Supporting Information

Compound **7**

A solution of 2'-O-(t-butyldimethylsilyl)-7β-O-trifluoromethanesulfonyl-paclitaxel **6**[2(a)] (240 mg, 0.237 mmole) in 2 mL of dry dimethylformamide was cooled in an acetone/ice bath at about -10°C under a dry nitrogen atmosphere. Powdered lithium thiomethoxide (30 mg, 2.5 equiv) were added and the reaction was then left stirring for 2 hr while maintaining the bath temperature below 0°C. The reaction was then quenched by adding a saturated solution of NH_4Cl with vigorous stirring. After partitioning the resulting mixture between EtOAc and water, the organic phase was separated and washed with water (3 times), brine and dried (Na_2SO_4). Removal of the solvents was followed by chromatography on a silica gel preparative tlc plate (2 mm, developed 3 times with a mixture of EtOAc : hexane = 1 : 3) to afford 82 mg (38%) of 2'-O-(t-butyldimethylsilyl)-7-deoxy-7α-thiomethylpaclitaxel: ^{1}H NMR ($CDCl_3$) δ -0.36 (s, 3H), -0.07 (s, 3H), 0.76 (s, 9H), 1.18 (s, 3H), 1.16 (s, 3H), 1.62 (s, 3H), 1.81 (s, 3H), 2.02 (s, 3H), 2.2-2.7 (m, 5H), 2.10 (s, 3H), 2.58 (s, 3H), 4.01 (d, 1H, J = 7.0 Hz), 4.32 (d, 1H, J = 8.3 Hz) 4.62 (d, 1H, J = 8.3 Hz), 4.66 (d, 1H, J = 1.7 Hz), 5.00 (m, 1H), 5.70 (d, 1H, J = 7.0 Hz), 5.78 (d, 1H, J = 9.7 Hz), 6.27 (m, 1H), 7.08 (d, 1H, J = 9.0 Hz), 7.26 - 7.61 (m, 12H), 7.74 (d, 2H, J = 7.3 Hz), 8.13 (d, 2H, J = 7.0 Hz); LRMS (ESI) 998 ($[M+H]^+$).

A solution of 2'-O-(t-butyldimethylsilyl)-7-deoxy-7•-thiomethylpaclitaxel (195 mg, 0.195 mmole) in dry THF (2 mL) and under a dry nitrogen atmosphere was cooled in an acetone/ice bath at about -10°C. A solution of tetrabutylammonium fluoride (0.22 mL, 1.0 M in THF, 1.1 equiv) was added. After 20 min, the reaction was quenched by adding a saturated solution of NH_4Cl with vigourous stirring. This was extracted with EtOAc (3 times) and the combined organic extracts were washed with brine and dried (Na_2SO_4). Removal of the solvents was followed by chromatography on a silica gel preparative tlc plate (2 mm, developed 3 times with a mixture of EtOAc : hexane = 3 : 2) to afford 140 mg (81%) of 7-deoxy-7α-thiomethylpaclitaxel **7**: ^{1}H NMR ($CDCl_3$) δ 1.16 (s, 3H), 1.17 (s, 3H), 1.80 (s, 3H), 1.88 (s, 3H), 2.09 (s, 3H), 2.18 (s, 3H) 2.3 - 2.6 (m, 5H), 2.41 (s, 3H), 3.42 (d, 1H, J = 4.6 Hz), 4.00 (d, 1H, J = 7.0 Hz), 4.28 (d, 1H, J = 8.2Hz), 4.61 (d, 1H, J = 4.6 Hz), 4.79 (dd 1H, J = 2.4, 4.6 Hz), 4.95 (m, 1H), 5.69 (d, 1H, J = 7.0 Hz), 5.84 (dd, 1H, J = 1.9, 9.5 Hz), 5.82 (m, 1H), 7.01 (d, 1H, J = 9.2 Hz), 7.19 (s, 1H), 7.32 - 7.62 (m, 11H), 7.74 (d, 2H, J = 7.7 Hz), 8.13 (d, 2H, J = 7.7 Hz); LRMS (negative ESI) 882 ($[M-H]^-$) .

