197. Syntheses of Bile Pigments

Part 15[1])

First Unequivocal Assignment of the Absolute Configuration of an Urobilinoid Bile Pigment by X-Ray Diffraction Analysis of its Synthetic Precursor

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(18.IX.87)

(−)-(4*S*,16*S*)-8,12-bis[de(2-carboxyethyl)]mesourobilin-IIIα hydrochloride (**8**) has been synthesized from the enantiomerically pure 1,4,5,10-tetrahydro-1-oxodipyrrin-9-carboxylic-acid precursor **6a** whose absolute configuration was determined by X-ray diffraction analysis of the *N*-[(*S*)-1-(1-naphthyl)ethyl] carboxamide **7b**. The present results prove unequivocally that an (*S,S*)-configurated urobilin chromophore displays a *negative Cotton* effect in the VIS absorption range. However, the helicity of the inherently dissymmetric chromophore remains undetermined.

Catabolism of heme, the chromophore of hemoglobin, which commences by the oxidative cleavage of the protoporphyrin IX macrocycle yielding protobiliverdin IXα, continues in humans and mammalians through a series of reduction processes brought about first enzymatically (to protobilirubin IXα) and completed by bacteria of the intestinal flora (mainly *Clostridia*) [2]. The final products of the reduction of protobilirubin IXα are urobilinogen and stercobilinogen which, upon oxidation by air, yield mesourobilin IXα (= urobilin; **1**) and stercobilin IXα (= stercobilin = 2,3,17,18-tetrahydrourobilin), respectively [3].

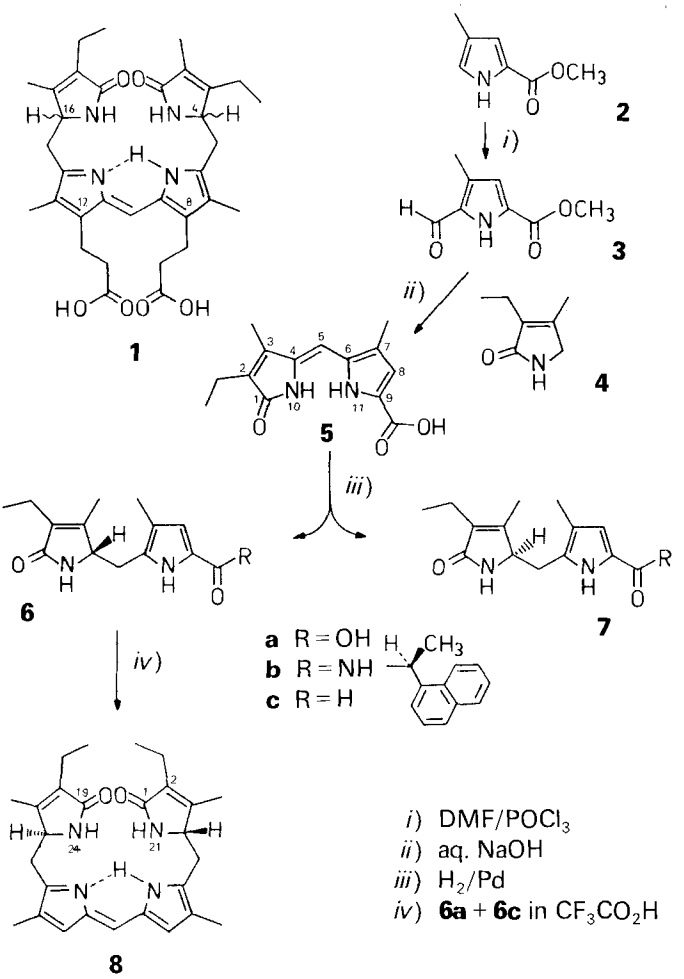
Although mesourobilinogen enters into the enterohepatic circulation [4], the biological significance for the fecal excretion of bile pigments in the form of urobilinoids rather than as conjugated protobilirubin remains obscure. On the other hand, interest for this class of bile pigments rose promptly, after the existence of the urobilin chromophore had been unequivocally demonstrated in both algal [5][6] and bacterial [7] photosynthetic accessory pigments of the phycoerythrin type.

Both urobilin (**1**) and stercobilin have been isolated from natural sources as optically active compounds which are characterized by the extremely high specific rotations of their hydrochlorides ($[\alpha]_D^{20} = +5000°$ for (+)-urobilin and $[\alpha]_D^{20} = -4000°$ for (−)-stercobilin) in the vicinity of the absorption of the dipyrrin chromophore [8]. This high optical

[1]) Part 14: [1].

[2]) Part of the Ph. D. work of *C.P.*, in progress. Universität Freiburg i. Ue. An abstract of this work has been presented at the autumn meeting of the Swiss Chemical Society in Bern, 16th October, 1987.

activity has been attributed by *Moscowitz et al.* [9] to the presence of an inherently dissymmetric dipyrrin chromophore of fixed chirality, which is stabilized by intramolecular H-bonding. In this model, the helicity of the dipyrrin chromophore is determined by the absolute configurations of the asymmetric atoms C(4) and C(16) (see **1**). Based on the examination of space-filling molecular models, it was thus suggested that the urobilin molecule, and hence the sense of twist of the dipyrrin chromophore, may coil into a left-handed helix, when both chirality centers assume the (*R*)-configuration and into a right-handed helix for the (*S,S*)-configuration [10]. In fact, however, the precise structures of the optically active conformers cannot be deduced from their CD spectra, since neither the relationship between the helicity (*P* or *M*) of the dipyrrin chromophore and the sign of the corresponding *Cotton* effect is known nor has the absolute configuration of optically active urobilins been proven unequivocally so far. Indeed, the assignments of the absolute configuration of optically active urobilins [11][12] and phycoerythrobilin [13] have been made on the basis of a questionable assignment of the absolute configuration



of (−)-stercobilin by ^{1}H-NMR spectroscopy [11], assuming the validity of *Moscowitz*'s model.

As, until now, our repeated attempts to obtain crystalline samples, suitable for an X-ray analysis, of (+)-mesourobilin IXα, (+)-mesourobilin IIIα, or some of their synthetic precursors had failed, we envisaged the synthesis of a 8,12-bis[de(2-carboxyethyl)] derivative of the latter (*i.e.* **8** or its enantiomer) from the optically active dipyrromethan-1(4*H*)-one precursors **6a** or **7a**, respectively. Our project was guided both by the assumption that, on entropic grounds, removal of the conformatively flexible propionic-acid residues at C(8) and C(12) might favour the crystallization of a C_2-symmetric urobilinoid such as **8**, and by the possibility of introducing at some advanced stage of the synthesis the propionic-acid chains in the free β-positions, thus enabling, if necessary, a chemical

