164. Syntheses of Bile Pigments

Part 18[1])

Synthesis and Conformational Studies of Oxa- and Thia-deaza-biliverdin Analogues

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Dedicated to Prof. Dr. *Charles W. Jefford* on the occasion of his 65th birthday

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Following the conventional methodology used for the synthesis of bile pigments, some oxa- and thia-deaza-biliverdin analogues were synthetized for the first time. Both UV/VIS spectroscopic and $^1H\{^1H\}$-NOE difference studies reveal that the oxa-deaza-biliverdin analogue **8a** occurs in apolar solvents in a partly 'stretched' conformation, whereas the corresponding thia derivative **8b** behaves rather like a genuine bile pigment. Unexpectedly, the helical-shaped conformation is also preponderant in a trioxa-trideaza-biliverdin analogue, which could be only characterized in its protonated form **14**.

Bile-pigment chromophores of phycobiliproteins – the light-harvesting pigments which are integral part of the photosynthetic apparatus of cyanobacteria and some microalgae – are characterized by two main spectroscopic properties: an enhanced absorption of VIS light with respect to the absorption in the near-UV range (*i.e.* $\varepsilon_{VIS}/\varepsilon_{UV} \approx 4$ for the not denatured biliprotein) and a high quantum yield of photoluminescence. Both properties contrast with those of the isolated bile-pigment chromophores which prefentially occur in helical-shaped conformations, in solution [2] [3]. It can be shown experimentally [4] that at least the enhanced extinction of the VIS absorption band is caused by the presence of 'stretched' conformations of the chromophore, as originally suggested by theoretical calculations [5] [6]. On the other hand, the low quantum yield of fluorescence of protobiliverdin dimethyl ester ($\Phi = 1.1 \cdot 10^{-4}$ in EtOH at room temperature [7]) may be explained by radiationless deactivation due either to rotation around exocyclic bonds [8] or to intramolecular proton jump between the N-atoms of the dipyrrin moiety of the helical-shaped molecules in the excited state [9]. The latter mechanism, however, seems to be a negligible deexcitation process in bilindiones [10]. Moreover, at room temperature, a part of the fluorescence arises from 'stretched' biliverdin chromophores which emit with a quantum yield of about two orders of magnitude higher than the corresponding coiled conformers [7].

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An obvious approach to investigate the influence of intramolecular H-bonding on the photophysical properties of bile-pigment chromophores consists in the replacement of the NH groups in the molecule either by N-alkyl groups or by divalent heteroatoms, such as an O- or S-atom. This approach was explored with dipyrrins as model chromophores of bile pigments [11] and, in the case of bile pigments themselves, with 22-methyl derivatives of biliverdins [12]. Both spectroscopic studies [12] and force-field calculations [13] of the latter reveal the preference of 'stretched' conformations in the absence of intramolecular H-bonding. However, the destabilization of the coiled conformers may be also a consequence of the steric demand of the 22-methyl group which equalizes the thermodynamic stability of (*Z*)- and (*E*)-isomers at the exocyclic C=C bonds. For this reason, the above mentioned studies should be complemented with the inspection of oxa-deaza and thia-deaza analogues of biliverdins in which steric effects are not determinative of their preferred conformations.

As, to our knowledge, such oxa and thia analogues of bile pigments have not been described before, the syntheses of derivatives **8a** and **8b**[4]) was envisaged in the scope of the present work. For the sake of comparison, the parent chromophore **7** has been also prepared. Particularly interesting in connection with our objective was furthermore the synthesis of the trioxa-trideaza-biliverdin derivative **14**, in which no NH groups at all are present.

Oxa-deaza- and Thia-deaza-biliverdin Analogues 8a,b. – The strategy followed for the preparation of the biliverdin analogues **8a** and **8b** parallels the conventional methodology used for the synthesis of bile pigments. Thus, oxo-pyrrole **2** [14] was condensed in the presence of KOH (*cf.* [15]) with the formyl-pyrrole **1** [16] to yield, after esterification, the 1,10-dihydro-1-oxo-11*H*-dipyrrin **4a** (*Scheme 1*). Under the same conditions, reaction of **2** with furfural (**3a**) and thiophene-2-carbaldehyde (**3c**) afforded the oxo-dipyrrin analogues **5a** and **5c**, respectively.

After reaction of **4a** with trimethyl orthoformate in the presence of CF_3COOH (*cf.* [17]), the obtained 9-formyl derivative **4b** was condensed with **4a** in acidic medium (*cf.* [18]) to yield the biliverdin derivative **7**. In the case of **5a** and **5c**, however, introduction of the CHO group on C(9) either using trimethyl orthoformate or by means of the *Vilsmeier-Haack* reaction failed. Therefore, **2** was reacted in the presence of NaOH with the known monoacetals **3b** and **3d** of furan-2,5-dicarbaldehyde [19] and thiophene-2,5-dicarbaldehyde [20], respectively, yielding, after acidic workup and subsequent reesterification, the desired formyl derivatives **5b** and **5d**, respectively.

Like genuine 11*H*-dipyrrin-1(10*H*)-ones [21] and dipyrrin analogues lacking an intramolecular H-bridge (!) [11], both aldehydes **5b** and **5d** are transformed into the corresponding (*E*)-isomers **6a** and **6b**, respectively, on irradiation with a high-pressure Hg lamp.

Finally, reaction of **5b** and **5d** with the same 9-[(*tert*-butoxy)carbonyl]-1,10-dihydro-1-oxo-11*H*-dipyrrin **4a**, in the presence of HCl, afforded the corresponding biliverdin analogues **8a** and **8b**, respectively.

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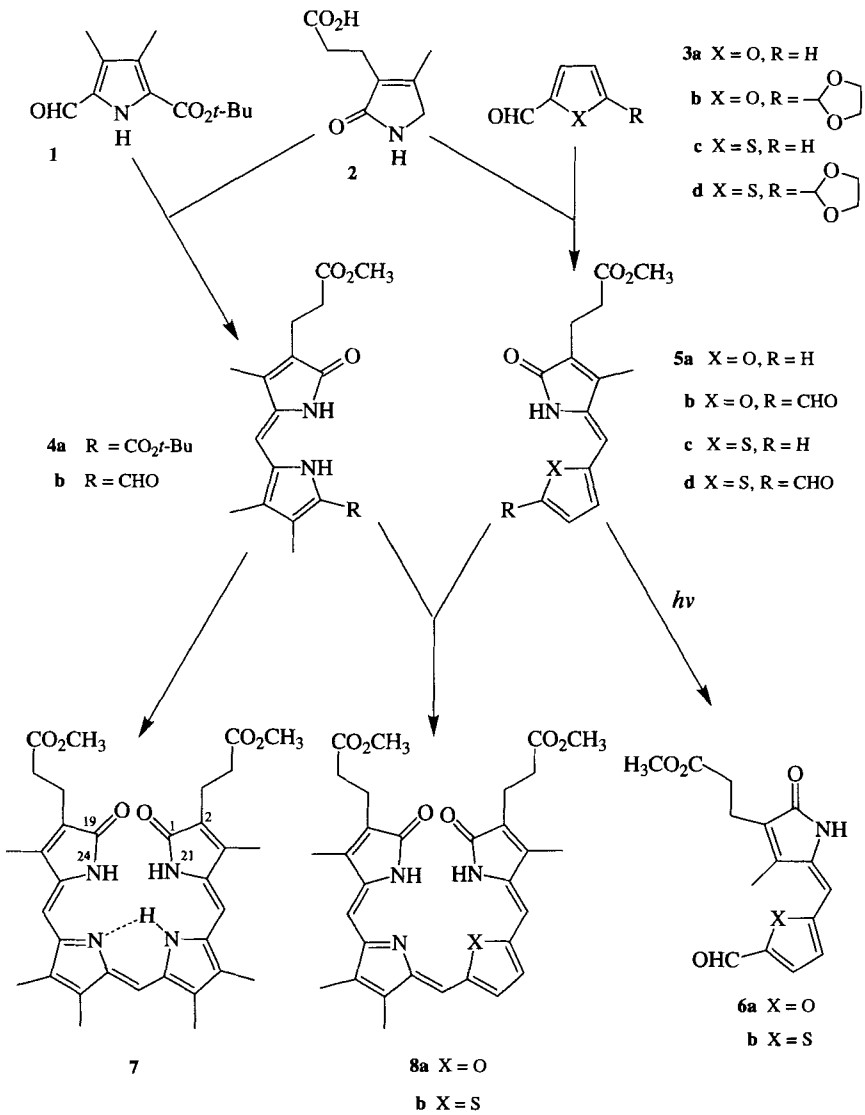
[4]) The particular substitution pattern of compounds **8a** and **8b** has been chosen in regard to their use as bile-pigment-like chromophores in bilindionostilbenoparacyclophanes (*cf.* [4]), the synthesis of which will be reported in a later communication in this series.

