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LONG CHAIN ALKYL PHENOLS FROM THE LIVERWORT *SCHISTOCHILA APPENDICULATA**

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Key Word Index *Schistochila appendiculata*; Jungermanniales; Hepaticae; long chain alkyl phenols; 3-undecyl, 3-tridecyl, 3-pentadecyl phenols; 6-undecyl, 6-tridecyl, 6-pentadecyl salicylic acids; potassium 6-undecyl, 6-tridecyl, 6-pentadecyl salicylates; 6-undecyl catechol; allergy; chemosystematics.

Abstract—3-Undecyl phenol, 6-undecyl salicylic acid and potassium 6-undecyl salicylate were isolated from the New Zealand liverwort *Schistochila appendiculata*. 3-Tridecyl and 3-pentadecyl phenol, 6-tridecyl and 6-pentadecyl salicylic acid, potassium 6-tridecyl and 6-pentadecyl salicylate and 6-undecyl catechol were also detected in the same species. The chemical constitution of *S. appendiculata* is quite similar to that of the brown algae *Caulocystis* species, and of the higher plants *Ginkgo biloba* and some of the *Anacardia* species. The allergic reaction brought on by *S. appendiculata* might be due to the presence of these phenolic compounds.

INTRODUCTION

The members of the Schistochilaceae are one of the most beautiful of all hepatics and there are about 32 species in the world [1]. *Schistochila appendiculata* is the largest of the Jungermanniales and its shoot may be up to 110 cm (× 2.6 cm) tall [1]. This species causes allergenic contact dermatitis. In our continuing search for biologically active substances from liverworts [2–4], we investigated the chemical constituents of the New Zealand *S. appendiculata* and isolated some new phenols possessing a linear alkyl side chain. These new phenols may be of value when considering the evolution of the Hepaticae.

In this paper, we wish to report the chemical structures of these phenols and to discuss the natures of the allergy inducing substances in, and the chemosystematics of, *S. appendiculata*.

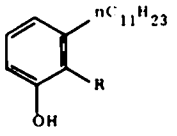
RESULTS AND DISCUSSION

The ether extract of dried *S. appendiculata* gave one major and two minor spots on TLC and five peaks on GC which were tentatively identified as undecyl (95%), tridecyl (3%) and pentadecyl phenol (0.2%), undecyl catechol (0.2%) and heptadecadienyl phenol (0.2%) by GC/MS and by comparison with the MS spectra of those reported for 3-tridecyl [5] and authentic 3-pentadecyl phenols. The extract was chromatographed on silica gel followed by Sephadex LH-20 to afford three alkyl phenols (**1**, **2** and **3**), corresponding to the three spots on TLC.

High resolution mass spectrometry showed that the molecular formula of **1** was $C_{17}H_{28}O$. The spectral data showed the presence of a hydroxyl group (3350 cm^{-1}), a benzylic methylene (δ2.53, *dd*, J = 7.7 Hz), a homobenzylic methylene (δ1.58, *m*) and an ethyl group (δ0.88, *t*, J = 7.1 Hz), four protons [6.63, *dd* (*br*), J = 7.6, 2.5 Hz, 6.65, *s* (*br*), 6.74 *d* (*br*), J = 7.6 Hz, 7.12, *ddd*, J = 7.6, 7.6, 1.3 Hz] on a 1,3-disubstituted benzene ring [5] and a long chain methylene group (δ1.25, *s*, 16H). The MS spectrum of **1** showed the base peak at *m/z* 108, indicating that the alkyl group was longer than C_2. These spectral data were quite similar to those of 3-tridecyl phenol (**6**) [5] and the authentic 3-pentadecyl phenol (**11**) isolated from *Ginkgo biloba*. Methylation of **1** gave a monomethyl ether (**4**), $C_{18}H_{30}O$ ([M]$^+$ 262, 3.78, 3H, *s*). Treatment of **1** with *meta*-chloroperbenzoic acid afforded a *para*-benzoquinone (**18**), $C_{17}H_{26}O_2$ ([M]$^+$ 262; 246 nm; 1665 cm^{-1}). From the above spectral and chemical evidence coupled with the molecular formula, the structure of **1** was established as 3-undecyl phenol. The arrangment of the benzene ring was further confirmed by a difference NOE examination of **2** (see Fig. 1). The isolated phenol (**1**) and its methylated product (**4**), however, contained two minor components, respectively, which were separable by GC. The MS spectra of the two components were identical to those of 3-tridecyl (**6**) and 3-pentadecyl phenol (**11**) in the parent phenol and to 3-tridecyl (**9**) and 3-pentadecyl methoxybenzene (**14**) in its methylated derivative.

