gallium chelate. A reexamination of the parabactin chelate using natural and our synthetic parabactin also indicated only two amide signals and one methyl signal. An exhaustive investigation of the previously prepared chelate suggested that the reported minor isomer was not the Λ cis-4,3 diastereomer but was in fact homoparabactin–gallium(III) chelate. Mass spectrometry of the parabactin sample used to make the parabactin–gallium(III) chelate utilized in our initial NMR study showed the molecular ions of the parabactin (*m/e* 620) and contaminating homoparabactin (*m/e* 634). After further examining the steps involved in the parabactin synthesis,[2] we determined that the problem arose from a sample of N^4-benzylspermidine contaminated with N^5-benzylhomospermidine. During the alkylation of *N*-(2-cyanoethyl)benzylamine with 4-chlorobutyronitrile,[13] small amounts of the symmetrical bisnitrile *N,N*-bis(3-cyanopropyl)benzylamine can be generated by reverse Michael reaction of acrylonitrile during the alkylation. Although small amounts of the contaminant could be carried through to the corresponding homospermidine, this higher boiling amine is normally separated by vacuum distillation. Alternatively, N^4-benzylspermidine can be prepared by using our recently reported polyamine reagents.[14] This efficient route precludes formation of the symmetrical contaminant and the associated separation problems.

In summary, agrobactin was prepared synthetically in a versatile high-yield synthesis, amenable to the generation of the nor- and homoagrobactin analogues. Furthermore, it appears from both parabactin– and agrobactin–gallium(III) chelates that the complexes exist exclusively as the Λ cis-3,4-isomer. This is an interesting finding since the free ligands have been shown to exist in solution in a number of different isomeric conformations arising from hindered rotation around the tertiary amide bond.

Experimental Section

All reagents, with the exception of gallium(III) nitrate nonahydrate (Alfa), were purchased from Aldrich Chemical Co. and were used without further purification. Sodium sulfate was employed as a drying agent. Melting points are uncorrected. Sephadex LH-20 was purchased from Pharmacia Fine Chemicals. Proton NMR spectra were recorded on a Varian T-60, EM-390, or a Nicolet NT-300 instrument, and unless otherwise noted, were run in $CDCl_3$ with chemical shifts given in parts per million downfield from an internal tetramethylsilane standard (coupling constants are in hertz). IR spectra were recorded on a Beckman Acculab 1 spectrophotometer. Elemental analyses were performed by Atlantic Microlabs, Atlanta, GA, or Galbraith Laboratories, Knoxville, TN.

2,3-Bis(benzyloxy)benzamide (4b). A solution of 2,3-bis(benzyloxy)benzoyl chloride (**4a**) (20.3 mmol)[11] in CH_2Cl_2 (80 mL) was added in portions to concentrated ammonium hydroxide (50 mL) and CH_2Cl_2 (30 mL) at 0 °C. After 1 day at room temperature, water (50 mL) was added, and the layers were separated. After two more extractions with CH_2Cl_2, the organic layer was washed with dilute $NaHCO_3$ and water and then dried and concentrated. Recrystallization with 50% aqueous ethanol afforded 6.19 g (92%) of **4b**, mp 130–132 °C: ^1H NMR δ 5.02 and 5.07 (2 s, 4 H), 6.0 (br, 2 H), 7.0–7.8 (m, 13 H); IR ($CHCl_3$) 3480 and 3360 (NH_2), 1670 (C=O) cm^{-1}. Anal. Calcd for $C_{21}H_{19}NO_3$: C, 75.65; H, 5.74; N, 4.20. Found: C, 75.75; H, 5.76, N, 4.19.

