SUPPORTING INFORMATION

Synthesis of Ecteinascidin ET-743 and Phtalascidin Pt-650 from Cyanosafracin B

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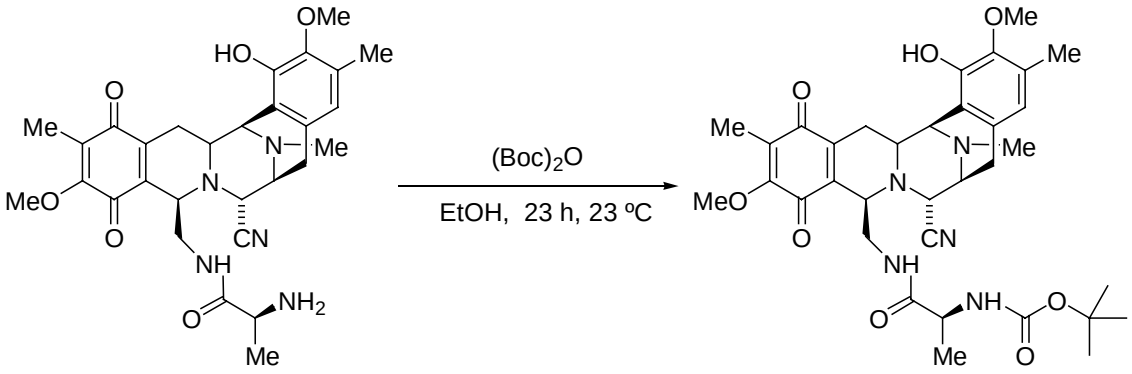
General Methods

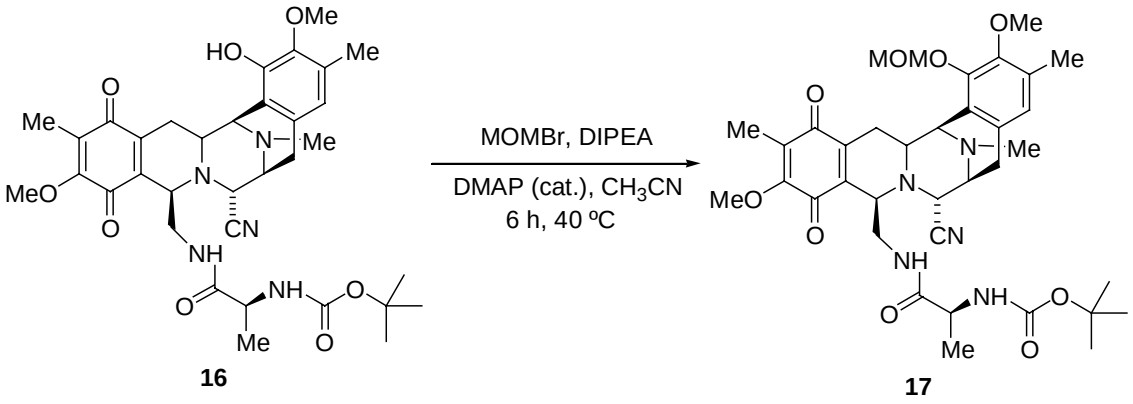
^{1}H and ^{13}C NMR spectra were recorded on a Varian AC300 instrument using $CDCl_3$. The shifts are reported in ppm (δ scale) and all *J* values are in Hz. TLC was performed on SDS precosted 60 F_{254} plates. The spots were visualized with UV light (254 nm). Column chormatography was performed using silica gel 60 (0.040-0.063 mm, SDS). Mass spectra were recorded on a HP Series 1100.



3 **16**

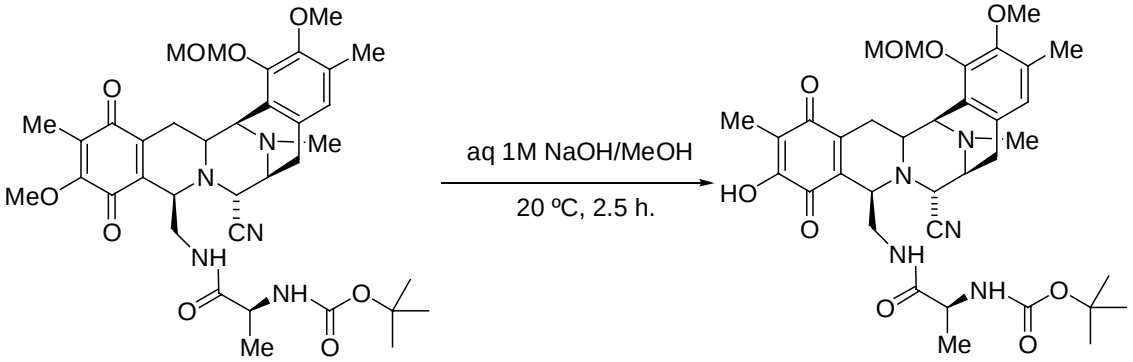
To a solution of **3** (21.53 g, 39.17 mmol) in EtOH (200 mL), $(Boc)_2O$ (7.7 g, 35.25 mmol) was added and the mixture was stirred for 23 h at 23 ºC. Then, the reaction was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2, Hex:EtOAc 6:4) to give **16** (20.6 g, 81%) as a yellow solid. Rf: 0.52 (EtOAc:$CHCl_3$ 5:2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.49 (s, 1H), 6. 32 (bs, 1H), 5.26 (bs, 1H), 4.60 (bs, 1H), 4.14 (d, *J*= 2.4 Hz, 1H), 4.05 (d, *J*= 2.4 Hz, 1H), 3.94 (s, 3H), 3.81 (d, *J*= 4.8 Hz, 1H), 3.7 (s, 3H), 3.34 (br d, *J*= 7.2 Hz, 1H), 3.18-3.00 (m, 5H), 2.44 (d, *J*= 18.3 Hz, 1H), 2.29 (s, 3H), 2.24 (s, 3H), 1.82 (s, 3H), 1.80-1.65 (m, 1H), 1.48 (s, 9H), 0.86 (d, *J*= 5.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 185.5, 180.8, 172.7, 155.9, 154.5, 147.3, 143.3, 141.5, 135.3,

130.4, 129.2, 127.5, 120.2, 117.4, 116.9, 80.2, 60.7, 60.3, 58.5, 55.9, 55.8, 54.9, 54.4, 50.0, 41.6, 40.3, 28.0, 25.3, 24.0, 18.1, 15.6, 8.5. ESI-MS m/z: 650.3 $(M+H)^+$.



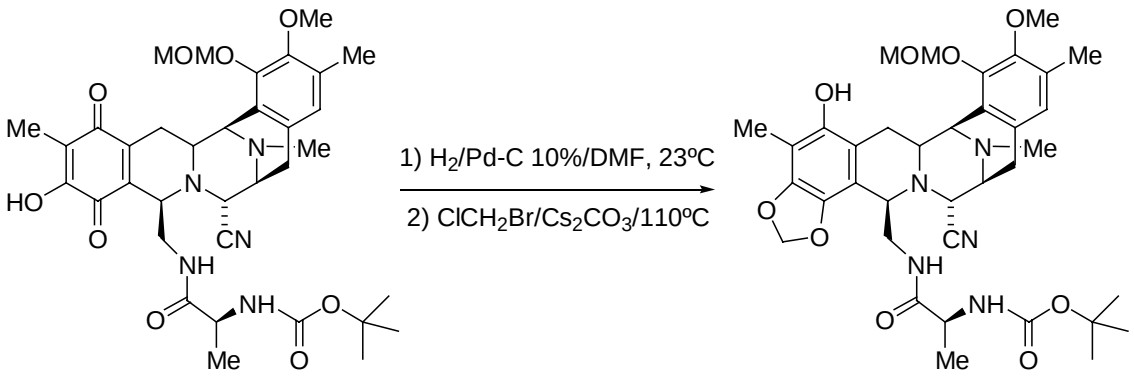
16 **17**

To a stirred solution of **16** (20.6 g, 31.75 mmol) in CH_3CN (159 mL), diisopropylethylamine (82.96 mL, 476.2 mmol), bromomethyl methyl ether (25.9 mL, 317.5 mmol) and dimethylaminopyridine (155 mg, 1.27 mmol) were added at 0 ºC. The mixture was stirred at 40 ºC for 6 h. The reaction was quenched at 0 ºC with HCl 0.1 N (750 mL) (pH= 5), and extracted with CH_2Cl_2 (2 x 400 mL). The organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography (SiO_2, gradient Hex:EtOAc 4:1 to Hex:EtOAc 3:2) to give **17** (17.6 g, 83%) as a yellow solid. Rf: 0.38 (Hex:AcOEt 3:7). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.73 (s, 1H), 5.35 (bs, 1H), 5.13 (s, 2H), 4.50 (bs, 1H), 4.25 (d, *J*= 2.7 Hz, 1H), 4.03 (d, *J*= 2.7 Hz, 1H), 3.97 (s, 3H), 3.84 (bs, 1H), 3.82-3.65 (m, 1H), 3.69 (s, 3H), 3.56 (s, 3H), 3.39-3.37 (m, 1H), 3.20-3.00 (m, 5H), 2.46 (d, *J*= 18 Hz, 1H), 2.33 (s, 3H), 2.23 (s, 3H), 1.85 (s, 3H), 1.73-1.63 (m, 1H), 1.29 (s, 9H), 0.93 (d, *J*= 5.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 185.4, 180.9, 172.4, 155.9, 154.5, 149.0, 148.4, 141.6, 135.1, 131.0, 129.9, 127.6, 124.4, 123.7, 117.3, 99.1, 79.3, 60.7, 59.7, 58.4, 57.5, 56.2, 55.9, 55.0, 54.2, 50.0, 41.5, 39.9, 28.0, 25.2, 24.0, 18.1, 15.6, 8.5. ESI-MS m/z: 694.3 $(M+H)^+$.



