

# On the Chemistry of Pyrrole Pigments, XCIV [1]: 1-(Dipyrrinon-9-yl)-3-(dipyrrinon-9-ylidene)-1- propene – A Novel *b*-Vinylogous Verdin Chromophore

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**Summary.** 1-(Dipyrrinon-9-yl)-3-(dipyrrinon-9-ylidene)-propene, a *b*-vinylogous verdin, was synthesized by condensation of 3-(dipyrrinon-9-yl)-propenal with a dipyrrinone unsubstituted in position 9. By condensing the latter with dimedone or squaric acid, *b*-vinylogous verdin pigments with restricted configurational and conformational degrees of freedom were obtained. The chemical and spectroscopic properties of these novel systems are discussed.

**Keywords.** 1-(Dipyrrinon-9-yl)-3-(dipyrrinon-9-ylidene)-propenes; *b*-Vinylogous verdin; Synthesis; Spectroscopy; Protonation.

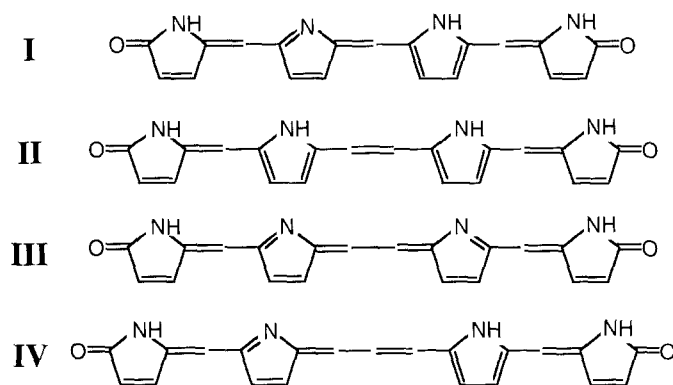
**Zur Chemie von Pyrrolpigmenten, 94. Mitt. [1]: 1-(Dipyrrinon-9-yl)-3-(dipyrrinon-9-yliden)-1-propen – Ein neuer *b*-vinyloger Verdinchromophor**

**Zusammenfassung.** 1-(Dipyrrinon-9-yl)-3-(dipyrrinon-9-yliden)-propen, ein *b*-vinyloges Verdin, wurde durch Kondensation von 3-(Dipyrrinon-9-yl)-propenal mit einem in Position 9 unsubstituierten Dipyrrinon dargestellt. Kondensation des Letzteren mit Dimedon oder Quadratsäure lieferte vinyloge Pigmente, welche in ihren konfigurationellen und konformationellen Freiheiten eingeschränkt sind. Die chemischen und spektroskopischen Eigenschaften dieser neuen Systeme werden diskutiert.

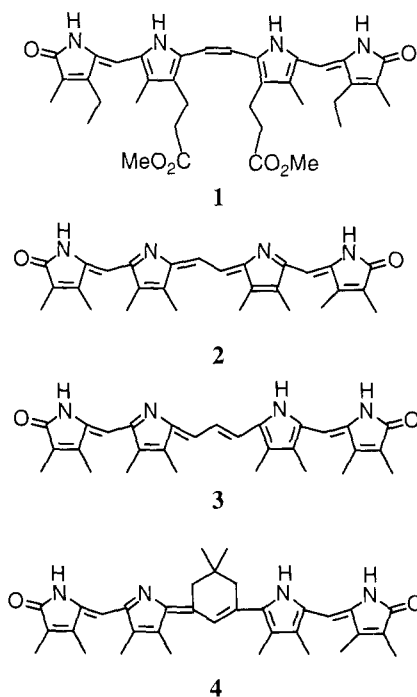
## Introduction

Most natural bile pigments are characterized by the verdin chromophore **I** [2]. It has been shown that this chromophore can be transformed into systems with shortened [3] or lengthened conjugation paths [1, 4, 5]. In the case of the latter, insertion of one carbon atom led to the two interesting novel *b*-homo-verdins **1** and **2** [1], which are of chromophore types **II** and **III**. The two chromophores **II** and **III** differ in their oxidation state. However, in **II** the two dipyrrinone “halves” are identical and the chromophoric system is related to that of the rubins. The type **III** chromophore has been found to be unique because of its two pyrrolenic nitrogen atoms, which again render the molecule formally mirror symmetric.

A true homologous chromophore related to the verdins is only possible by means of a vinylogous extension of the verdinoid chromophore type **I** into that of type **IV**.



Only in this case the two “halves” of the chromophore differ in their oxidation states as is the case in the verdins. Such novel chromophores are interesting with respect to a variety of applications, which range from possible metabolites of porphyrinoid radiation therapy agents to novel chelating agents [1]. Therefore, we set out to explore the chemistry of the chromophoric system **IV** by synthesizing the derivatives **3**, **4**, and **10**. They mainly differ in their diastereomeric degrees of freedom.

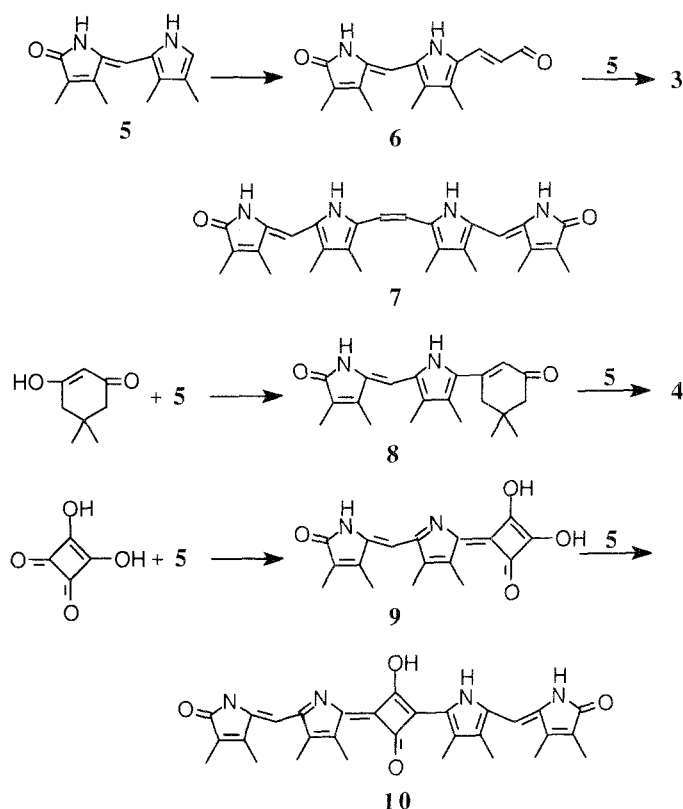


## Results and Discussion

### *Synthesis aspects*

The synthesis of **3** was achieved by first substituting the dipyrinone **5**, unsubstituted in position 9, by means of 3-dimethylaminoacrolein under the conditions used in the preparation of an analogous pyrrole derivative [6]. This reaction proceeded

with high yield to provide **6**. The latter underwent smooth acid catalyzed condensation with another mole of **5** to yield the desired homoverdinoid derivative **3**. Upon careful chromatography, a red pigment, which was produced as a trace by-product of the condensation reaction, could also be isolated. From its UV/Vis spectroscopic properties it was tentatively assigned the *b*-homo-verdinoid constitution **7**.

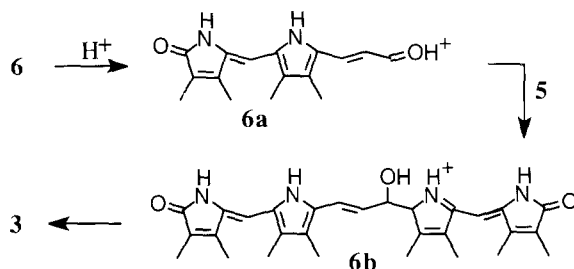


Although it has been previously reported that pyrroles with a free 2-position can be condensed with cyclohexane-1,3-dione or squaric acid [7, 8], the corresponding condensation of the dipyrriion **5** with dimedone proved to be rather difficult. The acid catalyzed (HBr) condensation of the two educts provided only about 5% of the blue pigment **4** together with 70% of the intermediate monocondensation product **8** after a lengthy reaction period of one week. The latter could be partially converted into **4** by acid catalyzed condensation with an additional mole of **5** after a reaction period of one week in a yield of only about 15%. The condensation of squaric acid with the dipyrriion **5** proceeded analogously. Thus, the mono-condensation product **9** was formed as an intermediate, and only upon prolonged treatment with an excess of squaric acid the interesting pigment **10** could be isolated. It should be mentioned that condensation of **5** with 1,3-pentanedione was not successful.