Ethyl 2,3-Bis(benzyloxy)benzimidate (5). To **4b** (6.99 g, 21.0 mmol) in CH_2Cl_2 (150 mL) was added triethyloxonium hexafluorophosphate (5.72 g, 23.1 mmol) and then more CH_2Cl_2 (50 mL). After stirring at least 1 day (room temperature, N_2), CH_2Cl_2 (50 mL) was added and the solution poured into ice-cold 1 M Na_2CO_3 (120 mL). The aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL), dried, and then concentrated. Recrystallization from hexane (55–60 °C) furnished 6.11 g (81%) of solid **5**, mp 42–43.5 °C: ^1H NMR δ 1.37 (t, 3 H, J = 7), 4.31 (q, 2 H, J = 7), 5.04 and 5.13 (2s, 4 H), 7.0–7.55 (m, 13 H), 8.58 (br s, 1 H); IR (neat) 3340 (NH) and 1640 (C=N) cm^{-1}.

Anal. Calcd for $C_{23}H_{23}NO_3$; C, 76.43; H, 6.41; N, 3.88. Found: C, 76.32; H, 6.45; N, 3.81.

Ethyl 2,3-Dihydroxybenzimidate (3). Into a solution of **5** (0.55 g, 1.52 mmol) in absolute, degassed ethanol (60 mL) was introduced 10% palladium on carbon (0.17 g), using acid-washed glassware. The suspension was stirred under a hydrogen atmosphere for 55 min. Hydrogen was removed at reduced pressure and replaced with argon. The suspension was heated to 80 °C and filtered under N_2 through a medium(10–15) frit, which was washed with hot ethanol (10–15 mL). Solvent removal gave 0.24 g of crude **3**, which was recrystallized from absolute ethanol to afford 0.200 g of **3** as light green needles in 73% yield, mp (sealed capillary) 193–195 °C dec: ^1H NMR (Me_2SO-d_6) δ 1.37 (t, 3 H, J = 7), 3.9–5.7 (br s and q, 5 H, J = 7), 6.3–7.2 (m, 3 H); IR (Nujol) 3100 and 1625 cm^{-1}.

Anal. Calcd for $C_9H_{11}NO_3$: C, 59.66; H, 6.12; N, 7.73. Found: C, 59.72; H, 6.15; N, 7.72.

Agrobactin (1a). Compounds **2** (0.128 g, 0.213 mmol) and **3** (0.17 g, 0.938 mmol, 4.4 equiv) were heated at reflux in dry, degassed methanol (20 mL) for 34 h. The cooled solution was dry packed onto LH-20 and eluted with 20% EtOH/benzene on an LH-20 column (22.4 g) to furnish 85 mg (61%) of **1a**. The NMR was identical with that reported for natural agrobactin.[9]

Anal. Calcd for $C_{32}H_{36}N_4O_{10}\cdot H_2O$: C, 58.71; H, 5.85; N, 8.56. Found: C, 58.85, H, 5.90; N, 8.54.

Acknowledgment. We wish to thank the National Institutes of Health for their generous support of this work (Grant No. AM 29936).

Registry No. **1a**, 70393-50-9; **2**, 82247-46-9; **3**, 96649-28-4; **4a**, 69146-58-3; **4b**, 96649-29-5; **5**, 96649-30-8.

Titanium Tetrachloride Promoted Reactions of Allylic Trimethylsilanes and Oxetane

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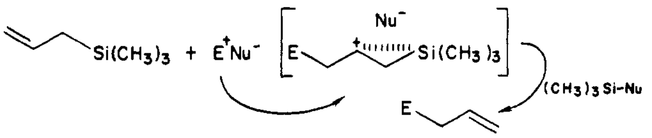
Many reactions of allylic trimethylsilanes involve electrophilic substitution with allylic rearrangement and loss of the trimethylsilyl group. These reactions may occur by addition of the electrophile to the carbon–carbon double bond to yield a carbocation intermediate which is stabilized by a *β*-trimethylsilyl group. Nucleophilic attack on silicon by an associated anion or solvent results in loss of the silyl group and formation of products.[1–3]



