NATURALLY OCCURRING BIOACTIVE BENZO[de]-1,6-NAPHTHYRIDINES FROM THE SEA SPONGE AAPTOS AAPTOS

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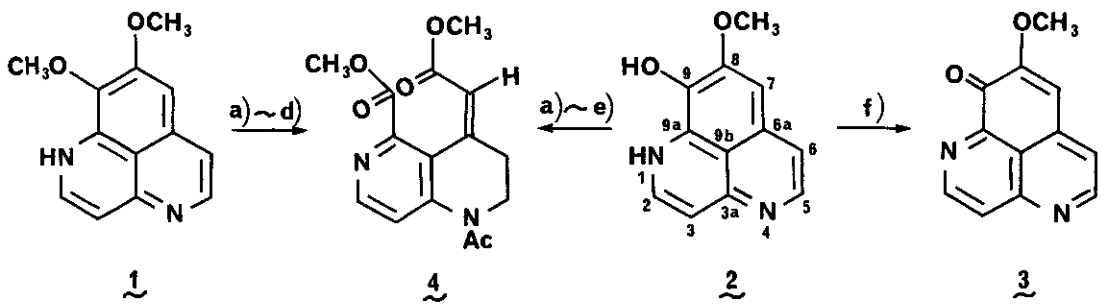
Numerous marine natural products with biological activities have been isolated from various marine organisms. It has been expected that natural products showing useful pharmacological actions will be obtained from marine organisms. We have investigated pharmacological actions of extracts of about three handred species of marine organisms collected at Okinawa island. Recently aaptamine 1 has been isolated from the sea sponge Aaptos aaptos as an α-adreoceptor blocking substance (Tetrahedron Lett, 23, 5555 (1982)). Continuous study on the constituents of the sea sponge led to the isolation of related substances, demethylaaptamine 2 and demethyloxyaaptamine 3 possessing the antimicrobial activities. These substances belong to a new class of heteroaromatic substance having benzo[de]-1,6-naphthyridine skelton.

Aaptos aaptos was collected at Okinawa island in July 1981. The ethanol soluble portion of methanol extracts of the sea sponge was chromatographed several times on a silica gel column to afford aaptamine 1 ($C_{13}H_{12}N_2O_2$), demethylaaptamine 2 (greenish yellow powder, mp 248-251°C, $C_{12}H_{10}N_2O_2$) and demethyloxyaaptamine 3 (yellow rods, mp 198-200°C, $C_{12}H_8N_2O_2$). Their yields were 0.17, 0.36 and 0.023%, respectively. The structures of 2 and 3 were elucidated on the basis of their spectral data and the following chemical interrelations. Successive degradation of 2 gave a dimethyl ester 4, which was identical with a degradation product of 1. Further, 2 was treated with a base under atomospheric oxygen to give 3 in 61% yield. These results suggest that 2 and 3 have the same skelton as 1 and that positions of substituents are the same with that of 1. It is also suggested that a substituent at 9 position of 2 is a hydroxy group. The position of a methoxy group was also supported by NOE observed between a proton at 7 position (δ 7.10, 1H,s) and a methoxy group (δ 3.98,3H,s).



1 4 2 3

a) PtO_2 / AcOH - conc HCl b) Ac_2O / Py c) O_3 / MeOH d) Me_2S
e) CH_2N_2 f) Na_2CO_3 / H_2O - MeOH