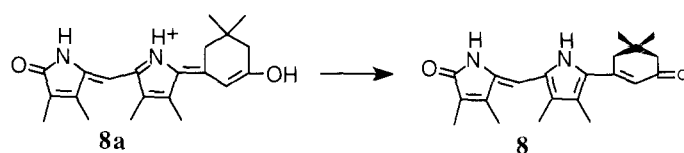
#### Mechanistic aspects

With respect to the mechanism of the formation of the pigment **3** it was suggested that the aldehyde functionality of **6** was protonated to form the intermediate species **6a** which was nucleophilically

attacked by **5** to yield **6b** in the way recently discussed [1, 2]. The latter then could lose water to yield the product **3**. Formation of the trace byproduct **7** could not readily be explained. It would involve loss of a CHO fragment from **6**, followed by an electrophilic attack of a molecule of **5**.



The formation of **4** could follow the same mechanism as that of **3**. However, it was remarkable that the reaction proceeded extremely slowly and almost stopped at the intermediate stage **8**. An explanation of this effect was based on the observation that compound **8** was red when it was just eluted from the chromatographic column (with  $\lambda_{\max} = 538$  and  $385$  nm in the eluent and  $\lambda_{\max} = 695$ ,  $581$ ,  $551$ ,  $425$ , and  $324$  nm upon acidification with trifluoroacetic acid). Upon workup and purification, this material turned yellow ( $\lambda_{\max} = 387$  nm and  $\lambda_{\max} = 438$  nm upon acidification). Obviously, the primary condensation reaction formed the tautomer **8a**, which became stabilized by protonation in the acidic reaction mixture. The chromophore of **8a** was found to be nearly coplanar by means of a PCMODEL [9] calculation. In contrast to this finding, **8** was derived to be twisted at the cyclohexene – dipyrrole single bond by about  $34^\circ$ . Of course, **8a** was not a suitable candidate to react with a second mole of **5**, which caused a severe retardation of the final condensation step. The chromophore of **8** closely resembled the one of **6**. The mechanistic details of the condensation of squaric acid with **5** to yield **10** via **9** may be envisaged in an analogous way.



#### Structural assignments

The constitutional, tautomeric, and configurational aspects [2] of the novel pigments were in accordance with their spectra. Thus, the molecular ion peak of **3** appeared in its mass spectrum at  $m/e = 468$ , and the fragmentation pattern also fitted the proposed constitution. Due to its limited solubility, a satisfactory  $^1\text{H}$  NMR spectrum of **3** could be obtained only in *TFA-d*. The data were characteristic of a symmetrical structure with the chemical shifts of the  $-\text{CH}=\text{}$  groups at  $6.45$  ppm, pointing to (*Z*) configurations at the two lactam ring exocyclic double bonds. A broad singlet for the  $-\text{CH}=\text{CH}-\text{CH}=\text{}$  protons was observed at  $7.54$  ppm. Of course, the configurations at the double bonds of this fragments could not be assigned. The  $^{13}\text{C}$  NMR spectrum displayed a  $\text{C}=\text{O}$  signal at  $173.24$  ppm, typical for a lactam tautomer [6]. Moreover, the IR spectra of **3** contained the typical lactam vibration at  $1699\text{ cm}^{-1}$  [2].

The molecular ion peak of **4** appeared in its mass spectrum at  $m/e = 537$ , and several characteristic fragments could be assigned. The  $^1\text{H}$  NMR spectrum of **4** could be measured in  $\text{CDCl}_3$ . Chemical shifts of two methyl groups at the cyclohexene moiety were found at 1.07 and 1.25 ppm. The  $^1\text{H}$  NMR spectrum displayed a singlet for  $-\text{CH}=\text{}$  in the 5,17-positions at 5.86 ppm. This chemical shift pointed to (*Z*) configurations at the two lactam ring exocyclic double bonds. The signal of the  $-\text{CH}=\text{}$  proton in position 11 was observed at 6.22 ppm. Nuclear *Overhauser* effects could be measured for protonated **4**, corroborating the predominance of the (*4Z,9E,11E,17Z*)-*12anti* arrangement. The  $^{13}\text{C}$  NMR spectrum exhibited a typical signal of the lactam  $\text{C}=\text{O}$  groups at 173.33 ppm [2] together with the appropriate number of pyrrole, alkene, and alkane signals. The lactam tautomerism of **4** was further corroborated by the IR spectrum which displayed the typical lactam vibration [2] at about  $1704\text{ cm}^{-1}$ .

The structural aspects of the intermediate **6** became obvious from its mass and NMR spectra. Thus, the (*5Z,10E*)-*5syn,9anti,11anti* lactam tautomer was derived to be the most predominant species. The spectroscopic details of the byproduct **7** were found to be in accordance with those of the derivative recently described [1]. The two intermediates **8** and **9** also allowed unequivocal structural assignments from their NMR and mass spectra, based on the characteristic dipyrinone and oxo-ring signals.

Due to solubility problems, NMR spectra of **10** could be obtained only in its protonated form or in pyridine as the solvent. The signals thus obtained were found to be in accordance with the (*4Z,9E,17Z*)-*5syn,12syn* or *12anti,16syn bis*-lactam species predominating in organic solvents. The constitutional assignment was also compatible with its mass spectrum.

*Absorption spectra, conformational aspects, protonation equilibria, and complexation of 3, 4, and 10*

The electronic absorption spectra of **3**, **4**, and **10** are illustrated in Fig. 1. Although they are of the same chromophoric type, their long wavelength band varied within a broad spectral range of nearly 200 nm. The configurationally constrained

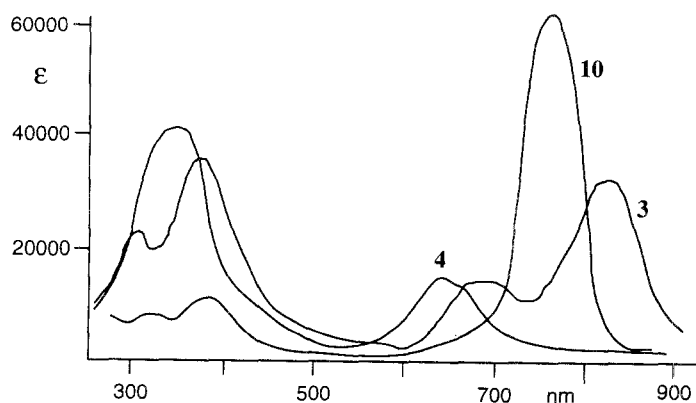
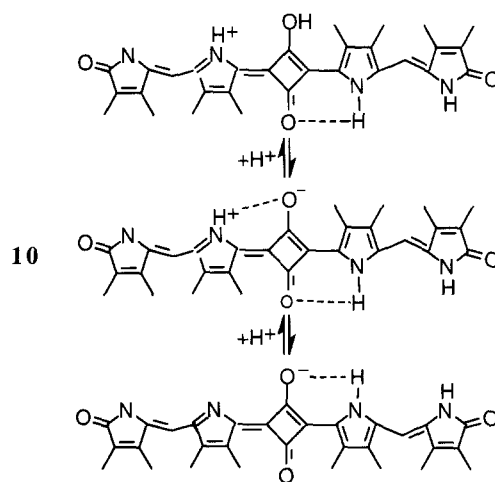


Fig. 1. Absorption spectra of the *b*-homoverdins **3**, **4**, and **10** in dichloromethane

derivative **4**, which according to a PCMODEL [9] calculation, is severely twisted ( $36^\circ$ ) at the exocyclic single bond between carbon atoms 12 and 13, absorbed in the region characteristic of verdins [2]. Obviously, the configurationally free parent system **3** could adopt an energetically low lying stretched and mostly planar arrangement; this explains its long wavelength band is shifted to about 820 nm. From PCMODEL [9] calculations, the (9*E*,11*E*) and (9*Z*,11*E*) diastereomers were derived to be the most stable ones. They were found to be characterized by dihedral angles of about  $0^\circ$  at the two adjacent single bonds, thus allowing for an unrestricted conjugation path within the chromophoric system. The (9*E*,11*Z*) and (9*Z*,11*Z*) diastereomers were calculated to be less stable by about 15 kJ/mole, with the two adjacent single bonds twisted by about  $25^\circ$ .