Scheme 1



Spectroscopic Behaviour of 8a, b in Solution. – The UV/VIS spectra of the biliverdin derivative **7** in different solvents, are represented in *Fig. 1*. As earlier observed by *Falk* and coworkers [22], the population of 'stretched' conformers in hexamethylphosphoric triamide (HMPA) is higher than in other organic solvents. On the contrary, the dramatic change of the relative intensities of short- and long-wavelength absorption bands of the oxa analogue **8a** observed when the solvent MeOH or HMPA is replaced by CH_2Cl_2 or $CHCl_3$ reveals a higher population of 'stretched' conformers in unpolar media

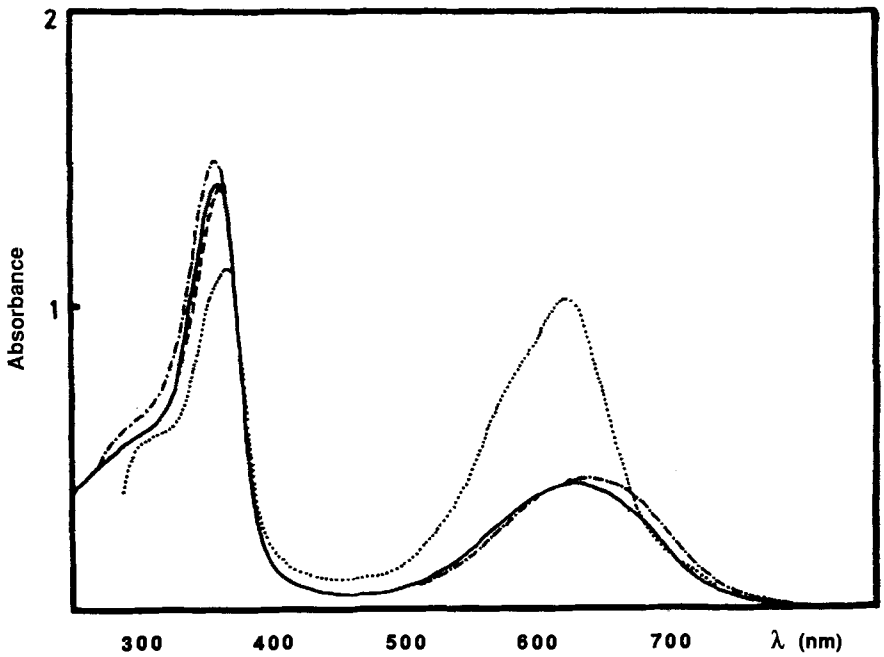


Fig. 1. *UV/VIS Spectra of* **7** *at room temperature in different solvents.*
—— CH_2Cl_2; ---- $CHCl_3$; –·–·– MeOH; ···· HMPA.

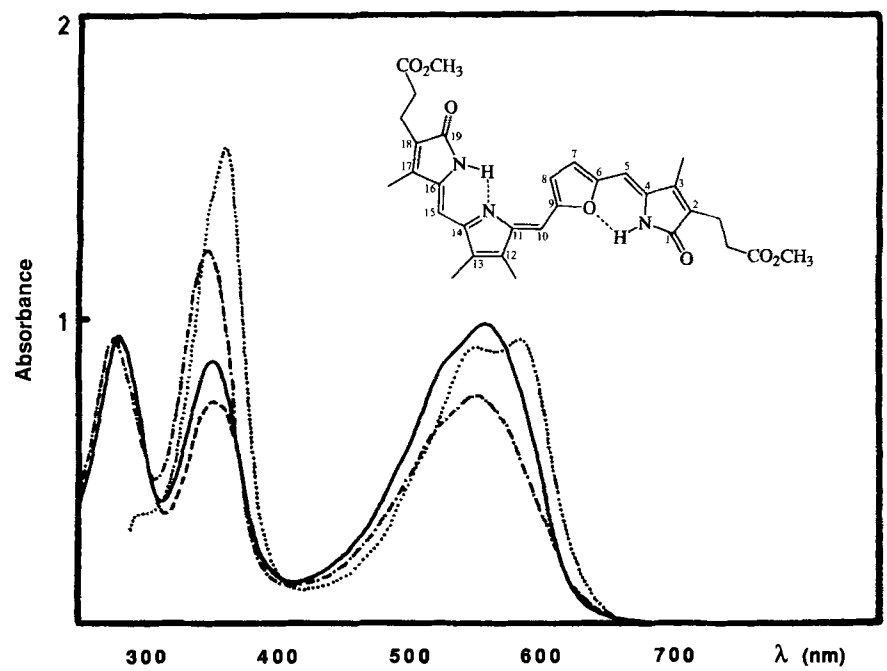


Fig. 2. *UV/VIS Spectra of* **8a** *at room temperature in different solvents.*
—— CH_2Cl_2; ---- $CHCl_3$; · ·–·– MeOH; ···· HMPA.

Table 1. *^{1}H-NMR Signals of* **8a** *Assigned by $^1H\{^1H\}$-NOE Difference Experiments*

Irradiated signal[a])	Enhanced signal[a])[b])	% Enhancement
7.25 (H–C(8))	6.65 (*d*, *J* = 3.7, H–C(7)); 6.70 (*s*, H–C(10))	5.5; 1.6
6.70 (H–C(10))	7.25 (*d*, *J* = 3.7, H–C(8)); 2.14 (*d*, *J* = 0.8, 3 H–C(12^1))	2.7; 10.2
6.65 (H–C(7))	5.94 (*s*, H–C(5)); 7.25 (*d*, *J* = 3.7, H–C(8))	4.3; 6.1
5.94 (H–C(5))	2.10 (*s*, 3 H–C(3^1))	9.3
5.91 (H–C(15))	2.04 (*s*, 3 H–C(13^1)); 2.15 (*s*, 3 H–C(17^1))	6.2; 8.0
2.04 (3 H–C(13^1))	5.91 (*s*, H–C(15))	3.3
2.15 (3 H–C(17^1))	5.91 (*s*, H–C(15)); 2.68 (*m*, 2 H–C(18^1))	2.6; 0.8
2.14 (3 H–C(12^1))	6.70 (*s*, H–C(10))	1.1
2.10 (3 H–C(3^1))	2.68 (*m*, 2 H–C(2^1)); 5.94 (*s*, H–C(5))	2.1; 3.8

[a]) δ in ppm ($CDCl_3$, 360.13 MHz) referred to Me_4Si as internal standard, *J* in Hz.

[b]) The other signals were assigned according to their multiplicities and chemical shifts: 10.31 (br. *s*, NH); 3.66 (*s*, 2 MeO); 2.61 (*m*, $CH_2(2^2)$, $CH_2(18^2)$).

(*cf. Fig. 2*). This assumption is corroborated by $^1H\{^1H\}$-NOE difference experiments, according to which a (4*Z*,10*Z*,15*Z*,5(6)*sp*,9(10)*ap*,14(15)*sp*)-conformation (*sp* = syn-periplanar, *ap* = antiperiplanar) is preponderant in $CDCl_3$ (*cf. Table 1*). Most likely, this geometry results from the repulsion of nonbonding electrons on the heteroatoms of the middle rings of the chromophore instead of a H-bridge between them, as well as from intramolecular H-bonding involving the lactam NH groups. Indeed, the small NOE

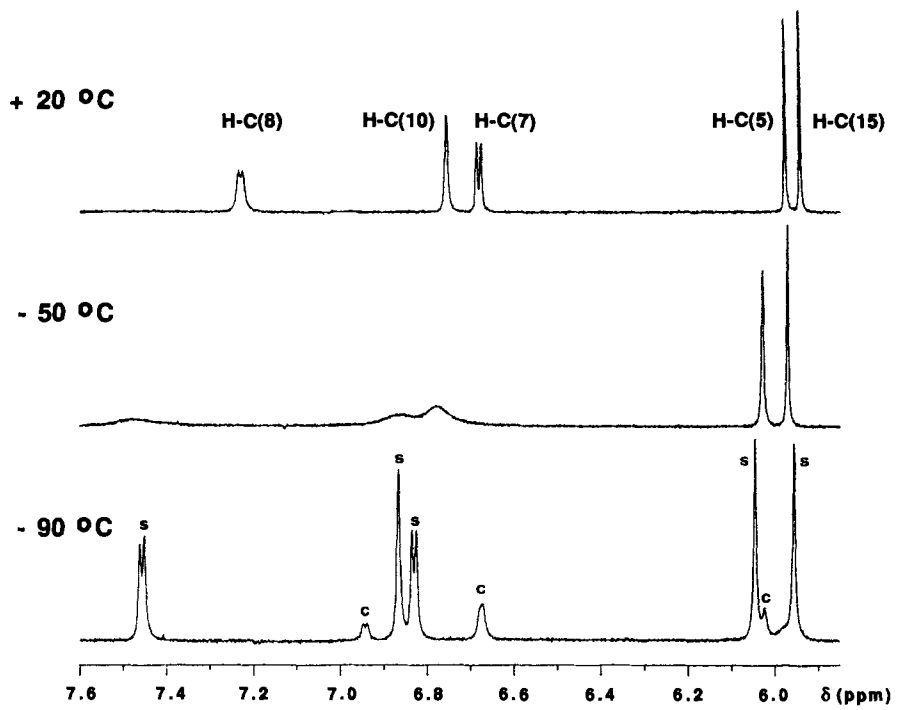


Fig. 3. *Detail of the ^{1}H-NMR spectrum of* **8a** *in CD_2Cl_2 at different temperatures.*
c: coiled conformer; s: = 'stretched' conformer.

