J = 11.0 Hz), 4.32 (1 H, dd, J = 6.0, 1.5 Hz), 6.61 (1 H, s), 6.7 (1 H, s); mass spectrum, m/z 335 (M^+); high resolution mass spectrum obsd m/z 335.1024 ($C_{17}H_{21}NO_2S_2$ (M^+) requires 335.1014). Anal. Calcd for $C_{17}H_{21}NO_2S_2$: C, 60.89; H, 6.26; N, 4.17. Found: C, 60.69; H, 6.36; N, 4.04.

1,4-Addition product of 1-cyclohexenecarbonitrile (cf. eq 1, $R_1 = R_2 = H$): cis, mp 133-134 °C; IR ($CHCl_3$) 2240 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.17-1.4 (3 H, m), 1.55-1.68 (1 H, m), 1.72-1.92 (3 H, m), 1.94-2.05 (2 H, m), 2.1-2.2 (2 H, m), 2.7-2.85 (1 H, m), 2.85-3.0 (4 H, m), 3.42 (1 H, ddd, J = 3.5, 2.9, 1.4,2.9 Hz), 4.0 (1 H, d, J = 10.8 Hz); mass spectrum, m/z 227 (M^+); high resolution mass spectrum, obsd m/z 227.0791 ($C_{11}H_{17}NS_2$ (M^+) requires 227.0801); trans, mp 120-131 °C; IR ($CHCl_3$) 2240 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.17-1.3 (3 H, m), 1.55-1.68 (1 H, m), 1.71-1.92 (3 H, m), 1.93-2.05 (2 H, m) 2.1-2.2 (2 H, m), 2.7-2.85 (1 H, m), 2 .85-2.95 (3 H, m), 3.04 (1 H, ddd, J = 12.1, 11.1, 4.0 Hz), 4.56 (1 H, d, J = 3.6 Hz).

Hydrolysis of the Product 3. A mixture of the dithiane (335 mg, 10 mmol), mercuric chloride (1.62 g, 6 mmol), and calcium carbonate (800 mg, 8 mmol) in aqueous 80% acetonitrile (20 mL) was allowed to stir at ambient temperature for 10 h. The dithiane-mercuric chloride complex separated as a flocculent white precipitate. The mixture was stirred and heated at 80 °C under nitrogen for 12 h, cooled, diluted with 150 mL of methylene chloride, and passed through a 1 in. silica bed, and the solvent was evaporated. The residue was extracted with ether/hexane, and the organic layer was washed with saturated NH_4Cl and brine, dried ($MgSO_4$), and evaporated to afford a colorless oil 90%: IR ($CHCl_3$) 2245, 1720 cm^{-1}; ^1H NMR δ 1.8-1.95 (1 H, m), 2.3-2.45 (1 H, m), 2.85 (2 H, t, J = 7.0 Hz), 3.05-3.1 (1 H, m), 4.3 (1 H, d, J = 7.0 Hz), 6.9 (1 H, d, J = 8.0 Hz), 7.2 (1 H, d, J = 8.0 Hz), 9.8 (1 H, s); mass spectrum, m/z 245 (M^+), 216 (M^+ - CHO).

Acknowledgment. We thank Dr. Steven Crowley for chemical literature searches and Ms. Joan Doerrer for typing this manuscript.

