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Inducing *anti*-Conformers of Biliverdin Chromophores by Reducing Sterical Hindrance

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Summary. Two different types of conformational changes of the biliverdin chromophore were accomplished by the concept of reducing sterical hindrance. On one hand, model compounds unsubstituted at position 7 and/or 13 adopt the semi-extended geometry with *anti*-conformation of the dipyrrinone moiety. On the other hand, stretching of the chromophore with *anti*-conformation of the dipyrrin substructure was achieved with a model compound unsubstituted at position 12. Both kinds of *anti*-conformations have been proved by 2D NMR and UV-Vis spectroscopy.

Keywords. Chromophores; Conformation; NMR spectroscopy; Tetrapyrroles; UV-Vis spectroscopy.

Introduction

Dissolved biliverdines or biliverdin-derived chromophores generally adopt a helical (all*Z*,all*syn*)-geometry, but bound to proteins many of them have been found to occur in a stretched geometry mostly in an (*anti*,*syn*,*anti*)-conformation [1–3]. The stretching of the chromophore is accompanied by changes in light absorption: while UV-absorption decreases, Vis-absorption increases. Accordingly, several ways of modifying chromophore geometry have been developed. First, chemical transformations such as chelating the tetrapyrrole [4], linking the lactams [5], or bridging adjacent rings [6–9] have been performed following the structure of bile pigments found in lepidopteran insects [10, 11] or sea snakes [12]. Second, changes in geometry could be achieved by using *HMPA* as the solvent [13].

In this paper we report on a new strategy for the *syn*/*anti*-change of the exocyclic single bonds of the tetrapyrrole chromophore just by reducing sterical hindrance (Scheme 1). Biliverdines substituted in all eight β-positions are found to occur exclusively in the (all*Z*,all*syn*)-geometry with the bulky substituents at the

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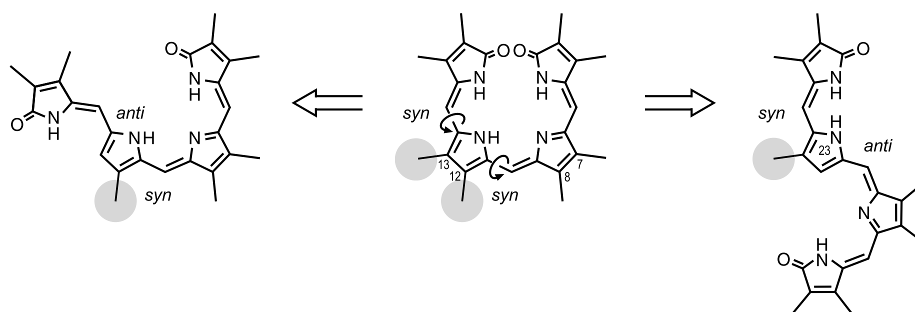


Scheme 1

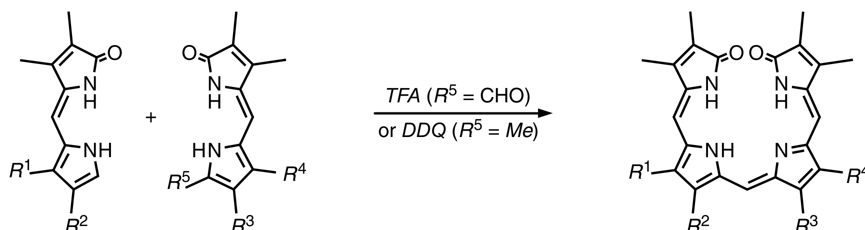
periphery and the small nitrogen-bound hydrogens in the center of the chromophore. Replacement of a β-substituent by hydrogen adjacent to the single bond of a *meso*-bridge will result in a sterical equivalence of the inside N-H and the outside C_β-H, enabling rotation from the *syn*- to the *anti*-conformation. Thus, biliverdines unsubstituted at position 7 or 13 can adopt the *anti*-conformation within the dipyrrinone substructure, whereas the *syn*/*anti*-change within the dipyrrin moiety can be accomplished by biliverdins unsubstituted at position 12 as shown for the 23*H*-tautomer in Scheme 1, or in position 8 for the 22*H*-tautomer.