between H–C(8) and H–C(10) is a consequence of the dynamic equilibrium between coild and 'stretched' conformers. As expected, this dynamic equilibrium becomes manifest at low temperatures, at which the coexistence of coiled and 'stretched' conformers as well as the preponderance of the latter (*ca.* 4:1) is revealed by ^{1}H-NMR spectroscopy (*cf. Fig. 3*). Accordingly, the ratio of the extinction coefficients of long- and short-wavelenght absorption bands of **8a** increases at low temperatures, thus confirming the lower energy content of the 'stretched' conformation of this compound (*cf. Fig. 4*).

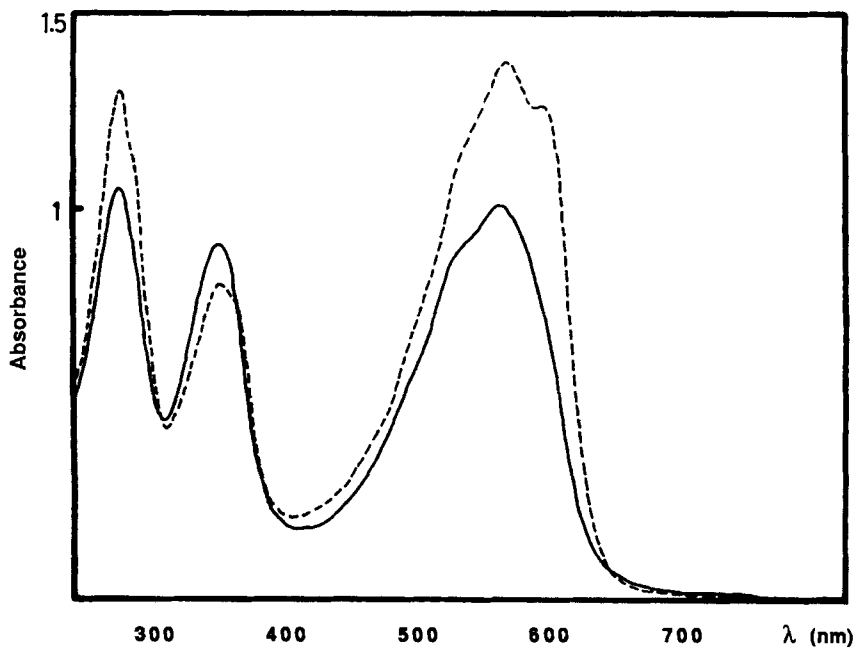


Fig. 4. *UV/VIS Spectra of* **8a** *in* CH_2Cl_2 *at different temperatures.* —— +20°; ---- –90°

Table 2. *^{1}H-NMR Signals of* **8b** *Assigned by $^1H\{^1H\}$-NOE Difference Experiments*

Irradiated signal[a])	Enhanced signal[a])[b])	% Enhancement
7.29 (H–C(8))	7.08 (*d*, *J* = 4.1, H–C(7)); 7.02 (*s*, H–C(10))	6.6; 8.4
7.08 (H–C(7))	6.29 (*s*, H–C(5)); 7.29 (*d*, *J* = 4.1, H–C(8))	7.1; 7.5
7.02 (H–C(10))	7.29 (*d*, *J* = 4.1, H–C(8)); 2.11 (*d*, *J* = 0.8, 3 H–C(12^1))	9.0; 6.5
6.29 (H–C(5))	7.08 (*d*, *J* = 4.1, H–C(7)); 2.15 (*s*, 3 H–C(3^1))	6.2; 9.2
5.90 (H–C(15))	2.15 (*s*, 3 H–C(3^1), 3 H–C(17^1)); 2.04 (*d*, *J* = 0.7, 3 H–C(13^1))	7.1; 6.4
2.15 (3 H–C(3^1), 3 H–C(17^1))	6.29 (*s*, H–C(5)); 5.90 (*s*, H–C(15))	2.5; 1.6
2.11 (3 H–C(12^1))	7.02 (*s*, H–C(10))	3.5
2.04 (3 H–C(13^1))	5.90 (*s*, H–C(15))	3.4

[a]) δ in ppm ($CDCl_3$, 360.13 MHz) referred to Me_4Si as internal standard; *J* in Hz.

[b]) The other signals were assigned according to their multiplicities and chemical shifts: 11.18, 8.18 (2 br. *s*, 2 NH); 3.66 (*s*, 2 MeO); 2.72 (*m*, 6 H) and 2.62 (*m*, 2 H; 2 CH_2CH_2COOMe); 2.04 (*d*, *J* = 0.7, 3 H–C(13^1)).

Like genuine bile pigments [23], the VIS absorption band of **8a** is shifted to longer wavelengths in acidic medium or in the presence of Zn^{II} ions (*cf. Exper. Part*).

The spectroscopic behaviour of the thia analogue **8b** is remarkable inasmuch as it rather corresponds to that of genuine biliverdins (see *Fig. 5*). Accordingly, the observed enhancement of the intensity of the H–C(10) signal upon irradiation at the resonance frequency of the proton on C(8) points out that coiled conformers of **8b** are preponderant in unplar solvents (*cf. Table 2*). In HMPA, the ratio of the extinction coefficients of long- and short-wavelength absorption bands is increased, but no hypsochromic shift of the VIS absorption is observed.

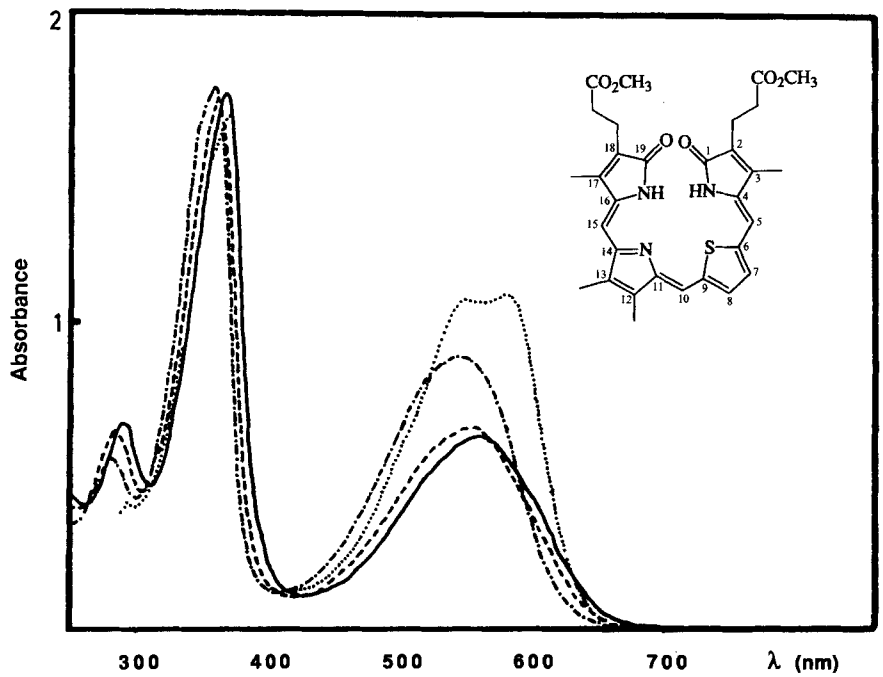


Fig. 5. *UV/VIS Spectra of* **8b** *at room temperature in different solvents.* —— CH_2Cl_2; ---- $CHCl_3$; –·–·– MeOH; ···· HMPA.

Trioxa-trideaza-biliverdin Analogue 14. – The structure found for the 22-oxa-22-deaza-biliverdin analogue **8a** suggests that replacement of all NH groups present in bile pigment molecules by O-atoms should increase the population of still more 'stretched' conformations in solution. Thus, the synthesis of a trioxa-trideaza-biliverdin analogue was envisaged on the basis of the well-documented use of commercially available 2-(trimethylsilyloxyl)furan (**9**) for the preparation of 4-ylidene-butenolides from a variety of both aliphatic and aromatic aldehydes [24] [25][5]).

