A Nozaki-Hiyama-Kishi Ni(II)/Cr(II) Coupling Approach to the Phomactins

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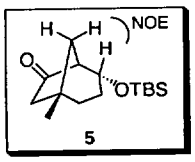
SUPPORTING INFORMATION

Materials and Methods

Reactions were carried out in oven- or flame-dried glassware under nitrogen atmosphere, unless otherwise noted. All commercial reagents were used without purification. Anhydrous THF, 1,2-dimethoxyethane (DME), and diethyl ether were freshly distilled under N_2 from sodium benzophenoneketyl. Pyridine, triethylamine, and diisopropylethylamine (Hünig's base) were distilled under N_2 from calcium hydride. N,N'-Dimethylformamide (DMF), dimethylsulfoxide (DMSO), and acetonitrile were distilled under N_2 from anhydrous calcium sulfate. All other solvents and reagents were used as received from chemical sources or otherwise noted. Except as otherwise indicated, all reactions were magnetically stirred and monitored by thin layer chromatography with Whatman 0.25-mm precoated silica gel plates or capillary GC with a Perkin-Elmer 8500 gas chromatograph fitted with a fused silica column. Flash chromatography was performed with silica gel 60 Å (particle size 230-400 Mesh ASTM) supplied by Silicycle. Yields refer to chromatographically and spectroscopically pure compounds, unless otherwise stated. Infrared spectra were recorded on a Nicolet IR/42 spectrometer. Proton and carbon NMR spectra were recorded on a Varian Gemini-300 spectrometer. Chemical shifts are reported relative to the residue peaks of solvent chloroform (δ 7.24 for ^1H and δ 77.0 for ^{13}C). High-resolution mass spectra were obtained at either the Michigan State University Mass Spectrometry Service Center with a JEOL-AX505 mass spectrometer (resolution 7000) or at the Mass Spectrometry Laboratory of the University of

South Carolina, Department of Chemistry & Biochemistry with a Micromass VG-70S mass spectrometer. Combustion analysis was performed by Robertson Microlit Laboratories, Inc., Madison, N.J. 07940. Melting points (m.p.) were determined uncorrected using a Thomas Hoover apparatus.

Experimental



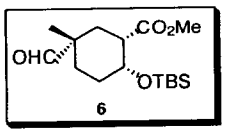
5

t-Butyldimethylsilyloxy bicyclo[3.2.1]octanone 5. A 0 °C solution of **4**[1] (0.57 g, 2.07 mmol) in MeOH (40 mL) was stirred with $NaBH_4$ (30 mg, 0.79 mmol) at 0 °C for 30 min. After being quenched with aq NH_4Cl, extracted with Et_2O, dried, and concentrated under high vacuum 0.57 g (99%) of crude benzodithiole methylbicyclo[3.2.1]octanol obtained as a light yellowish solid. This material was used without further purification. However, an analytical sample was prepared by recrystallization from cyclohexane, m.p. 97-100 °C. IR ($CHCl_3$) 3403 (broad), 3058, 1459, 1256, 1015 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.21-7.00 (m, 4 H), 3.72 (ddd, J = 13.1, 6.0, 2.8 Hz, 1 H), 2.74 (m, 1 H), 2.34 (s, 2 H), 2.04 (dtt, J = 13.9, 5.3, 1.6 Hz, 1 H), 1.96 (ddd, J =12.4, 5.3, 2.9 Hz, 1 H), 1.65 (m, 1 H), 1.46-1.38 (m, 2 H), 1.28 (d, J =12.1 Hz, 1 H), 1.05 (s, 3 H), OH not visible; ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.4, 137.5 126.0, 125.8, 122.6, 122.2, 74.4, 74.3, 55.6, 50.2, 43.8, 39.6, 38.0, 29.8, 26.4; HRMS (EI) m/z 278.0800 [(M^+); calcd for $C_{15}H_{18}OS_2$ 278.0799]. Anal. Calcd for $C_{15}H_{18}OS_2$: C, 64.70; H, 6.52. Found: C, 64.69; H, 6.78. (Note: a strong NOE was observed between the carbinol proton and the methylene bridge proton.)

To a solution of crude benzodithiole methylbicyclo[3.2.1]octanol prepared above (6.05 g, 21.8 mmol) and Hünig's base (4.55 mL, 3.37 g, 26.1 mmol) in CH_2Cl_2 (180 mL) was added TBSOTf (5.50 mL, 6.33 g, 24.0 mmol) dropwise at 0 °C. After the addition, the mixture was stirred at 0 °C for 30 min. The reaction mixture was quenched with aq NH_4Cl, extracted with ether, washed with aq $NaHCO_3$ and brine, dried, and concentrated under high vacuum to produce 8.40 g (99%) crude TBS ether as yellowish oil.

A solution of above crude product (1.01 g, 2.58 mmol) in a mixture of CH_3CN (7 mL) and acetone (3 mL) was added drop wise to a solution of NBS (2.8 g, 15.9 mmol) in aq acetonitrile (80%, 65 mL) at -5 °C. The stirring was continued for another 2-3 min before the reaction was quenched with aq 10% $Na_2S_2O_3$ (35 mL) and extracted with mixed solvent CH_2Cl_2-hexane (60 mL, 1:1). The organic layer was washed with brine, separated on silica gel (hexane/ether [10:1], R_f = 0.70) to furnish 0.43 g (61%) t-butyl-

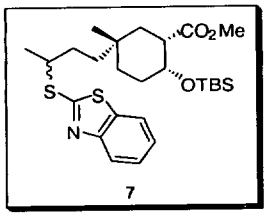
dimethylsilyloxy bicyclo[3.2.1]octanone **5** as a colorless oil. IR (neat) 1748, 1458, 1252, 1101, 839 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.79 (m, 1 H), 2.38 (m, 1 H), 2.08-1.40 (m, 8 H), 1.10 (s, 3 H), 0.82 (s, 9 H), 0.01 (s, 3 H), 0.00 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 216.9, 72.5, 56.0, 49.9, 41.8, 36.9, 36.7, 30.6, 26.6, 25.7, 18.1, -4.7, -4.8; HRMS (CI) m/z 269.1939 [(M^+ + H); calcd for $C_{15}H_{29}O_2Si$ 269.1937].



6

Aldehyde ester 6. To a solution of ketone **5** (1.55 g, 5.78 mmol) and HMPA (3 mL) in DME (30 mL) was added KHMDS (0.5 M in toluene, 14 mL, 7.0 mmol) dropwise at -40 °C. The resulting solution was allowed to warm slowly to rt over a period of 30 min and cool again to -25 °C before MeOTf (0.85 mL, 1.23 g, 7.5 mmol) was added dropwise. After the addition, the mixture was slowly warmed to rt and stirred at rt for 45 min before being quenched with aq $NaHCO_3$, extracted with ether, washed with brine, dried, and concentrated to furnish the intemediate enol ether as a light yellowish oil.