Epoxides react with Lewis acids to yield electrophiles that react regiospecifically with allylic trimethylsilanes to

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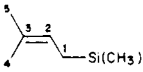
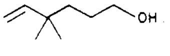
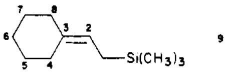
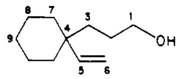
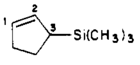
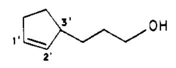
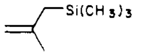
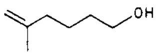
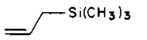
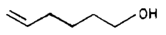
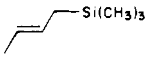
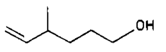
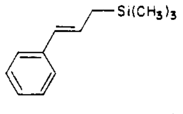
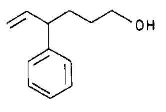
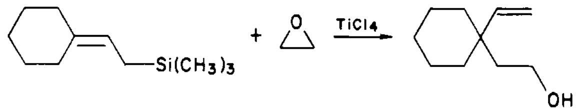
Table I. Titanium Tetrachloride Promoted Reaction of Allylic Trimethylsilanes with Oxetane[a]

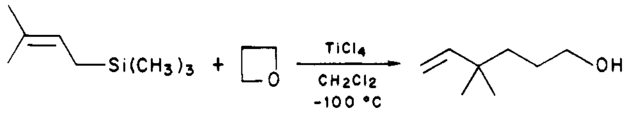
allylic trimethylsilane	product, 5-hexen-1-ol	yield	conversion
		85%	85%
		86%	86%
		55%	55%
		90%	90%
		69%	30%
		49%	49%
		85%	25%

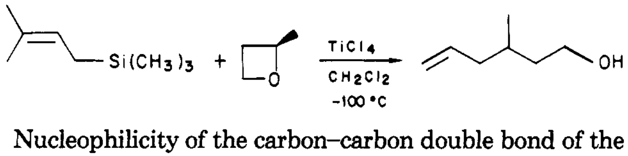
[a] Numbering for ^{13}C NMR assignments.

give homoallylic alcohols. Both intra- and intermolecular examples of this reaction are known.[4-6]

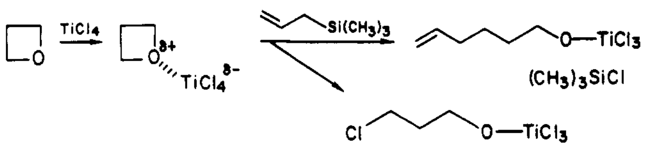


We would like to report that the titanium tetrachloride promoted reaction of allylic trimethylsilanes with oxetanes yields 5-hexen-1-ols as products (Table I). We anticipated that this reaction might be successful due to the similar strain energy of oxetanes and epoxides (25 kcal/mol)[10] as well as on the basis of our previous work on the reactions of oxetanes with dimethylsilylene,[11] (methylthio)trimethylsilane,[12] and trimethylsilyl cyanide.[13] Unfortunately, the reaction is limited to cyclic ethers that possess high ring strain, since similar reactions with tetrahydrofuran failed. The reaction is not catalytic in titanium tetrachloride, but requires a stoichiometric quantity of the Lewis acid. A variety of other Lewis acids, $ZnBr_2$, ZnI_2, $ZnCl_2{\cdot}2H_2O$, $SnCl_4$, $SnCl_2{\cdot}2H_2O$, and $BF_3{\cdot}Et_2O$, were found to be less efficient catalysts for this reaction. Low initial temperature (−100 °C) is essential for the success of the reaction. High regiospecificity is observed. For example, (γ,γ-dimethylallyl)trimethylsilane reacts with oxetane to yield 4,4-dimethyl-5-hexen-1-ol. Likewise, 2-methyloxetane reacts with allyltrimethylsilane to yield 3-methyl-5-hexen-1-ol, albeit in low yield.

