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NEW POLYBROMINATED METABOLITES FROM THE RED ALGA PTILONIA AUSTRALASICA

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Red algae of the family Bonnemaisoniaceae have yielded many acetate derived halogenated secondary metabolites. Haloforms, haloacetones, halopropenes and halobutenones are amongst the vast array of compounds detected in Asparagopsis taxiformis[1,2] and A. armata[3] and haloheptan-2-ones were isolated from Bonnemaisonia hamifera[4]. Two species of Delisea have been found to contain halogenated lactones of the general structure (1)[5,6], whilst halogenated oct-1-en-3-ones have been recently reported from Ptilonia australasica[7], D. fimbriata[8] and B. asparagoides[9] respectively.

We now report the isolation of a series of polybrominated metabolites from the dichloromethane soluble material of Ptilonia australasica collected in Tasmania. Chromatography of this extract (3% based on dry weight) on silica gel yielded two novel crystalline metabolites (2) and (3), together with a complex mixture of lower polarity which consisted of 1,1,2-tribromoalk-1-en-3-ones of general structure (4) which have been previously reported[5,7]. We now present evidence to support the structures of (2) and (3) and also spectral data to establish the identity of the individual components comprising the mixture of general structure (4).

The pentabromopyrone (2), representing 30% of the total extract, separated from hexane-ethyl acetate as colourless prisms m.p. 98-99°. The ^{1}H n.m.r. spectrum ($CDCl_3$) was particularly simple and showed only two resonances at δ1.28 (3H, t, J 7Hz) and 2.96 (2H, q, J 7Hz). ^{13}C n.m.r. spectroscopy showed resonances due to eight carbon atoms at 167.5 (s), 161.0 (s), 144.7 (s), 116.2(s), 115.3 (s), 58.8 (s), 41.3 (t) and 12.7 (q). The i.r. spectrum confirmed the presence of a conjugated carbonyl (ν_{max} 1655, 1572, 1543) and the u.v. spectrum (MeOH) showed bands at 238 (15,800), 247 (sh) and 275 (11,500) nm respectively. The molecular formula $C_8H_5O_2Br_5$, established by elemental analysis, was confirmed by m.s. which showed a six line symmetrical molecular ion cluster at m/e 528 (Br_5, 6) indicative of pentabromo-substitution. Major fragment ion clusters commenced at m/e 449 (Br_4, 100), 420 (Br_4, 15) and 291 (Br_2, 42%).

Structure (2) was established by reduction with zinc-acetic acid which at 100° (1 hr.) gave 2-propyl-4(1H)-pyrone (5) as the major product. This structure was confirmed by ^{1}H, ^{13}C n.m.r. (Table 1) and i.r. spectra (ν_{max} 1650, 1600 cm^{-1}). Reduction of (2) at 25° produced significant quantities of the partially reduced compounds (6), (7) and (8), the structures of which were established by mass spectral, ^{13}C and ^{1}H n.m.r. data (Table 1).

A second crystalline pyrone (3) m.p. 155-156° constituted 15% of the dichloromethane extract and analysed for $C_8H_5O_3Br_3$. The mass spectrum substantiated the molecular formula and showed a molecular ion cluster at m/e 386 (Br_3, 13), together with fragment ions at m/e 146 (Br, 14), 131 (Br, 15), 57 (100) and 29 (56%). The i.r. (ν_{max} 1720, 1650 cm^{-1}) and ^{13}C n.m.r. spectra showed the presence of two carbonyl groups and the n.m.r. spectral data (Table 1) established the structure of (3).

The least polar fraction, constituting 20% of the dichloromethane extract of P.australasica was shown by g.c. to be a complex mixture in which compounds (4a)-(4e) were major and readily detected. Separation of this fraction by HPLC on silica gel (CH_2Cl_2/pentane 1:1) allowed the isolation of compounds (4a) and (4b) in low yield. The structures of (4a) and (4b) were deduced from ^1H and ^{13}C n.m.r. data and mass spectral analysis. The general fragmentations found in the g.c./m.s. of (4a)-(4e) were most readily explained as arising from a common 1,1,2-tribromo-alk-1-en-3-one moiety.

1,1,2,4,4-Pentabromooct-1-en-3-one (4a) was the least polar of the two pure enones isolated. The ^1H n.m.r. spectrum indicated the presence of a linear C_4 side chain [$\delta(CDCl_3)$ 2.60 (2H,t, J 7Hz); multiplet centred at δ1.5 (4H); 0.96 (3H,t,J 7Hz)] whereas the ^{13}C n.m.r. spectrum showed eight carbon atoms. The ^{13}C n.m.r. chemical shifts of (4a) were 190.1(s), 115.8(s), 94.3(s), 63.3(s), 46.8(t), 29.3(t), 22.1(t) and 13.8(q) and the mass spectrum m/e 516 (Br_5, 0.1); 437 (Br_4, 0.3); 381 (Br_4, 0.15); 357 (Br_3, 0.15) and 289 (Br_3, 100%).