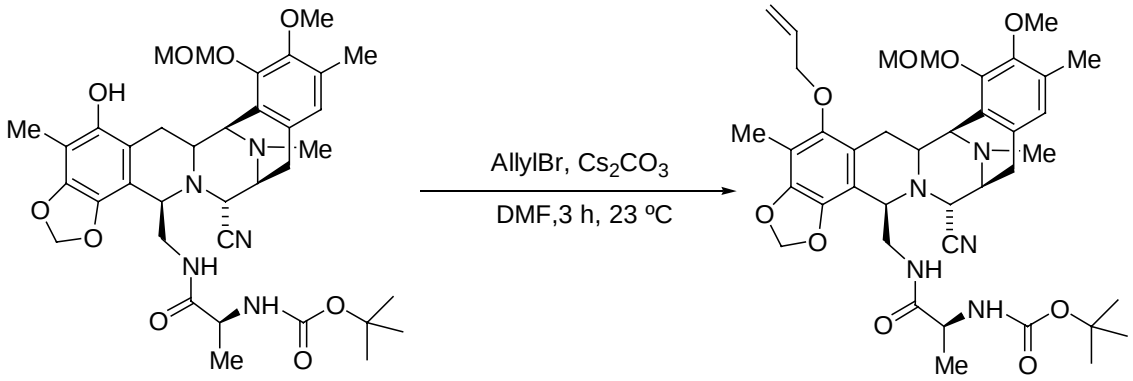
17 **4**

To a flask containing **17** (8 g, 1.5 mmol) in MeOH (1.6 L) an aqueous solution of NaOH 1 M (3.2 L) was added at 0 ºC. The reaction was stirred for 2.5 h at 20 ºC and then, quenched with HCl 6 M to pH = 5. The mixture was extracted with EtOAc (3 x 1L) and the combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography (SiO_2, gradient $CHCl_3$ to $CHCl_3$:EtOAc 2:1) to afford **4** (5.3 mg, 68%). Rf: 0.48 (CH_3CN:H_2O 7:3, RP-C18). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.73 (s, 1H), 5.43 (bs, 1H), 5.16 (s, 2H), 4.54 (bs, 1H), 4.26 (d, *J*= 1.8 Hz, 1H), 4.04 (d, *J*= 2.7 Hz 1H), 3.84 (bs, 1H), 3.80-3.64 (m, 1H), 3.58 (s, 3H), 3.41-3.39 (m, 1H), 3.22-3.06 (m, 5H), 2.49 (d, *J*= 18.6 Hz 1H), 2.35 (s, 3H), 2.30-2.25 (m, 1H), 2.24 (s, 3H), 1.87 (s, 3H), 1.45-1.33 (m, 1H), 1.19 (s, 9H), 1.00 (br d, *J*= 6.6 Hz 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 184.9, 180.9, 172.6, 154.7, 151.3, 149.1, 148.6, 144.7, 132.9, 131.3, 129.8, 124.5, 123.7, 117.3, 116.8, 99.1, 79.4, 59.8, 58.6, 57.7, 56.2, 55.6, 54.9, 54.5, 50.1, 41.6, 40.1, 28.0, 25.3, 24.4, 18.1, 15.7, 8.0. ESI-MS m/z: 680.3 $(M+H)^+$.



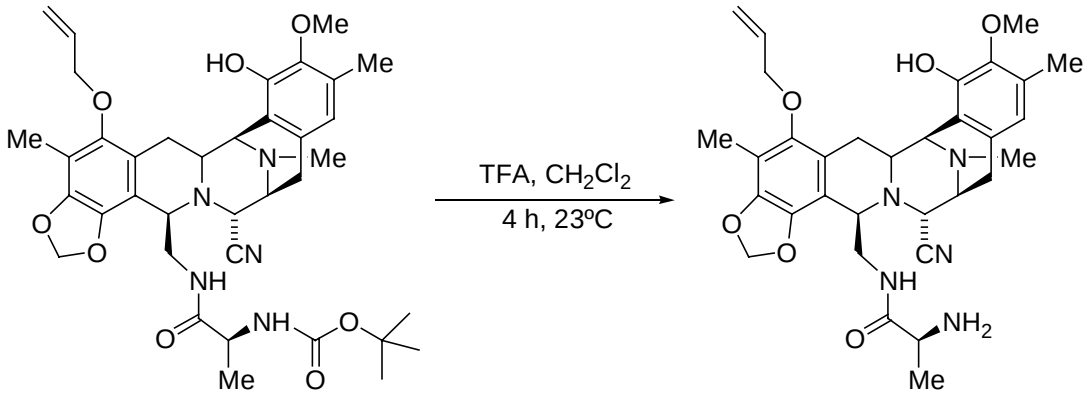
4 **5**

To a degassed solution of compound **4** (1.8 g, 2.64 mmol) in DMF (221 mL) 10% Pd/C (360 mg) was added and stirred under H_2 (atm. Pressure) for 2 h. The reaction was filtered through Celite under Argon to a flask containing anhydrous Cs_2CO_3 (2.58 g, 7.92 mmol). Then, bromochloromethane (3.40 mL 52.8 mmol), was added and the tube was sealed and stirred at 100 ºC for 2 h. The reaction was cooled, filtered through a pad of Celite and washed with CH_2Cl_2. The organic layer was dried over Na_2SO_4 and concentrated to afford **5** as a brown oil that was used in the next step with no further purification. Rf: 0.36 (Hex:EtOAc 1:5, SiO_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.68 (s, 1H), 6.05 (bs, 1H), 5.90 (s, 1H), 5.79 (s, 1H), 5.40 (bs, 1H), 5.31-5.24 (m, 2H), 4.67 (d, *J*= 8.1 Hz, 1H), 4.19 (d, *J*= 2.7 Hz, 1H), 4.07 (bs, 1H), 4.01 (bs, 1H), 3.70 (s, 3H), 3.67 (s, 3H), 3.64-2.96 (m, 5H), 2.65 (d, *J*=18.3 Hz, 1H), 2.33 (s, 3H), 2.21 (s, 3H), 2.04 (s, 3H), 2.01-1.95 (m, 1H), 1.28 (s, 9H), 0.87 (d, *J*= 6.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.1, 162.6, 154.9, 149.1, 145.7, 135.9, 130.8, 130.7, 125.1, 123.1, 117.8, 100.8, 99.8, 76.6, 59.8, 59.2, 57.7, 57.0, 56.7, 55.8, 55.2, 49.5, 41.6, 40.1, 36.5, 31.9, 31.6, 29.7, 28.2, 26.3, 25.0, 22.6, 18.2, 15.8, 14.1, 8.8. ESI-MS m/z: 694.3 $(M+H)^+$.



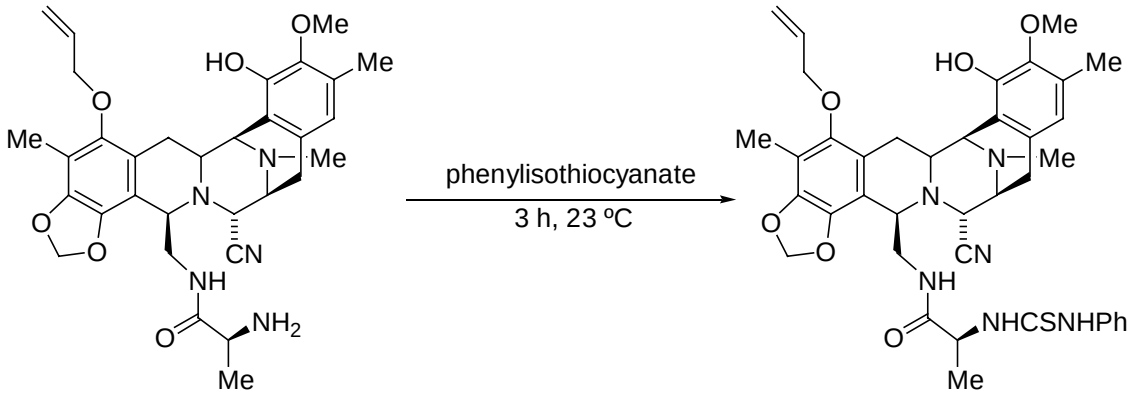
5 **6**

To a flask containing a solution of **5** (1.83 g, 2.65 mmol) in DMF (13 mL), Cs_2CO_3 (2.6 g, 7.97 mmol), and allyl bromide (1.15 mL, 13.28 mmol) were added at 0 ºC.The resulting mixture was stirred at 23 ºC for 3 h. The reaction was filtered through a pad of Celite and washed with CH_2Cl_2. The organic layer was dried and concentrated (Na_2SO_4). The residue was purified by flash column chromatography (SiO_2, $CHCl_3$:EtOAc 1:4) to afford **6** (1.08 mg, 56%) as a white solid. Rf: 0.36 ($CHCl_3$:EtOAc 1:3). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.70 (s, 1H), 6.27-6.02 (m, 1H), 5.94 (s, 1H), 5.83 (s, 1H), 5.37 (dd, J_1= 1.01 Hz, J_2= 16.8 Hz, 1H), 5.40 (bs, 1H), 5.25 (dd, J_1= 1.0 Hz, J_2= 10.5 Hz, 1H), 5.10 (s, 2H), 4.91 (bs, 1H), 4.25-4.22 (m, 1H), 4.21 (d, J= 2.4 Hz, 1H), 4.14-4.10 (m, 1H), 4.08 (d, J=2.4 Hz, 1H), 4.00 (bs, 1H), 3.70 (s, 3H), 3.59 (s, 3H), 3.56-3.35 (m, 2H), 3.26-3.20 (m, 2H), 3.05-2.96 (dd, J_1= 8.1 Hz, J_2=18 Hz, 1H), 2.63 (d, J=18 Hz, 1H), 2.30 (s, 3H), 2.21 (s, 3H), 2.09 (s, 3H), 1.91-1.80 (m, 1H), 1.24 (s, 9H), 0.94 (d, J= 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ172.0, 154.8, 148.8, 148.6, 148.4, 144.4, 138.8, 133.7, 130.9, 130.3, 125.1, 124.0, 120.9, 117.8, 117.4, 112.8, 112.6, 101.1, 99.2, 73.9, 59.7, 59.3, 57.7, 56.9, 56.8, 56.2, 55.2, 40.1, 34.6, 31.5, 28.1, 26.4, 25.1, 22.6, 18.5, 15.7, 14.0, 9.2. ESI-MS m/z: 734.4 $(M+H)^+$.