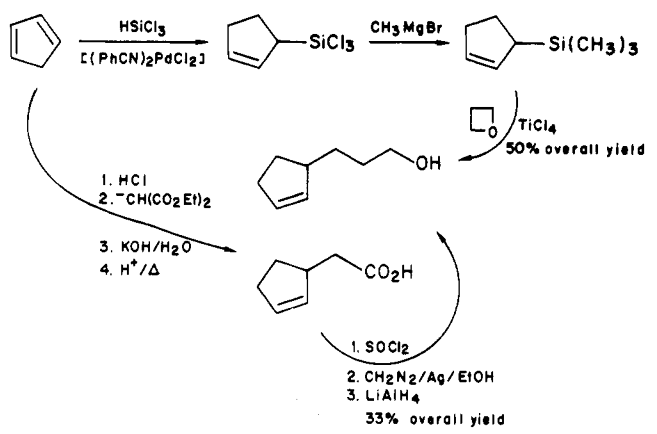




Nucleophilicity of the carbon–carbon double bond of the allylic trimethylsilane is essential for the success of the reaction. High yields are obtained with allylic trimethylsilanes in which the carbon–carbon double bond is substituted with alkyl groups, such as (2-methylallyl)trimethylsilane and (γ,γ-dimethylallyl)trimethylsilane. On the other hand, when the carbon–carbon double bond is less substituted or when its nucleophilicity is decreased by resonance, conversions are low. Thus cinnamyltrimethylsilane reacts with oxetane to give a high yield (85%) but low conversion (25%) of 4-phenyl-5-hexen-1-ol, based on 71% recovered starting material. We suggest that the reaction occurs by coordination of the Lewis acid, titanium tetrachloride, to the oxygen of the oxetane. The carbon–oxygen bonds of oxetane in this complex are highly polarized which renders these carbons electrophilic in character. This complex can react either with the carbon–carbon double bond of the allylic trimethylsilane to yield the product 5-hexen-1-ol or undergo reaction with chloride anion, possibly by an intramolecular process, to yield 3-chloropropanol. Due to this competing reaction 2 equiv of oxetane have been utilized. Excess oxetane is not recovered from the reaction but rather 3-chloropropanol.



Specific 5-hexen-1-ols have been prepared by various methods, which makes comparison difficult. Nevertheless, in certain cases the reaction of allylic trimethylsilanes with oxetanes provides not only significant savings in the number of synthetic operations but also higher overall yields. A comparison of the preparation of 3-(3′-cyclopentenyl)propanol by previous methods[7-9] to our reaction is outlined below.



We have utilized a two-step procedure[14] to prepare allyltrimethylsilane, (2-methylallyl)trimethylsilane, (*E*)-crotyltrimethylsilane, and cinnamyltrimethylsilane. In the first step, trichlorosilane and tri-*n*-butylamine[15-17] are re-

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acted with an allylic chloride to yield the allylic trichlorosilane. This is subsequently reacted with methylmagnesium bromide to give the desired allylic trimethylsilane. This reaction is quite regio- and stereoselective. Thus reaction of a mixture of (*E*)- and (*Z*)-1-bromo-2-butenes (crotyl bromides) and 2-bromo-1-butene (66:26:8) gave (*E*)-crotyltrimethylsilane and (*Z*)-crotyltrimethylsilane (97:3) in 84% overall yield. No 2-(trimethylsilyl)-1-butene is observed.