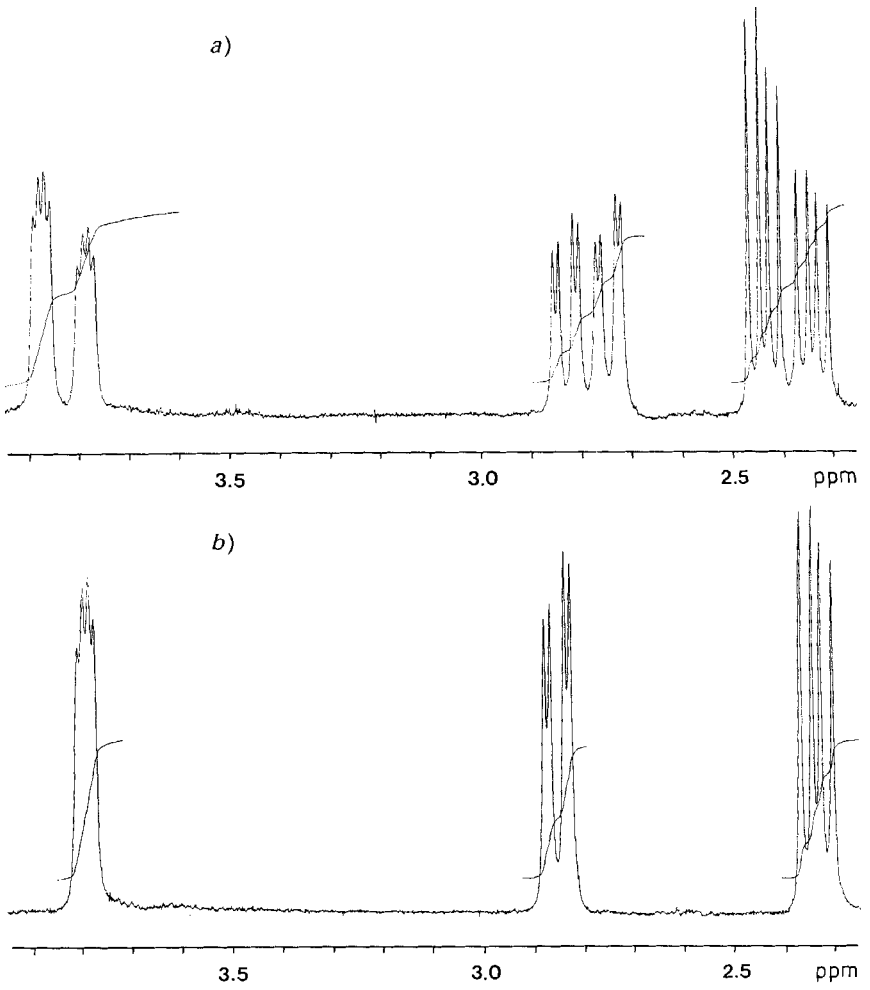


Fig. 1. *Detail of the* ^{1}*H-NMR spectrum* ($CDCl_3$): a) *of a mixture* **6b**/**7b** (9:11) *showing characteristic signals for the* (4S,9^{3}S)- *and* (4R,9^{3}S)-*diastereoisomers and* b) *of pure* (−)-(4S,9^{3}S)-*2-ethyl-1,4,5,10-tetrahydro-3,7-dimethyl-N-[1-(1-naphthyl)ethyl]-1-oxodipyrrin-9-carboxamide* (**6b**)

correlation between the absolute configuration of **8** and those of naturally occurring urobilins of the meso type.

The racemic mixture of dipyrromethan-1(4*H*)-ones **6a**/**7a** was obtained from the known methyl 4-methyl-1*H*-pyrrole-2-carboxylate (**2**) [14] and 3-ethyl-4-methyl-1*H*-pyrrol-2(4*H*)-one (**4**) [15] *via* **3** and **5** using conventional methodology (*cf.* [16]). For the resolution of the racemic mixture **6a**/**7a**, fractional crystallization of their strychnine salts proved to be superior to the use of brucine, quinine, cinchonidine, (+)-(*R*)- or (−)-(*S*)-1-

Table 1. *Fractional Atomic Coordinates* (× 10^4) *and Equivalent Isotropic Temperature Coefficients* (Å^2 × 10^4) *for* **7b**[a]). Values of U_{eq} were obtained as one third of the trace of the orthogonalized U_{ij} tensor.

	x/a	*y/b*	*z/c*	U_{eq}
N(1)	10720(9)	1779 fix	7103(6)	208(41)
C(2)	11865(10)	1326(5)	7595(7)	223(51)
O(3)	13640(7)	1335(3)	7308(5)	241(34)
C(4)	10625(11)	812(5)	8521(8)	201(46)
C(5)	11438(12)	268(5)	9261(8)	268(53)
C(6)	11882(11)	647(5)	10393(8)	306(54)
C(7)	8766(11)	958(5)	8489(7)	234(51)
C(8)	7009(11)	573(5)	9245(8)	310(57)
C(9)	8693(11)	1586(5)	7594(7)	184(46)
H(9)	8261(82)	1451(36)	6712(56)	74(170)
C(10)	7470(10)	2257(5)	8250(7)	190(48)
C(11)	7060(10)	2835(5)	7373(7)	186(46)
N(12)	5667(9)	2732(4)	6740(6)	195(41)
H(12)	4977(104)	2370(43)	6958(72)	134(247)
C(13)	7793(10)	3568(5)	7090(7)	169(46)
C(14)	9398(10)	3924(5)	7582(8)	244(51)
C(15)	6781(10)	3890(5)	6274(7)	194(46)
C(16)	5457(10)	3362(5)	6097(7)	177(45)
C(17)	3975(10)	3361(5)	5398(7)	165(45)
O(18)	3013(7)	2779(3)	5343(5)	240(34)
N(19)	3620(10)	4002(4)	4833(7)	224(45)
H(19)	3934(98)	4351(39)	5052(69)	1(234)
C(20)	2013(10)	4043(5)	4237(7)	181(46)
H(20)	1074(80)	3709(34)	4715(57)	1(170)
C(21)	1287(12)	4855(5)	4259(8)	294(52)
C(22)	2591(10)	3746(5)	2911(7)	236(50)
C(23)	4361(10)	3866(5)	2137(7)	214(48)
C(24)	4884(10)	3669(5)	888(8)	269(51)
C(25)	3597(11)	3306(5)	370(8)	260(49)
C(26)	1725(11)	3125(4)	1129(8)	274(53)
C(27)	406(11)	2717(5)	582(7)	291(53)
C(28)	−1403(11)	2548(5)	1333(8)	297(54)
C(29)	−1939(11)	2771(5)	2591(8)	317(54)
C(30)	−685(10)	3164(5)	3112(8)	246(49)
C(31)	1202(10)	3350(5)	2398(7)	193(44)
C(1L)	5033(13)	6030(5)	6024(9)	407(63)
O(2L)	5406(8)	5498(3)	4979(6)	317(37)
H(2L)	5597(83)	5661(37)	4214(60)	1(177)
C(3L)	3504(14)	5688(6)	7077(8)	500(72)
C(4L)	6823(13)	6228(5)	6409(9)	437(67)

[a]) Arbitrary numbering scheme (see *Fig. 2*).

phenylethylamine. However, a reliable determination of the enantiomeric purity of the free carboxylic acids or their corresponding methyl esters was thwarted by the insufficient resolution of the ^{1}H-NMR signals of both enantiomers in the presence of optically active shift reagents (*cf.* [17–19]).

More satisfactory proved to be the analysis by ^{1}H-NMR spectroscopy of the mixture of diastereoisomeric amides obtained, when the racemic mixture **6a**/**7a** was reacted with optically active amines under conditions which efficiently prevent racemization in peptide synthesis (*cf.* [20]). Among the nine amines examined: L-alanine methyl ester, (+)-(*R*)- and (−)-(*S*)-1-phenylethylamine, L-phenylalanine *tert*-butyl and benzyl ester, L-proline

Table 2. *Bond Lengths* (Å) *for* **7b**[a]). Estimated standard deviations are in the range of 0.009–0.014 Å.

