Supporting Information

Targeting FtsZ for anti-tuberculosis drug discovery: non-cytotoxic taxanes as novel anti-TB agents

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Synthetic procedures and characterization data for all compounds

General Methods: ^{1}H and ^{13}C NMR spectra were measured on a Bruker AC-250 NMR spectrometer or a Varian 300, 400, or 500 NMR spectrometer. Melting points were measured on a Thomas Hoover Capillary melting point apparatus and are uncorrected. Optical rotations were measured on a Perkin-Elmer Model 241 polarimeter. TLC was performed on Merck DC-alufolien with Kieselgel 60F-254 and column chromatography was carried out on silica gel 60 (Merck; 230-400 mesh ASTM). High-resolution mass spectra were obtained from the University of California, Riverside Mass Spectrometry Facility, Riverside, CA; or Mass Spectrometry Laboratory, University of Illinois at Urbana-Champaign, Urbana, IL. Purity was determined with Shimadzu HPLC (LC2010A) system. HPLC1: Phenomenex®, Jupiter, C18, 10μ, 250 x 4.6 mm column; 70:30 v/v $CH_3CN:H_2O$ over 10 min, followed by 70:30-90:10 v/v $CH_3CN:H_2O$ over 3 min, then hold at 90/10 v/v $CH_3CN:H_2O$ over 10 min; flow rate 1.0 mL/min; wavelength 254 nm. HPLC2: Waters, Nova-Pak®, C18, 3.9 x 150 mm column; 60:40 v/v $CH_3CN:H_2O$ over 10 min, followed by 60:40-90:10 v/v $CH_3CN:H_2O$ over 3 min, then hold at 90/10 v/v $CH_3CN:H_2O$ over 10 min; flow rate 1.0 mL/min; wavelength 254 nm. HPLC3: Phenomenex®, Curosil–B, 5μ, 250 x 4.60mm column, gradient 50:50-90:10 v/v $CH_3CN:H_2O$ over 15 min, then hold at 90/10 v/v $CH_3CN:H_2O$ for 10 min; flow rate 1.0 mL/min; wavelength 220 nm. HPLC4: Phenomenex®, Curosil–B, 5μ, 250 x 4.60mm column, gradient 20:80-90:10 v/v $CH_3CN:H_2O$ over 30 min, followed by 90:10 v/v $CH_3CN:H_2O$ over 5 min; flow rate 1.0 mL/min; wavelength 254 nm. HPLC5: Agilent, Zorbax, Eclipse XDB, C8, 5μ, 4.6 x 150mm column; 50:50 v/v $CH_3CN:H_2O$ over 10 min, followed by 50:50-90:10 v/v $CH_3CN:H_2O$ over 5 min, then hold at 90/10 v/v $CH_3CN:H_2O$ over 10 min; flow rate 0.5 mL/min; wavelength 254 nm.

Materials: The chemicals were purchased from Aldrich Co. and Sigma and purified before use by standard methods. Tetrahydrofuran was freshly distilled from sodium metal and benzophenone. Dichloromethane was also distilled immediately prior to use under nitrogen from calcium hydride. 10-Deacetylbaccatin III (DAB) and 14-b-hydroxy-10-deacetylbaccatin (14-OH-DAB) were obtained from Indena, SpA, Italy.

Acylation at the C-13 position

To a solution of **7**, 10-Bis (triethylsilyl)-10-deacetylbaccatin III **(1a), 7**, 10-Bis (triethylsilyl)-2-debenzoyl-2-(4-methoxybenzoyl)-10-deacetylbaccatin III **(1b)** or 7,9- Bis (triethylsilyl)-10-dehydro-7, 8-*seco*-10-deacetylbaccatin III **(9)** (0.15-0.2 M), DMAP (0.2 equiv) and the corresponding acid (2.2 equiv) in toulune/ dichloromethane (1/1) was added DIC (4.0 equiv) at room temperature with stirring. After stirring for 10-15 h, the solvent was evaporated *in vacuo*. Purification of the crude product by short silica gel chromatography using ethyl acetate/hexane (4:1) as eluant afforded TES protected C-13 coupling product contaminated by DIC-acid complex, which were directly used in the next step.

To a solution of TES protected C-13 coupling product in a (1:1) mixture of pyridine and acetonitrile (4 mL/100mg of starting material) at 0 ^{o}C was added a 70 % solution of HF in pyridine (1 mL/100 mg of starting material) with stirring. After stirring overnight at room temperature, the reaction was quenched with $NaHCO_3$ solution and extracted with ethyl acetate. The combined organic layers were washed with a saturated solution of copper sulfate and with water, then dried over magnesium sulfate, filtered and concentrated. Purification of the crude

product by silica gel chromatography (hexanes/EtOAc = 1/1) afforded to afford **2a-2b, 4a-4g, 10a-10d** as white solid.

13-[3-(2-Naphthyl)prop-2-enoyl]-10-deacetylbaccatin III (2a):[1]
Yield: 75 %; mp 189-192 ^{o}C; $[\alpha]_D^{20}$ -32.5 (*c* 0.40, $CHCl_3$); ^{1}HNMR (300 MHz, $CDCl_3$) δ 1.15 (s, 3H), 1.26 (s, 3H), 1.70 (m, 2H), 1.79 (s, 3H), 1.93 (m, 1H), 2.09 (s, 3H), 2.24 (m, 1H), 2.30 (s, 3H), 2.46 (dd, *J* = 9.2, 16.0 Hz, 1H), 2.65 (m, 1H), 4.02 (d, *J* = 7.0 Hz, 1H), 4.26 (m, 4H), 4.99(d, *J* = 8.3Hz, 1H), 5.31(s, 1H), 5.71 (d, *J* = 7.0 Hz, 1H), 6.19 (m, 1H), 6.61 (d, *J* = 16.0 Hz, 1H), 7.51 (m, 4H), 7.60 (m, 3H), 7.70 (d, *J* = 9.2 Hz, 1H), 7.89 (m, 2H), 8.03(m, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 9.8, 15.1, 2.02, 22.6, 26.5,36.5, 37.1, 42.9, 46.8, 57.7, 70.3, 72.1, 74.7, 76.6, 79.0, 81.0, 84.1, 117.1, 123.1, 126.4, 127.6, 127.8, 128.6, 128.9, 129.2, 130.0, 130.5, 131.4, 133.3, 134.4, 135.8, 139.3, 143.9, 146.6, 166.3, 166.9, 211.5. HRMS (FAB) *m/z* calcd for $C_{42}H_{44}O_{11}H^+$: 725.2962, Found: 725.2942 (Δ = -2.0 ppm). HPLC1: 5.38 min, purity > 97%; HPLC3: 8.56 min, purity > 97%. All data were in agreement with literature values.[1]

13-[3-(2-Naphthyl)prop-2-enoyl]-2-debenzoyl-2-(4-methoxybenzoyl)-10-deacetylbaccatin III (2b):

Yield: 88%; mp 190-192 ^{o}C; $[\alpha]_D^{20}$ -78.0 (*c* 0.67, $CHCl_3$); ^{1}HNMR (300 MHz, $CDCl_3$) δ 1.15 (s, 3H), 1.26 (s, 3H), 1.70 (m, 2H), 1.79 (s, 3H), 1.93 (m, 1H), 2.09 (s, 3H), 2.24 (m, 1H), 2.30 (s, 3H), 2.46 (dd, *J* = 9.2, 16.0 Hz, 1H), 2.65 (m, 1H), 3.86 (s, 1H), 4.02 (d, *J* = 7.0 Hz, 1H), 4.26 (m, 4H), 4.99 (d, *J* = 8.3Hz, 1H), 5.31 (s, 1H), 5.71 (d, *J* = 7.0 Hz, 1H), 6.19 (m, 1H), 6.61 (d, *J* = 16.0 Hz, 1H), 6.98 (d, *J* = 8.7 Hz, 2H), 7.59 (m, 2H), 7.73 (d, *J* = 7.2, 1H), 7.92 (m, 3H), 8.03 (m, 4H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 9.7, 15.8, 22.9, 29.9, 35.9, 36.5, 43.3, 55.7, 59.0, 70.4, 72.6, 74.7, 75.8, 79.5, 81.4, 114.2, 117.1, 121.7, 123.4, 127.2, 127.9, 128.1, 128.9, 129.2, 130.8, 131.6, 132.4, 133.2, 133.5, 134.7, 143.2, 147.0, 166.5, 170.1, 204.2. HRMS (FAB) *m/z* calcd for $C_{43}H_{44}O_{12}H^+$: 753.2911, Found: 753.2888 (Δ = -2.3 ppm). HPLC1: 5.31 min, purity > 96%; HPLC3: 8.29 min, purity > 96%.

