Total Synthesis of (+)-Phomactin A Using a *B*-Alkyl Suzuki Macrocyclization

Peter J. Mohr and Randall L. Halcomb*

*Department of Chemistry and Biochemistry, University of Colorado,
Boulder, CO 80309-0215*

Supporting Information

(5*R*)-5,6-dimethylcyclohex-2-enone (3). Diisopropyl amine (8.6 mL, 61.1 mmol) was added to THF (200 mL) at 0 °C, followed by the addition of *n*-butyl lithium (2.2M in hexanes, 58.3 mmol). The resulting solution was stirred for 20 min and then cooled to -78 °C. A -78 °C solution of (3*R*)-2,3-dimethylcyclohexanone (7.0 g, 55.5 mmol) in THF (100 mL) was then added dropwise by cannula. The resulting solution was stirred for 35 min at -78 °C, followed by the addition of triethylamine (15.4 mL, 111.0 mmol) and chlorotrimethylsilane (14.0 mL, 111.0 mmol). The solution was then stirred at -78 °C for 1 h, followed by warming to 0 °C over 30 min. The resulting 0 °C solution was then transferred by cannula to a solution of bromine (8.5 mL, 166.5 mmol) in THF (150 mL) at -78 °C. The resulting solution was stirred for 2 h at -78 °C, and quenched with 10% aqueous sodium thiosulfate (500 mL). The reaction mixture was then warmed to rt, extracted with ether (3 x 500 mL), washed with brine (2 x 500 mL), dried (Mg₂SO₄), filtered through a short plug of silica, and concentrated under vacuum to give (3*R*)-6-bromo-2,3-dimethylcyclohexanone. The crude bromide (11.3 g, 55.0 mmol) was then immediately diluted with DMF (200 mL) and the resulting solution was placed in an addition funnel attached to a 3-neck round bottom flask equipped with a condenser and filled with DMF (500 mL). Lithium carbonate (41 g, 555 mmol) was then added to the flask, followed by the careful addition of lithium bromide (48 g, 555 mmol) at a rate slow enough to maintain the internal temperature of the reaction mixture below 50 °C. The resulting white slurry was then slowly heated to exactly 100-105 °C, and stirred at this temperature for 1 h. The solution of crude bromide was then added dropwise from the addition funnel to the hot DMF solution and stirred for 3 h. The reaction was then cooled to 0 °C, quenched with water, extracted with pentane (7 x 500 mL), washed with brine (2 x 500 mL), dried (Mg₂SO₄), and concentrated under vacuum. Vacuum distillation (30 °C, 0.5 mm Hg) gave **3** (5.0 g, 73%) as a clear liquid.

(5*R*,6*S*)-5,6-dimethyl-6-vinylcyclohex-2-enone (4). Diisopropyl amine (0.65 mL, 4.6 mmol) was added to a solution of ether (20 mL) at 0 °C, followed by the addition of *n*-butyl lithium (2.3 M in hexanes, 4.4 mmol). The resulting solution was stirred for 20 min and then cooled to -78 °C. A solution of ketone **3** (0.5 g, 4.0 mmol) in ether (10 mL) was then added dropwise by

cannula. The resulting solution was stirred for 35 min at $-78\text{ }^{\circ}\text{C}$, followed by the fast dropwise addition of a $-78\text{ }^{\circ}\text{C}$ solution of phenylselenoacetaldehyde (1.2g, 6.0 mmol) in ether (10 mL). The resulting solution was stirred for 1 h at $-78\text{ }^{\circ}\text{C}$, followed by fast transfer by cannula into a rt solution of aqueous ammonium chloride (100 mL). The reaction was immediately extracted with ether (3 x 100 mL), washed with brine (100 mL), dried (Mg_2SO_4), and concentrated under vacuum. The crude β -hydroxyketone was then immediately diluted with CH_2Cl_2 (30 mL). The mixture was cooled to $0\text{ }^{\circ}\text{C}$, followed by the addition of triethylamine (2.1 mL, 15 mmol). A solution of methanesulfonyl chloride (0.9 mL, 12 mmol) in CH_2Cl_2 (10 mL) was then slowly added from an addition funnel. Upon completion of the addition, the reaction was warmed to rt, and stirred for 4 h. The reaction was then quenched with 1 M NaOH, extracted with ether (3 x 100 mL), washed with brine (100 mL), dried (Mg_2SO_4), and concentrated under vacuum. Vacuum distillation ($30\text{ }^{\circ}\text{C}$, 0.5 mm Hg) gave **4** (378 mg, 63%) as a clear liquid.