N(1)–C(2)	1.356	N(1)–C(9)	1.466	C(2)–O(3)	1.238
C(2)–C(4)	1.487	C(4)–C(5)	1.474	C(4)–C(7)	1.373
C(5)–C(6)	1.517	C(7)–C(8)	1.495	C(7)–C(9)	1.495
C(9)–H(9)	1.116	C(9)–C(10)	1.547	C(10)–C(11)	1.486
C(11)–N(12)	1.368	C(11)–C(13)	1.407	N(12)–H(12)	0.811
N(12)–C(16)	1.348	C(13)–C(14)	1.529	C(13)–C(15)	1.409
C(15)–C(16)	1.383	C(16)–C(17)	1.463	C(17)–O(18)	1.252
C(17)–N(19)	1.348	N(19)–H(19)	0.721	N(19)–C(20)	1.467
C(20)–H(20)	0.952	C(20)–C(21)	1.529	C(20)–C(22)	1.508
C(22)–C(23)	1.362	C(22)–C(31)	1.446	C(23)–C(24)	1.376
C(24)–C(25)	1.364	C(25)–C(26)	1.434	C(26)–C(27)	1.440
C(26)–C(31)	1.409	C(27)–C(28)	1.391	C(28)–C(29)	1.398
C(29)–C(30)	1.373	C(30)–C(31)	1.430	C(1L)–O(2L)	1.458
C(1L)–C(3L)	1.512	C(1L)–C(4L)	1.495	O(2L)–H(2L)	0.867

[a]) Arbitrary numbering scheme (see *Fig. 2*).

Table 3. *Bond Angles* (°) *for* **7b**[a]). Estimated standard deviations are in the range of 0.5–0.8°.

C(2)–N(1)–C(9)	111.4	C(21)–C(20)–C(22)	110.8	C(11)–N(12)–H(12)	115.3
N(1)–C(2)–C(4)	108.3	C(20)–C(22)–C(31)	119.7	H(12)–N(12)–C(16)	132.0
C(2)–C(4)–C(5)	121.7	C(22)–C(23)–C(24)	124.4	C(11)–C(13)–C(15)	106.8
C(5)–C(4)–C(7)	131.4	C(24)–C(25)–C(26)	120.0	C(13)–C(15)–C(16)	107.4
C(4)–C(7)–C(8)	126.6	C(25)–C(26)–C(31)	119.7	N(12)–C(16)–C(17)	117.8
C(8)–C(7)–C(9)	122.8	C(26)–C(27)–C(28)	118.5	C(16)–C(17)–O(18)	120.7
N(1)–C(9)–H(9)	101.4	C(28)–C(29)–C(30)	120.5	O(18)–C(17)–N(19)	120.1
C(7)–C(9)–H(9)	118.3	C(22)–C(31)–C(26)	118.9	C(17)–N(19)–C(20)	120.6
H(9)–C(9)–C(10)	108.8	C(26)–C(31)–C(30)	117.6	N(19)–C(20)–H(20)	104.7
C(10)–C(11)–N(12)	121.9	O(2L)–C(1L)–C(4L)	111.8	N(19)–C(20)–C(22)	110.9
N(12)–C(11)–C(13)	107.0	C(1L)–O(2L)–H(2L)	120.2	H(20)–C(20)–C(22)	107.8
C(11)–N(12)–C(16)	110.4	N(1)–C(2)–O(3)	125.6	C(20)–C(22)–C(23)	122.7
C(11)–C(13)–C(14)	125.3	O(3)–C(2)–C(4)	126.1	C(23)–C(22)–C(31)	117.6
C(14)–C(13)–C(15)	127.9	C(2)–C(4)–C(7)	106.9	C(23)–C(24)–C(25)	119.4
N(12)–C(16)–C(15)	108.3	C(4)–C(5)–C(6)	110.9	C(25)–C(26)–C(27)	119.4
C(15)–C(16)–C(17)	133.8	C(4)–C(7)–C(9)	110.6	C(27)–C(26)–C(31)	121.0
C(16)–C(17)–N(19)	119.2	N(1)–C(9)–C(7)	102.8	C(27)–C(28)–C(29)	121.0
C(17)–N(19)–H(19)	117.3	N(1)–C(9)–C(10)	113.1	C(29)–C(30)–C(31)	121.5
H(19)–N(19)–C(20)	117.0	C(7)–C(9)–C(10)	112.0	C(22)–C(31)–C(30)	123.6
N(19)–C(20)–C(21)	110.1	C(9)–C(10)–C(11)	114.1	O(2L)–C(1L)–C(3L)	107.5
H(20)–C(20)–C(21)	112.5	C(10)–C(11)–C(13)	130.9	C(3L)–C(1L)–C(4L)	113.1

[a]) Arbitrary numbering scheme (see *Fig. 2*).

methyl and benzyl ester, L-histidine methyl ester, and (−)-(*S*)-1-(1-naphthyl)ethylamine, the latter yielded the mixture of amides showing the best resolved ^{1}H-NMR signals for both diastereoisomeric components (see *Fig. 1*). In this way, the enantiomeric purity of the carboxylic acid **6a** which was properly separated by fractional crystallization of the corresponding strychnine salt was determined to be 98±2%. On the other hand, the enantiomeric carboxylic acid **7a** which could be only partially resolved by crystallization of its strychnine salt from the mother liquors yielded diastereoisomeric pure crystals of the amide **7b** in a quality suitable for X-ray diffraction studies[3]). Thus, the relative configuration of the two asymmetric C-atoms present in the molecule could be clearly established (see *Tables 1–3*). Since the absolute configuration of (−)-1-(1-naphthyl)-ethylamine has been unequivocally determined to be *S* [23][24], the (*R*)-configuration must be assigned to the *dextrorotatory* carboxylic acid **7a** (*cf. Fig. 2*). For the sake of comparison, the enantiomer **6a** was reacted with (+)-(*R*)-1-(1-naphthyl)ethylamine in order to obtain the corresponding amide whose analytical data proved to be identical with those of its enantiomer **7b** (*cf. Exper. Part*).

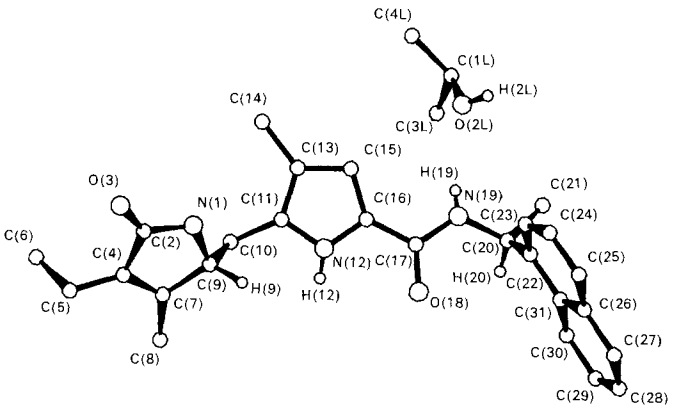


Fig. 2. *Structure of (+)-(4R,9^{3}S)-2-ethyl-1,4,5,10-tetrahydro-3,7-dimethyl-*N*-[1-(1-naphthyl)ethyl]-1-oxo-9-carboxamide* (**7b**)[3]). Arbitrary numbering scheme.