Compound **8**

Potassium thioacetate (7.30 gm, 10 equiv) was added to a stirred solution of 2'-O-(t-butyldimethylsilyl)-7β-O-trifluoromethanesulfonyl-paclitaxel **6** (7.07 g, 6.40 mmole) in 64 mL of absolute EtOH at room temperature under a dry nitrogen atmosphere. After stirring for 45 hr in the dark, the reaction was

partitioned between a mixture of EtOAc : hexane = 1 : 1 and water, the organic phase was separated and washed with water (2 times), brine and dried (Na_2SO_4). Removal of the solvents was followed by chromatography on a silica gel column (gradient elution with mixtures of EtOAc : hexane = 1 : 4 to 7 : 13) to afford 5.82 gm (89%) of 2'-O-(t-butyldimethylsilyl)-7-deoxy-7α-thioacetoxy paclitaxel **8**: ^{1}H NMR ($CDCl_3$) δ -0.33 (s, 3H), -0.05 (s, 3H), 0.78 (s, 9H), 1.12 (s, 3H), 1.17 (s, 3H), 1.8 - 2.4 (m, 4H), 2.04 (s, 3H), 2.13 (s, 3H), 2.43 (s, 3H), 2.63 (s, 3H), 3.89 (d, 1H, J = 7.0 Hz), 4.00 (m, 1H), 4.28 (d, 1H, J = 8.3 Hz), 4.64 (d, 1H, J = 8.4 Hz), 4.68 (d, 1H, J = 1.9 Hz), 4.85 (m, 1H), 5.69 (d, 1H, J = 7.0 Hz), 5.80 (br d, 1H, J = 8.5 Hz), 6.29 (m, 1H), 6.89 (s, 1H), 7.06 (d, 1H, J = 9.0 Hz), 7.3 - 7.6 (m, 11H), 7.74 (m, 2H), 8.15 (m, 2H); LRMS (ESI) 1026 ($[M+H]^+$).

Compound **9**

A solution of 2'-O-(t-butyldimethylsilyl)-7-deoxy-7α-thioacetoxy paclitaxel **8** (0.96 gm, 0.94 mmole) in anhydrous EtOH (50 mL) was sparged with dry nitrogen for 45 min. This solution was then saturated with anhydrous NH_3 and then left stirring at room temperature for 1hr. It was sparged with dry nitrogen for 20 min and the solvent was removed. The residue was chromatographed on a silica gel column (elution with 200 mL portions of hexane containing 50, 60, 70, 80 (twice) mL of EtOAc) to afford 0.57 gm (61%) of slightly impure 2'-O-(t-butyldimethylsilyl)-7-deoxy-7α-thiopaclitaxel **9**: ^{1}H NMR ($CDCl_3$) δ -0.34 (s, 3H), -0.07 (s, 3H), 0.76 (s, 9H), 1.15 (s, 3H), 1.18 (s, 3H), 1.84 (s, 3H), 1.97 (s, 3H), 2.1 - 2.6 (m, 4H), 2.17 (s, 3H), 2.63 (s, 3H), 2.93 (m, 1H), 3.70 (d, 1H, J = 13.0 Hz), 4.06 (d, 1H, J = 7.1 Hz), 4.26 (d, 1H, J = 8.4 Hz), 4.67 (m, 2H), 4.95 (m, 1H), 5.71 (d, 1H, J = 6.8 Hz), 5.78 (d, 1H, J = 8.9 Hz), 6.28 (m, 1H), 7.07 (d, 1H, J = 8.9 Hz), 7.2 - 7.6 (m, 12 Hz), 7.74 (d, 2H, J = 7.4 Hz), 8.15 (d, 2H, J = 7.9 Hz); LRMS (ESI) 984 ($[M+H]^+$).

Compound **12**

A solution of 2'-O-(t-butyldimethylsilyl)-7-deoxy-7α-thiopaclitaxel **9** (500 mg, 0.508 mmole) in dry toluene (20 mL) at room temperature was sparged with dry nitrogen for 20 min. 1,8-Diazabicyclo[5.4.0]undec-7-ene (0.152 mL, 2 equiv) was added and the reaction was placed in an oil bath at approximately 95°C. The isomerization of the starting material into its 7β-isomer was monitored by HPLC (Vydac 218TP reverse phase column, gradient elution: 75% aqueous CH_3CN to 100% CH_3CN over 9 min at 2 mL per min). After 18.5 hr, the ratio of 7α to 7β-thiol isomers was about 1 : 9 and the reaction was allowed to cool to room temperature and diluted with a mixture of EtOAc : hexane = 3 : 2. This was washed with saturated aqueous NH_4Cl (twice), brine, and then dried (Na_2SO_4). Removal of the solvents followed by radial chromatography (1 mm silica gel plate, gradient elution with mixtures of EtOAc :