The second compound (**2**) had the molecular formula $C_{18}H_{28}O_3$ (high resolution MS: 292.2074). Its spectral data indicated the presence of a *n*-undecyl group on a benzene ring and a chelated carboxylic group (1660 cm^{-1}; δ_H 10.90; δ_C 176.5), this latter finding showing that the carboxylic group and phenolic hydroxyl group were *ortho* to each other. These data were very similar to those of 6-tridecyl salicylic acid (**7**) isolated from the brown algae [5]. Methylation of **2** with MeI gave a methylated compound (**5**), $C_{20}H_{32}O_3$ ([M]$^+$ 320; 1738 cm^{-1}; δ3.81, 3.90 each 3H, *s*). On the above evidence, coupled with the molecular formula, the structure of **2** was confirmed as 6-

* Part 20 in the series "Chemosystematics of Bryophytes". For part 19, see Asakawa, Y., Takikawa, K., Tori, M. and Campbell, E. O. (1986) *Phytochemistry* **25**, 2543.



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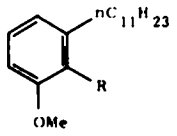
3 R = COOK



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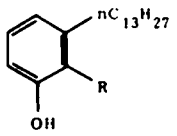

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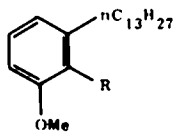

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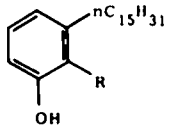

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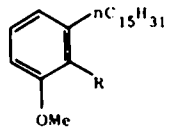

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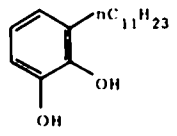

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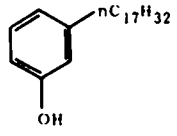

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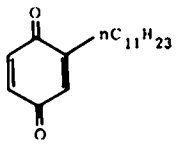

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undecyl salicylic acid from which **1** might be biosynthesized by decarboxylation. The methylated compound thus obtained, however, showed two additional minor peaks on GC, the MS spectra of which were identical to those of methyl 2-methoxy-6-tridecyl benzoate (**10**) and methyl 2-methoxy-6-pentadecyl benzoate (**15**), respectively. Thus the second compound isolated was a mixture of 6-undecyl, 6-tridecyl and 6-pentadecyl salicylic acids.

The ^{1}H NMR and MS spectral patterns of the most polar compound (**3**) were identical to those of 6-undecyl salicylic acid (**2**), but its IR spectrum was quite different from that of **2**. Methylation of **3** with MeI gave a mixture of methyl 2-methoxy-6-undecyl benzoate (**5**) (60% by GC), methyl 2-methoxy-6-tridecyl benzoate (**10**) (10%) and methyl 2-methoxy-6-pentadecyl benzoate (**15**) (0.7%). Thus the third isolated product appeared to be a mixture of 6-undecyl, 6-tridecyl and 6-pentadecyl salicylate salts. This was further confirmed by the strong IR band at 1590 cm^{-1} of the original salt. FAB/MS showed that the salicylates were in fact present as their monopotassium salts (*m/z* 331 [$C_{18}H_{27}O_3K$ + H]$^+$ and 423 [$C_{18}H_{27}O_3K$ + H + glycerine]$^+$. From the above data, the structure of the most polar compound was established as potassium 6-undecyl salicylate (**3**) in which a small amounts of potassium 6-tridecyl (**7**) and 6-pentadecyl salicylates (**13**) were present.

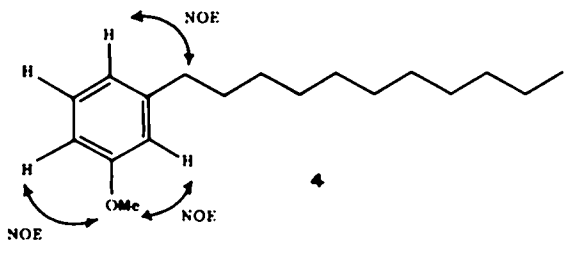

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Fig. 1.