Experimental Section

^{1}H and ^{13}C NMR spectra were obtained on an IBM-Bruker WP-270-SY or Jeolco 90-FQ spectrometer operating in the FT mode using 5% sample solutions in deuteriochloroform. Chloroform was utilized as the internal standard. ^{13}C NMR spectra were run with broadband proton decoupling. IR spectra were obtained on a Perkin-Elmer 281 spectrometer. Low-resolution mass spectra were obtained on a Hewlett-Packard 5985 GC/MS at an ionizing voltage of 70 eV. A 20 in. × $^1/_8$ in. 2% OV-101 on 100/120 mesh Chromosorb W column was used in the gas chromatrographic inlet of the mass spectrometer. GLPC analysis was performed on a Hewlett-Packard F&M 700 using a 12 ft × $^1/_4$ in. 20% PPE on a 80/100 mesh Chromosorb W column. Yields were calculated with either cyclohexanone or cyclohexanol as internal standard. All reactions were carried out under an atmosphere of purified nitrogen. Elemental analyses were done by Galbraith Laboratories, Knoxville, TN.

Many of the starting materials and products are known compounds. They had physical and spectral properties in complete agreement with literature values. In those cases where incomplete spectral data has been previously reported we have included this information, in particular ^{13}C NMR.

(γ,γ-Dimethylallyl)trimethylsilane[18] was prepared by a Wittig reaction between β-(trimethylsilyl)ethylidene triphenylphosphorane and acetone.[20] ^{13}C NMR δ 128.574 (C-3), 120.014 (C-2), 25.751 (C-1), 18.654 (C-5), 17.561 (C-4), −1.766 ($SiCH_3$).

[2-(Trimethylsilyl)ethylidene]cyclohexane[19] was likewise prepared by a Wittig procedure.[20] ^{13}C NMR δ 137.106 (C-3), 116.791 (C-2), 37.450 (C-8), 28.967 (C-4), 28.534 (C-7), 27.733 (C-5), 27.200 (C-6), 17.821 ($SiCH_2$), −1.736 ($SiCH_3$).

3-Cyclopentenyltrimethylsilane[21] was prepared by the 1,4-hydrosilation reaction of cyclopentadiene by trichlorosilane catalyzed by bis(benzonitrile)palladium(II) dichloride,[22] followed by reaction of 3-cyclopentenyltrichlorosilane with methylmagnesium bromide. ^{13}C NMR δ 132.344 (C-1), 127.798 (C-2), 34.934 (C-5), 32.957 (C-3), 25.1079 (C-4), −3.120 (CH_3Si).

Synthesis of Allyltrimethylsilanes by Reaction of Trichlorosilyl Anion with Allylic Chloride.[14] In a 250-mL three-necked round-bottom flask equipped with a reflux condenser, pressure equalizing addition funnel, and Teflon-covered magnetic stirring bar was placed 0.1 mol of tri-*n*-butylamine and 70 mL of ether. The flask was cooled to 0 °C. A solution of allyl halide, 0.1 mol, and trichlorosilane, 0.11 mol, was placed in the addition funnel. This solution was added to the stirred solution in the flask over 15 min. A precipitate is rapidly formed. The reaction is allowed to warm to room temperature overnight. The allyltrichlorosilane product is separated from the tri-*n*-butylammonium hydrochloride salts by trap to trap distillation under reduced pressure (0.1 mm). Addition of allyltrichlorosilane to an ether solution of methylmagnesium bromide (3.2 equiv) gave the corresponding allyltrimethylsilane.

(2-Methylallyl)trimethylsilane[23] was prepared as above by reaction of 2-methylallyl chloride with trichlorosilane. ^{13}C NMR δ −1.371 (CH_3Si), 25.053 ($SiCH_2$), 28.371 (CH_3), 103.155 ($C{=}CH_2$), 143.609 ($C{=}CH_2$).

Allyltrimethylsilane was purchased from Aldrich. ^{13}C NMR δ −2.075 (CH_3Si), 24.730 ($SiCH_2$), 112.611 ($HC{=}CH_2$), 135.555 ($HC{=}CH_2$).