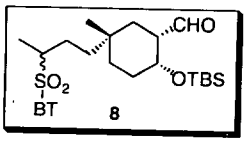
The above crude oil was instantly submitted to ozonolysis, and after purification on silica gel (hexane/ether [5:1], R_f = 0.38), 1.10 g (61% from **5**) aldehyde ester **6** was isolated as a colorless oil. IR (neat) 1736 (broad), 1466, 1258, 1072, 833 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.40 (s, 1 H), 4.40 (s, broad, 1 H), 3.64 (s, 3 H), 2.58-1.40 (m, 7 H), 1.08 (s, 3 H), 0.81 (s, 9 H), 0.01 (s, 3 H), 0.00 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.2, 173.4, 67.0, 51.6, 45.1, 43.3, 28.3, 26.1, 25.8, 25.6, 23.6, 16.5, -4.5, -5.5; HRMS (CI) m/z 315.2004 [(M^+ + H), calcd for $C_{16}H_{31}O_4Si$ 315.1992].



7

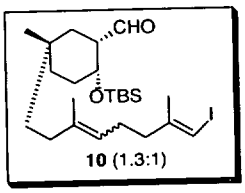
Benzothiazoyl sulfide ester 7. A solution of 0.96 g (3.06 mmol) of aldehyde ester **6** and 2.96 g (9.17 mmol) of phosphoranylideneacetone ylide in toluene (20 mL) was heated in a sealed tube for 20 h at 170 °C. After silica gel chromatography (hexane/ether [5:1], R_f = 0.29), 920 mg (85%) of the α,β-unsaturated ketone was obtained as a colorless oil. IR (neat) 1744, 1676, 1437, 1255, 1068 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.75 (d, J = 6.3 Hz, 1 H), 6.02 (d, J = 6.3 Hz, 1 H), 4.39 (s, broad, 1 H), 3.61 (s, 3 H), 2.50 (m, 1 H), 2.23 (s, 3 H), 2.00-1.20 (m, 6 H), 1.00 (s, 3 H), 0.80 (s, 9 H), 0.00 (s, 3 H), -0.04 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.4, 173.6, 158.2, 126.5, 67.1, 51.5, 44.0, 35.8, 31.1, 29.0, 28.9, 27.1, 25.6, 20.9, 17.9, -4.5, -5.5; HRMS (CI) m/z 355.2299 [(M^+ + H), calcd for $C_{19}H_{35}O_4Si$ 355.2305].

The α,β-unsaturated ketone prepared above (1.95 g, 5.51 mmol) was stirred with Pd-C (10%) in MeOH under H_2 at 45 °C for 24 h to afford 1.96 g (100%) crude light yellowish oil. The crude oil (0.54 g, 1.52 mmol) was dissolved in MeOH (40 mL), stirred with $NaBH_4$ (30 mg, 0.79 mmol) at 0 °C for 30 min. After being quenched with aq NH_4Cl, extracted with Et_2O, dried, and concentrated under high vacuum, 0.54 g (100%) crude alcohol was collected as a light yellowish oil. To a solution of this crude alcohol (0.94 g, 2.63 mmol) and 2-mercaptobenzothiazole (0.657 g, 3.93 mmol) was added Ph_3P (1.10 g, 4.20 mmol) in THF (50 mL) and DIAD (0.794 g, 3.93 mmol) dropwise at rt. The resulting mixture was stirred at rt for 12 h and at 40 °C for 12 h. The mixture was concentrated and purified on silica gel (hexane/ether [10:1], R_f = 0.45) to furnish 1.17 g (87% from the α,β-unsaturated ketone) benzothiazole sulfide ester **7** as a sticky yellowish oil as a single isomer. IR (neat) 3050, 1744, 1458, 1429, 1252 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.85 (d, J = 7.7 Hz, 1 H), 7.75 (d, J = 7.7 Hz, 1 H), 7.40-7.22 (m, 2 H), 4.36 (s, broad, 1 H), 3.90 (m, 1 H), 3.62 (s, 3 H), 2.47 (d, J = 12.9 Hz, 1 H), 1.80-1.00 (m, 13 H), 0.81 (s, 3 H), 0.80 (s, 9 H), 0.00 (s, 3 H), -0.03 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.2, 166.7, 153.3, 135.2, 125.9, 124.1, 121.5, 120.8, 67.7, 51.3, 45.2, 44.4, 43.1, 42.9, 32.3, 30.2, 30.0, 29.4, 25.6, 21.9, 21.2, 17.9, -4.5, -5.4; HRMS (CI) m/z 508.2383 [(M^+ + H), calcd for $C_{26}H_{42}NO_3S_2Si$ 508.2375].



Benzothiazoyl sulfone aldehyde 8. To a stirred solution of sulfide **7** (0.937 g, 1.85 mmol) in CH_2Cl_2 (55 mL) was added $NaHCO_3$ (710 mg, 8.45 mmol) and mCPBA (680 mg, 3.93 mmol) at -45 °C. This mixture was slowly warmed to rt over a period of about 2 h and stirred at rt for 14 h before being quenched with aq $Na_2S_2O_3$. The organic layer was washed with brine, dried, concentrated, and purified on silica gel (hexane/ether [1:1], R_f = 0.40) to produce 0.85 g (85%) the sulfone ester as a colorless oil. IR (neat) 3050, 1740, 1472, 1325, 833 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.20 (d, J = 7.5 Hz, 1 H), 7.99 (d, J = 7.5 Hz, 1 H), 7.58 (m, 2 H), 4.33 (s, broad, 1 H), 3.60 (s, 3 H), 3.50 (m, 1 H), 2.50-1.00 (m, 14 H), 0.80 (s, 3 H), 0.78 (s, 9 H), -0.01 (s, 3 H), -0.04 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.0, 165.1, 152.8, 136.8, 127.8, 127.5, 125.4, 122.2, 67.5, 60.5, 60.4, 51.3, 44.3, 42.6, 42.4, 32.4, 30.1, 29.9, 29.3, 25.6, 22.5, 17.9, -4.5, -5.5; HRMS (FAB) m/z 540.2287 [(M^+ + H); calcd for $C_{26}H_{42}NO_5S_2Si$ 540.2274].