Interestingly enough, in contrast to the findings for **4** the absorption spectrum of **3** displayed a strong solvatochromic effect. The long wavelength band was shifted from 820 nm in dichloromethane *via* 802 nm in methanol and 652 nm in dimethylsulfoxide to 640 nm in dimethylformamide. Accordingly, solvation could stabilize various different configurational and conformational ground states of **3** as compared with the stereochemically restricted **4**. However, the spectral solvent shifts of **3** did not correlate with solvent polarity parameters like  $E_T$  [10].

The absorption spectrum of **10** displayed a more or less solvent indifferent long wavelength band of high intensity in the red region which was similar to the one of a protonated species. Hence, it was concluded that **10** was actually present in solution as its zwitterion. This species could be derived from a PCMODEL [9] calculation to adopt a mostly planar (9*E*)-12*anti* arrangement, which was stabilized by the charge interaction of the zwitterion part on the one hand, and a hydrogen bond between the pyrrole NH and the carbonyl group of the squaric acid moiety on the other hand, as indicated in Scheme 1.



Scheme 1

Compounds **3** and **4** were characterized by  $pK_a$  values of  $1.8 \pm 0.2$  and  $3.9 \pm 0.2$ , and were thus slightly less basic than their verdinoid parent compounds of chromophore type **I** [2]. Due to its acidic squaric acid fragment, **10** displayed a more complicated dissociation behavior which is illustrated in Scheme 1. Thus, its

protonation-deprotonation behavior with  $pK_a$  values of 5.5 and 9.2 was found to be analogous to that of the natural bile pigment biliverdin, which in addition to its basic pyrroline nitrogen atom bears carboxylic acid functions.

The three novel pigments **3**, **4**, and **10** were found to chelate with a variety of metal ions, such as Zn(II), Mg(II), Fe(II), Ni(II), and Cu(II) in several solvents. This behavior could point to novel agents for facilitated transport of metal ions [2].

## Experimental

$^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra were recorded on the Bruker-AC 200 and WM-360 instruments. Proton and carbon signals assignments were achieved using NOE and  $^1\text{H}$ - $^{13}\text{C}$  COSY experiments. UV/Vis and IR spectra were run on the Hitachi-U-3210 and Biorad-FT-IR-45 spectrophotometers. Mass spectra were measured on the MAT 95 (Innsbruck) and Hewlett-Packard 5989A (Linz) instruments, and melting points were determined by means of a Kofler hot stage microscope (Reichert, Vienna). Aluminum oxide (active, type 90, neutral) and silica GF<sub>254</sub> were used for column chromatography. The dipyrinone **5** was prepared according to Ref. [11]. Spectrophotometric  $pK_a$  estimates were derived using sulfuric acid and trifluoroacetic acid dilution series in dichloromethane as described in [12].

(4Z,17Z)-1-(2,3,7,8-tetramethyl-10H-dipyrinon-9yl)-3-(2,3,7,8-tetramethyl-9H-dipyrinon-9-ylidene)-propene (**3**; C<sub>29</sub>H<sub>32</sub>N<sub>4</sub>O<sub>2</sub>)

A 25 ml round-bottom flask was charged with 20 mg **6** (0.07 mmol), 16 mg **5** (0.07 mmol), 5 ml methanol, 10 ml and 2 ml of a CH<sub>2</sub>Cl<sub>2</sub> solution of HBr (33%) in acetic acid. The reaction was monitored by periodically quenching an aliquot of the reaction mixture with saturated aqueous sodium bicarbonate and observing the disappearance of **5** and **6** and the appearance of **3** by TLC and UV/Vis spectra. After 3 h 20 ml CH<sub>2</sub>Cl<sub>2</sub> and 20 ml of a 10% solution of aqueous ammonia were added dropwise over 10 min to neutralize the acid. Then the organic layer was separated and the aqueous phase was extracted three times with 50 ml CH<sub>2</sub>Cl<sub>2</sub>. The combined organic phases were washed with 50 ml water and 30 ml brine. After drying over anhydrous sodium sulfate and removing the solvent, the residue was purified by means of flash chromatography over alumina (type 90, neutral) using CH<sub>2</sub>Cl<sub>2</sub>/ethyl acetate (v/v, 6/4) as the eluent. Three fractions (order: **6** > **3**, **7**) were eluted. Compound **7** was purified by crystallization from methanol and found to exhibit an UV/Vis spectrum similar to the one of a recently prepared derivative [1]. The blue-green band containing **3** was further purified by silica gel column chromatography using CH<sub>2</sub>Cl<sub>2</sub>/ethyl acetate/CCl<sub>4</sub> (v/v/v, 2/2/1). To further purify **3**, the solid product was dissolved in a minimum amount of CH<sub>2</sub>Cl<sub>2</sub>; then methanol was added until **3** started to precipitate. The mixture was kept for 4 h; the solid was filtered off and washed with acetone (0 °C) until the washings were colorless. The solid was again dissolved in dichloromethane and passed through a short aluminum oxide chromatographic column (active, type 90, neutral 3 × 5 cm). Compound **3** was finally crystallized from CH<sub>2</sub>Cl<sub>2</sub>-MeOH, yielding 18 mg (54%). M.p.: 270 °C (dec.);  $^1\text{H}$  NMR (200 MHz,  $\delta$ , TFA-d): 1.96 (s, 2CH<sub>3</sub>), 2.10 (s, 2CH<sub>3</sub>), 2.15 (s, 2CH<sub>3</sub>), 2.24 (s, 2CH<sub>3</sub>), 6.45 (s, -CH=), 7.45 (br s, -CH=CH-CH=), 11.48 (s, NH) ppm;  $^{13}\text{C}$  NMR (90 MHz,  $\delta$ , TFA-d): 9.38 (CH<sub>3</sub>), 10.04 (CH<sub>3</sub>), 10.72 (CH<sub>3</sub>), 11.90 (CH<sub>3</sub>), 104.08 (-CH=), 113.35, 115.25, 120.87, 126.51, 132.17, 135.05, 143.78, 148.35, 153.44, 168.2 (C=N), 172.24 (C=O) ppm; IR (KBr):  $\nu$  = 3344, 2980, 2900, 1699, 1680, 1670, 1600, 1551, 1393, 1327, 1274, 1164, 1084, 967 cm<sup>-1</sup>; UV/Vis (acetone):  $\lambda_{\text{max}}$  = 816 (65600), 728 (20500), 640 (20900), 396 (54000), 380 (42500) nm ( $\epsilon$ ); UV/Vis (acetone + TFA):  $\lambda_{\text{max}}$  = 795 (52500), 715 (31500), 367 (42300), 327 (14900) nm ( $\epsilon$ ); UV/Vis (CHCl<sub>3</sub>):  $\lambda_{\text{max}}$  = 824 (14400), 652 (35200), 400 (65500), 385 (64200), 313 (35900) nm ( $\epsilon$ ); UV/Vis (CHCl<sub>3</sub> + TFA):  $\lambda_{\text{max}}$  = 817 (12600), 733 (48400), 733 (48400), 401 (84800), 317 (27400) nm ( $\epsilon$ ); UV/Vis (Et<sub>3</sub>N):  $\lambda_{\text{max}}$  = 667 (21500), 399 (8400), 381 (23500), 332 (13400) nm ( $\epsilon$ ); UV/Vis (acetic acid):  $\lambda_{\text{max}}$  = 796 (53600), 392 (45800) nm ( $\epsilon$ ); UV/Vis (acetic acid + TFA):  $\lambda_{\text{max}}$  = 764 (57300), 392 (45000) nm ( $\epsilon$ ); UV/Vis (ethyl acetate):  $\lambda_{\text{max}}$  = 808 (51200), 724 (16300), 403 (28800) nm ( $\epsilon$ ); UV/Vis

