chloroform for extraction and acetonitrile for recrystallization. The reaction conditions and the isolated yields are listed in Table I. All of these compounds were characterized by comparing their melting points and NMR and mass spectra with those reported for the same structures. Important data of these products are shown below.

m-Iodotoluene: mp 27–28 °C (lit.[16] mp 28 °C); mass spectrum, *m/e* 218 (M^+).

p-Iodoacetophenone: mp 83–84 °C (lit.[16] mp 85 °C); mass spectrum, *m/e* 246 (M^+).

p-Diiodobenzene: mp 126–127 °C (lit.[15] mp 129 °C); mass spectrum, *m/e* 329 (M^+).

p-Iodoanisole: mp 49–50 °C (lit.[15] mp 51–52 °C); mass spectrum, *m/e* 234 (M^+).

A nickel powder with smaller particle size (<10 μm, Merck) was also employed in the exchange reaction between *p*-bromoacetophenone and KI. The same reaction conditions as those in Example 1 were followed except that the reaction time used was only 4 h. The reaction gave 75% of *p*-iodoacetophenone.

Example 2. A mixture of nickel powder (4.19 g, 71.4 mmol, 100 mesh), KI (4.75 g, 28.5 mmol), I_2 (0.181 g, 0.714 mmol), bromobenzene (1.50 mL, 14.3 mmol), and DMF (10 mL) in a round-bottom flask were first degassed and then heated at 150 °C with stirring for 21 h. To the solution was added 50 mL of a 3% dilute hydrochloric acid and 20 mL of a 1/1 (v/v) chloroform–*n*-pentane mixture. The nickel powder, which was absorbed on the magnetic stirring bar, was removed, and the organic layer was separated from the aqueous phase. The latter was further extracted by the same solvent mixture twice. The combined *n*-pentane–chloroform solution was washed with Na_2SO_3 solution and distilled water and dried over $MgSO_4$. The organic mixture was concentrated and analyzed by GC with chlorobenzene as the internal standard to give 83% of iodobenzene and 15% of unreacted bromobenzene. The relative amounts of iodobenzene and bromobenzene were further determined by ^1H NMR spectroscopy. The results of these two methods are in good agreement.

The reactions of *o*-bromobenzene with KI and aryl chlorides with KI or NaI were analyzed by the same method. The results are shown in Table II.

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Registry No. Ni, 7440-02-0; KI, 7681-11-0; NaI, 7681-82-5; KBr, 7758-02-3; KCl, 7447-40-7; NaBr, 7647-15-6; *p*-BrC_6H_4Me, 106-38-7; *m*-BrC_6H_4Me, 591-17-3; *o*-BrC_6H_4Me, 95-46-5; *p*-$BrC_6H_4C(O)CH_3$, 99-90-1; PhBr, 108-86-1; *p*-$Br_2C_6H_4$, 106-37-6; *p*-BrC_6H_4OMe, 104-92-7; *p*-ClC_6H_4Me, 106-43-4; *m*-ClC_6H_4Me, 108-41-8; *o*-ClC_6H_4Me, 95-49-8; *p*-$ClC_6H_4C(O)CH_3$, 99-91-2; *p*-ClC_6H_4OMe, 623-12-1; *p*-$ClC_6H_4NO_2$, 100-00-5; *p*-IC_6H_4Me, 624-31-7; PhCl, 108-90-7; *m*-IC_6H_4Me, 625-95-6; *o*-IC_6H_4Me, 615-37-2; *p*-$IC_6H_4C(O)Me$, 13329-40-3; PhI, 591-50-4; *p*-$I_2C_6H_4$, 624-38-4; *p*-IC_6H_4OMe, 696-62-8; *p*-$IC_6H_4NO_2$, 636-98-6.

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Charamin, a Quaternary Ammonium Ion Antibiotic from the Green Alga *Chara globularis*

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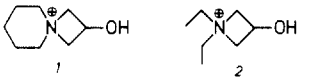
In view of the abundant current chemical investigations of marine algae,[2] freshwater plants have received only little attention from natural products chemists. Among freshwater and brackish water plants characean algae have been noted for their ability to dominate their ecosystems.[3] Earlier reports[4,5] have implicated the insecticidal[6,7] 4-(methylthio)-1,2-dithiolane and the herbicidal[5] 5-(methylthio)-1,2,3-trithiane in an allelopathic defense system in these organisms. Further investigations of *Chara globularis* Thuillier 1799 revealed a pronounced antibiotic activity associated with aqueous extracts of defatted plant material, exposing still another component of the chemical armory of this alga.