To a solution of the sulfone ester prepared above (435 mg, 0.81 mmol) in 30 mL CH_2Cl_2-Et_2O (4:1) was injected DIBAL (1.20 mL, 1.0 M in hexane, 1.20 mmol) dropwise at -80 °C. After the injection, the reaction was further stirred for 15 min before being quenched with MeOH (4 mL) and slowly warmed to 0 °C. To this cold solution was added dilute HCl. The mixture was extracted with Et_2O, washed with $NaHCO_3$ and brine, dried, concentrated, and purified on silica gel (hexane/ether [1:1], R_f = 0.52) to furnish 343 mg (83%) of aldehyde **8** as a colorless oil. IR (neat) 3063, 1727, 1472, 1254, 1146 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.59 (d, J = 3.6 Hz, 1 H), 8.20 (d, J = 7.4 Hz, 1 H), 7.99 (d, J = 7.4 Hz, 1 H), 7.59 (m, 2 H), 4.40 (s, broad, 1 H), 3.50 (m, 1 H), 2.30-2.10 (m, 2 H),1.60-1.10 (m, 12 H), 0.81 (s, 3 H), 0.80 (s, 9 H), 0.01 (s, 3 H), -0.02 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.6, 165.0, 152.8, 136.8, 127.9, 127.5, 125.4, 122.2, 66.1, 60.4, 60.3, 50.8, 42.4, 32.2, 30.9, 30.5, 29.1, 25.6, 22.6, 21.9, 17.9, -4.4, -5.3; HRMS (CI) m/z 510.2173 [(M + H^+); calcd for $C_{25}H_{40}NO_4S_2Si$ 510.2168].

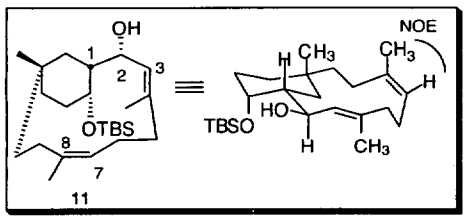


10 (1.3:1)

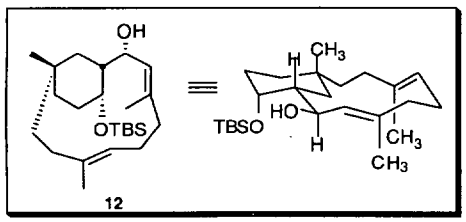
Vinyl iodide aldehyde 10. A solution of aldehyde **8** (230 mg, 0.452 mmol) and a trace amount of TSA (ca. 5 mg) in 2,2-dimethoxypropane was stirred at 65 °C for 5 h. The solution was cooled, diluted with ether, washed with aq $NaHCO_3$, dried, and filtered through a plug of silica gel. After concentration under high vacuum, 250 mg (100%) the crude acetal was isolated. To a solution of this crude acetal (720 mg, 1.30 mmol) in DME (25 mL) was injected NaHMDS (1.70 mL, 1.0 M in THF) at -78 °C and the resulting mixture was stirred at the same temperature for 45 min before a solution of (E)-5-iodo-4-methyl-4-pentenal **9**[2] (430 mg, 1.92 mmol) in DME (2 mL) was added dropwise. After complete addition, the solution was stirred at -78 °C for 1.0 h, slowly warmed to rt and stirred at rt for 20 min before being quenched with aq NH_4Cl, extracted with ether, washed with brine, dried, and concentrated to produced a sticky oil containing the vinyl iodide acetal. This crude oil was stirred in AcOH-THF-H_2O (12 mL + 4 mL + 4 mL) at 45 °C for 8 h. The resulting creamy liquid was diluted with ether, washed with water (7x), sodium bicarbonate and brine. After silica gel purification (hexane/ether [20:1], R_f = 0.27), 484 mg (72% from **8**) of an inseparable 1.3:1 E/Z mixture of geometric isomers of vinyl iodide aldehyde **10** was obtained as a colorless oil. IR (neat) 1728, 1472, 1253, 1069, 837 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.61 (s, 1 H), 5.81 (s, 1 H), 5.00 (m, 1 H), 4.41 (s, broad, 1 H), 2.30-1.90 (m, 7 H), 1.81 (s, 3 H), 1.63 (s, 3 H), 1.60-1.10 (m, 8

H), 0.84 (s, 3 H), 0.80 (s, 9 H), 0.01 (s, 3 H), -0.03 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.0, 147.6, 137.0, 123.0, 122.4, 74.8, 66.3, 51.0, 44.3, 44.1, 39.7, 39.4, 33.2, 32.3, 30.9, 30.6, 30.4, 29.2, 26.2, 26.1, 25.6, 23.9, 23.4, 21.5, 18.0, 16.2, -4.3, -5.2; HRMS (CI) m/z 519.2141 [(M^+ + H); calcd for $C_{24}H_{44}IO_2Si$ 519.2155].

NHK macrocyclization of 10. Preparation of Macrocycles 11 and 12. To a flask charged with $CrCl_2$ (470 mg, 3.82 mmol) and $Ni(acac)_2$ (2 mg, 0.008 mmol) was injected DMSO (10 mL) and THF (3 mL) at rt. The resulting slurry was stirred at rt for 10 min before a solution of aldehyde **10** (200 mg, 0.386 mmol, E/Z 1.3:1) in DMSO-THF (25 mL + 7 mL) was injected. The mixture was further stirred for 26 h at rt. The mixture was cooled in ice-water bath and quenched with 5% potassium serinate, extracted with ether, washed with brine, dried, and separated on silica gel (hexane/ether [10:1]) to furnish 41 mg (27%) of bicyclic allylic alcohol (E, Z) isomer **11** (R_f = 0.22, m.p. 100-101 °C) and 51 mg (33%) of the desired (E, E) isomer **12** (R_f = 0.20, m.p. 127-9 °C) both as colorless crystals in addition to 50 mg (25%) recovered vinyl iodide aldehyde **10**.



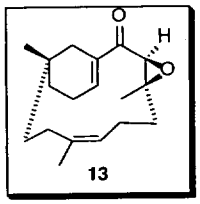
For **11**: IR ($CHCl_3$) 3461, 1462, 1260, 1069 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.39 (d, J = 9.0 Hz, 1 H), 5.12 (dd, J = 8.8, 5.2 Hz, 1 H), 4.80 (t, J = 8.8 Hz, 1 H), 4.38 (s, broad, 1 H), 3.90 (dt, J = 11.2, 4.0 Hz, 1 H), 2.50-2.30 (m, 3 H), 2.05-1.85 (m, 4 H), 1.71 (s, 3 H), 1.60 (s, 3 H), 1.60-1.10 (m, 8 H), 0.91 (s, 9 H), 0.78 (s, 3 H), 0.12 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.0, 136.6, 125.0, 123.0, 66.8, 45.9, 41.2, 36.8, 36.0, 34.3, 31.7, 30.0, 29.4, 27.4, 26.5, 25.8, 25.7, 22.8, 21.1, 18.0, -4.5, -5.3; HRMS (CI) m/z 391.3033 [(M^+ - H); calcd for $C_{24}H_{43}O_2Si$ 391.3032].