This is the first example of the isolation of long chain alkyl phenols from bryophytes although a number of different aromatic compounds have been found in the Hepaticae [6, 7]. 3-Undecyl phenol, 6-undecyl salicylic acid and the potassium salt of the long chain alkyl salicylic acid have not been found previously in nature although a crystalline salicylic acid derivative named anagigantic acid has been isolated from *Anacardium giganteum* (Anacardiaceae) and its structure tentatively proposed as 3-undecyl salicylic acid (**2**) [8]. The fruit of *Ginkgo biloba* causes a strong allergic reaction due to the presence of 6-pentadecenyl salicylic acid and 6-pentadecyl salicylic acid (**12**) and their decarboxylated compounds [9, 10]. Many Anacardiaceae species produce various types of *n*-C_{15} and *n*-C_{17} alkyl phenols which cause strong allergenic contact dermatitis [9, 10]. It is possible that the allergic reaction caused by *S. appendiculata* is due to the presence in this organism of linear alkyl side chain phenolic compounds.

The terpenoid constituents of the Hepaticae are similar to those of algae, in particular, the Phaeophyceae [11]. The present phenolic compounds which are found in both the Hepaticae and the Phaeophyceae may provide important chemical evidence when considering the evolutionary process among the algae and the lower terrestrial green plants.

Most Jungermanniales species biosynthesize terpenoids as the major components [6]. *S. appendiculata* is one of the most peculiar liverworts from the point of view of chemical constitution.

EXPERIMENTAL

TLC, GC and GC/MS were carried out as previously reported [12]. High resolution MS: 70 eV; FAB/MS: Accel. H.V., 5000 V. The solvents used for spectral determination were: TMS-$CDCl_3$

[^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz)]; EtOH (UV) and $CHCl_3$ (IR) unless otherwise stated.

Plant material. *Schistochila appendiculata* identified by E.O.C. was deposited in the Herbarium of Institute of Pharmacognosy, Tokushima Bunri University.

Extraction and isolation. *S. appendiculata* (18.60 g) collected in New Zealand, August 1984, was extracted with MeOH for 3 months. The crude extract, after removal of the solvent, was partitioned between Et_2O and H_2O. Evaporation of the Et_2O extract under vacuum gave a green oil (1.96 g). A small amount of the crude extract was subjected to TLC, GC and GC/MS. One major, non-polar and two minor, polar spots were detected by TLC. GC of the crude extract indicated 5 peaks in the ratio 95:3:0.2:0.2:0.2 (%). These components, in turn, were suggested to be undecyl, tridecyl and pentadecyl phenols, undecyl catechol (**16**) and heptadecenyl phenol (**17**), respectively, by direct comparison of their MS spectra with those of the reported tridecyl phenol (**6**) [5] and authentic pentadecyl phenol (**11**) or by analysis of their GC/MS spectra. *Undecyl catechol* (**16**): MS *m/z* (rel. int.): 264 (12) [M]$^+$, 132 (15) and 124 (100). *Heptadecenyl phenol* (**17**): MS *m/z* (rel. int.): 328 (15), 120 (40), 108 (100).