Lyophilized *Chara globularis* was defatted and extracted with water to produce, after lyophilization, 6.1% mainly organic material with the ability to significantly reduce the uptake of tritium-labeled glucose by a natural pond population of bacteria. Guided by the latter bioassay a convenient purification procedure consisting of cellulose column chromatography was established. The active fraction was partitioned between chloroform and water, leaving the activity in the aqueous phase. Repeated purification by HPLC gave thymidine, deoxyuridine, and an active compound. At a concentration of 4 μg/mL this material reduced the uptake of tritiated glucose by a natural population of bacteria to about 9% as compared to a control without antibiotic added. Noise- and off-resonance-decoupled ^{13}C NMR in D_2O served to identify the signals as due to methylene groups at 64.5 ppm and methine groups at 74.1 ppm. These values compare favorably with the values of 59.1 and 71.9 ppm observed for the methylene and methine carbons, respectively, of the four membered ring of 4-azoniaspiro[3.5]nonan-2-ol (**1**).[8] In pyridine-d_5 the ^1H NMR (90 MHz) exhibits a multiplet centered around 4.3 ppm comparable to a value of 4.2–4.9 (m, 5 H) or 4.5 ppm reported for the protons of the four-membered ring of **2** in acetonitrile-d_3[9] and dimethyl sulfoxide-d_6,[10] respectively. The multiplet (displaced to



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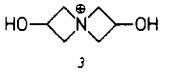

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3.6 ppm in D_2O) is resolved at 500 MHz into an ABX system: H_A 3.55 ppm (4 H, dd, J_{AB} 12.0 Hz, J_{AX} 6.2 Hz), H_B 3.64 ppm (4 H, dd, J_{AB} 12.0 Hz, J_{BX} 4.0 Hz), 3.77 ppm (2 H, m). The ^1H NMR spectrum in pyridine-d_5 indicates a water content of 7–8 molecules of H_2O per 10 ABX protons. The water content was substantiated by IR spectroscopy on the solid compound (KBr), where a strong broad absorption at 3000–3500 cm^{-1} (OH_2 stretch) after desiccation of the sample leaves two bands (OH stretch) at 3200 and 3360 cm^{-1} concomitant with decreased intensity of the weak bands at 1600–1630 (OH_2 scissoring) and 400–700 cm^{-1} (coordinated OH_2 rock, twist, and wag modes). The CH_2 deformation mode appears strongly at 1405 cm^{-1}. On the basis of these findings, we propose the structure of the active principle, charamin, to be 4-azoniaspiro[3,3]heptane-2,6-diol (**3**).

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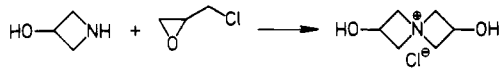
The sample of charamin used for the analytical studies has a minor impurity which could be removed by HPLC. This impurity was presumably an artifact since it could not be detected in the raw material. It was of no consequence with regard to the structure elucidation; however, it prohibited the determination of a reliable optical rotation value.

Charamin was synthesized (with concomitant formation of 1,3-dichloro-2-propanol) by the reaction of azetidin-3-ol, obtained by hydrogenolysis of 1-(diphenylmethyl)azetidin-3-ol,[11] with epichlorohydrin in analogy with the reported preparation of 1,1-diethyl-3-hydroxyazetidinium chloride.[10] The 500-MHz ^1H and ^{13}C NMR spectra of the



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natural and synthetic material were superimposable. The activity toward a natural bacteria population at a concentration of 4 μg/mL was about 60%. Work is in progress to optimize the synthetic procedure, to clarify the stereochemical identity (whether optical active or racemic) of the natural product, and to investigate the biological activity in more detail.

Experimental Section

The NMR measurements were obtained from a Bruker AM 500 spectrometer or a JEOL FX 90Q instrument. Samples were prepared in D_2O. IR spectra were recorded on a Perkin-Elmer 580 spectrometer and FAB mass spectra on a VG Masslab VG 20-250 Quadropole mass spectrometer fitted with a VG FAB source and probe. The primary beam of xenon atoms was produced from an ion gun operating at 1.0 mA, 8 kV.

