (3H, s, CH_3), 2.72 (2H, d, *J* 6, CH); δ_C (DMSO-d_6) 29.3 (t), 36.0 (t), 45.5 (d), 51.3 (q), 51.5 (q), 60.4 (d), 105.6 (s), 109.5 (d), 111.1 (d), 116.1 (d), 116.5 (d), 121.3 (d), 123.2 (d), 127.6 (s), 127.7 (d), 130.5 (s), 135.7 (s), 136.0 (s), 149.8 (s), 172.0 (2s); ν_{max}(KBr)/cm^{-1} 3361, 2522 br, 1722, 1655, 1618, 1415, 1206, 744; *m*/*z* (ESI) [M + H$^+$] 379. Found: HRMS (EI) *m*/*z* 378.1562. $C_{22}H_{22}N_2O_4$ requires *M*, 378.1580.

Diethyl 2-(indol-2′-yl)indoline-3,3′-diacetate 24c. Yield 99%, δ_H (300 MHz; DMSO-d_6) 11.11 (1H, s), 7.41 (1H, d, *J* 7.8), 7.30 (1H, d, *J* 8.0), 7.05–6.95 (4H, m), 6.64–6.57 (2H, m), 6.03 (1H, d, *J* 3.2), 4.80 (1H, dd, *J* 10.8 and 3.2), 4.05–3.76 (4H, m), 3.76 (2H, s), 3.70 (1H, dd, *J* 10.8 and 6.6), 2.70 (2H, d, *J* 6.6), 1.16 (3H, t, *J* 7.1), 1.06 (3H, t, *J* 7.1); δ_C (DMSO-d_6) 172.1 (2s), 149.8 (s), 136.3 (s), 135.4 (s), 129.6 (s), 128.3 (d), 128.0 (s), 124.0 (d), 122.3 (d), 119.6 (d), 119.3 (d), 118.5 (d), 110.9 (d), 109.4 (d), 105.8 (s), 61.2 (d), 60.9 (t), 60.6 (t), 46.1 (d), 37.4 (t), 30.1 (t), 14.1 (q), 14.0 (q); *m*/*z* (ESI) [M + H$^+$] 407. Found: HRMS (EI) *m*/*z* 406.1882. $C_{24}H_{26}N_2O_4$ requires *M*, 406.1893.

Dimethyl 2,2′-biindolyl-3,3′-dicarboxylate 26

DDQ (260 mg, 1.14 mmol) in 1,4-dioxane (7 ml) was added to a solution of the dimer **24b** of indole-3-acetic acid methyl ester (430 mg, 1.14 mmol) in 1,4-dioxane (15 ml) at room temperature. After 16 h the DDQ-2H was filtered off and the solvent was evaporated. The residue was recrystallized from propan-2-ol and filtration gave 261 mg (61%) of the product as a white solid, mp 196–197 °C; δ_H (DMSO-d_6) 11.35 (2H, s, NH), 7.50 (2H, app d, ArH), 7.41 (2H, app d, ArH), 7.18 (2H, app t, ArH), 7.06 (2 H, app t, ArH), 3.77 (4H, s, CH_2), 3.58 (3H, s, CH_3); δ_C (DMSO-d_6) 172.1 (q), 136.3 (q), 127.8 (q), 127.6 (q), 122.1 (s), 119.2 (s), 119.0 (s), 111.4 (s), 107.3 (q), 51.7 (q), 30.2 (t); *m*/*z* (ESI) [M + H$^+$] 377. Found: HRMS (EI) *m*/*z* 376.1408. $C_{22}H_{22}N_2O_4$ requires *M*, 376.1423.

The tetrahydroindolocarbazole 27

The diastereomerically pure bisindole **10b** (19 mg) was dissolved in TFA (1.5 ml) at room temperature and the solution stirred for 3 h. Water was added and the slightly yellow precipitate **26** (18 mg, 94%) was collected by filtration and washed with water, δ_H (DMSO-d_6) 11.05 (1H, s, NH), 7.38–7.45 (2H, m, ArH), 6.98–7.15 (4H, m, ArH), 6.70–6.80 (2H, m, ArH), 5.05 (1H, d, *J* 7.8, CH), 4.27 (1H, d, *J* 5.4, CH), 4.08 (1H, dd, *J* 11.5 and 5.4, CH), 3.67 (3H, s, CH_3), 3.60 (3H, s, CH_3), 3.03 (1H, dd, *J* 11.5 and 7.8, CH); δ_C (DMSO-d_6) 172.2 (s), 171.6 (s), 149.2 (s), 136.1 (s), 133.5 (s), 130.4 (s), 128.3 (d), 125.1 (s), 125.1 (d), 121.7 (d), 119.4 (d), 119.1 (d), 118.0 (d), 111.5 (d), 110.8 (d), 105.8 (s), 54.2 (d), 51.8 (q), 51.7 (q), 45.2 (d), 40.4 (d), 39.7 (d); ν_{max}(KBr)/cm^{-1} 3442, 1733, 1663, 1434, 1200, 1137, 757, 745, 723; *m*/*z* (ESI) [M + H$^+$] 377. Found: HRMS (EI) *m*/*z* 376.1405. $C_{22}H_{22}N_2O_4$ requires *M*, 376.1423.

Compound 28

Dissolution of **10b** (10 mg) in TFA (1 ml) at 40 °C gave the known[22] indolocarbazole **28** as a precipitate (8 mg).

Tetrahydroarcyriaflavin A 29

The succinimide[25] **18b** (15 mg) was dissolved in TFA (2.5 ml). After 15 min at room temperature 5 ml of water was added. The product of **28** (13 mg, 87%) was collected by filtration and washed with diethyl ether; δ_H (DMSO-d_6) 11.16 (1H, s), 10.90 (1H, s), 7.8 (1H, br s), 7.71 (1H, d, *J* 7.8), 7.29 (1H, d, *J* 7.9), 7.17 (1H, d, *J* 7.2), 7.04 (1H, app t), 6.94 (1H, app t), 6.88 (1H, app t), 6.58 (1H, app t), 6.50 (1H, d, *J* 7.6), 4.74 (1H, d, *J* 7.9), 4.29 (1H, dd, *J* 7.5 and 2), 4.10 (1H, dd, *J* 7.9 and 2), 4.01 (1H, d, *J* 7.5); δ_C (DMSO-d_6) 179.9 (s), 178.0 (s), 149.7 (s), 136.1 (s), 134.5 (s), 128.9 (s), 127.8 (d), 125.6 (s), 122.5 (d), 121.8 (d), 120.3 (d), 119.0 (d), 117.9 (d), 111.1 (d), 109.3 (d), 104.7 (s), 53.2 (d), 40.9 (d), 40.0 (d), 39.7 (d); *m*/*z* (ESI) [M + H$^+$] 330.

Arcyriaflavin A 4

The succinimide[25] **18b** (15 mg) was dissolved in TFA (5 ml). The solution was refluxed for 8 h, when water was added. The orange product (11 mg, 75%) was collected by filtration and washed with diethyl ether, mp >260 °C; δ_H (DMSO-d_6) 11.79 (2H, s), 10.97 (1H, s), 8.98 (2H, d, *J* 7.9), 7.79 (2H, d, *J* 8.2), 7.54 (2H, app t), 7.34 (2H, app t); δ_C (DMSO-d_6) 171.3 (s), 140.3 (s), 129.1 (s), 126.8 (d), 124.3 (d), 121.6 (s), 120.2 (d), 119.9 (s), 115.5 (s), 112.0 (d). These data are in agreement with those published.[26]

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