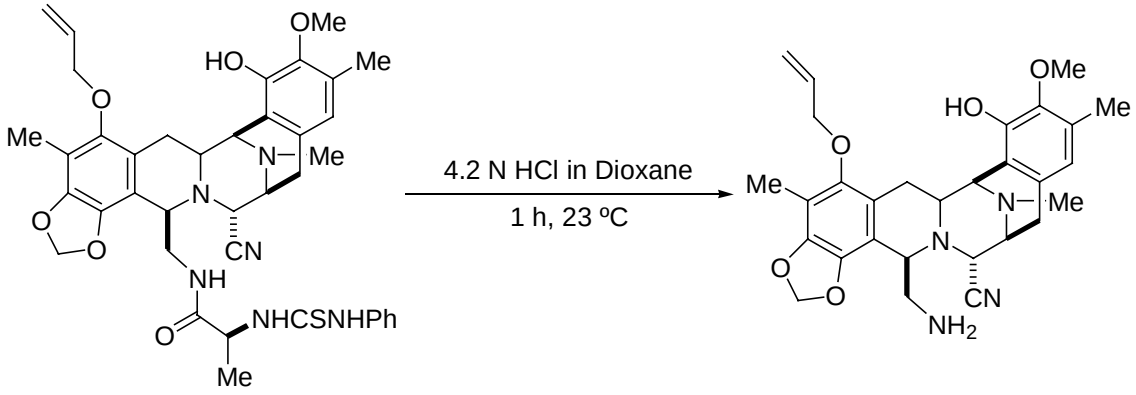
6 **18**

To a solution of **6** (0.1 g, 0.137 mmol) in CH_2Cl_2 (2 mL), TFA (0.411 mL, 5.48 mmol) was added and the mixture was stirred for 4 h at 23 ºC. The reaction was quenched at 0 ºC with saturated aqueous solution of $NaHCO_3$ (60 mL) and extracted with EtOAc (2 x 70 mL). The organic layers were dried over Na_2SO_4 and concentrated *in vacuo* to afford **18** (267 mg, 95%) as a white solid that was used in subsequent reactions with no further purification. Rf: 0.17 (EtOAc:MeOH 10:1, SiO_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.49 (s, 1H), 6.12-6.00 (m, 1H), 5.94 (s, 1H), 5.86 (s, 1H), 5.34 (dd, *J*= 1.0 Hz, *J*= 17.4 Hz, 1H), 5.25 (dd, *J*= 1.0 Hz, *J*= 10.2 Hz, 1H), 4.18-3.76 (m, 5H), 3.74 (s, 3H), 3.71-3.59 (m, 1H), 3.36-3.20 (m, 4H), 3.01-2.90 (m, 1H), 2.60 (d, *J*= 18.0 Hz, 1H), 2.29 (s, 3H), 2.24 (s, 3H), 2.11 (s, 3H), 1.97-1.86 (m, 1H), 0.93 (d, *J*= 8.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.5, 148.4, 146.7, 144.4, 142.4, 138.9, 133.7, 131.3, 128.3, 120.8, 117.9, 117.4, 113.8, 112.4, 101.1, 74.2, 60.5, 59.1, 56.5, 56.1, 56.3, 56.0, 55.0, 50.5, 41.6, 39.5, 29.5, 26.4, 24.9, 21.1, 15.5, 9.33. ESI-MS m/z: 590 $(M+H)^+$.



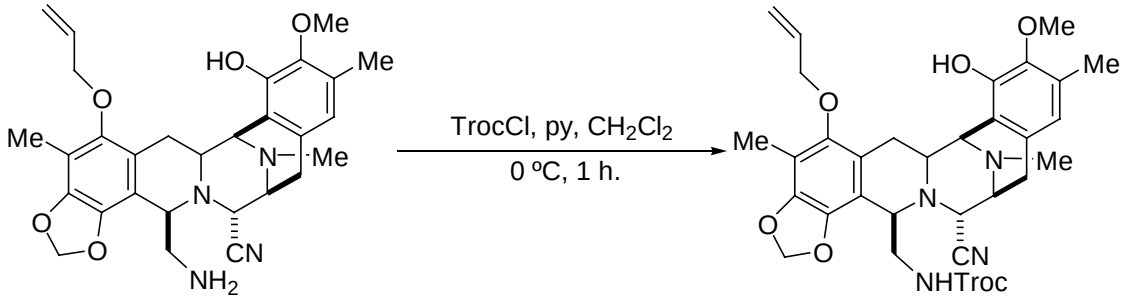
18 **19**

To a solution of **18** (250 mg, 0.42 mmol) in CH_2Cl_2 (1.5 mL), phenyl isothiocyanate (0.3 mL, 2.51 mmol) was added and the mixture was stirred at 23º C for 1 h. The reaction was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2, gradient Hexane to 5:1 Hex:EtOAc) to afford **19** (270 mg, 87%) as a white solid. Rf: 0.56 ($CHCl_3$:EtOAc 1:4). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00 (bs, 1H), 7.45-6.97 (m, 4H), 6.10 (s, 1H), 6.08-6.00 (m, 1H), 5.92 (s, 1H), 5.89 (s, 1H), 5.82 (s, 1H), 5.40 (dd, *J*= 1.5 Hz, *J*= 17.1 Hz, 1H), 3.38 (bs, 1H), 5.23 (dd, *J*= 1.5 Hz, *J*= 10.5 Hz, 1H), 4.42-4.36 (m, 1H), 4.19-4.03 (m, 5H), 3.71 (s, 3H), 3.68-3.17 (m, 4H), 2.90 (dd, *J*=7.8 Hz, *J*= 18.3 Hz, 1H), 2.57 (d, *J*= 18.3 Hz, 1H), 2.25 (s, 3H), 2.12 (s, 3H), 2.10 (s, 3H), 1.90 (dd, *J*= 12.3 Hz, *J*= 16.5 Hz, 1H), 0.81 (d, *J*= 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.4, 171.6, 148.6, 146.8, 144.3, 142.7, 138.7, 136.2, 133.6, 130.7, 129.8, 126.6, 124.2, 124.1, 120.9, 120.5, 117.7, 117.4, 116.7, 112.6, 112.5, 101.0, 74.0, 60.6, 59.0, 57.0, 56.2, 56.1, 55.0, 53.3, 41.4, 39.7, 26.3, 24.8, 18.3, 15.5, 9.2. ESI-MS m/z: 725.3 $(M+H)^+$.



19 **7**

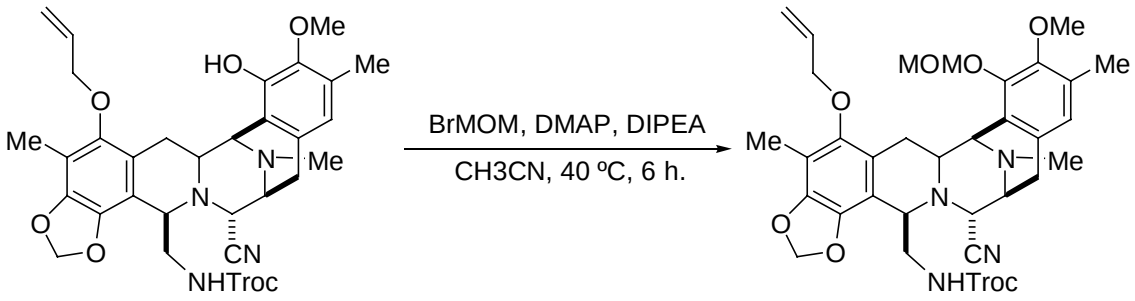
To a solution of **19** (270 mg, 0.37 mmol) in dioxane (1 mL), 4.2N HCl/dioxane (3.5 mL) was added and the reaction was stirred at 23 ºC for 1 h. Then, EtOAc (20 mL) and H_2O (20 mL) were added and the organic layer was decanted. The aqueous phase was basified with saturated aqueous solution of $NaHCO_3$ (60 mL) (pH=8) at 0 ºC and then, extracted with CH_2Cl_2 (2 x 50 mL). The combined organic extracts were dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by flash column chromatography (SiO_2, EtOAc:MeOH 5:1) to afford compound **6** (158 mg, 82%) as a white solid. Rf: 0.3 (EtOAc:MeOH 1:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.45 (s, 1H), 6.12-6.03 (m, 1H), 5.91 (s, 1H), 5.85 (s, 1H), 5.38 (dd, J_1= 1.2 Hz, J_2= 17.1 Hz, 1H), 5.24 (dd, J_1= 1.2 Hz, J_2= 10.5 Hz, 1H), 4.23-4.09 (m, 4H), 3.98 (d, J= 2.1 Hz, 1H), 3.90 (bs, 1H), 3.72 (s, 3H), 3.36-3.02 (m, 5H), 2.72-2.71 (m, 2H), 2.48 (d, J= 18.0 Hz, 1H), 2.33 (s, 3H), 2.22 (s, 3H), 2.11 (s, 3H), 1.85 (dd, J_1= 11.7 Hz, J_2= 15.6 Hz, 1H)); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.4, 146.7, 144.4, 142.8, 138.8, 133.8, 130.5, 128.8, 121.5, 120.8, 118.0, 117.5, 116.9, 113.6, 112.2, 101.1, 74.3, 60.7, 59.9, 58.8, 56.6, 56.5, 55.3, 44.2, 41.8, 29.7, 26.5, 25.7, 15.7, 9.4. ESI-MS m/z: 519.2 $(M+H)^+$.



7 **20**

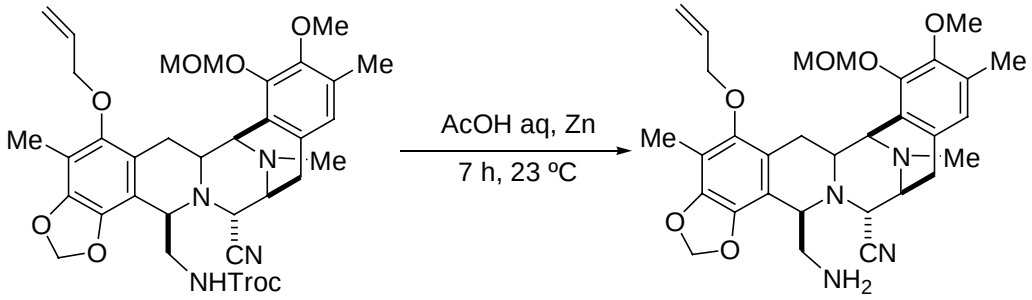
To a solution of **7** (0.64 g, 1.22 mmol) in CH_2Cl_2 (6.13 mL), pyridine (0.104 mL, 1.28 mmol) and 2,2,2-trichloroethyl chloroformate (0.177 mL, 1.28 mmol) were added at 0 ºC. The mixture was stirred at this temperature for 1 h and then, the reaction was quenched by

addition of HCl 0.1 N (10 mL) and extracted with CH_2Cl_2 (2 x 10 mL). The organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography (SiO_2, (Hex:EtOAc 1:2) to afford **20** (0.84 g, 98%) as a white foam solid. Rf: 0.57 (AcOEt: MeOH 5:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.50 (s, 1H), 6.10-6.00 (m, 1H), 6.94 (d, J= 1.5 Hz, 1H), 5.87 (d, J= 1.5 Hz, 1H), 5.73 (bs, 1H), 5.37 (dq, J_1= 1.5 Hz, J_2= 17.1 Hz, 1H), 5.26 (dq, J_1= 1.8 Hz, J_2= 10.2 Hz, 1H), 4.60 (d, J= 12 Hz, 1H), 4.22-4.10 (m, 4H), 4.19 (d, J= 12 Hz, 1H), 4.02 (m, 2H), 3.75 (s, 3H), 3.37-3.18 (m, 5H), 3.04 (dd, J_1= 8.1 Hz, J_2= 18 Hz, 1H), 2.63 (d, J= 18 Hz, 1H), 2.31 (s, 3H), 2.26 (s, 3H), 2.11 (s, 3H), 1.85 (dd, J_1= 12.3 Hz, J_2= 15.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.3, 148.5, 146.7, 144.5, 142.8, 139.0, 133.8, 130.7, 128.7, 121.3, 120.8, 117.8, 117.7, 116.8, 112.7, 101.2, 77.2, 74.3, 60.7, 59.9, 57.0, 56.4, 55.3, 43.3, 41.7, 31.6, 26.4, 25.3, 22.6, 15.9, 14.1, 9.4. ESI-MS m/z: 695.2 $(M+H)^+$.



