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Novel Chlorins with a δ-Lactone Ring fused at Ring D

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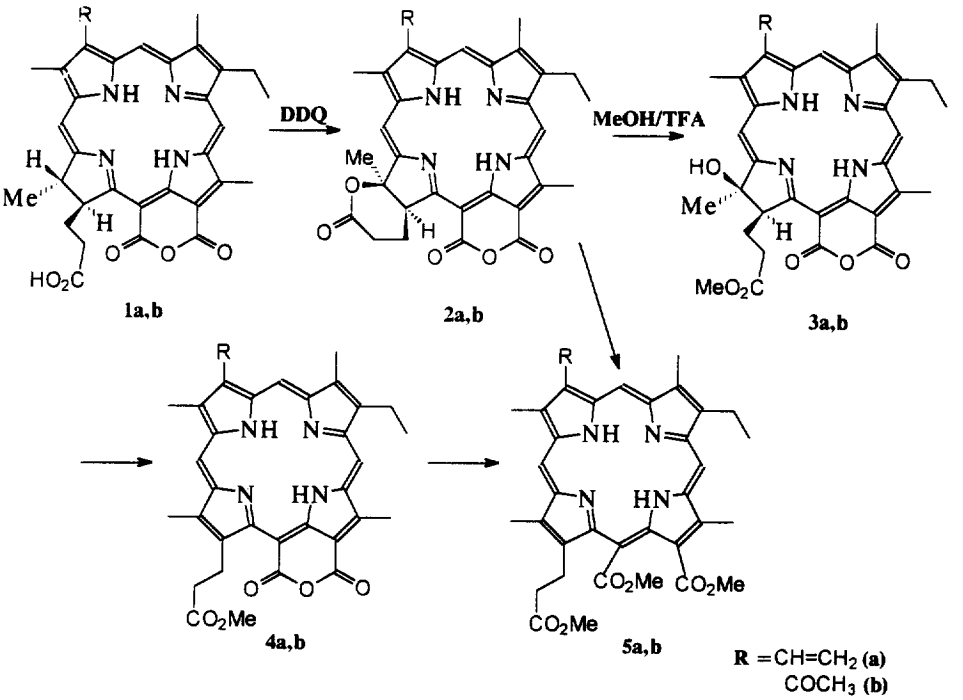
Abstract: Reaction of purpurins (**1a,b**) with DDQ resulted in oxidative ring closure at ring D to give novel δ-lactones (**2a,b**), mild treatment of which with TFA/methanol gave chlorins (**3a,b**) possessing a hydroxy group at C-18. Prolonged treatment of (**3a,b**) with TFA resulted in their dehydration and the formation of porphyrins (**4a,b**). © 1997 Elsevier Science Ltd.

It has been shown recently that some marine organisms contain metal-free chlorins possessing strong antioxidant activity.[1] A characteristic feature of these compounds is the presence of an additional seven-membered ring with one or two oxygen atoms.[2] It is interesting that about ten years before the first isolation of such compounds from natural sources[3], Eschenmoser *et al.* had reported the chemical synthesis of cyclo(pyro)pheophorbide *a*.[4] The additional ring was formed by a Claisen-type intramolecular condensation of the methyl ester of the propionic acid residue with the cyclopentanone ring.

However, the propionic acid residue is able to form rings at positions other than the 13^2-C of pyropheophorbide. Here we report a new reaction in which the 17-propionic acid group of purpurins in the presence of 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) reacts with position 18 of ring D. The use of DDQ for the dehydrogenation of hydrogenated porphyrins is widely applied. Thus we had used this reaction to dehydrogenate bacteriopurpurin to give 3-acetyl-3-devinylpurpurin 18 (**1b**), which was further transformed into the porphyrin (**4b**).[5] The new reaction interested us as both an approach to preparing novel chlorins at present unknown in nature and to elucidating the pathways of transformation of chlorins into porphyrins. As starting compounds in the present study we chose purpurin 18 (**1a**) and 3-acetyl-3-devinylpurpurin 18 (**1b**).

