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On the Chemistry of Pyrrole Pigments, XCIII [1]: 1,2-*bis*-(Dipyrrinon-9-ylidene)-ethane – a Novel *b*-Homoverdin Chromophore

Q.-Q. Chen and **H. Falk***

Institut für Chemie, Johannes Kepler Universität Linz, A-4040 Linz, Austria

Summary. Condensation of a 9-unsubstituted dipyrrinone with glyoxal in dichloromethane yielded a red pigment. It could be identified as 1,2-*bis*-(dipyrrinon-9-ylidene)-ethane which is an example of the hitherto unknown dehydro-*b*-homo-verdins. In addition, the corresponding mesobiliverdin-XIIIα could be isolated from the reaction mixture. The mechanistic aspects of this reaction are discussed. Absorption spectra, protonation equilibria, and complexation of the title compound with transition metal ions were investigated.

Keywords. 1,2-*bis*-(Dipyrrinon-9-ylidene)-ethane; *b*-Homoverdin; Dehydro-*b*-homoverdin; Mesobiliverdin; Protonation; Metal complexes; Absorption spectra.

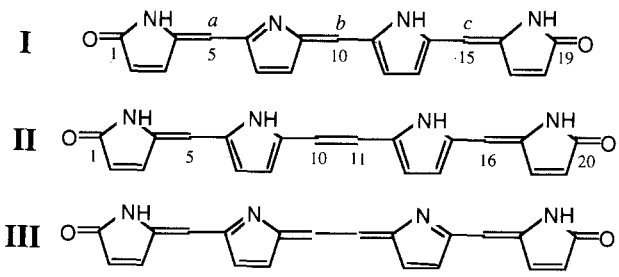
Zur Chemie von Pyrrolpigmenten, 93. Mitt. [1]: 1,2-*bis*-(Dipyrrinon-9-yliden)-ethan – ein neuer *b*-Homoverdin Chromophor

Zusammenfassung. Kondensation eines 9-unsubstituierten Dipyrrinons mit Glyoxal in Dichlormethan unter saurer Katalyse ergab ein rotes Pigment. Dieses konnte als 1,2-*bis*-(Dipyrrinon-9-yliden)-ethan identifiziert werden, welches ein Beispiel für die bislang nicht bekannten Dehydro-*b*-homoverdine darstellt. Darüber hinaus konnte dabei auch aus der Reaktionsmischung das entsprechende Mesobiliverdin-XIIIα isoliert werden. Die mechanistischen Aspekte der Bildungsreaktion werden diskutiert. Absorptionsspektren, Protonierungsgleichgewichte und die Komplexierung mit Übergangsmetallionen wurden untersucht.

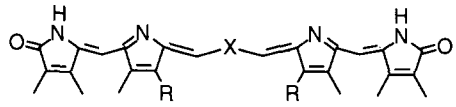
Introduction

The verdin chromophore **I** is present in a variety of bile pigments occurring in animals and plants. It may be expanded at position 10 into homologues, as has been recently discussed in detail [1]. By means of this formal operation two *b*-homoverdin chromophores **II** and **III**, which differ in their oxidation states, were obtained. Pigments of these kind are interesting with respect to their novel chromophoric systems and their structural peculiarities.

Recently, it has been demonstrated that treatment of 9-methyl-10*H*-dipyrrin-1-ones with bromine in dichloromethane solution resulted in red pigments of type **II** [2]. The first *b*-homoverdin extended at C-10, the linear pentapyrrole **1a**, has been previously synthesized by our group [3]. In this pentapyrrin system, a 3,4-dimethyl-



pyrrole-2,5-diyl moiety has been inserted between two dipyrrinone chromophores yielding a system which corresponds to the oxidation state of the chromophore **III**. Their analogs **1b–1d** and a *b*-homorubin derivative, with the latter corresponding to the *meso*-hydrogenated system **II**, have been recently prepared by *Lightner*'s group [4, 5]. However, *b*-homoverdin derivatives of the fundamental type **III** are still unknown to our knowledge. Therefore, a rational synthesis of a compound like **2**, which corresponds to chromophore **III**, was investigated and is reported in this paper.



