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 staurosporine¹ 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 others¹² 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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indole-3-acetic acid 5 afforded the trianion 6. Quenching an aliquot of the reaction mixture with D2O 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-3yl)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 diastereometric 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 $(200 \,^{\circ}C; N_2)$ 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



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 \pm -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



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 indolyl-magnesium 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 CH₂ group in the ¹³C NMR spectrum. The previous workers did not report any ¹³C NMR data and interpreted the CH₂ 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





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hydroindolocarbazole 27 (Scheme 7) in excellent yield.

upon treatment with TFA, and indeed 10 gave the tetra-



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

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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

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 NaHSO₃ (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 MgSO₄. 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; $\delta_{\rm H}$ (200 MHz; DMSO-d₆) 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, CH₃); $\delta_{\rm C}$ (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); v_{max} (KBr)/cm⁻¹ 3350, 1714, 1432, 1313, 1161, 749; *m*/*z* (ESI) [M + H⁺] 377. Found: HRMS (EI) *m*/*z* 376.1410. C₂₂H₂₀N₂O₄ requires *M*, 376.1423. Concentration of the 1,4-dioxane solution followed by flash chromatography (CH₂Cl₂-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 NaHSO3 (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 MgSO4. 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 (CH₂Cl₂-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; $\delta_{\rm H}$ (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); $\delta_{\rm C}$ (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); v_{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. C₂₀H₁₄N₂O₃ 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 (CH₂Cl₂–MeOH, 98:2) gave **12** (1.30 g, 80%), mp 184–187 °C; $\delta_{\rm H}$ (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, CH₂), 4.62 (2H, s, CH); $\delta_{\rm C}$ (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); $\nu_{\rm max}({\rm KBr})/{\rm cm}^{-1}$ 3400, 1775, 1695, 1460, 1430, 1395, 1345, 1155, 740 and 700; m/z (ESI) [M + H]⁺ 420. Found: HRMS (EI) m/z 419.1627. C₂₇H₂₁N₃O₂ 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 (CH₂Cl₂–MeOH, 98:2) to give **14** (0.27 g, 94%) as a red solid, $\delta_{\rm H}$ (200 MHz; Me₂CO-*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, CH₂); $\nu_{\rm max}$ (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 (CH₂Cl₂–MeOH, 98:2) gave **15** (0.73 g, 90%) as red solid, mp >260 °C; $\delta_{\rm H}$ (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, CH₂); $\nu_{\rm max}$ (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), HCO₂NH₄ (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 (CH₂Cl₂–MeOH, 95:5) gave **18a** (0.36 g, 55%) as a colourless foam, mp 239–242 °C; $\delta_{\rm H}$ (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, CH); $\delta_{\rm C}$ (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); $\nu_{\rm max}$ (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. C₂₀H₁₅N₃O₂ 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%); $\delta_{\rm H}$ (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); $\delta_{\rm C}$ (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.

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; $\delta_{\rm H}$ (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, CH₂), 2.61 (1H, dd, J 8.4 and 16.4, CHH), 2.70 (1H, dd, J 4.5 and 16.4, CHH); $\delta_{\rm C}$ (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); $\nu_{\rm max}({\rm KBr})/{\rm cm^{-1}}$ 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; $\delta_{\rm H}$ (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, CH₂), 3.71 (1H, dd, J 6 and 11, CHH), 3.58 (3H, s, CH₃), 3.51 (3H, s, CH₃), 2.72 (2H, d, J 6, CH); $\delta_{\rm C}$ (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); $v_{\rm max}$ (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. C₂₂H₂₂N₂O₄ requires *M*, 378.1580.

Diethyl 2-(indol-2'-yl)indoline-3,3'-diacetate 24c. Yield 99%, $\delta_{\rm H}$ (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); $\delta_{\rm C}$ (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. C₂₄H₂₆N₂O₄ 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; $\delta_{\rm H}$ (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, CH₂), 3.58 (3H, s, CH₃); $\delta_{\rm C}$ (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. C₂₂H₂₂N₂O₄ 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, $\delta_{\rm H}$ (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, CH₃), 3.60 (3H, s, CH₃), 3.03 (1H, dd, *J* 11.5 and 7.8, CH); $\delta_{\rm C}$ (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); $v_{\rm max}$ (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. C₂₂H₂₂N₂O₄ requires *M*, 376.1423.

Compound 28

Dissolution of **10b** (10 mg) in TFA (1 ml) at 40 $^{\circ}$ C gave the known²² indolocarbazole **28** as a precipitate (8 mg).

Tetrahydroarcyriaflavin A 29

The succinimide²⁵ **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; $\delta_{\rm H}$ (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); $\delta_{\rm C}$ (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); *mlz* (ESI) [M + H⁺] 330.

Arcyriaflavin A 4

The succinimide²⁵ **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; $\delta_{\rm H}$ (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); $\delta_{\rm C}$ (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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