(5R,6S)-3-methoxymethoxymethyl-4,5-dimethyl-4-vinylcyclohex-2-en-1-one (5). A solution of methoxymethoxytributylstannylmethane (650 mg, 1.8 mmol) and lithium chloride (400 mg, 9.4 mmol) in THF (10 mL) was stirred for 2 h at rt, and then cooled to $-78\text{ }^{\circ}\text{C}$. *n*-Butyl lithium (2.3 M in hexanes, 1.67 mmol) was then added and the resulting solution was stirred for 5 min at $-78\text{ }^{\circ}\text{C}$. A solution of ketone **4** (180 mg, 1.19 mmol) in THF (5 mL) at $-78\text{ }^{\circ}\text{C}$ was then added to the above solution quickly via cannula. The resulting solution was stirred for 30 min at $-78\text{ }^{\circ}\text{C}$, quenched with H_2O , extracted with ether (3 x 50 mL), dried (Mg_2SO_4), filtered, and concentrated under vacuum. Column chromatography (20:1 hexane:ethyl acetate) gave the tertiary allylic alcohol (284 mg, 70%) as a clear liquid. A solution of the alcohol in CH_2Cl_2 (11 mL) at rt was then stirred for 5 min. PCC (430 mg, 2.2 mmol) was then added in one portion and the resulting mixture was stirred at rt for 24 h. A second portion of PCC (430 mg, 2.2 mmol) was then added, and the reaction was stirred for an additional 24 h. The reaction mixture was then diluted with ether (50 mL), washed with 1.0 M NaOH (3 x 100 mL), dried (Mg_2SO_4), filtered, and concentrated under vacuum. Column chromatography (4:1 hexane:ethyl acetate) gave **5** (224 mg, 91%) as a clear liquid.

(1R,2S,4R,5S,6S)-6-methoxymethoxymethyl-4,5-dimethyl-5-vinyl-7-oxabicyclo

[4.1.0]heptan-2-ol (6). A solution of ketone **5** (200 mg, 0.89 mmol) and cerium trichloride (400 mg, 1.07 mmol) in methanol (9 mL) was cooled to $0\text{ }^{\circ}\text{C}$. Sodium borohydride (41 mg, 1.07 mmol) was then added slowly in one portion, and the resulting mixture was stirred for 30 min at $0\text{ }^{\circ}\text{C}$. The reaction was quenched with H_2O , extracted with ethyl acetate (3 x 50 mL), dried

(Mg₂SO₄), filtered, and concentrated under vacuum. A solution of the crude alcohol in CH₂Cl₂ (8 mL) was then cooled to 0 °C. *m*CPBA (162 mg, 0.8 mmol) was then added in one portion. The reaction was stirred for 1 h, and then quenched with saturated sodium bicarbonate, extracted with CH₂Cl₂ (3 x 50 mL), dried (Mg₂SO₄), filtered, and concentrated under vacuum. Column chromatography (2:1 hexane:ethyl acetate) gave **6** (173 mg, 81%) as a clear liquid.

(4*S*,5*R*)-2-bromo-3-methoxymethoxymethyl-4,5-dimethyl-4-vinylcyclohex-2-enone. Alcohol **6** (145 mg, 0.6 mmol) was dissolved in CH₂Cl₂ at 0 °C. Sodium bicarbonate (300 mg, 3.6 mmol) was then added, followed by the addition of Dess-Martin periodinane (508 mg, 1.2 mmol). The reaction was then warmed to rt, stirred for 1 h, quenched with 10% aqueous sodium thiosulfate (50 mL), extracted with ether (3 x 50 mL), washed with brine (2 x 50 mL), dried (Mg₂SO₄), and concentrated under vacuum. Column chromatography (9:1 hexane:ethyl acetate) gave the ketone (123 mg, 86%) as a clear liquid. A solution of the ketone (1.0 g, 4.2 mmol) in CH₂Cl₂ (84 mL) was then cooled to -78 °C. Magnesium bromide diethyl etherate (10.8 g, 42 mmol) was then added over 5 min. The reaction was stirred for 12 h at -78 °C, quenched into a saturated aqueous solution of ammonium chloride (200 mL), extracted into ethyl acetate (3 x 100 mL), washed with brine (100 mL), dried (Mg₂SO₄), filtered, and concentrated under vacuum. The crude bromohydrin **7** was dissolved in CH₂Cl₂ (42 mL) and the resulting solution was cooled to 0 °C. Pyridine (3.4 mL, 42 mmol) and trifluoroacetic anhydride (3.0 mL, 21 mmol) were then added simultaneously, and the resulting solution was stirred for 1 h at 0 °C. Triethylamine (10.1 mL, 84 mmol) was then added, and the reaction was stirred at 0 °C for 30 min, followed by stirring at rt for 2 h. The reaction was quenched with 1 M HCl (100 mL), extracted into CH₂Cl₂, washed with 1 M NaOH (100 mL) and brine (100 mL), dried (Mg₂SO₄), filtered, and concentrated under vacuum. Column chromatography (9:1 hexane:ethyl acetate) gave the vinyl bromide (1.0 g, 79%) as a clear liquid.

