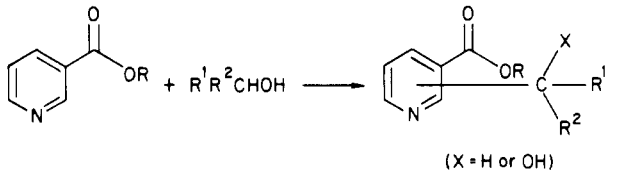
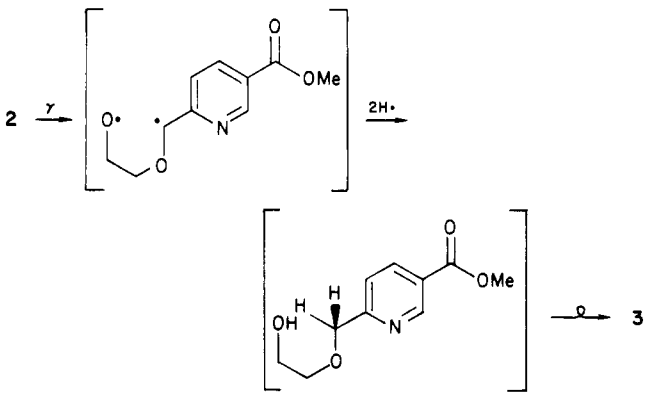


age[14] to give exclusively the methyl substituted products.



Under these radiative conditions, acetal **2** was transformed (ca. 80%) to **3** supporting such a homolytic or related degration hypothesis. This incredibly simple synthetic methodology appears to be a selective, and a clean procedure to alkylate α- and γ-sites on electron-deficient heteroaromatics.

Experimental Section

Irradiation was performed at the Louisiana State University Nuclear Science Center employing a ^{60}Co source (6×10^5 rad h^{-1}). ^1H NMR spectra used in comparison with literature spectra were recorded with an IBM NR-80 spectrometer. Unless specified otherwise, reagent grade reactants and solvents were obtained from chemical suppliers and used directly.

General γ-Irradiation Procedure. Methyl 6-Methylnicotinate (3). To a solution of methyl nicotinate (4.1 g, 30 mmol) in dioxolane (100 mL) was added concentrated H_2SO_4 (4.9 g, 50 mmol), and then the mixture was deaerated with nitrogen gas for 20 min. The solution was sealed in a Pyrex flask and placed in an aluminum bell jar (10 cm i.d. 50 mm wall), which was lowered into the radiation source (^{60}Co, 6×10^5 rad h^{-1}). After 7 days (1.0×10^7 rad), the excess dioxolane was removed in vacuo and the residue neutralized by aqueous Na_2CO_3 (10%). The aqueous layer was extracted with CH_2Cl_2, and then the organic extract was dried over anhydrous $MgSO_4$ and chromatographed (thick-layer chromatography; C_6H_{12}/EtOAc) to give unchanged methyl nicotinate (2.91 g, 71%), methyl 6-methylnicotinate [950 mg, 21%; mp 31 °C (lit.[15] mp 32 °C)], and methyl 4,6-dimethylnicotinate [250 mg, 5%; mp 43–44 °C (lit.[16] mp 44–45 °C)]. Each product was confirmed by ^1H NMR comparison with literature spectra;[7,13] the purity of each was >95%.

Acknowledgment. We acknowledge the National Science Foundation, the National Institutes of Health for partial support of this research, and Dr. Edward N. Lambremont, Director of the LSU Nuclear Science Center, for his technical assistance.

Registry No. 1, 93-60-7; 3, 5470-70-2; 4, 69971-44-4; dioxolane, 646-06-0.

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Stevensine,† a Novel Alkaloid of an Unidentified Marine Sponge