For **12**: IR ($CHCl_3$) 3378, 1458, 1252, 1057, 1020 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.05 (dt, J = 11.9, 1.5 Hz, 1 H), 4.97 (d, J = 10.2, 1 H), 4.37 (dd, J = 9.9, 8.6 Hz, 1 H), 4.10 (d, J = 2.4 Hz, 1 H), 2.50-1.90 (m, 6 H), 1.61 (s, 3 H), 1.55 (s, 3 H), 1.50-1.14 (m, 9 H), 0.90 (s, 9 H), 0.88 (s, 3 H), 0.07 (s, 3 H), 0.04 (s, 3 H), (OH not observed); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.1, 137.2, 129.3, 127.7, 69.4, 65.3, 43.4, 40.7, 40.3, 36.4, 34.6, 33.9, 33.0,

29.6, 25.9, 25.7, 20.7, 18.1, 15.9, 15.3, -4.6, -5.0; HRMS (CI) m/z 393.3183 [(M^+ + H); calcd for $C_{24}H_{45}O_2Si$ 393.3189].

The stereochemistries of **11** and **12** were initially assigned according to their 500 MHz ^1H NMR and NOE spectra, and later secured by single crystal X-ray analysis (vide infra). The strong NOE (about 5%) between the C(8)-methyl group and C(7) olefinic hydrogen atom in **11** proves the cis stererochemistry of this π-bond. While the absence of such NOE effects enables us to assign the trans stereochemistry of the same bond in **12**. The relatively large coupling constants (>8 Hz) between C(2)-H and C(1)-H in both **11** and **12** indicate the C(2) protons are in axial positions and therefore allowed us to assign the conformations and relative stereochemistry as shown.



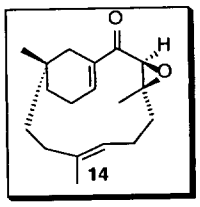
13

Epoxide 13. To a flask charged with a benzene (12 mL) solution of (E, Z) dienol **11** (70 mg, 0.178 mmol) and a trace amount of vanadyl acetylacetonate (0.5 mg, 0.0020 mmol) was added t-BuOOH (26 mg, 90%, 0.26 mmol) at rt and the resulting mixture was stirred at 35 °C for 40 min. The reaction was quenched by adding a few drops of dimethyl sulfide. The reaction mixture was concentrated and purified on silica gel (hexane/ether [2:1], R_f = 0.22) to furnish the epoxy alcohol (63 mg, 86%) as colorless crystals (m.p. 140-142 °C). IR ($CHCl_3$) 3472, 1482, 1379, 1252, 1028 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.00 (d, J = 11.5 Hz, 1 H), 4.15 (s, broad, 1 H), 3.43 (t, J = 9.4, 1 H), 2.66 (d, J = 9.4 Hz, 1 H), 2.55-2.40 (m, 2 H), 2.15-1.93 (m, 3 H), 1.70 (s, 3 H), 1.65-1.10 (m, 11 H), 1.25 (s, 3 H), 0.94 (s, 3 H), 0.91 (s, 9 H), 0.02 (s, 3 H), 0.01 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.5, 124.4, 69.8, 66.2, 64.6, 62.7, 42.5, 40.8, 39.5, 34.1, 33.2, 30.2, 29.5, 26.1, 25.8, 23.6, 21.1, 21.0, 18.0, -4.6, -5.1; HRMS (CI) m/z 409.3139 [(M^+ + H), calcd for $C_{24}H_{45}O_3Si$ 409.3138. (Note: the stereochemistry of the epoxide was supported by the observance of a strong NOE between the C(8)-methyl and the C(2)-H.)

To a solution of oxalyl chloride (37 mg, 0.282 mmol) in methylene chloride (5 mL) was added DMSO (42 mg, 0.56 mmol) at -78 °C. The resulting mixture was stirred at the same temperature for 10 min before a solution of the epoxy alcohol prepared above (96 mg, 0.235 mmol) in methylene chloride (10 mL) was added dropwise. The mixture was stirred for 55 min at -78 °C. i-Pr_2NEt (0.3 mL, 1.77 mmol) was then added and the reaction was allowed to slowly warm to rt. The mixture was washed with brine, dried,

concentrated and purified on silica gel (hexane/ether [3:2], R_f = 0.50) to furnish 83 mg (87%) the α-keto epoxide as colorless crystals (m.p. 136-138 °C). IR ($CHCl_3$) 1727, 1458, 1252, 1065, 1034 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.08 (d, J = 11.5 Hz, 1 H), 4.41 (s, broad, 1 H), 3.45 (s, 1 H), 2.70 (q, J = 12.2 Hz, 1 H), 2.54 (dd, J = 14.6, 10.0 Hz, 1 H), 2.40 (d, J = 13.2 Hz, 1 H), 2.26 (d, J = 13.2 Hz, 1 H), 2.18 (dt, J = 13.2, 3.3 Hz, 1 H), 2.00 (d, J = 13.0 Hz, 1 H), 1.75 (s, 3 H), 1.55 (m, 9 H), 1.18 (s, 3 H), 1.06 (s, 3 H), 0.81 (s, 9 H), 0.06 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.9, 136.9, 124.2, 64.4, 63.8, 63.0, 49.4, 40.3, 38.8, 34.2, 33.3, 30.7, 29.5, 26.3, 25.9, 23.3, 21.5, 19.3, 18.0, -4.7, -4.8; HRMS (CI) m/z 407.2982 [(M^+ + H); calcd for $C_{24}H_{43}O_3Si$ 407.2981].

A solution of the α-keto epoxide prepared above (15 mg, 0.037 mmol) in THF (6 mL) was stirred with TBAF (0.1 mL, 1.0 M in THF) at 0 °C for 8 min. The reaction mixture was quenched with aq NH_4Cl, extracted with ether, washed with Na_2CO_3, dried, concentrated and purified on silica gel (hexane/ether [2:1], R_f = 0.41) to furnish 7.5 mg (74%) of epoxide **13** as colorless crystals (m.p. 114-116 °C). IR ($CHCl_3$) 1696, 1622, 1458, 1379, 1200 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.63 (dd, J = 6.2, 3.3 Hz, 1 H), 4.98 (d, J = 11.9 Hz, 1 H), 3.82 (s, 1 H), 2.63 (m, 2 H), 2.48 (dd, J = 13.0, 6.9 Hz, 1 H), 2.20-2.00 (m, 4 H), 1.73 (m, 1 H), 1.60 (s, 3 H), 1.55-1.30 (m, 6 H), 1.06 (s, 3 H), 0.98 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.4, 137.3, 136.6, 136.3, 123.0, 63.6, 63.2, 38.5, 35.6, 33.6, 33.3, 31.8, 26.5, 26.2, 25.5, 23.2, 22.9, 18.9; HRMS (EI) m/z 274.1932 [(M^+); calcd for $C_{18}H_{26}O_2$ 274.1933].