(4*S*,5*R*)-2-bromo-3-(3,4-dimethoxybenzyloxymethyl)-4,5-dimethyl-4-vinyl cyclohex-2-enone (8). A solution of the above vinyl bromide (1.0 g, 3.3 mmol) in ether (33 mL) was prepared at rt. Magnesium bromide diethyl etherate (4.2 g, 16.5 mmol) and butanethiol (0.9 mL, 8.25 mmol) were then added. The reaction was stirred for 15 h at rt, quenched with sodium bicarbonate (50 mL), extracted into ethyl acetate (3 x 50 mL), washed with brine (3 x 50 mL), dried (Mg₂SO₄), filtered, and concentrated under vacuum. The crude alcohol was then dissolved in CH₂Cl₂ (16.5 mL) at rt. Camphorsulfonic acid (10 mg, 0.05 mmol) and 2-(3,4-dimethoxybenzyloxy)-3-nitropyridine (DMB-ONPy) (375 mg, 1.3 mmol) were then added, and the solution was stirred for 2 h. The addition of CSA and DMB-ONPy was then repeated on equimolar scale three (3) more times at 2 h intervals. After the final addition, the reaction was stirred for 12 h at rt. The

reaction was quenched with sodium bicarbonate (100 mL), extracted into CH_2Cl_2 (50 mL), dried (Mg_2SO_4), filtered, and concentrated under vacuum. Column chromatography (9:1 hexane:ethyl acetate) gave **8** (1.0 g, 77%) as a clear liquid.

(1S,4S,5R)-2-bromo-3-(3,4-dimethoxybenzyloxymethyl)-4,5-dimethyl-4-vinyl cyclohex-2-enol. A solution of ketone **8** (800 mg, 1.96 mmol) and cerium trichloride (875 mg, 2.35 mmol) in methanol (20 mL) was cooled to 0 °C. Sodium borohydride (101 mg, 2.35 mmol) was then added slowly in one portion, and the resulting mixture was stirred for 30 min at 0 °C. The reaction was quenched with H_2O , extracted with ethyl acetate (3 x 50 mL), dried (Mg_2SO_4), filtered, and concentrated under vacuum. Column chromatography (9:1 hexane:ethyl acetate) gave the pseudoequatorial alcohol (755 mg, 94%) as a clear liquid.

(1R,4S,5R)-2-bromo-3-(3,4-dimethoxybenzyloxymethyl)-4,5-dimethyl-4-vinyl cyclohex-2-enol. A solution of the pseudoequatorial alcohol (1.2 g, 2.9 mmol), triphenylphosphine (3.0 g, 11.7 mmol), and 4-nitrobenzoic acid (2.0 g, 11.7 mmol) in THF (29 mL) was cooled to -10 °C. Diethyl azodicarboxylate (1.9 mL, 11.7 mmol) was then added dropwise. The resulting mixture was warmed to rt and stirred for 12 h. The reaction was quenched with sodium bicarbonate (50 mL), extracted into ethyl acetate (3 x 50 mL), dried (Mg_2SO_4), filtered through a short plug of silica, and concentrated under vacuum. The crude benzoate was dissolved in methanol (29 mL) at rt. Sodium methoxide (0.5 M in methanol, 8.7 mmol) was then added dropwise, and the resulting solution was stirred for 1 h, quenched with ammonium chloride (50 mL), extracted into ethyl acetate (100 mL), washed with brine (100 mL), dried (Mg_2SO_4), and concentrated under vacuum. Column chromatography (4:1 hexane:ethyl acetate) gave the pseudoaxial alcohol (1.0 g, 86%) as a clear liquid.

(1R,4S,5R)-[2-bromo-3-(3,4-dimethoxybenzyloxymethyl)-4,5-dimethyl-4-vinyl cyclohex-2-en-1-yl]-tert-butyldimethylsilane (9). A solution of the above alcohol (1.8 g, 4.4 mmol) in DMF (44 mL) was stirred at rt for 5 min. Imidazole (1.5 g, 22 mmol) and TBS-Cl (1.0 g, 6.6 mmol) were then added. The resulting solution was heated to 40 °C for 2 h, cooled to rt,

quenched with H₂O, extracted into ethyl acetate (3 x 100 mL), dried (Mg₂SO₄), filtered, and concentrated under vacuum. Column chromatography (20:1 hexane:ether) gave **9** (2.1 g, 92%) as a clear liquid.

