A NEW HEXAGONAL CYCLIC ENOL PHOSPHATE OF 6-β-HYDROXYPROPIONYLLUMAZINES FROM THE MARINE SWIMMING POLYCHAETE, ODONTOSYLLIS UNDECIMDONTA

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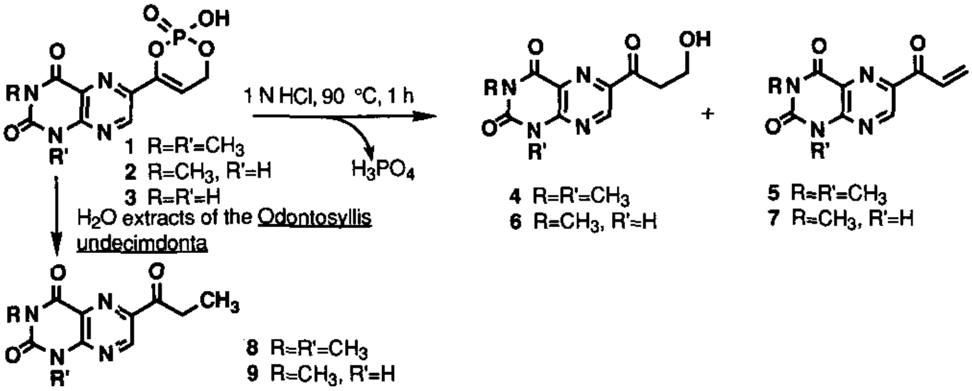
Abstract-A new hexagonal cyclic enol phosphate of 6-β-hydroxypropionyllumazine and its 3-methyl and 1,3-dimethyl derivatives were isolated from *Odontosyllis undecimdonta*.

The marine swimming polychaete, *Odontosyllis undecimdonta*, was found to contain considerable amounts of 6-propionyllumazine derivatives.[1] In efforts to isolate compounds related to lumazines from the same polychaete, a new type of cyclic phosphate of 6-β-hydroxypropionyllumazines was isolated, as discussed in the following.

Specimens of *Odontosyllis* were collected by hand using a fine mesh net at Namerikawa and Uozu sea shores in Toyama Bay[2] and stored in dry ice. The frozen specimens (*ca*. 5000 individuals) were lyophilized (*ca*. 10 g) and extracted with ether and MeOH. The MeOH extracts (2 g) were chromatographed on a silica gel column developed with AcOEt/acetone/MeCN/MeOH/H_2O (3:1:1:1:1) to afford a mixture of three crude metabolites. Repeated chromatography of the mixture on silica gel tlc using i) 80% MeCN ii) AcOEt/acetone/MeOH/H_2O (5:2:2:1) and iii)

MeOH/CH_2Cl_2(1:2) gave pure compounds (**1**) (14.7 mg),[3] (**2**) (45 mg),[4] and (**3**) (2.7 mg),[5] respectively. The structures of **1**, **2**, and **3** were deduced based on analysis of various spectral data and chemical conversions. The molecular formula of the major metabolite (**2**) was $C_{10}H_9N_4O_6P$ by HRms [FAB, m/z 313.0337, $(M+H)^+$, 0.8 mmu error]. The presence of P in **2** was confirmed from the ^{31}P nmr spectrum, in which a signal at δ -7.69 ppm was observed as a triplet (J=10.6 Hz, ^1H-^{31}P long range correlation from $-CH_2-O-PO_3-$). Reasonable resonances for an allylic structure of the C_3-side chain were observed in ^1H and ^{13}C as well as ^{31}P nmr spectra[4] of **2** suggesting the cyclic phosphate structure in **2**. The acid hydrolysis of **2**[6] gave phosphoric acid and an equilibrated mixture of a known compound of 6-β-hydroxypropionyl-3-methyllumazine (**6**)[1b] and its dehydrated form (**7**).[7] The structure of **2** would thus appear quite likely to be the hexagonal cyclic enol phosphate of 6-β-hydroxypropionyl-3-methyllumazine (**6**). The ^1H, ^{13}C, and ^{31}P nmr spectra of **1**[3] and **2**[4] were quite similar except for proton and carbon signals due to the N-methyl group. Acid hydrolysis of **1** under the same condition as for **2** gave 6-β-hydroxypropionyl-1,3-dimethyllumazine (**4**)[8] and its dehydrated form (**5**),[9] respectively. On the other hand, when compound (**3**) was methylated with MeI-K_2CO_3 in DMF (room temperature, 2 h), **1** was obtained via **2**. The structures of **1** and **3** were thus concluded to be that of the similar cyclic enol phosphate, as shown below.



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

4 R=R'=CH_3
6 R=CH_3, R'=H

5 R=R'=CH_3
7 R=CH_3, R'=H

8 R=R'=CH_3
9 R=CH_3, R'=H

Phosphates (**1**) and (**2**) were easily hydrolyzed with 1N HCl under heating to give 6-β-hydroxypropionyllumazines (**4**) and (**6**), respectively. When they were treated with water extracts of the above lyophilized *Odontosyllis undecimdonta* at room temperature, 6-propionyllumazines (**8**)[1a] and (**9**)[1a] were obtained in good yields. Further studies on this interesting reductive dephosphorylation are in progress.