Isolation of Charamin (3). Lyophilized *Chara globularis* (855 g dry weight) was extracted twice with petroleum ether (0.06% extract), three times with ethyl acetate (0.24% extract), and twice with water. All extractions were carried out at room temperature, and extractions with water were limited to 24 h in order to minimize any microbial growth during extraction. Lyophilization of the combined aqueous extracts left 51.84 g (6.1%) of crude material. The bioassay was performed in a standard procedure as follows: Filtered pond water (25 mL), 50 μL of test solution (2 mg/mL), and tritium-labeled glucose were incubated at 20 °C for 1 h. The bacteria were removed by filtration, and the activity was determined by scintillation counts. The activity was expressed relative to a control without test solution. The amount of [^{3}H]glucose added was adjusted to give a control sample with about 2000 cpm.

The crude material, which was mainly organic (C, 30.36%; H, 5.19; N, 5.16%; S; 1.09%; 26.65% combustion residue), reduced the tritium uptake to 12% and 21% on addition of 100 and 10 μL of test solution, respectively. Gel filtration (Sephadex G-25) did not significantly concentrate the active material. However, purification was achieved with cellulose chromatography (Avicel, Merck, 150 g) with 2-propanol/water (80:20) as eluent. Separation of 10 g of crude material afforded 249 mg, which after partition between water (5 mL), and chloroform (5 mL) left 71 mg of active material in the aqueous phase (reduction of tritium uptake to 20%). Repeated purification of this material by HPLC (RP-18, water/acetonitrile, 90:10 followed by 97:3) gave thymidine (0.03% of aqueous extract), deoxyuridine (0.07%), and the active material (0.4% of aqueous extract or 0.02% of dry plant material). Thymidine and deoxyuridine were identified by ^1H NMR, UV, and MS; all data were identical with the published values.

The active fraction had a minor impurity which affected the elemental analysis slightly. Calcd for $C_6H_{12}ClNO_2 \cdot 6H_2O$: C, 26.33; H, 8.78; N, 5.12; ionic Cl, 12.98. Found for charamin: C, 26.21; H, 6.75; N, 6.64; ionic Cl, 12.5.

Synthesis of Charamin (3). Preparation of the hydrochloride of azetidin-3-ol was performed in accordance with ref 11. The ^{13}C NMR spectrum exhibited signals at 63.7 (CH) and 57.5 (CH_2) ppm and ^1H NMR showed complex multiplets from 3.84–4.34 and 4.56–4.86 ppm, the latter multiplet superimposed on the intense HOD resonance. The IR spectrum (KBr) had strong absorptions at 3390, 3210, and 3015 cm^{-1} and medium strong bands at 1625, 1433, 1300, 1240, 1158, and 1085 cm^{-1}. A sample of the free amine was prepared by addition of potassium hydroxide (three pellets) to 4.6 mmol of hydrochloride dissolved in a small amount of water. Wet amine was then obtained by vacuum distillation (30 °C) into a reaction flask cooled in N_2 liquid. The reaction was performed by addition of epichlorohydrin (4 mmol) and stirring for 1 day at room temperature. ^{13}C NMR of the residue left by evaporation reveals the product to be a mixture of 1,3-dichloro-2-propanol (72.5 and 47.9 ppm) and charamin. Preparative HPLC on a RP-8 column with acetonitrile/water (10:90) with a refractive index detector yielded 65 mg (10%) of charamin. The synthetic product exhibited ^1H and ^{13}C data identical with those of the natural product and FAB MS gave the 4-azoniaspiro[3.3]heptane-2,6-diol cation at m/z 130.08 (calcd for $C_6H_{12}NO_2$, m/z 130.06).

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3-Ferrocenyl-2*H*-thiete and 3-Ferrocenyl-2*H*-thiete 1,1-Dioxide

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Previous attempts to prepare transition-metal complexes of thietes (thiacyclobutenes), as distinct from preparing thietes with an organometallic substituent, resulted in ring opening to give complexes of the rare α,β-unsaturated thioaldehydes (enethials).[1] We report here the synthesis of a thiete substituted by a ferrocenyl group, a stable species in which the thiacyclobutene ring is intact. The synthesis involves an enamine derived from 3-acetylferrocene. Ferrocenyl enamines are uncommon, the examples **1** and **2** being prepared by special methods.[2,3] Treatment of ferrocenyl ketones with amines in the presence of aluminum chloride[4] or titanium tetrachloride[5] gave iminium salts with secondary amines and imines with primary amines; no mention was made of enamine formation. Acetylferrocene did not react with the dimethylamine–aluminum chloride complex[4] but gave enamine **3** on treatment with aniline–DMF–$POCl_3$.[3]

The original procedure of White and Weingarten[6] for the preparation of enamines, which involved addition of titanium tetrachloride to a solution of amine and ketone

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