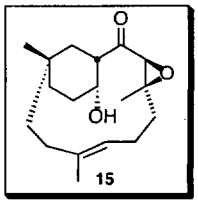


Phomactin C/D analog 14. To a flask charged with a benzene (16 mL) solution of (E, E) dienol **12** (90 mg, 0.230 mmol) and a trace amount of vanadyl acetylacetonate (0.7 mg, 0.0026 mmol) was added t-BuOOH (33 mg, 90%, 0.33 mmol) at rt and the resulting mixture was stirred at rt for 10 min. The reaction was quenched by adding a few drops of dimethyl sulfide. The reaction mixture was concentrated and purified on silica gel (hexane/ether [2:1], R_f = 0.29) to furnish the epoxy alcohol (94 mg, 100%) as colorless crystals (m.p. 166-168 °C). IR ($CHCl_3$) 3488, 1460, 1252, 1061, 1038 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.10 (d, J = 11.5 Hz, 1 H), 4.07 (d, J = 2.0 Hz, 1 H), 3.39 (t, J = 9.3, 1 H), 2.60 (d, J = 9.3 Hz, 1 H), 2.40-2.00 (m, 6 H), 1.63 (s, 3 H), 1.60-1.21 (m, 10 H), 1.20 (s, 3 H), 0.95 (s, 3 H), 0.88 (s, 9 H), 0.02 (s, 3 H), 0.00 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.9, 127.2, 70.1, 69.7, 64.9, 63.3, 42.4, 40.2, 38.9,

36.2, 34.5, 33.3, 31.5, 29.4, 25.8, 24.7, 20.8, 18.0, 17.5, 15.7, -4.6, -5.1; HRMS (CI) m/z 409.3127 [(M^+ + H); calcd for $C_{24}H_{45}O_3Si$ 409.3138]. (Note: the stereochemistry of the epoxide was supported by the observance of a 3% NOE between the C(8)-methyl and the C(2)-H.)

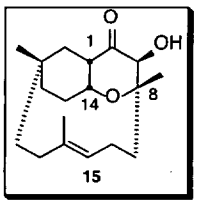
To a solution of oxalyl chloride (14 mg, 0.109 mmol) in methylene chloride (5 mL) was added DMSO (16 mg, 0.22 mmol) at -78 °C. The resulting mixture was stirred at the same temperature for 10 min before a solution of the epoxy alcohol prepared above (37 mg, 0.091 mmol) in methylene chloride (10 mL) was added dropwise. The mixture was stirred for 55 min at -78 °C. i-Pr_2NEt (0.12 mL, 0.69 mmol) was then added and the reaction was allowed to slowly warm to rt. The mixture was washed with brine, dried, concentrated and purified on silica gel (hexane/ether [3:2], R_f = 0.50) to furnish 35 mg (95%) the α-keto epoxide as colorless crystals (m.p. 106-107 °C). IR ($CHCl_3$) 1723, 1252, 1061, 1039, 833 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.18 (d, J = 11.5 Hz, 1 H), 4.38 (s, broad, 1 H), 3.38 (s, 1 H), 2.55 (d, J = 8.7 Hz, 1 H), 2.40 (t, J = 13.9 Hz, 1 H), 2.35 (t, J = 11.5 Hz, 1 H), 2.28 (ddd, J = 13.9, 3.3, 1.7 Hz, 1 H), 2.21 (dt, J = 13.9, 3.3 Hz, 1 H), 2.10 (m 1 H), 1.70 (s, 3 H), 1.60-1.20 (m, 9 H), 1.08 (s, 3 H), 1.03 (s, 3 H), 0.81 (s, 9 H), 0.02 (s, 6 H); ^{13}C (125 MHz, $CDCl_3$) δ 203.9, 138.0, 127.4, 67.8, 64.0, 63.4, 49.2, 39.8, 39.1, 36.2, 34.6, 33.3, 32.3, 29.2, 25.9, 24.7, 21.1, 18.0, 15.6, 15.4, -4.7, -4.8; HRMS (CI) m/z 407.2970 [(M^+ + H); calcd for $C_{24}H_{43}O_3Si$ 407.2981].

A solution of the α-keto epoxide prepared above (30 mg, 0.074 mmol) in THF (12 mL) was stirred with TBAF (0.2 mL, 1.0 M in THF) at 0 °C for 8 min. The reaction mixture was quenched with aq NH_4Cl, extracted with ether, washed with Na_2CO_3, dried, concentrated and purified on silica gel (hexane/ether [1:1], R_f = 0.50) to furnish 15 mg (74%) of phomactin C/D analog **14** as colorless crystals (m.p. 103-105 °C). IR ($CHCl_3$) 1692, 1622, 1462, 1192, 1140 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.89 (d, J = 1.5 Hz, 1 H), 5.20 (d, J = 10.8 Hz, 1 H), 3.75 (s, 1 H), 2.80 (d, J = 17.0 Hz, 1 H), 2.40-2.05 (m, 6 H), 1.96 (d, J = 17.0 Hz, 1 H), 1.62 (m, 1 H), 1.59 (s, 3 H), 1.40-1.20 (m, 5 H), 1.13 (s, 3 H), 1.05 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.2, 138.0, 136.3, 136.1, 124.7, 64.7, 63.4, 38.4, 35.3, 35.0, 33.3, 32.4, 30.3, 28.2, 24.8, 23.1, 16.0, 14.6; HRMS (EI) m/z 274.1932 [(M^+); calcd for $C_{18}H_{26}O_2$ 274.1933].



Epoxide 15. Dienol **12** was epoxidized as desribed above. A solution of the resultant epoxy alcohol (75 mg, 0.183 mmol) in THF (9 mL) was stirred with TBAF (0.25 mL, 1.0 M in THF) at 55 °C for 6.0 h. The reaction mixture was cooled and quenched with aq NH_4Cl, extracted with ether, washed with Na_2CO_3, dried, concentrated under high vacuum to furnish 55 mg crude epoxy diol as colorless solid. (Note: the stereochemistry of the epoxide was supported by the observance of a strong NOE between the C(8)-methyl and the C(2)-H.)