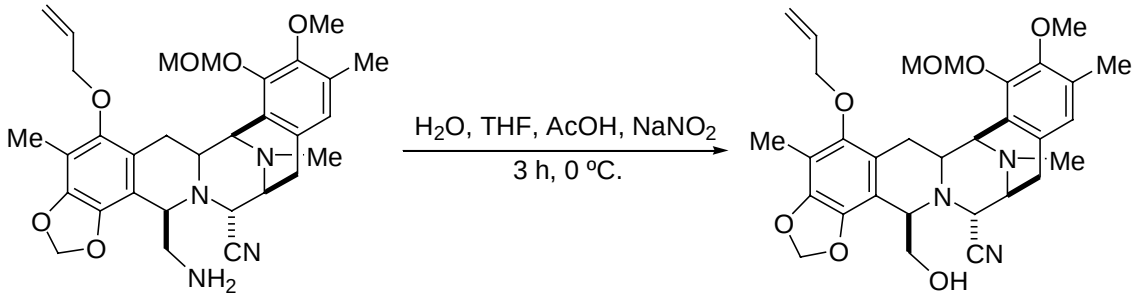
20 **21**

To a solution of **20** (0.32 g, 0.46 mmol) in CH_3CN (2.33 mL), diisopropylethylamine (1.62 mL, 9.34 mmol), bromomethyl methyl ether (0.57 mL, 7.0 mmol) and dimethylaminopyridine (6 mg, 0.046 mmol) were added at 0 ºC. The mixture was heated at 40 ºC for 6 h. Then, the reaction was diluted with dichloromethane (30 mL) and poured in an aqueous solution of HCl at pH=5 (10 mL). The organic layer was dried over Na_2SO_4 and the solvent was eliminated under reduced pressure to give a residue which was purified by flash column chromatography (SiO_2, Hex:AcOEt 2:1) to afford **21** (0.304 g, 88%) as a white foam solid. Rf: 0.62 (Hex:AcOEt 1:3). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.73 (s, 1H), 6.10 (m, 1H), 5.94 (d, J= 1.5 Hz, 1H), 5.88 (d, J= 1.5 Hz, 1H), 5.39 (dq, J_1= 1.5 Hz, J_2= 17.1 Hz, 1H), 5.26 (dq, J_1= 1.8 Hz, J_2= 10.2 Hz, 1H), 5.12 (s, 2H), 4.61 (d, J= 12 Hz, 1H), 4.55 (t, J= 6.6 Hz, 1H), 4.25 (d, J= 12 Hz, 1H), 4.22-4.11 (m, 4H), 4.03 (m, 2H), 3.72 (s, 3H), 3.58 (s, 3H), 3.38-3.21 (m, 5H), 3.05 (dd, J_1= 8.1 Hz, J_2= 18 Hz, 1H), 2.65 (d, J= 18 Hz, 1H), 2.32 (s, 3H), 2.23 (s, 3H), 2.12 (s, 3H), 1.79 (dd, J_1= 12.3 Hz, J_2= 15.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.3, 148.6, 148.4, 144.5, 139.0, 133.6, 130.6, 130.1, 125.07, 124.7, 124.0, 121.1, 117.7, 112.6, 101.2, 99.2, 77.2, 74.4, 74.1, 59.8, 59.8, 57.7, 57.0, 56.8, 56.68, 55.3, 43.2, 41.5, 26.4, 25.2, 15.9, 9.3. ESI-MS m/z: 739 $(M+H)^+$.



21 **8**

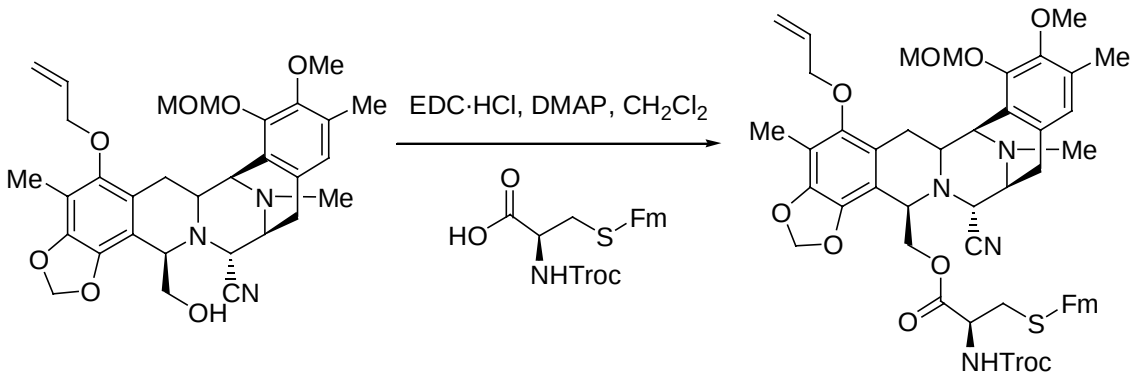
To a suspension of **21** (0.304 g, 0.41 mmol) in 90% aqueous acetic acid (4 mL), powder Zinc (0.2 g, 6.17 mmol) was added and the reaction was stirred for 7 h at 23 ºC. The mixture was filtered through a pad of Celite which was washed with CH_2Cl_2. The organic layer was washed with an aqueous saturated solution of $NaHCO_3$ (pH = 8) (15 mL) and dried over Na_2SO_4. The solvent was eliminated under reduced pressure to give **8** (0.191 g, 83%) as a white solid. Rf: 0.3 (EtOAc:MeOH 5:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.68 (s, 1H), 6.09 (m, 1H), 5.90 (d, J= 1.5 Hz, 1H), 5.83 (d, J= 1.5 Hz, 1H), 5.39 (dq, J_1= 1.5 Hz, J_2= 17.1 Hz, 1H), 5.25 (dq, J_1= 1.5 Hz, J_2= 10.2 Hz, 1H), 5.10 (s, 2H), 4.22-4.09 (m, 3H), 3.98 (d, J= 2.4 Hz, 1H), 3.89 (m, 1H), 3.69 (s, 3H), 3.57 (s, 3H), 3.37-3.17 (m, 3H), 3.07 (dd, J_1= 8.1 Hz, J_2= 18 Hz, 1H), 2.71 (m, 2H), 2.48 (d, J= 18 Hz, 1H), 2.33 (s, 3H), 2.19 (s, 3H), 2.17 (s, 3H), 1.80 (dd, J_1= 12.3 Hz, J_2= 15.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.5, 148.2, 144.3, 138.7, 133.7, 130.7, 129.9, 125.0, 123.9, 121.3, 117.9, 117.5, 113.6, 112.0, 101.0, 99.2, 74.0, 59.8, 59.7, 58.8, 57.6, 57.0, 56.2, 55.2, 44.2, 41.5, 31.5, 26.4, 25.6, 22.5, 16.7, 14.0, 9.2. ESI-MS m/z: 563.1 $(M+H)^+$.



8 **9**

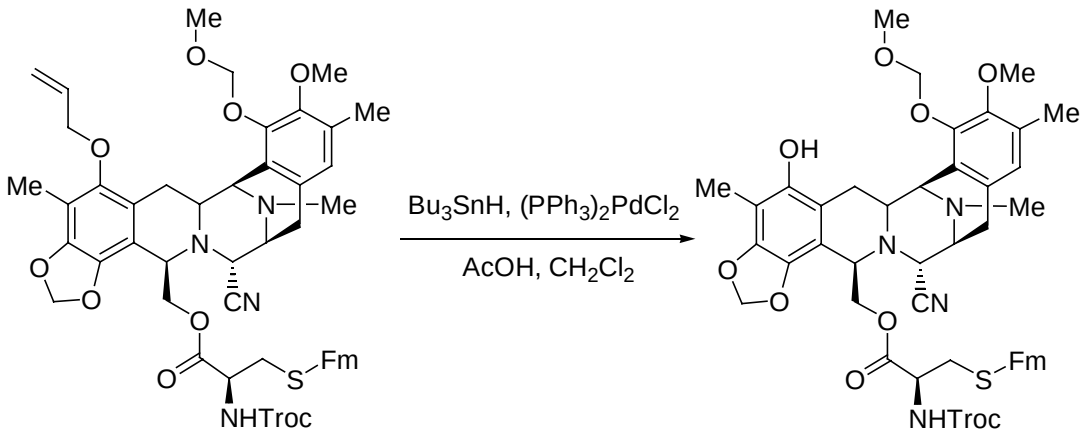
To a solution of **8** (20 mg, 0.035 mmol), in H_2O (0.7 mL) and THF (0.7 mL), $NaNO_2$ (12 mg, 0.17 mmol) and 90% aq. AcOH (0.06 mL) were added at 0 ºC and the mixture was stirred at 0 ºC for 3 h. After dilution with CH_2Cl_2 (5 mL), the organic layer was washed with H_2O (1 mL), dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography (SiO_2, Hex:EtOAc 2:1) to afford **9** (9.8 mg, 50%) as a white solid. Rf: 0.34 (Hex:EtOAc 1:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.71 (s, 1H), 6.11 (m, 1H), 5.92 (d, J= 1.5 Hz, 1H), 5.87 (d, J= 1.5 Hz, 1H), 5.42 (dq, J_1= 1.5 Hz, J_2= 17.1

Hz, 1H), 5.28 (dq, J_1= 1.5 Hz, J_2= 10.2 Hz, 1H), 5.12 (s, 2H), 4.26-4.09 (m, 3H), 4.05 (d, J= 2.4 Hz, 1H), 3.97 (t, J= 3.0 Hz, 1H), 3.70 (s, 3H), 3.67-3.32 (m, 4H), 3.58 (s, 3H), 3.24 (dd, J_1= 2.7 Hz, J_2= 15.9 Hz, 1H), 3.12 (dd, J_1= 8.1 Hz, J_2= 18.0 Hz, 1H), 2.51 (d, J= 18 Hz, 1H), 2.36 (s, 3H), 2.21 (s, 3H), 2.12 (s, 3H), 1.83 (dd, J_1= 12.3 Hz, J_2= 15.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.7, 148.4, 138.9, 133.7, 131.1, 129.4, 125.1, 123.9, 120.7, 117.6, 117.5, 113.2, 112.3, 101.1, 99.2, 74.0, 63.2, 59.8, 59.7, 57.9, 57.7, 57.0, 56.5, 55.2, 41.6, 29.6, 26.1, 25.6, 22.6, 15.7, 9.2. ESI-MS m/z: 564.1 $(M+H)^+$.