hexane = 1 : 4 to 7 : 13) afforded 344 mg (69%) of 2'-O-(t-butyldimethylsilyl)-7-deoxy-7β-thiopaclitaxel **12**: ^{1}H NMR ($CDCl_3$) δ -0.31 (s, 3H), -0.05 (s, 3H), 0.79 (s, 9H), 1.17 (s, 3H), 1.20 (s, 3H), 1.69 (s, 3H), 1.8 - 2.2 (m, 3H), 1.91 (s, 3H), 2.40 (dd, 1H, J = 9.3, 15.3 Hz), 2.21 (s, 3H), 2.56 (s, 3H), 2.68 (m, 1H), 3.84 (d, 1H, J = 6.7 Hz), 4.17 (d, 1H, J = 8.4 Hz), 4.32 (d, 1H, J = 8.4 Hz), 4.65 (d, 1H, J = 2.1 Hz), 4.94 (d, 1H, J = 9.3 Hz), 5.69 (m, 2H), 6.23 (m, 1H), 6.28 (s, 1H), 7.05 (d, 1H, J = 8.8 Hz), 7.3 - 7.6 (m, 11H), 7.73 (d, 2H, J = 7.2 Hz), 8.11 (d, 2H, J = 7.2 Hz); LRMS (ESI) 984 ($[M+H]^+$).

Compound **13**

A solution of 2'-O-(t-butyldimethylsilyl)-7-deoxy-7β-thiopaclitaxel **12** (234 mg, 0.238 mmole) in dry THF (3 mL) and under a dry nitrogen atmosphere was cooled in an ice bath. A solution of tetrabutylammonium fluoride (0.26 mL, 1.0 M in THF, 1.1 equiv) was added. After 5 min, the reaction was quenched by adding a saturated solution of NH_4Cl with vigourous stirring. This was extracted with EtOAc (2 times) and the combined organic extracts were washed with brine and dried (Na_2SO_4). Removal of the solvents was followed by column chromatography on silica gel (elution with 100 mL portions of hexane containing 30, 35, 40, 45, 50, 55 mL of EtOAc) to afford 115 mg (56%) of 7-deoxy-7β-thiomethylpaclitaxel **13**: ^{1}H NMR ($CDCl_3$) δ 1.19 (s, 3H), 1.18 (s, 3H), 1.69 (s, 3H), 1.76 (s, 3H), 1.8 - 2.3 (m, 4H), 2.21 (s, 3H), 2.36 (s, 3H), 2.66 (m, 1H), 3.53 (m, 1H), 3.61 (br s, 1H), 3.79 (d, 1H, J = 6.6 Hz), 4.15 (d, 1H, J = 8.4 Hz), 4.29 (d, 1H, J = 8.4Hz), 4.77 (br s, 1H), 4.90 (d, 1H, J = 8.8 Hz), 5.67 (d, 1H, J = 6.6 Hz), 5.78 (br d, 1H, J = 8.1 Hz), 6.16 (m, 1H), 6.24 (s, 1H), 7.02 (d, 1H, J = 8.8 Hz), 7.2 - 7.6 (m, 11H), 7.74 (d, 2H, J = 8.0 Hz), 8.09 (d, 2H, J = 8.0 Hz); LRMS (negative ESI) 868 ($[M-H]^-$) .

Compound **11**

Bromomethyl methyl ether (0.006 mL, 1.1 equiv) was added to a solution of 2'-O-(t-butyldimethylsilyl)-7-deoxy-7β-thiopaclitaxel **12** (61 mg, 0.062 mmole) and 1,8-diazabicyclo[5.4.0]undec-7-ene (0.152 mL, 1.5 equiv) in dry CH_2Cl_2 (1 mL) and under a dry nitrogen atmosphere. After 10 min, the reaction was diluted with a mixture of EtOAc : hexane = 3 : 2. It was then washed with saturated aqueous NH_4Cl (twice), brine, and dried (Na_2SO_4). Removal of the solvents was followed by radial chromatography (1 mm silica gel plate, gradient elution with mixtures of EtOAc : hexane = 1 : 4 to 7 : 13) to afford 43 mg (67%) of 2'-O-(t-butyldimethylsilyl)-7-deoxy-7β-thiomethoxymethylpaclitaxel: ^{1}H NMR ($CDCl_3$) δ -0.32 (s, 3H), -0.04 (s, 3H), 0.78 (s, 9H), 1.17 (s, 3H), 1.22 (s, 3H), 1.73 (s, 3H), 2.0 - 2.4 (m, 3H), 2.01 (s, 3H), 2.18 (s, 3H), 2.56 (s, 3H), 2.84 (m, 1H), 3.34 (s, 3H), 3.37 (m, 1H), 3.89 (d, 1H, J = 6.7 Hz), 4.18 (d, 1H, J = 8.5 Hz), 4.34 (d, 1H, J = 8.5 Hz), 4.62 (d, 1H, J = 11.9 Hz), 4.65 (d, 1H, J = 1.8 Hz), 4.70 (d, 1H, J = 11.9 Hz), 4.96 (d, 1H, J = 8.3 Hz), 5.66 (d, 1H, J = 6.7 Hz), 5.72 (d, 1H, J = 8.9 Hz), 6.24 (m, 1H), 6.49 (s, 1H), 7.06 (d,

1H, J = 8.9 Hz), 7.3 - 7.6 (m, 11H), 7.73 (d, 2H, J = 7.9 Hz), 8.11 (d, 2H, J = 7.9 Hz); LRMS (ESI) 1028 ($[M+H]^+$).

