Supporting Information

Mechanism-Based Tumor-Targeting Drug Delivery System. Validation of Efficient Vitamin Receptor-Mediated Endocytosis and Drug Release

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General Methods: ^{1}H NMR spectra were measured on a Varian 300 or Varian 400 NMR spectrometer. TLC was performed on Merck DC-aluminfolien with Kieselgel 60F-254 and column chromatography was carried out on silica gel 60 (Merck; 230-400 mesh ASTM). Solvents were purified either by distillation after drying over respective drying agents according to the standard protocols or by a PureSolv^{TM} system (Innovative Technology, Inc) under N_2. De-gassed solvents were applied whenever necessary. Analytical HPLC was performed on a Shimadzu L-2010A with CH_3CN and H_2O as the mobile phase. The columns for HPLC were Waters Nova-Pak® (C18, 3.9 x 150 mm) and Phenomenex® (Curosil–B, 5μ, 250 x 4.60 mm), and the wavelength of UV detector was set at either 254 nm or 220 nm. High-resolution mass spectrometry (HRMS) analyses were conducted at the Mass Spectrometry Laboratory of the University of Illinois at Urbana-Champaign. Dark room, aluminum foil, and inert nitrogen atmosphere were applied whenever necessary. As the staining agent on TLC for biotin derivatives, 4-*N*,*N*-dimethylaminocinnamaldehyde solution was used.[1]

Materials: Tetrahydrofuran (THF) was freshly distilled from sodium metal and benzophenone. Dichloromethane (DCM) was distilled immediately prior to use under nitrogen from calcium hydride. *N*,*N*-Dimethylformamide (DMF) was distilled over 4A molecular sieves under reduced pressure. Dimethyl sulfoxide (DMSO, anhydrous), 4-(*N*,*N*-dimethylamino)pyridine (DMAP), *N*,*N'*-dicyclohexylcarbodiimide (DCC), *N*,*N'*-diisopropylcarbodiimide (DIC), diisopropyl azodicarboxyate (DIAD), *N*-hydroxysuccinimide (HOSu) and all other chemicals were used as received. 3'-Dephenyl-3'-(2-methyl-1-propenyl)-10-(cyclopropanecarbonyl)docetaxel (**SB-T-1214**) was prepared by the literature method.[2]

Synthetic Procedures and Characterization Data for Intermediates and Conjugates

Biotinylhydrazine (5)[3]

To a suspension of biotin (300 mg, 1.23 mmol) in MeOH (3 mL) was added $SOCl_2$ (0.30 mL, 4.0 mmol), and the solution was stirred overnight at room temperature to give a clear solution. After evaporation of the solvent and excess $SOCl_2$ under reduced pressure, biotin methyl ester (296 mg) was obtained in 93% yield as a white solid: ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.4-1.7 (m, 6 H), 2.34 (t, *J* = 7.2 Hz, 2 H), 2.76 (d, *J* = 13.2 Hz, 1 H), 2.91 (dd, *J* = 13.2, 4.8 Hz, 1 H), 3.17 (m, 1 H), 3.67 (s, 3 H), 4.32 (m, 1 H), 4.52 (m, 1 H), 5.08 (s, 1 H), 5.37 (s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.5, 28.4, 33.6, 40.0, 50.1, 51.6, 55.4, 62.2, 63.8, 164.0, 174.3. All data were in agreement with literature values.[3]

Biotin methyl ester (296 mg, 1.14 mmol) was dispersed in MeOH (2.5 mL), and hydrazine (0.30 mL, 10 mmol) was added with stirring. After stirring for 16 h, the solution was concentrated under reduced pressure and diluted with water (50 mL). The aqueous layer was washed by chloroform (30 mL x 3), and concentrated *in vacuo* to give **5** (296 mg, 100% yield) as a white solid: ^{1}H NMR (400 MHz, D_2O) δ 1.40 (m, 2 H), 1.5-1.7 (m, 4 H), 2.3 (t, *J* = 7.2 Hz, 2 H), 2.8 (d, *J* = 13.2 Hz, 1 H), 3.0 (dd, *J* = 13.2, 4.8 Hz, 1 H), 3.4 (m, 1 H), 4.4 (m, 1 H), 4.6 (m, 1 H); ^{13}C NMR (100 MHz, D_2O) δ 25.0, 27.8, 28.0, 33.6, 39.9, 55.5, 60.5, 62.3, 165.6, 175.8. Data were in agreement with literature values.[3]

Fluoresceinthiocarbamoylbiotinylhydrazine (**2**)

To a solution of **5** (52 mg, 0.2 mmol) in dimethylsulfoxide (DMSO, 1.0 mL) was added fluorescein isothiocynate (FITC, 130 mg, 0.3 mmol) with stirring. The resulting yellow solution was stirred for 36 h at room temperature. The reaction mixture was directly subjected to purification by column chromatography on silica gel using (i) ether (50 mL), (ii) 5% MeOH in DCM (100 mL), and (iii) 10 % MeOH in DCM (100 mL) sequentially, as eluents to give biotin-FITC conjugate **2** (120 mg, 93% yield) as yellow solid: ^{1}H NMR (300 MHz, CD_3OD) δ 1.4-1.8 (m, 6 H), 2.35 (t, *J* = 7.5 Hz, 2 H), 2.68 (d, *J* = 12.9 Hz, 1 H), 2.90 (dd, *J* = 12.9, 4.8 Hz, 1 H), 3.20 (m, 1 H), 4.29 (m, 1 H), 4.47 (m, 1 H), 6.57 (m, 2 H), 6.67 (m, 2 H), 6.76 (m, 2 H), 7.15 (d, *J* = 8.4 Hz, 1 H), 7.87 (dd, *J* = 8.4, 1.8 Hz, 1 H), 8.13 (d, *J* = 1.8 Hz, 1 H). ^{13}C NMR (100 MHz, CD_3OD): δ 26.27, 29.63, 29.90, 34.69, 41.21, 57.09, 61.74, 63.45, 103.70, 111.71, 113.96, 121.83, 125.60, 128.82, 130.54, 133.60, 142.36, 150.27, 154.38, 161.71, 166.16, 170.98, 175.77, 184.16. HRMS (ESI) *m/e* calcd for $C_{31}H_{30}N_5O_7S_2^+$ (M + H^+): 647.1581. Found: 648.1587 (Δ = 0.9 ppm).

3-(Pyridin-2-yldisulfanyl)propanoic acid (**7**)[4]

2,2'-Bipyridyl disulfide (**6**, 3.75 g, 17.0 mmol) was dissolved in 99.5% ethanol (15 mL), and glacial acetic acid (0.4 mL, 8.5 mmol) was added. To this solution was added dropwise 3-sulfhydrylpropanoic acid (0.90 g, 8.5 mmol) in ethanol (5.0 mL) at 0 °C with vigorous stirring. The mixture was stirred for 12 h at room temperature. Then, the reaction mixture was concentrated under reduced pressure and the residue was purified on a neutral alumina column using CH_2Cl_2/MeOH/glacial acetic acid (20/2/1) as the eluent to give **7** (1.30 g, 78 %) as white solid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.79 (t, *J* = 6.9 Hz, 2 H), 3.06 (t, *J* = 6.9 Hz, 2 H), 7.14 (m, 1 H), 7.66 (m, 1 H), 8.48 (dd, *J* = 3.3, 1.2 Hz, 1 H), 10.4 (br, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 33.8, 34.1, 120.5, 121.2, 137.4, 149.4, 159.2, 176.1. Data were in agreement with the reported values.[4]

Triisopropylsilyl 3-(pyridin-2-yldisulfanyl)propanoate (**8**)

To a solution of **7** (562 mg, 2.6 mmol) and triethylamine (TEA, 0.60 mL, 4.2 mmol) in CH_2Cl_2 (10 mL) was added chlorotriisopropylsilane (TIPSCl, 0.75 mL, 3.4 mmol) dropwise at 0 ^oC. After stirring at room temperature for 1 h, the reaction mixture was diluted with ether (60 mL). The organic layer was separated, washed by saturated aqueous $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated under reduced pressure. Flash chromatography of the residue on silica gel using hexanes/EtOAc (20/1) as the eluent gave **8** (900 mg, 93 % yield) as colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.05 (d, *J* = 7.2 Hz, 18 H), 1.29 (m, 3H), 2.80 (t, *J* = 7.2 Hz, 2 H), 3.04 (t, *J* = 7.2 Hz, 2 H), 7.09 (m, 1 H), 7.66 (m, 2 H), 8.45 (d, *J* = 8.4 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.07, 17.93, 34.04, 35.51, 119.94, 120.92, 137.26, 149.84, 160.13, 171.61. HRMS (ESI) *m/e* calcd for $C_{17}H_{30}NO_2S_2Si^+$ (M + H^+): 372.1487. Found: 372.1485 (Δ = -0.5 ppm).

3H-Benzo[b]thiophen-2-one (**10**)[5]

To a solution of thianaphthene-2-boronic acid (**9**, 3.09 g, 17 mmol) in EtOH (30 mL) was added hydrogen peroxide (30%, 5.6 mL) dropwise with stirring. The color of the reaction mixture changed from pink to red. After stirring for 8 h, the reaction mixture was carefully concentrated under reduced pressure, diluted with water (100 mL), and extracted with $CHCl_3$ (70 mL x 3). The combined organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. Flash

chromatography of the residue on silica gel using hexanes/EtOAc (20/1) as the eluent gave **10** (2.25 g, 86 % yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.98 (s, 2 H), 7.2-7.4 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 46.9, 122.7, 124.5, 125.9, 128.1, 132.0, 136.7, 202.6. HRMS (ESI) *m/e* calcd for $C_8H_7OS^+$ ($M + H^+$): 150.0139. Found: 150.0138 (Δ = -0.7 ppm).

