Supporting Information

A New Synthetic Route to Phomoidride B and Its Derivatives

Experimental Section

Technical notes

Nuclear magnetic resonance (^{1}H NMR (400 MHz), ^{13}C NMR (100 MHz)) spectra were determined on a JEOL-LA400 instrument. Chemical shifts for ^{1}H NMR are reported in parts per million downfields from tetramethylsilane (δ) as the internal standard and coupling constants are in hertz (Hz). The following abbreviations are used for spin multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Chemical shifts for ^{13}C NMR were reported in ppm relative to the center line of a triplet at 77.0 ppm for deuteriochloroform.

Infrared spectra (IR) were recorded on a JASCO FT/IR-410.

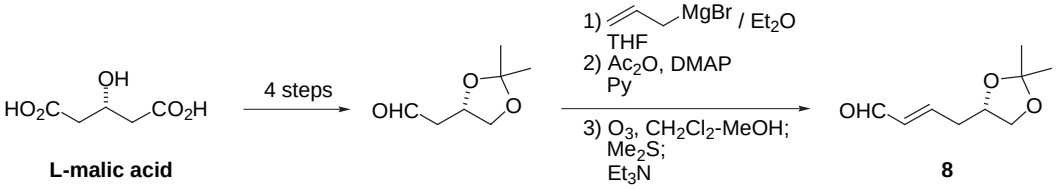
Mass spectral data were obtained on a JEOL JMS-Gcmate MS-DIP20.

Analytical thin layer chromatography (TLC) was performed on Merck precoated analytical plates, 0.25 mm thick, silica gel 60 F_{254}. Preparative TLC separations were performed on Merck precoated analytical plates, 0.25 mm or 0.50 mm thick, silica gel 60 F_{254}. Compounds were eluted from the adsorbent with 10% methanol in chloroform or with ethyl acetate.

Flash column chromatography separations were performed on KANTO CHEMICAL Silica Gel 60 (40-100 mesh), unless otherwise noted.

All non-aqueous reactions were carried out in oven-dried glass apparatuses under a slightly positive pressure of argon. Toluene, dichloromethane, DMSO, Me_2S, chlorotrimethylsilane and HMPA were distilled from calcium hydride. All other solvents were used after dried over molecular sieves 3A or 4A. All other reagents were commercially available and used without further purification.

Aldehyde 8



L-malic acid **8**

L-malic acid was converted to (3*S*)-3,4-*O*-isopropylidene-3,4-dihydroxybutanal[1] in 4 steps.

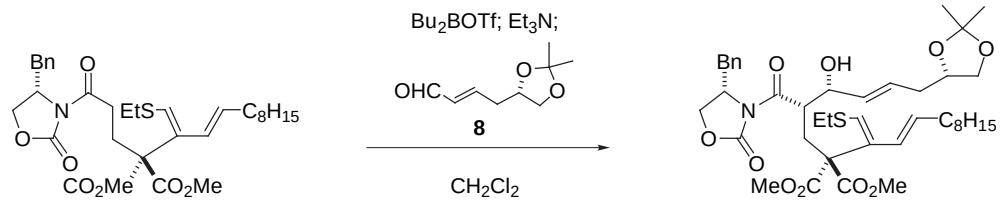
To a solution of the foregoing aldehyde (29 g, 201 mmol) in THF (200 mL) was added allyl magnesiumbromide (402 mmol, 1.0 M in Et_2O) at 0 °C. After stirring for 1 hour at 0 °C, the reaction was quenched by saturated aqueous NH_4Cl under ice-cooling and the mixture was filtered through Celite. The filtrate was extracted with ethyl acetate and the combined organic layer was washed with brine, then dried over $MgSO_4$. The solvent was removed under reduced pressure and the resulting crude product was used in the next reaction without purification.

To a solution of the foregoing crude product in pyridine (40 mL) were added Ac_2O (16 mL, 251 mmol) and DMAP (200 mg, 1.6 mmol) at 0 °C. After stirring for 1 hour at room temperature, 3 N HCl was added and the mixture was extracted with ethyl acetate. The combined organic layer was washed with saturated aqueous $NaHCO_3$ and brine, then dried over $MgSO_4$. The solvent was removed under reduced pressure and the resulting crude

product was used in the next reaction without purification.

To a solution of the foregoing crude product in CH_2Cl_2 (250 mL)-MeOH (250 mL) was added O_3 at –78 °C. After stirring for 2.5 hours at –78 °C, Me_2S (52 mL, 708 mmol) was added. The mixture was stirred for 30 min at 0 °C, and Et_3N (59 mL, 426 mmol) was added. After stirring for 1 hour at 0 °C, water was added and extracted with CH_2Cl_2. The combined organic layer was washed with brine, then dried over $MgSO_4$. The solvent was removed under reduced pressure and the resulting residue was purified by silica gel chromatography (ethyl acetate/hexane = 3/7) to afford optically active aldehyde **8** (14 g, 82 mmol, 41%, 3 steps): ^{13}C NMR ($CDCl_3$) δ 192.80, 153.21, 123.12, 108.52, 74.01, 68.69, 36.46, 26.78, 25.45; ^{1}H NMR ($CDCl_3$) δ 9.54 (1H, d, *J* = 7.8 Hz), 6.83-6.90 (1H, m), 5.20 (1H, td, *J* = 5.2, 15.5 Hz), 4.28-4.31 (1H, m), 4.12 (1H, dd, *J* = 8.2, 6.3 Hz), 3.62 (1H, dd, *J* = 8.2, 5.9 Hz), 2.59-2.64 (2H, m), 1.44 (3H, s), 1.37 (3H, s); IR (film, cm^{-1}) 2987, 2942, 1700, 1654, 1373, 1217, 1156, 1063, 982, 855; $[\alpha]_D^{25}$–8.53° (c = 0.85, $CHCl_3$); Anal. Calcd for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.79; H, 8.25.