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	X	R
a	3,4-dimethyl-2,5-pyrrole-diyl	CH_3
b	3,4-dimethyl-2,5-pyrrole-diyl	$CH_2CH_2CO_2CH_3$
c	1,4-phenyl-diyl	$CH_2CH_2CO_2CH_3$
d	1,3-phenyl-diyl	$CH_2CH_2CO_2CH_3$
2	single bond	CH_3

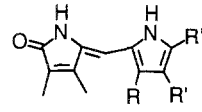
Results and Discussion

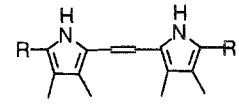
Synthetic Aspects

To synthesize a compound with type **III** chromophore, one could envisage several routes. For example, the pigment **2** could in principle be prepared by dehydrogenation of the corresponding pigment of chromophore type **II**. To study this possibility, 1,2-*bis*-dipyrrinonyl-ethenes were the first synthesis target. Following the disconnection approach [6], the synthesis of 1,2-*bis*-dipyrrinonyl-ethenes might be conducted on two convergent routes. The first one would involve the dimerization of a suitably substituted dipyrrinone, the second one would start with a *bis*-pyrrolyl-ethene derivative to which the lactam rings would be attached in the final step.

To follow the first route, it was tried to achieve the self-coupling of the 9-formyl-dipyrrinone **3** by using *McMurry* conditions [7] with $TiCl_4/Zn$ as the reducing agent. This system has been previously used to convert 5-pyrrole-aldehydes

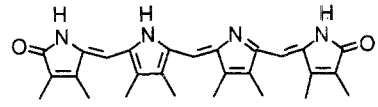
into 1,2-*bis*-pyrrolyl-ethenes [1, 8]. Unfortunately, the reaction did not result in the desired product under a variety of conditions. This could be either due to the lowered activity of the aldehyde group of **3**, or more probable, to a deactivation of the catalyst upon complexation with the lactam group.





	R	R′	R″
3	C_2H_5	CH_3	CHO
4	CH_3	CH_3	H
5	CH_3	CH_3	$COOBu^t$

	R
6a	$CH{=}CH(COOC_2H_5)CN$
6b	CHO



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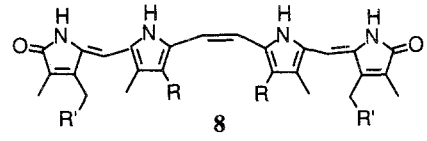

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R: **a**, $CH_2CH_2COOCH_3$; **b**, CH_2COOCH_3; **c**, C_2H_5; **d**, CH_3
R′: **a**–**c**, CH_3; **d**, H

Another route to produce **2** is the condensation of 3,4-dimethyl-pyrrolin-2-one [9] with 1,2-*bis*-(3,4-dimethyl-5-formyl-pyrrolyl)-ethene **6b** which was prepared by hydrolysis of **6a** [1]. The failure of this reaction under a variety of conditions obviously resulted from the low reactivity of the aldehyde group which is linearly conjugated to the respective second pyrrole.

Thus, we were left with the recently developed method of reacting 9-methyl-10*H*-dipyrrinone-1-ones with bromine in dichloromethane, resulting in 1,2-*bis*-dipyrrinonyl-ethenes **8a**–**8c** [2]. Using this recipe, we were able to synthesize the precursor **8d** in reasonable yield. Dehydrogenation of **8d** using *DDQ* produced **2** in 65% yield.

Unexpectedly, **2** could also be synthesized by condensation of glyoxal with dipyrrinone **4** which is unsubstituted in position 9. This reaction behavior could not be anticipated, since it is known from the times of *H. Fischer* that acid catalyzed condensations of α-free alkyl pyrroles with glyoxal lead to the formation of dipyrrins [10]. Indeed, besides **2** the verdinoid product **7**, expected from *Fischer*'s observations, could also be isolated from the reaction mixture. It is interesting to note that the yields of the reaction critically depends on the solvent and the kind of acid used to catalyze the reaction (Table 1, Experimental). The most appropriate conditions for

the formation of the dehydro-*b*-homoverdin **2** compared to the verdinoid derivative **7** were found to be dichloromethane as the solvent, two mole equivalents of glyoxal, and 33% hydrogen bromide in acetic acid to catalyze the condensation and the monomerization of the glyoxal polymer. According to Table 1, there occurred also an optimum in the reaction time. The best results were achieved by quenching the reaction mixture by addition of ammonia after about two minutes. Upon prolonged reaction times, the formation of the verdinoid derivative became more prominent.