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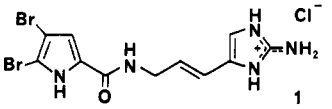
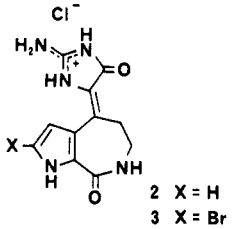
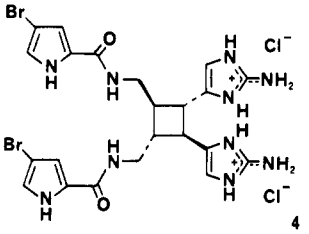
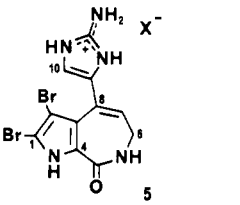
Marine sponges have yielded relatively few alkaloids.[1,2] Perhaps the best known group of sponge alkaloids is the "oroidin group", C_{11} compounds exemplified by oroidin (**1**) from *Agelas oroides*[3] and the yellow compounds **2** and **3** from *Phakellia flabellata*,[4] *Axinella verrucosa*,[5] *Acanthella aurantica*, and *Hymeniacidon aldis*.[6] Our study of an unidentified[7] Micronesian sponge has resulted in the isolation of sceptrin (**4**)[8] and a new metabolite, stevensine (**5**), which possesses the 6,7-dihydropyrrolo[2,3-*c*]azepin-8-one ring system.









The methanol-soluble material from the unidentified Micronesian sponge was chromatographed on Sephadex LH-20 with methanol as eluant to obtain sceptrin (**4**, 0.19% dry weight) and stevensine (**5**, 0.10% dry weight). Stevensine (**5**) was obtained as an amorphous orange solid, soluble only in polar solvents such as methanol, DMF, and Me_2SO. When heated, **5** decomposed slowly over a wide temperature range which did not prove diagnostically useful. The UV spectrum of **5** exhibited maxima at 258 (ϵ 11 600) and 220 nm (ϵ 17 200) similar to those of metabolites of the oroidin class. Infrared spectroscopy was of limited value but did indicate the presence of a carboxamide (1650, 1450 cm^{-1}) as well as broad absorption in the N–H region (3600–2800 cm^{-1}). Electron-impact mass spectrometry did not yield reproducible spectra, but high-resolution FAB mass spectrometry indicated a molecular formula of $C_{11}H_{10}Br_2N_5O$, highly suggestive of an oroidin-like structure. Decoupling of the ^1H NMR spectra of stevensine (Me_2SO-d_6) revealed a =CH—CH_2—NH— subunit in addition to exhangeable protons at δ 7.43 and a one-proton singlet at δ 6.90 (δ 6.81 in CD_3OD). When stevensine was treated with aqueous Na_2CO_3, a new substance with similar NMR, IR, and UV data was obtained, indicating that stevensine (**5**) was an amine salt that had been converted into its free base. In the ^1H NMR spectrum of the free base, the aromatic single was shifted upfield to δ 6.45 (from δ 6.81) consistent with the assignment of this resonance to an imidazole C–H. Commercially obtained 2-aminoimidazole sulfate shows a similar upfield shift of 0.24 ppm when converted to its free base (δ 6.86

† Stevensine is named for the late Robert V. Stevens.
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to δ 6.62 in CD_3OD). The bromine atoms were assigned to the pyrrole ring of **5**, which is related to oroidin (**1**) by oxidative cyclization. The ^{13}C NMR spectrum contained 11 signals including key resonances occurring at δ 161.5 (amide carbonyl), 147.0, 126.0, and 111.6 (2-aminoimidazole ring) and was entirely consistent with this structural assignment.

Experimental Section

Extraction and Chromatography. The specimen was collected by hand (Scuba, −15 m) at Ponape, Carolina Islands. The sponge (76.1 g dry weight) was soaked in methanol at ca. 0 °C for ca. 6 months, after which the solvent was evaporated to leave of an amorphous light orange solid (18.7 g). This residue was sequentially extracted with 2 × 400 mL portions of hexane. CH_2Cl_2, EtOAc, and methanol. The methanol soluble material was chromatographed on Sephadex LH-20 using methanol as the eluant. The fractions were monitored by TLC on silica using a CH_3OH/CH_2Cl_2/concentrated NH_4OH (6:3:1) solvent system. Rechromatography of the active fractions (antimicrobial assay) gave sceptrin (**4**, 144 mg, 0.19% dry weight) and stevensine (**5**, 80 mg, 0.10% dry weight) as amorphous orange solids.