To a solution of oxalyl chloride (50 mg, 0.393 mmol) in methylene chloride (8 mL) was added DMSO (65 mg, 0.83 mmol) at -78 °C and the resulting mixture was stirred at the same temperature for 10 min before a solution of crude epoxy diol prepared above (55 mg, 0.188 mmol) in methylene chloride (6 mL) was added dropwise and stirred for 90 min at -78 °C. i-Pr_2NEt (0.4 mL, 2.3 mmol) was then added and the reaction was allowed to slowly warm to rt. The mixture was washed with brine, dried, concentrated and purified on silica gel (hexane/EtOAc [4:1], R_f = 0.50) to furnish 41 mg (77%) of 14-hydroxy-2-keto epoxide **15** as colorless crystals (m.p. 194-196 °C). IR ($CHCl_3$) 3528, 1711, 1381, 1140, 1090 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.20 (d, J = 11.0 Hz, 1 H), 4.28 (s, broad, 1 H), 3.45 (s, 1 H), 2.69 (d, J = 13.4 Hz, 1 H), 2.65 (t, J = 2.2 Hz, 1 H), 2.53 (dt, J = 13.4, 3.3, Hz, 1 H), 2.42 (m, 2 H), 2.22 (dt, J = 14.2, 3.7 Hz, 1 H), 2.10 (m, 2 H), 1.73 (ddd, J = 14.2, 6.5, 3.3 Hz, 1 H), 1.70 (s, 3 H), 1.60-1.30 (m, 7 H), 1.10 (s, 3 H), 1.03 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.6, 138.4, 127.1, 67.1, 64.0, 63.5, 48.6, 39.4, 38.7, 36.0, 34.9, 32.8, 32.5, 27.3, 24.6, 20.2, 15.6, 14.9; HRMS (EI) m/z 292.2039 [(M^+); calcd for $C_{18}H_{28}O_3$ 292.2038].



Phomactin A analog 16. A solution of 14-hydroxy-2-keto epoxide **15** (7.5 mg, 0.026 mmol) and a few crystals of p-TSA in toluene (10 mL) was stirred at 65 °C for 3.5 h. The solution was cooled and purified on silica gel (hexane/ether [3:1], R_f = 0.66) to furnish 6.0 mg (80%) of phomactin A analog **16** as colorless crystals (m.p. 115-117 °C). IR ($CHCl_3$) 3482, 1705, 1456, 1074, 911, 733 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.57 (d, J = 11.7 Hz, 1 H), 4.41 (d, J = 4.4 Hz, 1 H), 3.82 (m, 1 H), 3.41 (d, J = 4.4 Hz, 1 H), 2.50 (m, 3 H), 2.37 (m, 3 H), 2.15 (dm, J = 15.9 Hz, 1 H), 2.00-1.70 (m, 4 H), 1.60 (s, 3 H), 1.56-1.20 (m, 3 H), 1.01 (s, 3 H), 0.98 (dd, J = 13.5, 6.0 Hz, 1 H), 0.83 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.5, 130.2,

129.0, 83.3, 71.5, 68.9, 49.4, 38.7, 37.7, 36.3, 32.5, 31.4, 29.7, 28.3, 25.8, 24.4, 19.1, 15.4; HRMS (EI) m/z 292.2026 [(M^+); calcd for $C_{18}H_{28}O_3$ 292.2038]. (Note: The stereochemical assignments of **16** were primarily based on the reaction mechanism and were supported by a strong NOE observed between the C(8)-Me and the C(14)-H. Furthermore the coupling data suggests a cis relationship between the C(14) and C(1) protons.)

X-Ray Single Crystal Structure Determination of NHK product 11

Data Collection

Colorless crystals were obtained from the recrystallization in petroleum ether (b.p. 60-90 °C). A crystal (approximate dimensions 0.8 x 1.3 x 1.9 mm) was placed onto the tip of a fine glass capillary and mounted on a Bruker SMART 1 K system for a data collection at 173(2) K. A preliminary set of cell constants was calculated from reflections harvested from three sets of 20 frames. These initial sets of frames were oriented such that orthogonal wedges of reciprocal space were surveyed. This produced an initial orientation matrix determined from 95 reflections. Final cell constants were calculated from the xyz centroids of 8192 strong reflections from the actual data collection after integration (SAINT 5.00 1998).

The data collection was carried out using MoKα radiation (graphite monochromator) with a frame time of 19 seconds and a detector distance of 5.05 cm. A full sphere of reciprocal space was surveyed to a resolution of 0.75 A. Four runs of frames were collected with 0.30° scans in ω at 4 different ϕ settings and a detector position of –28° in 2θ. An additional partial run of frames was collected in order to model possible decay, however, no decay was observed. Data were corrected for absorption (SADABS, Sheldrick 1999).

Structure Solution and Refinement

The structure was solved and refined using SHELXS-97. The space group $I4_1/a$ was determinted based on systematic absence and intensity statistics. A direct-methods solution was calculated which provided all non-hydrogen atoms the E-map. All non-hydrogen atoms were refined with anisotropic displacement parameters. All hydrogen atoms were placed in ideal positions and refined independently

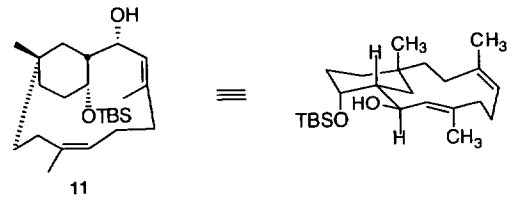
with isotropic displacement parameters. The final full matrix least squares refinement converged to R_1 = 0.0486 and wR2 = 0.1431 (F, all 6247 data, F>4σ).

Data collection and structure solution were conducted at the Crystallography Service Laboratory, Chemistry Department, Michigan State University. All calculations were performed using SGI 02 R10000 workstations using the SHELXTL V5.0 suite of program.

Table 1. Crystal Data and Structure Refinement for **11**

Identification code	[A45]
Empirical formula	$C_{24}H_{44}O_2Si$
Formula weight	392.68
Temperature	173(1) K
Wavelength	0.71073 Å
Crystal system	tetragonal
Space group	I4(1)/a (# 88)
Unit cell dimensions	a = 29.316 (4) Å b = 29.316 (4) Å c = 12.019 (2) Å alpha = 90 degree beta = 90 degree gamma = 90 degree
Volume	10329 (3) $Å^3$
Z	16
Density (calculated)	1.010 Mg/m^3
Absorption coefficient	0.105 mm^{-1}
F (000)	3488
Crystal size	1.9 x 1.3 x 0.8 mm
Theta range for data collection	1.39 to 28.27 degree
Index ranges	$-37 \le h \le 37$, $-38 \le k \le 38$, $-15 \le l \le 15$
Reflections collected / unique	58259 / 6247 [R (int) = 0.0405]
Completeness to theta = 28.27	97.6%
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6247 / 0 / 421
Goodness-of-fit on F^2	1.042
Final R indices [I>2sigma(I)]	R1 = 0.0486, wR2 = 0.1310
R indices (all data)	R1 = 0.0645, wR2 = 0.1431
Extinction coefficient	0.00003 (12)
Largest diff. peak and hole	0.724 and –0.258 $e.Å^{-3}$