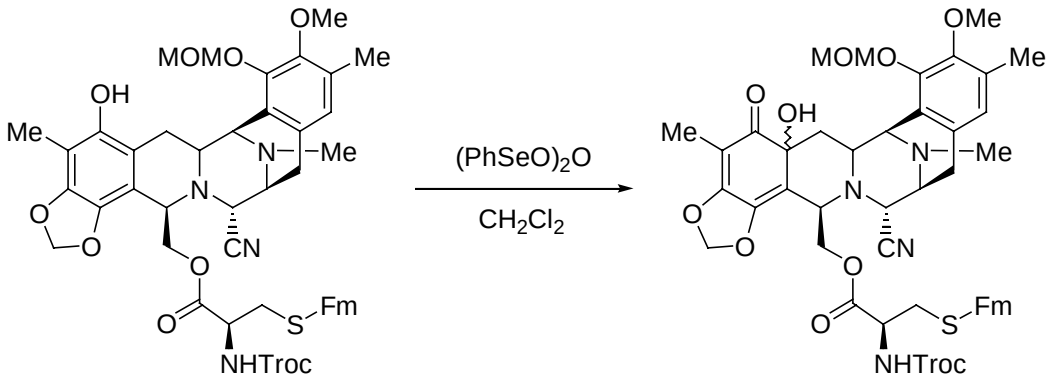
7 **8**

A mixture of compound **9** (585 mg, 1.03 mmol) and the cysteine derivative (1.47 mg, 3.11 mmol) were azeotroped with anhydrous toluene (3 x 10 mL). To a solution of **9** and the cysteine derivative in anhydrous CH_2Cl_2 (40 mL) was added DMAP (633 mg, 5.18 mmol) and EDC·HCl (994 mg, 5.18 mmol) at 23 ºC. The reaction mixture was stirred at 23 ºC for 3 h. The mixture was partitioned with saturated aqueous solution of $NaHCO_3$ (50 mL) and the layers were separated. The aqueous layer was washed with CH_2Cl_2 (50 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated. The crude was purified by flash column chromatography (EtOAc/hexane 1:3) to obtain **11** (1.00 g, 95%) as a pale cream yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72 (m, 2H), 7.52 (m, 2H), 7.38 (m, 2H), 7.28 (m, 2H), 6.65 (s, 1H), 6.03 (m, 1H), 5.92 (d, J= 1.5 Hz, 1H), 5.79 (d, J= 1.5 Hz, 1H), 5.39 (m, 1H), 5.29 (dq, J= 10.3 Hz, J= 1.5 Hz, 1H), 5.10 (s, 2H), 4.73 (d, J= 11.9 Hz, 1H), 4.66 (d, J= 11.9 Hz, 1H), 4.53 (m, 1H), 4.36-3.96 (m, 9H), 3.89 (t, J= 6.4 Hz, 1H), 3.71 (s, 3H), 3.55 (s, 3H), 3.33 (m, 1H), 3.20 (m, 2H), 2.94 (m, 3H), 2.59 (m, 1H), 2.29 (s, 3H), 2.23 (s, 3H), 2.02 (s, 3H), 1.83 (dd, J= 16.0 Hz, J= 11.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.7, 154.0, 148.8, 148.4, 145.7, 144.5, 140.9, 139.0, 133.7, 130.9, 130.6, 127.6, 127.0, 124.8, 124.6, 124.1, 120.8, 119.9, 118.2, 117.7, 117.3, 112.7, 112.1, 101.3, 99.2, 74.7, 73.9, 64.4, 59.8, 57.7, 57.0, 56.8, 55.4, 53.3, 46.7, 41.4, 36.5, 34.7, 31.5, 26.4, 24.9, 22.6, 15.7, 14.0, 9.1. ESI-MS m/z: 1021.2 $(M+H)^+$.



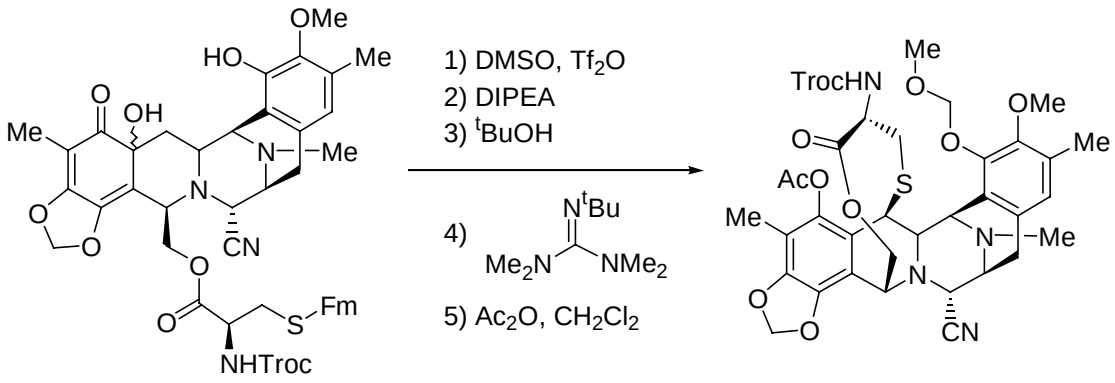
8 **21**

To a solution of **11** (845 mg, 0.82 mmol), acetic acid (500 mg, 8.28 mmol) and $(PPh_3)_2PdCl_2$ (29 mg, 0.04 mmol) in anhydrous CH_2Cl_2 (20 mL) at 23 ºC was added, dropwise, Bu_3SnH (650 mg, 2.23 mmol). The reaction mixture was stirred at this temperature for 15 min., bubbling was over. The crude was quenched with H_2O (50mL) and extracted with CH_2Cl_2 (3 x 50 mL). The organic layers were dried over Na_2SO_4, filtered and concentrated. The crude was purified by flash column chromatography (EtOAc/hexane in gradient from 1:5 to 1:3). to obtain compound **22** (730 mg, 90%) as a pale cream yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72 (m, 2H), 7.56 (m, 2H), 7.37 (m, 2H), 7.30 (m, 2H), 6.65 (s, 1H), 5.89 (s, 1H), 5.77 (s, 1H), 5.74 (s, 1H), 5.36 (d, *J*= 5.9 Hz, 1H), 5.32 (d, *J*= 5.9 Hz, 1H), 5.20 (d, *J*= 9.0, 1H), 4.75 (d, *J*= 12.0 Hz, 1H), 4.73 (m, 1H), 4.48 (d, *J*= 11.9 Hz, 1H), 4.08 (m, 4H), 3.89 (m, 1H), 3.86, (t, *J*= 6.2 Hz, 1H), 3.70 (s, 3H), 3.69 (s, 3H), 3.38 (m, 1H), 3.25 (m, 1H), 3.02-2.89 (m, 4H), 2.67 (s, 1H), 2.61 (s, 1H), 2.51 (dd, *J*= 14.3 Hz, *J*= 4.5 Hz, 1H), 2.29 (s, 3H), 2.23 (s, 3H), 1.95 (s, 3H), 1.83 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.2, 152.5, 148.1, 146.2, 144.4, 144.3, 143.3, 139.6, 134.6, 129.7, 129.6, 126.2, 125.6, 123.4, 123.3, 121.6, 118.5, 116.3, 110.7, 110.2, 105.1, 99.4, 98.5, 75.2, 73.3, 61.7, 58.4, 57.9, 56.3, 56.1, 55.1, 54.7, 53.9, 51.9, 45.2, 40.1, 35.6, 33.3, 24.8, 23.3., 14.5, 7.3. ESI-MS m/z: 981.2 $(M+H)^+$.



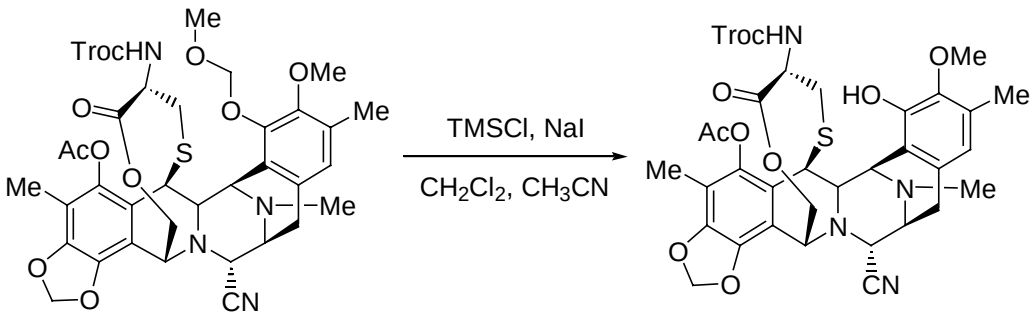
22 **12**

To a solution of **22** (310 mg, 0.32 mmol), in anhydrous CH_2Cl_2 (15 mL) at -10 ºC was added a solution of benzeneseleninic anhydride 70% (165 mg, 0.32 mmol), in anhydrous CH_2Cl_2 (7 mL), *via* cannula, keeping the temperature at -10 ºC. The reaction mixture was stirred at -10 ºC for 5 min. A saturated aqueous solution of $NaHCO_3$ (30 mL) was added at this temperature. The aqueous layer was washed with more CH_2Cl_2 (40 mL). The organic layers were dried over Na_2SO_4, filtered and concentrated. The crude was purified by flash column chromatography (EtOAc/hexane in gradient from 1:5 to 1:1) to obtain **12** (287 mg, 91%) as a pale cream yellow solid and as a mixture of two isomers (65:35) wich were used in the next step. ^{1}H NMR (300 MHz, $CDCl_3$) δ(Mixture of isomers) 7.76 (m, 4H), 7.65 (m, 4H), 7.39 (m, 4H), 7.29 (m, 4H), 6.62 (s, 1H), 6.55 (s, 1H), 5.79-5.63 (m, 6H), 5.09 (s, 1H), 5.02 (d, *J*= 6.0 Hz, 1H), 4.99 (d, *J*= 6.0 Hz, 1H), 4.80-4.63 (m, 6H), 4.60 (m, 1H), 4.50 (m, 1H), 4.38 (d, *J*= 12.8 Hz, *J*= 7.5 Hz, 1H), 4.27 (dd, *J*= 12.8 Hz, *J*= 7.5 Hz, 1H), 4.16-3.90 (m, 10H), 3.84 (s, 3H), 3.62 (s, 3H), 3.50 (s, 3H), 3.49 (s, 3H), 3.33-2.83 (m, 14H), 2.45-2.18 (m, 2H), 2.21 (s, 6H), 2.17 (s, 6H), 1.77 (s, 6H), 1.67 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (Mixture of isomers) 168.6, 168.4, 158.6, 154.8, 152.8, 152.5, 147.3, 147.2, 146.8, 144.1, 144.0, 140.8, 139.7, 137.1, 129.8, 129.3, 128.4, 128.7, 126.5, 125.5, 123.7, 123.6, 123.5, 123.4, 122.2, 121.3, 118.3, 115.8, 115.5, 110.2, 106.9, 103.5, 103.2, 100.1, 99.6, 97.9, 97.7, 93.8, 73.4, 70.9, 69.2, 64.9, 62.5, 59.3, 58.9, 58.4, 56.7, 56.3, 56.2, 55.4, 55.2, 55.1, 54.9, 54.7, 54.3, 54.1, 53.8, 52.8, 45.5, 40.5, 40.0, 39.8, 35.8, 35.5, 33.9, 33.7, 30.1, 28.8, 24.2, 24.1, 21.2, 14.5, 14.4, 12.7, 6.0, 5.7. ESI-MS m/z: 997.2 $(M+H)^+$.