13-[3-(2-Naphthyl)prop-1-enoyl]-10-deacetylbaccatin III (4a):

Yield: 80%; mp 234-235 ^{o}C; $[\alpha]_D^{20}$ –133.3 (*c* 0.8, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.15 (s, 3H), 1.26 (s, 3H), 1.70 (m, 2H), 1.79 (s, 3H), 1.93 (m, 1H), 2.09 (s, 3H), 2.24 (m, 1H), 2.30 (s, 3H), 2.46 (dd, *J* = 9.2, 16.0 Hz, 1H), 2.65 (m, 1H), 4.02 (d, *J* = 7.0 Hz, 1H), 4.26 (m, 4H), 4.99(d, *J* = 8.3Hz, 1H), 5.29(s, 1H), 5.71 (d, *J* = 7.0 Hz, 1H), 6.21 (m, 1H), 6.61 (d, *J* = 16.0 Hz, 1H), 7.48 (m, 2H), 7.60(m, 4H), 7.82 (d, *J* = 7.2 Hz, 1H), 7.94 (m, 2H), 8.28(m, 1H), 8.71 (d, *J* = 16 Hz, 1H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 10.0, 15.4, 20.4, 22.8, 26.7, 29.9, 36.7, 37.3, 43.2, 47.0, 58.0, 70.6, 72.3, 74.8, 76.6, 79.0, 81.2, 84.3, 119.7, 123.4, 125.3, 125.7, 126.7, 127.5, 128.9, 129.1, 129.5, 130.3, 131.4, 131.7, 134.0, 136.1, 139.5, 143.8, 166.4, 167.2, 170.1, 211.5. HRMS (FAB) *m/z* calcd for $C_{42}H_{44}O_{11}H^+$: 725.2962, Found: 725.2969 (Δ = 0.7 ppm). HPLC1: 5.25 min, purity > 98%; HPLC3: 8.54 min, purity > 98%.

13-[4-Phenoxycinnamoyl]-10-deacetylbaccatin III (4b):

Yield: 83%; mp 188-191 ^{o}C; $[\alpha]_D^{20}$ –137 (*c* 1.6, $CHCl_3$); ^{1}H NMR (300 MHz, Acetone-d_6) δ 1.15 (s, 3H), 1.27 (s, 3H), 1.71 (m, 2H), 1.45 (m, 3H), 1.78 (s, 3H), 1.93 (m, 1H), 2.09 (s, 3H), 2.24 (m, 1H), 2.30 (s, 3H), 2.46 (dd, *J* = 9.2, 16.0 Hz, 1H), 2.65 (m, 1H), 3.99 (d, *J* = 7.0 Hz,

1H), 4.26 (m, 4H), 4.99(d, J = 8.3Hz, 1H), 5.27 (s, 1H), 5.71 (d, J = 7.0 Hz, 1H), 6.20 (m, 1H), 6.60 (d, J = 16.0 Hz, 1H), 7.06 (d, J = 6.4 Hz, 2H), 7.10 (d, J = 5.7 Hz, 2H), 7.23 (m, 1H), 7.44 (m, 2H), 7.48 (m, 2H), 7.62 (m, 1H), 7.78 (d, J = 6.3Hz, 2H), 7.84 (m, 1H), 8.09 (d, J = 5.5 Hz, 2H); ^{13}C NMR (75 MHz, Acetone-d_6) δ 9.6, 13.8, 14.3, 20.2, 22.2, 26.4, 37.1, 43.4, 47.1, 58.0, 70.3, 72.0, 74.7, 75.2, 76.3, 78.0, 81.2, 84.4, 116.5, 118.5, 119.9, 124.5, 128.7, 129.4, 130.1, 130.3, 130.5, 130.7, 133.3, 136.9, 138.1, 145.3, 156.4, 160.1, 165.9, 166.3, 170.1, 205.6, 211.0. HRMS (FAB) *m/z* calcd for $C_{44}H_{46}O_{12}H^+$: 767.3068, Found: 767.3057 (Δ = -1.0 ppm). HPLC1: 6.07 min, purity > 96%; HPLC3: 9.42 min, purity > 96%.

13- [4-Phenylthiophenyl)-10-deacetylbaccatin III (4c):
Yield: 81%; mp 190-192 °C; $[\alpha]_D^{20}$ –170.1 (*c* 1.1, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.14 (s, 3H), 1.23 (s, 3H), 1.75 (m, 2H), 1.78 (s, 3H), 1,88 (m, 1H), 1.86 (m, 1H), 2.03 (s, 3H), 2.24 (m, 4H), 2.42 (m, 1H), 2.62 (m, 1H), 3.99 (d, J = 7.0 Hz, 1H), 4.26 (m, 4H), 4.99(d, J = 8.3Hz, 1H), 5.26 (s, 1H), 5.68 (d, J = 7.0 Hz, 1H), 6.15 (m, 1H), 6.43 (d, J = 16.0 Hz, 1H), 7.34 (m, 1H), 7.39 (m, 3H), 7.44 (m, 2H), 7.48 (m, 6H), 7.59 (m, 1H), 7.76 (d, J = 15.6 Hz, 1H), 8.05 (d, J = 7.2 Hz, 2H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 10.0, 15.3, 20.4, 22.8, 26.7, 29.9, 36.7, 37.3, 43.1, 47.0, 58.0, 70.4, 72.4, 75.0, 79.2, 81.3, 84.3, 116.8, 128.7, 128.9, 129.0, 129.2, 129.5, 129.8, 130.2, 131.9, 133.5, 133.9, 136.0, 139.5, 141.7, 145.9, 166.5, 167.1, 170.0, 211.7. HRMS (FAB) *m/z* calcd for $C_{44}H_{46}O_{11}SH^+$: 783.2839, Found: 783.2856 (Δ = 1.7 ppm). HPLC1: 7.23 min, purity > 98%; HPLC3: 10.15 min, purity > 98%.

13-[3-(6-Methoxy-2-naphthyl)prop-2-enoyl]-10-deacetylbaccatin III (4d):
Yield: 75%; mp: 218-220 °C; ^{1}HNMR (300 MHz, $CDCl_3$) δ 1.14 (s, 3H), 1.25 (s, 3H), 1.63 (m, 2H), 1.78 (s, 3H), 1.90 (m, 2H), 2.09 (s, 3H), 2.25 (m, 1H), 2.30 (s, 3H), 2.44 (m, 1H), 2.65 (m, 1H), 3.95 (s, 3H), 4.01 (d, J = 7.2 Hz, 1H), 4.26 (m, 4H), 4.99(d, J = 8.3Hz, 1H), 5.29(s, 1H), 5.71 (d, J = 7.0 Hz, 1H), 6.17 (m, 1H), 6.61 (d, J = 16.0 Hz, 1H), 7.18 (m, 2H), 7.45(m, 2H), 7.57 (m, 1H), 7.66 (m, 1H), 7.78 (m, 2H), 7.94 (m, 2H), 8.06 (m, 2H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 10.0, 15.4, 20.4, 22.9, 26.7, 29.9, 36.8, 37.3, 43.1, 47.0, 55.7, 58.0, 70.4, 72.4, 75.0, 79.2, 81,2, 84.3, 106.3, 116.2, 119.9, 124.1, 128.0, 128.9, 129.5, 130.3, 130.5, 133.9, 136.0, 136.2, 140.0, 147.0, 159.4, 166.7, 167.1, 170.2, 211.8. HRMS (FAB) m/z calcd for $C_{43}H_{46}O_{12}H^+$: 755.3068, Found: 755.3058 (_ = -0.9 ppm). HPLC1: 5.20 min, purity > 98%; HPLC3: 8.38 min, purity > 98%.

