63. Syntheses of Bile Pigments

Part 16[1])

Synthesis of a Vinyl-Substituted 2,3-Dihydrobilinedione: Possible Role of this New Class of Bile Pigments in Phycobilin Biosynthesis

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The total synthesis of racemic *cis*-2,3,18^1,18^2-tetrahydroprotobiliverdin IXα dimethyl ester (**19b**), which is identical with the dimethyl ester of *rac*-**4**, is described (*Scheme 2*). Under virtually neutral conditions, in solution, this bile pigment isomerized within a few min to racemic *Z*-phycocyanobilin dimethyl ester (*rac*-**5b**). Likewise, acid-catalyzed allyl rearrangement of 3-vinyl-substituted *cis*- and *trans*-2,3-dihydrodipyrrin-1(10*H*)-ones **11c** and **13c**, respectively, yielded the corresponding ethylidene derivatives. In this case, however, the *E*-isomer was formed stereoselectively from both substrates. The above results prove that, if protobiliverdin IXα (**2**) is transformed enzymatically to its 2,3,18^1,18^2-tetrahydro derivative, the latter would isomerize spontaneously to phycocyanobilin. The biosynthesis of bacteriochlorophyll a and b from a common precursor bearing a vinyl group at C(8) may be straightforwardly explained in the same way.

Phycobiliproteins are high-molecular-weight globular proteins found in cyanobacteria as well as in red and cryptomonad algae (*Rhodophytae* and *Cryptophytae*, resp.). Their function appears to be that of accessory light-harvesting pigments which, ultimately, act as photosensitizers of chlorophyll a in the primary process of photosynthesis [2]. Until now, the best known of these chromoproteins is C-phycocyanin whose structure has been determined by X-ray-diffraction methods [3]. Its chromophore molecules which are released from the covalently bounded apoprotein by an elimination reaction yielding phycocyanobilin (**6**) belong to the class of bile pigments, as do, by definition, the prosthetic groups of all biliproteins.

As demonstrated some years ago by *Troxler et al.* [4–7], the biosynthesis of the phycocyanin chromophore in the unicellular rhodophyte *Cyanidium caldarium* parallels the catabolic pathway of hemoglobin in mammalians in that CO is evolved in stoichiometric amounts and at comparable rates as the bile pigment prosthetic group is formed. More recently, incorporation of haem (**1**) [8] and protobiliverdin IXα (**2**) [9–11] into phycocyanin in *C. caldarium* has been demonstrated using ^{14}C-labeled substrates. The findings that upon incubation of *C. caldarium* with 5-aminolevulinic acid, protobiliverdin IXα [12], 3^1-hydroxymesobiliverdin IXα [13], and phycocyanobilin (**6**) [14] [15] can be

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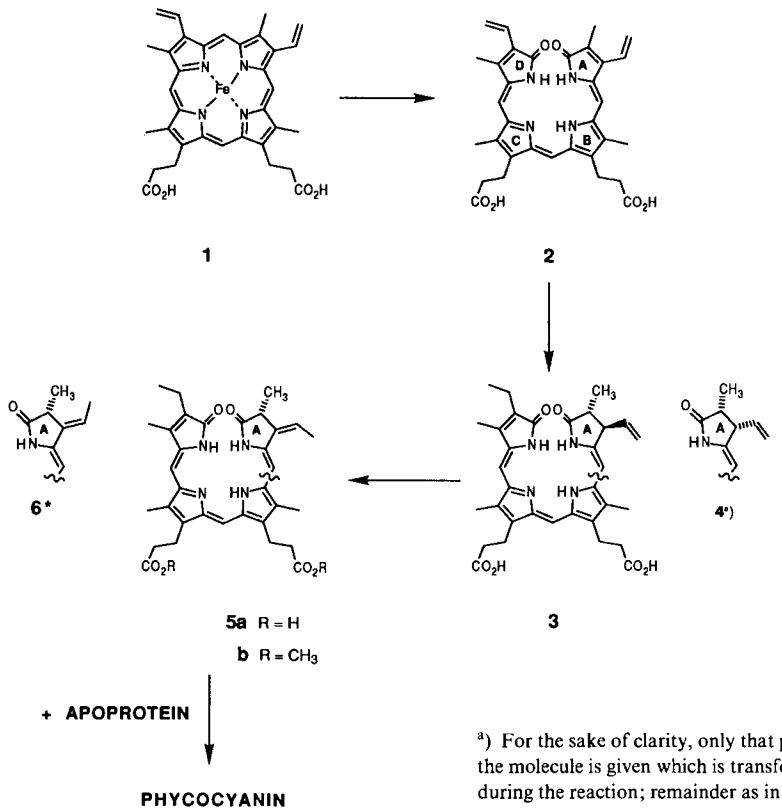
Scheme 1. *Suggested Biogenetic Pathway for the Prosthetic Group of Phycocyanin*



[a]) For the sake of clarity, only that part of the molecule is given which is transformed during the reaction; remainder as in **3**.

isolated from the culture medium suggest that binding of the apoprotein to the bile pigment prosthetic group takes place at the end of the phycocyanin biosynthesis.

Thus, provided that phycocyanobilin (**6**) is a precursor of the prosthetic group of phycocyanin [16], two reduction steps (at the 18-vinyl group and at ring A) must be present between phycocyanin and protobiliverdin IXα (**2**). As the transformation of **2** into **6** appears to be dependent on pyridine nucleotides as electron carriers [10], either an *anti*-[17] or a *syn*-stereoselective [18][2]) formal 1,2-addition of hydrogen to the C(2)=C(3) bond is much more likely than a 1,4-hydrogenation of the conjugated diene formed by the endocyclic double bond and the vinyl group at ring A of **2** (*cf. Scheme 1*). Hence, it must be followed that the vinyl-substituted 2,3-dihydro-22*H*-biline-1,19(21*H*,24*H*)-dione derivative **3**[3]) or its *cis*-isomer **4**[3]) are highly probable intermediates in the enzymatic transformation of **2** into phycocyanobilin [12]. Even though bile pigments of the type represented by **3** and **4** have not been isolated until now from natural sources,

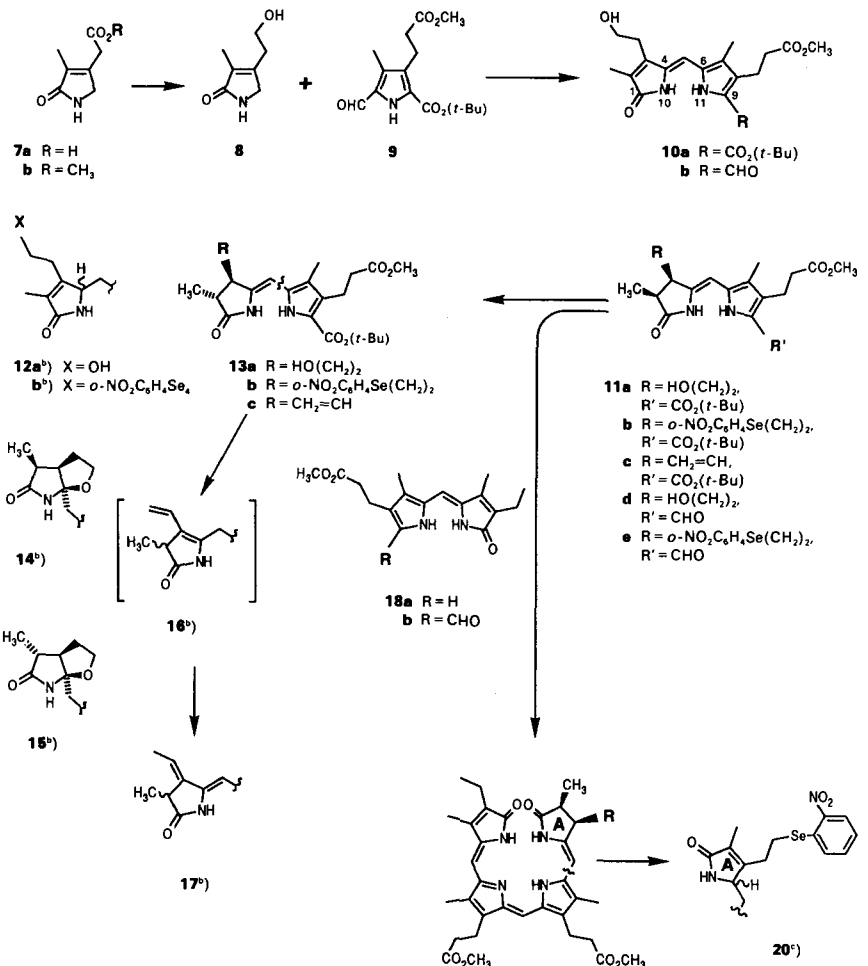
[2]) We thank Prof. *S.A. Benner* (Laboratory of Organic Chemistry, Swiss Federal Institute of Technology (ETH), Zürich) for giving us indication to this reference.

[3]) In both formulae **3** and **4**, the known absolute configuration of phycocyanobilin at C(2) [19] has been taken into consideration.

the knowledge of the spectroscopic data and chemical properties of synthetic compounds of this kind could be interesting for the study of phycocyanin biosynthesis.

In order to prepare compound **3** (as the racemic dimethyl ester), the conventional methodology used for convergent synthesis of bile pigments was envisaged [20], whose crucial step is the acid-catalysed condensation of the known methyl 5′-formyl-isoneoxanthobilirubinate (**18b**) [21] with the *trans*-3-vinyl-2,3-dihydrodipyrrin-1(10*H*)-one **13c**[4]). As for the synthesis of the latter, however, there is no precedent in the literature, the

Scheme 2[a])



[a]) All formulae represent racemates.

[b]) For the sake of clarity, only that part of the molecule is given which is transformed during the reaction; remainder as in **13**.

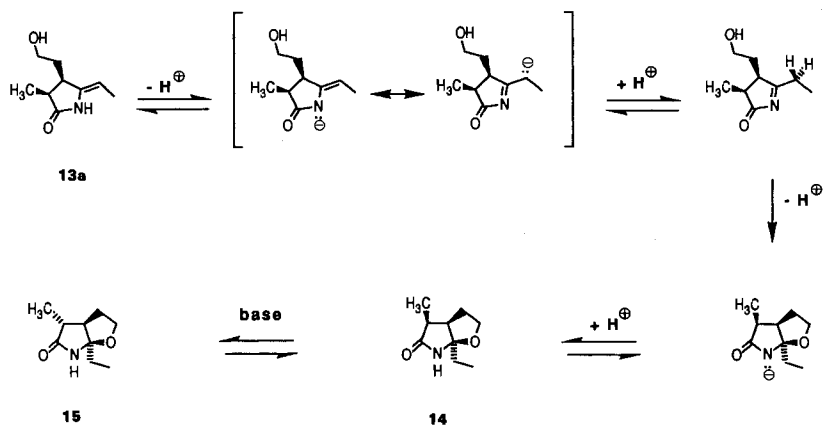
[c]) Remainder as in **19**.