(2E)-tert-butyl-(3-methyloct-2-en-6-yn-1-yl)oxy-diphenylsilane (11). Zinc dust (870 mg, 13.4 mmol) and triphenylphosphine (3.5 g, 13.4 mmol) were added to CH₂Cl₂ (20 mL) at 0 °C. The mixture was stirred for 5 min, followed by the addition of carbon tetrabromide (4.4 g, 13.4 mmol). The reaction mixture was then stirred for 1 h at 0 °C, followed by the addition of aldehyde **10** (1.0 g, 2.68 mmol) in CH₂Cl₂ (7 mL). After warming to rt, the reaction was stirred for 5 h, diluted with hexane (50 mL), decanted, and the resulting solids were redissolved in CH₂Cl₂ (50 mL). The hexane wash was repeated four (4) times, the combined washes were filtered through a short silica plug with 9:1 hexane:ethyl acetate, and then concentrated under vacuum. The crude dibromide was then dissolved in ether (27 mL) and cooled to 0 °C, followed by the dropwise addition of *n*-butyllithium (2.3 M in hexane, 6.4 mmol). The reaction was stirred for 1 h at 0 °C, quenched with H₂O, extracted with ethyl acetate (3 x 50 mL), dried (Mg₂SO₄), filtered through a short plug of silica, and concentrated under vacuum. The crude alkyne was then dissolved in THF (27 mL) and cooled to -78 °C. *n*-butyllithium (2.3 M in hexane, 3.2 mmol) was then added dropwise, and the resulting solution was stirred at -78 °C for 30 min, followed by the addition of iodomethane (1.7 mL, 26.8 mmol). The resulting solution was allowed to slowly warm to rt, and then stirred for an additional 3 h. The reaction was quenched with H₂O, extracted with ethyl acetate (3 x 50 mL), dried (Mg₂SO₄), filtered, and concentrated under vacuum. Column chromatography (20:1 hexane:ether) gave **11** (816 mg, 81%) as a clear liquid.

(2E)-tert-butyl-dimethyl-(3-methyl-oct-2-en-6-yn-1-yl)oxy-silane. Alkyne **11** (16.1 g, 44.4 mmol) was dissolved in THF (222 mL) at rt. TBAF (1.0 M in THF, 53.2 mmol) was then added and the solution was stirred for 1 h at rt. The reaction was quenched with H₂O, extracted with ethyl acetate (3 x 200 mL), dried (Mg₂SO₄), filtered, and concentrated under vacuum. A solution of the crude alcohol in DMF (150 mL) was then stirred at rt for 5 min. Imidazole (6.0 g, 89

mmol) and TBS-Cl (7.4 g, 48.8 mmol) were then added. The resulting solution was stirred at rt for 12 h, quenched with H₂O, extracted with ethyl acetate (3 x 300 mL), dried (Mg₂SO₄), filtered, and concentrated under vacuum. Column chromatography (20:1 hexane:ether) gave the TBS ether (10.5 g, 94%) as a clear liquid.

(2E,6E)-tert-butyl-(7-iodo-3-methyl-octa-2,6-dienyloxy)-dimethylsilane (12). The above alkyne (50 mg, 0.19 mmol) was dissolved in freshly distilled benzene (4 mL). Bis(cyclopentadienyl)zirconium chloride hydride (153 mg, 0.59 mmol) was then added in one portion, and the resulting solution was heated to exactly 40 °C for 12 h in the dark. The reaction was then cooled to rt, and iodine (120 mg, 0.48 mmol) in benzene (5 mL) was added until a dark purple color persisted. The reaction was then stirred for an additional 5 min, diluted with pentane (20 mL), and filtered through celite. The reaction was quenched with 10% sodium thiosulfate, extracted with ethyl acetate (3 x 50 mL), dried (Mg₂SO₄), filtered, and concentrated under vacuum. Immediate column chromatography (hexane, then 40:1 hexane:ethyl acetate) gave **12** (47 mg, 65%) as a clear liquid.

(2E,6E)-7-iodo-3-methylocta-2,6-dien-1-ol. Silyl ether **12** (0.5 g, 1.3 mmol) was dissolved in THF (13 mL) at rt. TBAF (1 M in THF, 2.6 mmol) was then added and the solution was stirred for 30 min at rt. The reaction was quenched with H₂O, extracted with ethyl acetate (3 x 50 mL), dried (Mg₂SO₄), filtered, and concentrated under vacuum. Column chromatography (20:1 hexane:ether) gave the free alcohol (318 mg, 92%) as a clear liquid.