Structural Assignment of **2**

The constitutional, tautomeric, and configurational aspects [11] of **2** could be derived from its NMR, IR, and mass spectra. Thus, the molecular ion peak of **2** appeared in its mass spectrum at $m/e = 454$, and the peaks at m/e 332, 227, and 214 corresponded to the characteristic fragments shown in Fig. 1. Accordingly, the constitution of **3** followed unequivocally from this fragmentation pattern.

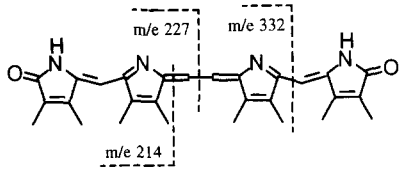


Fig. 1. Mass fragmentation of **2** (EI)

Due to its rather limited solubility in common organic solvents like chloroform, methanol, dimethyl sulfoxide, acetone, dioxane, dimethylformamide, and pyridine, the ^{1}H NMR spectrum of **2** could be recorded only in dichloromethane-d_2 and trifluoroacetic acid-d solutions. The ^{13}C NMR spectrum could even be measured only with a saturated solution in trifluoroacetic acid-d and rather long acquisition times (200 hrs). The ^{1}H NMR spectrum displayed a singlet of the –CH= protons in the 5,16-positions at 5.90 (dichloromethane-d_2) and 6.31 ppm (trifluoroacetic acid-d). This chemical shift pointed to (*Z*) configurations at the two exocyclic double bonds. The signal of the =CH–CH= protons in positions 10,11 were observed at 7.73 (dichloromethane-d_2) and 7.92 ppm (trifluoroacetic acid-d). However, due to the C_2 symmetry of the molecule coupling of these protons is absent, and a stereochemical assignment for this double bond (*Z,Z vs. Z,E* ≡ *E,Z vs. E,E*) could therefore not be achieved. In addition to the signals discussed above, the characteristic methyl protons could be easily identified by means of NOE measurements and chemical shift arguments. The ^{13}C NMR spectrum exhibited a typical signal of the C=O groups of the lactam fragments at 172 ppm [11] together with the appropriate number of pyrrole, alkene, and alkane signals. The lactam tautomerism of **2** was corroborated by the IR spectrum which clearly revealed the typical lactam vibration at about 1703 cm^{-1} [11]. Moreover, the NMR and IR data were in accordance with the constitutional assignment derived from the mass spectroscopic data.

The structural assignment of **7** followed easily from its ^{1}H NMR spectrum. It exhibited the characteristic signals of the methyl, methylene, and methine groups of a (*Z,Z,Z*)-mesobiliverdin-XIIIα derivative [11–13]. Moreover, the absorption spectrum of **7** contained the typical two band system of verdins at 630 and 360 nm.

Electronic Absorption Spectra, Protonation and Complexation of **2**

The absorption spectrum of **2** illustrated in Fig. 2 came as a surprise. The long wavelength band was observed at 533 nm in dichloromethane and was thus hypsochromically shifted with respect to the one of the verdinoid system **7a** (640 nm) and even slightly hypsochromically displaced from one of the *b*-homoverdinoid precursor **8d** (540 nm) which contains one double bond less. As has been discussed for the *b*-homoverdins [2], this hypsochromic shift can be correlated to considerable twisting at the single bonds joining the two dipyrrinoid 'halves' of the molecule. Indeed, PCMODEL [15] calculations indicated that, regardless of the configurations at the two double bonds in positions 9 and 11, and *synclinal* conformation with a dihedral angle of about 50° at the 10–11 single bond is slightly more stable than the nearly coplanar *antiperiplanar* conformation. This dihedral deformation leads to a significant hindrance of conjugation and accordingly to a strong hypsochromic shift of the absorption bands.

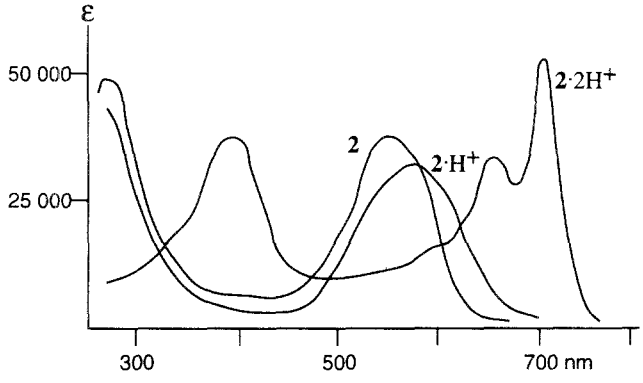


Fig. 2. UV/Vis spectra of **2**, **2**·H^+, and **2**·$2H^+$ in dichloromethane solutions