Formylation of **6a** with trimethyl orthoformate in the presence of CF_3COOH (*cf.* [12]) afforded the aldehyde **6c** which was condensed with **6a** using the conventional procedure (*cf.* [16]) to yield (−)-(4*S*,16*S*)-8,12-bis[de(2-carboxyethyl)]mesourobilin-IIIα hydrochloride (**8**) in 50% yield. In the temperature range −35 to +25°, the CD spectrum ($CHCl_3$) of **8** shows that the (4*S*,16*S*)-configurated urobilin chromophore gives rise to a *negative*

[3]) Amide **7b** crystallized with 1 molecule of i-PrOH per asymmetric unit. Crystal data: $C_{26}H_{29}N_3O_2 \cdot C_3H_7OH$, space group $P2_1$, cell constants $a = 7.204(1)$, $b = 17.722(4)$, $c = 11.001(3)$ Å, $\beta = 75.61(2)°$, $V = 1360.6(4)$ Å^3, $Z = 2$, $d_c = 1.132$; lattice parameters determined by least-squares refinement of the positions of 48 reflections with $10 \leq 2\theta \leq 15°$; data collection on a modified *Stoe* 4-circle diffractometer (MoK_α-radiation, $\lambda = 0.71069$ Å) at 98(1) K, ω-scan technique, scan width 1.5°, max. $\sin\theta/\lambda = 0.595$ Å^{-1}, 2538 unique reflections (2575 with $F_o > 4\sigma(F_o)$); structure solved with direct methods and tangent expansion (SHELX86 [21]); refinement (SHELX76 [22]) of all 35 non-H-atoms anisotropic, of 5 H-atoms isotropic, and the remaining H-atoms riding with temperature coefficient free, $R = 0.072$, $R_w = 0.057$ ($\omega_i = 1/\sigma^2(F)$), max. shift in last refinement cycle $\Delta/\sigma = 3.1$, largest peak in final *F-Fourier* syntheses 0.4 eÅ^{-3}.

Cotton effect (*cf. Fig. 3*), in agreement with the tentative assignment of the absolute configuration of (+)-mesourobilin IXα (**1**) by *Brockmann et al.* [11]. Although the X-ray diffraction analysis of **7b** establishes for the first time experimentally the relationship between the absolute configuration of urobilinoids and the sign of the *Cotton* effect in their CD curves, the preferred conformation of the optically active chromophores cannot be inferred from our results. It must be pointed out, however, that if a right-handed (*P*-configurated) helical dipyrrin chromophore is conditioned by the (4*S*,16*S*)-configuration of the urobilin molecule as postulated by *Moscowitz et al.* [10], the relationship between helicity of the chromophore and sign of the *Cotton* effect in urobilinoids must be opposite, as in the case of helicenes[4]).

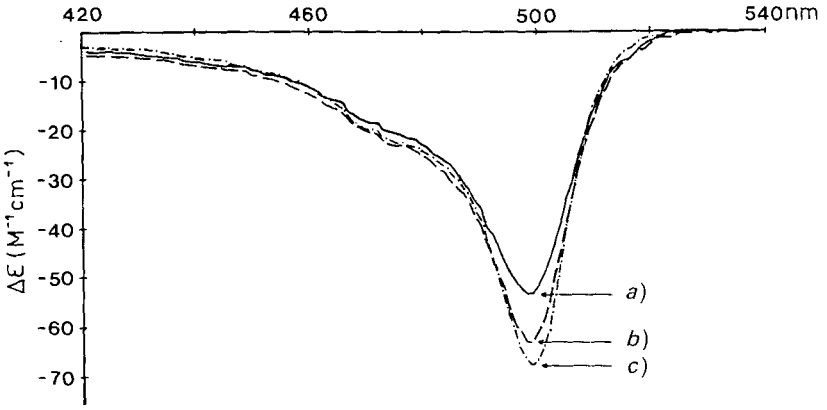


Fig. 3. *Temperature-dependent CD curves* ($CHCl_3$) *of (−)-(4S,16S)-8,12-bis[de(2-carboxyethyl)]mesourobilin-IIIα hydrochloride* (**8**; $c = 1.47 \times 10^{-5}$ M). *a*) 298 K, *b*) 268 K, *c*) 238 K.

In their study of the circular dichroism of urobilinoids, *Moscowitz et al.* [10] observed that in MeOH/glycerol 9:1 at low temperatures, at least two chiral species with opposite CD curves are present in the solution. This effect was explained by an increase of the population of some (possibly unfolded) conformers, in which the dipyrrin chromophore assumes the opposite chirality from that present in intramolecularly H-bonded molecules. Actually, when dissolved in MeOH in the absence of acid, the urobilin hydrochloride **8** is partially deprotonated by the solvent (*cf. Fig. 4*). At room temperature, both the hydrochloride and the free base display negative *Cotton* effects, although at different wavelengths (λ_{max} 516 and 437 nm, resp.). A study of the relationship between the conformation of the urobilin chromophore and its chiroptical properties is, at present, in progress using a model for 'stretched' bile-pigment chromophores recently performed in our laboratory [1].

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[4]) In the case of helicenes, where specific rotations are in the same order of magnitude as in urobilinoids, the relationships between the helicity of the inherently dissymmetric chromophore and the sign of the *Cotton* effect could be correctly predicted by MO calculations using the π-SCF approximation [25] [26]. Thus, for instance, in agreement with experimental evidence [27], (−)-hexahelicene is *M*-configurated. To the best of our knowledge, such calculations have not yet been carried out for urobilinoids.

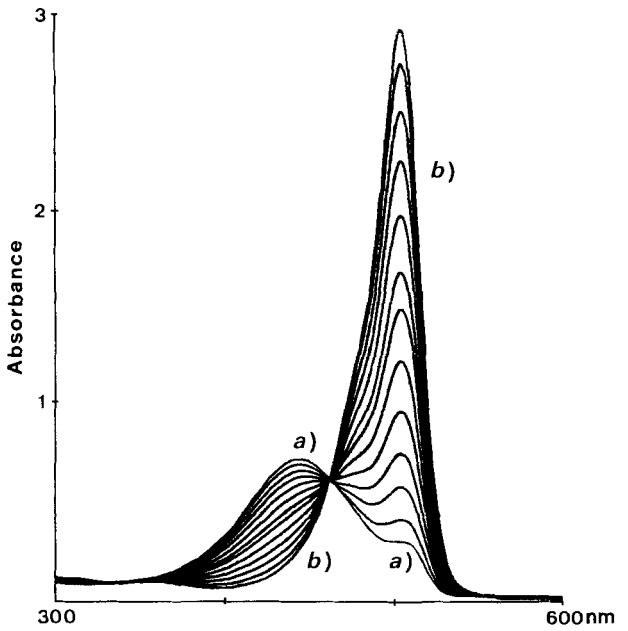

Fig. 4. *Change of the VIS spectrum of 8,12,-bis[de(2-carboxyethyl)]mesourobilin-IIIα hydrochloride* (**8**) *in MeOH. a*) 4.43 × 10^{-5} M in MeOH; *b*) gradual addition of 10^{-3} N HCl/MeOH.

Financial support of this work by the *Swiss National Science Foundation* (Project No. 2.436-0.84) and the *Austrian Science Foundation* (Project No. 4873) is gratefully acknowledged. We thank Dr. *T. A. Jenny* for his help in interpretation of the spectra.