Results and Discussions

Synthesis Aspects

With regard to the structure determination of the chromophore geometry by means of NMR-spectroscopic methods model-compounds **1**–**4** were chosen. Their ^{1}H NMR spectra only consist of singlets or singlet like signals minimizing the probability of signal overlap and facilitating stereochemical assignments by N*O*E cross-peaks of proper intensities.

In principle, two synthetic methods were used to obtain bilindiones with different substitution patterns (Scheme 2). On the one hand biliverdins **1**–**3** were prepared by means of an acid catalyzed condensation [14] of the 9-unsubstituted



		R^1	R^2	R^3	R^4	R^5	
5	**7**	*Me*	*Me*	*Me*	*Me*	CHO	**1**
6	**7**	H	*Me*	*Me*	*Me*	CHO	**2**
6	**8**	H	*Me*	*Me*	H	CHO	**3**
5	**9**	*Me*	*Me*	H	*Me*	*Me*	**4**

Scheme 2

dipyrrinones **5** and **6** with the 9-formyldipyrrinones **7** and **8**. On the other hand biliverdin **4** was synthesized from 9-methyldipyrrinone **9** and the 9-unsubstituted dipyrrinone **5** by oxidative coupling with *DDQ* [15].

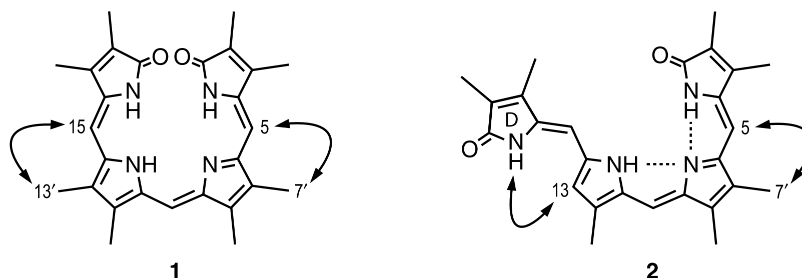
Syn/anti Change Within the Dipyrrinone Moiety

Bilindione **1** carrying methyl groups in all β-positions was used as a reference chromophore with (allZ,all*syn*)-geometry. Its stereochemistry was confirmed by N*O*ESY cross-peaks between the methine hydrogens and the methyl groups adjacent to the corresponding *meso*-bridges (Scheme 3). Moreover, the intensity-ratio of 3:1 of its maximum absorptions in the UV- and Vis-region is characteristic for (allZ,all*syn*)-bilindiones.

With respect of the *syn/anti* change within the dipyrrinone substructure model-compounds **2** and **3** were investigated. Biliverdin **2** being unsubstituted at position 13 should be capable of adopting the "semi-extended" (5*syn*,10*syn*,14*anti*)-conformation. However, for biliverdin **3** being unsubstituted at position 7 as well as 13 rotation around both of the adjacent *meso*-single bonds principally could result in a "fully-extended" (5*anti*,10*syn*,14*anti*)-geometry.

Concerning heptamethylbilindione **2** the N*O*ESY experiments clearly prove that the semi-extended geometry is adopted in both $CDCl_3$ and *HMPA*-d_{18}. Dissolved in $CDCl_3$ the (14*anti*)-conformation is indicated by the broadened signal around 7.6 ppm which has to be assigned to the non hydrogen-bridged H-N24 of lactam D. However, when *HMPA*-d_{18} is used as the solvent this signal is sharpened and of proper intensity resulting in a strong N*O*E cross-peak with the signal of H-C13 (Scheme 3).