The protonation equilibrium of **2** was found to consist of a two step system characterized by strongly differing absorption spectra. The effect was rather small for the mono protonation with a spectrophotometrically estimated [16] pK_a^I of 4.0 ± 0.3. This value was thus observed in a region common to pyrroleninic nitrogen atoms contained in linear tetrapyrroles [11]. However, upon full protonation ($pK_a^{II} = 0.1 \pm 0.1$), the long wavelength band shifted dramatically (Fig. 2). Upon addition of base the spectral changes proved to be reversible. This behavior was similar to that found for the *b*-homoverdins like **8** [2]. It was ascribed to a stretching and planarization of the chromophore.

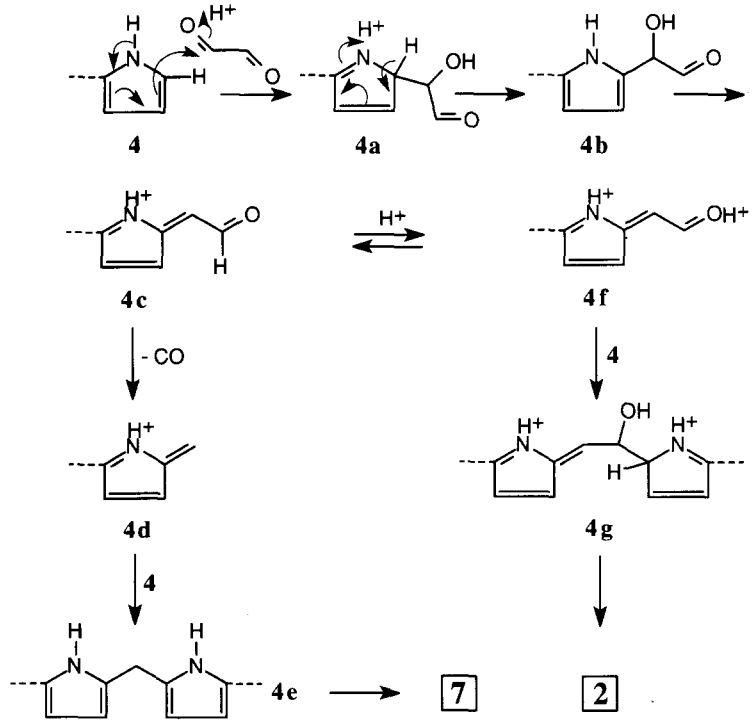
Transition metal ions Zn(II), Fe(II), Ni(II), and Cu(II) were observed to form complexes with the pigment **2** in dichloromethane, methanol, and dimethyl sulfoxide. However, as exemplified with a series of absorption spectra of solutions with varying relative amounts of ligand and Zn(II) ions, there seemed to exist a complicated cascade of different complexes. Thus, at low relative zinc concentrations a species absorbing at about 580 nm predominated. Upon increasing the relative zinc concentration this was followed by a species absorbing at about 640 nm, a further one at about 700 nm, and finally one at about 620 nm. The nature of these complexes could not be derived, but it was obvious that – due to the unique ligand geometry and two pyrroleninic type nitrogens together with two lactam nitrogen atoms – **2** could form complexes ranging from $\mathbf{2}_2$·Zn to polymeric systems. A

qualitative impression of the complexation behavior of **2** will be gained from an inspection of Table 2 (Experimental) where the species characterized by their absorption spectra were those formed at a high relative metal ion concentration.

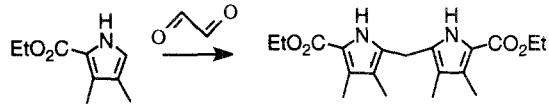
Mechanistic Aspects

With respect to the reaction mechanism for the formation of **2**, we suggested that in the first step the dipyrrinone **4** attacked the protonated glyoxal in the usual way of a nucleophilic addition [11] to yield **4a**. This intermediate would be first transformed into the substituted system **4b** which could then loose water to yield the conjugated azafulvenium intermediate **4c**. This particle has two options to react. The first possibility would be an intramolecular hydride shift to a species which then would split off carbon monoxide to give the azafulvenium ion **4d**. The latter is known to be a powerful electrophilic agent [11] which could attack another molecule of **4** to form the dipyrrylmethane derivative **4e**. Finally the verdin **7** is formed by aerial oxidation.