(2-Sulfhydrylphenyl)acetic acid (**11**)

To a solution of **10** (310 mg, 2.0 mmol) in THF (10 mL) was added LiOH hydrate (508 mg, 12 mmol) in H_2O (10 mL) at 60 ˚C. After stirring for 16 h and cooling down to room temperature, the reaction was quenched by adding H_2O (2 mL) and diethyl ether (10 mL). The pH was adjusted to 2 by 2M hydrochloric acid. The organic layer was separated, washed with saturated NaCl, and dried over Na_2SO_4. After the solvent was removed *in vacuo*, the residue was subjected to column chromatography on silica gel (eluent: hexanes/EtOAc = 10/1) to give **11** (302 mg, 90 % yield) as golden crystals: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.49 (s, 1 H, S-H), 3.83 (s, 2 H), 7.18-7.29 (m, 3 H), 7.41 (m, 1 H), 10.10 (br, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 39.85, 126.94, 128.25, 130.74, 131.00, 132.41, 133.33, 176.16. HRMS (ESI) *m/e* calcd for $C_8H_8O_2S$: 168.02450. Found: 168.02445(Δ = -0.3 ppm).

2-[(3-Oxo-3-triisopropylsiloxypropyl)disulfanyl]phenylacetic acid (**12**)

To a solution of **8** (900 mg, 2.4 mmol) in THF (10 mL) was added **11** (407 mg, 2.4 mmol) in THF (6 mL) dropwise at 0 ^{o}C with stirring. After stirring for 3 h, the solvent was removed *in vacuo* and the crude product was purified on a silica gel column using hexanes/EtOAc (3/1) as the eluent to give **12** (868 mg, 84 %) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.22 (d, J = 7.2 Hz, 18 H), 1.31 (m, 3H), 2.76 (t, J = 6.9 Hz, 2 H), 2.92 (t, J = 6.9 Hz, 2 H), 3.90 (s, 2 H), 7.28 (m, 3 H), 7.77 (d, J = 8.4 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 12.05, 17.93, 33.78, 35.53, 39.09, 128.23, 128.62, 131.06, 131.18, 134.00, 137.00, 171.85, 176.55. HRMS (ESI) *m/e* calcd for $C_{20}H_{33}O_4S_2Si^+$: 429.1590. Found: 429.1601 (Δ = 2.6 ppm).

Triisopropylsilyl 3-[2-(4-methyl-2-oxo-2H-1-benzopyran-7-yloxycarbonylmethyl)phenyl-disulfanyl]propanoate (**14**)

To a solution of **12** (113 mg, 0.26 mmol), DMAP (16 mg, 0.13 mmol) and 7-hydroxy-4-methylcoumarin (**13**, 142 mg, 0.78 mmol) in THF (2 mL) was added DCC (56 mg, 0.26 mmol) at 0 ^{o}C with stirring. After stirring for 3 h, the precipitate was filtered off and the reaction mixture was concentrated *in vacuo*. The residue was purified on a silica gel column using hexanes/EtOAc (8/1) as the eluent to give **14** (80 mg, 50 % yield) as colorless gel: Compound **14** was found to exist as a mixture of rotamers in $CDCl_3$, CD_3OD or DMSO-d^6; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.22 (m, 18 H), 1.31 (m, 3H), 2.40-2.42 (m, 3 H), 2.77 (t, J = 7.2 Hz, 1.6 H), 2.96 (t, J = 6.8 Hz, 1.6 H), 3.04 (m, 0.8 H), 3.90 (s, 0.4 H), 4.14 (s, 1.6 H), 6.25 (m, 1 H), 7.04-7.12 (m, 2 H), 7.20-7.33 (m, 3 H), 7.56 (m, 1 H), 7.80 (d, J = 8.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.02, 17.90, 18.85 (CH_3), 33.84, 35.43, 39.53, 110.50, 114.69, 118.03, 118.16, 125.50, 128.54, 128.76, 131.31, 131.33, 133.87, 136.75, 152.01, 153.28, 154.30, 160.58, 168.97, 171.51. Some other peaks should belong to the rotamer: δ 17.85 (TIPS CH_3), 32.88, 34.02, 40.93 (linker, Ar-CH_2), 114.75, 118.12, 125.55, 127.99, 128.29, 134.87, 136.58, 153.01, 169.67, 170.72.

3-[2-(4-Methyl-2-oxo-2H-1-benzopyran-7-yloxycarbonylmethyl)phenyldisulfanyl]-propanoic acid (**15**)

To a solution of **14** (105 mg, 0.18 mmol) in pyridine (1.6 mL) and acetonitrile (1.6 mL) was added HF/pyridine (70% weight, 0.80 mL) at 0 ^{o}C with stirring. After stirring for 5 h, the reaction was quenched by adding EtOAc (60 mL). The organic layer was separated, washed by water, saturated aqueous $CuSO_4$ and brine, dried over $MgSO_4$, and concentrated. The crude product was purified on a silica gel column (eluent: hexanes/EtOAc = 1/1.5) to give **15** (40 mg, 57% yield) as white solid: Compound **15** was found to exist as a mixture of rotamers in $CDCl_3$; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.43 (m, 3 H), 2.77 (t, *J* = 7.2 Hz, 1.4 H), 2.95 (t, *J* = 7.2 Hz, 1.4 H), 3.04 (m, 1.2 H), 3.90 (s, 0.7 H), 4.14 (s, 1.3 H), 6.26 (m, 1 H), 7.04-7.12 (m, 2 H), 7.20-7.33 (m, 3 H), 7.56 (d, *J* = 8.4 Hz, 1 H), 7.80 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.86 (HMC CH_3), 32.84, 33.69, 39.51 (linker, Ph-CH_2), 110.51, 114.64, 118.10, 118.19, 125.56, 128.56, 128.83, 131.04, 131.42, 133.71, 136.53, 152.21, 153.27, 154.25, 160.80, 169.03, 176.88. Some other peaks should belong to the rotamer: δ 32.89, 34.06, 39.10, 110.54, 114.72, 118.10, 125.55, 128.36, 128.71, 130.78, 131.34, 133.91, 136.69, 152.16, 153.00, 160.73, 169.75, 176.52.

2,5-Dioxopyrrolidin-1-yl 3-[2-(4-methyl-2-oxo-2H-1-benzopyran-7-yloxycarbonylmethyl)-phenyldisulfanyl]propanoate (**16**)

To a solution of **15** (40 mg, 0.093 mmol) and HOSu (11 mg, 0.093 mmol) in DCM (0.25 mL) and pyridine (0.25 mL) was added DCC (20 mg, 0.098 mmol) at 0 ^{o}C with stirring. After stirring for 18 h, the reaction mixture was filtered on Celite to remove precipitated dicyclohexylurea and concentrated *in vacuo*. The residue was purified on a silica gel column (eluent: hexanes/EtOAc = 2/1~3/1) to give **16** (33 mg, 67% yield) as white waxy solid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.42 (m, 3 H), 2.81-2.85 (s and s, 4 H), 3.02 (m, 4 H), 4.0-4.2 (s and s, 2 H), 6.25 (m, 1 H), 7.04-7.12 (m, 2 H), 7.20-7.33 (m, 3 H), 7.56 (d, *J* = 8.4 Hz, 1 H), 7.80 (m, 1H).

4-Methyl-2-oxo-2H-chromen-7-yl 2-[(3-biotinylhydrazinyl-3-oxopropyl)disulfanyl]phenyl-acetate (**3**)

To a solution of **16** (75 mg, 0.14 mmol) in DMSO (1.0 mL) was added **5** (33 mg, 0.13 mmol). After stirring for 16 h at room temperature, the reaction mixture was directly subjected to purification on a silica gel column (eluent: DCM/MeOH = 10/1) to give **3** (48 mg, 56% yield) as white powder: ^{1}H NMR (300 MHz, CD_3OD) δ 1.4-1.8 (m, 6 H, biotin side chain), 2.25 (t, *J* = 7.2 Hz, 2 H, biotin), 2.48 (m, 3 H, HMC), 2.65-2.73 [m, 3 H, biotin (1H) and linker (2H)], 2.90 (m, 1 H, biotin), 3.0 (m, 2 H, linker), 3.20 (m, 1 H, biotin), 3.86 and 4.21 (s, 2 H, integrations were 0.78 and 1.24, respectively, linker), 4.27(m, 1 H, biotin), 4.45 (m, 1 H, biotin), 6.32 (m, 1 H, HMC), 7.15 (m, 2 H, linker), 7.2-7.4 [m, 3 H, linker (1H) and HMC (2H)], 7.78 [m, 2 H, linker (1H) and HMC (1H)]; ^{13}C NMR (100 MHz, DMSO-d^6) δ 18.16 (HMC), 25.02, 28.01, 28.08 (25.1-28.1 biotin), 32.68, 32.92 (linker two carbons), 33.41 (biotin), 38.57 (linker, Ar-CH_2), 39.86 (biotin), 55.39, 59.19, 61.04 (55.4-61.0 biotin), 109.85, 113.85, 117.69, 118.19, 126.58 (109.8-126.6 HMC), 127.59, 128.67, 130.15, 131.63, 133.78, 136.15 (127.6-136.2 linker), 152.76, 152.90, 153.55, 159.58 (152.8-159.6 HMC), 162.71 (biotin), 168.82 (amide), 169.64 (amide), 170.90 (ester). Some other peaks should belong to the rotamer: δ 32.57, 37.83, 109.97, 113.81, 117.62, 118.30, 126.46, 127.88, 128.14, 130.69, 136.29, 152.68, 152.92, 153.50, 159.57, 162.67, 168.19, 169.64, 171.00; (HMC = 7-hydroxy-4-methylcoumarin). HRMS (ESI) *m/e* calcd for $C_{31}H_{35}N_4O_7S_3^+$ ($M + H^+$): 671.1662. Found: 671.1674 (Δ = 1.8 ppm).

Methyl 2-(6-hydroxy-3-oxo-3H-xanthen-9-yl)benzoate (17)[6]

Concentrated sulfuric acid (1.5 mL) was added dropwise to a suspension of fluorescein (2.00 g, 6.00 mmol) in methanol (6.0 mL). The resulting suspension was refluxed for 14 h. The reaction mixture was cooled to room temperature and diluted with EtOAc (100 mL). The organic layer was separated, washed with 5 % aqueous $NaHCO_3$ three times, water and brine. After drying over $MgSO_4$ and filtration, the solvent was removed *in vacuo* to dryness to afford **17** (1.88 g, 86 % yield) as a red solid: ^{1}H NMR (300 MHz, CD_3OD) δ 3.60 (s, 3 H), 6.66 (dd, *J* = 9.2, 2.0 Hz, 2 H), 6.74 (d, *J* = 1.5 Hz, 2 H), 7.00 (d, *J* = 9.2 Hz, 2 H), 7.43 (d, *J* = 7.6 Hz, 1 H), 7.79 (td, *J* = 7.2, 1.4 Hz, 1 H), 7.84 (td, *J* = 7.2, 1.4 Hz, 1 H), 8.29 (d, *J* = 7.4 Hz, 1 H).