Hexamethylbilindione **3** also adopts a semi-extended geometry set up in a rapid equilibrium between two species of structural identity. The ^{1}H NMR spectrum of **3** recorded at room temperature shows a set of time-averaged signals resulting from pairs of singlets, which can be observed separated at −90°C in the case of the lactam NHs and the hydrogens at position 7 and 13 (Fig. 1). At this temperature the singlet of H-C5/H-C15 and each of the three singlets corresponding to the methyl groups at the positions 2/18, 3/17, and 8/12 are broadened significantly in comparison with the singlet of H-C10. According to the N*O*ESY experiment the equilibrium of the (5*syn*,10*syn*,14*anti*) and (5*anti*,9*syn*,14*syn*)-conformers is obvious by two cross-peaks of H-C7/H-C13 indicating close proximity to both H-C5/H-C15 as well as H-N21/H-N24. Thus, the conformational equilibrium of **3**



Scheme 3

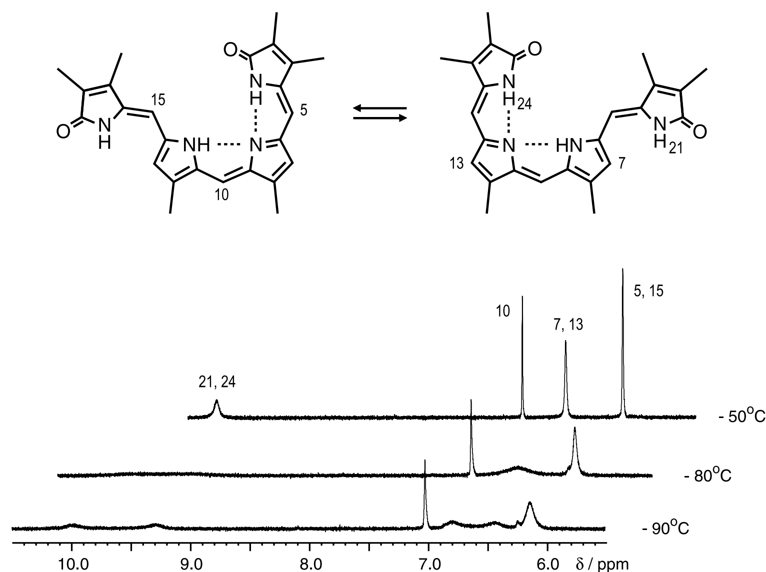


Fig. 1. Conformational dynamics of **3** (top) shown by the temperature dependence of its ^{1}H NMR spectrum in *THF*-d_8 (bottom)

is degenerated in terms of the semi-extension within the dipyrrinone units and in terms of tautomerism within the dipyrrin substructure.

Since it was not possible to observe the fully-extended geometry not even in a solvent with high donor power such as *HMPA* it has to be concluded that the (*syn*,*syn*)-conformation of the tripyrrinone substructure is stabilized by two hydrogen bridges, whereas the lactam not involved is able to rotate towards the *anti*-position. Due to this stability we further conclude that the interconversion of the semi-extended conformers runs *via* an (allZ,all*syn*)-intermediate, where the hydrogen-bridge system can easily oscillate by tautomerization within the dipyrrin moiety. Concerning light absorption semi-extension leads to a phenotype UV-Vis spectrum, which is characterized roughly by a 1:1 ratio of the maximum absorptions in the UV- and Vis-region.

Syn/anti Change Within the Dipyrrin Moiety

Heptamethylbilindione **4** unsubstituted at position 12 was found to be a suitable model-compound for studying the *syn/anti*-change of the dipyrrin subunit. With respect to the unsymmetrical substitution pattern each of the two (all*syn*)-tautomers **4a** and **4b** can be transformed into the structurally different (*syn*,*anti*,*syn*)-conformers **4c** and **4d** by rotation around the single bonds in position 9 or 10 (Fig. 2).

The comparison of the UV-Vis spectra of heptamethylbilindione **4** dissolved in chloroform, *DMF*, *DMSO*, and *HMPA* shows significant changes depending on the donor power of the solvent: an increase in donor power results in hyperchromicity of the Vis-absorption and in hypochromicity of the UV-absorption, indicating no stretching of the chromophore in $CHCl_3$, partial stretching in *DMF* and *DMSO*, and complete stretching in *HMPA*.