The procedure was as follows: a solution of purpurin 18 (3 mg) in chloroform (15 ml) was treated with excess DDQ for 45 min at room temperature. After purification by TLC, the lactone (**2a**) was obtained in 51% yield. The electronic absorption spectrum showed an intense maximum at 699 nm and a Soret band at 411 nm (see figure). The product appeared to be quite stable and did not decompose during storage. Its mass spectrum[6] contained an abundant peak of a molecular ion with *m/z* 562. Confirmation of the structure of the lactone was provided by its ^{1}H NMR spectrum[7]. In contrast to that of the starting purpurin 18, it did not contain a quartet at δ 4.38 ppm (1H), and the doublet at δ 1.73 ppm (3H) was replaced with a singlet at δ 2.15 ppm, thus indicating the absence of a proton at position 18 and the presence of an angular 18-CH_3 group.

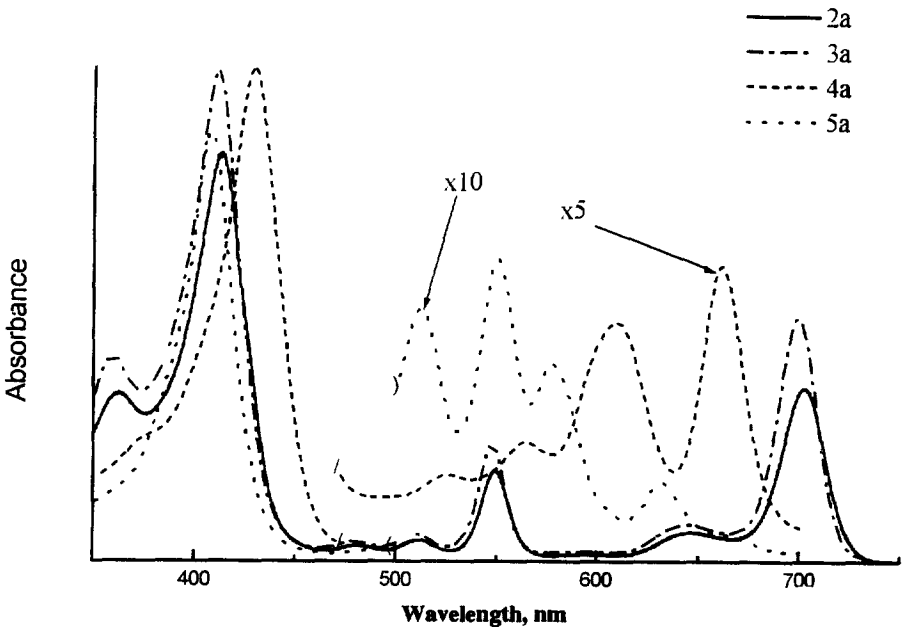
The oxidative reaction with 3-acetyl-3-devinylpurpurin 18 (**1b**) proceeded similarly. In the absorption spectrum of the lactone (**2b**) obtained, the major band was shifted hypsochromically by 6 nm with respect to that in the starting purpurin (λ_{max} 725 nm).[5] The mass spectrum contained an abundant [M+1] peak with *m/z* 579.7. The ^{1}H NMR spectrum did not show a signal for 18-H; and the 18-methyl group gave a singlet at δ 2.18 ppm.



An interesting effect was observed on cleaving the lactones (**2a, 2b**) with TFA and methanol under mild conditions. Instead of the expected porphyrins, we obtained more polar compounds, which on the basis of their mass and ^{1}H NMR spectra were formulated as the previously unknown chlorins with an extra hydroxy group on ring D. 18-Hydroxypurpurin 18 (**3a**) and 18-hydroxy-3-acetyl-3-devinylpurpurin 18 (**3b**) showed peaks with *m/z* 594.1 and 610.6, respectively, in their mass spectra; the ^{1}H NMR spectrum of the chlorin (**3a**) contained an additional singlet at δ 4.78 ppm, which was assigned to the proton of the hydroxy group. The 18-methyl group was still represented by a singlet (not a doublet characteristic of the natural chlorins) at δ 1.83 ppm. Compound (**3b**) had the corresponding resonances at δ 4.80 and δ 1.85 ppm, respectively.

Compounds (**3a**) and (**3b**) exhibited electronic absorption spectra (see figure) characteristic of purpurins (intense absorption bands at 702 and 725 nm, respectively). Despite the presence of the hydroxy group, these compounds appeared to be reasonably stable: no dehydration was observed during chromatography on silica, crystallization, and storage. These properties make these substances valuable as promising intermediates in the synthesis of new photosensitizers and, possibly, as model systems to mimic primary processes of natural photosynthesis.