***tert*-Butyl 4-hydroxybutanoate (19)**[7]

To a solution of 4-*tert*-butoxy-4-oxobutanoic acid (**18**) (2.12 g, 12.2 mmol) in dry THF (18 mL) at 0 ^{o}C was added BH_3•Me_2S (2.0 M, 6.55 mL, 13.1 mmol) dropwise with stirring. After stirring at room temperature for 24 h, the reaction was quenched by adding EtOAc (100 mL). The organic layer was separated, washed with water and brine, dried over $MgSO_4$, and concentrated *in vacuo* to give **19** (1.92 g, 98 % yield) as a colorless liquid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.41 (s, 9 H), 1.82 (m, 2 H), 2.31 (t, *J* = 6.3 Hz, 2 H), 2.50 (bs, 1 H), 3.64 (t, *J* = 6.3 Hz, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 27.78, 27.98, 32.31, 61.97, 80.43, 173.41.

***tert*-Butyl 4-[9-(2-methoxycarbonylphenyl)-3-oxo-3H-xanthen-6-yloxy]butanoate (20)**[6]

To a suspension of **17** (200 mg, 0.58 mmol), **19** (278 mg, 1.74 mmol) and triphenylphosphine (454 mg, 1.74 mmol) in 50 % THF/CH_3CN (4 mL) was added DIAD (0.33 mL, 1.74 mmol). The mixture was stirred for 3 h and then concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (eluent: 5% MeOH in DCM) to give **20** (197 mg, 70 % yield) as an orange solid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.45 (s, 9 H), 2.17 (m, 2 H), 2.42 (t, *J* = 6.3 Hz, 2 H), 3.65 (s, 3 H), 4.18 (t, *J* = 6.3 Hz, 2 H), 6.66 (dd, *J* = 9.2, 2.0 Hz, 2 H), 6.74 (d, *J* = 1.5 Hz, 2 H), 7.00 (d, *J* = 9.2 Hz, 2 H), 7.43 (d, *J* = 7.6 Hz, 1 H), 7.79 (td, *J* = 7.2, 1.4 Hz, 1 H), 7.84 (td, *J* = 7.2, 1.4 Hz, 1 H), 8.29 (d, *J* = 7.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.70, 28.42, 32.04, 52.68, 68.04, 80.91, 101.15, 106.04, 113.96, 115.09, 117.84, 129.13, 130.47, 130.59, 130.85, 131.41, 132.30, 132.43, 132.98, 134.92, 150.43, 154.52, 159.22, 163.63, 165.88, 172.44, 185.92.

4-[9-(2-Methoxycarbonylphenyl)-3-oxo-3H-xanthen-6-yloxy]butanoic acid (21)

To a solution of **20** (230 mg, 0.471 mmol) in DCM (2.3 mL) was added dropwise trifluoroacetic acid (TFA, 2.3 mL) with stirring. The mixture was stirred at room temperature for 2 h and ether (10 mL x 2) was added to precipitate out the product. The upper ether layer was removed by decantation and the precipitate was dried *in vacuo*. The crude product was purified on a silica gel column (eluent: 3% MeOH in DCM) to give **21** (215 mg, 94 % yield) as an orange solid: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.28 (m, 2 H), 2.68 (t, 2 H), 3.69 (s, 3 H), 4.40 (t, 2 H), 7.37 (m, 7 H), 7.89 (m, 2 H), 8.42 (d, *J* = 7.5 Hz, 1 H), 12.26 (s, br, 1 H).

2'-*tert*-Butyldimethylsilyl-SB-T-1214 (22)

To a mixture of **SB-T-1214**[2,8] (343 mg, 0.40 mmol), *tert*-butyldimethylsilyl chloride (TBDMSCl, 302 mg, 2.0 mmol) and imidazole (273 mg, 4.0 mmol) was added dry DMF (0.54 mL). After stirring the mixture at room temperature for 4 h, the reaction was quenched by adding

EtOAc (90 mL). The resulting solution was washed by water and brine, dried over $MgSO_4$, and concentrated. The crude product was purified on a silica gel column (eluent: hexanes/EtOAc = 2.5/1) to give **22** (330 mg, 85% yield) as a white solid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.080 (s, 3 H), 0.12 (s, 3 H), 0.98-1.05 (m, 2 H), 1.13-1.21 (m, 2 H), 1.15 (s, 3 H), 1.26 (s, 3 H), 1.35 (s, 9 H), 1.37 (s, 9 H), 1.66 (s, 3 H), 1.74-1.79 (m, 8 H), 1.86 (m, 1 H), 1.87 (s, 3 H), 2.2-2.4 (m, 2 H), 2.41 (s, 3 H), 2.55 (m, 1 H), 2.58 (d, *J* = 3.9 Hz, 1 H), 3.81 (d, *J* = 7.2 Hz, 1 H), 4.17 (d, *J* = 8.1 Hz, 1 H), 4.23 (d, *J* = 3.6 Hz, 1 H), 4.30 (d, *J* = 8.1 Hz, 1 H), 4.40 (m, 1 H), 4.78 (m, 2 H), 4.95 (d, *J* = 7.8 Hz, 1 H), 5.21 (d, *J* = 8.4 Hz, 1 H), 5.65 (d, *J* = 7.2 Hz, 1 H), 6.19 (t, *J* = 7.2 Hz, 1 H), 6.28 (s, 1 H), 7.49 (t, *J* = 8.1 Hz, 2 H), 7.61 (t, *J* = 7.2 Hz, 1 H), 8.11 (d, *J* = 8.4 Hz, 2 H).

7-(4-Fluorescein-butanoyl)-2'-*tert*-butyldimethylsilyl-SB-T-1214 (23)

To a solution of **22** (120 mg, 0.124 mmol), DMAP (15.1 mg, 0.124 mmol) and **21** (107 mg, 0.247 mmol) in DCM (5 mL) and DMF (2 mL) was added DIC (0.038 mL, 0.248 mmol) at room temperature with stirring. The mixture was stirred overnight at room temperature. The white precipitate was filtered off through Celite, and rinsed with DCM. The DCM filtrates were combined and concentrated under reduced pressure. The crude product was purified on a silica gel column (eluent: 2% MeOH in DCM) to afford **23** (115.8 mg, 70 % yield) as an orange solid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.07 (s, 3 H), 0.10 (s, 3 H), 0.92 (s, 9 H), 0.99 (m, 2 H), 1.06 (m, 2 H), 1.16 (s, 3 H), 1.22 (s, 3 H), 1.34 (s, 9 H), 1.66 (m, 1 H), 1.73 (s, 3 H), 1.77 (s, 3 H), 1.79 (s, 3 H), 1.93 (s, 3 H), 2.09 (m, 2 H), 2.15 (m, 1 H), 2.29 (m, 1 H), 2.40 (s, 3 H), 2.46 (m, 2 H), 2.57 (m, 2 H), 3.61 (s, 3 H), 3.69 (s, 1 H), 3.95 (d, *J* = 6.8 Hz, 1 H), 4.10 (m, 2 H), 4.17 (d, *J* = 8.4 Hz, 1 H), 4.23 (d, *J* = 3.2 Hz, 1 H), 4.30 (d, *J* = 8.4 Hz, 1 H), 4.74 (m, 1 H), 4.80 (m, 1 H), 4.93 (d, *J* = 8.8 Hz, 1 H), 5.22 (d, *J* = 8.0 Hz, 1 H), 5.60 (dd, *J* = 10.8, 7.2 Hz, 1 H), 5.66 (d, *J* = 6.8 Hz, 1 H), 6.13 (t, *J* = 8.8 Hz, 1 H), 6.29 (s, 1 H), 6.49 (s, 1 H), 6.54 (d, *J* = 10 Hz, 1 H), 6.73 (m, 1 H), 6.86 (m, 2 H), 6.96 (t, *J* = 2.4 Hz, 1 H), 7.28 (d, *J* = 7.2 Hz, 1 H), 7.46 (t, *J* = 8.0 Hz, 2 H), 7.64 (m, 3 H), 8.08 (d, *J* = 8.8 Hz, 2 H), 8.22 (m, 1 H).

7-(4-Fluorescein-butanoyl)-SB-T-1214 (24)

Compound **24** (38 mg, 0.0275 mmol) was added to 1% hydrochloric acid in ethanol (2.36 mL) and the mixture was stirred at room temperature overnight. The reaction mixture was diluted with ethyl acetate (60 mL) and washed with $NaHCO_3$ and water. The organic layer was separated, dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The crude product was purified on a silica gel column (eluent: 2 % MeOH in DCM) to afford **24** (24 mg, 93 % yield) as an orange solid: ^{1}H NMR ($CDCl_3$, 500 MHz): δ 0.86-0.92 (2 H, m, CH_2-*c*-Pr), 0.99 (1 H, m, CH_2-*c*-Pr), 1.06 (1 H, m, CH_2-*c*-Pr), 1.17 (3 H, s, C-16), 1.23 (3H, s, C-17), 1.34 (9 H, s, Boc), 1.67 (1 H, m, CH-*c*-Pr), 1.75 (6 H, s, H-3' isobutyl), 1.80 (3 H, s, C-19), 1.85 (4 H, m, H-6b), 1.99 (3 H, s, C-18), 2.14 (3 H, m, H-6b, CH_2-fluorescein), 2.37 (3 H, s, 4-OAc), 2.37-2.53 (4 H, m, H-14ab, CH_2-fluorescein), 2.58 (1 H, m, H-6a), 3.25 (1 H, bs, OH), 3.62 (3 H, s, OMe), 3.96 (1 H, d, *J*= 7.0 Hz, H-3), 4.18 (3 H, m, H-20b, OCH_2-fluorescein), 4.26 (1 H, d, *J*= 2.5, H-5), 4.31 (1 H, d, *J*= 8.0, H-20a), 4.75 (1 H, m, H-7), 4.96 (1 H, d, *J*= 9.0 Hz, H-2), 5.00 (1 H, bs, NH), 5.32 (1 H, bm, H-2'), 5.62-5.68 (2 H, m, H-3' , H-3'-isobutyl), 6.13 (1 H, t, *J*= 9.0 Hz, H-13), 6.31 (1 H, s, H-10), 6.86 (3 H, m, fluorescein), 7.01 (1 H, d, *J*= 9.5 Hz, fluorescein), 7.04 (1 H, d, *J*= 9.0 Hz, fluorescein), 7.22 (1 H, d, *J*= 5.0 Hz, fluorescein), 7.31 (1 H, d, *J*= 7.0 Hz, fluorescein), 7.46 (2 H, t, *J*= 8.0 Hz), 7.60 (1 H, t, *J*= 7.5 Hz), 7.71 (1 H, d, *J*= 8.0 Hz, fluorescein), 7.77 (1 H, d, *J*= 7.5 Hz, fluorescein), 8.08 (2 H, d, *J*= 8.0 Hz), 8.28 (1 H, d, *J*= 7.0 Hz, fluorescein); ^{13}C (125 MHz, $CDCl_3$): δ 8.7, 8.8, 10.8, 12.4, 14.6, 18.5, 21.1, 23.4, 25.7, 26.2, 28.2, 29.6, 29.9, 30.0,