13-[3-(2-Naphthyl)propanoyl]-10-deacetylbaccatin III (4e):[1]
Yield: 80 %; mp: 181-184 °C; $[\alpha]_D^{20}$ –76.9 (*c* 0.26, $CHCl_3$); IR ($CDCl_3$, cm^{-1}) 3449, 3331, 2919, 2837, 1708, 1619, 1443, 1367, 1308, 1267, 1238, 1161, 1138, 1108, 1067, 1020, 985, 961, 709; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.10 (s, 3 H), 1.20 (s, 3 H), 1.26 (s, 3 H), 1.73 (m, 3 H), 1.81 (s, 3 H), 1.90 (m, 1 H), 2.17 (d, J = 8.7 Hz, 1 H), 2.22 (s, 1 H), 2.56 (m, 1 H), 2.82 (dd, J = 7.0, 14.3 Hz, 2 H), 3.20 (t, J = 7.0 Hz, 2 H), 3.45 (m, 1 H), 3.90 (d, J = 7.0 Hz, 1 H), 4.17 (m, 3 H), 4.94 (d, J = 9.2 Hz, 1 H), 5.19 (s, 1 H), 5.64 (d, J = 6.7 Hz, 1 H), 6.18 (t, J = 8.3 Hz, 1 H), 7.36 (d, J = 7.5 Hz, 1 H), 7.46 (m, 4 H), 7.62 (m, 2 H), 7.80 (m, 3 H), 8.04 (d, J = 7.5 Hz, 2 H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 9.8, 14.5, 20.3, 22.5, 24.9, 25.6, 26.3, 29.7, 31.0, 33.8, 35.9, 36.0, 36.9, 42.9, 46.1, 49.2, 57.6, 60.4, 69.8, 71.9, 74.6, 74.9, 78.8, 80.9, 84.1, 125.6, 126.2, 126.5, 126.7, 127.4, 127.6, 128.3, 129.2, 130.0, 132.2, 133.6, 133.7, 135.6, 137.5, 139.0, 166.9, 169.6, 172.2, 211.4. HRMS (FAB) *m/z* calcd for $C_{42}H_{46}O_{11}H^+$: 727.3118, Found: 727.3130 (Δ = 1.2 ppm). HPLC1:

5.06 min, purity > 96%; HPLC3: 8.61 min, purity > 96%. All data were in agreement with literature values.[1]

13-[4-Benzoylcinnamoyl]-10-deacetybaccatin III (4f):
Yield: 82%; mp: 208-210 ^{o}C; $[\alpha]_D^{20}$ –93.4 (*c* 0.7, EtOAc); ^{1}H NMR (300 MHz, Acetone-d_6) δ 1.14 (s, 3H), 1.25 (s, 3H), 1.70 (m, 2H), 1.46 (m, 3H), 1.79 (s, 3H), 1.93 (m, 1H), 2.09 (s, 3H), 2.24 (m, 1H), 2.30 (s, 3H), 2.46 (dd, J=9.2, 16.0 Hz, 1H), 2.65 (m, 1H), 3.99 (d, *J* = 7.0 Hz, 1H), 4.26 (m, 4H), 4.99(d, *J* = 8.3Hz, 1H), 5.27 (s, 1H), 5.71 (d, *J* = 7.0 Hz, 1H), 6.19 (m, 1H), 6.59 (d, *J* = 16.0 Hz, 1H), 7.36 (d, *J* = 8.8 Hz, 1H), 7.46 (m, 3H), 7.59 (m, 1H), 7.71 (d, *J* = 8.0, 2H), 7.91 (m, 5H), 8.06 (d, *J* = 7.2, 2H); ^{13}C NMR (75 MHz, Acetone-d_6) δ 9.6, 14.4, 20.2, 22.2, 26.4, 37.1, 43.4, 47.1, 58.1, 70.7, 72.0, 74.7, 75.2, 76.3, 77.9, 81.2, 84.4, 120.24, 128.5, 128.7, 129.9, 130.1, 130.6, 132.9, 137.1, 137.6, 137.9, 138.2, 139.3, 144.7, 148.8, 165.9, 166.0, 170.1, 195.2, 208.6, 211.0. HRMS (FAB) *m/z* calcd for $C_{45}H_{46}O_{12}H^{+}$: 779.3068, Found: 779.3073 (Δ = 0.5 ppm). HPLC1: 4.81 min, purity > 96%; HPLC3: 8.17 min, purity > 96%.

13-[4-(4-Ethoxybenzoyl)cinnamoyl]-10-deacetybaccatin III (4g):
Yield: 85%; mp 192-195 ^{o}C; $[\alpha]_D^{20}$ –100.0 (*c* 0.2, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.14 (s, 3H), 1.25 (s, 3H), 1.70 (m, 2H), 1.46 (m, 3H), 1.79 (s, 3H), 1.93 (m, 1H), 2.09 (s, 3H), 2.24 (m, 1H), 2.30 (s, 3H), 2.46 (dd, *J* = 9.2, 16.0 Hz, 1H), 2.65 (m, 1H), 3.99 (d, *J* = 7.0 Hz, 1H), 4.14 (m, 2H), 4.26 (m, 4H), 4.99(d, *J* = 8.3Hz, 1H), 5.27 (s, 1H), 5.71 (d, *J* = 7.0 Hz, 1H), 6.19 (m, 1H), 6.59 (d, *J* = 16.0 Hz, 1H), 6.96 (d, *J* = 8.8 Hz, 1H), 7.46 (m, 2H), 7.59 (m, 1H), 7.67 (d, *J* = 8.0, 2H), 7.91 (m, 5H), 8.05 (d, *J* = 7.2, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.0, 14.9, 15.3, 20.4, 22.8, 26.7, 29.9, 36.7, 37.3, 43.2, 47.0, 58.0, 64.1, 70.7, 72.4 75.0, 79.1, 81.3, 84.3, 114.4, 119.3, 128.1, 128.9, 129.5, 129.7, 130.3, 130.6, 132.8, 133.9, 136.2, 137.2, 139.3, 140.4, 145.5, 163.2, 166.1, 167.2, 170.0, 193.2, 194.8, 211.7; HRMS (FAB) *m/z* calcd for $C_{47}H_{50}O_{13}H^{+}$: 823.3330, Found: 823.3325 (Δ = -0.4 ppm). HPLC1: 5.49 min, purity > 96%; HPLC3: 8.75 min, purity > 96%.

13-[3-(2-Naphthyl) prop-2-enoyl]-10-dehydro-7, 8-*seco*-10-deacetylbaccatin III (10a):
Yield: 70 %; mp: 157-160 ^{o}C; $[\alpha]_D^{20}$ –178.4 (*c* 3.48, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00-7.60 (m, 13 H), 6.70 (bs, 1 H), 6.50 (m, 1 H), 6.12 (m, 1H, H-13), 5.64 (d, 1H, *J* = 9 Hz), 5.40 (bs, 2H), 4.40 (bs, 2H), 3.90 (bs, 2H), 2.90-1.80 (m, 15H), 1.27 (s, 3H) 1.15 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.5 (10-C), 169.4 (4-Ac), 167.4 (1'-C), 166.5 (2-benz.), 149.0 (9-C), 146.8 (3'-C), 142.5 (11-C), 136.8 (12-C), 134.7 (arom), 134.0 (arom), 133.5 (arom), 131.7 (arom), 130.0 (arom), 129.8 (arom), 129.6 (arom), 129.1(arom), 128.7 (arom), 128.0 (arom), 127.7 (arom), 127.4 (arom), 127.0 (arom), 124.4 (8-C), 123.4 (arom), 117.2 (2'-CH), 88.2 (5-CH), 86.4 (4-C), 80.3 (1-C), 75.1 (20-CH_2), 74.9 (2-CH), 69.3 (13-CH), 60.0 (7-CH_2), 48.7 (3-CH), 43.0 (15-C), 37.2 (6-CH_2), 29.9(14-CH_2), 25.3 (16-CH_3), 21.3 (4-Ac), 20.9 (17-CH_3), 15.1 (18-CH_3), 14.6 (19-CH_3). HRMS (FAB) *m/z* calcd for $C_{42}H_{44}O_{11}H^{+}$: 725.2962, Found: 725.2958 (Δ = -0.4 ppm). HPLC1: 5.03 min, purity > 98%; HPLC3: 8.11 min, purity > 98%.

13-[3-(6-Methoxy-2-naphthyl) prop-2-enoyl]-10-dehydro-7, 8-*seco*-10-deacetylbaccatin III (10b):
Yield: 64%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00-7.40 (m, 10H), 7.18 (m, 2H), 6.65 (bs, 1H), 6.50 (s, 1H), 6.12 (m, 1H, H-13), 5.64 (d, 1H, *J* = 9 Hz), 5.40 (bs, 2H), 4.40 (bs, 2H), 3.90 (bs,

5H), 2.90-1.40 (m, 15H), 1.27 (s, 3H) 1.15 (s, 3H). HRMS (FAB) *m/z* calcd for $C_{43}H_{46}O_{12}H^+$: 755.3068, Found: 755.3061 (_ = -0.7 ppm). HPLC2: min, purity > 95%; HPLC5: 6.70 min, purity > 95%.