(THF):  $\lambda_{\max}$  = 816 (65600), 728 (20500), 640 (20900), 396 (54000), 318 (20800) nm ( $\epsilon$ ); UV/Vis (THF + TFA):  $\lambda_{\max}$  = 807 (88400), 726 (49500), 397 (59300), 317 (19300) nm ( $\epsilon$ ); UV/Vis (pyridine):  $\lambda_{\max}$  = 648 (45000), 401 (52000), 385 (45500), 329 (25000) nm ( $\epsilon$ ); UV/Vis (dioxane):  $\lambda_{\max}$  = 816 (8700), 408 (8000) nm ( $\epsilon$ ); UV/Vis (dioxane + TFA):  $\lambda_{\max}$  = 814 (80600), 400 (59300), 316 (18800) nm ( $\epsilon$ ); UV/Vis (CH<sub>3</sub>CN):  $\lambda_{\max}$  = 808 (8300), 392 (12300) nm ( $\epsilon$ ); UV/Vis (CH<sub>3</sub>CN + TFA):  $\lambda_{\max}$  = 802 (13300), 706 (17000), 373 (22400) nm ( $\epsilon$ ); UV/Vis (1,2-dichloroethane):  $\lambda_{\max}$  = 820 (49100), 734 (16000), 403 (3300), 323 (11200) nm ( $\epsilon$ ); UV/Vis (1,2-dichloroethane + TFA):  $\lambda_{\max}$  = 819 (49600), 731 (19500), 399 (32700), 322 (7800) nm ( $\epsilon$ ); UV/Vis (CH<sub>2</sub>Cl<sub>2</sub>):  $\lambda_{\max}$  = 820 (17550), 631 (12900), 381 (37100), 316 (18290) nm ( $\epsilon$ ); UV/Vis (CH<sub>2</sub>Cl<sub>2</sub> + TFA):  $\lambda_{\max}$  = 797 (46200), 399 (42100), 319 (17900) nm ( $\epsilon$ ); UV/Vis (CH<sub>2</sub>Cl<sub>2</sub> + Zn<sup>2+</sup>):  $\lambda_{\max}$  = 807 (36900), 732 (31800), 401 (18300) nm ( $\epsilon$ ); UV/Vis (CH<sub>2</sub>Cl<sub>2</sub> + Fe<sup>2+</sup>):  $\lambda_{\max}$  = 808 (17300), 690 (39800), 354 (11200) nm ( $\epsilon$ ); UV/Vis (CH<sub>2</sub>Cl<sub>2</sub> + Ni<sup>2+</sup>):  $\lambda_{\max}$  = 839 (46300), 753 (22600), 393 (46400) nm ( $\epsilon$ ); UV/Vis (CH<sub>2</sub>Cl<sub>2</sub> + Mg<sup>2+</sup>):  $\lambda_{\max}$  = 813 (6100), 670 (33700), 398 (31700) nm ( $\epsilon$ ); UV/Vis (CH<sub>2</sub>Cl<sub>2</sub> + Cu<sup>2+</sup>):  $\lambda_{\max}$  = 852 (5600), 768 (16800), 436 (18500) nm ( $\epsilon$ ); UV/Vis (MeOH):  $\lambda_{\max}$  = 802 (12800), 709 (33000), 373 (35000) nm ( $\epsilon$ ); UV/Vis (MeOH + TFA):  $\lambda_{\max}$  = 760 (48800), 387 (20900), 312 (17000) nm ( $\epsilon$ ); UV/Vis (MeOH + Zn<sup>2+</sup>):  $\lambda_{\max}$  = 835 (18600), 782 (16900), 400 (22400) nm ( $\epsilon$ ); UV/Vis (MeOH + Fe<sup>2+</sup>):  $\lambda_{\max}$  = 805 (88000), 710 (30000), 372 (20000) nm ( $\epsilon$ ); UV/Vis (MeOH + Ni<sup>2+</sup>):  $\lambda_{\max}$  = 764 (12700), 380 (25200), 312 (39600) nm ( $\epsilon$ ); UV/Vis (MeOH + Cu<sup>2+</sup>):  $\lambda_{\max}$  = 850 (2300), 736 (5000), 455 (10000) nm ( $\epsilon$ ); UV/Vis (DMSO):  $\lambda_{\max}$  = 652 (44800), 400 (58800), 309 (29900) nm ( $\epsilon$ ); UV/Vis (DMSO + TFA):  $\lambda_{\max}$  = 794 (110200), 404 (46500), 315 (27400) nm ( $\epsilon$ ); UV/Vis (DMSO + Zn<sup>2+</sup>):  $\lambda_{\max}$  = 853 (61600), 770 (14900), 432 (35300), 332 (8200) nm ( $\epsilon$ ); UV/Vis (DMSO + Fe<sup>2+</sup>):  $\lambda_{\max}$  = 651 (19700), 325 (15600) nm ( $\epsilon$ ); UV/Vis (DMSO + Ni<sup>2+</sup>):  $\lambda_{\max}$  = 797 (107400), 404 (46200) nm ( $\epsilon$ ); UV/Vis (DMSO + Mg<sup>2+</sup>):  $\lambda_{\max}$  = 651 (42700), 400 (58400), 320 (20400) nm ( $\epsilon$ ); UV/Vis (DMSO + Cu<sup>2+</sup>):  $\lambda_{\max}$  = 867 (37200), 779 (3700), 441 (15600) nm ( $\epsilon$ ); UV/Vis (DMF):  $\lambda_{\max}$  = 640 (44200), 397 (59900), 311 (28450) nm ( $\epsilon$ ); UV/Vis (DMF + TFA):  $\lambda_{\max}$  = 779 (114760), 400 (42700), 316 (27200) nm ( $\epsilon$ ); MS (70 eV):  $m/e$  (%) = 468 (M<sup>+</sup>, 25), 431 (18), 404 (19), 345 (16), 313 (53), 272 (68), 243 (70), 224 (12), 215 (41), 197 (25), 148 (22), 105 (79), 91 (100). The  $pK_a$  value was estimated to  $1.8 \pm 0.2$  from a spectrophotometric titration. The **3** and **3**·H<sup>+</sup> species were characterized by long wavelength absorption bands at 820 (1.0) and 800 (2.1) nm (relative intensity).

(5Z,9E,11E,17Z)-1-(2,3,7,8-Tetramethyl-10H-dipyrrinon-9-yl)-3-(2,3,7,8-tetramethyl-9H-dipyrrinon-9-ylidene)-5,5'-dimethyl-cyclohexene (**4**; C<sub>34</sub>H<sub>40</sub>N<sub>4</sub>O<sub>2</sub>)

**Method A.** 100 mg **5** (0.46 mmole), 156 mg **8** (0.46 mmole), 150 ml CH<sub>2</sub>Cl<sub>2</sub>, and 50 ml methanol were added to a flask filled with argon. The mixture was stirred for 30 min under an argon atmosphere; then, 5 ml HBr (33% in acetic acid) were added. The mixture was then stirred under reflux. The reaction was monitored by periodically quenching an aliquot of the reaction mixture with saturated aqueous sodium bicarbonate and observing the disappearance of starting material and the appearance of **4** (blue-green color) by TLC (eluent: CH<sub>2</sub>Cl<sub>2</sub>/ethyl acetate/CCl<sub>4</sub> = 2/1/1 (v/v/v)). After about one week, the mixture was allowed to cool down to room temperature. 40 ml Aqueous ammonia (15%) was added to quench the reaction, and the mixture was vigorously stirred for a few minutes. The organic layer was separated and the aqueous layer was extracted with 3 × 50 ml. The combined organic layers were washed with 2 × 80 ml saturated aqueous sodium bicarbonate solution, 2 × 80 ml water, 80 ml brine, and then dried over anhydrous sodium sulfate. After removing the solvent, the residue was dissolved in the minimum amount of CH<sub>2</sub>Cl<sub>2</sub> and chromatographed on a silica G-60 column with CH<sub>2</sub>Cl<sub>2</sub>/ethyl acetate/CCl<sub>4</sub> = 2/1/1 (v/v/v) as the eluent. After removing the solvent, the crude product was purified according to the procedure described above for **3**. Yield 37 mg **4** (15%).