The structure of (4b) followed from spectral data. The ^1H n.m.r. showed an AB system at δ6.92 (1H,d,J 16Hz) and δ6.50 (1H,d,J 16Hz) of a trans-enone and an ethyl group [δ2.54 (2H,q, J 7Hz) and δ1.24 (3H,t,J 7Hz)]. The ^{13}C n.m.r. showed eight resonances at 186.2(s), 151.2(d), 131.0(s), 125.4(d), 93.7(s), 65.7(s), 42.5(t) and 12.2(q) and the mass spectrum showed a molecular ion cluster commencing at m/e 514 (Br_5, 1.8) with fragment ions at 435 (Br_4, 48), 406 (Br_4, 2.0), 356 (Br_3, 53), 289 (Br_3, 100) and 131 (Br, 72%) fully consistent with the proposed structure.

The structures of compounds (4c)-(4e) were inferred from g.c./m.s. results of the total non-polar fraction (SE30, 1m, programmed 140-220° at 2°/min.). Compound (4c) had a retention time of 2 min. and showed 382 (Br_4, 10, M^+), 289 (Br_3, 100), 260 (Br_3, 20), 182 (Br_2, 20), 131 (Br, 25%); (4c) [RT, 3.6 min.] showed m/e 360 (Br_3, 0.1, M^+), 304 (Br_3, 63), 289 (Br_3, 56), 260 (Br_3, 17), 225 (Br_2, 49), 131 (Br, 29), 99 (100%) and finally compound (4e) [RT, 8 mins.] showed m/e 438 (Br_4, 0.1, M^+), 382 (Br_4, 11), 359 (Br_3, 5), 289 (Br_3, 100) and 131 (Br, 14%). Compounds (4a) and (4b) had retention times of 12.6 and 13.8 minutes respectively.

All compounds described have shown significant activity against bacteria, yeasts and fungi.

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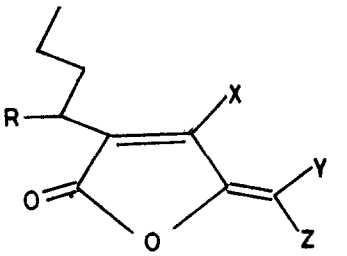
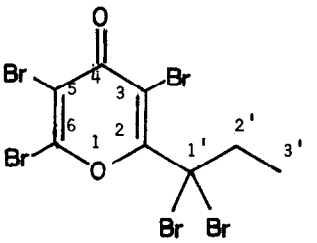
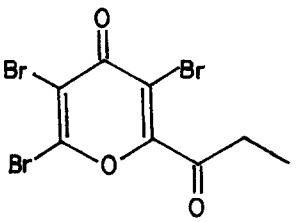


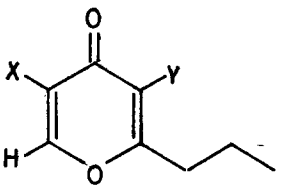
(1) R=H, OH or OAc
XYZ=3Br; 2Br,H; Br,Cl,H; Br,I,H



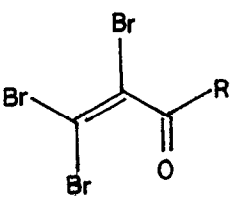


(3)

(2)



(5) X = Y = H
(6) X = Br, Y = Br
(7) X = H, Y = Br
(8) X = Br, Y = H



(4a) R = $CBr_2CH_2CH_2CH_2CH_3$
(4b) R = CH ‡ $CHCBr_2CH_2CH_3$
(4c) R = CH_2Br
(4d) R = $CH_2CH_2CH_2CH_2CH_3$
(4e) R = $CHBrCH_2CH_2CH_2CH_3$

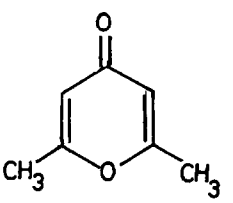


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TABLE 1.

^{13}C N.M.R. SHIFTS[A] (^{1}H N.M.R. CHEMICAL SHIFTS[A])

COMPOUND	C2	C3	C4	C5	C6	C1'	C2'	C3'
(9)	165.4	113.5	179.6	113.5	165.4	19.6	-	-
(2)	144.7†	116.2*	167.5	115.3*	161.0†	58.8	41.3 (2.96,q)	12.7 (1.28,t)
(3)	146.1	117.1*	192.8	112.5*	155.4	192.8	33.8 (3.00,q)	7.3 (1.24,t)
(7)	154.0 (7.64,d, J 6Hz)	114.5 (6.28,d, J 6Hz)	#	115.3	#	35.8 (2.80,t)	20.0 (1.72, sextet)	13.5 (δ1.00,t)
(8)	169.7 (8.60,s)	115.2	173.0	112.7 (6.16,s)	169.7	35.1 (2.48,t)	20.1 (1.66, sextet)	13.4 (0.98,t)
(6)	152.7 (8.04,s)	112.7	168.0	112.7	167.3	35.8 (1.80,t)	20.0 (1.72, sextet)	13.5 (1.00,t)
(5)	155.1 (7.64,d, J 6Hz)	116.6* (6.18,dd, J 6,2.5Hz)	179.2 (6.08,d, J 2.5Hz)	114.8*	169.6	35.6 (2.44,t)	20.0 (1.66, sextet)	13.5 (0.96,t)

[A] $CDCl_3$, δ values respectively; # not observed; *interchangeable;

†based on peak intensities due to bromine effects[10].

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