33.4, 35.5, 43.2, 45.9, 46.9, 51.5, 52.5, 56.1, 68.4, 71.6, 71.9, 73.6, 74.4, 75.1, 76.3, 78.6, 79.7, 80.6, 83.9, 100.7, 104.8, 115.2, 116.1, 117.0, 120.9, 127.3, 128.5, 128.6, 128.7, 129.1, 129.5, 130.1, 130.2, 130.8, 130.9, 131.2, 132.0, 132.5, 132.8, 133.7, 134.0, 141.2, 155.4, 155.8, 159.6, 165.3, 165.5, 166.8, 170.1, 171.8, 171.9, 172.9, 202.4; HRMS (FAB$^+$, *m/z*): Calcd. for $C_{70}H_{77}NO_{21}\cdot H^+$, 1268.5061; Found, 1268.5072 (Δ = 0.8 ppm).

7-Fluorescein-SB-T-1214-2'-Linker-CO_2TIPS (25)

To a solution of **24** (84 mg, 0.066 mmol), **12** (34 mg, 0.079 mmol) and DMAP (8 mg, 0.066 mmol) in DCM was added DIC (0.020 mL, 0.132 mmol) at 0 ^oC with stirring. The reaction was stopped after 4 h with incomplete conversion when side reaction was observed by TLC analysis. The precipitate was filtered off through Celite, and rinsed with DCM. The DCM filtrates were combined and concentrated. Column chromatography of the residue on silica gel using hexanes/EtOAc (1/2~1/4) as the eluent gave **25** (65 mg, 71 % yield) as yellow powder: ^1H NMR (300 MHz, $CDCl_3$) δ 0.98-1.05 (m, 2 H), 1.07 (d, *J* = 6.9 Hz, 18 H), 1.13-1.21 (m, 2 H), 1.15 (s, 3H), 1.26 (s, 3H), 1.29 (m, 3 H), 1.35 (s, 9 H), 1.62 (m, 2 H), 1.65 (s, 3 H), 1.67 (s, 3 H), 1.72 (m, 1 H), 1.75 (s, 3 H), 1.92 (s, 3 H), 2.12 (m, 2 H), 2.24 (m, 2 H), 2.32 (s, 3 H), 2.41 (m, 2 H), 2.52 (m, 1 H), 2.72 (t, *J* = 6.6 Hz, 2 H), 2.91 (t, *J* = 6.6 Hz, 2 H), 3.58 (d, *J* = 0.9 Hz, 3 H), 3.87 (m, 2 H), 4.02-4.14 (m, 4 H), 4.26 (d, *J* = 8.4 Hz, 1 H), 4.7-4.9 (m, 4 H), 5.04 (d, *J* = 8.4 Hz, 1 H), 5.55 (dd, *J* = 10.5, 6.9 Hz, 1 H), 5.63 (d, *J* = 6.9 Hz, 1 H), 6.11 (t, *J* = 7.2 Hz, 1 H), 6.25 (s, 1 H), 6.41 (s, 1 H), 6.47 (d, *J* = 9.9 Hz, 1 H), 6.68 (dd, *J* = 9.0, 2.1 Hz, 1 H), 6.80 (m, 2 H), 6.92 (t, *J* = 2.1 Hz, 1 H), 7.27 (m, 4 H), 7.43 (t, *J* = 7.8 Hz, 2 H), 7.54-7.73 (m, 4 H), 8.06 (d, *J* = 8.4 Hz, 2 H), 8.19 (dd, *J* = 8.1, 1.5 Hz, 1 H).

7- Fluorescein-SB-T-1214-2'-Linker-CO_2H (26)

To a solution of **25** (65 mg, 0.039 mmol) in pyridine (1 mL) and CH_3CN (1 mL) was added HF/pyridine (70% wt, 0.50 mL) at 0 ^oC with stirring. After stirring for 5 h at room temperature, the reaction mixture was diluted with EtOAc and washed thoroughly by saturated aqueous $CuSO_4$ (20 mL x 4), water and brine. The organic layer was separated, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified on a silica gel column (eluent: hexanes/EtOAc = 1/4~1/8) to give **26** (43 mg, 80% yield) as yellow powder: ^1H NMR (300 MHz, $CDCl_3$) δ 0.98-1.05 (m, 2 H), 1.13-1.21 (m, 8 H), 1.35 (s, 9 H), 1.62 (m, 2 H), 1.72-1.78 (m, 10 H), 1.97 (s, 3 H), 2.12 (m, 2 H), 2.3-2.6 (m, 8 H), 2.68 (t, *J* = 6.9 Hz, 2 H), 2.95 (m, 2 H), 3.62 (d, *J* = 0.9 Hz, 3 H), 3.94 (m, 2 H), 4.02-4.25 (m, 4 H), 4.33 (d, *J* = 8.7 Hz, 1 H), 4.90-4.97 (m, 4 H), 5.12 (d, *J* = 8.4 Hz, 1 H), 5.58 (dd, *J* = 10.5, 6.9 Hz, 1 H), 5.69 (d, *J* = 6.9 Hz, 1 H), 6.17 (t, *J* = 7.2 Hz, 1 H), 6.28 (s, 1 H), 6.58-6.62 (m, 2 H), 6.74 (dd, *J* = 9.0, 2.1 Hz, 1 H), 6.88 (m, 2 H), 7.03 (t, *J* = 1.8 Hz, 1 H), 7.27 (m, 4 H), 7.43 (t, *J* = 7.8 Hz, 2 H), 7.54-7.73 (m, 4 H), 8.06 (d, *J* = 8.4 Hz, 2 H), 8.19 (dd, *J* = 8.1, 1.5 Hz, 1 H). MS (ESI) *m/e* calcd for $C_{81}H_{88}NO_{24}S_2^+$ (M + H^+): 1522.5. Found: 1522.4; *m/e* calcd for $C_{81}H_{87}NNaO_{24}S_2^+$ (M + Na^+): 1544.5. Found: 1544.4.

7-Fluorescein-SB-T-1214-2'-Linker-OSu (27)

To a solution of **26** (43 mg, 0.028 mmol) and HOSu (16 mg, 0.14 mmol) in THF was added DCC (14 mg, 0.068 mmol) at 0 ^oC with stirring. After stirring for 36 h at room temperature, the reaction mixture was filtered and the filtrate concentrated *in vacuo*. The residue was purified on a silica gel column to give **27** (45 mg, 99% yield) as orange powder: ^1H NMR (300 MHz, $CDCl_3$): δ 0.98-1.05 (m, 2 H), 1.13-1.21 (m, 8 H), 1.34 (s, 9 H), 1.62 (m, 2 H), 1.72-

1.78 (m, 10 H), 1.97 (s, 3 H), 2.12 (m, 2 H), 2.3-2.6 (m, 8 H), 2.83 (s, 4 H), 3.02 (m, 4 H), 3.62 (d, *J* = 0.9 Hz, 3 H), 3.94 (m, 2 H), 4.02-4.25 (m, 4 H), 4.33 (d, *J* = 8.7 Hz, 1 H), 4.90-4.97 (m, 4 H), 5.12 (d, *J* = 8.4 Hz, 1 H), 5.57 (dd, *J* = 10.5, 6.9 Hz, 1 H), 5.67 (d, *J* = 6.9 Hz, 1 H), 6.17 (t, *J* = 7.2 Hz, 1 H), 6.28 (s, 1 H), 6.45 (d, *J* = 2.1 Hz, 1 H), 6.52 (dd, *J* = 9.6, 1.8 Hz, 1 H), 6.72 (dd, *J* = 9.0, 2.4 Hz, 1 H), 6.85 (m, 2 H), 6.96 (t, *J* = 2.4 Hz, 1 H), 7.27 (m, 4 H), 7.47 (t, *J* = 7.8 Hz, 2 H), 7.54-7.73 (m, 4 H), 8.09 (d, *J* = 8.4 Hz, 2 H), 8.24 (dd, *J* = 8.1, 1.5 Hz, 1 H). MS (ESI) *m/e* calcd for $C_{85}H_{91}N_2O_{26}S_2^+$ (M + H^+): 1619.5. Found: 1619.5; *m/e* calcd for $C_{85}H_{90}N_2NaO_{26}S_2^+$ (M + Na^+): 1641.5. Found: 1641.5.