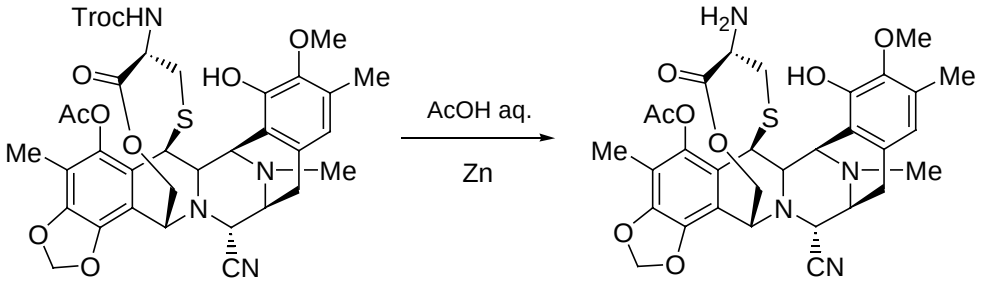
12 **13**

The reaction flask was flamed twice, purged vacuum/Argon several times and kept under Argon atmosphere. To a solution of DMSO (39.1 μL, 0.55 mmol, 5 equivs.) in anhydrous CH_2Cl_2 (4.5 mL) was dropwise added triflic anhydride (37.3 μL, 0.22 mmol, 2 equivs.) at -78 ^oC . The reaction mixture was stirred at -78 ^oC for 20 minutes, then a solution of **9** (110 mg, 0.11 mmol, HPLC: 91.3%) in anhydrous CH_2Cl_2 (1 mL, for the main addition and 0.5 mL for wash) at -78 ^oC was added, *via* canula. During the addition the temperature was kept at -78 ^oC in both flasks and the color changed from yellow to brown. The reaction mixture was stirred at -40 ^oC for 35 minutes. During this period of time the solution was turned from yellow to dark green. After this time, $^iPr_2NEt$ (153 μL, 0.88 mmol, 8 equivs.) was dropwise added and the reaction mixture was kept at 0 ^oC for 45 minutes, the color of the solution turned to brown during this time. Then ^{t}BuOH (41.6 μL, 0.44 mmol, 4 equivs.) and 2-^{t}Butyl-1,1,3,3-tetramethylguanidine (132.8 μL, 0.77 mmol, 7 equivs.) were dropwise added and the reaction mixture was stirred at 23 ^oC for 40 minutes. After this time, acetic anhydride (104.3 μL, 1.10 mmol, 10 equivs.) was dropwise added and the reaction mixture was kept at 23 ^oC for 1 hour more. Then the reaction mixture was diluted with CH_2Cl_2 (20mL) and washed with aqueous saturated solution of NH_4Cl (50mL), $NaHCO_3$ (50mL), and NaCl (50mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash column chromatography (eluent: ethyl acetate/hexane gradient from 1:3 to 1:2) to afford compound **13** (54 mg, 58%) as a pale yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.85 (s, 1H), 6.09 (s, 1H), 5.99 (s, 1H), 5.20 (d, *J*= 5.8 Hz, 1H), 5.14 (d, *J*= 5.3 Hz, 1H), 5.03 (m, 1H), 4.82 (d, *J*= 12.2, 1H), 4.63 (d, *J*= 12.0 Hz, 1H), 4.52 (m, 1H), 4.35-4.17 (m, 4H), 3.76 (s, 3H), 3.56 (s, 3H), 3.45 (m, 2H), 2.91 (m, 2H), 2.32 (s, 3H), 2.28 (s, 3H), 2.21 (s, 3H), 2.12 (m, 2H), 2.03 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 168.5, 167.2, 152.7, 148.1, 147.1, 144.5, 139.6, 139.1, 130.5, 129.0, 123.7, 123.5, 123.3, 118.8, 116.5, 112.1, 100.6, 97.8, 73.3, 60.5, 59.4, 59.2, 58.3, 57.6, 57.4, 56.1, 53.3, 53.1, 40.6, 40.0, 31.0, 22.2, 18.9, 14.4, 8.1. ESI-MS m/z: 843.1 $(M+H)^+$.



13 **23**

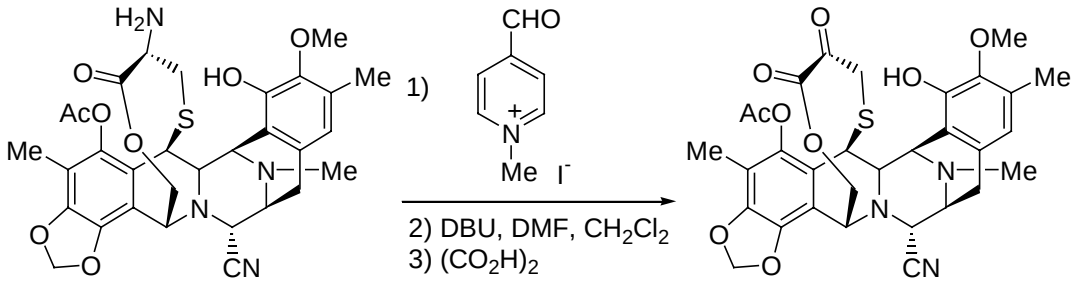
To a solution of **13** (12 mg, 0.014 mmol)in dry CH_2Cl_2 (1.2 mL) and HPLC grade CH_3CN (1.2 mL) was added at 23 ^oC sodium iodide (21 mg, 0.14 mmol) and freshly distilled (over calcium hydride at atmospheric pressure) trimethylsilyl chloride (15.4 mg, 0.14 mmol). The reaction mixture turned to orange colour. After 30 min the solution was diluted with dichloromethane (10 mL) and was washed with a freshly aqueous saturated solution of $Na_2S_2O_4$ (3 x 10 mL). The organic layer was dried over Na_2SO_4, filtered and concentrated. It was obtained compound **23** (13 mg, quantitative) as pale yelow solid wich was used without further purification. ^1H NMR (300 MHz, $CDCl_3$) δ 6.85 (s, 1H), 6.09 (s, 1H), 5.99 (s, 1H), 5.27 (d, *J*= 5.8 Hz, 1H), 5.14 (d, *J*= 5.3 Hz, 1H), 5.03 (d, *J*= 11.9 Hz, 1H), 4.82 (d, *J*= 12.2, 1H), 4.63 (d, *J*= 13.0 Hz, 1H), 4.52 (m, 1H), 4.34 (m, 1H), 4.27 (bs, 1H), 4.18 (m, 2H), 3.76 (s, 3H), 3.56 (s, 3H), 3.44 (m, 1H), 3.42 (m, 1H), 2.91 (m, 2H), 2.32 (s, 3H), 2.28 (s, 3H), 2.21 (s, 3H), 2.03 (s, 3H). ESI-MS m/z: 799.1 $(M+H)^+$.



23 **24**

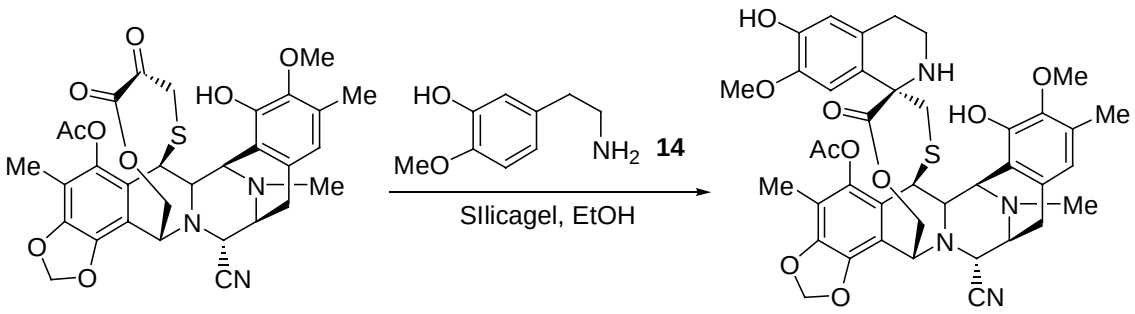
To a solution of **23** (13 mg, 0.016 mmol) in a mixture of acetic acid/H_2O (90:10, 1 mL) was added powder Zinc (5.3 mg, 0.081 mmol) at 23 ºC. The reaction mixture was heated at 70 ºC for 6 h. After this time, was cooled to 23 ºC, diluted with CH_2Cl_2 (20 mL) and washed with saturated aqueous solution of $NaHCO_3$ (15 mL) and aqueous solution of Et_3N (15 mL). The organic layer was dried over Na_2SO_4, filtered and concentrated. The residue was purified purified by flash column chromatography with Silica-NH_2 (eluent: ethyl acetate/hexane gradient from 0:100 to 50:50) to afford compound **24** (6.8 mg, 77% for two

steps) as a pale yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.51 (s, 1H), 6.03 (dd, *J*= 1.3 Hz, *J*= 26.5 Hz, 2H), 5.75 (bs, 1H), 5.02 (d, *J*= 11.6 Hz, 1H), 4.52 (m, 1H), 4.25 (m, 2H), 4.18 (d, *J*= 2.5 Hz, 1H), 4.12 (dd, *J*= 1.9 Hz, *J*= 11.5 Hz, 1H), 3.77 (s, 3H), 3.40 (m, 2H), 3.26 (t, *J*= 6.4 Hz, 1H), 2. 88 (m, 2H), 2.30-2.10 (m, 2H), 2.30 (s, 3H), 2.28 (s, 3H), 2.18 (s, 3H), 2.02 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.1, 168.4, 147.8, 145.4, 142.9, 140.8, 140.1, 131.7, 130.2, 129.1, 128.3, 120.4, 118.3, 117.9, 113.8, 111.7, 101.7, 61.2, 59.8, 59.2, 58.9, 54.4, 53.8, 54.4, 41.3, 41.5, 34.1, 23.6, 20.3, 15.5, 9.4. ESI-MS m/z: 623.2 $(M+H)^+$.