A solution of tetrabutylammonium fluoride (0.57 mL, 1.0 M in THF, 1.1 equiv) was added to a solution of 2'-O-(t-butyldimethylsilyl)-7-deoxy-7β-thiomethoxymethyl paclitaxel (511 mg, 0.516 mmole) in dry THF (5 mL) that was in an ice bath and maintained under a dry nitrogen atmosphere. After 5 min, the reaction was quenched by adding a saturated solution of NH_4Cl with vigourous stirring. This was extracted with EtOAc (3 times) and the combined organic extracts were washed with brine and dried (Na_2SO_4). Removal of the solvents was followed by column chromatography on silica gel (elution with 100 mL portions of hexane containing 30, 35, 40, 45, 50, 55 60 mL of EtOAc) to afford 365 mg (77%) of 7-deoxy-7β-thiomethoxymethyl paclitaxel **11**: ^1H NMR ($CDCl_3$) δ 1.16 (s, 3H), 1.22 (s, 3H), 1.56 (s, 3H), 1.85 (s, 3H), 2.18 (s, 3H), 2.0 - 2.4 (m, 3H), 2.35 (s, 3H), 2.82 (m, 1H), 3.31 (m, 1H), 3.32 (s, 1H), 3.66 (d, 1H, J = 4.6 Hz), 3.82 (d, 1H, J = 6.5 Hz), 4.15 (d, 1H, J = 8.3 Hz), 4.30 (d, 1H, J = 8.3Hz), 4.58 (d, 1H, J = 11.9 Hz), 4.70 (d, 1H, J = 11.9 Hz), 4.77 (dd, 1H, J = 2.6, 4.6 Hz), 4.92 (d, 1H, J = 9.3 Hz), 5.62 (d, 1H, J = 6.7 Hz), 5.79 (m, 1H), 6.15 (m, 1H), 6.46 (s, 1H), 7.07 (d, 1H, J = 8.9 Hz), 7.3 - 7.6 (m, 11H), 7.76 (m, 2H), 8.08 (d, 2H); LRMS (ESI) 914 ($[M+H]^+$) .

Compound **14**

Iodomethane (0.100 mL, 1.1 equiv) was added to a solution of 7-deoxy-7β-thiopaclitaxel **13** (1.30 gm, 1.49 mmole) and 1,8-diazabicyclo[5.4.0]undec-7-ene (0.33 mL, 1.5 equiv) in dry CH_2Cl_2 (14 mL) and under a dry nitrogen atmosphere. After 5 min, the reaction was diluted with CH_2Cl_2, washed with saturated aqueous NH_4Cl, water, and dried (Na_2SO_4). Removal of the solvents was followed by radial chromatography (2 mm silica gel plate, gradient elution with mixtures of EtOAc : hexane = 1 : 4 to 1 : 3) afforded 1.04 gm (79%) of 7-deoxy-7β-thiomethylpaclitaxel **14**: ^1H NMR ($CDCl_3$) δ 1.16 (s, 3H), 1.21 (s, 3H), 1.70 (s, 3H), 1.84 (s, 3H), 2.09 - 2.27 (m, 3H), 2.12 (s, 3H) 2.19 (s, 1H), 2.35 (s, 3H), 2.73 (m, 1H), 3.04 (dd, 1H, J = 6.5, 11.8 Hz), 3.67 (m, 1H), 3.80 (d, 1H, J = 6.6 Hz), 4.14 (d, 1H, J = 8.4 Hz), 4.30 (d, 1H, J = 8.4 Hz), 4.77 (br s, 1H), 4.94 (d, 1H, J = 8.1 Hz), 5.61 (d, 1H, J = 6.6 Hz), 5.78 (dd, 1H, J = 2.4, 8.9 Hz), 6.14 (m, 1H), 6.53 (s, 1H), 7.07 (d, 1H, J = 8.9 Hz), 7.3 - 7.6 (m, 11H), 7.75 (d, 2H, J = 7.2 Hz), 8.08 (d, 2H, J = 7.2 Hz); LRMS (negative ESI) 882 ($[M-H]^-$) .