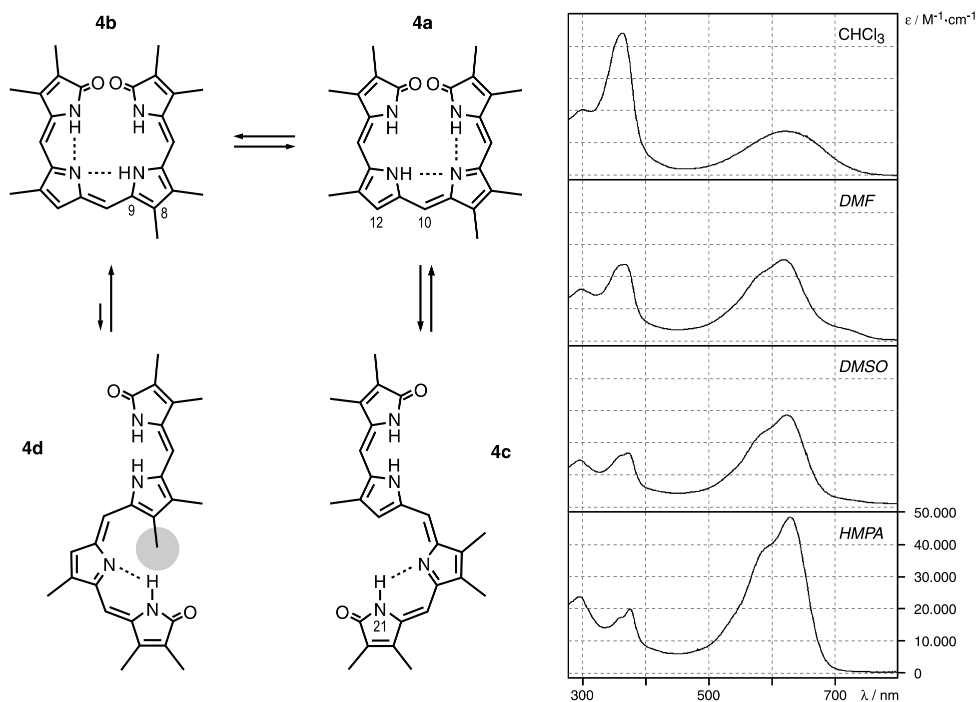


Fig. 2. Equilibrium of **4** in terms of tautomerism (**4a**/**4b**) and in terms of *syn*/*anti*-conformation (**4a**/**4c** and **4b**/**4d**) (left); UV-Vis spectra of **4** in $CHCl_3$, *DMF*, *DMSO*, and *HMPA* (right)

Accordingly, no cross-peak between H-C10 and H-C12 could be detected in the 2D-N*O*ESY spectra using *HMPA*-d_{18} as the solvent. However, a cross-peak clearly visible between H-C12 and H-N21 provides evidence for the (10*anti*)-conformation. Thus, conformer **4d** can be excluded when *HMPA* is the solvent and the mode of stretching seems to be controlled by the sterical differences between the small hydrogen at position 12 and the bulkier methyl group at position 8. The influence of the solvent can be interpreted by the assumption that aprotic polar solvents of high donor power are able to replace the intramolecular hydrogen-bridge of the pyrromethene subunit by an intermolecular one where the oxygen of the solvent binds towards the dipyrrinone NHs in a urea like structure [16].

In summary, we presented a new strategy for the stretching of biliverdin chromophores via conformational changes of their exocyclic single bonds. The results indicate that sterical requirements of definite β-substituents and the donor strength of the solvent in use can induce changes in chromophore geometry in such a way that the absorption characteristics of protein bound bilindiones can be mimicked.

Experimental

All chemicals were reagent grade. *THF* was distilled from Na benzophenone ketyl. Flash column chromatography was performed on silica gel 60 (Merck, 0.063–0.200 mm) or Al_2O_3 90 (Merck, 0.063–0.200 mm). NMR spectra were recorded on a Brucker Avance DRX-500 spectrometer. Assignments of ^1H and ^{13}C NMR signals were achieved using N*O*ESY and HSQC experiments under

standard instrument parameters. IR and UV-Vis spectra were recorded using a Bruker Tensor 27 and a Varian Cary 100 spectrometer. MS detection was performed using a quadrupole system Hewlett Packard 5989B and a pneumatically assisted electrospray ionisation interface Hewlett Packard 59987A. Compounds **1**, **5**, and **7** were prepared according to Refs. [17–19].