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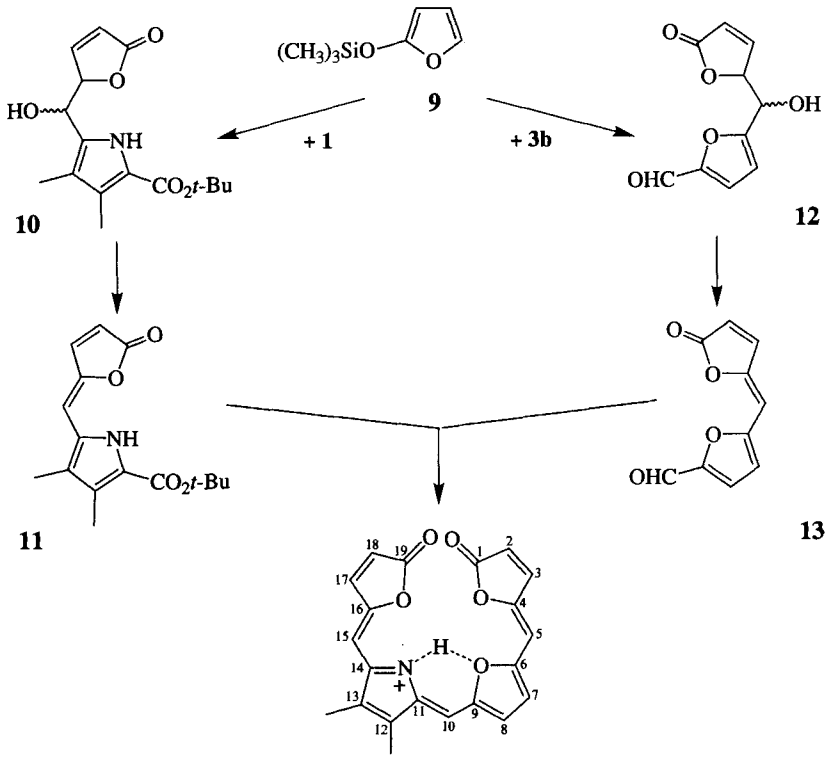
[5]) We thank Prof. *C. W. Jefford*, Department of Organic Chemistry, University of Geneva, for having provided us with valuable experimental details concerning the handling of 2-(trimethylsilyloxy)furan.

Scheme 2



Actually, reaction of **9** with formyl-pyrrole **1** in the presence of tin(IV) chloride as a *Lewis*-acid catalyst led to a mixture of three separable components: hydroxy derivative **10** (diastereoisomer mixture) as well as the (*Z*)-isomer **11** and its (*E*)-isomer (not shown; *Scheme 2*). Through dehydration of **10**, and additional quantity of **11** and its (*E*)-isomer could be obtained. From the combined fractions, pure **11** was isolated and characterized by spectroscopic methods including $^1H\{^1H\}$-NOE difference experiments (*cf. Exper. Part*). Under the same conditions, reaction of **9** with the monoacetal **3b** of furan-2,5-dicarbaldehyde led to **12** (diastereoisomer mixture) which was transformed into a 3:2 mixture of (*Z*)-isomer **13** and the corresponding (*E*)-isomer. After chromatographic separation, the pure (*Z*)-isomer **13** was reacted with **11**, in the presence of CF_3COOH, to afford **14** in 96% yield as a deep-blue crystalline compound. The low ratio $\varepsilon_{VIS}/\varepsilon_{UV} = 0.4$ measured in CD_2Cl_2/CF_3CO_2H suggests an equilibrium in favour of coiled conformers (*cf. Fig. 6*). Indeed, $^1H\{^1H\}$-NOE difference experiments confirm that the molecule occurs in a (4*Z*,10*Z*,15*Z*,5(6)*sp*,9(10)*sp*,14(15)*sp*)-conformation in the same solvent. Particularly, the helical-shaped geometry of the chromophore is substantiated by NOE correlations between H–C(5) and H–C(7) and between CH_3–C(13) and H–C(15), as well as by the reciproque responses on H–C(8) and CH_3–C(12) upon irradiation at the

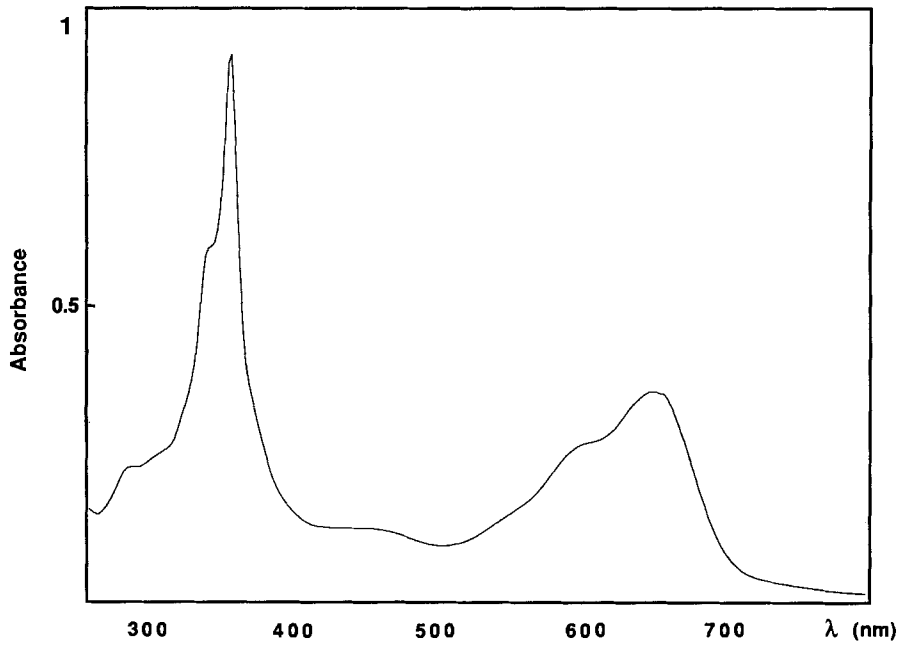


Fig. 6. *UV/VIS Spectrum of* **14** *at room temperature in* CH_2Cl_2/CF_3CO_2H

Table 3. *^{1}H-NMR Signals of* **14** *Assigned by $^1H\{^1H\}$-NOE Difference Experiments*

Irradiated signal[a])	Enhanced signals[a])	% Enhancement
7.83 (H–C(17))	6.41 (*s*, H–C(15)); 6.71 (*dd*, *J* = 5.5, 0.8, H–C(18))	3.3; 5.0
7.82 (H–C(3))	6.58 (*dd*, *J* = 5.4, 0.8, H–C(2)); 7.10 (*s*, H–C(5))	4.1; 4.0
7.71 (H–C(8))	7.52 (*d*, *J* = 4.0, H–C(7)); 7.39 (*s*, H–C(10))	3.9; 3.7
7.52 (H–C(7))	7.10 (*s*, H–C(5)); 7.71 (*d*, *J* = 4.0, H–C(8))	1.0; 2.4
7.39 (H–C(10))	7.71 (*d*, *J* = 4.0, H–C(8)); 2.41 (*s*, 3 H–C(12^1))	4.4; 7.9
7.10 (H–C(5))	7.82 (*d*, *J* = 5.7, H–C(3)); 7.52 (*d*, *J* = 4.0, H–C(7))	8.0; 1.0
6.71 (H–C(18))	7.83 (*d*, *J* = 5.7, H–C(17))	8.5
6.58 (H–C(2))	7.82 (*d*, *J* = 5.7, H–C(3))	6.4
6.41 (H–C(15))	2.25 (*s*, 3 H–C(13^1)); 7.83 (*d*, *J* = 5.7, H–C(17))	4.6; 5.1
2.41 (3 H–C(12^1))	7.39 (*s*, H–C(10)); 2.25 (*s*, 3 H–C(13^1))	4.1; 1.0
2.25 (3 H–C(13^1))	2.41 (*s*, 3 H–C(12^1)); 6.41 (*s*, H–C(15))	0.6; 3.1

[a]) δ in ppm (CD_2Cl_2/CF_3CO_2D, 360.13 MHz) referred to Me_4Si as internal standard; *J* in Hz.

resonance of H–C(10) (*cf. Table 3*). Unfortunately, attempts to deprotonate **14** using either Et_3N or poly(4-vinylpyridine) in CH_2Cl_2 led only to intractable mixtures. In this respect, the behaviour of the free base corresponding to **14** is reminiscent of that of tetraoxa-tetradeaza-porphin, which until now is only known as dication [26–28].

In spite of the different extend of intramolecular H-bonding, none of the bile pigment analogues examined in the present work displays a perceptible higher lumininescence than biliverdin itself. In conclusion, therefore, the present work emphasizes that quench-

ing of the fluorescence of bile-pigment chromophores is not due to intramolecular proton tunnelling within the dipyrrin chromophore in the excited state. Unfortunately, however, the deprotonated form of the trioxa-trideaza-biliverdin analogue **14** is too unstable to permit a study of the photoluminiscence of this interesting molecule.

