96. On the Novel Free Porphyrins Corallistin B, C, D, and E: Isolation from the Demosponge *Corallistes* sp. of the Coral Sea and Reactivity of Their Nickel(II) Complexes toward Formylating Reagents

by **Michele D'Ambrosio**[a]), **Antonio Guerriero**[a]), **Cécile Debitus**[b]), **Olivier Ribes**[b]), and **Francesco Pietra**[a])*

[a]) Istituto di Chimica, Università di Trento, I–38050 Povo-Trento
[b]) ORSTOM, B.P. A5, Noumea, Nouvelle Calédonie

(5.IV.93)

Reported here are the novel free porphyrins corallistin B, C, D, and E, isolated as methyl esters **2a**, **3a**, **4a**, and **5a**, respectively, from the sponge *Corallistes* sp. (Lithistida) collected at the basis of the south New Caledonian coral reef. A protocol is also established for formylation of their Ni^{II} complexes, which show a different reactivity pattern toward $DMF/POCl_3$ from metal complexes of deuteroporphyrins. Together with corallistin A, previously isolated as the methyl ester **1a**, and the known deuteroporphyrin IX (isolated as **6a**) also present in the sponge, the new corallistins, which may be thought to derive from protoporphyrin *via* heme, account for an amazing 60% of the EtOH extract from the sponge.

1. Introduction. – Free porphyrins are known from geological sources such as oil shale [1] and coal [2] and have, therefore, been called geoporphyrins. They are thought to have taken origin from chlorophylls [3], which is particularly evident when a five-, six-, or seven-membered carbocycle is annelated to the tetrapyrrole unit [1] [3].

In the living world, 'false' free porphyrins have been known for a long time such as uroporphyrin I and coproporphyrin I, which co-occur with coproporphyrin III and protoporphyrin IX in various living invertebrates [4]. Moreover, an unspecified protoporphyrin was extracted from deep-sea medusae of the classes Schyphozoa and Hydrozoa, which also contain other, unidentified porphyrins [5].

More recently, also free chlorins of unusual structure were isolated from marine invertebrates. This is the case of bonellin from the Enteropneusta marine worm *Bonellia viridis,* where it induces larvae to develop into male worms [6], tunichlorin from the ascidian *Trididemnum solidum* [7], 13^2,17^3-cyclopheophorbide enol from the sponge *Darwinella oxeata* (Dendroceratida) [8], and both chlorophyllone A [9a] and chlorophyllonic acid A methyl ester [9b] from the short-necked clam, *Ruditapes philippinarum.* Having chlorin structure, these compounds in invertebrates are considered to be of dietary origin.

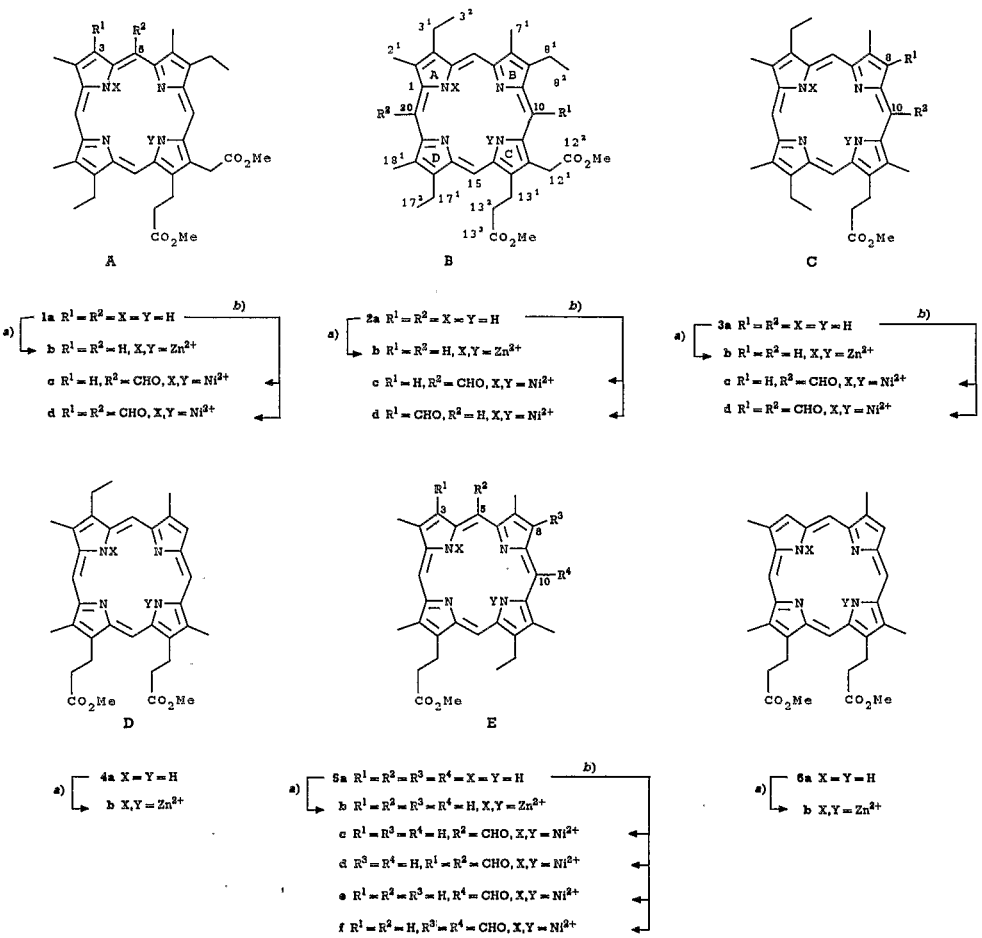
The first unusual free porphyrin found in a living organism is corallistin A, present in huge amounts in the demosponge *Corallistes* sp. (Lithistida), from which it was isolated as methyl ester **1a** [10]. Its structure, derived from NMR and mass spectra [10], was confirmed by total synthesis [11].