Figure 1. ORTEP Drawing of the Structure of Compound **11**



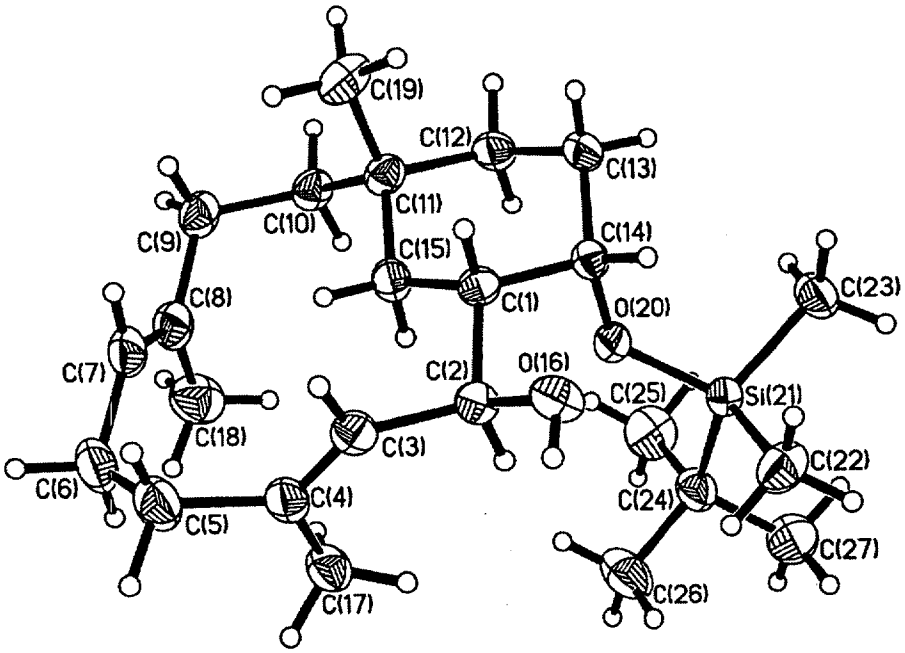


Table 2. Atomic Coordinates (x 10^4), Equivalent Isotropic Displacement Parameters (A^2 x 10^3), and Occupancies for Compound **11**

	x	y	z	U (eq)	Occ
C (1)	9511 (1)	6306 (1)	-2482 (1)	30 (1)	1
C (2)	9280 (1)	6766 (1)	-2178 (1)	30 (1)	1
C (3)	9177 (1)	7028 (1)	-3234 (1)	37 (1)	1
C (4)	8770 (1)	7041 (1)	-3754 (1)	40 (1)	1
C (5)	8741 (1)	7183 (1)	-4976 (2)	51 (1)	1
C (6)	8794 (1)	6772 (1)	-5774 (2)	64 (1)	1
C (7)	8453 (1)	6402 (1)	-5591 (2)	60 (1)	1
C (8)	8509 (1)	5946 (1)	-5478 (2)	57 (1)	1
C (9)	8949 (1)	5673 (1)	-5624 (2)	52 (1)	1
C (10)	9117 (1)	5377 (1)	-4614 (2)	44 (1)	1
C (11)	9458 (1)	5609 (1)	-3800 (1)	36 (1)	1
C (12)	9540 (1)	5302 (1)	-2772 (2)	40 (1)	1
C (13)	9804 (1)	5543 (1)	-1832 (2)	39 (1)	1
C (14)	9574 (1)	5992 (1)	-1476 (1)	31 (1)	1
C (15)	9239 (1)	6057 (1)	-3389 (1)	32 (1)	1
O (16)	9590 (1)	6999 (1)	-1440 (1)	40 (1)	1
C (17)	8328 (1)	6875 (1)	-3224 (2)	47 (1)	1
C (18)	8089 (1)	5664 (1)	-5270 (3)	73 (1)	1
C (19)	9910 (1)	5706 (1)	-4412 (2)	51 (1)	1
O (20)	9131 (1)	5895 (1)	-1009 (1)	33 (1)	1
Si (21)	8997 (1)	5899 (1)	331 (1)	33 (1)	1
C (22)	9131 (1)	6464 (1)	976 (2)	53 (1)	1
C (23)	9322 (1)	5441 (1)	1081 (2)	50 (1)	1
C (24)	8361 (1)	5787 (1)	341 (2)	43 (1)	1
C (25)	8254 (1)	5338 (1)	-260 (2)	65 (1)	1
C (26)	8112 (1)	6184 (1)	-241 (3)	70 (1)	1
C (27)	8190 (1)	5756 (1)	1555 (2)	64 (1)	1

U (eq) is defined as one third of the trace of the orthogonalized Uij tensor.

X-Ray Single Crystal Structure Determination of NHK product 12

Data Collection

Colorless crystals were obtained from the recrystallization in petroleum ether (b.p. 60-90 °C). A crystal (approximate dimensions 0.2 x 0.3 x 0.5 mm) was placed onto the tip of a fine glass capillary and mounted on a Bruker SMART 1 K system for a data collection at 173(2) K. A preliminary set of cell constants was calculated from reflections harvested from three sets of 20 frames. These initial sets of frames were oriented such that orthogonal wedges of reciprocal space were surveyed. This produced an initial orientation matrix determined from 144 reflections. Final cell constants were calculated from the xyz centroids of 6710 strong reflections from the actual data collection after integration (SAINT 5.00 1998).

The data collection was carried out using MoKα radiation (graphite monochromator) with a frame time of 26 seconds and a detector distance of 5.05 cm. A full sphere of reciprocal space was surveyed to a resolution of 0.75 A. Four runs of frames were collected with 0.30° scans in ω at 4 different ϕ settings and a detector position of –28° in 2θ. An additional partial run of frames was collected in order to model possible decay, however, no decay was observed. Data were corrected for absorption (SADABS, Sheldrick 1999).

Structure Solution and Refinement

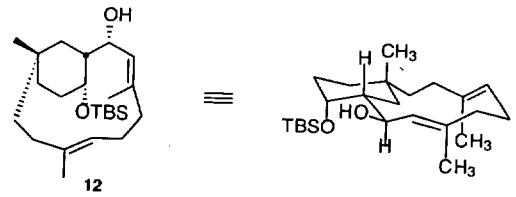
The structure was solved and refined using SHELXS-97. The space group $I4_1/a$ was determinted based on systematic absence and intensity statistics. A direct-methods solution was calculated which provided all non-hydrogen atoms the E-map. All non-hydrogen atoms were refined with anisotropic displacement parameters. All hydrogen atoms were placed in ideal positions and refined independently with isotropic displacement parameters. The final full matrix least squares refinement converged to R_1 = 0.0403 and wR2 = 0.1026 (F, all 6293 data, F>4σ).

Data collection and structure solution were conducted at the Crystallography Service Laboratory, Chemistry Department, Michigan State University. All calculations were performed using SGI 02 R10000 workstations using the SHELXTL V5.0 suite of program.