Experimental Part

General: Anal. TLC: plates precoated with silica gel *60* PF_{254} (*E. Merck*, D-6100 Darmstadt). Prep. TLC: plates (20 × 20 or 100 × 20 cm) precoated with silica gel *60* $PF_{254+366}$ (*E. Merck*). Column chromatography (CC): silica gel *60*, 0.040–0.063 mm (*E. Merck*). M.p.: *Kofler* hot stage melting point apparatus (*Thermovar, C. Reichert AG*, Vienna); not corrected. IR: *Perkin-Elmer 599* spectrophotometer; KBr pellets unless otherwise specified; wave numbers in cm^{-1}. UV/VIS: *Perkin-Elmer-320* spectrophotometer; λ_{max} (log ε) in nm. CD: *Jobin-Yvon-Auto-Dichrograph-Mark-V*; band amplitudes are given as specific ellipticity (θ) and wavelengths (λ) in nm, $CHCl_3$ solns. unless otherwise specified. Specific optical rotations ($[\alpha]_D^{20}$): *Perkin-Elmer-241-MC* polarimeter; concentrations *c* in g/100 ml. ^{1}H-NMR (360.13 MHz) and ^{13}C-NMR (90.56 MHz): *Bruker AM 360* instrument equipped with a data system *Aspect 3000*; chemical shifts in ppm (δ) are referenced to internal TMS; $CDCl_3$ (77.05 ppm) and (D_6)DMSO (39.5 ppm), *J* values in Hz; the spectra were recorded by Mrs. *E. Bard-Trieschmann*. EI-MS (*m/z* (rel. intensity)): *Vacuum Generator Micromass 7070 E* instrument (70 eV) equipped with a data system *DS 11-250*; assignments have not been verified by HR-MS or by means of isotope-labeled derivatives. Elemental analyses; *Perkin-Elmer-240*CHN analyser; performed by Mr. *F. Nydegger*.

*Methyl 5-Formyl-4-methyl-1*H*-pyrrole-2-carboxylate* (**3**). A soln. of *Vilsmeier*'s reagent (prepared by dropwise addition of $POCl_3$ (21 g) to DMF (40 ml) at 10° and subsequent stirring for 15 min at r.t.) was added dropwise to a soln. of methyl 4-methyl-1*H*-pyrrole-2-carboxylate [14] (17 g) in ice-cooled DMF (80 ml). Then, the mixture was allowed to attain r.t., heated for 15 min at 100°, poured into aq. NaOAc soln. (800 ml, 1.25M), and allowed to stand overnight at r.t. The precipitate was separated by filtration and recrystallized from hexane to yield **3** as needles (18 g, 88%). M.p. 124–126°. IR: 3280*s*, 2930*w*, 1710*s* (ester, C=O), 1680*s* (formyl, C=O), 1550*m*, 1485*w*, 1465*m*,

1425*m*, 1390*w*, 1380*w*, 1340*m*, 1255*s*, 1110*w*, 1000*w*, 935*w*, 835*m*. UV/VIS: 297 (4.35), 228 (4.05). ^{1}H-NMR ($CDCl_3$): 9.79 (*s*, CHO, NH); 6.71 (*dq*, *J*(NH,CH) = 1.1, *J*(CH,CH) = 0.5, H–C(3)); 3.89 (*s*, CH_3O); 2.39 (*d*, *J* = 0.5, CH_3–C(4)). ^{13}C-NMR ($CDCl_3$): 178.92 (*d*, CHO); 160.73 (*s*, ester CO); 131.24 (*s*); 130.89 (*s*); 127.16 (*s*); 116.76 (*d*, H–C(3)); 52.10 (*q*, CH_3O); 10.54 (*q*, CH_3–C(4)). MS: 165 (85, $M^{+\cdot}$), 136 (31, $M^{+\cdot} - CH_3O$), 107 (100, $M^{+\cdot} - COOCH_3$–H), 78 (16, 107 – CO, – H), 53 (31, 78–CH_3). Anal. calc. for $C_8H_9NO_3$ (167.16): C 57.48, H 5.42, N 8.37; found: C 57.71, H 5.50, N 8.31.

2-Ethyl-1,10-dihydro-3,7-dimethyl-1-oxodipyrrin-9-carboxylic Acid[5] (**5**). A soln. of **3** (7.21 g) and 3-ethyl-4-methyl-1*H*-pyrrol-2(4*H*)-one [15] (5.35 g) in 4N aq. NaOH (260 ml) was refluxed for 1 h, then cooled and acidified with 3N aq. HCl. The precipitate was separated by filtration, washed with H_2O and dried *in vacuo* over P_4O_{10}. The crude **5** (10 g, 90%) of m.p. 259–265° was used without further purification in the next reaction. IR: 3360*m* (NH), 3180*m* (br., OH), 2960*w*, 2920*w*, 2860*w*, 1670*s* (C=O), 1600*m*, 1485*w*, 1470*m*, 1420*w*, 1400*m*, 1370*w*, 1270*m*, 1230*m*, 1180*w*, 1120*w*, 1060*w*, 990*w*, 960*w*, 920*w*, 890*w*, 840*w*, 830*w*, 760*w*, 740*w*, 710*w*, 680*w*, 670*w*, 650*w*. UV/VIS (CH_3OH): 402 (sh), 338 (4.20), 270 (sh), 253 (3.97), 246 (sh). UV/VIS (CH_3OH + H_2SO_4): 398 (sh), 378 (4.16), 276 (3.83), 253 (4.01), 246 (sh). UV/VIS (CH_3OH + $Zn(OAc)_2$): 435 (4.01), 412 (4.10), 392 (sh), 268 (sh), 260 (4.03). ^{1}H-NMR ((D_6)DMSO): 11.31 (br. *s*, H–N(11)); 10.41 (br. *s*, H–N(10)); 6.62 (*d*, *J*(NH,CH) = 1.7, H–C(8)); 5.89 (*s*, H–C(5)); 2.24 (*q*, *J* = 7.5, CH_3CH_2–C(2)); 2.10 (*s*, CH_3–C(7)); 2.06 (*s*, CH_3–C(3)); 1.0 (*t*, *J* = 7.5, CH_3CH_2–C(2)). ^{13}C-NMR ((D_6)DMSO): 172.17 (*s*, C(1)); 161.39 (*s*, COOH); 141.28 (*s*, C(3)); 133.83 (*s*); 131.81 (*s*); 128.60 (*s*); 124.53 (*s*); 122.96 (*s*); 116.92 (*d*, C(8)); 96.03 (*d*, C(5)); 16.35 (*t*, CH_3CH_2–C(2)); 13.28 (*q*); 11.22 (*q*); 9.24 (*q*). MS: 260 (4, $M^{+\cdot}$), 216 (29, $M^{+\cdot} - CO_2$), 201 (19), 179 (29), 135 (75), 94 (100, 3-methylazafulvenium ion), 85 (15), 71 (28).

rac-*2-Ethyl-1,4,5,10-tetrahydro-3,7-dimethyl-1-oxodipyrrin-9-carboxylic Acid* (**6a**/**7a**). A suspension of **5** (10 g) in CH_3OH (3.46 l) containing KOH (3.46 g) was hydrogenated on 10% Pd/C (3.27 g) at 1 atm and r.t. until the soln. became colorless (*ca.* 150 min). The catalyst was removed by filtration on *Celite* and the filtrate acidified to pH 2 by bubbling SO_2 into the soln. About ½ of the solvent was then evaporated under reduced pressure and H_2O (900 ml) added to the residue. The product was separated by filtration and dried *in vacuo* over P_4O_{10} to yield 6.45 g (64%) of crude **6a**/**7a** which was used without further purification for resolution. Crystallization from EtOH yielded a pure sample of m.p. 220–222°.