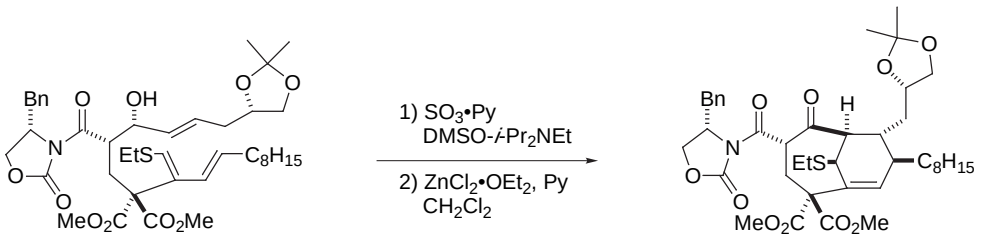
Aldol Adduct 9



7 **9**

To a solution of **7** (0.86 g, 1.5 mmol) in CH_2Cl_2 (7.4 mL) at –78 °C was added Bu_2BOTf (0.70 mL, 2.1 mmol), which was fleshly prepared from tributylborane and trifluromethanesulfonic acid. The mixture was stirred at –78 °C for 1 hour, then Et_3N (0.41 mL, 3.0 mmol) was added. After stirring at –78 °C for 30 min and further stirring at 0 °C for 30 min, a solution of the aldehyde **8** (0.27 g, 1.6 mmol) in CH_2Cl_2 (3.0 mL) was added dropwise. After stirring at 0 °C for 1 hour, water was added and the mixture was extracted with ethyl acetate. The combined organic layer was washed with brine, then dried over $MgSO_4$. The solvent was removed under reduced pressure and the resulting residue was purified by silica gel chromatography (ethyl acetate/hexane = 2/3) to afford the adduct **9** (0.79 g, 1.0 mmol, 71%): ^{13}C NMR ($CDCl_3$) δ173.90, 170.63, 170.24, 154.09, 136.32, 134.95, 132.66, 131.50, 131.31, 129.69, 129.47, 128.91, 128.71, 127.09, 125.90, 124.67, 108.92, 75.47, 75.11, 68.91, 65.89, 61.57, 56.23, 52.99, 52.89, 44.94, 37.52, 36.48, 32.73, 32.51, 32.12, 29.45, 29.38, 29.14, 28.76, 26.88, 25.66, 17.92, 15.19; ^{1}H NMR ($CDCl_3$) δ 7.23–7.26 (5H, m), 6.26 (1H, s), 5.81 (1H, d, *J* = 15.1 Hz), 5.56–5.76 (3H, m), 5.38–5.42 (2H, m), 4.60–4.69 (1H, m), 4.49 (1H, br t, *J* = 6.4 Hz), 4.27 (1H, br t, *J* = 5.6 Hz), 4.07–4.16 (1H, m), 4.03 (2H, dd, *J* = 8.1, 5.9 Hz), 3.75 (3H, s), 3.72 (3H, s), 3.59 (2H, m), 2.85 (1H, dd, *J* = 15.1, 8.0 Hz), 2.79 (1H, br d, *J* = 1.7 Hz, OH), 2.70 (2H, q, *J* = 7.4 Hz), 2.63–2.72 (2H, m), 2.42–2.48 (1H, m), 2.34 (1H, d, *J* = 14.3 Hz), 2.22–2.30 (1H, m), 2.05 (2H, br q, *J* = 6.9 Hz), 1.92–2.00 (2H, m), 1.62–1.65 (3H, m), 1.22–1.42 (6H, m), 1.40 (3H, s), 1.33 (3H, s), 1.29 (3H, t, *J* = 7.4 Hz); IR (film, cm^{-1}) 3481, 2989, 2927, 2935, 2360, 2339, 2329, 1780, 1734, 1436, 1387, 1212, 1065, 968; $[\alpha]_D^{25}$+2.87° (c = 1.17, $CHCl_3$); Anal. Calcd for $C_{41}H_{57}NO_{10}S$: C, 65.14; H, 7.60; N, 1.85. Found: C, 65.23; H, 7.52; N, 1.76.