Financial support of this work from the *Swiss National Science Foundation* (project No. 2.320-0.82) is gratefully acknowledged. NMR Spectra on the *Brucker-AM-360* instrument and mass spectra were recorded by *F. Fehr* and *F. Nydegger*, respectively. We thank Prof. *T.A. Jenny* for his help in interpretation of the spectra. Elemental analyses were carried out by *Ciba Geigy AG*, Forschungszentrum, CH-1723 Marly.

Experimental Part

General. See [29]. *N,N'*-Dicyclohexylcarbodiimide (DCC), 4-(dimethylamino)pyridine (DMAP), furan-2-carbaldehyde, thiophene-2-carbaldehyde, 2-(trimethylsilyloxy)furan and other reagents were purchased from *Fluka Chemie AG*. Solvents for chemical reactions and chromatography were generally dried and distilled prior to use. Reactions were monitored by TLC on *E. Merck* silica gel *60* F_{254} (0.2 mm) precoated Al foils. Prep. TLC: plates (20 × 20 or 20 × 100 cm, 1.2 mm thick, activated for 2 h at 100°) precoated with silica gel *60* $F_{254+366}$ (*E. Merck*). Flash chromatography (FC) (*cf.* [30]): *E. Merck* silica gel *60* (40–63 μm). UV/VIS Spectra: MeOH solns. unless otherwise specified; λ_{max} (log ε) in nm. IR Spectra: in cm^{-1}. ^1H (360.13 MHz) and ^{13}C-NMR (90.56 MHz): chemical shifts δ in ppm, rel. to Me_4Si as internal standard, measured in $CDCl_3$; *J* values in Hz; dipyrrin or bilin numbering. NOE: δ of enhanced signal (% enhancement, irradiation frequency). Mass spectra: EI at an acceleration voltage of 70 eV, FAB (at 6 kV) in 3-nitrobenzyl alcohol with Ar at 8 kV; *m/z* and relative intensities (%) in parentheses.

*Methyl (Z)-5-{{5-[(*tert*-Butoxy)carbonyl]-3,4-dimethyl-1*H*-pyrrol-2-yl}methylidene}2,5-dihydro-4-methyl-2-oxo-1*H*-pyrrole-3-propanoate* (= *Methyl (Z)-9-[(*tert*-Butoxy)carbonyl]-1,10-dihydro-3,7,8-trimethyl-1-oxo-11*H*-dipyrrin-2-propionate*; **4a**). A soln. of 2,5-dihydro-4-methyl-2-oxo-1*H*-pyrrole-3-propanoic acid [14] (**2**; 3.65 g, 0.02 mol) and *tert*-butyl 5-formyl-3,4-dimethyl-1*H*-pyrrole-2-carboxylate [16] (**1**; 4.82 g, 0.02 mol) in MeOH/H_2O 3:1 (200 ml) containing NaOH (10 g) was stirred for 60 h at r.t. Thereafter, the mixture was carefully acidified (pH 3.0) with 3N aq. HCl and the obtained precipitate separated by filtration, washed with H_2O, and dried *in vacuo* over P_4O_{10}. The crude product (7.8 g, 96%) was dissolved in CH_2Cl_2 (140 ml) containing MeOH (20 ml), DCC (5.8 g), and DMAP (0.4 g) and the mixture stirred for 24 h at r.t. Then, the precipitated dicylohexylurea was filtered off, the filtrate evaporated, and the residue crystallized from AcOEt/MeOH: 6.5 g of **4a**. M.p. 228–230°. UV/VIS: 257 (4.25), 385 (4.48). IR: 3440*m*, 3340*w*, 2950*m*, 1735*m*, 1690*s*, 1440*m*, 1370*m*, 1280*m*, 1260*m*, 1180*m*, 1150*m*. ^1H-NMR: 9.62, 9.50 (2 br.*s*, 2 NH); 5.98 (*s*, H–C(5)); 3.62 (*s*, MeO); 2.76 (*t*, $CH_2(2^1)$); 2.62 (*t*, $CH_2(2^2)$); 2.22, 2.14, 2.06 (3*s*, 3 Me); 1.55 (*s*, *t*-Bu). ^{13}C-NMR: 173.68, 173.52 (2*s*, 2CO); 160.98 (*s*, COO); 143.18, 134.34, 129.57, 127.31, 125.96, 123.97, 123.62 (7*s*, quat. C's); 98.76 (*d*, C(5)); 80.61 (*s*, Me_3C); 51.42 (*q*, MeO); 32.58 (*t*, $C(2^2)$); 28.47 (*q*, (Me_3C); 19.10 (*t*, $C(2^1)$); 10.72, 9.77, 9.44 (3*q*, 3 Me). EI-MS: 388 (27, M^+), 332 (100), 272 (63). Anal. calc. for $C_{21}H_{28}N_2O_5$ (388.46): C 64.93, H 7.26, N 7.21; found: C 64.80, H 7.28, N 7.30.

*Methyl (Z)-5-[(Formyl-3,4-dimethyl-1*H*-pyrrol-2-yl)methylidene]-2,5-dihydro-4-methyl-2-oxo-1*H*-pyrrole-3-propanoate* (= *Methyl (Z)-9-Formyl-1,10-dihydro-3,7,8-trimethyl-1-oxo-11*H*-dipyrrin-2-propionate*; **4b**). A soln. of **4a** (388 mg, 1 mmol) in CF_3CO_2H (15 ml) was stirred for 15 min at r.t. and then cooled in an ice-bath. Trimethyl orthoformate (10 ml) was added at once and the mixture stirred for further 15 min at 0°. Thereafter H_2O (500 ml) was added, the product extracted with CH_2Cl_2 (2 × 100 ml), the combined org. phase shaken with aq. $NaHCO_3$ soln. and evaporated, and the residue crystallized from AcOEt/MeOH: **4b** (259 mg, 79%). M.p. 213–215°. UV/VIS: 266 (4.39), 395 (4.48). IR: 3340*m*, 3000*m*, 2960*w*, 2930*w*, 1770*m*, 1640*m*, 1610*s*, 1455*m*, 1440*m*, 1400*m*, 1265*m*. ^1H-NMR: 10.98, 10.82 (2 br. *s*, 2 NH); 9.60 (*s*, CHO); 5.89 (*s*, H–C(5)); 3.65 (*s*, MeO); 2.73 (*t*, $J = 6$, $CH_2(2^1)$); 2.62 (*t*, $J = 6$, $CH_2(2^2)$); 2.27, 2.13, 2.04 (3*s*, 3 Me). ^{13}C-NMR: 176.97 (*d*, CHO); 173.26, 173.05 (*s*, 2 CO); 143.05, 136.12, 132.94, 132.61, 131.27, 129.95, 124.43 (7*s*, quat. C's); 96.25 (*d*, C(5)); 51.49 (*q*, MeO); 32.47 (*t*, $C(2^2)$); 19.21 (*t*, $C(2^1)$); 9.73, 8.95, 8.87 (3*q*, 3 Me). EI-MS: 316 (100, M^+), 256 (82). Anal. calc. for $C_{17}H_{20}N_2O_4$ (316.36): C 64.54, H 6.37, N 8.86; found: C 64.55, H 6.41, N 8.83.

*Methyl (Z)-5-[(Furan-2-yl)methylidene]-2,5-dihydro-4-methyl-2-oxo-1*H*-pyrrole-3-propanoate* (**5a**). A soln. of **2** [14] (3.36 g, 0.02 mol) in H_2O (50 ml) containing NaOH (6.0 g) was treated with a soln. of furan-2-carbaldehyde (**3a**; 1.74 ml, 0.02 mol) in MeOH (100 ml). After stirring for 4 h at r.t., the mixture was acidified (pH 2.0) with 3N aq.