Registry No. 1, 36049-90-8; *cis*-2, 98218-24-7; *trans*-3, 98218-25-8; *cis*-4, 98218-26-9; *trans*-4, 98218-27-0; *cis*-5, 98218-28-1; *trans*-5, 98218-29-2; *cis*-6, 98218-30-5; *trans*-6, 98218-31-6; *cis*-7, 98218-32-7; *trans*-7, 98218-33-8; *cis*-8, 98218-34-9; *trans*-8, 98218-35-0; 9, 98218-36-1; 1,3-dithiane, 505-23-7; 3,4-dihydro-5,6-dimethoxy-1-naphthalenecarbonitrile, 89047-59-6; 3,4-dihydro-1-naphthalenecarbonitrile, 73599-59-4; 3,4-dihydro-5-methoxy-1-naphthalenecarbonitrile, 98218-37-2; 3,4-dihydro-6-methoxy-1-naphthalenecarbonitrile, 6398-50-1; 3,4-dihydro-6,7-dimethoxy-1-naphthalenecarbonitrile, 85221-58-5; 1-cyclohexenecarbonitrile, 1855-63-6; *cis*-2-(1,3-dithian-2-yl)cyclohexanecarbonitrile, 98218-38-3; *trans*-2-(1,3-dithian-2-yl)cyclohexanecarbonitrile, 98218-39-4; *trans*-1-cyano-1,2,3,4-tetrahydro-5,6-dimethoxy-2-naphthalenecarboxaldehyde, 98218-40-7.

^{60}Co γ-Irradiation:[1] Homolytic Alkylation of Methyl Nicotinate

George R. Newkome* and Charles R. Marston

Department of Chemistry, Louisiana State University, Baton Rouge, Louisiana 70803-1804

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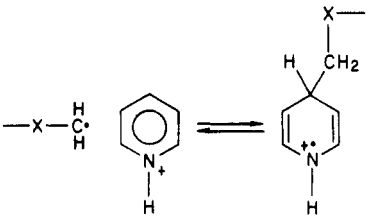
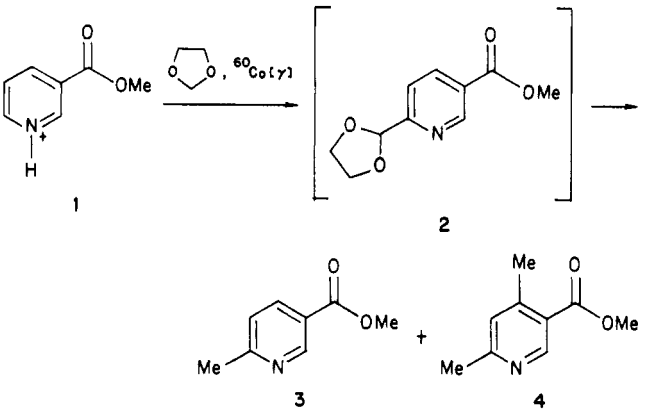
Recent developments in homolytic substitution reactions induced by chemical[2-4] and photochemical[5,6] methods have generated new, simple avenues for rapid direct functionalization of heterocycles. In contrast, γ-irradiation-induced alkylation and hydroxyalkylation procedures have been less frequently employed[7,8] due to limited availability of radiation sources. As with many radical processes, the indiscriminate nature of the reactive intermediate can lead to a product distribution with limited synthetic value. However, the nucleophilic character[9] of radicals, generated via γ-irradiation and specifically those with α-heteroatoms,[10-12] can be utilized for the homolytic alkylation of protonated electron-deficient heteroaromatics.[7,8,13]



During our evaluation of new methodologies to functionalize alkyl 6-methylnicotinates, the direct transformation of **1** to acetal **2** by a γ-ray-induced alkylation was attempted. We herein report the facile methylation of protonated methyl nicotinate via ^{60}Co γ-ray-induced homolytic substitution by 1,3-dioxolane.



Treatment of a deaerated solution of methyl nicotinate (**1**), sulfuric acid, and dioxolane with ^{60}Co γ-irradiation (overall dose; 1.0×10^7 rad) gave a clean mixture of methyl 6-methyl- (**3**, 21%)[13] and methyl 4,6-dimethyl-(**4**, 5%)[7,8] nicotinates. The only other ingredient was unchanged starting ester (71%). In contrast, analogous chemically induced reactions[2-4] gave exclusively the acetal products. On the basis of the work of Sugimori[7,8] in which **1** was γ-irradiated in the presence of diverse alcohols, mixtures of alkyl and α-hydroxyalkyl derivatives were realized; in unexpected contrast, no trace of acetal products was herein observed.

