to remove traces of acetic acid: mp 121–124 °C dec; R_f (IV) 0.82, R_f (V) 0.60; IR (KBr) 3200–3000 (COOH and NH), 1760 (ester C=O), 1660 (amide C=O), 1630 cm^{-1} (C=C); NMR (CD_3OD) δ 7.7–7.3 (m, 6 H, HC=C and ArH), 4.3 (m, 1 H, α-H), 3.8 (s, 3 H, $COOCH_3$), 3.0–2.8 (m, 2 H, β-CH_2).

Anal. Calcd for $C_{14}H_{16}N_2O_5 \cdot {}^1/_2H_2O$: C, 55.75; H, 5.64; N, 9.29. Found: C, 55.76; H, 5.74; N, 9.22.

Acknowledgment. We gratefully acknowledge the partial financial support of this work by Research Corporation, Summer, 1979.

Registry No. **2**, 79043-73-5; **3**, 68763-45-1; **4**, 79043-74-6; **5**, 79043-75-7; **6**, 79043-76-8; *N*-(*tert*-butoxycarbonyl)-L-aspartic acid β-benzyl ester, 7536-58-5; L-phenylalanine, 63-91-2.

Leucettidine, a Novel Pteridine from the Calcareous Sponge *Leucetta microraphis*[1]

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Received June 16, 1981

Leucettidine, 6-(1-hydroxypropyl)-3-methylpteridine-2,4(1*H*)-dione (1), has been isolated from dichloromethane and acetone extracts of *Leucetta microraphis*, a calcareous sponge from low-light zones in Bermudan waters. The structure of leucettidine was deduced by analysis of spectral data and the absolute configuration was proposed on the basis of comparison of optical rotation data of leucettidine and other pteridines of known configuration.

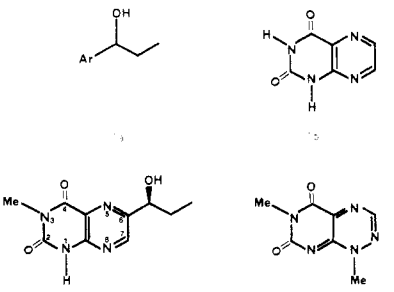
The last 15 years have witnessed a rapid growth of research interest in marine natural products. The chemistry of sponges has attracted much of this attention and work by numerous groups has yielded a plethora of novel compounds, many of which exhibit interesting pharmacological activity. Most of the research on sponges has been focused on the Demospongiae, a major class of widely distributed siliceous sponges.[2]

The class Calcispongiae (Calcarea), on the other hand, has been largely overlooked. Herein we describe leucettidine, a minor metabolite of *Leucetta microraphis*, a calcareous sponge common in Bermudan waters. Leucettidine, a levorotatory, amorphous solid, was isolated from dichloromethane and acetone extracts of the freeze-dried sponge by a combination of adsorption chromatography and gel filtration. We have assigned structure 1 to this metabolite on the basis of the evidence discussed below.

Discussion

The one-proton singlet at δ 8.76 in the ^1H NMR spectrum of leucettidine is indicative of a heteroaromatic ring, while the long wavelength and relatively low molar extinction coefficients of the ultraviolet absorption maxima suggest a bicyclic heteroaromatic chromophore. High-resolution mass spectrometry supported this conclusion, revealing a molecular ion of formula $C_{10}H_{12}N_4O_3$, consistent with seven sites of unsaturation. There was very little fragmentation of the molecular ion or the base peak, which further supported the basic skeletal assignment. NMR decoupling experiments led us to partial structure **1a**, incorporating a 1-(1-hydroxypropyl) group. The chemical shift of the alcohol-bearing methine, at δ 4.84, indicates that this moiety is most likely attached to the aromatic nucleus. This assumption was substantiated by observation of mass spectral α cleavage on but one side of the alcohol, giving rise to the base peak at m/e 207 ($M^+ - 29$). The only other nonaromatic protons in the ^1H NMR spectrum of **1** appear as a methyl singlet at δ 3.63.