HCl and the obtained precipitate separated by filtration, washed with H_2O, and dried *in vacuo* over P_4O_{10}. The crude product (4.81 g, 97%) was suspended in CH_2Cl_2 (50 ml) containing MeOH (5 ml), DCC (4 g), and DMAP (0.2 g) and the mixture stirred for 12 h at r.t. The precipitated dicyclohexylurea was then filtered off, the filtrate evaporated, and the residue crystallized from benzene/hexane: 4.3 g (82%) of **5a**. M.p. 115–117°. UV/VIS: 224 (3.90), 352 (4.50). IR: 3450*m*, 3000*m*, 2950*w*, 1730*s*, 1690*s*, 1435*m*, 1405*w*, 1380*m*, 1170*m*, 1145*m*, 1015*m*. ^{1}H-NMR: 8.27 (br. *s*, NH); 7.48 (*ddd*, J = 1.8, 0.6, 0.4, H–C(5′)); 6.46 (*dd*, J = 3.4, 1.8, H–C(4′)); 6.42 (*ddd*, J = 3.4, 0.6, 0.5, H–C(3′)); 5.89 (br. *s*, CH=C(5)); 3.65 (*s*, MeO); 2.69, 2.63 (2*m*, 2 CH_2); 2.10 (*s*, Me–C(4)). ^{13}C-NMR: 173.16, 171.18 (2*s*, 2 CO); 151.65, 143.37, 135.65, 129.97, (4*s*, quat. C's); 141.65 (*d*, C(5′)); 112.15, 111.67 (2*d*, C(3′), C(4′)); 96.06 (*d*, *C*H=C(5)); 51.55 (*q*, MeO); 32.36 (*t*, C(3^2)); 19.38 (*t*, C(3^1)); 9.59 (*q*, *Me*–C(4)). EI-MS: 261 (53, M^+), 230 (18), 202 (37), 201 (100). Anal. calc. for $C_{14}H_{15}NO_4$ (261.28): C 64.36, H 5.79, N 5.36; found: C 64.52, H 5.79, N 5.41.

*Methyl (Z)-5-[(5-Formylfuran-2-yl)methylidene]-2,5-dihydro-4-methyl-2-oxo-1*H*-pyrrole-3-propanoate* (**5b**). To a soln. of **2** [14] (3.36 g, 0.02 mol) in H_2O (50 ml) containing NaOH (5.0 g), 5-(1,3-dioxolan-2-yl)furan-2-carbaldehyde [19] (**3b**; 3.36 g, 0.02 mol) was added and the mixture stirred for 4 h at r.t. The product (4.84 g, 88%) was isolated and esterified overnight as described for **5a**: 4.28 g (74%) of **5b**. M.p. 153–155° (from C_6H_6/hexane). UV/VIS: 253 (4.26), 380 (4.42). IR (nujol): 3320*m*, 3250*m*, 1735*s*, 1695*s*, 1665*s*, 1645*s*. ^{1}H-NMR: 9.63 (*s*, CHO); 8.49 (br. *s*, NH); 7.26 (*d*, J = 3.8, H–C(4′)); 6.57 (*d*, J = 3.8, H–C(3′)); 5.90 (*s*, CH=C(5)); 3.66 (*s*, MeO); 2.66 (*m*, 2 CH_2); 2.12 (*s*, Me–C(4)). NOE: 9.63 (2.1, 7.26); 7.26 (3.7, 6.57); 6.57 (3.5, 7.26; 3.5, 5.90); 5.90 (3.9, 6.57; 3.5, 2.12); 2.66 (3.1, 2.12); 2.12 (7.9, 5.90). ^{13}C-NMR: 176.56 (*d*, CHO); 173.01, 171.31 (2*s*, 2 CO); 156.58, 152.62, 141.86, 139.98, 131.73 (5*s*, quat. C's); 122.82 (*d*, C(4′)); 113.05 (*d*, C(3′)); 94.09 (*d*, *C*H=C(5)); 51.62 (*q*, MeO); 32.19 (*t*, C(3^2)); 19.46 (*t*, C(3^1)); 9.70 (*q*, *Me*–C(4)). EI-MS: 289 (28, M^+), 258 (14), 230 (22), 229 (100). Anal. calc. for $C_{15}H_{15}NO_5$ (289.29): C 62.28, H 5.23, N 4.84; found C: 62.41, H 5.22, N 4.70.

*Methyl (Z)-2,5-Dihydro-4-methyl-2-oxo-5-[(thien-2-yl)methylidene]-1*H*-pyrrole-3-propanoate* (**5c**). A soln. of **2** [14] (1.69 g, 0.01 mmol) in H_2O (20 ml) containing NaOH (3.0 g) was treated with a soln. of thiophene-2-carbaldehyde (**3c**; 1.12 g, 0.01 mol) in MeOH (50 ml). After stirring for 24 h at r.t., the crude product (2.50 g, 95%) was isolated and esterified during 3 h as described for **5a**: 2.0 g (76%) of **5c**. M.p. 146–147° (from C_6H_6/hexane). UV/VIS: 233 (3.75), 350 (4.44). IR: 3440*m*, 3000*m*, 2950*m*, 1730*s*, 1690*s*, 1435*s*, 1390*m*, 1170*m*, 1140*m*. ^{1}H-NMR: 7.63 (br. *s*, NH); 7.38 (*ddd*, J = 5.1, 1.1, 0.6, H–C(5′)); 7.13 (*ddd*, J = 3.7, 1.1, 0.8, H–C(3′)); 7.08 (*dd*, J = 5.1, 3.7, H–C(4′)); 6.29 (br. *s*, CH=C(5)); 3.66 (*s*, MeO); 2.69, 2.63 (2*m*, 2 CH_2); 2.13 (*s*, Me–C(4)). ^{13}C-NMR: 173.13, 171.87 (2*s*, 2 CO); 142.86, 138.11, 136.01, 130.05 (4*s*, quat. C's); 128.28, 128.11, 126.62 (3*d*, 3 =CH–); 102.10 (*d*, *C*H=C(5)); 51.55 (*q*, MeO); 32.29 (*t*, C(3^2)); 19.41 (*t*, C(3^1)); 9.73 (*q*, *Me*–C(4)). EI-MS: 277 (58, M^+), 246 (15), 217 (100), 204 (15). Anal. calc. for $C_{14}H_{15}NO_3S$ (277.34): C 60.63, H 5.45, N 5.05; found: C 60.80, H 5.55, N 5.07.

*Methyl (Z)-5-[(5-Formylthien-2-yl)methylidene]-2,5-dihydro-4-methyl-2-oxo-1*H*-pyrrole-3-propanoate* (**5d**). A soln. of **2** [14] (1.69 g, 0.01 mmol) in H_2O (20 ml) containing NaOH (3.0 g) was treated with a soln. of 5-(1,3-dioxolan-2-yl)thiophene-2-carbaldehyde [20] (**3d**; 1.84 g, 0.01 mol) in MeOH (50 ml). After stirring overnight at r.t., the crude product (2.83 g, 97%) was isolated and esterified during 20 h as described for **5a**: 2.76 g (93%) of **5d**. M.p. 170–172° (from C_6H_6). UV/VIS: 258 (4.03), 376 (4.49). IR (nujol): 3310*m*, 3230*m*, 1740*s*, 1695*s*, 1660*s*, 1620*s*. ^{1}H-NMR: 9.88 (*s*, CHO); 8.26 (br. *s*, NH); 7.73 (*d*, J = 4.0, H–C(4′)); 7.27 (*d*, J = 4.0, H–C(3′)); 6.23 (*s*, CH=C(5)); 3.66 (*s*, MeO); 2.68 (*m*, 2 CH_2); 2.15 (*s*, Me–C(4)). NOE: 9.88 (4.9, 7.73); 7.73 (5.0, 7.27); 7.27 (5.9, 7.73; 3.4, 6.23); 6.23 (3.3, 7.27; 3.8, 2.15); 2.68 (3.0, 2.15); 2.15 (8.2, 6.23). ^{13}C-NMR: 182.14 (*d*, CHO); 173.01, 172.06 (2*s*, 2 CO); 147.36 (*s*, C(5′)); 143.27, 143.03, 139.55, 131.62 (4*s*, remaining quat. C's); 136.85 (*d*, C(4′)); 128.51 (*d*, C(3′)); 100.73 (*d*, *C*H=C(5)); 51.63 (*q*, MeO); 32.14 (*t*, C(3^2)); 19.51 (*t*, C(3^1)); 9.82 (*q*, *Me*–C(4)). EI-MS: 305 (45, M^+), 274 (18), 245 (100). Anal. calc. for $C_{15}H_{15}NO_4S$ (305.36): C 59.00, H 4.95, N 4.59; found: C 58.93, H 4.94, N 4.58.

*Methyl (E)-5-[(5-Formylfuran-2-yl)methylidene]-2,5-dihydro-4-methyl-2-oxo-1*H*-pyrrole-3-propanoate* (**6a**). A degassed soln. of **5b** (0.2 g, 0.7 mmol) in MeOH (100 ml) was irradiated under Ar for 1 h with a high-pressure Hg lamp (*L-3*, *Quarzlampengesellschaft*, Hanau). From the residue obtained after evaporation, 49 mg (25%) of **6a** along with 120 mg of **5b** were isolated by chromatography (silica gel, CH_2Cl_2/AcOEt 3:1). Recrystallization from C_6H_6/hexane afforded pure **6a**. Yellow solid. M.p. 83–85°. UV/VIS: 254 (4.21), 380 (4.48). ^{1}H-NMR: 9.60 (*s*, CHO); 8.22 (br. *s*, NH); 7.26 (*d*, J = 3.6, H–C(4′)); 6.58 (*d*, J = 3.6, H–C(3′)); 6.16 (*s*, CH=C(5)); 3.68 (*s*, MeO); 2.73 (*t*, CH_2(3^1)); 2.62 (*t*, CH_2(3^2)); 2.36 (*s*, Me–C(4)). EI-MS: 289 (42, M^+), 258 (18), 229 (100). Anal. calc. for $C_{15}H_{15}NO_5$ (289.29): C 62.28, H 5.23, N 4.84; found: C 62.31, H 5.30, N 4.89.