13-[(4-Phenylthiophenyl)-10-dehydro-7, 8-*seco*-10-deacetylbaccatin III (10c):
Yield 68 %; mp: 139-140 ^oC ; ^1H NMR (400 MHz, $CDCl_3$) δ 8.00 (bs, 2 H), 7.75 (d, 1 H, *J* = 16 Hz), 7.60 (m, 1 H), 7.45 (m, 5 H), 7.37 (m, 3 H), 7.22 (m, 3 H), 6.50 (bs, 2 H), 6.13 (m, 1 H, 13-H), 5.63 (d, 1 H, *J* = 8 Hz), 5.30 (bs, 2 H), 4.40 (bs, 2 H), 3.80 (bs, 2 H), 2.90-1.80 (m, 15 H), 1.27 (s, 3 H) 1.15 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.2 (10-C), 169.1 (1'-C), 167.2 (4-Ac), 166.2 (2-benz), 149.0 (9-C), 145.7 (3'-C), 142.2 (11-C), 141.3 (12- C), 133.8 (arom), 133.2 (arom), 133.0 (arom), 131.7 (arom), 129.5 (arom), 129.3 (arom), 129.0 (arom), 128.8 (arom), 128.7 (arom), 128.3 (arom), 124.1 (8-C), 116.4 (2'-C), 88.1 (5-CH), 86.1 (4-C), 80.2 (1-C), 75.0 (20-CH_2), 74.6 (2-CH), 68.9 (13-CH), 59.9 (7-CH), 44.4 (3-CH), 42.7 (15-C), 36.9 (6-CH_2), 29.7 (14-CH_2), 25.1 (16-CH_3), 22.1 (4-Ac), 20.7 (17-CH_3), 14.8 (18-CH_3), 14.4 (19-CH_3). HRMS (FAB) *m/z* calcd for $C_{44}H_{46}O_{11}SH^+$: 783.2839, Found: 783.2830 (_ = -0.9 ppm). HPLC1: 6.60 min, purity > 97%; HPLC3: 10.14 min, purity > 97%.

13-[4-Phenoxycinnamoyl]-10-dehydro-7, 8-*seco*-10-deacetylbaccatin III (10d):
Yield: 60%; mp: 135-137 ^oC ; ^1H NMR (400 MHz, $CDCl_3$) δ 8.00 (bs, 2 H), 7.75 (d, *J* = 16 Hz, 1 H), 7.60-7.30 (m, 7 H), 7.18 (m, 2 H), 7.00 (m, 3 H), 6.50 (bs, 2 H), 6.13 (m, 1 H, H-13), 5.63 (d, 1 H, J = 8 Hz), 5.30 (bs, 2 H), 4.40 (bs, 2 H), 3.80 (bs, 2 H), 2.90-1.80 (m, 15 H), 1.27 (s, 3 H) 1.15 (s, 3 H). HRMS (FAB) *m/z* calcd for $C_{44}H_{46}O_{12}H^+$: 767.3068, Found: 767.3060 (_ = -0.8 ppm). HPLC2: min, purity > 95%; HPLC4: 24.37 min, purity > 95%.

Acylation at the C-10 position

Method A:
To a solution of **2a** or **2b (**0.04M) in THF were added $CeCl_3$ (0.1 equiv) and corresponding acid anhydride (10 equiv). After 4-5h, the mixture was diluted with EtOAc, washed with H_2O and brine, dried over anhydrous $MgSO_4$ and concentrated. Purification of the crude product by silica gel chromatography (hexanes/EtOAc = 2/1 to 1/1) afforded **3ac**, **3ad**, **3bc**, and **3bd** as white solid.

10-Hexanoyl-13-[3-(2-naphthyl)prop-2-enoyl]-10-deacetylbaccatin III (3ac):
Yield: 91%; mp 134-136 ^oC; $[\alpha]_D^{20}$ -100 (*c* 1.4, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 0.96 (m, 3H), 1.16 (s, 3H), 1.28 (m, 5H), 1.33(m, 2H), 1.56(m, 2H), 1.69 (m, 2H), 1.79 (m, 3H), 1.93 (m, 1H), 2.03 (s, 3H), 2.24 (m, 3H), 2.42 (s, 3H), 2.46 (dd, *J* = 9.2, 16.0 Hz, 1H), 2.66 (m, 1H), 3.90 (d, *J* = 6.8 Hz, 1H), 4.26 (m, 3H), 4.99(d, *J* = 8.3Hz, 1H), 5.71 (d, *J* = 7.0 Hz, 1H), 6.19 (m, 1H), 6.39 (s, 1H), 6.61 (d, *J* = 16.0 Hz, 1H), 7.51 (m, 4H), 7.70 (d, *J* = 9.2 Hz, 1H), 7.89 (m, 2H), 8.03(m, 3H); ^{13}C NMR (100MHz, $CDCl_3$) δ 9.7, 14.1, 15.8, 21.6, 22.5, 22.9, 24.7, 27.1, 31.5, 34.4, 35.9, 36.5, 43.3, 46.2, 59.0, 70.4, 72.6, 75.1, 75.8, 76.7, 79.5, 81.4, 84.6, 117.1, 123.4, 127.3, 127.9, 128.1, 128.9, 128.9, 129.2, 129.4, 130.3, 130.8, 131.6, 133.2, 133.5, 133.9, 134.7, 143.3, 147.0, 166.5, 167.2, 170.1, 174.3, 204.1; HRMS (FAB) *m/z* calcd for $C_{48}H_{54}O_{12}H^+$:

823.3694, Found: 823.3687 (Δ = -0.7 ppm). HPLC1: 14.97 min, purity > 98%; HPLC3: 12.75 min, purity > 98%.

10-Benzoyl-13-[3-(2-naphthyl)prop-2-enoyl]-10-deacetylbaccatin III (3ad):
Yield: 90%; mp 172-174 ^{o}C; $[\alpha]_D^{20}$ -76.7 (*c* 2,7, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.25 (m, 5H), 1.39 (s, 3H), 1.75 (m, 3H), 1.97 (m, 1H), 2.06 (s, 3H), 2.24 (m, 1H), 2.30 (s, 3H), 2.47 (dd, *J* = 9.2, 16.0 Hz, 1H), 2.65 (m, 1H), 3.99 (d, *J* = 7.0 Hz, 1H), 4.29 (m, 2H), 4.62(m, 1H), 5.06(d, *J* = 8.3Hz, 1H), 5.76 (d, *J* = 7.0 Hz, 1H), 6.29 (m, 1H), 6.65 (m, 2H), 7.50 (m, 7H), 7.61(m, 3H), 7.70 (d, *J* = 9.2 Hz, 1H), 7.89 (m, 2H), 8.09(m, 5H); ^{13}C NMR (100MHz, $CDCl_3$) δ 9.7, 15.9, 21.9, 22.9, 27.3, 36.0, 36.6, 43.4, 46.3, 59.0, 70.4, 72.7, 75.2, 76.4, 76.7, 79.6, 79.6, 81.4, 84.7, 117.1, 123.4, 127.2, 127.9, 128.1, 128.8, 128.9, 129.2, 129.4, 130.2, 130.3, 130.8, 131.6, 133.1, 133.5, 133.9, 134.0, 134.7, 143.7, 147.1, 166.5, 166.7, 167.2, 170.1, 203.9. HRMS (FAB) *m/z* calcd for $C_{49}H_{48}O_{12}H^+$: 829.3234, Found: 829.3242(Δ = 1.8 ppm). HPLC1: 11.14 min, purity > 96%; HPLC3: 12.14 min, purity > 96%.

10-Hexanoyl-13-[3-(2-naphthyl)prop-2-enoyl]-10-deacetyl- 2-debenzoyl-2-(4-methoxybenzoyl)-10-deacetylbaccatin III (3bc):
Yield: 95%; mp 115-118 ^{o}C; $[\alpha]_D^{20}$ -92.1 (*c* 1.26, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.96 (m, 3H), 1.16 (s, 3H), 1.28 (m, 5H), 1.33(m, 2H), 1.56(m, 2H), 1.69 (m, 2H), 1.79 (m, 3H), 1.93 (m, 1H), 2.03 (s, 3H), 2.24 (m, 3H), 2.42 (s, 3H), 2.46 (dd, *J* = 9.2, 16.0 Hz, 1H), 2.66 (m, 1H), 3.86 (s, 1H), 3.90 (d, J=6.8 Hz, 1H), 4.26 (m, 3H), 4.99(d, J=8.3Hz, 1H), 5.71 (d, *J* = 7.0 Hz, 1H), 6.19 (m, 1H), 6.39 (s, 1H), 6.61 (d, *J* = 16.0 Hz, 1H), 6.98(d, *J* = 8.7 Hz, 2H), 7.59(m, 2H), 7.75(d, *J* = 7.2, 1H), 7.93(m, 3H), 8.03(m, 4H); ^{13}C NMR (100MHz, $CDCl_3$) δ 9.7, 14.1, 15.8, 21.6, 22.5, 22.9, 24.7, 27.0, 29.9, 31.5, 34.4, 35.9, 36.5, 43.3, 46.2, 55.7, 59.0, 70.4, 72.6, 74.7, 75.8, 79.5, 81.4, 84.6, 114.2, 117.2, 121.7, 123.4, 127.2, 127.9, 128.1, 128.9, 129.2, 130.8, 131.6, 132.4, 133.2, 133.5, 134.7, 143.3, 147.0, 164.2, 166.5, 167.0, 170.1, 174.3, 204.1. HRMS (FAB) *m/z* calcd for $C_{49}H_{56}O_{13}H^+$: 853.3799, Found: 853.3814 (Δ = 1.5 ppm). HPLC1: 15.18 min, purity > 97%; HPLC3: 12.57 min, purity > 97%.