Interest in corallistin A stems from its mysterious role at such high concentrations in a marine sponge which lives in low-light conditions at the basis of the south New Caledonian coral reef, and from its potential interest for tumor phototherapy [12]. In fact, the potential of similar porphyrins as phototherapeutic agents was also evaluated through

their ability to act as photosensitizers in generating singlet oxygen [13]. This stimulated us to examine this sponge further, obtaining four new corallistins which accompany the long known deuteroporphyrin IX. The structures are fully elucidated here on the basis of the NMR and mass spectra of the free porphyrin methyl esters, their Zn^{II} complexes, and formylation products of their Ni^{II} complexes.

2. Results and Discussion. – In analogy with corallistin A, isolated as methyl ester **1a** [10], the new corallistins B, C, D, and E were isolated as methyl esters **2a**, **3a**, **4a**, and **5a**, respectively, from the sponge *Corallistes* sp. (*Scheme*). Their ^{1}H-NMR spectra, revealing ring currents from low-field resonances for the *meso*-protons and high-field resonances for the NH protons (*Exper. Part*), are consistent with porphyrin structures. A thorough ^{1}H- and ^{13}C-NMR spectral analysis carried out on the Zn^{II} complexes revealed, in

Scheme



a) $Zn(AcO)_2$. *b*) 1. $Ni(AcO)_2$; 2. $DMF/POCl_3$.

combination with MS data, that the various corallistins differ as to the substitution pattern at the peripheral positions. Examination of the data in *Tables 1* and *2* and the *Exper. Part* clearly indicates that corallistin B methyl ester (**2a**) possesses one Et substituent more than corallistin A methyl ester (**1a**). Differential NOE experiments (*Exper. Part*) established that this Et substituent is at C(3) in **2a**.

Continuing the above analysis, in corallistin C methyl ester (**3a**), H-atoms have taken the place of both the C(12²) OOMe group and the Et–C(8) group of **2a**. Moreover, corallistin D methyl ester (**4a**) possesses, with respect to **3a**, one propanoyl chain more, which has replaced Et–C(17) of **3a**. Finally, corallistin E methyl ester (**5a**) is related to **3a** by the loss of Et–C(3) and exchange of the substituents between C(13) and C(17).

Table 1. *^{13}C-NMR Data* ($CDCl_3$) *for the Zinc(II) Complexes of the Methyl Esters* **2b**, **3b**, **4b**, **5b**, *and* **6b** *of Corallistin B–E and Deuteroporphyrin IX, Respectively*