The formation of the dipyrryl-methane **4e** as the primary species was corroborated by the finding that upon acid catalyzed condensation of **9** with glyoxal the product was dipyrrylmethane **10**. In this case the product was stabilized against oxidation by the two carboxyl groups. In the case of alkyl substituted pyrroles, the product is a dipyrrin as has been observed by *Fischer* [10]. Alternatively, **4c** could also be protonated at the carbonyl group to provide **4f** which could be attacked by a further



molecule of **4** in the same way as in the case of the formation of **4a** to produce **4g**. Acid catalyzed loss of water would then render **2**.



9 **10**

Experimental

^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker-AC 200 instrument. Proton and part of the carbon, signals assignments were achieved using N*O*E and ^{1}H–^{13}C COSY. UV Vis and IR spectra were run on Hitachi-U-3210 and Biorad-FT-IR-45 spectrophotometers. Mass spectra were measured on a Hewlett-Packard 5989A instrument; melting points were determined by means of a Kofler hot stage microscope (Reichert, Vienna). Aluminum oxide (active, type 90, neutral) and silica G_{60} were used for column chromatography. Spectrophotometric pK_a estimates were derived using sulfuric acid and trifluoroacetic acid dilution series as described in Ref. [16].

(5Z,16Z)-1,2-bis-(2,3,7,8-Tetramethyl-dipyrrin-1-one-9-ylidene)-ethane (**2**: $C_{28}H_{30}N_4O_2$)

Method A: 200 mg 2,3,7,8-tetramethyl-dipyrrin-1-one (**4**, 0.93 mmol; [17]) and 105 mg glyoxal polymer (1.85 mmol) were added to 250 ml dichloromethane. The mixture was stirred for 30 min under an argon atmosphere; then, 2 ml hydrogen bromide (33% in acetic acid) were added. After stirring for additional 2 min, 30 ml aqueous ammonia (15%) were added to quench the reaction, and the mixture was vigorously stirred for few minutes. The organic layer was separated and washed with aqueous saturated sodium bicarbonate (2 × 50 ml), water (2 × 50 ml), brine (50 ml), and then dried over anhydrous sodium sulfate. After removing the solvent, the residue was dissolved in the minimum amount of dichloromethane and chromatographed on a silica G-60 column with CH_2Cl_2/ethyl acetate/CCl_4 = 2/1/1 (v/v/v) as the eluent. Two fractions (order: **2** > **7**) were eluted. To purify **2** further, the solid product was dissolved in a minimum amount of dichloromethane; then, methanol was added until **2** started to precipitate. The mixture was kept standing for 4 h, the solid was filtered off, washed with acetone (0 °C) and then with chloroform until the washings were colourless. The solid was again dissolved in dichloromethane and passed through a short aluminium oxide chromatographic column (active, type 90, neutral 3 × 5 cm). Compound **7** was purified by crystallization from dichloromethane-methanol. This procedure yielded 29 mg **2** (28%) and 31 mg **7** (30%). To obtain the results contained in Table 1 the reactions were monitored by periodically quenching an aliquot of the reaction mixture with aqueous saturated sodium bicarbonate and following the disappearance of **4** and the appearance of **2** by means of thin layer chromatography.

Method B: 100 mg 9-Butoxylcarbonyl-2,3,7,8-tetramethyl-dipyrrin-1-one (**5**, 0.32 mmol) was carefully dissolved in 3 ml trifluoroacetic acid under an argon atmosphere at 25 °C. After stirring for 25 min, a solution of 37 mg glyoxal polymer (0.63 mmol) in 50 ml dichloromethane was added. After 10 min, 20 ml aqueous ammonia (15%) were added to quench the reaction. Workup and purification were as described for method A. The yields were 7 mg **2** (20%) and 11 mg **7** (30%).

Method C: 5 mg **8d** (0.01 mmol) were dissolved in 50 ml tetrahydrofuran and 37 mg *DDQ* (0.016 mmol), and 1 ml trifluoroacetic acid were added at once. The solution was stirred for 90 min and worked up and purified according to method A. Yield 3.2 mg (65%).