The molecular formula and the ultraviolet absorption data are best accomodated by a pteridinedione chromophore, as shown in **1b**.[3] The intense, broad carbonyl absorption at 1710 cm^{-1} in the infrared spectrum of **1** supports this suggestion; a model compound, the antibiotic toxoflavin, **2**,[4] has two overlapping infrared absorptions between 1710 and 1720 cm^{-1}.



Further examination of, and correlation of our data with, the pteridine literature has led us to propose structure **1** for leucettidine. Placement of the methyl group on the nitrogen at position 3 of the pteridine nucleus is prompted by chemical shift data for various methyl-substituted pteridines (**3**–**5**)[5] and analogues (**6**–**7**).[6] The hydroxypropyl

(1) (a) Contribution No. 869 from the Bermuda Biological Station. (b) A preliminary report of this work was presented at the 41st Meeting of the Montana Academy of Sciences, April 1981.

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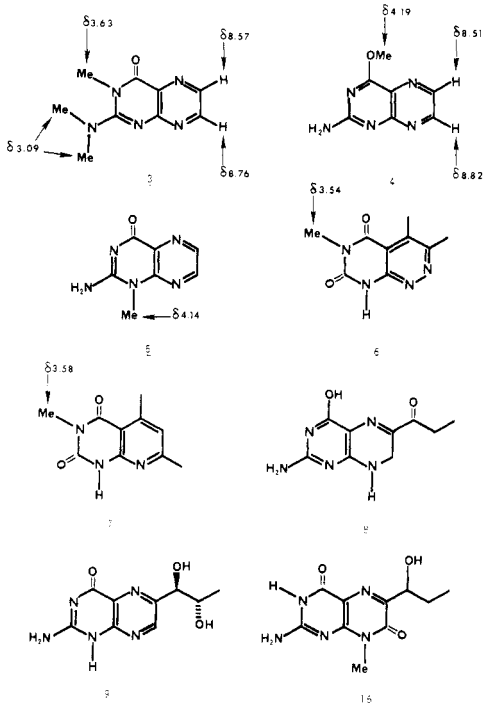
0022-3263/81/1946-4782$01.25/0

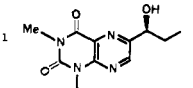
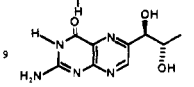
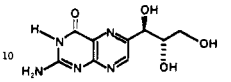
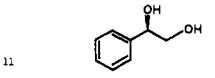
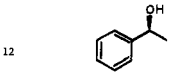
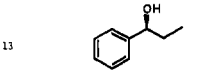
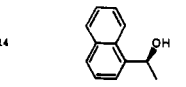
moiety is placed at C-6 because the aromatic proton in **1** resonates at δ 8.76, in agreement with the assignments[5] for H-7 in **3** and **4**. In addition, the majority of naturally occurring, alkyl-substituted pteridines possess propyl substituents at C-6, as in isosepiapterin (**8**) and biopterin (**9**).



Having examined the optical rotations and absolute configurations of several model compounds, we propose the *S* configuration for the alcoholic methine of **1**. Both L-biopterin (**9**)[7] and L-neopterin (**10**)[8] exhibit the same sign and a similar magnitude of optical rotation as leucettidine, suggesting the same configuration at the α carbon of the propyl substituents in all three molecules. To gauge the contribution of the chiral β carbons in **9** and **10** to the optical rotations, we examined (*R*)-(−)-phenylethane-1,2-diol (**11**);[9] this levorotatory compound possesses a magnitude of optical rotation similar to those of **9** and **10**, indicating that the contribution from the chiral β carbons is small compared to that of the α carbons. Finally, we assessed the importance of the hydroxyl groups on the β carbons by considering the simpler models (*S*)-(−)-1-phenylethanol (**12**),[10] (*S*)-(−)-phenylpropanol (**13**),[10] and (*S*)-(−)-1-naphthylethanol (**14**).[11] Since these compounds are all levorotatory, the contribution of the aromatic systems must exceed that of a β-hydroxyl group. Leucettidine, therefore, possesses the *S* configuration at its lone chiral center. Table I summarizes the data described above.