	2b	**3b**	**4b**	**5b**	**6b**
C(1)	147.56 (*s*)	147.83 (*s*)	147.19 (*s*)	148.62 (*s*)	147.50 (*s*)
C(2)	135.01 (*s*)	135.03 (*s*)	134.74 (*s*)	140.37 (*s*)	139.89 (*s*)
C(3)	142.04 (*s*)	142.39 (*s*)	142.00 (*s*)	129.20 (*d*)	128.99 (*d*)
C(4)	146.69 (*s*)	146.23 (*s*)	145.84 (*s*)	147.47 (*s*)	146.29 (*s*)
C(5)	96.27 (*d*)	95.91 (*d*)	96.65 (*d*)	100.49 (*d*)	100.37 (*d*)
C(6)	147.92 (*s*)	147.66 (*s*)	147.35 (*s*)	148.79 (*s*)	147.59 (*s*)
C(7)	134.90 (*s*)	139.94 (*s*)	139.77 (*s*)	140.79 (*s*)	140.43 (*s*)
C(8)	142.54 (*s*)	128.90 (*d*)	128.73 (*d*)	129.12 (*d*)	128.85 (*d*)
C(9)	146.27 (*s*)	146.90 (*s*)	146.68 (*s*)	148.29 (*s*)	147.34 (*s*)
C(10)	97.02 (*d*)	100.05 (*d*)	99.70 (*d*)	99.60 (*d*)	99.64 (*d*)
C(11)	145.06 (*s*)	147.25 (*s*)	146.99 (*s*)	149.18 (*s*)	147.92 (*s*)
C(12)	131.42 (*s*)	136.48 (*s*)	136.14 (*s*)	135.80 (*s*)	136.36 (*s*)
C(13)	139.56 (*s*)	138.07 (*s*)	137.93 (*s*)	142.98 (*s*)	138.42 (*s*)
C(14)	144.68 (*s*)	146.42 (*s*)	145.84 (*s*)	148.09 (*s*)	146.54 (*s*)
C(15)	96.75 (*d*)	97.00 (*d*)	95.38 (*d*)	95.98 (*d*)	95.60 (*d*)
C(16)	146.05 (*s*)	146.83 (*s*)	145.68 (*s*)	147.55 (*s*)	146.16 (*s*)
C(17)	142.33 (*s*)	142.48 (*s*)	137.85 (*s*)	138.44 (*s*)	138.04 (*s*)
C(18)	134.90 (*s*)	135.32 (*s*)	135.96 (*s*)	136.89 (*s*)	136.60 (*s*)
C(19)	147.76 (*s*)	147.83 (*s*)	146.70 (*s*)	147.76 (*s*)	146.60 (*s*)
C(20)	96.37 (*d*)	96.42 (*d*)	96.10 (*d*)	97.24 (*d*)	96.87 (*d*)
Me–C(2)	11.03 (*q*)	11.29 (*q*)	11.12 (*q*)	13.84 (*q*)	13.48 (*q*)
C(3¹)	19.31 (*t*)	19.56 (*t*)	19.39 (*t*)	–	–
C(3²)	17.55 (*q*)	17.71 (*q*)	17.64 (*q*)	–	–
Me–C(7)	11.31 (*q*)	13.63 (*q*)	13.53 (*q*)	13.78 (*q*)	13.55 (*q*)
C(8¹)	19.59 (*t*)	–	–	–	–
C(8²)	17.70 (*q*)	–	–	–	–
C(12¹)	32.49 (*t*)	11.52 (*q*)	11.40 (*q*)	11.40 (*q*)	11.50 (*q*)
C(12²)	172.32 (*s*)	–	–	–	–
*Me*OOC(12²)	52.22 (*q*)	–	–	–	–
C(13¹)	21.79 (*t*)	21.83 (*t*)	21.59 (*t*)	19.99 (*t*)	21.68 (*t*)
C(13²)	37.33 (*t*)	37.14 (*t*)	36.97 (*t*)	17.96 (*q*)	36.95 (*t*)
C(13³)	173.81 (*s*)	173.79 (*s*)	173.68 (*s*)	–	173.69 (*s*)
*Me*OOC(13³)	51.77 (*q*)	51.73 (*q*)	51.67 (*q*)	–	51.68 (*q*)
C(17¹)	19.67 (*t*)	19.70 (*t*)	21.59 (*t*)	22.24 (*t*)	21.62 (*t*)
C(17²)	17.70 (*q*)	17.71 (*q*)	36.97 (*t*)	37.48 (*t*)	36.98 (*t*)
C(17³)	–	–	173.68 (*s*)	173.92 (*s*)	173.69 (*s*)
*Me*OOC(17³)	–	–	51.67 (*q*)	51.70 (*q*)	51.68 (*q*)
Me–C(18)	11.23 (*q*)	11.38 (*q*)	11.36 (*q*)	11.40 (*q*)	11.38 (*q*)

Table 2. *^{1}H-NMR Data* ($CDCl_3$) *for the Zinc(II) Complexes* **2b**, **3b**, **4b**, **5b**, *and* **6b** *of Corallistin B–E and Deuteroporphyrin IX, Respectively*[a])

	2b	**3b**	**4b**	**5b**	**6b**
Me–C(2)	3.20	3.33	3.37	3.45	3.47
H–C(3)	–	–	–	8.58	8.60
$CH_2(3^1)$	3.60	3.76	3.81	–	–
$Me(3^2)$	1.64	1.71	1.73	–	–
H–C(5)	9.23	9.44	9.53	9.39	9.38
Me–C(7)	3.40	3.60	3.62	3.58	3.58
H–C(8)	–	8.79	8.84	8.77	8.74
$CH_2(8^1)$	3.87	–	–	–	–
$Me(8^2)$	1.74	–	–	–	–
H–C(10)	9.42	9.49	9.56	9.49	9.42
Me–C(12)	–	3.46	3.48	3.47	3.44
$CH_2(12^1)$	4.81	–	–	–	–
$MeOOC(12^2)$	3.76	–	–	–	–
$CH_2(13^1)$	4.19	4.21	4.21	3.89	4.15
$CH_2(13^2)$	3.15	3.13	3.11	–	3.08
$Me(13^2)$	–	–	–	1.76	–
$MeOOC(13^3)$	3.70	3.71	3.65	–	3.66
H–C(15)	9.35	9.43	9.40	9.28	9.15
$CH^2(17^1)$	3.81	3.87	4.18	4.09	4.06
$CH_2(17^2)$	–	–	3.14	3.04	3.02
$Me(17^2)$	1.73	1.76	–	–	–
$MeOOC(17^3)$	–	–	3.68	3.67	3.67
Me–C(18)	3.34	3.42	3.42	3.29	3.29
H–C(20)	9.20	9.38	9.39	9.19	9.19

[a]) *J* Values within the Et and the CH_2CH_2COOMe groups are 7.5 and 8.0 Hz, respectively. Allylic couplings between Me protons and peripheral protons are 1.2 Hz.