Diels-Alder Product 4

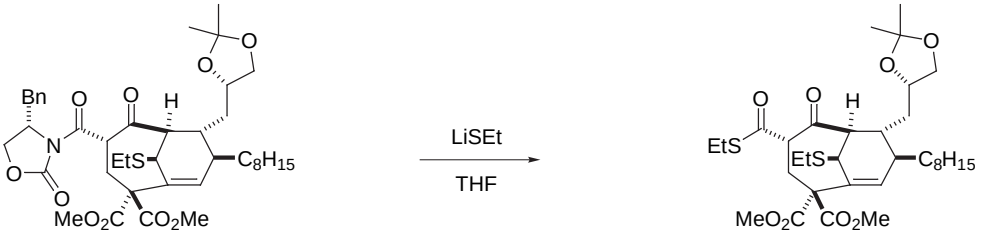


9 **4**

To a solution of **9** (21 g, 28 mmol) in DMSO (150 mL) and *i*-Pr_2NEt (150 mL) was added SO_3·Py (20 g, 128 mmol) at room temperature. After stirring for 2 hours, saturated aqueous $NaHCO_3$ was added and the mixture was extracted with ethyl acetate. The combined organic layer was washed with brine, then dried over $MgSO_4$. The solvent was removed under reduced pressure and the resulting residue was purified by silica gel chromatography (ethyl acetate/hexane = 2/3) to afford the enone (15 g, 20 mmol, 73%): ^{13}C NMR ($CDCl_3$) δ 194.77, 169.97, 169.81, 168.78, 153.48, 143.59, 135.85, 134.08, 132.25, 131.46, 130.08, 129.78, 129.37, 128.93, 127.17, 127.02, 124.65, 109.19, 74.24, 68.89, 66.17, 61.09, 55.59, 53.90, 53.01, 52.94, 37.89, 36.77, 32.76, 32.47, 30.91, 29.43, 29.41, 29.18, 28.76, 26.86, 25.58, 17.90, 15.12; ^1H NMR ($CDCl_3$) δ 7.24–7.36 (5H, m), 6.88–7.00 (1H, m), 6.62 (1H, dt, *J* = 15.6, 1.5 Hz), 6.32 (1H, d, *J* = 0.8 Hz), 5.90 (1H, dd, *J* = 15.1, 0.8 Hz), 5.72 (1H, dt, *J* = 15.1. 6.8 Hz), 5.37–5.43 (2H, m), 5.22 (1H, d, J = 8.7 Hz), 4.68–4.75 (1H, m), 4.24 (1H, quintet, *J* = 6.5 Hz), 4.05–4.16 (3H, m), 3.76 (3H, s), 3.74 (3H, s), 3.60 (1H, dd, *J* = 8.0, 6.5 Hz), 3.49 (1H, dd, *J* = 13.4, 3.2 Hz), 3.18 (1H, dd, *J* = 15.1, 8.7 Hz), 2.71 (2H, q, *J* = 7.4 Hz), 2.56–2.68 (3H, m), 2.43–2.51 (1H, m), 2.05 (2H, br q, *J* = 6.7 Hz), 1.91–1.99 (2H, m), 1.62–1.65 (3H, m), 1.24-1.43 (6H, m), 1.42 (3H, s), 1.35 (3H, s), 1.30 (3H, t, *J* = 7.4 Hz); IR (film, cm^{-1}) 2984, 2928, 2855, 2738, 1732, 1698, 1693, 1633, 1435, 1454, 1370, 1352, 1251, 1214, 1063, 968, 762, 703; $[\alpha]_D^{26}$+75.2° (c = 1.44, $CHCl_3$); Anal. Calcd for $C_{41}H_{55}NO_{10}S$: C, 65.32; H, 7.35; N, 1.86. Found: C, 65.69; H, 7.28; N, 1.82.

In a flask was placed $ZnCl_2$ (20 g, 27 mmol). The flask was heated *in vaccuo* until practically all of the salt melted. The flask was cooled and filled with argon. The salt was suspended with CH_2Cl_2 (270 mL). To this suspension was added diethyl ether (11 mL, 107 mmol). After stirring for 2 hours, pyridine (0.43 mL, 5.4 mmol) was added and a solution of the foregoing enone in CH_2Cl_2 (100 mL) was added by cannula. After stirring for 3 hours, saturated aqueous $NaHCO_3$ was added and the mixture was extracted with CH_2Cl_2. The combined organic layer was washed with brine, then dried over $MgSO_4$. The solvent was removed under reduced pressure and the resulting residue was purified by silica gel chromatography (ethyl acetate/hexane = 2/3) to afford **4** (18 g, 24 mmol, 88%): ^{13}C NMR ($CDCl_3$) δ 207.82, 170.25, 170.10, 170.02, 153.49, 137.56, 135.29, 135.00, 131.42, 129.58, 128.97, 127.32, 124.81, 108.79, 73.65, 69.74, 66.20, 65.20, 62.67, 55.23, 55.04, 53.24, 53.02, 44.04, 41.68, 41.31, 37.90, 37.88, 32.50, 32.36, 31.40, 29.54, 29.17, 29.17, 27.69, 26.94, 25.69, 17.94, 14.17; ^1H NMR ($CDCl_3$) δ 7.18–7.37 (5H, m), 5.61 (1H, dd, *J* = 3.9, 1.4 Hz), 5.39–5.44 (2H, m), 4.74–4.81 (1H, m), 4.69 (1H, dd, *J* = 11.2, 1.4 Hz), 4.26 (1H, t, *J* = 8.9 Hz), 4.19–4.23 (1H, m), 4.13 (1H, dd, *J* = 8.9, 3.2 Hz), 3.95 (1H, dd, *J* = 8.0, 5.8 Hz), 3.85 (3H, s), 3.80 (3H, s), 3.43 (1H, t, *J* = 8.0 Hz), 3.40 (1H, dd, *J* = 3.0, 1.4 Hz), 3.22 (1H, dd, *J* = 13.4, 3.2 Hz), 3.03 (1H, d, *J* = 2.7 Hz), 2.98 (1H, dd, *J* = 15.9, 1.4 Hz), 2.83–2.92 (2H, m), 2.61 (2H, qd, *J* = 7.3, 1.0 Hz), 1.91–2.00 (3H, m), 1.57-1.81 (6H, m), 1.20–1.42 (8H, m), 1.39 (3H, s), 1.33 (3H, s), 1.23 (3H, t, *J* = 7.3 Hz); IR (film, cm^{-1}) 2979, 2930, 2856, 1779, 1733, 1709, 1454, 1369, 1225, 1115, 1060, 968, 860; $[\alpha]_D^{26}$+58.9° (c = 0.95, $CHCl_3$); Anal. Calcd for $C_{41}H_{55}NO_{10}S$: C, 65.32; H, 7.35; N, 1.86. Found: C, 65.03; H, 7.44; N, 1.80.