(2*S*,3*R*,6*E*)-[3-(4-iodo-pent-3-enyl)-3-methyloxiranyl]-methanol. A solution of CH₂Cl₂ (4 mL) was cooled to -20 °C. Molecular sieves (4A, 60 mg) were then added. Freshly distilled isopropyl D-tartrate (37 □L, 0.18 mmol) and freshly distilled titanium isopropoxide (44 □L, 0.15 mmol) were then added sequentially, followed by the dropwise addition of *tert*-butylhydroperoxide (6.0 M in decane, 4.5 mmol). The resulting mixture was stirred for 30 min at -20 °C. A solution of the above allylic alcohol (400 mg, 1.5 mmol) in CH₂Cl₂ (3 mL) was then added dropwise to the above solution at a rate slow enough to maintain the temperature below -15 °C. Upon completion of the addition, the resulting mixture was stirred at -20 °C for 2 h. Citric acid monohydrate (30 mg, 0.15 mmol) was then added in 2 mL of a 1:1 acetone:ether mixture. The reaction was then allowed to warm to rt, stirred for 30 min, filtered through celite, and concentrated. Column chromatography on neutral silica (9:1 hexane:ethyl acetate) gave the epoxide (342 mg, 81%, 85%ee) as a clear liquid.

(2*S*,3*R*,6*E*)-3-(4-iodopent-3-enyl)-3-methyl-oxirane-2-carbaldehyde (13). A 0 °C solution of the above alcohol (20 mg, 0.07 mmol) in CH₂Cl₂ (0.8 mL) and DMSO (1.0 mL) was stirred for 5 min. Triethylamine (25 μ L, 0.18 mmol) was added, followed by the addition of sulfur trioxide pyridine complex (25 mg, 0.18 mmol). The resulting solution was stirred at 0 °C for 1 h. The reaction mixture was then quenched with H₂O, extracted with ethyl acetate (3 x 50 mL), dried (Mg₂SO₄), filtered, and concentrated under vacuum. Column chromatography on neutral silica (20:1 hexane:ethyl acetate) gave **13** (16 mg, 82%) as a clear liquid.

Addition Product. A solution of vinyl bromide **9** (50 mg, 0.095 mmol) in ether (2 mL) was cooled to -78 °C. *t*-Butyl lithium (1.5 M in pentane, 0.195 mmol) was added dropwise and the resulting solution was stirred at -78 °C for 30 min. TMEDA (30 μ L, 0.195 mmol) was then added, and the resulting solution was stirred for 5 min. A -78 °C solution of aldehyde **13** (40 mg, 0.143 mmol) in ether (1 mL) was then added, and the resulting solution was stirred for 5 min at -78 °C. The reaction was quenched with H₂O, extracted with ethyl acetate (3 x 50 mL), dried (Mg₂SO₄), filtered, and concentrated under vacuum. Column chromatography (9:1 hexane:ethyl acetate) gave the alcohol (35 mg, 51%) as a clear liquid.

Ketone (14). A solution of the above alcohol (30 mg, 0.03 mmol) in CH_2Cl_2 (5 mL) at rt was stirred for 5 min. Sodium bicarbonate (34 mg, 0.411 mmol) was then added, followed by the addition of Dess-Martin periodinane (36 mg, 0.081 mmol). The resulting solution was stirred at rt for 1 h, quenched with 10% $\text{Na}_2\text{S}_2\text{O}_3$ and stirred for 30 min. The reaction was diluted with H_2O , extracted with ethyl acetate (3 x 50 mL), dried (Mg_2SO_4), filtered, and concentrated under vacuum. Column chromatography (9:1 hexane:ethyl acetate) gave **14** (20 mg, 90%) as a clear liquid.

Oxadecalin (15). A solution of ketone **14** (50 mg, 0.068 mmol) in THF (4 mL) was cooled to 0 °C. TBAF (1.0 M in THF, 0.68 mmol) was added dropwise and the resulting solution was stirred for 30 min at 0 °C. The reaction mixture was then quenched with H_2O , extracted with ethyl acetate (3 x 10 mL), dried (Mg_2SO_4), filtered, and concentrated under vacuum. The crude alcohol was then diluted with a 1% HCl solution in *tert*-amyl alcohol (4 mL). The resulting solution was stirred at rt for 2 h, quenched with sodium bicarbonate, extracted with ethyl acetate (3 x 50 mL), dried (Mg_2SO_4), filtered, and concentrated under vacuum. Column chromatography (2:1 hexane:ethyl acetate) gave **15** (25 mg, 60%) as a clear liquid.