More forcing treatment of the 18-hydroxypurpurins (**3a**) and (**3b**) with TFA resulted in dehydration, thus giving the purpuroporphyrins (**4a**) and (**4b**) with unusual absorption spectra (see figure). Along with the Soret band, these spectra also contained intense maxima at 661 (**4a**) and 662 nm (**4b**). The mass spectra of the purpuroporphyrins (**4a**) and (**4b**) showed molecular ions at *m/z* 576.6 and 592.6 nm, respectively. The ^{1}H NMR spectra of (**4a**) and (**4b**) were of the usual porphyrin type. Treatment of the lactones (**2a**) and (**2b**) with methanolic alkali followed by esterification with diazomethane afforded porphyrins (**5a**) and (**5b**).



UV-Vis spectra ($CHCl_3$) of purpurin-18-lactone (**2a**), 18-hydroxypurpurin 18 methyl ester (**3a**), purpuroporphyrin 18 methyl ester (**4a**) and chloroporphyrin p_6 methyl ester (**5a**).

The formation of lactones (**2a, 2b**) here is reminiscent of the formation of lactones from open-chain amides in the corrinoid series under various oxidative conditions. In that series γ-lactones (both fused and spiro) appear to be formed preferentially.[8]

It should be emphasized that the cyclization described here is observed for compounds with a free propionic acid residue. When oxidizing methyl esters of purpurin 18 and 3-acetyl-3-devinylpurpurin 18 with DDQ, we obtained porphyrins (**4a**) and (**4b**) directly. Hence, dehydrogenation of chlorins to porphyrins with DDQ depends on the nature of the substituent at position 17 and can follow two pathways.

The ability of the propionic acid residue to give stable six-membered lactones at ring D should be taken into consideration when performing oxidative transformations of chlorophyll derivatives, and could possibly be relevant in the search for new naturally-occurring or naturally-derived chlorins.

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REFERENCES AND NOTES

1. Montforts, F.-P.; Gerlach, B.; Höper, F., *Chem. Rev.*, **1994**, *94*, 327-347.

2. Ma, L.; Dolphin, D., *J. Org. Chem.*, **1996**, *61*, 2501-2510.

3. Karuso, P.; Berquist, P.R.; Buckleton, J.S.; Cambie, R.C.; Clark, G.R.; Rickard, C.E.F., *Tetrahedron Lett.*, **1986**, *27*, 2177-2180.

4. Falk, H.; Hoornaert, G.; Isenring, H.P.; Eschenmoser, A., *Helv. Chim. Acta*, **1975**, *58*, 2347-2356.

5. Kozyrev, A.N.; Efremov, A.; Efremova, O.; Perepyolkin, P. Yu.; Mironov, A.F. *Proc. Soc.Photo-Opt. Instrum. Eng.*, **1994**, *2325*, 297-305.

6. Mass spectra were measured on a MSBKh instrument (SELMI, Sumy, Ukraine). Ionization was caused by ^{252}Cf fission products, and a time-of-flight monitoring ion analyzer was employed.

7. ^1H NMR data (Bruker MSL 200, $CDCl_3$, δ, ppm):

Purpurin 18 δ-lactone (17^4, 18)(2a): 9.61 s, 9.51 s, 8.90 s (5-H, 10-H, 20-H), 7.90 dd (3^1-CH), 6.23dd, 6.28 dd (3^2-CH_2), 5.58 dd (17-H), 3.72 s (12-CH_3), 3.62 q (8^1-CH_2), 3.38 s (2-CH_3), 3.17 s (7-CH_3), 2.96 m (17^1-CH_2), 2.46 m (17^2-CH_2), 2.23 m (17^1, 17^2-CH_2), 2.16 s (18-CH_3), 1.64 t (8^2-CH_3).

3-Acetyl-3-devinylpurpurin 18 δ-lactone (17^4, 18) (2b): 10.18 s, 9.73 s, 9.00 s (5-H, 10-H, 20-H), 5.62 dd (17-H), 3.70 s (12-CH_3), 3.63 s (2-CH_3), 3.59 q (8^1-CH_2), 3.20 s (3-CH_3), 3.17 s (7-CH_3), 2.98 m (17^1-CH_2), 2.49 m (17^2-CH_2), 2.23 m (17^1, 17^2-CH_2), 2.18 s (18-CH_3), 1.69 t (8^2-CH_3).