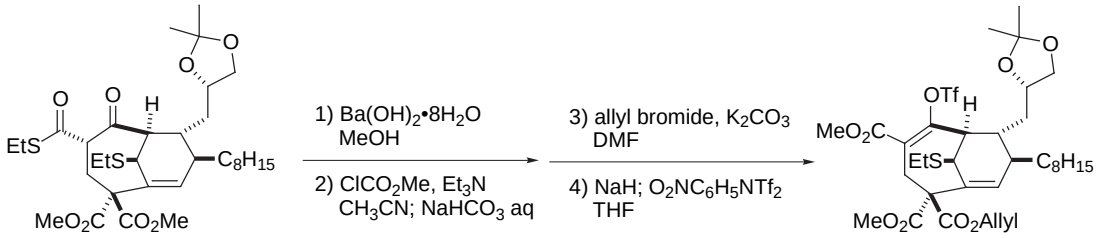
Thiol Ester 10



4 **10**

To a solution of ethanethiol (1.8 mL, 24 mmol) in THF (80 mL) was added 1.5 M *n*-BuLi in hexane (16 mL, 22 mmol) at 0 °C. After stirring for 10 min, a solution of **4** (6.0 g, 8.0 mmol) in THF (30 mL) was added. After stirring at 0 °C for 30 min, water was added and the mixture was extracted with ethyl acetate. The combined organic layer was washed with brine, then dried over $MgSO_4$. The solvent was removed under reduced pressure then the resulting residue was purified by silica gel chromatography (ethyl acetate/hexane = 2/8) to afford **10** (3.8 g, 6.0 mmol, 75%): ^{13}C NMR ($CDCl_3$) δ 206.73, 195.26, 170.15, 169.78, 137.61, 135.03, 131.22, 124.83, 108.99, 73.37, 69.38, 63.94, 62.66, 60.94, 53.27, 52.97, 44.07, 43.70, 41.11, 37.21, 32.38, 32.27, 31.46, 29.41, 29.07, 28.99, 27.49, 26.82, 25.49, 23.75, 17.86, 14.33, 14.04; ^1H NMR ($CDCl_3$) δ 5.56 (1H, d, *J* = 4.2 Hz), 5.41-5.44 (2H, m), 4.25-4.32 (1H, m), 4.02 (1H, dd, *J* = 7.9, 5.9 Hz), 3.83 (3H, s), 3.78 (3H, s), 3.71-3.74 (1H, m), 3.40-3.45 (2H, m), 3.03 (1H, d, *J* = 2.4 Hz), 2.89-3.00 (2H, m), 2.85 (1H, dd, *J* = 15.4, 3.9 Hz), 2.75 (1H, d, *J* = 15.4 Hz), 2.56-2.64 (2H, m), 1.97-2.09 (3H, m), 1.61-1.87 (5H, m), 1.09-1.47 (9H, m), 1.41 (3H, S), 1.34 (3H, S), 1.26 (3H, t, *J* = 7.4 Hz), 1.21 (3H, d, *J* = 6.2 Hz); IR (film, cm^{-1}) 2931, 2856, 1738, 1732, 1703, 1455, 1435, 1379, 1369, 1259, 1219, 1062, 969, 860; $[\alpha]_D^{24}$+18.3° (c = 0.60, $CHCl_3$); Anal. Calcd for $C_{33}H_{50}O_8S$: C, 62.04; H, 7.89. Found: C, 61.89; H, 7.77.

Enol Triflate 14



10 **14**

To a solution of **10** (3.8 g, 5.9 mmol) in MeOH (60 mL) was added $Ba(OH)_2 \cdot 8H_2O$ (17 g, 53 mmol) at room temperature. After stirring for 24 hours, 10% citric acid was added at 0 °C until the pH of the solution was adjusted to *ca*. 3 and the mixture was extracted with ethyl acetate. The combined organic layer was washed with brine three times, then dried over Na_2SO_4. The solvent was removed under reduced pressure and the resulting crude product was used in the next reaction without purification.

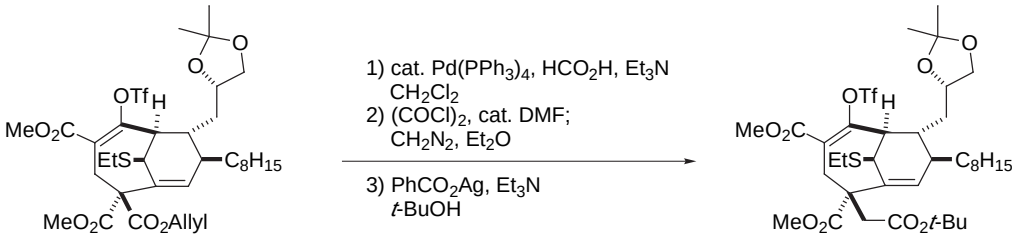
To a solution of the foregoing crude product in CH_3CN (60 mL) were added $ClCO_2Me$ (1.1 mL, 15 mmol) and Et_3N (2.3 mL, 17 mmol) at 0 °C. The ice bath was removed, and the mixture was stirred for 30 min at room temperature, and then aqueous $NaHCO_3$ was added. After stirring for 1 hour at room temperature, 10% citric acid was added and the mixture was extracted with ethyl acetate. The combined organic layer was washed with brine, then dried over Na_2SO_4. The solvent was removed under reduced pressure and the resulting crude product was used in the next reaction without purification.

To a solution of the foregoing crude product in DMF (60 mL) were added allyl

bromide (1.3 mL, 15 mmol) and K_2CO_3 (1.6 g, 12 mmol) at room temperature. After stirring for 10 min, saturated aqueous NH_4Cl was added and the mixture was extracted with ether. The combined organic layer was washed with brine, then dried over $MgSO_4$. The solvent was removed under reduced pressure and the resulting crude product was used in the next reaction without purification.

To a solution of the foregoing crude product in THF (1.0 mL) was added NaH (1.2 g, 60% purity, 30 mmol) at room temperature. After stirring for 1 hour, the triflating reagent ($O_2NC_6H_4NTf_2$) (6.0 g, 15 mmol) was added. After stirring for 30 min at room temperature, water was added and the mixture was extracted with ether. The combined organic layer was washed with brine, then dried over $MgSO_4$. The solvent was removed under reduced pressure and the resulting residue was purified by silica gel chromatography (ethyl acetate/hexane = 1/9) to afford **14** (3.2 g, 4.2 mmol, 71%, 4 steps): ^{13}C NMR ($CDCl_3$) δ 169.60, 168.93, 166.78, 152.48, 137.24, 133.81, 131.26, 130.93, 124.75, 124.61, 119.67, 109.44, 73.16, 69.93, 66.56, 64.30, 58.37, 52.94 52.93, 52.53, 44.70, 44.21, 41.21, 37.99, 33.30, 32.38, 32.35, 29.45, 29.15, 29.09, 27.54, 26.82, 25.47, 17.85, 14.29; ^{1}H NMR ($CDCl_3$) δ 5.87 (1H, ddt, *J* = 17.3, 10.1, 5.8 Hz), 5.40-5.41 (3H, m), 5.32 (1H, dd, *J* = 17.3, 1.5 Hz), 5.26 (1H, dd, *J* = 10.3, 1.5 Hz), 4.65 (2H, d, *J* = 5.8 Hz), 4.27-4.32 (1H, m), 4.12 (1H, dd, *J* = 7.7, 6.2 Hz), 3.83 (1H, d, *J* = 16.3 Hz), 3.80 (3H, s), 3.78 (3H, s), 3.52 (1H, t, *J* = 7.7 Hz), 3.37 (1H, br s), 3.34 (1H, d, *J* = 16.3 Hz), 3.24 (1H, br s), 2.62-2.72 (2H, m), 1.78-2.10 (5H, m), 1.56-1.73 (5H, m), 1.16-1.43 (7H, m), 1.41 (3H, s), 1.34 (3H, s), 1,25 (3H, t, *J* = 7.3 Hz); IR (film, cm^{-1}) 2985, 2930, 2857, 1735, 1422, 1380, 1370, 1247, 1214, 1137, 1063, 850; $[\alpha]_D^{24}$–43.9° (c = 1.09, $CHCl_3$); Anal. Calcd for $C_{35}H_{49}O_{11}S_2F_3$: C, 54.82; H, 6.44. Found: C, 54.57; H, 6.44.