In view of the potential utility of new porphyrins as phototherapeutic agents, we thought useful to functionalize the nucleus of the corallistins with groups that would allow further elaboration. To this purpose, we took the formylation reaction into consideration. Previous formylations of porphyrins invested on the *Vilsmayer* reaction albeit in different schemes. Thus, *Johnson* and *Oldfield* carried out the formylation of Ni^{II} complexes of etioporphyrins with $DMF/POCl_3$, isolating only products of monoformylation at *meso*-positions [14]. *Brockmann et al.* used the same reagent on Cu^{II} complexes of deuteroporphyrins carrying out the reactions at two different temperatures; at 0° they obtained only monoformylation products, at either a *meso*- or a β-position in about the same yields, whereas at 80° they obtained diformylated derivatives, which must have arisen *via* β-monoformylated intermediates [15]. *Nichol* used the same reagent, too, on Fe^{III} complexes; he observed with mesoporphyrins only monoformylation at C(10), with deuteroporphyrins products of both monoformylation at C(10) and diformylation at C(2) and C(10), and with protoporphyrins only formylation at the vinyl substituents [16]. *Montforts et al.* exposed Cu^{II} complexes of deuteroporphyrins to trimethyl orthoformate, observing only monoformylation products at C(3) or C(8) [17].

The above examples show that formylation may offer a general entry into new porphyrins functionalized at the nucleus, but that the methodology of *Johnson* and *Oldfield* [14], though most promising, is insufficiently investigated. Thus, we chose this

methodology [14] to carry out formylation of the Ni^{II} complexes of the corallistin methyl esters. Carrying out the reactions at 50°, we observed only monoformylation of the Ni^{II} complex of corallistin B methyl ester (**2a**) either at C(20) to give **2c**, or at C(10) to give **2d**. Formylations under similar conditions of the Ni^{II} complexes of **1a**, **3a**, and **5a** proved to be less selective, giving also products of further formylation at peripheral positions. Thus, the Ni^{II} complex of **1a** underwent formylation at the most reactive position C(5) (→monoformylated **1c**), and at the second most reactive position C(3) (→diformylated **1d**). With the Ni^{II} complex of **3a**, the most reactive and the second most reactive positions proved to be C(10) and C(8) (→**3c** and **3d**, resp.). Finally, we found that with the Ni^{II} complex of **5a**, the positions C(5) and C(10) compete for monoformylation giving both **5c** and **5e**, followed by diformylation of the former at C(3) (→**5d**) and of the latter at C(8) (→**5f**). The formylated Ni^{II} porphyrins were characterized by their ^{1}H-NMR spectra (*Table 3*).

Our results show that in the Ni^{II} complexes of the corallistin methyl esters, *meso*-positions are preferred to peripheral positions by the formylating reagent. In fact, while

Table 3. *^{1}H-NMR Chemical Shifts* ($CDCl_3$) *for the Formylation Products* **1c,d**, **2c,d**, **3c,d**, *and* **5c–f**, *of the Nickel(II) Complexes of the Methyl Esters of Corallistin A, B, C, and E, Respectively* [a])

	1c	**1d**	**2c**	**2d**	**3c**	**3d**	**5c**	**5d**	**5e**	**5f**
Me–C(2)	3.44	3.64	3.32	3.25	3.35	3.27	3.42	3.05	3.39	3.26
H–C(3)	9.57	–	–	–	–	–	9.51	–	8.60	8.16
$CH_2(3^1)$	–	–	3.72	3.67	3.78	3.27	–	–	–	–
$Me(3^2)$	–	–	1.68	1.70	1.71	1.60	–	–	–	–
OHC–C(3)	–	11.19	–	–	–	–	–	10.69	–	–
H–C(5)	–	–	9.29	9.22	9.52	9.25	–	–	9.33	8.66
OHC–C(5)	11.96	10.39	–	–	–	–	11.96	9.64	–	–
Me–C(7)	3.35	3.37	3.27	3.25	3.47	3.50	3.43	3.23	3.38	3.15
H–C(8)	–	–	–	–	9.59	–	8.67	8.40	9.52	9.52
$CH_2(8^1)$	3.74	3.81	3.74	3.84	–	–	–	–	–	–
$Me(8^2)$	1.69	1.72	1.68	1.70	–	–	–	–	–	–
OHC–C(8)	–	–	–	–	–	11.08	–	–	–	10.82
H–C(10)	9.56	9.62	9.46	–	–	–	–	9.10	–	–
OHC–C(10)	–	–	–	11.59	12.01	10.15	9.29	–	11.91	9.77
Me–C(12)	–	–	–	–	3.40	3.28	3.28	3.28	3.32	3.18
$CH_2(12^1)$	4.83	4.89	4.78	4.79	–	–	–	–	–	–
$MeOOC(12^2)$	3.75	3.77	3.74	3.75	–	–	–	–	–	–
$CH_2(13^1)$	4.19	4.24	4.13	4.04	4.10	4.03	3.77	3.72	3.71	3.64
$CH_2(13^2)$	3.15	3.06	3.13	3.08	3.06	3.04	–	–	–	–
$Me(13^2)$	–	–	–	–	–	–	1.70	1.70	1.64	1.65
$MeOOC(13^3)$	3.70	3.72	3.70	3.70	3.70	3.69	–	–	–	–
H–C(15)	9.53	9.60	9.36	9.33	9.52	9.32	9.43	9.11	9.36	9.09
$CH_2(17^1)$	3.79	3.83	3.70	3.67	3.80	3.77	4.09	3.92	4.06	3.97
$CH_2(17^2)$	–	–	–	–	–	–	3.07	2.98	3.05	3.02
$Me(17^2)$	1.71	1.72	1.68	1.70	1.70	1.70	–	–	–	–
$MeOOC(17^3)$	–	–	–	–	–	–	3.68	3.69	3.67	3.70
Me–C(18)	3.32	3.34	3.33	3.25	3.35	3.33	3.33	2.97	3.31	3.21
H–C(20)	9.48	9.55	–	9.30	9.54	9.35	9.44	8.60	9.41	9.07
OHC–C(20)	–	–	11.98	–	–	–	–	–	–	–