[4]) For nomenclature, see [22].

approach *via* selenide **13b** was chosen on account of the advantages of this method for the synthesis of other vinyl-substituted bile pigments [23–25]. The synthesis of **13b** started with **7a** which was obtained in poor yield by reductive cyclisation [26] of the cyanohydrine of diethyl 2-methyl-3-oxoglutarate. After esterification and reduction of the ester group of **7b**, the obtained (hydroxyethyl)pyrrolone **8** was condensed with the known formylpyrrolecarboxylate **9** [27] to yield the dipyrrin-1(10*H*)-one derivative **10a**. Catalytical hydrogenation of the latter on $Pd/CaCO_3$ (*cf.* [28]) afforded a mixture of the desired *cis*-2,3-dihydro derivative **11a** and its 4,5-dihydrodipyrrin-1(10*H*)-one isomer **12a** in 52 and 26% yield, respectively. As it is known that *cis*-2,3-dihydrodipyrrin-1(10*H*)-ones can be epimerized to the corresponding *trans*-isomers on treatment with a strong base [28] [29], **11a** was reacted with NaOMe in MeOH with the aim to obtain the corresponding *trans*-2,3-dihydrodipyrrin-1(10*H*)-one **13a**. Instead of **13a**, however, a mixture of the two epimeric bicyclic lactams **14** and **15** was obtained in almost quantitative yield under basic conditions. In the presence of acid, **11a** isomerized also quantitatively, but only **14** was formed. A similar reaction has been reported earlier by *Falk* and *Zrunek* [30].

As extensively proved by *Grubmayr et al.* [31] [32], the formation of **14** and **15** is due to a general reactivity of enelactams, which is particularly favoured when nucleophilic addition to the double bond occurs intramoleculary (see *Scheme 2*).

Scheme 3. *Suggested Mechanism for the Formation of* **14** *and* **15** *from* **13a** *Under Basic Conditions*[a])



[a]) All formulae represent racemates.

The structures of the bicyclic lactams **14** and **15** are proved by their spectroscopic data (s. *Exper. Part*). Particularly, the ^{1}H-NMR signals assigned to the CH_2 protons of the condensed tetrahydrofuran ring differ clearly from that of the hydroxyethyl group in **11a**. Moreover, the two-spin system at 3.0 ppm for a CH_2 bridge and the *d* for the Me group at C(2) agree unequivocally with structures **14** and **15**. The relative configurations of both epimers are established essentially by the mutual NOE's between H–C(3) and Me-C(2) which is observed in the case of the *trans*-isomer **15** but not of the *cis*-isomer **14**.

In order to overcome the difficulties raised by the OH group of **11a**, the transformation of the latter into the *trans*-isomer was postponed to the synthesis of selenide **11b**, which is required for the introduction of a vinyl group at C(3). Thus, reaction of **11a** with *o*-nitrophenyl selenocyanate in THF containing tributylphosphine (*cf.* [33]) afforded the corresponding *cis*-selenide **11b** which could be isomerized in acidic $CHCl_3$ to a mixture

12b/**13b** in 73% overall yield. However, the relative quantities of both products fluctuated strongly, and, as yet, no reproducible reaction conditions could be found which favour the formation of the desired *trans*-2,3-dihydrodipyrrin-1(10*H*)-one **13b**. Nevertheless, after treatment of the latter with H_2O_2 in THF, the *trans*-vinyl derivative **13c** was obtained. In acidic $CHCl_3$, however, **13c** was transformed quantitatively into the (*E*)-ethylidine isomer **17**. The *same* compound **17** was obtained when the *cis*-2,3-dihydrodipyrrin-1(10*H*)-one **11b** was transformed into the corresponding *cis*-vinyl derivative **11c**, and the latter was dissolved in $CHCl_3$ containing a trace of CF_3COOH. When CF_3CO_2D was used, deuterium labeling was observed at the ethylidene Me group (33%) as well as at the CH bridge (*ca.* 30%) and the C(2) position of the lactam ring (*ca.* 30%) of **17**. These results agree with the formation of a 2,5-dihydrodipyrrin-1(10*H*)-one derivative **16** whose characteristic signals were indeed observed transitorily in the ^{1}H-NMR spectrum of the reaction mixture.

Particularly, the signals assigned to the *ABX* system characteristic for the vinyl group at 6.53 (H_X–C(3^1)), 5.096 (H_A–C(3^2), $J(X,A) = 10.8$, $J(A,B) = 0.9$), and 5.089 ppm (H_B–C(3^2), $J(X,B) = 17.7$, $J(A,B) = 0.9$) are shifted with respect to those of **13c**, as it would be expected for a conjugated double bond in **16**.

In the face of the extreme lability of the vinyl compounds **11c** and **13c**, the cleavage of the *t*-Bu ester group under acidic conditions or by treatment with Me_3SiI [34] tourned out to be hopeless at this stage of the synthesis. Therefore, the reaction sequence was recommenced with dipyrrinone **10a** which was transformed into the corresponding aldehyde **10b** and subsequently hydrogenated to the *cis*-2,3-dihydrodipyrrin-1(10*H*)-one **11d**. Attempts to condense the latter with methyl isoneoxanthobilirubinate (**18a**) failed to yield the desired bile pigment because of the ready intramolecular addition of the OH group to the exocyclic double bond (*cf.* **13a** → **14**). Thus, **11d** was transformed first into selenide **11e** which subsequently was condensed with **18a** in the presence of phosphoryl bromide and 2,6-di(*tert*-butyl)-4-methylpyridine (*cf.* [28]) to afford the bile-pigment derivative **19a**. Attempts to transform the latter into the *trans*-isomer, under acidic conditions, quantitatively led to the formation of the biliviolinoid pigment **20**, in analogy with the known isomerization of bilirhodins into urobilins [35]. After oxidation of **19a** with H_2O_2 in THF, only a blue pigment could be isolated which was identified with an authentic sample of racemic (*Z*)-phycocyanobilin dimethyl ester (*rac*-**5b**) [25]. However, when the crude reaction mixture was analyzed by ^{1}H-NMR spectroscopy, the expected tetrahydrobiliverdin **19b**, which is identical with the dimethylester of *rac*-**4**, could be detected in addition to *rac*-**5b**, and its spectrum could be obtained by substraction of the signals of the latter (*cf. Exper. Part*). Noteworthy, on isomerization, **19b** yielded racemic (*Z*)-phycocyanobilin dimethyl ester (*rac*-**5b**), whereas the migration of the vinyl double bond in both *cis*- and *trans*-2,3-dihydrodipyrrin-1(10*H*)-one **11c** and **13c**, respectively, led stereoselectively to the formation of the corresponding (3*E*)-ethylidene derivatives. On the other hand, the migration of the vinyl double bond in the dipyrrinone series required acidic conditions, whereas the isomerization of the bile pigment **19b** took place in virtually neutral solutions.

Owing to the inherent lability of the vinyl group at the reduced lactam ring of all compounds so far investigated[5]), incubation experiments using isotopically labeled **3** as a substrate would not be conclusive. Actually, since **11c**, **13c**, and **19b** isomerized into the

[5]) Also vinylchlorins isomerize readily to the corresponding ethylidene derivatives [36].

corresponding 3-ethylidene derivatives at room temperature, incorporation of **3** into phycocyanin *via* phycocyanobilin (**6**) would not prove that the latter compound has been formed enzymatically (see *Scheme 1*). Therefore, the synthesis of the bile pigment **3** was abandoned. Nevertheless, the above results prove that, if **3** would be formed enzymatically from protobiliverdin IXα (**2**), it would be transformed spontaneously into **6**. Moreover, it is interesting to observe that (*Z*)-phycocyanobilin (**5**), which is obtained in the racemic form as the product of isomerization of **19b**, is also produced *primarily* when **2** is incubated with crude cell-free extracts of *C. caldarium* [10]. On the other hand, on the basis of the above results, the biosynthesis of the bacteriochlorophylls a and b may be straightforwardly explained by hydrogenation and rearrangement, respectively, of a common precursor (analogous to **3**) bearing a vinyl group at C(8).

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Experimental Part

General. TLC: plates (20 × 20 cm) precoated with silica gel *60* $PF_{254+366}$ (*E. Merck*, D-6100 Darmstadt); products eluted from the stationary phase with CH_2Cl_2/MeOH 2:1, unless otherwise specified. M.p.: *Kofler* hot stage melting point apparatus (*Thermovar, C. Reichert AG*, Vienna), not corrected. IR: *Perkin-Elmer-IR-599* spectrometer; KBr pellets, unless otherwise specified; in cm^{-1}. UV/VIS: *Perkin-Elmer-320* spectrophotometer; λ_{max} ($\log \varepsilon$) in nm. ^1H- and ^{13}C-NMR: at 360.13 and 100.61 MHz, resp.; *Bruker-AM-360* instrument equipped with a data system *Aspekt 3000;* chemical shifts in ppm rel. to int. TMS, coupling constants *J* in Hz; NOE's in % enhancement, irradiation frequency is preceded by the sign ↯; unless otherwise specified, $CDCl_3$ as solvent, filtered through neutral alumina (*Woelm N-Super I*, Typ *4200* for column chromatography). NMR spectra were recorded by Miss *E. Trieschmann*. MS: *Vacuum Generators Micromass 7070 E* instrument equipped with a data system *DS 11-250;* EI ionization at 70 eV; FAB ionisation with Ar at 8 kV, at an acceleration voltage of 6 kV. Elemental analyses were performed with a *Perkin-Elmer-240* CHN analyser by Mr. *F. Nydegger*.

*2,5-Dihydro-4-methyl-5-oxo-1*H*-pyrrole-3-acetic Acid* (**7a**) *and Methyl 2,5-Dihydro-4-methyl-5-oxo-1*H*-pyrrole-3-acetate* (**7b**). H_2SO_4 (30 g; $d = 1.365$) was added dropwise to an ice-cooled aq. soln. of NaCN (18 g in 45 ml), and after 15 min stirring at 0–5°, neat dimethyl 2-methyl-3-oxoglutarate (39 g) [37] was added within 10 min. Then, the mixture was allowed to stand for 1 h at r.t. before it was extracted with Et_2O. The org. layer was washed with 5% H_2SO_4 soln. and evaporated. The obtained crude cyanohydrine was dissolved in Ac_2O (590 ml) and hydrogenated for 2 h at 100°/70 bar over *Raney*-Ni[6] (4 g). Thereafter, the mixture was heated in the autoclave for 6 h at 180°. The catalyst was filtered off, the solvent evaporated, and the residue refluxed in 2N aq. H_2SO_4 soln. (120 ml) for 2 h. The mixture was filtered, Na_2CO_3 added until pH 3 was attained, and the soln. boiled with charcoal, filtered, and evaporated. The residue was extracted with hot i-PrOH (400 ml), the solvent evaporated, and the oily product crystallized from CH_2Cl_2 by chilling the soln. to −20°: 2.86 (10%) of **7a**. M.p. 171–172° (from i-PrOH). The acid **7a** (2.8 g) was esterified with MeOH (50 ml) containing 4% H_2SO_4 soln. After 1 h at r.t., CH_2Cl_2/H_2O 1:1 (200 ml) was added, the aq. phase extracted with CH_2Cl_2 (4 × 20 ml), the combined org. phase filtered through CH_2Cl_2-soaked filter paper and evaporated, and the residue crystallized from AcOEt: **7b** (2.78 g, 91%). M.p. 110°. IR: 3200*s*, 3070*w*, 2950*w*, 2910*w*, 2842*w*, 2820*w*, 1747*s*, 1685*s*, 1665*s*, 1440*m*, 1405*w*, 1395*w*, 1365*w*, 1340*w*, 1320*m*, 1195*s*, 1178*s*, 1160*m*, 1085*w*, 1055*w*, 993*m*, 920*w*, 890*w*, 767*m*, 758*m*, 740*w*, 710*w*, 690*w*, 605*w*, 580*w*, 377*w*, 295*w*. ^1H-NMR: 8.01–7.91 (*s*, NH); 3.98 (*q*, $J(CH_3{-}C(4),2) = 1.8$, $CH_2(2)$); 3.72 (*s*, CH_3OOC); 3.42 (*s*, CH_2COO); 1.84 (*t*, $J(CH_3{-}C(4),2) = 1.8$, $CH_3{-}C(4)$). ^{13}C-NMR: 175.7 (*s*, C(5)); 169.7 (*s*, COO); 144.2 (*s*, C(3)); 131.7 (*s*, C(4)); 52.2 (*q*, $C(CH_3OOC)$); 49.1 (*t*, C(2)); 33.5 (*t*, CH_2COO); 8.5 (*q*, $CH_3{-}C(4)$). EI-MS: 169 (31, M^+), 110 (100), 96 (25), 82 (43). Anal. calc. for $C_8H_{11}NO_3$ (169.18): C 56.80, H 6.55, N 8.28; found: C 56.84, H 6.49, N 8.22.