*General Procedure for the Preparation of the Biliverdins **2** and **3***

A solution of **6** (88 μmol) and **7** or **8** (88 μmol) in 1 cm^3 of *TFA* was stirred for 4 h at 45°C. After adding 5 cm^3 of CH_2Cl_2, 4 cm^3 of *Me*OH, and 50 cm^3 of H_2O the mixture was extracted with CH_2Cl_2. All extracts were combined and washed with saturated aqueous $NaHCO_3$. After evaporating the solvent the residue was subjected to column chromatography (Al_2O_3, 0.02% triethylamine in CH_2Cl_2) to afford **2** or **3** as a blue solid.

(4Z,9Z,15Z)-2,3,7,8,12,17,18-Heptamethylbilin-1,19-(21H,24H)-dione (**2**, $C_{26}H_{28}N_4O_2$)

Yield 31%; mp > 300°C; ^{1}H NMR (500 MHz, $CDCl_3$, 25°C): δ = 7.64 (s broad, H-N24), 6.71 (s, H-C10), 6.30 (s, H-C13), 6.11 (s, H-C15), 5.92 (s, H-C5), 2.30 (s, CH_3-C12), 2.18 (s, CH_3-C17), 2.16 (s, CH_3-C8), 2.12, 2.06 (2s, CH_3-C7, CH_3-C3), 1.95, 1.91 (2s, CH_3-C2, CH_3-C18) ppm; N*O*ESY (500 MHz, $CDCl_3$, 25°C): CH_3-C3 ↔ H-C5 ↔ CH_3-C7, CH_3-C8 ↔ H-C10 ↔ CH_3-C12 ↔ CH-C13, H-C15 ↔ CH_3-C17; ^{1}H NMR (500 MHz, *HMPA*-d_{18}, 25°C): δ = 10.22 (s, H-N24), 9.97 (s broad, H-N), 7.19 (s, H-C13), 6.64 (s, H-C10), 6.00 (s, H-C15), 5.82 (s, H-C5), 1.95 (s, CH_3-C12), 1.80 (s, CH_3-C8, CH_3-C3, CH_3-C17), 1.71 (s, CH_3-C7), 1.50, 1.44 (2s, CH_3-C2, CH_3-C18) ppm; N*O*ESY (500 MHz, *HMPA*-d_{18}, 25°C): CH_3-C2 ↔ CH_3-C3 ↔ H-C5 ↔ CH_3-C7 ↔ CH_3-C8 ↔ H-C10 ↔ CH_3-C12 ↔ H-C13 ↔ H-N24, H-C15 ↔ CH_3-C17 ↔ CH_3-18; IR (KBr): $\bar{\nu}$ = 1700, 1674, 1587 cm^{-1}; UV-Vis ($CHCl_3$): λ_{max} (ε) = 621 (28600), 371 (45600) nm (mol^{-1} dm^3 cm^{-1}); UV-Vis (*HMPA*): λ_{max} (ε) = 634 (28500), 374 (41800) nm (mol^{-1} dm^3 cm^{-1}); MS (ESIp): m/z = 429 [M + H$^+$].

(4Z,9Z,15Z)-2,3,8,12,17,18-Hexamethylbilin-1,19-(21H,24H)-dione (**3**, $C_{25}H_{26}N_4O_2$)