[a]) *J* Values within the Et and the CH_2CH_2COOMe groups are 7.5 and 8.0 Hz, respectively. Allylic couplings between Me protons and peripheral protons are 1.2 Hz.

several products of monoformylation at *meso*-positions were isolated (**1c**, **2c**, **2d**, **3c**, **5c**, **5e**), no product was observed of monoformylation at peripheral positions. Apparently, the formylating agent seeks preferentially *meso*-positions which are not flanked by two alkyl- or carboxyalkyl-substituted β-pyrrolic C-atoms. When all β-positions are substituted, such as in **2a**, formylation only occurs very sluggishly and results in poor yields. However, once a *meso*-position has undergone formylation, peripheral C-atoms can react (→**1d**, **3d**, **5d**, **5f**) and, interestingly, the β-position closest to the formylated *meso*-position is formylated, as observed with **5d** and **5f**. This is at variance with previous cases. Thus, both *Bockman et al.* with Cu^{II} deuteroporphyrin complexes [15] and *Nichol* with Fe^{III} deuteroporphyrin complexes [16] observed that diformylation takes place at positions far apart from one another along the porphyrin nucleus, resulting in 3,10- or 3,8-diformylated products. In conclusion, our observations establish a protocol for the chemical functionalization of the corallistins which may be of guidance in the synthesis of functionalized porphyrins with a pattern of substitution different from that observed from other porphyrins. This may be of interest in view of devising biologically active porphyrins.

We thank Prof. *C. Lévi, Musée National d'Histoire Naturelle,* Paris, for the sponge identification. This work was carried out within the collaborative program '*ORSTOM-CNRS* on Marine Substances of Biological Interest'. The work in Trento was supported by *MURST* (Progetti di Interesse Nazionale) and *CNR*, Roma.

Experimental Part

1. *General.* See [10]. Moreover, NOE (differential, in $CDCl_3$) is indicated as irradiated proton(s)→ % NOE on the observed proton(s).

2. *Isolation of the Corallistins and Preparation of Zinc(II) Complexes.* The sponge was collected at the basis of the south New Caledonian coral reef at a depth of 350 m [10]. The residue from the treatment of the EtOH extract of the sponge with CH_2N_2 [10] was further examined by HPLC (hexane/AcOEt/(i-Pr)NH_2 93:7:0.2), isolating materials at t_R 9, 10.2, 15.5, and *ca.* 18 min, which correspond to *corallistin C methyl ester* (**3a**), *E methyl ester* (**5a**), *B methyl ester* (**2a**), and a mixture of the *corallistin A methyl ester* (**1a**), *corallistin D methyl ester* **4a**, and *deuteroporphyrin IX methyl ester* (**6a**), respectively. Pure **2a** was obtained by further subjecting the above sample to reversed-phase HPLC (MeOH/H_2O 96:4, t_R 16.3 min). On treatment with $Zn(AcO)_2$ [10], the above samples of **2a**, **3a**, and **5a** gave their Zn^{2+} complexes **2b**, **3b**, and **5b** which were collected by reversed-phase HPLC (MeOH/H_2O 97:3, t_R 13.2, 13.6, and 11.5 min, resp.). Separately, the mixture **1a**/**4a**/**6a** was treated with $Zn(AcO)_2$ [10] to give, after separation by reversed-phase HPLC (MeOH/H_2O 92:8), the Zn^{2+} complexes **6b**, **1b**, and **4b** at t_R 9.3, 10.5, and 11.5 min, resp.

3. *Formylated Nickel(II) Complexes.* A soln. of **5a** (45 mg), **3a** (32 mg), or **2a**/**1a** 9:1 (52 mg) each in 20 ml of $CHCl_3$ was added to a soln. of 4 mol-equiv. of $Ni(AcO)_2 \cdot 4H_2O$ in 30 ml of ethyleneglycol. The mixtures were heated under reflux for 1 h, whereby **5a**, **3a**, and **1a** were completely, and **2a**, after 1 additional h, for only 80%, bound by Ni^{II}. Each mixture was then cooled, diluted with 3 volumes of H_2O, and extracted 3 times with $CHCl_3$. Evaporation of the org. phase gave the Ni^{II} porphyrin. Then, freshly distilled $POCl_3$ (1.4 ml) was added dropwise to dry DMF (1 ml) cooled in an ice-bath, this soln. left at r.t. for 0.5 h and then warmed on a water bath at 50°, and the above Ni^{II} porphyrin dissolved in 30 ml of dried 1,2-dichloroethane added. Each mixture was stirred for 0.5 h at 50°, then sat. aq. NaOAc soln. (40 ml) added with stirring, which was continued for further 2 h at 50°. The mixtures were cooled, the aq. phase extracted with $CHCl_3$, and the combined org. phase evaporated. The residues were subjected to reversed-phase HPLC (MeCN) to give **5c**/**5e** (8.5 mg), **5d**/**5f** (4.0 mg), **3c** (10 mg), **3d** (17 mg), unreacted corallistin B methyl ester Ni^{II} complex (15 mg), **2c** (1 mg), **2d** (0.5 mg), **1c** (2 mg), and **1d** (1 mg), resp.