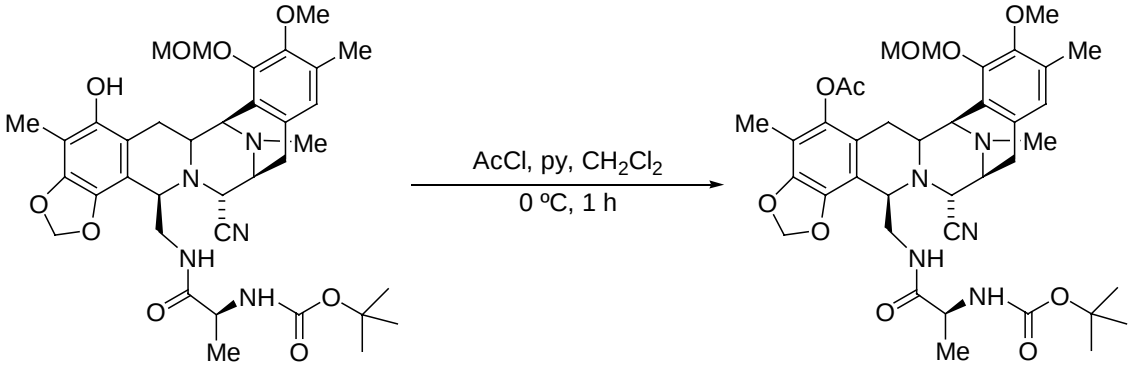
24 **25**

A solution of *N*-methyl pyridine-4-carboxaldehyde iodide (378 mg, 1.5 mmol) in anhydrous DMF (5.8 mL) was treated with anhydrous toluene (2 x 10 mL) to eliminate the amount of water by azeotropic removal of the toluene. A solution of **24** (134 mg, 0.21 mmol), previously treated with anhydrous toluene (2 x 10 mL), in anhydrous CH_2Cl_2 (distilled over CaH_2, 7.2 mL) was added, *via* cannula, at 23 ^{o}C to this orange solution. The reaction mixture was stirred at 23 ºC for 4 hours. After this time DBU (32.2 µL, 0.21mmol) was dropwise added at 23 ºC and it was stirred for 15 minutes at 23 ºC. A freshly saturated aqueous solution of oxalic acid (5.8 mL) was added to the reaction mixture and was stirred for 30 minutes at 23 ºC. Then the reaction mixture was cooled to 0 ºC and $NaHCO_3$ was portionwise added followed by addittion of aqueous saturated solution of $NaHCO_3$. The mixture was extracted with Et_2O. K_2CO_3 was added to the aqueous layer and it was extrated with Et_2O. The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The crude was purified by flash column chromatography (AcOEt/hexane from 1/3 to 1/1) to afford compound **25** (77 mg, 57%) as pale yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.48 (s, 1H), 6.11 (d, *J*= 1.3 Hz, 1H), 6.02 (d, *J*= 1.3 Hz, 1H), 5.70 (bs, 1H), 5.09 (d, *J*= 11.3 Hz, 1H), 4.66 (bs, 1H), 4.39 (m, 1H), 4.27 (d, *J*= 5.6 Hz, 1H), 4.21 (d, *J*= 10.5 Hz, 1H), 4.16 (d, *J*= 2.6 Hz, 1H), 3.76 (s, 3H), 3.54 (d, *J*= 5.1 Hz, 1H), 3.42 (d, *J*= 8.5 Hz, 1H), 2.88-2.54 (m, 3H), 2.32 (s, 3H), 2.24 (s, 3H), 2.14 (s, 3H), 2.04 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 186.7, 168.5, 160.5, 147.1, 146.4, 142.9, 141.6, 140.7, 130.4, 129.8, 121.7 (2C), 120.0, 117.8, 117.1, 113.5, 102.2, 61.7, 61.4, 60.3, 59.8, 58.9, 54.6, 41.6, 36.9, 29.7, 24.1, 20.3, 15.8, 14.1, 9.6. ESI-MS m/z: 622.2 $(M+H)^+$.



25 **Et-770**

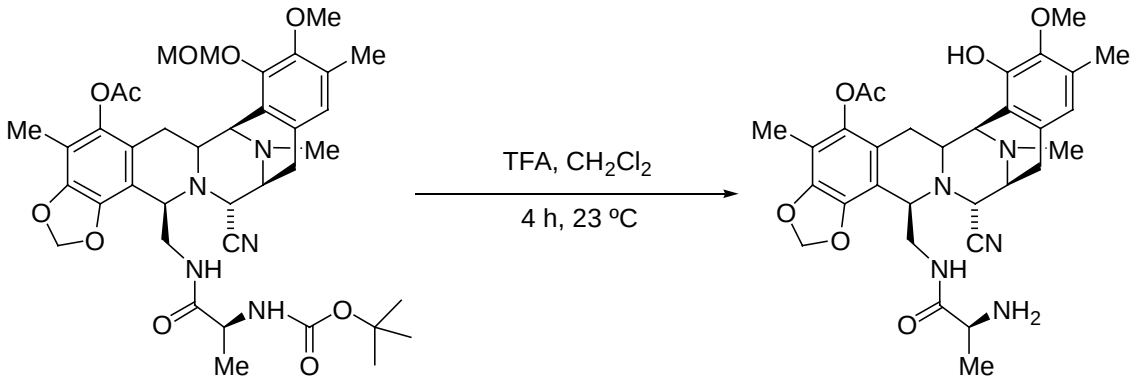
To a solution of **25** (49mg, 0.08 mmol) and 2-[3-hydroxy-4-methoxyphenyl]ethylamine **14** (46.2 mg, 0.27 mmol) in EtOH (2.5 ml) was added silicagel (105 mg) at 23 ºC. The reaction mixture was stirred at 23 ºC for 12 h. It was diluted with hexane and poured into a column of chromatography (AcOEt/hexane from 1/3 to 1/1) to afford **Et-770** (55 mg, 90%) as a pale yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.60 (s, 1H), 6.47 (s, 1H), 6.45 (s, 1H), 6.05 (s, 1H), 5.98 (s, 1H), 5.02 (d, *J*=11.4 Hz, 1H), 4.57 (bs, 1H), 4.32 (bs, 1H), 4.28 (d, *J*= 5.3 Hz, 1H), 4.18 (d, *J*= 2.5 Hz, 1H), 4.12 (dd, *J*= 2.1 Hz, *J*= 11.5 Hz, 1H), 3.78 (s, 3H), 3.62 (s, 3H), 3.50 (d, *J*= 5.0 Hz, 1H), 3.42 (m, 1H), 3.10 (ddd, *J*= 4.0 Hz, *J*= 10.0 Hz, *J*= 11.0 Hz, 1H), 2.94 (m, 2H), 2.79 (m, 1H), 2.61 (m, 1H), 2.47 (m, 1H), 2.35 (m, 1H), 2.32 (s, 3H), 2.27 (s, 3H), 2.20 (s, 3H), 2.09 (m, 1H), 2.04 (s, 3H). ESI-MS m/z: 771.2 $(M+H)^+$.



5 **26**

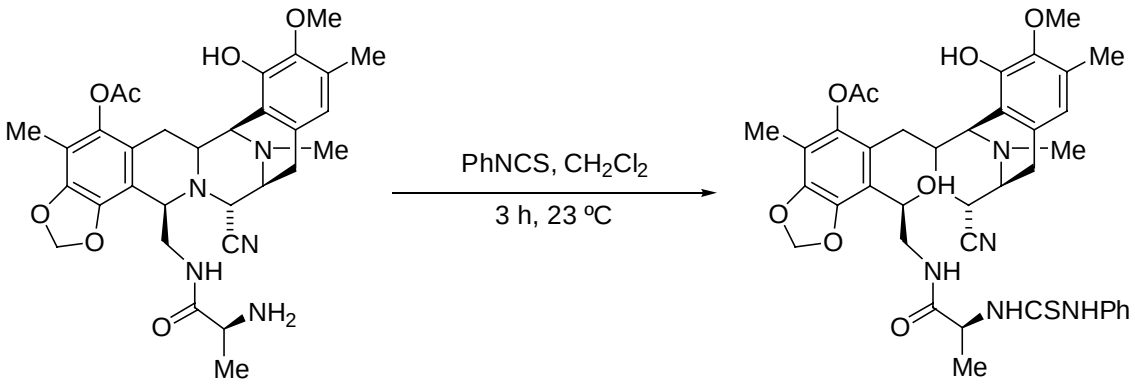
To a solution of **5** (300 mg, 0.432 mmol) in CH_2Cl_2 (2 mL), acethyl chloride (30.7 µL, 0.432 mmol) and pyridine (34.9 µL, 0.432 mmol) were added at 0 ºC. The reaction mixture was stirred for 1 h at this temperature and then, the solution was diluted with CH_2Cl_2 (15 mL) and washed with HCl 0.1 N (15 mL). The organic layer was dried over Na_2SO_4, filtered, and the solvent was eliminated under reduced pressure to afford **26** (318 mg, 100%) as a white solid that was used in subsequent reactions with no further purification. Rf: 0.5 (EtOAc:MeOH 5:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.66 (s, 1H), 5.93 (d, *J*= 1.2 Hz, 1H), 5.83 (d, *J*= 1.2 Hz, 1H), 5.42 (t, *J*= 6.6 Hz, 1H), 5.07 (d, *J*= 5.7 Hz, 1H), 4.98 (d, *J*=

5.7 Hz, 1H), 4.16 (d, *J*= 1.8 Hz, 1H), 4.11 (d, *J*= 2.7 Hz, 1H), 3.98 (bs, 1H), 3.73-3.61 (m, 2H), 3.64 (s, 3H), 3.52-3.48 (m, 1H), 3.50 (s, 3H), 3.33 (d, *J*= 9.6 Hz, 1H), 3.17-3.14 (m, 1H), 2.97-2.87 (m, 1H), 2.75-2.70 (d, *J*= 16.8 Hz, 1H), 2.26 (s, 6H), 2.16 (s, 3H), 1.96 (s, 3H), 1.70 (dd, J_1= 11.7 Hz, J_2= 15.6 Hz, 1H), 1.33 (s, 9H), 0.59 (d, *J*= 6.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$)) δ 172.0, 168.3, 162.3, 148.2, 144.4, 140.4, 140.2, 130.9, 130.5, 125.3, 123.4, 120.8, 117.6, 112.7, 111.7, 101.4, 99.1, 79.2, 59.5, 58.8, 57.5, 57.4, 56.4, 55.5, 55.0, 41.3, 39.0, 28.2, 26.4, 24.6, 19.9, 18.4, 15.4, 9.1. ESI-MS m/z: 736.3 $(M+H)^+$.