**Method B:** As a byproduct of the condensation of **5** and dimedone as described in the preparation of **8** (see below).

M.p.: 280 °C (dec.); <sup>1</sup>H NMR (200 MHz,  $\delta$ , CDCl<sub>3</sub>): 1.07 (s, CH<sub>3</sub>(CH<sub>3</sub>)C= of cyclohexene), 1.25 (s, CH<sub>3</sub>(CH<sub>3</sub>)C= of cyclohexene), 1.78 (s, 2-CH<sub>2</sub>-), 2.03 (s, 3CH<sub>3</sub>), 2.05 (s, 3CH<sub>3</sub>), 2.14 (s, 2CH<sub>3</sub>),



5.86 (s, 2-CH=–5,17), 6.64 (s, –CH=–11) ppm;  $^1\text{H}$  NMR (200 MHz,  $\delta$ ,  $\text{CDCl}_3 + \text{TFA-d}$ ): 1.07 (s,  $\text{CH}_3(\text{CH}_3)\text{C=}$  of cyclohexene), 1.41 (s,  $(\text{CH}_3)_2\text{C=}$  of cyclohexene), 1.92 (s, 2- $\text{CH}_2$ -), 1.97 (s,  $\text{CH}_3$ -2,20), 2.16 (s,  $\text{CH}_3$ -3,19), 2.26 (s,  $\text{CH}_3$ -7,15), 2.52 (s,  $\text{CH}_3$ -8,14), 6.30 (s, 2-CH=–5,17), 7.63 (s, –CH=–11), 10.45 (br. s, NH), 10.65 (br. s, NH) ppm; NOE: 3,19 $\leftrightarrow$ 5,17 $\leftrightarrow$ 7,15; 11 $\leftrightarrow$ 8,14; 2,20 $\leftrightarrow$ 3,19;  $^{13}\text{C}$  NMR (90 MHz,  $\delta$ ,  $\text{CDCl}_3$ ): 9.06 (2 $\text{CH}_3$ ), 10.04 (2 $\text{CH}_3$ ), 10.12 (2 $\text{CH}_3$ ), 10.30 (2 $\text{CH}_3$ ), 21.06 ( $(\text{CH}_3)_2\text{C=}$ ), 30.23 ( $(\text{CH}_3)_2\text{C=}$ ), 54.21 (– $\text{CH}_5$ -), 97.18 (–CH=), 114.50 (–CH=), 128.41, 129.46, 135.01, 135.41, 141.18, 141.40, 142.24, 150.30, 152.22, 173.33 (C=O) ppm; IR (KBr):  $\nu = 2962, 2851, 1704, 1680, 1591, 1453, 1398, 1259, 1226, 1090, 1021, 938 \text{ cm}^{-1}$ ; UV/Vis ( $\text{CH}_2\text{Cl}_2$ ):  $\lambda_{\text{max}} = 627$  (9800), 367 (32500) nm ( $\epsilon$ ); UV/Vis ( $\text{CH}_2\text{Cl}_2 + \text{TFA}$ ):  $\lambda_{\text{max}} = 684$  (17700), 653 (18100), 357 (34600), 300 (14200) nm ( $\epsilon$ ); UV/Vis ( $\text{CH}_2\text{Cl}_2 + \text{Zn}^{2+}$ ):  $\lambda_{\text{max}} = 700$  (13400), 652 (15900), 405 (15900), 350 (30500), 277 (39000) nm ( $\epsilon$ ); UV/Vis ( $\text{CH}_2\text{Cl}_2 + \text{Fe}^{2+}$ ):  $\lambda_{\text{max}} = 710$  (11800), 650 (16000), 362 (35200) nm ( $\epsilon$ ); UV/Vis ( $\text{CH}_2\text{Cl}_2 + \text{Ni}^{2+}$ ):  $\lambda_{\text{max}} = 696$  (9600), 653 (18100), 357 (34600), 300 (14200) nm ( $\epsilon$ ); UV/Vis ( $\text{CH}_2\text{Cl}_2 + \text{Mg}^{2+}$ ):  $\lambda_{\text{max}} = 650$  (12300), 361 (28700) nm ( $\epsilon$ ); UV/Vis ( $\text{CH}_2\text{Cl}_2 + \text{Cu}^{2+}$ ):  $\lambda_{\text{max}} = 795$  (8000), 412 (21900) nm ( $\epsilon$ ); UV/Vis (MeOH):  $\lambda_{\text{max}} = 655$  (13200), 363 (36600) nm ( $\epsilon$ ); UV/Vis (MeOH + TFA):  $\lambda_{\text{max}} = 665$  (12700), 661 (36400) nm ( $\epsilon$ ); UV/Vis (MeOH +  $\text{Zn}^{2+}$ ):  $\lambda_{\text{max}} = 690$  (25200), 634 (17400), 362 (35800) nm ( $\epsilon$ ); UV/Vis (MeOH +  $\text{Fe}^{2+}$ ):  $\lambda_{\text{max}} = 672$  (23500), 352 (70800), 328 (84900) nm ( $\epsilon$ ); UV/Vis (MeOH +  $\text{Ni}^{2+}$ ):  $\lambda_{\text{max}} = 692$  (24600), 356 (42500) nm ( $\epsilon$ ); UV/Vis (MeOH +  $\text{Mg}^{2+}$ ):  $\lambda_{\text{max}} = 692$  (29700), 388 (43700), 331 (37300) nm ( $\epsilon$ ); UV/Vis (MeOH +  $\text{Cu}^{2+}$ ):  $\lambda_{\text{max}} = 785$  (8500), 409 (23000), 317 (20400) nm ( $\epsilon$ ); UV/Vis (DMSO):  $\lambda_{\text{max}} = 632$  (16500), 368 (43000), 326 (21600) nm ( $\epsilon$ ); UV/Vis (DMSO + TFA):  $\lambda_{\text{max}} = 693$  (31600), 644 (25000), 365 (43700) nm ( $\epsilon$ ); UV/Vis (DMSO +  $\text{Zn}^{2+}$ ):  $\lambda_{\text{max}} = 691$  (27600), 644 (22600), 366 (42000) nm ( $\epsilon$ ); UV/Vis (DMSO +  $\text{Fe}^{2+}$ ):  $\lambda_{\text{max}} = 636$  (14400), 356 (93100) nm ( $\epsilon$ ); UV/Vis (DMSO +  $\text{Ni}^{2+}$ ):  $\lambda_{\text{max}} = 636$  (16000), 628 (9700), 370 (42700) nm ( $\epsilon$ ); UV/Vis (DMSO +  $\text{Mg}^{2+}$ ):  $\lambda_{\text{max}} = 632$  (17300), 372 (44200) nm ( $\epsilon$ ); UV/Vis (DMSO +  $\text{Cu}^{2+}$ ):  $\lambda_{\text{max}} = 803$  (9000), 414 (24900) nm ( $\epsilon$ ); UV/Vis (DMF):  $\lambda_{\text{max}} = 652$  (14000), 368 (43000) nm ( $\epsilon$ ); UV/Vis (DMF + TFA):  $\lambda_{\text{max}} = 665$  (30600), 363 (41000) nm ( $\epsilon$ ); MS (FAB):  $m/e$  (%) = 537 (2, M + 1), 461 (5), 443 (100), 442 (65), 427 (6), 327 (12), 322 (4), 318 (5), 216 (15), 201 (5); MS (EI):  $m/e$  (%) = 483 (2), 442 (100), 427 (23), 422 (22), 332 (2), 318 (2), 304 (5), 274 (1), 221 (5), 216 (10), 201 (2), 156 (2). The  $pK_a$  value was estimated to  $3.0 \pm 0.2$  from a spectrophotometric titration. The **4** and **4**· $\text{H}^+$  species were characterized by long wavelength absorption bands at 627 (1.0) and 630 (2.0) and 705 (1.8) nm (relative intensity).

