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6-Propionyllumazines from the Marine Polychaete, Odontosyllis undecimdonta

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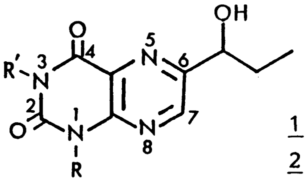
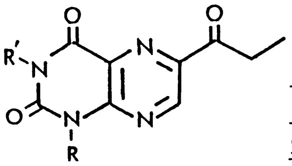
6-Propionyllumazine and its 3-methyl and 1,3-dimethyl derivatives have been isolated from the swimming polychate, Odontosyllis undecimdonta.

In 1981 Cardellina and Meinwald[1)] isolated a minor metabolite of 6-substituted lumazine derivative from Leucetta microraphis, a calcareous sponge common in Bermudan waters, and named it leucettidine. Its structure was proposed as 1 based on analysis of various spectral data. However, in 1984 Pfleiderer[2)] revised the structure of leucettidine to 6-(1-hydroxypropyl)-1-methyllumazine (2) by comparison of the natural product with an authentic sample prepared by an unambiguous synthesis.

Recently, we isolated three 6-substituted lumazine derivatives from the luminescent marine polychaete called "fire worm", Odontosyllis undecimdonta,[3)] collected at Toyama-Bay in Japan.



1 : R=H, R'=CH_3
2 : R=CH_3, R'=H



3 : R=H, R'=CH_3
4 : R=R'=CH_3
5 : R=R'=H

The structures of three natural products were deduced from various spectral data involving high resolution mass spectra[4)] on 6-propionyllumazine derivatives to determine the empirical formula for $C_{10}H_{10}O_3N_4$ and $C_{11}H_{12}O_3N_4$, and ^1H and ^{13}C-NMR spectra[5)] to elucidate the nature of the substituents such as the -CO-CH_2CH_3 group coupled with the basic nucleus of the lumazine framework. From the above physical properties, the structures of two of three derivatives were assigned as 3-methyl-6-propionyllumazine (3) and 1,3-dimethyl-6-propionyllumazine (4), respectively, and were characterized by comparison of their physical data (TLC, NMR, and UV spectra) with those of authentic samples prepared by the known method.[6)] The structure of the remaining metabolite was deduced as 6-propionyllumazine (5) by NMR analysis[7)] in conjunction with high resolution mass spectrometry.[7)] When 5 was methylated with MeI-K_2CO_3 in DMF (rt, 1 h), the known compound of 1,3-dimethyl-6-propionyllumazine (4)[6)] was obtained via the 3-methyl derivative (3).

Isolation of these lumazine derivatives possessing the propionyl substituent at C-6 position from the natural source is the first example. Whether compounds 3, 4, and 5 are related to the luminescent system in Odontosyllis bioluminescence is not yet known. Studies on the roles of 6-propionyllumazines on Odontosyllis and on the characterization of other fluorescent substances are in progress.

Isolation of 6-propionyllumazine derivatives was accomplished as follows: freeze-dried worms (6 g, ca. 3000 individuals) were ground and subsequently emitted a bright luminescence after being placed in 120 ml of water. The suspended worms were repeatedly ground and squeezed until luminescence could no longer be detected and then evaporated to dryness in vacuo. The contents thus obtained were extracted with MeOH. The MeOH extracts (2 g) were taken up in MeOH-CH_2Cl_2 (1:10) and the solvents were removed. Separation of the soluble portion in MeOH-CH_2Cl_2 (680 mg) through Toyopearl$^{8)}$ column using MeOH afforded three fractions containing 3, 4, and 5, which were separated on silica-gel TLC plates using MeOH-CH_2Cl_2 (1:20 for 3 and 4, and 1:10 for 5). Further TLC purification of each fractions using AcOEt-benzene-MeOH (10:6:1) gave pure compound 3 (31.2 mg), 4 (29.9 mg), and 5 (7.7 mg), respectively.

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References

1) J. H. Cardellina II and J. Meinwald, J. Org. Chem., 46, 4782 (1981).

2) a) W. Pfleiderer, Tetrahedron Lett., 25, 1031 (1984); b) W. Pfleiderer, Tetrahedron, 44, 3373 (1988).

3) This swimming worm appeared at the surface of the water in some abundance for only a few minutes begining shortly after sunset and spawned during 30 minutes. The spawning can be observed only once a year for about three weeks from the end of September to the middle of October at Toyama-Bay.

4) 3: High-resolution MS Found: m/z 234.0768; $C_{10}H_{10}O_3N_4$ requires 234.0752; 4: High-resolution MS Found: m/z 248.0905; $C_{11}H_{12}O_3N_4$ requires 248.0909.

5) 3: mp 227-228 °C (lit.$^{2b)}$); UV (MeOH) λ_{max} 249 nm (log ε 4.09), 272(4.03), 328(4.00); UV (MeOH-NaOH) λ_{max} 256 nm (log ε 4.05), 313(4.24), 372(3.97); ^{1}H-NMR (270 MHz, DMSO-d_6) δ 1.12(3H, t, J=7.4 Hz), 3.16(2H, q, J=7.4 Hz), 3.29 (3H, s), 9.10(1H, s), 12.64(1H, br s, NH); ^{13}C-NMR (DMSO-d_6) δ 7.5(q), 27.6(q), 30.3(t), 125.5(s), 142.5(s), 146.7(d), 150.0(s), 150.1(s), 160.0(s), 199.6(s); 4: mp 146-147 °C (lit.$^{6)}$); UV (MeOH) λ_{max} 251 nm (log ε 4.11), 280(4.07), 332(3.98); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.24(3H, t, J=7.3 Hz), 3.33(2H, q, J=7.3 Hz), 3.57(3H, s), 3.76(3H, s), 9.28(1H, s); ^{13}C-NMR ($CDCl_3$) δ 7.5(q), 29.2(q), 29.8(q), 31.3(t), 125.7(s), 143.4(s), 147.0(d), 149.7(s), 150.4(s), 159.3(s), 200.4(s).

6) R. Baur, E. Kleiner, and W. Pfleiderer, Liebigs Ann. Chem., 1984, 1798.

7) 5: mp 278-280 °C (decomp); UV (MeOH) λ_{max} 241 nm (log ε 3.87), 273(4.05), 327(3.96); UV (MeOH-NaOH) λ_{max} 242 nm (log ε 3.90), 312(4.21), 368(3.90); ^{1}H-NMR (270 MHz, DMSO-d_6) δ 1.12(3H, t, J=7.4 Hz), 3.15(2H, q, J=7.4 Hz), 9.08(1H, s), 11.85(1H, br s, NH), 12.32(1H, br s, NH); ^{13}C-NMR (DMSO-d_6) δ 7.6(q), 30.1(t), 126.3(s), 141.7(s), 146.7(d), 150.9(s), 152.9(s), 160.7(s), 199.6(s); High-resolution MS Found: m/z 220.0593; $C_9H_8O_3N_4$ requires 220.0596.

8) TSK gel TOYOPEARL HW-40C, Tosoh Corporation.

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