*1,5-Dihydro-4-(2-hydroxymethyl)-3-methyl-2*H*-pyrrol-2-one* (**8**). A soln. of **7b** (1.85 g) in THF (70 ml) was treated with a suspension of $LiAlH_4$ (1.85 g) in dry Et_2O (40 ml). After 1 h at r.t., the ice-cold mixture was acidified with 2N H_2SO_4 and then neutralized with sat. aq. Na_2CO_3 soln., the soln. filtered, and the residue extracted with

[6]) Commercial *Raney*-Ni was washed successively with MeOH (3×) and AcOH (2×) before use.

CH_2Cl_2 in a *Soxhlet* apparatus. The obtained soln. was combined with the filtrate and evaporated. Crystallization of the residue from i-PrOH yielded 1.21 g (78%) of **8**. M.p. 115–116°. IR: 3220*s*, 3180*s*, 2940*m*, 2915*w*, 2893*w*, 2880*w*, 2400*w*, 2360*w*, 1675*s*, 1660*s*, 1450*m*, 1420*w*, 1392*w*, 1370*w*, 1355*w*, 1335*w*, 1315*w*, 1240*w*, 1180*w*, 1148*w*, 1100*w*, 1075*w*, 1050*m*, 990*w*, 972*w*, 930*w*, 870*w*, 845*w*, 775*m*, 722*m*, 670*w*, 595*w*, 558*w*, 505*w*, 445*w*, 340*w*. ^{1}H-NMR ($CDCl_3 + CD_3OD$): 3.94 (*q*, $J(CH_3{-}C(3),5) = 1.8$, $CH_2(5)$); 3.73 (*t*, $J(CH_2C(4), CH_2OH) = 6.4$, CH_2OH); 2.64 (*t*, $J(CH_2C(4), CH_2OH) = 6.4$, $CH_2{-}C(4)$); 1.80 (*t*, $J(CH_3{-}C(3),5) = 1.8$, $CH_3{-}C(3)$). ^{13}C-NMR ($CDCl_3 + CD_3OD$): 177.2 (*s*, C(2)); 152.7 (*s*, C(4)); 129.6 (*s*, C(3)); 60.7 (*t*, CH_2OH); 49.8 (*t*, C(5)); 31.7 (*t*, $CH_2{-}C(4)$); 8.5 (*q*, $CH_3{-}C(3)$). EI-MS: 141 (27, M^+), 123 (60), 110 (100), 96 (46), 82 (48). Anal. calc. for $C_7H_{11}NO_2$ (141.17): C 59.51, H 7.85, N 9.92; found: C 59.41, H 7.95, N 10.02.

*(Z)-9-(*tert*-Butoxycarbonyl)-3-(2-hydroxyethyl)-8-[2-(methoxycarbonyl)ethyl]-2,7-dimethyldipyrrin-1(10*H*)-one* (**10a**). To a soln. of **8** (1.0 g) and *tert*-butyl 5-formyl-3-[2-(methoxycarbonyl)ethyl]-4-methylpyrrole-2-carboxylate [27] (2.1 g) in MeOH (5 ml), 4N aq. KOH (30 ml) was added and the mixture stirred overnight at r.t. Thereafter, the soln. was acidified by passing a gentle stream of SO_2. The obtained yellow precipitate was collected by filtration, washed with H_2O, dried, and dissolved in MeOH (80 ml). A soln. of *N,N*-dicyclohexylcarbodiimide (0.90 g) and 4-(dimethylamino)pyridine (35 mg) and CH_2Cl_2 (20 ml) was added and the mixture stirred for 3 h at r.t. The soln. was diluted with CH_2Cl_2 and shaken successively with H_2O (1×), 5% AcOH soln. (3×), and H_2O (1×). The org. layer was dried by filtration through cotton and evaporated. Crystallization of the residue from i-PrOH yielded 1.95 g (66% from **8**) of **10a**. M.p. 176–178°. UV/VIS (MeOH): 401 (sh), 384 (4.47), 280 (sh), 259 (4.36), 253 (sh). UV/VIS (MeOH + $Zn(AcO)_2$): 4.38 (4.36), 418 (4.40), 271 (sh), 265 (4.34). IR: 3320*m*, 3180 (br.), 2970*w*, 2920*m*, 2850*w*, 1733*m*, 1685*s*, 1667*s*, 1550*w*, 1440*m*, 1390*w*, 1360*m*, 1270*m*, 1250*m*, 1155*m*, 1130*m*, 1110*w*, 1050*w*, 965*w*, 885*w*, 845*w*, 770*w*, 755*w*, 720*w*, 700*w*, 675*w*, 580*w*. ^{1}H-NMR: 9.72–9.66 (*s*, NH); 8.96–8.91 (*s*, NH); 5.83 (*s*, H–C(5)); 4.11–3.90 (*s*, OH); 4.06 (*t*, $J(3^1,3^2) = 5.4$, $CH_2(3^2)$); 3.68 (*s*, $CH_3O(8^4)$); 2.92–2.88 (*m*, $CH_2(8^1)$); 2.76 (*t*, $J(3^1,3^2) = 5.4$, $CH_2(3^1)$); 2.45–2.40 (*m*, $CH_2(8^2)$); 1.94 (*s*, $CH_3(7^1)$); 1.84 (*s*, $CH_3(2^1)$); 1.57 (*s*, $(CH_3)_3C(9^3)$). ^{13}C-NMR ($CDCl_3 + CD_3OD$): 173.5, 173.3 (*s*, C(1), $C(8^3)$); 161.5 (*s*, $C(9^1)$); 142.8 (*s*, C(3)); 134.6 (*s*, C(4)); 129.0, 128.9, 128.3 (*s*, C(2), C(6), C(8)); 122.8, 122.4 (*s*, C(7), C(9)); 97.6 (*d*, C(5)); 81.6 (*s*, $C(9^3)$); 61.7 (*t*, $C(3^2)$); 51.5 (*q*, $C(8^5)$); 35.0 (*t*, $C(8^2)$); 28.5 (*t*, $C(3^1)$); 28.4 (*q*, $(CH_3)_3C(9^3)$); 20.9 (*t*, $C(8^1)$); 9.0 (*q*, $C(7^1)$); 8.5 (*q*, $C(2^1)$). EI-MS: 418 (78, M^+), 362 (100), 345 (12), 331 (38), 318 (56), 302 (100), 288 (34).

*(Z)-9-Formyl-3-(2-hydroxyethyl)-8-[2-(methoxycarbonyl)ethyl]-2,7-dimethyldipyrrin-1(10*H*)-one* (**10b**). A soln. of **10a** (100 mg) in CF_3COOH (40 ml) was stirred for 10 min at r.t. Then, triethyl orthoformate (25 ml) was added and the mixture stirred for 15 min. After dilution with CH_2Cl_2, the mixture was poored into ice-cold aq. Na_2CO_3 soln., the org. layer separated, the aq. phase once extracted with CH_2Cl_2, the combined org. phase shaken successively with aq. Na_2CO_3 soln. (1×) and H_2O (2×), filtered through a cotton plug, evaporated, and the product isolated by prep. TLC on silica gel using CH_2Cl_2/AcOEt/MeOH 20:20:7: 48 mg (58%) of **10b**. M.p. 212–213°. UV/VIS (MeOH): 415 (sh), 395 (4.40), 269 (4.27), 260 (sh). UV/VIS (MeOH + $Zn(OAc)_2$): 453 (4.40), 428 (4.36), 405 (sh), 280 (sh), 275 (4.34). IR: 3480 (br.), 3330*m*, 2950*w*, 2920*w*, 2870*w*, 1735*m*, 1680*s*, 1655*s*, 1635*s*, 1555*w*, 1500*w*, 1450*m*, 1440*m*, 1390*w*, 1365*m*, 1350*w*, 1300*w*, 1250*m*, 1200*w*, 1165*m*, 1110*w*, 1050*w*, 970*w*, 905*w*, 875*w*, 755*w*, 715*w*, 675*w*, 640*w*. ^{1}H-NMR ($CDCl_3 + CD_3OD$): 9.57 (*s*, H–C(10)); 6.02 (*s*, H–C(5)); 3.78 (*t*, $J(3^1,3^2) = 6.7$, $CH_2(3^2)$); 3.67 (*s*, $CH_3O(8^4)$); 3.04 (*t*, $J(8^1,8^2) = 7.6$, $CH_2(8^1)$); 2.79 (*t*, $J(3^1,3^2) = 6.7$, $CH_2(3^1)$); 2.58 (*t*, $J(8^1,8^2) = 7.6$, $CH_2(8^2)$); 2.10 (*s*, $CH_3(7^1)$); 1.93 (*s*, $CH_3(2^1)$). ^{13}C-NMR ($CDCl_3 + CD_3OD$): 177.9 (*d*, $C(9^1)$); 173.6, 173.2 (*s*, C(1), $C(8^3)$); 143.2 (*s*, C(3)); 136.2 (*s*, C(4)); 134.4, 132.7, 130.6, 129.7, 123.7 (*s*, C(2), C(6), C(7), C(8), C(9)); 96.8 (*d*, C(5)); 61.6 (*t*, $C(3^2)$); 51.8 (*q*, $C(8^5)$); 35.2 (*t*, $C(8^2)$); 28.3 (*t*, $C(3^1)$); 19.3 (*t*, $C(8^1)$); 8.9, 8.6 (*q*, $C(2^1)$, $C(7^1)$). EI-MS: 346 (47, M^+), 328 (17), 318 (16), 287 (10), 272 (10), 227 (10), 208 (23), 140 (100).