(S)-Enantiomer **6a**. The racemic mixture **6a**/**7a** (6.42 g) was added in small portions at 40° under Ar to a stirred suspension of 8.18 g of (–)-strychnine (*Aldrich-Chemie GmbH*, D-7924 Steinheim a. A.) in CH_3OH (1125 ml). After a clear soln. was obtained, impurities were removed by filtration, and the filtrate was kept at –20° for 16 h. The jelly-like precipitate thus obtained was separated by filtration, washed with cold CH_3OH and dried *in vacuo* over P_4O_{10} for 24 h to yield 5.54 g (76%) of a mixture of diastereoisomeric strychnine salts of $[\alpha]_D^{20} = -59°$ (*c* = 0.1, CH_3OH). Sixfold crystallization of the latter from CH_3OH afforded one pure diastereoisomer of $[\alpha]_D^{20} = -68°$ whose crystals of m.p. 132–135° contain 1 mol of CH_3OH per mol even after drying at 60°/0.1 Torr over P_4O_{10} for 48 h. Anal. calc. for $C_{36}H_{44}N_4O_6$ (628.77): C 68.77, H 7.05, N 8.91; found: C 68.84, H 7.10, N 9.00.

The mother liquors contained mainly the strychnine salt of **7a** from which it could be obtained impure ($[\alpha]_D^{20} = +46°$) by the procedure described below.

The strychnine salt of **6a** (1.06 g) was dissolved in AcOH (6.4 ml) at 35° under Ar and H_2O added dropwise until the mixture became turbid. The mixture was then chilled to 0° and more H_2O added (*ca.* 40 ml total) until precipitation of the product was completed. After storage in the refrigerator for 16 h, the precipitate was separated by filtration, washed with H_2O, and dried overnight *in vacuo* over P_4O_{10} to yield 386 mg (82%) of crystalline **6a**. M.p. 214–216° (from CH_3OH). $[\alpha]_D^{20} = -75°$ (*c* = 0.1, CH_3OH). IR: 3360*m* (br.), 3300*m*, 2960*w*, 2920*w*, 2860*w*, 1680*s* (C=O), 1630*w*, 1470*m*, 1420*m*, 1390*w*, 1320*w*, 1270*m*, 1250*m*, 1210*m*, 1190*m*, 1170*w*, 1140*w*, 1120*w*, 1060*w*, 990*w*, 970*w*, 830*w*, 770*w*. UV (CH_3OH): 272 (4.17). ^{1}H-NMR ((D_6)DMSO): 11.11 (br. *s*, H–N(11)); 7.75 (br. *s*, H–N(10)); 6.44 (*d*, *J*(NH,CH) = 2.3, H–C(8)); 4.05 (*dd*, *J*(4,5*A*) = 5.3, *J*(4,5*B*) = 7.1, H–C(4)); 2.83 (*dd*, *J*(4,5*A*) = 5.3, *J*(5*A*,5*B*) = 14.3, H_A–C(5)); 2.60 (*dd*, *J*(4,5*B*) = 7.1, *J*(5*A*,5*B*) = 14.3, H_B–C(5)); 2.05 (*q*, *J* = 7.5, CH_3CH_2–C(2)); 1.92 (*s*, CH_3–C(7)); 1.81 (*s*, CH_3–C(3)); 0.87 (*t*, *J* = 7.5, CH_3CH_2–C(2)). ^{13}C-NMR ((D_6)DMSO): 172.82 (*s*, C(1)); 161.68 (*s*, COOH); 151.06 (*s*, C(3)); 133.35 (*s*); 130.37 (*s*); 120.42 (*s*); 116.96 (*s*); 115.98 (*d*, C(8)); 59.10 (*d*, C(4)); 29.01 (*t*, C(5)); 16.00 (*t*, CH_3CH_2–C(2)); 12.95 (*q*); 11.68 (*q*); 10.94 (*q*). MS: 262 (7, $M^{+\cdot}$), 218 (22, $M^{+\cdot} - CO_2$), 138 (100, 3-methyl-5-carboxyazafulvenium ion), 120 (92), 94 (100, 138 – CO_2), 81 (20), 65 (32). Anal. calc. for $C_{14}H_{18}N_2O_3$ (262.3): C 64.10, H 6.92, N 10.68; found: C 63.98, H 6.77, N 10.57.

(4S,9'S)-2-Ethyl-1,4,5,10-tetrahydro-3,7-dimethyl-N-[1-(1-naphthyl)ethyl]-1-oxodipyrrin-9-carboxamide (**6b**). To a soln. of enantiomerically pure **6a** (109 mg) and 72 mg of (–)-(*S*)-1-(1-naphtyl)ethylamine (*Fluka AG*,

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[5] For nomenclature, *cf.* [28].

CH-9470 Buchs) in DMF (4 ml), dry *N*-hydroxybenzotriazole (56 mg) and *N*-[3-(dimethylamino)propyl]-*N'*-ethylcarbodiimide hydrochloride (96 mg) were added. The mixture was stirred at r.t. for 14 h and, then, diluted with CH_2Cl_2 (30 ml). The soln. was washed successively with 0.1N aq. $NaHCO_3$, 2N aq. citric acid, 0.1N aq. $NaHCO_3$, and finally with H_2O, and dried ($MgSO_4$). After evaporation of the solvent, the product was purified by prep. TLC using AcOEt/CH_2Cl_2 2:1 to yield 111 mg (65%) of **6b**. M.p. 128–130°. $[\alpha]_D^{20} = -80°$ ($c = 0.1$, $CHCl_3$). IR: 3420*m* (br.), 3280*m* (br.), 3060*w*, 2960*m*, 2920*m*, 2860*w*, 1680*s*, 1630*s*, 1580*m*, 1530*s*, 1510*m*, 1460*w*, 1410*w*, 1400*w*, 1380*w*, 1370*w*, 1340*w*, 1310*w*, 1280*w*, 1260*w*, 1240*m*, 1190*w*, 1170*w*, 1120*w*, 1090*w*, 1080*w*, 1060*w*, 980*w*, 950*w*, 910*w*, 860*w*, 830*w*, 800*m*, 780*m*. UV ($CHCl_3$): 284 (4.36). ^{1}H-NMR ($CDCl_3$): 10.3 (br. *s*, H–N(11)); 8.05, 7.84, 7.75, 7.51–7.37 (4*m*, naphthyl-H); 6.62 (br. *s*, H–N(10)); 6.23 (*d*, *J*(NH,CH) = 2.3, H–C(8)); 6.14 (*d*, *J* = 7.6, CONH); 5.94 (*dq*, *J*(NH,CH) = 7.6, *J*(CH,CH) = 6.9, C*H*–NH); 3.83 (*dd*, *J*(4,5*A*) = 4.0, *J*(4,5*B*) = 8.6, H–C(4)); 2.88 (*dd*, *J*(4,5*A*) = 4.0, *J*(5*A*,5*B*) = 14.5, H_A–C(5)); 2.35 (*dd*, *J*(4,5*B* = 8.6, *J*(5*A*,5*B*) = 14.5, H_B–C(5)); 2.14 (*q*, *J* = 7.5, CH_3CH_2–C(2)); 1.90 (*s*, CH_3–C(7)); 1.85 (*s*, CH_3–C(3)); 1.63 (*d*, *J* = 6.9, CH_3–C(9^3)); 0.95 (*t*, *J* = 7.5, CH_3CH_2–C(2)). ^{13}C-NMR ($CDCl_3$): 174.25 (*s*, C(1)); 160.53 (*s*, CONH); 151.06 (*s*, C(3)); 138.93 (*s*, naphthyl-C); 134.25 (*s*); 133.83, 130.86 (2*s*, naphthyl-C); 128.81 (*s*); 128.60, 127.92, 126.34, 125.66, 125.21 (5 *d*, naphthyl-CH); 123.69 (*s*); 123.26, 122.25 (2 *d*, naphthyl-CH); 117.33 (*s*); 111.61 (*d*, C(8)); 59.87 (*d*, C(4)); 44.87 (*d*, C*H*–NH); 28.71 (*t*, C(5)); 21.33 (*q*, CH_3–C(9^3)); 16.47 (*t*, CH_3CH_2–C(2)); 12.95 (*q*); 11.79 (*q*); 10.98 (*q*). MS: 415 (27, M^+), 292 (97), 291 (100, 5-[*N*-[1-(1-naphthyl)ethyl]carbamoyl]-3-methylazafulvenium ion), 259 (14), 170 (76) 156 (100), 155 (100, 1-(1-naphthyl)ethyl cation), 137 (100, 5-carbamoyl-3-methylazafulvenium ion), 120 (41), 93 (44, 3-methylazafulvenium ion-H).