10-Benzoyl-13-[3-(2-naphthyl)prop-2-enoyl]-10-deacetyl 2-debenzoyl-2-(4-methoxybenzoyl)-10-deacetylbaccatin III (3bd):
Yield: 96%; mp 148-150 ^{o}C; $[\alpha]_D^{20}$ -84.1 (*c* 2.1, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.25 (m, 5H), 1.39 (s, 3H), 1.75 (m, 3H), 1.97 (m, 1H), 2.06 (s, 3H), 2.24 (m, 1H), 2.30 (s, 3H), 2.47 (dd, *J* = 9.2, 16.0 Hz, 1H), 2.65 (m, 1H), 3.86 (s, 1H), 3.99 (d, *J* = 7.0 Hz, 1H), 4.29 (m, 2H), 4.62(m, 1H), 5.06(d, *J* = 8.3Hz, 1H), 5.76 (d, *J* = 7.0 Hz, 1H), 6.29 (m, 1H), 6.65 (m, 2H), 6.97 (d, *J* = 9.0 Hz, 2H), 7.57(m, 3H), 7.66 (m, 4H), 7.73 (d, *J* = 7.2, 1H), 7.93(m, 3H), 8.02(m, 4H), 8.14(m, 3H); ^{13}C NMR (100MHz, $CDCl_3$) δ 9.7, 15.9, 21.9, 22.9, 27.3, 29.9, 36.0, 36.5, 43.4, 46.3, 55.7, 59.0, 70.5, 72.7, 74.8, 76.4, 76.8, 79.5, 81.4, 84.7, 114.2, 117.2, 121.7, 123.4, 127.2, 127.9, 128.1, 128.7, 128.8, 128.9, 129.2, 129.4, 130.2, 130.4, 131.6, 132.4, 133.1, 133.5, 133.8, 133.9, 134.7, 143.6, 147.0, 164.2, 166.5, 166.7, 167.0, 170.1, 203.9; HRMS (FAB) *m/z* calcd for $C_{50}H_{50}O_{13}H^+$: 859.3330, Found: 859.3314 (Δ = -1.6 ppm). HPLC1: 11.13 min, purity > 97%; HPLC3: 12.03 min, purity > 97%.

Method B:
To a solution of 13-[3-(2-naphthyl)prop-2-enoyl]-10-deacetylbaccatin III **(2a) (**60 mg, 0.083mmol) and imidazole (17 mg, 0.249 mmol) in *N,N*-dimethylformamide (DMF, 1.0 mL) was

added chlorotriethylsilane (0.035 mL, 0.208 mmol) dropwise via syringe at 0 °C. The reaction mixture was stirred for 1 h at room temperature and diluted with EtOAc (50 mL). The mixture was then washed with H_2O (20 mL x 3), brine (20 mL), dried over anhydrous $MgSO_4$ and concentrated. The crude product was purified on a silica gel column using hexanes/EtOAc (1/1) as eluant to give7-triethylsilyl-13-[3-(2-naphthyl)prop-2-enoyl]-10-deacetylbaccatin III as a white solid (59 mg, 85%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.81(m, 6H), 1.00 (m, 9H), 1.15 (s, 3H), 1.26 (s, 3H), 1.70 (m, 2H), 1.79 (s, 3H), 1.93 (m, 1H), 2.09 (s, 3H), 2.24 (m, 1H), 2.30 (s, 3H), 2.46 (dd, *J* = 9.2, 16.0 Hz, 1H), 2.65 (m, 1H), 4.02 (d, *J* = 7.0 Hz, 1H), 4.26 (m, 3H), 4.51(m, 1H), 4.99(d, *J* = 8.3Hz, 1H), 5.31(s, 1H), 5.71 (d, *J* = 7.0 Hz, 1H), 6.19 (m, 1H), 6.61 (d, *J* = 16.0 Hz, 1H), 7.51 (m, 4H), 7.60(m, 3H), 7.70 (d, *J* = 9.2 Hz, 1H), 7.89 (m, 2H), 8.03(m, 3H); ^{13}C NMR (100MHz, $CDCl_3$) δ 9.6, 15.9, 21.5, 22.9, 27.0, 36.0, 36.4, 43.2, 46.1, 52.8, 55.7, 59.0, 70.4, 72.5, 74.7, 76.5, 76.8, 78.7, 79.5, 81.4, 84.6, 106.5, 114.2, 117.1, 121.7, 123.4, 127.2, 127.9, 128.0 ,128.9, 129.2, 130.8, 131.6, 132.4, 132.8, 133.5, 134.7, 144.2, 147.0, 156.0, 164.2, 166.5, 167.0, 170.1, 204.4.

To a solution of 7-triethylsilyl-13-[3-(2-naphthyl)prop-2-enoyl]-10-deacetylbaccatin III or 7-Triethylsilyl -10-deacetylbaccatin III in THF (0.055 M) was added 1.0-1.1 equiv of LiHMDS at -40 °C. After the reaction mixture was stirred for 10 min, 1.2 equiv of an alkanoyl chloride was added drop wise at -40 °C. The mixture was warmed to 0 °C over a period of 30-60 min and then quenched by NH_4Cl. After diluted with EtOAc, the mixture was then washed with H_2O, brine, dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. This crude protected coupling product was dissolved in acetonitrile/pyridine (1/1, 0.4 mL/10 mg of reactant) and cooled to 0 °C. The HF/pyridine (70/30) was added dropwise (0.1 mL/10 mg of reactant). The mixture was stirred at 0 °C for 1 h and then at room temperature overnight. After the disappearance of starting material on TLC analysis, the reaction was quenched with saturated $NaHCO_3$. The reaction mixture was extracted with EtOAc, and the extracts were washed with saturated $CuSO_4$ (2 x 15 mL) and water (2 x 15 mL) and dried over anhydrous $MgSO_4$. Evaporation of the solvent followed by purification of the crude product by flash chromatography (silica gel; hexane/EtOAc = 1/2) afforded **3aa**, **3ab**, **3ba**, **3bb,** and **6** as white solid.

10- *N,N*-Dimethylcarbamyl-13-[3-(2-naphthyl)prop-2-enoyl]-10-deacetylbaccatin III (3aa): Yield: 86%; mp 179-180 °C; $[\alpha]_D^{20}$ -99.1 (*c* 0.82, $CHCl_3$); ^{1}HNMR (300 MHz, $CDCl_3$) δ 1.17 (s, 3H), 1.26 (s, 3H), 1.70 (m, 2H), 1.91 (m, 1H), 2.04 (s, 2H), 2.25 (m, 1H), 2.32 (s, 3H), 2.46 (dd, *J* = 9.2, 16.0 Hz, 1H), 2.60 (m, 1H), 3.00 (m, 6H), 3.89 (d, *J* = 7.0 Hz, 1H), 4.25 (m, 3H), 4.52(m, 1H), 5.03(d, *J* = 8.3Hz, 1H), 5.68 (d, *J* = 7.0 Hz, 1H), 6.21 (m, 1H), 6.32 (s, 1H), 6.62 (d, *J* = 16.0 Hz, 1H), 7.54 (m, 4H), 7.61(m, 3H), 7.72 (d, *J* = 9.2 Hz, 1H), 7.87 (m, 2H), 8.04(m, 3H); ^{13}C NMR (100MHz, $CDCl_3$) δ 9.5, 15.9, 22.0, 22.9, 27.3, 35.7, 36.3, 36.5, 36.9, 43.3, 46.1, 58.9, 66.4, 70.4, 72.9, 75.3, 76.6, 76.7, 79.7, 81.4, 84.8, 117.1, 123.4, 127.2, 127.9, 128.1, 128.9, 128.9, 129.2, 129.5, 130.3, 130.8, 131.6, 133.4, 133.5, 133.9, 134.7, 143.8, 147.0, 150.3, 156.4, 159.8, 166.6, 167.2, 170.0, 182.2, 206.0; HRMS (FAB) *m/z* calcd for $C_{45}H_{49}NO_{12}H^+$: 796.3333, Found: 796.3326(Δ = -0.7 ppm). HPLC1: 7.69 min, purity > 96%; HPLC3: 10.37 min, purity > 96%.