From a faster-migrating zone, a second compound (12 mg, 13%) was isolated and characterized as the 3^2-*O*-formate of **10b**. UV/VIS (MeOH): 415 (sh), 395 (4.45), 268 (4.27), 260 (sh). UV/VIS (MeOH + $Zn(OAc)_2$): 454 (4.49), 429 (4.43), 405 (sh), 284 (sh), 276 (4.33). IR: 3340*m*, 2960*w*, 2930*w*, 2858*w*, 1740*m*, 1720*m*, 1680*s*, 1655*s*, 1560*w*, 1500*w*, 1450*w*, 1395*w*, 1365*w*, 1350*w*, 1280*w*, 1260*m*, 1245*m*, 1200*m*, 1173*m*, 1060*w*, 1030*w*, 980*w*, 930*w*, 910*w*, 875*w*, 790*w*, 758*w*, 715*w*, 675*w*, 640*w*, 605*w*, 580*w*. ^{1}H-NMR: 11.00–10.86 (*s*, NH); 10.85–10.73 (*s*, NH); 9.76 (*s*, H–C(9^1)); 8.07 (*s*, H–C(3^4)); 6.08 (*s*, H–C(5)); 4.32 (*t*, $J(3^1,3^2) = 7.1$, $CH_2(3^2)$); 3.68 (*s*, $CH_3O(8^4)$); 3.09 (*t*, $J(8^1,8^2) = 7.7$, $CH_2(8^1)$); 2.93 (*t*, $J(3^1,3^2) = 7.1$, $CH_2(3^1)$); 2.61 (*t*, $J(8^1,8^2) = 7.7$, $CH_2(8^2)$); 2.17 (*s*, $CH_3(7^1)$); 2.04 (*s*, $CH_3(2^1)$). ^{13}C-NMR: 177.9 (*d*, $C(9^1)$); 173.6, 172.7 (*s*, C(1), $C(8^3)$); 160.7 (*d*, $C(3^4)$); 141.0 (*s*, C(3)); 135.0 (*s*, C(4)); 134.1, 132.3, 131.2, 130.4, 124.6 (*s*, C(2), C(6), C(7), C(8), C(9)); 97.0 (*d*, C(5)); 62.5 (*t*, $C(3^2)$); 51.7 (*q*, $C(8^5)$); 35.2 (*t*, $C(8^2)$); 24.1 (*t*, $C(3^1)$); 19.4 (*t*, $C(8^1)$); 9.0, 8.8 (*q*, $C(2^1)$, $C(7^1)$). EI-MS: 374 (100, M^+), 346 (26), 328 (7), 315 (22), 300 (26), 287 (10).

*(Z,2*RS*,3*SR*)-9-(*tert*-Butoxycarbonyl)-2,3-dihydro-3-(2-hydroxyethyl)-8-[2-(methoxycarbonyl)ethyl]-2,7-dimethyldipyrrin-1(10*H*)-one* (**11a**). A soln. of **10a** (100 mg) in 15 ml of benzene/MeOH 4:1 was hydrogenated over 5% $Pd/CaCO_3$ (200 mg) for 6 h at r.t. and atmospheric pressure. The catalyst was removed by filtration and the

solvent evaporated. Prep. TLC of the residue on silica gel using CH_2Cl_2/AcOEt/MeOH 20:20:7 yielded two main products, **12a** (see below) and **11a** (52 mg, 52%). UV/VIS (MeOH): 311 (4.28), 248 (sh), 229 (4.11). UV/VIS (MeOH + $Zn(OAc)_2$): 356 (4.24), 311 (3.96), 290 (3.95), 280 (3.92), 235 (4.26). IR: 3430 (br.), 3300 (br.), 2970*m*, 2930*m*, 2870*w*, 1715*s*, 1673*s*, 1560*w*, 1490*w*, 1435*m*, 1390*m*, 1365*m*, 1280*m*, 1250*m*, 1167*m*, 1135*m*, 1112*m*, 1055*m*, 960*w*, 845*w*, 775*w*. ^{1}H-NMR: 9.34 (*s*, NH); 8.66 (*s*, NH); 5.38 (*d*, $J(3,5) = 0.8$, H–C(5)); 3.84–3.76 (*m*, $CH_2(3^2)$); 3.67 (*s*, $CH_3O(8^4)$); 3.20 (*dddd*, $J(3,5) = 0.8$, $J(2,3) = 8.2$, $J(3,3^1_A) = 6.7$, $J(3,3^1_B) = 8.1$, H–C(3)); 2.99–2.94 (*m*, $CH_2(8^1)$); 2.83–2.75 (*s*, OH); 2.79 (*dq*, $J(2,2^1) = 7.4$, $J(2,3) = 8.2$, H–C(2)); 1.94 (*s*, $CH_3(7^1)$); 1.85 (*dddd*, $J(3^1_A,3^1_B) = 14.0$, $J(3,3^1_A) = 6.7$, $J(3^1_A,3^2_A) \approx J(3^1_A,3^2_B) \approx 7$, H_A–C(3^1)); 1.71 (*dddd*, $J(3^1_A,3^1_B) = 14.0$, $J(3,3^1_B) = 8.1$, $J(3^1_B,3^2_A) \approx J(3^1_B,3^2_B) \approx 7$, H_B–C(3^1)); 1.52 (*s*, $(CH_3)_3C(9^3)$); 1.16 (*d*, $J(2,2^1) = 7.4$, $CH_3(2^1)$). ^{13}C-NMR: 180.7 (*s*, C(1)); 173.7 (*s*, C(8^3)); 161.5 (*s*, C(9^1)); 140.6 (*s*, C(4)); 129.1, 128.7 (*s*, C(6), C(8)); 119.8, 117.9 (*s*, C(7), C(9)); 92.4 (*d*, C(5)); 80.9 (*s*, C(9^3)); 59.9 (*t*, C(3^2)); 51.4 (*q*, C(8^5)); 40.2, 39.6 (*d*, C(2), C(3)); 35.1 (*t*, C(8^2)); 31.1 (*t*, C(3^1)); 28.4 (*q*, $(CH_3)_3C(9^3)$); 21.0 (*t*, C(8^1)); 10.6 (*q*, C(2^1)); 9.1 (*q*, C(7^1)). EI-MS: 420 (5, M^+), 364 (7), 322 (18), 307 (13), 281 (25), 225 (28), 149 (100).

*(Z,2RS,3SR)-9-(*tert*-Butoxycarbonyl)-2,3-dihydro-8-[2-(methoxycarbonyl)ethyl]-2,7-dimethyl-3-[2-(2-nitrophenylseleno)ethyl]dipyrrin-1(10*H*)-one* (**11b**). To a soln. of **11a** (50 mg) and 2-nitrophenyl selenocyanate (50 mg) in THF (2 ml), 85% tributylphosphine (63 µl) was added and the mixture stirred for 30 min at r.t. Prep. TLC of the mixture on silica gel using CH_2Cl_2/AcOEt 1:2 yielded 53 mg (74%) of **11b**. UV/VIS (MeOH): 382 (3.58), 313 (4.26), 251 (4.31), 230 (4.27). UV/VIS (MeOH + $Zn(OAc)_2$): 360 (4.35), 314 (3.87), 255 (sh), 237 (4.45). IR: 3300 (br.), 2975*m*, 2930*m*, 2870*w*, 1720*s*, 1672*s*, 1590*w*, 1565*w*, 1510*m*, 1440*m*, 1390*w*, 1365*m*, 1330*m*, 1300*m*, 1275*m*, 1250*m*, 1167*m*, 1135*m*, 1050*w*, 1040*w*, 980*w*, 960*w*, 850*w*, 780*w*, 730*m*, 700*w*, 648*w*. ^{1}H-NMR: 9.10–9.02 (*s*, NH); 8.63–8.53 (*s*, NH); 8.30 (*dd*, $J(3^6,3^7) = 8.4$, $J(3^6,3^8) = 1.2$, H–C(3^6)); 7.53 (*ddd*, $J(3^8,3^9) = 8.0$, $J(3^7,3^8) = 6.4$, $J(3^6,3^8) = 1.2$, H–C(3^8)); 7.49 (*dd*, $J(3^8,3^9) = 8.0$, $J(3^7,3^9) = 2.0$, H–C(3^9)); 7.34 (*ddd*, $J(3^6,3^7) = 8.4$, $J(3^7,3^8) = 6.4$, $J(3^7,3^9) = 2.0$, H–C(3^7)); 5.42 (*d*, $J(3,5) = 0.9$, H–C(5)); 3.67 (*s*, $CH_3O(8^4)$); 3.21 (*dddd*, $J(3,5) = 0.9$, $J(2,3) = 8.2$, $J(3,3^1_A) = 6.3$, $J(3,3^1_B) = 8.2$, H–C(3)); 3.09–2.98 (*m*, $CH_2(3^2)$); 3.00–2.95 (*m*, $CH_2(8^1)$); 2.89 (*dq*, $J(2,2^1) = 7.4$, $J(2,3) = 8.2$, H–C(2)); 2.53–2.48 (*m*, $CH_2(8^2)$); 2.11–1.88 (*m*, $CH_2(3^1)$); 1.93 (*s*, $CH_3(7^1)$); 1.53 (*s*, $(CH_3)_3C(9^3)$); 1.21 (*d*, $J(2,2^1) = 7.4$, $CH_3(2^1)$). NOE: 5.42 (4.5, ↗ 3.21); 3.21 (4.8, ↗ 2.89); 2.89 (7.2, ↗ 3.21; 4.2, ↗ 1.21); 2.11–1.88 (2.6, ↗ 3.21); 1.21 (1.0, ↗ 3.21; 5.6, ↗ 2.89). ^{13}C-NMR: 180.4 (*s*, C(1)); 173.5 (*s*, C(8^3)); 161.1 (*s*, C(9^1)); 147.0, 132.7 (*s*, C(3^4), C(3^5)); 139.2 (*s*, C(4)); 133.7, 129.0, 126.4, 125.6 (*d*, C(3^6), C(3^7), C(3^8), C(3^9)); 128.8, 127.9 (*s*, C(6), C(8)); 120.2, 118.3 (*s*, C(7), C(9)); 93.1 (*d*, C(5)), 80.8 (*s*, C(9^3)); 51.4 (*q*, C(8^5)); 43.8 (*d*, C(3)); 39.6 (*d*, C(2)); 35.1 (*t*, C(8^2)); 28.4 (*q*, $(CH_3)_3C(9^3)$); 27.9 (*t*, C(3^2)); 23.3 (*t*, C(3^1)); 21.0 (*t*, C(8^1)); 10.0 (*q*, C(2^1)); 9.2 (*q*, C(7^1)). FAB-MS (*o*-nitrophenyl octyl ether): 605 ($M^+ + 1$).

