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HALOGENATED METABOLITES INCLUDING BROMINATED 2-HEPTANOLS AND 2-HEPTYL ACETATES FROM THE TETRASPOROPHYTE OF THE RED ALGA BONNEMAISONIA HAMIFERA

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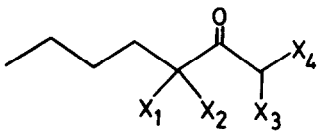
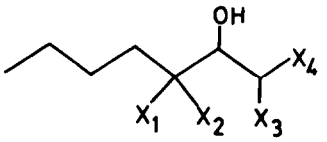
Algae belonging to the genus Bonnemaisonia are known to produce α-halogenated ketones and a spectrum of halogenated compounds, formally derived from the ketones by reduction or Favorskii-type rearrangements.[1]

During a study of the tetrasporophyte of Bonnemaisonia hamifera Har. (collected near Aarhus, Denmark) we have demonstrated the presence of the halogen substituted 2-heptanones 1-8 and 2-heptanols 9-11, the corresponding acetates 12-14, the epoxide 15, and the acids 16-18. Of these, 6, 8, 10-14 and 18 appear to be novel as natural products, whereas 1-4 and 7 have been described from the gametophyte of the same alga,[1a] 9, 15, 16 and 17 from B. nootkana (Esp.) Silva.[1b] The overlap in the chemical patterns supports a close relationship between the two morphologically similar species.

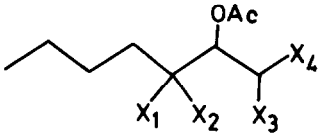
A pentane extract of the diluted alcoholic extract of the frozen alga was chromatographed on a Merck prepacked silicagel column (2 % ether in pentane); the fractions were analyzed by GC-MS. The ketones 1-8 were easily identified from their characteristic electron impact (EI) MS fragmentation pattern,[1a] their chemical ionisation (CI) MS quasimolecular peaks (M+1, isobutane), and by comparison (GC, MS and liquid chromatography) with synthetic samples prepared by bromination of 2-heptanone followed by fractionation of the product mixture by liquid chromatography. Samples of the bromo-iodo-ketones 7 and 8 were obtained on brief treatment of the bromoketones 2 and 3 with KI in MeOH. The possibility of 7 and 8 being artefacts, similarly formed upon reaction with iodide ions in the alga during the extraction procedure, cannot be ruled out.



1 - 8

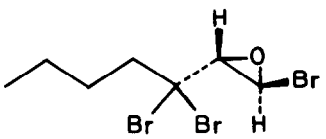


9 - 11

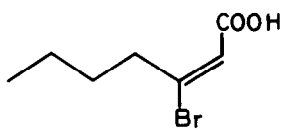


12 - 14

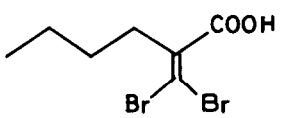
	X_1	X_2	X_3	X_4	% (wet weight)
1	Br	Br	Br	Br	0.05
2	Br	Br	Br	H	
3	Br	H	Br	Br	0.004
4	Br	H	Br	H	< 0.001
5	Br	Br	H	H	< 0.001
6	H	H	Br	Br	< 0.001
7	Br	Br	I	H	< 0.001
8	I	H	Br	Br	< 0.001
9	Br	Br	Br	Br	0.01
10	Br	Br	Br	H	< 0.001
11	Br	H	Br	Br	< 0.001
12	Br	Br	Br	Br	0.008
13	Br	Br	Br	H	
14	Br	H	Br	Br	0.004



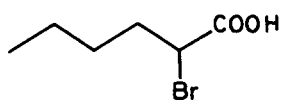
15 (0.02%)



16 (0.001%)



17



18 (< 0.001%)

Again, the brominated 2-heptanols 9-11 and the corresponding acetates 12-14 of unknown stereochemical identity, were identified from their EI-MS fragmentation patterns, CI-MS quasimolecular peaks (M+1) and by comparison (GC, MS and liquid chromatography)with synthetic, racemic specimens. In the EI mass spectra of the alcohols 9-11 no molecular peaks were observed. The highest mass ions detected were those due to loss of Br followed by loss of HBr and/or H_2O. Oxonium and alkyl ions resulting from α-cleavage revealed the substitution pattern. In the acetates 12-14, the acetyl ion gave rise to the base peak; no molecular peaks were observed. Again, ions resulting from α-cleavage (acetoxonium ions) were useful for distinguishing between isomers, while the gross structure followed from the fragments formed by loss of Br from the molecular ion with subsequent loss of HBr and/or HOAc.