10-Methoxycarbonyl-13-[3-(2-naphthyl)prop-2-enoyl]-10-deacetylbaccatin III (3ab): Yield: 83%; mp 170-171 °C; $[\alpha]_D^{20}$ -122.0 (*c* 4.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.26 (s, 3H), , 1.72 (s, 3H), 1.91 (m, 1H), 2.08 (s, 3H), 2.24 (m, 1H), 2.32 (s, 3H), 2.47 (dd, *J* = 9.2,

16.0 Hz, 1H), 2.62 (m, 1H), 3.88 (s, 3H), 4.25 (m, 2H), 4.46(m, 1H), 5.01(d, *J* = 8.3Hz, 1H), 5.69 (d, *J* = 7.0 Hz, 1H), 6.21 (m, 3H), 6.61 (d, *J* = 16.0 Hz, 1H), 7.51 (m, 4H), 7.60(m, 3H), 7.70 (d, *J* = 9.2 Hz, 1H), 7.89 (m, 2H), 8.04(m, 3H); ^{13}C NMR (100MHz, $CDCl_3$) δ 9.7, 15.9, 21.5, 22.9, 27.0, 36.0, 36.5, 43.2, 46.1, 55.8, 59.0, 70.3, 72.5, 75.1, 77.6, 78.7, 79.5, 81.3, 84.6, 117.1, 123.4, 127.2, 127.9, 128.1, 128.9, 128.9, 129.2, 129.4, 130.3, 130.8, 131.6, 132.8, 133.5, 133.9, 134.7, 144.2, 147.1, 156.0, 166.5, 167.2, 170.2, 204.3; HRMS (FAB) *m/z* calcd for $C_{44}H_{46}O_{13}H^+$: 783.3017, Found: 783.3013(Δ = -0.3 ppm). HPLC1: 7.16 min, purity > 98%; HPLC3: 10.32 min, purity > 98%.

10-Cyclohexanecarbonyl-13-[3-(2-naphthyl)prop-2-enoyl]-10-deacetyl-2-debenzoyl-2-(4-methoxybenzoyl)-10-deacetylbaccatin III (3ba):
Yield: 80%; mp 148-150 ^oC; $[\alpha]_D^{20}$ -111.0 (*c* 0.83, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.15 (s, 3H), 1.26 (s, 3H), 1.40(m, 6H), 1.70 (m, 2H), 1.79 (m, 7H), 1.93 (m, 1H), 2.09 (s, 3H), 2.24 (m, 2H), 2.32 (s, 3H), 2.46 (dd, *J* = 9.2, 16.0 Hz, 1H), 2.65 (m, 1H), 3.86 (s, 1H), 3.89 (d, *J* = 7.0 Hz, 1H), 4.25 (m, 2H), 4.50(m, 1H), 5.01(d, *J* = 8.3Hz, 1H), 5.69 (d, *J* = 7.0 Hz, 1H), 6.22 (m, 1H), 6.36 (s, 1H), 6.63 (d, *J* = 16.0 Hz, 1H), 6.97 (d, *J* = 9.0 Hz, 2H), 7.57(m, 3H), 7.66 (m, 4H), 7.73 (d, *J* = 7.2, 1H), 7.93(m, 3H), 8.03(m, 4H), 8.14(m, 3H); ^{13}C NMR (100MHz, $CDCl_3$) δ 9.7, 15.8, 21.7, 22.9, 25.5, 25.7, 26.0, 27.1, 28.9, 29.5, 35.9, 36.5, 43.2, 43.3, 46.2, 55.7, 59.0, 70.4, 72.7, 74.7, 75.6, 77.7, 79.5, 81.4, 84.6, 114.2, 117.2, 121.7, 123.4, 127.2, 127.9, 128.1, 128.9, 129.2, 130.8, 131.6, 132.4, 133.3, 133.5, 134.7, 143.1, 147.0, 164.2, 166.5, 167.0, 170.1, 176.4, 204.1; HRMS (FAB) *m/z* calcd for $C_{50}H_{56}O_{13}H^+$: 865.3799, Found: 865.3771 (Δ = -2.8 ppm). HPLC1: 15.62 min, purity > 96%; HPLC3: 12.90 min, purity > 96%.

10-Methoxycarbonyl-13-[3-(2-naphthyl)prop-2-enoyl]-10-deacetyl-2-debenzoyl-2-(4-methoxybenzoyl)-10-deacetylbaccatin III (3bb):
Yield: 88%; mp 165-166 ^oC; $[\alpha]_D^{20}$ -96.4 (*c* 1.3, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.17 (s, 3H), 1.26 (s, 3H), , 1.72 (s, 3H), 1.91 (m, 1H), 2.08 (s, 3H), 2.24 (m, 1H), 2.32 (s, 3H), 2.47 (dd, *J* = 9.2, 16.0 Hz, 1H), 2.62 (m, 1H), 3.86 (s, 1H), 3.88 (s, 3H), 4.25 (m, 2H), 4.46(m, 1H), 5.01(d, *J* = 8.3Hz, 1H), 5.69 (d, *J* = 7.0 Hz, 1H), 6.21 (m, 3H), 6.61 (d, *J* = 16.0 Hz, 1H), 6.97 (d, *J* = 9.0 Hz, 2H), 7.57(m, 3H), 7.66 (m, 4H), 7.73 (d, *J* = 7.2 Hz, 1H), 7.94(m, 3H), 8.02(m, 4H), 8.14(m, 3H); ^{13}C NMR (100MHz, $CDCl_3$) δ 9.6, 15.9, 21.5, 22.9, 27.0, 36.0, 36.4, 43.2, 46.1, 52.8, 55.7, 59.0, 70.4, 72.5, 74.7, 76.5, 76.8, 78.7, 79.5, 81.4, 84.6, 106.5, 114.2, 117.1, 121.7, 123.4, 127.2, 127.9, 128.0 ,128.9, 129.2, 130.8, 131.6, 132.4, 132.8, 133.5, 134.7, 144.2, 147.0, 156.0, 164.2, 166.5, 167.0, 170.1, 204.4. HRMS (FAB) *m/z* calcd for $C_{45}H_{48}O_{14}H^+$: 813.3122, Found: 813.3118 (Δ = -0.5 ppm). HPLC1: 7.06 min, purity > 98%; HPLC3: 10.17 min, purity > 98%.

10-[3-(2-Naphthyl)prop-2-enoyl]-10-deacetylbaccatin III (6):
Yield: 80%; mp 176-179 ^oC; $[\alpha]_D^{20}$ -53.05 (c 2.62, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.18 (m, 6 H), 1.69 (m, 5 H), 1.89 (s, 2 H), 1.97 (m, 2 H), 2.09 (s, 3 H), 2.19 (s, 3 H), 2.24 (m, 5 H), 2.35 (m, 6 H), 2.60 (m, 1 H), 3.93 (d, *J* = 6.8 Hz, 1 H), 4.17 (d, *J* = 8.0 Hz, 1 H), 4.31 (d, *J* = 8.4 Hz, 1 H), 4.54 (m, 1H), 4.91 (m, 1H), 5.01 (d, *J* = 10 Hz, 1 H), 5.66 (d, *J* = 6.8 Hz, 1 H), 6.49 (s, 1 H), 6.68 (d, *J* = 16.0 Hz, 1 H), 7.45-7.93 (m, 11 H), 8.10 (d, *J* = 7.6 Hz, 2 H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 9.7, 15.9, 21.4, 22.8, 27.4, 35.9, 38.9, 43.0, 46.4, 59.0, 68.2, 72.6, 75.2, 76.5, 76.7, 79.4, 81.1, 84.8, 117.3, 123.8, 127.0, 127.7, 128.0, 128.8, 128.9, 129.0, 129.6, 130.4, 130.7, 131.9, 132.2, 133.5, 133.9, 134.7, 146.8, 147.0, 167.2, 167.3, 170.9, 204.4. HRMS (FAB) *m/z*

calcd for $C_{42}H_{44}O_{11}H^+$: 725.2962, Found: 725.2973 (Δ = 1.1 ppm). HPLC1: 5.23 min, purity > 96%; HPLC3: 8.73 min, purity > 96%.

Method C:
To a magnetically stirred solution of 7-triethylsilyl -13-[3-(2-naphthyl) prop-2-enoyl]-10-deacetylbaccatin III in dry DMF/CH_2Cl_2 (1/2) were added corresponding amino acid (2.5 equiv), DMAP (1.5 equiv), and DIC (3.5 equiv) at room temperature under N_2. After stirring for overnight, the solvent was removed on a rotary evaporator and the residue was purified by short silica gel chromatography using ethyl acetate/hexane (2:1) as eluant to afford TES protected C-10 coupling product contaminated by DIC-acid complex, which were directly used in the next step.
To a solution of TES protected C-10 coupling product in a (1:1) mixture of pyridine and acetonitrile (4 mL/100mg of starting material) at 0 ^oC was added a 70 % solution of HF in pyridine (1 mL/100 mg of starting material) with stirring. After stirring overnight at room temperature, the reaction was quenched with $NaHCO_3$ solution and extracted with ethyl acetate. The combined organic layers were washed with a saturated solution of copper sulfate and with water, then dried over magnesium sulfate, filtered and concentrated. Purification of the crude product by silica gel chromatography (hexanes/EtOAc/TEA = 1/2/0.1) afforded to afford **7a, 7b** as white solid.