(*Z*)- and (*E*)-crotyltrimethylsilane[24] (97:3) were prepared by reaction of crotyl bromide, a mixture comprised of (*Z*)- and (*E*)-1-bromo-2-butenes and 3-bromo-1-butene (66:26:8), with trichlorosilane as above in 84% yield. ^{13}C NMR δ, [(*Z*)-crotyltrimethylsilane] 126.475, 121.213, 18.065 (CH_3), 12.512 ($SiCH_2$), −1.794 ($SiCH_3$), [(*E*)-crotyltrimethylsilane] 127.066, 123.135, 22.636 (CH_3), 17.902 ($SiCH_2$), −1.991 ($SiCH_3$).

Cinnamyltrimethylsilane[19] was prepared by reaction of cinnamyl bromide with trichlorosilane as above. ^{13}C NMR δ 139.959, 128.844, 128.595, 127.924, 126.379, 125.912, 24.130, −1.692.

2-Methyloxetane was prepared from 1,3-butanediol by literature methods, bp 60 °C (760 mm), lit. bp 60–61 °C (760 mm).[25,26] It had spectral properties in complete agreement with previous values.[27]

Oxetane was purchased from Aldrich.

General Procedure for the Synthesis of 5-Hexen-1-ols. Allyltrimethylsilane (3.8 mmol), oxetane (7.6 mmol), and 10 mL of dry methylene chloride were placed in a 25-mL three-necked round-bottom flask equipped with a reflux condenser, pressure equalizing addition funnel, and Teflon-covered magnetic stirring bar. The flask was cooled to −100 °C, at which time titanium tetrachloride (3.8 mmol, 0.42 mL) dissolved in 5 mL of methylene chloride was added via the addition funnel to the stirred reaction mixture. A pale yellow precipitate immediately formed. The reaction mixture was allowed to warm to room temperature overnight. After workup with cold 0.1 N potassium hydroxide, the reaction mixture was analyzed by GLPC.

Reaction of (γ,γ-dimethylallyl)trimethylsilane with oxetane as above gave 4,4-dimethyl-5-hexen-1-ol[28,29] in 83% yield. ^{13}C NMR δ 148.296 (C-5), 110.387 (C-6), 63.563 (C-1), 38.699 (C-2), 36.198 (C-3), 28.099 (C-4), 26.738 ($2CH_3$).

Reaction of [2-(trimethylsilyl)ethylidene]cyclohexane with oxetane gave 1-vinyl-1-(3′-hydroxypropyl)cyclohexane in 86% yield. ^{1} NMR δ 5.59 (d of d, J = 18, 10 Hz, H), 5.06 (d of d, J = 10, 1.8 Hz, 1 H), 4.89 (d of d, J = 18, 1.8 Hz, 1 H), 3.57 (t, J = 7.2 Hz, 2 H), 1.7–1.0 (m, 15 H); ^{13}C NMR δ 146.596 (C-5), 112.675 (C-6), 63.345 (C-1), 39.429 (C-4), 37.127 (C-2), 35.976 (C-3), 27.116 (C-7), 26.640 (C-8), 22.238 (C-9); MS, *m/z* 150 (M − 18, 1.6%), 109 (39.4%), 67 (100%). Anal. Found: C, 78.32%; H, 12.07%. Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.98%.

Reaction of 3-cyclopentenyltrimethylsilane with oxetane as above gave 3-(3′-cyclopentenyl)propanol in 55% yield.[9] ^{13}C NMR δ 134.916 (C-2′), 130.337 (C-1′), 63.160 (C-1), 45.424 (C-3′), 32.129 (C-5′), 31.931 (C-4′), 31.160 (C-2), 29.366 (C-3).

Reaction of (2-methylallyl)trimethylsilane with oxetane as above gave 5-methyl-5-hexen-1-ol in 90% yield.[30] ^{13}C NMR δ 145.6 (C-5), 109.953 (C-6), 62.750 (C-1), 37.613 (C-4), 32.576 (CH_3), 24.505 (C-2), 22.187 (C-3).