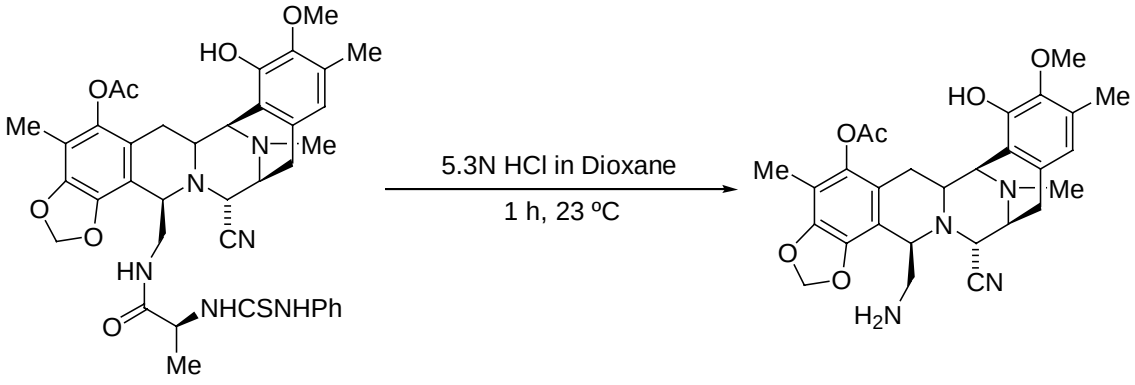
26 **27**

To a solution of **26** (318 mg, 0.432 mmol) in CH_2Cl_2 (2.16 mL), trifluoroacetic acid (1.33 mL, 17.30 mmol) was added and the reaction mixture was stirred for 4 h at 23 ºC. The reaction was quenched at 0 ºC with saturated aqueous solution of $NaHCO_3$ (60 mL) and extracted with CH_2Cl_2 (2 x 70 mL). The combined organic layers were dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by flash column chromatography (SiO_2, EtOAc:MeOH 20:1) to afford **27** (154 mg, 60%) as a white solid. Rf: 0.22 (EtOAc:MeOH 5:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.47 (s, 1H), 6.22 (bs, 1H), 5.95 (d, *J*= 1.2 Hz, 1H), 5.88 (d, *J*= 1.2 Hz, 1H), 4.08-4.06 (m, 2H), 4.01 (bs, 1H), 3.69 (s, 3H), 3.49 (d, *J*= 3.6 Hz, 1H), 3.33 (d, *J*= 8.1 Hz, 1H), 3.26-3.22 (m, 1H), 2.95 (dd, J_1= 8.1 Hz, J_2= 18 Hz, 1H), 2.80-2.76 (m, 2H), 2.58 (d, *J*=18Hz, 1H), 2.29 (s, 3H), 2.27 (s, 3H), 2.21 (s, 3H), 1.96 (s, 3H), 1.77 (dd, J_1= 12.3 Hz, J_2= 15.6 Hz, 1H), 0.90 (d, *J*=6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.8, 169.0, 146.8, 144.4, 142.8, 140.5, 140.2, 131.1, 128.8, 120.8, 120.5, 117.1, 112.9, 111.6, 101.5, 60.3, 59.0, 56.5, 56.3, 55.6, 55.1, 50.2, 41.6, 39.5, 26.8, 26.3, 24.9, 20.2, 15.4, 9.2. ESI-MS m/z: 592.3 $(M+H)^+$.



27 **28**

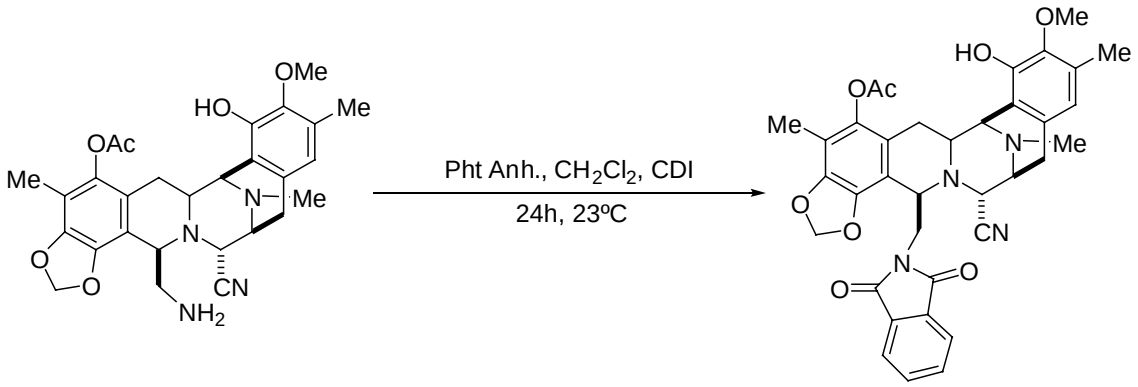
To a solution of **27** (154 mg, 0.26 mmol) in CH_2Cl_2 (1.3 mL), phenylisothiocyanate (186 µL, 1.56 mmol) was added and the mixture was stirred at 23º C for 3 h. The reaction was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2, gradient Hexane to Hex:EtOAc 1:1) to afford **28** (120 mg, 63%) as a white solid. Rf: 0.41 (EtOAc:MeOH 5:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.17 (s, 1H), 7.49-7.44 (m, 3H), 7.31-7.24 (m, 3H), 7.05 (d, *J*= 6.9 Hz, 1H), 5.98 (d, *J*= 1.2 Hz, 1H), 5.87 (d, *J*= 1.2 Hz, 1H), 5.52 (bs, 1H), 4.54 (t, *J*= 6.6 Hz, 1H), 4.15 (d, *J*= 2.1 Hz, 1H), 4.03 (d, *J*= 2.7 Hz, 2H), 3.80 (bs, 1H), 3.66 (s, 3H), 3.40 (bs, 1H), 3.32 (d, *J*= 7.8 Hz, 1H), 3.16 (d, *J*= 11.7 Hz, 1H), 2.82-2.61 (m, 3H), 2.29 (s, 3H), 2.20 (s, 3H), 2.01 (s, 3H), 1.99 (s, 3H), 1.80 (dd, J_1= 12.0 Hz, J_2= 15.9 Hz, 1H), 0.62 (d, *J*= 6.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.5, 171.9, 168.7, 146.7, 144.5, 142.6, 140.6, 140.3, 136.3, 131.0, 129.9, 128.9, 126.7, 124.4, 120.9, 120.6, 117.7, 116.6, 112.7, 111.9, 101.4, 60.4, 58.7, 57.5, 56.1, 55.7, 55.1, 53.3, 41.4, 38.8, 26.3, 24.4, 20.2, 18.1, 15.3, 9.2. ESI-MS m/z: 727.3 $(M+H)^+$.



28 **15**

To a solution of **28** (120 mg, 0.165 mmol) in dioxane (0.9 mL), 5.3N HCl/dioxane (1.8 mL) was added and the reaction was stirred at 23 ºC for 1 h. Then, CH_2Cl_2 (10 mL) and H_2O (5 mL) were added to this reaction and the organic layer was decanted. The aqueous phase was basified with saturated aqueous solution of $NaHCO_3$ (20 mL) (pH = 8) at 0 ºC and

then, extracted with CH_2Cl_2 (2 x 15 mL). The combined organic extracts were dried over Na_2SO_4, and concentrated *in vacuo* to afford **15** (75 mg, 87%) as a white solid that was used in subsequent reactions with no further purification. Rf: 0.23 (EtOAc:MeOH 5:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.43 (s, 1H), 5.94 (d, *J*= 1.2 Hz, 1H), 5.87 (d, *J*= 1.2Hz, 1H), 4.10 (d, *J*= 2.1 Hz, 1H), 3.98 (d, *J*= 2.4 Hz, 1H), 3.91 (bs, 1H), 3.69 (s, 3H), 3.34-3.25 (m, 2H), 3.05 (dd, J_1= 1.8 Hz, J_2= 8.1 Hz, 1H), 2.80-2.73 (m, 3H), 2.46 (d, *J*= 18 Hz, 1H), 2.30 (s, 3H), 2.28 (s,3H), 2.20 (s, 3H), 1.98 (s, 3H), 1.79 (dd, J_1= 12.6 Hz, J_2= 16.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.7, 146.7, 144.4, 142.9, 140.4, 130.4, 128.9, 121.1, 120.8, 117.8, 116.8, 113.6, 111.5, 101.4, 67.6, 60.5, 59.8, 58.4, 56.6, 55.8, 55.3, 43.6, 41.8, 31.3, 25.6, 20.2, 15.6, 9.2. ESI-MS m/z: 521.3 $(M+H)^+$.



15 **2**

To a solution of **15** (10 mg, 0.02 mmol) in CH_2Cl_2 (0.4 mL) was added phtalic anhydride (2.84 mg, 0.02 mmol) and the reaction mixture was stirred for 2 h at 23 ºC. Then, carbonyldiimidazole (0.5 mg, 0.003 mmol) was added and the mixture was stirred at 23 ºC for 24 h. Then, carbonyldiimidazole (2.61 mg, 0.016 mmol) was added and the reaction was stirred at 23 ºC for an additional 17h. The solution was diluted with CH_2Cl_2 (10 mL) and washed with HCl 0.1 N (5 mL). The organic layer was dried over Na_2SO_4, filtered, and the solvent was eliminated under reduced pressure. The residue was purified by flash column chromatography (RP-18, CH_3CN:H_2O 60:40) to afford **2** (11.7 mg, 93%) as a white solid. Rf: 0.37 (CH_3CN:H_2O 7:3, RP-18). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72–7.68 (m, 2H), 7.67-7.63 (m, 2H), 6.38 (s, 1H), 5.69 (d, *J*= 1.2 Hz, 1H), 5.64 (d, *J*= 1.2Hz, 1H), 5.30 (bs, 1H), 4.25-4.21 (m, 2H), 4.02 (d, *J*= 2.1 Hz, 1H), 3.64-3.62 (m, 5H), 3.33 (d, *J*= 8.4 Hz, 1H), 3.21-3.16 (m, 1H), 3.02 (dd, J_1= 8.1 Hz, J_2= 18 Hz, 1H), 2.76 (dd, J_1= 1.8 Hz, J_2= 15.6 Hz, 1H), 2.63 (d, *J*= 17.7 Hz, 1H), 2.29 (s, 3H), 2.28 (s,3H), 2.21 (s, 3H), 2.0 (s, 3H), 1.73 (dd, J_1= 12.0 Hz, J_2= 15.3 Hz, 1H)); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.5, 167.6, 146.2, 144.2, 142.5, 141.0, 140.5, 133.4, 131.8, 130.7, 128.2, 120.9, 120.8, 117.9, 116.4, 113.6, 101.1, 60.4, 60.0, 57.0, 56.3, 55.6, 55.4, 41.6, 41.5, 26.5, 25.2, 20.2, 15.7, 9.4. ESI-MS m/z: 651.2 $(M+H)^+$.