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ISOLATION AND STRUCTURES OF TWO NEW PYRAZINES, PALYTHAZINE AND ISOPALYTHAZINE FROM PALYTHOA TUBERCULOSA

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Two new compounds possessing a pyrazine ring system were isolated from the zoanthid Palythoa tuberculosa. These compounds have now been named palythazine and isopalythazine and assigned to structures 1 and 2, respectively, by means of spectral analysis and synthesis.

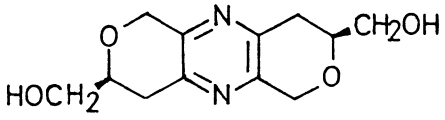
In the course of our continuous research on the UV-absorbing substances[1] at 310-360 nm from Palythoa tuberculosa, we found and isolated two new pyrazines, palythazine and isopalythazine. Now, we wish to report herein the isolation and structures of these compounds.

75% EtOH extracts of Palythoa tuberculosa were concentrated carefully under reduced pressure. The aqueous oily material obtained by evaporation was charged on TSK-G3000S (polystyrene gel) column which was washed with water. The aqueous eluate contains mycosporine-Gly[2], palythine[3], palythinol[4] and palythene[4]. The subsequent eluates of 50% ethanol were combined and concentrated to afford a mixture containing new pyrazines. This was separated by column chromatography with silicic acid monitered by UV absorption. The eluate of MeOH-$CHCl_3$ (15%, V/V) was concentrated to give crystalline compounds, which were treated with 3,5-dinitrobenzoyl chloride in pyridine at 50°. Two products produced by this reaction were separated by preparative TLC with silicic acid, and then each product was hydrolyzed with methanolic KOH solution giving palythazine (m.p. 169-170°) and isopalythazine (m.p. 216-219°). The ester of palythazine showed the larger Rf value on TLC plate than one of isopalythazine.

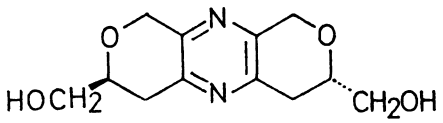
Both compounds possess the same molecular formula, $C_{12}H_{16}N_2O_4$, which was secured by high-resolution mass spectrometry, respectively. The PMR and CMR (Table 1) spectra indicate that palythazine and isopalythazine have the symmetrical structures. However, the result from ORD measurement indicates that two compounds are optically active. Since the UV spectrum of palythazine shows the absorption maxima at 286 and 303 nm, the presence of pyrazine ring system is suggested. Treatment of palythazine with zinc dust in acetic acid afforded a keto alcohol 3. Therefore, two plausible structures 1 and 2 were derived from above data. Furthermore, palythazine and isopalythazine could be assigned to structures 1 and 2, respectively, on the basis of the following observation. The difference of chemical shifts between C-2 and C-3 in each CMR spectrum reflects the degree of equivalence among the carbon atoms on pyrazine ring system as shown in table 2. The difference of chemical shifts in palythazine is 0.10 ppm and in the case of isopalythazine it is 1.44 ppm.

In order to confirm the ring system of palythazine and isopalythazine, we at-

tempted to derive these compounds from the suitable starting material such as kojic acid 4. Obtained results were depicted in Scheme 1. Cyclization of tetrahydrokojic acid 5 was achieved by treatment with ammonium acetate[5]. Except two products, (±)-palythazine and (±)-isopalythzine, we obtained two additional compound 6 and 7. As mentioned in the isolation of palythazine and isopalythazine, these products were purified by separation by preparative TLC as the 3,5-dinitrobenzoates, and then by hydrolysis of each ester. Determination of absolute configuration and biosynthetic pathway of 1 and 2 are under progress.



1 Palythazine

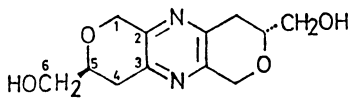


2 Isopalythazine

Table 1. ^{13}C Chemical shifts[a] (δ in ppm) of palythazine and isopalythazine.

Carbon number	1	2	3	4	5	6
Palythazine 1	68.34	147.88[b]	147.98[b]	32.08	76.32	64.29
Isopalythazine 2	68.37	147.20[c]	148.64[c]	31.95	76.32	64.28
Multiplicity	t	s	s	t	d	t

[a]Internal standard; dioxane (67.4 ppm) [b,c]Assignment may be reversed.



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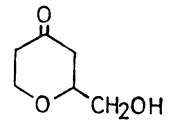

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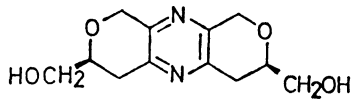

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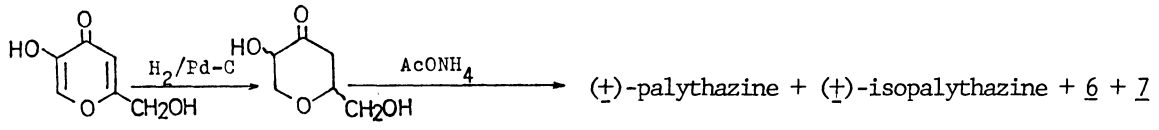
Table 2. Difference between chemical shifts of C-2 and C-3 in the CMR spectrum of each alkylated pyrazines and p-quinones.

Compounds	Δδ in ppm
2,5[a]-Dimethylpyrazine	7.7
2,6-Dimethylpyrazine	12.2
2,5-Dihydroxymethylpyrazine	10.8
2,6-Dihydroxymethylpyrazine	14.8
2,5-Di-tert-butyl-p-quinone[6]	18.7
2,6-Di-tert-butyl-p-quinone[6]	27.6

[a]These numbers differ from numbering in the case of palythazine and isopalythazine.

Scheme 1.



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References: 1) Y.Hirata, D.Uemura, K.Ueda, and S.Takano, Pure Appl.Chem.,51,1875 (1979). 2) S.Ito and Y.Hirata, Tetrahedron Lett.,2429(1977). 3) S.Takano, D.Uemura, and Y.Hirata, Tetrahedron Lett.,2299(1978). 4) S.Takano, D.Uemura, and Y.Hirata, Tetrahedron Lett.,4909(1978). S.Takano, A.Nakanishi, D.Uemura, and Y.Hirata, Chemistry Lett.,419(1979). 5) T.Kosuge and K.Sugiyama, unpublished work. 6) S.Berger and A.Rieker, Tetrahedron,28,3123(1972).

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