Reaction of allyltrimethylsilane with oxetane as above gave 5-hexen-1-ol in 69% yield based on recovered starting material (61%).[31] ^{13}C NMR δ 138.594 (C-5), 114.432 (C-6), 62.708 (C-1), 33.376 (C-4), 32.268 (C-2), 25.136 (C-3).

Reaction of crotyltrimethylsilane with oxetane as above gave 4-methyl-5-hexen-1-ol[32] in 49% yield. ^{13}C NMR δ 144.658 (C-5), 112.777 (C-6), 62.669 (C-1), 37.965 (C-4), 32.978 (C-2), 30.811 (C-3), 20.356 (CH_3).

Reaction of cinnamyltrimethylsilane with oxetane as above gave 4-phenyl-5-hexen-1-ol in 85% yield based on recovered starting material (71%). IR 3500–3200 cm^{-1} (OH); ^{1}H NMR δ 7.32–7.08 (m, 5 H), 5.94 (d of d of d, J = 19, 13.3, 7.9 Hz, 1 H), 5.05 (d of d of d, J = 19, 2.2 Hz, 1 H), 4.99 (d of d, J = 13.3, 2.2

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Hz, 1 H), 3.61 (t, $J = 6.6$ Hz, 2 H), 3.26 (d of t, $J = 8.6, 7.9$ Hz, 1 H), 1.82–1.25 (m, 4 H), 1.19 (br, s, 1 H); ^{13}C NMR δ 144.293, 142.216, 128.487, 127.642, 126.252, 114.120, 62.887, 49.704, 31.664, 30.878. Anal. Found: C, 81.97%; H, 9.14%. Calcd for $C_{12}H_{16}O$: C, 81.77%; H, 9.15%.

Reaction of 2-methyloxetane with allyltrimethylsilane as above gave 3-methyl-5-hexen-1-ol in 20% yield.[33]

Preparative Reaction of (2-Methylallyl)trimethylsilane with Oxetane. A stirred solution of (2-methylallyl)trimethylsilane, 9.3 g (0.073 mol), and 9.5 mL of oxetane in 25 mL of CH_2Cl_2 which was cooled to −100 °C under an atmosphere of nitrogen was prepared. To this was added over about 15 min 8.5 mL of titanium tetrachloride (0.073 mol) dissolved in 15 mL of CH_2Cl_2. The reaction was then stirred overnight while it gradually warmed to room temperature. The resulting mixture was then slowly poured into cold 0.1 N potassium hydroxide. The resulting suspension was extracted 3 times with about 60 mL of CH_2Cl_2. The organic solution was dried over anhydrous magnesium sulfate and filtered and the solvent removed by evaporation under reduced pressure. The product mixture was filtered through a short column of alumina. A 1:1 mixture of ether/petroleum ether was used as the eluent. This process serves to remove any titanium residues. Failure to follow this procedure may result in isomerization of the carbon–carbon double bond of the product. The volatile material was distilled through a 66-cm vacuum-jacketed column which was packed with a spiral glass band. 3-Chloropropanol distilled at 60–62 °C (25 mm). The desired product 5-methyl-5-hexen-1-ol distilled at 53–54 °C (9 mm), lit. bp 74–76 °C (15 mm).[34] Its spectra were in complete agreement with those previously reported. A yield of 5.4 g (0.048 mol), 69% , was obtained.