Yield 60%; mp > 300°C; ^{1}H NMR (500 MHz, *DMSO*-d_6, 30°C): δ = 9.70 (s, H-N21, H-N24), 6.76 (s, H-C10), 6.60 (s, H-C7, H-C13), 6.05 (s, H-C5, H-C15), 2.09 (s, CH_3-C8, CH_3-C12), 1.91 (s, CH_3-C3, CH_3-C17), 1.64 (s, CH_3-C2, CH_3-C18) ppm; N*O*ESY (500 MHz, *DMSO*-d_6, 30°C): (H-N21, H-N24) ↔ (H-C7, H-C13) ↔ (CH_3-C8, CH_3-C12), H-C10 ↔ (CH_3-C8, CH_3-C12), (H-C7, H-C13) ↔ (H-C5, H-C15) ↔ (CH_3-C3, CH_3-C17) ↔ (CH_3-C2, CH_3-C18); ^{1}H NMR (500 MHz, *THF*-d_8, −50°C): δ = 9.52 (s, H-N21, H-N24), 6.96 (s, H-C10), 6.59 (s, H-C7, H-C13), 6.11 (s, H-C5, H-C15), 2.30 (s, CH_3-C8, CH_3-C12), 2.16 (s, CH_3-C3, CH_3-C17), 1.87 (s, CH_3-C2, CH_3-C18) ppm; IR (KBr): $\bar{\nu}$ = 1681, 1584 cm^{-1}; UV-Vis ($CHCl_3$): λ_{max} (ε) = 616 (29500), 366 (42200) nm (mol^{-1} dm^3 cm^{-1}); UV-Vis (*DMF*): λ_{max} (ε) = 612 (41400), 366 (56100) nm (mol^{-1} dm^3 cm^{-1}); UV-Vis (*HMPA*): λ_{max} (ε) = 619 (49500), 370 (61900) nm (mol^{-1} dm^3 cm^{-1}); MS (ESIp): m/z = 415 [M + H$^+$].

(4Z,9Z,15Z)-2,3,7,8,13,17,18-Heptamethylbilin-1,19-(21H,24H)-dione (**4**, $C_{26}H_{28}N_4O_2$)

A solution of 20.3 mg of **5** (94 μmol) and 20.3 mg of **9** (94 μmol) in 5 cm^3 of absolute *THF* was cooled to 0°C. Then a solution of 42.6 mg of *DDQ* (190 μmol) in 10 cm^3 of absolute *THF* was added dropwise within 30 minutes. The reaction mixture was poured into a cold mixture of 15 cm^3 of $CHCl_3$ and 25 cm^3 of aqueous triethylamine (1%). After extracting with $CHCl_3$, the combined extracts were washed with aqueous L-ascorbic acid (1%), with H_2O, and dried (Na_2SO_4). After evaporation of the solvent the residue was subjected to column chromatography (first Al_2O_3, $CHCl_3$:*Me*OH = 100:1, and then silica gel, $CHCl_3$:*Me*OH = 100:1) to afford 7.0 mg of **4** (17%) as a blue solid. mp 162–165°C

(dec); ^{1}H NMR (500 MHz, $CDCl_3$, 40°C): $\delta = 6.63$ (s broad, H-C12), 6.62 (s, H-C10), 5.91 (s, H-C15), 5.86 (s, H-C5), 2.18 (s, CH_3-C13), 2.13 (s, CH_3-C8), 2.08 (s, CH_3-C17), 2.04 (s, CH_3-C3), 2.01 (s, CH_3-C7), 1.84, 1.82 (2s, CH_3-C2, CH_3-C18) ppm; N*O*ESY (500 MHz, $CDCl_3$, 40°C): (CH_3-C2, CH_3-C18) ↔ (CH_3-C3, CH_3-C17), CH_3-C3 ↔ H-C5 ↔ CH_3-C7, CH_3-C8 ↔ H-C10, H-C12 ↔ CH_3-C13 ↔ H-C15 ↔ CH_3-C17; ^{1}H NMR (500 MHz, *HMPA*-d_{18}, 25°C): $\delta = 11.8$ (s broad, H-N), 10.5 (s, H-N21), 10.0 (s, H-N), 6.87 (s, H-C12), 6.48 (s, H-C10), 5.92 (s, H-C5), 5.69 (s, H-C15), 1.89 (s, CH_3-C13), 1.82 (s, CH_3-C3), 1.81 (s, CH_3-C17), 1.75 (s, CH_3-C8), 1.72 (s, CH_3-C7), 1.51, 1.46 (2s, CH_3-C2, CH_3-C18) ppm; N*O*ESY (500 MHz, *HMPA*-d_{18}, 25°C): (CH_3-C2, CH_3-C18) ↔ (CH_3-C3, CH_3-C17), CH_3-C3 ↔ H-C5 ↔ CH_3-C7, CH_3-C8 ↔ H-C10, H-N21 ↔ H-C12 ↔ CH_3-C13 ↔ H-C15 ↔ CH_3-17; IR (KBr): $\bar{\nu} = 3319$, 1703, 1663, 1559, 1323, 1206 cm^{-1}; UV-Vis ($CHCl_3$): λ_{max} (ε) = 625 (14000), 366 (44300) nm ($mol^{-1}\,dm^3\,cm^{-1}$); UV-Vis (*DMF*): λ_{max} (ε) = 620 (22700), 368 (23000) nm ($mol^{-1}\,dm^3\,cm^{-1}$); UV-Vis (*DMSO*): λ_{max} (ε) = 626 (27500), 375 (15700) nm ($mol^{-1}\,dm^3\,cm^{-1}$); UV-Vis (*HMPA*): λ_{max} (ε) = 631 (48000), 377 (19500) nm ($mol^{-1}\,dm^3\,cm^{-1}$); MS (ESIp): $m/z = 429$ [M + H$^+$].