4. *5-Formylcorallistin A Methyl Ester Nickel(II) Complex* (= *Diacetato{methyl 8,17-Diethyl-5-formyl-12-[(methoxycarbonyl)methyl]-2,7,18-trimethylporphyrin-13-propanoato}nickel(II)*; **1c**). NOE: 3.32→11% on 9.48; 3.35→14% on 11.96; 3.44→12% on 9.48 and 11% on 9.57; 3.74→1% on 3.35 and 12% on 9.56; 9.56→5% on

4.83; 3.79→7% on 9.53 and 1% on 3.32; 4.19→4% on 4.83 and 9% on 9.53; 9.48→4% on 3.32 and 4% on 3.44; 9.57→2.5% on 3.44 and 6% on 11.96; 11.96→10% on 9.57 and 4% on 3.35.

5. *3,5-Diformylcorallistin A Methyl Ester Nickel(II) Complex* (= *Diacetato{methyl 8,17-Diethyl-3,5-diformyl-12-[(methoxycarbonyl)methyl]-2,7,18-trimethylporphyrin-13-propanoato}nickel(II)*; **1d**). NOE: 3.34→8% on 9.55; 3.37→10% on 10.39; 3.64→5% on 9.55 and 3% on 11.19; 3.81→1% on 3.37 and 7% on 9.62; 3.83→7% on 9.60 and 1% on 3.34; 4.24→4% on 4.89 and 7% on 9.60; 4.89→12% on 9.62 and 12% on 4.24; 9.55→2% on 3.34 and 1% on 3.64; 9.62→5% on 4.89; 10.39→7% on 11.19 and 4% on 3.37; 11.19→1% on 3.64 and 8% on 10.39.

6. *Corallistin B Methyl Ester* (= *Methyl 3,8,17-Triethyl-12-[(methoxycarbonyl)methyl]-2,7,18-trimethylporphyrin-13-propanoate*; **2a**). MS: 594 (100, M^+), 579 (12, $[M-15]^+$), 521 (16).

7. *Corallistin B Methyl Ester Zinc(II) Complex* (= *Diacetato{methyl 3,8,17-Triethyl-12-[(methoxycarbonyl)methyl]-2,7,18-trimethylporphyrin-13-propanoato}zinc(II)*; **2b**). NOE: 3.20→12% on 3.60; 3.34→5% on 9.20; 3.60→1% on 9.23; 3.40→5% on 9.23 and 2% on 3.87; 3.81→3% on 9.35 and 1% on 3.34; 3.87→1% on 3.40 and 3% on 9.42; 4.81→7% on 9.42 and 1% on 4.19; 4.19→4% on 9.35 and 2% on 4.81.

8. *20-Formylcorallistin B Methyl Ester Nickel(II) Complex* (= *Diacetato{methyl 3,8,17-Triethyl-20-formyl-12-[(methoxycarbonyl)methyl]-2,7,18-trimethylporphyrin-13-propanoato}nickel(II)*; **2c**). NOE: 3.27→10% on 9.29; 3.32→10% on 11.98; 3.33→11% on 11.98; 3.70→5% on 9.36; 3.72→5% on 9.29; 3.74→5% on 9.46; 4.78→7% on 9.46; 4.13→4% on 9.36; 9.29→2% on 3.27; 9.46→2% on 4.78.

9. *10-Formylcorallistin B Methyl Ester Nickel(II) Complex* (= *Diacetato{methyl 3,8,17-Triethyl-10-formyl-12-[(methoxycarbonyl)methyl]-2,7,18-trimethylporphyrin-13-propanoato}nickel(II)*; **2d**). NOE: 3.25→7% on 9.22 and 12% on 9.30; 3.67→9% on 9.22 and 7% on 9.33; 3.84→10% on 11.59; 4.04→9% on 9.33; 4.79→2% on 11.59; 9.22→6% on 3.25; 9.30→2% on 3.25.

10. *Corallistin C Methyl Ester* (= *Methyl 3,17-Diethyl-2,7,12,18-tetramethylporphyrin-13-propanoate*; **3a**). UV ($CHCl_3$): 619 (1500), 565 (3100), 530 (5100), 497 (8400), 399 (126500). MS: 509 (100, M^+), 494 (16, $[M-15]^+$), 436 (60).

11. *Corallistin C Methyl Ester Zinc(II) Complex* (= *Diacetato(methyl 3,17-Diethyl-2,7,12,18-tetramethylporphyrin-13-propanoato)zinc(II)*; **3b**). NOE: 3.33→4% on 9.41; 3.76→1% on 3.33 and 5% on 9.44; 3.60→3% on 9.44 and 3% on 8.79; 8.79→1% on 3.60 and 3% on 9.49; 9.49→5% on 8.79 and 3% on 3.46; 3.46→7% on 9.49; 4.21→1% on 3.46 and 5% on 9.43; 3.87→4% on 9.43 and 1% on 3.42; 3.42→4% on 9.38.