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REFERENCES AND NOTES

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2. This swimming polychaete appeared on the surface of water in some abundance about thirty minutes after sunset and luminesced and spawned for approximately thirty minutes. Specimens were collected from the end of September to end of October.
3. **1**: Pale yellow prisms (H_2O-MeOH), mp 220-227 °C (decomp.); ^1H nmr (400 MHz, DMSO-d6) δ 3.33 (3H, s), 3.56 (3H, s), 4.63 (2H, dd, J_{HH}=2.7 Hz, J_{HP}=10.8 Hz), 6.08 (1H, q, J_{HH}=2.7 Hz, J_{HP}=2.7 Hz), 8.80 (1H, s); ^{13}C nmr (25 MHz, CD_3OD) δ 29.3, 29.8, 66.5 (d, J_{CP}=5.9 Hz), 105.0 (d, J_{CP}=11.7 Hz), 127.7, 144.4 (d, J_{CP}=8.8 Hz), 144.6, 147.4 (d, J_{CP}=5.9 Hz), 148.9, 152.0, 162.3; ^{31}P nmr (162 MHz, D_2O, H_3PO_4=0 ppm) δ -7.52 (t, J_{PH}=10.8 Hz); ms (FAB, negative ion) m/z 325 $(M-H)^-$.
4. **2**: Pale yellow needles (H_2O-MeOH), mp 230-235 °C (decomp.); ^1H nmr (400 MHz, DMSO-d6) δ 3.25 (3H, s), 4.57 (2H, dd, J_{HH}=2.8 Hz, J_{HP}=10.6 Hz), 5.97 (1H, br s), 8.67 (1H, s); ^{13}C nmr (100 MHz, CD_3OD) δ 28.4, 66.5 (d, J_{CP}=5.9 Hz), 104.5 (d, J_{CP}=11.7 Hz), 127.0, 144.7 (d, J_{CP}=8.8 Hz), 145.5, 147.6 (d, J_{CP}=4.9 Hz), 148.9, 151.9, 163.2; ^{31}P nmr (162 MHz, D_2O, H_3PO_4=0 ppm) δ -7.69 (t, J_{PH}=10.6 Hz); ms (FAB, positive ion) m/z

313 $(M+H)^+$, (FAB, negative ion) m/z 311 $(M-H)^-$; HRms (FAB) Found: m/z 313.0337. Calcd for $C_{10}H_{10}N_4O_6P$: 313.0345.

5. **3**: Pale yellow crystalline solid, mp 225-235 °C (decomp.); ^1H nmr (400 MHz, DMSO-d6) δ 4.57 (dd, J_{HH}=2.0 Hz, J_{HP}=10.4 Hz), 5.95 (1H, m), 8.64 (1H, s), 11.47 (2H, br s).
6. This reaction was conducted in a nmr tube and monitored progress for the hydrolysis by measuring changes in signals in the ^{31}P nmr spectrum. A solution of **2** (10.0 mg) in 3 ml of 1N DCl was heated at 90 °C in a nmr tube (10 mmΦ). During hydrolysis, a triplet at δ -7.69 ppm due to the phosphate gradually contracted and disappeared completely after 1 h. The intensity of a signal at δ 0 ppm due to phosphoric acid markedly increased. Evaporation followed by the usual work up and separation of the resulting reaction products on silica gel tlc using $MeOH/CH_2Cl_2$ (1:10) gave **6** (4.2 mg) and **7** (1.9 mg), respectively.
7. **7**: ^1H Nmr (400 MHz, $CDCl_3$) δ 3.55 (3H, s), 6.05 (1H, dd, J=1.8, 10.6 Hz), 6.73 (1H, dd, J=1.8, 17.2 Hz), 7.90 (1H, dd, J=10.6, 17.2 Hz), 9.09 (1H, br s), 9.34 (1H, s).

   An equilibrium mixture (2.5:1) of **6** and **7** was obtained when a solution of **6** (or **7**) in 90% TFA was heated at 70 °C for 1 h.
8. Compound (**4**) was characterized by a comparison of physical data with those of an authentic sample prepared from synthetic 6-β-methoxypropionyl-1,3-dimethyllumazine[1b] by acid hydrolysis (90% TFA, 70 °C, 3 h). **4**: Light yellow prisms, mp 169-170 °C; ^1H nmr (400 MHz, $CDCl_3$) δ 3.54 (2H, t, J=5.5 Hz), 3.57 (3H, s), 3.77 (3H, s), 4.08 (2H, t, J=5.5 Hz), 9.30 (1H, s).
9. **5**: ^1H Nmr (400 MHz, $CDCl_3$) δ 3.57 (3H, s), 3.78 (3H, s), 6.04 (1H, dd, J=1.8, 10.6 Hz), 6.72 (1H, dd, J=1.8, 17.6 Hz), 7.92 (1H, dd, J=10.6, 17.6 Hz), 9.38 (1H, s).

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