10-*N, N*-Dimethylglycyl-13-[3-(2-naphthyl)prop-2-enoyl]-10-deacetylbaccatin III (7a):
Yield: 75%; mp 145-146 ^oC; $[\alpha]_D^{20}$ -103.6 (*c* 3.3, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.15 (s, 3H), 1.26 (s, 3H), 1.70 (m, 2H), 1.79 (s, 3H), 1.93 (m, 1H), 2.09 (s, 3H), 2.24 (m, 7H), 2.30 (s, 3H), 2.46 (dd, *J* = 9.2, 16.0 Hz, 1H), 2.65 (m, 1H), 3.45 (s, 2H), 3.91 (d, *J* = 7.0 Hz, 1H), 4.26 (m, 4H), 4.52(m, 1H), 5.02(d, *J* = 8.3Hz, 1H), 5.71 (d, *J* = 7.0 Hz, 1H), 6.24 (m, 1H), 6.43(s, 1H), 6.63 (d, *J* = 16.0 Hz, 1H), 7.49 (m, 4H), 7.58(m, 3H), 7.71 (d, *J*= 9.2 Hz, 1H), 7.90 (m, 2H), 8.09(m, 3H); ^{13}CNMR (100MHz, $CDCl_3$) δ 9.8, 15.8, 21.6, 22.9, 23.7, 27.0, 35.9, 36.5, 42.4, 43.3, 45.3, 46.1, 59.0, 60.2, 70.3, 72.5, 75.1, 76.0, 76.7, 79.5, 81.3, 84.6, 117.1, 123.3, 127.2, 127.9, 128.1, 128.9, 128.9, 129.3, 129.4, 130.3, 130.8, 131.6, 132.9, 133.5, 134.0, 134.7, 143.7, 147.1, 166.5, 167.2, 170.1, 171.3, 203.8. HRMS (FAB) *m/z* calcd for $C_{46}H_{51}NO_{12}H^+$: 810.3490, Found: 810.3476 (Δ = -1.4 ppm). HPLC1: 5.51 min, purity > 95%; HPLC3: 8.46 min, purity > 95%.

10-*N,N*-Diethyl-β-alaninyl-13-[3-(2-naphthyl)prop-2-enoyl]-10-deacetylbaccatin III (7b):
Yield: 62%; mp 114-115 ^oC; $[\alpha]_D^{20}$ -106.3 (*c* 0.8, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.15 (s, 3H), 1.26 (s, 3H), 1.70 (m, 2H), 1.79 (s, 3H), 1.93 (m, 1H), 2.09 (s, 3H), 2.24 (m, 1H), 2.30 (s, 3H), 2.46 (dd, *J* = 9.2, 16.0 Hz, 1H), 2.65 (m, 1H), 3.00 (m, 2H), 4.02 (d, *J* = 7.0 Hz, 1H), 4.26 (m, 3H), 4.51(m, 1H), 4.58(m, 1H), 5.02 (d, *J* = 8.3Hz, 1H), 5.71 (d, *J* = 7.0 Hz, 1H), 6.19 (m, 1H), 6.40 (s, 1H), 6.67 (d, *J* = 16.0 Hz, 1H), 7.51 (m, 4H), 7.60(m, 3H), 7.71 (d, *J* = 9.2 Hz, 1H), 7.99 (m, 2H), 8.09(m, 3H); ^{13}CNMR (75 MHz, $CDCl_3$) δ 9.5, 11.9, 15.6, 21.4, 22.6, 23.7, 26.8, 29.7, 32.0, 35.6, 36.2, 42.9, 45.6, 46.8, 47.9, 58.7, 68.1, 70.1, 72.4, 74.7, 76.6, 79.3, 81.2, 84.4, 116.8, 123.1, 126.4, 127.6, 127.8, 128.6, 128.9, 129.2, 130.0, 130.5, 131.4, 133.3, 134.4, 135.8, 139.3, 143.9, 146.8, 166.3, 166.9, 169.9, 173.1, 203.8. HRMS (FAB) *m/z* calcd for $C_{49}H_{57}NO_{12}H^+$: 852.3959, Found: 852.3969(Δ = 0.9 ppm). HPLC1: 6.45 min, purity > 95%; HPLC3: 8.43 min, purity > 95%.

Acylation at the C-7 position

Method A:
To a solution of 13-Ac baccatin III (0.15 M), DMAP (0.2 equiv) and the corresponding acid (1.2 equiv) in dichloromethane was added DCC (1.5 equiv) at room temperature with stirring. After stirring for 15 h, the solvent was evaporated *in vacuo*. Purification of the crude product by silica gel chromatography using ethyl acetate/hexane (1:1) as eluant afforded **5** as a white solid.

7-[3-(2-Naphthyl)acryloyl]-13-acetylbaccatin III (5):[1]
Yield: 95%; mp 181-184 ^{o}C; $[\alpha]_D^{20}$ -56.25 (*c* 0.16, CH_2Cl_2); ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.20 (s, 6 H), 1.69 (s, 1 H), 1.90 (s, 3 H), 1.97 (m, 1 H), 2.02 (s, 3 H), 2.05 (s, 3 H), 2.24 (m, 5 H), 2.35 (s, 3 H), 2.73 (m, 1 H), 4.02 (d, *J* = 7.0 Hz, 1 H), 4.19 (d, *J* = 8.1 Hz, 1 H), 4.34 (d, *J* = 8.1 Hz, 1 H), 5.01 (d, *J* = 8.6 Hz, 1 H), 5.72 (m, 2 H), 6.17 (t, *J* = 8.3 Hz, 1 H), 6.40 (s, 1 H), 6.46 (d, *J* = 16.0 Hz, 1 H), 7.45-7.93 (m, 11 H), 8.09 (d, *J* = 7.6 Hz, 2 H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 10.91, 14.77, 20.59, 20.70, 21.23, 22.47, 26.35, 33.44, 35.55, 43.10, 47.13, 56.26, 69.55, 71.69, 74.51, 75.18, 76.33, 78.82, 80.85, 84, 87.21, 118.30, 123.87, 126.55, 127.07, 127.71, 128.46, 128.55, 128.65, 129.17, 129.92, 130.04, 132.13, 132.62, 133.25, 34.16, 141.44, 144.83, 165.73, 166.94, 168.55, 169.49, 170.22, 202.36. HRMS (FAB) *m/z* calcd for $C_{46}H_{48}O_{13}H^+$: 809.3168, Found: 809.3173 (Δ = -0.5 ppm). HPLC1: 10.58 min, purity > 98%; HPLC3: 12.84 min, purity > 98%. All data were in agreement with literature values.[1]

Method B:
To a magnetically stirred solution of 13-[3-(2-naphthyl)prop-2-enoyl]-10-deacetylbaccatin III **(2a)** or 13-[3-(2-naphthyl)prop-2-enoyl]baccatin III in dry CH_2Cl_2 were added corresponding acid (1.0 equiv), DMAP (1.0 equiv), and DIC (2.0 equiv) at room temperature under N_2. After stirring for overnight, the solvent was removed on a rotary evaporator and the residue was purified using silica gel chromatography with hexane/EtOAc/TEA (1:2:0.1) as the eluant to afford **8a, 8b** as white solid.

7-*N*,*N*-Dimethylglycyl-13-[3-(2-naphthyl)prop-2-enoyl]-10-deacetylbaccatin III (8a):
Yield: 80%; mp 171-176 ^{o}C; $[\alpha]_D^{20}$ -47.1 (*c* 0.7, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.15 (s, 3H), 1.26 (s, 3H), 1.70 (m, 2H), 1.79 (s, 3H), 1.93 (m, 1H), 2.09 (s, 3H), 2.24 (m, 7H), 2.30 (s, 3H), 2.46 (dd, *J* = 9.2, 16.0 Hz, 1H), 2.65 (m, 1H), 3.14 (s, 2H), 4.10 (d, *J* = 7.0 Hz, 1H), 6.19 (m, 1H), 6.61 (d, *J* = 16.0 Hz, 1H), 7.51 (m, 4H), 7.60 (m, 3H), 7.70 (d, *J* = 9.2 Hz, 1H), 7.89 (m, 2H), 8.03 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 8.1, 11.1, 20.3, 22.8, 26.6, 27.7, 30.0, 33.8, 36.8, 39.8, 43.0, 45.2, 46.6, 53.4, 60.1, 70.4, 72.2, 74.8, 75.0, 79.2, 80.9, 93.9, 117.4, 123.4, 127.2, 128.1, 130.8, 131.2, 133.5, 134.0, 134.7, 135.6, 140.0, 146.8, 166.5, 167.1, 170.1, 211.5. HRMS (FAB) *m/z* calcd for $C_{46}H_{51}NO_{12}H^+$: 810.3490, Found: 810.3476 (Δ = -1.4 ppm). HPLC1: 5.43 min, purity > 95%; HPLC3: 8.41 min, purity > 95%.