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Registry No. Allyltrichlorosilane, 107-37-9; methylmagnesium bromide, 75-16-1; allyltrimethylsilane, 762-72-1; (2-methylallyl)trimethylsilane, 18292-38-1; 2-methylallyl chloride, 563-47-3; trichlorosilane, 10025-78-2; (*Z*)-1-bromo-2-butene, 39616-19-8; (*E*)-1-bromo-2-butene, 29576-14-5; 3-bromo-1-butene, 22037-73-6; (*Z*)-crotyltrimethylsilane, 17486-13-4; (*E*)-crotyltrimethylsilane, 17486-12-3; cinnamyltrimethylsilane, 19752-23-9; cinnamyl bromide, 4392-24-9; 2-methyloxetane, 2167-39-7; oxetane, 503-30-0; titanium tetrachloride, 7550-45-0; (γ,γ-dimethylallyl)trimethylsilane, 18293-99-7; 4,4-dimethyl-5-hexen-1-ol, 86549-26-0; 2-(trimethylsilyl)ethylidenecyclohexane, 63922-76-9; 1-vinyl-1-(3′-hydroxypropyl)cyclohexane, 96746-39-3; 3-cyclopentenyltrimethylsilane, 14579-08-9; 3-(3′-cyclopentenyl)propanol, 2910-50-1; 5-hexen-1-ol, 821-41-0; 4-methyl-5-hexen-1-ol, 25906-56-3; 4-phenyl-5-hexen-1-ol, 96746-40-6; 3-methyl-5-hexen-1-ol, 25913-87-5; 5-methyl-5-hexen-1-ol, 5212-80-6.

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5-*epi*-Ilimiquinone, a Metabolite of the Sponge *Fenestraspongia* Sp.

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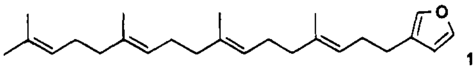
Our research on the chemical constituents of sponges from Palau has been directed primarily toward the structural elucidation of novel antimicrobial agents. Crude extracts of a sponge tentatively identified as a species of *Fenestraspongia*[1] exhibited in vitro antimicrobial activity and inhibited cell division in the fertilized sea urchin egg assay. Extracts of the sponge material contained the inactive metabolite furospinulosin-1 (1)[2] and the active metabolites ilimaquinone (2)[3] and 5-*epi*-ilimaquinone (3). In this note we report the structural elucidation of 5-*epi*-ilimaquinone (3) (Chart I).

Chart I



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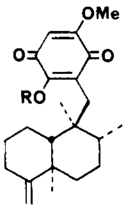

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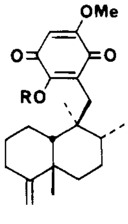

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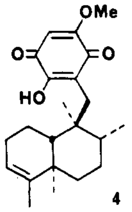

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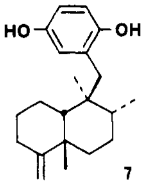

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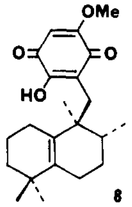

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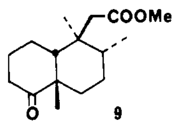

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Specimens of *Fenestraspongia* sp. were collected near Urukthapel Island, Palau, and were stored frozen until required. Chromatography of a methanolic extract on Sephadex LH-20 using 1:1 dichloromethane–methanol as eluant separated the major inactive metabolite furospinulosin-1 (1, 0.4% dry weight) from a 6:4 mixture of ilimaquinone (2) and 5-*epi*-ilimaquinone (3) (2.1% dry weight). We had previously encountered a number of sponge samples from Palau that contained ilimaquinone (2) mixed with 10–20% isospongiaquinone (4),[4,5] but the active mixture from this sponge contained two compounds both having an exocyclic methylene group. The ^1H NMR spectrum contained the signals expected for ilimaquinone (2) at δ 5.86 (s, 1 H), 4.45 (br s, 1 H), 4.43 (br s, 1 H), and 3.87 (s, 3 H) together with an additional set of signals at δ 5.87 (s, 1 H), 4.70 (br s, 1 H), 4.67 (br s, 1 H), and 3.88 (s, 3 H) in the low-field region. These data suggested that

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(1) The sponge was in an unusually poor condition for identification but has the basic characteristics of the genus *Fenestraspongia* Bergquist.

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(5) The arguments presented in ref 4 for the relative stereochemistry of isospongiaquinone (4) appear to be correct and have not been challenged. We have adopted the proposed relative stereochemistry although the authors were more cautious.

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