t-Butyl Ester 15



14 **15**

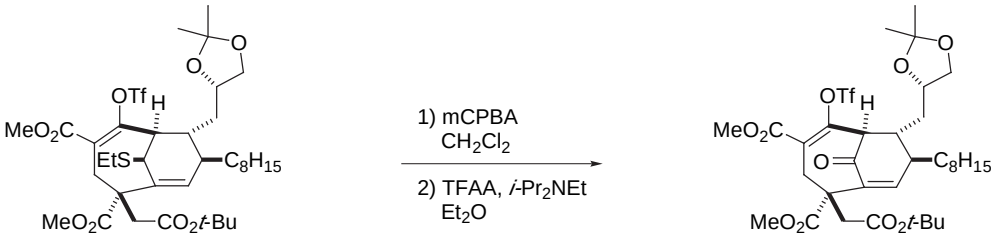
To a solution of **14** (1.0 g, 1.3 mmol) and $Pd(PPh_3)_4$ (0.30 g, 0.26 mmol) in CH_2Cl_2 (13 mL) were added formic acid (0.49 mL, 13 mmol) and Et_3N (2.2 mL, 16 mmol) at room temperature. After stirring for 1 hour, 10% citric acid was added and the mixture was extracted with ethyl acetate. The combined organic layer was washed successively with 10% citric acid and brine, then dried over Na_2SO_4. The solvent was removed under reduced pressure and the resulting crude product was used in the next reaction without purification.

The foregoing crude product was dissolved in CH_2Cl_2 (10 mL). To this solution were added $(COCl)_2$ (0.57 mL, 6.5 mmol) and DMF (10 μL). After stirring for 20 min, the solvent was removed under reduced pressure and the resulting residue was dissolved in ether. This mixture was added to a solution of CH_2N_2 (prepared from Diazald (5.5 g, 26 mmol)) in ether. After stirring for 10 min, aqueous AcOH was added. Then the pH of the solution was adjusted to *ca.* 7 with saturated aqueous $NaHCO_3$ and the mixture was extracted with ether. The combined organic layer was washed with brine, then dried over $MgSO_4$. The solvent was removed under reduced pressure and the resulting residue was purified by neutral silica gel chromatography (ethyl acetate/hexane = 2/8) to afford diazoketone (0.50 g, 0.63 mmol, 64%, 2 steps): ^{13}C NMR ($CDCl_3$) δ 188.60, 171.33, 166.94, 151.79, 138.52, 134.15, 131.34, 125.19, 124.84, 109.49, 73.21, 69.99, 68.63, 58.14, 55.28, 53.17, 53.16, 52.71, 44.75, 44.37,

41.39, 37.88, 33.22, 32.27, 31.36, 29.51, 29.28, 29.07, 27.92, 26.88, 25.52, 17.92, 14.32; ^{1}H NMR ($CDCl_3$) δ 5.65 (1H, s), 5.63 (1H, br s), 5.40-5.43 (2H, m), 4.25-4.28 (1H, m), 4.13 (1H, dd, *J* = 8.0, 6.1 Hz), 3.80 (3H, s), 3.79 (3H, s), 3.73 (1H, d, *J* = 16.1 Hz), 3.46 (1H, t, *J* = 8.0 Hz), 3.43 (1H, br s), 3.34 (1H, d, *J* = 16.1 Hz), 3.22 (1H, br s), 2.58-2.67 (2H, m), 1.75-2.04 (5H, m), 1.57-1.70 (7H, m), 1.23-1.41 (5H, m), 1.40 (3H, s), 1.34 (3H, s), 1.25 (3H, t, *J* = 6.2 Hz); IR (film, cm^{-1}) 2931, 2857, 2111, 1732, 1641, 1422, 1349, 1246, 1215, 1138, 851; $[\alpha]_D^{30}$–32.4° (c = 1.97, $CHCl_3$); Anal. Calcd for $C_{33}H_{45}N_2O_{10}S_2F_3$: C, 52.79; H, 6.04; N, 3.73. Found: C, 52.91; H, 6.01; N, 3.55.