Table 1. Crystal Data and Structure Refinement for **12**

Identification code	[A44]
Empirical formula	$C_{24.02}H_{44}Cl_{0.07}O_2Si$
Formula weight	395.20
Temperature	173(1) K
Wavelength	0.71073 Å
Crystal system	tetragonal
Space group	I4(1)/a (# 88)
Unit cell dimensions	a = 24.146 (4) Å
	b = 29.146 (4) Å
	c = 12.129 (2) Å
	alpha = 90 degree
	beta = 90 degree
	gamma = 90 degree
Volume	10303 (3) $Å^3$
Z	16
Density (calculated)	1.019 Mg/m^3
Absorption coefficient	0.112 mm^{-1}
F (000)	3507
Crystal size	0.2 x 0.3 x 0.5 mm
Theta range for data collection	1.40 to 28.28 degree
Index ranges	$-38 \le h \le 38, -38 \le k \le 37, -16 \le l \le 15$
Reflections collected / unique	60391 / 6293 [R (int) = 0.0549]
Completeness to theta = 28.28	98.3%
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6293 / 0 / 427
Goodness-of-fit on F^2	1.007
Final R indices [I>2sigma(I)]	R1 = 0.0403, wR2 = 0.0908
R indices (all data)	R1 = 0.0711, wR2 = 0.1026
Extinction coefficient	0.00018 (6)
Largest diff. peak and hole	0.282 and –0.202 $e.Å^{-3}$

Figure 1. ORTEP Drawing of the Structure of Compound **12**



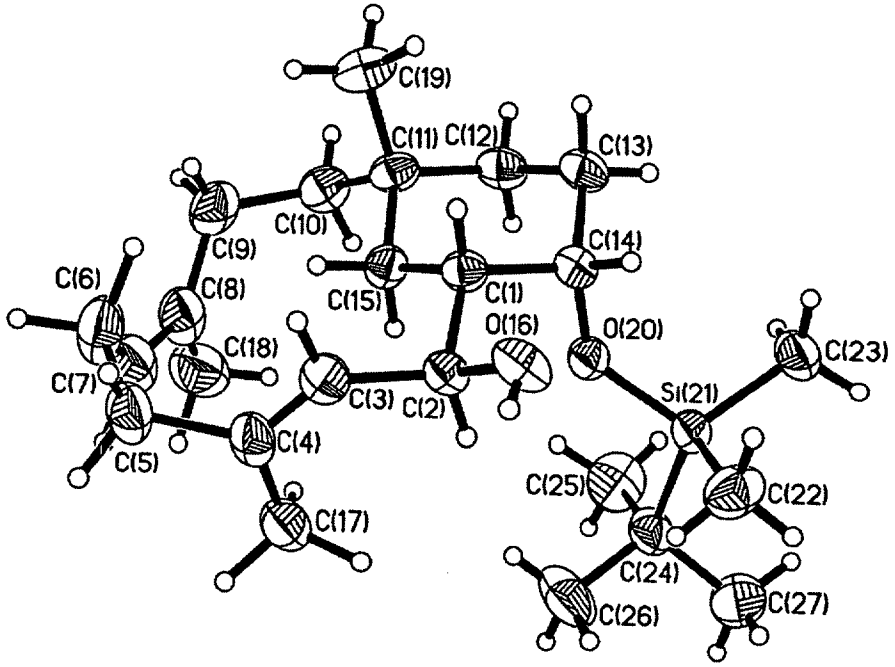


Table 2. Atomic Coordinates (x 10^4), Equivalent Isotropic Displacement Parameters (A^2 x 10^3), and Occupancies for Compound **12**

	x	y	z	U (eq)	Occ
C (1)	9541 (1)	6259 (1)	-2294 (1)	24 (1)	1
C (2)	9303 (1)	6724 (1)	-2090 (1)	25 (1)	1
C (3)	9216 (1)	6963 (1)	-3175 (1)	29 (1)	1
C (4)	8816 (1)	6984 (1)	-3715 (1)	31 (1)	1
C (5)	8792 (1)	7140 (1)	-4911 (1)	43 (1)	1
C (6)	8598 (1)	6768 (1)	-5699 (1)	46 (1)	1
C (7)	8876 (1)	6328 (1)	-5693 (1)	39 (1)	1
C (8)	8739 (1)	5905 (1)	-5427 (1)	37 (1)	1
C (9)	9075 (1)	5505 (1)	-5424 (1)	36 (1)	1
C (10)	9176 (1)	5273 (1)	-4298 (1)	31 (1)	1
C (11)	9503 (1)	5526 (1)	-3497 (1)	27 (1)	1
C (12)	9557 (1)	5242 (1)	-2434 (1)	30 (1)	1
C (13)	9811 (1)	5504 (1)	-1514 (1)	31 (1)	1
C (14)	9584 (1)	5967 (1)	-1244 (1)	25 (1)	1
C (15)	9289 (1)	5990 (1)	-3189 (1)	27 (1)	1
O (16)	9601 (1)	6980 (1)	-1372 (1)	33 (1)	1
C (17)	8366 (1)	6832 (1)	-3227 (1)	37 (1)	1
C (18)	8252 (1)	5781 (1)	-5130 (2)	51 (1)	1
C (19)	9975 (1)	5592 (1)	-4042 (2)	43 (1)	1
O (20)	9131 (1)	5887 (1)	-814 (1)	27 (1)	1
Si (21)	8989 (1)	5912 (1)	504 (1)	26 (1)	1
C (22)	9123 (1)	6491 (1)	1082 (2)	42 (1)	1
C (23)	9310 (1)	5468 (1)	1304 (1)	40 (1)	1
C (24)	8353 (1)	5793 (1)	509 (1)	35 (1)	1
C (25)	8255 (1)	5330 (1)	-51 (2)	52 (1)	1
C (26)	8101 (1)	6174 (1)	-126 (2)	51 (1)	1
C (27)	8173 (1)	5780 (1)	1703 (2)	51 (1)	1
Cl (28)	9605 (3)	7360 (3)	-7175 (7)	67 (3)	0.066 (2)
C (29)	10000	7500	-6250	62 (15)	0.066 (2)

U (eq) is defined as one third of the trace of the orthogonalized Uij tensor.

REFERENCES and NOTES

(1) From methacrolein (3 steps, 40% overall yield) Rigby, J. H.; Kotnis, A.; Kramer, J. J. Org. Chem. **1990**, 55, 5078-5088.

(2) (a) Roush, W. R.; Barda, D. A. Tetrahedron Lett. **1997**, 38, 8781-8784. (b) Zheng, Y. F.; Oehlschlager, A. C. J. Org. Chem. **1994**, 59, 5803-5809.