

Structure of Dibromophakellin, a New Bromine-containing Alkaloid from the Marine Sponge *Phakellia flabellata*

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Summary The structure of a new bromine-containing guanidine alkaloid, dibromophakellin, isolated from the marine sponge *Phakellia flabellata* has been elucidated.

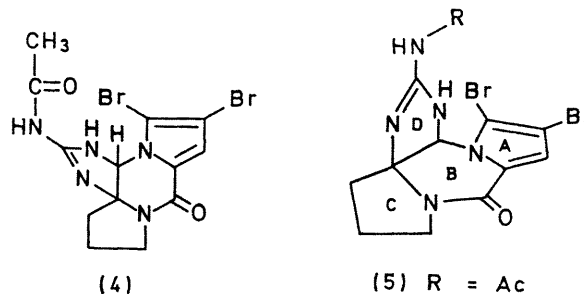
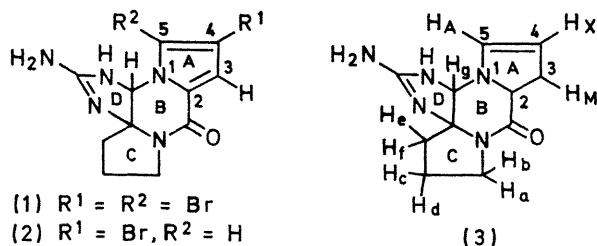
DIBROMOPHAKELLIN (1), $C_{11}H_{11}N_5OBr_2$, m.p. 237—245° (decomp.) and $[\alpha]_D^{25} -203^\circ$, is a new bromine-containing alkaloid isolated from the marine sponge *Phakellia flabellata*, found on the Great Barrier Reef. Although this alkaloid contains a guanidine unit in the five-membered ring D, it does not exhibit the usual high basicity of guanidinium compounds. In fact, dibromophakellin is a weakly basic substance, having a pK_a ca. 7.7 (20% methyl cellosolve). Guanidines, on the other hand, are extremely strong bases¹ and have a $pK_a > 13.4$. In this communication, we present evidence for the assignment of structure (1) to dibromophakellin.

The i.r. spectrum of (1) [ν_{max} (KBr) 3400br, 2975, 2950, 1675, 1640, 1587, 1550, 1490, 1435, 972, and 741 cm^{-1}] revealed the presence of amino and methylene groups, an amide function, and a heteroaromatic ring (pyrrole). The u.v. spectrum [λ_{max} (MeOH) 233 (ϵ 8877) and 281 nm (8813)] suggested the presence of a pyrrole ring bearing a carbonyl function at the α -position.² The presence of a guanidine moiety was indicated by the fragments³ at m/e 374, 372, 370 ($M - NH_3$) and 349, 347, 345 ($M - NH_2CN$) in the mass spectrum and the i.r. band at 1640 cm^{-1} (C=N). In agreement with these data, dibromophakellin contained three D_2O -exchangeable protons.

On catalytic hydrogenation, dibromophakellin readily underwent reductive debromination with the uptake of two moles of hydrogen to give phakellin (3) $C_{11}H_{13}ON_5$, m.p. 285° (decomp.) A detailed analysis of the 220 MHz n.m.r. spectrum of the hydrochloride of (3) revealed the complete structure of the phakellin skeleton. Thus, the three multiplets (d of d, AMX system) at 7.45 (1H, J_{AX} 3 and J_{AM} 1.8 Hz, H_A), 6.86 (1H, J_{MX} 4 and J_{MA} 1.8 Hz, H_M), and 6.43 p.p.m. (1H, J_{XM} 4 and J_{XA} 3 Hz, H_X) required the presence of the 1,2-disubstituted pyrrole ring A. From the bands at 3.70 (q, 1H, J_{gem} 18 and J_{vic} 8 Hz, H_a), 3.56 (q, 1H, J_{gem} 18 and J_{vic} 8 Hz, H_b), 2.5—2.15 (two closely-spaced complex multiplets, 2H, H_c and H_d), and 2.1 p.p.m. (br q, 2H, H_e and H_f), the presence of the partial structure

$CH_2 \cdot CH_2 \cdot CH_2 \cdot N \cdot C=O$ in the pyrrolidine ring c, was inferred.

In the absence of olefinic protons, the singlet at 6.18 p.p.m. (1H) was assigned to the hydrogen (H_g) on the carbon atom bearing two electron-withdrawing groups, the guanidine moiety and the pyrrole nitrogen. Finally, a broad D_2O -exchangeable band at 4.0—5.0 p.p.m. (4H) was assigned to the protons of the guanidinium ion. Thus, the n.m.r. spectrum of phakellin is in accord with the suggested structure (3).



The n.m.r. spectrum of dibromophakellin was almost identical with that of (3), except that it had only one pyrrole proton appearing as a singlet at 6.88 p.p.m. Since this singlet represents the proton at C-3 of the pyrrole ring, C-4 and C-5 of this ring in dibromophakellin must be substituted by the two bromine atoms. Dibromophakellin, therefore, has the structure (1). The structure of dibromophakellin has also been confirmed by X-ray diffraction analysis of a single crystal of the monoacetyl derivative (4), [$C_{13}H_{13}N_5O_2Br_2$, m.p. 240—250° (decomp.); λ_{max} (MeOH),

231 (ϵ 18,072) and 283 nm (8328); and ν_{\max} (KBr), 1708 cm^{-1} (C=O of the acetyl group)]. The crystals were orthorhombic with $a = 15.336$, $b = 12.725$, $c = 7.767$ Å; space group $P2_12_12_1$. The structure was solved by conventional heavy-atom methods and has been refined to an R factor of 0.053. The salient features of the X-ray defined structure are shown in (5). As expected, the five-membered

ring D, containing the guanidine moiety, was almost perpendicular to the plane of the other three rings.

The sponge *Phakellia flabellata* also produces the closely-related alkaloid 4-bromophakellin (2) m.p. 170—180° (decomp.)

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