Biotin-Linker-Taxoid- Fluorescein conjugate (**4**)

To a solution of **27** (45 mg, 0.022 mmol) in DMSO (0.15 mL) was added **5** (5.4 mg, 0.020 mmol) at room temperature with stirring. After stirring for 24 h, the reaction mixture was directly loaded onto silica gel column and column chromatography using 6% MeOH in DCM as the eluent afforded **4** (24 mg, 82% yield) as orange powder: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.80-1.10 [m, 4 H: cyclopropyl (2H) and biotin (2H)], 1.13-1.41 [m, 21 H: biotin (4H), cyclopropyl (2H), C17 (3H), C16 (3H) and Boc (9H)], 1.5-1.8 [m, 12 H: OH, cyclopropyl (1H), C6 (1H), C5' (6H) and C19 (3H)], 1.95 (s, 3 H, C18), 2.1-2.74 [m, 15 H: C7-tether (2H at 2.10 ppm), biotin (2H at 2.26 ppm), Ac (3H), C6 (1H), C14 (2H), C7-tether (2H), biotin (1H at 2.60 ppm) and linker (2H)], 2.85 (m, 1 H, biotin), 2.95 (m, 2 H, linker), 3.10 (m, 1 H, biotin), 3.62 (d, *J* = 1.2 Hz, 3 H, OCH_3), 3.94-4.20 [m, 6 H: C3 (1H), linker (2H), C20 (1H) and C7-tether (2H)], 4.33 [m, 2 H: C20 (1H) and biotin (1H)], 4.47 (m, 1 H, biotin), 4.90-5.2 (m, 5 H: C2', C3', C4', C5 and NH of taxoid), 5.59 (dd, *J* = 10.5, 6.9 Hz, 1 H, C7), 5.68 (d, *J* = 6.9 Hz, 1 H, C2), 5.83 (s, 1 H, urea NH at biotin), 6.16 (t, *J* = 7.2 Hz, 1 H, C13), 6.28 (s, 1 H, C10), 6.54 (d, *J* = 1.5 Hz, 1 H, fluorescein), 6.62 (dd, *J* = 9.6, 1.8 Hz, 1 H, fluorescein), 6.66 (br, 1 H, urea NH at biotin), 6.75 (dd, *J* = 9.0, 2.4 Hz, 1 H, fluorescein), 6.88 (m, 2 H, fluorescein), 7.02 (t, *J* = 2.1 Hz, 1 H, fluorescein), 7.27-7.35 [m, 4 H: fluorescein (1H) and linker (3H)], 7.43 (t, *J* = 7.8 Hz, 2 H, taxoid), 7.54-7.73 [m, 4 H: taxoid (1H), fluorescein (2H) and linker (1H)], 8.06 (d, *J* = 8.4 Hz, 2 H, taxoid), 8.19 (dd, *J* = 8.1, 1.5 Hz, 1 H, fluorescein), 9.13 (br, 1 H, hydrazide), 9.31 (br, 1 H, hydrazide); ^{13}C NMR (100 MHz, $CDCl_3$) δ 8.98, 11.05, 13.05, 14.68, 18.73, 21.58, 22.60, 23.88, 25.28, 25.62, 25.95, 26.45, 27.96, 28.08, 28.45, 30.48, 33.16, 33.44, 33.45, 35.63, 38.90, 40.62, 43.45, 47.04, 49.21, 52.61, 55.66, 56.19, 60.57, 62.08, 68.25, 71.71, 71.99, 74.76, 75.14, 75.23, 76.49, 78.82, 80.09, 80.92, 84.07, 100.92, 105.64, 114.70, 114.89, 117.43, 119.94, 128.20, 128.81, 129.12, 129.47, 129.92, 130.33, 130.45, 130.68, 131.31, 132.57, 132.87, 133.61, 133.80, 134.70, 136.81, 138.32, 141.72, 152.16, 154.83, 155.38, 159.50, 164.19, 164.80, 165.71, 166.92, 168.64, 169.89, 170.05, 170.64, 172.03, 172.15, 172.81, 173.05, 185.82, 202.61. HRMS (ESI) *m/e* calcd for $C_{91}H_{104}N_5O_{25}S_3^+$ (M + H^+): 1762.6177. Found: 1762.6162 (Δ = -0.9 ppm).

SB-T-1214-linker-CO_2TIPS (**28**)

To a mixture of **SB-T-1214** (42 mg, 0.049 mmol), DMAP (1 mg, 0.010 mmol) and **12** (22 mg, 0.051 mmol) in DCM (2.5 mL) was added DIC (9.2 μL, 0.059 mmol). The mixture was stirred for 4 h at room temperature and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (eluent: hexanes/EtOAc = 3/1) to give **28** (85 mg, 85 % yield) as white solid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.13 (s, 3 H), 1.14 (s, 3 H), 1.25 (s, 4 H), 1.22 (d, *J* = 7.2 Hz, 18 H), 1.31 (m, 3H), 1.34 (s, 9 H), 1.66 (s, 3 H), 1.71 (s, 1 H), 1.75 (s, 6 H), 1.82 (s, 1 H), 1.86 (m, 1 H), 1.91 (s, 3 H), 2.31 (s, 1 H), 2.33 (s, 1 H), 2.37 (s, 3 H), 2.60 (m, 2 H), 2.87 (d, *J* = 6 Hz, 2 H), 2.97 (d, *J* = 6 Hz, 2 H), 3.80 (d, *J* = 7.2 Hz, 1 H), 4.17 (s, 2 H), 4.19

(d, *J* = 8.7 Hz, 1 H), , 4.30 (d, *J* = 8.7 Hz, 1 H), 4.43 (dd, *J* = 10.6, 6.6 Hz, 1 H), 4.9-5.0 (m, 4 H), 5.19 (s, 1 H), 5.66 (d, *J* = 7.2 Hz, 1 H), 6.17 (t, *J* = 8.7 Hz, 1 H), 6.29 (s, 1 H), 7.34 (m, 3 H), 7.47 (t, *J* = 7.5 Hz, 2 H), 7.60 (t, *J* = 7.3 Hz, 1 H), 7.80 (d, *J* = 7.2 Hz, 1 H), 8.10 (d, *J* = 7.4 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 1.22, 9.32, 9.53, 9.75, 13.21, 13.90, 15.00, 18.75, 19.32, 22.42, 22.63, 23.69, 25.80, 25.94, 26.91, 28.44, 29.90, 30.86, 32.84, 33.54, 35.67, 35.95, 43.40, 45.84, 49.20, 58.71, 64.56, 72.05, 72.37, 75.05, 75.45, 75.66, 76.62, 79.51, 80.07, 81.22, 84.70, 120.15, 128.57, 128.85, 129.20, 129.51, 130.38, 131.03, 131.27, 132.12, 132.76, 133.82, 136.70, 138.16, 143.58, 155.13, 166.58, 167.21, 168.39, 169.20, 169.86, 171.19, 175.30, 204.30.

SB-T-1214-linker-CO_2H (**29**)

To a solution of **28** (50 mg) in pyridine/acetonitrile (1:1) (2 mL) was added dropwise HF/pyridine (70:30, 0.5 mL) at 0 °C, and the mixture was stirred for 12 h at room temperature. The reaction mixture was diluted with ethyl acetate (30 mL), washed with saturated aqueous $CuSO_4$ solution (30 mL x 3) and water (30 mL), dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (eluent: hexanes/EtOAc = 1/1) to afford the **29** (39 mg, 89 % yield) as white solid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.13 (s, 3 H), 1.14 (s, 3 H), 1.25 (s, 4 H), 1.34 (s, 9 H), 1.66 (s, 3 H), 1.71 (s, 1 H), 1.75 (s, 6 H), 1.82 (s, 1 H), 1.86(m, 1 H), 1.91 (s, 3 H), 2.31 (s, 1 H), 2.33 (s, 1 H), 2.37 (s, 3 H), 2.60 (m, 2 H), 2.87 (d, J = 6 Hz, 2 H), 2.97 (d, J = 6 Hz, 2 H), 3.80 (d, J = 7.2 Hz, 1 H), 4.17 (s, 2 H), 4.19 (d, J = 8.7 Hz, 1 H), , 4.30 (d, J = 8.7 Hz, 1 H), 4.43 (dd, J = 10.6, 6.6 Hz, 1 H), 4.9-5.0 (m, 4 H), 5.19 (s, 1 H), 5.66 (d, J = 7.2 Hz, 1 H), 6.17 (t, J = 8.7 Hz, 1 H), 6.29 (s, 1 H), 7.34 (m, 3 H), 7.47 (t, J = 7.5 Hz, 2 H), 7.60 (t, J = 7.3 Hz, 1 H), 7.80 (d, J = 7.2 Hz, 1 H), 8.10 (d, J = 7.4 Hz, 2 H).

SB-T-1214-Linker-OSu (**30**)

To a solution of **29** (107 mg, 0.097 mmol) and HOSu (14 mg, 0.12 mmol) in pyridine (0.25 mL) was added DCC (24 mg, 0.11 mmol) at 0 ^{o}C. After stirring the mixture for 24 h at 4 ^{o}C, the reaction mixture was filtered and the filtrate concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (eluent: hexanes/EtOAc = 2/1~1/2) to give **30** (100 mg, 86% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.13 (s, 3 H, H16), 1.14 (s, 3 H, H17), 1.25 (s, 4 H, H10 cyclopropane), 1.34 (s, 9 H, Boc), 1.66 (s, 3 H, H19), 1.71 (s, 1 H, cyclopropane), 1.75 (s, 6 H, isobutenyl), 1.82 (s, 1 H, OH), 1.86(m, 1 H, H6a), 1.91 (s, 3 H, H18), 2.31 (s, 1 H, H 6), 2.33 (s, 1 H, OH), 2.37 (s, 3 H, OAc), 2.60 (m, 2 H, H 14), 2.83 (s, 4 H, OSu), 2.87 (d, J =6 Hz, 2 H, CH_2-CO_2Su), 2.97 (d, J =6 Hz, 2 H, S-CH_2), 3.80 (d, J = 7.2 Hz, 1 H, H3), 4.17 (s, 2 H, Ph-CH_2-CO_2), 4.19 (d, J = 8.7 Hz, 1 H, H20a), , 4.30 (d, J = 8.7 Hz, 1 H, H20b), 4.43 (dd, J = 10.6, 6.6 Hz, 1 H, H7), 4.9-5.0 (m, 4 H, H3', H4'isobutenyl, H5, H2'), 5.19 (s, 1 H, NH), 5.66 (d, J = 7.2 Hz, 1 H, H2), 6.17 (t, J = 8.7 Hz, 1 H, H13), 6.29 (s, 1 H, H10), 7.34 (m, 3 H, Ph linker), 7.47 (t, J = 7.5 Hz, 2 H, Bz), 7.60 (t, J = 7.3 Hz, 1 H, Bz), 7.80 (d, J = 7.2 Hz, 1 H, Ph linker), 8.10 (d, J = 7.4 Hz, 2 H, Bz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 1.22, 9.32, 9.53, 9.75, 13.21, 13.90, 15.00, 18.75, 19.32, 22.42, 22.63, 23.69, 25.80, 25.94, 26.91, 28.44, 29.90, 30.86, 32.84, 33.54, 35.67, 35.95, 43.40, 45.84, 49.20, 58.71, 64.56, 72.05, 72.37, 75.05, 75.45, 75.66, 76.62, 79.51, 80.07, 81.22, 84.70, 120.15, 128.57, 128.85, 129.20, 129.51, 130.38, 131.03, 131.27, 132.12, 132.76, 133.82, 136.70, 138.16, 143.58, 155.13, 166.58, 167.21, 168.39, 169.20, 169.86, 171.19, 175.30, 204.30. HRMS (FAB) *m/e* calcd for $C_{60}H_{72}N_2O_{20}S_2{\cdot}H^+$: 1205.4198. Found: 1205.4188 (Δ = -0.8 ppm).