*(Z,2RS,3SR)-9-(*tert*-Butoxycarbonyl)-3-ethenyl-2,3-dihydro-8-[2-(methoxycarbonyl)ethyl]-2,7-dimethyldipyrrin-1(10*H*)-one* (**11c**). To a soln. of **11b** (50 mg) in THF (7.5 ml), 30% H_2O_2 (0.15 ml) was added and the mixture stirred for 2 h at r.t. Then, the soln. was diluted with CH_2Cl_2 and shaken successively with sat. aq. Na_2CO_3 soln. (1×) and H_2O (2×). The org. phase was filtered through a cotton plug and evaporated and the residue purified by prep. TLC on silica gel using CH_2Cl_2/AcOEt 2:1 to yield 30 mg (94%) of **11c**. UV/VIS (MeOH): 316 (4.23), 250 (sh), 227 (4.14). UV/VIS (MeOH + $Zn(OAc)_2$): 358 (4.25), 305 (sh), 295 (sh), 273 (4.04), 237 (4.28). IR ($CHCl_3$): 3420 (br.), 3000*w*, 2980*w*, 2950*w*, 2930*w*, 2860*w*, 1725*s*, 1673*s*, 1490*w*, 1450*w*, 1435*m*, 1390*w*, 1367*m*, 1337*m*, 1290*m*, 1265*m*, 1250*m*, 1210*m*, 1160*m*, 1137*m*, 1050*w*, 1035*w*, 990*w*, 960*w*, 925*w*, 865*w*, 840*w*. ^{1}H-NMR: 8.84–8.76 (*s*, NH); 8.16–8.08 (*s*, NH); 5.75 (*ddd*, $J(3^1_X,3^2_A) = 10.6$, $J(3^1_X,3^2_B) = 15.7$, $J(3,3^1_X) = 8.9$, H_X–C(3^1)); 5.265 (*d*, $J(3,5) = 0.8$, H–C(5)); 5.260 (*dd*, $J(3^2_A,3^2_B) = 1.6$, $J(3^1_X,3^2_A) = 10.6$, H_A–C(3^2)); 5.253 (*dd*, $J(3^2_A,3^2_B) = 1.6$, $J(3^1_X,3^2_B) = 15.7$, H_B–C(3^2)); 3.71 (*ddd*, $J(3,5) = 0.8$, $J(3,3^1_X) = 8.9$, $J(2,3) = 7.5$, H–C(3)); 3.67 (*s*, $CH_3O(8^4)$); 3.00–2.95 (*m*, $CH_2(8^1)$); 2.81 (*dq*, $J(2,3) = 7.5$, $J(2,2^1) = 7.6$, H–C(2)); 2.53–2.48 (*m*, $CH_2(8^2)$); 1.94 (*s*, $CH_3(7^1)$); 1.55 (*s*, $(CH_3)_3C(9^3)$); 1.17 (*d*, $J(2,2^1) = 7.6$, $CH_3(2^1)$). EI-MS: 402 (65, M^+), 346 (100), 327 (16), 315 (36), 302 (18), 286 (62), 272 (25).

*(Z,2RS,3SR)-9-Formyl-2,3-dihydro-3-(2-hydroxyethyl)-8-[2-(methoxycarbonyl)ethyl]-2,7-dimethyldipyrrin-1(10*H*)-one* (**11d**). Pure **10b** (100 mg) was hydrogenated according to the procedure described above for **11a**, to yield 47 mg (47%) of **11d**. M.p. 157–159°. UV/VIS (MeOH): 350 (4.12), 265 (sh), 243 (4.08). UV/VIS (MeOH + $Zn(OAc)_2$): 405 (4.22), 296 (sh), 260 (4.20). IR: 3450*m*, 3340*m*, 2960*m*, 2930*m*, 2870*w*, 1740*s*, 1715*s*, 1660*s*, 1600*s*, 1542*m*, 1505*w*, 1440*m*, 1380*w*, 1355*m*, 1325*m*, 1285*m*, 1265*m*, 1250*m*, 1212*w*, 1180*m*, 1110*w*, 1070*w*, 1055*w*, 920*w*, 830*w*, 795*w*, 725*w*, 615*w*, 600*w*, 535*w*, 505*w*, 415*w*. ^{1}H-NMR: 11.34–10.54 (*s*, NH); 10.87–10.07 (*s*, NH); 9.50 (*s*, H–C(10)); 5.43 (*d*, $J(3,5) = 0.8$, H–C(5)); 3.87–3.77 (*m*, $CH_2(3^2)$); 3.67 (*s*, $CH_3O(8^4)$); 3.25 (*dddd*, $J(3,5) = 0.8$, $J(2,3) = 8.2$, $J(3,3^1_A) = 6.7$, $J(3,3^1_B) = 8.1$, H–C(3)); 3.03 (*t*, $J(8^1,8^2) = 7.7$, $CH_2(8^1)$); 2.82 (*dq*, $J(2,2^1) = 7.4$, $J(2,3) = 8.2$, H–C(2)); 2.56 (*t*, $J(8^1,8^2) = 7.7$, $CH_2(8^2)$); 2.01 (*s*, $CH_3(7^1)$); 1.88 (*dddd*, $J(3^1_A,3^1_B) = 14.0$, $J(3,3^1_A) = 6.7$, $J(3^1_A,3^2_A) \approx J(3^1_A,3^2_B) \approx 7$, H_A–C(3^1)); 1.74 (*dddd*, $J(3^1_A,3^1_B) = 14.0$, $J(3,3^1_B) = 8.1$, $J(3^1_B,3^2_A) \approx J(3^1_B,3^2_B) \approx 7$, H_B–C(3^1)); 1.20 (*d*, $J(2,2^1) = 7.4$, $CH_3(2^1)$). ^{13}C-NMR: 181.4 (*s*, C(1)); 176.5 (*d*, C(9^1));

173.4 (*s*, C(8^3)); 142.6 (*s*, C(4)); 135.9, 134.7, 128.7, 119.4 (*s*, C(6), C(7), C(8), C(9)); 91.4 (*d*, C(5)); 59.5 (*t*, C(3^2)); 51.8 (*q*, C(8^5)); 40.9, 39.4 (*d*, C(2), C(3)); 35.5 (*t*, C(8^2)); 31.3 (*t*, C(3^1)); 19.5 (*t*, C(8^1)); 10.7 (*q*, C(2^1)); 8.8 (*q*, C(7^1)). EI-MS: 348 (33, M^+), 125 (100), 110 (47), 96 (60).

*(Z,2*RS*,3*SR*)-9-Formyl-2,3-dihydro-8-[2-(methoxycarbonyl)ethyl]-2,7-dimethyl-3-[2-(2-nitrophenylseleno)-ethyl]dipyrrin-1(10*H*)-one* (**11e**) was prepared from **11d** (47 mg) following the procedure described above for **11b**. The product was isolated by prep. TLC using CH_2Cl_2/AcOEt/MeOH 20:20:7: 51 mg (71%). M.p. 195–197°. UV/VIS (MeOH): 410 (sh), 358 (4.06), 284 (4.25). UV/VIS (MeOH + $Zn(OAc)_2$): 406 (4.20), 257 (4.33). IR: 3420 (br.), 3320*m*, 3110*w*, 3030*w*, 2940*w*, 2860*w*, 1738*s*, 1725*s*, 1660*s*, 1602*s*, 1565*w*, 1545*w*, 1510*s*, 1450*m*, 1438*m*, 1385*w*, 1330*s*, 1300*m*, 1265*m*, 1255*m*, 1230*w*, 1195*m*, 1165*m*, 1095*m*, 1040*m*, 985*w*, 920*w*, 855*w*, 830*w*, 785*w*, 760*w*, 720*m*, 705*w*, 690*w*, 680*w*, 650*w*, 600*w*, 530*w*. ^{1}H-NMR ($CDCl_3$ + CD_3OD): 9.44 (*s*, H–C(10)); 8.30 (*dd*, $J(3^6,3^8) < 1$, $J(3^6,3^7) = 8.0$, H–C(3^6)); 7.54–7.52 (*m*, H–C(3^8), H–C(3^9)); 7.36 (*ddd*, $J(3^6,3^7) = 8.0$, $J(3^7,3^8) = 5.2$, $J(3^7,3^9) = 3.4$, H–C(3^7)); 5.46 (*d*, $J(3,5) = 0.9$, H–C(5)); 3.67 (*s*, $CH_3O(8^4)$); 3.26 (*dddd*, $J(3,5) = 0.9$, $J(2,3) = 8.2$, $J(3,3^1_A) = 6.3$, $J(3,3^1_B) = 8.2$, H–C(3)); 3.07–2.91 (*m*, $CH_2(3^2)$); 3.02 (*t*, $J(8^1,8^2) = 7.6$, $CH_2(8^1)$); 2.89 (*dq*, $J(2,3) = 8.2$, $J(2,2^1) = 7.4$, H–C(2)); 2.57 (*t*, $J(8^1,8^2) = 7.6$, $CH_2(8^2)$); 2.15–1.92 (*m*, $CH_2(3^1)$); 1.96 (*s*, $CH_3(7^1)$); 1.23 (*d*, $J(2,2^1) = 7.4$, $CH_3(2^1)$). ^{13}C-NMR ($CDCl_3$ + CD_3OD): 180.6 (*s*, C(1)); 176.4 (*d*, C(9^1)); 173.1 (*s*, C(8^3)); 147.1, 132.6 (*s*, C(3^4), C(3^5)); 141.2, 135.7, 134.2, 128.8, 119.6 (*s*, C(4), C(6), C(7), C(8), C(9)); 133.8, 129.1, 126.6, 125.9 (*d*, C(3^6), C(3^7), C(3^8), C(3^9)); 91.6 (*d*, C(5)); 51.8, (*q*, C(8^5)); 44.5 (*d*, C(3)); 39.3 (*d*, C(2)); 35.5 (*t*, C(8^2)); 28.1 (*t*, C(3^2)); 23.3 (*t*, C(3^1)); 19.4 (*t*, C(8^1)); 10.1 (*q*, C(2^1)); 8.8 (*q*, C(7^1)). FAB-MS (*o*-nitrophenyl octyl ether): 532 ($M^+ + 1$).

rac-*9-(*tert*-Butoxycarbonyl)-4,5-dihydro-3-(2-hydroxyethyl)-8-[2-(methoxycarbonyl)ethyl]-2,7-dimethyl-dipyrrin-1(10*H*)-one* (**12a**) was obtained in 26% yield (26 mg) as a by-product of the hydrogenation of **10a** (see above, preparation of **11a**). UV/VIS (MeOH): 280 (4.26). IR: 3360 (br.), 2970*w*, 2920*w*, 2860*w*, 1735*m*, 1675*s*, 1500*w*, 1445*m*, 1390*w*, 1367*m*, 1280*m*, 1250*w*, 1165*m*, 1140*m*, 1110*w*, 1053*w*, 960*w*, 850*w*, 775*w*. ^{1}H-NMR: 9.84–9.77 (*s*, NH); 6.85–6.80 (*s*, NH); 4.30 (*dd*, $J(4,5_A) = 4.0$, $J(4,5_B) = 11.0$, H–C(4)); 3.87–3.80 (*m*, H_A–C(3^2)); 3.76–3.69 (*m*, H_B–C(3^2)); 3.67 (*s*, $CH_3O(8^4)$); 3.10 (*dd*, $J(5_A,5_B) = 14.5$, $J(4,5_A) = 4.0$, H_A–C(5)); 2.97–2.93 (*m*, $CH_2(8^1)$); 2.73 (*ddd*, $J(3^1_A,3^1_B) = 14.4$, $J(3^1_A,3^2_A) = 5.6$, $J(3^1_A,3^2_B) = 3.6$, H_A–C(3^1)); 2.52–2.42 (*m*, $CH_2(8^2)$, H_B–C(3^1), H_B–C(5)); 1.93 (*s*, $CH_3(7^1)$); 1.78 (*s*, $CH_3(2^1)$); 1.51 (*s*, $(CH_3)_3C(9^3)$). ^{13}C-NMR: 174.6 (*s*, C(1)); 173.7 (*s*, C(8^3)); 161.3 (*s*, C(9^1)); 153.8 (*s*, C(3)); 130.2, 129.2, 128.7 (*s*, C(2), C(6), C(8)); 119.2, 117.4 (*s*, C(7), C(9)); 80.7 (*s*, C(9^3)); 60.8 (*t*, C(3^2)); 59.4 (*d*, C(4)); 51.5 (*q*, C(8^5)); 35.2 (*t*, C(8^2)); 30.0, 29.5 (*t*, C(3^1), C(5)); 28.4 (*q*, $(CH_3)_3C(9^3)$); 21.1 (*t*, C(8^1)); 8.8, 8.5 (*q*, C(2^1), C(7^1)). EI-MS: 420 (44, M^+), 280 (70), 224 (100), 192 (33), 164 (18), 140 (10).