The remainder of the extract (1.90 g) was chromatographed on silica gel using a *n*-hexane–EtOAc gradient and divided into two fractions. The first fraction (*n*-hexane–EtOAc, 4:1) (1.205 g), was further chromatographed on Sephadex LH-20 using $CHCl_3$–MeOH (1:1) to give 3-*undecyl phenol* (**1**) (830 mg) as a viscous oil. $C_{17}H_{28}O$ (high resolution MS: found 248.2226; calc. 248.2140); UV λ_{max} nm (log ε): 217 (3.88), 273 (3.37) and 279 (3.32); IR ν_{max}^{liq} cm^{-1}: 3350, 1610, 1590, 1460, 1452, 1263, 1150, 772 and 687; ^{1}H NMR: δ0.88 (3H, J = 7.1 Hz), 1.25 (16H, *s*), 1.58 (2H, *m*), 2.53 (2H, *dd*, J = 7.7 Hz), 5.30 [1H, *s* (*br*), OH], 6.63 [1H, *dd* (*br*), J = 7.6, 2.5 Hz], 6.65 [1H, *s* (*br*)], 6.74 [1H, *d* (*br*) J = 7.6 Hz] and 7.12 (1H, *ddd*, J = 7.6, 7.6, 1.3 Hz); ^{13}C NMR: δ14.12 (Me, *q*), 22.71 (CH_2, *t*), 29.36 (CH_2 × 2, *t*), 29.54 (CH_2, *t*), 29.61 (CH_2, *t*), 29.66 (CH_2, *t*), 29.69 (CH_2, *t*), 31.31 (CH_2, *t*), 31.94 (CH_2, *t*), 35.84 (CH_2, *t*), 112.52 (Ph CH, *d*), 115.36 (Ph CH, *d*), 121.01 (Ph CH, *d*), 144.99 (Ph C, *s*), 155.31 (Ph-C, *s*); MS *m/z* (rel. int.): 248 (11) [M]$^+$, 121 (10), 108 (100). The alkyl phenol thus obtained, however, included a small amount of two long chain alkyl phenols whose MS spectra were identical to those reported for 3-tridecyl phenol (**6**) [5] and the authentic 3-pentadecyl phenol (**11**). The ratio of **1**:**6**:**11** as determined by GC was 95:3:0.2 (%). The second fraction (374 mg) was further chromatographed on Sephadex LH-20 ($CHCl_3$–MeOH, 1:1) to give two alkyl phenols, **2** (180 mg) and **3** (101 mg), as white crystals. 6-*Undecyl salicylic acid* (**2**): mp 81–82°; $C_{18}H_{28}O_3$ (high resolution MS: found 292.2074; calc. 292.2038); UV λ_{max} nm (log ε): 213 (4.17), 242 (3.62) and 309 (3.43); IR ν_{max}^{KBr} cm^{-1}: 3300–2400, 1660 (OCO···HO), 1605, 1446, 1303, 1242 and 1212; ^{1}H NMR: δ0.86 (3H, *t*, J = 6.8 Hz), 1.25–1.40 (*ca* 16H, *s*), 1.61 (2H, *dddd*, J = 7.8 Hz), 2.98 (2H, *dd*, J = 7.8 Hz), 6.78 [1H, *d* (*br*), J = 7.6 Hz], 6.87 [1H, *d* (*br*), J = 8.3 Hz], 7.35 (1H, *dd*, J = 8.3, 7.6 Hz) and 10.90 [1H, *s* (*br*), hydrogen bonded OH]; ^{13}C NMR: δ14.13 (Me), 22.71, 29.39, 29.52, 29.69, 29.72, 29.80, 29.84, 31.95, 32.01, 36.49 (each CH_2), 110.43, 115.91, 122.83 (each Ph CH), 135.49, 147.94, 163.62 (each Ph C) and 176.53 (COOH); MS *m/z* (rel. int.): 292 (29) [M]$^+$, 149 (100). *Potassium 6-undecyl salicylate* (**3**): mp 201–204° (decomp.); UV λ_{max} nm (log ε): 212.5 (3.88), 240 sh (3.31) and 302 (3.18); IR ν_{max}^{KBr} cm^{-1}: 1590, 1500, 1468, 1408, 1330, 1270, 830, 820, 780, 710, 700 and 593; ^{1}H NMR (CD_3OD): δ0.89 (3H, *t*, J = 6.8 Hz), 1.24–1.26 (*ca* 16H, *s*), 1.58 (2H, *m*), 3.08 (2H, *dd*, J = 7.8 Hz), 4.92 [1H, *s* (*br*), OH], 6.64 (1H, *dd*, J = 7.6, 1.2 Hz), 6.66 (1H, *dd*, J = 8.1, 1.2 Hz) and 7.09 (1H, *dd*, J = 8.1, 7.6 Hz); ^{13}C NMR: δ14.39 (Me), 23.47, 30.21, 30.50 (each CH_2), 30.60 (CH_2 × 3), 30.83, 32.79, 33.05, 36.04 (each CH_2), 114.83, 118.62, 122.24 (each Ph CH), 131.89, 147.39, 161.85 (each Ph–C) and 178.16 (COO); MS *m/z* (rel. int.): 292 (5) [M − K + 1]$^+$, 274 (4), 248 (14), 108 (100); FAB/MS: *m/z* (rel. int.): 331 (1) [M + H]$^+$, 423 (16) [M + H + glycerine]$^+$.

