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Studies on Steroids. XXXIX.[1] Sterol Profiles of Red Algae. (2)[2]

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Five species of red algae were examined for sterols. Desmosterol was identified in *Porphyra tenera*, *Ptilota pectinata* and *Rhodymenie palmate* and the last algae was found to contain liagosterol (I) and cholesta-5,25-dien-3β,23-diol (II)

In the previous report,[2] we have described the sterol components in twelve different species of red algae belonging to orders Gelidiales, Cryptonemiales and Gigartinales. In that investigations a variety of 5,6-dihydrosterol (stanol) in which cholestanol was the major one, was identified in four species. Another noteworthy was that desmosterol was not detected in any of these twelve species although this sterol has appeared to be widely distributed in red algae.[4] Desmosterol may be a suitable starting compound for synthesis of biologically active steroids, *e.g.*, active forms of vitamin D_3.[5] Now we have extended the search for sterols to orders Bangiales (1 species) and Rhodymeniales (4 species).

In the same manner as described previously,[2] sterols in unsaponifiable fractions of algae were analyzed as their trimethylsilyl ethers by means of gas chromatograph–mass spectrometry (GC–MS) technique. Table I shows the estimations of cholesterol and desmosterol contents in the algae. GC patterns of *Odonthalia corymbifera* and *Laurencia nipponica* were extremely simple, indicating cholesterol almost the sole sterol in these species. *Porphyra tenera* (commercial *Nori*) contained desmosterol in addition to cholesterol. The other two algae, *i.e.*, *Ptilota pectinata* and *Rhodymenia palmata* (dulse) showed complex sterol profiles. Besides cholesterol and desmosterol the following sterols were detected in *P. pectinata*: 24-dimethylchola-5,22-dien-3β-ol, 24-methylenecholesterol and isofucosterol. *R. palmata* may be one of the most extensively studied algae on sterol components, and desmosterol has been reported as the

Table I. Amounts of Cholesterol and Desmosterol in Algae[a]

Algae	Cholesterol (%)	Desmosterol (%)
Bangiales		
Porphyra tenera Kjellman (Asakusanori)	0.006	0.002
Rhodymeniales		
Odonthalia corymbifera J. Agardh (Hakesanokogirihiba)	0.004	—
Laurencia nipponica (Urasozo)	0.18	—
Ptilota pectinata Kjellman (Kushibenihiba)	0.01	0.003
Rhodymenia palmata Greville (Darusu)	0.001	0.003

a) Estimated gas chromatographically and expressed in % concentrations based on dry weight of algae.

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[2] Part 1: I. Chardon-Loriaux, M. Morisaki, and N. Ikekawa, *Phytochemistry*, **15**, 723 (1976).
[3] Location: *Ookayama, Meguro-ku, Tokyo, 152, Japan.*
[4] *a*) G.F. Gibbons, L.J. Goad, and T.W. Goodwin, *Phytochemistry*, **6**, 677 (1967); *b*) A. Alcaide, M. Devys, and M. Barbier, *ibid.*, **7**, 329 (1968); *c*) D.R. Idler, A. Saito, and P. Wiseman, *Steroids*, **11**, 465 (1968); *d*) J.P. Ferezou, M. Devys, J.P. Allais and M. Barbier, *Phytochemistry*, **12**, 593 (1974).
[5] N. Ikekawa, M. Morisaki, N. Koizumi, Y. Kato, and T. Takeshita, *Chem. Pharm. Bull.* (Tokyo), **23** 695 (1975); N. Ikekawa and M. Morisaki, *Farumashia*, **10**, 319 (1974).

major one in British,[4a] Canadian[4c] and French[4d] dulse. In accordance with these previous findings, *R. palmata* presently harvested in the sea near to Hokkaido, Japan has also been found to contain this sterol as the principal one. GC-MS analysis (Fig. 1) indicated the coexistence of 22-dehydrocholesterol, cholesterol and 24-methylenecholesterol.

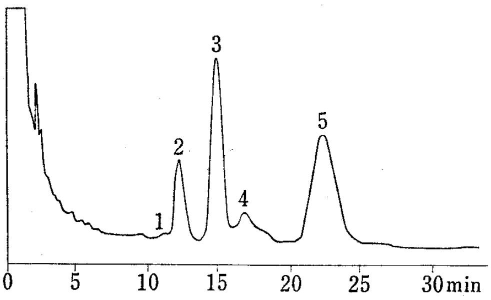

Fig. 1. Gas Chromatogram of Sterol Trimethylsilyl (TMS) Ethers from *Rhodymenia palmata*

Shimadzu GC-5A was used with column, 1.5% OV-17 (1.5 m × 3 mm i.d.) on Shimalite W; temperature, 230°; flame ionization detector. Peaks 1, 2, 3 and 4 were identified as TMS ethers of 22-dehydrocholesterol, cholesterol, desmosterol and 24-methylenecholesterol, respectively by comparison with authentic samples in retention time and fragmentation patterns of mass spectra. Peak 5 was found to be a mixture of isofucosterol, liagosterol (I) and cholesta-5,25-diene-3β,23-diol (II) from mass chromatographic analysis shown in Fig. 2.