12. *10-Formylcorallistin C Methyl Ester Nickel(II) Complex* (= *Diacetato(methyl 3,17-Diethyl-10-formyl-2,7,12,18-tetramethylporphyrin-13-propanoato)nickel(II)*; **3c**). NOE: 3.35→10% on 9.54; 3.78→2% on 3.35 and 8% on 9.52; 9.52→1% on 3.47; 3.47→4% on 9.52 and 1% on 9.59; 3.80→7% on 9.52 and 2% on 3.35; 9.59→5% on 12.01; 12.01→4% on 9.59 and 1% on 3.40; 3.40→8% on 12.01; 4.10→3% on 3.40 and 6% on 9.52; 9.52→1% on 4.10.

13. *8,10-Diformylcorallistin C Methyl Ester Nickel(II) Complex* (= *Diacetato(methyl 3,17-Diethyl-8,10-diformyl-2,7,12,18-tetramethylporphyrin-13-propanoato)nickel(II)*; **3d**). NOE: 3.27→1% on 9.35; 3.28→1% on 10.15 and 1% on 4.03; 3.33→2% on 9.35; 3.60→1% on 3.27 and 2% on 9.25; 3.50→2% on 9.25 and 1% on 11.08; 3.77→5% on 9.32 and 1% on 3.33; 4.03→1% on 3.28 and 4% on 9.32; 9.25→1% on both 3.60 and 3.50; 9.32→3% on 4.03 and 4% on 3.77; 9.35→2% on 3.33 and 1% on 3.27; 10.15→2% on 11.08 and 1% on 3.28.

14. *Corallistin D Methyl Ester* (= *Dimethyl 3-Ethyl-2,7,12,18-tetramethylporphyrin-13,17-dipropanoate*; **4a**). MS: 566 (100, M^+), 551 (5, $[M-15]^+$), 493 (36).

15. *Corallistin D Methyl Ester Zinc(II) Complex* (= *Diacetato(methyl 3-Ethyl-2,7,12,18-tetramethylporphyrin-13,17-dipropanoato)zinc(II)*; **4b**). NOE: 3.37→5% on 9.39; 3.81→1% on 3.37 and 5% on 9.53; 3.62→5% on 9.53 and 6% on 8.84; 8.84→1% on 3.62 and 6% on 9.56; 9.56→7% on 8.84 and 3% on 3.48; 4.21→2% on 3.48 and 5% on 9.40; 4.18→5% on 9.40 and 2% on 3.42; 3.42→5% on 9.39; 9.39→2% on 3.37.

16. *Corallistin E Methyl Ester* (= *Methyl 13-Ethyl-2,7,12,18-tetramethylporphyrin-17-propanoate*; **5a**). UV ($CHCl_3$): 619 (1400), 565 (2700), 530 (4300), 497 (7800), 398 (118600). MS: 480 (100, M^+), 465 (9, $[M-15]^+$), 407 (64).

17. *Corallistin E Methyl Ester Zinc(II) Complex* (= *Diacetato(methyl 13-Ethyl-2,7,12,18-tetramethylporphyrin-17-propanoato)zinc(II)*; **5b**). NOE: 3.29→4% on 9.19; 3.45→4% on both 9.19 and 8.58; 3.47→5% on 9.49; 3.58→5% on 9.39 and 3% on 8.77; 3.89→1% on 3.47 and 5% on 9.28; 4.09→3% on 9.28 and 1% on 3.29; 9.39→10% on 8.58 and 2% on 3.58; 9.49→6% on 8.77 and 2% on 3.47.

18. *5-Formylcorallistin E Methyl Ester Nickel(II) Complex* (= *Diacetato(methyl 13-Ethyl-5-formyl-2,7,12,18-tetramethylporphyrin-17-propanoato)nickel(II)*; **5c**). NOE: 3.28→7% on 9.29; 3.33→5% on 9.44; 3.42→4% on 9.44 and 7% on 9.51; 3.43→8% on 11.96 and 5% on 8.67; 3.77→1% on 3.28 and 7% on 9.43; 4.09→9% on 9.43 and 2% on 3.33; 8.67→1% on 3.43 and 5% on 9.29; 9.29→4% on 8.67; 9.44→2% on both 3.33 and 3.40; 9.51→1% on 11.96; 11.96→4% on 9.51.

19. *3,5-Diformylcorallistin E Methyl Ester Nickel(II) Complex* (= *Diacetato(methyl 13-Ethyl-3,5-diformyl-2,7,12,18-tetramethylporphyrin-17-propanoato)nickel(II)*; **5d**). NOE: 2.97→4% on 8.60; 3.05→4% on 8.68 and 3% on 10.69; 3.23→4% on 9.64 and 3% on 8.40; 3.28→6% on 9.10; 3.72→1% on 3.28 and 4% on 9.11; 3.92→6% on 9.11 and 1% on 2.97; 8.40→6% on 9.10; 8.60→2% on 2.97 and 1% on 3.05; 9.10→3% on 8.40 and 2% on 3.28; 9.64→4% on 10.69 and 2% on 3.23; 10.69→1% on 3.05 and 3% on 9.64.

20. *10-Formylcorallistin E Methyl Ester Nickel(II) Complex* (= *Diacetato(methyl 13-Ethyl-10-formyl-2,7,12,18-tetramethylporphyrin-17-propanoato)nickel(II)*; **5e**). NOE: 3.31→6% on 9.41; 3.32→8% on 11.91; 3.39→4% on 9.41 and 4% on 8.60; 3.71→1% on 3.32 and 8% on 9.36; 4.06→8% on 9.36 and 1% on 3.31; 8.60→1% on 3.39 and 6% on 9.33; 9.33→6% on 8.60 and 4% on 3.38; 3.38→8% on 9.33 and 6% on 9.52; 9.36→2% on 4.06; 9.41→4% on both 3.31 and 3.39; 9.52→4% on 11.91; 11.91→2% on 9.52 and 3% on 3.32.