Bronze colored crystals; m.p.: 225 °C (dec.); ^{1}H NMR (200 MHz, δ, CD_2Cl_2): 1.99 (s, CH_3-2,19), 2.15 (s, CH_3-3,18), 2.17 (s, CH_3-8,13), 2.31 (s, CH_3-7,14), 6.31 (s, –CH= at 5,5'), 7.92 (s, =CH–CH=) ppm;

Table 1. Yields (%) of **2** and **7** from the reaction of **4** with glyoxal with acids at 25 °C

Solvent	**4**:glyoxal (mol)	acid	time (min)	**2**	**7**
CH_2Cl_2	1:0.5	HBr[a]	180	~0	20
CH_2Cl_2	1:1	HBr[a]	120	5	20
CH_2Cl_2	1:1.5	HBr[a]	60	10	35
CH_2Cl_2	1:2	HBr[a]	1.5	18	25
CH_2Cl_2	1:2	HBr[a]	3	28	30
CH_2Cl_2	1:2	HBr[a]	10	12	25
CH_2Cl_2	1:2	HBr[a]	30	8	35
CH_2Cl_2	1:2	HBr[a]	3	10	25
CH_2Cl_2	1:2	TFA	30	8	22
CH_2Cl_2	1:2	TsOH	30	8	33
CH_2Cl_2	1:2	$BF_3 \cdot OEt_2$	2 days	6	20
THF	1:2	HBr[a]	30	~0	15
CH_3OH	1:2	HBr[a]	30	8	20
CH_3COOH	1:2	HBr[a]	30	15	30
dioxane	1:2	HBr[a]	2 days	~0	25

[a] 33% in acetic acid

^{1}H NMR (200 MHz, δ, CF_3COOD): 1.97 (s, CH_3-2,19), 2.09 (s, CH_3-8,13), 2.11 (s, CH_3-3,18), 2.19 (s, CH_3-7,14), 5.90 (s, -CH= at 5,5'), 7.73 (s, =CH–CH=) ppm; ^{1}H NMR (200 MHz, δ, *DMSO*-d_6 + 1 drop CF_3COOD): 1.89 (s, CH_3-2,19), 1.95 (s, CH_3-3,18), 2.18 (s, CH_3-8,13), 2.22 (s, CH_3-7,14), 5.75 (s, =CH–), 6.21 (s, =CH–CH=) ppm; ^{13}C NMR (90 MHz, δ, *DMSO*-d_6 + 1 drop CF_3COOD): 8.27 (CH_3-7,14), 8.65 (CH_3-2,19), 9.74 (CH_3-8,13), 11.02 (CH_3-3,18), 94.01 (CH), 128.67 (C-pyrr.), 130.22 (C-pyrr.), 132.01 (C-pyrr.), 133.02 (C-pyrr.), 137.45 (C-pyrr.), 146.85 (C-pyrr.), 154.28 (C-pyrr.), 163,10 (C-pyrr.), 172.14 (C=O) ppm; *NOE* (CD_2Cl_2): =CH–CH=↔CH_3-8,13, –CH=↔CH_3-3,7,14,18; IR (KBr): ν = 3262, 2857, 1703, 1624, 1602, 1446, 1391, 1335, 1283, 1211 cm^{-1}; UV/Vis (CH_2Cl_2): λ_{max} = 533 (35800), 366 (3700), 284 (50000) nm (ε); UV/Vis (CH_3OH): λ_{max} = 524 (3300), 379 (2800), 271 (82600) nm (ε); UV/Vis (*DMSO*): λ_{max} = 540 (16900), 408 (5500), 288 (19800) nm (ε).

To obtain the data of Table 2, **2** was dissolved in the given solvent and a drop of a concentrated methanolic solution of the following metal salts was added: $Zn(OAc)_2$, $NiCl_2 \cdot 4H_2O$, $Cu(OAc)_2$, $FeSO_4 \cdot 7H_2O$. Upon addition of trifluoroacetic acid to the complexes, the spectrum of the protonated system (Fig. 2) was obtained. MS (70 eV): *m/e* (%) = 456 (57, M + 2), 455 (85, M + 1), 454 (100, M^+), 439 (38), 411 (8), 395 (5), 332 (6), 278 (4), 261 (37), 227 (25, 1/2 M^+), 214 (6), 203 (22).