rac-*9-(*tert*-Butoxycarbonyl)-4,5-dihydro-8-[2-(methoxycarbonyl)ethyl]-2,7-dimethyl-3-[2-(2-nitrophenylse-leno)ethyl]dipyrrin-1(10*H*)-one* (**12b**) was obtained as a by-product of the isomerization of **11b** (see below, preparation of **13b**). UV/VIS (MeOH): 389 (3.44), 280 (4.23), 254 (4.19). IR: 3300 (br.), 2970*w*, 2920*m*, 2850*w*, 1735*m*, 1675*s*, 1590*w*, 1565*w*, 1510*m*, 1450*m*, 1435*m*, 1390*w*, 1365*m*, 1330*m*, 1300*m*, 1275*m*, 1250*m*, 1165*m*, 1135*m*, 1055*w*, 1037*w*, 960*w*, 850*w*, 780*w*, 730*m*. ^{1}H-NMR: 9.57–9.50 (*s*, NH); 8.29 (*dd*, $J(3^6,3^7) = 8.3$, $J(3^6,3^8) = 1.3$, H–C(3^6)); 7.55 (*ddd*, $J(3^8,3^9) = 8.1$, $J(3^7,3^8) = 6.8$, $J(3^6,3^8) = 1.3$, H–C(3^8)); 7.50 (*dd*, $J(3^8,3^9) = 8.1$, $J(3^7,3^9) = 1.6$, H–C(3^9)); 7.35 (*ddd*, $J(3^6,3^7) = 8.3$, $J(3^7,3^8) = 6.8$, $J(3^7,3^9) = 1.6$, H–C(3^7)); 6.90–6.82 (*s*, NH); 4.30 (br. *d*, $J(4,5_A) < 1$, $J(4,5_B) = 9.1$, H–C(4)); 3.66 (*s*, $CH_3O(8^4)$); 3.06 (*dd*, $J(5_A,5_B) = 14.6$, $J(4,5_A) = 4.4$, H_A–C(5)); 3.08–2.98 (*m*, H_A–C(3^1), $CH_2(3^2)$); 2.97–2.92 (*m*, $CH_2(8^1)$); 2.71–2.63 (*m*, H_B–C(3^1)); 2.55 (*dd*, $J(4,5_B) = 9.2$, $J(5_A,5_B) = 14.6$, H_B–C(5)); 2.50–2.46 (*m*, $CH_2(8^2)$); 1.94 (*s*, $CH_3(7^1)$); 1.80 (*s*, $CH_3(2^1)$); 1.51 (*s*, $(CH_3)_3C(9^3)$). ^{13}C-NMR: 174.1 (*s*, C(1)); 173.6 (*s*, C(8^3)); 161.2 (*s*, C(9^2)); 153.2 (*s*, C(3)); 147.2, 132.1 (*s*, C(3^4), C(3^5)); 133.7, 129.0, 126.6, 125.9 (*d*, C(3^6), C(3^7), C(3^8), C(3^9)); 130.8, 128.8, 128.3 (*s*, C(2), C(6), C(8)); 119.5, 117.4 (*s*, C(7), C(9)); 80.8 (*s*, C(9^3)); 58.3 (*d*, C(4)); 51.4 (*q*, C(8^5)); 35.1 (*t*, C(8^2)); 28.5 (*q* + *t*, $(CH_3)_3C(9^3)$, C(5) or C(3^2)); 25.7 (*t*, C(3^2) or C(5)); 23.8 (*t*, C(3^1)); 21.0 (*t*, C(8^1)); 9.0, 8.8 (*q*, C(2^1), C(7^1)). FAB-MS (*o*-nitrophenyl octyl ether): 605 ($M^+ + 1$).

*(Z,2*RS*,3*RS*)-9-(*tert*-Butoxycarbonyl)-2,3-dihydro-8-[2-(methoxycarbonyl)ethyl]-2,7-dimethyl-3-[2-(2-ni-trophenylseleno)ethyl]dipyrrin-1(10*H*)-one* (**13b**). Pure **11b** (50 mg) was dissolved in $CHCl_3$ (2 ml) which was previously shaken with 4N aq. HCl. The soln. was allowed to stand at r.t. for 2 h, then shaken repeatedly with H_2O, filtered through $CHCl_3$-soaked filter paper, and evaporated. By prep. TLC of the residue on silica gel using CH_2Cl_2/AcOEt 2:1, two main products, **13b** and **12b** (see above), were separated from a faster and a slower migrating zone. Although the united yield amounted to up to 98%, the relative yields were not reproducible. **13b:** UV/VIS (MeOH): 384 (3.55), 313 (4.26), 251 (4.30), 230 (4.25). UV/VIS (MeOH + $Zn(OAc)_2$): 361 (4.35), 311 (3.79), 255 (sh), 238 (4.44). IR: 3300 (br.), 2980*m*, 2930*m*, 2870*w*, 1740*s*, 1650*s*, 1590*w*, 1565*w*, 1215*m*, 1445*m*, 1395*w*, 1370*m*, 1335*m*, 1305*m*, 1275*m*, 1250*m*, 1170*m*, 1135*m*, 1055*w*, 1040*w*, 985*w*, 962*w*, 910*w*, 850*w*, 785*w*, 730*m*, 705*w*, 650*w*. ^{1}H-NMR: 8.74–8.65 (*s*, NH); 8.29 (*dd*, $J(3^6,3^7) = 8.3$, $J(3^6,3^8) = 1.3$, H–C(3^6)); 7.96–7.88 (*s*, NH);

7.53 (*ddd*, $J(3^8,3^9)=8.1$, $J(3^7,3^8)=6.6$, $J(3^6,3^8)=1.3$, H–C(3^8)); 7.49 (*dd*, $J(3^8,3^9)=8.1$, $J(3^7,3^9)=1.9$, H–C(3^9)); 7.35 (*ddd*, $J(3^6,3^7)=8.3$, $J(3^7,3^8)=6.6$, $J(3^7,3^9)=1.9$, H–C(3^7)); 5.32 (*d*, $J(3,5)=1.5$, H–C(5)); 3.67 (*s*, $CH_3O(8^4)$); 3.06 (*ddd*, $J(3^2_A,3^2_B)=11.6$, $J(3^1_A,3^2_A)=5.7$, $J(3^1_B,3^2_A)=9.4$, H_A–C(3^2)); 3.00–2.96 (*m*, $CH_2(8^1)$); 2.96 (*ddd*, $J(3^2_A,3^2_B)=11.6$, $J(3^1_A,3^2_B)=9.5$, $J(3^1_B,3^2_B)=5.8$, H_B–C(3^2)); 2.89 (*dddd*, $J(3,5)=1.5$, $J(2,3)=5.0$, $J(3,3^1_A)\approx J(3,3^1_B)\approx 5.9$, H–C(3)); 2.53–2.49 (*m*, $CH_2(8^2)$); 2.47 (*dq*, $J(2,3)=5.0$, $J(2,2^1)=7.3$, H–C(2)); 2.23–2.04 (*m*, $CH_2(3^1)$); 1.94 (*s*, $CH_3(7^1)$); 1.55 (*s*, $(CH_3)_3C(9^3)$); 1.35 (*d*, $J(2,2^1)=7.3$, $CH_3(2^1)$). NOE: 5.32 (2.6, ↯ 2.89); 3.06 (1.7, ↯ 5.32); 3.00–2.96 (2.4, ↯ 5.32); 2.89 (0.5, ↯ 2.47; 1.4, ↯ 1.35); 2.47 (1.7, ↯ 2.89; 2.2, ↯ 1.35); 2.23–2.04 (3.2, ↯ 5.32; 2.6, ↯ 2.89); 1.94 (3.5, ↯ 5.32); 1.35 (3.0, ↯ 2.89; 1.2, ↯ 2.47). ^{13}C-NMR: 180.1 (*s*, C(1)); 173.6 (*s*, C(8^3)); 161.1 (*s*, C(9^1)); 147.1, 132.6 (*s*, C(3^4), C(3^5)); 139.8 (*s*, C(4)); 133.7, 129.0, 126.5, 125.7 (*d*, C(3^6), C(3^7), C(3^8), C(3^9)); 129.0, 128.0 (*s*, C(6), C(8)); 120.3, 118.2 (*s*, C(7), C(9)); 92.1 (*d*, C(5)); 80.9 (*s*, C(9^3)); 51.4 (*q*, C(8^5)); 47.0 (*d*, C(3)); 41.4 (*d*, C(2)); 35.1 (*t*, C(8^2)); 32.6 (*t*, C(3^2)); 28.4 (*q*, $(CH_3)_3C(9^3)$); 22.2 (*t*, C(3^1)); 21.0 (*t*, C(8^1)); 16.9 (*q*, C(2^1)); 9.3 (*q*, C(7^1)). FAB-MS (*o*-nitrophenyl octyl ether): 605 ($M^+ + 1$).