The broad peak at retention time of 22.5 min has been revealed to be consisted of three sterols when analyzed by GC equipped with a glass capillary column coated with OV-17 or OV-101. By mass chromatographic studies[6] of this portion (Fig. 2), these sterols were identified as isofucostelol, liagosterol (I)[7] and its isomer (II). The structure of the latter two sterols were further confirmed by the complete agreement of retention time on GC and mass spectra with those of authentic samples.[8] Liagosterol (I) has recently been isolated from *Liagora distenta* and *Scinaia furcellata* belonging to the order Nemalionales and has been proposed to be confined to plant of this order. Cholesta-5,25-diene-3β,23-diol (II) may be to our knowledge a new sterol to algae. The cooccurrence of these sterols (I and II) with desmosterol

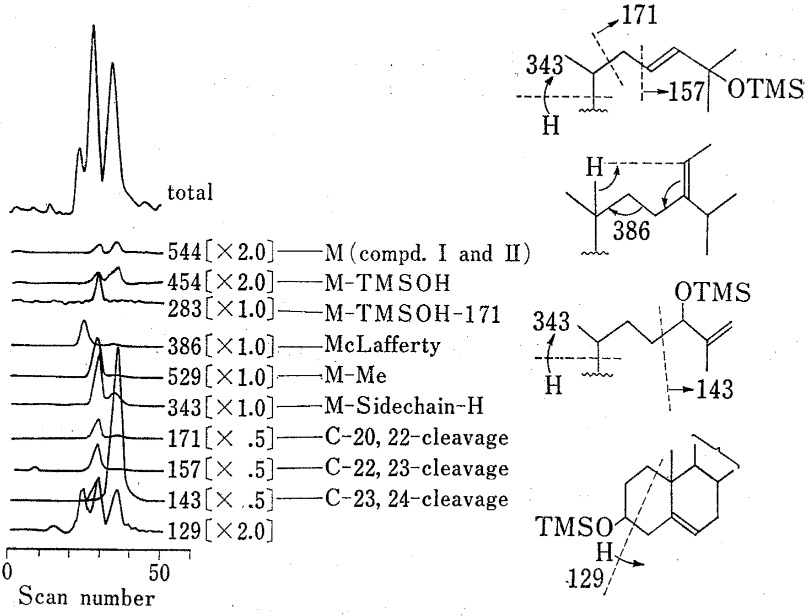

Fig. 2. Mass Chromatogram of Peak 5 in Fig. 1 (retention time, 17—23 min; mass range, *m/e* 100—600)

Shimadzu-LKB 9000 Gas Chromatograph-Mass Spectrometer connected to a computor system PAC-300 DG was used with column, OV-17 (40 m × 0.25 mm i.d.) SCOT glass capillary column at 250°; carrier gas inlet pressure, 1.2 K; make up gas, 25 ml/min; injection port temperature, 320°; separator temperature, 320°; ion source temperature, 290°; electron energy, 20 eV; accelerating voltage, 3.5 kV; trap current, 60 μA.

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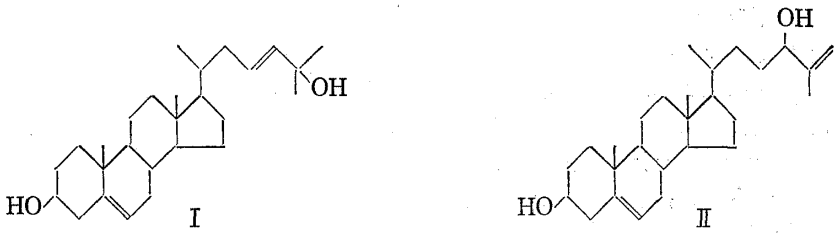
7) E. Fattorusso, S. Magno, C. Santacrose, D. Scica, G. Impellizzeri, S. Mangliafico, G. Oriente, M. Piattelli, and S. Sciuto, *Phytochemistry*, **14**, 1579 (1975).

8) M. Morisaki, J. Rubio-Lightbourn and N. Ikekawa, *Chem. Pharm. Bull.* (Tokyo), **21**, 457 (1973).



I

II

Chart

in *R. palmata* seems to suggest that I and II might be biosynthesized from desmosterol *via* photosensitized oxygenation or related mechanism. However, the possibility that these diols (I and II) would be artifact produced from desmosterol during air-drying of algae or extraction/isolation procedures, should be also considered.

Experimental

The algae were harvested at Muroran bay, Hokkaido, Japan, and identified by Profs. T. Nakamura and M. Tatewaki, Hokkaido University. Extraction of sterols and the analysis of their trimethylsilyl ethers by GC-MS were carried out as previously described.[2] Mass chromatography was performed with Shimadzu-LKB 9000 Gas Chromatograph-Mass Spectrometer equipped with GC-MASS PAC-300 DG data processing system; OKITAC-4300C minicomputer with 12K core, a typewritten digital plotter, a magnetic disk and an interface. For details see Fig. 2 legend.

Acknowledgement We are indebted to Profs. T. Nakamura, and M. Tatewaki, Hokkaido University, for collection and identification of algae. Thanks are also due to Shimadzu Co., Ltd. for analysis by mass chromatography.

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Studies on the Synthesis of Cardiotonic Steroids. II.[1] Synthesis of 17β-(3-Furyl)-5β,14β-androstane-3β,14β-diol

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17β-(3-Furyl)-5β,14β-androstane-3β,14β-diol, a promissing relay compound leading to digitoxigenin, was synthesized starting with 3β-acetoxy-5β-pregn-14-en-20-one.

Our continuous interest in the exploration of new synthetic routes to naturally occurring cardenolide led us to establish the effective synthetic method of the title compound,[3] since the compound is known to be convertible to digitoxigenin.[4] The starting material employed for this objective was 3β-acetoxy-5β-pregn-14-en-20-one (**1**) that proved the attractive intermediate in our previous digitoxigenin synthesis.[1] Derivation of furan ring from the side chain of **1** and subsequent formation of 14β-hydroxy group have completed the present approach as described below.

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