TES ether. A solution of alcohol **15** (80 mg, 0.13 mmol) in DMF (2 mL) was stirred at rt for 5 min. Imidazole (100 mg, 0.7 mmol) and TES-Cl (0.2 mL, 0.39 mmol) were then added. The resulting solution was stirred at rt for 2 h, quenched with H_2O , extracted with ethyl acetate (3 x 50 mL), dried (Mg_2SO_4), filtered, and concentrated under vacuum. Column chromatography (9:1 hexane:ethyl acetate) gave the TES ether (78 mg, 83%) as a clear liquid.

Tricyclic core. A solution of the above oxadecalin (33 mg, 0.045 mmol) in CH_2Cl_2 (2 mL) and H_2O (0.1 mL) was stirred at rt for 5 min. DDQ (13 mg, 0.054 mmol) was then added, and the resulting solution was stirred for 30 min. The reaction mixture was then filtered through a silica plug, washed with sodium bicarbonate, extracted with ether (3 x 10 mL), dried (Mg_2SO_4), filtered, and concentrated under vacuum. Immediate column chromatography (9:1 hexane:ethyl acetate) gave the tricyclic core (22 mg, 87%) as a clear liquid.

TMS ether (16). The above tricyclic core (20 mg, 0.034 mmol) in CH_2Cl_2 was cooled to $-78\text{ }^\circ\text{C}$. Pyridine (13 μl , 0.17 mmol) and trimethylsilyl trifluoromethanesulfonate (12 μl , 0.068 mmol) were then added, and the reaction was stirred for 10 min at $-78\text{ }^\circ\text{C}$. The reaction was quenched with sodium bicarbonate, extracted with ether (3 x 10 mL), dried (Mg_2SO_4), filtered, and concentrated under vacuum. Column chromatography (20:1 hexane:ethyl acetate) gave **16** (14 mg, 81%) as a clear liquid. ^1H NMR (400 MHz, CD_3OD) δ 6.13-6.08 (m, 1H), 5.69 (dd, 1H, $J = 17.4, 10.7$ Hz), 5.15 (dd, 1H, $J = 10.7, 1.2$ Hz), 5.01 (dd, 1H, $J = 17.4, 0.83$ Hz), 4.56 (dd, 1H, $J = 13.6, 2.3$ Hz), 4.27 (dd, 1H, $J = 13.6, 0.83$ Hz), 4.16-4.12 (m, 1H), 3.31 (s, 1H), 2.31-2.30 (m, 3H), 2.15-1.98 (m, 2H), 1.82-1.70 (m, 3H), 1.55-1.50 (m, 2H), 1.22 (s, 3H), 1.03 (s, 3H), 0.96 (t, 9H, $J = 7.9$ Hz), 0.85 (d, 3H, $J = 6.5$ Hz), 0.74-0.57 (m, 6H), 0.07 (s, 9H). ^{13}C NMR (126 MHz, CD_3OD) δ 145.7, 144.7, 142.7, 133.5, 114.6, 111.0, 93.0, 80.7, 79.6, 72.8, 62.6, 41.5, 40.5, 35.7, 33.8, 27.5, 25.1, 17.1, 16.4, 15.0, 7.2, 5.9, 1.3; $[\alpha]_D^{28} = -12.2$ ($c = 0.125$, CHCl_3); ESI m/z : 669 ($\text{M} + \text{Na}$).

Tetracycle. Alkene **16** (10 mg, 0.015 mmol) was placed in freshly distilled and degassed THF (1 mL). 9-BBN (0.5 M in THF, 0.3 mmol) was added dropwise, and the resulting mixture was heated to $40\text{ }^\circ\text{C}$ for 2 h. The reaction was then cooled to rt, followed by the addition of H_2O (0.1

mL), vigorous stirring for 5 min, and then dilution with THF (4 mL). The resulting alkyl borane solution was then placed in a syringe and added over 1 h via syringe pump to a solution of thallium carbonate (33 mg, 0.075 mmol), triphenylarsine (9 mg, 0.030 mmol) and [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II) (12 mg, 0.015 mmol) in 10 mL of a THF:DMF:H₂O mixture (6:3:1) at 40 °C. Upon completion of the addition, the reaction was cooled to rt, and stirred for an additional 12 h. The reaction was then filtered through celite with 4:1 hexane:ethyl acetate, diluted with H₂O (30 mL), extracted with ethyl acetate (3 x 50 mL), dried (Mg₂SO₄), filtered through a plug of silica, and concentrated under vacuum. Column chromatography (20:1 hexane:ether) gave the tetracycle (3 mg, 37%) as a clear liquid.