*(Z,2RS,3RS)-9-(*tert*-Butoxycarbonyl)-3-ethenyl-2,3-dihydro-8-[2-(methoxycarbonyl)ethyl]-2,7-dimethyldipyrrin-1(10H)-one* (**13c**). According to the method described for **11c**, 29 mg (87%) of **13c** were obtained from 50 mg of **13b** as a pale yellow oil. UV/VIS (MeOH): 314 (4.25), 250 (sh), 226 (4.16). UV/VIS (MeOH + $Zn(OAc)_2$): 359 (4.27), 310 (3.88), 295 (3.91), 270 (4.03), 236 (4.29). IR: 3450*s*, 2980*m*, 2930*m*, 2860*w*, 1740*s*, 1715*s*, 1692*s*, 1672*s*, 1560*w*, 1440*m*, 1420*w*, 1395*w*, 1385*w*, 1365*m*, 1335*m*, 1275*s*, 1250*m*, 1178*m*, 1160*m*, 1135*s*, 1115*m*, 1090*w*, 1055*w*, 1010*w*, 995*w*, 960*w*, 925*w*, 875*w*, 847*w*, 815*w*, 800*w*, 770*w*, 685*w*, 630*w*, 610*w*, 550*w*, 520*w*. ^{1}H-NMR: 8.95–8.85 (*s*, NH); 8.50–8.40 (*s*, NH); 5.78 (*ddd*, $J(3^1_X,3^2_A)=10.4$, $J(3^1_X,3^2_B)=16.3$, $J(3,3^1_X)=8.6$, H_X–C(3^1)); 5.268 (*dd*, $J(3^2_A,3^2_B)<1$, $J(3^1_X,3^2_A)=10.4$, H_A–C(3^2)); 5.260 (*dd*, $J(3^2_A,3^2_B)<1$, $J(3^1_X,3^2_B)=16.3$, H_B–C(3^2)); 5.256 (*d*, $J(3,5)=1.8$, H–C(5)); 3.67 (*s*, $CH_3O(8^4)$); 3.22 (*ddd*, $J(3,5)=1.8$, $J(2,3)=J(3,3^1)=8.6$, H–C(3)); 3.00–2.95 (*m*, $CH_2(8^1)$); 2.53–2.48 (*m*, $CH_2(8^2)$); 2.50 (*dq*, $J(2,3)=8.6$, $J(2,2^1)=7.2$, H–C(2)); 1.94 (*s*, $CH_3(7^1)$); 1.53 (*s*, $(CH_3)_3C(9^3)$); 1.27 (*d*, $J(2,2^1)=7.2$, $CH_3(2^1)$). ^{13}C-NMR: 178.8 (*s*, C(1)); 173.6 (*s*, C(8^3)); 160.8 (*s*, C(9^1)); 139.7 (*s*, C(4)); 136.0 (*d*, C(3^1)); 129.1, 127.9 (*s*, C(6), C(8)); 120.1, 118.2 (*s*, C(7), C(9)); 119.0 (*t*, C(3^2)); 92.2 (*d*, C(5)); 80.8 (*s*, C(9^3)); 52.8 (*d*, C(3)); 51.4 (*q*, C(8^5)); 42.2 (*d*, C(2)); 35.0 (*t*, C(8^2)); 28.5 (*q*, $CH_3)_3C(9^3)$); 21.0 (*t*, C(8^1)); 14.0 (*q*, C(2^1)); 9.3 (*q*, C(7^1)). EI-MS: 402 (18, M^+), 346 (100), 315 (10), 286 (25).

*(2RS,3SR,4SR)-9-(*tert*-Butoxycarbonyl)-4,3-(epoxyethano)-2,3,4,5-tetrahydro-8-[2-(methoxycarbonyl)ethyl]-2,7-dimethyldipyrrin-1(10H)-one* (**14**) was obtained in 95% yield (19 mg) when **11a** (20 mg) was treated with acidic $CHCl_3$ under the conditions described above for **13b**. UV/VIS (MeOH): 280 (4.12). IR: 3420 (br.), 3290 (br.), 2970*m*, 2930*m*, 2870*w*, 1735*m*, 1685*s*, 1500*w*, 1445*m*, 1420*w*, 1390*w*, 1365*m*, 1277*m*, 1255*m*, 1240*m*, 1165*m*, 1142*w*, 1112*m*, 1050*w*, 1030*w*, 960*w*, 910*w*, 845*w*, 775*w*. ^{1}H-NMR: 9.23–9.17 (*s*, NH); 6.17–6.11 (*s*, NH); 3.96 (*ddd*, $J(3^1_A,3^2_A)=4.2$, $J(3^1_B,3^2_A)=7.2$, $J(3^2_A,3^2_B)=8.9$, H_A–C(3^2)); 3.76 (*ddd*, $J(3^1_A,3^2_B)=6.5$, $J(3^1_B,3^2_B)=8.9$, $J(3^2_A,3^2_B)=8.9$, H_B–C(3^2)); 3.67 (*s*, $CH_3O(8^4)$); 3.05 (*d*, $J(5_A,5_B)=14.9$, H_A–C(5)); 3.01–2.97 (*m*, $CH_2(8^1)$); 2.97 (*d*, $J(5_A,5_B)=14.9$, H_B–C(5)); 2.71 (*ddd*, $J(2,3)=9.0$, $J(3,3^1_A)=4.4$, $J(3,3^1_B)=9.0$, H–C(3)); 2.66 (*dq*, $J(2,3)=9.0$, $J(2,2^1)=7.0$, H–C(2)); 2.53–2.48 (*m*, $CH_2(8^2)$); 1.95 (*s*, $CH_3(7^1)$); 1.95–1.82 (*m*, $CH_2(3^1)$); 1.55 (*s*, $(CH_3)_3C(9^3)$); 1.17 (*d*, $J(2,2^1)=7.0$, $CH_3(2^1)$). NOE: 6.17–6.11 (1.0, ↯ 3.76); 3.96 (21.2, ↯ 3.76; 2.1, ↯ 1.95–1.82); 3.76 (24.1, ↯ 3.96; 1.9, ↯ 1.95–1.82); 3.05 (1.5, ↯ 2.71–2.66); 2.97 (1.5, ↯ 2.71–2.66); 2.71 (10.2, ↯ 1.95–1.82); 2.66 (10.2, ↯ 1.95–1.82; 3.2, ↯ 1.17); 1.95–1.82 (4.9, ↯ 3.96; 3.8, ↯ 3.76; 8.4, ↯ 2.71–2.66; 1.5, ↯ 1.17); 1.17 (5.5, ↯ 2.71–2.66; 9.4, ↯ 1.95–1.82). ^{13}C-NMR: 177.6 (*s*, C(1)); 173.6 (*s*, C(8^3)); 160.9 (*s*, C(9^1)); 128.0, 127.0 (*s*, C(6), C(8)); 119.5, 118.0 (*s*, C(7), C(9)); 97.6 (*s*, C(4)); 80.7 (*s*, C(9^3)); 67.1 (*t*, C(3^2)); 51.4 (*q*, C(8^5)); 46.2 (*d*, C(3)); 38.1 (*d*, C(2)); 35.2 (*t*, C(8^2)); 34.5, 27.4 (*t*, C(3^1), C(5)); 28.5 (*q*, $(CH_3)_3C(9^3)$); 21.0 (*t*, C(8^1)); 11.7 (*q*, C(2^1)); 8.9 (*q*, C(7^1)). EI-MS: 420 (5, M^+), 347 (6), 322 (9), 305 (8), 281 (72), 254 (17), 225 (83), 140 (100).

*(2RS,3RS,4RS)-9-(*tert*-Butoxycarbonyl)-4,3-(epoxyethano)-2,3,4,5-tetrahydro-8-[2-(methoxycarbonyl)ethyl]-2,7-dimethyldipyrrin-1(10H)-one* (**15**). Pure **11a** (50 mg) was dissolved in 0.5M NaOMe in MeOH (3 ml) and refluxed under N_2 for 2 h. The mixture was diluted with H_2O and extracted with CH_2Cl_2, the org. layer shaken twice with H_2O, filtered through a cotton plug, and evaporated, and the residue separated by prep. TLC on silica gel using CH_2Cl_2/AcOEt/MeOH 20:20:7. Two products, **14** (see above) and **15**, were obtained in 84% yield. Under the same conditions, the latter was obtained in 26% yield (26 mg) from **12a** (100 mg) as the sole product. UV/VIS (MeOH): 280 (4.12). IR: 3460*w*, 3300 (br.), 2980*m*, 2940*m*, 2870*w*, 1740*s*, 1690*s*, 1580*w*, 1500*w*, 1450*m*, 1425*m*, 1395*w*, 1370*m*, 1280*m*, 1255*m*, 1170*m*, 1145*m*, 1115*m*, 1045*m*, 1035*m*, 990*w*, 962*w*, 910*w*, 850*w*, 780*w*, 740*w*, 620*w*, 600*w*, 530*w*, 470*w*. ^{1}H-NMR: 9.23–9.12 (*s*, NH); 6.24–6.19 (*s*, NH); 4.03 (*ddd*, $J(3^1_B,3^2_A)<1$, $J(3^2_A,3^2_B)=9.1$, $J(3^1_A,3^2_A)=7.1$, H_A–C(3^2)); 3.83 (*ddd*, $J(3^2_A,3^2_B)=9.1$, $J(3^1_A,3^2_B)=11.5$, $J(3^1_B,3^2_B)=5.0$, H_B–C(3^2)); 3.67 (*s*, $CH_3O(8^4)$); 3.03, 2.97 (*2d*, $J(5_A,5_B)=14.8$, H_A–C(5), H_B–C(5)); 3.00–2.95 (*m*, $CH_2(8^1)$); 2.53–2.48 (*m*, $CH_2(8^2)$); 2.33 (*dd*, $J(2,3)=4.4$, $J(2,2^1)=7.2$, H–C(2)); 2.31 (*ddd*, $J(3,3^1_B)<1$, $J(2,3)=4.4$, $J(3,3^1_A)=8.8$, H–C(3)); 1.96 (*s*, $CH_3(7^1)$); 2.00–1.89 (*m*, H_A–C(3^1)); 1.73 (*dddd*, $J(3^1_A,3^1_B)=12.5$, $J(3^1_B,3^2_B)=5.0$, $J(3^2_A,3^1_B)<1$, $J(3,3^1_B)<1$, H_B–C(3^1)); 1.55 (*s*, $(CH_3)_3C(9^3)$); 1.17 (*d*, $J(2,2^1)=7.2$, $CH_3(2^1)$). NOE: 4.03 (0.7, ↯ 1.73); 3.83 (2.6, ↯ 1.73); 3.03

(1.1, ≠ 1.17); 2.97 (1.1, ≠ 1.17); 2.33 (6.6, ≠ 1.73; 4.5, ≠ 1.17); 2.31 (6.6, ≠ 1.73; 4.5, ≠ 1.17); 1.96 (11.3, ≠ 1.73). ^{13}C-NMR: 178.7 (*s*, C(1)); 173.6 (*s*, C(8^3)); 160.9 (*s*, C(9^1)); 128.1, 126.8 (*s*, C(6), C(8)); 119.6, 118.0 (*s*, C(7), C(9)); 97.7 (*s*, C(4)); 80.7 (*s*, C(9^3)); 66.8 (*t*, C(3^2)); 51.4 (*q*, C(8^5)); 50.1 (*d*, C(3)); 43.4 (*d*, C(2)); 35.8, 28.5 (*t*, C(3^1), C(5)); 35.2 (*t*, C(8^2)); 33.5 (*q*, (CH_3)$_3$C(9^3)); 20.9 (*t*, C(8^1)); 17.5 (*q*, C(2^1)); 8.9 (*q*, C(7^1)). EI-MS: 420 (11, M^+), 347 (14), 305 (20), 289 (27), 281 (100), 254 (8), 225 (100), 140 (100).