Biotin-Linker-SB-T-1214 (**1**)

To a solution of **30** (32 mg, 0.030 mmol) in DMSO (0.15 mL) was added **5** (7.0 mg, 0.027 mmol) at room temperature. After stirring the mixture for 48 h, the reaction mixture was directly loaded onto a silica gel column. Column chromatography of the residue (eluent: 7% MeOH in DCM) afforded **1** (25 mg, 81% yield) as white powder: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.95 (m 2 H), 1.10-1.25 (m, 9 H), 1.36-1.43 (m, 10 H), 1.57-1.98 (m, 19 H), 2.1-2.74 (m, 8 H), 2.60-2.72 (m, 3 H), 2.85-3.00 (m, 3 H), 3.10 (m, 1 H), 3.28 (br, 1 H), 3.80 (d, *J* = 7.2 Hz, 1 H), 4.00 (m, 2 H), 4.16 (d, *J* = 8.4 Hz, 1 H), 4.30 (m, 2 H), 4.39 (m, 1 H), 4.47 (m, 1 H), 4.9-5.2 (m, 5 H), 5.67 (d, *J* = 6.8 Hz, 1 H), 6.00 (s, 1 H), 6.16 (t, *J* = 7.2 Hz, 1 H), 6.32 (s, 1 H), 6.94 (s, 1 H), 7.2-7.4 (m, 3 H), 7.46 (t, *J* = 7.8 Hz, 2 H), 7.59 (t, *J* = 7.8 Hz, 1 H), 7.79 (d, *J* = 8.0 Hz, 2 H), 8.06 (d, *J* = 8.4 Hz, 2 H), 9.23 (br, 1 H), 9.61 (br, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 9.31, 9.44, 9.83, 13.24, 14.95, 18.68, 22.22, 22.67, 25.41, 25.96, 26.81, 28.23, 28.47, 33.34, 33.46, 35.70, 35.92, 38.89, 40.66, 43.39, 46.10, 49.21, 55.80, 58.58, 60.47, 62.12, 72.02, 75.19, 75.27, 75.66, 76.56, 79.29, 80.00, 81.24, 84.65, 120.03, 128.09, 128.80, 129.51, 130.30, 130.49, 131.27, 132.88, 133.44, 133.78, 136.94, 138.26, 142.89, 155.23, 164.79, 167.06, 168.60, 169.71, 170.00, 170.68, 172.08, 174.98, 204.06. HRMS (ESI) *m/e* calcd for $C_{66}H_{85}N_5O_{19}S_3H^+$:1348.5079. Found: 1348.5087 (Δ = 0.6 ppm).

References

(1) McCormick, D. B.; Roth, J. A. *Analytical Biochemistry* **1970**, *34*, 226-36.
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1HNMR

Parameter	Value
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2 Origin	Varian
3 Spectrometer	inova
4 Solvent	CDCl3
5 Temperature	25.0
6 Pulse Sequence	s2pul
7 Experiment	1D
8 Number of Scans	480
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11 Pulse Width	0.0000
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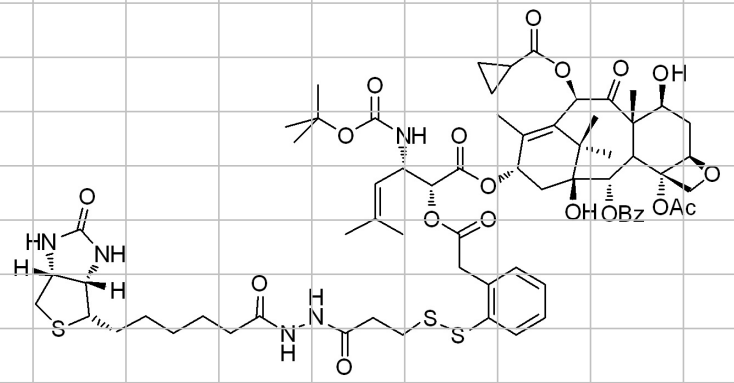

f1 (ppm)

13CNMR

Parameter	Value
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3 Spectrometer	inova
4 Solvent	CDCl3
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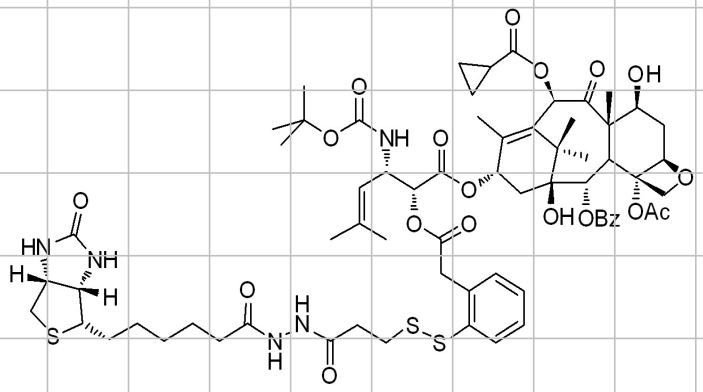
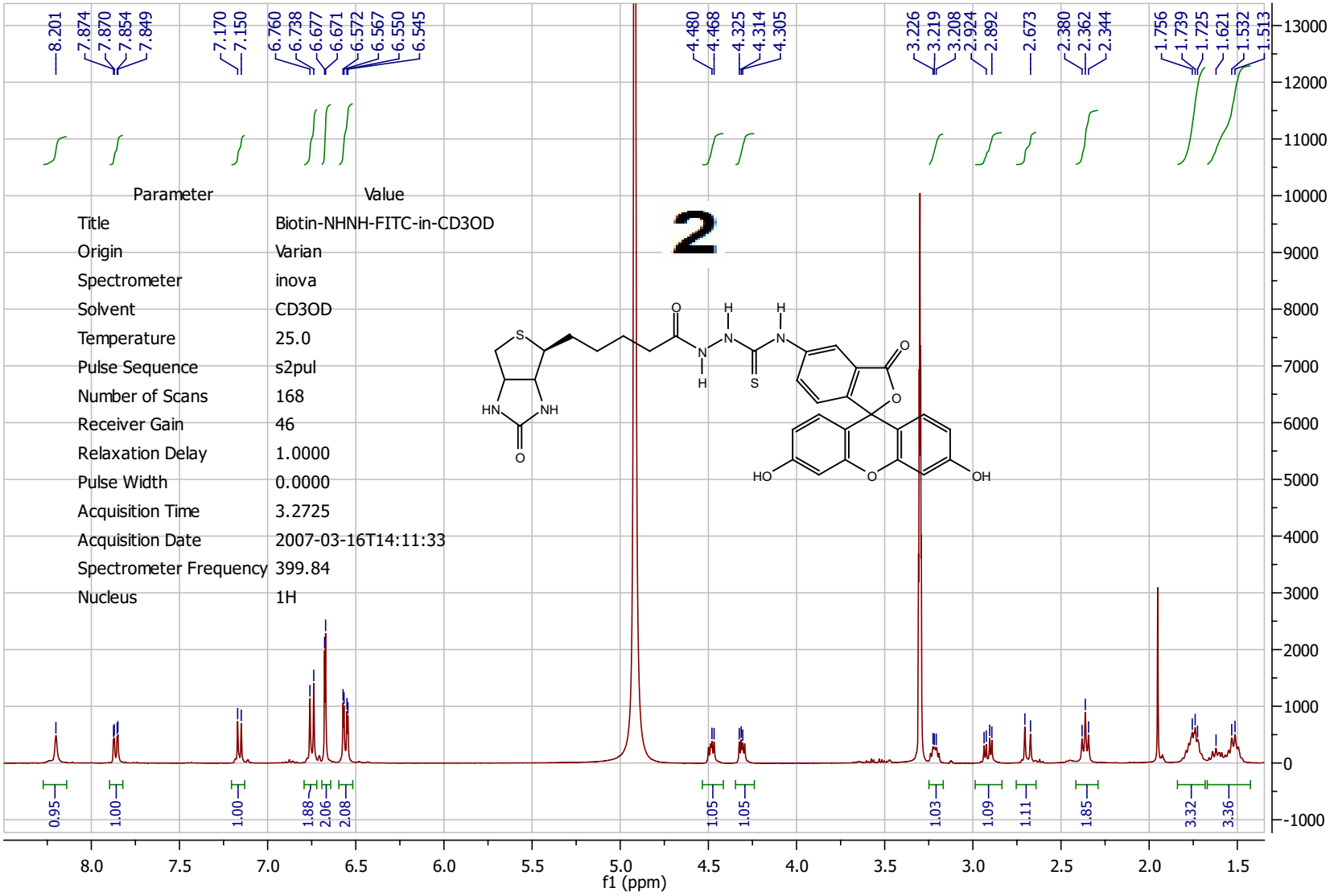
1