9-Butoxycarbonyl-2,3,7,8-tetramethyl-dipyrrin-1-one (**5**; $C_{18}H_{24}N_2O_3$)

To a mixture of 1 g 2-butoxylcarbonyl-3,4-dimethyl-5-formyl-pyrrole (4.5 mmol) [18], 0.50 g 3,4-dimethyl-pyrrolinone-2 (4.5 mmol) [9], and 20 ml methanol, 10 ml aqueous potassium hydroxide (4 *N*) were added. After refluxing for 3 h the solution was kept at 0 °C overnight. The precipitate was filtered off and crystallized from 95% methanol, yielding 0.85 g **5** (60%); m.p.: 250–252 °C; ^{1}H NMR (200 MHz, δ, $CDCl_3$): 1.59 (s, $OC(CH_3)_3$), 1.77 (s, CH_3-2), 2.20 (s, CH_3-8), 2.25 (s, CH_3-3), 2.28 (s, CH_3-7), 5.96 (s, –CH=), 9.26 (br s, 2 NH-10,11) ppm; *NOE* ($CDCl_3$): –CH=↔CH_3-3,7, CH_3-8↔CH_3-7, and $OC(CH_3)_3$; IR (KBr): ν = 3449, 3384, 2920, 1683, 1450, 1560, 1441, 1281 cm^{-1}; UV/Vis (CH_2Cl_2): λ_{max} = 382 (17000), 262 (31800) nm (ε); UV/Vis (CH_3OH): λ_{max} = 384 (21300), 270 (23700) nm (ε); UV/Vis

Table 2. UV/Vis data (λ_{max}, nm) of **2** complexed with metal ions in different solvents

	dichloromethane		methanol		dimethylsulfoxide	
	λ_{max}	ε	λ_{max}	ε	λ_{max}	ε
Zn(II)	622	44000	680	8300	708	25800
	404	10100	390	2600	663	22500
	291	34000	273	13300	453	3900
					400	4100
					303	11200
Fe(II)	745	53700	742	15100	580	8700
	642	99700	644	18400	528	11600
	369	202400	596	162300	336	60900
	289	396600	370	30400		
Ni(II)	742	10200	628	2800	784	3922
	570	45200	561	3400	532	10200
	389	47000	389	6600	423	16400
	280	205000	283	4200	260	81000
Cu(II)	706	12200	741	1500	773	1700
	396	21100	653	16300	404	4200
	267	191400	602	25400		
			329	29700		

(*DMSO*): λ_{max} = 404 (24200), 261 (26500) nm (ε); MS (70 eV, 210 °C): *m/e* (%) = 316 (24, M^+), 260 (100), 242 (73), 214 (46), 199 (70), 134 (7).

1,2-bis-(3,4-Dimethyl-5-formyl-pyrrolyl)-ethene (**6b**; $C_{16}H_{18}N_2O_2$)

To a mixture of 2 g 1,2-*bis*-(5-(2-cyano-2-ethoxycarbonylvinyl)-3,4-dimethyl-pyrrol-2-yl)-ethene (**6a**, 4.3 mmol [1]) and 50 ml methanol, 22 g KOH (0.39 mol = 90 equivalents) were slowly added for 10 min. The solution was then heated under reflux for 3 h in an argon atmosphere. After cooling, 100 ml of water were added and the mixture was carefully neutralized with 10% HCl and extracted with chloroform (3 × 60 ml). The organic phase was washed successively with water (2 × 50 ml), saturated aqueous sodium bicarbonate (40 ml), and brine (40 ml); 0.35 g **6b** were obtained (30%) after drying over anhydrous sodium sulfate, removing the solvent, and crystallizing from 95% methanol; m.p.: 180–182 °C; ^{1}H NMR (200 MHz, δ, $CDCl_3$): 1.92 (s, CH_3-3,3'), 2.26 (s, CH_3-4,4'), 6.39 (s, –CH=CH–), 9.35 (s, NH-1,1'), 9.47 (s, CHO) ppm; NOE ($CDCl_3$): –CH=CH– ↔ CH_3-3,3', –CH=CH– ↔ NH-1,1'; ^{13}C NMR (90 MHz, δ, $CDCl_3$): 9.28 (CH_3-3,3') 11.48 (CH_3-4,4'), 65.12 (–CH=CH–), 123.78 (C_{pyrr}), 129.57 (C_{pyrr}), 133.35 (C_{pyrr}), 135.01 (C_{pyrr}), 176.45 (CHO) ppm; IR (KBr): ν = 3450, 3320, 2970, 1746, 1698, 1541, 1220 cm^{-1}; UV/Vis (CH_2Cl_2): λ_{max} = 379 (20100), 280 (7600) nm (ε); UV/Vis (CH_3OH): λ_{max} = 368 (15200), 273 (67700) nm (ε); UV/Vis (*DMSO*): λ_{max} = 415 (33000), 279 (7800) nm (ε); MS (70 eV, 210 °C): *m/e* (%) = 270 (33, M^+), 212 (100), 197 (33).