Leucettidine represesnts a departure from the usual substitution patterns of pteridines in that is has no amino group of C-2 and, along with isosepiapterin (**8**), and 6-(1-hydroxypropyl)-8-methylisoxanthopterin (**15**), recently characterized from the firefly *Photinus pyralis*,[12] it appears to be among the very few naturally occurring pteridines with a monooxygenated propyl side chain.

Table I. Comparison of Optical Rotations of Leucettidine and Model Compounds

compound	$[\alpha]_D$, deg	ref
1 	-35.9	
9 	-65	7
10 	-53	8
11 	-47.9	9
12 	-54.9	10
13 	-55.5	10
14 	-76	11

Momzikoff and his co-workers have recently reported the presence of several previously known pteridines in diatoms,[13] copepods,[14] and tunicates.[15] Since sponges are filter feeders, **1** may be obtained directly from a dietary source, produced by the metabolic action of *L. microraphis* on substrates in its diet, or synthesized de novo by the sponge as a secondary metabolite.

Experimental Section

Infrared spectra were recorded on a Perkin-Elmer Model 257 grating infrared spectrophotometer, ultraviolet spectra on a Beckman DB-6 spectrophotometer, and optical rotations on a Perkin-Elmer Model 141 polarimeter. NMR spectra were obtained on a Varian EM-390 spectrometer; chemical shifts are reported in parts per million (δ units) downfield from tetramethylsilane (δ = 0) as an internal standard. Mass spectra were obtained on an Associated Electronic Industries MS-902 mass spectrometer operating at 70 eV.

Collection and Extraction. *Leucetta microraphis* was collected in September 1979 from shallow caves and under rock overhangs in Harrington Sound, Bermuda, at depths of 3–12 ft. The sponges were freeze-dried (650-g dry weight), chopped, and extracted successively with petroleum ether, dichloromethane, acetone, and methanol.

Isolation of Leucettidine (1). Silica gel chromatography of the dichloromethane (2.57 g) and acetone (1.25 g) extracts, using similar hexane–ethyl acetate–methanol eluant combinations, yielded 10 fractions from each extract. Fractions 6 and 7 from each chromatography, eluted with ethyl acetate and ethyl acetate–methanol (9:1), respectively, were shown by TLC to contain a polar, UV-active component. Repeated gel filtration of these fractions through Sephadex LH-20 with CH_2Cl_2–MeOH (1:1) provided a total of 17 mg of leucettidine (**1**): $[\alpha]_D$−35.9° (*c* 1.26, MeOH); mass spectrum, *m/e* 236.0910 (M^+, 9%, calcd for $C_{10}H_{12}N_4O_3$, 236.0909), 218 (3), 207 (100), 192.0626 (10%, calcd for $C_8H_8N_4O_2$, 192.0647), 136.0512 (12%, calcd for $C_6H_6N_3O$, 136.0511); λ_{max} (MeOH) 334 nm (ϵ 4200), 238 (8500); λ_{max} (MeOH + NaOH) 344 nm (ϵ 4600), 292 (3000), 246 (14 200), 218 (10 400); ν_{max} ($CHCl_3$) 3340, 3140, 2900, 2840, 1718 (sh), 1710, 1582, 1548,

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1489, 1450, 1362, 1316, 1288, 1068, 979, 950 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.76 (1 H, s), 4.84 (1 H, dd, J = 7, 5 Hz), 3.63 (3 H, s), 1.85 (2 H, m), 0.97 (3 H, t, J = 6.5 Hz).

Acknowledgment. We thank Mr. Francis Connor for assistance with the field work and Dr. Klaus Ruetzler of the Smithsonian Institution for identifying the sponge. H. B. Wilkinson and Continental Corporation Fellowships awarded to J.H.C. by the Bermuda Biological Station supported the field work.

Registry No. 1, 79121-29-2.

Notes

Molecular Rearrangements. 19. Thermolysis and Photolysis of *N*-Arylbenzenesulfonamides

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The cleavage of sulfonamides had been frequently used since the famous Hinsberg reaction was discovered[1] for identification and separation of amine mixtures. Three modes of bond cleavages were known, involving the S–N, C–S, or C–N bond[2] according to the type of reagent used.