*Methyl (E)-5-[(5-Formylthien-2-yl)methylidene]-2,5-dihydro-4-methyl-2-oxo-1*H*-pyrrole-3-propanoate* (**6b**) was obtained in 26% yield by photoisomerization of **5d** (0.2 g, 0.6 mmol), as described for **6a**. M.p. 128–130°. UV/VIS: 262 (4.11), 364 (4.35). ^{1}H-NMR: 9.88 (*s*, CHO); 8.58 (br. *s*, NH); 7.68 (*d*, J = 3.8, H–C(4′)); 7.09 (*dd*,

J = 3.8, 1.2, H–C(3′)); 6.44 (*d*, J = 1.2, CH=C(5)); 3.67 (*s*, MeO); 2.20–2.08 (*m*, 2 CH_2); 2.02 (*s*, Me–C(4)). EI-MS: 305 (52, M^+), 289 (20), 274 (16), 245 (100), 229 (40). Anal. calc. for $C_{15}H_{15}NO_4S$ (305.36): C 59.00, H 4.95, N 4.59; found: C 59.20, H 5.11, N 4.33.

*Dimethyl (4Z,10Z,15Z)-1,19,21,24-Tetrahydro--3,7,8,12,13,17-hexamethyl-1,19-dioxo-22*H*-bilin-2,18-dipropanoate* (**7**). A soln. of **4a** (130 mg, 0.33 mmol) in CF_3CO_2H (5 ml) was stirred at r.t. for 15 min before a soln. of **4b** (106 mg, 0.33 mmol) in CH_2Cl_2 (5 ml) was added at once. After stirring overnight, $POCl_3$ (2.0 ml) was added and the mixture refluxed for 2 h. Then the mixture was diluted with CH_2Cl_2 (100 ml), washed with sat. aq. $NaHCO_3$ soln. and H_2O, dried ($MgSO_4$), and evaporated and the residue recrystallized from MeOH: pure **7** (122 mg, 64%). M.p. 257–259°. UV/VIS (CH_2Cl_2): 367 (4.72), 635 (4.14). IR: 3430*w*, 3005*m*, 2960*m*, 2930*m*, 2870*w*, 1735*s*, 1700*s*, 1635*w*, 1595*m*, 1440*m*, 1395*m*. ^{1}H-NMR: 6.53 (*s*, H–C(10)); 5.77 (*s*, H–C(5), H–C(15)); 3.65 (*s*, 2 MeO); 2.51 (br. *s*, 4 CH_2); 2.10, 2.07, 1.99 (3*s*, 6 Me). ^{13}C-NMR: 173.47, 173.03 (2*s*, 4 CO); 149.66, 141.92, 141.36, 140.68, 134.75, 130.98, 127.71 (7*s*, quat. C's); 114.50 (*d*, C(10)); 97.01 (*d*, C(5), C(15)); 51.38 (*q*, 2 MeO); 31.47 (*t*, $C(2^2)$, $C(18^2)$); 19.00 (*t*, $C(2^1)$, $C(18^1)$); 9.56, 9.43 (2*q*, 6 Me). EI-MS: 586 (100, M^+), 288 (35). Anal. calc. for $C_{33}H_{38}N_4O_6$ (586.69): C 67.56, H 6.53, N 9.55; found: C 67.48, H 6.70, N 9.53.

*Dimethyl (4Z,10Z,15Z)-1,19,21,24-Tetrahydro-3,12,13,17-tetramethyl-1,19-dioxo-22-oxa-22-deazabilin-2,18-dipropanoate (= Methyl 5-{{5-{{5-{{2,5-Dihydro-4-[2-(methoxycarbonyl)ethyl]-3-methyl-5-oxo-1*H*-pyrrol-2-yli-dene}methyl}furan-2-yl}methylidene}-3,4-dimethyl-5*H*-pyrrol-2-yl}methylidene}-1,5-dihydro-4-methyl-2-oxo-1*H*-pyrrole-3-propanoate;* **8a**). A soln. of **4a** (1.293 g, 3.3 mmol) in CF_3CO_2H (10 ml) was stirred at r.t. for 15 min before a soln. of **5b** (963 mg, 3.3 mmol) in CH_2Cl_2 (50 ml) was added at once. Stirring was continued for 3 h, mixture diluted with CH_2Cl_2 (200 ml), the soln. washed with sat. aq. $NaHCO_3$ soln. and H_2O, dried ($MgSO_4$), and evaporated, and the residue recrystallized from AcOEt: 1.50 g of pure **8a**. M.p. 238–240°. From the mother liquor, additional 0.3 g were isolated. Total yield: 1.80 g (97%). UV/VIS: 280 (4.45), 355 (4.59), 550 (4.28). UV/VIS (MeOH + H^+): 286, 352, 668; $Q^{668}/_{352} = 0.56$. UV/VIS (MeOH + Zn^{2+}): 288, 360, 430 (sh), 700; $Q^{700}/_{360} = 0.22$. UV/VIS (CH_2Cl_2): 286 (4.30), 361 (4.75), 551 (4.30). IR (nujol): 3320*w*, 3220*w*, 3140*w*, 1745*m*, 1725*m*, 1675*s*, 1625*m*, 1605*s*. ^{1}H-NMR: *Table 1*. ^{13}C-NMR: 173.13 (*s*, 2 COO); 171.52, 171.09 (2*s*, C(1), C(19)); 170.34, 154.64, 153.89, 153.35, 146.61, 141.52, 140.71, 138.02, 134.40, 132.37, 130.40 (11*s*, quat. C's); 120.35, 115.98, 113.49, 96.43, 95.12 (5*d*, CH='s); 51.59 (*q*, 2 MeO); 32.35, 32.28 (2*t*, $C(2^2)$, $C(18^2)$); 19.37 (*t*, $C(2^1)$, $C(18^1)$); 9.83, 9.73, 9.68, 9.61 (4*q*, 4 Me). EI-MS: 559 (10, M^+), 359 (8), 321 (30), 222 (20), 44 (100). Anal. calc. for $C_{31}H_{33}N_3O_7$ (559.62): C 66.53, H 5.94, N 7.51; found: C 66.38, H 6.05, N 7.38.

*Dimethyl (4Z,10Z,15Z)-1,19,21,24-Tetrahydro-3,12,13,17-tetramethyl-1,19-dioxo-22-thia-22-deazabilin-2,18-dipropanoate (= Methyl 5-{{5-{{5-{{2,5-Dihydro-4-[2-(methoxycarbonyl)ethyl]-3-methyl-5-oxo-1*H*-pyrrol-2-yli-dene}methyl}thien-2-yl}methylidene}-3,4-dimethyl-5*H*-pyrrol-2-yl}methylidene}-1,5-dihydro-4-methyl-2-oxo-1*H*-pyrrole-3-propanoate;* **8b**) was prepared from **4a** (1.293 g, 33 mmol) and **5d** (1.017 g, 3.3 mmol) as described for **8a**: 1.70 g (89%). Blue solid. M.p. 259–262° (from AcOEt). UV/VIS: 284 (4.15), 360 (4.64), 546 (4.33). UV/VIS (MeOH + H^+): 288, 366, 630; $Q^{630}/_{366} = 0.69$. UV/VIS (MeOH + Zn^{2+}): 287, 364, 570, 616; $Q^{570}/_{364} = 0.49$. UV/VIS (CH_2Cl_2): 286 (4.30), 361 (4.75), 551 (4.30). IR (nujol): 1730*m*, 1690*m*, 1675*s*, 1620*m*, 1585*m*. ^{1}H-NMR: *Table 2*. ^{13}C-NMR: 173.25 (*s*, 2 COO); 171.79, 171.63 (2*s*, C(1), C(19)); 168.83, 153.21, 146.88, 146.77, 142.89, 141.33, 140.92, 139.93, 137.58, 132.89, 130.46 (11*s*, quat. C's); 134.64, 128.63, 121.27, 101.89, 95.85 (5*d*, CH='s); 51.56 (*q*, 2 MeO); 32.37, 32.30 (2*t*, $C(2^2)$, $C(18^2)$); 19.48 (*t*, $C(2^1)$, $C(18^1)$); 9.93, 9.74, 9.57 (3*q*, 4 Me). EI-MS: 575 (17, M^+), 224 (8), 143 (12), 99 (18), 56 (100). Anal. calc. for $C_{31}H_{33}N_3O_6S$ (575.68): C 64.68, H 5.78, N 7.30; found: C 64.40, H 5.98, N 7.36.