(5Z,10E)-3-(2,3,7,8-Tetramethyl-10H-dipyrriion-9-yl)-prop-2-enal (**6**;  $\text{C}_{16}\text{H}_{18}\text{N}_2\text{O}_2$ )

0.25 g 3-Dimethylaminoacrolein (2.5 mmol, 1.1 mole equiv., Aldrich) was introduced into a 250 ml flask which was cooled to  $-80^\circ\text{C}$ . Then, 0.39 g  $\text{POCl}_3$  (2.5 mmol, 1.1 mole equiv.) were added dropwise during 15 min. After stirring for 20 min, 50 ml dry  $\text{CH}_2\text{Cl}_2$  were added to the mixture and the solution was allowed to warm to  $-5^\circ\text{C}$ . A solution of 0.5 g **5** (2.3 mmol) dissolved in 50 ml  $\text{CH}_2\text{Cl}_2$  was added dropwise over 10 min. The color of the solution quickly turned orange–red. Before a solution of 1 g sodium acetate in 50 ml water was added, the mixture was stirred for another 30 min at room temperature. Then the organic layer was separated and the aqueous phase was extracted 3  $\times$  with 50 ml. The combined organic phases were washed with 50 ml water and 30 ml brine. After drying over anhydrous sodium sulfate and removing the solvent, the residue was purified by flash chromatography over alumina (type 90, neutral) and crystallized from  $\text{CH}_2\text{Cl}_2$ -hexane, yielding 0.44 g **6** (70%). M.p.:  $245^\circ\text{C}$  (dec.);  $^1\text{H}$  NMR (200 MHz,  $\delta$ ,  $\text{CDCl}_3$ ): 1.93 (s,  $\text{CH}_3$ -2), 2.12 (s,  $\text{CH}_3$ -3,7), 2.16 (s,  $\text{CH}_3$ -8), 6.08 (s, –CH=), 6.82 (dd,  $J_1 = 7.9 \text{ Hz}$ ,  $J_2 = 15.6 \text{ Hz}$ , –CH=CH–CHO), 7.39 (d,  $J = 15.6 \text{ Hz}$ , –CH=CH–CHO), 9.51 (d,  $J = 7.9 \text{ Hz}$ , –CH=CH–CHO), 10.32 (s, NH), 11.16 (s, NH) ppm;  $^{13}\text{C}$  NMR (90 MHz,  $\delta$ ,  $\text{CDCl}_3$ ): 8.86 ( $\text{CH}_3$ ), 9.32 ( $\text{CH}_3$ ), 9.33 ( $\text{CH}_3$ ), 9.90 ( $\text{CH}_3$ ), 98.80 (–CH=), 105.12 (–CH=CH–CHO), 109.53 (–CH=CH–CHO), 129.83, 133.25, 134.07, 142.76, 148.53, 153.78, 167.88 (C=N), 172.31 (C=O), 178.52 (CHO); NOE ( $\text{CDCl}_3$ ): –CH= $\leftrightarrow$  $\text{CH}_3$ -3 +  $\text{CH}_3$ -7;  $\text{CH}_3$ -8 $\leftrightarrow$  $\text{CH}_3$ -7; CH=CH–CHO $\leftrightarrow$ NH-12; IR (KBr):  $\nu = 3340, 2980, 2910, 2860, 1681, 1606, 1562, 1423, 1348, 1271, 1173, 1126, 1076, 955, 947 \text{ cm}^{-1}$ ; UV/Vis ( $\text{CH}_2\text{Cl}_2$ ):  $\lambda_{\text{max}} = 456$  (23600), 276 (129900) nm ( $\epsilon$ ), UV/Vis ( $\text{CH}_3\text{OH}$ ):  $\lambda_{\text{max}} = 450$  (24660), 299 (19700) nm ( $\epsilon$ ); UV/Vis (DMSO):  $\lambda_{\text{max}} = 461$  (36300), 302 (29900) nm ( $\epsilon$ ); MS (70 eV,  $250^\circ\text{C}$ ):  $m/e$  (%) = 270 ( $\text{M}^+$ , 100), 237 (12.4), 227 (5).

*9-(5,5'-Dimethyl-cyclohexen-1-one-3-yl)-2,3,7,8-tetramethyl-10H-dipyrin-1-one (8; C<sub>21</sub>H<sub>26</sub>N<sub>2</sub>O<sub>2</sub>)*

500 mg **5** (2.31 mmol), 972 mg 6,6'-dimethyl-cyclohexane-1,3-dione (dimedone; 6.9 mmol, 3.0 mole equiv., Aldrich), 100 ml dry CH<sub>2</sub>Cl<sub>2</sub>, and 100 ml dry methanol were charged to a three neck flask filled with argon. The mixture was stirred for 30 min under an argon atmosphere; then, 5 ml HBr (33% in acetic acid) were added and the mixture was stirred under reflux. The reaction was monitored by periodically quenching an aliquot of the reaction mixture with saturated aqueous sodium bicarbonate and observing the disappearance of **5** and the appearance of **4** (blue–green color) by TLC (eluent: CH<sub>2</sub>Cl<sub>2</sub>/ethyl acetate/CCl<sub>4</sub> = 2/1/1 (v/v/v)). After about one week, the reaction mixture was allowed to cool down to room temperature. 40 ml aqueous ammonia (15%) were added to quench the reaction and the mixture was vigorously stirred for a few minutes. The organic layer was separated and the aqueous layer was extracted three times with 50 ml CH<sub>2</sub>Cl<sub>2</sub>. The combined organic layers were washed twice with 80 ml aqueous saturated sodium bicarbonate and 80 ml water, once with 80 ml brine, and dried over anhydrous sodium sulfate. After removing the solvent, the residue was dissolved in the minimum amount of CH<sub>2</sub>Cl<sub>2</sub> and chromatographed on a silica G-60 column with CH<sub>2</sub>Cl<sub>2</sub>/ethyl acetate/CCl<sub>4</sub> = 2/1/1 (v/v/v) as the eluent. Compound **4** was further purified as described above. This procedure yielded 20 mg **4** (5%) and 183 mg **8** (70%). It should be noted that the color of compound **8** was red (in the eluent solution: λ<sub>max</sub> = 538, 385, 322 nm; in eluent solution + TFA: λ<sub>max</sub> = 695, 581, 551, 425, 324 nm; in eluent solution + Zn<sup>2+</sup>: λ<sub>max</sub> = 692, 615, 564, 399, 340, 294 nm) when just eluted from the chromatography column. It became yellow when it was worked up by removing the solvent and crystallizing from methanol. M.p.: 250 °C (dec.); <sup>1</sup>H NMR (200 MHz, δ, CDCl<sub>3</sub>): 1.07 (s, CH<sub>3</sub>(CH<sub>3</sub>)C= of cyclohexene), 1.35 (s, CH<sub>3</sub>(CH<sub>3</sub>)C= of cyclohexene), 2.04 (s, 4CH<sub>3</sub>), 2.11 (s, 4CH<sub>3</sub>), 2.22 (s, -CH<sub>2</sub>-), 2.78 (s, -CH<sub>2</sub>-), 6.10 (s, -CH= -5), 6.81 (s, -CH= of cyclohexene), 10.30 (br. s, NH), 10.36 (br s, NH), ppm; <sup>13</sup>C NMR (90 MHz, δ, CDCl<sub>3</sub>): 8.62 (CH<sub>3</sub>), 9.38 (CH<sub>3</sub>), 9.86 (CH<sub>3</sub>), 10.13 (CH<sub>3</sub>), 23.44 (CH<sub>3</sub>(CH<sub>3</sub>)C=), 26.38 (CH<sub>3</sub>(CH<sub>3</sub>)C=), 32.56 ((CH<sub>3</sub>)<sub>2</sub>C=), 51.66 (CH<sub>2</sub>), 53.45 (CH<sub>2</sub>), 101.09 (-CH=), 121.05 (-CH=), 124.23, 125.00, 129.72, 130.16, 135.16, 147.63, 148.32, 172.00 (C=O at pyrrolyl ring), 174.16, 180.98 (C=O) ppm; IR (KBr): ν = 3353, 3159, 2856, 2736, 1656, 1637, 1575, 1347, 1270, 1174, 1088, 1022, 938 cm<sup>-1</sup>; UV/Vis (CH<sub>2</sub>Cl<sub>2</sub>): λ<sub>max</sub> = 387 (18300) nm (ε); UV/Vis (CH<sub>2</sub>Cl<sub>2</sub> + TFA): λ<sub>max</sub> = 438 (21000) nm (ε); UV/Vis (MeOH): λ<sub>max</sub> = 396 (21700) nm (ε); UV/Vis (DMSO): λ<sub>max</sub> = 394 (30100) nm (ε); MS (70 eV, 235 °C): m/e (%) = 338 (2, M<sup>+</sup>), 257 (2), 245 (14), 233 (3), 217 (100), 216 (21), 126 (13), 124 (9).