21. *8,10-Diformylcorallistin E Methyl Ester Nickel(II) Complex* (= *Diacetato(methyl 13-Ethyl-8,10-diformyl-2,7,12,18-tetramethylporphyrin-17-propanoato)nickel(II)*; **5f**). NOE: 3.15→2% on 8.66 and 4% on 10.82; 3.18→3% on 9.77; 3.21→5% on 9.07; 3.26→2% on 8.16 and 7% on 9.07; 3.64→1% on 3.18 and 5% on 9.09; 3.97→7% on 9.09 and 1% on 3.21; 8.16→2% on 8.66; 8.66→3% on 8.16 and 2% on 3.15; 9.07→2% on 3.21 and 2% on 3.26; 9.77→4% on 10.82 and 2% on 3.18; 10.82→1% on 3.15 and 4% on 9.77.

22. *Deuteroporphyrin IX Methyl Ester* (= *Dimethyl 2,7,12,18-Tetramethylporphyrin-13,17-dipropanoate*; **6a**). MS: 538 (100, $M^{+\cdot}$), 523 (4, $[M-15]^{+}$), 465 (42).

23. *Deuteroporphyrin IX Methyl Ester Zinc(II) Complex* (= *Diacetato(methyl 2,7,12,18-Tetramethylporphyrin-13,17-dipropanoato)zinc(II)*; **6b**). NOE: 3.29→4% on 9.19; 3.44→2% on 9.42; 3.47→1% on both 9.19 and 8.60; 3.58→3% on 9.38 and 1% on 8.74; 4.06→3% on 9.15 and 1% on 3.29; 4.15→4% on 9.15 and 1% on 3.44; 9.15→2% on 4.06 and 4% on 4.15; 9.19→2% on 3.47 and 1% on 3.29; 9.38→1% on 3.58; 9.42→1% on 3.44.

REFERENCES

[1] I. Verne-Mismer, R. Ocampo, H.J. Callot, P. Albrecht, *Tetrahedron Lett.* **1990,** *31,* 1751.
[2] R. Bonnet, P.J. Burke, A. Reszka, *Fuel* **1987,** *66,* 515.
[3] M.I. Chicarelli, J.R. Maxwell, *Tetrahedron Lett.* **1986,** *27,* 4653.
[4] G.Y. Kennedy, *Ann. N. Y. Acad. Sci.* **1975,** *244,* 662.
[5] R. Bonnet, E.J. Head, P.J. Herring, *J. Mar. Biol. Ass. U.K.* **1979,** *59,* 565.
[6] A. Pelter, J.A. Ballantine, V. Ferrito, V. Jaccarini, A.F. Psaila, P.J. Schembri, *J. Chem. Soc., Chem. Commun.* **1976,** 999.
[7] K.L. Rinehart, V. Kishore, R.C. Bible, R. Sakai, D.W. Sullins, K.M. Li, *J. Nat. Prod.* **1988,** *51,* 1; K.L. Rinehart, *Pure Appl. Chem.* **1989,** *61,* 521.
[8] P. Karuso, P.R. Bergquist, J.S. Buckleton, R.C. Cambie, G.R. Clark, C.E.F. Rickard, *Tetrahedron Lett.* **1986,** *27,* 2177.
[9] a) K. Sakata, K. Yamamoto, H. Ishikawa, A. Yagi, H. Etoh, K. Ina, *Tetrahedron Lett.* **1990,** *31,* 1165; b) K. Yamamoto, K. Sakata, N. Watanabe, A. Yagi, L.S. Brinen, J. Clardy, *ibid.* **1992,** *33,* 2587.
[10] M. D'Ambrosio, A. Guerriero, C. Debitus, O. Ribes, B. Richer de Forges, F. Pietra, *Helv. Chim. Acta* **1989,** *72,* 1451.
[11] P. Yon-Hin, A.I. Scott, *Tetrahedron Lett.* **1991,** *32,* 4231.
[12] K.R. Adams, M.C. Berenbaum, R. Bonnett, A.N. Nizhnik, A. Salgado, M.A. Valles, *J. Chem. Soc., Perkin Trans. 1* **1992,** 1465; T. Ando, Y. Suzuki, R. Geka, K. Irie, K. Koshimizu, T. Takemura, S. Nakajima, I. Sakata, *Tetrahedron Lett.* **1991,** *32,* 5107.
[13] N. Ono, M. Bougauchi, K. Maruyama, *Tetrahedron Lett.* **1992,** *33,* 1629.
[14] A.W. Johnson, D. Oldfield, *J. Chem. Soc. (C)* **1966,** 794.
[15] H. Brockmann, Jr., K.-M. Bliesener, H.H. Inhoffen, *Liebigs Ann. Chem.* **1968,** *718,* 148.
[16] A.W. Nichol, *J. Chem. Soc. (C)* **1970,** 903.
[17] F.P. Montforts, G. Scheurich, A. Meier, G. Haake, F. Höper, *Tetrahedron Lett.* **1991,** *32,* 3477.