$C_{67}H_{87}N_5O_{19}S_3$

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Origin Varian
Spectrometer inova
Solvent CD3OD
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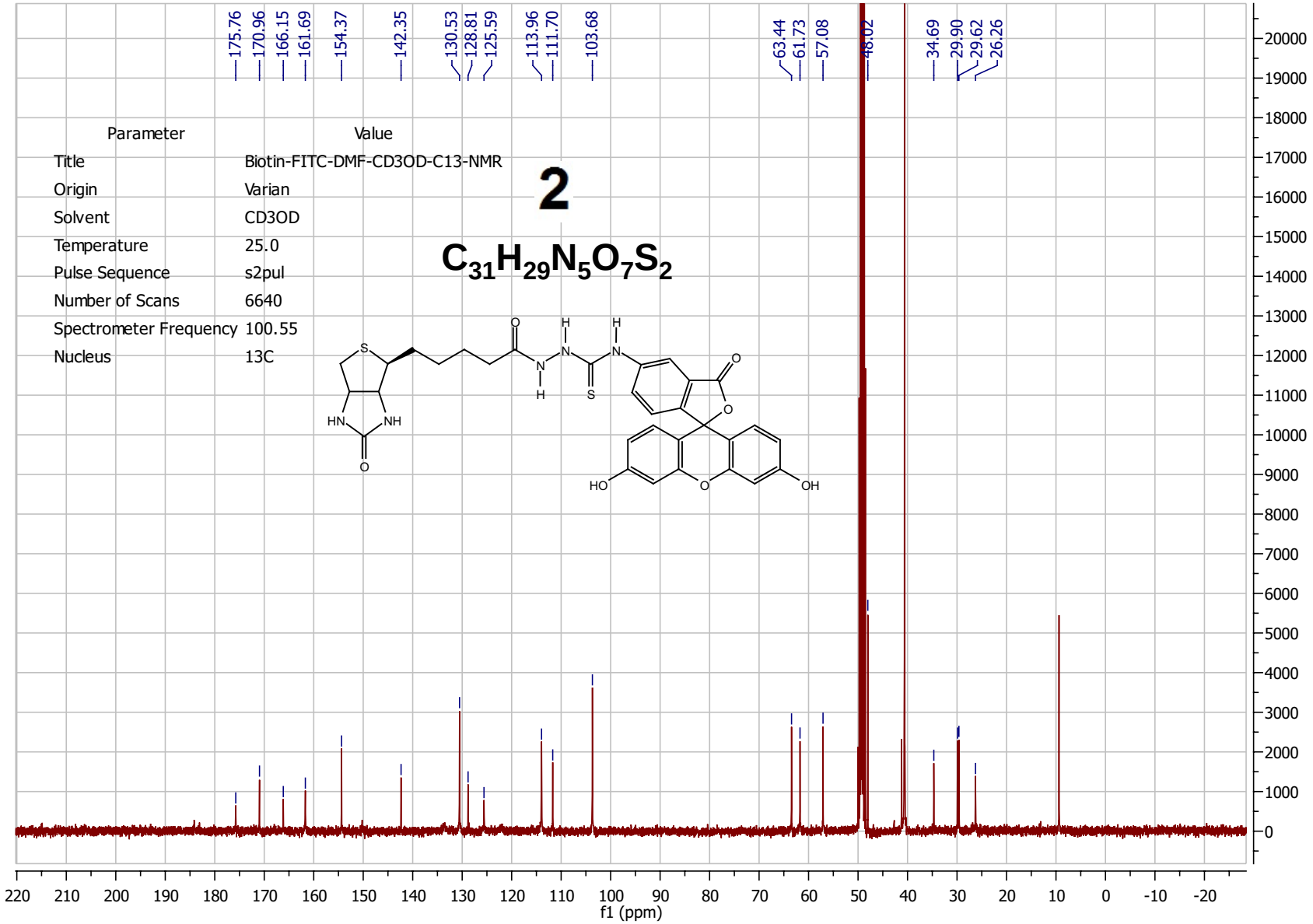
f1 (ppm)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Origin Varian
Solvent CD3OD
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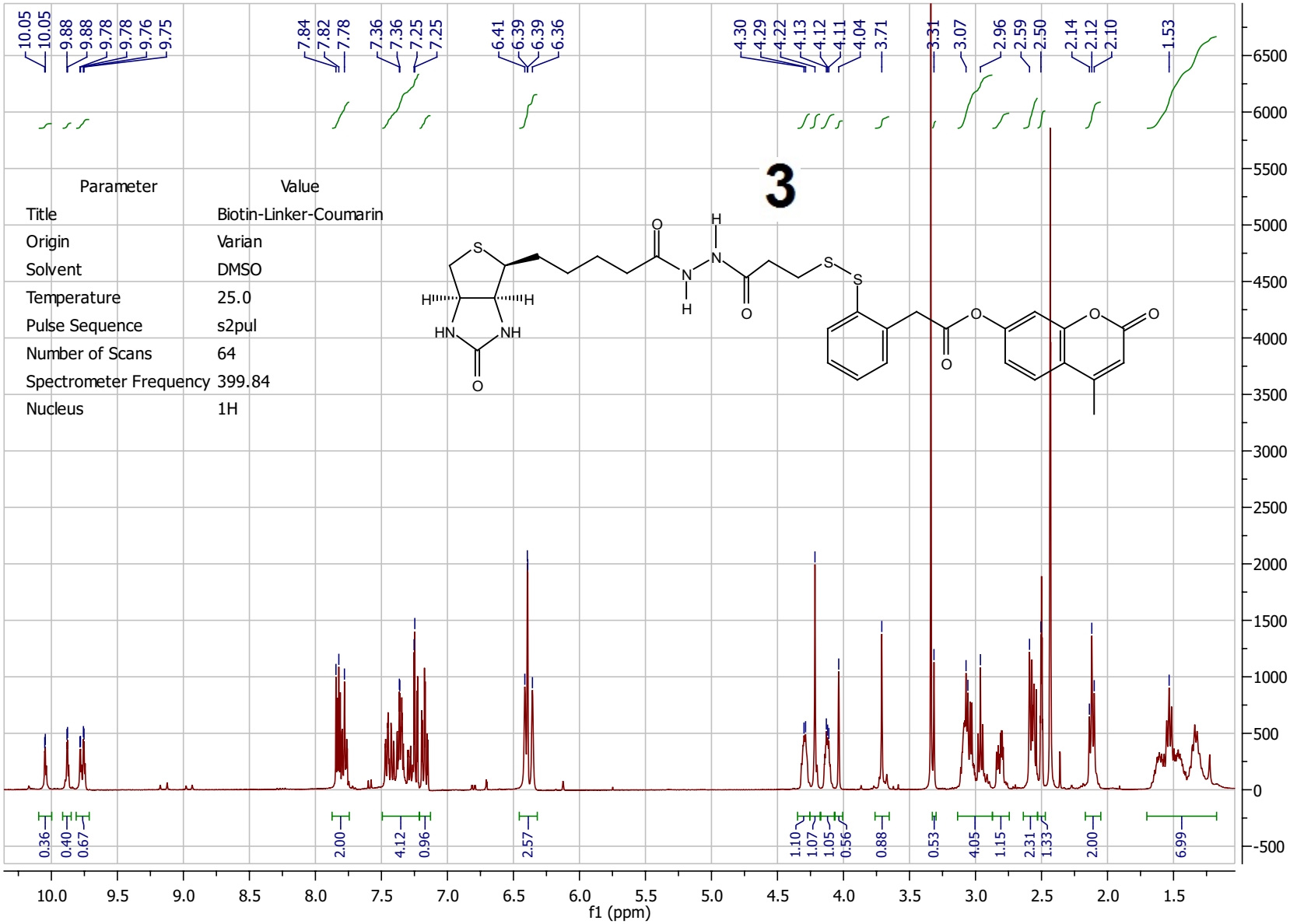
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3.31
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2.12
2.10
1.53
3
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Origin Varian
Solvent DMSO
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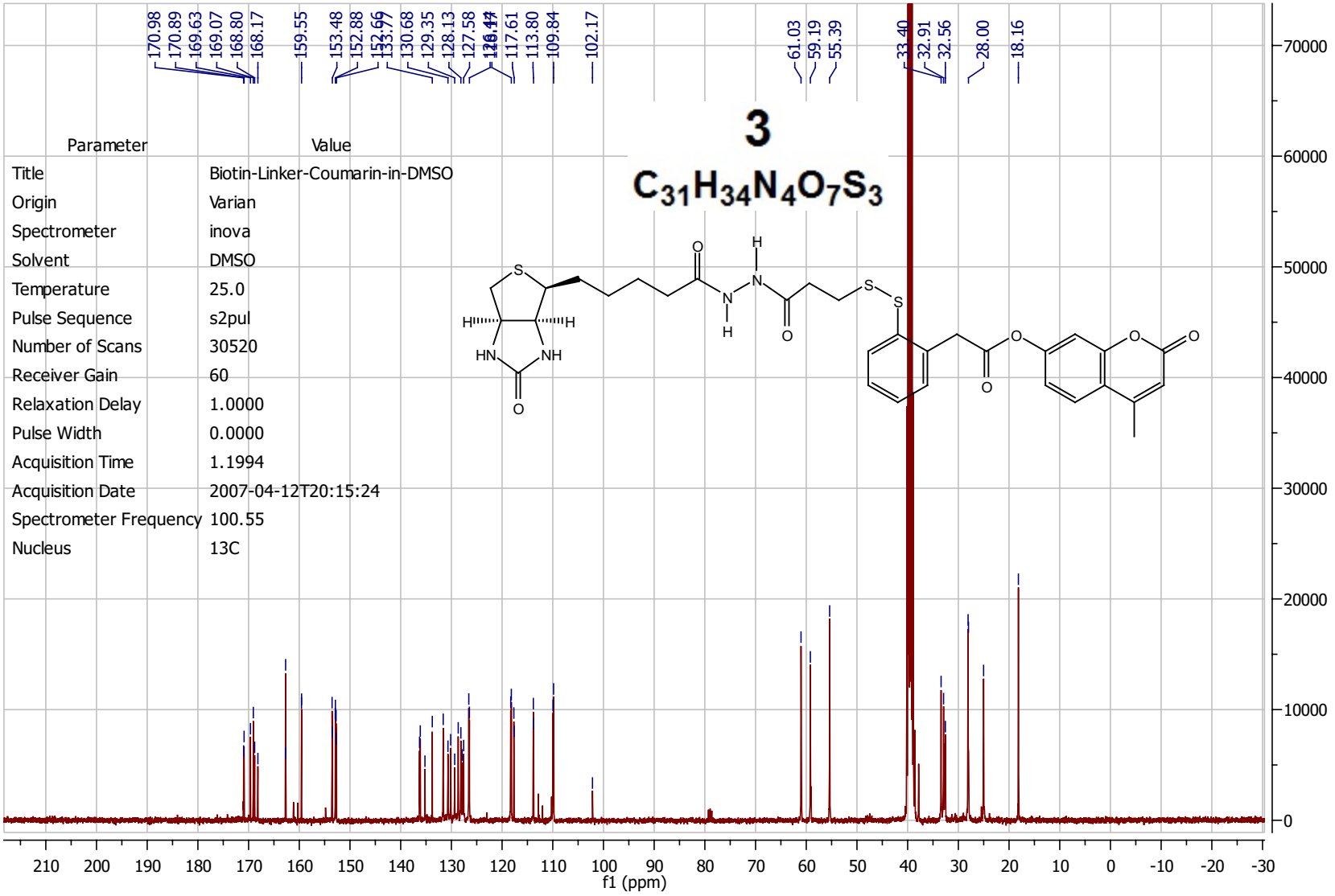
f1 (ppm)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Origin Varian
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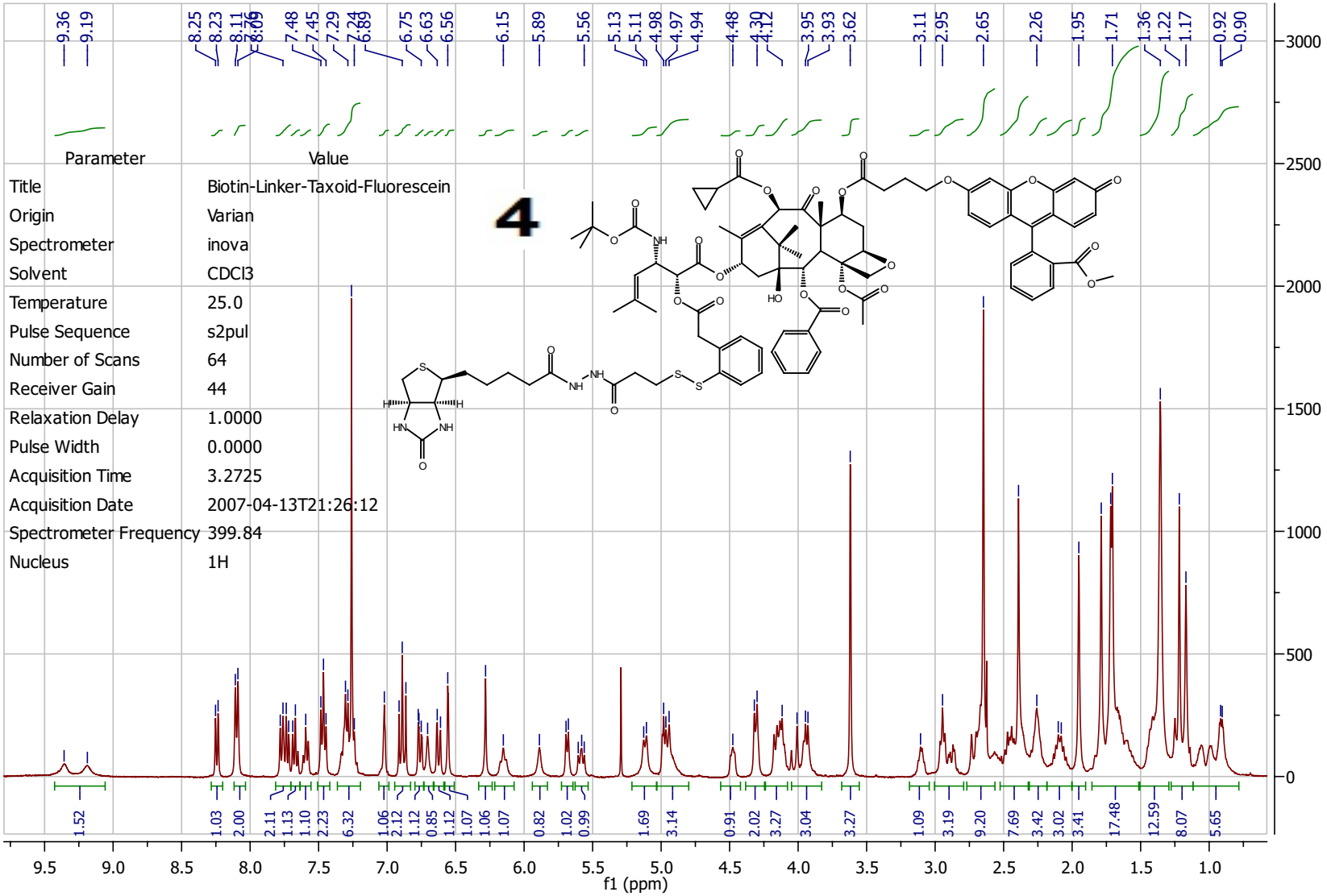
f1 (ppm)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Origin Varian
Spectrometer inova
Solvent CDCl3
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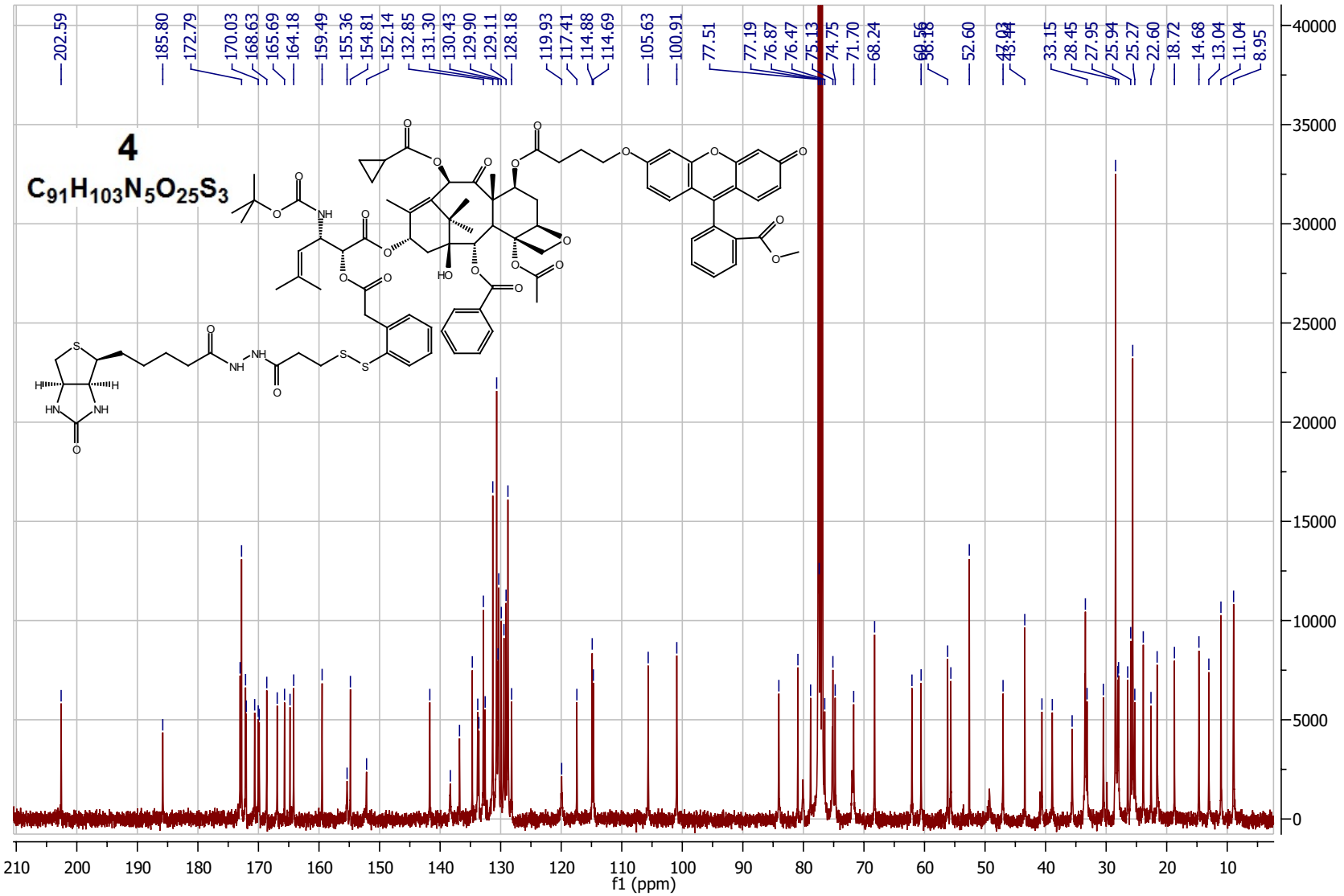
f1 (ppm)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100
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80
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60
50
40
30
20
10
f1 (ppm)