Phomactin A (1). A solution of the above tetracycle (2 mg, 0.0038 mmol) in THF (2 mL) was cooled to 0 °C. TBAF (1.0 M in THF, 0.02 mmol) was added dropwise and the resulting solution was stirred for 30 min at 0 °C. The reaction mixture was then quenched with H₂O, extracted with ethyl acetate (3 x 10 mL), dried (Mg₂SO₄), filtered, and concentrated under vacuum. Column chromatography (9:1 hexane:ether) gave phomactin A (**1**) (1 mg, 78%) as a clear liquid. ¹H NMR (500 MHz, CD₃OD) δ 5.37 (d, 1H, *J* = 11.7 Hz), 4.64 (dd, 1H, *J* = 12.9, 1.2 Hz), 4.47 (d, 1H, *J* = 12.9 Hz), 4.07 (broad s, 1H), 3.57 (s, 1H), 2.81-2.73 (m, 1H), 2.46-2.37 (m, 2H), 1.96-1.88 (m, 2H), 1.79-1.67 (m, 3H), 1.65 (s, 3H), 1.67-1.57 (m, 2H), 1.51 (dt, 1H, *J* = 15.3, 3.9 Hz), 1.22 (s, 3H), 0.92 (d, 3H, *J* = 7.1 Hz), 0.91 (s, 3H); ¹³C NMR (126 MHz, CD₃OD) δ 144.6, 131.3, 131.3, 128.7, 109.9, 81.0, 74.6, 71.8, 62.5, 38.5, 38.3, 37.6, 34.5, 34.1, 27.8, 25.8, 21.8, 19.5, 16.4, 14.9; [α]_D²⁸ = + 81.3 (*c* = 0.20, CHCl₃); ESI *m/z*: 357 (M + Na), 373 (M + K).

UCB VKR-3008 H1 Standard Parameters

Pulse Sequence: s2pul1

File: pjm.9.012.e.01h.fid (Varian Data)

Date: Mar 26 2002

Acquisition Parameters:

Nucleus: H1 at 299.955 MHz

Solvent: CDCl3

tof 600.0

sw 4000.0 Hz (13.335 ppm)

pw 11.25 usec

d1 0.100 sec

np 24000

ac 3.000 sec

ba/ss 4/0

nt/ct 32/8

Processing Parameters:

lb 0.15

fm 65536

lp/rp -33.7/-44.2

ppm/cm 0.41

4

UCB Varian Inova-500
Standard Proton Parameters
NMRAC 4N Probe

Pulse Sequence: s2pul

File: pjm.9.122.e.01h.fid (Varian Data)
Date: Jul 22 2002

Acquisition Parameters:

Nucleus: H1 at 500.370 MHz
Solvent: CDCl3
tof 273.7
sw 6505.1 Hz (13.001 ppm)
pw 2.10 usec
d1 0.100 sec
np 39030
ac 3.000 sec
bs/ss 4/0
nt/ct 32/12

Processing Parameters:

lb 0.15
fm 65536
lp/rp 2.9/-93.4
ppm/cm 0.41

UCB VXR-300S H1 Standard Parameters

Pulse Sequence: szpul

File: pjm.8.024.a.01H.fid (Varian Data)

Date: Nov 26 2001

Acquisition Parameters:

Nucleus: H1 at 299.955 MHz

Solvent: CDCl3

tof 600.0

sw 4000.0 Hz (13.335 ppm)

pw 11.25 usec

d1 0.100 sec

np 24000

ac 3.000 sec

bs/ss 4/0

nt/ct 32/16

Processing Parameters:

lb 0.15

fn 65536

lp/rp -26.8/-32.0

ppm/cm 0.41

11 -> 12

Pulse Sequence: s2puls

Acquisition Parameters:

```

Nucleus: 1H at 500.370 MHz
Solvent: CDCl3
temp: 273.7
sw 6505.1 Hz (13.001 ppm)
pw 2.10 usec
d1 0.100 sec
np 39030
ac 3.000 sec
bs/ss 4/0
nt/ct 32/16

```

Processing Parameters:

lb	0.15
fn	65536
lp/rp	-7.3/-13.6
ppm/cm	0.41

11 --> 12

UCB Varian Inova-500
Standard Proton Parameters
MULORAC 4M Probe

Pulse Sequence: s2pul

File: pjm.10.005.c.01h.fid (Varian Data)
Date: Sep 13 2002

Acquisition Parameters:

Nucleus: H1 at 500.373 MHz
Solvent: Acetone
f0 273.7
sw 6505.1 Hz (13.001 ppm)
pw 2.10 usec
d1 0.100 sec
np 39030
ac 3.000 sec
bs/ss 4/0
ns/ct 32/20