*(4*R,*9*^{3}*S)-Enantiomer* **7b**. According to the procedure described for **6b**, 248 mg (54%) of **7b** were obtained from 290 mg of partially resolved **7a** (see above). Crystals suitable for X-ray analysis were obtained by recrystallization from i-PrOH. **7b** · i-PrOH: M.p. 202–208° $[\alpha]_D^{20} = +143°$ ($c = 0.093$, $CHCl_3$). UV ($CHCl_3$): 284 (4.39). ^{1}H-NMR ($CDCl_3$): 9.84 (br. *s*, H–N(11)); 8.03, 7.82, 7.77, 7.48–7.39 (4 *m*, naphthyl-H); 6.28 (*d*, *J*(NH,CH) = 2.2, H–C(8)); 6.20 (br. *s*, H–N(10)); 6.08 (*d*, *J* = 7.6, CONH); 5.86 (*dq*, *J*(NH,CH) = 7.6, *J*(CH,CH) = 6.9, C*H*–NH); 4.02 (*sept. d*, *J*(CH,OH) = 3.2, *J*(CH,CH) = 6.0, $(CH_3)_2CH$OH); 3.94 (*dd*, *J*(4,5*A*) = 3.5, *J*(4,5*B*) = 8.5, H–C(4)); 2.85 (*dd*, *J*(4,5*A*) = 3.5, *J*(5*A*,5*B*) = 14.6, H_A–C(5)); 2.44 (*dd*, *J*(4,5*B*) = 8.5, *J*(5*A*,5*B*) = 14.6, H_B–C(5)); 2.19 (*q*, *J* = 7.5, CH_3CH_2–C(2)); 1.97 (*s*, CH_3–C(7)); 1.91 (*s*, CH_3–C(3)); 1.60 (*d*, *J* = 6.9, CH_3–C(9^3)); 1.30 (*d*, *J* = 3.2, $(CH_3)_2CHO$*H*); 1.21 (*d*, *J* = 6.0, $(CH_3)_2$CHOH); 0.98 (*t*, *J* = 7.5, CH_3CH_2–C(2)). ^{13}C-NMR ($CDCl_3$): 174.33 (*s*, C(1)); 160.43 (*s*, CONH); 151.03 (*s*, C(3)); 138.75 (*s*, naphthyl-C); 134.42 (*s*); 133.61, 130.94 (2 *s*, naphthyl-C); 128.51, 127.92, 126.42, 125.72, 125.20 (5 *d*, naphthyl-CH); 123.80 (*s*); 123.27, 122.25 (2 *d*, naphthyl-CH); 117.25 (*s*); 111.81 (*d*, C(8)); 64.35 (*d*, $(CH_3)_2$CHOH); 59.82 (*d*, C(4)); 44.70 (*d*, C*H*–NH); 28.66 (*t*, C(5)); 25.34 (*q*, $(CH_3)_2$CHOH); 21.03 (*q*, CH_3–C(9^3)); 16.55 (*t*, CH_3CH_2–C(2)); 12.96 (*q*); 11.87 (*q*); 11.05 (*q*). MS: 415 (56, M^+), 292 (100), 291 (100, 5-{*N*-[1-(1-naphthyl)ethyl]carbamoyl}-3-methylazafulvenium ion), 261 (26), 257 (29), 155 (100, 1-(1-naphthyl)ethyl cation), 137 (43, 5-carbamoyl-3-methylazafulvenium ion), 124 (13), 93 (24, 3-methylazafulvenium ion-H).

*(4*S,*9*^{3}R*)-2-Ethyl-1,4,5,10-tetrahydro-3,7-dimethyl*-N-*[1-(1-naphthyl)ethyl]-1-oxodipyrrin-9-carboxamide* was obtained (274 mg, 86%) following the procedure described for **6b**, from 200 mg of **6a** and 132 mg of (+)-(*R*)-1-(1-naphthyl)ethylamine (*Sigma Chemie GmbH*, D-8028 Taufkirchen). M.p. 203–209° (from i-PrOH). $[\alpha]_D^{20} = -158°$ ($c = 0.096$, $CHCl_3$). UV ($CHCl_3$): 283 (4.39). ^{1}H-NMR ($CDCl_3$): 10.12 (br. *s*, H–N(11)); 7.99, 7.81, 7.75, 7.48–7.35 (4 *m*, naphthyl-H); 6.37 (br. *s*, H–N(10)); 6.29 (*d*, *J*(NH,CH) = 2.2, H–C(8)); 6.15 (*d*, *J* = 6.9, CONH); 5.80 (*dq*, *J*(NH,CH) = 6.9, *J*(CH,CH) = 6.9, C*H*–NH); 4.02 (*sept.*, *J* = 6.1, $(CH_3)_2CH$OH); 3.93 (*dd*, *J*(4,5*A*) = 3.5, *J*(4,5*B*) = 8.5, H–C(4)); 2.78 (*dd*, *J*(4,5*A*) = 3.5, *J*(5*A*,5*B*) = 14.6, H_A–C(5)); 2.44 (*dd*, *J*(4,5*B*) = 8.5, *J*(5*A*,5*B*) = 14.6, H_B–C(5)); 2.17 (*q*, *J* = 7.5, CH_3CH_2–C(2)); 1.96 (*s*, CH_3–C(7)); 1.88 (*s*, CH_3–C(3)); 1.55 (*d*, *J* = 6.9, CH_3–C(9^3)); 1.20 (*d*, *J* = 6.1, $(CH_3)_2$CHOH); 0.96 (*t*, *J* = 7.5, CH_3CH_2–C(2)). ^{13}C-NMR ($CDCl_3$): 174.35 (*s*, C(1)); 160.47 (*s*, CONH); 151.08 (*s*, C(3)); 138.80 (*s*, naphthyl-C); 134.34 (*s*); 133.78, 130.69 (2 *s*, naphthyl-C); 128.49, 127.85, 126.37, 125.67, 125.18 (5 *d*, naphthyl-CH); 123.77 (*s*); 123.24, 122.22 (2 *d*, naphthyl-CH); 117.19 (*s*); 111.94 (*d*, C(8)); 64.27 (*d*, $(CH_3)_2$CHOH); 59.83 (*d*, C(4)); 44.69 (*d*, C*H*–NH); 28.58 (*t*, C(5)); 25.31 (*q*, $(CH_3)_2$CHOH); 21.02 (*q*, CH_3–C(9^3)); 16.52 (*t*, CH_3CH_2–C(2)); 12.96 (*q*); 11.84 (*q*); 11.02 (*q*).