1HNMR

Parameter	Value
1 Title	Taxoid-Fluorescein
2 Origin	Varian
3 Spectrometer	inova
4 Solvent	CDCl3
5 Temperature	25.0
6 Pulse Sequence	s2pul
7 Experiment	1D
8 Number of Scans	400
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11 Pulse Width	0.0000
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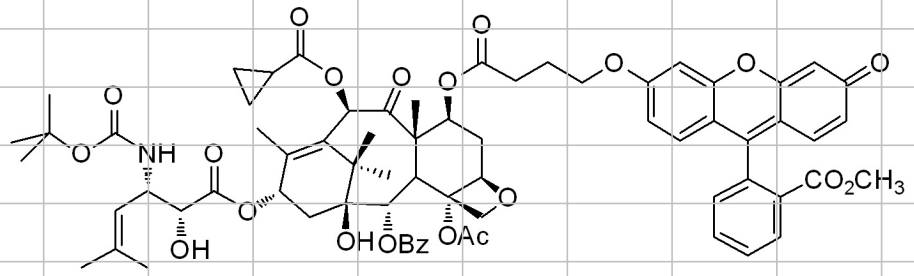

f1 (ppm)

13CNMR

Parameter	Value
1 Title	Taxoid-Fluorescein
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3 Spectrometer	inova
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6 Pulse Sequence	s2pul
7 Experiment	1D
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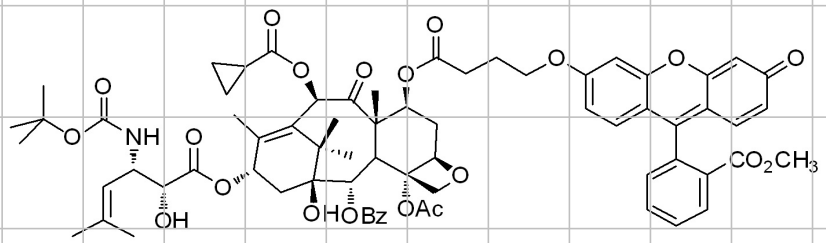
24

$C_{70}H_{77}NO_{21}$



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f1 (ppm)