*(Z)-1-(2,3,7,8-tetramethyl-10H-dipyrin-1-one-9-yl)-2-hydroxy-1-cyclobuten-4-one (9; C<sub>17</sub>H<sub>16</sub>N<sub>2</sub>O<sub>4</sub>)*  
*and (Z,E,Z)-1-(2,3,7,8-tetramethyl-10H-dipyrinon-1-one-9-yl)-3-(2,3,7,8-tetramethyl-10H-dipyrin-1-one-9-ylene)-2-hydroxy-1-cyclobuten-4-one (10; C<sub>30</sub>H<sub>30</sub>N<sub>4</sub>O<sub>4</sub>)*

*Method A.* 100 mg **5** (0.46 mmol), 211 mg 3,4-dihydroxycyclobut-1-en-1,2-dione (squaric acid; 1.85 mmol, 4.0 mole equiv., Aldrich), 150 ml dichloromethane, and 50 ml methanol were added to a flask filled with argon. The mixture was stirred for 30 min under an argon atmosphere. Then, 5 ml HBr (33% in acetic acid) were added. The mixture was stirred at room temperature and monitored by periodically quenching an aliquot of the reaction mixture with aqueous saturated sodium bicarbonate and observing the disappearance of the starting material and the appearance of **10** (blue–green color) by TLC (eluent: CH<sub>2</sub>Cl<sub>2</sub>/ethyl acetate/CCl<sub>4</sub> = 2/1/1, v/v/v). After about three days, a crystalline solid of bronze color had precipitated. The mixture was taken up with 200 ml CH<sub>2</sub>Cl<sub>2</sub>, 40 ml aqueous ammonia (15%) were added to quench the reaction, and the mixture was vigorously stirred for a few minutes. The organic layer – together with the solid – was separated and the solvent was removed under vacuum. The residue was washed with 20 ml methanol, 20 ml acetone, and finally with 20 ml CH<sub>2</sub>Cl<sub>2</sub>. The washings were retained for further work-up. The solid residue was purified by carefully dissolving it in a minimum amount of TFA and filtering to remove the insoluble materials. 20 ml MeOH were very slowly added to the resulting green solution. The mixture was cooled for 24 h at -20 °C. Then the bronze colored solid was collected and washed with 3 ml triethylamine and 5 ml acetone. To further purify the solid it was dissolved in a minimum amount of TFA, precipitated with 20 ml acetone, filtered, and washed

with 3 ml pyridine and 5 ml methanol. This procedure yielded 73 mg (93%) **10**. After removing the solvent *in vacuo*, the solution from above was treated with the minimum amount of  $\text{CH}_2\text{Cl}_2$  and chromatographed on a silica G-60 column with  $\text{CH}_2\text{Cl}_2$ /ethyl acetate/ $\text{CCl}_4 = 2/1/1$ , v/v/v, as the eluent. After removing the solvent on a rotary evaporator, the crude product was crystallized from  $\text{CH}_2\text{Cl}_2$ -hexane. This procedure yielded 10 mg (21%) **9**.

*Method B.* Condensation of **5** with **9** according to the preparation of **4** and purifying the product as given above. This afforded **10** in 95% yield.

Compound **9** was found to be soluble in methanol, *DMF*, *DMSO*, pyridine; slightly soluble in acetone,  $\text{CHCl}_3$ , acetic acid, ethyl acetate; insoluble in  $\text{CHCl}_3$ . M.p.: 250 °C;  $^1\text{H}$  NMR (200 MHz,  $\delta$ , *DMSO*- $d_6$ ): 1.79 (s,  $\text{CH}_3$ -2), 2.05 (s,  $\text{CH}_3$ -7), 2.06 (s,  $\text{CH}_3$ -3), 2.26 (s,  $\text{CH}_3$ -8), 5.97 (s,  $-\text{CH}=\text{}$ ), 8.82 (br s, NH), 8.95 (s, NH) ppm; NOE (*DMSO*- $d_6$ ):  $-\text{CH}=\leftrightarrow\text{CH}_3$ -3,7,  $\text{CH}_3$ -2 $\leftrightarrow\text{CH}_3$ -3;  $^{13}\text{C}$  NMR (90 MHz,  $\delta$ , *DMSO*- $d_6$ ): 8.42 ( $\text{CH}_3$ ), 9.21 ( $\text{CH}_3$ ), 9.62 ( $\text{CH}_3$ ), 10.35 ( $\text{CH}_3$ ), 97.51 ( $-\text{CH}=\text{}$ ), 120.24 (C-1 of cyclobutene), 123.31 ( $\text{C}_{\text{pyrr}}$ ), 126.02 ( $\text{C}_{\text{pyrr}}$ ), 126.57 ( $\text{C}_{\text{pyrr}}$ ), 133.00 ( $\text{C}_{\text{pyrr}}$ ), 141.82 ( $\text{C}_{\text{pyrr}}$ ), 165.51 ( $\text{C}_{\text{pyrr}}$ ), 172.22 (C-2 of cyclobutene), 173.10 (C=O of lactams), 191.34 (C=O), 194.07 (C=O) ppm; IR (KBr):  $\nu = 3602, 3328, 2863, 1773, 1678, 1595, 1585, 1497, 1459, 1384, 1310, 1163, 1069 \text{ cm}^{-1}$ ; UV/Vis (*DMSO*):  $\lambda_{\text{max}} = 494$  (9000), 462 (8800), 318 (6400) nm ( $\epsilon$ ); UV/Vis (*DMSO* +  $\text{Zn}^{2+}$ ):  $\lambda_{\text{max}} = 494$  (8400), 464 (8400), 370 (6400) nm ( $\epsilon$ ); UV/Vis (*DMSO* + *TFA*):  $\lambda_{\text{max}} = 467$  (9600) nm ( $\epsilon$ ); UV/Vis (MeOH):  $\lambda_{\text{max}} = 452$  (13100) nm ( $\epsilon$ ); UV/Vis (MeOH + *TFA*):  $\lambda_{\text{max}} = 464$  (13900), 440 (14800) nm ( $\epsilon$ ). It should be noted that this compound was red in  $\text{CH}_2\text{Cl}_2$ /ethyl acetate/ $\text{CCl}_4$  (2/2/1, v/v/v) when it was just eluted from the chromatographic column. Its UV/Vis spectrum at this time was characterized as: UV/Vis (in the eluent solution):  $\lambda_{\text{max}} = 539$  (0.89), 367 (0.51), 319 (0.91) nm (*A*); UV/Vis (in the eluent solution +  $\text{Zn}^{2+}$ ):  $\lambda_{\text{max}} = 586$  (0.69), 546 (0.66), 404 (0.44), 324 (0.89) nm (*A*); UV/Vis (in the eluent solution + *TFA*):  $\lambda_{\text{max}} = 582$  (0.83), 550 (0.83), 405 (0.37), 363 (0.49), 324 (0.92) nm (*A*).