To a solution of the foregoing diazoketone (0.56 g, 0.74 mmol) in *t*-BuOH (5.0 mL) were added silver benzoate (0.35 g, 1.6 mmol) and Et_3N (0.11 mL, 0.74 mmol). After stirring at 50 °C for 15 min, saturated aqueous $NaHCO_3$ was added and the mixture was extracted with ethyl acetate. The combined organic layer was washed with brine, then dried over $MgSO_4$. The solvent was removed under reduced pressure and then the resulting residue was purified by silica gel chromatography (ethyl acetate/hexane = 2/8) to afford **15** (0.50 g, 0.63 mmol, 86%): ^{13}C NMR ($CDCl_3$) δ 173.46, 169.28, 167.19, 152.66, 140.27, 131.57, 131.56, 131.51, 1124.95, 124.15, 109.60, 81.57, 70.20, 58.23, 53.51, 52.71, 52.49, 52.48, 44.95, 44.15, 42.75, 41.15, 38.07, 33.87, 33.14, 32.65, 29.71, 29.39, 29.04, 28.09 (three carbons), 28.01, 27.00, 25.69, 18.07, 14.54; ^{1}H NMR ($CDCl_3$) δ 5.60 (1H, d, *J* = 2.2 Hz), 5.41-5.43 (2H, m), 4.27-4.29 (1H, m), (1H, dd, *J* = 7.9, 5.9 Hz), 3.95 (1H, d, *J* = 16.0 Hz), 3.75 (3H, s), 3.74 (3H, s), 3.51 (1H, t, *J* = 7.9 Hz), 3.36 (1H, br s), 3.19 (1H, br s), 2.98 (1H, d, *J* = 16.6 Hz), 2.69 (1H, d, *J* = 13.2 Hz), 2.54-2.66 (2H, m), 2.43 (1H, d, *J* = 13.2 Hz), 1.97-2.07 (3H, m), 1.76-1.83 (2H. m), 1.58-1.71 (7H, m), 1.20-1.46 (5H, m), 1.42 (9H, s), 1,34 (3H, s), 1.30 (3H, s), 1.24 (3H, t, *J* = 7.3 Hz) ; IR (film, cm^{-1}) 2931, 2857, 1738, 1419, 1369, 1247, 1213, 1154, 984, 849; $[\alpha]_D^{26}$–11.4° (c = 1.80, $CHCl_3$); Anal. Calcd for $C_{37}H_{55}O_{11}S_2F_3$: C, 55.76; H, 6.96. Found: C, 55.55; H, 6.89.

Ketone 16



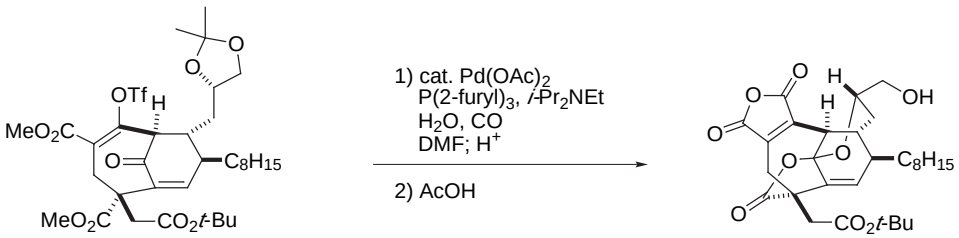
15 **16**

To a solution of **15** (0.49 g, 0.62 mmol) in CH_2Cl_2 (7.0 mL) was added mCPBA (0.15 g, 75% purity, 0.62 mmol) at –20 °C. After stirring for 5 min, saturated aqueous $Na_2S_2O_3$ and $NaHCO_3$ were added and the mixture was extracted with CH_2Cl_2. The combined organic layer was washed with brine, then dried over Na_2SO_4. The solvent was removed under reduced pressure and the resulting crude product was used in the next reaction without purification.

To a solution of the foregoing crude product in ether (12 mL) were added *i*-Pr_2NEt (1.1 mL, 6.2 mmol) and TFAA (0.43 mL, 3.1 mmol) at 0 °C. After stirring for 30 min, saturated aqueous $NaHCO_3$ was added and the mixture was stirred for 1 hour. The mixture was extracted with ethyl acetate and the combined organic layer was washed with brine, then dried over $MgSO_4$. The solvent was removed under reduced pressure and the resulting residue was purified by silica gel chromatography (ethyl acetate/hexane = 3/7) to afford **16** (0.42 g, 0.57 mmol, 92%, 2 steps): ^{13}C NMR ($CDCl_3$) δ 201.39, 170.32, 168.69, 165.50, 152.57, 140.39, 135.82, 131.22, 124.92, 123.93, 109.45, 81.94, 72.51, 69.75, 61.12, 52.91,

52.80, 51.51, 51.50, 40.82, 39.62, 38.36, 38.12, 34.86, 32.54, 32.40, 29.39, 28.98, 27.94 (three carbons), 27.04, 26.75, 25.54. 17.91; ^{1}H NMR ($CDCl_3$) δ 5.86 (1H, d, *J* = 2.4 Hz), 5.40-5.42 (2H, m), 4.09-4.14 (1H, m), 4.06 (1H, dd, *J* = 7.8, 6.1 Hz), 3.79 (3H, s), 3.78 (3H, s), 3.43-3.47 (2H, m), 3.16 (1H, d, *J* = 15.6 Hz), 3.07 (1H, d, *J* = 15.6 Hz), 3.01 (1H, d, *J* = 16.1 Hz), 2.52 (1H, q, *J* = 6.1 Hz), 2.39 (1H, d, *J* = 16.1 Hz), 1.97-1.98 (2H, m), 1.51-1.68 (7H, m), 1.22-1.46 (7H, m), 1.44 (9H, s), 1.38 (3H, s), 1.32 (3H, s); IR (film, cm^{-1}) 2984, 2932, 2858, 1734, 1428, 1214, 1154, 1077, 843; $[\alpha]_D^{23}$–25.3° (c = 1.39, $CHCl_3$); Anal. Calcd for $C_{35}H_{49}O_{12}SF_3$: C, 55.99; H, 6.58. Found: C, 55.80; H, 6.68.

γ-Lactone Acetal 17

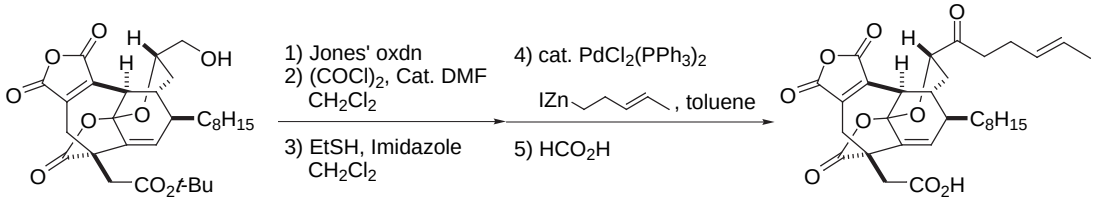


16 **17**

To a solution of **16** (0.12 g, 0.16 mmol) in DMF (2.0 mL) were added $Pd(OAc)_2$, (17 mg, 0.08 mmol), $P(2\text{-furyl})_3$ (92 mg, 0.40 mmol), *i*-Pr_2NEt (0.20 mL, 1.2 mmol) and H_2O (0.22 mL, 12 mmol). After stirring under CO atmosphere (1.0 atm) at 90 °C for 3 hours, 1 N HCl was added and the mixture was extracted with ether. The combined organic layer was washed with brine, then dried over $MgSO_4$. The solvent was removed under reduced pressure and the resulting crude product was used in the next reaction without purification.