Methylation of **1**. Compound **1** (50 mg) in Me_2CO (4 ml) was treated with MeI (0.1 ml) in the presence of anhydrous K_2CO_3 for 1.5 hr. Work up as usual gave the monomethyl ether **4** (47 mg): $C_{18}H_{30}O$; UV λ_{max} nm (log ε): 218 (3.59), 271 (3.07) and 278 (3.05); IR ν_{max} cm^{-1}: 1605, 1589, 1490, 1468, 1260, 1150, 1045, 772 and 692; ^{1}H NMR: δ0.88 (3H, *t*, J = 7.0 Hz), 1.26 (16H, *s*), 1.60 (2H, *m*), 2.57 (2H, *dd*, J = 7.0 Hz), 3.78 (3H, *s*), 6.71 (1H, *dd*, J = 7.6, 2.5 Hz), 6.72 [1H, *s* (*br*)], 6.77 [1H, *d* (*br*), J = 7.6 Hz] and 7.17 (1H, *ddd*, J = 7.6, 7.6, 1.3 Hz); MS *m/z* (rel. int.): 262 (18) [M]$^+$, 122 (100), 91 (10). The methyl ether (**4**) included **9** and **14** as minor components. The ratio of **4**:**9**:**14** was estimated by GC to be 95:3:0.2 (%).

Methylation of **2**. Compound **2** (45 mg) was treated in the same manner as described above to afford methyl 2-methoxy-6-undecyl benzoate (**5**) (43 mg): $C_{20}H_{32}O_3$; UV λ_{max} nm (log ε): 210.5 (4.12), 278 (3.52) and 272 sh (3.46); IR ν_{max}^{liq} cm^{-1}: 1738, 1600, 1583, 1469, 1430, 1265, 1107, 1070, 822 and 740; ^{1}H NMR: δ0.88 (3H, *t*, J = 7.0 Hz), 1.25 (*ca* 16H, *s*), 1.57 (2H, *m*), 2.53 (2H, *dd*, J = 7.0 Hz), 3.81 (3H, *s*), 3.90 (3H, *s*), 6.75 (1H, *d*, J = 8.3 Hz), 6.81 (1H, *d*, J = 7.6 Hz) and 7.26 (1H, *dd*, J = 8.3, 7.6 Hz); MS *m/z* (rel. int.): 320 (17) [M]$^+$, 289 (23), 180 (41), 161 (100), 91 (9). The methyl ester (**5**), however, contained two minor methylated components which were detected by GC and GC/MS. The MS spectra of these components were consistent with those of methyl 2-methoxy-6-tridecyl benzoate (**10**) and methyl 2-methoxy-6-pentadecyl benzoate (**15**), respectively. The ratio of **5**:**10**:**15** as measured by GC was 60:17:0.2 (%).

Methylation of **3**. Compound **3** (45 mg) in Me_2CO (4.5 ml) was methylated with MeI (0.3 ml). Work-up as usual gave a product (42 mg) whose spectral data were identical to those of methyl 2-methoxy-6-undecyl benzoate (**5**). GC and GC/MS showed that the methyl ester (**5**) contained two minor components, methyl 2-methoxy-6-tridecyl benzoate (**10**) and methyl 2-methoxy-6-pentadecyl benzoate (**15**). The ratio of **5**:**10**:**15** as measured by GC was 60:10:0.2 (%).

Oxidation of **1**. To compound **1** (150 mg) in $CHCl_3$ (6 ml) was added *m*-chloroperbenzoic acid (171 mg) and the soln was refluxed for 23 hr [13, 14]. The reaction mixture was filtered to remove excess benzoic acid and the product, after removal of the solvent, was chromatographed on Sephadex LH-20 ($CHCl_3$–MeOH) to afford 2-undecyl-1,4-benzoquinone (**18**) (5 mg): $C_{17}H_{26}O_2$; UV λ_{max} nm (log ε): 204 (3.51) and 246 (3.93); IR ν_{max} cm^{-1}: 1665, 1600, 1468, 1292, and 902; ^{1}H NMR: δ0.88 (3H, *t*, J = 7.0 Hz), 1.22–1.27 (16H, *s*), 1.49 (2H, *m*), 2.41 (2H, *dd*, J = 7.0 Hz), 6.56 (1H, *ddd*, J = 7.7, 2.4 Hz), 6.70 (1H, *dd*, J = 10.0, 2.4 Hz) and 6.75 (1H, *d*, J = 10.0 Hz); MS *m/z* (rel. int.): 262 (28) [M]$^+$, 149 (27), 136 (26), 123 (100).

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