Processing Parameters:

lb 0.15
fm 65536
lp/zp -0.9/54.4
ppm/cm 0.41

UCB Varian Inova-500
Standard Proton Parameters
NMRAC 4N Probe

Pulse Sequence: szpul

File: pjm.10.005.a.01h.fid (Varian Data)
Date: Sep 13 2002

Acquisition Parameters:

Nucleus: H1 at 500.370 MHz
Solvent: CDCl3
tof 273.7
sw 6505.1 Hz (13.001 ppm)
pw 2.10 usec
d1 0.100 sec
np 39030
ac 3.000 sec
ba/ss 4/0
ne/ct 128/24

Processing Parameters:

lb 0.15
fn 65536
lp/rp 3.7/-12.2
ppm/cm 0.41

UCB Varian Inova-500
Standard Proton Parameters
NALORAC 4N Probe

Pulse Sequence: s2puls

File: pjm.10.007.a.01H.fld (Varian Data)
Date: Sep 15 2002

Acquisition Parameters:

```

Nucleus: H1 at 500.370 MHz
Solvent: CDCl3
Temp: 273.7
F1: 6505.1 Hz (13.001 ppm)
P1: 2.10 usec
d1: 0.100 sec
NP: 39030
ac: 3.000 sec
bs/ss: 4/0
nt/ct: 32/12

```

Processing Parameters:

lb 0.15
fn 65536
lp/yp 1.1/-7.5
ppm/cm 0.41

UCB Varian Inova-500
Standard Proton Parameters
MILORAC 4N Probe

Pulse Sequence: zgpg30

File: pjm.10.009.a.01H.fid (Varian Data)
Date: Sep 16 2002

Acquisition Parameters:

Nucleus: H1 at 500.370 MHz
Solvent: CDCl3
tof 273.7
sw 6505.1 Hz (13.001 ppm)
pw 2.10 usec
dl 0.100 sec
mp 39030
ac 3.000 sec
ba/ss 4/0
re/ct 1000/116

Processing Parameters:

lb 0.15
fn 65536
lp/rp 10.7/-15.9
ppm/cm 0.41

UCB Varian Inova-500
Standard Proton Parameters
NALORAC 4N Probe

Pulse Sequence: s2pul1

File: pjm.10.054.a.01h.fid (Varian Data)
Date: Nov 19 2002

Acquisition Parameters:

Nucleus: H1 at 500.370 MHz
Solvent: CDCl3
tof 273.7
sw 6505.1 Hz (13.001 ppm)
pw 2.10 usec
d1 0.100 sec
rp 39030
ac 3.000 sec
bs/ss 4/0
nt/ct 32/12

Processing Parameters:

lb 0.15
fm 65536
lp/rp 5.9/-14.8
ppm/cm 0.41

STANDARD 1H OBSERVE

Pulse Sequence: s2pul1

File: pjm.10.057.a.01h.fid (Varian Data)

Date: Dec 5 2002

Acquisition Parameters:

Nucleus: H1 at 400.158 MHz
 Solvent: CD3OD
 tof 0.0
 sw 6000.6 Hz (14.996 ppm)
 pw 2.39 usec
 d1 0.500 sec
 np 42004
 at 3.500 sec
 bs/ss 4/0
 nt/ct 1000/39

Processing Parameters:

lb 0.20
 fn 131072
 lp/rp 4.7/162.3
 ppm/cm 0.41

Pulse Sequence: s2pul

File: **pjm.10.058.a.01H.fid** (Varian Data)
Date: **Nov 22 2002**

Acquisition Parameters:

```

Inclusion: H1 at 400.157 MHz
Solvent: C6D6
tOff      0.0
sw         6000.6 Hz (14.996 ppm)
pw         4.73 usec
d1         0.500 sec
np         36004
ap         3.000 sec
ds/ss      4/0
nt/ct     32/8

```

Processing Parameters:

lb 0.20
fn 131072
lp/rd 1.4/-168.5
ppm/cm 0.41

16 → 1

UCB Varian Inova-500
Standard Proton Parameters
MILORAC 4M Probe

Pulse Sequence: szpul

File: pjm.10.059.a.01h.f1d (Varian Data)
Date: Nov 22 2002

Acquisition Parameters:

Nucleus: H1 at 500.372 MHz
Solvent: CD3OD
tof 273.7
sw 6505.1 Hz (13.001 ppm)
pw 2.10 usec
d1 0.100 sec
np 39030
ac 3.000 sec
ba/ss 4/0
nt/ct 1000/128

Processing Parameters:

lb 0.15
fn 65536
lp/rp 5.9/-88.2
ppm/cm 0.41