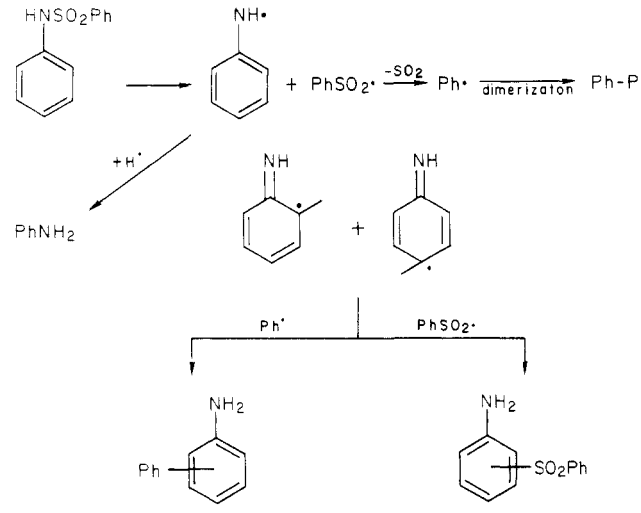
The *N*-phenylsulfonyl group of *N*,*N*-bis(*p*-toluenesulfonyl)aniline has been observed to migrate[3] under the influence of anhydrous aluminium chloride to the aniline nucleus, and this also occurs when solutions of sulfonamides in nitrobenzene or aniline are refluxed[3] or when alkylithium is used as a promoter.[4]

Recently, photolysis of *N*-alkylarenesulfonamides was found to produce the free alkylamine in good yield in addition to other products.[5,6] On the other hand, irradiation of *N*-arylarenesulfonamides induced the Fries-type rearrangement, yielding the diaryl sulfones and the free arylamines together with unidentified byproducts.[6a] Far less is known about the behavior or sulfonamides on thermolysis.

The present work describes the behavior of *N*-arylbenzenesulfonamides on thermolysis and photolysis. Heating *N*-phenylbenzenesulfonamide in a nitrogen atmosphere at ca. 300 °C for 15 h gave sulfur dioxide, aniline, biphenyl, carbazole and a mixture of isomeric *o*- and *p*-aminobiphenyl together with trace amounts of *o*- and *p*-aminobiphenyl sulfones.

The process appears to involve the homolytic fission of an S–N bond to form anilino and phenylsulfonyl radical pairs. The ease of bond rupture parallels the decrease in bond dissociation energy values, being 184, 167, and 116 kcal mol^{-1} (at 25 °C) for the C–N, C–S, and N–S bonds, respectively.[7]

Scheme I



As shown by Scheme I, the anilino radicals abstract hydrogen to form aniline or are subjected to attack by phenylsulfonyl radicals in ortho and para positions forming *o*- and *p*-aminophenyl sulfones. Moreover, the phenylsulfonyl radicals can favorably extrude sulfur dioxide, forming phenyl radicals that couple with the anilino radical in the ortho or para position to form the isomeric aminobiphenyls, whereas dimerization of phenyl radicals leads to the formation of biphenyl.

The appearance of only trace amounts of aminophenyl phenyl sulfones so identified in the products can be interpreted in terms of their thermal instability under such pyrolytic conditions. To confirm this, we heated the isomeric aminophenyl phenyl sulfones and found that sulfur dioxide was extruded in addition to the formation of biphenyl and a mixture of *o*- and *p*-aminobiphenyls and aniline.

It may be suggested that biphenyl can arise from deamination of aminobiphenyls.[8] However, this possibility was ruled out by the observed stability of the isomeric aminobiphenyls under the pyrolytic conditions used. This was further confirmed by the absence of ammonia or ammonium salts among the products.

Possible routes for carbazole formation are cyclization of either *o*-aminobiphenyl (route a of Scheme II) or 2,2′-diaminobiphenyl regarded as the ortho dimer of the anilino radicals (route b of Scheme II).

However, the absence of either ammonia or 2,2′-diaminobiphenyl among the products strongly favors the

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