*(*rac*,3*E*,4*Z*)-9-(*tert*-Butoxycarbonyl)-3-ethylidene-2,3-dihydro-8-[2-(methoxycarbonyl)ethyl]-2,7-dimethyldipyrrin-1(10*H*)-one* (**17**). Pure **11c** or **13c** was dissolved in $CDCl_3$ in a NMR tube and 1 drop of CF_3CO_2D added. In both cases, conversion into **17** was complete after 2–3 h. ^{1}H-NMR: 8.74–8.63 (*s*, NH); 7.95–7.85 (*s*, NH); 6.19 (*dq*, $J(2,3^1) = 2.3$, $J(3^1,3^2) = 7.3$, H–C(3^1)); 5.68 (*s*, H–C(5)); 3.68 (*s*, $CH_3O(8^4)$); 3.22 (*dqq*, $J(2,2^1) = 7.5$, $J(2,3^1) = 2.3$, $J(2,3^2) = 1.0$, H–C(2)); 3.02–2.96 (*m*, $CH_2(8^1)$); 2.55–2.50 (*m*, $CH_2(8^2)$); 1.98 (*s*, $CH_3(7^1)$); 1.85 (*dd*, $J(2,3^2) = 1.0$, $J(3^1,3^2) = 7.3$, $CH_3(3^2)$); 1.56 (*s*, $(CH_3)_3C(9^3)$); 1.39 (*d*, $J(2,2^1) = 7.5$, $CH_3(2^1)$). NOE: 6.19 (13.5, ≠ 5.68); 5.68 (13.2, ≠ 6.19). EI-MS: 402 (10, M^+), 380 (23), 360 (15), 346 (28), 335 (18), 320 (45), 305 (100).

*(*Z*,*Z*,*Z*,2*RS*,3*SR*)-18-Ethyl-8,12-bis[2-(methoxycarbonyl)ethyl]-2,7,13,17-tetramethyl-3-[2-(2-nitrophenylseleno)ethyl]-22*H*-biline-1,19(21*H*,24*H*)-dione* (**19a**). To an ice-cooled soln. of **11e** (10 mg) and methyl isoneoxanthobilirubinate [38] (**18a**, 5.7 mg) in $CHCl_3$ (10 ml), 0.5 ml of a freshly prepared soln. of 2,6-di(*tert*-butyl)-4-methylpyridine (1.025 g) and phosphoryl bromide (1.43 g) in $CHCl_3$ (25 ml) [28] was added and the mixture stirred for 40 min at 0° under N_2. Then, the soln. was diluted with CH_2Cl_2 and shaken successively with aq. $NaHCO_3$ soln. (1×) and H_2O (4×). The org. layer was filtered through a cotton plug, evaporated and the product isolated by prep. TLC on silica gel using CH_2Cl_2/AcOEt 1:1. Extraction of the blue zone at R_f 0.8 with acetone gave 9 mg (58%) of **19a**. UV/VIS ($CHCl_3$): 590 (4.17), 348 (4.54), 275 (4.33), 260 (4.38). IR ($CHCl_3$): 3470 (br.), 3410*w*, 3000*m*, 2960*w*, 2930*w*, 1710*s*, 1630*w*, 1593*w*, 1510*w*, 1437*m*, 1415*m*, 1362*s*, 1305*w*, 1215 (br.), 1165*w*, 1090*m*, 980*w*, 960*w*, 900*w*, 860*w*. ^{1}H-NMR: 8.29 (*dd*, $J(3^6,3^7) = 8.3$, $J(3^6,3^8) = 1.3$, H–C(3^6)); 7.55 (*dd*, $J(3^8,3^9) = 8.1$, $J(3^7,3^9) = 1.4$, H–C(3^9)); 7.50 (*ddd*, $J(3^8,3^9) = 8.1$, $J(3^7,3^8) = 6.9$, $J(3^6,3^8) = 1.3$, H–C(3^8)); 7.32 (*ddd*, $J(3^6,3^7) = 8.3$, $J(3^7,3^8) = 6.9$, $J(3^7,3^9) = 1.4$, H–C(3^7)); 6.69 (*s*, H–C(10)); 5.98 (*s*, H–C(15)); 5.54 (*d*, $J(3,5) = 0.7$, H–C(5)); 3.673, 3.666 (2*s*, $CH_3O(8^4)$, $CH_3O(12^4)$); 3.38 (*dddd*, $J(3,5) = 0.7$, $J(2,3) = 8.1$, $J(3,3^1_A) \approx J(3,3^1_B) \approx 7$, H–C(3)); 3.12–2.99 (*m*, $CH_2(3^2)$); 2.95 (*t*, $J(12^1,12^2) = 7.5$, $CH_2(12^1)$); 2.90 (*t*, $J(8^1,8^2) = 7.5$, $CH_2(8^1)$); 2.87 (*dq*, $J(2,3) = 8.1$, $J(2,2^1) = 7.5$, H–C(2)); 2.56 (*t*, $J(12^1,12^2) = 7.5$, $CH_2(12^2)$); 2.54 (*t*, $J(8^1,8^2) = 7.5$, $CH_2(8^2)$); 2.30 (*q*, $J(18^1,18^2) = 7.5$, $CH_2(18^1)$); 2.17–2.03 (*m*, $CH_2(3^1)$); 2.12 (*s*, $CH_3(13^1)$, $CH_3(17^1)$); 1.96 (*s*, $CH_3(7^1)$); 1.14 (*d*, $J(2,2^1) = 7.5$, $CH_3(2^1)$); 1.10 (*t*, $J(18^1,18^2) = 7.5$, $CH_3(18^2)$). FAB-MS (*o*-nitrophenyl octyl ether): 817 ($M^+ + 1$).

*(*Z*,*Z*,*Z*,2*RS*,3*SR*)-3-Ethenyl-18-ethyl-8,12-bis[2-(methoxycarbonyl)ethyl]-2,7,13,17-tetramethyl-22*H*-biline-1,19(21*H*,24*H*)-dione* (**19b**). To a soln. of **19a** (9 mg) in THF (2 ml), 30% H_2O_2 (0.06 ml) was added and the mixture allowed to stand for 2 h at r.t. Then, CH_2Cl_2 which was previously shaken with sat. aq. $NaHCO_3$ soln. was added, the soln. washed successively with ice-cold aq. $NaHCO_3$ soln. (2×) and H_2O (1×), the org. layer filtered through a cotton plug and evaporated. The residue (composed of **19b** and racemic (*Z*)-phycocyanobilin dimethyl ester (*rac*-**5b**)) was dissolved in $CDCl_3$ and investigated by ^{1}H-NMR. Transformation of **19b** into *rac*-**5b**, which was identified with an authentic sample [25], was complete after chromatography on silica gel using CH_2Cl_2/AcOEt 2:1. On substraction of the signals of *rac*-**5b**, the difference ^{1}H-NMR of **19b** could be obtained: 6.66 (*s*, H–C(15)); 5.98 (*s*, H–C(10)); 5.82 (*ddd*, $J(3^1_X,3^2_A) = 9.3$, $J(3^1_X,3^2_B) = 16.9$, $J(3,3^1_X) = 9.4$, H_X–C(3^1)); 5.43 (*d*, $J(3,5) = 1.4$, H–C(5)); 5.26 (*dd*, $J(3^2_A,3^2_B) = 1.7$, $J(3^2_B,3^1_X) = 16.9$, H_B–C(3^2)); 5.25 (*dd*, $J(3^2_A,3^2_B) = 1.7$, $J(3^2_A,3^1_X) = 9.3$, H_A–C(3^2)); 3.89 (*ddd*, $J(2,3) \approx 9.4$, $J(3,3^1_X) = 9.4$, $J(3,5) = 1.4$, H–C(3)); 3.67, 3.66 (2*s*, $CH_3O(8^4)$, $CH_3O(12^4)$); 2.94, 2.89 (2*t*, $J(8^1,8^2) = J(12^1,12^2) = 7.6$, $CH_2(8^1)$, $CH_2(12^1)$); 2.81 (*dq*, $J(2,2^1) = 7.6$, $J(2,3) \approx 9.4$, H–C(2)); 2.55, 2.54 (2*t*, $J(8^1,8^2) = J(12^1,12^2) = 7.6$, $CH_2(8^2)$, $CH_2(12^2)$); 2.33 (*q*, $J(18^1,18^2) = 7.6$, $CH_2(18^1)$); 2.11 (*s*, $CH_3(13^1)$, $CH_3(17^1)$); 1.99 (*s*, $CH_3(7^1)$); 1.104 (*d*, $J(2,2^1) = 7.6$, $CH_3(2^1)$); 1.102 (*t*, $J(18^1,18^2) = 7.6$, $CH_3(18^2)$).

*(*rac*,Z,Z)-18-Ethyl-4,5-dihydro-8,12-bis[2-(methoxycarbonyl)ethyl]-2,7,13,17-tetramethyl-3-[2-(2-nitrophenylseleno)ethyl]-22*H*-biline-1,19(21*H*,24*H*)-dione* (**20**) was obtained in nearly quantitative yield when **19a** was treated with acidic $CHCl_3$ under the conditions described for **13b**. UV/VIS ($CHCl_3$): 564 (4.30), 400 (sh), 329 (4.43), 255 (4.26). IR ($CHCl_3$): 3440*w*, 3000*w*, 2950*w*, 2930*w*, 2858*w*, 1730*m*, 1690*s*, 1630*w*, 1595*m*, 1515*m*, 1455*w*, 1438*m*, 1395*w*, 1360*w*, 1335*m*, 1305*m*, 1270*m*, 1165*m*, 1095*w*, 1060*w*, 1035*w*, 965*w*, 910*w*, 865*w*, 830*w*. ^{1}H-NMR: 8.27 (*dd*, $J(3^6,3^8) < 1$, $J(3^6,3^7) = 8.2$, H–C(3^6)); 7.466 (*dd*, $J(3^8,3^9) = 8.2$, $J(3^7,3^9) = 2.8$, H–C(3^9)); 7.463 (*ddd*, $J(3^6,3^7) < 1$, $J(3^8,3^9) = 8.2$, $J(3^7,3^8) = 5.6$, H–C(3^8)); 7.30 (*ddd*, $J(3^6,3^7) = 8.2$, $J(3^7,3^8) = 5.6$, $J(3^7,3^9) = 2.8$, H–C(3^7)); 7.08 (*s*, NH); 6.77 (*s*, H–C(10)); 5.92 (*s*, H–C(15)); 4.61–4.53 (br., H–C(4)); 3.67, 3.64 (2*s*, $CH_3O(8^4)$, $CH_3O(12^4)$); 3.13 (*dd*, $J(5_A,5_B) = 5.2$, $J(4,5_A) = 5.0$, H_A–C(5)); 3.03–2.94 (*m*, $CH_2(3^2)$); 2.94–2.87 (*m*, $CH_2(8^1)$, $CH_2(12^1)$, H_B–C(5), H_A–C(3^1)); 2.67–2.58 (*m*, H_B–C(3^1)); 2.53 (*t*, $J(12^1,12^2) = 7.6$, $CH_2(12^2)$); 2.50 (*t*, $J(8^1,8^2) = 7.6$, $CH_2(8^2)$); 2.37 (*q*, $J(18^1,18^2) = 7.6$, $CH_2(18^1)$); 2.11 (*s*, $CH_3(17^1)$); 2.07 (*s*, $CH_3(13^1)$); 1.95 (*s*, $CH_3(7^1)$); 1.76 (*s*, $CH_3(2^1)$); 1.10 (*t*, $J(18^1,18^2) = 7.6$, $CH_3(18^2)$). FAB-MS (*o*-nitrophenyl octyl ether): 817 ($M^+ + 1$).

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