Compound **10** was found to be insoluble in methanol, acetone,  $\text{CH}_2\text{Cl}_2$ ,  $\text{CHCl}_3$ , and ethyl acetate; slightly soluble in pyridine, *DMF*, *DMSO*, and acetic acid, easily soluble in M.p.: 280 °C (dec.);  $^1\text{H}$  NMR (200 MHz,  $\delta$ ,  $\text{CDCl}_3$  + *TFA*- $d$ ): 2.13 (s, 2 $\text{CH}_3$ ), 2.16 (s, 2 $\text{CH}_3$ ), 2.19 (s, 2 $\text{CH}_3$ ), 2.31 (s, 2 $\text{CH}_3$ ), 3.80 (s, OH), 5.30 (s, 2- $\text{CH}=\text{}$ ) ppm;  $^1\text{H}$  NMR (200 MHz,  $\delta$ , pyridine- $d_5$ ): 2.03 (s, 2 $\text{CH}_3$ ), 2.04 (s, 2 $\text{CH}_3$ ), 2.07 (s, 2 $\text{CH}_3$ ), 2.13 (s, 2 $\text{CH}_3$ ), 3.75 (s, OH), 6.73 (s, 2- $\text{CH}=\text{}$ ) ppm;  $^{13}\text{C}$  NMR (90 MHz,  $\delta$ ,  $\text{CDCl}_3$  + *TFA*- $d$ ): 9.00 ( $\text{CH}_3$ ), 9.25 ( $\text{CH}_3$ ), 9.80 ( $\text{CH}_3$ ), 10.45 ( $\text{CH}_3$ ), 99.51 ( $-\text{CH}=\text{}$ ), 120.24 (C-1,3 of cyclobutene), 124.31 ( $\text{C}_{\text{pyrr}}$ ), 125.02 ( $\text{C}_{\text{pyrr}}$ ), 129.57 ( $\text{C}_{\text{pyrr}}$ ), 138.00 ( $\text{C}_{\text{pyrr}}$ ), 144.82 ( $\text{C}_{\text{pyrr}}$ ), 145.33 ( $\text{C}_{\text{pyrr}}$ ), 165.51 ( $\text{C}_{\text{pyrr}}$ ), 172.22 (C-2 of cyclobutene), 173.10 (C=O, lactam), 191.34 (C=O of cyclobutene) ppm; IR (KBr):  $\nu = 3449, 2980, 2915, 1694, 1630, 1592, 1486, 1420, 1394, 1340, 1294, 1260, 1214, 1147, 1091, 933 \text{ cm}^{-1}$ ; UV/Vis ( $\text{CH}_2\text{Cl}_2$ ):  $\lambda_{\text{max}} = 760$  (65000), 372 (5000) nm ( $\epsilon$ ); UV/Vis ( $\text{CH}_2\text{Cl}_2$  + *TFA*):  $\lambda_{\text{max}} = 760$  (65000), 730 (131200), 402 (23500) nm ( $\epsilon$ ); UV/Vis ( $\text{CH}_2\text{Cl}_2$  +  $\text{Zn}^{2+}$ ):  $\lambda_{\text{max}} = 760$  (71100), 412 (19600) nm ( $\epsilon$ ); UV/Vis (*DMF*):  $\lambda_{\text{max}} = 760$  (27800), 700 (39100), 410 (12500), 356 (9600) nm ( $\epsilon$ ); UV/Vis (*DMF* +  $\text{Zn}^{2+}$ ):  $\lambda_{\text{max}} = 788$  (102000), 710 (33400), 429 (6000), 338 (11500) nm ( $\epsilon$ ); UV/Vis (*DMF* + *TFA*):  $\lambda_{\text{max}} = 759$  (59800), 407 (13200), 365 (10200) nm ( $\epsilon$ ); UV/Vis (*DMSO*):  $\lambda_{\text{max}} = 775$  (16700), 733 (16000), 413 (3000), 369 (3000), 320 (2400) nm ( $\epsilon$ ); UV/Vis (*DMSO* +  $\text{Zn}^{2+}$ ):  $\lambda_{\text{max}} = 774$  (16800), 736 (16200), 412 (3000), 365 (3000), 317 (2100) nm ( $\epsilon$ ); UV/Vis (*DMSO* + *TFA*):  $\lambda_{\text{max}} = 772$  (23400), 375 (3000), 322 (2000) nm ( $\epsilon$ ); MS (EI):  $m/e$  (%) = 513 (1), 512 (4), 510 (1;  $\text{M}^+$ ), 494 (1), 391 (65), 377 (1), 230 (35), 216 (58), 201 (26), 187 (20), 123 (100), 110 (40), 94 (85), 79 (50). The  $pK_a$  values were estimated to  $5.5 \pm 0.2$  and  $9.2 \pm 0.2$  from a spectrophotometric titration in *DMF*. The  $\mathbf{10}^{\pm}$ ,  $\mathbf{10}^-$ , and  $\mathbf{10} \cdot \text{H}^+$  species were characterized by long wavelength absorption bands at 760 (1.0), 803 (1.0), and 759 (2.3) nm (relative intensity).

## Acknowledgements

A *Lise-Meitner* postdoctoral fellowship of the *Fonds zur Förderung der wissenschaftlichen Forschung* to Q.-Q. C. is gratefully acknowledged. Doz. Dr. K. Grubmayr (Univ. Linz) helped with inspiring discussions; the MS were kindly measured by Doz. Dr. K. Ongania (Univ. Innsbruck) and DI. K. Haider (Univ. Linz).

## References

- [1] Part XCIII: Chen Q-Q, Falk H (1995) *Monatsh Chem* **126**: 1097
- [2] Falk H (1989) *The chemistry of linear oligopyrroles and bile pigments*. Springer, Wien New York
- [3] Falk H, Flödl H, Wagner UG (1988) *Monatsh Chem* **119**: 739; Falk H, Flödl H (1988) *Monatsh Chem* **119**: 1155
- [4] Chen Q-Q, Ma J-S, Wang C-Q, Liu Y-Y, Yan F, Cheng L-J, Jin S, Falk H (1995) *Monatsh Chem* **126**: 983
- [5] Chen Q-Q, Falk H, Micura R (1995) *Monatsh Chem* **126**: 473
- [6] Gosman M, Franck B (1986) *Angew Chem* **98**: 1107 (1986) *Angew Chem Int Ed Engl* **25**: 1100; Franck B, Gosmann M (1988) DOS 3635820 (Vinyloge Porphyrine), BASF AG, *Chem Abstr* **109**: 94748; Beckman VS, Wessel T, Franck B, Hönle W, Borrmann H, Schnering HGV (1990) *Angew Chem* **102**: 1439
- [7] Treibs A, Herrmann E (1954) *Liebigs Ann Chem* **589**: 287
- [8] Falk H, Hofer O, Leodolter A (1975) *Monatsh Chem* **106**: 983
- [9] PCMODEL v 5.0 (1994) Serena Software, Bloomington, USA
- [10] Reichardt C (1988) *Solvent effects in organic chemistry*. Verlag Chemie, Weinheim
- [11] Dobeneck H, Graf W, Ettl W (1962) *Hoppe Seyler's Z Physiol Chem* **329**: 168; Shroud DP, Puzicha G, Lightner DA (1992) *Synthesis* **1992**: 328
- [12] Albert A, Serjeant EP (1984) *The determination of ionization constants*. Chapman & Hall, London

*Received May 2, 1995. Accepted May 15, 1995*