The foregoing crude product was dissolved in 80% aqueous acetic acid (2.0 mL). After stirring at 70 °C for 4 hours, toluene was added and the solvent was removed under reduced pressure. The resulting crude product was purified by PTLC (ethyl acetate/hexane = 1/1) to afford **17** (30 mg, 0.054 mmol, 34%, 2 steps): ^{13}C NMR ($CDCl_3$) δ 175.57, 167.83, 164.61, 164.46, 141.79, 140.27, 140.19, 131.11, 129.33, 125.03, 105.38, 82.80, 72.09, 64.59, 47.56, 43.38, 43.12, 40.79, 39.00, 36.09, 35.94, 34.83, 32.37, 29.35, 29.02, 27.89 (three carbons), 26.77, 17.92; ^{1}H NMR ($CDCl_3$) δ 5.66 (1H, d, *J* = 2.0 Hz), 5.32–5.45 (2H, m), 4.29–4.36 (1H, m), 3.79–3.86 (1H, m), 3.55–3.63 (1H, m), 3.58 (1H, br s), 3.16 (1H, d, *J* = 16.7 Hz), 3.03 (1H, dd, *J* = 19.5, 1.2 Hz), 2.74 (1H, d, *J* = 16.7 Hz), 2.67 (1H, dd, *J* = 19.5, 2.2 Hz), 2.28–2.39 (1H, m), 2.32 (1H, dd, *J* = 13.2, 6.8 Hz), 2.24 (1H, br d, *J* = 4.9 Hz), 1.85–1.97 (2H, m), 1.88 (1H, dd, *J* = 13.2, 9.8 Hz), 1.62–1.66 (3H, m), 1.45 (9H, s), 1.15–1.37 (9H, m); IR (film, cm^{-1}) 2928, 2856, 1734, 1368, 1263, 1156, 995, 759, 733; $[\alpha]_D^{27}$+7.20° (c = 0.85, $CHCl_3$); Anal. Calcd for $C_{30}H_{38}O_9$: C, 66.40; H, 7.06. Found: C, 66.62; H, 7.05.

Phomoidride B (1)



17 Phomoidride B (**1**)

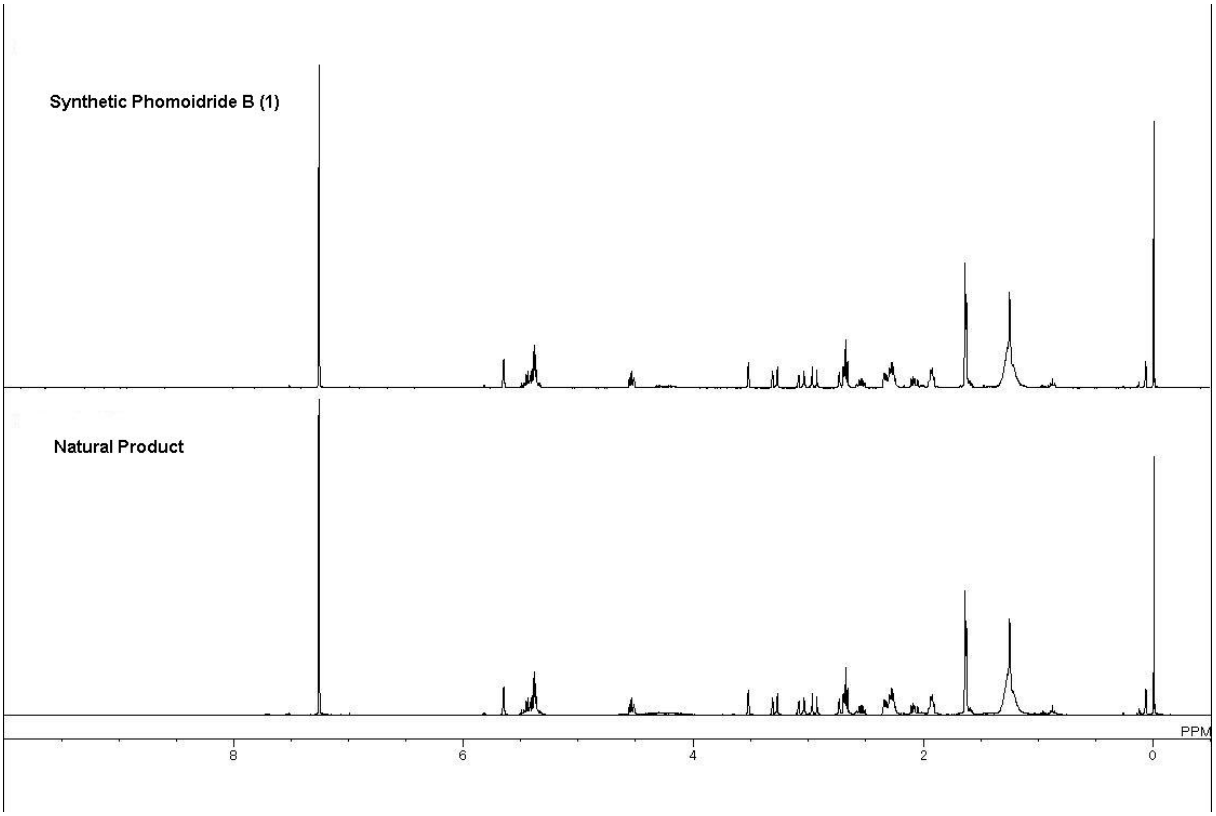
To a solution of **17** (12 mg, 0.022 mmol) in acetone (0.2 mL) was added 0.9 M Jones' reagent (0.24 mL, 0.22 mmol). After stirring for 2 hours, 1 N HCl was added and the mixture was extracted with ethyl acetate. The combined organic layer was washed with brine,

then dried over Na_2SO_4. The solvent was removed under reduced pressure and the resulting crude product was used in the next reaction without purification.