Apparently under the harsh "mega dose" γ-irradiation[7,8] conditions and a readily available hydrogen atom source, the acetal **2** can undergo a facile double homolytic cleav-

(1) Chemistry of Heterocyclic Compounds Series, 110. For previous related part in the series, see: Newkome, G. R.; Kiefer, G. E.; Majestic, V. K. *J. Org. Chem.* **1983**, *48*, 5112.
(2) Zorin, V. V.; Zelechonok, Yu. B.; Zlotskii, S. S.; Rakhmankulov, D. L. *Khim. Geterotsikl. Soedin.* **1984**, 25; *Dokl. Akad. Nauk SSSR* **1984**, *279*, 386; *Zh. Org. Khim.* **1985**, *21*, 193.
(3) Gardini, G. P. *Tetrahedron Lett.* **1972**, 4113.
(4) Minisci, F. *Synthesis* **1973**, 1.
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(12) Gardini, G. P.; Minisci, F.; Palla, G.; Arnone, A.; Galli, R. *Tetrahedron Lett.* **1971**, 59.
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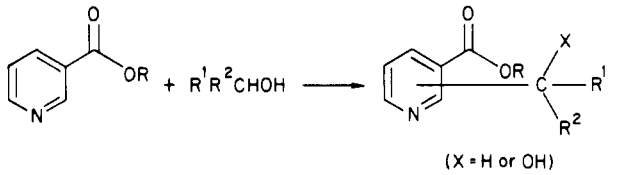
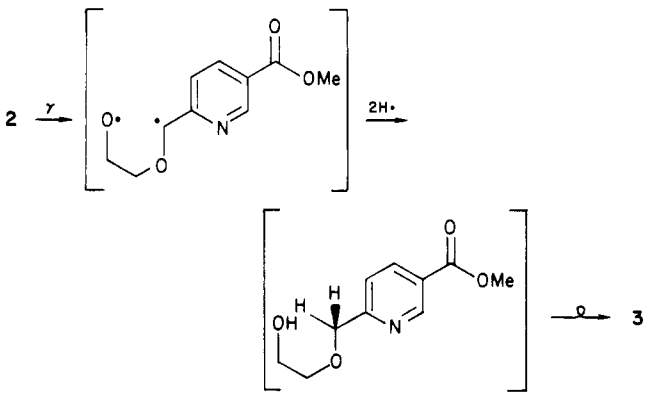


age[14] to give exclusively the methyl substituted products.



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

Kim F. Albizati‡ and D. John Faulkner*

Scripps Institution of Oceanography (A-012F), University of California, San Diego, La Jolla, California 92093

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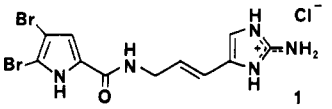
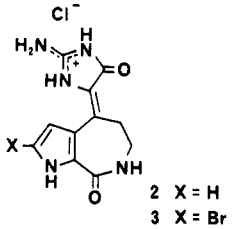
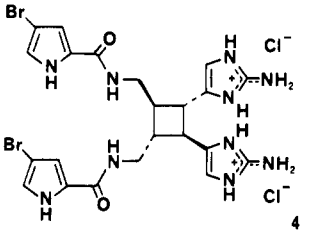
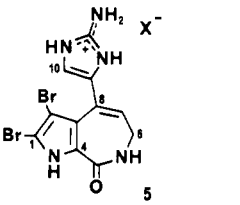
Marine sponges have yielded relatively few alkaloids.[1,2] Perhaps the best known group of sponge alkaloids is the "oroidin group", C_{11} compounds exemplified by oroidin (**1**) from *Agelas oroides*[3] and the yellow compounds **2** and **3** from *Phakellia flabellata*,[4] *Axinella verrucosa*,[5] *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.
‡ Current address: Wayne State University, Detroit, MI.

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