*(–)-(*S*)-2-Ethyl-1,4,5,10-tetrahydro-3,7-dimethyl-1-oxodipyrrin-9-carbaldehyde* (**6c**). A soln. of **6a** (50 mg) in CF_3COOH (25 ml) was stirred under Ar for 12 min at r.t. Then, the mixture was cooled in an ice-bath for 5 min, and 5 ml of trimethyl orthoformate were added at once. The soln. was stirred for a further 12 min at r.t. and then diluted with CH_2Cl_2 (25 ml). The mixture was washed repeatedly with H_2O until the aq. layer was neutral, dried ($MgSO_4$), and the solvent evaporated. The product (45 mg, 96%) was used without further purification. Crystallization of the residue from CH_2Cl_2/hexane yielded a pure sample of m.p. 212–216°. $[\alpha]_D^{20} = -97°$ ($c = 0.04$, CH_3OH). UV (CH_3OH): 308 (4.27), 255 (3.79). IR: 3260*m*, 3100*w*, 3060*w*, 3040*w*, 2960*m*, 2920*m*, 2860*w*, 2820*w*,

2790*w*, 1660*s*, 1630*s*, 1580*w*, 1510*w*, 1470*m*, 1420*m*, 1370*w*, 1350*m*, 1315*w*, 1290*m*, 1220*w*, 1200*w*, 1170*w*, 1150*m*, 1120*w*, 1060*w*, 980*w*, 890*w*, 860*w*, 820*w*, 800*w*, 770*w*, 750*w*, 720*w*. ^{1}H-NMR ($CDCl_3$): 10.54 (br. *s*, H–N(11)); 9.29 (*s*, CHO); 6.90 (br. *s*, H–N(10)); 6.73 (*d*, *J*(NH,CH) = 2.3, H–C(8)); 4.11 (*dd*, *J*(4,5*A*) = 3.9, *J*(4,5*B*) = 9.1, H–C(4)); 3.16 (*dd*, *J*(4,5*A*) = 3.9, *J*(5*A*,5*B*) = 14.6, H_A–C(5)); 2.58 (*dd*, *J*(4,5*B*) = 9.1, *J*(5*A*,5*B*) = 14.6, H_B–C(5)); 2.23 (*q*, *J* = 7.5, CH_3CH_2–C(2)); 2.08 (*s*, CH_3–C(7)); 1.99 (*s*, CH_3–C(3)); 1.02 (*t*, *J* = 7.5, CH_3CH_2–C(2)). ^{13}C-NMR ((D$_6$)DMSO): 177.47 (*d*, CHO); 172.68 (*s*, C(1)); 150.74 (*s*, C(3)); 134.94 (*s*); 133.41 (*s*); 130.76 (*s*); 121.86 (*d*, C(8)); 118.63 (*s*); 58.70 (*d*, C(4)); 29.23 (*t*, C(5)); 15.94 (*t*, CH_3CH_2–C(2)); 12.85 (*q*); 11.61 (*q*); 10.79 (*q*). MS: 246 (11, M^+), 179 (8), 167 (12), 152 (43), 135 (20), 122 (100, 5-formyl-3-methyl-azafulvenium ion), 94 (24, 122–CO).

*(4S,16S)-2,18-Diethyl-3,7,13,17-tetramethyl-4,5,15,16-tetrahydro-22*H*-bilin-1,19(21*H*,24*H*)-dione Hydrochloride* (**8**). A soln. of **6a** (20.2 mg) and **6c** (19 mg) in CF_3COOH (1.8 ml) was stirred for 10 min under N_2 at r.t. The mixture was then cooled in an ice-bath, and after 5 min, 1 ml of CH_3OH was added. Stirring was continued for 1 h at r.t. before the solvent was evaporated. The residue was purified by column chromatography on silica gel with CH_2Cl_2/AcOH/CH_3OH 90:2:8. The orange fraction containing the desired product was shaken repeatedly with 2N aq. HCl, the org. layer separated, and the solvent evaporated at r.t. The product (18.4 mg, 50%) contains less than 3% of its (4*R*,16*S*)-diastereoisomer (by ^{1}H-NMR). M.p. 135–140° (dec.). $[\alpha]_D^{20} = -5000°$ ($c = 7.04 \cdot 10^{-4}$, $CHCl_3$). UV ($CHCl_3$): 500 (4.81), 353 (3.70). UV (CH_3OH): 503 (3.82), 445 (4.20). IR ($CHCl_3$): 3670*w*, 3420*w*, 2990*m*, 2960*m*, 2920*m*, 2860*w*, 1680*s* (C=O), 1620*s* (C=C), 1510*m*, 1450*w*, 1400*w*, 1320*m*, 1300*m*, 1280*s*, 1250*m*, 1180*m*, 1150*m*, 960*s*. ^{1}H-NMR ($CDCl_3$): 13.83 (br. *s*, H–N(22), H–N(23)); 7.00 (*s*, H–C(10)); 6.88 (*s*, H–C(8), H–C(12)); 6.81 (br. *s*, H–N(21), H–N(24)); 4.57 (*dd*, *J*(*AB*) = 4.4, *J*(*AX*) = 7.8, H_A–C(4), H_A–C(16)); 3.59 (*dd*, *J*(*AB*) = 4.4, *J*(*BX*) = 13.7, H_B–C(5), H_B–C(15)); 2.81 (*dd*, *J*(*AX*) = 7.8, *J*(*BX*) = 13.7, H_X–C(5), H_X–C(15)); 2.19 (*q*, *J* = 7.5, CH_3CH_2–C(2), CH_3CH_2–C(18)); 2.07 (*s*, CH_3–C(3), CH_3–C(17)); 2.06 (*d*, ^4J = 0.4, CH_3–C(7), CH_3–C(13)); 0.97 (*t*, *J* = 7.5, 2 CH_3CH_2). ^{13}C-NMR ($CDCl_3$): 173.92 (*s*, C(1), C(19)); 154.61 (*s*); 150.73 (*s*); 134.96 (*s*); 134.26 (*d*, C(10)); 128.72 (*s*); 127.69 (*s*); 127.55 (*d*, C(8), C(12)); 59.64 (*d*, C(4), C(16)); 30.06 (*t*, C(5), C(15)); 16.83 (*t*, CH_3CH_2–C(2), CH_3CH_2–C(18)); 12.98 (*q*); 12.27 (*q*), 11.06 (*q*). EI-MS (free base): 446 (4, M^+), 322 (55, 5-{[5-[(4-ethyl-2,5-dihydro-3-methyl-5-oxo-1*H*-pyrrol-2-yl)methyl]-4-methyl-2*H*-pyrrol-2-ylidene]-methyl}-3-methylazafulvenium ion), 199 (100, 5-[(4,5-dimethyl-2*H*-pyrrol-2-ylidene)methyl]-3-methylazafulvenium ion), 149 (8), 94 (7, 3-methylazafulvenium ion). CD ($1.47 \cdot 10^{-5}$ M): 499 (−174800). CD (CH_3OH+HCl, $2.22 \cdot 10^{-5}$ M): 516 (−56300). CD ($CHCl_3$, $1.47 \cdot 10^{-5}$ M; at different temp., see *Fig. 4*): 298 K (−174800), 268 K (−206800), 238 K (−222600).

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