(4Z)-2,3,8-Trimethyldipyrrin-1(10H)-one (**6**, $C_{12}H_{14}N_2O$)

A solution of 204 mg of **10** (0.829 mmol) in 3.5 cm^3 of *TFA* was stirred at 60°C for 1 h. After adding 10 cm^3 of CH_2Cl_2, 10 cm^3 of *Me*OH, and 100 cm^3 of H_2O the mixture was extracted with CH_2Cl_2. All extracts were combined, washed with aqueous $NaHCO_3$ (5%) and dried (Na_2SO_4). After evaporating the solvent the residue was subjected to column chromatography (silica gel, CH_2Cl_2:*Me*OH = 40:1) to afford 142 mg of **6** (85%) as a yellow solid. mp 213°C (dec); ^{1}H NMR (500 MHz, *DMSO*-d_6, 25°C): $\delta = 10.66$ (s broad, H-N11), 9.51 (s, H-N10), 6.65 (s broadened, H-C9), 6.50 (s broadened, H-C7), 5.96 (s, H-C5), 2.01 (s, CH_3-C8), 1.99 (s, CH_3-C3), 1.75 (s, CH_3-C2) ppm; ^{13}C NMR (125 MHz, *DMSO*-d_6, 25°C): $\delta = 172.4$ (C1), 141.6, 131.9, 127.4, 125.2, 120.1 (C2, C3, C4, C6, C8), 119.3 (C9), 113.1 (C7), 100.1 (C5), 12.2 (C-C8), 9.9 (C-C3), 8.7 (C-C2) ppm; IR (KBr): $\bar{\nu} = 3352$, 3187, 3148, 3003, 2916, 1682, 1641, 1580 cm^{-1}; UV-Vis (*DMF*): λ_{max} (ε) = 383 (13400) nm ($mol^{-1}\,dm^3\,cm^{-1}$); MS (ESIp): $m/z = 203$ [M + H$^+$].

(4Z)-2,3,8-Trimethyl-9-formyldipyrrin-1(10H)-one (**8**, $C_{13}H_{14}N_2O_2$)

To a stirred solution of 50 mg of **6** (247 μmol) in 1 cm^3 of *TFA* at 0°C 0.4 cm^3 of methyl orthoformate were added at once. After stirring for 3 min at 0°C the reaction mixture was stirred without cooling for another 3 min and poured into 20 cm^3 of H_2O. The green precipitate was filtered off with suction, washed with H_2O, cold methanol, and CH_2Cl_2. After drying 51 mg of **8** (90%) were obtained as a yellow-green solid. mp 278°C (dec); ^{1}H NMR (500 MHz, *DMSO*-d_6, 40°C): $\delta = 11.45$ (s, H-N11), 9.64 (s, H-N10), 9.39 (s, CHO), 6.56 (d, $J = 2.2$ Hz, H-C7), 5.89 (s, H-C5), 2.13 (s, CH_3-C8), 1.83 (s, CH_3-C3), 1.61 (s, CH_3-C2) ppm; ^{13}C NMR (125 MHz, *DMSO*-d_6, 40°C): $\delta = 177.6$ (C-C9), 172.8 (C1), 141.9, 137.9, 134.5, 132.8, 130.2, 127.6 (C2, C3, C4, C6, C8, C9), 114.3 (C7), 97.5 (C5), 11.0 (C-C8), 9.8 (C-C3), 8.7 (C-C2) ppm; IR (KBr): $\bar{\nu} = 3248$, 3027, 2918, 2849, 1686, 1611, 1487, 1426, 1364 cm^{-1}; UV-Vis (*DMF*): λ_{max} (ε) = 402 (15800), 382 (17800) nm ($mol^{-1}\,dm^3\,cm^{-1}$); MS (ESIp): $m/z = 231$ [M + H$^+$].

