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ISOAPLYSIN-20, A NATURAL BROMINE-CONTAINING DITERPENE, FROM APLYSIA KURODAI

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Although great efforts have been made to isolate bromo-compounds from sea weeds as well as from sea animals, only a few bromine-containing diterpenes have been found.[1,2] Aplysin-20 (1) is the first one that has been isolated from Aplysia kurodai collected in Hokkaido (in September).[1] We here describe the isolation and structure of a new bromine-containing diterpene, isoaplysin-20, in connection with aplysin-20 (1) which co-occurs in the same sea hare.[3]

According to the same procedure as described in the case of aplysin,[4] the hexane extracts of Aplysia kurodai were chromatographed on silica gel [Wako Pure Chemicals; hexane-ether (10 : 1)] and then on alumina [Wako Pure Chemicals; hexane-ether (4 : 5)] to give aplysin-20.[1] Further elution with hexane-ether (3 : 7) afforded a mixture of aplysin-20 and isoaplysin-20 (ratio, 5 : 1), which was separated by preparative TLC [Kieselgel PF_{254}; hexane-EtOAc (2 : 1)] to give a small amount of isoaplysin-20 (2) from the more polar fraction. The physical data of 2 is as follows: mp 195-198° (from MeOH); $C_{20}H_{35}O_2Br$; ν_{max}(Nujol) 3550, 3430 and 3260sh.cm^{-1}; δ0.93(3H, s), 0.95(3H, s), 0.98(3H, s), 1.04(3H, s), 1.32(3H, s) and 3.74-4.01(3H, complex);[5] m/e 370 and 368(M^+- H_2O), 355, 353, 312, 310, 299, 297, 289, 230 and 228.

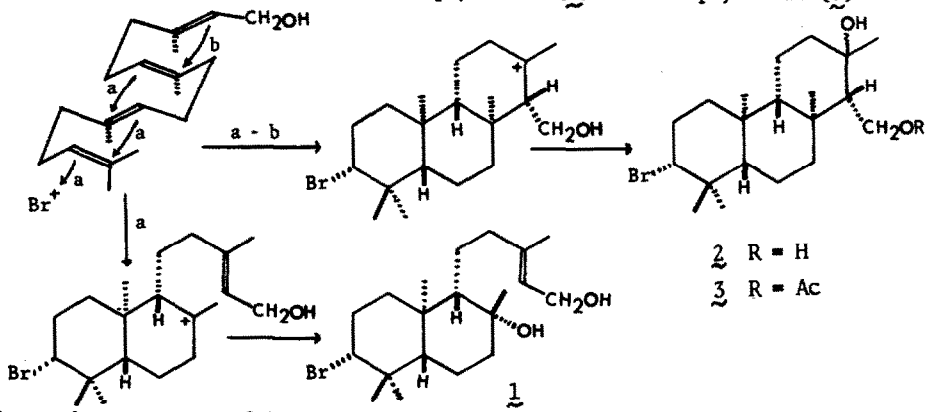
Aplysin-20 (1) is a bicyclic diterpene with one double bond,[1] while isoaplysin-20 (2) is a tricyclic one that has no double bond. As seen in the case of 1, the latter also has five methyl groups, one of which is attached to the carbon atom bearing a tertiary OH group. However, none of them should be attached to a double bond.

On acetylation with Ac_2O-pyridine (room temp., overnight), isoaplysin-20 was readily converted into the corresponding monoacetate (3); mp 135°; $C_{27}H_{37}O_3Br$ [m/e 430 and 428(M^+)]; ν_{max}(film) 3500, 1735 and 1250cm^{-1}; δ0.92(3H, s), 0.97(3H, s), 1.03(6H, s), 1.20(3H, s), 2.01(3H, s), 3.90

(1H, dd, J= 10, 6Hz), 4.26(1H, d, J= 8Hz) and 4.26(1H, d, J= 4Hz). The NMR spectrum of 3 has two doublets (H_a and H_b) at δ4.26, both of which become a sharp singlet on irradiation at δ1.65, indicating the presence of a secondary acetoxymethyl group (AcO-CH_aH_b-$\overset{|}{C}$H-). Furthermore, it should be noted that the NMR signal at δ3.90 can be due to a Br-$\overset{|}{C}$H-CH_2- grouping, as seen in the case of aplysin-20 (1).[1]

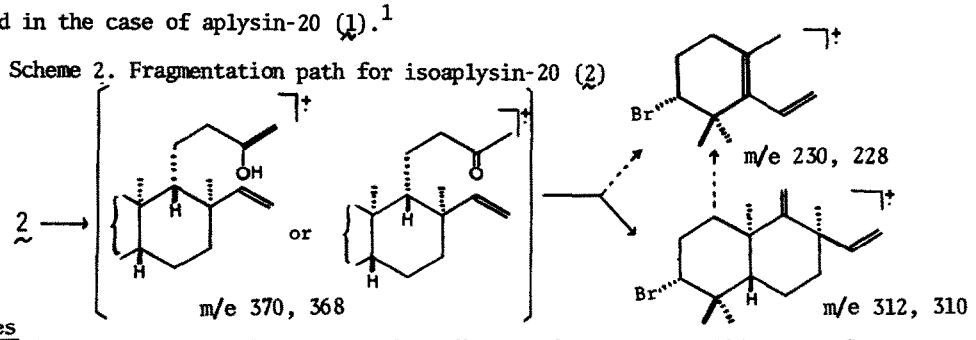
From these data, together with co-occurrence of aplysin-20 (1), the most tentative structure of isoaplysin-20 can be represented by 2. The biogenesis of these two bromine-containing diterpenes is shown in Scheme 1.

Scheme 1. Biogenesis of aplysin-20 (1) and isoaplysin-20 (2)



In fact, the structure of isoaplysin-20 (2) is compatible with its mass spectrum, as shown in Scheme 2. Although isoaplysin-20 has two OH groups, a pair of the fragment peaks corresponding to an ion (M^+ - $2H_2O$) are not observed or quite weak in their intensities, while these peaks are found in the case of aplysin-20 (1).[1]

Scheme 2. Fragmentation path for isoaplysin-20 (2)



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3. These bromine-containing diterpenes seem to be produced in the sea weeds eaten by Aplysia kurodai. In near future, they will be found in sea weeds.
4. S. Yamamura and Y. Hirata, Tetrahedron 19, 1485 (1963).
5. NMR spectra were taken on a JEOL PS-100 NMR spectrometer using $CDCl_3$ as the solvent.