18-Hydroxypurpurin 18 methyl ester (3a): 9.62 s, 9.39 s, 8.82 s (5-H, 10-H, 20-H), 7.86 dd (3^1-CH), 6.22 dd (3^2-CH_2), 6.21 dd (3^2-CH_2), 5.32 dd (17-H), 4.78 s (18-OH), 3.79 s (12-CH_3), 3.62 q (8^1-CH_2), 3.34 s (17^4-CH_3), 3.26 s (2-CH_3), 3.17 s (7-CH_3), 2.35 m (17^1, 17^2 -CH_2), 1.83 s (18-CH_3), 1.66 t (8^2-CH_3).

18-Hydroxy-3-acetyl-3-devinylpurpurin 18 methyl ester (3b): 10.00 s, 9.70 s, 9.00 s (5-H, 10-H, 20-H), 5.38 dd (17-H), 4.80 s (18-OH), 3.83 s (12-CH_3), 3.66 q (8^1-CH_2), 3.57 s (17^4-CH_3), 3.30 s (2-CH_3), 3.20 s (3-CH_3), 3.19 s (7-CH_3), 2.60 m (17^2-CH_2), 2.26 m (17^1-CH_2), 1.85 s (18-CH_3), 1.66 t (8^2-CH_3).

Purpuroporphyrin 18 methyl ester (4a): 9.43 s, 9.30 s, 8.85 s (5-H, 10-H, 20-H), 7.93 dd (3^1-CH), 6.26, 6.18 dd (3^2-CH_2), 3.88 t (17^1-CH_2), 3.78 q (8^1-CH_2), 3.52 s (17^4-CH_3), 3.43 s, 3.33 s, 3.28 s, 3.20 s (2-CH_3, 7-CH_3, 12-CH_3, 18-CH_3), 3.10 t (17^2-CH_2), 1.62 t (8^2 -CH_3).

3-Acetyl-3-devinylpurpuroporphyrin 18 methyl ester (4b): 10.35 s, 9.36 s, 8.85 s (5-H, 10-H, 20-H), 3.89 (q, 8^1-CH_2), 3.88 (t, 17^1-CH_2), 3.72 s (17^4-CH_3), 3.60 s, 3.53 s, 3.53 s, 3.34 s, 3.28 s (2-CH_3, 7.CH_3, 12-CH_3, 18-CH_3, 3^1-CH_3), 3.05 t (17^2-CH_2), 1.59 t (8^2-CH_3).

Chloroporphyrin p_6 trimethyl ester (5a): 10.10 s, 10.05 s, 9.93 s (5-H, 10-H, 20-H), 8.08 dd (3^1-CH), 6.22, 6.11 dd (3^2-CH_2), 4.42 s, 4.30 s (13-CH_3, 15-CH_3), 4.04 t (17^1 -CH_2), 4.01 q (8^1-CH_2), 3.80 s (17^4-CH_3), 3.67 s 3.61 s, 3.54 s, 3.52 s (2-CH_3, 7-CH_3, 12-CH_3, 18-CH_3), 3.07 t (17^2-CH_2), 1.80 t (8^2-CH_3).

3-Acetyl-3-devinylchloroporphyrin p_6 trimethyl ester (5b): 10.27 s, 9.85 s, 9.67 s (5-H, 10-H, 20-H), 4.46 s, 4.32 s (13-CH_3, 15-CH_3), 4.06 t (17^1-CH_2), 3.98 q (8^1-CH_2), 3.80 s (17^4-CH_3), 3.63 s, 3.59 s, 3.50 s, 3.47 s (2-CH_3, 7-CH_3, 12-CH_3, 18-CH_3), 3.16 s (3^1-CH_3), 3.03 t (17^2-CH_2), 1.76 t (8^2-CH_3).

8. Bonnett, R. Reactions of the Corrin Macrocycle. In *Vitamin B_{12}. Volume 1: Chemistry*; Dolphin, D., Ed.; John Wiley: New York and Chichester, 1982; pp. 226-230.

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