Stevensine (5): IR (film) 3400, 1650, 1450 cm^{-1}; UV (CH_3OH) 258 (ε 11 600), 220 (ε 17 200) nm; ^1H NMR (360 MHz, Me_2SO-d_6) δ 8.21 (br t, 1 H, amide N*H*), 7.43 (s, 1 H, pyrrole N–H), 6.90 (s, 1 H, H-10), 6.21 (t, J = 7 Hz, 1 H, H-7), 3.48 (br m, 2 H, $-CH_2-$); (CD_3OD) δ 6.81 (s, 1 H, H-10), 6.27 (t, J = 7 Hz, 1 H, H-7), 3.50 (d, J = 7 Hz, 2 H, $-CH_2-$); ^{13}C NMR (50 MHz, Me_2SO-d_6) δ 161.5 (s, C-5), 147.0 (s, C-11), 128.5 (s, C-4), 126.0 (s, C-9), 125.9 (d, C-7), 124.6 (s, C-3), 120.9 (s, C-8), 111.6 (d, C-10), 107.6 (s, C-1), 97.7 (s, C-2), 37.2 (t, C-6); high-resolution fast atom bombardment mass spectrum, obsd m/z 385.9248, $C_{11}H_{10}Br_2N_5O$ requires 385.9252.

Acknowledgment. This research was supported by grants from the National Institutes of Health (AI-11969 and CA07458 to K.F.A.).

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Organic Disulfides and Related Substances. 44. Preparation and Characterization of 1-Adamantyl Hydrodisulfide as a Stable Prototype of the Series[1a]

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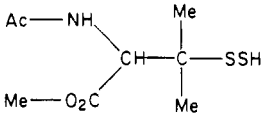
Two recent papers have described the preparation and characterization of hydrodisulfide derivatives of penicillamine.[2,3] Reasons were outlined in these papers for interest in hydrodisulfides as a class and, in particular, for seeking especially stable hydrodisulfides. The present paper reports the preparation and characterization of 1-adamantyl hydrodisulfide and compares the shelf life with that reported for the penicillamine derivatives **1**[2] and **2**.[3]

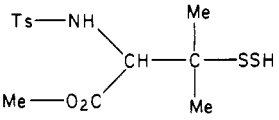
Table I. ^{13}C Chemical Shifts (δ) of 1-Adamantane Derivatives[a]

compd	C-1	C-2	C-4	C-3
AdSH	47.56	43.18	35.79	30.11
AdSSAd	47.32	43.10	36.20	30.11
AdCl	68.74	47.72	35.63	31.73
AdSCl	51.05	40.74	36.04	29.46
AdSSAc	50.16	42.11	35.80	29.79
AdSSH	46.73	41.56	36.16	29.82
AdSS-2,4-DNP	52.98	42.77	35.84	30.04
AdSSSSAd	50.73	42.93	36.13	30.03

[a] Ad = 1-adamantyl (tricyclo[3.3.1.1]decan-1-yl).



1



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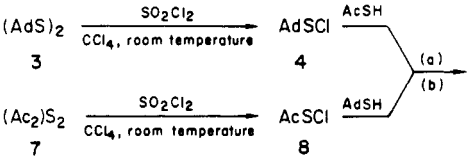
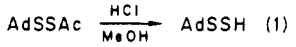
The preparation of 1-adamantyl hydrodisulfide was achieved by acid-catalyzed methanolysis[4] of the acetyl disulfide derivative **5** (eq 1). The required acetyl disulfide derivative **5** should be available by two routes, by the

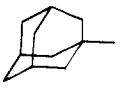


3 4 7 8



5 6

Ad =



reaction of adamantanesulfenyl chloride with thioacetic acid (eq 1a) or by the reaction of 1-oxoethanesulfenyl chloride with 1-adamantanethiol (eq 1b). We examined both of these routes and found the second more satisfactory.

Attempts to convert 1-adamantyl disulfide (**3**) to sulfenyl chloride **4** followed by reaction of the sulfenyl chloride with thioacetic acid gave product mixtures from which it was difficult to separate the desired product. Efforts were made to improve the preparation of **4** by a study of the chlorinolysis of **3** by both Cl_2 and SO_2Cl_2, since it had been reported earlier that the chlorinolysis of another tertiary disulfide, *tert*-butyl disulfide, gave different products at −20 and 45 °C.[5] Initially, a GC method was used to assess S–S vs. S–C cleavage under various conditions by determining the amount of the S–C bond cleavage product, 1-chloroadamantane. However, we found that the GC method could not be used because 1-adamantanesulfenyl

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