7-*N*,*N*-Diethyl-β-alanyl-10-acetyl-13-[3-(2-naphthyl)prop-2-enoyl]-10-deacetylbaccatin III (8b):
Yield: 72%; mp 114-115 ^{o}C; $[\alpha]_D^{20}$ -106.3 (*c* 0.8, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.15 (s, 3H), 1.26 (s, 3H), 1.70 (m, 2H), 1.79 (s, 3H), 1.93 (m, 1H), 2.09 (s, 3H), 2.24 (m, 1H), 2.30 (s, 3H), 2.46 (dd, *J* = 9.2, 16.0 Hz, 1H), 2.65 (m, 1H), 3.00 (m, 2H), 4.02 (d, *J* = 7.0 Hz, 1H), 4.26 (m, 3H), 4.51(m, 1H), 4.58(m, 1H), 5.02 (d, *J* = 8.3Hz, 1H), 5.71 (d, *J* = 7.0 Hz, 1H),

6.19 (m, 1H), 6.40 (s, 1H), 6.67 (d, J = 16.0 Hz, 1H), 7.51 (m, 4H), 7.60(m, 3H), 7.71 (d, J = 9.2 Hz, 1H), 7.99 (m, 2H), 8.09(m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 9.5, 11.9, 15.6, 21.4, 22.6, 23.7, 26.8, 29.7, 32.0, 35.6, 36.2, 42.9, 45.6, 46.8, 47.9, 58.7, 68.1, 70.1, 72.4, 74.7, 76.6, 79.3, 81.2, 84.4, 116.8, 123.1, 126.4, 127.6, 127.8, 128.6, 128.9, 129.2, 130.0, 130.5, 131.4, 133.3, 134.4, 135.8, 139.3, 143.9, 146.8, 166.3, 166.9, 169.9, 173.1, 203.8. HRMS (FAB) *m/z* calcd for $C_{51}H_{59}NO_{13}H^+$: 894.4065, Found: 894.4061 (Δ = -0.4 ppm). HPLC1: 7.12 min, purity > 95%; HPLC3: 10.13 min, purity > 95%.

Evaluation of Biological Activities

Bacterial Strain. $H37_{Rv}$, the drug sensitive laboratory strain of *Mycobacterium tuberculosis* (MTB) as well as IMCJ946.K2, a multi-drug resistant MTB strain were used in this study. IMCJ 946.K2 is resistant to isoniazid (INH), rifampicin (RFP), ethambutol (EB), streptomycin (SM), kanamycin (KM), ethionamide (ETH), *p*-aminosalicylic acid (PAS), cycloserine (CS) and enviomycin (EVM).

Growth of Bacteria. The MTB strains were grown in MycoBroth (Kyokuto pharmaceutical Co., Ltd, Tokyo, Japan). When cultures reached an optical density of 0.4 to 0.5 at 530 nm (Vi-spec, Kyokuto pharmaceutical Co., Ltd), 100 µL of bacterial suspension was transferred to a tube containing fresh MycoBroth and grown until an optical density of 0.4 to 0.5 was reached.

Antibacterial Activity. The minimum inhibitory concentration (MIC_{99}) was determined by the Microplate Alamar Blue assay[2] with some modifications. Stock solutions of the compounds were prepared in DMSO at a concentration of 10 mM, and diluted into the culture broth to give the final desired concentration before every experiment. The optical density of the cultures in MycoBroth was adjusted to 0.16 - 0.2 at 530 nm (equal to that of a no. 1 McFarland standard) with MycoBroth, and further diluted 1:50 in Middlebrook 7H9 broth (Difco, Becton Dickinson and Company, Sparks, MD) supplemented with 10% of BBL™ Middlebrook OADC Enrichment (Becton Dickinson and Company) and 0.2% glycerol (7H9 broth). One hundred microliters of 7H9 broth was dispensed in each well of sterile 96-well flat bottom-plates (Nalge Nunc International, Naperville, IL), and serial twofold dilutions of each compound were prepared directly in the plate. One hundred microliters of inoculum was added to each well, yielding a final volume of 200 µL per well. The wells filled with 7H9 broth served as drug-free (inoculum-only) controls. One hundred microliters of 7H9 broth was added to all outer-perimeter wells of 96-well plates to minimize evaporation of the medium in the test wells during incubation. The plates were sealed with Parafilm and were incubated with 5 % CO_2 at 37°C for 6 days. After 7 days of incubation, 50 µL of freshly prepared 1:1 mixture of 10 x Alamar Blue (Trek Diagnostic Systems, Inc., Westlake, OH) reagent and 7H9 broth containing 10% Tween 80 (Sigma Chemical Co., St. Louis, MO) was added to each well, and the plates were further incubated overnight. A change in color from blue to pink indicated the growth of bacteria. The MIC_{99} was defined as the lowest drug concentration of compound that prevented this change in color.

Cytotoxicity Assay. The human breast cancer-derived cell line MCF7 was provided by K. Yasuda, Dokkyo University, Tochigi, Japan, while the human lung cancer cell line A549 was purchased from Riken BioResource Center, Tsukuba, Japan. Cells were plated at 5 x 10^4 /well in

96-well plates, and cultured for 3 days in the presence of serial diluted compounds. At the end of this time, the number of viable cells was determined by a quantitative colorimetric staining assay using a tetrazolium salt (MTT, Sigma Chemical Co.)[3] The inhibitory concentration (IC_{50}) of each compound was determined as the concentration required to inhibit 50% of the growth of the MCF7 and A549 cells.

References

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Scanning Electron Microscopy

SEM Ultrastructual analysis of *M. tuberculosis* treated with FtsZ inhibitors. Treated bacteria were fixed with 2.5% glutaraldehyde in buffer consisting of 0.1 M sodium cacodylate, 5 mM $CaCl_2$ and 5 mM $MgCl_2$ (pH 7.2). Complete fixation was accomplished incubation for 1 hr at room temperature followed by repeated washing with 0.1 M sodium cacodylate buffer followed by overnight fixation at 4C. Cells were post-fixed processed by rinsing in 0.1M Sodium cacodylate buffer followed by 1 hr treatment with 1% OsO_4 in the same buffer. The bacteria were then pelleted and subsequently dehydrated in a graded series of acetone (25-100%). The cells were then examined with JOEL JEM -100CX electron microscope (JOEL Ltd. Japan).

Figure S1. Electron micrographs of MTB cells before (Cntrol) and after treatment with TRA **3aa** and TRA **10a**

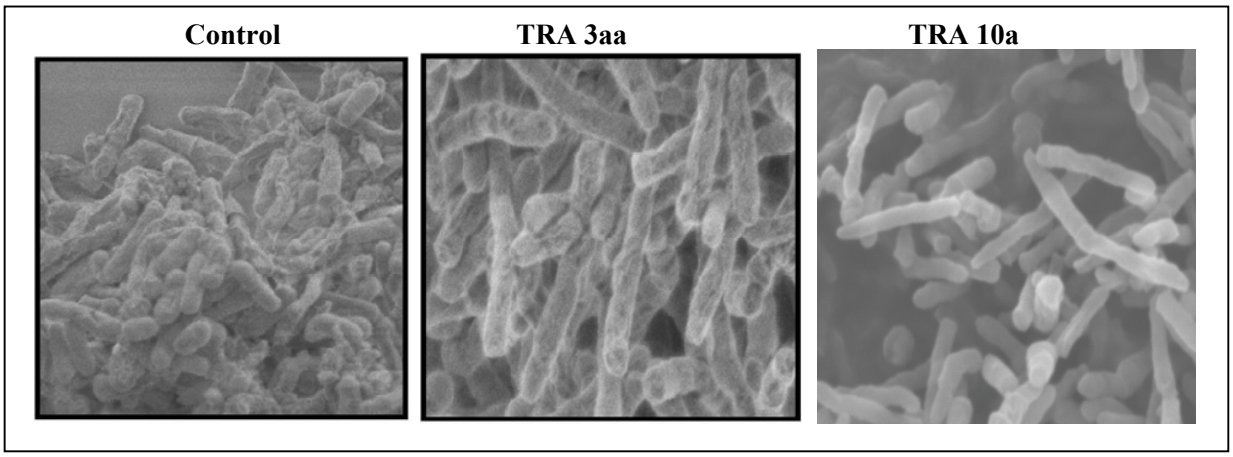

Figure S2. Brightfield Nomarski Differential Interference Contrast images of *M. tuberculosis* treated with **10a**. (**A-D**) show typical filamentation and prolongated cells resulting from prolonged treatment and (**C-D**) arrows depict the multi-partial constructions along the bacterial filament consistent with bacterial morphology resulting from FtsZ inhibition. All images were acquired by wide-field microscopy using a Zeiss200M inverted microscope and 100X PlanApochromatoil immersion objective in conjunction with a 1.6 optical magnification lens. Each image was obtained from cells treated at the minimum inhibitory concentration of **10a**.