(4Z)-2,3,7,9-Tetramethyldipyrrin-1(10H)-one (**9**, $C_{13}H_{16}N_2O$)

In a mixture of 6 cm^3 of *Et*OH and 6 cm^3 of 4 *N* NaOH 222 mg of 3,4-dimethyl-3-pyrrolin-2-one [20] (2.0 mmol) and 248 mg of 3,5-dimethylpyrrole-2-carbaldehyde [21] (2.0 mmol) were dissolved and refluxed for 1.5 h. After cooling to 0°C the precipitate was filtered off with suction, washed with a small quantity of cold *Me*OH, and dried under vacuum. Product **9** (200 mg, 46%) was obtained as yellow needles. mp 287–290°C (dec); ^{1}H NMR (500 MHz, *DMSO*-d_6, 25°C): $\delta = 10.39$ (s broad,

H-N), 9.77 (s broad, H-N), 5.91 (s, H-C5), 5.72 (s, H-C8), 2.21 (s, CH_3-C9), 2.07 (s, CH_3-C7), 2.06 (s, CH_3-C3), 1.77 (s, CH_3-C2) ppm; ^{13}C NMR (125 MHz, *DMSO*-d_6, 25°C): $\delta = 172.3$ (C1), 141.8, 132.3, 129.1, 124.0, 123.8, 122.9 (C2, C3, C4, C6, C7, C9), 110.1 (C8), 98.1 (C5), 13.3 (C-C9), 11.6 (C-C7), 10.0 (C-C3), 8.7 (C-C2) ppm; IR (KBr): $\bar{\nu} = 3340$, 2915, 1675, 1637, 1579, 1477, 1380 cm^{-1}; UV-Vis (*Me*OH): λ_{max} (ε) = 405 (23800), 265 (4800), 233 (6600) nm (mol^{-1} dm^3 cm^{-1}).

(4Z)-9-Carboxy-2,3,8-trimethyldipyrrin-1(10H)-one (**10**, $C_{13}H_{14}N_2O_3$)

In a mixture of 2 cm^3 of *Et*OH and 2 cm^3 of 4 *N* NaOH 111 mg of 3,4-dimethyl-3-pyrrolin-2-one [20] (1.0 mmol) and 181 mg of ethyl 5-formyl-3-methylpyrrol-2-carboxylate [18] (1.0 mmol) were dissolved and stirred at 85°C for 6 h. The solution was diluted with 6 cm^3 of H_2O and saturated with SO_2. The precipitate was filtered off, washed with H_2O, and dried. Product **10** (211 mg, 86%) was obtained as a yellow-brown solid. mp 175°C (dec); ^{1}H NMR (500 MHz, *DMSO*-d_6, 25°C): $\delta = 11.38$ (s broad, H-N), 9.73 (s, H-N), 6.70 (s, H-C7), 6.11 (s, H-C5), 2.23 (s, CH_3-C8), 1.99 (s, CH_3-C3), 1.77 (s, CH_3-C2) ppm; ^{13}C NMR (125 MHz, *DMSO*-d_6, 25°C): $\delta = 172.7$, 162.7 (C1, C-C9), 141.8, 135.7, 130.6, 128.4, 126.8, 120.7 (C2, C3, C4, C6, C8, C9), 113.8 (C7), 98.5 (C5), 13.2 (C-C8), 9.8 (C-C3), 8.7 (C-C2) ppm; IR (KBr): $\bar{\nu} = 3371$, 3170, 1681, 1487, 1436, 1403, 1350, 1282 cm^{-1}; UV-Vis (*DMF*): λ_{max} (ε) = 391 (15400), 372 (17000) nm (mol^{-1} dm^3 cm^{-1}); MS (ESIn): $m/z = 245$ $[M - H^+]$.

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