The alcohols 9-11 were prepared by reduction of the ketones 1-3,[1b] in our hands proceeding more satisfactorily with $BH_3 \cdot$ THF. Acetylation (CH_3COCl, pyridine) gave the acetates 12-14. The synthetic specimens of 11 and 14 were obtained as mixtures of diastereomers, which could be separated by liquid chromatography. They had virtually identical mass spectra, and assignment of relative configuration to the natural products was not possible. NMR data, 90 MHz, ($CDCl_3$, signals from the butyl groups omitted): 9, δ 3.11 (1H, d, J=10), exchangeable; 4.36 (1H, dd, J = 10 and 1.2); 6.50 (1H, d, J = 1.2), 12, δ 2.28 (3H, s); 5.90 (1H, d, J = 2.1); 6.17 (1H, d, J = 2.1). The alcohols and acetates 10, 11, 13 and 14 showed complex AA'B and ABX patterns for the C1, C2 and C3 protons.

The epoxide 15 had the spectral data: 90 MHz NMR (C_6D_6): δ 4.99 (1H, d, J = 1.0); 3.33 (1H, d, J = 1.0). MS (EI), m/e (%): 269 (6, M-Br); 227 (1, $C_5H_9Br_2$); 133 (8, C_4H_6Br); 119 (44, C_3H_4Br). M+1 (CI): 349. McConnell and Fenical[1b] earlier assigned trans-configuration to a compound isolated from B. nootkana with a different shift of the low field epoxide ring proton (4.51) and a vicinal coupling constant between the ring protons of 3 Hz. Since in 1,2-disubstituted epoxides the vicinal coupling is reportedly smaller in the trans-isomers,[3] we prefer trans-configuration for 15 and hence suggest cis-configuration for the compound of McConnell and Fenical. The small coupling constant in both compounds is most likely due to the electronegative substituents. A minor constituent of the extract having a mass spectrum identical with that of 15 but with a higher retention time, is tentatively assigned the cis-configuration. The structure of 15 was confirmed by synthesis from 9 using excess NaH in ether (30 min, rt.). Chromatographic work up gave 15 (30 %), identical (GC, MS, and NMR) with the natural product.

The bromoacids 16-18 were present in the extract as ethyl esters probably formed during the EtOH treatment. A few mg of the ethyl ester of 16 was isolated and had the spectral data: 90 MHz NMR ($CDCl_3$) (protons on C4 and C2): δ 3.08 (2H, t, J = 7); 6.29 (1H, s). MS (EI) m/e (%): 234 (2, M^+); 205 (2, M-Et); 189 (21, M-OEt); 177 (2, M-C_4H_9); 155 (100, M-Br). The NMR-data are consistent with the E-configuration,[1b] whereas a less abundant compound with virtually identical mass spectrum, but higher retention time is probably the Z-isomer. The ethyl esters of 17 and 18 had the MS (EI) data m/e (%): 17, 312 (1, M^+); 283 (1, M-Et); 270 (7, M-C_3H_6); 267 (14, M-OEt); 242 (6, M-C_3H_6-C_2H_4); 233 (20, M-Br); 205 (34, M-Br-C_2H_4; 187 (21, M-OEt-HBr); 18, 222 (0.6, M^+): 177 (3, M-OEt); 166 (40, M-C_4H_8); 149 (2, M-COOEt); 143 (23, M-Br), and were identical (GC, MS) with synthetic samples made from 1[1b] and 18, respectively.

All the halogenated metabolites reported in this communication formally belong to the C_7 series. The Z-isomer of acid 16 together with 17, are the products claimed to arise from

'a biological Favorsky rearrangement' of 3 and 1 respectively;[1b] the detection of the isomer 16, however, casts doubt on the stereospecific course claimed for this reaction.

Several species of both red and brown algae appear to possess a highly developed potential for acetylation[4] in keeping with the here reported occurrence of 12-14.

Species of Asparagopsis, another genus within the family Bonnemaisoniaceae, contain large amounts of halomethanes,[5] proposed to arise from properly substituted ketones by a biological equivalent of the haloform reaction.[6] The occurrence of acid 18, suggests a similar Activity in B. hamifera; hence a study of the more volatile constituents of the tetrasporophyte is in progress.

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3. L. M. Jackman and S. Sternhell, Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry, 2. ed., Pergamon Press, 1969, page 287.

4. Several examples in: D. J. Faulkner, Tetrahedron, 1977, 33, 1421. For a more recent example see: J. H. Cardellina and R. E. Moore, Phytochemistry, 1978, 17, 554.

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