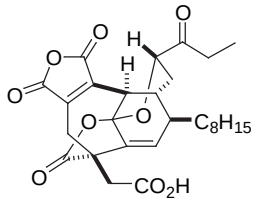
The foregoing crude product was dissolved in CH_2Cl_2 (0.50 mL). To this solution were added $(COCl)_2$ (9.0 μL, 0.11 mmol) and DMF (0.60 μL). After stirring for 20 min, the solvent was removed under reduced pressure and the resulting residue was dissolved in CH_2Cl_2 (0.50 mL). To this mixture were added ethanethiol (32 μL, 0.44 mmol) and imidazole (15 mg, 0.22 mmol). After stirring for 1 hour, 1 N HCl was added and the mixture was extracted with ether. The combined organic layer was washed with brine, then dried over $MgSO_4$. The solvent was removed under reduced pressure and the resulting residue was purified simply by neutral silica gel pad (ethyl acetate/hexane = 5/5) to afford thiol ester **19** (7.8 mg, 0.013 mmol, *ca.* 63%).

To a mixture of the foregoing thiol ester (4.3 mg, 0.0072 mmol) and $PdCl_2(PPh_3)_2$ (2.5 mg, 0.0036 mmol) was added 1.0 M (*E*)-3-pentenylzinc iodide in THF, then THF was removed under reduced pressure and the resulting residue was dissolved in toluene (0.1 mL). After stirring for 3 hours, 1 N HCl was added and the mixture was extracted with ether. The combined organic layer was washed with brine, then dried over $MgSO_4$. The solvent was removed under reduced pressure and the resulting residue was purified by GPC to afford ketone **20** (3.4 mg, 0.0056 mmol, *ca.* 78%).

The foregoing ketone was dissolved in formic acid (0.20 mL). After the mixture was stirred for 1 hour, formic acid was removed under reduced pressure to afford phomoidride B (**1**) quantitatively (3.0 mg, 0.0056 mmol). A part of the product was purified by reverse phase HPLC separation (C18, CH_3CN/0.1% aqueous H_3PO_4 = 65/35) to give pure phomoidride B: ^{13}C NMR ($CDCl_3$) δ 207.60, 175.29, 173.75, 154.37, 164.28, 141.52, 140.31, 139.78, 131.01, 129.27, 129.25, 126.17, 125.02, 104.84, 75.12, 47.28, 43.19 (two carbons), 40.21, 38.26, 37.25, 36.07, 35.42, 35.21, 32.32, 29.27, 28.91, 26.77, 26.02, 17.96, 17.89; ^1H NMR ($CDCl_3$) δ 5.66 (1H, d, *J* = 1.7 Hz), 5.32-5.52 (4H, m), 4.54 (1H, t, *J* = 8.3 Hz), 3.53 (1H, s), 3.29 (1H, d, *J* = 17.8 Hz), 3.06 (1H, d, *J* = 19.5 Hz), 2.95 (1H, d, *J* = 17.8 Hz), 2.71 (1H, dd, *J* = 19.5, 2.0 Hz), 2.68 (1H, t, *J* = 7.2 Hz), 2.55 (1H, dt, *J* = 13.7, 7.1 Hz), 2.34 (1H, br d, *J* = 7.1 Hz), 2.24-2.32 (3H, m), 2.08 (1H, dd, *J* = 13.7, 9.0 Hz), 1.89-1.96 (2H, m), 1.61-1.65 (6H, m), 1.15-1.33 (8H, m); IR (film, cm^{-1}) 3324, 3020, 2927, 2855, 1793, 1767, 1721, 1441, 1412, 1263, 1176, 1135, 1066, 1000, 966, 948, 930, 789, 737; $[\alpha]_D^{27}$–10.0° (c = 0.25, CH_2Cl_2); MS (EI) *m/z* 552 (M^+); HRMS (EI) calcd for $C_{31}H_{36}O_9$ 552.2359, found 552.2362.



Ethylketone Analog 22



Ethylketone analog (**22**)

^{13}C NMR ($CDCl_3$) δ 209.02, 171.12, 164.35, 141.65, 140.18, 139.74, 131.06, 130.27, 129.41, 125.07, 124.10, 104.99, 75.16, 47.28, 43.27, 40.01, 37.06, 36.13, 35.53, 35.38, 32.37, 31.94, 31.76, 29.71, 29.31, 28.94, 26.83, 17.92; ^{1}H NMR ($CDCl_3$) δ 5.66 (1H, d, *J* = 1.7 Hz), 5.37-5.40 (2H, m), 4.56 (1H, t, *J* = 8.2 Hz), 3.53 (1H, s), 3.26 (1H, d, *J* = 17.7 Hz), 3.06 (1H, d, *J* = 19.3 Hz), 2.96 (1H, d, *J* = 17.7 Hz), 2.62-2.71 (3H, m), 2.32-2.35 (1H, m), 2.05-2.11 (4H, m), 1.91-1.98 (2H, m), 1.63-1.68 (6H, m), 1.25-1.33 (6H, m), 1.07 (2H, t, *J* = 8.9 Hz); IR (film, cm^{-1}) 3324, 3020, 2958, 2926, 2850, 1790, 1724, 1266, 1011, 999, 946, 765, 720; $[\alpha]_D^{23}$–15.4° (c = 0.84, $CHCl_3$); MS (FAB) *m/z* 512 $(M)^+$; HRMS (FAB) calcd for $C_{28}H_{32}O_9$ 512.2046, found 512.2051.

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(1) Saito, S.; Hasegawa, T.; Inaba, M.; Nishida, R.; Fujii, T.; Nomizu, S.; Moriwake, T. *Chem. Lett.* **1984**, 1389.