tert-*Butyl 5-[(2,5-Dihydro-5-oxofuran-2-ylidene)methyl]-3,4-dimethyl-1*H*-pyrrole-2-carboxylate* (**11**). $SnCl_4$ (1 ml) was added to a soln. of 2-(trimethylsilyloxy)furan (**9**; 3.5 ml, 21 mmol) and **1** [16] (4.47 g, 20 mmol) in CH_2Cl_2 (30 ml) previously cooled under Ar to −80°. The mixture was stirred at −80° for 3 h, then 6M aq. HCl (10 ml) and H_2O (10 ml) were added, and stirring was continued for 3 h at r.t. The org. layer was separated, the aq. phase extracted with CH_2Cl_2 (3 × 50 ml), and the combined org. extract dried ($MgSO_4$) and evaporated. The residue was fractionated by FC (silica gel): 0.66 g (11%; eluted with CH_2Cl_2) of a 97:3 mixture of **11** (R_f 0.48) and its (*E*)-isomer (R_f 0.58) and 5.20 g (85%; eluted with AcOEt) of **10** as an oil (R_f 0.21, using hexane/AcOEt as eluant). This oil was dissolved in CH_2Cl_2 (60 ml), and Et_3N (10.5 ml), Ac_2O (4.9 ml), and DMAP (0.28 g) were added. The mixture was stirred for 1 h at r.t. Then, the mixture was shaken with H_2O and 1M aq. HCl, the org. layer separated, the aq. phase extracted with CH_2Cl_2 (2 × 50 ml), the combined org. extract washed with H_2O (2 × 50 ml), dried ($MgSO_4$), and evaporated, and the residue filtered through silica gel (60 g) using CH_2Cl_2: yellow 94:7 mixture (4.70 g, 96%) of **11** and its (*E*)-isomer, which were separated by FC (silica gel).

(Z)-Isomer **11**: Total yield: 4.94 g (86%). M.p. 155–156.5° (from AcOEt). UV/VIS (CH_2Cl_2): 410 (4.47). IR (CH_2Cl_2): 3460*m*, 2980*m*, 2940*m*, 1760*s*, 1700*s*, 1640*s*, 1350*s*, 1110*s*. ^{1}H-NMR: 9.65 (br. *s*, NH); 7.45 (*d*, J = 5.32

H–C(3')); 6.11 (*dd*, J = 5.32, J = 0.73, H–C(4')); 6.00 (*s*, CH=C(2')); 2.24 (*s*, Me–C(3)); 2.08 (*s*, Me–C(4)); 1.59 (*s*, *t*-Bu). NOE: 7.45 (4.3, 6.00); 6.11 (4.1, 7.45); 6.00 (4.5, 7.45; 2.6, 2.08); 2.24 (1.7, 2.08); 2.08 (5.3, 6.00; 2.0, 2.24). ^{13}C-NMR: 169.11 (*s*, C(5')); 160.29 (*s*, COO); 145.83 (*s*, C(2)); 143.39 (*d*, C(3')); 125.97, 125.91, 125.38, 124.19, (4*s*, remaining quat. C's); 116.52 (*d*, C(4')); 101.70 (*d*, *C*H=C(2')); 81.22 (*s*, Me_3C); 28.38 (*q*, *Me*$_3$C); 10.21 (*q*, *Me*–C(4)); 9.04 (*q*, *Me*–C(3)). EI-MS: 289 (49, M^+), 233 (100), 187 (93). Anal. calc. for $C_{16}H_{19}NO_4$ (289.34): C 66.42, H 6.62, N 4.84; found: C 66.24, H 6.61, N 4.85.

(E)-Isomer of **11**: Total yield: 201 mg (3.5%). M.p. 166–168° (from hexane/AcOEt). ^{1}H-NMR: 8.81 (br. *s*, NH); 7.74 (*dd*, J = 5.52, 0.59, H–C(3')); 6.56 ('*d*', CH=C(2')); 6.30 (*dd*, J = 5.50, 1.76, H–C(4')); 2.22 (*s*, Me–C(3)); 2.04 (*s*, Me–C(4)); 1.57 (*s*, *t*-Bu).

5-[(2,5-Dihydro-5-oxofuran-2-ylidene)methyl]furan-2-carbaldehyde (**13**). As described for **11**, from **9** (3.5 ml, 21 mmol) and **3b** [19] (3.36 g, 20 mmol). The sole product **12** was purified by FC (hexane/AcOEt 1:2) and the obtained oil (2.83 g, 68%) dehydrated as described for **11**: 2:3 mixture of (*E*)-isomer and (*Z*)-isomer **13** (1.98 g, 77%). Identical R_f 0.56 (hexane/AcOEt 1:3). Pure **13** was obtained by crystallization from CH_2Cl_2. M.p. 184–186°. ^{1}H-NMR: 9.63 (*s*, CHO); 7.49 (*d*, J = 5.37, H–C(3')); 7.30 (*d*, J = 3.88, H–C(3)); 7.24–7.21 (*m*, H–C(4)); 6.30 (*dd*, J = 5.45, 0.55, H–C(4')); 6.12 (*s*, CH–C(5)). NOE: 7.49 (2.3, 6.12); 6.30 (1.1, 7.49); 6.12 (2.9, 7.49). ^{13}C-NMR: 177.36 (*d*, CHO); 168.53 (*s*, C(5')); 153.51 (*s*); 152.19 (*s*, C(2)); 150.22 (*s*); 143.62 (*d*, C(3')); 123.31 (*d*, C(3)); 120.41 (*d*, C(4')); 116.66 (*d*, C(4)); 100.75 (*d*, *C*H=C(2')). EI-MS: 190 (100, M^+), 161 (5), 133 (52), 105 (25), 79 (24). Anal. calc. for $C_{10}H_6O_4$ (190.15): C 63.16, H 3.18; found: C 63.02, H 3.13.

The ^{1}H-NMR data of the (*E*)-isomer of **13** could be obtained from the 360.13 MHz spectrum of the isomers mixture. ^{1}H-NMR: 9.62 (*s*, CHO); 8.31 (*dd*, J = 5.84, 0.96, H–C(3')); 7.24–7.21 (*m*, H–C(3)); 6.65 (*d*, J = 3.70, H–C(4)); 6.41–6.40 (*m*, H–C(4'), CH=C(2')). NOE: 7.24–7.21 (1.9, 6.6); 6.65 (1.0, 8.31); 6.41–6.40 (1.9, 6.6).

(4Z,10Z,15Z)-1,19,21,24-Tetrahydro-12,13-dimethyl-21,22,24-trioxa-21,22,24-trideazabilin-1,19-dione Hydrotrifluoroacetate (*= 5-[(2,5-Dihydro-5-oxofuran-2-ylidene)methyl]-2-{{5-[(2,5-dihydro-5-oxofuran-2-ylidene)-methyl]furan-2-yl}methylidene}-3,4-dimethyl-2*H*-pyrrol-1-ium Trifluoroacetate*; **14**). A soln. of **11** (116 mg, 0.4 mmol) in dry CH_2Cl_2 (10 ml) was added within 10 h to a stirred soln. of **13** (76 mg, 0.4 mmol) in dry CH_2Cl_2 (10 ml) containing CF_3CO_2H (1 ml), under Ar. After the addition was complete, stirring was continued for 24 h at r.t. Thereafter, the solvent was evaporated and the deep-blue residue repeatedly redissolved in dry CH_2Cl_2 (2 × 15 ml) and the soln. evaporated. The remaining residue was suspended in Et_2O, filtered, and washed successively with anh. Et_2O (2 × 10 ml) and pentane (2 × 10 ml): 183 mg (96%) of **14**. M.p. > 350°. UV/VIS (CF_3COOH): 336 (sh, 4.58), 352 (4.74), 594 (sh, 4.24), 636 (4.31). UV/VIS (CH_2Cl_2/CF_3COOH): 344 (sh, 4.56), 360 (4.75), 604 (sh, 4.20), 658 (4.35). ^{1}H-NMR: *Table 3*. ^{13}C-NMR (CD_2Cl_2/FC_3CO_2D): 171.34, 167.82 (2*s*, C(1), C(18)); 161.40, 158.41, 154.92, 154.32, 153.18, 147.67, 138.73, 133.99 (8*s*, quat. C's); 145.53, 145.01, 134.74, 124.53, 122.40, 122.15, 118.94, 101.80, 98.28 (9*d*, CH='s); 10.56 (*q*, *Me*–C(12)); 9.35 (*q*, *Me*–C(13)). FAB-MS: 362 (100, $[M - CF_3CO_2]^+$), 308 (5), 281 (8). HR-FAB-MS: 362.1028 ($[C_{21}H_{16}NO_5]^+$; calc. 362.1028).

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