(Z,Z,Z)-2,3,7,8,12,13,17,18-Octamethyl-1,19,21,24-tetrahydro-1,19-dioxo-22H-bilin (**7**)

M.p.: 305 °C (dec.; Ref. [19]: 300 °C); IR, UV/Vis, and ^{1}H NMR agreed with the data of Ref. [19]; ^{13}C NMR (90 MHz, δ, $CDCH_3$): 8.57 (CH_3–), 9.51 (CH_3–), 9.58 (CH_3–), 9.80 (CH_3–), 96.50 (–CH= at 5,15), 113.89 (–CH= at 10), 127.85 (C_{pyrr}), 128.98 (C_{pyrr}), 134.95 (C_{pyrr}), 140.80 (C_{pyrr}), 140.87 (C_{pyrr}), 141.73 (C_{pyrr}), 149.81 (C_{pyrr}), 172.56 (C=O) ppm.

(Z,Z,Z)-1,2-bis-(2,3,7,8-Tetramethyl-dipyrrin-1-one-9-yl)-ethane (**8d**; $C_{28}H_{32}N_4O_2$)

Prepared from 2,3,7,8,9-pentamethyl-dipyrrinone [17] according to the method reported recently [2] in 23% yield; m.p.: 280 °C (dec.); ^{1}H NMR (200 MHz, δ, pyridine-d_5): 1.85 (s, $2CH_3$), 1.92 (s, $2CH_3$), 2.01 (s, $2CH_3$), 2.08 (s, $2CH_3$), 6.21 (s, 2–CH=), 8.25 (s, –CH=CH–) ppm; UV/Vis ($CHCl_3$): $\lambda_{max} = 286$ (29300), 540 (41000) nm (ε). UV/Vis ($CHCl_3 + ZnOAc_2$): $\lambda_{max} = 389$ (38000), 672 (34500), 708 (34600) nm (ε); UV/Vis ($CHCl_3$ + trifluoroacetic acid): $\lambda_{max} = 312$ (24200), 392 (29000), 750 (143000) nm (ε); IR (KBr): $\nu = 3443$, 2929, 1699, 1634, 1580, 1493, 1385, 1372, 1283, 1105 cm^{-1}.

2,2'-di-(Ethoxycarbonyl)-3,3'-4-4'-tetramethyl-dipyrr-5,5'-yl-methane (**10**, $C_{19}H_{26}N_2O_4$)

To a mixture of 0.4 g glyoxal polymer (6 mmol) and 10 ml acetic acid, a solution of 2.0 g ethyl-3,4-dimethyl-pyrrole-2-carboxylate (**9**, 12 mmol [20]) in 10 ml acetic acid and 1 ml hydrogen bromide (33% in acetic acid) was added successively. The mixture was stirred for 3 h at room temperature. Water (50 ml) was added, the mixture then extracted with dichloromethane (2 × 50 ml) and the organic phase was thoroughly washed with 20 ml sodium bicarbonate, water (2 × 20 ml), and 20 ml brine. After drying over anhydrous sodium sulfate and removing the solvent, the residue was crystallized from 95% methanol, yielding 1.24 g **10** (60%). M.p.: 242–244 °C; ^{1}H NMR (200 MHz, δ, $CDCl_3$): 1.26 (t, $J = 7.5$ Hz, $2CH_2CH_3$), 1.74 (s, $2CH_3$), 2.18 (s, $2CH_3$), 4.20 (q, $J = 7.5$ Hz, $2CH_2CH_3$), 4.96 (s, $-CH_2-$), 9.07 (br s, 2NH) ppm; ^{13}C NMR (90 MHz, δ, $CDCl_3$): 6.46 (CH_2CH_3), 10.53 (CH_3), 14.24 (CH_3), 37.80 (CH_2CH_3), 59.95 ($-CH_2-$), 118.21 (C_{pyrr}), 118.40 (C_{pyrr}), 127.55 (C_{pyrr}), 130.86 (C_{pyrr}), 161.62 ($COOC_2H_5$); IR (KBr): $\nu = 3420$, 1720, 1690, 1570 cm^{-1}; UV/Vis (CH_2Cl_2): $\lambda_{max} = 380$ (12300); MS (70 eV, 210 °C): m/e (%) = 345 (M^+, 100), 299 (90), 283 (20), 225 (25), 210 (15), 179 (25).

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